



# Topical (Microbicide) Pre-Exposure Prophylaxis (PrEP)

## What is topical pre-exposure prophylaxis (PrEP)?

Topical PrEP is the use of a microbicide—a gel, lubricant, douche, or enema infused with antiretrovirals (ARVs)—applied to the vagina and/or rectum in order to prevent sexual transmission of HIV.<sup>1</sup> For the purposes of this bulletin, topical PrEP will specifically refer to the use of a water-based gel lubricant containing a 1% formulation of tenofovir.<sup>2</sup>

## How does topical PrEP work?

Topical PrEP is believed to “block” HIV in vaginal and rectal tissue, impeding the virus from entering cells.<sup>1</sup>

## What is the evidence supporting topical PrEP?

### Topical PrEP for heterosexual women

- In the CAPRISA 004 trial, topical PrEP demonstrated *partial* effectiveness at preventing HIV acquisition among high-risk, heterosexual South African women.<sup>3</sup> Study participants were instructed to insert the gel vaginally up to 12 hours before sex, as well as soon after sex. Women were provided with testing, counseling, and education for HIV and other sexually transmitted infections (STIs). Overall, those on topical PrEP were 39% less likely to contract HIV than those who were not utilizing topical PrEP.<sup>3</sup>
- Conversely, the VOICE study, a different trial that targeted heterosexual women in Uganda, Zimbabwe,

and South Africa, did not show topical PrEP to be effective at protecting women from HIV.<sup>4</sup> Future research is needed to determine topical PrEP’s potential to be implemented at scale.

### Topical PrEP for men who have sex with men (MSM)

- Evidence regarding topical PrEP used rectally by MSM is emerging. Thus far, studies have not assessed the efficacy of topical PrEP for MSM, but instead have been more exploratory and/or focused on the acceptability and safety of the intervention.
- In one small study whose findings were released in February 2011, men and women using a rectal gel containing tenofovir were compared to men and women using a placebo gel. Next, samples of rectal tissues were exposed to HIV and examined in a laboratory. Findings revealed that the rectal tissues of those who used topical PrEP blocked HIV much more effectively than the rectal tissues of those who used the placebo gel.<sup>5</sup> However, the acceptability of the gel was limited due to the high glycerin content of the formulary. Glycerin is commonly used as a laxative and was reported to interfere with the pleasure and comfort of the receptive partner during anal sex.<sup>6</sup>
- Another study, entitled MTN 007, utilized a tenofovir-based lubricant with less glycerin, which was found to be both acceptable and safe.<sup>7</sup>
- MTN 007 and other studies on topical PrEP used in anal intercourse involved small sample sizes and were not designed to test efficacy. Findings must therefore be interpreted with caution. More research is needed before provision of topical PrEP for MSM is rolled out.<sup>1</sup>

## What is next for topical PrEP and MSM?

Additional studies are under way globally to further determine the potential of topical PrEP as a viable HIV prevention tool for MSM. A few studies that focus specifically on MSM include

- **MTN 017:** A clinical trial examining the safety and acceptability of a reformulated rectal microbicide with lower levels of glycerin among MSM and transgender women in the United States, South Africa, Peru, Puerto Rico, and Thailand.<sup>1</sup>
- **Project Gel:** A study of rectal microbicide safety and acceptability among young MSM in the United States and Puerto Rico.<sup>8</sup>
- **CHARM (Combination HIV Antiretroviral Rectal Microbicide Program):** A five-year study looking at the safety and acceptability of three tenofovir-based rectal microbicides.<sup>9</sup>

Although there are ongoing trials to determine the efficacy of vaginal microbicides, there are no ongoing or near-term plans for trials designed to determine the efficacy of rectal microbicides.

## What are the considerations and limitations of oral PrEP as an HIV prevention strategy for MSM?

Topical PrEP has the potential to be an important resource in the HIV prevention toolkit for MSM. If topical PrEP proves to be efficacious in future clinical trials and is brought to market, it may offer a viable option for MSM who lack access to condoms, MSM who cannot use condoms due to severe stigma/safety reasons, or MSM who refuse to use condoms for reasons related to pleasure or personal preference.

Moreover, topical PrEP will likely be formulated as a water-based lubricant—hence offering the added benefits of increasing sexual pleasure for both the insertive and receptive partner during anal sex while helping to reduce the risk of anal tissue tearing. However the cost of such a lubricant could also be prohibitive in resource-limited contexts.

The implementation of topical PrEP has the potential to be both complicated and costly. The possible limitations of topical PrEP are similar to those of systemic PrEP, including potential challenges around adherence and individual health behavior, overall costs of the intervention if approved, and equitable

access, as well as possible adverse events, side effects, and drug resistance.<sup>1</sup> Unlike systemic PrEP, which utilizes a medication approved for use by the US Food and Drug Administration, topical PrEP for MSM is still in the exploratory phase of product development. As noted earlier, current studies are still examining the safety and acceptability of topical PrEP. If subsequent studies further demonstrate safety and acceptability for MSM, efficacy trials (studies to determine if topical PrEP is effective at preventing HIV) will need to be conducted before it is brought to market and delivered through health systems.

## What does recent research on overall knowledge of PrEP amongst MSM tell us?

From June through August 2010, the Global Forum on MSM and HIV (MSMGF) conducted a global study on access to and knowledge of HIV prevention strategies—including lubricants, rectal microbicides and PrEP<sup>11</sup>—among over 5000 gay men and other MSM worldwide.<sup>10</sup> Results from this survey highlighted key findings regarding access to water-based lubricants, as well as knowledge of and attitudes toward microbicides and PrEP.

### Access to water-based lubricants

- When asked how accessible water-based lubricants were in the respondent's community, only 29% of respondents reported that lubricants were "easily accessible." Over 35% of those surveyed believed that water-based lubricants were "close to impossible to access" or "not available" in their community.
- Only 23% of those residing in the Global South (Asia, Middle East, Africa, Latin America) reported easy access to water-based lubricants compared to 51% in the Global North (Europe, North America, Australia/New Zealand) ( $p < .0001$ ).

### Knowledge and understanding of rectal microbicides

- Only 27% of the entire sample reported being "very knowledgeable" or "somewhat knowledgeable" of the potential of rectal microbicides to prevent the transmission of HIV among gay men and other MSM.

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<sup>1</sup>For more information, see the MSMGF's Technical Bulletin on Systemic PrEP at <http://www.msmgf.org/index.cfm/id/81/Publications/>.

<sup>11</sup>Survey asked about PrEP in general and did not specify "topical" or "systemic" PrEP.

- Those in the Global South reported being less knowledgeable about the potential of rectal microbicides to prevent HIV than respondents from the Global North (23% vs 43% reported being “very knowledgeable” or “somewhat knowledgeable” respectively,  $p < .0001$ ).
- Respondents overall were overwhelmingly interested in learning more about rectal microbicides. Of all respondents, 94% “strongly agreed” or “somewhat agreed” with the statement, “I would like to learn more about the proper use of rectal microbicides to prevent transmission of HIV among gay men/MSM.”

## Knowledge and understanding of PrEP

- Only 31% of the entire sample reported being “very knowledgeable” or “somewhat knowledgeable” of PrEP to prevent the transmission of HIV among gay men and other MSM.
- Respondents in the Global South were significantly less knowledgeable about PrEP than respondents from the Global North (25% vs 57% reported being “very knowledgeable” or “somewhat knowledgeable” respectively,  $p < .0001$ ).
- Only 28% of all respondents correctly answered the question, “PrEP should only be used by HIV-negative persons.” Moreover, only 39% responded to the following true/false question correctly, “PrEP is different from post-exposure prophylaxis (PEP) in that it is taken BEFORE exposure to HIV” (3% responded incorrectly and 58% answered “I don’t know”).
- Overall, participants expressed a strong desire to learn more about PrEP. Approximately 93% of respondents “strongly agreed” or “somewhat agreed” with the statement, “I would like to learn more about Pre-Exposure Prophylaxis (PrEP) to prevent transmission of HIV among gay men/MSM.”

## Perceptions and attitudes regarding PrEP

- In total, only 35% of respondents “strongly agreed” or “somewhat agreed” with the statement, “I believe that PrEP should be used by gay men/MSM to prevent HIV infection.”
- About a quarter of respondents indicated that they “would be comfortable with the idea of taking antiretroviral medications every day in order to prevent HIV,” signaling skepticism about PrEP and potentially low demand for the intervention in the future.

## Conclusion

Going forward, more operations and social science research will be needed to better understand adherence rates of topical PrEP in “real world settings” as opposed to clinical trial conditions. The threat of risk compensation among MSM (for example, the availability of topical PrEP leading to decreased condom use) will also need to be explored.<sup>1</sup>

If topical PrEP proves to be efficacious in the future, successful implementation for MSM will require that several necessary conditions are met:

- **Improvement of access to water-based lubricants for MSM globally:** Findings from the MSMGF’s global survey highlighting poor MSM access to water-based lubricants raises key questions about potential implementation of PrEP for MSM globally. Current reports of little to no access to water-based lubricants among MSM signal potential challenges for future implementation of topical PrEP. Hence, in the near term, greater investment and efforts are needed to improve distribution of and access to free water-based lubricants for MSM.
- **Engagement and mobilization of MSM communities:** Communities of MSM must organize around sexual health issues and identify sexual health needs. Efforts to address these needs must be adequately resourced in a sustained manner, and they must include competent and accessible health care services, HIV testing and treatment opportunities, and mental health services.
- **Awareness building and education around PrEP:** Considerable efforts should be made to improve overall understanding, awareness, and knowledge of topical PrEP within MSM communities. Researchers, both clinical and social, need to actively engage MSM communities in the design and implementation of studies, and results must be conveyed effectively to MSM communities. Not only will this improve the overall quality of research, but it will also establish the necessary groundwork to prepare MSM communities for implementation.
- **Health systems strengthening and cultural competency to serve MSM:** To further prepare for the possibility of topical PrEP implementation, efforts must be made to strengthen health systems and train providers so that they better understand the unique needs of MSM, helping them to provide culturally competent

and higher-quality services.<sup>11</sup> Finally, MSM must feel safe attending clinics in order to access interventions such as topical PrEP. This underscores the importance of an enabling sociopolitical environment that mitigates HIV stigma and homophobia. Country-level and multi-lateral support of policies and legislation that decriminalize homosexuality, mitigate HIV stigma, and address homophobia are all essential components to ensuring that new interventions targeting MSM are implemented successfully.

Topical PrEP may eventually be another important HIV prevention strategy in our toolkit of interventions targeting gay men/MSM. However, if topical PrEP proves to be efficacious in future studies, it will not be a “silver bullet;” PrEP will need to be utilized as part of a comprehensive HIV prevention package that includes behavioral and structural interventions as well (eg, community-based outreach; condom and condom-compatible lubricant promotion; counseling and testing; campaigns and policies that reduce HIV stigma and homophobia; and STI prevention, screening, and treatment).<sup>12</sup>

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