Defining and Measuring the Effective Use of PrEP Think Tank Meeting Report

June 18-19, 2019, Washington, D.C.

Executive Summary

Setting the stage on oral PrEP continuation and success

While oral PrEP as HIV prophylaxis prevents transmission by 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.

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.

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 the 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.





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 PrEP use, 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.

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 programs and 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 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.
- 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 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.

Background: The challenge of measuring PrEP continuation

While daily oral pre-exposure prophylaxis (PrEP) of a single pill containing tenofovir disoproxil fumarate (TDF) + emtricitabine (FTC) is a highly effective method for preventing HIV transmission, its efficacy is dependent on the maintenance of effective concentrations of the drugs during periods of exposure to the virus¹²³. As retention, adherence, and continuation of PrEP during riskier periods is therefore fundamental to achieving optimal outcomes for individuals and populations, faithfully documenting and attending to effective use is of prime importance.

Central to the challenge of documenting PrEP continuation, however, is the reality that existing definitions of continuation from which monitoring and evaluation of programs and delivery have been constructed, rely on three potentially faulty assumptions, including that; a) HIV risk is ongoing, perhaps indefinitely; b) self-report of HIV risk is reliable, despite evidence to the contrary; and c) the number of pills recorded as dispensed or remaining at follow-up are an accurate reflection of pills taken⁴⁵. Implementers and modelers are increasingly attempting to overcome the complexity and uncertainty that these potentially faulty assumptions introduce in their efforts to build programs that have a positive public health impact in a cost-effective manner.

In fact, most guidance documents acknowledge that individuals may have periods, or "seasons", of risk, and therefore recommend the offer of PrEP explicitly during these periods for most populations. To make matters more complicated, the WHO considers "event driven" (ED) PrEP a reasonable option for those with rectal exposure, therefore allowing non-contiguous PrEP⁶. These guidance documents also acknowledge that self-reported risk may be the only available marker for a PrEP indication for assessing proper use. This is especially true in health systems without the resources to document a person's medical history and work from an objective proxy for risk, such as diagnoses of sexually transmitted

⁶ What's the 2+1+1? Event-driven oral pre-exposure prophylaxis to prevent HIV for men who have sex with men: Update to WHO's recommendation on oral PrEP - Technical Brief. WHO. July 2019





¹ Anderson, Peter L et al. "Emtricitabine-tenofovir concentrations and pre-exposure prophylaxis efficacy in men who have sex with men." Science translational medicine vol. 4,151 (2012): 151ra125. doi:10.1126/scitranslmed.3004006

² Baeten JM, et al. "Antiretroviral prophylaxis for HIV prevention in heterosexual men and women." N Engl J Med. 2012 Aug 2;367(5):399-410. ³ Molina JM, et al. "On Demand PrEP With Oral TDF-FTC in MSM: Results of the ANRS Ipergay Trial" [abstract 23LB]. Conference on Retroviruses and Opportunistic Infections; 2015 Feb 23–26; Seattle, WA, USA

⁴ Monitoring, Evaluation, and Reporting Indicator Reference Guide (MER) 2.0 (Version 2.3). September 2018

⁵ WHO implementation tool for pre-exposure prophylaxis of HIV infection. July 2017

infections (STIs) or pregnancy and many newly expanding PrEP programs are located in regions of the globe were resources are too limited to faithfully document self-reported risk, let alone such objective biomedical proxies.

In low income countries, PrEP demonstration projects are now transitioning into ongoing PrEP delivery programs and entirely new PrEP delivery services have been launched, resulting in substantial increases in PrEP initiations. However, many of the very same programs are seeing significant numbers of individuals who quickly discontinue PrEP after starting⁷⁸.

Addressing this vexing problem will be challenging, but it is not without precedent, as users of many health products – particularly those designed to prevent disease or pregnancy – discontinue or struggle to maintain perfect adherence to them, and where assumptions about effective use have become built into indicators.

Therefore, while assessing risk can be particularly useful for gauging broader epidemiological snapshots of generalized epidemics within particular geographies or within key populations, or even matching use patterns in those trying ED PrEP, high-level indicators are likely to remain disaggregated from concerns about risk.

The early stages of PrEP roll-out largely focused on building and expanding the number of people offered and starting PrEP, with methods for documenting, measuring and evaluating these numbers taking precedence. It is only recently that significant attention is being paid to PrEP continuation. While demonstration projects and PrEP providers expanding ramp-up in the field have documented early discontinuation rates in many cases, the methods employed by them have varied.

Ultimately, high-level indicators of effective PrEP use will be unlikely to address the direct link between risk and use patterns explicitly as a primary variable, at least across a cohort. This is due to a number of factors, but resource limitations and doubts among some about the usefulness of HIV risks assessments to document effective use predominate. Likewise, sophisticated measures of adherence are unlikely to be employed outside of clinical trials and demonstration projects.

Monitoring (in)correct/(in)effective use, however, is essential for locating where PrEP delivery is going well, or where additional focus and possibly resources should be directed. Therefore, indicators that are the simplest, easiest to collect, and of the greatest value must take precedence

⁸ Kagaayi J, et al. "Preexposure prophylaxis: acceptability and retention in South Western Uganda." Abstract 993. CROI 2019. March 4-7 2019, Seattle, Washington, USA





⁷ Mugwanya K, et al. "Persistence with PrEP use in African adolescents and young women initiating PrEP." Abstract 993. CROI 2019. March 4-7 2019, Seattle, Washington, USA

The need to define successful and effective PrEP use is made even more clear when one considers that the available data often fails to distinguish any gaps that may occur between PrEP initiation, prescription refills or visits, and a restart. Equally important is the observation that while PrEP programs in adolescent girls and young women (AGYW) have ramped up quickly, documented use-patterns within the countries with the earliest PrEP adoption suggest that discontinuation rates may be more common and more erratic in the first years following the roll out of PrEP programs. This has been true even in the United States, where PrEP expansion occurred first and which has a strong public health infrastructure and a reasonable level of PrEP awareness of among those at risk.⁹¹⁰

There is a risk that some policymakers and stakeholders will point to low continuation rates as a reason to question whether PrEP is a worthwhile investment. However, taken in context –compared to high-income settings as well as to ART scale-up and continuation rates of contraception – it is crucial not to prematurely assess PrEP programs in sub-Saharan Africa based on rates of continuation alone.

It should not be forgotten that PrEP is a relatively new prevention intervention and that important questions remain unanswered, including how best and in whom to use it alongside other existing methods, such as behavior change, condom distribution, VMMC, and the offer of ART in people with HIV for secondary prevention. As the scale up of PrEP programs is now occurring at a rapid pace in multiple countries, a variety of stakeholders in the global response to the HIV epidemic have noted the lack of a commonly shared and simple measurement of successful PrEP that is both relevant and scalable from the site to the national level. Stakeholders involved in PrEP scale up have been working, with varying levels of coordination to address this unmet need.

As PrEP programs mature and consolidate, there is a unique opportunity to work closely with stakeholders at the global and country level to: 1) recalibrate expectations on time required to document impact and in the meantime to: 2) agree on a harmonized method to measure impact and 3) devise simple models to measure persistence/duration of use at the site/sub-national/program level that reflects the realities of varying risk periods and multiple episodes of use.

Moving toward solutions for the definition and measurement of successful PrEP continuation

Offering PrEP to those at risk for HIV acquisition has the potential to slow or reverse the number of new infections over time within the populations with high uptake of the intervention. Emerging data from the United States, Australia and the London, England, suggest this may be possible. The uptake of PrEP in these areas—beginning in 2012 in the United States and more recently in Australia and London—has

¹⁰ Scott HM, et al. "Racial/Ethnic and HIV risk category disparities in PrEP discontinuation among patients in publicly-funded primary care clinics." 2019 Aug 20. [Epub ahead of print]





⁹ Serota DP, et al. "Pre-exposure prophylaxis uptake and discontinuation among young black men who have sex with men in Atlanta, Georgia: A prospective cohort study." Clin Infect Dis. 2019 Sep 10. pii: ciz894 [Epub ahead of print]

corresponded with year-over-year reductions in new HIV cases, at least among subgroups of men who have sex with men (MSM), where the epidemic is highly concentrated.¹¹¹²

These data, including a recently reported analysis of country-wide data from the United States, suggest a strong correlation between increases in generalized PrEP use among greater numbers of at-risk individuals (but not inherently tied to contiguous PrEP use in the individual) and a reduction in new HIV diagnoses, over and above what would be expect from increasing numbers of people with HIV with fully suppressed virus due to ART¹³.

Determining how best to define and measure the impact of PrEP programs in low- and middle-income countries, however, particularly programs focused on adolescent girls and young women (AGYW), is an enduring challenge. Intermittent PrEP use may be less forgiving in women compared to men¹⁴¹⁵, and it may be more difficult to observe significant reductions in the number of new HIV diagnoses in a generalized epidemic. However, efforts are underway to better understand and measure both oral PrEP impact and continuation rates.

To assess the challenges commonly confronted by funding and evaluation bodies in constructing PrEP indicators and efforts by modelers and implementers to adapt them, as well as to identify potential methods for measuring effective use, Jhpiego and the Prevention Market Manager (PMM), funded by the Bill & Melinda Gates Foundation, and implemented by AVAC and the Clinton Health Access Initiative (CHAI), co-convened a Think Tank on Defining and Measuring Effective Use of PrEP in Washington, D.C. on June 18 - 19, 2019.

Under the assumption that wider distribution of PrEP can enhance existing HIV prevention programs, an effective marker toward measuring the impact of PrEP is required. PrEP continuation is increasingly viewed as indispensable to establish the impact of PrEP. However, there are divergent views on the definition of successful PrEP continuation, and existing methods to measure it are only beginning to be developed and implemented. Coalescing around a shared definition of successful PrEP continuation and proposing a simple measurement of impact was the primary focus of the Think Tank.

Think Tank Background and Rationale

¹² Grulich AE, et al. "Population-level effectiveness of rapid, targeted, high-coverage roll-out of HIV pre-exposure prophylaxis in men who have sex with men: the EPIC-NSW prospective cohort study." Lancet HIV. 2018 Nov;5(11):e629-e637

¹⁴ Thompson CG, et al. "Antiretroviral pharmacology in mucosal tissues." J Acquir Immune Deficiency Syndrome. 2013;63 Suppl 2:S240-7 ¹⁵ Karim SS, et al. "Drug concentrations after topical and oral antiretroviral pre-exposure prophylaxis: implications for HIV prevention in women." Lancet. 2011;378(9787):279-81





¹¹ Nwokolo N, et al. "Rapidly declining HIV infection in MSM in central London." Lancet HIV. 2017 Nov;4(11):e482-d483

¹³ Mera-Giler R, et al. "PrEP Significantly Reduces the Rate of New HIV Diagnoses in US Metropolitan Statistical Areas Independent of Treatment as Prevention (2012–2017)." IDWeek 2019, Washington, D.C.

In June 2019, a small group of PrEP experts gathered to discuss definitions of PrEP continuation, successful use, personal and population 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 Jhpiego and the PMM, a joint project between AVAC and CHAI, which was formed to facilitate an efficient and effective rollout of HIV prevention products. The Think Tank resulted in a set of preliminary recommendations as well as a thorough review of current methods used and measurement options for consideration.

Goals and Key Discussion Points for the Meeting

The goals of the meeting was to develop action-oriented recommendations and activities for follow-up based on a review of methods already in use for measuring continuation and defining successful implementation. Tied to this goal were the following objectives:

- 1. Explore and discuss ongoing efforts to utilize and expand on PEPFAR and WHO PrEP continuation indicators across populations and program types and the challenges in using existing indicators;
- 2. Identify the strengths and weaknesses of the various models and their practical applicability for implementation in other settings and populations;
- 3. Examine the pathway toward the design, validation and adoption of definitions of continuation and impact in the field of family planning and contraception and its applicability to oral PrEP delivery; and
- 4. Determine whether a reconceptualized definition of PrEP continuation could improve the quality and practicality of M&E efforts and predict epidemic impact

Although PrEP continuation indicators are evolving and improving, feedback from implementing partners and policymakers prior to the meeting confirmed the challenges on the ground in measuring and supporting PrEP continuation across many settings. Therefore, the conveners set out to build opportunities for knowledge transfer and discussion among diverse stakeholder groups, including implementers, M&E experts, representatives from normative bodies, and funders and to determine how to recalibrate the definition of successful PrEP continuation in ways that could benefit multiple stakeholders. A total of 27 participants attended the Think Tank (Appendix A) and the meeting agenda (Appendix B) was constructed to generate the answers to specific questions, which were posed to the participants and included:

- 1. What current definitions are most widely used to measure PrEP implementation, including starts, stops, restarts and continuation?
- 2. What approaches have modelers and implementers taken to address M&E challenges?
- 3. What can we learn from other health sectors on measuring continued use?
- 4. Can we reconceptualize definitions of successful PrEP continuation and metrics to measure it?





- 5. Which definitions and M&E methodologies rise to the top for exploration and implementation, and what questions remain unanswered?
- 6. What additional work must be done to test and validate new definitions and measurements of successful continuation?

Think Tank Discussion Highlights

Clearly, funders and implementers must use data to guide decisions about whether a disease prevention product is likely to have a positive impact on public health crises and whether the intervention can be employed in a cost-effective manner. Unfortunately, such data are often incomplete and crises may be of such magnitude that it would be unethical to refrain from providing products about which data are lacking. Nevertheless M&E is crucial to ensuring that current and ongoing performance of product delivery programs are monitored to the degree possible, despite frequently limited resources.

Normative bodies such as the WHO and the Centers for Disease Control and Prevention (CDC) in the United States have highlighted HIV risk as an obligatory factor when determining who should be offered PrEP (WHO and CDC). However, evolving indicators for PrEP continuation rest on the assumption that risk is ongoing and therefore contiguous daily use is necessary until ongoing risk is no longer present. At the time of the Think Tank, it was highly anticipated that the WHO would soon issue a directive on ED PrEP, which did subsequently occur. This makes newly introduced indicators for PrEP continuation both overly complex and likely divorced from the capacity to measure when actual risk is being covered and therefore the possibility that a beneficial impact for the individual and the population is being achieved. The Think Tank was designed to more fully explore these challenges and limitations and to bring the expertise of varying stakeholders to bare on devising potential solutions for further study.

Yet, periods of risk for HIV acquisition ebb and flow for most individuals, and decades of data from the fields of HIV prevention – and especially sexual and reproductive health – underscore the challenge of developing a simple, reliable and valid indicator linking continuous provision and use of a specific intervention (e.g. PrEP, condoms, etc.) with a reasonable assumption of increased or diminished risk. With PrEP, this equates to vulnerability to HIV acquisition and with contraceptives, unintended pregnancy, and the reality that risk and use are intermittent in both cases underscores the complexity with developing a reliable benchmark to measure program impact.

Efforts to devise such indicators are in early stages given the recent roll-out of PrEP outside of biomedical studies and demonstration projects. For instance, PEPFAR recently added a measure of current use (e.g. CURR) as an indicator to help distinguish continuation from new starts, (e.g. NEW). The WHO now recommends defining the success of a PrEP program by the number of eligible people who





initiate oral PrEP, the number of those who continue PrEP for at least <u>three consecutive months</u>, and the number of people prescribed PrEP who seroconvert.

Neither of these approaches, however, automatically lend themselves to an obvious and practical method for distinguishing starts and stops as an actual PrEP failure or success. Under these models, it would be difficult for a funder, program administrator or implementer, to gauge whether a 30%, 60% or 90% continuation rate represents actual success in terms of ensuring adequate protection for clients during periods of high risk, (in other words impact) without reliable and comparable risk assessment. Furthermore, these measures only apply to an individual's first PrEP use; for those with multiple periods of initiation, use and restarts, second and subsequent uses have no measure of continuation. To the extent that continuation may improve or decline with successive uses, continuation rates at first use may be biased. In all, widescale and full adoption of an oral PrEP continuation measurement is incomplete.

Therefore, the participants discussed models for measuring PrEP continuation that are in current operation (See Appendixes C and D), including contiguous and cumulative use, understanding that there are several shortcomings to any model that fails to document and discriminate between new initiations, current clients taking PrEP, return for a first follow-up visit and the average duration of use.



Measurements of PrEP Use – Challenges and Solutions



A number of measures are being employed by different groups. Some models attempt to follow individual PrEP-takers longitudinally for better accuracy. most cross-sectional for ease of data collection an analysis (e.g. number of clients served in a reporting period, number of clients served cumulatively to date, etc.). Each has strengths and weakness as documented below (Appendix C).

In short, however, while certain indicators, such as clients served is easy to measure, it is nearly impossible to disaggregate actual current users for the purposes of establishing continuation rates. Other measures, such as use-patterns may be far more helpful, but are much more difficult to collect, document and analyze.

Country presentations and experiences

There was considerable overlap among the country-level models presented and discussed, which included sites in South Africa, Zambia, the Kingdom of Eswatini, Kenya, Uganda, Vietnam and the United States. Each attempt to assess programmatic impact and not simply continuation alone as the end goal.

Putting aside the case of the United States, for which there exists a much more extensive database and discussed in detail below, each of the other models sought to ensure both data robustness and integrity, particularly as they transitioned from smaller formal demonstration projects to ongoing PrEP delivery programs. Given the resource limitations that existed within many of the programs, each data collection methods had to balance: a) recording the least number of variables possible while still yielding meaningful outputs ; along with, b) ensuring the greatest ease in data collection, input and analysis.

In all of the non-U.S. models, the date of a medical visit and a PrEP prescription were recorded. Some models also included additional inputs, including HIV-status at the time of a visit, self-assessed HIV risk, and in Vietnam, client-level data, such as reasons for discontinuation.

All of the models revealed low continuation rates among most populations, and in fact, later analyses in several found that the original PrEP continuation estimates were much lower than previously believed. Nevertheless, each model offered useful tools to consider. Highlights included:

- utilizing the results of HIV antibody tests can serve as a lose measure of covered risk (e.g. newly positive diagnoses in persons otherwise adjudicated as continuing PrEP use or continued negative diagnoses in persons with intermittent use or missed visits);
- introducing indictors that accurately reflect restarts; and,

Learning from SRH and contraception use measurement

• collecting and recording client-level data to allow for more accurate assumptions of covered risk periods.



j; jhpiego

Beyond serving as an example for the length of time it can take to achieve optimal public health targets, the field of sexual and reproductive health lends itself to other helpful comparisons to attempts to devise a simple measurement for PrEP continuation. For instance, PrEP expands the number of available HIV prevention options, all of which may be used separately or in combination, and the preference for one option over others may fluctuate. Therefore, experience with devising simple measurements to estimate the impact of providing contraceptives, where many options exist, may offer useful analogies.

Too little effort has been given to examining the long pathway toward developing and validating the standardized definitions and M&E methods in wide use today for contraception, as well as the lessons that might be learned. In particular, as data on the real-world effectiveness of individual contraceptive methods became richer, the ability to make more accurate predictions about the degree of protection an intervention offered allowed the field to consolidate around a formula called Couple-years of prevention (CYP). The CYP formula is straightforward in that it relies on defining a particular average duration of pregnancy protection per "dose" of a particular contraceptive method, whether short or long-acting. Although this method has weaknesses, especially the fact that it only reflects the bulk delivery of products and not delivery to individuals, its simplicity and practicality make it an attractive model for thoughtful discussion as definitions and measures of success for PrEP continue to evolve. Actual use and temporal associations of use and risk would require defined assumptions to forecast PrEP protection.

With WHO guidance on the use of event-driven oral PREP with TDF+FTC in MSM was introduced in July 2019, and new forms of PrEP on the mid-term horizon (especially long-acting products), we may have much to learn from the oral contraceptive field. These innovations in PrEP use, will demand different approaches to linkages between continuation and impact. While expanded choice will demand different approached, the CYP model does suggest a pathway for the development of simple indicators when multiple options are available.

Defining a threshold for PrEP Impact

Research conducted by Gilead Sciences in conjunction with the CDC may serve as a useful model, at least for the purposes of validating assumptions about PrEP prevalence and population-level epidemiological impact. In short, their analysis of pharmacy fill data, de-identified medical data and HIV surveillance databases has documented a correlation between the steep increase in the prevalence of PrEP use in the United States between 2012 and 2017 and a corresponding drop in new HIV cases.

While the literature has documented this correlation in the past (Graph # 1), a recent presentation incorporating additional data into the Gilead/CDC model asserts that the magnitude of the independent





effect of PrEP uptake on reduced new HIV diagnoses across the cohort was twice that of increased numbers of people with HIV taking ART since the introduction of PrEP in the United States (Graph # 2).



Graph #1

Graph # 2

HIV Prevention

Market Manager

AVAC

Accelerating Product Introduction Informing Product Development

Reducing Time to Impact

Supported by the Bill & Melinda Gates Foundation





Permission: Mera, et al. IDWeek2019

While the vast reach and robustness of such data may never be available to stakeholders doing work in low-income settings, this type of research could indicate which types of proxies for population-level impact could prove most useful as an adjunct to more simple PrEP use measurements. As such, while a model without the robustness of the data produced by Gilead and the CDC would suffer from some of the same weaknesses of the CYP model employed for decades for contraceptive use, it could also benefit from the simplicity of bulk dispensation as a measurement.



Couple Years Protection

CYP is based on the volume of various methods (units) dispensed and not people.



United States/Gilead

Impact Measure

Demonstrated a strong correlation between PrEP prevalence and a reduction in new infections

Model vulnerable in early months/years as PrEP oll-out can increase testing, which increases the likelihood of new diagnoses

If prevalence (# of pills dispensed in total) climbs slowly, more detailed information to understand reasons for PrEP refusal or discontinuation would be required. Pathway to a Coarse Measurement

Can we define a proxy measure of impact (i.e number of new HIV cases) as we refine models/indicators to monitor effective use?





Potential

Solution

The data from Gilead was produced by first assessing at least one filled TDF+FTC prescription that could be confidently adjudicated as indicated for PrEP, based on an algorithm excluding use for other indications. In each year, from 2012 through 2017, PrEP use was tracked by gender, age and geography, with 80% of pharmacies in the United States reporting data and a significant number of metropolitan public health authorities providing surveillance data, including HIV diagnoses and estimated ART use among those living with HIV. The analysis calculated the need for PrEP based on the rate of new cases in prior years, PrEP use in the current year and the number of new HIV cases. The resulting PrEP-to-need ratio (PnR) was calculated, which simultaneously linked PrEP prevalence to the number of new HIV cases, but also offered a dynamic measure of the degree of coverage that the model estimates is needed—and potentially met—in specific populations over time.

Discussions and considerations for next steps

Perhaps the three most provocative questions posed during the closing day of the meeting were:

- 1. How relevant is early PrEP discontinuation when one has the long view in mind?
- 2. Can any simple M&E methods be developed to allow for the definition of success to reflect periods of risk covered by PrEP (whether used continuously or episodically)?
- 3. Could a course measurement of the overall prevalence of PrEP use in a population, region or country which when other prevention methods are included was dubbed by meeting attendees as the "community prevention load" become a reasonable predictor that PrEP is meaningfully contributing to reduced HIV incidence?

As to the first, meeting attendees familiar with the dissemination of new products and services into communities commented that early adopters frequently choose not to continue utilizing the interventions, but that this kind of saturation can significantly increase awareness of and familiarity and comfort with the intervention within a population in a short amount of time. The Gilead data bears this out to some degree. Whereas early discontinuation was common in the first period of analysis following the approval of PrEP in the United States from 2012 to 2014, subsequent periods of analysis revealed that as PrEP saturation continued to climb, so too did the rates of PrEP continuation. To the extent continuation may improve with successive uses, continuation rates based solely upon first use may be negatively biased.

Meeting participants were less sanguine that current definitions, indictors and M&E models for continuous PrEP use could be easily adapted in low-resource settings to account for successful episodic use, whereby individuals take PrEP only when they are at actual risk of HIV infection. While more sophisticated models that successfully incorporate additional variables, such as HIV seroconversions, risk assessments and recorded reasons for discontinuation could provide a foundation for adaptation of the more minimal indicators in the future, this will take time and the impact of any single product or





intervention on new HIV diagnoses will suffer from the inability to strongly attribute the impact independently.

For instance, increased HIV testing rates in addition to or apart from increased ART uptake among people with HIV are just two factors that could lead to an apparent reduction in new HIV diagnoses that could be misattributed to PrEP coverage. As well, assumptions about the association between use, perceived risk, actual risk and any temporal associations are undefined.

Finally, a significant amount of time was spent exploring the conceptual model utilized by Gilead Sciences, whereby a pathway to a single indicator, being total PrEP prevalence, could be a valid and reliable proxy for PrEP success in a population, region or country. While this model is similarly vulnerable to gaps in data or data reliability, particularly trustworthy models for HIV incidence, it is similar to the model used in contraception, where the calculation of the overall level of protection is based on distribution and does not rely on counting the number of individuals using contraception.

The direct link between CYP and the potential decrease in unwanted pregnancies at the individual, community and country level can be difficult to establish and rely upon. For instance:

- The model relies on a blend of efficacy and effectiveness data for the methods, that is included in the estimates for how continuation rates could contribute to impact.
- Discontinuations for all reasons, including switching or combining methods, or changes in desire for pregnancy or becoming pregnant, are aggregated.
- The model doesn't reveal whether the contraceptive methods are accessible and acceptable to all individuals, nor does it provide any indication of the quality of services.

A model proposed by the data from Gilead and the CDC that has shown a strong correlation between total PrEP prescriptions and diminishing incidence, the answers to these questions, as well as HIV incidence data, become less relevant as the cumulative distribution of PrEP reaches a certain threshold.

The course impact measurement this allows, which could be adopted by nearly any program, with the proviso that multiple factors (e.g. expanded ART coverage and viral suppression, VMMC, etc.) may contribute to any observable reduction in new HIV diagnoses, is as follows:

- Numerator: Number of new HIV cases
- Denominator: Number of individuals at risk ([adults with PrEP indication alive at beginning of each period × 1 year] – [new HIV diagnoses × average time exposed] – [persons on PrEP × average time exposed with PrEP]).

While PrEP scale-up may initially lead to a more rapid increase in HIV testing, and therefore identification of new HIV cases, the impact of HIV testing is expected to diminish over time. As well, pilot programs and demonstration projects to model estimates of HIV incidence, could become less necessary





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or require less precision, provided that estimates in analogous settings and populations are available. Also, attributing a beneficial impact on reducing the number of new HIV cases to PrEP alone will be somewhat speculative regardless of the sophistication and depth of multiple data sources, given the variability of use of other prevention methods within a population. This mimics and is underscored by the limitation of CYP in contraceptive delivery as a proxy for beneficial impact.

In short, if PrEP volume alone, regardless of continuation, could provide a reasonable and simple method for estimating the impact of PrEP, it could offer solutions to many of the disadvantages of existing indicators. It requires only three variables: the number of pills dispensed regardless of PrEP continuation rates; the number of new HIV infections over periods of time; and, the number of individuals estimated to be at risk.

Next steps and timelines

Meeting participants recognized the need to continue these discussions and to bring in a wider stakeholder base to determine what additional areas for exploration are needed. The Think Tank model simultaneously pushes for concrete, measurable outcomes linked to time-based deliverables while also being flexible enough to produce outcomes that might be different than originally anticipated. The interdisciplinary expertise from different health sectors and contexts generated richer solutions compared to a meeting with HIV prevention experts. Consensus was achieved on developing a model with the following elements:

- has a clear pathway to demonstrating or predicting the likely relationship between a simple measure (PrEP prevalence) to impact;
- could be adopted nearly universally; and
- could be less vulnerable to the addition of new PrEP options, including episodic or event-driven use

Proposed next steps are detailed below, not least of which is the plan to move forward with a subsequent meeting that could focus on research strategies to enhance continuation and, potentially, provide underlying data necessary to increase confidence in the course measurement for a specific population or country.

Proposed next steps include:

• Develop and circulate report for review, highlighting standardized descriptions of M&E models and program implementation for consideration, modification and adoption by other implementers.





- Provide information and recommendations to influence stakeholders who determine indicators and other data variables used in the short- and mid-term to measure PrEP continuation (e.g. PEPFAR and WHO).
- Develop recommendations to promote the inclusion of PrEP use and awareness questions in large population surveys, such as those conducted by the DHS and other surveillance based surveys.
- Continue dialogue with and additional stakeholders, especially implementers, providers, civil society and experts on other analogous health topics (e.g. contraception) to validate/determine the utility of proposed measures.
- Work with product developers to determine how the Think Tank outcomes can be used to guide research and product development of novel PrEP interventions.





Appendix A

Think Tank on Defining and Measuring Effective Use of PrEP Washington, D.C., U.S.A. June 18 - 19, 2019

Meeting Attendees

- Mary Aikenhead, Bill & Melinda Gates Foundation
- Stella Alamo Talisuna, Centers for Disease Control and Prevention
- Jennifer Albertini, S/GAC
- Rutendo Bothma, Wits Reproductive Health and HIV Institute
- Charles Brown, Preventive Care International
- Alison Cheng, USAID
- Shona Dalal, World Health Organization
- Emily Dorward, USAID
- Evan Doyle, Clinton Health Access Initiative
- Robyn Eakle, USAID
- Brooke Fokker, Boston University
- Julie Franks, ICAP at Columbia University
- Anabel Gomez, AVAC
- Kimberly Green, PATH
- Stephano Gudukeya, Population Services International/Zimbabwe
- Matthew Hamilton, Avenir Health
- Cheryl Hendrickson, Health Economics and Epidemiology Research Office
- Anita Hettema, Clinton Health Access Initiative
- Aparna Jain, Population Council
- Sarah Jenkins, Clinton Health Access Initiative
- Robertino Mera, Gilead Sciences
- Abednego Musau, Jhpiego
- Pragna Patel, Centers for Disease Control and Prevention
- Sangeeta Rana, USAID
- Jason Reed, Jhpiego
- Michelle Rodolph, World Health Organization
- Jessica Rodrigues, AVAC

Support:

• David Evans, Independent Consultant



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Appendix B

Think Tank Agenda Defining and Measuring Effective Use of PrEP

Day One: Tuesday, June 18, 2019		
Time	Session Title	Facilitator/Moderator
9:00 am	Opening remarks and introductions	Jessica Rodrigues, PMM/AVA
9:15am	Meeting objectives and format	David Evans, Consultant
9:30am	Current definitions most widely used to measure oral PrEP	Shona Dalal, WHO
	implementation	Robyn Eakle, USAID
		Jason Reed, Jhpiego
10:30am	Break	
10:45am	Challenges with current PrEP M&E approaches and interim "solutions"	Jason Reed (overview)
		Methods
		Evan Doyle
		Robertino Mera
		Cherly Hendrickson/Brooke
		Nichols
		Matthew Hamilton
		Q&A
		Implementers
		Kimberly Green
		Charles Brown
12:30pm	What can we learn from other health sectors on measuring continued used?	Aparna Jain, Population Council
1.00pm	Lunch	
2:00pm	Reconceptualizing definitions of successful oral PrEP continuation	Jessica Rodrigues,
•	and metrics to measure it	PMM/AVAC
3:00pm	Break	
3.30pm	Which definitions and M&E methodologies are rising to the top and where do questions remain?	David Evans, Consultant
4:30pm	Wrap-up	Robyn Eakle, USAID

Day Two: Wednesday, June 19, 2019			
9:00am	Recap of Day One		David Evans, Consultant
9.00am	Recap of Day Offe		Daviu Evalis, Colisuitant





9:15am	Work that remains to test and validate new definitions and measurements of success.	Jessica Rodrigues, PMM/AVAC
10:15am	Break	
10:45am	Reviewing and agreeing on what metrics can be proposed and to whom	Jessica Rodrigues, PMM/AVA
11:45am	Follow up and action	David Evans, Consultant
12:30pm	Closing remarks	
1:00pm	Lunch and end of meeting	





Appendix C

Table 1: Measures of PrEP Use

Cross-	-sectional Measures
No. Cl	ients Served in Reporting Period (FY)
Pros	
•	Relatively easy to measure
•	Already collected for purposes of reporting PREP_NEW
Cons	
•	Does not reflect the duration of use, e.g., a client receiving 1 PrEP prescription and a client
	receiving 9 PrEP prescriptions each count as "1", though their duration of use (refills as proxy)
	is not possibly the same
•	Does not reflect the periodicity of use, e.g., 2 clients receiving 6 PrEP prescriptions are counted
	the same, even if the first takes PrEP for 180 days in a row and the other discontinues and
	restarts PrEP every other month
Comn	nents
•	Current PREP_NEW indicator does not define whether/when a client discontinuing and
	restarting PrEP at a later date is again counted as PREP_NEW
No. Cl	ients Served Cumulatively/To Date
Pros	
•	Relatively easy to measure
•	Already collected for purposes of reporting PREP_CURR
Cons	
•	Does not reflect the duration of use, e.g., a client receiving 1 PrEP prescription and a client
	receiving 9 PrEP prescriptions would each count as "1", though their duration of use (refills as
	proxy) is not the same
Comn	nents
•	A client counts toward PrEP_CURR as long as they receive at least 2 PrEP prescriptions in two
	different fiscal years (FY), regardless of whether their use of PrEP was continuous or separate
	by one or more periods of non-use. Thus, PREP_CURR doesn't reflect continuous use; rather
	it is really a measure of the number of clients only receiving 1 prescription or only receiving
	prescriptions in a single reporting period/FY
Volum	ne PrEP (bottles/pills) Distributed (in Reporting Period or Cumulatively)
Pros	
•	Relatively easy to measure
Cons	
•	Does not reflect the number of clients served
•	No indication of patterns of use (discontinuation(s) and restart(s))
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	HIV Provention Acceleration Product Introduction





Comments

• When combined with No. Clients Served, can derive PrEP coverage (if denominator/population size known)

No. Visits Provided, by Visit Type

Pros

• Relatively easy to measure

Cons

- Does not allow for characterization of client groups/providers/sites with high non-adherence for the purposes of intervention
- Does not readily account for variability introduced by multi-month dispensing, since no single duration between visits equates to timeliness of follow-up prescriptions

Comments

• Poses challenges if determination of visit type (refill vs. restart) requires manual calculation based upon time elapsed since prior visit and number of pills dispensed at prior visit

Individual and aggregate client PrEP use/Use Patterns over time

Pros

- Provides information about duration of use, duration of non-use, including across an infinite number of discontinuation(s) and restart(s)/use cycles (patterns)
- Identification and characterization client groups/providers/sites with high non-adherence possible for purposes of intervention

Cons

- Relatively harder to measure; requires client-level data that include two data points for *every* visit: 1) visit date; and, 2) volume of PrEP dispensed
- Maintaining client-level longitudinal data typically requires an electronic database for feasibility

Comments

• Follow-up visits in an electronic database can be automatically differentiated (refill vs. restart) based upon the two data points—date and PrEP volume dispensed—captured at every visit





Appendix D

Measuring PrEP Continuation Methods and Models





Organization/Project: Jilinde

Country:	Kenya	
Definition of PrEP	The Jilinde project is testing whether a simple data collection method can	
continuation	predict both effective use (e.g. all risk asks covered by PrEP) and days of	
being utilized:	contiguous use. Currently, the pathway toward this proposes cumulative	
	days rather than contiguous days covered.	
Description of	• Examines each subsequent visit after a new start (NEW) to determine	
methodology:	whether a client is there for a refill (CURR) or restart	
	• The numerator is number of pills to provide continuous daily coverage	
	+/- forgiveness with the denominator being a specific time period.	
	• If the number of days since the last visit is within the forgiveness window	
	based on the number of pills dispensed, a client is designated as a refill.	
	 If the number of days since the last visit is beyond the forgiveness 	
	window based on the number of pills dispensed, a client is designated as	
	a restart.	
Key variables:	Date and pill count	
Advantages:	Limited number of variables	
	Can provide a baseline from which to examine risk-based analysis and	
	client-level discussions	
Disadvantages:	Demands accurate tracking of client-level data	
	 Without client-reported risk data there is no way to determine the 	
	relevancy of distinguishing between a refill or restart	
	• The method for data entry can be cumbersome at the site level,	
	particularly when paper-based records are the norm.	





Organization/Project: CHAI

Country:	South Africa, Kenya (piloting), and Zimbabwe (piloting)	
Definition of PrEP	Estimation of average months of PrEP use among a cohort of PrEP users	
continuation	within a specified evaluation period (quarterly or annually) from monthly	
being utilized:	cross-sectional visit tallies.	
Description of	 First, <u>unique clients taking PrEP</u> in a given evaluation period (e.g. 1 	
methodology:	quarter or 1 year) is estimated by counting a subset of initiation, follow-	
	up, and restart visits with prescription periods overlapping with the	
	period of evaluation. Aims of this exercise are to:	
	\circ Account for all clients seen at the facility during the evaluation	
	period	
	 Account for all clients not seen at the facility but are assumed to 	
	be taking their prescription as directed based on timing of last	
	visit	
	 Ensure no clients are double counted 	
	Second, <u>average months of PrEP use</u> among unique clients taking PrEP in	
	the evaluation period is estimated by counting a subset of initiation,	
	follow-up, and restart visits, multiplying by the number of prescription	
	months that fall within the evaluation period (i.e., total client-months on	
	PrEP), and dividing total client-months by unique clients. Aims of this	
	exercise are to:	
	\circ Only count total time during the evaluation period where unique	
	clients are assumed to be taking their prescription as directed	
	 Account for all clients seen at the facility during the evaluation period 	
	 Account for all clients not seen at the facility but are assumed to 	
	be taking their prescription as directed based on timing of last	
	visit	
	Key assumptions:	
	Length of prescription-months issued to the client will be standardized	
	and dictated by visit type (e.g., for South Africa: initiation = 1 month,	
	follow-up = 3 months, and re-start = 1 month prescription).	
	Client will take the full duration of their prescription, making no	
	assumptions on daily adherence.	





	 Visit occurring on any day of the month denotes prescription coverage
	for that entire month (i.e., assumes all visits in a given month happen on
	first day of the month).
Key variables:	 Monthly initiation, follow-up, and restart visit tallies
Advantages:	 Data inputs are relatively easy-to-collect, manage, and report on at
	facility-level and nationally via routine M&E systems.
	 Allows national programs to rapidly and routinely compare trends in
	"PrEP load" and duration of use across populations and geographies
	over time.
	 Allows for estimates of 1) population coverage and 2) average time
	coverage, which can be used to estimate relative impact on infections
	averted.
Disadvantages:	 Doesn't account for clients who take PrEP on-demand.
	 Doesn't account for clients who seek PrEP at multiple delivery sites
	within the same evaluation period.
	 'Unique clients' will be an approximation when estimated annually,
	given that restarts with a previous visit occurring in the same evaluation
	period will be double counted. In South Africa, this is accounted for by
	diving annual restart visits by two before incorporating into the unique
	client estimation (likely most appropriate after the program has reached
	a maintenance phase).





Organization/Project: HE²RO/Boston University

Country:	Data modeled with reference to South Africa and Zambia
Definition of PrEP	Incorporates the HIV status, assessed risk and whether PrEP was dispensed
continuation	at an initiation visit and the same three measures with the addition of return
being utilized:	for a follow-up visit as the four data points to determine "success."
Description of	 Analyzed PrEP policy and monitoring & evaluation tools from two
methodology:	countries. Both countries routinely report PrEP dispensing, follow-up
	visits, and HIV status at quarterly visits.
	• South Africa, which does not capture assessed risk, was compared with
	Zambia, which does routinely assess risk.
	• Over a stipulated time period, each PrEP initiate is determined to be a
	'success' or 'non-success' based on indicators above.
	 The number of "PrEP successes" is compared to the number of total
	PrEP-initiates to determine a program success ratio
	 These ratios can then be compared among programs that target the
	same (key) populations
Key variables:	 Date, pill count, assessed risk, and HIV status
Advantages:	The addition of HIV status and assessed risk can lead to more accurate
	reflections of program success and impact
	 The methodology is well suited to longer periods of evaluation (e.g.
	yearly)
	Easily interpretable metric to monitor effectiveness of PrEP programs
	using routinely collected clinical data
	 Can be used as an outcome measure in cost-effectiveness analyses.
	 Allows for comparisons of PrEP program scale-up strategies and, if
	widely adopted, will allow comparative studies of different approaches
	to PrEP service delivery
	 Can serve as a measure of implementation at the site, program, and
	country level, or for any population that has access to PrEP under the
	same eligibility and implementation guidelines
	Can be applied and compared between a data-rich setting and a data-
	limited setting if warranted. This could allow for comparisons among
	trials or demonstration projects in addition to routine care, provided
	that they are conducted within the same country or transmission group.





Disadvantages:	 Relies on existing assessment of HIV infection risk, if formal risk assessment is done, which differs across programs and guidelines in various countries
	 The methodology does not take the pre-PrEP cascade of care into account
	 The methodology assumes only daily PrEP – doesn't take into account intermittent PrEP
	 Cross-country comparison will remain a challenge due to differences in guidelines for PrEP, models for M&E and routine data collection procedures.





Organization/Project: Arm Yourself (CHAI)

Country:	Kingdom of Eswatini	
Definition of PrEP	PrEP status active and attendance at follow-up visit within 7 days of	
continuation	scheduled visit date at 1, 3 and 6 months based on refill periods that	
being utilized:	assumed daily continuous use.	
Description of	 Demonstration project that was able to follow unique clients at all time 	
methodology:	points and to document reasons for PrEP refusal, discontinuation and self-assessed HIV risk.	
	 Initial roll-out depended on client report of discontinuation, while scale- up distinguished restarts within or outside of 12 months for simpler evaluation of estimated program impact 	
	Bisk question pairs is short and incorporated into visits	
Key variables:	HIV status Initiation data initiation type (first initiation restart=12	
Rey variables.	 First initiation date, initiation type (inst initiation, restart<12 months, restart ≥ 12 months, refill date, # month that refill was provided, PrEP status (active, LTFU, seroconverted, PrEP STOP) and 	
	follow-up date.	
Advantages:	 Simplified assessment allows for better accuracy at distinguishing troublesome patterns of continuation from longer periods lost to follow- up 	
	Incorporation of a simple risk assessment into the clinic visit allows for	
	more accurate determination of discontinuation during periods of risk	
	(e.g. failure) or during no risk (e.g. success), client-level counseling, and	
Disaduantagas:	evolution of client-level interventions.	
Disadvantages:	As with other models, risk assessments have limitations	
	Requires multiple data points tracked to an individual client to determine success.	





Organization/Project: Prepped for PrEP, USAID/PATH Healthy Markets project (PATH)

Country:	Vietnam	
Definition of PrEP	Continuation is measured by distinguishing between clients who start PrEP,	
continuation	are currently on PrEP at the end of the reporting period, the number of	
being utilized:	clients inclusive of the newly enrolled who received PrEP in the reporting	
	period and the number of users who continue on PrEP for three months	
	after initiation.	
Description of	An evolving country-level scale-up beginning in 2018 following	
methodology:	demonstration projects initiated in 2017.	
	Client-level data is collected at visits with the predominant providers of	
	PrEP services being community-led clinics.	
	 Program partners are offered the choice to use to use a paper-based 	
	logbook or digital data capture enabled by an app (but moving to an	
	entirely digital system).	
Key variables:	• New starts, on PrEP, stopped PrEP, reasons for stopping, re-start, HIV	
	status at testing, PrEP_CURR, and clients retained	
Advantages:	 In addition to standard per-visit collection, such as distinguishing new 	
	starts, data collection on clients' reasons for discontinuation or restarts	
	combined with HIV test results at quarterly visits allows for finer analysis	
	of true continuation patterns and program retention.	
	 Better ability to distinguish actual risk periods covered by PrEP from 	
	episodic use, and therefore program and quality improvement, and the	
	ability to determine impact when assessing discontinuation patterns.	
	 Utilization of community-led service providers allows for richer data 	
	collection and better retention and data capture of risk and reasons for	
	stopping and restarting.	
Disadvantages:	As with other models, risk assessments have limitations	
	 Requires multiple data points tracked to an individual client to 	
	determine success.	





Organization/Project: Gilead Sciences

Country:	United States	
Definition of PrEP	Total number of PrEP scripts filled per month by individual clients/patients.	
continuation	Continuous use deemed unimportant based on the number and accuracy of	
being utilized:	supporting data from regional incidence and prevalence reports.	
Description of	 Anonymized client-level demographic, medical and prescription fill data 	
methodology:	from 80% of retail or mail order pharmacies throughout the United	
	States are transmitted to researchers.	
	 Concomitant use of any other ART, diagnosis of HIV disease, 	
	symptomatic infection, HIV-2 infection, non-specific serologic evidence	
	or opportunistic infection diagnoses are exclusionary factors for HIV.	
	PrEP prevalence broken down by population geographic regions of the	
	country and compared with localized HIV surveillance data to determine	
	whether bulk prevalence could be correlated with changes in new HIV	
	cases.	
	 Secondary analysis combined data from 46 research projects that 	
	collected dried blood spots to ascertain HIV incidence.	
Key variables:	 PrEP prevalence calculated by the number of unique PrEP users and the 	
	total prescriptions filled by population and region.	
	 Secondary analysis utilized additional variables that included new or 	
	prevalent HIV cases from public health surveillance data and incidence	
	data from studies and demonstration projects.	
Advantages:	 With the number variables and reliability of the data, allows for a 	
	relatively accurate assessment of the threshold by which PrEP	
	prevalence may actually contribute to diminishing HIV incidence.	
	The number of variables also allows for population-level analysis of PrEP	
	uptake and prevalence and links to HIV incidence and prevalence data.	
	 Could provide a model for a course measure of success (discussed 	
	further below).	
	 Relies solely on data routinely collected for other purposes and 	
	therefore places no additional demands on partners.	
Disadvantages:	Requires data from resources, such as highly accurate claims data and	
	incidence and prevalence data, that are unrealistic in most low- and	
	middle-income countries, including accurate data on HIV incidence by	
	country, region or population.	





As well, stakeholders involved with the development and implementation of methods for measuring and evaluating PrEP continuation must contend with the reality that PrEP efficacy is defined in biological terms as episodes of risk fully covered by optimal drug blood concentrations. Therefore, measurements that record continguous visits and dispensed medication as a proxy for coverage may be equally likely to overestimate the beneficial impact of PrEP in the individual or cohort if individuals don't take it during episodes of risk) as to underestimate the impact of PrEP if individuals do not maintain contiguous visits



