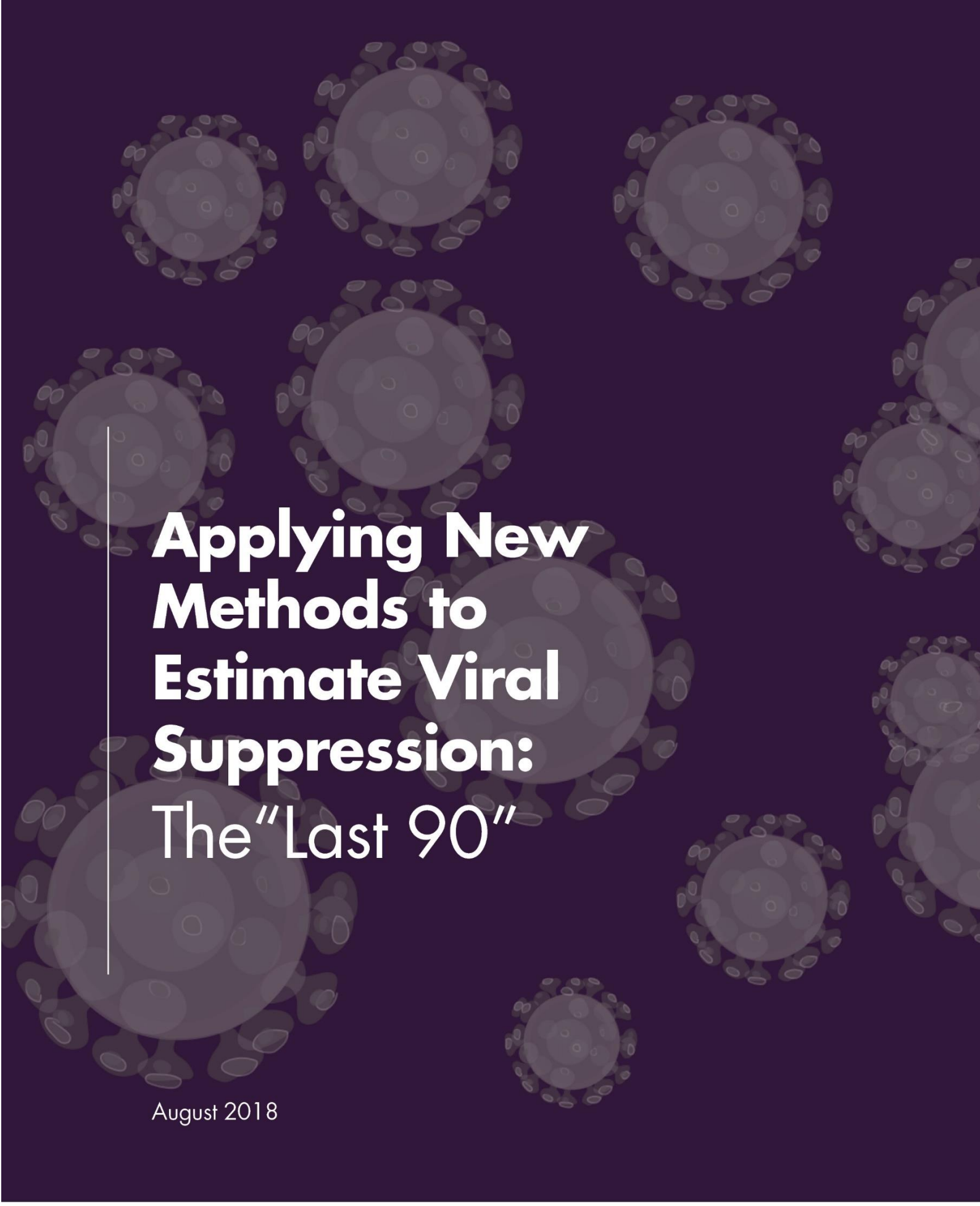

Applying New Methods to Estimate Viral Suppression: The "Last 90"

August 2018

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MEASURE Evaluation

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August 2018

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This publication was produced with the support of the United States Agency for International Development (USAID) under the terms of MEASURE Evaluation cooperative agreement AID-OAA-L-14-00004. MEASURE Evaluation is implemented by the Carolina Population Center, University of North Carolina at Chapel Hill in partnership with ICF International; John Snow, Inc.; Management Sciences for Health; Palladium; and Tulane University. Views expressed are not necessarily those of USAID or the United States government. TR-18-271

ISBN: 978-1-64232-052-7

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ACKNOWLEDGMENTS

We thank the United States Agency for International Development (USAID) and the United States President's Emergency Plan for AIDS Relief (PEPFAR) for supporting this research and the preparation of these guidelines..

Sabrina Zadrozny (Carolina Population Center, University of North Carolina at Chapel Hill [UNC]) and Sharon Weir, of the USAID- and PEPFAR-funded MEASURE Evaluation project, served as principal authors, with contributions from Jessie Edwards (UNC School of Medicine) and Michael Herce (UNC Gillings School of Public Health). The authors thank all colleagues who reviewed the document and/or provided feedback: Heidi Reynolds, Zahra Reynolds, and Elizabeth Sutherland (MEASURE Evaluation). The authors also thank collaborators in the Dominican Republic and Cameroon for their inspiration and the successful field application of the approach.

We thank the knowledge management team at MEASURE Evaluation for editorial and production services.

Suggested citation:

Zadrozny, S., Weir, S., Edwards, J., & Herce, M. (2018). Applying new methods to estimate viral suppression: The "last 90." Chapel Hill, NC, USA: MEASURE Evaluation, University of North Carolina.

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FIGURES

ABBREVIATIONS

ART	antiretroviral therapy
CHAMP	Continuum of Prevention, Care and Treatment of HIV/AIDS for Most-at-Risk-Populations
CI	confidence interval
FAPPS	Formulario de Aplicación a Programas de Políticas Sociales
FSW	female sex worker
IBBS	integrated HIV biobehavioral surveillance
KP	key population
LINKAGES	Linkages across the Continuum of HIV Services for Key Populations Affected by HIV
MSM	men who have sex with men
PEPFAR	United States President's Emergency Plan for AIDS Relief
UNAIDS	Joint United Nations Programme on HIV/AIDS
USAID	United States Agency for International Development
VL	viral load
WHO	World Health Organization

EXECUTIVE SUMMARY

The goal of HIV prevention, care, and treatment programs is to maximize the time that people living with HIV spend alive, well, and with a suppressed viral load.

The purpose of these guidelines is to describe an operational protocol for applying new methods to estimate viral suppression—the "last 90" of the 90-90-90 cascade[1]—at the clinical, programmatic, regional, or national level. These approaches can be used for any population living with HIV and can be tailored to focus on population subgroups or key populations (KPs).

The last 90 is an "ambitious treatment target to help end the AIDS epidemic," according to the Joint United Nations Programme on HIV/AIDS (UNAIDS) (UNAIDS, 2017). The United States Agency for International Development (USAID), through the United States President's Emergency Plan for AIDS Relief (PEPFAR), is working to achieve the 90–90–90 global goals by 2020.

USAID reports that more than 36.7 million people are living with HIV worldwide (USAID, 2018). Its Office of HIV/AIDS provides global leadership to respond to the epidemic and supports country efforts to meet the challenge. MEASURE Evaluation, funded by USAID and PEPFAR, works across the globe to strengthen health information systems, conduct research and evaluation, and develop global guidance and tools to improve the response to the epidemic in low-resource settings. The project works with USAID and countries to ensure cost-effective, sustainable, and integrated HIV and AIDS programming, using evidence-informed approaches and innovations.

Tools such as the Viral Load Calculator described in this document are among the solutions the project supports to improve data, so as to better describe the epidemic in any locale. In this way, enhanced strategies can be developed to achieve local and global goals. MEASURE Evaluation's activities take a holistic view of health information systems and the complex contexts that attend HIV and AIDS issues, underpinned by our own research and applications of best practices to advance the field.

What is the Viral Load Calculator?

These guidelines describe the Viral Load Calculator, which is a strategy to estimate viral suppression at a clinical, programmatic, regional, or national level in the presence of missing data. The method described combines biobehavioral survey data with routinely collected programmatic data to estimate viral suppression, the "last-90."

What is the purpose of this tool?

The purpose of this tool is to improve the estimation of the "last 90" (i.e., viral suppression) in resource-limited settings.

[1] "90-90-90" refers to the global goal that, by 2020, 90 percent of those who are HIV-positive will have been diagnosed, 90 percent of those diagnosed will be on antiretroviral therapy (ART), and 90 percent of those on ART will be virally suppressed (Joint United Nations Programme on HIV/AIDS [UNAIDS], 2017).

What is the motivation?

World Health Organization (WHO) guidelines recommend routine viral load (VL) testing to monitor treatment success and adherence for people living with HIV. VL scale-up is important for patient care. Resources are limited in low- and middle-income countries, and many barriers to routine VL testing exist. The challenges to obtaining representative VL data from a higher proportion of patients are limited laboratory resources, infrequent VL measurements, missed VL appointments, and variable patient compliance with a VL indication. Until such barriers to routine VL testing are removed, the Viral Load Calculator approach offers a solution for programs and reporting entities to use information for continuous quality improvement and for accurately estimating viral suppression.

In some resource-limited settings, VL data may be extensively missing. Nevertheless, clinics, programs, counties, districts, and countries must report indicators of viral suppression for purposes of monitoring and evaluation and to satisfy the requirements of national governments and funding agencies. Even high-quality HIV care and treatment programs report the proportion of patients with a suppressed VL without also reporting contextual information that would illuminate the data (e.g., loss of funding, shifting of priorities, national campaigns, coordination with other agencies, and limited laboratory resources).

What is new here?

The Viral Load Calculator uses well-established, evidence-based epidemiologic methods in a new way to estimate viral suppression for programs that have missing data. (See the section below titled

Underlying Theory**.**) These operational guidelines describe how to use routine data from treatment databases; collect additional data from a sample of those missing a VL measure; and extrapolate estimates of viral suppression for the entire population of interest.

When might this tool be useful?

When estimates of viral suppression are desired for HIV care and treatment programs, but many VL results are missing; and when some program clients who are missing VL results can be sampled, surveyed, and offered a VL test.

How does this tool work?

With this approach, we leverage elements from missing data methods and a two-stage study design. For the first stage, we identify a target population (longitudinal routine programmatic data). For the second stage, we deploy a small, rapid sampling biobehavioral survey of a consecutive sample of the target population with missing VL data for a discrete period of time. We then combine estimates of viral suppression from the target population that has extensive missing data with estimates of viral suppression in the sample to calculate an improved estimate of viral suppression.

Can programs use this tool instead of implementing routine viral load monitoring?

No. This is a public health monitoring, quality improvement, and reporting tool. It is not useful for patient-level clinical decision making. This tool cannot tell providers which patient's treatment is successful or who is experiencing treatment failure. However, the approach may be useful for programmatic decision making and tracking progress in removing barriers to and scaling up VL testing for more clients.

Can this tool help programs provide better care for their patients living with HIV?

Yes! Sampling patients with missing VL data in conjunction with a brief survey can offer more detailed behavioral and demographic information about the type of patient not getting VL testing or not achieving viral suppression. This information can be used to inform clinicians and to improve care and VL testing among these patients.

Has this tool been used previously?

Yes. We applied the method in two different settings (i.e., Dominican Republic and Cameroon), with different sampling schemes for patients missing VL tests, at different scales, using simple adaptable methods.

How does the Viral Load Calculator tool fit into the context of the WHO guidelines recommending routine viral load testing?

The WHO guidelines recommend routine VL surveillance, with VL testing occurring six months after diagnosis and every twelve months thereafter. Scale-up of routine VL testing has been slow; however, estimates of viral suppression are important endpoints for evaluating programmatic success. This approach bridges the gap while scale-up is underway, providing relevant program-level data that can inform epidemic control initiatives.

1. INTRODUCTION

Background

Patient engagement in HIV care and treatment is critical to achieve epidemic control and maintain the health and quality of life of people living with HIV. People living with HIV face barriers to HIV testing, linkage to services, initiation of antiretroviral therapy (ART), retention in care, and, as a result, viral suppression (Cohen, Chen, McCauley, Gamble, Hosseinipour, Kumarasamy, … Fleming, 2011). Strengthening the continuum of HIV-related services, especially for KP groups, is important both to improve survival and to prevent onward transmission (Zulliger, Barrington, Donastorg, Perez, & Kerrigan, 2015). Monitoring the indicators of HIV care and treatment at different stages along the continuum of care is important to reduce "leakages" or the cascading loss of patients engaged in care at each stage.

The main goals of programs focusing on HIV care and treatment are to:

- Engage high-risk people.
- Reduce the time between HIV acquisition and diagnosis.
- Conduct partner tracing to identify high risk and recently infected people and/or to offer pre-exposure prophylaxis.
- Reduce the time from diagnosis to linkage to care and treatment initiation.
- Improve retention in care and treatment.
- Reduce the time to viral suppression.
- Maximize the time spent virally suppressed.

HIV-1 VL is an important clinical endpoint (Quinn, Wawer, Sewankambo, Serwadda, Li, Wabwire-Mangen, …Gray, 2000; Attia, Egger, Müller, Zwahlen, & Low, 2009). Viral suppression reduces onward transmission and improves the long-term health and quality of life of people living with HIV. Viral suppression is also an important component of the UNAIDS 90-90-90 declaration, which states that by 2020, 90 percent of people living with HIV should know their status, 90 percent of people who know their status should be sustained on combination ART, and 90 percent of treated patients should achieve viral suppression (UNAIDS, 2017; UNAIDS, 2015). If the 2020 targets of 90-90-90 are reached, a gap in progress towards viral suppression remains (UNAIDS, 2015). If achievable, 27 percent of people living with HIV would not have a suppressed VL. More ambitious, fast-track targets of 95-95-95 for 2030 have been identified as an attempt to outpace the epidemic.

Viral suppression can be achieved with optimal ART (Vernazza, Gilliam, Dyer, Fiscus, Eron, Frank, & Cohen, 1997; Dyer, Kazembe, Vernazza, Gilliam, Maida, Zimba, … Eron, 1998; Vernazza, Troiani, Flepp, Cone, Schock, Roth, … Eron, 2000; Castilla, Del Romero, Hernando, Marincovich, García, & Rodríguez, 2005; Porco, Martin, Page-Shafer, Cheng, Charlebois, Grant, & Osmond, 2004). In response to the WHO guidelines recommending early initiation of ART, WHO also recommends implementation of routine monitoring of ART with VL testing of all patients six months after ART initiation and then every twelve months thereafter (WHO, 2013; WHO, 2014a; Médecins sans Frontières, 2013). Many barriers currently exist for the implementation of routine VL testing in resource-limited settings (Roberts, Cohn, Bonner, & Hargreaves, 2016). Routine VL implementation falls short of the scale and testing

frequency recommended by national and international guidelines (WHO, 2014b). For example, in many resource-constrained settings, laboratory resources are limited, the availability of point-of-care diagnostic technology is still nascent, and sample collection and transportation systems are strained. As a result, scheduled VLs are missed and VL results are infrequently recorded in patient records to guide clinical and program management. Moreover, the availability of VL data is context specific and depends on visit intervals; the availability of phlebotomy or dried blood spot sample collection kits; the cost of VL assays; VL monitoring guidelines; the availability of VL reagents; and mechanisms for delivering and recording VL results in program records.

Consequently, VL measurements are likely to be differentially missing, where "missingness" is meaningful (i.e., associated with measured patient characteristics that result in biased estimates of viral suppression). Missing VL data impede the ability of programs to evaluate the performance of care and treatment efforts, particularly for KPs, who may face additional barriers to accessing VL testing. When VL data are missing, the full HIV care and treatment cascade and the indicators for the 90-90-90 and 95-95-95 targets are biased. Scale-up of VL testing to the national level may eventually be feasible with the strengthening of health and laboratory systems, decreased test prices, and better availability of point-of-care testing resources. In the interim, a bridging strategy is needed to help programs understand progress toward the critical "last 90."

These operational guidelines describe a rapid sampling-based approach to estimate viral suppression in resource-constrained settings, and in the presence of missing data, to inform estimates of viral suppression during the interim period as this routine VL monitoring scales up.

Justification

Estimates of the "last-90"—that is, viral suppression—are often based only on patients with available VL data. Routine programmatic data (i.e., data collected during the course of HIV care and treatment) can be leveraged to strengthen estimates of viral suppression with either 1) population-based biobehavioral surveys or 2) a short biobehavioral validation survey.

The new methods proposed in these guidelines are based on an efficient two-stage design and leverage ongoing efforts to maximize information with minimal burden for participants, program staff, and existing monitoring and evaluation efforts. This Viral Load Calculator was initially developed by The University of North Carolina at Chapel Hill and applied under different conditions in the Dominican Republic and Cameroon under the Linkages across the Continuum of HIV Services for Key Populations Affected by HIV (LINKAGES) Project (Edwards, 2017; Zadrozny, 2018). LINKAGES is a five-year cooperative agreement funded by PEPFAR. Realizing that other countries could benefit from the application of the tool, PEPFAR and USAID invested in the adaptation of this approach into a methodological guidance that is adaptable to all epidemiological contexts.

In the two country projects that motivated the preparation of these guidelines, the proportion of people on treatment who had achieved viral suppression had been underestimated. After making adjustments using this new approach, the proportion achieving viral suppression increased. People missing VL measures were more likely to be virally suppressed and responding well to treatment. In programmatic and clinical data, when VLs are used diagnostically, results are missing differentially (Rich, Miller, Niyigena, Franke, Niyonzima, Socci, … Binagwaho, 2012). Prior to scale-up of routine VL testing, our findings confirmed evidence that VL testing is often used as a diagnostic tool for treatment failure and therefore sicker patients are more likely to have recent VL results.

We can leverage estimates of viral suppression from a sample of patients missing VL data to obtain a more accurate, representative estimate of viral suppression among a larger population in the care and treatment program, if we assume that the sample of patients who were missing VL measures is representative of all patients missing VL measures. Incorporating additional data from a sample of patients missing data allows us to make adjustments to the 90-90-90 indicators that address issues of bias from missing data and are critically important for documenting success in achieving epidemic control. In the two settings in which implementation of the approach has been completed, successful achievement of viral suppression has been underestimated.

This work will improve the ability of public and private sector clinics, programs, regions or countries to:

- Monitor the HIV care and treatment cascade with the goal of optimizing care for KPs and other priority populations.
- Allow countries with incomplete information on viral suppression to estimate the entire cascade by leveraging available information.
- Implement the Viral Load Calculator for use in larger populations or subpopulations of interest.
- Support PEPFAR in monitoring progress toward meeting the global 90-90-90 targets and improve the accuracy of measures used to evaluate programs.

Overview of the Guidelines

The purpose of these guidelines is to describe the use of the Viral Load Calculator to estimate viral suppression from routine HIV care and treatment data, using a two-stage study design.

The Overview section provides a description of the underlying theory behind the Viral Load Calculator. This section introduces the two-stage study design in the context of HIV care and treatment. It also frames the dearth of VL results in routine data as a missing data problem, with solutions linked to traditional missing data approaches. It also presents a big-picture outline of how the Viral Load Calculator works.

In the section entitled "Step 1: Analyze Existing Data," we describe how to define the target population (stage 1 of the two-stage design). We also outline how to analyze existing routine data to understand the state of VL data among patients in the target population. We provide examples of complete case estimates of viral suppression and estimates of the best-case and worst-case scenarios using available data.

For "Step 2: Strategically Collect New Information," we briefly describe two sampling strategies (stage 2 of the two-stage design) for a subset of the target population. We also explain possible approaches to varying the sampling strategy, highlighting the dynamic nature of the Viral Load Calculator.

In the section called "Step 3: Estimate the 'Last 90,'" the two stages are combined to obtain a more precise estimate of the "last 90." Here, we detail the cornerstone of the Viral Load Calculator, describing options for integrating data elements from each stage to estimate the proportion of the target population with a suppressed VL.

In the section entitled "Examples in Practice," we briefly describe the design of and findings from the application of the Viral Load Calculator in the Dominican Republic and Cameroon.

The section called "Extending the Viral Load Calculator" presents two ways that data from the Viral Load Calculator approach can be extended: 1) to develop a nomogram, a tool to estimate viral suppression using a correction factor from the Viral Load Calculator, which can be used over time even while the problem of missing data improves; or 2) to estimate longitudinal viral suppression if a longitudinal HIV care and treatment cascade is desired.

We reflect on the strengths, limitations, challenges, and setting-specific variations in the Conclusions section.

2. OVERVIEW: THE VIRAL LOAD CALCULATOR

In resource-constrained settings, many patients in HIV care and treatment programs do not have documentation of a VL measure in the past six to twelve months.

Routinely collected data from HIV care and treatment programs confront (at least) two issues:

1. Missing VL data
2. Available data may sometimes not be representative of the target population (i.e., those who are presenting unwell are more likely to receive a VL test and have their results recorded).

How It Works

The Viral Load Calculator is a tool for monitoring clinic, program, district, or national-level progress on achieving viral suppression. There are three components to implementation, which are discussed in detail in the sections that follow.

The Viral Load Calculator uses two complimentary types of information to calculate a third type of information: a population-level estimate of viral suppression.

Step 1. Quantify the missing VL data in the target population (i.e., the population for which you want to estimate viral suppression).

Step 2. Sample patients retained in care who are missing VL data to estimate viral suppression in the target population.

Step 3. Apply an algorithm to estimate the proportion of the total program population that is suppressed.

This approach to estimating viral suppression was developed for use in resource-constrained settings in which many VL data are missing. In subsequent sections, we describe how to implement a rapid sampling approach to estimate viral suppression at the clinic, program, regional, or national level in settings in which VL data are missing.

Underlying Theory

This Viral Load Calculator is a methodologically sound tool that was born from strong epidemiologic theory. It was inspired by strategies to estimate mortality when loss to follow-up is prevalent (Geng, Emenyonu, Bwana, Glidden, & Martin, 2008). The logic leading to the development of the Viral Load Calculator combines theory supporting traditional missing data methods (Rubin, 1996) and two-stage study design (Breslow & Chatterjee, 1999; Zhao & Lipsitz, 1992).

Two-stage studies offer a cost-efficient approach for obtaining detailed behavioral data or costly biological specimens for a sample of patients in the context of a larger cohort or population. Two-stage studies are useful in settings with extensive missing VL data. The first stage represents a target population or existing cohort. The second stage represents a sample of participants drawn from the target population. Costly biologic specimens and detailed behavioral data are only collected from the smaller, second stage sample.

First Stage

For the Viral Load Calculator, the target population (stage 1) can be a population drawn from an existing HIV cohort, a clinic or program with longitudinal medical records with HIV care and treatment data, or a national HIV care and treatment database.

Ideally, data from the first stage of the study will rely on routine data collected in an electronic HIV care and treatment database during HIV care visits, including information on age, sex, nationality, visit dates, WHO stage, treatment duration, ART regimen, and biomarker values, including CD4 cell count and VLs, when available.

Second Stage

This sample of patients is nested in the target population. Sampling may be conducted separately through a population-based survey, and if the populations overlap, can be linked at a later date to the target population with unique identifier codes (i.e., identical unique codes can be used in both the target population and the sample to link patients if not all are nested in the clinic/program/cohort).

In the second stage, difficult to obtain data (e.g., detailed behavioral information, biological samples) will augment routinely collected program data, which has some missing VL results. During the second stage, a subset of participants is sampled to measure VLs from new or existing dried blood spots or stored plasma samples. Targeted sampling for additional VL testing will ensure that programs can make inferences about the HIV care and treatment cascade for patients in care. Linking these data sources allows for the leveraging of rich behavioral information to improve programmatic estimates of viral suppression among KPs.

Missing Data Methods

We used long-standing missing data approaches as a basis for comparison for validating the Viral Load Calculator. Typical programmatic estimates rely on a **complete case analysis** to calculate event probabilities using only data available. The complete case approach assumes that people with missing data have the same probability of having the event as patients who are not missing data. In low- and middle-income settings, we know that patients who are missing VL data are generally much different than patients who have VL results recorded. Using multiple imputations or inverse probability weights, available data can be used to explain differences between the people who are missing data compared with the people who have data available.

A description of each step and how each step is implemented follows. Areas of flexibility in the approach are identified, including modifications that can be made to suit different scenarios depending on the available data, regional priorities, and contextual influences.

3. STEP 1: ANALYZE EXISTING DATA

Using routinely collected data from HIV care and treatment programs, the care and treatment of people over time can be analyzed using the unique code that the program assigns to track patients/clients (i.e., an internal program number or unique identifier).

Identify the Target Population

The first stage of the two-stage study design requires the identification of the target population. For the purpose of estimating viral suppression for an HIV care and treatment cascade, the target population includes the population of people living with HIV who are linked to care with data available at an HIV care and treatment program. This data source enumerates the target population and provides basic information on access to HIV care and treatment services. However, routine data are usually missing two important pieces of information: 1) VL data are often incomplete; and 2) information on HIV risk behavior or KP status is often also lacking. These absent pieces of information can be understood through the second stage of the two-stage study design.

Estimate the Proportion Suppressed in the Target Population with a Viral Load Measurement

The data analysis involves the creation of an HIV care and treatment cascade using all available relevant data for the target population to enumerate the proportion of program patients living with HIV who:

- Are linked to care (i.e., living with HIV and have a record in the routine data).
- Have initiated ART.
- Have been retained in care (more than six or twelve months, depending on the population and local definitions of retention in care).
- Have a suppressed VL (≤ 1000 copies/mL) measured in the past six to twelve months.

Indicators are calculated as conditional probabilities for the target population (Figure 1). The analysis includes: 1) the overall proportion of patients in these categories, with the number of patients living with HIV as the denominator for the first indicator; and 2) the nested proportion of each category, with the preceding step of the continuum as the denominator (Figure 2).

Figure 1. Viral Load Calculator definitions

Key Definitions

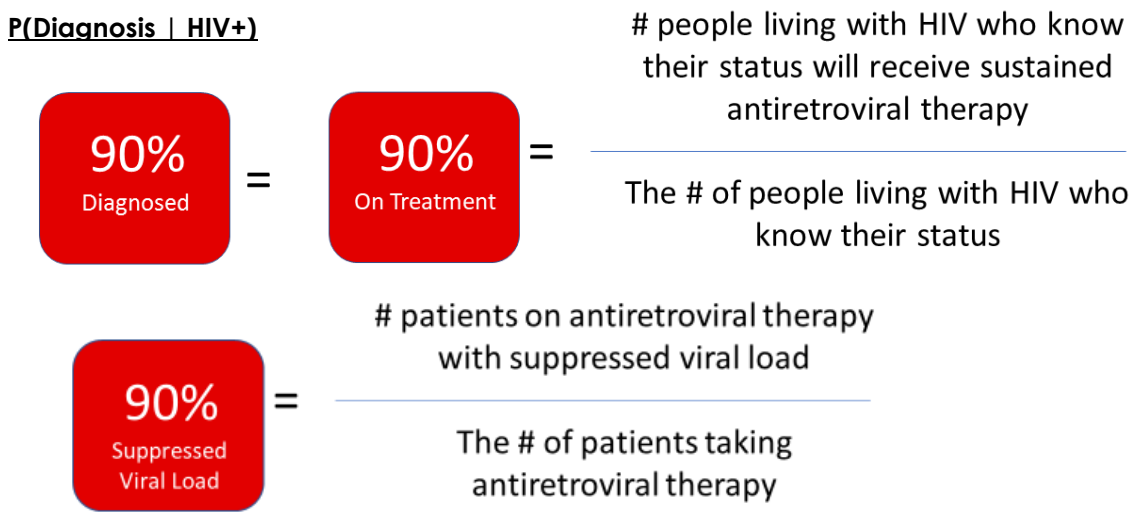
Target Population. The population for which it might be possible to draw an inference or the population we want an estimate to represent.

Conditional Probability. The probability of an event for a subset of the population or the probability of an event given the occurrence of another event. A conditional probability is often written as an equation in the following format:

$$P(A|B) = \frac{P(A \cap B)}{P(B)}.$$

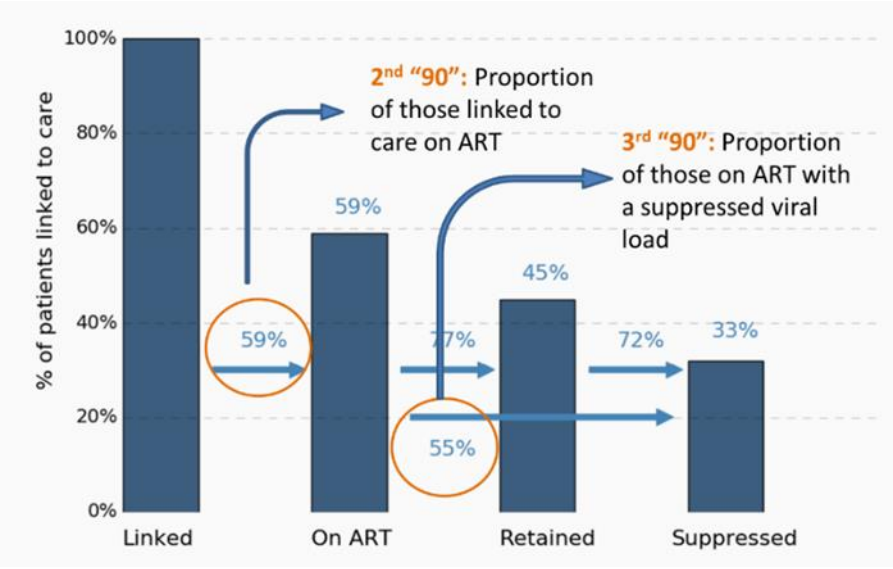
Where the left side of the equation reads: "the probability of A given B" = "the probability of A and B divided by the probability of B."

Figure 2. Numerators and denominators for indicators of the 90-90-90 targets



An example of a modified HIV care and treatment cascade is provided in **Error! Reference source not found.** in which a complete case approach is used to estimate that 72 percent of retained patients had a suppressed VL. With this complete case approach, the estimate of viral suppression was 72 percent, however, in our example many patients were missing VL results. We chose an illustrative example where only 9 percent of patients who were retained also had a VL result available in the six months prior to the desired time frame.

Figure 3. Example of a modified HIV care and treatment cascade with overall and cascade proportions estimated from prior subsets



Explore Uncertainty Associated with Assumptions

If we use available data from the program in our illustrative example to estimate viral suppression, the estimate of the proportion of patients suppressed is unbiased ONLY if we have VL results from a representative sample of patients. That is, if patients who are missing a VL measure are similar in disease stage, gender, risk behaviors, and treatment initiation to patients who are not missing a VL measure.

If we calculate logical bounds for the observed proportion of patients living with HIV who are linked to care, on ART, and have a suppressed VL. (**Error! Reference source not found.** provides an example of how to do this), we can explore the uncertainty associated with the complete case analysis of viral suppression (i.e., in the presence of missing data).

This calculation provides a worst-case and best-case scenario corresponding with the assumptions that all patients who have initiated ART who have a missing VL test are either all not suppressed (worst-case) or that they are all suppressed (best-case).

Error! Reference source not found. provides an example illustrating the calculation of bounds, continuing the example from **Error! Reference source not found.**, where the estimate of the proportion of the population with a suppressed VL was based on just 9 percent of patients who were retained in care. For the worst-case scenario, we assume that 91 percent of retained patients who were missing VL data did not have a suppressed VL. For the best-case scenario, we assumed that 91 percent of retained patients who were missing VL data had a suppressed VL.

Figure 4. Sample calculation for worst-case and best-case scenarios for the complete case analysis of viral suppression

Bounds for missing data

Viral suppression for patients living with HIV, linked to care, on ART, and retained in care:

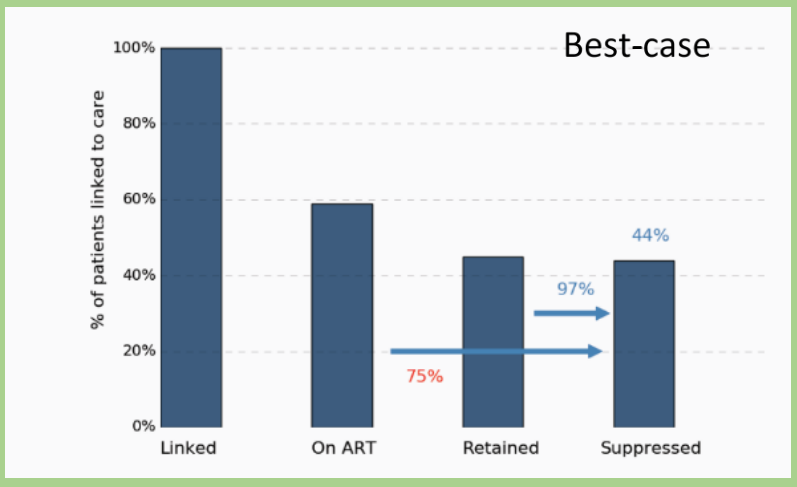
Observed: 77% retained among all on ART
72% suppressed VL among retained patients with VL data
x 9% of patients with data (i.e., not missing a VL result in the past six months)
5% with VL data AND suppressed

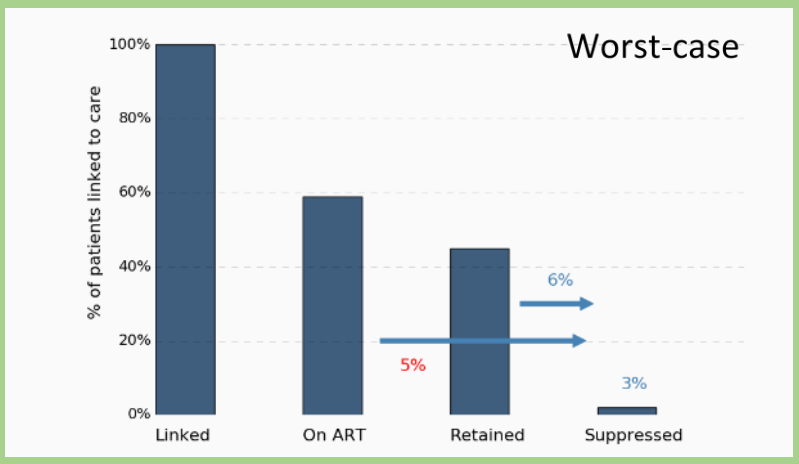
Worst-case: 77% retained in care among all on ART
0% suppressed for all those missing VL data
x 91% of patients missing VL data
0% without a VL AND (assumed) suppressed

5% + 0% = **5%** suppressed assuming all missing VL results are not suppressed

Best-case: 77% retained in care among all on ART
100% suppressed for all those missing VL data
x 91% of patients missing VL data
70% without a VL AND (assumed) suppressed

5% + 70% = **75%** suppressed assuming all missing VL results are suppressed





4. STEP 2: STRATEGICALLY COLLECT NEW INFORMATION

In the context of extensive missing VL data, the collection of information and measurement of VLs for a subset of patients who are missing data can provide a more informed estimate of VL for the HIV care and treatment program. The purpose of a validation sample is to compare the probability of viral suppression between patients with and without a routinely collected VL measurement, and to use this information to account for the missing data in the routinely collected VL information. In Step 2, the process of collecting demographic, behavioral, and VL data on a randomly sampled subset of patients retained in care with missing VL data is described.**Error! Reference source not found.** Figure 5 is a graphic presentation of the approach.

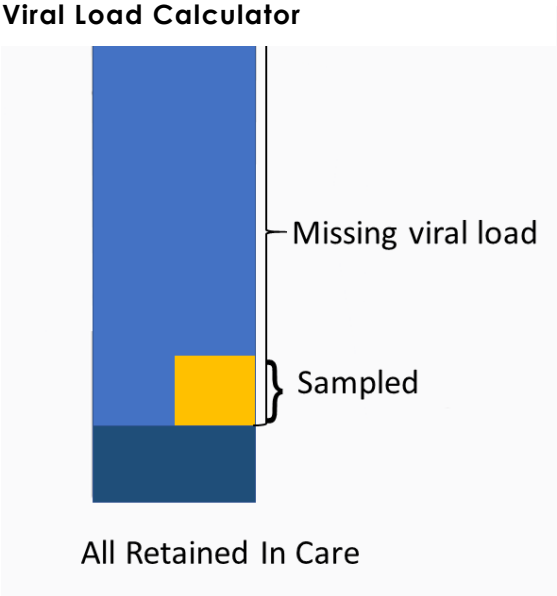
Sampling

For the second stage of the study, patients with missing VL data are sampled; their VL is measured; and additional data on HIV risk behavior and KP status are collected. Sampling can be conducted in several ways. Two options are presented.

A. **Rapid, random sampling**. A random consecutive sample of patients in care at a sample of sites is taken. Ideally, for the two-stage approach, routinely collected data will be augmented by targeted additional data collection. This option involves a brief survey, blood draw, coordination with a lab for VL testing, and access to routine programmatic data for a discrete period.

B. **Link to existing, ongoing population-based biobehavioral studies**. For this option, a sample of patients from existing population-based surveys is leveraged to coordinate with routine data using a unique identifier code (i.e., a code generated by the participant/client to link data from routine HIV care and treatment databases with population-based surveys, such as the integrated HIV biobehavioral surveillance [IBBS], while maintaining confidentiality). This sampling approach requires overlap in time, space, and people, between the routine database and the population-based survey. This approach requires an assumption of similar eligibility criteria between the population-based survey and KP data from the routine data collected by the HIV care and treatment database. The definitions are often not standardized, but the assumptions can be explored by comparing the populations using available data. Efforts to align definitions across data sources will facilitate connectedness and allow for the use of two-stage sampling designs to inform programmatic estimates of viral suppression or other HIV care and treatment endpoints.

Figure 5. Visual representation of the sampling strategy for stage two of the Viral Load Calculator



Regardless of the sampling approach, after a sample of patients is obtained with measured VL and some demographic and behavioral data, check for similarity where data are available for patients in the sample compared with patients in the overall target population for measured characteristics (e.g., when available,

compare data from the target population with data from the sample for median age, time since diagnosis, time on ART, KP status, type of employment, socioeconomic indicators, number of children).

Context-Specific Possibilities for Varying the Implementation of Step 2

Step 2 involves taking a sample of patients missing VL data and obtaining more detailed biological (e.g., VL results), demographic, and behavioral data for those patients than are available in the routine data. Step 2 can be adapted to align with the setting, available data, funding level, sampling strategy, and local priorities. Options for modifying this step are:

- Take a random, consecutive sample of patients for a discrete period of time for all clinics or a sample of clinics. This assumes that patients who consecutively arrive at the clinic and are sampled for the described period (e.g., one month, six weeks) are similar to patients who go to the clinic during other periods.
- Randomly sample all existing patients in the target population from the routine database who are missing VL data and request their presence for plasma sampling to participate in this data quality evaluation for quality improvement (i.e., regardless of whether they are scheduled to come to a clinic).
- If an existing population-based study (e.g., IBBS) exists for the target population that is reached by the program of interest, align research interests, request the collection of plasma samples for VL testing, and facilitate the linkage of records between the study and the program to maximize overlap.
- Instead of randomly sampling patients from the program solely, employ different sampling methods using the program as the initial recruiting site for additional participants (e.g., respondent-driven sampling). This assumes the sampling approach allows overlap between participants in the study and clients in the program, and that the program will recruit from the same target population. This approach may also allow for exploration of characteristics of the target population that may not be accessing HIV prevention, care, and treatment services.
- PEPFAR sets a threshold for viral suppression at 1,000 c/ml for operational feasibility across different testing platforms and sample collection modalities. However, the threshold for viral suppression should be selected to provide the most clinically meaningful information and which is associated with the lowest risk of treatment failure or developing other HIV-related complications for the desired setting.

To ensure representation, a random sample of all participants is taken who then have VL data and behavioral data collected. Realistically, funding is in short supply and, therefore, priorities for treatment and research should be aligned to maximize the utility of routine programmatic data and survey data.

5. STEP 3: ESTIMATE THE "LAST 90"

To estimate the "last 90," an algorithm is applied to calculate the proportion of the total program population that is suppressed.

As we saw in the complete case example in step 1, the presence of uncertainty about missing VL results in routine programmatic data leads to inaccurate estimates of viral suppression. Taking a sample of patients who are missing VL data from the target population and obtaining VL results on all patients in the sample allows for the calculation of a more informed, less biased estimate, with greater certainty.

Collect Three Component Data Elements

Collect three component data elements to estimate viral suppression at the program or clinic level. Use a simple series of calculations (e.g., an algorithm) to obtain a ratio, "r," which can be used as a correction factor to estimate the proportion of all retained patients with a suppressed VL.

Step 3 requires the following three pieces of information:

- w= The proportion of patients on ART who have a suppressed VL (among those with a measurement)
- m= The proportion of those on ART with missing VLs
- s= The proportion suppressed among the sampled patients on ART

These three data elements can be used to calculate the ratio, r, which represents the proportion suppressed, such that:

$$r = \frac{P(supression|sample)}{P(suppression|routine\ data)} = \frac{s}{w}$$

Calculate the Proportion of Patients with a Suppressed Viral Load for the Entire Program

The proportion of patients from the program or clinic with a suppressed VL can be calculated using the aggregate data described above or from a weighted analysis where the weights (see Figure 6) are calculated for each observation.

The following equation can be used to estimate viral suppression in the routine data, where many VL data are missing:

$$y = w(rm - m + 1)$$

Alternatively, weights based on the number of people in each category can be calculated for each observation using the formula given above and in Figure 6. Using the proposed sampling approach, patients with a VL measured through routine care receive a weight of 1; patients missing VL data and

who are not in the validation study are excluded; and patients in the validation study are up-weighted to represent all patients who are missing recent VL data and who are on ART in the national database (Figure 7). Weights for each patient in the validation study can be calculated as the number on ART missing a recent VL measurement in the database divided by the number included in the validation study who were also on ART.

Figure 6. Example: Estimating viral suppression using the Viral Load Calculator

Viral Load Calculator estimate of viral suppression

Use these component data elements to estimate the proportion suppressed in programmatic data. Using the data from the example above (**Error! Reference source not found.**), let $w = 0.55$, $m = 0.91$, $s = 0.85$ and the ratio $r = (0.85/0.55) = 1.55$

$$y = w(rm - m + 1)$$

$$y = 0.55[(1.55)(0.91) - 0.91 + 1]$$

$$y = 0.55[1.41 - 0.91 + 1]$$

$$y = 0.55[1.50]$$

$$y = 0.83$$

Figure 7. Weights assigned to patients in the target population to estimate viral suppression for programs where many data are missing

People with VL in routine data	$W = 1$
People in sample, missing VL in routine data	$W = \frac{\text{\# missing VL in routine data}}{\text{\# in the sample}}$
People missing VL in routine data	$W = 0$

Context-Specific Possibilities for Varying the Implementation of Step 3

Step 3 involves the calculation of the "last 90" leveraging VL results from a sample of patients who are missing VL data in the routine database to obtain a more informed estimate of viral suppression. This can be done using the algorithm or weighting scheme described above. Options for modifying this step are:

- The weighting approach can vary based on the amount of overlapping data available from both stages. Weights described here are simply based on the number of patients missing VL results in the target population and the number of patients with VL data from the sample. If additional, more specific information is available for patients in both the first and second stage of the study, more specific weights can be developed to account for the distribution of patient characteristics.

6. EXAMPLES IN PRACTICE

The Viral Load Calculator has been implemented using two different approaches, in two different settings—the Dominican Republic and Cameroon. A description of the two cases and a discussion of the differences between each approach follow.

Dominican Republic

In the Dominican Republic, for people living with HIV who are enrolled in HIV care and treatment, data are collected and stored in a national database called the Formulario de Aplicación a Programas de Políticas Sociales (FAPPS), which is administered by the Servicio Nacional de Salud. The FAPPS database contains one record per person per visit to an HIV care and treatment facility. Basic demographic and clinical information are recorded. The FAPPS also contains information on the deaths of patients with HIV.

Two-Stage Study Design

The proportion of patients retained on ART who had a suppressed VL in the Dominican Republic was estimated in January 2017 using a two-stage study. The approach used an efficient two-stage design and leveraged a rapid sample of program participants from a subset of sites to maximize information with minimal burden for participants and program staff.

The first stage of the two-stage study included people living with HIV who were enrolled in HIV care and treatment, and who had clinical data and patient characteristics recorded in FAPPS. Patients were considered "retained on ART" if they had a documented clinic visit in which they received ART in the last six months. For the purposes of this project in the Dominican Republic, to identify a clinically meaningful threshold for practitioners, viral suppression was defined as having a VL below 200 copies/mL. Many patients who were retained on ART did not have a VL measured in the last six months.

For the second stage, a consecutive sample of patients received VL testing during the assessment period. In this second stage of the two-stage study, clinical data from the first stage were augmented with a nested sample of program participants who completed a biobehavioral validation study, called the LINKAGES Viral Load Assessment. This validation study was conducted between January 25, 2017 and March 15, 2017. In this validation sample, VLs were measured for an unselected consecutive sample of 1,052 patients returning for follow-up visits at nine public and private clinics.

Results

For the first stage, of the 9,483 patients who were enrolled in the FAPPS database between June 2013 and January 2017 and were retained on ART in January 2017, only 22 percent (n=2,068) had a VL recorded in the database in the past six months.

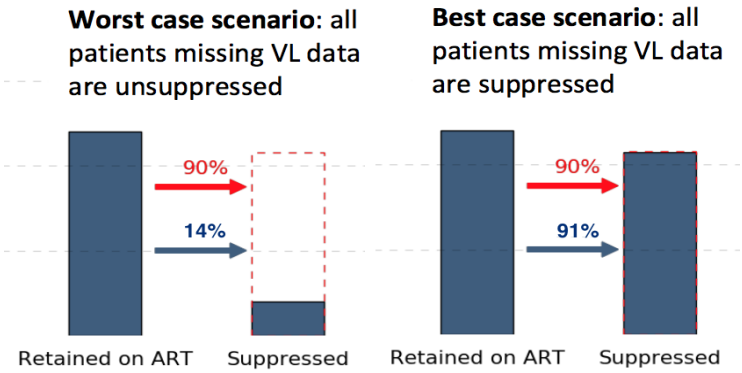
For the second stage, after restricting participants to those from the first stage who had attended one of nine clinics during a six-week period, the validation study included a sample of 517 patients who started ART, were retained on ART, and who did not have a VL result in the past six months.

To estimate viral suppression in the target population (i.e., participants in the first stage), we compared results from five statistical approaches to estimate the proportion of patients with a suppressed VL.

A. In the **complete case analysis**, among the participants who had a VL in FAPPS enrolled during the follow-up period, the proportion suppressed was estimated as the proportion with a VL below 200 copies/mL among patients retained on ART with recent VL measurement in the FAPPS database. Using only data from the FAPPS, the estimated proportion suppressed was 55.7 percent (95% confidence interval [CI]: 53.6, 57.9) (Figure 10).

B. For the best- and worst-case scenarios, we assumed that all patients missing VL data had suppressed and unsuppressed VLs, respectively. Logical bounds on the possible proportion suppressed were wide. The proportion suppressed was 14 percent in the worst-case scenario, and 91 percent in the best case scenario (**Error! Reference source not found.**).

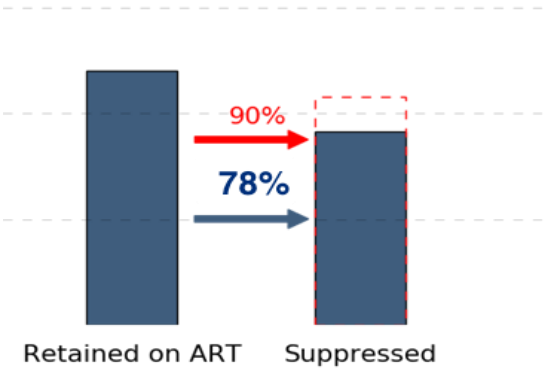
Figure 8. Worst- and best-case scenarios for viral suppression with missing data



C. Standard missing data approaches (i.e., **multiple imputation** and **inverse probability weighting**) were used to account for missing VL data using only VL data and covariates found in the FAPPS database. Using the standard missing data approaches, the results were similar to findings from the complete case analysis, likely because the variables contained in FAPPS insufficiently accounted for differences between people with and without VL data (Figure 10).

D. In the validation study alone (i.e., the second stage), 85 percent (95% CI: 82, 88) were suppressed (Figure 10). One foundational assumption about this validation study was that it was representative of all patients missing a recent VL measurement.

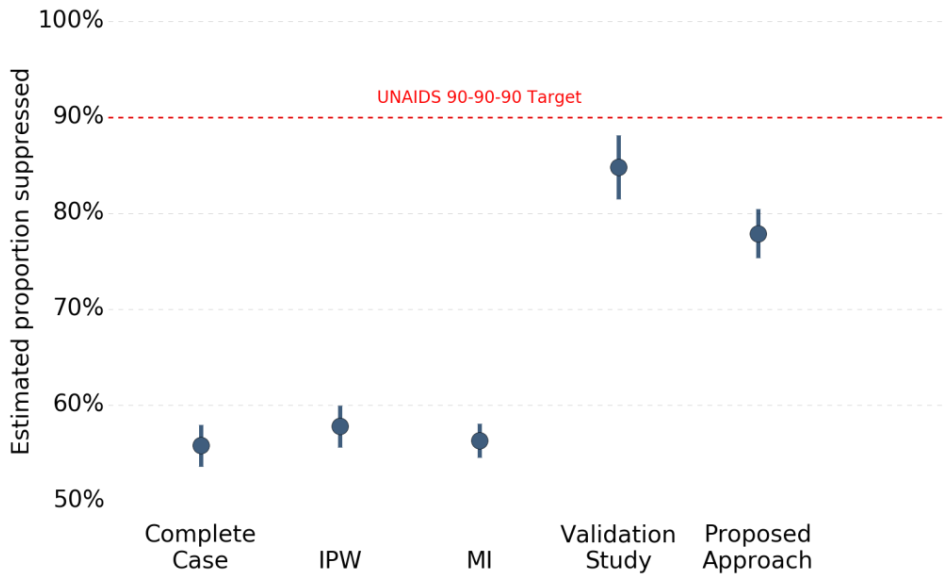
Figure 9. Estimated proportion suppressed under the proposed sampling approach and comparison with UNAIDS 90-90-90 targets in the Dominican Republic, 2017



E. Using the Viral Load Calculator (i.e., "proposed approach"), patients with VL measured through routine care received a weight of 1, patients missing VL data and not in the validation study were excluded, and patients in the validation study were up-weighted to represent all patients who were missing recent VL data and retained on ART in the national database. Weights for patients in the validation study were the number on ART missing a recent VL measurement in the database divided by the number on ART in the validation study (Figure 7). Combining information from the validation study and the clinical database and with the Viral Load Calculator, the estimated overall proportion suppressed was 78 percent (95% CI: 75, 81) (Figure 9) — a notable change from the complete case estimate of 55.7 percent (Figure 10).

The proportion suppressed in the validation sample was much higher than the proportion suppressed in the clinical database, suggesting that patients with suspected treatment failure may have been preferentially referred for VL testing. In resource-constrained settings using a targeted VL testing strategy or gradually scaling up routine VL monitoring, implementing a sampling approach to estimate viral suppression will allow for more accurate and efficient monitoring of HIV treatment program effectiveness.

Figure 10. Estimated proportion suppressed under selected methods to handle missing VL data in the Dominican Republic, 2017



Cameroon

Similar to the project in the Dominican Republic, the activity in Cameroon was designed as a traditional two-stage study (Figure 11). Instead of conducting a biobehavioral survey of a sample of patients, overlap was leveraged between the Continuum of Prevention, Care and Treatment of HIV/AIDS for Most-at-Risk-Populations (CHAMP) program in Cameroon and an existing population-based IBBS study, which collected plasma samples from patients with the intent of analyzing VL results at a later date.

Two-Stage Study Design

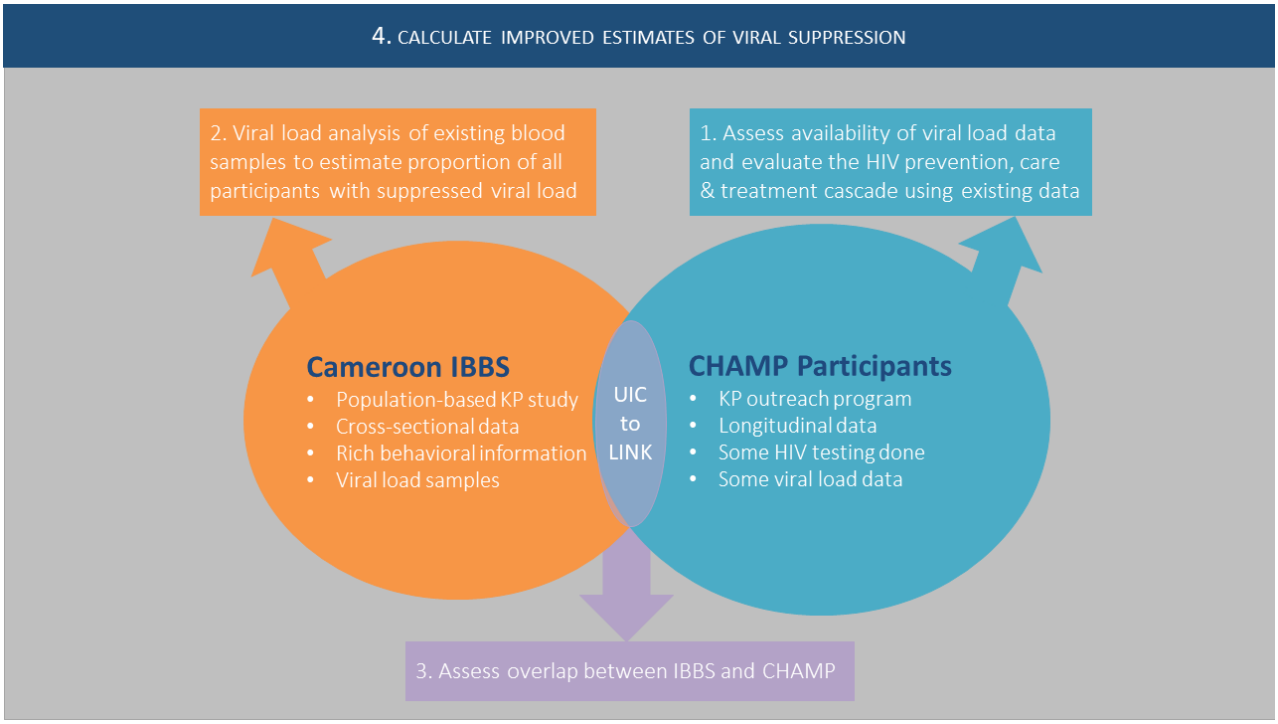
The first stage consisted of an existing cohort of KP members who use the HIV prevention, care, and treatment services of the CHAMP program in Cameroon. CHAMP is a five-year, USAID-funded program under cooperative agreement number AID-624–A–14-00003. The program runs from April 2014 through March 2019. CHAMP supports the United States Government's objective in Cameroon in the domain of HIV/AIDS "to increase Cameroonian capacity for sustained HIV prevention, care and treatment" (CARE, 2015).

The second stage was a study of IBBS participants, some of whom were also CHAMP clients, who had plasma samples stored for VL measurement. We can match clients in the CHAMP program who also participated in the IBBS study using the unique identifier codes employed by both the IBBS study and by CHAMP to track prevention, care, and treatment activities in the CHAMP program database (CommCare) during the same period and in similar geographic catchment areas.

Patients were considered to be on ART if they had a documented clinic visit in which they received ART from the CHAMP program between November 2015 and November 2016. Viral suppression was defined as having a VL below 1,000 copies/mL.

Viral suppression was estimated only for 1) clients from the CHAMP program with VL data available (complete case); 2) IBBS participants who were HIV-positive and on ART; 3) the population included in both the CHAMP program and the IBBS study (validation sample); and 4) using the Viral Load Calculator to leverage VL data from all participants from the IBBS study to inform estimates of viral suppression among CHAMP clients who were missing VL results.

Figure 11. Visual representation of study aims and the respective data sources used



Results

First, we examined the availability of VL data among female sex workers (FSW) and men who have sex with men (MSM) clients enrolled in the CHAMP program between November 2015 and November 2016 (i.e., the target population). VL data were extremely limited. Among the 1,440 MSM and FSWs clients in the target population, 600 (42 percent) had ever received antiretrovirals; of these, 395 (66 percent) had had a blood draw for VL testing; and only 24 (4 percent) of clients on ART who had a blood draw also had VL results available in the CommCare database.

The validation population included data from the 83 IBBS participants with VL results from stored plasma who had started on ART and were also CHAMP clients.

A. In the complete case analysis, using only data from CHAMP, the estimated proportion suppressed was 63 percent(Figure 12). Due to the extensive missing data, the logical bounds on the possible proportion suppressed were wide. In the worst-case scenario, the proportion suppressed was 2.5 percent, and in the best-case scenario, the proportion suppressed was 98 percent (Figure 12). These extreme scenarios, where we assumed all missing VL data were either

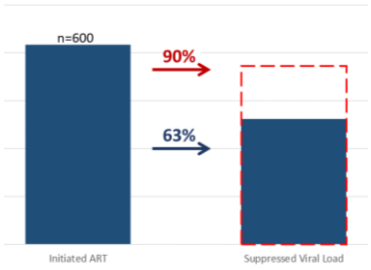
unsuppressed or suppressed, were included to illustrate the amount of uncertainty involved in estimates based on the existing routine data only.

B. For the complete IBBS population living with HIV who had initiated ART, viral suppression was 83 percent (data not shown).

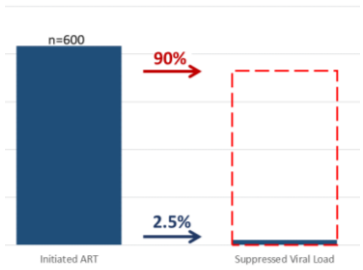
C. For the validation population, viral suppression was 86 percent (data not shown). (The validation population included IBBS participants who were also CHAMP clients).

D. Using the Viral Load Calculator approach, which combined information from the validation population and the target population from the CHAMP program, the estimated overall proportion suppressed was 72 percent (95% CI: 65, 80) (Figure 13)—a significant change from the 63 percent finding in the complete case analysis (Figure 12).

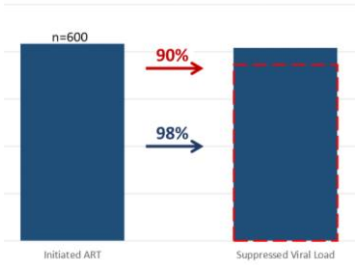
Figure 12. Viral suppression in CHAMP clients estimated using A) complete case analysis; B) worst-case scenario; and C) best-case scenario



a) Complete-case: estimated viral suppression using only available (limited) VL data from CHAMP



b) Worst-case scenario: assumed that all patients missing VL data in CHAMP were unsuppressed

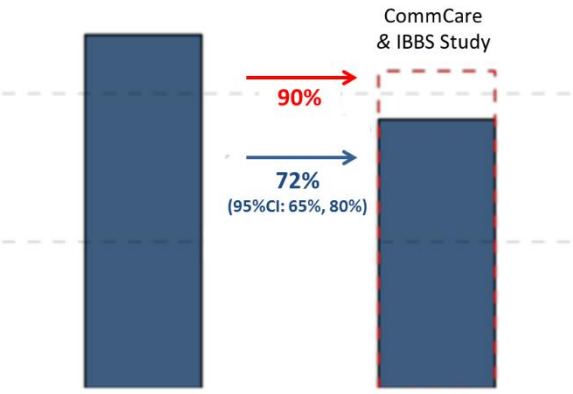


c) Best-case scenario: assumed that all patients missing VL data in CHAMP were suppressed

Conclusions from Cameroon

The proportion suppressed in the sample from the IBBS study was much higher than the proportion suppressed in the target population, suggesting that at the time, CHAMP patients with suspected treatment failure may have been preferentially referred for VL testing or were more likely to have linked laboratory results.

Figure 13. Results from the Viral Load Calculator in Cameroon



7. EXTENDING THE VIRAL LOAD CALCULATOR

The Viral Load Calculator approach to estimating viral suppression in the presence of extensive missing data can be used over time by the same program in conjunction with 1) a nomogram or 2) longitudinal estimates of viral suppression.

Nomogram

A nomogram is a simple tool to identify the relatedness of numbers by connecting numbers along a straight line. Although web-based calculators are useful for well-resourced areas, a simple tool like the nomogram can be used in resource-limited settings.

Description

Once the Viral Load Calculator is done for a program, the correction factor can be calculated. As routine VL testing scales up, the proportion of missing data (presumably) decreases over time. Once the correction factor is identified for a particular program, it can be used to estimate program-level viral suppression with differing proportions of missing data.

Using the formula from Figure 6, we developed a simple nomogram for use by programs to estimate a correction factor, which can be used to multiply by the proportion of patients with a suppressed VL who are observed, at differing levels of missing data.

$$y = w(rm - m + 1)$$

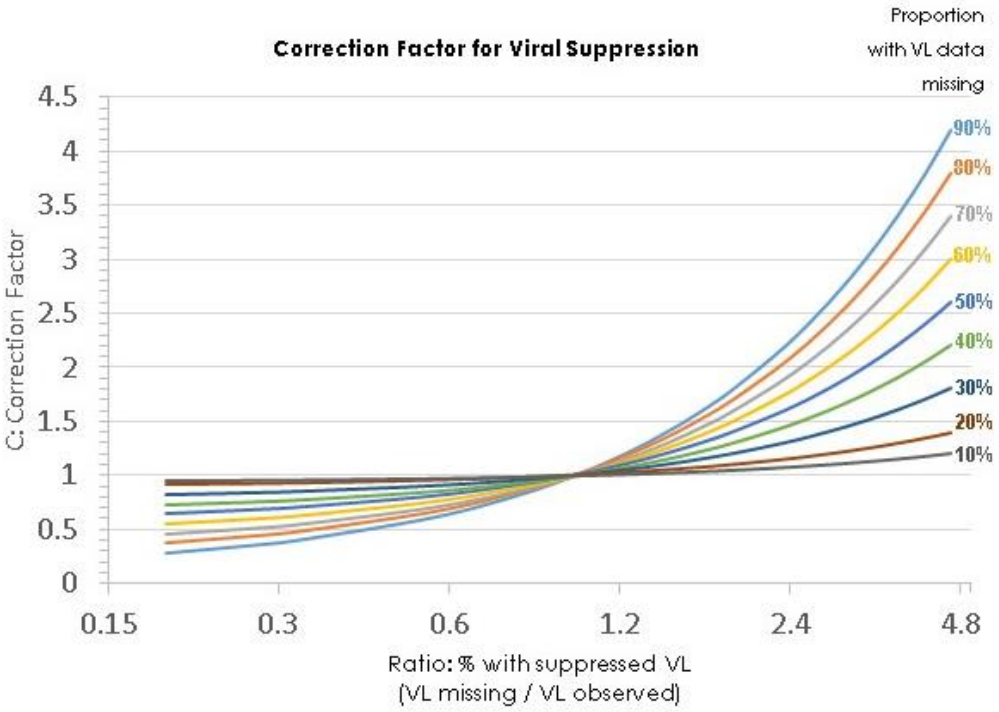
The nomogram identifies a correction factor (i.e., a multiplier) based on known data to estimate outcomes when some data are missing. The nomogram (Figure 14) allows a program to estimate viral suppression based on:

- m= the proportion of missing VL data in the routine database at a particular period after entry into care.
- w= the proportion with a suppressed VL among patients on ART, retained in care, and who have VL data (observed).
- s= the estimated proportion of viral suppression among patients on ART, retained in care, and who are missing VL results in the routine database, but were included in the validation sample (sampled).
- r=s/w= the ratio of viral suppression for patients who were missing versus not missing VL data.

After the Viral Load Calculator is completed for a program, the ratio, r, can be used in future years as routine monitoring of VL data increases and missing data decrease. Each year, under the assumption that the ratio, r, is constant over time, the program can calculate the correction factor, C, based on the proportion of missing data. The program-level indicators of viral suppression among patients who initiated ART and were retained in care is then multiplied by the correction factor to calculate an estimate of viral suppression that accounts for missing viral suppression data (i.e., a corrected estimate of viral

suppression). Once the levels of missing data change (e.g., an increase or decrease of more than 10 percent), the Viral Load Calculator should be implemented again to obtain an updated ratio for accurate programmatic evaluation.

Figure 14. Nomogram to identify the correction factor for estimating viral



Example

We suggest using a nomogram to estimate viral suppression because the proportion with a suppressed VL in the target population is a weighted average of virally suppressed patients with VL data and patients missing VL data.

Figure 15. Example using a nomogram to estimate viral suppression

Nomogram: Estimating viral suppression over time

The hypothetical program, called HIV-GO, implemented the Viral Load Calculator in 2016. At that time, 90 percent of patients (m) in the program were missing VL results in the prior 12 months, and among the 10 percent with data, 37 percent (w) were suppressed. In the validation sample of patients missing programmatic estimates of VL data, 80 percent (s) had a suppressed VL. ($r = \frac{80}{37}$ =2.16)

Routine VL testing began in 2016. At the end of 2017, 40 percent of patients were missing a VL test result, and among the 60 percent with data, 50 percent were suppressed.

- Using the nomogram in Figure 14, identify a correction factor ($C = 1.4$)
- Multiply C by the proportion suppressed among the observed= $1.4 * 50\%$
- To obtain a corrected estimate of viral suppression = 70%

Considerations

Although scale-up of routine VL monitoring is underway, there are many obstacles delaying its complete implementation. In the interim, program estimates of viral suppression will underestimate the proportion of patients with a suppressed VL. For patients who have initiated ART and are retained in care, VL data are differentially missing. VL testing is often used diagnostically to understand the causes of poor health, such as nonadherence or to identify treatment failure. VL results are generally missing more frequently among healthier patients who are doing well and do not need additional biological information to facilitate quality care.

As missing data decreases, the ratio, r, may approach 1 because a greater distribution of patients will be captured with the increased implementation coverage of routine VL testing. Eventually, as routine VL testing has greater coverage and fewer VL data are missing, the ratio may dip below 1 to the point that those missing VL data may have greater morbidity or mortality. To understand which proportion of missing data is associated with the inversion of the suppression ratio, we will need to monitor trends in missingness as VL testing increases coverage.

Longitudinal Estimates

If the goal of an HIV care and treatment program is to improve the amount of time in care, alive, and with a suppressed VL, then monitoring VL trends over time is an important programmatic tool. We propose using this approach as a key indicator for monitoring program improvement by measuring the following indicators:

- The length of time between HIV diagnosis and viral suppression
- The proportion suppressed at different stages of the HIV care and treatment continuum

In this section, we describe the benefits of including an element of time in monitoring VL results in routine programmatic data.

Time to Viral Suppression from Entry into HIV Care

If viral suppression is an important clinical endpoint of HIV care and treatment, then monitoring the time from entry to care to viral suppression is an important indicator of programmatic success. Instead of reporting counts of people at different stages of clinical care, this indicator monitors the ability of a program to enroll, treat, retain, and properly care for people living with HIV.

Time to viral suppression is a consistent measure of quality care that is particularly important for vulnerable and marginalized populations. Programs that successfully retain, treat, and achieve viral suppression for KP groups may not meet traditional reporting thresholds and yields. Instead, they may focus on providing a trusted, supportive environment for providing care to and retaining difficult-to-reach populations. This level of quality care will not be apparent through cross-sectional counts. It will be better understood through longitudinal, case-based monitoring of HIV care and treatment. This longitudinal measure of time to viral suppression, using a traditional Kaplan-Meier estimate of time to viral suppression in longitudinal routine data, paints a more complete picture of the quality of care offered by HIV care and treatment programs.

Estimate the Proportion Suppressed at any Given Time Since Entry to Care

Once viral suppression is achieved, we can also measure the time patients in the program spend with a suppressed VL. Increasing the proportion of time in which patients have a suppressed VL is a measurable indicator of work that programs are doing to reduce the probability of onward transmission.

Using data collected for the Viral Load Calculator, we can also estimate the time patients spend with a suppressed VL by augmenting routinely collected data from the target population with data from a validation sample. VL and other important information can be obtained from the validation sample.

Although the sample is cross-sectional in calendar time, patients with varying lengths of time since entry into care participate. Under the assumption that the conditional probability of viral suppression given that a patient is alive, retained in care, and on treatment was constant across calendar time, we use VLs obtained during the validation study to represent VLs among all patients missing VL data in the routine database. We can then estimate the restricted mean time patients in HIV care and treatment spend with a suppressed VL.

This analysis can be depicted graphically to provide information about the average time patients spend with a suppressed VL, the time on treatment, and the gap in which patients are on treatment but do not have a suppressed VL. We can then compare the probability of suppression, given that a patient is on treatment, over time between KP groups and the general population.

8. CONCLUSIONS

How Will This Tool Help HIV Care and Treatment Programs Take Better Care of their Patients?

Facilitate Communication of Program Results

Longitudinal measures of the 90-90-90 indicators can provide a more accurate picture of how programs have supported patients over time. In following individual people, we understand how quickly patients are linked to care and initiate ART, how long patients are retained in care, and their time to viral suppression.

Incorporating aspects of time in these measures can also benefit programs by putting their data into context. In response to changing priorities, funding, guidelines, and social context, patient trajectories and patterns of HIV care and treatment also change. Incorporating time in reports can illuminate which changes are effective and which changes have proven challenging.

Continuous Quality Improvement

Programmatic use of data collected as a part of routine HIV care and treatment is highly variable depending on the program, funding, resources for monitoring and evaluation, data collection tools, the social context, and reporting requirements.

Some programs meet regularly to review data about particular aspects of their program and to brainstorm changes. Regional and national reporting is time and resource intensive; however, the reporting efforts offer opportunities to review data regularly and identify challenges, strengths, and limitations.

For programs in areas where routine VL monitoring is supported, this Viral Load Calculator can quantify the success of the VL monitoring or identify challenges with community distribution of ART, ART adherence, and retention in HIV care and treatment. The Viral Load Calculator can also be used to identify disparities in the quality of care if disaggregated by gender, age, location, and behavioral risk factors.

Strengths and Limitations

Strengths of the Viral Load Calculator tool are:

- It uses routinely collected and continuously updated clinical program data.
- Some data are available on all program participants.
- Dynamic reflection of real-world program conditions.
- Adaptable to leverage efficiency and to address program needs.
- Can be leveraged to identify disparities in care for program improvement.

The main limitation of the tool is that it is highly dependent on the sampled population and how well the sample represents the population of patients with missing VL data.

Recommendations and Future Directions

Future Implementation

As these operational guidelines for the Viral Load Calculator are implemented in various settings, the authors welcome feedback to refine this new method in settings with different levels of missing VL data. We will need to explore modifications in the interpretation of findings as VL testing becomes more available. As VL data become routinely available, use of the Viral Load Calculator may shift. For example, in a population with very few missing VL data, those missing VL results may shift toward including a harder to reach, sicker population (i.e., instead of having missing VL results for healthier patients as most programs now do).

The logistics of implementing the Viral Load Calculator as a measurement and evaluation tool involve writing a protocol to apply this tool in an another geographic region selected for a field test; identifying priorities; obtaining a data use agreement with programs in the selected country to allow for the analysis of data from the country's treatment database; targeted data collection (funding permitting) based on an assessment of missing data; analysis; and a final report on the estimation of cascades of KPs in the selected country.

Collaborative Data Sharing and Use of Unique Identifiers to Link People Living with HIV across Programs and Population-Based Studies

It will be necessary to review accessibility and connectivity of available data, protocols for new data collection, and protocols for analysis. In the future, further analyses can be performed to assess "leakage" in the cascade; for example, who is lost and why and what can be done to improve the number and proportion who remain in care, on treatment, and virally suppressed. Selection of the country will need to take into account the amount of additional information that needs to be collected and the cost of data collection. In addition, it may be helpful to assess the reasons for delayed time to viral suppression and the timing of the loss of viral suppression.

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This publication was produced with the support of the United States Agency for International Development (USAID) under the terms of MEASURE Evaluation cooperative agreement AID-OAA-L-14-00004. MEASURE Evaluation is implemented by the Carolina Population Center, University of North Carolina at Chapel Hill in partnership with ICF International; John Snow, Inc.; Management Sciences for Health; Palladium; and Tulane University. Views expressed are not necessarily those of USAID or the United States government. TR-18-271

ISBN: 978-1-64232-052-7

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