

Evaluating, Scaling up and Enhancing Strategies for Supporting **PrEP** Continuation and Effective Use

THINK TANK MEETING REPORT

September 29, 2020

HIV Prevention
Market Manager

Accelerating Product Introduction
Informing Product Development
Reducing Time to Impact



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Executive Summary

Background

Oral PrEP is approved in many countries for use as an HIV prevention option. As of June 2020, approximately 650,000 people were using oral PrEP worldwide, far short of the UNAIDS target of three million users by the end of 2020. Most country guidelines feature daily oral PrEP, with event-driven (ED) PrEP now being added. Studies and experiences from country PrEP¹ programs have highlighted individual, health system and structural factors that hinder continued use of oral PrEP. Although not entirely similar in magnitude or context, many of the same barriers exist across populations and geographic regions. Many individuals struggle to maintain daily use, and programs have reported high rates of discontinuation of oral PrEP. However, there is emerging consensus that effective PrEP use does not have to be continuous, as cycling on and off of PrEP based on periods of risk is not unusual and is often appropriate according to individual needs. Discontinuation, when intentional, can be a feature of effective PrEP use. However, many people stop using PrEP for reasons that can be mitigated, such as limited access to health facilities, quality of care, cost and not having health insurance.

About the PrEP think tanks

In June 2019, the Prevention Product Manager (PMM; a joint partnership between AVAC and the Clinton Health Access Initiative, CHAI) and Jhpiego convened a think tank to discuss options for defining and measuring PrEP continuation. Recommendations from the think tank included modifications to current PrEP indicators, recognizing that a single definition of correct or effective use might not be possible given fluctuating and variable HIV risk. A second think tank was held in September 2020 with the theme *Evaluating, Enhancing and Scaling up Strategies for Supporting PrEP Continuation and Effective Use*. This think tank explored effective and promising strategies for helping people to stay on PrEP, strategies that can be scaled up across populations and locations.

Improving PrEP coverage and strategies for enhancing PrEP continued use

The Sustainable East Africa Research in Community Health (SEARCH) study, taking place in Kenya and Uganda, reported at the International AIDS Conference 2020 that, after offering PrEP at a population level, modest levels of PrEP coverage were associated with significantly lower-than-expected HIV infections among PrEP users. The study saw a 74 percent reduction in new infections among PrEP initiators compared to recent controls in the same study communities in the year prior to PrEP availability. It also reported that most users discontinue oral PrEP at least once. The think tank explored commonly used approaches for enhancing continuation, including counseling-based approaches, Mhealth (technology-based interventions, e.g., text messaging, pill reminder alerts), community- or home-based approaches, Information, Education and Communication (IEC) materials and peer-based strategies. At the think tank, participants discussed the question of whether rapidly expanding PrEP availability would be sufficient to achieve the full impact seen in the SEARCH study.

¹ In this report we use the term “PrEP” to refer to all HIV pre-exposure prophylaxis prevention products. Where the reference is to daily oral PrEP/Truvada, this is represented as “oral PrEP”.

Continued use in the context of the HIV prevention pipeline

New HIV prevention technologies are promising and will add to the method mix. Identifying strategies to overcome barriers to continued use and to support individuals to stay on PrEP during seasons of risk will be relevant to the new HIV prevention products including but not limited to the Dapivirine Vaginal Ring and cabotegravir long-acting injectable (pending regulatory approval). Although long-acting methods may address adherence challenges, some barriers to continued use are likely to persist and new ones may arise, including injection site pain, limited access to a health facility or discomfort using a vaginally inserted product. For the most part, longer-acting methods will remove the burden of daily pill taking, but it is possible that taking pills may still be part of the experience of using CAB-LA to cover the tail.

Additional products currently in the research pipeline and closest to being available are all in pill form: tenofovir alafenamide (F/TAF) and the dual prevention pill or monthly pill (islatravir). Understanding continuation challenges and improving the effective use of oral PrEP now can help to identify and circumvent structural and delivery-related barriers to continued use and support new technologies as they come online, and can also help to inform monitoring and measurement considerations for these future products.

Key considerations and recommendations from the think tank:

- 1** Following lessons from SEARCH as well as those reported from Australia, the United Kingdom and the United States, access to oral PrEP should be rapidly expanded to achieve scale in order to capitalize on its full potential impact.
- 2** New products will not resolve all barriers to continued use. Even as PrEP product options expand, programs and policies—including indicators for measuring continued use—must be responsive to the reality of event-driven, episodic and intermittent use.
- 3** Monitoring and evaluation of effective and continued PrEP use should be strengthened by improving indicators used to collect meaningful data (e.g., “where do you see very early stopping and/or long delays between stopping and restarting?”) while minimizing the reporting burden on programs.
- 4** Promising strategies and those showing effectiveness should be identified for integration and rapid uptake in the scale-up of national PrEP programs. In particular, there is good evidence that Mhealth interventions are effective across populations but may require additional investments to further pilot and evaluate them and bring them to scale.
- 5** Community-led and -based services have demonstrated higher uptake and continued use compared to facility-based approaches. The former are also more amenable to testing innovative approaches but tend to be donor dependent, which may affect the continuation of services. Continued investments in these services are critical in offering options that respond to user preferences.
- 6** Continued investments in implementation science research on oral PrEP are needed, especially in low- and middle-income countries. Research to identify, evaluate, cost and scale up impactful and client-centered interventions for continuation will inform interventions and the scale-up of future biomedical prevention products.



Introduction

Background

Approximately 650,000 people were using oral PrEP worldwide as of June 2020.² While progress has been made in expanding access, the UNAIDS target of three million users by the end of 2020 will not be reached. Additionally, despite high oral PrEP initiation levels, HIV prevention benefits are not being fully realized, since many users do not return for their refill or are delayed in doing so. Critical questions remain around the barriers to and facilitators of uptake and continued use in those with greatest vulnerability to HIV infection. This is particularly the case where oral PrEP rollout is recent in low- and middle-income countries. Most concerning is low adherence on PrEP among adolescent girls and young women (AGYW) in sub-Saharan Africa,³ who continue to be disproportionately affected by HIV in generalized epidemics. These challenges are not unique to resource-poorer settings, particularly in the initial stages of PrEP introduction and implementation. In the United States, oral PrEP continuation is lower among younger and Black MSM.⁴

Although limited evidence exists with regards to the most effective strategies to support PrEP adopters to continue on PrEP, promising practices and innovative strategies have begun to emerge. Early lessons learned from more mature oral PrEP delivery programs are showing promise in populations where continuation has previously been quite poor, including continuation past one month among: cisgender females in Africa (>84 percent continuation),⁵ adolescents (47 percent continuation),⁶ transgender women (64 percent continuation)⁷ and Black MSM (64 percent continuation).⁸ Measures of continuation vary greatly across studies,⁹ and terms that have emerged to describe an individual's use of PrEP over time are outlined below.

Terminologies of PrEP Use

TERMINOLOGY	DEFINITION
Continuation/continued use	The ability to use a method effectively over time
Effective use	Having drug concentrations to achieve maximum protection from HIV infection
Adherence	Taking medication as prescribed to achieve sufficient drug concentrations to confer protection in a 24-hour period
Persistence	Use as recommended, over a period of weeks, months or years

² www.prepwatch.org

³ Celum CL *et al.* 22 July 2019. *HIV Pre-Exposure Prophylaxis for Adolescent Girls and Young Women in Africa: From efficacy trials to delivery.* *J Int AIDS Soc.* Suppl 4.

⁴ Kanny D *et al.* National HIV Behavioral Surveillance Study Group. Rep. 20 Sept. 2019. *Racial/Ethnic Disparities in HIV Preexposure Prophylaxis Among Men Who Have Sex with Men: 23 urban areas, 2017.* *MMWR Morb Mortal Wkly.* 68(37):801-806.

⁵ Celum C *et al.* 4-7 March 2019. *Adherence 3 Months After PrEP Initiation Among Young African Women in HPTN 082.* Conference on Retroviruses and Opportunistic Infections (CROI), Seattle, WA.

⁶ Hosek S *et al.* 1 Nov. 2017. *Safety and Feasibility of Antiretroviral Preexposure Prophylaxis for Adolescent Men Who Have Sex With Men Aged 15 to 17 Years in the United States.* *JAMA Pediatrics.* 171(11):1063-1071.

⁷ Phanuphak N *et al.* Nov. 2018. *Princess PrEP Program: The first key population-led model to deliver pre-exposure prophylaxis to key populations by key populations in Thailand.* *Sex Health.* 15(6):542-555.

⁸ Wheeler D. 2019. *Pre-Exposure Prophylaxis Initiation and Adherence Among Black Men Who Have Sex with Men (MSM) in Three US Cities: Results from the HPTN 073 study.* *Journal of the International AIDS Society.* 22:e25223.

⁹ Stankevitz K *et al.* 1 Oct. 2020. *Oral Preexposure Prophylaxis Continuation, Measurement and Reporting.* *AIDS.* 34(12):1801-1811.

Understanding and enhancing PrEP continued use

Barriers that hinder oral PrEP continuation are well documented in clinical trials, demonstration projects and program implementation. They can be categorized into biopsychosocial, health system, sociological and ecological factors, as well as limited scale-up. The barriers include product-related side effects and branding, risk perception, societal and self-stigma, family and partner support, provider knowledge and willingness to prescribe PrEP and access to efficient, culturally appropriate, people-centered PrEP services. Although not entirely similar in magnitude or context, many of the same barriers exist across different populations¹⁰ and geographic regions.

Continued use in the context of the HIV prevention pipeline

New HIV prevention technologies are promising and will add to the method mix. Identifying strategies to overcome barriers to continued use and to support individuals to stay on PrEP during seasons of risk will be relevant to the next generation of HIV prevention products. Early results from HPTN 083 and HPTN 084 showed that using injectable cabotegravir (CAB-LA) every two months was safe and highly effective among men who have sex with men (MSM), transgender men who have sex with men and cisgender women. Another HIV prevention product in the pipeline is the Dapivirine Vaginal Ring, a monthly, topical ARV-based method and the first topical, women-controlled prevention method. In July 2020, the Dapivirine Vaginal Ring received a positive opinion from the European Medicines Agency for use by women in low- and middle-income countries outside the European Union, and it recently received WHO prequalification.

Although long-acting methods may address adherence challenges, some barriers to continued use are likely to persist, and new ones may arise, including injection site pain, limited access to a health facility or discomfort using a vaginally inserted product. For the most part, longer-acting methods will remove the burden of daily pill taking, but it is possible that taking pills may still be part of the experience of using CAB-LA to cover the tail. Additional products currently in the research pipeline and closest to being available are all in pill form: tenofovir alafenamide (F/TAF) and the dual prevention pill or monthly pill (islatravir). Understanding continuation challenges and improving the effective use of oral PrEP now can help to identify and circumvent structural and delivery-related barriers to continued use to support new technologies as they come online, and can also help to inform monitoring and measurement considerations for these future products.

Modest levels of PrEP coverage can reduce HIV infections

Encouraging results from the SEARCH¹¹ and ECHO¹² studies demonstrate that modest levels of PrEP coverage can significantly reduce HIV infections among persons at elevated risk of HIV. The SEARCH study reported a 74 percent reduction in new infections among PrEP initiators (compared to recent controls prior to PrEP access) across study sites. In the ECHO study, a 25 percent uptake of oral PrEP by women study participants produced a more than 50 percent fall in the rate of HIV infection. Recent research also reinforces the understanding that most people navigate seasons of risk effectively and will use PrEP when they need it. As a result, PrEP use may be episodic, long-term or event-driven, depending on an individual's circumstances. The SEARCH study reported that most users discontinued oral PrEP at least once. Therefore, the concept of continuation and effective PrEP

¹⁰ Eakle R *et al.* July 2019. *Understanding User Perspectives of and Preferences for Oral PrEP for HIV Prevention in the Context of Intervention Scale-up: A synthesis of evidence from sub-Saharan Africa.* *J Int AIDS Soc.* 22 Suppl 4 (Suppl 4).

¹¹ Koss CA, Havlir DV, Ayieko J, Kwarisiima D, Kabami J, Atukunda M, *et al.* *Lower than expected HIV incidence among men and women at elevated HIV risk in a population-based PrEP study in rural Kenya and Uganda: Interim results from the SEARCH study.* International AIDS Conference. Abstract OAC0805.

¹² Evidence for Contraceptive Options and HIV Outcomes (ECHO) Trial Consortium. 2019. *HIV Incidence Among Women Using Intramuscular Depot Medroxyprogesterone Acetate, a Copper Intrauterine Device, or a Levonorgestrel Implant for Contraception: A randomized, multicentre, open-label trial.* *Lancet.* 394(10195):303-313. doi:10.1016/S0140-6736(19)31288-7. Published correction appears 27 July 2019. *Lancet.* 394(10195):302.

use must be reevaluated and adapted to fit these realities. Few studies have been published on interventions that effectively support oral PrEP adherence and continuation.¹³ Some strategies that directly address these barriers have demonstrated effectiveness.^{14,15} Additionally, promising interventions to support the continued use of oral PrEP have been implemented in demonstration projects, research studies and national scale-up programs.

About PMM think tanks

The Prevention Market Manager (PMM) is a partnership of AVAC and the Clinton Health Access Initiative (CHAI), funded by the Bill & Melinda Gates Foundation. PMM works to reduce the time from regulatory approval to uptake of biomedical prevention products to ensure that they are available as quickly as possible to the people who need them the most. PMM has designed a series of think tanks that bring together a broad range of experts on PrEP and analogous health interventions to spur action and generate solutions to address key issues and persistent challenges to effective implementation. PMM convened the first think tank together with Jhpiego in June 2019 on *Defining and Measuring Effective Use of PrEP*. It explored some of the different methods to measure the impact and continued use of oral PrEP, both at the population level and the individual level. While a universal threshold for success for effective use was not identified, think tank participants concluded that effective use of PrEP does not have to be continuous and long-term, because HIV risk may be episodic or infrequent. Therefore, assessing PrEP continuation required broadening the definition to account for cycling on and off PrEP based on periods of risk.

The second think tank, *Evaluating, Scaling up and Enhancing Strategies for Supporting PrEP Continuation and Effective Use*, aimed to identify innovative strategies and promising practices that could be or are currently being implemented to overcome common barriers to continuation and effective use with strategies that can be adapted across populations and contexts.

The specific objectives were to:

- ▶ Examine strategies using effective models for supporting and improving continuation that can be adapted across populations and settings,
- ▶ Identify potential solutions to address barriers to continuation to maximize the impact of new biomedical prevention options,
- ▶ Connect the recommendations on measuring and monitoring effective PrEP use and impact with programmatic strategies to support continuation and
- ▶ Inform future investments to improve HIV prevention programs.

Discussions sought to answer the following questions:

- ▶ How do the SEARCH study results impact how we think about and measure continuation and PrEP impact?
- ▶ How do we reconceive the definition of success in the context of PrEP while also ensuring accurate messaging about the importance of effective use to potential and current PrEP users?
- ▶ What barriers to PrEP continuation are shared across populations and preventive care delivery models?
- ▶ What interventions have proved most promising to support PrEP adopters in continuing use, including interventions from other health sectors?
- ▶ What implementation science research is needed in order to pave the way for the accelerated and impactful introduction of new products?

¹³ AVAC. 2019. *A Review of Strategies For Evaluating, Scaling up and Enhancing Strategies for Supporting PrEP Continuation and Effective Use*.

¹⁴ Repack CJ. 17 July 2019. *A Promising PrEP Navigation Intervention for Transgender Women and Men Who Have Sex with Men Experiencing Multiple Syndemic Health Disparities*. *J Community Health*. 44(6):1193-1203.

¹⁵ Ridgeway K. 2 Jan. 2018. *Interventions to Improve Antiretroviral Therapy Adherence Among Adolescents in Low- and Middle-Income Countries: A systematic review of the literature*. *PLoS One*. 13(1):e0189770.



DISCUSSION POINTS

Redefining and measuring PrEP success

► Improved indicators for oral PrEP success will inform the design of implementation programs

In the second think tank, participants revisited discussions on what should be routinely measured by oral PrEP programs and why. There was consensus among participants that two broad areas required greater understanding: a) at the client domain, how people were using PrEP in terms of frequency and duration and how this corresponded to risk; b) at the population level, how coverage could be used as a way to better assess and measure impact. The collective use measures do not adequately capture a phenomenon like restarting, and the models have assumed an indefinite static risk after PrEP initiation and have not accounted for the prospect of people switching HIV prevention methods. The participants reviewed the global indicators created by WHO and PEPFAR, since the majority of countries collect data on these indicators.

Global indicators to measure PrEP use

The WHO indicators address continuity of use for 90 or more consecutive days, thus providing a measure of continuation, but they leave many unknowns about whether use for less than 90 days is effective if risk is episodic. The PEPFAR indicator PrEP_CURR measures the proportion of individuals who have returned for refills or restarts by considering at least one additional prescription of PrEP after the first three or more months of initiation. This measure does not capture the total volume distributed, and it does not identify suboptimal use of PrEP, such as very early discontinuation or extended durations off PrEP. There are no commonly agreed upon indicators to measure discontinuation, duration off PrEP, cyclical use and event-driven use. Dunbar *et al.* have highlighted some of the measurement challenges in oral PrEP delivery as well as the lack of common definitions, and they propose a common lexicon for uptake and coverage along the oral PrEP cascade.¹⁶

WHO and PEPFAR PrEP Continuation Indicators



World Health Organization

Indicator: Continuation on PrEP

Indicator description: Percentage of PrEP users who continued on oral PrEP for three consecutive months after having initiated PrEP in the previous 12 months

Source: WHO/CDS/HIV/18.10. 2018. *WHO Implementation Tool for Pre-Exposure Prophylaxis (Prep) of HIV Infection. Module 5: Monitoring and evaluation.* Geneva: World Health Organization. Licence: CC BY-NC-SA 3.0 IGO. <https://www.who.int/hiv/pub/prep/prep-implementation-tool/en/>.



PEPFAR

Indicator: PrEP_CURR

Indicator description: Percentage of PrEP users who continued on oral PrEP for three consecutive months after having initiated PrEP in the previous 12 months

Source: Sept. 2020. *PEPFAR Monitoring, Evaluation, and Reporting Indicator Reference Guide. MER 2.0 (Version 2.5).* <https://www.state.gov/wp-content/uploads/2019/10/PEPFAR-MER-Indicator-Reference-Guide-Version-2.4-FY20.pdf>.

¹⁶ Dunbar *et al.* Nov. 2018. *Understanding and Measuring Uptake and Coverage of Oral Pre-Exposure Prophylaxis Delivery Among Adolescent Girls and Young Women in Sub-Saharan Africa.* *Sex Health.* 15(6):513-521.

Considerations for measuring PrEP use

Recommendations from the think tank:

- PrEP use should be viewed flexibly, given that risk is variable from person to person and fluctuates over time.
- Since only effective use provides protection for all, monitoring for it is a reasonable goal of global public health programs.
- No single measure was found to meet all needs, and there were ongoing gaps in:
 - > knowledge about very early discontinuation, late discontinuation or failing to restart,
 - > information about changes in use patterns,
 - > understanding of risk with increasing PrEP use experience and
 - > understanding about prevention method switching.
- Impact modeling may be possible by simply measuring PrEP coverage of individuals offered PrEP and HIV incidence, and then associating those two data points, so long as robust data are available to help account for confounding of treatment scale-up and viral suppression.

Johns Hopkins University Affiliate Suggested Changes to Indicators

- 1** Add an indicator for distribution of PrEP (i.e., number of pills/bottles distributed combined with number of individuals prescribed PrEP/population size) as a proxy or initial step to measure impact based on PrEP coverage, similar to the approach used in the US and other high-income settings.
- 2** Support the use of cross-sectional and longitudinal approaches for collecting data on continuous use to:
 - > monitor for effective use.
 - > compare and contrast feasibility, data quality and impact planning to target programmatic interventions.
- 3** Support program evaluations/implementation science to
 - > identify the reasons for oral PrEP discontinuation and, if related to program quality, identify effective interventions and strategies,
 - > improve the quality of PrEP programs and
 - > better understand episodic or sporadic use.

➤ High saturation of oral PrEP use at scale contributes to reduce HIV incidence

Participants engaged with the data from the SEARCH study, which implemented a population-level PrEP intervention in 16 communities in rural Kenya and Uganda from 2016 to 2020. The SEARCH study was a community cluster randomized trial that began in 2013 to test the hypothesis that universal access to HIV testing and ART using a multi-disease, patient-centered care model would reduce new HIV infections and improve community health compared to a country guideline approach, which at the time did not include immediate start of ART. Oral PrEP was introduced in 2016-2017 to assess whether adding oral PrEP could further reduce HIV incidence among persons at elevated HIV risk. During population-level HIV testing, the study offered universal access to PrEP with enhanced counseling for individuals at elevated HIV risk. Rapid or same-day PrEP start was offered with flexible service delivery, with options for follow-up visits at facility or community-based sites.¹⁷ The study was conducted before the launch of national guidelines for oral PrEP. It analyzed data along the PrEP cascade, with the following measures as proportions:

¹⁷ Havlir, D et al. 2019. *HIV Testing and Treatment with the Use of a Community Health Approach in Rural Africa*. N Engl J Med 2019; 381:219-229

- > **Proportion at elevated HIV risk using three categories:** being in a sero-different partnership, risk score, self-identified risk
- > **Oral PrEP uptake:** measured as receipt of PrEP pills; from those who started PrEP, the study evaluated the following:
 - Program engagement: follow-up visit attendance during scheduled visit weeks, based on the date of oral PrEP initiation
 - Oral PrEP refills
 - Self-reported adherence based on a three-day recall: at least one dose of last three scheduled doses taken
 - Current self-assessed HIV risk (yes/no) among persons attending follow-up visits

The study also analyzed the HIV incidence rate among oral PrEP initiators who engaged in the program and had repeat HIV testing after PrEP initiation, and it compared the observed HIV incidence to what would have been the expected HIV incidence in this population in the absence of PrEP.

› Study results:

- > **HIV risk:** Of the 74,541 individuals who tested negative for HIV, 21 percent were at elevated risk of HIV. Among individuals at elevated HIV risk, 5,447 (35 percent) initiated PrEP, and of this group, 79 percent engaged in the PrEP program. About half were women and 29 percent were between the ages of 15 and 24 years.
- > **PrEP uptake** was significantly higher among sero-different partners, older adults and those in polygamous marriages and lower among youth and mobile individuals.
- > **PrEP continued use** (Figure 1): Among participants, 83 percent stopped (no refill in a visit period or refill ≥ 30 days late) PrEP at least once, and half of these later restarted. About 30 percent were still taking PrEP at six months. Among persons who reported current HIV risk at follow-up visits, over 90 percent received PrEP refills, which suggests that individuals may be able to effectively navigate “seasons of risk”.

- › **Impact of oral PrEP:** In eight of the 16 study communities with data on HIV incidence from the year before PrEP availability, HIV incidence among PrEP initiators was 74 percent lower compared to matched controls in the same communities from the year prior to oral PrEP availability.

The study also analyzed the HIV incidence rate among oral PrEP initiators who engaged in the program and had repeat HIV testing after PrEP initiation, and it compared the observed HIV incidence to what would have been the expected HIV incidence in this population in the absence of PrEP.

The results suggest that offering universal access to PrEP with rapid start and flexible service delivery (such as changing opening hours and having telephone contact with providers) are promising approaches to reduce incidence in generalized epidemic settings. The results also point to the value of measuring PrEP coverage at the population level to assess impact.

› Population-based surveys provide additional data on PrEP awareness and access

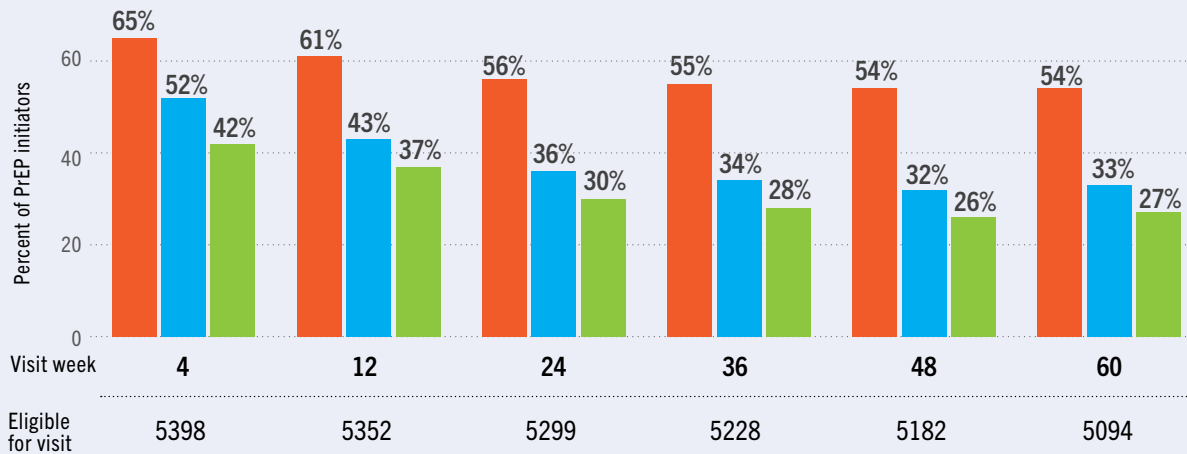
The Population-Based HIV Impact Assessment (PHIA) studies funded by PEPFAR and implemented by ICAP are nationally representative household surveys to assess the status of the HIV epidemic and the impact of national programs. The primary objective is to assess national HIV incidence, prevalence and viral load suppression.

Recent and planned PHIA studies have incorporated indicators on PrEP awareness and adherence. At the think tank, participants reviewed data from an unnamed, unpublished country to see how PHIA studies are now able to evaluate PrEP awareness and scale-up.¹⁸ In this country, 27 percent of adults had heard

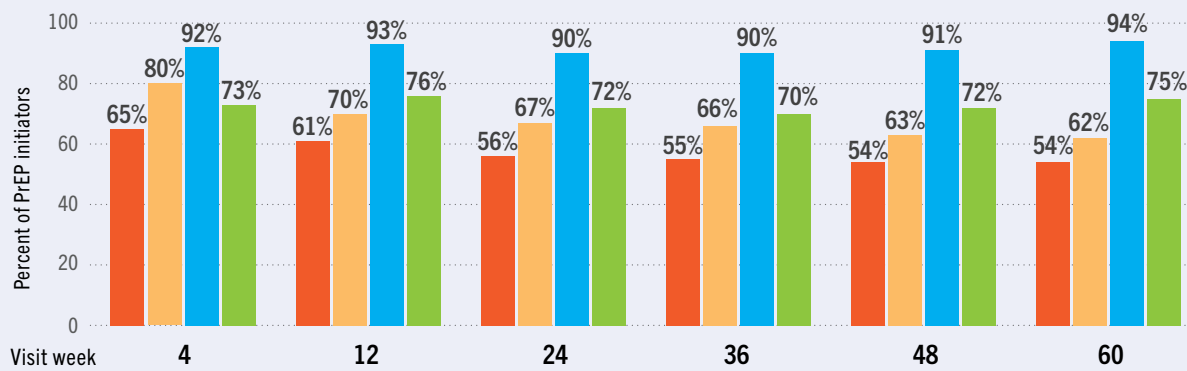
¹⁸ At the time of the think tank, the researchers could not disclose the name of the country, as the data ownership was with the country's Ministry of Health and the data had not been made public.

Figure 1: PrEP program engagement, refills, self-reported adherence among adherence among PrEP initiators, overall and by self-assessed current HIV risk through week 60

A Overall



B Participants reporting self-assessed current HIV risk at follow-up visits, and the proportion receiving refills and self-reporting adherence

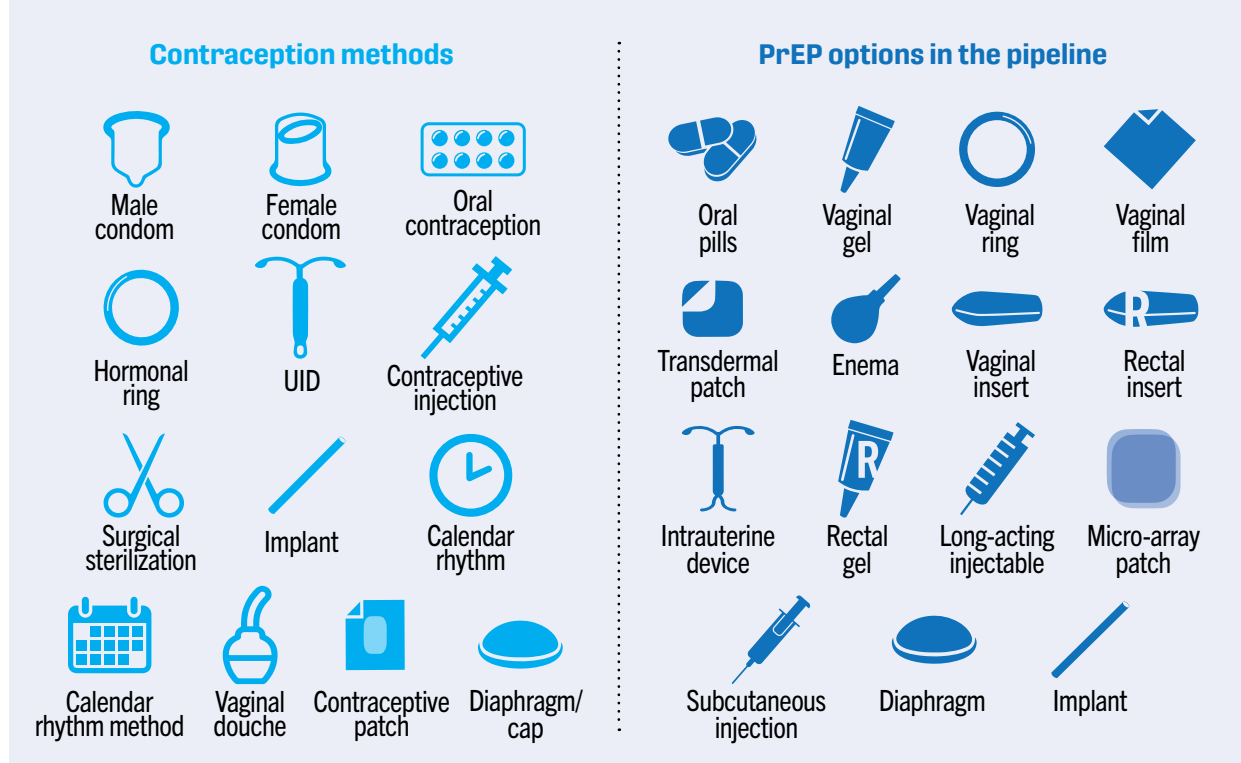


1	3512/5398	3986/5352	2987/5299	2893/5228	2784/5182	2758/5094
2	2826/3512	2297/3286	1987/2987	1919/2893	1752/2784	1711/2758
3	2605/2826	2130/2297	1785/1987	1735/1919	1600/1752	1601/1711
4	2053/2826	1747/2297	1428/1987	1349/1919	1267/1752	1277/1711

■ Program engagement
 ■ Self-assessed risk
 ■ Medication refill
 ■ Self-reported adherence
1 Program engagement / PrEP initiators eligible for visit
2 Self-assessed current risk / engaged in program
3 Medication refill / self-assessed current risk
4 Adherence / self-assessed current risk

of PrEP, including 31 percent of men and 24 percent of women. One percent of the nationally representative sample of HIV-negative adults reported having ever used PrEP. Self-reported adherence in the previous 30 days indicated high levels of PrEP adherence. For this country, there was high acceptability and adherence but low coverage, indicating the need for scaled-up distribution and continuation models. The PHIA provides a useful avenue for collecting complementary data on PrEP uptake, coverage, acceptance and adherence. Combined with program data and qualitative research data, they present a comprehensive picture of what's happening with PrEP use in a country in order to better guide effective PrEP programs. Additional data will become available following the second round of PHIA surveys, which include questions on PrEP use and adherence.

The PrEP landscape is evolving to mirror the family planning field, with more options and in a way that could shift how continued use is measured and supported



Promising programmatic strategies to support continuation

➤ Continued use is important as the PrEP landscape expands

While adherence refers to the daily phenomenon of taking medication as prescribed to achieve sufficient drug concentrations to confer protection, continued use refers to the ability to use a method effectively over time. Even if a new product addresses common adherence challenges, it may not remove the barriers to continued use. The PrEP landscape could potentially evolve to be similar to the family planning landscape, for which there is a large range of options, product switching, considerably high discontinuation and less rigorous follow-up. Agreeing upon the most productive measures of continued use will become increasingly important. While oral PrEP is the only product currently available, a number of other products are in the pipeline.

When they are eventually available, the Dapivirine Vaginal Ring or injectable CAB-LA would remove the burden of taking a daily pill. Adherence is typically easier with longer-acting products, but individuals may face continuation challenges similar to those observed with oral PrEP in different ways. Longer-acting methods may also pose new barriers to continued use:

- These new products will likely be administered by a trained health provider at a clinic, which requires users to visit a health facility for the same number of visits as oral PrEP.
- Oral PrEP is available now, while the ring and CAB-LA are not yet approved for use and, depending on the regulatory process, may not be available for a couple of years.
- In the case of CAB-LA, if someone discontinues injections and remains at risk of acquiring HIV, the current regimen requires that they take oral PrEP to “cover the tail”, where there is enough CAB-LA drug in the body to generate ARV resistance. As a result, taking pills may be part of the CAB-LA experience.

- Additional products in the research pipeline are all in pill form, including F/TAF and the dual prevention pill or monthly pill (islatravir). Efforts to improve effective use of PrEP remain highly relevant.

Understanding the continuation challenges with oral PrEP now can help to identify and circumvent some of the same issues for future products. As the HIV prevention pipeline grows and diversifies, understanding and resolving barriers and patterns of use and supporting people to use PrEP effectively become more important, while monitoring and measuring PrEP use (starting, switching, cycling on and off or discontinuation) may become more complicated.

➤ **Effective oral PrEP continuation strategies are adaptable across populations and locations**

AVAC/PMM conducted a literature review and interviews on strategies designed to support oral PrEP continued use ahead of the Think Tank. The aim was to elicit deeper and more nuanced data on promising continuation models. Eighteen key informant interviews were conducted and 12 published studies were found that assessed interventions to support oral PrEP continuation during periods of risk. The most commonly used measures of continued use were self-reports and pill counts. Overall, the studies reported declining adherence over time. The majority were conducted in the United States with populations of MSM and transgender women, with far fewer studies conducted in high HIV burden countries or among AGYW. Stigma, unsupportive partners, health system issues such as queuing for refills, clinical monitoring, daily pill burden and one-month drug supplies were highlighted as common barriers to continued PrEP use. Similar barriers were reported in the SEARCH study, which also found that facilitators of PrEP use included positive interactions with providers, support around the management of side effects, out-of-facility visits and using PrEP to support achieving one's life goals. Some successful interventions adapted from antiretroviral treatment adherence improvement programs among people living with HIV showed promise across populations of women and MSM on oral PrEP in Africa and the United States, respectively.^{19,20} Mhealth interventions—particularly bidirectional texts to increase awareness, send virtual reminders and provide peer- or provider-initiated support and counseling—were the most promising strategies for supporting continued use of PrEP across different populations and settings. Among women, counseling interventions delivered by health providers or lay counselors were promising strategies. A number of ongoing studies listed in [ClinicalTrials.gov](https://clinicaltrials.gov) may provide additional evidence of the scalability of PrEP continuation strategies across populations and geographic regions.

¹⁹ Psaros C et al. 2014. *An Intervention to Support HIV Preexposure Prophylaxis Adherence in HIV-Serodiscordant Couples in Uganda*. *Journal of Acquired Immune Deficiency Syndromes*. 66(5): 522–529.

²⁰ Mayer KH et al. 2017. *Optimizing Pre-Exposure Antiretroviral Prophylaxis Adherence in Men Who Have Sex with Men: Results of a pilot randomized controlled trial of “life-steps for PrEP”*. *AIDS Behav*. 21:1350–1360. <https://doi.org/10.1007/s10461-016-1606-4>.



MEETING HIGHLIGHTS AND RECOMMENDATIONS

The think tank generated some considerations and recommendations for: 1) measuring PrEP continuation, 2) programmatic strategies for enhancing continued PrEP use and 3) areas for further research and proposed recommendations for future donor investments.

› Redefining and measuring PrEP continuation

The first think tank was dedicated to detailed discussions and recommendations on measuring effective PrEP use. In the second think tank, the recommendations for measuring the continued use of PrEP centered on improving shortcomings identified in the current indicators used in collecting data, while remaining cognizant of what is realistic in national programs, especially in limited-resource settings. Since the first think tank, there have been positive developments with regards to indicators for measuring PrEP. For example, PEPFAR COP 21 guidance has shifted the PrEP_CURR indicator to be reported quarterly instead of annually.

OPPORTUNITIES/CONSIDERATIONS

- › Indicators of PrEP continued use that are based on ART retention fall short, since HIV risk is not universally continuous. Cohort monitoring (monitoring groups of people or sub-populations) within the population at the country level is a better way to assess the PrEP cascade, but it is not practical in national programs and requires electronic patient databases.
- › As the number of PrEP users increases, longitudinal follow-up, though challenging, would be ideal to also monitor method switching as new products become available.
- › Programs must balance between the need for data and the reporting burden on resource-constrained programs, identifying indicators that can be collected in short, insightful, targeted studies that follow people over time, in addition to global indicators that are cross-sectional, collected at one point in time.
- › PEPFAR indicators are prescriptive and have limited ability to generate program insights in order to intervene as necessary.
- › National programs can be encouraged to measure PrEP coverage at the population level as a way to assess impact.
- › Additional questions should be included in PHIA to assess event-driven PrEP in line with updated WHO strategic information guidelines.
- › Client-level continuation rates should be viewed not as a measure of program success but as information to support people to use PrEP effectively.

► Promising strategies for scaling up PrEP and supporting PrEP continuation at scale

From the literature and discussions, the most commonly used approaches for enhancing continuation can be categorized as: counseling-based, Mhealth, community/home-based, IEC materials and peer strategies. Mhealth and peer approaches are the most common strategies for enhancing continued use across populations and settings. Overcoming barriers to PrEP to improve continued use will, however, require that effective strategies are also implemented down the cascade of PrEP delivery: identifying who needs PrEP, increasing uptake and coverage and improving the quality of care clients receive.

OPPORTUNITIES/CONSIDERATIONS

- Strategies to improve PrEP uptake:
 - > Peer-led approaches are promising strategies for AGYW to debrief on their struggles with oral PrEP adherence and continuation and discuss how to overcome the challenges.
 - > Mobile clinics have worked well for oral PrEP initiation with AGYW in South Africa. Courier delivery of a prevention package that includes oral PrEP, an HIV self-test kit and a pregnancy testing kit is in early implementation.
 - > Lessons from the SEARCH study, scoping review and experience in scale up programs suggest that community-wide awareness and stigma reduction interventions promote PrEP uptake, especially among AGYW.
- Client-centered delivery to support continuation:
 - > Community-led service, i.e., delivery outside of facilities (such as at drop-in centers) or by peers, shows higher PrEP uptake and continued use among key populations and AGYW due to factors such as convenience for clients and accessible providers.
 - > Within facilities, there is a need to diversify PrEP delivery across departments (i.e., ART, family planning or outpatient clinics). This has worked well in national programs to strengthen facility-based uptake and continuation.
 - > PrEP users require flexibility in the time and places where PrEP is offered and in delivering continuation support tailored to clients' needs when, how and where they want. For example, AGYW prefer that services are not in facilities, are delivered by young providers and that they do not have to wait in line along with other adult clients perceived as their parents.
 - > Integration of PrEP and other services (e.g., family planning, NCDs, hormone replacement therapy) enhances continued use.
 - > Use of case management approaches that have been successful in other areas of HIV programming can be explored to support PrEP effective use.
- Product-related strategies:
 - > Discreet and portable packaging of PrEP increases clients' ability to keep use confidential. For example, the SEARCH study used blister packs and envelopes to overcome packaging-related concerns related to PrEP use.
 - > Simpler branding and packaging distinct from that of ARV drugs is recommended as a stigma reduction strategy.
- Improved understanding of HIV risk:
 - > Risk perception: multiple studies and implementation experience show that risk perception is linked to initiating and staying on oral PrEP. Creating spaces where people feel comfortable

and safe discussing the context of their relationships honestly can be an entry point to helping individuals understand their risk and then choose an HIV prevention option that fits their needs and circumstance. This may improve continued use.

- > Better risk stratification: segmentation into programs to identify who should be on PrEP or other prevention methods and better identification of risk profiles of individuals that show better or worse continuation outcomes can help develop more tailored strategies to support individuals at risk and struggling with PrEP continuation.
- ▶ Person-centered messaging:
 - > Holistic PrEP communication and messaging that focus on benefits such as empowerment or control over sexual health and sexuality are likely to resonate more with people who may benefit from using PrEP.
- ▶ Strategies to improve access:
 - > Simplified delivery (pharmacy models, home delivery, peer outreach) and monitoring (including strategies piloted during COVID-19 lockdowns) have the potential to increase PrEP use.
 - > Client experience is a critical determinant of uptake and continuation, and programs should consider client involvement in co-creating designs of delivery models and continuation support strategies.
- ▶ Revisions to national guidelines:
 - > Multi-month dispensing is recommended for inclusion in national guidelines.

▶ Considerations for future research and program investments

The published research on PrEP continuation and effective use is more prolific in the United States, with far less publication from low- and middle-income HIV endemic countries. Participants saw an opportunity to conduct rigorous research in ongoing programs that are scaling up in other geographic regions in order to address common barriers to oral PrEP continued use and to the use of potential PrEP products in the pipeline.

RECOMMENDATIONS FOR FUTURE RESEARCH

- ▶ Implementation science to improve program delivery:
 - > Evaluate PrEP continuation strategies in ongoing country programs and implementation science.
 - > Provide opportunities for rapid iteration and piloting of ideas.
 - > Integrate implementation science into actual program implementation settings as opposed to research-driven models.
 - > PrEP is an HIV prevention intervention, but as it is layered within a treatment oriented health system. Support further research to explore the question, “what would a system oriented around maintaining health and well-being look like?”
- ▶ Research to better understand factors associated with continuation:
 - > Conduct research to better understand reasons for low continuation, motivations behind higher continuation, what users need and how best to integrate interventions into community settings.

Behavioral economics or social psychology frameworks may be useful for such research to better understand how to support individuals as they anticipate and overcome barriers to continuation and to design effective interventions.

- > With the expanding options and evidence across populations and settings of event-driven, intermittent use and switching, conduct further research to better understand patterns and different methods by which people are using oral PrEP in order to inform appropriate strategies to enhance continued use and mitigate barriers for future PrEP products.
- > Conduct research to better understand individual versus service delivery factors that result in intentional versus unintentional breaks in PrEP use. Intentional discontinuation, for example, is when an individual stops using PrEP due to reduced HIV risk, while unintentional discontinuation is often related to access barriers.
- > Pursue a better understanding of factors that influence higher continuation in community-run services as compared to public sector clinics.
- ▶ Further research on effectiveness and scalability of promising strategies:
 - > Further develop and evaluate promising Mhealth strategies that can be supported in low-resourced, low-tech settings as part of a combination prevention. There is a need for more studies to better measure Mhealth in order to demonstrate attribution and set country standards for Mhealth and to expand use beyond interaction with the PrEP user, to include areas such as Mhealth for demand creation and interfacing with popular applications among populations for whom PrEP is targeted (e.g., dating apps).
 - > Expand the scope of program data for continuation strategies implemented in programs, particularly in low- and middle-income high HIV burden countries for which there is lower publication output.
- ▶ Invest in the sustainability of community-based PrEP delivery platforms.



KEY CONSIDERATIONS FOR PROGRAMS

Think tank discussions elicited a number of key issues for which further deliberations, solutions, research and resources are required in the short term. These include:

- 1** In response to lessons from SEARCH as well as data reported from Australia, the United Kingdom and the United States,^{21,22,23} access to oral PrEP should be rapidly expanded to reach scale in order to capitalize on the full potential impact.
- 2** With only one product approved, the evidence is clear that daily use (continuous or event-driven) is only one of the ways that people will use PrEP. New products will not resolve all barriers to continued use. Even as PrEP product options expand, programs and policies—including indicators for measuring continued use—must be responsive to the reality of event-driven, episodic and intermittent use.
- 3** Monitoring and evaluation of effective and continued PrEP use should be strengthened by improving indicators to collect meaningful data (e.g., discerning where is there very early stopping and/or long delays between stopping and restarting) while minimizing reporting burden on programs. As PrEP programs mature, it is critical that the indicators collected are useful and robust enough to understand and measure population-level impact as well as to inform programmatic decisions and interventions to support individuals to use PrEP in ways that are most effective for them. Further, WHO can provide ongoing global guidance on indicators as the field evolves. Integrating PrEP questions into PHIA— an effort which is underway—presents another opportunity to collect population-level data on effective and continued use.
- 4** The published and program data evidence points to the implementation of innovative PrEP continuation strategies.²⁴ Promising and effective strategies should be identified for integration and rapid uptake into the scale-up of national PrEP programs. In particular, there is strong evidence that Mhealth interventions are effective across populations but may require additional investments to further pilot, evaluate and bring them to scale.
- 5** Community-led and community-based services have demonstrated higher uptake and continued use compared to facility approaches. They are also more amenable to testing innovative approaches but tend to be donor dependent, which may affect the continuation of services. Continued investments in these services are critical in offering options that respond to user preferences.
- 6** Continued investments in implementation science research on oral PrEP are needed, especially in low- and middle-income countries. Research to identify, evaluate, cost and scale up impactful and client-centered interventions for continuation will inform interventions and the scale-up of future biomedical prevention products.

²¹ https://www.avac.org/sites/default/files/resource-files/EndEpidemic_nov2019.pdf.

²² Mera R et al. 20 Dec. 2019. *Estimation of New HIV Diagnosis Rates Among High Risk, PrEP Eligible Individuals Using HIV Surveillance Data at the Metropolitan Statistical Area Level in the United States*. *Journal of the International AIDS Society*. <https://onlinelibrary.wiley.com/doi/full/10.1002/jia2.25433>.

²³ <https://www.croiconference.org/abstract/rapid-reduction-hiv-diagnoses-after-targeted-prep-implementation-nsw-australia/>.

²⁴ Sushena Reza-Paul, Lisa Lazarus, Raviprakash Maiya, Partha Haldar, B. B. Rewari, M. S. Venugopal, Syed Hafeez Ur Rahman, K. T. Venukumar, Manjula Ramaiah, Akram Pasha, Mukta Sharma, Richard Steen & Robert Lorway (2020): *The Ashodaya PrEP project: Lessons and implications for scaling up PrEP from a community-led demonstration project among female sex workers in Mysore, India*, *Global Public Health*, DOI: 10.1080/17441692.2020.1724316.



MEETING AGENDA

Objectives

- Present and examine strategies for supporting and improving continuation from effective models that can be adapted across populations and settings.
- Identify potential solutions to address barriers to continuation in order to maximize the impact of new biomedical prevention options that are currently in trials or under development.
- Connect the recommendations on measuring and monitoring effective PrEP use and impact with programmatic strategies to support continuation.

TIME	SESSION TITLE	SESSION OBJECTIVES	FACILITATOR/MODERATOR AND SESSION TYPE
8:00am	Opening remarks and introductions	Review of meeting objectives, expected outcomes and logistics	Jessica Rodrigues, PMM/AVAC
8:10am	Review outcomes/ recommendations on defining and measuring the success of PrEP and recent research that demonstrates the impact of PrEP	<ul style="list-style-type: none"> > Making the case for measuring the impact of PrEP at the population level > Balancing messaging on impact with support for continued use at the individual level and current indicators that don't answer either question > Considerations for surveillance studies, donor reporting, national health systems 	Facilitator: Robyn Eakle, USAID Presenters: <ul style="list-style-type: none"> > Jason Reed, Jhpiego > Catherine Koss & James Ayieko, SEARCH study > Jessica Justman, ICAP Q&A
9:15am	BREAK		
9:25am	<ul style="list-style-type: none"> > Strategies to support continued use > Feedback on findings to fill in gaps 	<ul style="list-style-type: none"> > Relevance of programmatic interventions to support effective use > Presentation of summary of findings from literature review and interviews > Filling in gaps in findings based on collective knowledge and ongoing research 	Facilitator: Josie Presley, BMGF Presenters: <ul style="list-style-type: none"> > Jessica Rodrigues, PMM/AVAC > Wanjiru Mukoma, Consultant Q&A
10:00am	Deeper dive into types of interventions to support continued and effective use	<ul style="list-style-type: none"> > Better understanding of interventions that can be applied from different sectors > Considerations for programs, donor investments and future research 	Interactive small groups: <ol style="list-style-type: none"> 1. Research 2. Facility-based approaches 3. Community-based approaches 4. Mhealth
10:50am	Wrap-up and next steps		Jessica Rodrigues



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