World Health Organization

HIV STRATEGIC INFORMATION FOR IMPACT

USER MANUAL

CASCADE DATA USE MANUAL

TO IDENTIFY GAPS IN HIV AND HEALTH SERVICES FOR PROGRAMME IMPROVEMENT

JUNE 2018

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ABBREVIATIONS

ALT	Alanine aminotransferase
APRI	Aspartate aminotransferase-to-platelet ratio index
ART	Antiretroviral therapy
ARV	Antiretrovirals
DAA	Direct-acting antivirals
HBV	Hepatitis B virus
HBeAg	Hepatitis E antigen
HBsAg	Hepatitis B surface antigen
HCV	Hepatitis C virus
HTC	HIV testing and counselling
IBBS	Integrated bio-behavioural survey
KP	Key population
KPLHIV	Key population member living with HIV
MSM	Men who have sex with men
NAT	Nucleic acid test
NGO	Non-governmental organization
PEPFAR	President's Emergency Plan for AIDS Relief
PLHIV	People living with HIV
PMTCT	Prevention of mother-to-child transmission
PrEP	Pre-exposure prophylaxis
PW	Pregnant women
PWID	People who inject drugs
STI	Sexually transmitted infection
TB	Tuberculosis
UNAIDS	United Nations Joint Programme on HIV/AIDS
VMMC	Voluntary medical male circumcision
WHO	World Health Organization

EXECUTIVE SUMMARY

Purpose

This guide supports the use of data to identify and fill gaps in services in order to improve HIV and health programmes. Following from the Consolidated Strategic Information Guidelines, high-level indicators are organized along a cascade of services which are linked to achieve outcomes. The guide supports the ways in which these cascade data are analysed and used to identify gaps and better link services.

Countries, programme managers, health workers and other stakeholders have indicated the importance of consolidating World Health Organization (WHO) guidance for constructing HIV cascades into a single document. This manual addresses not only the HIV care and treatment cascade but also cascades for HIV prevention interventions, such as prevention of mother-to-child transmission, and for co-infections with hepatitis B virus (HBV), hepatitis C virus (HCV) and tuberculosis (TB).

The use of cascades is integral to achieving the 90-90-90 global HIV targets *(1)* and represents one of the key monitoring strategies for supporting expansion and linkage of HIV care, treatment and prevention services *(2)*.

This manual provides guidance on:

1. **Constructing various HIV cascades,** and identifying and interpreting reasons for gaps and linkages along the cascade.
2. **Understanding how cascades can be used** to assess whether interventions have been effective and are well linked to each other along a results chain in order to achieve outcomes.
3. **Understanding how biases in the data** used to construct the cascades can affect interpretation of the findings.
4. **A step-by-step approach to developing and interpreting findings** from cascades for HIV care and treatment, HIV prevention and HIV co-infections with HBV, HCV and TB.
5. **Disaggregating cascades** for key and other populations and subnational geographical areas for local planning.
6. **Aligning definitions and use of cascades and indicators** so they can be used between national programmes, partners (e.g. the Global Fund, PEPFAR), and at national, district and facility levels.

The cascade data use manual is intended for national and subnational AIDS control programmes and includes an embedded MS Excel tool that takes the data entered by users and converts them into cascade figures. It aims to support WHO consolidated guidelines, and how they are used operationally for cascade data, to identify gaps for programme improvement.

1. BACKGROUND

The widespread scale-up of HIV prevention, care and treatment worldwide has led to the possibility of ending the AIDS epidemic as a public health threat by 2030 *(1)*. In particular, the Joint United Nations Programme on HIV/AIDS (UNAIDS) estimates that this can be achieved if by 2020 90% of all persons living with HIV (PLHIV) are aware of their HIV status, 90% of all people who know their status are receiving antiretroviral therapy (ART), and 90% of those on ART are virally suppressed *(2)*. There are parallel global goals to reduce HIV incidence to less than 500 000 new infections in 2020 and to fewer than 200 000 in 2030 *(2)* and to eliminate mother-to-child transmission to ≤50 new paediatric infections per 100 000 live births *(3)*.[1]

Reaching these goals requires using data more actively to identify gaps and strengthen linkages in a cascade of indicators of HIV prevention, care and treatment to improve programmes (Box 1.1).

1.1 Cascades – focusing data on gaps and linkages in services

Box 1.1 What is a cascade?

Cascades are frameworks for monitoring gaps in programme services needed to achieve goals and health outcomes. Cascades consist of a results chain or a series of sequential events in which each event is linked to achieve a health outcome. Cascades are usually depicted as vertical bar graphs where the total affected population is in the left-hand column. The ultimate goal is depicted in the right-hand column. The height of the columns in-between show the number of people reached by the sequence of actions needed to achieve the goal. Comparing the columns highlights the gaps and linkages at each step (e.g. between testing and treatment or between treatment and viral suppression). The height of the columns can be represented either as a number or as a proportion of the left-hand column (i.e. the total affected population). The analysis of data in a cascade framework can then be used to assess the gaps and linkages needed at each stage to achieve an outcome (e.g. between testing, treatment and viral suppression). Indicators are not analysed in isolation, but as part of an overall framework or results chain, to describe and improve a health programme.

Cascades are frameworks for quantifying the magnitude of the gaps in HIV diagnosis, treatment, care and prevention among persons with, or at risk of, HIV infection. The purpose of cascades is:

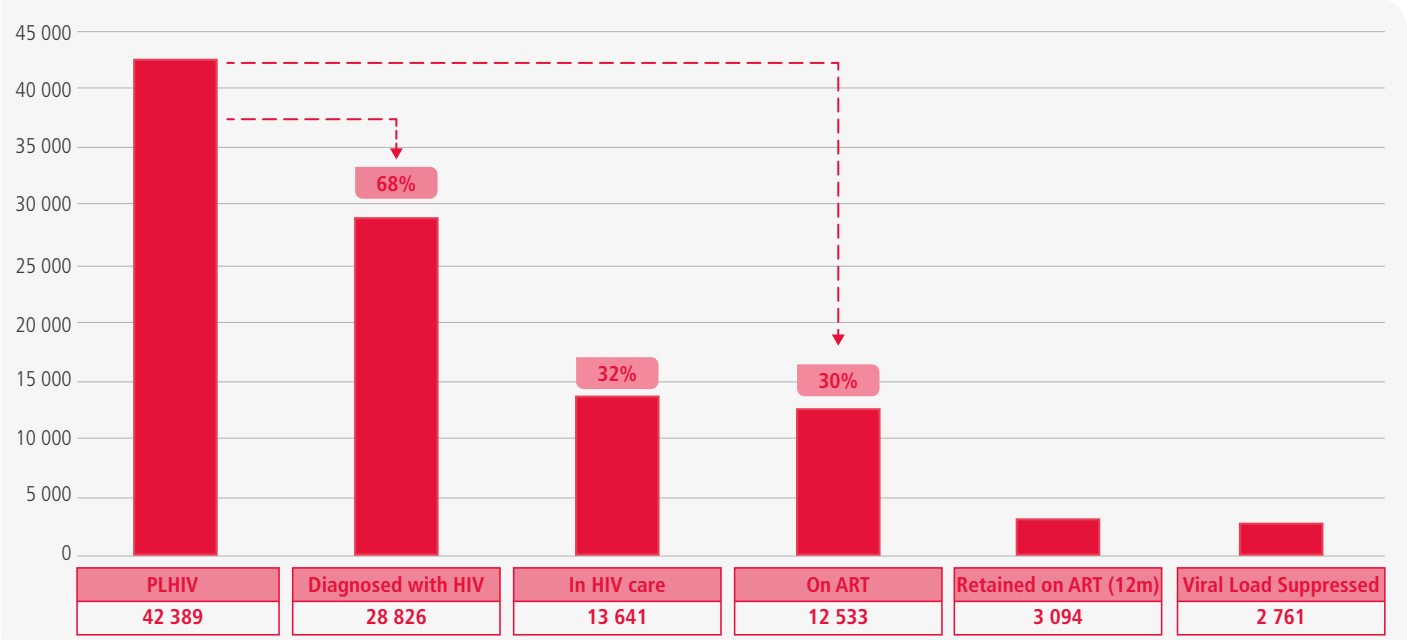
- to quantify the magnitude of the **gaps** along the continuum of HIV prevention, diagnosis, care and treatment;
- to identify where, along the steps of the continuum, programmes can **improve linkage** and retention of people in HIV prevention, care and treatment;
- to identify and analyse causes of the gaps and **priorities to fill them**;
- to **link programme services to their goals and outcomes** (e.g. the 90-90-90 targets[2] to achieve reductions in mortality and incidence);
- to provide information for **planning, prioritizing and designing** targeted interventions and for improving the existing monitoring and evauation system; and
- to improve the **quality of prevention, diagnosis, care and treatment** focused on the package of services a person requires.

Cascades consist of a series of sequential events in which each event is contingent on having achieved the preceding event until the final outcome is reached (Figure 1.1). HIV cascades have been constructed so that the final outcome is one that will have a positive effect on reducing HIV incidence, morbidity and mortality.

[1] The definition for elimination of mother-to-child transmission of HIV is ≤50 new paediatric infections per 100 000 live births and a transmission rates of <5% in breastfeeding populations or <2% in non-breastfeeding populations.

[2] By 2020, 90% of all people living with HIV will know their HIV status. By 2020, 90% of all people with diagnosed HIV infection will receive sustained antiretroviral therapy. By 2020, 90% of all people receiving antiretroviral therapy will have viral suppression.

Figure 1.1 Using the cascade to highlight gaps and linkages in HIV services - Philippines

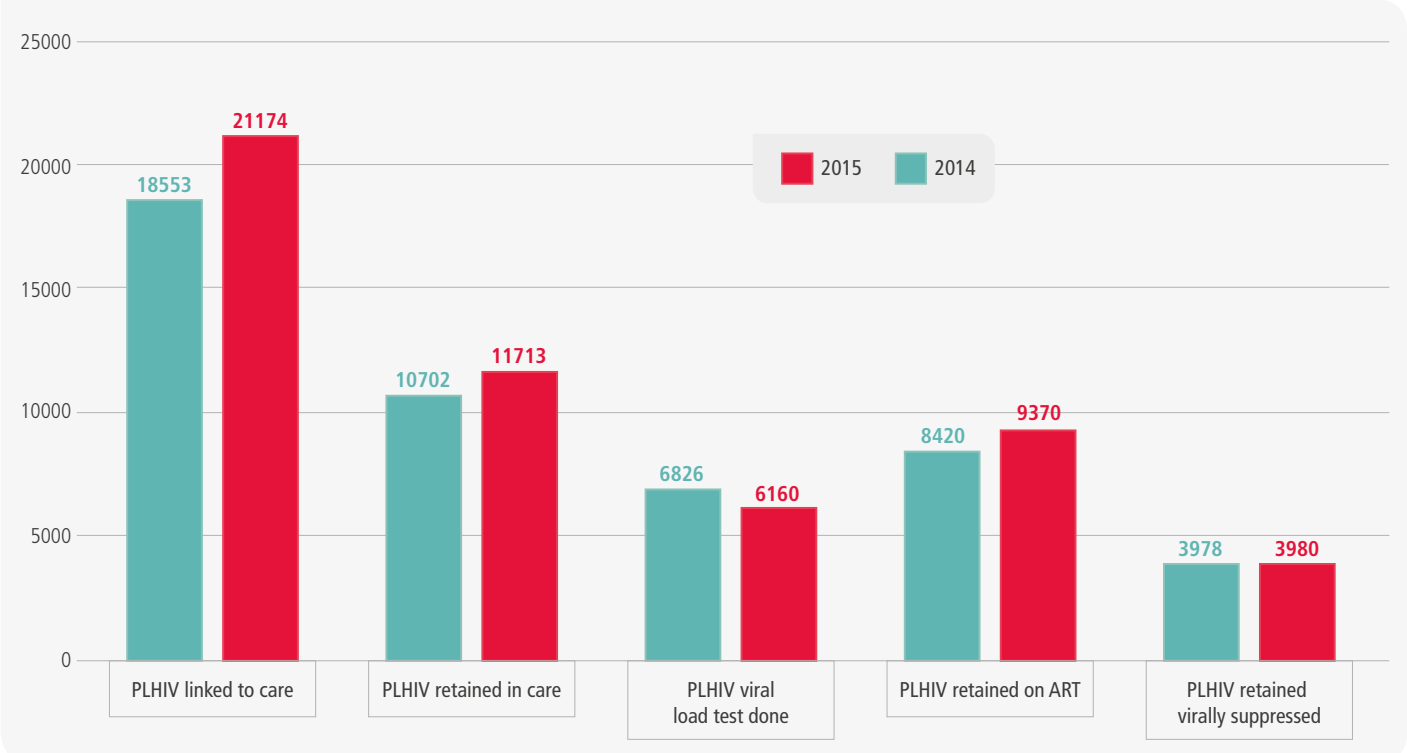


The events included in cascades are referred to as *indicators*. The indicators are defined and prioritized in the WHO Consolidated Strategic Information Guidelines. This cascade data use manual supports how to analyse them and use them to improve programmes.

1.1.1 Using data to identify programme gaps at national and sub national levels

The value of calculating the cascade indicators is that they can offer an efficient way to visualize and identify programmatic gaps in need of intervention in order to achieve the final goal. Monitoring care cascade indicators over time is a useful way to judge the impact of new or additional efforts to increase programme impact (Figure 1.2).

Figure 1.2 Using the cascade to show how programme gaps are closed over time - Jamaica



HIV cascades have been used most commonly for measuring and monitoring indicators along the HIV care continuum *(4)* although they are increasingly applied to HIV co-infections such as chronic hepatitis B virus (HBV) infection, hepatitis C virus (HCV) infection and tuberculosis and to HIV-infected pregnant women, as well as to HIV prevention programmes that go beyond the prevention of perinatal transmission.

HIV cascades can be constructed for the general population or for key populations (KP). Cascades can use national or subnational data and can be disaggregated by sex, age, KP, geographical region and even at the individual clinic level. A beneficial by-product of constructing cascades is that the analytic process may also identify areas where the quality and availability of data to monitor HIV care, treatment and prevention can be improved (Figures 1.3, 1.4).

Figure 1.3 Using standard cascades to highlight subnational gaps, Thailand

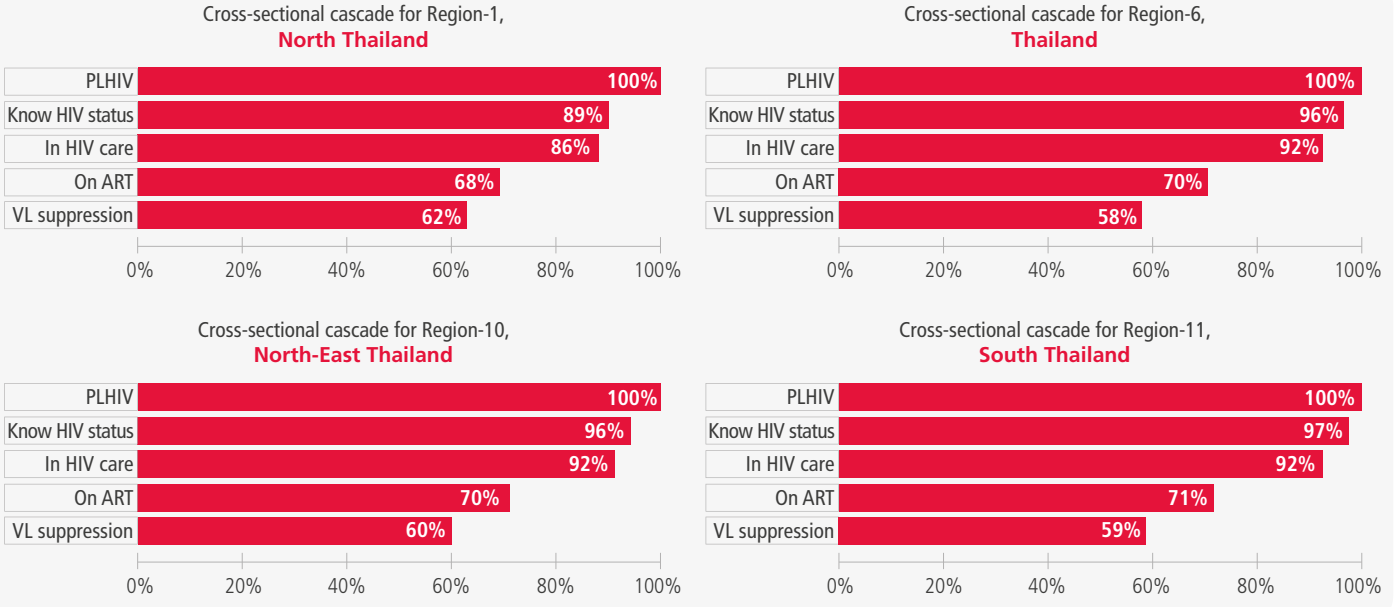


Figure 1.4 County-level cascade analysis to identify and fill programme gaps in the 90-90-90 targets, Kenya

County	1st 90			2nd 90					3rd 90	
	Linked to care, past 1 year (%)	PLHIV identified (%)	Currently in care, past 1 year (%)	PMTCT: on HAART (%)	Enrolled Started on ART (%)	In care and on ART (%)	PLHIV currently on ART (%)	Currently on ART, past 1 year (%)	Viral load suppression rate (%)	PLHIV virally suppressed (%)
Kakamega	81	89	3	98	64	92	92	17	84	52
Kericho	53	90	8	93	37	66	66	11	82	48
Kiambu	52	58	4	79	46	91	59	5	88	31
Kilifi	60	91	10	89	60	90	91	20	84	24
Kirinyaga	59	80	9	95	59	89	78	14	87	38
Kisii	97	54	13	95	91	87	52	13	78	44
Kisumu	64	70	5	98	56	89	69	15	86	58
Kitui	61	77	1	92	51	102	88	11	83	44
Kwale	89	47	10	67	72	93	48	22	79	7
Laikipia	68	76	7	92	55	86	73	8	87	33
Lamu	73	76	-2	93	65	95	81	11	81	26
Machakos	69	74	14	92	54	94	77	17	85	43
Makueni	60	67	20	85	42	93	70	19	85	39
Mandera	30	2	-77	12	25	92	2	-69	60	1
Marsabit	149	41	-52	84	85	131	59	4	80	22
Meru	58	75	0	86	46	89	75	9	87	65

In general, cascade indicators represent the targets that we want to achieve. An ideal cascade is flat: 100% of people with HIV have been diagnosed, treated and achieved virological suppression. For this reason, indicators that may appear reasonable for inclusion in a cascade may be omitted. For instance, for prevention of mother-to-child transmission (PMTCT), indicators such as the proportion of pregnant women offered HIV testing have been omitted before the number of pregnant women with HIV infection because there will be a large drop-off in the cascade from the number testing negative.

1.2 Types of cascades

This section provides an introduction to the cascades which can be used to highlight different programme gaps. It shows the basic indicators that are used (usually 3-5) which can be standardized and disaggregated. The following chapters provide more detail, which should be used when there are programme benefits. Limiting the number of indicators in cascade analysis is recommended to simplify data collection so long as it allows greater disaggregation and use of routine data for programme improvement.

1.2.1 Cascades for HIV care and treatment

Cascades for HIV care and treatment were first used in 2005 *(7,8)* and later came into general use *(9,10)* and have become ubiquitous in HIV care and treatment monitoring programmes. Excellent early guidance came from WHO's Western Pacific Regional Office and Eastern Mediterranean Regional Office *(11,12)*. These cascades are based on the linked sequence of steps for care and treatment to achieve outcomes of reduced mortality and incidence:

- They typically start with the estimated number of PLHIV in a given country or subnational region. This should be disaggregated by gender (and where possible age), geographical region, HIV-TB, and KP, so that the cascade indicates which populations should be reached and which can link effectively to outreach and prevention;
- This is followed by the number of people who have been diagnosed, including additional analysis of positivity yield[3] in different areas;
- Next comes the number of persons who have been started on antiretroviral therapy (ART), with supporting analysis of adherence rates and retention;
- The final bar of the cascade shows the number of persons who are virologically suppressed (Figure 1.1), with additional analysis of the coverage of viral load testing.

An additional bar may be added for the number of persons who have been linked to care.

These four steps are sufficient for overall cascade analysis. To understand the gaps at each stage and to improve programmes, the steps require additional analysis– of the stage the epidemic is at, the testing strategies to increase diagnosis, where losses to follow-up are occurring and for which population group, and the coverage and representativeness of viral load suppression data. Cascade analysis is about data analysis to improve the programme, and not just about reporting the numbers.

A simple cascade framework of a few well defined steps supports this data analysis and allows the same framework to be used at national, district and facility levels and among different populations. The major value of a consistent cascade framework is to promote data use, comparison by time, person and place, and actions to improve the programme.

Percentages can also be used on cascades to indicate the proportion of persons who have achieved the goal divided by the total number affected and, for instance, to assess progress towards the 90-90-90 targets (Figures 1.5 and 1.6).

[3] Positivity yield refers to the number of positive tests per persons tested. So, if there is an average of 14 positive tests for every 100 persons tested, the positivity yield is 14%.

Figure 1.5 Cascade analysis to quantify progress and gaps towards the 90-90-90 targets

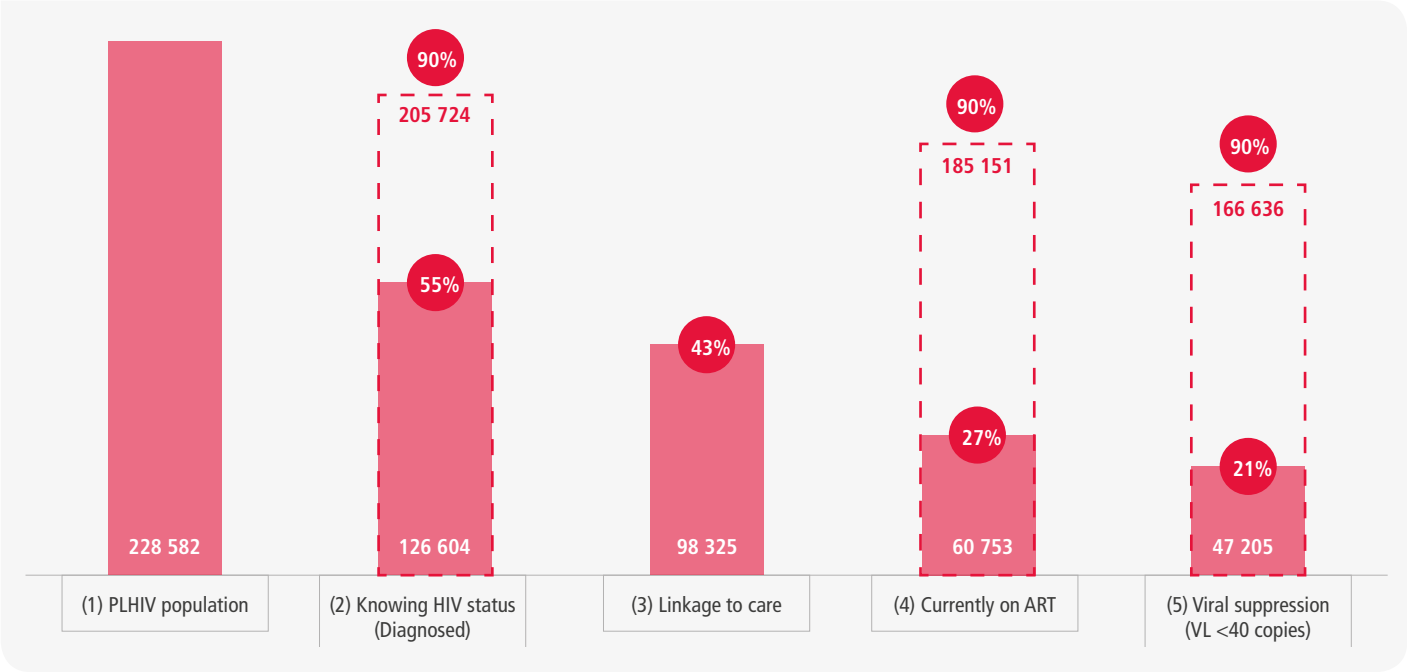
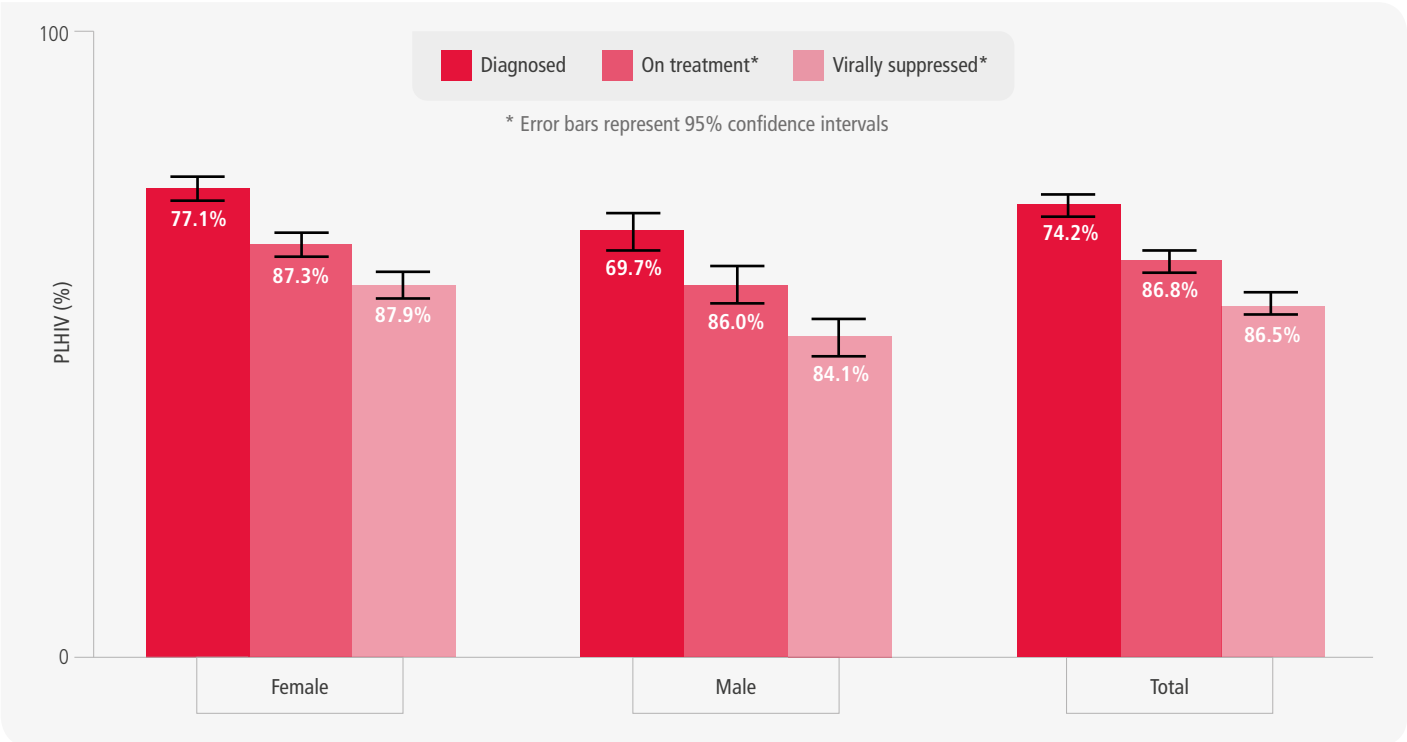


Figure 1.6 Surveys also provide population-level data for cascades, used by PEPFAR and Global Fund to identify gaps for funding, ZIMPHIA, Zimbabwe

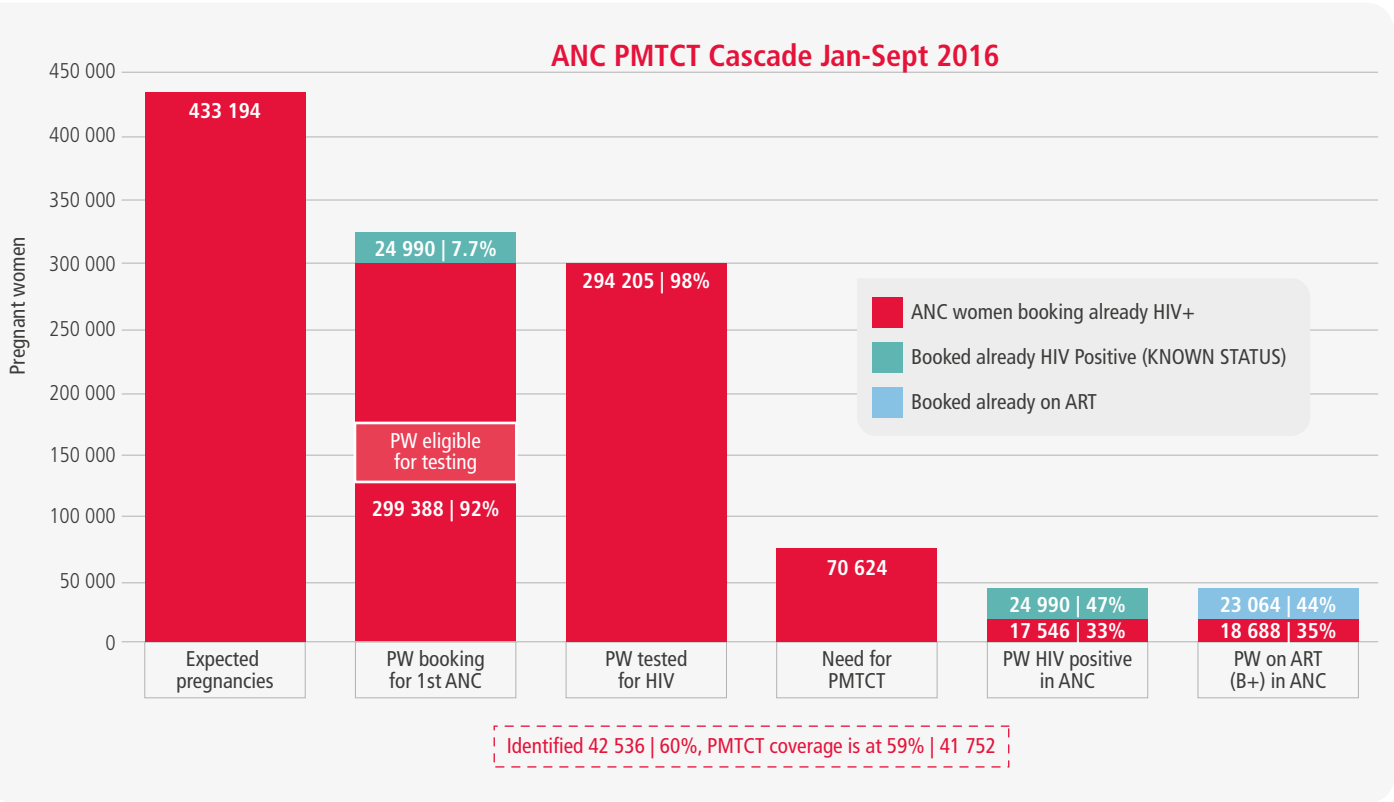


1.2.2 Cascades for HIV prevention

Cascades can also be used to depict HIV prevention efforts, where a sequence of actions is particularly important in achieving outcomes. There is increasing work on prevention cascades *(12-18)*, yet these have not yet been standardized and at this stage are not specifically included in this manual. However, in analysing the health sector cascade, it is important to include prevention and to ensure balanced priority-setting of actions to fill gaps in both prevention and treatment. Three areas are included in this manual:

- The **cascade for care and treatment offers opportunities for linking to prevention interventions.** Links to prevention should be assessed at each stage, particularly when testing (i.e. for persons testing negative or positive) and when providing community adherence to people on treatment and their partners;
- In general, the **start of the cascade for care and treatment should disaggregate data on PLHIV** and should develop differentiated strategies that reach key and at-risk populations, combining outreach prevention and treatment. This link is critical for prevention and for generating the flow of diagnoses for the treatment cascade;
- **Cascades to monitor PMTCT of HIV** are a special subset of prevention cascades. PMTCT cascades incorporate both treatment (of mothers) and prevention (in infants) with the goals of both prevention of HIV transmission to the baby and enrolment of infected mothers and babies into care and treatment. However, as a prevention cascade, its primary endpoint is the number of uninfected infants (Figure 1.7). PMTCT cascades are described in detail in Chapter 4.

Figure 1.7 PMTCT cascade used on a quarterly basis to identify and fill gaps in the programme, Zimbabwe



The primary aim of prevention is to prevent people from becoming infected. In contrast to the HIV care and treatment cascade that starts with the number of PLHIV, prevention cascades generally start with the number of uninfected people at risk for HIV infection; people can then be followed across various prevention programmes with an endpoint of not becoming infected.

1.2.2.1 Combination of prevention and care: linking prevention to care at each stage of the health sector cascade

Every step of the care and treatment cascade offers an opportunity to provide prevention interventions. For instance, the sexual and needle-sharing partners of PLHIV are at an especially high risk of infection and they would be part of the group at risk for HIV infection. Risk is greatest in the early stage of in infection, during the earliest period of ART before viral load falls and during periods of ART failure when viral load rises again *(19)*. In particular:

- Strategies for diagnosis should provide both prevention and linkage to care services.
- Testing positive provides opportunities for prevention for index cases and their partners.
- Programmes for retention on treatment and maintainenance of viral suppression (including gaps in viral suppression) also provide opportunities for delivery of prevention to individuals and communities.
- The importance of prevention should be emphasized at each clinical encounter with PLHIV who need access to prevention commodities, and their partners should be referred for outreach prevention interventions.

1.2.2.2 The first 90[4] – an opportunity for linkage to care and to prevention

The **first step of the care and treatment cascade – HIV testing services** – offers opportunities:

- for persons diagnosed with HIV to enter into care and achieve viral suppression;
- for persons who test negative but are at risk to be referred to prevention services.

In this cascade, testing has three stages (to which additional steps can be added if they have programmatic value):

1. **Risk yield** – number and proportion of uninfected people at elevated risk of infection that are identified and differentiated by age, sex and KP;
2. **Referral to relevant prevention services** – number and proportion of those at risk referred to relevant prevention services. This should be based on differentiation of, for instance, pre-exposure prophylaxis (PrEP), voluntary medical male circumcision (VMMC) and KP programmes;
3. **Retesting (and retention)** – number and proportion of people retained in the prevention intervention and retested for HIV after a defined period (e.g. after 3, 6 or 12 months). This provides the outcome in terms of keeping at-risk persons free from infection, and also gives insight into HIV incidence rates.

HIV testing can be focused on the **positivity yield** – the proportion of people diagnosed per total tested. Similarly, prevention can be focused on the proportion of uninfected people at elevated risk of infection who are identified. This **risk yield** is analogous to positivity yield and can help focus on and differentiate between prevention programmes on individuals and population groups at the highest risk of incident infection.

Assessing level of risk can be approached by a series of screening questions (Box 1.2). If the answer to any of the questions is yes, the person should be considered at high risk of HIV infection.

This can be presented as a stacked bar graph, where those who are found to be infected move into care and treatment, those at high risk of infection or who are members of key or priority populations receive intensive prevention follow-up, those at some risk receive more modest interventions and those with little or no risk receive counselling and condoms (Figure 1.8).

Training is required so that persons in testing services can engage with prevention and risk among persons testing negative, to refer those in need to differentiated prevention services. This requires programmes to **reduce stigma and ensure sensitive conversations**, which do not provide a significant burden to the services. In practice, the screening questions should be provided both sensitively and confidentially and it should not take more than two minutes to assess differentiated prevention referral opportunities).

Box 1.2 Examples of questions for establishing level of risk for persons found to be uninfected at HIV testing services

- Do you have an HIV-infected sexual partner?
- Have you had ≥2 sexual partners within the last 12 months?
- Have you had sex with a sex worker in the last 12 months?
- Have you had a sexually transmitted infection (STI) in the last 12 months?
- Behaviour questions for KPs or priority populations: have you injected drugs, had sex with other men (for men only), had sex for money, or had an STI in the last 12 months, are you a transgendered person, or have you been a prisoner?

[4] By 2020, 90% of all people living with HIV will know their HIV status.

The second stage is **referral to relevant prevention services** for those at risk (in particular KP services, PrEP, VMMC, and referral to community-based prevention in local areas of high risk). Prevention should be differentiated on the basis of risk, geographical and individual, to provide the necessary focus to prevention programmes. Differentiation of outreach and prevention should occur before testing, in determining the appropriate strategy, sites and populations for outreach prevention. It should also inform testing strategies on the basis of both positivity and risk yields. The key indicator is the number and proportion of those at risk referred to relevant prevention services. Differentiated prevention linkages should be measured and built into programmes at this stage:

- Consider PrEP.
- Notifiy partners.
- Refer men to VMMC and other prevention programmes for men.
- Refer to KP programmes.
- Refer to STI or HCV treatment, or HBV and HPV care.
- Referral to a community prevention organization for support.

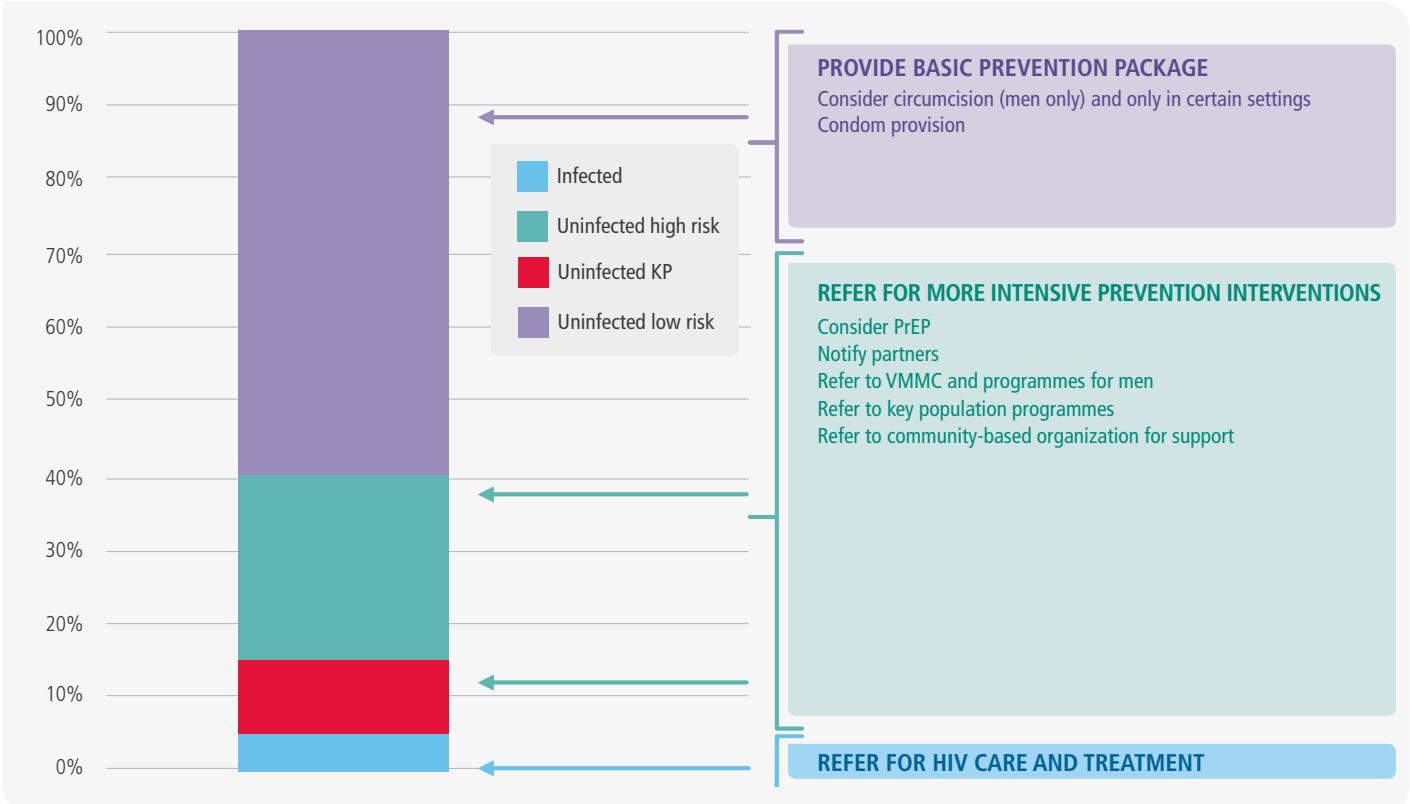
For self-testing, the key stage will the confirmation of the test, where linkages to prevention will be of greatest programmatic relevance. At every other level of the care and treatment cascade, the prevention focus should be on viral suppression – starting ART, retaining PLHIV in care and ensuring that viral replication is suppressed.

Additional data that can be collected, which will allow for further differentiation of risk and provide estimates to prevention programmes of the numbers of persons requiring follow-up, can include age group, circumcision status (men only), condom use, PrEP use, sex and geographical area (Box 1.3).

Box 1.3 Additional question topics to further characterize risk among persons found to be uninfected in HIV testing services

- Perception of risk of infection (this is often the best entry question to the assessment, and allows you to listen to the client; it also has value in client-centred prevention cascades)
- Engagement in risk behavious, such as injecting drug use, male to male sex, tattooing
- Age group
- Circumcision status
- Condom use (always, sometimes, never)
- Pre-exposure prophylaxis use
- Sex
- Geographical area

Figure 1.8 Prevention differentiation by risk at HIV testing services



The final stage is **retention in quality prevention services and retesting** after the recommended period (3, 6 or 12 months) to measure that the person remains uninfected as the outcome. The quality of the prevention package should be defined according to agreed standards, but the outcome of prevention should be retesting and remaining uninfected. The indicator at this stage is:

- retention in the prevention programme and retesting (at a defined time of 3, 6 or 12 months depending on the programme).

This stage will require a separate monitoring system in the prevention or KP programmes, which is not always linked to the testing service. The information on the initial test should be referred to the prevention service, along with subsequent HIV tests.

This provides a basic but important prevention link to the core health sector cascade for referring priority populations of young men or women or KPs to differentiated prevention services.

The risk yield should also be monitored across different sites to help differentiate, advocate for and focus evidence-based prevention efforts.

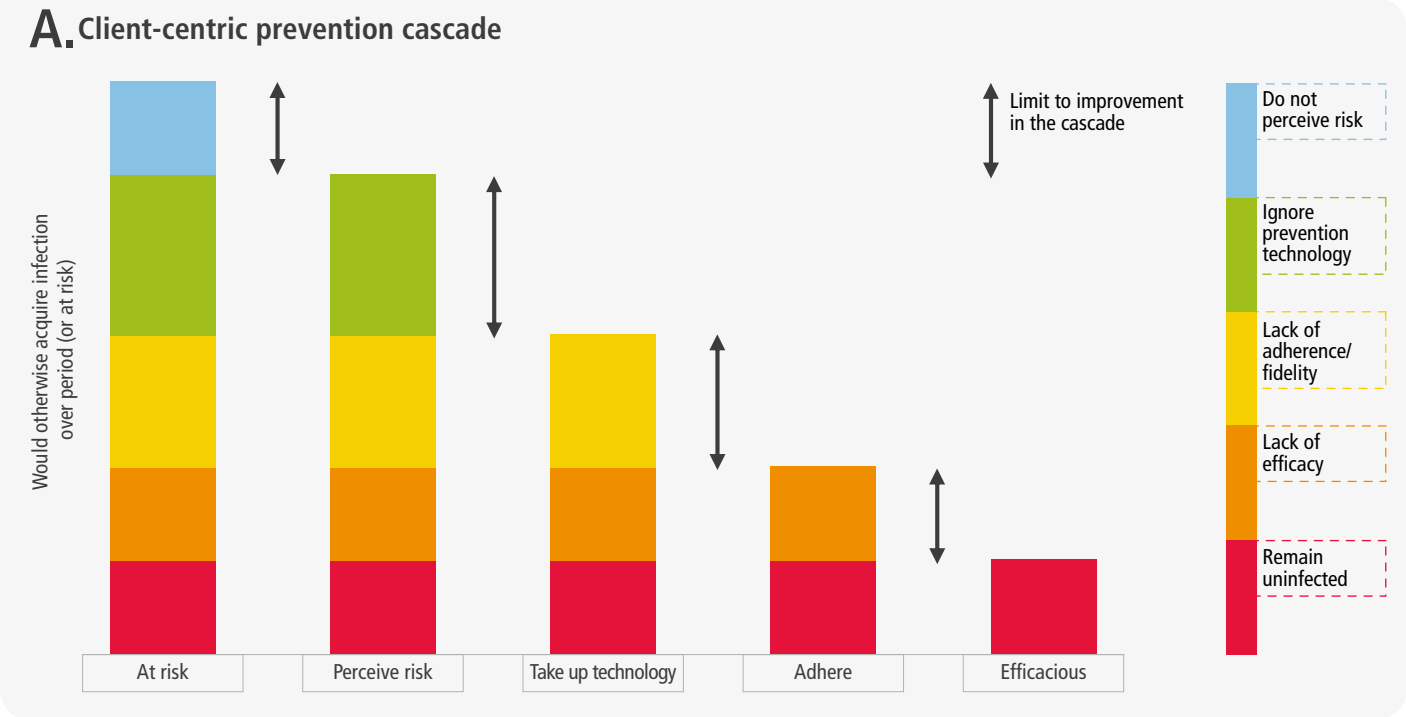
1.2.2.3 Linking to separate cascades for individual prevention services

As the prevention cascades are developed for separate services they can further fill in the stages between the three Rs of risk yield, referral and retesting (with retention in the prevention programme). This cascade data use manual focuses on the health sector cascade, stressing the importance of linkage to separate prevention cascades.

Such prevention cascades are being developed with a client-centric or an intervention-centric focus, with some key steps, which, as they are standardized, will be further referred to in this manual. The challenge is to keep them practical with some standardized steps so they can be used routinely for programme improvement.

The client-centric prevention cascade highlights the gaps in using prevention interventions from the number of persons at risk, the number who perceive they are at risk, the number who take up intervention, the number who adhere to the intervention and the number who achieve the outcome (Figure 1.9).

Figure 1.9 Gaps in client uptake and effective use of prevention



The intervention-centric cascade focuses on risk and the need for an intervention, a linkage to the service, retention in the service and outcomes relating to no infection. The three Rs for testing presented above – i.e. risk yield, referral, retesting (with retention) – also fit into the intervention-centric framework.

This manual stresses the importance of linking clinical care to prevention. Prevention cascades are also delivered as a sequence of steps towards a health outcome. Prevention, as much as treatment, needs data to identify the gaps in delivery and to focus and retain people in its programmes.

The cascades should be simple, with few standard steps with general relevance (additional data can always be provided for each step) and additional complexity added only if it has programmatic benefits. A simple framework from a consultation on prevention cascades is shown in Figure 1.10 which highlights the steps and gaps in delivering effective prevention services. Figure 1.11 provides a practical example from Zimbabwe.

Figure 1.10 Simple framework highlighting steps in delivering prevention

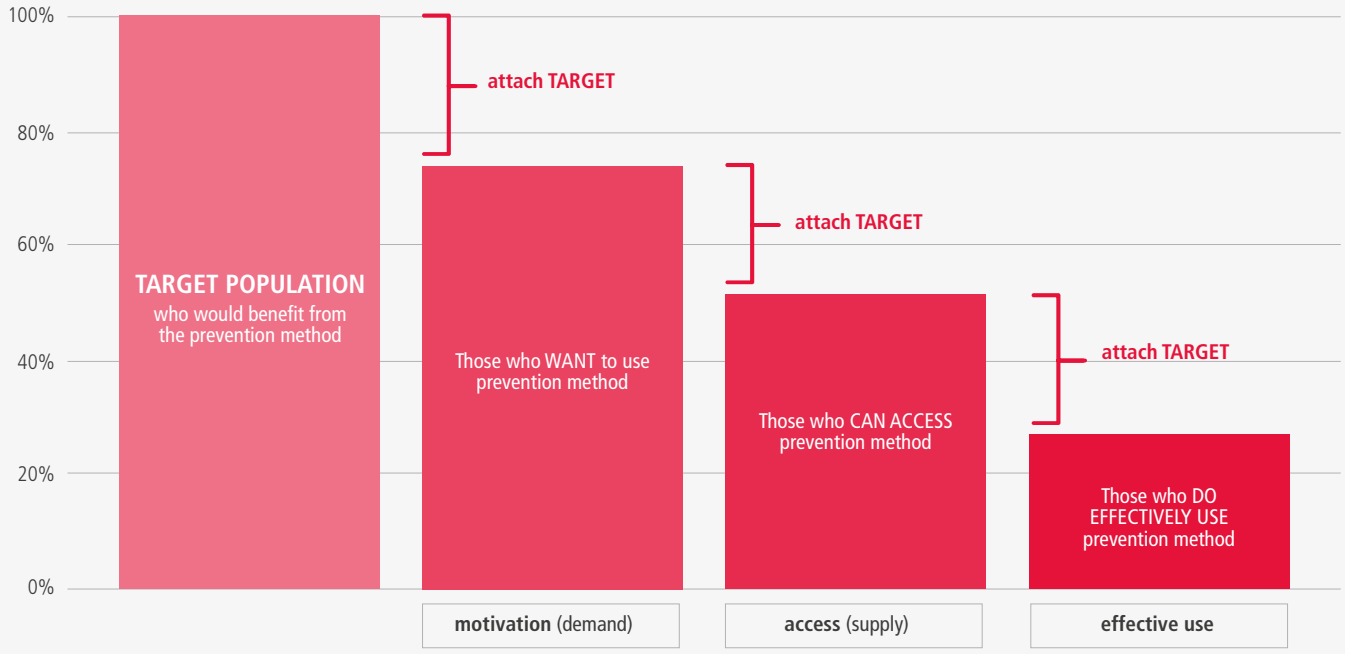
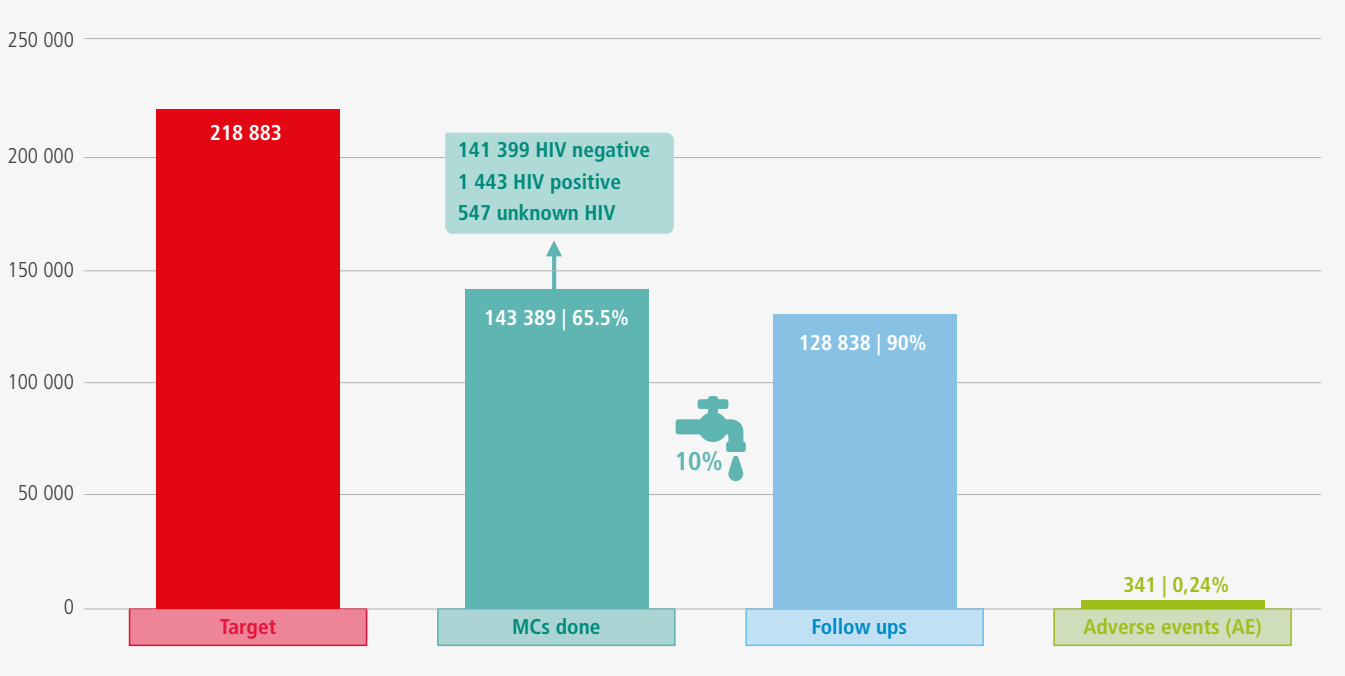


Figure 1.11 A VMMC cascade used to monitor gaps in the delivery of individual prevention services, Zimbabwe



1.2.2.4 PMTCT cascades

The prevention of mother to child transmission cascades have both treatment (of mothers) and prevention (in infants) as their goals. The first stage should be assessed with the core health-sector care cascade, using the following indicators:

1. Number of pregnant women living with HIV.
2. Number and proportion of HIV-infected pregnant women attending at least 1 antenatal care visit.
3. Number and proportion of HIV-infected pregnant women receiving ART.
4. Number of live infants born to HIV-infected women.

In addition, the retention and adherence of mothers to treatment for the years after birth are key measures for follow-up and disaggregation in the core cascade data. The following indicators also focus on infants, ensuring that a cascade of services are delivered to achieve health outcomes:

1. Number and proportion of HIV-exposed infants receiving antiretroviral prophylaxis.
2. Number and proportion of HIV-exposed infants evaluated for HIV infection using an HIV DNA test by 2 months of age.
3. Number and proportion of HIV-exposed infants who test negative by 2 months of age.
4. Number and proportion of HIV-exposed infants tested for HIV after breastfeeding cessation.
5. Number and proportion of HIV-exposed infants who test HIV-negative after breastfeeding cessation.

The PMTCT cascade shows the importance of addressing links to prevention as part of the core care cascade, and of ensuring necessary disaggregations. It also shows the need for additional cascade indicators to link services to outcomes for specific prevention components, as described in detail in Chapter 4.

Kenya has used the first four indicators of the PMTCT cascade with routine data at county level to identify women missing from PMTCT programmes, to provide differentiated support to sub-counties in need, and to rapidly close programme gaps. In this case, the use of cascade data was a major intervention in itself in closing the initial PMTCT gaps and linking missing women to the programme.

1.2.3 Cascades for key populations

Treatment and prevention cascades should be differentiated and disaggregated. Disaggregation can be done geographically from subnational units down to facility levels. Cascades can also be disaggregated by KPs so that individual cascades can be constructed separately for each defined population. These cascades can be national, subnational or facility-based and are described in detail in Chapter 3.

The cascade data use manual puts an important priority on KP cascades because there are often important gaps in access and services in such populations (Figures 1.12 and 1.13). Cascades can be developed using programme data (e.g. subnationally for implementing programmes), as well as linked to and as part of the national programme). Some programmes use referral slips to ensure that links between outreach and clinical services can be monitored, while data are kept separately for reasons of data security and confidentiality. KP cascades present challenges, but the data are important for promoting access for these populations.

Figure 1.12a Cascade analysis among commercial sex workers <25 years of age, Zimbabwe

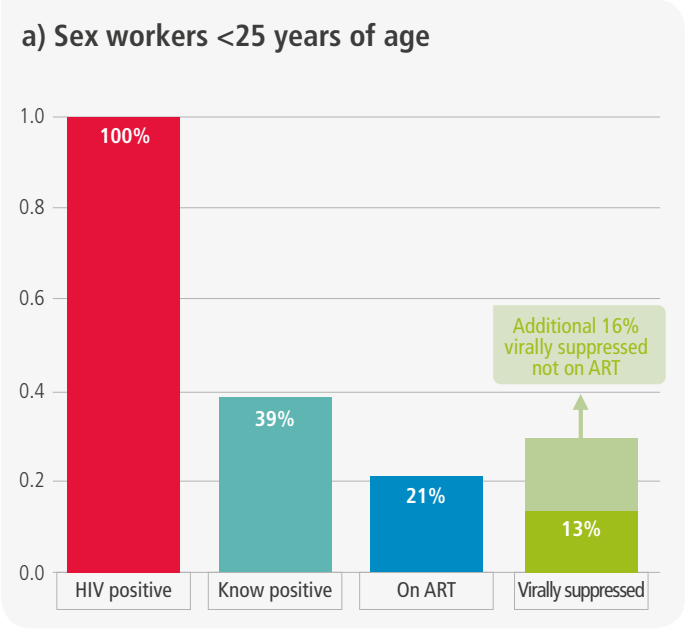


Figure 1.12b Cascade analysis among commercial sex workers ≥25 years of age, Zimbabwe

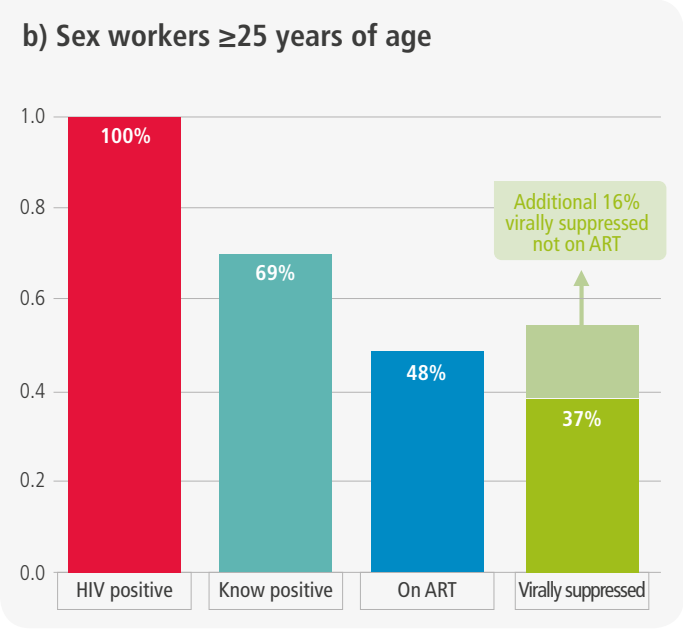
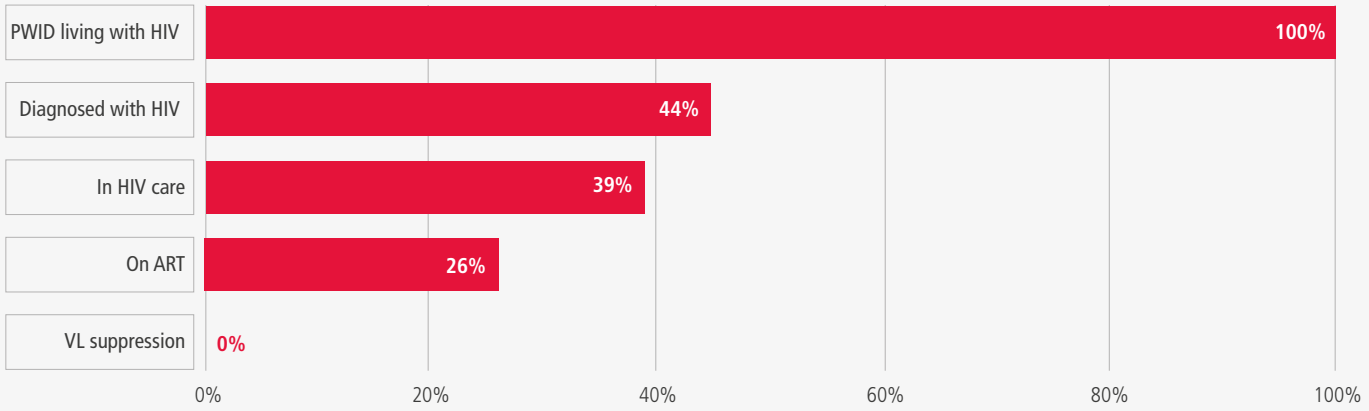


Figure 1.13 Cascade analysis to monitor access to HIV services among people who inject drugs, Ukraine



1.2.4 Cascades for care and treatment of HIV co-morbidities

Cascade analyses can be used to track populations with co-infections. First, cascade analysis is an opportunity to provide standard analyses and dashboards (e.g. in district health information systems) for several conditions.

For tuberculosis (TB), there are three routine indicators that can be used to identify cascade gaps and two additional indicators (A) where additional data from patient records or surveys are available, namely:

1. Estimated incident TB cases (new and relapse), data provided by WHO
   A. New and relapse TB patients detected
2. TB patients notified (new and relapse), reported routinely by countries
   A. New and relapse TB patients started on treatment
3. TB patients treated successfully (new and relapse), reported routinely.

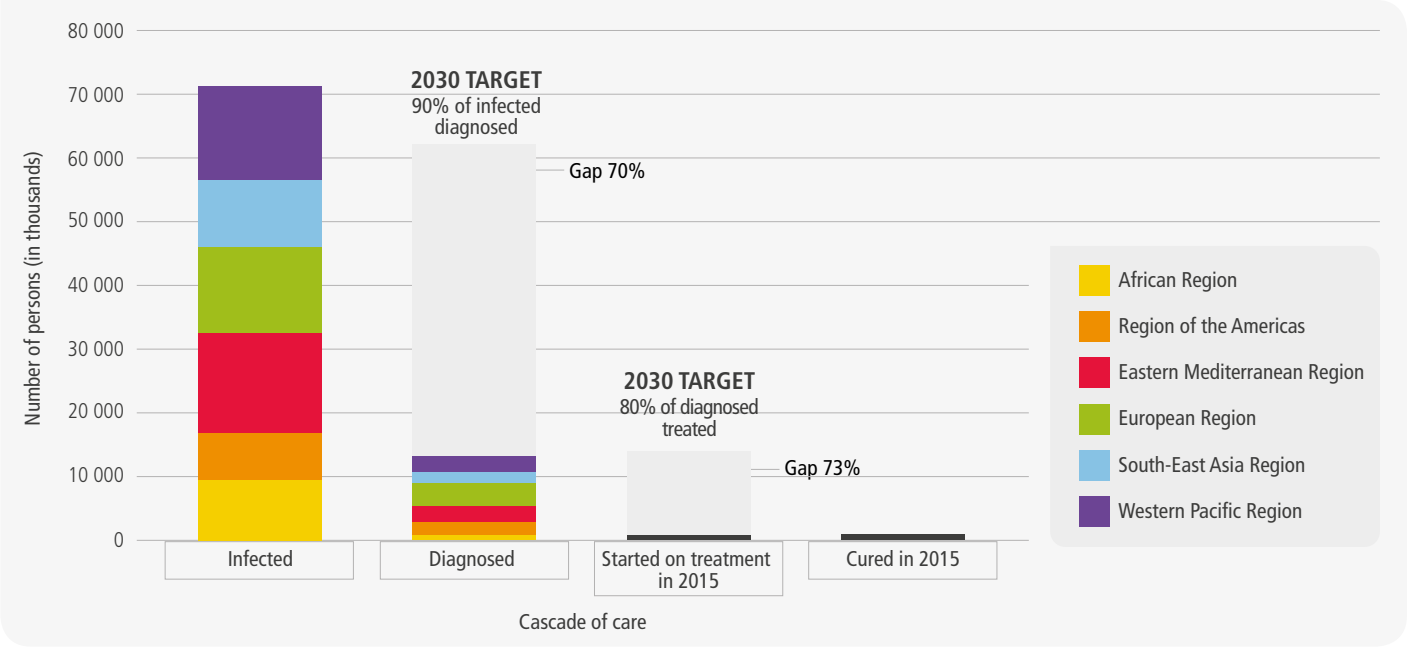
Similarly for HBV and HCV, there are standard cascade indicators that should be assessed to identify programme gaps, namely:

1. People infected with HBV and in a separate cascade with HCV
2. Diagnosis – the number of people who are diagnosed and the proportion of infected persons
3. Treatment – the number of people started on treatment, usually lifelong treatment for HBV or short-term curative treatment for HCV
4. Treatment outcomes – for HBV the number of people on treatment who have viral suppression; for HCV the number of people completing treatment who are cured.

These basic cascades should be addressed, where possible, in country cascade analysis and in building in standard dashboards into district health information systems.

Chapter 5 describes cascades for HIV-HBV, HIV-HCV and HIV-TB co-infection. Unlike care and treatment cascades for HIV, these cascades are usually only longitudinal. In these cascades, there is a screening indicator that precedes the cascade and defines the co-infected population; this indicator is not part of the cascade. For instance, all HIV-infected patients should be screened for TB, and all patients with active TB should be screened for HIV. Those that are diagnosed with co-infection with both HIV and TB become the base population that is then followed through the cascade (Figure 1.14).

Figure 1.14 Cascade for HCV by WHO region, highlighting the gaps that need filling in HIV co-morbidities by 2020 and 2030



1.3 Cross-sectional and longitudinal cascade analysis

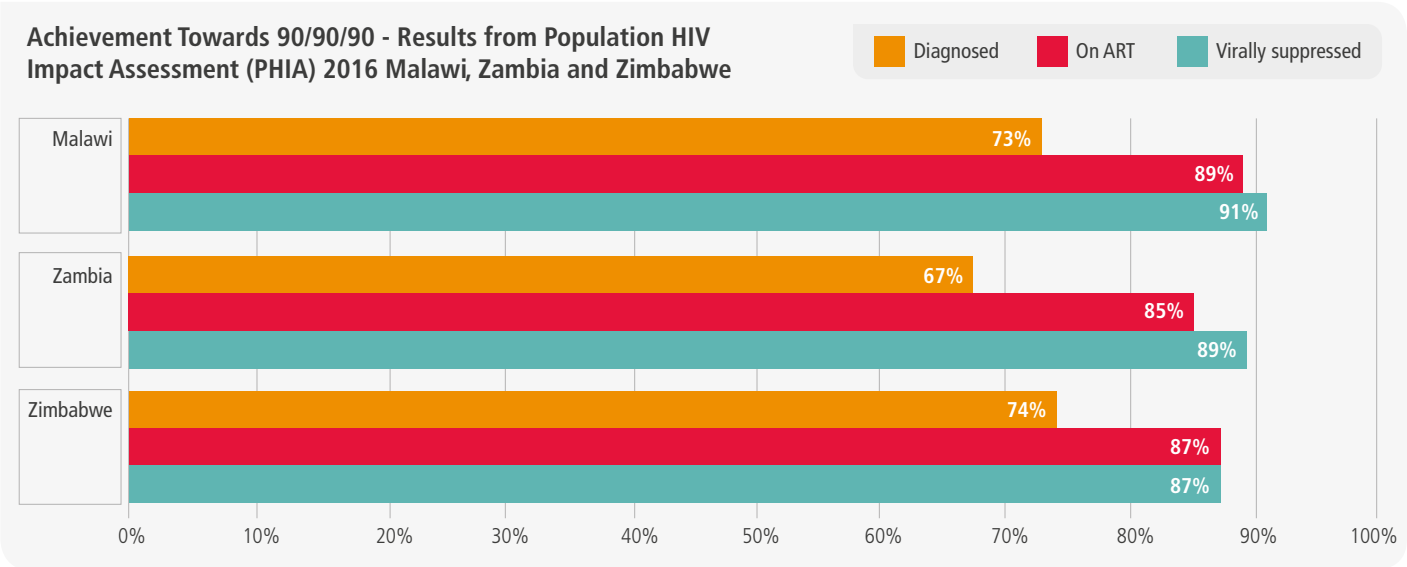
The two general types of cascade analyses are cross-sectional cascades and longitudinal cascades (Box 1.4).

Cascade analyses can be performed using data that reflect indicators at a specific point in time. This type of cascade is the most common and is referred to as a "cross-sectional HIV cascade".

Where there are strong individual-level reporting systems, including case reporting, HIV cascades can also be developed using data that follow persons along the indicators over time. This type of cascade is called a "longitudinal cascade" or a "cohort cascade". Longitudinal cascades reflect the outcomes from individuals during a specific time frame, with a specified beginning and a specified end. For example, a longitudinal cascade could include persons newly diagnosed with HIV in 2014 and results reported after 12 or 24 months of follow-up.

Cross-sectional cascades are generally the more useful for national programmes because they provide national estimates of the 90-90-90 targets (Figure 1.15). They are also normally easier to construct and use in a standard way at national, district and facility levels. Countries should prioritize construction of national and subnational cross-sectional cascades.

Figure 1.15 Cascades are used as a part of funding proposals for PEPFAR and the Global Fund in Malawi, Zambia and Zimbabwe



Cross-sectional cascades typically use data from multiple sources that do not account for in- and out-migration in the population but use readily accessible data and are simple to construct and interpret (Figure 1.16).

Most national longitudinal cascades use data from robust case surveillance systems that continuously un-duplicate and update individual records. Such systems do not exist widely in high-burden resource-constrained areas. Furthermore, cascade analysis using longitudinal data can be more complicated than analyses used in cross-sectional analysis.

Box 1.4 Cascade definitions

Cross-sectional cascade: A cascade that measure indicators at a specific point in time. All living persons with a specific trait (HIV infection, risk of HIV infection, HIV co-infection) are included regardless of whether they are currently in care or not.

Longitudinal cascade: A cascade that records data at multiple points in time. In longitudinal cascades, individuals are in cohorts and are followed until they reach a specified endpoint (e.g. viral suppression). This is also called a **cohort cascade**.

Denominator-denominator cascade: A cascade in which data are linked at the individual patient level across stages. For instance, in a cohort of patients with HIV-HCV co-infection, an individual patient is followed through each stage of the cascade.

Denominator-numerator cascade: A cascade in which data are linked at the individual patient level within each stage – for instance, the proportion of patients known to be on ART that have achieved viral suppression.

Single-source cascade: A cascade from which all data come from a single source – for instance, a cohort of patients with diagnosed HIV infection.

Multiple-source cascade: A cascade from which data come from multiple sources – for instance, in a prevention cascade when the numerator comes from the number of voluntary male medical circumcisions that have been performed and the denominator comes from a behavioural survey that estimates the number of 15-24-year-old men with multiple sexual partners.

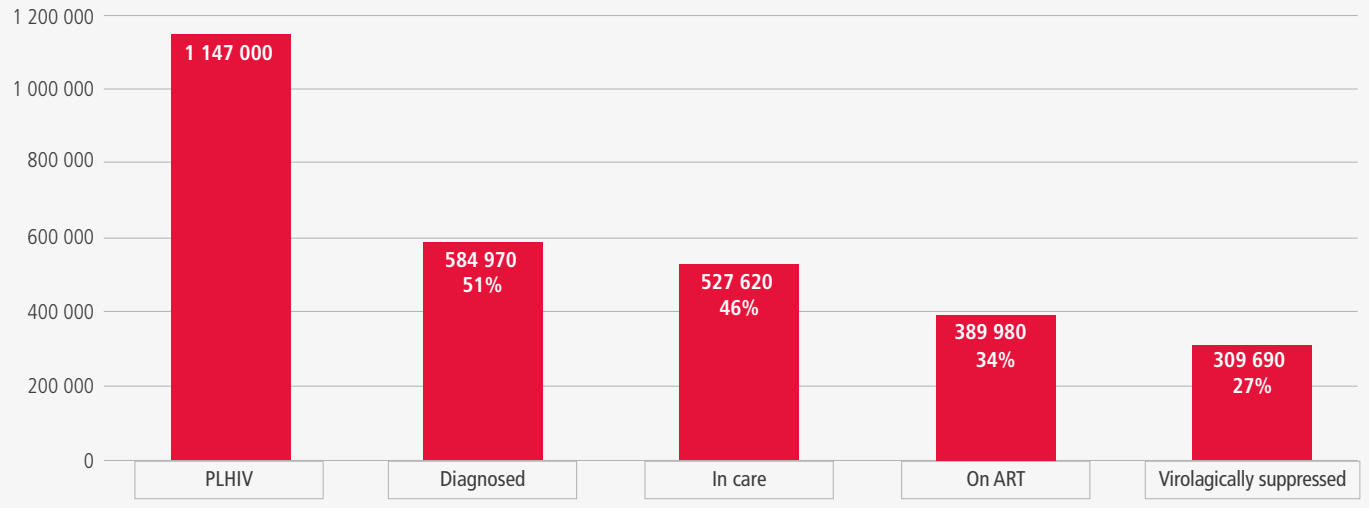
Prevalence-based HIV continuum: A cascade that includes the number of living persons, whether diagnosed or not, at each step of the cascade as a proportion of the total number with the condition *(5)*. This is equivalent to a **cross-sectional cascade**.

Diagnosis-based HIV continuum: A cascade that includes the number of living persons who are diagnosed with the condition (e.g. HIV, co-infection, elevated risk) as the denominator at each step of the cascade *(5)*. This is the equivalent of a **longitudinal cascade**.

Adapted from Haber N, Dillay D, Porter K, Bärninghausen T. Constructing the cascade of HIV care: methods for measurement. Curr Opin HIV AIDS. 2016;11:102-8.

In contrast to cross-sectional cascades, longitudinal cascades begin with the number of persons who have been diagnosed with HIV and follow these same people over time to see how many eventually access care and go on to become virally suppressed (Figure 1.17). For instance, in a longitudinal cascade the first indicator could be the number of persons newly diagnosed with HIV from 1 January 2015 through 31 December 2015. The second indicator would be the number and percentage of those persons who entered care within three months of diagnosis (or some other time frame of interest such as one month) among those who were newly diagnosed with HIV in 2015. Key to these assessments is the availability and quality of the data. Given that many nationally available data are imperfect, it is important to understand and document the limitations of the data and to note how these limitations may have an impact on, or may bias, interpretation of the findings. Understanding data limitations is also necessary for improving future data availability and quality. At a minimum, data for cascade analysis should be evaluated for quality and potential biases. In many settings, in order to overcome limitations in data availability and quality, cascade analysis requires the use of multiple data sources rather than a single data source. While this approach may still produce meaningful results, the analysis will need to take account of possible bias arising from differences in the timing and the populations monitored. Section 7 provides guidance on evaluating data quality and the use of multiple data sources for cascade analysis.

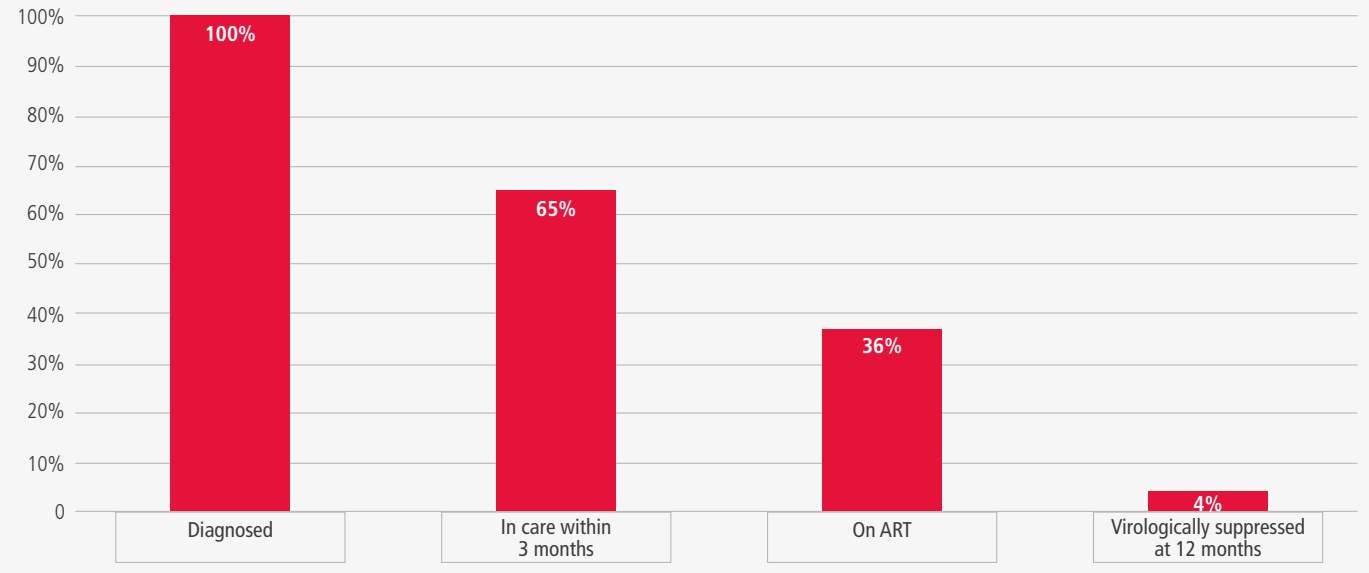
Figure 1.16 Cross-sectional national cascade, Kenya AIDS Indicator Survey, 2012*



Source: Kenya AIDS Indicator Survey, 2012: Final Report. Nairobi: National AIDS and STI Control Programme (NASCOP);2014
* The estimate for PLHIV comes from the Spectrum AIDS Indicator Model.

The selection of the denominator or denominators used in the cascade analysis depends on the indicators of interest. At global level, the preferred approach to constructing a cascade is to use a single denominator. This type of cascade is sometimes called a denominator-denominator cascade.

Figure 1.17 Longitudinal care cascade, La Romana, Dominican Republic, 2011



Adapted from: Ref. (6).

This manual provides guidance on how to calculate core indicators for cross-sectional and longitudinal care cascades using a denominator-denominator approach. For each of these cascades, the indicators and the potential data sources for the denominator and numerators are presented. The manual also provides guidance on how to approach situations in which specific data are unavailable by using supplemental (i.e. not core) indicators.

The guidance is practical in order to support data use, often with imperfect data, and to identify programme gaps and linkages. The data should be used to improve programmes and the quality of data continually. Cascade data use is an important step to improving both the quality of programmes and the quality and practical use of data.

2. HIV CARE AND TREATMENT CASCADES

Countries should prioritize cross-sectional cascade analysis at national and subnational levels and for KP. This provides an overall view of programme gaps. Where there are strong individual-level reporting systems, including case reporting, these can be supplemented by analysis of individual-level, longitudinal cascades.

Cross-sectional cascades measure related indicators at a specific point in time. Typically, the number in the left-hand column (e.g. PLHIV) is estimated, and multiple sources are used to calculate the various steps in the cascade. All living persons with a specific trait (HIV infection, risk of HIV infection, HIV co-infection) are included regardless of whether they are currently in care or not.

Cross-sectional cascades typically include four steps and indicators, although frequently a fifth (the number of PLHIV that are in HIV care) is added. These indicators are shown in Box 2.1.

Box 2.1 Cross-sectional cascade indicators

- Estimated number of PLHIV as of a specified date (typically the end of the most recent year for which data are available, which should be disaggregated geographically, by sex, age and KP).
- Number and percentage of the number of PLHIV who are aware of their status (also referred to as PLHIV who have been diagnosed with HIV).
- Number and percentage of the number of PLHIV who are receiving HIV care (including ART).[5]
- Number and percentage of the number of PLHIV who are on ART.
- Number and percentage of the number of PLHIV who are virologically suppressed (<1000 copies/mL).

Cross-sectional cascades are typically constructed using data from multiple sources, such as modelled estimates of the number of PLHIV from the Spectrum AIDS Indicator Model *(1)* and clinical registry data for the number of PLHIV in care, on ART and virologically supressed. Additionally, data that were collected at different times will often be needed to construct the cascade. For these reasons, it is important to document the source and year of the data that contribute to each column in the cascade. For all analyses, the most recent and most robust data should be used.

2.1 Core indicators and data sources

Indicator 1. Number of PLHIV (typically the estimated number of PLHIV)

HIV estimation models such as the Spectrum AIDS Indicator Model *(1)*, population-based surveys of the general population or size estimation exercises from surveys of KPs can be used to determine the first indicator. Uncertainty ranges around the estimate should be included if available. Estimates from the UNAIDS-supported Spectrum modelling tool are the preferred data source for this indicator. If estimates of the number of PLHIV are derived from a data source other than Spectrum, the methods and the uncertainty of the corresponding estimates should be described.

This first indicator is typically presented as a number and represents 100%. This number serves as the denominator for all subsequent indicators.

Indicator 2. Number and percentage of PLHIV who are aware of their HIV status

Case-based surveillance data. In countries with well-functioning, mature HIV reporting systems (see criteria below), the number of persons reported to the national case-based surveillance system, minus the number of deaths, can serve as a proxy for the number of PLHIV who are aware of their HIV status. This assumes that, with rapid HIV testing, nearly all people who are diagnosed with HIV learn their status, and with a well-functioning mature HIV reporting system, all people diagnosed are subsequently reported.

When using case-based surveillance data for cascade analysis, it is important to allow time for delays in reporting. Countries with delays in reporting should make sure that there is sufficient time between the end of the reporting period and the construction of the cascade to allow for possible reporting delay.

[5] This is an optional cascade indicator.

In addition to allowing for reporting delays, countries should conduct an evaluation of the quality, completeness and timeliness of reporting no more than 2 years prior to cascade analysis. The case-based reporting system should meet high performance standards (e.g. at least 85% complete and 65% of cases reported within 6 months of diagnosis, or other standards that are deemed sufficiently high).

It is also recommended that countries only use case-based surveillance to calculate the proportion of PLHIV who know their status if the surveillance system meets the following criteria:

- The system has been in operation for at least three years. More recent systems may not have fully captured people who were diagnosed earlier.
- Reports of people diagnosed with HIV who have subsequently died can be excluded from the indicator.
- Incoming reports are matched against records in the surveillance registry to distinguish new or existing information on a previously reported person from reports on persons not previously reported.

How the system meets these criteria should be documented as part of the evaluation.

Modelling. An alternative to using case-based surveillance is to model the proportion of PLHIV that are undiagnosed using the European Centre for Disease Control model, which uses CD4 counts at diagnosis as a way of estimating duration of infection and the probability that someone remains undiagnosed *(2)*. As with any data presented in a cascade, its source should be cited.

Population-based survey data. Population-based HIV serosurveys or integrated bio-behavioural surveys in KPs that both test participants for HIV infection and ask them if they have been diagnosed with HIV can be used as an estimate of the number of persons who are aware of their infection. It is important to note that these self-reported data may underestimate the proportion of persons who know that they are HIV-infected because some participants who know that they are infected may not disclose this information to the interviewer. Surveys that are limited to people who attend clinics or attend certain programmes, such as needle and syringe exchanges, will be very unlikely to be representative of the entire population and, as such, will suffer from selection bias.

In surveys that ask the respondents directly whether they are HIV-infected, the numerator is the number of participants who state that they are HIV-infected and whose HIV test result from the survey confirms their infection. Participants who are found to be HIV-infected from testing in the survey but report never having been tested or report having been tested prior to the survey but who did not receive their test results are considered to be unaware of their infection and should not be included in the numerator. The denominator in these studies is the number of people who test positive regardless of whether they know their status or not. In many study designs this number may be weighted to adjust for sampling.

Alternatively, some surveys do not ask participants to disclose their serostatus, but they do ask participants if they have been tested for HIV. In settings where indirect estimation of knowledge of status from survey data is required to construct this indicator, it is useful to refer to the global AIDS monitoring guidelines *(3)* for more detailed instruction.

In cascade analysis, preference is generally given to the most recent data to ensure reasonable indicator estimates. For this reason, it is recommended that surveys be no more than 3 years old for use in cascade analysis. When using older survey data, it is possible that the proportion of people who reported knowing their status at the time of the survey is now exceeded by the current proportion of people on treatment. Moreover, in general in population-based household surveys, the sample size is powered to provide robust prevalence estimates at the national and, at times, subnational levels. However, given rapid scale-up in many countries, older survey data may indeed underestimate the number of PLHIV who know their status.

Indicator 3. Number and percentage of PLHIV who are receiving HIV care (including ART)

In countries that have adopted and implemented treatment for all PLHIV, this indicator should eventually be the same as the number of PLHIV on ART. However, in some countries it may still be important to measure this indicator since not all PLHIV are eligible for ART. As such, this is an optional element. This indicator provides the opportunity to monitor persons in care who are not yet on ART and to determine how this varies across populations and time. When reporting this indicator, we recommend that national programmes note whether they have expanded the criteria for initiating ART to treat everyone or whether they are using a different recommendation.

There are three possible data sources for the numerator: 1) case-based surveillance, 2) programme data and 3) population-based surveys. Evidence of care includes documentation of clinical staging, a CD4 or viral load test, ART initiation or ART use. Selecting which of these data to use will depend on their completeness, quality and recency.

Case-based surveillance data. The considerations regarding use of data from case-based surveillance described for indicator 2 also apply to indicator 3. Obtaining the number of persons in care from a case-based surveillance database generally requires definitions that include some time frame restrictions. For example, if the cross-sectional cascade is measuring persons in care as of 31 December 2014, it would probably not make sense to include persons who were in care in 2010 but not in 2014. Therefore, when using case-based surveillance data, it is recommended that this indicator should refer to a specified time period. Case-based surveillance data should be used only if reporting of sentinel events is robust. If not, the value of this indicator will be underestimated.

Programme data. Programme data that indicate clinical staging, receipt of a CD4 or HIV viral load test or use of ART are all indicative of receiving HIV care at least once. Data may come from registers, electronic medical records or other patient monitoring systems. As with all programme data when used beyond the facility level, the number of persons in care is likely to be overestimated because programme data are submitted in aggregate and the possibility of duplicate reports cannot be excluded. Additionally, the number of those who have died needs to be subtracted from these estimates. These data should also reflect the specific period of time assessed in the cascade, such as the 6 months or year prior to data analysis.

Population-based survey data. The considerations regarding use of data from population-based surveys described for indicator 2 also apply to indicator 3. Population-based surveys that collect information on receipt of care usually include a time frame (e.g. receipt of care in the 12 months prior to the survey). For population-based surveys, the recency of the survey remains even more important.

Indicator 4. Number and percentage of PLHIV in care who are on ART

There are three possible data sources for the numerator: 1) case-based reporting, 2) programme data and 3) survey data that measure the number of PLHIV in care who are on ART directly. Additionally, population-based surveys may be able to estimate this through questions about self-reported access in the absence of direct testing for antiretrovirals (ARV).

Case-based surveillance data. The considerations regarding use of data from case-based surveillance described for indicators 2 and 3 also apply to indicator 4. In countries where persons on ART are routinely monitored using viral load testing, evidence of a viral load test can be used as a proxy for being on ART.

Programme data. Programme data that indicate ART initiation or a viral load test in situations where viral load testing is performed only on persons who are on ART should be used for the numerator. Clinical and pharmacy records may be useful data sources. It is important to take into account pharmacy protocols for patients on ART since in some settings some or all patients may receive medication refills at intervals greater than one month. These people should still be included as on ART. Note that use of pre- and post-exposure prophylaxis is not included in this indicator. Keep in mind that programme data obtained from aggregate data are likely to overestimate this indicator. Countries should document the national guidelines on criteria for ART and, for countries that require a clinical or immunological threshold for ART, documentation of the estimated number and proportion of ART-eligible persons who are on ART may be worth including.

Population-based survey data. Population-based surveys that collect information on ART usually include a time frame, and the question of ART use is asked only among persons who report being in care. While self-report of receiving ART is typically used for calculating this indicator, tests for the presence of antiretroviral agents may also be conducted in some surveys. Survey participants whose laboratory tests indicate HIV infection and the presence of ART should also be counted as receiving ART (as well as being included as knowing their status and being in care) even if these participants denied having HIV infection. As with indicators 3 and 4, timeliness of survey data is a major concern in the face of rapid expansion of ART programmes.

Indicator 5. Number and percentage of PLHIV who are virally suppressed (<1000 copies/mL)[6]

There are four possible data sources for the numerator: 1) case-based reporting, 2) programme data, 3) laboratory data and 4) population-based or drug-resistance surveys.

For the first three sources, countries should construct this indicator only in settings where viral load testing has been routinely available to all populations during the time period covered by the cascade. Episodic viral load testing (i.e. to identify possible treatment failure or to determine when to initiate treatment) will lead to substantial underestimation of viral suppression levels. In situations where patients are monitored using routine viral load measurements but only in sentinel or selected sites, the proportion suppressed at these sites may be used to represent national suppression proportions, but a detailed explanation of the source of the data should be noted. If a national indicator is to be extrapolated from limited sentinel surveillance, great care must be taken to ensure that the results found in participating clinics are representative of all ART clinics in the country.

Case-based surveillance data. Keeping in mind the same considerations regarding use of data from case-based surveillance described previously, the numerator is the number of persons on ART whose most recent viral load test result is <1000 copies/mL.

Programme data. Data may come from registers, medical records or other patient monitoring systems. The numerator is the number of persons whose most recent viral load test result is <1000 copies/mL.

Laboratory data. In some countries, viral load testing takes place at a selected number of specialized laboratories. If there is a national laboratory with unduplicated laboratory records, the numerator is the number of persons whose most recent HIV viral load test result is <1 000 copies/mL.

Population-based survey data or drug-resistance surveys. The numerator is the number of persons whose viral load test result is <1000 copies/mL. This can also be estimated from nationally representative surveys of PLHIV in care and on ART.

[6] An additional factor to consider is that approximately 12% of persons who are not yet on ART may be virally suppressed at any given point in time (4). Additional advice on whether and how to account for this will be forthcoming.

2.2 Examples of cross-sectional cascades

2.2.1. Cross-sectional HIV care and treatment cascade from Kenya

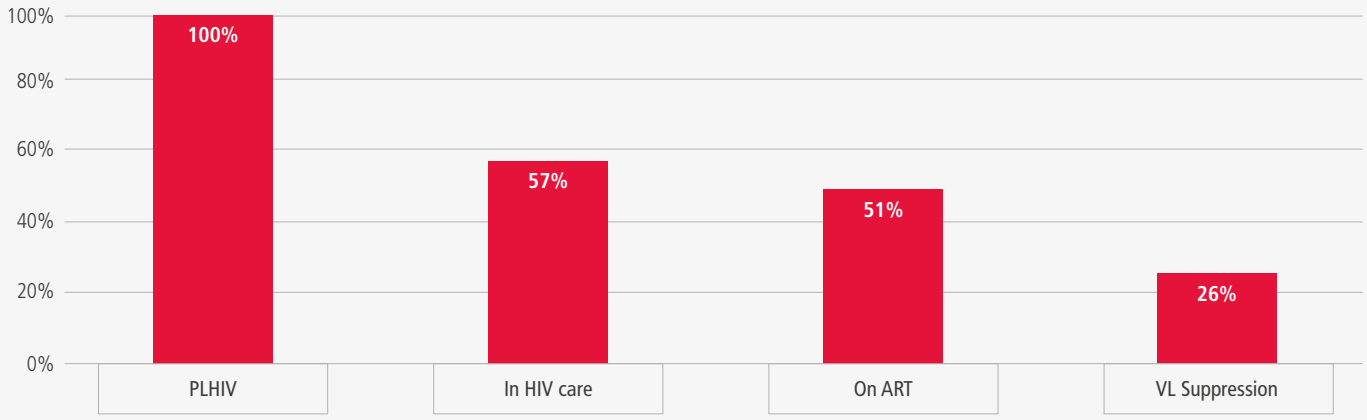
The data used to construct the HIV care cascade for Kenya using data from 2015 are shown below (Table 2.1); the cascade is shown in Figure 2.1. Unlike the Kenyan cascade shown in Figure 1.16, which is derived from a national household-based survey, the cascade shown in Figure 2.1 is much more typical in that it uses multiple sources to construct the care and treatment cascade. Figure 2.1 uses Spectrum to estimate the number of PLHIV, programme data to count the number of PLHIV in care and on ART, and cross-sectional estimates from the Kenyan AIDS Indicator Survey (KAIS 2012) for the proportion of persons who have reached virological suppression.

The findings from this cascade analysis highlight a number of areas for improved epidemiological data and programme service delivery. First, it shows that there is no current national estimate of the number of people who have been diagnosed with HIV and who know their results. This is a data gap that can be filled by case-based surveillance, modelled estimates or data from cross-sectional surveys. Secondly, while the cascade shows that the proportions of PLHIV who were in care and on ART were similar, it also found that a low proportion of PLHIV are virally suppressed. The comparability of these data can be questioned, but basic policy implications may include the need have data on HIV testing available for analysis, to increase the uptake of ART, and to obtain better estimates of the proportion of persons on ART who have achieved viral suppression. Because this is a cross-sectional cascade, it is possible that insufficient follow-up time may be responsible to some degree for the low suppression rate.

Table 2.1 Cross-sectional national-level HIV care and treatment cascade, Kenya, 2015

Indicator	Data source and year data obtained	Absolute number	Percentage
Estimated number of PLHIV	Spectrum (2015)	1 630 939	100%
Aware/diagnosed	None	Not available	Not available
In HIV care	Programme registers (2015)	931 518	57%
On ART	Programme registers (2015)	823 738	51%
Viral suppression	Kenya AIDS Indicator Survey, 2012	428 628	26%

Figure 2.1 Cross-sectional national-level HIV care and treatment cascade, Kenya, 2014

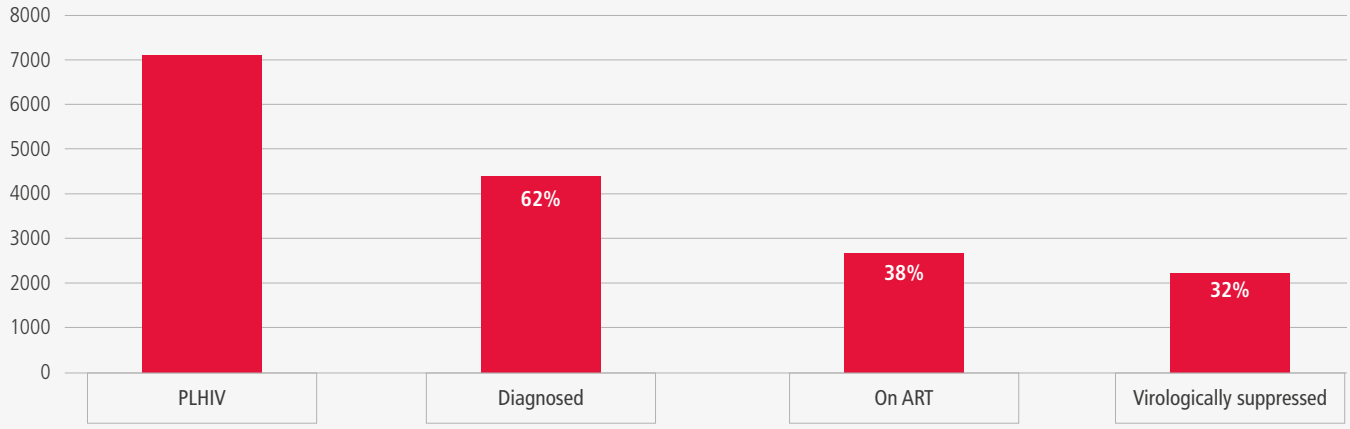


Source: Developed and presented at the WHO Global HIV Cascade Workshop: Measuring and Tracking People Along the HIV Health Sector Cascade, November 2015, Marrakech.

2.2.2 Cross-sectional HIV care and treatment cascade, Georgia

Georgia's cross-sectional cascade was constructed in 2015 from multiple data sources (Figure 2.2) *(5)*. The number of PLHIV was estimated from Spectrum; all other data came from the national HIV information system. In 2015 an estimated 61% of PLHIV had been diagnosed, 38% were on ART and 32% were virologically suppressed. These results suggest gaps in diagnosis and treatment. Notably, of the 2685 patients who had begun ART, 2274 (85%) had achieved virological suppression.

Figure 2.2 Cross-sectional national-level HIV care and treatment cascade, Georgia, 2015

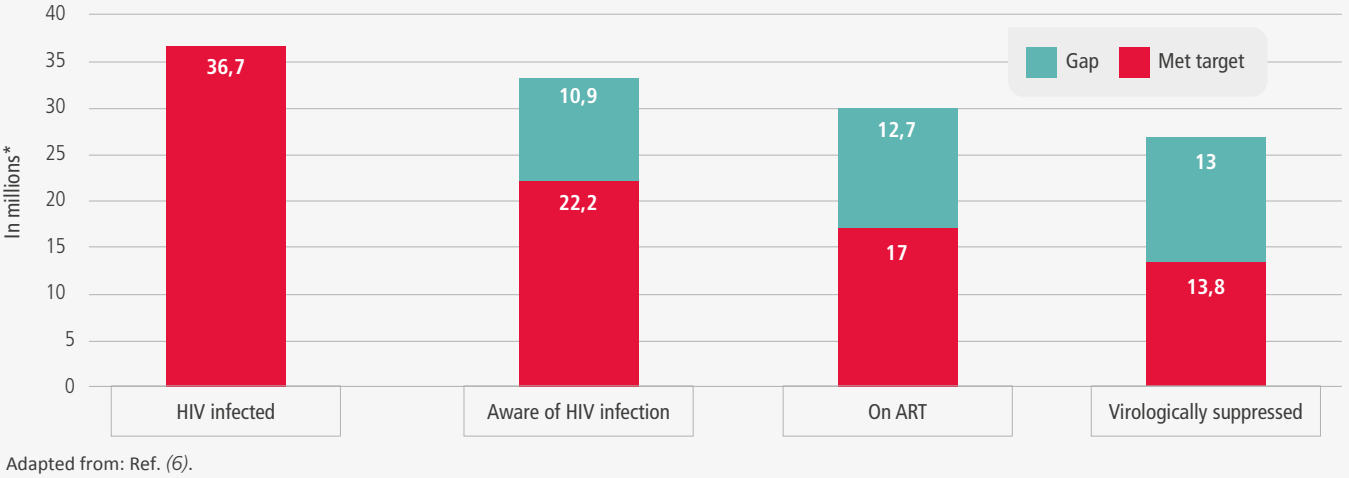


Source: Ref. *(5)*.

2.2.3 Estimated worldwide HIV care and treatment cascade, 2016

In its 2016 global report on HIV, WHO estimated a worldwide cascade from national-level data (Figure 2.3) *(6)*. Of the 36.7 million people estimated to be living with HIV at the end of 2015, 22.2 million (60%) knew that they were infected, 17.0 million (46%) had begun ART and 13.8 million (38%) had suppressed viral replication. The largest gap was in diagnosis, with 40% of PLHIV unaware that they were infected. The other gaps were smaller: 23% of those diagnosed had not been started on ART, and 19% of those that had started ART had not achieved viral suppression.

Figure 2.3 Cross-sectional HIV care and treatment cascade, Worldwide, 2015*



Adapted from: Ref. *(6)*.

3. DISAGGREGATED HIV CASCADE ANALYSIS

3.1 Cascades for subnational units

Existing HIV strategic information systems and planning of the HIV response are overwhelmingly focused at the national level. Disaggregation of surveillance and programmatic data is important for understanding which population groups and geographical areas have the greater burden of HIV and experience different access and coverage with services. HIV care cascades should, whenever possible, be disaggregated by sex, age (<1, 1-4, 5-14, 15-24 and ≥25 years), pregnancy status and geographical areas *(1)*.

Understanding variations in HIV service coverage by subpopulations is important for improving the effectiveness of the HIV response. Information on age and pregnancy status is usually collected in ART registries and HIV patient monitoring systems, but information on risk categories is typically not available from routine monitoring systems.

Subnational units can include regions, provinces, health district catchment areas and even individual clinics. Comparing cascade performance between various regions or even clinics can help identify better performers and worse performers. Interventions can then be implemented to improve the quality of service (e.g. where there are large gaps in the proportion of people diagnosed with HIV who begin ART).

3.2 Cascades for key populations

KPs include female sex workers, people who inject drugs (PWID), MSM, transgender people and people living in prisons or other closed settings (Table 3.1) *(2)*. Many factors – including criminalization, stigma, discrimination, lack of treatment literacy and awareness – can limit KP access to HIV testing, treatment and care services. Constructing separate cascades for KP groups is crucial in understanding progress towards achieving the 90-90-90 targets. General population data often mask different results within smaller subgroups of KPs, and successful control of transmission in the general population may be undermined by lack of progress in improving KPs' access to prevention and care. In addition KPs can often have problems with retention.

3.2.1 Defining the scope of KP cascade analysis.

It is important to define the population that will be included in the cascade analysis. For instance, will the cascade analysis consider all MSM, or only those engaging in higher-risk behaviours? How will "high risk" be defined? What time period will be used? In many settings, programmes and services already define which populations they are trying to reach, and these definitions can be used. A decision must also be made as to whether the analysis will be at facility level or at subnational or national level. National-level data are rarely disaggregated by KPs; it is often more feasible to use subnational data to monitor KPs' access along the cascade.

Table 3.1 Definitions of key populations

Key population	Definition
Men who have sex with men (MSM)	All men who engage in sexual and/or romantic relations with other men
People in prisons and other closed settings	Persons who are detained in criminal justice and prison facilities, including adult and juvenile males and females, during investigation of a crime, while awaiting trial, after conviction, before sentencing and after sentencing. This definition may be applied to persons detained because of immigration or refugee status, those without charges, and those retained for compulsory treatment in rehabilitation centres.
People who inject drugs	Persons who inject psychotropic (or psychoactive) substances for nonmedical purposes. Injection includes intravenous, intramuscular and subcutaneous routes.
Sex workers	Male, female and transgender adults (age ≥18 years) who receive money or goods in exchange for sexual services on a regular or occasional basis.
Transgender persons	Persons whose gender identity and expression does not conform to the norms and expectations traditionally associated with the sex assigned to them at birth.

Source: Ref. *(2)*.

3.2.2 Core key population cross-sectional care and treatment indicators and data sources

Indicator 1. Number of key population members living with HIV

Estimates of KP size and of the number of KP members living with HIV (KPLWH) may be available through community-based surveys or through HIV estimation models such as SPECTRUM or the Asian Epidemic Model *(3)*. However, national-level estimates can be difficult to conduct, may have large uncertainty ranges and are costly, limiting their availability and quality. In many cases, subnational or local-level data may be more readily available and of a higher quality than national estimates; moreover, consideration should be given to conducting KP cascade analysis at local level.

This indicator serves as the denominator for all subsequent indicators and should be calculated separately for each KP that will be considered in the cascade analysis.

Indicator 2. Number and percentage of key population members living with HIV who are aware of their status

Two potential data sources exist: case-based surveillance and community-based surveys.

Case-based surveillance data. As described above, the number of people reported as being members of a KP to the national case-based surveillance system, minus the number of deaths, can serve as a proxy for the number of KPLWH who are aware of their HIV status. Case report forms and systems include probable routes of transmissions (e.g. vaginal, anal or oral sex or injecting drug use), and these can be used to disaggregate surveillance data. However, these categorizations will not always match KP categories of interest. For example, these could not be used if data were to be disaggregated to better understand sex workers or transgender people. Further, people's risk behaviours may change between diagnosis and other sentinel events; someone may become infected by sharing a contaminated needle/syringe but subsequently stop injecting, thereby leaving a KP category and leading to an overestimate of PWID in the cascade analysis.

Community-based survey. Integrated bio-behavioural surveys (IBBS) include blood or saliva tests for HIV and a questionnaire. Relevant questions for this indicator include: "Have you been tested for HIV in the last X months?" and "I don't want to know the results, but did you receive the results of that test?" (i.e. participant is not asked to disclose status) or "What was the result of that test?" (i.e. participant is asked to disclose status).

If the survey does not ask participants to disclose the results of their HIV test, the calculation is as follows:

> % of KP members living with HIV and aware of status = number of seropositive participants who report having had an HIV test and having received the results in last [x] months divided by the number of seropositive participants.

If the survey asks participants to disclose the results of their HIV test, the calculation is as follows:

> % of KP members living with HIV and aware of status = number of seropositive participants who report having had a positive HIV test and receiving the results in last [x] months divided by the number of seropositive participants.

Because these surveys are often conducted in small geographical areas and often use quasi-random sampling methods, such as respondent-driven sampling, the results may not necessarily be representative of the national situation. Care must be taken in extrapolating results to larger geographical levels.

Indicator 3. Number and percentage of key population members living with HIV who are receiving HIV care (including ART)

There are three possible data sources for this indicator:

Case-based surveillance. If case-based surveillance systems collect longitudinal data on clinic care, ART initiation or laboratory test results, they can be used to estimate this indicator. In this situation, KPLWH who are reported to have been enrolled in care, initiated ART or had laboratory results recorded can be considered to be receiving HIV care.

Programme data. Pre-ART and ART programmes collect information for patient monitoring, such as clinical stage, CD4 or viral load tests, which indicate entry into care (see previous description) before someone commences ART. However, these programmes may not collect information about risk behaviour, KP category or transmission route. Reasons for this include concerns about misuse of data on criminalized behaviour collected in patient records, lack of privacy in clinical settings and lack of relevance of some information for patient monitoring. As such, it may not be possible to disaggregate programme data by KP.

Community-based survey data. IBBS data can be used to estimate the percentage of a KP that is receiving care. To calculate this indictator using community-based IBBS, the following numerator and denominator can be used:

> Numerator: Number who answer "yes" to one or more of these questions: Are you receiving ART? Have you received CD4 count results in the prior [x] months? Have you received viral load test in the last [x] months?
>
> Denominator: Number of seropositives in the sample.

All these results should be disaggregated by gender to understand coverage in different KPs.

Indicator 4. Number and percentage of key population members living with HIV in care and who are on ART

As with Indicator 3, three possible data sources exist for this indicator:

Case-based surveillance. The considerations regarding use of data from case-based surveillance described for indicators 2 and 3 also apply to indicator 4.

Programme data. Where possible, this indicator can be calculated using programme data which indicate ART initiation disaggregated by KP. However, as described above, ART programmes may not routinely collect data that would allow disaggregation by KP (such as KP category or risk behaviours) due to concerns about confidentiality, misuse of data, stigma and discrimination. Since pharmacies will not routinely collect information about KP category or risk behaviours, pharmacy data is unlikely to be helpful for calculating this this indicator.

Community-based surveys. IBBS questionnaires include questions such as "Are you currently receiving ART?" and the proportion of those seropositive who answer "yes" gives the indicator value. In some surveys, biological samples have also been used to test for the presence of ART.

As with indicator 3, all these results should be disaggregated by gender to understand coverage in different KP.

Indicator 5. Number and percentage of key population members living with HIV who are virally suppressed (<1000 copies/mL)

There are three possible data sources for this indicator:

Case-based surveillance. The considerations regarding use of data from case-based surveillance described for indicators 2 and 3 also apply to this indicator. The numerator is the number of KPLWH who are on ART and whose most recent viral load test result is <1000 copies/mL.

Programme data. As described above, patient monitoring systems may not collect information about KP category or risk behaviours. However, if available, these data can be used to disaggregate by KP.

Community-based and drug-resistance surveys. Estimates of viral load suppression rates are often available through national acquired HIV drug resistance surveillance systems or drug resistance surveys, although it is unlikely that these systems also collect data that will allow disaggregation by KP or HIV risk behaviour.

The value for this indicator can be estimated by using a special survey in which viral load testing using whole blood samples is done in a representative sample of KPLWH who have been receiving ART for 12 months (±3 months) or as part of an IBBS. It should be noted that, when using IBBS and dried blood spots, the reliable limit of quantification with dried blood spot is higher than that of plasma and thus it may be necessary to set a different "threshold" for defining viral suppression when using dried blood spot. To calculate this the formula would be: % of the KP with viral suppression 12 ±3 months after initiating treatment = number of respondents who have viral load < 1000 copies per mL (or more if using dried blood spot, see above) divided by number of respondents (HIV-infected and initiated ART 12 ±3 months ago).

As with indicator 3, all these results should be disaggregated by gender to understand coverage in different KP.

3.2.3 Core key population longitudinal care and treatment cascades

In KP longitudinal cascades, a cohort of KPLWH is followed for a period of time, usually after first HIV diagnosis. This requires a means (such as a unique identifier code) to link individual data at diagnosis with enrolment in care, ART and viral suppression. The analysis can be at national or subnational levels; in particular, this type of analysis may be useful to enable KP-led or community-based KP programmes to better understand retention and treatment outcomes for their clients. Other advantages of conducting longitudinal cascades for KPs include more accurate data with no double counting. The drawbacks of this type of analysis include the fact that data requirements may be unrealistic in many settings and the analysis may take two or more years to complete. Unique identifier codes are usually required for longitudinal cascade analysis, but consideration must be given to their acceptability for members of the KP.

It is important to consider the time frame for this analysis. If the cohort consists of all of one KP group's members diagnosed in one year, such as 1 January to 31 December 2017, the analysis must also be able to include all those enrolled in care and/or on ART a year after diagnosis (i.e. up to December 2018) and all those who achieved viral suppression within 1 year of initiating ART (i.e. up to December 2019) (Table 3.2).

Table 3.2 Time frames for outcomes in longitudinal cohort studies

Diagnosed	1 January 2017 – 31 December 2017
Enter care within 1 year after diagnoses	1 January 2017 – 31 December 2018
Initiate ART within 1 year after diagnosis	1 January 2017 – 31 December 2018
Virally suppressed within 12 months after initiating ART	1 January 2017 – 31 December 2019

Indicator 1. Number of key populations newly diagnosed in one calendar year

The value for this indicator forms the denominator for subsequent ones. There are two possible data sources for this indicator:

Case-based surveillance. Case-based surveillance data can be used for this indicator. As described above, HIV case-reporting usually includes details of probable route of transmission, such as injecting drug use, heterosexual sex or homosexual sex but does not allow disaggregation of data for transgendered persons, female sex workers or prisoners. It is also important to note that the route of transmission may not always indicate that someone is a member of a particular KP of interest; for instance, a person may have been exposed to HIV through a contaminated needle or syringe, but this does not necessarily mean that the person regularly injects drugs. However, for MSM and PWID, the probable route of transmission can be used as a proxy for KP category.

Programme data. Services or programmes operated by community groups or NGOs often serve one or more KP groups, providing on-site prevention and testing services but referring clients onwards for treatment and care. For these smaller programmes or services, longitudinal cascade analysis at service level can be a good way to monitor and evaluate the service's success in linking newly diagnosed KPLWH to treatment and care services and supporting them to remain in treatment. For this indicator, smaller services would need to be collecting data which allows disaggregation by KP group and would also need to record the date of positive diagnosis. To the extent that these data can be aggregated regionally or nationally, a regional or national estimate of the number of people newly diagnosed by KP group can be constructed.

Indicator 2. Number and percentage of key populations members newly diagnosed with HIV in one calendar year who entered care within 12 month of diagnosis

The second indicator is the number and proportion of KPLWH who enter care within 12 months of diagnosis by KP status. There are three possible data sources for this indicator:

Case-based surveillance. Case-based surveillance reports can be used to estimate this indicator if they provide a date of first being seen at an HIV care facility. Where ART is initiated as close to diagnosis as possible, the date of ART initiation can serve as a proxy for this indicator. These data may be obtained from ART registers as well as from a case-based reporting system.

Programme data. If clinical records contain the date of HIV diagnosis and the date of first clinic visit after diagnosis (or ART initiation), these records can be used to calculate this variable. Smaller programmes or services providing prevention and/or HIV testing and counselling services to one or more KP groups may wish to conduct a service-level longitudinal cascade analysis. To calculate this indicator, there would need to be a way to link individual data about clients who were diagnosed with HIV in the specified time period and those who received care within 12 months of diagnosis. In most situations, care will be provided at a different site. There are several ways to link the data – such as sharing unique identifier codes between services or linking client databases using individual identification data such as name or date of birth. Evidence of entry into care includes clinical staging, CD4 or viral load test result.

Laboratory data. In some situations, the first recorded laboratory test after diagnosis can be used as a proxy for first visit. This is especially true for countries where ART eligibility is still based on CD4 count and clinical criteria. These data will have to be directly linked with clinical records in order to construct this indicator.

Indicator 3. Number and percentage of key population members newly diagnosed with HIV in one calendar year who initiated ART within 12 months of diagnosis

This indicator measures the coverage of ART within one year of diagnosis. In countries where all patients with diagnosed HIV infection initiate ART, this indicator may be used in place of indicator 2. In countries that do not yet have universal ART, it is a marker of how long PLHIV are waiting until they begin ART. There are two possible data sources for this indicator:

Case-based surveillance data. To be used for this variable, start dates of ART will need to be reported to the national case-based surveillance system or matched to case data from ART registries using unique identifiers.

Programme data. To the extent that national ART registries contain date of HIV diagnosis, they can be used to estimate this indicator. Smaller programmes or services could include this indicator in a facility-level cascade analysis for a KP. This would require a unique identifier code shared or linked between the diagnostic services and treatment programmes.

Indicator 4. Number and percentage of key population members newly diagnosed with HIV in one calendar year who were virally suppressed within 12 months of initiating ART

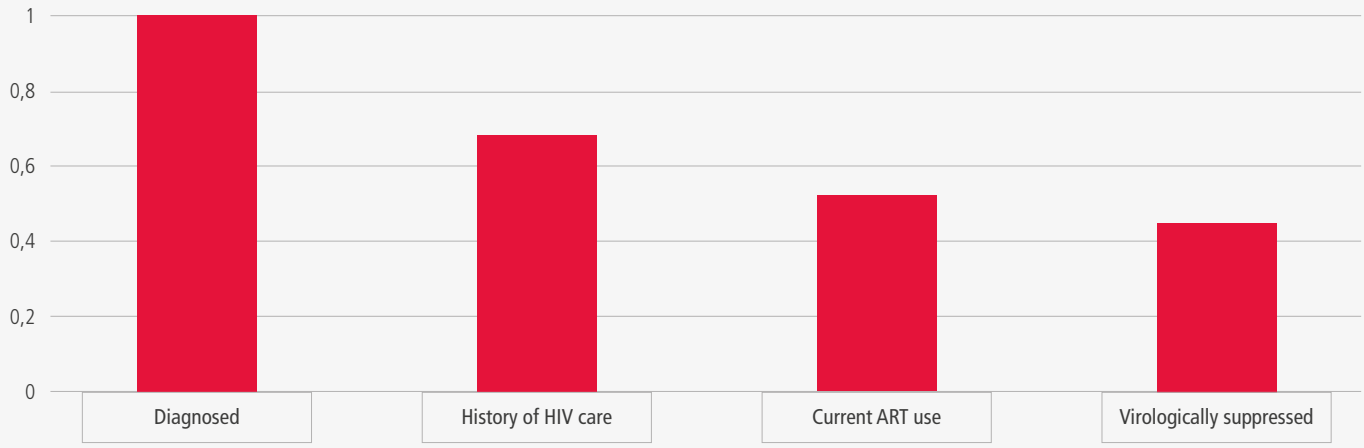
This indicator is used to judge problems in initiating ART, early problems with adherence leading to virological failure and, less commonly, primary ART resistance. In longitudinal analysis, the number and proportion of PLHIV who initiated ART within a given time period are followed for one year and the proportion that is virologically suppressed is measured (plasma viral load <1000 copies/mL). Virological suppression should be measured only in settings in which viral load testing is conducted as part of routine patient monitoring. In settings where viral load testing is done primarily to document the need to change the ART regimen, the proportion of patients who are virologically suppressed will be underestimated. There are two possible sources of these data:

Case-based surveillance data. Case-based surveillance data may be used if they capture viral loads or if they can match to central laboratory data using unique identifiers.

Programme data. This indicator can also be ascertained from medical records, and this is likely to be the simplest way to obtain these data for facility-level cascades.

3.3 Example of a key population cascade

Figure 3.1 HIV care cascade, female sex workers, Lilongwe, Malawi, 2014 (N=138)



Adapted from: Ref. *(4)*.

An example of a cross-sectional care cascade for a KP is shown in Figure 3.1. This cascade focused on care and treatment of female sex workers in Lilongwe, Malawi *(4)*. A venue-based survey of 200 female sex workers was conducted from July to September 2014. Participants were tested for HIV antibody using point-of-care tests, and those who were found to be positive were tested for CD4 counts and viral loads. Participants self-reported if they had ever been in care and if they were currently on ART. The overall seroprevalence was 69%. Of these, 69% had a history of HIV care, 52% reported current ART use and 45% had achieved virological suppression.

4. PREVENTION, CARE AND TREATMENT CASCADE FOR PREVENTION OF MOTHER-TO-CHILD TRANSMISSION

A number of strategies exist for PMTCT. Historically these have included antiretroviral prophylaxis of the mother and baby, antiretroviral therapy of mother and prophylaxis of baby, caesarean section and avoidance of breast-milk *(1)*. WHO now recommends that all HIV-infected pregnant or breastfeeding women who are not already on ART should begin ART for life *(2)*. Additionally, newborn infants whose mothers are receiving ART and are breastfeeding should receive 6 weeks of daily nevirapine (NVP). If they are receiving replacement feeding, they should be given 4-6 weeks of infant prophylaxis with daily NVP (or twice-daily zidovudine [AZT]). HIV-exposed infants should be tested for HIV infection at 4-6 weeks of age using an HIV virological test and at 9 months of age and at 3 months after breastfeeding cessation using an HIV antibody test *(2)*. Breastfed infants who are at high risk of acquiring HIV[7] should receive prophylaxis with AZT (twice daily) and NVP (once daily) for the first 6 weeks of life, whether they are breastfed or formula-fed. Breastfed infants who are at high risk of acquiring HIV, including those first identified as having been exposed to HIV during the postpartum period, should continue infant prophylaxis for an additional 6 weeks (for a total of 12 weeks of infant prophylaxis) using either AZT (twice daily) plus NVP (once daily) or NVP alone. WHO also recommends that all pregnant women should be screened for HIV at the first antenatal care visit and, in high-prevalence settings (>1%), should be retested in the third trimester, postpartum and/or during labour in accordance with national guidelines *(3)*.

The PMTCT cascade involves prevention, care and treatment of two people – the mother and the child – and is probably best visualized as a two longitudinal cascades. All pregnant women who have not previously been diagnosed with HIV infection need to be screened. While this is not part of a cascade per se, WHO recommends that HIV testing be considered for all pregnant women in all settings to ensure that appropriate measures can be taken to prevent vertical transmission of HIV to the child. PMTCT cascade indicators are shown in Box 4.1.

The number of pregnant women living with HIV infection forms the first column of the PMTCT cascade. The cascade then continues through the number of mothers who are on ART (both those already on ART and those newly started on ART).

Then the focus switches to the newborn infant. The next column is the number of infants born to women living with HIV (HIV-exposed infants). By limiting this number to live births the cascade removes losses due to spontaneous abortions, stillbirths and captures multiple gestations. This value will likely be larger than the previous column as not all women living with HIV will have received ARVs. The next column is the number of HIV-exposed infants who receive antiretroviral prophylaxis, which is followed by the number of HIV-exposed infants who are evaluated for HIV.

Box 4.1 Prevention, care and treatment indicators for mother-to-child transmission of HIV

- Number of pregnant women living with HIV.
- Number and proportion of HIV-infected pregnant women attending at least 1 antenatal care visit.
- Number and proportion of HIV-infected pregnant women receiving ART.
- Number of live-birth infants born to HIV-infected women. (For a cross sectional, population-level cascade this value will be higher than the value in the previous bar as not all women living with HIV will have received ART.)
- Number and proportion of HIV-exposed infants receiving antiretroviral prophylaxis.
- Number and proportion of HIV-exposed infants evaluated for HIV infection using an HIV DNA test by 2 months of age.
- Number and proportion of HIV-exposed infants that test negative by 2 months of age.
- Number and proportion of HIV-exposed infants tested for HIV after breastfeeding cessation.
- Number and proportion of HIV-exposed infants that test HIV-negative after breastfeeding cessation.

[7] High-risk infants are defined as those who were: 1) born to women with established HIV infection who have received less than 4 weeks of ART at the time of delivery, or 2) born to women with established HIV infection with viral load >1000 copies/mL in the four weeks before delivery, if viral load measurement is available, or 3) born to women with incident HIV infection during pregnancy or breastfeeding, or 4) identified for the first time during the postpartum period, with or without a negative HIV test prenatally.

Infection at 6 to 8 weeks and found negative. The final column is the number of uninfected HIV-exposed children after breastfeeding cessation. It is critical that programmes follow mothers and children until after breastfeeding – i.e. after the period of important risk of exposure to HIV infection through breastfeeding. All pregnant women and children found to have HIV infection should be started on ART and analysed in care and treatment cascades, as described in section 4.2. As discussed in Section 1, because the endpoint of the PMTCT cascade is uninfected children after the period of risk (post-breastfeeding), it is critical to include infected children, including infants, in HIV care and treatment cascades.

A generic PMTCT cascade is shown in Figure 4.1.

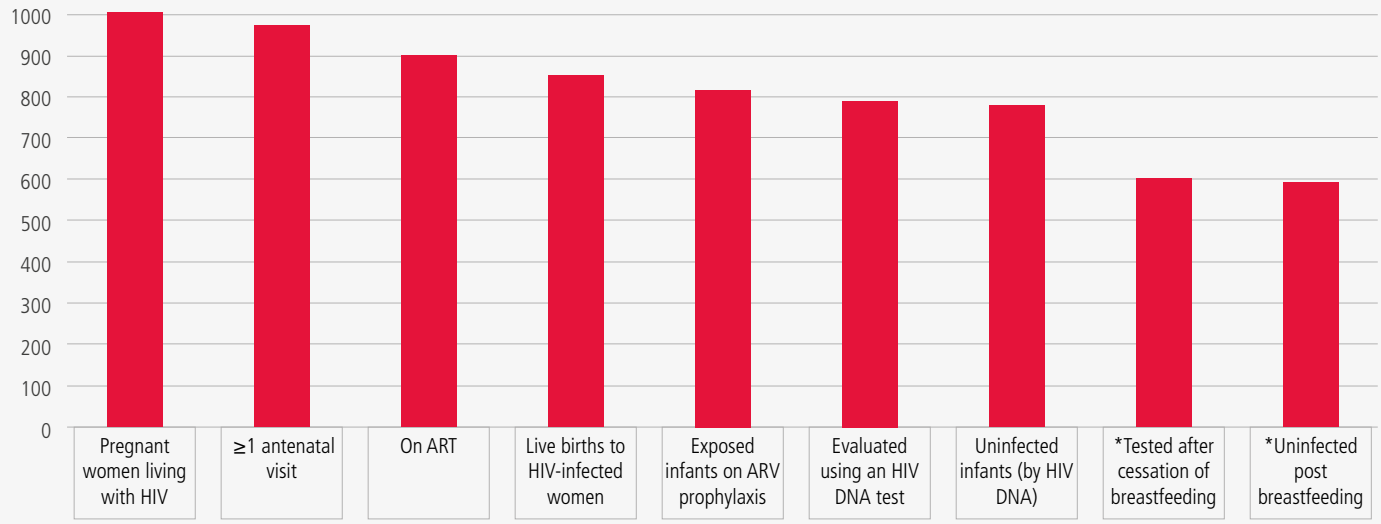
4.1 Core indicators and data sources

The sources used for the PMTCT cascade will depend on whether you are creating a longitudinal or cross sectional cascade.

Indicator 1. Number of pregnant women living with HIV infection

This includes all women who are infected with HIV and are pregnant. It includes those who were diagnosed with HIV before pregnancy, those diagnosed during the current pregnancy and those who are undiagnosed. To get a population-level estimate, including women who are undiagnosed this number would come from modelled estimate such as Spectrum. Spectrum estimates the number of births to women living with HIV so the value will not include women who have miscarried late in the pregnancy. Both Spectrum and programmatic data will exclude women who have miscarried early in their pregnancy Alternatively a programme cascade can be developed and this first number can be obtained from special studies of pregnant women in care at facilities, or regional or national estimates may be possible (e.g. by sampling antenatal care facilities and multiplying the prevalence by the number of births in the country). The number may also be estimated from national seroprevalence studies (women found to be HIV-infected and pregnant). Only thesite level data are useful for creating a longitudinal cascade.

Figure 4.1 Generic longitudinal prevention of mother-to-child transmission cascade



ART: antiretroviral therapy; ARV: antiretroviral.
*Optional indicator

The number of HIV-infected pregnant women should also be added to national and regional estimates and analysed in care and treatment cascades.

Indicator 2. Number and proportion of HIV-infected pregnant women attending at least one antenatal visit

This indicator reflects how completely the estimated number and proportion of HIV-infected women access antenatal care. This number will probably need to be estimated but, in areas where electronic health records are available, it may be possible to count it directly. The unit of measurement for the indicator is pregnant HIV-infected women and not the number of visits. For the proportion, the numerator is the number of HIV-infected women who attended at least one antenatal care visit, and the denominator is the estimated number of pregnant HIV-infected women, both those previously diagnosed and those diagnosed during the current pregnancy. This value could also be calculated from household surveys using the indicator "proportion of women with a birth in the past three years who had at least one ANC visit" and disaggregating the indicator by HIV status.

Indicator 3. Number and proportion of pregnant women with HIV infection who are on ART

This indicator refers specifically to women who are receiving effective antiretroviral medicines.[8] Most countries report these data from facilities to the national level. Another potential source is national ART registries, but they will have to include pregnancy status as a specific variable.

Indicator 4. Number of live births to women living with HIV and receiving ART

This indicator will be larger than the number of women receiving ARVs and thus should be separated from the previous column either by a line or by changing the colors of the bar. Because not every HIV-infected woman has one live-born infant, this indicator recalibrates the denominator for the remainder of the cascade and creates a new unit of analysis – i.e. the number of live-born HIV-exposed infants. It should exclude women living with HIV on ART who have had spontaneous or therapeutic abortions or stillbirths. It should include additional infants who are products of multiple gestations (e.g. the second twin). These values could come from modelled estimates or they can be calculated from data obtained from antenatal care facilities, which will record spontaneous and therapeutic abortions, and from facilities that provide obstetrical care that will record stillbirths and multiple gestations. Again, if regional or national samples of facilities are available, this number may be estimated at levels above that of the facility.

Indicator 5. Number and proportion of HIV-exposed newborn infants on antiretroviral prophylaxis

Every infant born to a woman with known HIV infection who is being breastfed should receive antiretroviral prophylaxis with 6 weeks of daily NVP. If they are receiving replacement feeding, these infants should be given 4-6 weeks of infant prophylaxis with daily NVP (or twice-daily AZT whether or not their mothers are on ART *(2)* or are otherwise at high risk for transmission).[9] The number of infants receiving antiretroviral prophylaxis will need to come from facilities that provide obstetrical care and can link an infected mother to an HIV-exposed infant. National ART registries may be used to estimate this if ages or dates of birth are recorded. The denominator for this indicator is the number of HIV-infected pregnancies that lead to live-born children.

Indicator 6. Number and proportion of HIV-exposed infants who are tested for HIV infection

WHO recommends that every HIV-exposed infant should be tested for HIV infection at between 6 and 10 weeks using an HIV virological test *(2)*. For a longitudinal analysis this number is best determined through a cohort analysis of HIV-exposed infants. For cross-sectional analysis this indicator is usually reported from facilities to the national level in a health information system or routine reporting forms. As testing is usually centralized in large regional or national laboratories, an estimate may also be generated from laboratory-based surveillance. Note that the number of infants testing positive is being measured rather than the number of positive tests. If expressed as a proportion, this indicator uses the same denominator as indicator 4, all HIV exposed children. Because maternal-child HIV transmission can occur through breastfeeding even among women on ART, albeit at low rates *(4)*, WHO also recommends that children be retested for HIV infection using an antibody test 3 months after they complete breastfeeding or at 18 months of age. For purposes of constructing a PMTCT cascade, however, both early infant diagnosis at 6-8 weeks of age and post-breastfeeding diagnosis are included. Programmes should follow up infants to the post-breastfeeding period to report a final outcome.

Indicator 7. Number and proportion of 2-month-old HIV-exposed infants that are uninfected

This indicator is the number of HIV-exposed infants found to be uninfected by HIV virological testing. If calculating a proportion, the denominator for this could be either the number of live-born HIV-exposed infants or the number of HIV-exposed infants who are tested at 6-8 weeks of age using an HIV virological test. Infants that are determined to be infected should enter the national or regional care and treatment cascade.

[8] In earlier WHO recommendations, this was referred to as Option B plus, as opposed to Option B (short-course three-drug antiretroviral prophylaxis through the completion of breastfeeding) or Option A (earlier forms of one- and two-drug therapy during pregnancy and the immediate postpartum period).

[9] Breastfed infants whose mothers are not on ART should receive 12 weeks of prophylaxis.

Indicator 8. Number and proportion of HIV-exposed infants tested for HIV after breastfeeding cessation

WHO also recommends that infants who are breastfed should be retested 3 months after the cessation of breastfeeding using an HIV antibody test. This number can come either from PMTCT programme data or potentially from laboratory-based reporting. If calculating a cascade, the denominator can be either the number of live-born HIV-exposed infants or the number of HIV-exposed infants who tested negative using an HIV virological test. It may be difficult to separate antibody test results from all other tests in children tested for this indication. For this reason, this indicator may be considered optional.

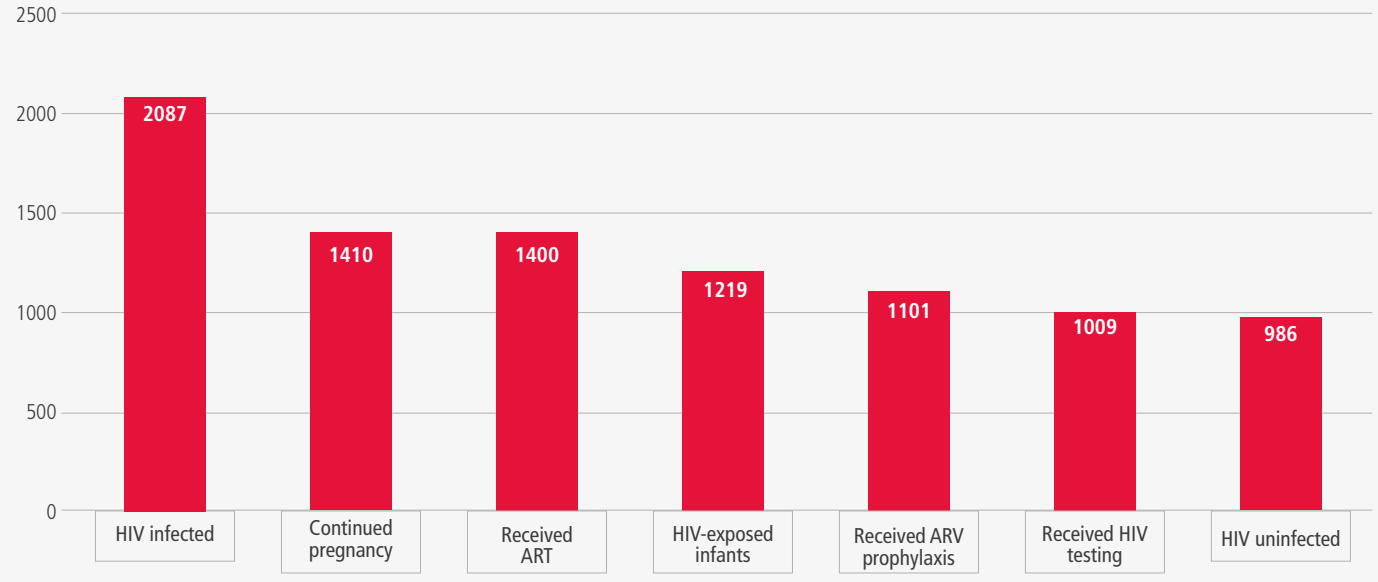
Indicator 9. Number and proportion of HIV-exposed infants who test HIV-negative after breastfeeding cessation

The final column is the number of HIV-exposed infants who test HIV-negative after breastfeeding is completed. This represents the prevention outcome – i.e. the number of HIV-exposed infants who were not infected. WHO recommends that testing should occur 3 months after cessation of breastfeeding but national programmes may recommend different timing. If calculating a cascade, the denominator should be the number of live-born HIV-exposed infants or the number of HIV-exposed infants tested after cessation of breastfeeding. Given difficulties with identifying laboratory results as with indicator 8, this indicator may also be considered optional.

The cascades described here are primarily focused on women that enter into the PMTCT programme. It is also critical to get information on women who are not in the health care setting and thus it is important to also estimate population-level cascades. Finally women who become infected with HIV during the breastfeeding period are missed altogether in these cascades so while the programme might appear strong based on the PMTCT cascade, if efforts are not made to protect women and their children during breastfeeding transmission rates will remain high.

4.2 Examples of prevention, care and treatment cascades for maternal-child transmission

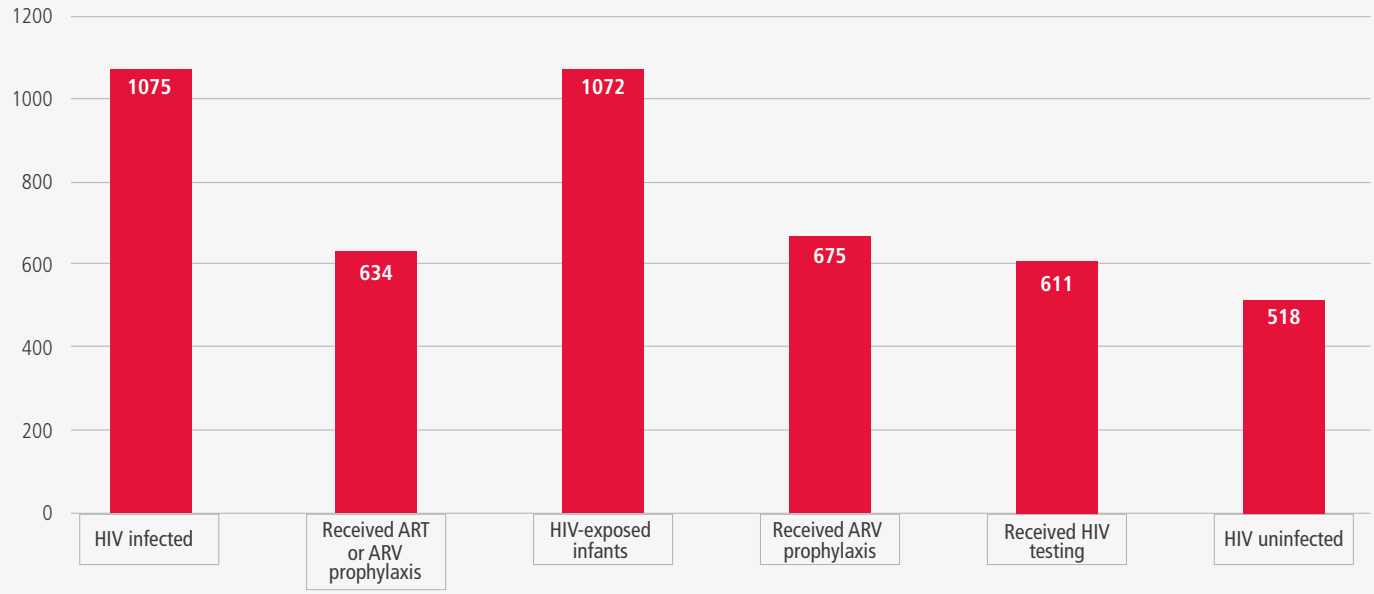
Figure 4.2 Prevention of mother-to-child transmission longitudinal cascade, China, 2011



ART: antiretroviral therapy; ARV: antiretroviral.
Adapted from: Ref. *(5)*.

Zeng and colleagues reviewed 114 published reports regarding the PMTCT cascade in China, covering the period 2002-2011 *(5)*. By 2011, the Chinese guidelines called for triple- or quadruple-drug ART beginning at 14 weeks of gestation with AZT and lamivudine twice daily during labour and 7 days of NVP postpartum. For HIV-exposed infants, the guidelines called for AZT and NVP four times daily until 6 weeks of age *(6)*. They estimated that 90.3% of pregnant women who had been seen in antenatal clinics had been tested for HIV in 2011. Of the 2087 found to be HIV-infected, 1410 (67.9%) elected to continue their pregnancy; 1209 (86.2%) of these women received ART or antiretroviral prophylaxis during pregnancy or delivery. They gave birth to 1219 HIV-exposed infants, of whom 1101 (90.3%) received antiretroviral prophylaxis, and 1009 (82.8%) had been retained in care and tested for HIV by 18 months of age. Twenty-three infants were diagnosed with HIV infection, leaving 986 (80.8% of live-born HIV-exposed infants or 97.7% of tested infants) who were uninfected. The estimated transmission rates for those not seen in antenatal care, or seen in antenatal care but not tested, were substantially higher (31.6% and 31.9%, respectively). Including estimates of HIV infections in infants born to mothers who did not attend antenatal care, those who were not tested for HIV, those who discontinued antenatal care and those who did not have their infants tested for HIV, the overall transmission rate was 11.7%. This cascade is shown in Figure 4.2. Two things are of particular note. Firstly, a large proportion (32.4%) of women elected not to continue their pregnancies, necessitating another step in the cascade. Secondly, the authors estimated that 187 (89.0%) of the 210 HIV-infected infants born in China in 2011 had dropped out of care at some point along the cascade. These data offer a clear example of the need to keep women and infants in care to achieve the full benefits of PMTCT.

Figure 4.3 Prevention of mother-to-child transmission longitudinal cascade, Zimbabwe, 2012



Adapted from: Ref. *(7)*.

A second example comes from Zimbabwe *(7)*. Zambia began an accelerated national PMTCT Programme in 2010, based on WHO's 2010 guidelines *(8)*. These guidelines called for Option A, which recommended that all eligible (i.e. CD4 ≤350 or WHO clinical stage 3-4) HIV-infected pregnant women should initiate lifelong ART and that HIV-infected women not eligible for ART and their exposed infants should receive antiretroviral prophylaxis in the prenatal and perinatal periods and during breastfeeding. In 2012, 8800 women were identified in a sample of 157 clinics from five provinces; 94% attended antenatal clinic at least once, and 92% knew their HIV status during pregnancy. Of these, 1075 women (12%) were found to be infected, and 59% of them reported receiving ART or antiretroviral prophylaxis. These 1075 women had 1072 live-born babies. Of these HIV-exposed infants, 63% received antiretroviral prophylaxis, and 57% were tested for HIV; of those tested, 93 (15.2%) were infected with HIV (Figure 4.3). This cascade suggests both the need for improvements in the proportion of women seen in antenatal clinics and diagnosed with HIV infection who are offered ART and a similar need for improvement in the proportion of infants who receive antiretroviral prophylaxis and are tested for HIV.

5. CARE AND TREATMENT CASCADES FOR HIV CO-MORBIDITIES

5.1 HIV-hepatitis B virus co-infection

HBV is transmitted through contact with contaminated blood, blood products or equipment used in or outside of medical settings. It is also transmitted sexually, perinatally and, unlike HIV or HCV, horizontally. Perinatal transmission of HBV is especially prevalent in sub-Saharan Africa and East Asia. Co-infection with HIV is common. It is estimated that between 5% and 15% of PLHIV worldwide have chronic HBV infection (1-4). In countries where HBV is predominantly acquired either perinatally or horizontally in childhood, the prevalence of infection among PLHIV is the same as it is in the general population. In countries with more concentrated epidemics and lower HBV prevalence (<2%), HBV infection is typically acquired later, either sexually or parenterally, and is higher than in the general population *(5)*. PLHIV who are co-infected with chronic HBV infection progress more rapidly to cirrhosis and hepatocellular carcinoma, have higher hepatic-related morbidity and are less easily treated than people with chronic HBV infection who do not also have HIV *(6)*. WHO (LINK 2.7) and UNAIDS (Global AIDS monitoring indicator 10.6) recommend that all persons with HIV should be screened for chronic HBV infection and have an indicator to measure the completeness of screening *(7,8)*. Those who are positive for the hepatitis B surface antigen (HBsAg) should be further evaluated and, if eligible for anti-HBV treatment and such treatment is available, should be offered curative HBV treatment *(6,8)*. Therapy for chronic HBV infection typically consists of nucleoside or nucleotide analogues, and WHO currently recommends initial therapy with either tenofovir or entecavir.

The HIV-HBV co-infection cascade should be measured longitudinally, starting with the number of people with diagnosed HIV-HBV co-infection who are eligible for treatment. Because of the eligibility criterion, which must be determined clinically, cross-sectional cascades are less useful. The indicators are shown in Box 5.1. As with other care and treatment cascades, the HIV-HBV cascade can be disaggregated by geography (e.g. at the clinic level) or by population (e.g. among MSM).

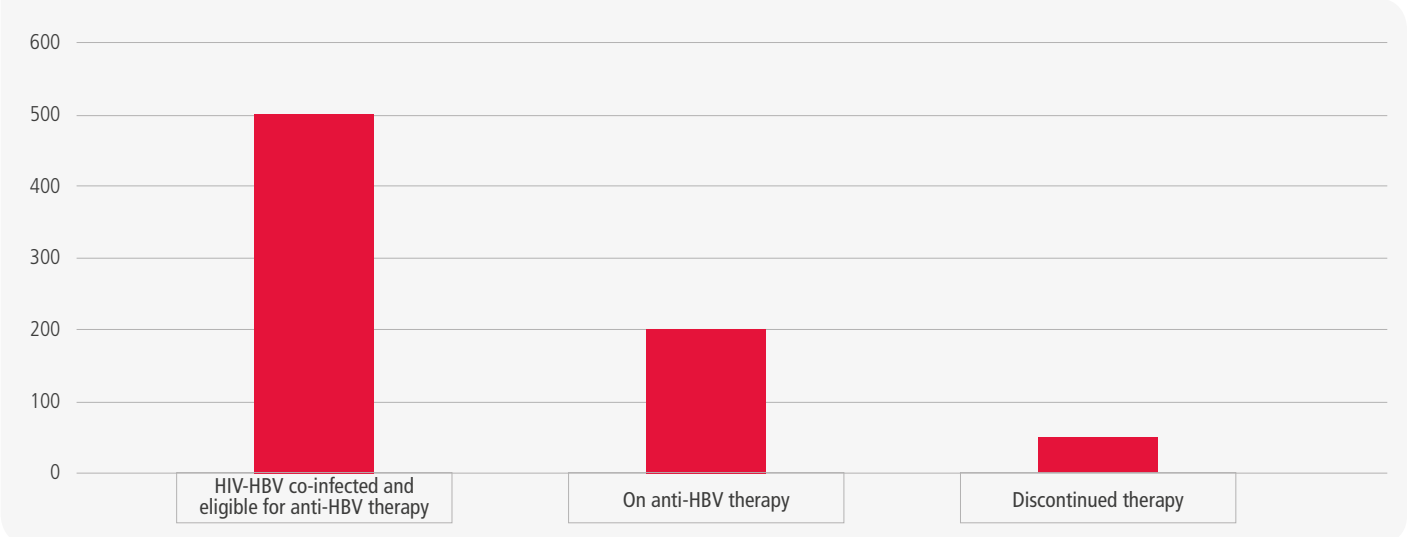
Box 5.1 HIV-HBV co-infected care and treatment cascade indicators

- Number, and percentage of number, of HIV-HBV co-infected people who have been diagnosed with co-infection and are eligible for anti-HBV therapy.
- Number, and percentage of number, of HIV-HBV co-infected people who are on anti-HBV therapy (treatment coverage).
- Number, and percentage of number, of HIV-HBV co-infected people who have discontinued therapy for chronic HBV infection (treatment effectiveness).

All PLHIV should be screened for chronic HBV infection using the HBsAg test. PLHIV who are HBsAg-positive are defined as chronically infected with hepatitis B and require additional evaluation to determine eligibility for treatment. The number and proportion of PLHIV that have been screened for HBsAg is not part of the cascade but is an important care indicator *(6)* and should can be used to define the estimated number of people with co-infection.

A generic HIV-HBV cascade is shown in Figure 5.1.

Figure 5.1 Generic HIV-HBV treatment cascade



5.1.1 Core indicators and data sources

Indicator 1. Number of HIV-HBV co-infected people who are eligible for anti-HBV therapy

The number of people who are co-infected will most likely be estimated from national surveys or by extrapolating cohort-based data to the national level. For instance, if the prevalence of chronic HBV infection in a highly-screened population of PLHIV is 5.1%, then that number could be used to construct a national estimate by multiplying the estimated number of PLHIV by 0.051. If more than one data source is available, national programmes could use the median of the different prevalence measurements to estimate a national prevalence. In some countries, HBsAg positivity may be reportable on HIV case-based surveillance forms and could potentially be used to estimate the national prevalence of co-infection.

Eligibility for anti-HBV therapy depends on a number of factors. In general, all patients with chronic HBV infection and clinical evidence of compensated or decompensated cirrhosis should be treated. Adults >30 years of age who do not have clinical evidence of cirrhosis (aspartate aminotransferase-to-platelet ratio index [APRI] score ≤2) but who have persistently abnormal alanine aminotransferase (ALT) levels and evidence of high-level HBV replication (HBV DNA >20 000 IU/mL regardless of hepatitis B e antigen [HBeAg]) status should also be treated *(5)*. In one community-based study, conducted in the United States of America among persons who had immigrated from Viet Nam, 13% of those with chronic hepatitis B were eligible for treatment *(9)*.

Indicator 2. Number and proportion on anti-HBV therapy

The number of people with co-infection who have received or are receiving anti-HBV therapy can be estimated by chart reviews of cohorts of patients with known co-infection. This is the equivalent of Global AIDS Monitoring indicator 10.7 *(8)* and corresponds to treatment coverage *(10)*. For both cross-sectional and longitudinal analysis, patients who have been successfully treated, as well as those currently on treatment for chronic HBV infection, should be counted. In some countries, where drugs specific to the treatment of chronic HBV infection, such as entecavir, are centrally controlled by the Ministry of Health, surveys of clinics that have received these drugs may be helpful in understanding which patients are co-infected with HIV and which are not. However, since WHO recommends starting antiviral treatment for HBV with either tenofovir or entecavir, and as tenofovir is also used extensively as first-line therapy for HIV infection, surveys of entecavir dispensing will not provide complete information on HBV treatment but may provide information on the centres that are treating chronic HBV infection.

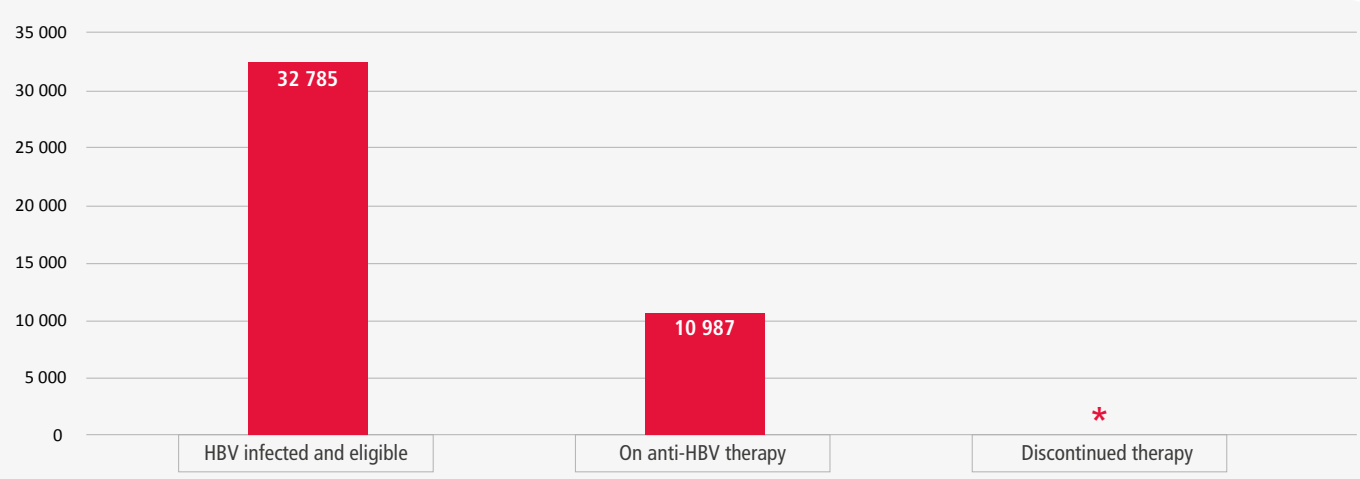
Indicator 3. Number and proportion discontinuing therapy

The number of people with HIV-HBV co-infection who have discontinued antiviral therapy because of prolonged HBV suppression can be estimated either from chart reviews of patients who have received anti-HBV therapy or from national pharmaceutical surveillance of patients who started and stopped entecavir therapy. This corresponds to treatment effectiveness *(10)*. Only a subset of patients (those with APRI scores ≤2) can be considered for discontinuation; those with APRI scores >2 should continue antiviral therapy for life. Other criteria that WHO suggests for discontinuing anti-HBV therapy are loss of HBeAg and seroconversion to anti-HBe (among persons initially HBeAg-positive), persistently normal ALT levels and persistently undetectable HBV DNA levels for at least one year.

5.1.2 Examples of HIV-HBV co-infection cascades.

There are few examples of cascades for HIV-HBV co-infection. Liou & Nguyen *(11)* reviewed treatment cascades for HBV mono-infection and suggested that there was a major gap between the number of people with diagnosed chronic HBV infection and the number who were evaluated and received therapy. In 15 studies that they reviewed, the median proportion of eligible patients who received antiviral therapy was 50.4%.

Figure 5.2 HBV care and treatment continuum, Australia, 2012



*Number who discontinued therapy not reported
Adapted from: Ref. *(12)*.

A study of HBV (with and without HIV co-infection) from Australia is illustrative (Figure 5.2) *(12)*. An estimated 218 567 persons are living with chronic HIBV infection in Australia. Of these, 32 785 (15.0%) are estimated to be eligible for treatment; 10 987 (33.5%) are on treatment. Neither the number that discontinued therapy nor the number with non-detectable HIV DNA was reported.

5.2 HIV-hepatitis C virus co-infection

HCV is transmitted primarily through contact with contaminated blood, blood products or injection equipment used in or outside of medical settings. However, infrequent sexual transmission of HCV has been reported, primarily among MSM, as has rare perinatal transmission. The shared transmission routes place persons with HIV infection at higher risk for HCV than the general population. PLHIV who have HCV infection are at higher risk for hepatitis fibrosis and hepatic decompensation, even if their HIV infection has been controlled *(13,14)*. However, PLHIV appear to have high responses to therapy with direct-acting antiviral drugs (DAA) similar to those in persons with HCV mono-infection *(13,14)*. WHO (LINK.28) and UNAIDS (Global AIDS monitoring indicator 10.8) recommend that all persons with HIV should be screened for HCV infection and that there should be an indicator to measure the completeness of screening *(8,15)*. If treatment is available, patients with HIV-HCV co-infection should be assessed for eligibility and offered curative HCV treatment *(16)*. Newer forms of treatment using DAAs are as short as 8 weeks and result in cure rates higher than 90%. WHO recommends that persons who are seropositive for HCV should be further evaluated using a nucleic acid test (NAT) for HCV ribonucleic acid (RNA) and that those who are NAT-negative should be excluded from further consideration because they have spontaneously cleared their infection. This is particularly important in patients with HIV-HCV co-infection because of the risk of false-negative HCV serological test results which may occur in up to 6% using a second-generation anti-HCV enzyme immunoassay *(17,18)*. The risk of false-negative HCV serological results appears to occur more commonly among PLHIV with advanced immunosuppression and during early HCV infection *(19,20)*. Additional baseline evaluation should include an assessment of liver fibrosis, using either the aspartate aminotransferase-to-platelet ratio index (ARPI) or the fibrosis-4 (FIB-4) score when biopsy or other more resource-intense tests such as elastography and genotyping as different HCV genotypes require different DAA regimens *(16)*.

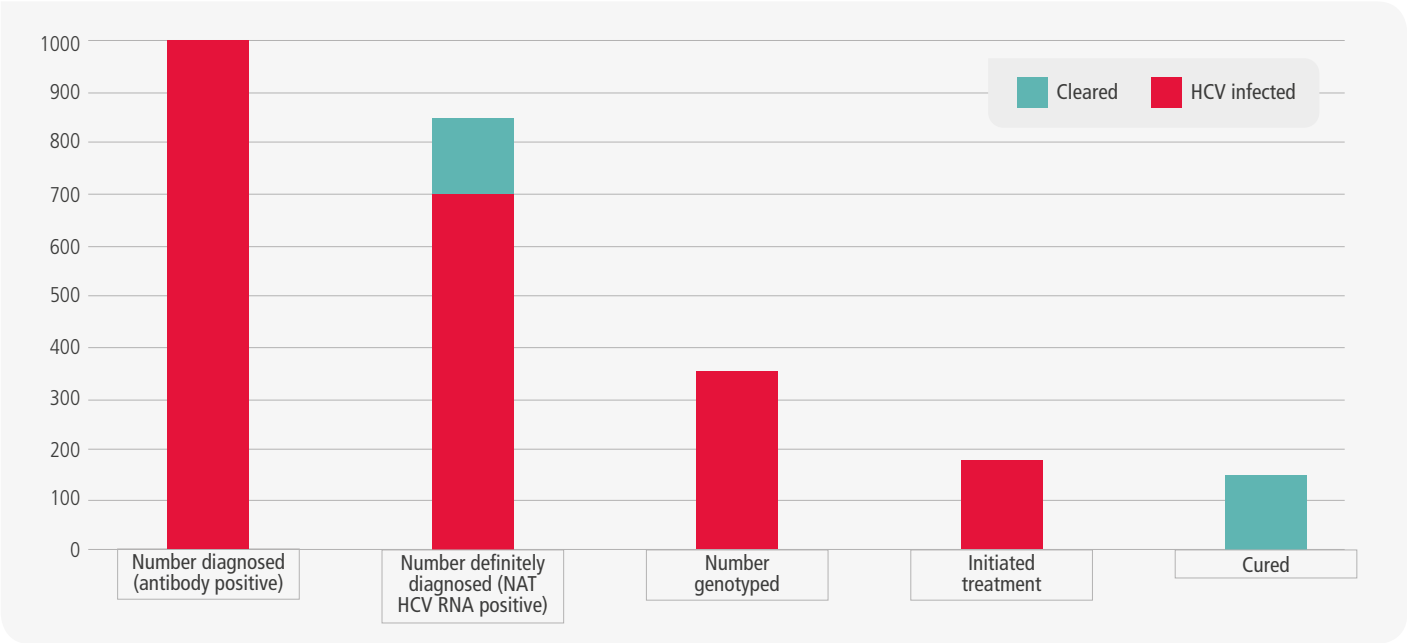
The cascade indicators for HIV-HCV co-infection are somewhat more complex than those in the HIV-HBV care cascade because of simplified eligibility criteria, the possibility of spontaneous remission in 15-45% of patients *(21,22)*, and the very strong possibility of a cure (as measured by sustained virological response]). The HIV-HCV co-infection cascade should be measured longitudinally, starting with the number of people with diagnosed HIV-HCV co-infection and then following with the number that are eligible for treatment, as defined by a positive NAT for HCV RNA. Because of this eligibility criterion, which must be determined clinically, cross-sectional cascades are less useful. The indicators are shown in Box 5.2. As with other care and treatment cascades, the HIV-HCV cascade can be disaggregated by geography (e.g. at the clinic level) or by population (e.g. among PWID).

Box 5.2 HIV-HCV co-infected care and treatment cascade indicators

- Number of PLHIV who have been diagnosed with HCV co-infection.
- Number and percentage that are positive for NAT HCV RNA.
- Number and percentage that are genotyped.
- Number and percentage of HIV-HCV co-infected people who have initiated or completed anti-HCV therapy (treatment initiation).
- Number and percentage of number of HIV-HCV co-infected people have achieved a sustained virological response (cure).

An example of an HIV-HCV treatment cascade is shown in Figure 5.3.

Figure 5.3 Generic HIV-HCV co-infection treatment cascade



5.2.1 Core indicators and data sources

Indicator 1. Number of PLHIV who have been diagnosed with HCV co-infection

The HIV-HCV cascade will most likely focus on cohorts of patients in individual clinics or in specific populations, such as PWID. If countries are interested in national estimates of the number of people who are co-infected, these are probably most easily obtained from case reporting in countries where HCV positivity is reportable on HIV case-based surveillance forms. In other countries, estimates may be extrapolated from cohort-based data to the national level. For instance, in a country with a concentrated epidemic, if the prevalence of HCV infection in a highly-screened population of PLHIV is 15.6%, then that number could be used to construct a national estimate by multiplying the estimated number of PLHIV by 0.156. If more than one data source is available, national programmes could use the median of the different prevalence measurements to estimate national prevalence. If there are large differences in HCV prevalence, for instance among PWID where typically it is higher and among MSM where it is lower, a synthetic estimate can be constructed by multiplying the prevalence of HIV-HCV co-infection in HIV-infected PWID by the estimated number of PWID who are living with HIV and averaging that with a similar estimate among MSM. However, it is estimated the number of PLHIV who are co-infected with HCV forms the left-hand column of the cascade.

Indicator 2. Number and percentage who are positive for NAT HCV RNA

The number and percentage of people who are eligible for HCV therapy is determined by the NAT for HCV RNA. A certain proportion of people, estimated to be between 15% and 45% *(22)*, will spontaneously clear their infection and will not require further evaluation. This can also be expressed in the cascade so that those who have been evaluated and are eligible plus those who have been evaluated and have spontaneously cleared their HIV infection are shown in a stacked bar graph. The number and percentage that have not been evaluated is the difference between the first and second columns.

Indicator 3. Number and percentage who are genotyped

People with HIV-HCV co-infection who are eligible for HCV therapy need to have their HCV strain genotyped to ensure that the correct DAAs are used. For instance, therapy for genotypes 1 and 4 in HCV-infected patients without cirrhosis involves lepidasvir/sofosburvir or daclatasvir/sofosbuvir; ribavirin may be added if there is evidence of cirrhosis *(16)*.

Indicator 4. Number and percentage of HIV-HCV co-infected people who have initiated or completed anti-HCV therapy

Once genotyping is completed, patients should start DAA therapy. This includes patients who have previously failed therapy with interferon- and ribavirin-based regimens. This is the equivalent of Global AIDS monitoring indicator 10.9 *(8)* and corresponds to treatment initiation *(10)*. Since DAA therapy is of such short duration (in the order of 12-24 weeks), the proportion of people in the cohort who have completed therapy, whether they have benefited or not, should also be included in this column. This variable should be collected from chart reviews or, potentially, from pharmacy records.

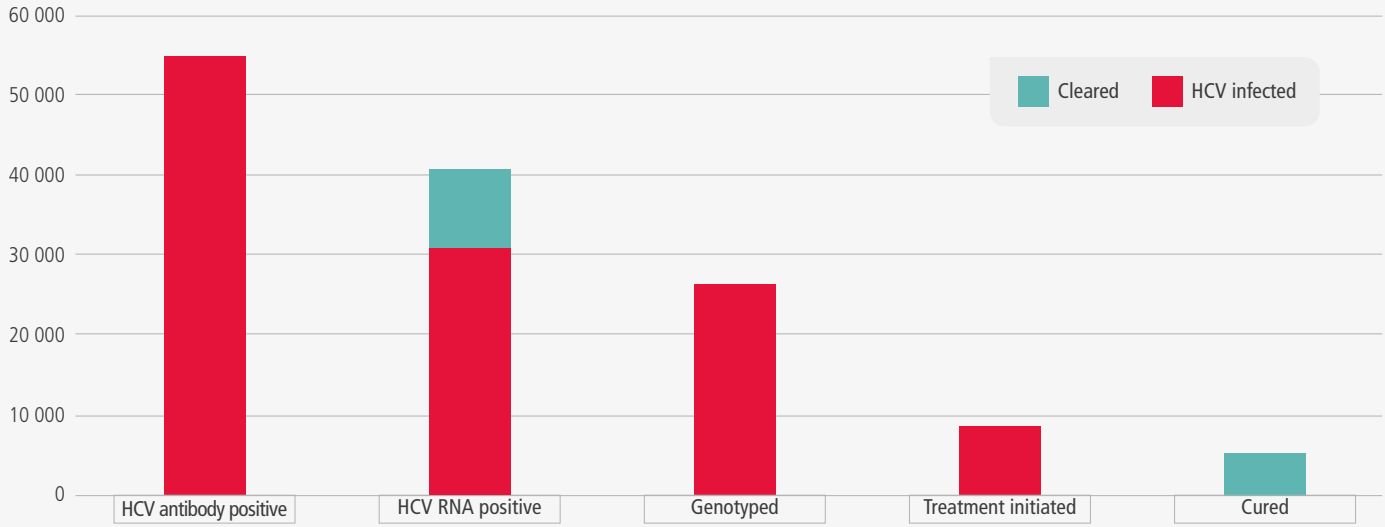
Indicator 5. Number and percentage of number of HIV-HCV co-infected people who have achieved sustained virological response

WHO recommends that patients who have completed a course of DAAs for HCV infection should be assessed with an NAT for HCV DNA 12 weeks after they complete therapy. This corresponds to cure for chronically infected patients *(10)*. Those who are negative are considered to have a sustained virological response and are considered cured. This should be measured directly in chart reviews.

5.2.2 Examples of HIV-HCV co-infection cascades.

There are few published examples of HIV-HCV care and treatment cascades. An example of a cascade for HCV mono-infection (Figure 5.4) comes from the province of British Columbia in Canada, which has a concentrated epidemic with foci among both MSM and PWID. The provincial Ministry of Health estimated that at the time of the study there were 73 203 people living with HCV in the province of British Columbia. Of these, 54 902 (75%) had been diagnosed. Of those with diagnosed infection, 40 656 (74.1%) had been tested for HCV RNA; it is of interest that 9842 (17.9%) were found to have spontaneously cleared their infection. Of the remaining 30 814, 26 300 (85.4%) had been genotyped, 8532 (27.7%) had begun treatment and 5197 (16.9%) had been cured *(23)*. Overall, 27.4% of those who had been diagnosed with co-infection had either cleared HCV spontaneously or had achieved a sustained virological response with therapy. Janjua and colleagues *(23)* also provide some data on HIV-HCV co-infection. Of the estimated 75 023 patients living with HCV, 3178 (5.8%) had HIV infection as well. Of these, 2605 (82.0%) had been tested for HCV RNA *(23)*.

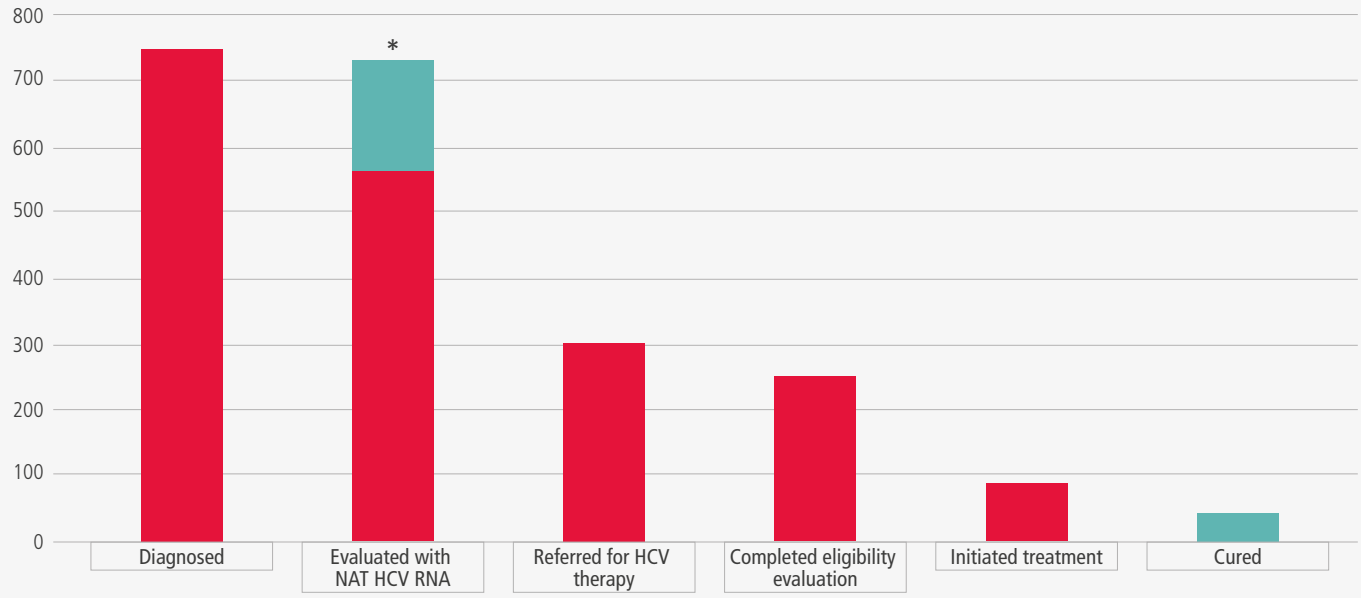
Figure 5.4 Provincial HCV treatment cascade, British Columbia, Canada, 2012



Adapted from: Ref. *(23)*.

Another example comes from a clinic-based cohort at the University of California, San Diego in the United States of America *(24)*. Of 4725 PLHIV followed at the centre from 2008 to 2012, 4534 (96.0%) had been screened for HCV. A total of 748 (16.5%) had HCV antibody and 562 (75.1%) had active infection. Of these 562, 303 (53.9%) were referred for care. The most important independent risk factor for not being referred for HCV therapy was being out of HIV care. Of the 303 referred for care, 250 (82.5%) completed eligibility evaluation, 88 (29.0%) initiated therapy and 41 (13.5%) were cured (Figure 5.5). It should be noted that many of these data were collected prior to the advent of DAA.

Figure 5.5 HIV-HCV co-infection care and treatment cascade, San Diego, United States of America, 2008-2012



NAT HCV RNA: nucleic acid test for hepatitis C virus ribonucleic acid.
* Of the 172 patients who cleared HCV infection prior to being evaluated for HCV therapy, 138 had spontaneously cleared infection and 34 had previously been treated successfully with interferon.
Adapted from: Ref. *(24)*.

5.3 HIV-associated tuberculosis

The countries with the highest burden of HIV infection are also heavily affected by TB. Persons with HIV infection are at elevated risk of active TB and at elevated risk of mortality if they develop active TB *(25)*. TB may account from one third to 40% of HIV-related mortality *(26,27)*. WHO estimates that there were 1.2 million new cases of active TB among PLHIV in 2015, almost 60% of which were not reported to have reached care *(27,28)*. TB remains the leading cause of death for PLHIV, so early diagnosis and initiation of treatment are crucial to ensure survival. For this reason, all PLHIV should be screened for TB at every medical encounter using an algorithm containing fever, cough of any duration, weight loss and night sweats *(29)*. Persons with active TB should be screened for HIV before beginning therapy *(30)*. The WHO-recommended rapid molecular tuberculosis diagnostic test, Xpert MTB/RIF, should be used as the first test if TB is suspected. PLHIV in whom active TB has been ruled out should receive TB preventive treatment while those with confirmed disease should receive TB treatment as well as ART *(31)*.

Box 5.3 HIV-associated tuberculosis and treatment cascade indicators

- Number of PLHIV in care.
- Number and proportion of PLHIV in HIV care that are screened symptomatically for active TB.
- Number and proportion of PLHIV in HIV care that are screened symptomatically for active TB and that screen positive.
- Number and proportion of PLHIV in HIV care that screened positive for symptoms of active TB and were tested for TB.
- Number and proportion of PLHIV that are diagnosed with active TB.
- Number and proportion of PLHIV with active TB that have initiated therapy for active TB.
- Number and proportion of PLHIV with active TB that have completed therapy for active TB.*

*This is not routinely measured for the subset of TB patients with HIV infection and should be considered optional.

WHO recommends a set of core national indicators as essential for identifying gaps in the cascade of intensified tuberculosis case-finding among people living with HIV who enter the health-care system through HIV care settings *(31,32)*. Globally, WHO recommends countries to report a number of HIV-TB indicators that reflect combined efforts by the TB and HIV programmes to ensure that a person enters care and receives ART during TB treatment. WHO also recommends countries to report three indicators that are important for analysing the cascade of case detection versus the provision of TB preventive therapy. These are the same as the UNAIDS global AIDS monitoring indicators 10.1, 10.2 and 10.3 *(8)*.

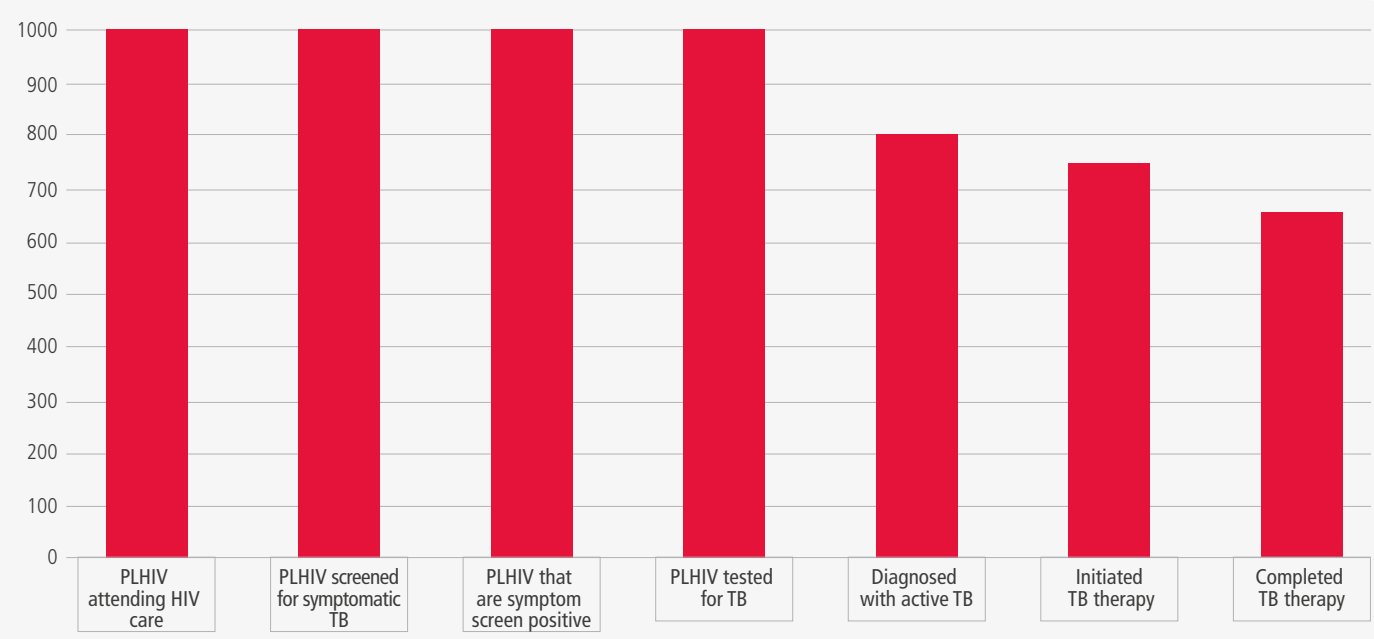
There are two different ways to construct an HIV-TB care and treatment cascade. The first is from the point of view of HIV care services and starts with TB case-finding among PLHIV attending HIV care (see section 5.3.1). The second is among people attending TB care and includes screening and treatment for HIV (see section 5.3.2). We also present a third cascade which examines isoniazid preventive therapy among PLHIV in care who have screened negative for active TB.

5.3.1 Cascade of intensified TB case-finding among people attending HIV care.

For this care and treatment cascade the indicators start with the number of PLHIV in HIV care or treatment settings, as opposed to the estimated number of PLHIV with active TB, which is estimated by the SPECTRUM AIDS Impact Model *(33)*. TB screening should be a routine investigation for anyone attending HIV care. The subsequent indicators are the number of PLHIV who have been screened for TB, those who have a positive symptoms screen, those who have a diagnostic test and those who are started on treatment (Box 5.3). The purpose of this set of indicators is to assess the effectiveness of mechanisms established by the National AIDS Control Programme and the National Tuberculosis Programme to ensure that all PLHIV presenting to HIV care and treatment facilities who are screened for tuberculosis undergo the appropriate investigations if found to have symptoms, and receive treatment if found to have tuberculosis.

An example of a generic HIV-TB care and treatment cascade is shown in Figure 5.6.

Figure 5.6 Generic cascade for treatment of active TB in PLHIV



PLHIV: people living with HIV; TB: tuberculosis.

Indicator 1. Number of PLHIV in HIV care (including PMTCT)

The first indicator is the number of people who are enrolled in HIV care (including PMTCT) and who are seen for care during the reporting period. These data can be obtained from the ART and pre-ART registers.

Indicator 2. Number and proportion of PLHIV in HIV care that are screened symptomatically for active tuberculosis

The second indicator helps programmes to assess the extent of implementation of the recommendation to screen all PLHIV in HIV care for the presence of any of the four symptoms at every visit to HIV care and treatment facilities. With paper-based systems, a mechanism for systematic recording and reporting of all events should be established (e.g. a cough register).

Indicator 3. Number and proportion of PLHIV in HIV care that are screened symptomatically for active tuberculosis and that screen positive

The third indicator helps identify people attending HIV care who are eligible for a TB diagnostic test. As with indicator 2, a mechanism for recording and reporting of all events needs to be established to capture these data and ensure that persons with presumed TB can be tracked through the process of TB diagnosis and treatment. In settings where electronic medical records with unique patient identifiers exist, these data can be incorporated.

Indicator 4. Number and proportion of PLHIV in HIV care that screened positive for symptoms of active TB and were tested for tuberculosis

The fourth indicator helps assess the level of integration or strength of referral links between the HIV and TB services. As with indicators 1 and 2, in the absence of electronic medical records with unique patient identifiers, a mechanism needs to be established. This necessitates close coordination between the National AIDS Control Programme and the National Tuberculosis Programme but responsibility for systematic recording, reporting and follow-up of data lies with the National AIDS Control Programme.

Indicator 5. Number and proportion of PLHIV that are diagnosed with active tuberculosis

The fifth indicator is the number and percentage of people attending HIV care that have been investigated and diagnosed with TB during the reporting period. This is a subset of all PLHIV who have TB; others may have presented through the TB care system. In accordance with WHO recommendations, this should be done with the Xpert MTB/RIF test *(34)*. A mechanism should be established to capture these data unless electronic medical records are in place.

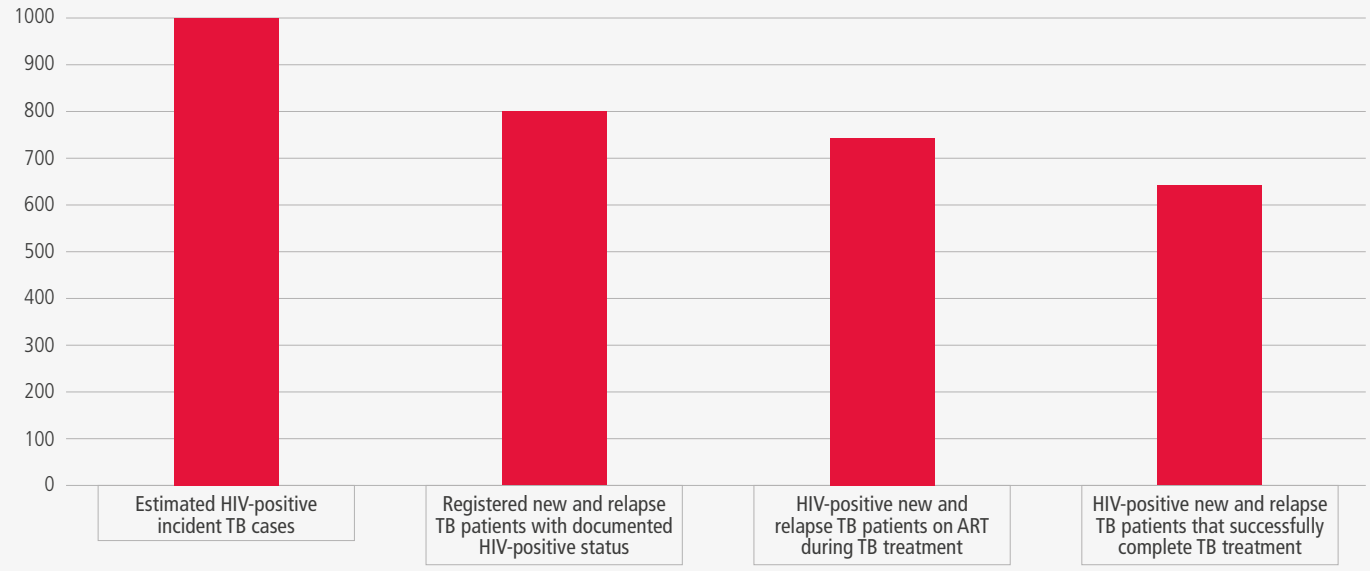
Indicator 6. Number and proportion of PLHIV that have initiated therapy for active tuberculosis

The sixth indicator is the number and percentage of PLHIV attending HIV care who were found to have active TB and who have initiated TB therapy. This is the equivalent of Global AIDS monitoring indicator 10.1 *(8)*. While this is ideally done in combination with ART, this indicator does not require simultaneous ART. These data are available from the tuberculosis register but, as with the other indicators above in the cascade, the subset of data on patients entering through the HIV system should be recorded and closely tracked by the National AIDS Control Programme. Where a country has an electronic case-based system with unique identifiers, tuberculosis treatment outcomes should also be tracked.

Indicator 7. Number and proportion of PLHIV with active TB that have completed therapy for active TB

This is an optional indicator that is unlikely to be obtained from routine HIV or TB data. Countries wishing to collect data on this indicator will be likely to require special studies involving review of medical records.

Figure 5.7 Generic treatment cascade for treatment of HIV and TB



5.3.2 Cascade of HIV-TB care and treatment that can use TB indicators

Another way to construct the HIV-TB care and treatment cascade is shown in Figure 5.7. This is constructed from the perspective of national TB programmes, and the data in this cascade can be found from TB indicators. This cascade begins with the estimated number of PLHIV that are estimated to have incident TB in a particular reporting period. It then moves to the estimated number of new and relapsed TB patients who have HIV infection to the number of TB patients on ART during their TB treatment, and finally to the number who have successfully completed TB therapy.

5.3.3 Cascade of case detection and provision of tuberculosis preventive therapy among people who are newly enrolled in HIV care.

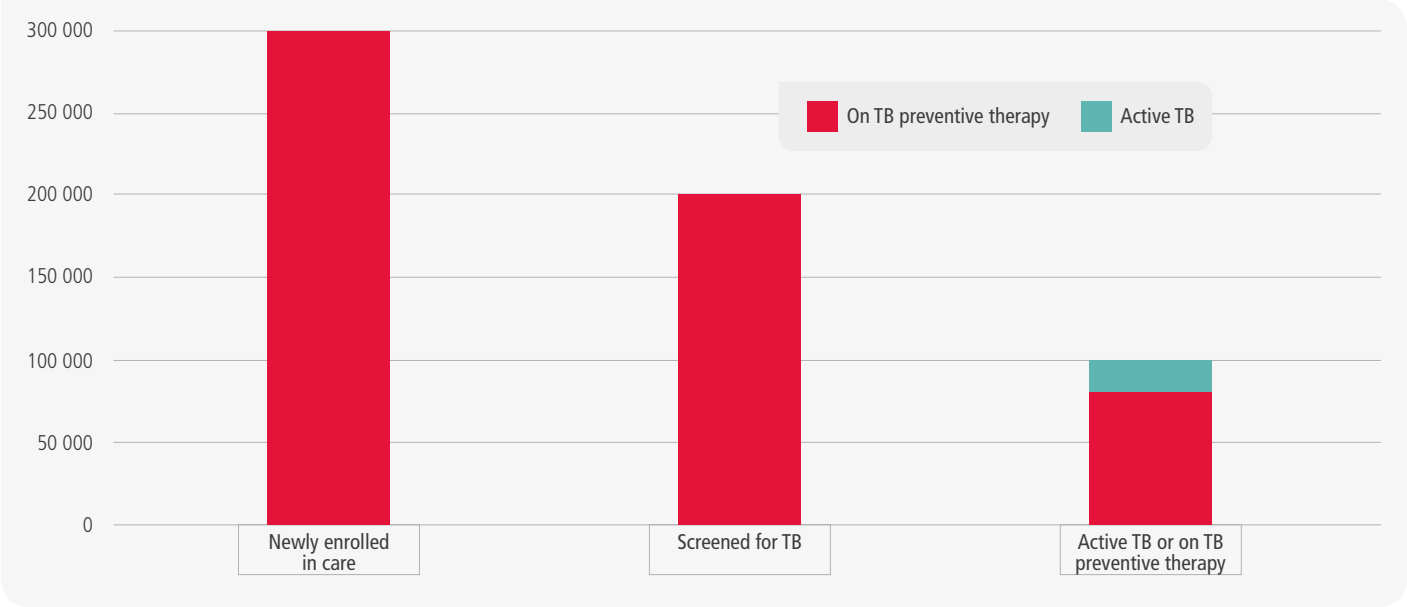
An additional cascade can be constructed for PLHIV who have been evaluated and are found not to have active TB. This cascade starts with the number of people who are newly enrolled in HIV care (pre-ART or ART register during the reporting period). All PLHIV should be screened for TB and, if they are found not to have any signs and are eligible, they should be started on TB preventive therapy. Those who do present with a symptom should be further investigated for TB with diagnostic tests. If after undergoing further investigations for TB they are found not to have active TB, they should also receive TB preventive therapy. Thus, the sum of the indicator for people living with HIV newly enrolled in HIV care with active disease plus the indicator for PLHIV started on TB preventive therapy should come to close to the total number of PLHIV newly enrolled in HIV care (Box 5.4).

Box 5.4 Indicators for cascade of tuberculosis case detection and provision of tuberculosis preventive treatment

- Number of PLHIV newly enrolled in HIV care.
- Number and proportion of PLHIV newly enrolled in HIV care who have been screened for TB.
- Number and proportion of PLHIV newly enrolled in care with active TB.
- Number and proportion of PLHIV newly enrolled in care started on TB preventive therapy.

A generic cascade for tuberculosis preventive therapy is shown in Figure 5.8. In this example, two thirds of PLHIV newly enrolled in care have been screened for TB. However, only half of these have either been diagnosed with TB and started on therapy or have begun TB preventive therapy.

Figure 5.8 Generic cascade for prevention of TB in PLHIV



Indicator 1. Number of PLHIV newly enrolled in HIV care (including PMTCT)

This indicator relates to the number of PLHIV who are registered in the pre-ART or ART register during the reporting period. The source of these data is the patient HIV care/ART card or the pre-ART or ART registers.

Indicator 2. Number and proportion of PLHIV newly enrolled in HIV care who have been screened for tuberculosis

This indicator measures the number of PLHIV newly enrolled in care who have been screened for TB regardless of whether they were ultimately found to have TB or not.

Indicator 3. Number and proportion of PLHIV newly enrolled in care with active tuberculosis disease

This indicator measures the burden of active tuberculosis among people who are newly enrolled in HIV care, and also indirectly measures the extent of effort to detect HIV-associated TB early. These data should be available in the pre-ART and ART registers, as well as in the TB register at the basic management unit. The difference between the indicator 1 and the sum of indicators 2 and 3 is the gap in TB preventive therapy.

Indicator 4. Number and proportion of PLHIV newly enrolled in care started on tuberculosis preventive therapy

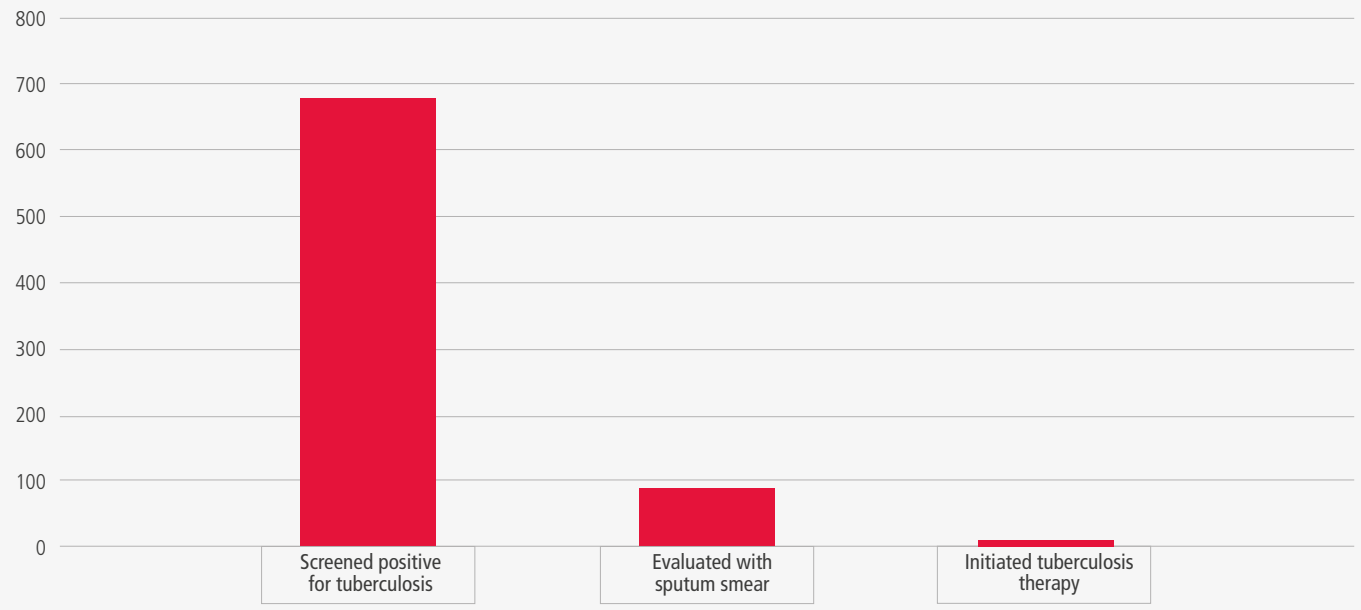
This indicator measures the extent to which PLHIV are started on TB preventive treatment. It includes patients who initially screened negative and those who screened positive but who were subsequently found not to have active TB. These data can be extracted from the patient HIV care/ART card, pre-ART register or ART register.

5.3.4 Examples of HIV-TB care and treatment cascades.

There are some published examples of HIV-TB care and treatment cascades. Most use the number of patients with reported TB as the starting point and then examine the number that have been tested for HIV, the number that are infected and the number that start ART. Consequently, these cascades are HIV treatment cascades for patients with tuberculosis. An example of this comes from Lessels and colleagues, who reviewed worldwide data through 2013 on the diagnosis and treatment of HIV-tuberculosis co-infection from the vantage point of tuberculosis patients *(35)*. They reported that, in the WHO African Region, 76% of patients with active tuberculosis had been screened for HIV but that, in the South-East Asia, Western Pacific and Eastern Mediterranean regions, fewer than 50% had been screened. Of those that had been identified as being co-infected 70% worldwide had begun ART.

An example of the HIV-tuberculosis care cascade in HIV patients comes from Roy and colleagues in Uganda. Of 2613 newly-diagnosed PLHIV, 2439 (93%) were screened for active tuberculosis. Of these, 682 (28%) had positive screens; however, only 90 (13%) had a sputum smear ordered but, of these, all but two began tuberculosis therapy (Figure 5.9) *(36)*. These findings demonstrate a large drop-off between screening positive for tuberculosis and evaluation of sputum. The authors suggested that much of this difference was due to mistaken diagnoses of malaria or bacterial infections.

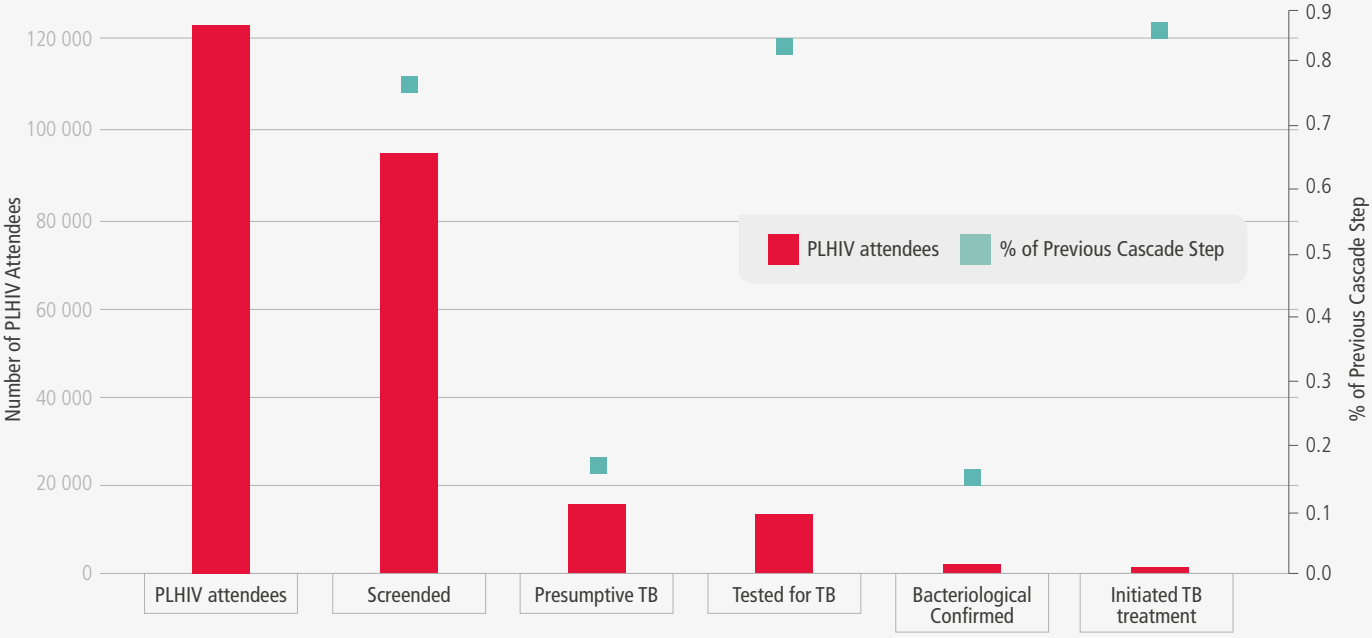
Figure 5.9 HIV-tuberculosis care and treatment cascade, Uganda, 2012-2013



Adapted from: Ref. *(36)*.

Another example comes from Swaziland. In this cascade presentation, of more than 120 000 PLHIV attending care, approximately 75% were screened for TB and 11% had presumptive TB. Only about 15% of those who were subsequently tested for TB had bacteriologically-confirmed TB, and 85% of these started TB treatment (Figure 5.10). There were modest gaps in the proportion with presumptive TB who were tested (around 80%) and the proportion with bacteriologically-confirmed TB started on therapy (about 85%). However, while bacteriological confirmation is important, in PLHIV with suspected TB about 40% of bacteriologically negative cases subsequently become clinically-confirmed cases *(37,38)*. Thus, while Swaziland's addition of bacteriologically-confirmed provides additional data, a substantial proportion of TB cases diagnosed by other means are not included.

Figure 5.10 HIV-tuberculosis care and treatment cascade, Swaziland



From: Ref. *(38)*.

6. INDIVIDUAL-LEVEL LONGITUDINAL CASCADES

The core indicators to be included in an individual-level longitudinal cascade are shown in Box 6.1. These indicators should be assessed for a given time frame such as one calendar year. Supplemental indicators, which are described in the annex, primarily apply to analysis of data over a longer period of time (e.g. 24, 36, 48 or 60 months). Typically, longitudinal cascades follow a cohort of persons diagnosed with HIV within a specified time frame, such as a single year. Longitudinal cascades allow for time-dependent indicators. For example, linkage to care can be measured as the proportion of newly diagnosed persons who enter care within 12 (3, or 6) months of diagnosis. Similarly, the indicator of persons initiating ART can be measured as the proportion of persons who are in care and who initiate ART within one month.

Box 6.1 Indicators for a longitudinal care cascade among persons newly diagnosed with HIV

- Number of people diagnosed with HIV during the period of the cascade (e.g. between 1 January and 31 December 2014).
- Number and percentage of people diagnosed with HIV during the cascade time period that have been successfully linked to care within 12 months of diagnosis (or other specified time period such as within 1, 2 or 3 months of diagnosis).
- Number and percentage of people diagnosed with HIV who initiated ART within 12 months of diagnosis (or other specified time period such as within 1, 2 or 3 months of diagnosis).
- Number and percentage of people diagnosed with HIV who were virally suppressed within 12 months of initiating ART.

A longitudinal cascade can be constructed at national and subnational levels in countries that have well-established individual-level data from HIV case-based surveillance or patient monitoring systems. In countries where such systems are not available, a longitudinal cascade can be made at a facility level by using a patient monitoring system that records outcomes of people who are diagnosed with HIV and receive HIV care and treatment.

In constructing these cascades there is a need to be able to link individual patients' records across various datasets, such as HIV testing, care and treatment, pharmacy and laboratory reports; this will require de-duplication of records. Facility-level patient monitoring systems collect patients' names and dates of birth which together can be used to un-duplicate records. Additionally, longitudinal cascades can be constructed for different demographic groups and KPs and can be used to determine inequities in care. Guidance on unique identifiers may be useful for countries where systems are currently inadequate for de-duplication of records *(1)*.

An advantage of longitudinal cascades is that they permit measurement of the cascade indicators over a specified time period. This can facilitate assessment of the impact of interventions when the time that such interventions were implemented is known. Comparing trends in indicators over time is also easier when cascades are created for discrete time periods. Examples of indicators used in longitudinal care cascades are shown in Table 6.1.

Table 6.1 Indicators included in longitudinal care cascades

Longitudinal care cascade among persons newly diagnosed with HIV	Longitudinal care cascade among PLHIV	Longitudinal care cascade among persons newly initiating ART
Number of people newly diagnosed with HIV in one calendar year	Number of PLHIV as of the end of a calendar year	Number of patients who initiated ART within a specified time period
Number and percentage of people newly diagnosed with HIV in one calendar year who entered care within 12 months of diagnosis	Number and percentage of PLHIV who are in care	Number and percentage of persons who initiated ART within a specified time period and who were retained on ART 12 months after ART initiation.
Number and percentage of people newly diagnosed with HIV in one calendar year who initiated ART within 12 months of diagnosis	Number and percentage of PLHIV who are receiving ART	Number and percentage of patients who initiated ART within a specified time period and who were virally suppressed within 12 months of initiating ART
Number and percentage of people newly diagnosed with HIV in one calendar year who were virally suppressed within 12 months of diagnosis	Number and percentage of PLHIV who are virally suppressed	

There are at least three different types of longitudinal care cascades that can be constructed: 1) longitudinal care cascades among persons newly diagnosed with HIV (the most common), 2) longitudinal care cascades among PLHIV and 3) longitudinal care cascade among persons on ART. A longitudinal cascade among persons newly diagnosed with HIV is one way to determine accurately the efficiency of linkage to care because it tracks people from diagnosis into care. Longitudinal cascades are also helpful for assessing the time required to move from diagnosis to care to ART initiation and to viral suppression. Box 6.1 lists the core indicators for the different types of longitudinal cascades presented in this manual.

This longitudinal cascade begins with all PLHIV newly diagnosed with HIV in one year (e.g. from 1 January to 31 December 2014); as such, it represents an annual cohort. To allow sufficient follow-up time for persons in the cohort to achieve indicators within 12 months following diagnosis, the data used should be available through to 31 December 2015 (i.e. 12 months after cohort membership closed). Longitudinal HIV patient monitoring systems allow the calculation of retention on ART and viral load suppression for longer periods after ART initiation (e.g. 24, 36 or 60 months and longer). At each stage, however, the indicator should be a subset of the prior indicator – i.e. cohort members must have completed one step before proceeding to the next. When determining which longer-term indicators to include in the cascade, consider the situation where a person is diagnosed on the last day of the year of the cascade (e.g. 31 December 2014) and then determine the duration of follow-up. If ART retention at 24 months after initiation is to be calculated, a person diagnosed on 31 December 2014 must have 24 months of follow-up time. This means that data must be available through 31 December 2016. Guidance on supplemental indicators for a longitudinal care cascade among persons newly diagnosed with HIV is included in the annex.

These types of analyses can be used to generate important public health data. For instance, in the United States of America, estimated times from diagnosis to linkage to care, from linkage to care to engagement in care, and from engagement in care to virological suppression are 3.1 months, 3.6 months and 14.6 months, respectively *(2)*. In a another study from Melbourne, Australia, the estimated duration of infectiousness, time from infection to virological suppression fell from 49.0 months for patients diagnosed between 2007 and 2009 to 9.6 months for those diagnosed between 2013 and 2015 *(3)*.

6.1 Longitudinal care cascade among persons newly diagnosed with HIV

In a longitudinal care cascade, indicators are either met or are not met. This means that within the annual cohort, persons who, for instance, do not enter care within 12 months of diagnosis are no longer part of the cascade cohort. Because persons may sometimes enter care more than 12 months following diagnosis, programmes may wish to use additional methods to analyse the time to entering care. This can be done, for example, by calculating the average time from diagnosis to care. This type of analysis is important but is not used in cascade analysis.

In this cascade, the first indicator is a number and constitutes 100%. This number serves as the denominator for all subsequent indicators in the cascade. As with other indicators, it is recommended to present both the number and proportion for each indicator.

6.1.1 Indicators and data sources

Indicator 1. Number of people newly diagnosed with HIV in one calendar year

For national or subnational cascades, HIV case-based surveillance data should be used. A facility-level cascade can be constructed if data on dates of HIV diagnosis are complete and a database is available that links the date of diagnosis to care with ART records. In some settings a laboratory database or information management system may have unduplicated records of new HIV diagnoses. The indicator is the number of persons newly diagnosed in a specified year. This includes persons who have died or were lost to follow-up. Case-based surveillance and, in some situations, programme data should include the date of diagnosis. The date of diagnosis is used to identify cases that are included in the cohort (i.e. persons who were diagnosed within a specified calendar year). The date of diagnosis is used to determine the starting point for measuring time to achieve subsequent indicators.

Indicator 2. Number and percentage of people newly diagnosed with HIV in one calendar year who entered care within 12 months of diagnosis

There are three possible data sources for the numerator: 1) case-based surveillance data, 2) programme data and 3) laboratory data.

Case-based surveillance or programme data (patient monitoring data). This indicator represents entry into care, not retention in care. As such, it will include all persons with any evidence of a care visit provided that the visit occurred within 12 months of diagnosis. Case-based surveillance or programme data should indicate the date on which a patient first entered care. Evidence of care includes the date of a documented clinical assessment such as a WHO clinical stage, a CD4 or viral load test requisition or result, or an indication of initiating ART. In the situation where there may be multiple dates of clinical staging, CD4 or viral load testing, the earliest date of any of these indications of care should be used as the date of entry into care. For this indicator, it is recommended to measure the number and proportion of persons who were diagnosed in a given year who entered care within 12 months of diagnosis. Countries may select a shorter or longer time period if needed for programmatic purposes.

Laboratory data. In settings with a national, subnational or facility-level database with unduplicated records, laboratory data that include dates of tests can be used to identify the first CD4 or viral load test. In situations where laboratory test dates are available in case-based surveillance, programme and laboratory databases, the first CD4 or viral load test should be used to determine persons who entered care within 12 months of diagnosis.

Indicator 3. Number and percentage of people newly diagnosed with HIV in one calendar year who initiated ART within 12 months of diagnosis

There are two possible data sources for the numerator:
1) case-based surveillance data and 2) programme data (patient monitoring data)

Case-based surveillance or programme data. This indicator should also include a time frame. With the recommendations for initiating ART regardless of clinical or immunological criteria, the date of entry into care should also be the date of ART initiation. However, because not all patients will be willing to start treatment immediately and because other factors may limit the availability of ART, some delay between entry into care and ART initiation should be allowed.

Indicator 4. Number and percentage of persons newly diagnosed with HIV in one calendar year who were virally suppressed within 12 months of diagnosis

This indicator should be measured only in settings where viral load testing is performed as part of routine patient monitoring and not primarily to confirm the need to change ART regimens.

There are three possible data sources for the numerator:
1) case-based surveillance data, 2) programme data (patient monitoring data) and 3) laboratory data.

Case-based surveillance or programme data. This indicator must allow for 12 months of follow-up time after ART initiation and data should be obtained from settings where viral load testing is performed as part of routine patient monitoring. The numerator is the number of persons newly diagnosed with HIV during the specified time period whose most recent viral load test result is <1000 copies/mL.

Laboratory data. In settings with a national, subnational or facility-level database or laboratory information management system with unduplicated records, the numerator is the number of newly-diagnosed persons during the specified time period whose most recent viral load test result was <1000 copies/mL.

6.2 Longitudinal care cascade among all PLHIV (previous and new diagnoses)

The longitudinal HIV care cascade can be constructed as described above but could also include people previously diagnosed and alive as of the end of the reporting period (Box 6.2). Outcomes of these persons are then reported for a period of one year (or longer) and include retention in care and viral load suppression in the subsequent year. For example, a care cascade can be constructed for PLHIV who were diagnosed up to 31 December 2013 as of 31 December 2014.

Box 6.2 Indicators for a longitudinal care cascade among people living with HIV

- Number of PLHIV as of the end of a calendar year.
- Number and percentage of PLHIV who are in care as of the end of the calendar year.
- Number and percentage of PLHIV who are receiving ART as of the end of the calendar year.
- Number and percentage of PLHIV who are virally suppressed as of the end of the calendar year.

6.2.1 Indicators and data sources

In this cascade, the first indicator is the number of persons diagnosed with HIV and alive as of a specified date, such as the end of a calendar year.This number serves as the denominator for all subsequent indicators. All indicators must pertain to a specific calendar year.

Indicator 1. Number of PLHIV as of the end of a calendar year

For national or subnational cascades, HIV case-based surveillance data should be used. A facility-level cascade can be constructed if data on dates of HIV diagnosis and deaths are complete. A recent population-based survey may also be used provided that it ascertained indicator data.

Indicator 2. Number and percentage of PLHIV who are in care

There are three possible data sources for the numerator: 1) case-based surveillance, 2) population-based surveys and 3) programme data.

Persons who are in care and clinically stable may be seen only twice a year. As such, the indicator should include evidence of persons who received any care in the most recent year. For intance, if the cascade is constructed for PLHIV as of 31 December 2014, to be considered in care there must be evidence of receipt of care in 2014. The evidence of receipt of care differs depending on the data source. The numerator is the number of persons (or percentage if using survey data) with evidence of care in the most recent year of the cascade analysis.

Case-based surveillance data. Case-based surveillance data may be used if these data ascertain deaths. In general, mortality data collected only from facilities and not through vital registries are incomplete. Evidence of care using case-based surveillance data may include a report of a WHO clinical stage, ART initiation or a CD4 or viral load test result in the most recent year included in the cascade analysis.

Population-based survey data. A recent survey in which participants indicated whether they were HIV-infected and were asked if they were in care and when their most recent clinic visit took place (or were asked questions that permitted determination of whether the participant was in care during the most recent year) can be included in the cascade analysis.

Programme data. Programmes that have cumulative data and that ascertain deaths may be used. Typically these data do not include vital registries and, as such, deaths will be underreported. Evidence of receipt of care using programme data includes documentation of a WHO clinical stage, ART initiation, or a CD4 or viral load test result in the most recent year of the cascade.

Indicator 3. Number and percentage of PLHIV who are receiving ART

There are three possible data sources for the numerator: 1) case-based surveillance, 2) population-based surveys and 3) programme data.

Case-based surveillance data. Case-based surveillance data may be used if these data ascertain deaths. In general, deaths collected only from facilities and not through vital registries are incomplete. Evidence of ART initiation may be available from case-based surveillance data but typically cannot definitively indicate ongoing use of ART. As such, a proxy such as a viral load test that indicates viral suppression may be used.

Population-based survey data. Using a recent survey in which participants indicated whether they were HIV-infected and currently using ART may be used. If the survey measures the presence of ART in the blood, the percentage of participants who are HIV-infected and have evidence of ART can be used for this indicator. If laboratory tests for the presence of ART are not conducted, self-report of ART use may be appropriate; however, this may overestimate the proportion of persons on ART because of reporting bias.

Programme data. Programmes that have cumulative data and that ascertain deaths may be used. Typically these data do not include vital registries and, as such, deaths will be underreported. Evidence of ART use may be obtained from medical or pharmacy records.

Indicator 4. Number and percentage of PLHIV who are virally suppressed

There are three possible data sources for the numerator: 1) case-based surveillance, 2) population-based surveys and 3) programme data.

Case-based surveillance data. Case-based surveillance data may be used if they ascertain deaths. In general, deaths collected only from facilities and not through vital registries are incomplete. The numerator is the number of PLHIV whose most recent viral load test result indicates a viral load test result of <1000 copies/mL.

Population-based survey data. A recent survey in which HIV-infected participants are tested for HIV RNA may be used. The indicator is the percentage of PLHIV who have a viral load test result of <1000 copies/mL.

Programme data. Programmes that have cumulative data and that ascertain deaths may be used. Typically these data do not review vital registries and, as such, deaths will be underreported. Evidence of viral suppression (<1000 copies/mL) may be obtained from medical records.

6.3 Longitudinal care cascades among persons newly initiating ART

In countries that lack case-based surveillance data and cannot link data from diagnosis to care or initiation of ART at an individual level, it may still be possible to calculate indicators with persons starting on ART. In this situation, an annual cohort will include all HIV-diagnosed individuals newly initiated on ART during a specified time period, such as from 1 January to 31 December 2014 (Box 6.3). Although in this manual retention indicators are considered to be supplemental, it is recommended that – for this cascade – retention on ART 12 months after ART initiation should be included as a core indicator.

Box 6.3 Indicators for a longitudinal care cascade among persons newly initiating ART

- Number of patients who initiated ART within a specified time period (e.g. at time of diagnosis, or within 1, 2 or 3 months of diagnosis).
- Number and percentage of patients who initiated ART within a specified time period who were retained on ART 12 months after ART initiation.
- Number and percentage of patients who initiated ART within a specified time period who were virally suppressed within 12 months of initiating ART.

6.3.1 Indicators and data sources

Indicator 1. Number of patients who initiated ART within a specified time period

Although this cascade can be constructed with data from a number of sources, the cascade should be used primarily in settings where the only data source is programme data. Some countries may have national databases with individual-level programme data that can be used for this cascade. If data are not available at the national level, facility-level data may be used. There must be at least 12 months of follow-up time for this cascade.

The first indicator is the number of persons who initiated ART within a specified time period.

Indicator 2. Number and percentage of persons who initiated ART within a specified time period who were retained on ART 12 months after ART initiation

Using the data source from indicator 1, calculate the number of patients from indicator 1 who were in care 12 months after ART initiation. For example, if indicator 1 is the number of persons who initiated ART between 1 January 2014 and 31 January 2014, indicator 2 is the number of those specific patients who are still in care and on ART as of 31 January 2015.

Indicator 3. Number and percentage of patients who initiated ART within a specified time period who were virally suppressed within 12 months of initiating ART

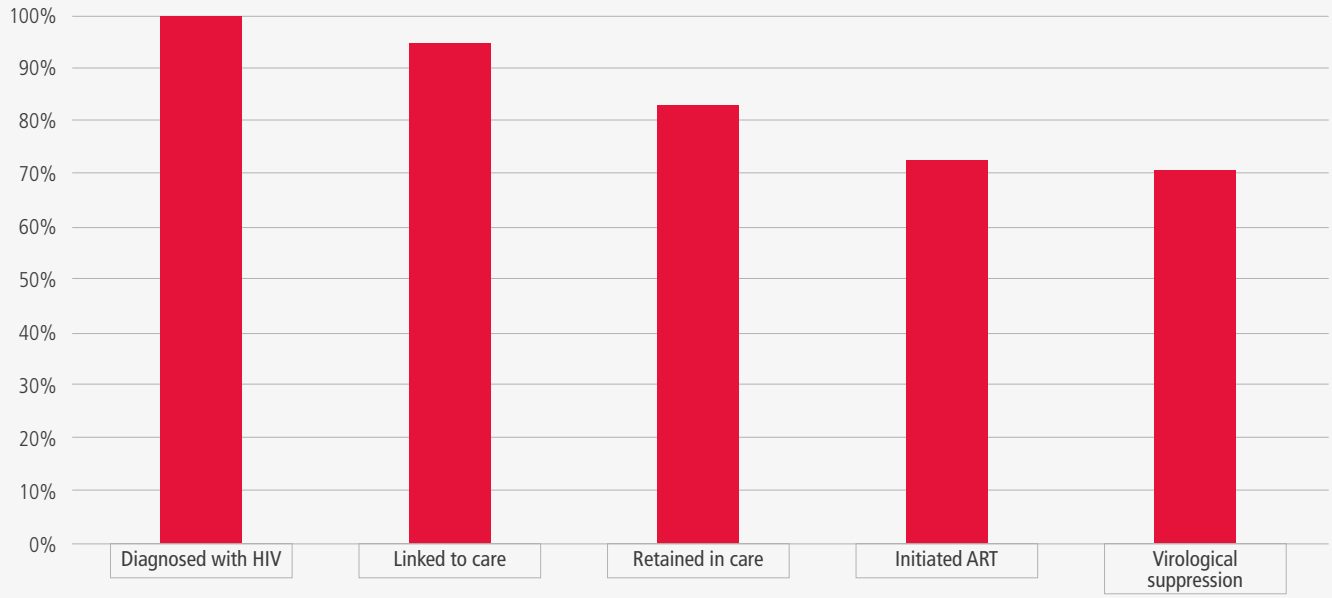
Using the data source from indicator 1, calculate the number of patients from indicator 1 who were in care 12 months after ART initiation. For example if indicator 1 is the number of persons who initiated ART between 1 January 2014 and 31 January 2014, indicator 3 is the number of those specific patients who are still in care and on ART as of 31 January 2015 and who are virologically suppressed (<1000 copies/mL). Virological suppression should be measured only in settings where viral load testing is conducted as part of routine patient monitoring. In settings where viral load testing is done primarily to document the failure of ART, the proportion of patients who are virologically suppressed will be underestimated.

6.4 Examples of longitudinal cascades

6.4.1 Longitudinal HIV care and treatment cascade from Denmark

In Denmark the details of all patients diagnosed with HIV are entered into a national cohort study, the Swedish-Danish HIV Cohort *(4)*. Data on diagnoses come from the national HIV surveillance system. Patients are considered linked to care when they are seen at a Danish HIV treatment centre and are enrolled in the cohort. "Retained in care" is defined as having been seen in the previous 13 months, and "suppression" iss defined as <500 copies/mL. Among patients diagnosed from 1995 to 2010, 95% were linked to care, 88% were retained in care, 73% initiated ART and 70% achieved viral suppression (at a level of 500 copies/mL) (Figure 6.1). This would suggest that there were gaps in patients beginning ART but, once ART had begun, 96% of patients were virologically suppressed.

Figure 6.1 Longitudinal national-level HIV care and treatment cascade, Denmark, 1995-2010*



*Total diagnosed = 5519.
From: Ref. *(4)*.

7. WORKING WITH IMPERFECT DATA

The ability to interpret the results of the cascade analysis depends heavily on the availability and quality of the data that go into the cascade. High-quality data are valid, complete, timely and representative. However, all data are subject to limitations.

Recognizing and understanding how these limitations have an impact on the findings from cascade analysis is important for proper interpretation.

7.1 Strengths and limitations of commonly used data sources

7.1.1 Modelled data

Most countries use the Spectrum AIDS Impact Model to estimate HIV prevalence and the number of people living with HIV *(1)*. For estimating the HIV prevalence in settings with a generalized epidemic, Spectrum relies primarily on data from antenatal care sentinel surveillance with refinement of estimates using data from household and KP surveys and ART and PMTCT programmes. In concentrated epidemics, estimates may be derived either from serosurveys among KPs along with estimates of sizes of these populations or from case-based surveillance and AIDS-related mortality data. A strength of Spectrum is that it provides reasonably robust estimates when compared to other data sources and is able to capture uncertainty around estimates, taking into account the quality and availability of data. The primary limitation of Spectrum is that it relies on accurate inputs that are representative of the underlying population that is being modelled. If other methods exist to estimate the population of interest, the strengths and limitations of those approaches should be considered. For population-specific cascades, if data from a recent population-based survey with high response rates (≥75%) are available, these may be used in place of Spectrum.

7.1.2 Case-based surveillance data

Comprehensive case-based surveillance data include reports of persons newly diagnosed with HIV, follow-up sentinel events including reviews (or computer matching) with vital registration to identify deaths, and laboratory reporting. High-quality case-based surveillance systems are routinely evaluated and have high rates of data completeness, accuracy and timeliness and have strong systems to un-duplicate reports. A strength of case-based surveillance data for cascade analysis is that they provide population-based, representative, individual-level data that can be used for longitudinal cascades. Weaknesses are that case-based surveillance provides no data on the number of PLHIV. Additionally, in many settings data from case-based surveillance may be incomplete (especially in settings that rely on passive reporting) for both newly-diagnosed persons and for sentinel events such as ART initiation. Case-based surveillance systems need to collect a sufficient number of personal identifiers to be able to un-duplicate records (which is necessary to avoid overestimates). Case-based surveillance systems may not be able to adjust for death as well as in- and out-migration. Keeping deceased patients in the numerator and denominators when constructing care cascades can lead to very inaccurate estimates. In situations where deaths are ascertained but the number of deaths differs from mortality estimates from Spectrum, the latter should be used.

7.1.3 Programme data

In many settings programme data are the only source of information on HIV care and treatment (for instance, patient monitoring systems). Individual-level (that is, un-duplicated) programme data are available at the facility level and can be used for longitudinal cascades. However, at the subnational and national levels individual-level data may not be available, thereby resulting in overestimates of persons in care and on ART because patients are counted twice in the numerators. This can also impede disaggregated cascade analysis. In many programmes, data from HIV testing and counselling programmes cannot be linked to care and ART programme data. The result is that programme data typically cannot determine true linkage to care.

7.1.4 Laboratory data

In low-income and in some middle-income countries, routine monitoring of patients on ART using viral load testing is not yet conducted. In these countries, viral load testing in adults is typically used to confirm treatment failure and, if used for cascade analysis, would underestimate viral suppression. Most settings do not have methods to link viral load data directly from laboratories to case-reporting systems because the technology to link individual records is not available. As such, results from viral load testing are available only from patient monitoring systems or directly from laboratories. Case-based surveillance data that do not obtain laboratory reports directly from the laboratories may have incomplete data on viral suppression. Determining whether a person has an undetectable viral load also varies according to the sensitivity of the assays used. For this reason, suppression at a value of <1000 copies/mL should be used rather than undetectable viral load. The testing threshold value should be reported for levels other than <1000 copies/mL. In addition, viral load testing may be delayed due to shortages of staff and reagents.

7.1.5 Population-based survey data

Population-based surveys are designed to provide representative estimates of HIV prevalence *(2)*. National household-based surveys provide reasonable and representative HIV prevalence estimates for the general population if they are based on proper sampling methods and have a high response rate (≥75%). Household surveys are generally under-powered to provide accurate HIV prevalence estimates of KPs which are generally only a small proportion of the general population and because reports of risk behaviours are obtained through self-report and may be subject to social desirability bias. A major impediment to using survey data for cascade analysis is that surveys are conducted only periodically and, as such, the data may not be timely. If surveys are recent, they are likely to be among the best sources of data for cross-sectional cascades.

7.2 Common biases and limitations in data used for cascade analysis

7.2.1 Selection bias

This occurs when populations are sampled, such as in surveys, and refers to the likelihood that persons who are selected to be in a study are different from those who are not selected or who refuse to participate. For instance, recruiting for a household survey during the day may result in a selection bias by missing persons who are at work.

7.2.2 Representativeness

This refers to the degree to which the persons who are included in the estimate (such as the sample in surveys or reported cases in case-based surveillance) truly represent those who were not included. For instance, in a survey of sex workers, if the recruitment is only from brothels then the findings may not be representative of street-based sex workers. Another example is sentinel HIV surveillance from antenatal clinics, which does not include women who are not pregnant or who are pregnant but do not attend antenatal clinics.

7.2.3 Surveillance bias

This occurs when a surveillance system monitors only a subset of the population. Populations that are monitored will have an outcome that is counted, whereas populations that are not under surveillance will be missed. This can occur because of differences in HIV testing services, which in turn can result in missed diagnoses from areas in which testing is not widely available.

7.2.4 Incomplete data

This is a common problem with case-based surveillance data, particularly in settings where active and direct laboratory-based reporting are not used. Incomplete data indicates that not all data is available on all persons reported to the surveillance system.

7.2.5 Recall bias/social desirability bias

Self-reported information, whether it is from a medical record or a survey, may be inaccurate. This is particularly true if someone is asked to recall something that happened a long time ago (such as the date of HIV diagnosis) or when persons are disinclined to provide truthful information because of stigma. For instance, participants in surveys may not wish to disclose that they are HIV-positive although they are aware of their infection. Social desirability bias may be particularly problematic in KPs, when individuals may be reticent to discuss their behaviours.

7.2.6 Old data

Outdated data can adversely affect the validity of the cascade results, particularly in situations that are rapidly changing. For instance, data on the proportion of people with diagnosed HIV infection who are on antiretroviral therapy derived from a national survey may quickly be out of date as diagnostic testing and treatment availability expands.

7.3 Multiple data sources

In cross-sectional cascade analyses a single data source may not provide all the information needed for all cascade indicators. Consequently, more than one data source may be required, which can introduce additional biases and precludes the use of a single method of expressing uncertainty regarding the estimates. For instance, if the HIV prevalence and number of people living with HIV comes from Spectrum and the proportion virally suppressed comes from laboratory records, it is far from simple to relate the 95% confidence intervals for Spectrum estimates to confidence intervals for the proportion virally suppressed. Moreover, the use of multiple data sources (or aggregate data) does not permit the linking of individual records and therefore the findings cannot be interpreted as meaning that the same person is included in all indicators. As a result, the use of multiple data sources may produce findings that are illogical (e.g. the estimate of the number of persons on ART may exceed the number estimated to be aware of their infection). This can happen because of the biases associated with the different data sources, particularly if the data were obtained in different years.

Table 7.1 Indicators, sources and quality scoring for cross-sectional data

Indicator	Description of indicators	Quality of indicators
PLHIV	Estimated number of PLHIV	Spectrum = green Estimates from nationally representative survey = yellow Other = red Note that the default source is Spectrum
Diagnosed with HIV	Number of PLHIV who have been diagnosed and are alive	Case-based surveillance with adjustments for mortality = green Nationally representative surveys = yellow Other = red
In HIV care	Number of PLHIV who received HIV care in the past 12 months (including ART)	Case-based surveillance = green Nationally representative survey (self report) = yellow Other = red
On ART	Number of PLHIV currently receiving ART	Case-based surveillance = green Nationally representative survey (self report) = yellow ART log = yellow Other = red
Virological suppression	Number of PLHIV on ART who have a suppressed viral load (<1000 copies per mL)	Case-based surveillance = green Nationally representative survey (lab) = yellow Laboratory log of viral load results (unduplicated) = yellow Other = red

ART: antiretroviral therapy; PLHIV: people living with HIV.

In addition to these considerations regarding combining data from multiple sources, a situation will occasionally arise in which there are multiple sources for the same data (e.g. estimates of the number of HIV-infected persons from both HIV-testing and counselling programmatic data and from a national household survey). In constructing cascades the most reliable data should be chosen (i.e. data that are most likely to be valid, complete, timely and representative of the population for which the cascade is being constructed). This process is referred to as triangulation *(3)*. If multiple data sources are available, they should be noted along with the reason why one data source was chosen over another. The information in Chapter 8 is aimed at guiding users through the process of understanding data sources and their limitations and strengths.

7.4 Assessing data quality

High-quality data are valid, complete, timely and representative of the population of interest. Cascade analysis in many settings relies on modelled, survey and aggregated programme data, each of which have strengths and weaknesses. Early in the process of cascade analysis it is necessary to review the quality, inherent biases and gaps in available data. The highest-quality data should be used. A useful tool for assessing data quality is the "green, yellow, red" scale described in Table 7.1.

As part of cascade analysis, the data sources, the dates on which the data were obtained and biases should be presented, and the impact that these limitations have on the interpretation of the findings should be discussed. When the data sources include confidence limits or other measures of uncertainty, these should also be presented. Note that on the spread sheets included with this manual there are columns in which to describe the sources of data and to score their quality.

8. INTERVENTIONS TO IMPROVE DATA QUALITY FOR CASCADE ANALYSIS

Cascade analysis should be used to identify the priority problems that lead to inadequate data quality and to improve the quality. All data sources should be routinely evaluated for completeness, accuracy and timeliness. Dissemination of data is critical to ensure that findings are used and to ensure continued resource support for collection, analysis and dissemination of strategic information. Some key activities that can improve common data sources for cascade analysis are shown in Table 8.1.

Table 8.1 Suggested methods to improve data quality

Data source	Methods to improve quality
Spectrum	
Household surveys	Routinely ask participants to disclose their serostatus in addition to testing participants for HIV.
	Ask participants who self-report HIV infection if they are in care and on ART and test blood specimen for the presence of ARV.
	Conduct surveys more frequently than every five years.
	Conduct outreach prior to the survey to improve participation rates.
	Disseminate data using media that community members are likely to see and that acknowledges appreciation of participants and community leaders.
Surveys in key populations	Use robust sampling methods to obtain a representative sample.
	Routinely ask participants to disclose their serostatus in addition to testing them for HIV.
	Ask participants who self-report HIV infection if they are in care and on ART, and/or test blood specimen for the presence of antiretrovirals.
	Conduct surveys more frequently than every five years.
	Obtain buy-in from the target community to improve participation rates.
	Disseminate data using media that the community members are likely to see and that acknowledges appreciation of participants and community leaders.
Case-based surveillance	Conduct laboratory-based reporting.
	Implement or expand use of active surveillance methods.
	Implement a national identifier.
	Improve vital statistics to ascertain and remove deaths for better estimates of HIV prevalence.
	Routinely educate providers about the importance of case-based surveillance.
	Use standardized reporting forms and reporting at all facilities, including those in the private sector, that collect demographic, risk and personal identifier data for constructing disaggregated cascades and for de-duplicating records.
	Ensure that facilities have reporting protocols available for staff, that all new staff receive training on reporting requirements, and that data are routinely evaluated at facility, subnational and national levels with appropriate corrective action and supportive supervision.
	Disseminate findings to persons who report cases and to the broader community and end-users to ensure continued support for high-quality surveillance.
Programme data	Implement individual-level reporting from facilities to subnational and national levels.
	Implement methods to permit de-duplication of records – such as collecting names and national identifiers in all registers, medical records, laboratory logs, information management systems and requisition forms.
	Routinely educate providers on the clinical and programme importance of quality data.
	Provide feedback to those who complete programme reports on the quality of their data.

9. INTERPRETING AND USING DATA FROM CASCADE ANALYSES

The first step in reviewing findings from cascade analysis is to gain an understanding of the data's strengths and limitations. This is done initially as part of cascade analysis and is discussed in Chapter 7 of this manual. As the cascade data sources and findings are reviewed, there will be situations where additional information is needed to interpret the cascade results more fully.

9.1 Analysing cascade data

9.1.1 Assess plausibility

An initial review of the cascade should focus on whether the estimates appear to be reasonable in view of what is known. For instance, as one moves from the first towards the last, each indicator should be a proportion of the preceding indicator. It is possible for an indicator to amount to 100% of the previous indicator but not to exceed it. Implausible findings require further investigation and most likely will need to be revised using different data sources.

The source documents used to construct the cascade, as well as other sources, should be reviewed to help assess plausibility and to refine estimates. For instance, when interpreting a national cascade, it may help to look at subnational reports for indicator data to see if the national findings make sense. If the national numbers are lower than those from a summation of all subnational reports, then the national cascade data may be inaccurate. The estimates of persons currently on ART may come from programme monitoring reports but could be corroborated using pharmacy records. Results from research should also be reviewed to see if the cascade estimates are reasonable. Using multiple data sources can be useful to identify plausibility (or uncertainty) limits whereby indicators include lower and upper estimates around the point estimate.

Once the cascade estimates have been refined, the cascade results should be reviewed to identify the indicators that do not meet global targets, to prioritize areas for improvement and to make actionable recommendations and timelines.

9.1.2 Determine the most important findings

Begin by reviewing the cascade of the general population or KP. Next, identify the indicators in greatest need of intervention. Comparing the difference between the indicator and the target values should help to guide prioritization of programme areas in greatest need of intervention. For instance, in a cross-sectional cascade analysis, if 79% of PLHIV are on ART but only 50% have achieved virological suppression, countries should focus on understanding the factors – such as poor ART adherence – that impede achievement of viral suppression and should identify steps to improve adherence and hence suppression rates instead of trying to increase uptake of ART.

9.1.3 Identify populations most adversely affected

If available, review the cascade disaggregated by sex, age, geography, KP or other important variable to identify the indicators and populations in greatest need of intervention.

9.1.4 Consider the factors to address and the potential interventions

Review each indicator in need of improvement and the possible factors that may contribute to low indicator values and consider possible interventions.

9.2 Addressing gaps in the cascade

Multiple strategies have been evaluated to improve cascade performance. Broadly they group into 1) improving the proportion of PLHIV who have been diagnosed, 2) improving linkage to care following diagnosis, 3) improving ART coverage and 4) improving viral suppression.

9.2.1 Improving diagnosis

If a cascade shows a large difference between the estimated number of PLHIV and the number diagnosed (or reported in countries that employ case-based surveillance), a number of potential strategies can be employed (Box 9.1). In addition to seeking to improve diagnosis, another factor to consider is whether the number of PLHIV may have been overestimated. This may be particularly problematic in small and medium-sized countries with concentrated epidemics.

Box 9.1 Strategies for improving the proportion of PLHIV that have been diagnosed

- Better target and strategically expand HIV testing services in terms of population subgroups and geographical areas. Set priorities for HIV testing in terms of population groups (KPs, adolescents, infants, pregnant women, others) and geographical areas.
- Raise awareness of a need for HIV testing and emphasize the benefits of treatment for prevention among those at risk of HIV.
- Expand testing options such as self-testing, partner and peer referrals for testing or increased use of provider-initiated testing.
- Depending on the setting, raise awareness among providers working at various service entry points (e.g. TB, STI, antenatal care, well-child clinics) of a need to offer HIV testing to clients and provide test kits and reporting forms.
- Consider approaches that can be used to increase testing coverage in communities (e.g. NGOs, outreach sites, workplaces, schools/colleges, social media, sports or entertainment events).
- Determine provider attitudes and behaviours that may impede the offering or uptake of testing (e.g. stigma, confidentiality, linkage to and benefits of treatment, staff self-efficacy, competence in counselling and testing).
- Address structural factors to reduce barriers to testing (e.g. lack of transportation, inconvenient service hours).

9.2.2 Improving linkage to care

If there is a large gap between the proportion of PLHIV that have been diagnosed and the proportion that have entered care (or are on ART if the linkage-to-care indicator is not used), there are several options for improving the linkage. Gaps may exist either because PLHIV are not entering care after diagnosis or because they are not staying in care (Box 9.2).

Box 9.2 Strategies for improving linkage to care following diagnosis

- Implement same-day linkage through integration of facility-based testing and care services.
- Use patient navigators, especially for persons tested outside of treatment facilities.
- Expand or develop integrated services.
- Identify and address patient-level barriers to enrolment in care (e.g. stigma, family support), community-level barriers (stigma, discrimination) and structural barriers (laws, location of services).

9.2.3 Improving ART coverage

Improved ART coverage results from more rapid initiation of ART, as is envisioned in WHO guidelines *(1)*, or improved retention once patients start therapy (Box 9.3).

Box 9.3 Strategies for improving ART coverage

- Examine the need for additional financial and human resources.
- Identify methods such as data systems for improved supply chain.
- Eliminate required psychosocial and medical eligibility assessments before ART initiation.
- Provide patient counselling and support to address concerns about stigma and discrimination.
- Reduce frequency of ART refills and follow-up visits.
- Decentralize care and treatment services.
- Expand clinic and pharmacy hours.
- Use patient navigators/case managers to assist patients with transportation or other personal barriers to obtaining ART or attending the clinic.
- Provide home delivery of ART refills.
- Use SMS reminders for improved ART adherence.
- Conduct community education campaigns on the benefits of ART and the importance of adherence.
- Diagnose and treat impeding co-morbidities such as substance use and mental health disorders.

9.2.4 Improving viral suppression

WHO defines the virological suppression indicator as the proportion of patients who have fewer than 1000 copies/μL. To achieve this, adherence to ART is crucial. While there may be some low-level background primary ART resistance, most PLHIV on ART who fail to achieve virological suppression within 6 months of initiation are much more likely to show secondary rather than primary resistance and are most amenable to adherence counselling as a first-line intervention. Nevertheless, it must be borne in mind that supply chain problems – stock-outs and other issues that effect availability and accessibility – are common in low- and middle-income countries and may account for widespread failure to achieve virological suppression. Potential interventions are listed in Box 9.4.

Box 9.4 Strategies for improving the proportion of PLHIV on ART that are virologically suppressed

- Develop laboratory capacity for routine viral load testing.
- Implement effective and efficient methods for specimen transport and return of results.
- Ensure adequate supply reagents and other supplies.
- Conduct laboratory quality assurance.
- Ensure that patients receive their results in a timely manner.
- Improve knowledge of status and ART uptake and adherence.
- Monitor drug resistance through surveillance and address through improved ART adherence.

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ANNEX: SUPPLEMENTAL INDICATORS

1. Supplemental indicators for a cross-sectional HIV care cascade

Countries may wish to consider three other indicators, although these do not use PLHIV as the denominator. For this reason, they are presented separately from the basic indicators.

1.1 Supplemental indicators and data sources

Supplemental indicator 1. Number and proportion of PLHIV who initiated and are retained on antiretroviral therapy 12 months after initiation

There are three data sources for the numerator: 1) case-based surveillance, 2) population-based surveys and 3) programme data.

Case-based surveillance data. To calculate this indicator there must have been at least 12 months of follow-up. For example, if the cascade reporting period is 1 January 2014 to 31 December 2014, data must be collected at least up to the end of 2015 in order to allow for persons who initiated ART at the end of 2014 to have had at least 12 months of follow-up. The numerator is the number of persons on ART during a specified time period (e.g. as of 31 December 2014), and the denominator is the number of persons who initiated ART in 2014, were receiving ART for 12 or more months after beginning ART and were alive as of 31 December 2015.

Programme data. This indicator is best calculated when constructing a cascade for a given period of time (i.e. as of a specific date) rather than cumulatively. As with case-based surveillance data, the numerator will be number of persons who initiated ART within the specified time frame and who were retained on ART 12 months later. In addition to requiring at least 12 months of follow-up time for persons who initiated ART at the end of the cascade time frame, monthly cohorts should be analysed; the numerator will be those who remain on ART 12 months after initiation, and the denominator will be persons who initiated ART in the specified month.

Population-based survey data. Surveys that ask participants if they are HIV-infected (with the dates of diagnosis, entry into care and ART initiation) and whether they are currently on ART can be used to calculate participants who initiated ART if the timing of the survey allows for at least 12 months of follow-up from the date of ART initiation. The denominator is the number of persons who initiated ART at least 12 months prior to the survey, and the numerator is the number of persons who reported currently receiving ART. This analysis generally requires the ability to construct and compare dates.

Supplemental indicator 2. Number and proportion of PLHIV who on ART who had a viral load test result in 12 or fewer months after ART initiation

There are three data sources for the numerator: 1) case-based surveillance, 2) population-based surveys and 3) programme data.

Case-based surveillance data. The use of case-based surveillance must allow for at least 12 months of follow-up. The numerator is the number of persons on ART who had a viral load test within the 12 months after initiation, and the denominator is the number of PLHIV who initiated ART and had at least 12 months of follow-up as of the end of the follow-up period.

Programme data. This indicator is best calculated when constructing a cascade for a given period of time (i.e. as of a specific date) rather than cumulatively. The numerator is the number of persons on ART who had a viral load test within the 12 months after ART initiation in a specified time period (e.g. 1 January 2014 to 31 December 2014), and the denominator is the number of PLHIV who initiated ART and were alive and in care at least 12 months after initiating ART (e.g. as of 31 December 2014).

Population-based survey data. Surveys of participants who disclose that they are HIV-infected can be used to calculate this indicator if the survey obtains the dates of diagnosis, entry into care and ART initiation and asks if and when these persons had their most recent viral load test. The denominator is persons who initiated ART at least 12 months prior to the survey, and the numerator is the number who reported that their most recent viral load test was within 12 months of ART initiation. This analysis generally requires the ability to construct and compare dates.

Supplemental indicator 3. Number and proportion of persons who are on ART who achieved viral suppression (<1000 copies/mL) 12 or fewer months after initiating ART

Case-based surveillance data. Time frames including follow-up time must be taken into consideration when calculating this indicator. For example, if the cascade reporting period is 1 January 2014 to 31 December 2014, the numerator is the number of persons whose last viral load test as of 31 December 2015 was <1000 copies/mL), and the denominator is the number of persons who initiated ART in 2014 and were alive as of 31 December 2015.

Programme data. This indicator is best calculated when constructing a cascade for a given period of time (i.e. as of a specific date) rather than cumulatively. The numerator is the number of persons on ART who had a viral load test within 12 months after ART initiation in a specified time period (e.g. 1 January 2014 to 31 December 2014) and whose most recent result was <1000 copies/mL. The denominator is the number of PLHIV who initiated ART and were alive and in care at least 12 months after initiating ART (e.g. as of 31 December 2014).

Population-based survey data. Surveys can be used to calculate this indicator if the survey asks participants if they are HIV-infected (and obtains the dates of diagnosis, entry into care and ART initiation) and also asks if and when they had their most recent viral load test and the result of that test (suppressed or unsuppressed). The denominator is persons who initiated ART at least 12 months prior to the survey, and the numerator is the number who reported that their most recent viral load test was within 12 months after ART initiation and that the most recent result indicated that they were suppressed. Although definitions of viral suppression may differ, it is acceptable to use the survey results without knowing what the definitions of suppressed were. This analysis generally requires the ability to construct and compare dates.

2. Supplemental indicators for a longitudinal (cohort) HIV care cascade

2.1 Supplemental indicators and data sources

Supplemental indicator 1. Number and proportion of people diagnosed with HIV in one calendar year who are retained on ART 12 months after ART initiation (or longer [e.g. 24, 36, 48, 60 months etc.] if data are available)

It is likely that only programme data such as those from patient monitoring systems can be used for this indicator.

This indicator requires at least 12 months of follow-up after allowing for initiating ART within one month of diagnosis. Consider a patient who is diagnosed on 31 December 2014 and initiates ART on 30 January 2015. In order for it to be possible for a patient to be retained on ART for at least 12 months after starting ART, data must be available at least through to the end of January 2016. Therefore, the availability of data must be considered before the most appropriate retention time frame for examination can be selected.

The numerator is persons diagnosed with HIV during the specified period who are alive and on ART 12 months after initiation of ART. For example, if the denominator is the number of persons diagnosed in 2014, data from patient monitoring systems must be available through to the end of 2015. For calculating a longer retention period, such as 24 months, follow-up patient monitoring data must be available to the end of 2016.

Supplemental indicator 2. Number and proportion of people diagnosed with HIV in one calendar year and on ART who received viral load testing 6-12 months after ART initiation

This indicator may be of value in settings where viral load testing may not be conducted in a timely manner. In this situation, this supplemental indicator may be used in place of the core indicator 4 on viral suppression. The time frame was selected because WHO guidelines recommend measuring viral load 6 months after ART initiation and allowing for some delays in obtaining viral load tests. This indicator should be measured only in settings where patients are routinely monitored using viral load results.

It is likely that only programme data, such as those from patient monitoring systems, can be used for this indicator. However, in settings with laboratory databases or information management systems with un-duplicated records of viral load test requests, results and dates, data may be obtained from these systems.

The numerator is the number of persons diagnosed with HIV during the specified period and who initiated ART and had evidence of a viral load test result 6-12 months after initiating ART. Evidence of viral load testing includes documentation of a request for a viral load test in the laboratory database or a test result in the patient monitoring system. This indicator requires at least 12 months of follow-up.

Supplemental indicator 3. Number and percentage of people newly diagnosed with HIV in one calendar year who are virally suppressed longer than 12 months after ART initiation (e.g. 24, 36, 48, 60 months etc.)

There are three possible data sources for the numerator: 1) case-based surveillance data, 2) programme data (patient monitoring data) and 3) laboratory data.

Case-based surveillance or programme data. This indicator must allow for more than 12 months of follow-up after ART initiation (e.g. 24, 36, 48 or 60 months) and should be obtained from settings where viral load testing is carried out as part of routine patient monitoring. A specific time period will need to be determined, and there must be a sufficient period of follow-up to measure this indicator. The numerator is the number of persons newly diagnosed in the specified time period who are alive 12 or more (e.g. 24) months after ART initiation and whose viral load test result closest to 24, 36, 48 or 60 months after diagnosis is <1000 copies/mL. The denominator is the number of persons on ART for 24, 36, 48 or 60 months.

Laboratory data. In settings with a national, subnational or facility-level laboratory database or information management system with un-duplicated records and that can be linked to programme data that can identify persons on ART for 24, 36, 48 or 60 months, the numerator is the number of persons whose most recent viral load is less than 1000 copies/mL. The denominator is the number of persons on ART for 24, 36, 48 or 60 months.

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