Chapter 2

Global Mortality and Morbidity of HIV/AIDS

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INTRODUCTION

The HIV/AIDS epidemic has seen dramatic shifts since the first cases were described in 1981. Initially perceived as a disease among gay men or Haitians in Western countries, HIV transmission has been reported in virtually all parts of the world. Prevalence levels in the 1990s reached more than 30 percent among adults in many Sub-Saharan African cities, and no accessible, effective treatment was available. Although treatment was available for a limited number of people in wealthier settings shortly after the studies on triple therapy in 1996, mortality nevertheless soared, particularly in Sub-Saharan Africa, slashing the hard-won gains in life expectancy resulting from social and economic development and advances in medical technology and nutrition (United Nations Population Division 2004) by more than a decade within a few years.

Since 2000, remarkable progress has been made in the diagnosis and treatment of persons living with HIV/AIDS. With medications now affordable at a cost of approximately US$129–$568 per person per year even in the hardest hit countries (Bendavid and others 2010; Menzies, Berruti, and Blandford 2012; PEPFAR 2013; UNAIDS 2015a; Walensky and others 2013), 17 million people were receiving antiretroviral therapy (ART) in 2015. The international targets are to treat nearly three-quarters of those living with HIV/AIDS by 2030 (UNAIDS 2012, 2014b, 2015b, 2016b; WHO 2013c).

ART has reduced HIV/AIDS morbidity and mortality significantly (Cohen and others 2011; Danel and others 2015; INSIGHT START Study Group 2015; Kitahata and others 2009; Lopez-Cortes, Gutierrez-Valencia, and Ben-Marzouk-Hidalgo 2016; Lundgren, Babiker, and Neaton 2016; Médecins Sans Frontières 2013; Montaner and others 2006; SMART Study Group and others 2006; Sterne and others 2009; Violari and others 2008). In high-income countries (HICs), access to early treatment has led to near-normal life expectancy for persons living with HIV/AIDS (Johnson and others 2013; May and others 2014; Rodger and others 2013; Samji and others 2013). As a result, the focus of clinical care of HIV/AIDS in these settings has shifted from treatment of a usually fatal infectious disease with multiple comorbidities (see chapter 4 [Harripersaud and others 2017] and chapter 11 [Bloom and others 2017] of this volume) to management of a chronic condition and prevention of illness, death, and transmission for individuals who remain adherent to treatment (Attia and others 2009; Cohen and others 2011; Das and others 2010; Fang and others 2004; Montaner and others 2010).

New Focus on Treatment and Care

Treatment access and care recommendations have dramatically changed all over the world since the second edition of *Disease Control Priorities in Developing Countries* (Jamison and others 2006) (Bertozzi and others 2006; WHO 2010, 2013a, 2015b). Accumulating evidence definitively demonstrates that treatment reduces morbidity and mortality, irrespective of disease stage or

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immunological competence, for example, CD4 level (Danel and others 2015; INSIGHT START Study Group 2015; Kitahata and others 2009). Treatment simultaneously prevents onward transmission (chapter 5 in this volume, Holmes and others 2017; Attia and others 2009). Accordingly, the dream of ending the epidemic as a public health threat by 2030 (UNAIDS 2015d) no longer seems impossible.

Expanded Surveillance

The drive to end the epidemic has resulted in the expansion of surveillance. In addition to tracking the burden of incidence, prevalence, and mortality, programs now track success in meeting the 90-90-90 targets as part of their efforts to monitor and evaluate the continuum of care (IAPAC 2016; UNAIDS 2014e, 2015c, 2016b).

The new focus on care in treatment is reflected in the recent changes in the World Health Organization's (WHO) guidelines (2015b) and demonstrated by the 90-90-90 campaign of the Joint United Nations Programme on HIV/AIDS (UNAIDS), which recommend treating infected individuals as soon as possible. These 90-90-90 targets propose achievement of the following by 2020:

- Ninety percent of all people living with HIV/AIDS will know their HIV/AIDS status
- Ninety percent of people with diagnosed HIV/AIDS infection (or 81 percent of all people living with HIV) will receive sustained ART
- Ninety percent of all people receiving ART will be virally suppressed—that is, will achieve 73 percent population-based suppression in people living with HIV (UNAIDS 2014a). Achieving 90-90-90 is the first step to ensuring access to treatment for nearly everyone by 2030, which could lead to ending AIDS as a public threat, as well as the virtual elimination of HIV transmission in many settings (Granich 2016).

The UNAIDS Fast-Track Targets for 2020 (Stover and others 2016) include reducing by 75 percent the number of people newly infected annually (compared with 2010), with zero new infections among children, and reducing the annual number of people dying from HIV/AIDS-related causes to fewer than 500,000. These targets are the next steps to the even more challenging yet achievable 95-95-95 goals for 2030, when annual deaths related to HIV/AIDS should be fewer than 200,000 and incidence should be reduced by 90 percent (compared with 2010).

Some may argue that this is an aspirational slogan, but assessing accomplishments in care is consistent with recent recommendations by the U.S. Centers for Disease Control (CDC) (AIDS.gov 2017). In addition, these targets are subject to meaurement challenges (many of which are described subsequently); however, they are critical to address success in epidemic control. Although measurement of disease burden is informative, it falls short of meeting needs in public health for which the influences of positive health—such as successes in care and treatment—must also be tracked (Thacker and others 2006).

In addition to monitoring regional burdens, more precise surveillance tools, including geospatial mapping and targeted surveillance, have uncovered microepidemics concentrated in small regions and in key, vulnerable populations, which heretofore might have been missed. The availability of such detailed surveillance data at subnational and smaller local levels has revealed the microepidemics defined by locality or risk group that fuel generalized epidemics in Sub-Saharan Africa (Tanser and others 2014). Although we address this phenomenon in this chapter, more extensive detail about the concentration of infection among key populations and risk groups is provided in chapter 8 of this volume (Wilson and Taaffe 2017).

Chapter Content

This chapter is divided into two sections. The first describes the distribution of surveillance indicators for effective monitoring of national HIV/AIDS programs. These indicators include the conventional, key outcomes of mortality and morbidity—incidence, prevalence, and disability-adjusted life years (DALYs)—as well as more recent indicators that reflect the pivot to ending the epidemic: tracking 90-90-90 targets and examining surveillance in smaller units of analysis, including microepidemics and key populations. The second part of the chapter addresses challenges in the measurement of all of these indicators.

Subsequent chapters in this volume address current cost-effective approaches for treatment (chapter 5, Holmes and others 2017), prevention of mother-to-child transmission (chapter 6, John-Stewart and others 2017), and combination prevention (chapter 7, Garnett and others 2017). The burden, prevention, and management of HIV/AIDS-related comorbidities, including other sexually transmitted infections and tuberculosis, are discussed in chapter 10 (Chesson and others 2017) and chapter 11 (Bloom and others 2017) of this volume. The goal of this chapter is not to provide a complete review of available data on burden, but rather to situate this volume—volume 6, *Major Infectious Diseases*—of the third edition of *Disease Control Priorities* (*DCP3*) in the context of an HIV/AIDS epidemic and response that is at a turning point.

DISTRIBUTION OF KEY EPIDEMIC MEASURES: MORTALITY, INCIDENCE, PREVALENCE, AND DALYS

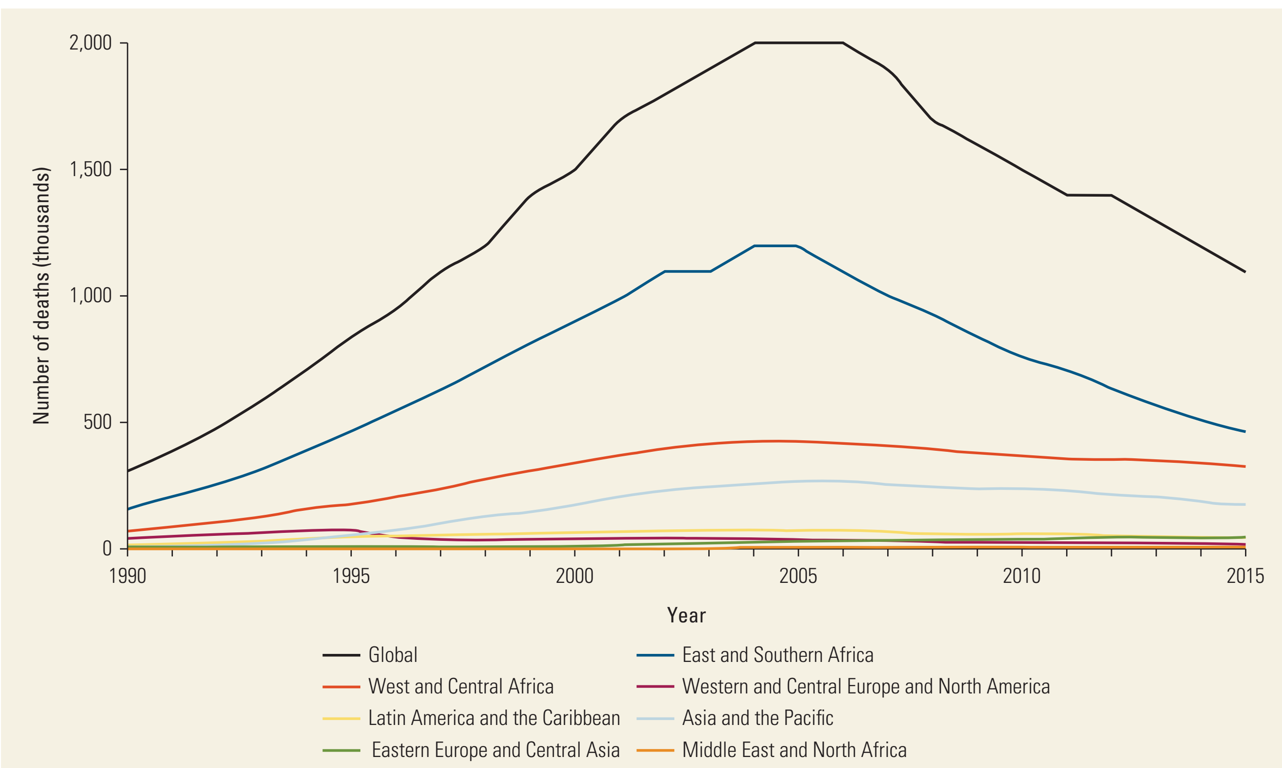
Given the outsized importance of HIV/AIDS among donors and global health organizations, a variety of sources for burden of disease estimates at global and national levels exist, such as UNAIDS, the WHO, and the Institute for Health Metrics and Evaluation (UNAIDS 2016a; Wang and others 2016; WHO 2013b). To maintain consistency with the other volumes in the *DCP3* series and the chapters that follow in this volume, we focus primarily on data from two sources, UNAIDS and the WHO's Global Health Estimates, supplemented with country-specific studies, where relevant, for illustrative purposes. No estimate is without limitations, and the UNAIDS and WHO figures are no exception. These limitations are discussed in a later section, titled "Measurement: Challenges in Surveillance."

Global and Regional Trends in Mortality

Global trends in AIDS-related mortality reveal the remarkable success of HIV treatment and other prevention. Deaths peaked at just more than 2 million per year from 2004 to 2005 (figure 2.1) and have been steadily declining since, driven primarily by gains in Sub-Saharan Africa. The 1.1 million individuals who lost their lives to AIDS in 2015 represent the lowest number since 1998, and this number was 45 percent lower than at the peak of the epidemic (UNAIDS 2016a, 2016b). Despite this progress, high-burden countries will need to accelerate access to ART treatment to avert millions of premature AIDS deaths and new HIV infections (Granich and others 2015).

Despite these gains, AIDS remains a significant cause of death, and global trends mask persistent regional and subregional variation. AIDS is the sixth-leading cause of death globally and the leading cause in Sub-Saharan Africa, a fact that has not changed since 2000, despite the 41 percent decline in the region's AIDS-related mortality rate. AIDS was responsible for one in nine deaths in the WHO's African region in 2012 (WHO 2013b). In contrast to declining rates in Sub-Saharan Africa, AIDS-related mortality rates per 100,000 population from 2000 to 2012 increased from 3.6 to 10.2 in Europe, from 2.7 to 5.6 in the Eastern Mediterranean Region, and from 1.6 to 3.2 in the

Figure 2.1 Number of Deaths Related to AIDS, 1990–2015



Source: Based on UNAIDS 2016a.
Note: AIDS = acquired immune deficiency syndrome.

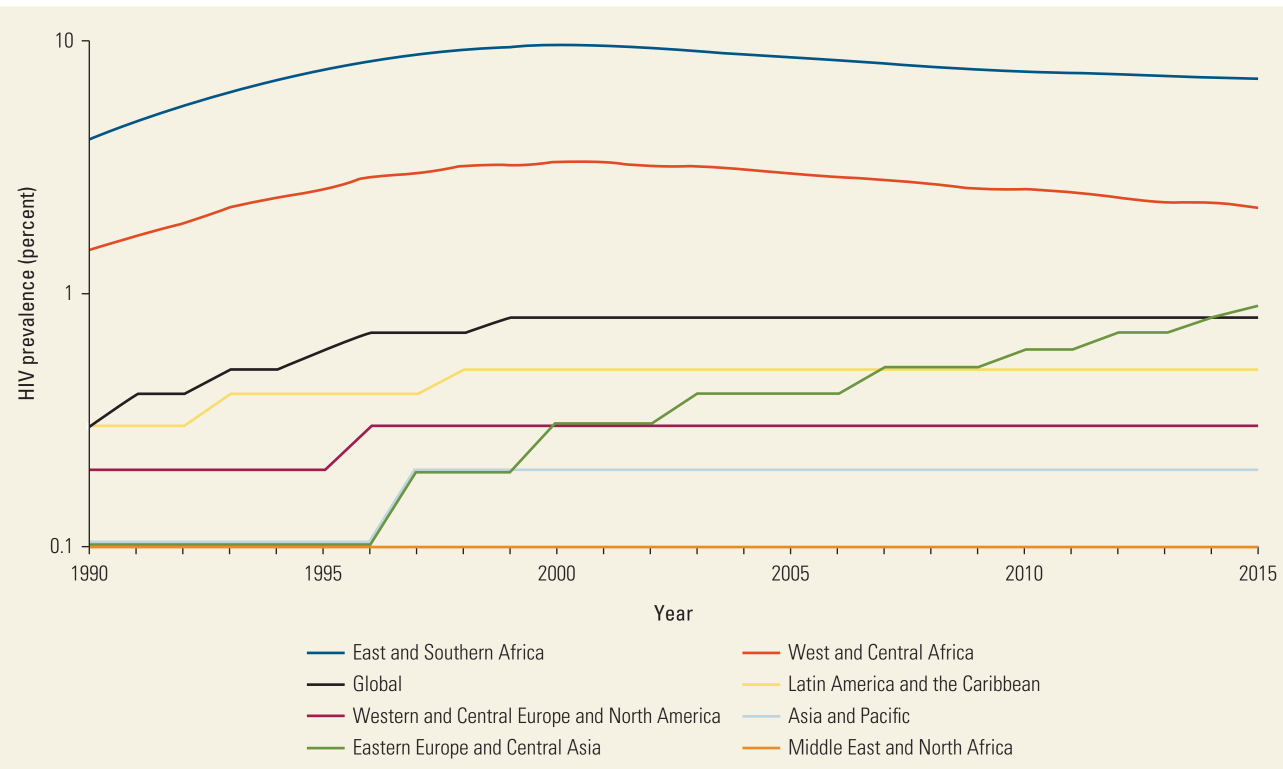
Western Pacific Region. The numbers of AIDS-related deaths in Europe and the Eastern Mediterranean Region have also been steadily increasing and have tripled since 2000 (WHO 2013b).

Morbidity: Incidence and Prevalence

Trends in HIV/AIDS prevalence are similar to those of mortality, although one must note that by definition, increased treatment results in increased prevalence. In the current era of massive global antiretroviral scale up, with plans for reaching millions more (UNAIDS 2012, 2014b; WHO 2013c), there are critical drivers of changing morbidity in persons living with the disease. Most important, with earlier initiation of ART and improved access to care, persons with HIV are living longer (Kitahata and others 2009; Sterne and others 2009; SMART Study Group and others 2006; U.S. National Institutes of Health 2015; Violari and others 2008) and therefore are experiencing the health consequences of aging. This is an outcome of improved treatment options and increased access to interventions that lead to longer lives. Global prevalence rates peaked in 2001, three years earlier than AIDS-related mortality peaked, and they have been slowly declining or have plateaued over the past decade in most regions (figure 2.2). The trends in prevalence reveal that HIV/AIDS remains a predominantly East and Southern Africa health challenge, with a 2014 prevalence of 7.4 percent, more than triple that of the western and central part of the continent. However, low prevalence rates in low disease burden settings still present major challenges, even, for example, in the United States (Del Rio 2015). More to the point, although prevalence rates are currently low in Eastern Europe and Central Asia, they are the only regions where prevalence rates are still rising, with rates increasing from 0.1 percent in 1990 to 0.8 percent in 2014.

A central focus of the new UNAIDS goals is a 75 percent reduction in new infections (compared with 2010) by 2030. Models of incidence suffer from significant methodological limitations, which are discussed later in this chapter in the section on measurement challenges. Incident infections have fallen substantially since their peak of an estimated 3.5 million per year in 1997 to 2.1 million in 2015. However, current projections from UNAIDS and the Institute of Health Metrics and

Figure 2.2 Trends in HIV Prevalence, by Region, 1990–2015



Source: Based on UNAIDS 2016a.
Note: HIV = human immunodeficiency virus.

Evaluation indicate that, in general, the world is not yet on track to meet the UNAIDS goal (UNAIDS 2016a; Wang and others 2016); new infections declined 14 percent globally between 2010 and 2014 (UNAIDS 2016a). Although HIV prevalence remains heavily concentrated in Africa, other regions have also emerged as important sources of new infections (figure 2.3). Between 1990 and 2015, the proportion of incident infections in East and Southern Africa steadily declined from 59 percent to 46 percent, and those in Eastern Europe and Central Asia and Asia and the Pacific steadily increased from 1 percent to 9 percent and from 10 percent to 15 percent, respectively. While these relative relationships are informative, the assumptions underlying incidence models, and thus current and future projections, are likely to be revised as new empirical data improve our knowledge about the effect of ART scale-up on HIV-transmission rates in these regions.

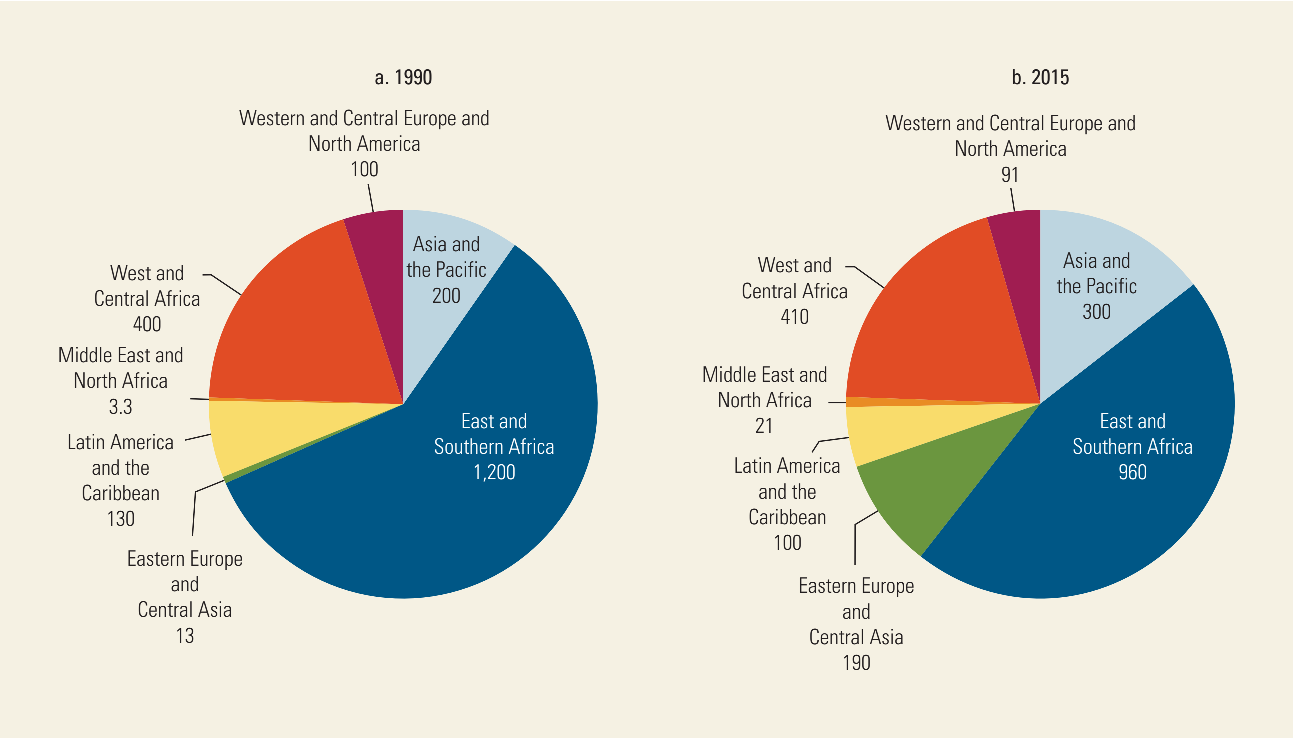
Morbidity: Disability-Adjusted Life Years

In 2012, 91.9 million DALYs were lost worldwide because of HIV/AIDS, second only to diarrhea in terms of morbidity from infectious disease and seventh overall, but nevertheless representing a 9.6 percent decrease from 2000. In 2012, by region, Africa accounted for 66.8 million DALYs lost (72.7 percent); South-East Asia, 11.8 million (12.8 percent); Europe, 4.5 million (4.9 percent); Eastern Mediterranean, 2.0 million (2.2 percent); Western Pacific, 3.3 million (3.6 percent); and the Americas, 3.5 million (3.8 percent). HIV/AIDS is still the leading cause of morbidity in Africa, but DALYs lost declined 19.2 percent since 2000 (WHO 2013b). The Global Burden of Disease data present lower absolute values for DALYs (69.4 million in 2013), but show a similar decline from 2000 to 2013 (IHME 2016b).

As with mortality and incidence, these regional numbers mask significant subregional variation. In the African region, 31 percent of all DALYS lost in Botswana were due to HIV/AIDS (324,000), compared to 6.9 percent of DALYs in Ethiopia (3,353,000) and 4.3 percent of DALYs in Eritrea (126,000) (WHO 2013b).

The trends in global DALYs show both the promise of ART and the gap that remains in getting effective treatment to all who need it and ensuring adherence among those receiving it. The decline in DALYs is driven largely by reductions in AIDS deaths, and thus the pattern of DALYs lost because of HIV/AIDS parallels that for

Figure 2.3 Proportion of Incident HIV Infections, by Region, 1990 and 2015
thousands



Source: Based on UNAIDS 2016a.
Note: HIV = human immunodeficiency virus.

mortality (Wang and others 2016). Although deaths decreased 18 percent between 2000 and 2012, morbidity declined by only 9.6 percent (UNAIDS 2016a; WHO 2013b). One contributing factor is that a small but important portion of morbidity is due to years lived with disability, which has plateaued since 2005, driven in part by the estimated 46 percent of HIV-positive individuals globally who are not currently on ART (IHME 2016a; UNAIDS 2016b; Wang and others 2016). Among those who are, fewer than half remain virally suppressed three years after initiating treatment (UNAIDS 2015b; WHO 2015a). A better understanding of the structure and composition of epidemics, including global resource allocation for AIDS (Granich and others 2016) within countries, is an essential next step as the world shifts from trying to manage the epidemic to trying to end it.

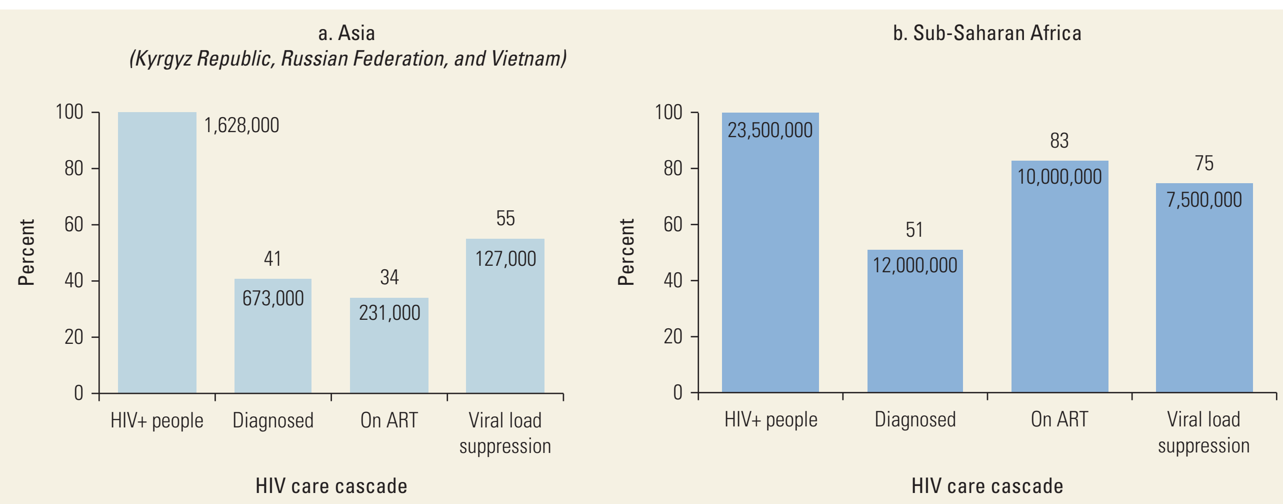
REACHING THE 90-90-90 TARGETS

Tracking progress toward the achievement of the 90-90-90 targets is a central challenge for surveillance efforts, particularly in measurement, given the lack of individual cohort data from most regions. Moreover, the methods used to determine the national cascades included in estimating regional cascades often vary and often do not follow the WHO recommendations. The lack of viral load data necessary for estimating the final component of the cascade is particularly problematic because the data are not available to most people living with HIV (UNAIDS 2014e). As such, regional cascade results should be viewed with considerable caution. Nevertheless, even these suboptimal estimates reveal critical trends. Perhaps more important, especially with regard to comparative estimates across countries or regions or over time, the data enforce the value of monitoring the health outcomes that are essential for epidemic control.

Preliminary estimates from Levi and others (2016), based on data from 69 countries for which data were available, show that progress is uneven.

Progress in achieving the first 90 percent in predominantly high-income regions is encouraging; in six out of nine countries across North America, Australasia, and Western Europe, 80 percent or more of individuals know their HIV status. In the majority of these countries, the most significant gap is the proportion of HIV-positive individuals who currently receive ART. Conversely, in lower-income regions, the need for scaled-up testing services coupled with demand creation to meet the first 90 percent target is great. For example, data from Levi and others (2015) for countries where full treatment cascades were available in the African and Asian regions suggest that fewer than half of all HIV-positive individuals are aware of their status (figure 2.4). In Sub-Saharan Africa, the majority of those who know they are HIV-positive are successfully initiated on ART, and roughly 75 percent achieve viral suppression. For the Kyrgyz Republic, the Russian Federation, and Vietnam, fewer than 35 percent of those who know they are HIV-positive are successfully

Figure 2.4 Cascade of HIV Care in Africa and Asia



Sources: Adapted from data from Levi and others 2015; UNAIDS 2015e.
Note: ART = antiretroviral therapy; HIV = human immunodeficiency virus. The numbers above each bar represent the number of individuals at that stage as a proportion of the number of individuals at the preceding stage. Sub-Saharan Africa viral load data from Botswana, Burkina Faso, Cameroon, Côte d'Ivoire, Kenya, Malawi, Mali, Mozambique, Nigeria, Senegal, South Africa, Tanzania, Uganda, Zambia, and Zimbabwe.

initiated on ART, and among these, only about half are virally suppressed. Data such as these, which are essential to inform program planners where to effectively invest resources, illustrate the uneven progress of regions toward achievement of the 90-90-90 targets. These data also reinforce how success cannot be realized without consideration of the complete cascade. Although rates of viral suppression among those on ART in the 15 Sub-Saharan African countries with data available are high, the very low rates of diagnosis mean that, overall, fewer than 32 percent of HIV-positive individuals in those countries are virally suppressed.

REGIONAL MICROEPIDEMICS AND KEY POPULATIONS

Regional Microepidemics

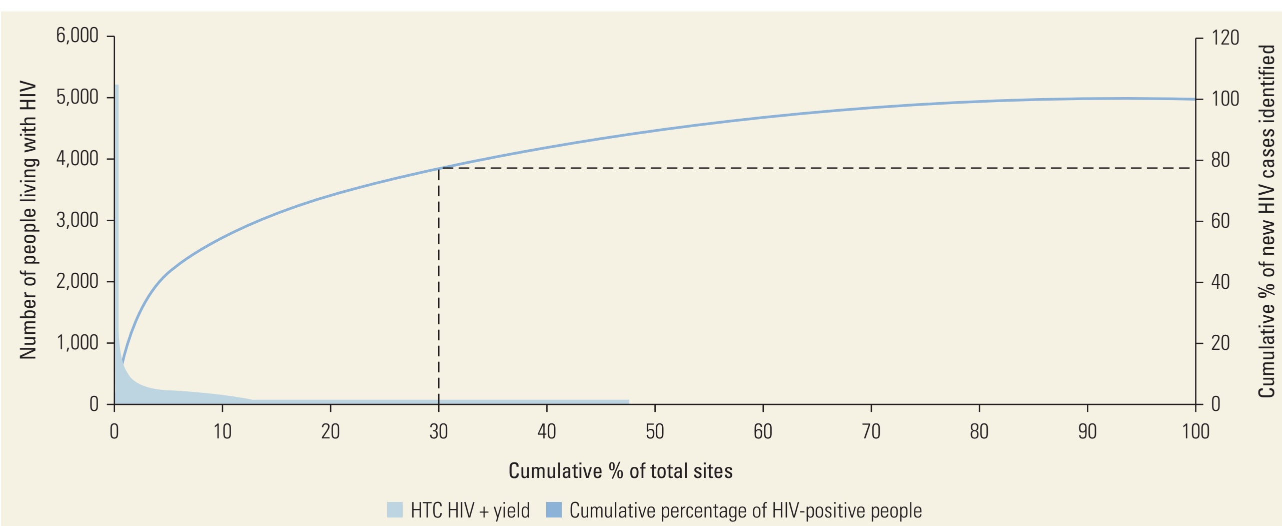
Global and regional estimates conceal significant country-level heterogeneity and within-country variability that is characterized by microepidemics—pockets of illness concentrated among specific populations and smaller subnational geographic regions. In Brazil, most AIDS cases and HIV infections occur in fewer than 10 percent of the country's 5,570 municipalities (UNAIDS 2014c). In India, national prevalence was only 0.4 percent in 2011, but 71 of 672 districts had a prevalence of ≥ 1.0 percent. Three-quarters of these 71 districts are located in the southern and northeastern parts of the country (National AIDS Control Organisation 2012).

Similarly, although the epidemic is disproportionately concentrated in countries of East and Southern Africa, pockets of high rates of transmission within countries are driving the spread of the disease. Data from 1,724 sites supported by the President's Emergency Plan for AIDS Relief (PEPFAR) and community-based services in Zimbabwe show that from October 2013 to September 2014, approximately 80 percent of all newly diagnosed people living with HIV/AIDS were identified by only 30 percent of sites (figure 2.5).

One of the earliest studies to investigate subnational analyses examined geospatial data on HIV/AIDS in KwaZulu-Natal, South Africa (MEASURE Evaluation 2016; Tanser and others 2009). Within a relatively homogeneous population, where age-adjusted prevalence was 27 percent for women and 14 percent for men, local prevalence had notable spatial variation, with three very-high-prevalence clusters (approximately 36 percent) along the main national road and three relatively low-prevalence clusters (6 percent) (Tanser and others 2009). In another study, Magadi (2013) examined spatial distribution of HIV/AIDS infection in relation to various demographic factors. She found that the urban poor in Sub-Saharan Africa had significantly higher rates of infection than did their urban nonpoor counterparts and that the well-documented higher risk among women was amplified among the urban poor.

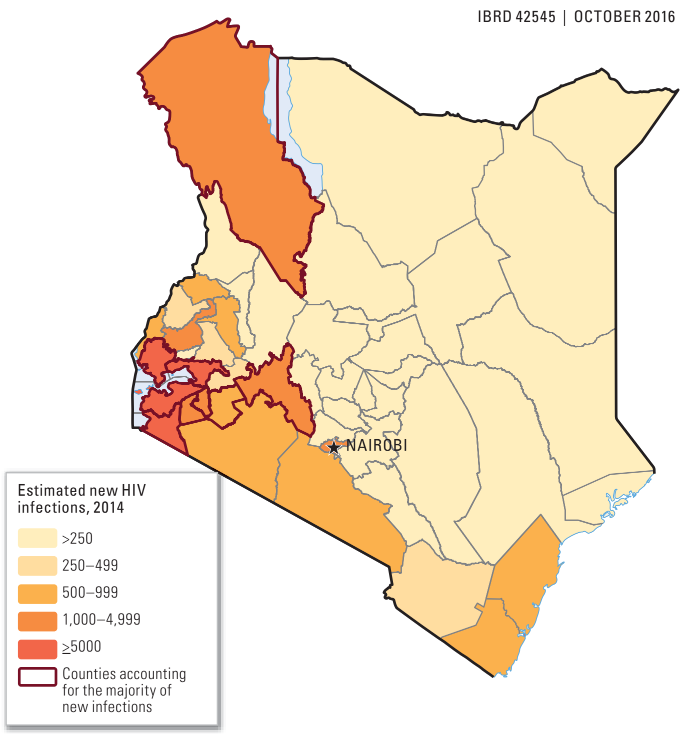
Anderson and others (2014) modeled and demonstrated the importance of targeting prevention services, including early treatment, to microepidemics. For example, in Kenya, just 9 of 47 counties represented an

Figure 2.5 HIV Diagnoses Yield from PEPFAR-Supported Testing Sites, Zimbabwe, 2013–14



Source: UNAIDS 2015d.
Note: HIV = human immunodeficiency virus; HTC = HIV testing and counseling; PEPFAR = President's Emergency Plan for AIDS Relief.

Map 2.1 Estimated New Infections in Kenya, 2014



Source: UNAIDS 2015d.

estimated 65 percent of all new infections, and HIV prevalence varied substantially across counties, from less than 1 percent to 22 percent in 2014 (map 2.1) (UNAIDS 2015d). Similar uneven regional variation can also be seen in the United States (map 2.2) and in many other countries. Using these data to model the rollout of prevention programs, Anderson and others (2014) demonstrated that a focused approach using local epidemiologic data to direct prevention programs would achieve greater effect than would a uniform approach for the same amount of investment. Such focused surveillance is necessary for a more targeted response to the epidemic and is the hallmark of PEPFAR 3.0 and the pivot to a data-driven approach that strategically targets microepidemics, hot spots, and key populations.

Key Populations

Defining Key Populations

The emergence of smaller, subnational regions as substantial contributors to incident infections is due in part to the presence of key populations, traditionally defined as people who inject drugs, commercial sex workers, and men who have sex with men (MSM), (addressed more fully in chapter 8 of this volume [Wilson and Taaffe 2017]), and more recently, young women and mobile migrant populations in Sub-Saharan Africa. Given that issues related to stigma, discrimination, and punitive legislations make tracking these groups extremely challenging, some patterns are clear. High rates of transmission among people who inject drugs and among sex workers are the main drivers of new infections in the Middle East and North Africa, and MSM is the main contributor in Latin America and the Caribbean. In Pakistan, transmission to female spouses of HIV-positive injection drug users and bisexual men, and subsequently to children through mother-to-child transmission, is a critical source of new infections in these regions. Patterns vary substantially across countries in Eastern Europe and Central Asia with respect to the relative contribution of such key populations (Gouws and Cuchi, on behalf of the International Collaboration on Estimating HIV Incidence by Modes of Transmission 2012), which is limited by the severe lack of data and signficant issues in surveillance discussed subsequently. Similarly, the pattern within Africa is mixed. In Kenya, HIV/AIDS overall prevalence among key populations is extremely high at 5.3 percent: 29 percent among sex workers, 18 percent among MSM, and 18 percent among people who inject drugs (UNAIDS 2015d, 2016a).

Other key populations include prisoners and individuals in the military, for whom regional statistics are sorely lacking. The risk of infection among transgender people has recently emerged as a public health emergency. Although the global picture of HIV/AIDS among transgender people is varied—with HIV prevalence ranging from 8 percent to 68 percent—transgender people are among the groups most affected by HIV/AIDS, particularly in the Latin America and the Caribbean and Asia and the Pacific regions (WHO 2011).

These studies highlight the assumption that significant proportions of new HIV infections, even in Sub-Saharan Africa, may occur among key populations (Hirnschall 2015). This means that no way exists to fully end the epidemic without addressing infections in these key populations, even though stigma, social norms, and legal restrictions present formidable challenges to identifying and engaging them in programs for prevention or care (Wilson and Taaffe 2017).

A deeper dive into the statistics in the United States reveals that minority race, especially African Americans, constitutes another key population. African Americans are overrepresented among people living with HIV in every region in the United States. In contrast, Asians and Caucasians constitute the proportion of the population with the lowest infection rates. Notably, adjusting for poverty reduces the magnitude of these differences,

Map 2.2 Rates of Persons Ages 25–34 Years Living with HIV/AIDS Diagnosis, by County, United States, 2013

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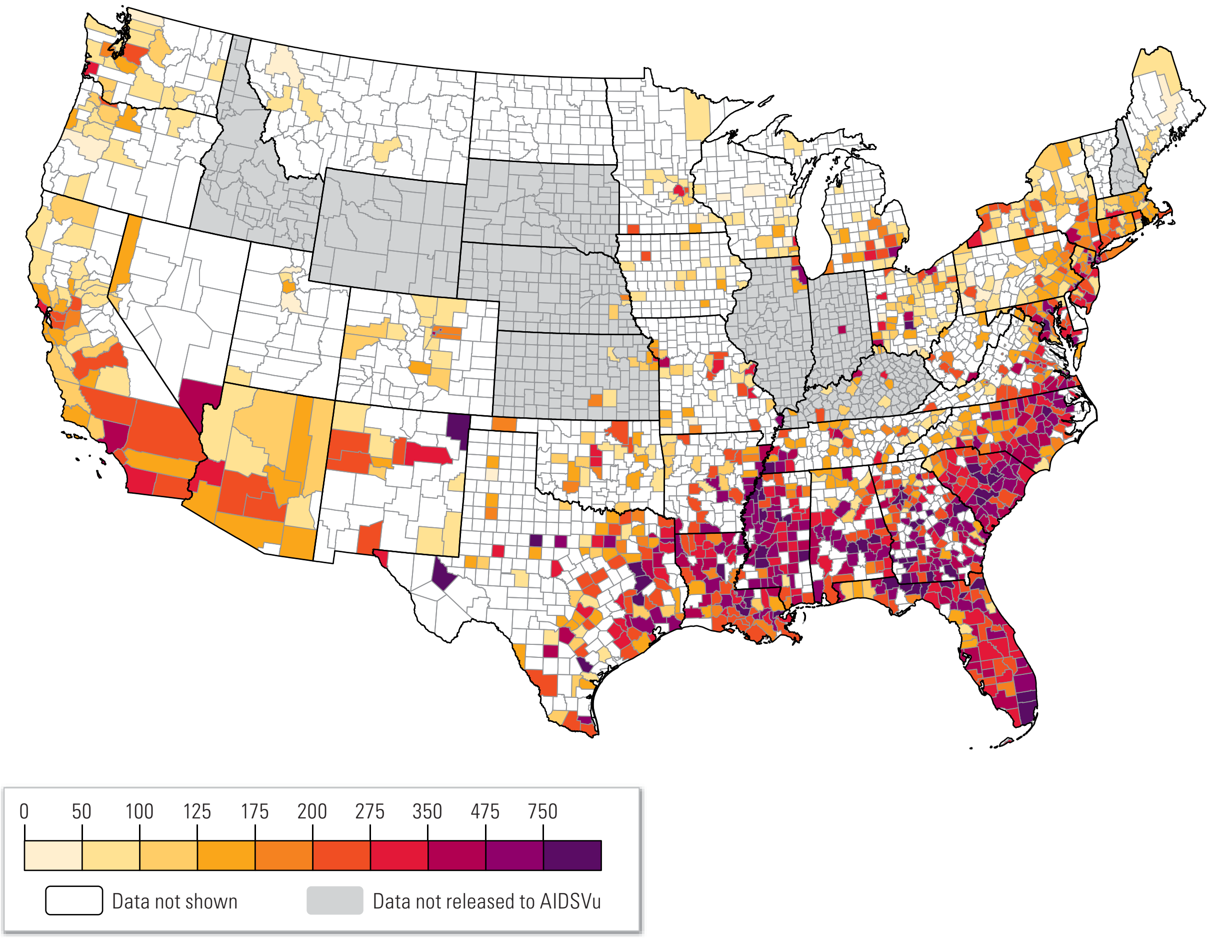

Source: AIDSVu 2016.
Note: AIDS = acquired immune deficiency syndrome; HIV = human immunodeficiency virus.

but it did not change the trends based on race and ethnicity (Del Rio 2015). These same trends are mirrored in AIDS cases and in access to HIV-specific health services (Del Rio 2015) and show that many of the challenges and surveillance needs in LMICs discussed in this chapter are also relevant to HICs, and substantial opportunities exist for cross-learning.

Reaching 90-90-90 Targets among Key Populations

Not surprisingly, the success in meeting 90-90-90 targets also varies by key populations; factors such as stigma and discrimination present even greater obstacles to linking these populations to care. One study of people living with HIV/AIDS in the United States found that only 59 percent of transgender participants, compared to 82 percent of participants with a birth-assigned gender, were accessing ART (Melendez and others 2006). HIV/AIDS-related stigma also creates a barrier to getting tested for many key populations. In one study in the United States, 73 percent of transgender women who tested HIV-positive were previously unaware of their status (U.S. CDC 2011), a figure that can be far greater in other parts of the world. Similarly, in the Asia and Pacific region, fewer than half of the key populations know their HIV status (figure 2.6).

MEASUREMENT: CHALLENGES IN SURVEILLANCE

Prevalence and Incidence

Any summary report of morbidity and mortality is only as good as available data and the methodologies used for collection. The accuracy of estimates of prevalence, incidence, and disease-specific mortality are challenging for any health outcome, especially in low-income, high-mortality countries where vital registration and

Figure 2.6 HIV Testing Coverage among Key Populations, Asia and Pacific Region, 2007–12

Source: UNAIDS 2014a.
Note: HIV = human immunodeficiency virus.

cause-of-death data may be lacking or incomplete (Lopman and others 2006; Mathers and others 2005; Murray and Lopez 2013). As a result, almost all global or large regional estimates of morbidity and mortality require some modeling, the results of which can vary depending on assumptions and sources of data (Flaxman, Vos, and Murray 2015; UNAIDS 2014d). For example, for generalized epidemics, UNAIDS estimates are based on routine surveillance of antenatal clinics, augmented with results from population-based household surveys, where available (UNAIDS 2013). These estimates can lead to oversampling of urban populations and provide no direct information on HIV/AIDS prevalence rates in men. These data are supplemented by models of transmission from Spectrum (UNAIDS 2016c) and models of progression from the International Epidemiologic Databases to Evaluate AIDS. These data sources tend to underrepresent high-risk groups within the general population, and UNAIDS estimates for concentrated epidemics rely on extrapolating from individual studies of key populations (Mahy 2016; UNAIDS 2013).

A salient example of the limitations and fragility of these surveillance methods is the revised estimate by UNAIDS of infection and mortality among adolescents presented at the 2016 meeting of the International AIDS Society (Mahy 2016). On the basis of more robust empirical data on the relative demographic growth of adolescents, the effect of prevention of mother-to-child transmission programs, and ART coverage among adolescents, estimates of adolescent HIV/AIDS-related mortality were revised. Significantly, HIV/AIDS-specific causes of death are now ranked eighth in the leading causes of death in this age group, down from second before these revisions.

Moreover, regardless of the accuracy of surveillance tools, population-based prevalence estimates invariably suffer from survey methodological limitations, such as representativeness and potential nonresponse bias (Flaxman, Vos, and Murray 2015). These challenges can be particularly salient for HIV/AIDS because of social reasons, such as the persistent stigma and discrimination that come with a diagnosis (Tanser and others 2014) or with identification as a person in a key population that is at exceptionally high-risk (see chapter 8 in this volume [Wilson and Taaffe 2017]) and with the methodological challenges of assessing an asymptomatic infection for which representative sampling is imperative.

Most surveillance is primarily designed to assess mortality and prevalence. However, epidemics change; although incidence is associated with prevalence, other factors, such as migration, mortality, survival rates, and the inherent epidemic trajectory, attenuate the legitimacy of using prevalence as a measure of incidence (Brookmeyer 2010). Incidence rates modeled from prevalence are also constrained by the time between surveys, as well as in-and-out population mobility and migration that is especially critical for men in Sub-Saharan Africa who often migrate for work (Brookmeyer 2010; Busch and others 2010; Hallett and others 2008; Marston, Harriss, and Slaymaker 2008). Although incidence rates obtained from prospective data are most robust, these rates are subject to the potential for nonrandom loss to follow-up where sicker individuals are more likely to be lost. Newer surveillance methods using a geospatial approach to monitoring, combined with more reliable incidence assays, can provide more robust estimates to identify weaker performance sites or regions where enhanced efforts are warranted. Data from PEPFAR-supported, ongoing, population-based HIV/AIDS impact assessments—a multicountry initiative to measure the reach and impact of programs in PEPFAR-supported countries through population-based surveys to estimate incidence, prevalence, and viral load suppression among adults and children in Malawi, Uganda, Zambia, and Zimbabwe—should be well-suited to this purpose (ICAP 2016).

Loss to Follow-Up

Loss to follow-up also affects facility-based HIV/AIDS surveillance estimates. Even at care and treatment clinics that have individual-level patient data, high rates of loss to follow-up undermine estimates of facility-based survival and mortality (Egger and others 2011; Geng, Bangsberg, and others 2010; Geng, Glidden, and others 2010; Geng, Nash, and others 2010; Geng and others 2008; Geng and others 2012; Geng and others 2013). Attempts to validate HIV/AIDS-related mortality have been attempted through verbal autopsies (Lopman and others 2006) and actual autopsies (Coulibaly and others 1994; Domoua and others 1995; Greenberg and others 1995; Lucas, Diomande, and others 1994; Lucas, Hounnou, and others 1994). However, verbal autopsies lack external validity and must be tailored to specific context, and actual autopsies present a major challenge to scale-up. Unfortunately, the costs and efforts required to intensively track all missing patients is likely to be prohibitive in most settings.

Geng and others (2015) offer a viable alternative: intensively trace a manageable *random* sample of the individuals lost to follow-up and incorporate their weighted outcomes into the available clinic sample. The power of this approach is evident in a review they conducted of mortality from 14 clinics in Eastern Africa. Sample-corrected estimates of three-year mortality in each clinic ranged from 2 times to more than 10 times higher compared to the naïve (that is, unadjusted) estimates (Geng, Odeny, and Lyamuya 2016; Geng and others 2015). Similar results are apparent from additional analyses in the same clinics also by Geng, Odeny, and Lyamuya (2016) examining retention in care. Using only routine clinic data without supplementation by tracing, after two years of ART, they found 26 percent of patients were reported as lost to follow-up; sampled corrected estimates revealed that 14 percent of the clinic population who were presumed lost had actually transferred their care elsewhere. Although such data can be used to correct facility or regional estimates, they require individual data collection.

Cohort approaches allow for accountability for each patient started on treatment, and with the push toward 90-90-90, programs that use unique identifiers for those diagnosed with HIV coupled with a national cohort will be able to better account for retention—including transfers from clinic to clinic and other outcomes, regardless of geographic location. As in other transmissible infectious diseases programs that are responsible for providing access to successful treatment, this approach will ensure access to life-saving treatment, prevent transmission, and allow follow-up for everyone on ART.

Surveillance at Smaller Units of Analysis: Microepidemics and Key Populations

Regional and subnational variation discussed throughout this chapter is in addition to mapping infection by key populations (Wilson and Taaffe 2017). The principle of "knowing your epidemic" (UNAIDS 2008) has shifted to "know your local epidemics," and the practice of monitoring data at the country or province level has shifted to collecting data at the community and facility levels (UNAIDS 2014c). These more precise pictures of the epidemic permit local governments to set priorities, devote resources, and design programs that clearly match local epidemic realities and to determine whether HIV/AIDS services are appropriately matched, sufficient, and best packaged.

To facilitate these kinds of analyses, the UNAIDS Reference Group on Estimates, Modelling and Projections is reconsidering assumptions underlying the Spectrum model that drives surveillance estimates. The group is working toward standardizing the data collection that underlies spatial analysis, as well as the optimal methods and the frequency of use of such methods, recognizing the need for user-friendly programs to make these estimates possible (UNAIDS Reference Group on Estimates, Modelling and Projections 2013). Other modeling efforts will also be helpful to provide a critique of the standard approaches as we learn more about the effect on incidence and prevalence of key interventions such as treatment, circumcision, and other prevention methods. Supplemental phylogenetic studies assess the contribution of high-risk groups and provide critical knowledge about transmission dynamics and the accuracy of targeting those at risk. However, the cost and technical capacity for such studies currently prohibit their widespread use. A related ongoing challenge is the best method for empirical estimation of population sizes of hidden high-risk groups (Tanser and others 2014). In settings nearing HIV elimination, future efforts will likely rely on the most current phylogentic studies to identify new cases in clusters combined with traditional public health outbreak control methods to end ongoing transmission.

MEASUREMENT: CHALLENGES IN ASSESSING THE 90-90-90 TARGETS

The tremendous benefits in early treatment and viral suppression, both for improving individual health and stemming transmission, have led to the 90-90-90 framing of the HIV/AIDS response, led by UNAIDS, PEPFAR, and other organizations. Surveillance efforts now aim to track the success in meeting these targets; methodologies for doing so have been standardized to the extent possible to permit regional and national comparisons using numerous population-based household surveys—primarily the Demographic and Health Surveys for 24 countries conducted between 2007 and 2013 and for the first 90 percent.

- Given the methodological issues and potential biases related to survey data, getting a robust estimate of the true percentage of people in a population who are infected remains a challenge, although the use of biologic sampling and careful attention to regional variations have improved newer surveys.

- The first 90 percent, HIV diagnosis, is estimated using the number of people diagnosed with HIV divided by the estimate of people living with HIV. UNAIDS produces annual estimates for the denominator (number of people living with HIV).
- The second 90 percent, treatment coverage, is estimated using the annual country figure for the number of people on treatment (N) divided by the number of people diagnosed with HIV. UNAIDS produces annual and midyear estimates for treatment coverage (Stover and others 2014; UNAIDS 2016c).
- The third 90 percent is derived from the universal viral load indicator that is defined in the Global AIDS Response Progress reports and is the percentage of people on ART who are virally suppressed, but it is the estimate for which the data are weakest. Viral load data are often not available for everyone on treatment, and surrogate measures such as the proportion of samples in the national lab that meet viral suppression criteria are often used for estimates (UNAIDS 2015c).

As noted previously, accurate estimates can only be derived using a cohort approach. Valid measurement of these targets requires that individuals be followed longitudinally from the time they are tested until the time they are virally suppressed. This level of granularity would also provide more robust estimates of microepidemics and key populations in both prevalence and incidence. This level is essential for monitoring long-term follow-up.

CONCLUSIONS

As HIV/AIDS programmatic efforts transition to a unified focus on ending the epidemic by 2030 (UNAIDS 2015d), new demands, including accurate monitoring of 90-90-90 goals, are being placed on monitoring and surveillance strategies. Broad measures of national prevalence and mortality are no longer sufficient to guide interventions that will need to increase in efficiency to effectively target hard-to-reach populations. Data needed to target key populations and microepidemics will need to be collected through subnational surveillance methods, which have both time and budget implications. Expanding resources for surveillance and monitoring of a disease that is already one of the best documented in history may not be appealing in an era of ever-increasing competing priorities, but it will be necessary if programs are to be targeted in order to maximize their effect. Improved surveillance systems and techniques must be responsive to and informed by effective interventions for treatment and other prevention interventions.

Notably, however, the critical nature of this approach is not new. It parallels the need for targeted active case-finding, long recognized as a critical aspect of epidemic control for diseases such as smallpox (Kerrod and others 2005), severe acute respiratory syndrome (Cheng and others 2013), Ebola virus (Tom-Aba and others 2015), and tuberculosis (Yuen and others 2015). The ability to accomplish disease control is a global good and requires an ongoing international effort; neither risk nor infection respects political boundaries, and our ability to improve public health is directly dependent on the weakest link in the chain.

NOTE

World Bank Income Classifications as of July 2014 are as follows, based on estimates of gross national income (GNI) per capita for 2013:

- Low-income countries (LICs) = US$1,045 or less
- Middle-income countries (MICs) are subdivided:
  (a) lower-middle-income = US$1,046 to US$4,125
  (b) upper-middle-income (UMICs) = US$4,126 to US$12,745
- High-income countries (HICs) = US$12,746 or more.

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