

Think Tank on Defining and Measuring Effective Use of PrEP
Executive Summary
June 2019

Background: setting the stage on oral PrEP continuation and success

As defined and recommended by WHO, effective use includes daily oral PrEP for all populations at high risk of HIV, with an option for intermittent or “event driven” (ED) dosing for men who have sex with men. Existing methods for monitoring and evaluation (M&E), however, don’t allow non-daily use to be considered effective use. Defining effective use of PrEP, which may require continued daily use for many but not all, has therefore been challenging.

While oral PrEP as HIV prophylaxis prevents transmission up to 99% when taken as recommended, many struggle to maintain effective use during periods of risk, thereby diminishing protection for the individual, reducing the potential for population-level impact and complicating efforts by donors and program implementers to monitor and evaluate PrEP delivery in many settings.

Monitoring (in)correct/(in)effective use is essential to identify the programs, providers, and locations where individuals, particularly sub-populations, may be deriving sub-optimal protection, and then intervene appropriately to improve effective use. Measuring effective use of an intervention use – as defined by normative agencies and donors – is critical for many public health domains, and drives implementer monitoring of program performance and reporting to national governments and funding agencies. Ensuring that indicators are of optimal value to the broadest array of stakeholders is essential.

In this nascent phase of PrEP scale-up, various programs’ monitoring and evaluation (M&E) approaches are evolving as experience is gained. Monitoring for (in)effective/(in)correct use requires an understanding of: 1) the duration and intermittency of PrEP use; and, 2) the duration and intermittency of HIV risk. Indicators of PrEP use are typically measured by cross-sectional (e.g. a single snapshot in time) and client-level longitudinal approaches, operating under the assumption that prescription refills equate to actual use (See Table 1 Measures of PrEP Use). The second consideration, HIV risk, is not routinely measured over time and is, for simplicity, assumed by current indicators to be consistent and ongoing between follow-up visits, despite data proving that episodic risk is common.

In an individual with highly frequent, indefinite risk to HIV, measurement of effective PrEP use is straightforward: effective use equates to uninterrupted, continuous use for long periods. In reality, many clients have sufficiently infrequent or episodic periods of HIV risk. Therefore, either ED-PrEP or short-term cycles of oral daily PrEP use with discontinuation(s), followed by PrEP restart(s), would, in actuality, be effective use.

**HIV Prevention
Market Manager** Accelerating Product Introduction
Informing Product Development
Reducing Time to Impact



Supported by the Bill & Melinda Gates Foundation



Many stakeholders have borrowed effectiveness definitions from antiretroviral therapy (ART) programming and indicators, whereby anything less than recommended daily use is associated with significant consequences, such as the development of drug resistance or increased morbidity and mortality. However, PrEP is not synonymous to ART in that risk is not universally continuous. Therefore, applying this narrow definition of proper adherence to PrEP, may lead implementers and other stakeholders to deem programs as failures if large proportions of the individuals in a cohort stop using PrEP for any duration after starting.

Furthermore, the PrEP continuation indicator adopted by WHO is currently restricted to measurement at an individual's first use, even if s/he has subsequent restarts. To more appropriately characterize the full spectrum of effective PrEP use as a function of use equivalent to risk, a broader definition for correct/effective PrEP use is necessary.

In addition to monitoring for program improvement purposes, estimating duration of use (person-time use) is essential to forecasting epidemic impact and defining, as well as measuring, success of the intervention within a cohort. Such modeling activities must also make assumptions about periodicity and typology of exposure risk, which may not be captured by routine PrEP M&E systems. From the standpoint of indicators, contiguous days' use would be the only proper definition of successful use among those with frequent, ongoing risk (assumed or measured). Among those with infrequent, short-term risk, intermittent dosing may confer equivalent protection from HIV acquisition, to the extent that episodic use and risk sufficiently overlap.

Defining PrEP Success

Though a single definition of correct/effective use is preferred by scale-up programs for routine M&E purposes, devising one that suits both PrEP clients with ongoing/frequent risk and those with episodic/infrequent risk may not be possible. For example, the results of applying a universal definition could be misleading, potentially undercounting the number of risk events actually covered in those with episodic/infrequent use if continuous use is the sole definition of success.

Measures of correct/effective use can provide important information to target interventions to improve current and future PrEP delivery (including next-generation products), client engagement and quality of care. Irrespective of the type of measure adopted by programs, whether cross-sectional or longitudinal, there is an impetus to begin to define and measure community or population level impact on HIV incidence drawing on and adapting the approaches used in contexts such as the United States, and other settings with access to robust and accurate sources of linked HIV testing and PrEP prescription data.

Of note, data from the U.S. correlates HIV incidence with PrEP coverage levels, the latter based upon PrEP prescriptions, without any measurements or assumptions related to actual use, actual risk, and overlap. PrEP coverage is a function of the number of people at risk of HIV, the number of PrEP

prescriptions filled for an individual at HIV risk, and an average duration of use (PrEP prescription filled as a proxy of use). This calculation has the ability to define a threshold of PrEP use at which point new infections may be reduced in a given context. Ideally, this calculation could be applied to contexts outside of the US, though the different epidemic dynamics—concentrated vs. generalized—and incidence surveillance capacities would require careful consideration.

The PrEP Continuation and Success Think Tank

In June 2019, a small group of PrEP experts gathered to discuss definitions of continuation and successful use and impact and how best to measure them. This Think Tank was comprised of PEPFAR agency representatives, implementing partners, partners working outside of the PEPFAR space, other funders, and mathematicians. The meeting was hosted by the Prevention Market Manager (AVAC and CHAI) and Jhpiego. The Think Tank has produced a set of preliminary recommendations as well as a thorough review of current methods used and measurement options for consideration.

Recommendations

The Think Tank group has proposed a set of recommendations based on the current understanding of PrEP implementation and taking into account infrastructure and implementation realities on the ground. These recommendations are the following:

1. PrEP continuation should be considered fluid, and successful use on an individual level will depend on the individual's needs and state of risk at given points in time. PrEP continuation and ART retention are not analogous; PREP_CURR and TX_CURR require different interpretations.
2. While HIV risk can be continuous or episodic, only continuous PrEP use provides protection for all. For this reason, preferring continuous use—and monitoring for it—may be the goal of routine M&E. PrEP continuation can be primarily measured by tracking the date(s) and volume(s) of PrEP dispensed. For most programs, this can be a cross-sectional measurement.
 - a. Client-level longitudinal measurement for a subset of programs/sites is recommended to assess the validity of the cross-sectional measurement and allow for characterization of clients/providers/sites with high non-adherence for purposes of intervention (important to distinguish short-term users such as sero-discordant couples or women who are pregnant or breastfeeding).
3. Successful PrEP implementation/impact may be assessed by reaching a certain threshold of PrEP use in a given community achieving saturation, as long as sufficient information is available regarding PrEP coverage and HIV incidence in sub-populations.

These recommendations can be used across geographies and contexts as well as oral PrEP regimens (including event-driven) and future HIV preventative technologies in the pipeline. At this time, the Think Tank recommends that these definitions and measurement methods be incorporated into oral PrEP programming and supported by normative bodies to ensure continuity and comparability.

Modifications to current PrEP indicators/M&E approaches for consideration:

- Report PrEP_NEW every 3 months with disaggregation by key population and age, and pregnancy/breastfeeding status
- Add an indicator to measure 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 U.S and other high-income settings. This could potentially be relevant and applicable to future PrEP technologies.
- Pilot test, or discuss with national TWGs the potential for piloting, an impact indicator (see above) based on distribution in settings where PrEP is sufficiently scaled-up
- Support use of cross-sectional and longitudinal approaches for collecting data on effective use to compare and contrast feasibility, data quality and impact planning to target programmatic interventions.
- Support program evaluations and implementation science to identify the reasons for oral PrEP discontinuation and if related to program quality, identify effective interventions and strategies to improve the quality of PrEP programs and to better to understand episodic or sporadic use.

**HIV Prevention
Market Manager** Accelerating Product Introduction
Informing Product Development
Reducing Time to Impact



Supported by the Bill & Melinda Gates Foundation

