Treatment and care: unprecedented progress, remaining challenges
Key findings

- The number of people receiving antiretroviral drugs in low- and middle-income countries has increased 10-fold in only six years, reaching almost 3 million people by the end of 2007.
- The rapid expansion of treatment access in resource-limited settings is saving lives, improving quality of life, and contributing to the rejuvenation of households, communities, and entire societies.
- Intensified action is needed to ensure timely delivery of HIV treatment to children, who are significantly less likely than adults to receive antiretroviral drugs.
- Globally, coverage of antiretroviral treatment for women is higher than or equal to that of men.
- The populations most at risk of HIV exposure, such as injecting drug users, face considerable barriers to HIV treatment access, often as a result of institutionalized discrimination.
- Low testing rates reduce the impact of HIV treatment, because individuals who are diagnosed late in the course of infection have a poorer prognosis. A number of countries, however, are successfully using a range of approaches to increase knowledge of HIV serostatus.
- Despite the existence of affordable medications, too few people living with both HIV and tuberculosis are receiving treatment for both conditions. This situation contributes to substantial, avoidable morbidity and mortality.
- Weaknesses in health-care systems are slowing the scale-up of HIV treatment programmes, underscoring the need for intensified action to strengthen these systems. Antiretroviral therapy scale-up is helping to drive significant improvements in health-care infrastructure in resource-limited settings.
- Among the developments needed to ensure the sustainability of HIV treatment are more affordable second- and third-line therapies, as well as greater success in preventing new HIV infections.
The decision of the global community to push towards universal access to HIV prevention, treatment, care, and support represents a moral commitment of historic proportions. Never before has the world attempted, on such a large scale, to bring broad-based chronic disease management to resource-limited settings. Until this decade, low- and middle-income countries were forced to wait 10–20 years—sometimes for more than a generation—before breakthrough health technologies were broadly available. Slightly more than a decade after the emergence of combination antiretroviral therapy, millions of individuals in resource-limited settings are now benefiting from these medications.

Global commitment to make HIV treatments available in resource-limited settings is bearing fruit. In only six years, the number of people receiving antiretroviral drugs in low- and middle-income countries has increased more than 10-fold (Figure 5.2). In settings where HIV was invariably fatal only a short time ago, introduction of life-preserving therapies has rejuvenated households, revived entire communities, and re-energized the broader response to the epidemic (Sanders, 2008).

Many actors share credit in this achievement, most notably people living with HIV themselves, whose advocacy helped achieve what was once considered impossible.

Notwithstanding these considerable achievements, substantially greater progress will be required to move towards universal access to HIV treatment and care. The number of new HIV infections continues to outstrip the increase each year in the number of people on antiretroviral drugs by 2.5 to 1. Thus, the long-term sustainability of even the current pace of treatment scale-up may be jeopardized.

Children are not benefiting equally from the momentous treatment advances, being less likely than adults to receive antiretroviral drugs. In addition, hundreds of thousands of people who are coinfected with HIV and tuberculosis die needlessly each year due to inadequate tuberculosis diagnostic services, failure to deliver affordable medications to those who need them, and rising rates of tuberculosis drug resistance.

This chapter summarizes the achievements to date in expanding access to HIV treatment

![Figure 5.2]

**Number of people receiving antiretroviral drugs in low- and middle-income countries, 2002–2007**

- North Africa and the Middle East
- Eastern Europe and Central Asia
- East, South and South-East Asia
- Latin America and the Caribbean
- Sub-Saharan Africa

Source: Data provided by UNAIDS & WHO, 2008.
in low- and middle-income countries. It discusses challenges in ensuring equal access to antiretroviral drugs, as well as non-antiretroviral components of HIV treatment and care, including management of opportunistic illnesses and other conditions. Finally, the chapter identifies the impediments to more rapid and broad-based scale-up, and summarizes what is known about how to overcome these obstacles.

**Progress in reducing HIV-related illness and death**

The impact of antiretroviral drugs on the management of HIV infection has been startling, with improvements in health proving to be far more marked and enduring than anticipated when combination antiretroviral therapy first emerged in the mid-1990s. Recent studies in Denmark suggest that a young man newly diagnosed with HIV is likely to live an additional 35 years with available medications, a tripling of the life expectancy for people with HIV (Lohse et al., 2007). In slightly more than a decade, the introduction of combination antiretroviral therapy has saved an estimated three million years of life in the United States alone (Walensky et al., 2006).

As more is learnt about antiretroviral therapy management through clinical trials and through the accumulation of greater clinical experience, health outcomes as a result of therapy are improving further still. Data derived from national HIV treatment and care monitoring in the United Kingdom, for example, indicates that median time to treatment failure for patients on first-line regimens that include one or more protease inhibitors ranges from 4.3 years to 6.5 years; however, patients started on a regimen containing two nucleoside reverse transcriptase inhibitors (NRTI) and one non-nucleoside reverse transcriptase inhibitor (NNRTI) had a median time before treatment failure of 13.2 years (Beck et al., 2008a). As Chapter 6 explains, increased access to antiretroviral drugs is also improving quality of life for millions of people, benefiting households, communities, and societies.

The growing availability of antiretroviral drugs is lessening the burden of HIV-related mortality.

**FIGURE 5.3** Estimated number of adult and child deaths due to AIDS globally, 1990–2007

Source: Data from UNAIDS and WHO, 2008.
Lillian Mworeko was 29 when she was diagnosed with HIV. It was the day her husband died.

“I was already in shock at the death of my husband, so my results did not bother me so much”, she says. “But later on, after the burial, the reality of being HIV-positive came to me. Here I was, a young widow, with a small child, and I was struggling to cope alone.”

Alone and having no money, Mworeko sought help from support groups and networks in her hometown in Uganda. She began to learn more about HIV. As she gained confidence she was able to get the support she needed from her family and friends.

“I became courageous, I knew life has to continue,” she says.

Her courage stood her in good stead when, some years later, she and her new partner decided to have a child together. She did a lot of reading and research to ensure that she would not transmit the virus to her unborn child. By this time she was already on antiretroviral treatment, but it was not the recommended regimen to prevent mother-to-child transmission. “I had several discussions with my doctors and they had to change my drugs, to conduct tests on my CD4 and viral loads”, she says. “I discussed my serostatus with my doctor. He was so supportive. At one time, I thought I was going to need a caesarean, then I changed my mind. I got a lot of support... it is mainly because I shared with them.”

Mworeko was also helped by other HIV-positive women who had started a motherhood programme called the Mama’s Club. They talked about the challenges they faced and the measures and precautions needed to prevent vertical transmission. The support and interaction with other women was invaluable. But even so, there were shocks in store for Mworeko when she got her new baby home. She had decided to bottle-feed the baby to be absolutely certain that she would not transmit HIV in her breast milk. “I thought it was cheap to be on PMTCT programme”, says Mworeko, “but I did not know the price of formula feed. It is expensive and he went through four tins of food a week in the first weeks.”

Mworeko considers herself fortunate in having access to antiretroviral therapy and medical support provided by her workplace. “It has given me hope and when I look at life now, it is more positive than before... there were times when I was not sure of the next day, but now, I look at life positively, I’ve decided to go back to school, to go higher in my career, so that the contribution I make towards the community is higher.”
in low- and middle-income countries, as it did in high-income countries a decade ago (Figure 5.3). In rural South Africa, substantial declines in mortality were reported in 2006, as these drugs became increasingly available (Nyirenda et al., 2007). After decades of increasing mortality, the annual number of AIDS deaths globally has declined in the past two years, in part as a result of the substantial increase in HIV treatment access in recent years.

Antiretroviral therapy has been also found to be a cost-effective or cost-saving intervention in high-, middle- and lower-income countries. (Harling, 2005.) Most of the cost-effectiveness studies performed to date, have only included direct costs. If indirect costs are included, Highly Active Antiretroviral Therapy (HAART) in many countries is likely to be a cost-saving intervention as it enables people living with HIV to remain well, and socially and economically active (Badri, 2006).

In spite of promising signs that improved treatment access is yielding results in low- and middle-income countries, treatment success rates may be somewhat lower in resource-limited settings than in high-income settings. At both 6 and 12 months after initiation of antiretroviral therapy, mortality rates for individuals in low- and middle-income countries are at least 28% higher than those for patients in high-income countries (Antiretroviral Therapy in Lower Income Countries Collaboration, 2006). When long-term survival is estimated, although the benefits of antiretroviral therapy in low- and middle-income countries are considerable, they are still less than those enjoyed in high-income countries (Beck, 2008b).

A number of factors are likely to contribute to this, such as more advanced clinical disease in resource-limited settings at the start of therapy and a higher incidence of co-occurring conditions (Beck, 2008b). In the interests of global
equity, at the same time as efforts focus on the scaling up of antiretroviral drugs in low- and middle-income countries, attention must also be focused on understanding and addressing the sources of suboptimal outcomes for many patients in resource-limited settings.

**Antiretroviral management in resource-limited settings**

As of December 2007, an estimated 3 million people in low- and middle-income countries were receiving antiretroviral drugs, which represents 31% of those who need the medications, and is a 45% increase over 2006. Increases in treatment coverage have been extraordinary in many countries (Figure 5.4). For example, in Namibia, where treatment coverage was less than 1% in 2003, 88% of individuals in need were on antiretroviral drugs in 2007. In Rwanda, antiretroviral therapy coverage increased from 1% in 2003 to almost 71% in 2007, aided by a 40-fold growth in the number of antiretroviral treatment sites. Antiretroviral therapy coverage in Thailand rose from 4% in 2003 to 61% in 2007 (UNGASS Indicator 4, 2008).

Figure 5.5 shows percentage coverage of antiretroviral therapy between males and females for generalized and concentrated epidemic countries, based on modelled estimates of male

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**Figure 5.5**

Comparison of antiretroviral therapy coverage in 2007 between males and females (for countries with reported data on the number of people on treatment for both sexes separately)

- **Countries with generalized epidemics**
- **Countries with concentrated or low epidemics**

Source: Data from UNAIDS and WHO, 2008.

Note: Coverage estimates are based on applying the ratio of number of males and number of females receiving antiretroviral therapy to the final projected value of all people receiving antiretroviral therapy as of December 2007. This provides December 2007 estimates of number of males and females receiving antiretroviral therapy that are then divided by the estimated number of males and females in need of antiretroviral treatment respectively.
and female need. In most countries, women are receiving more than expected coverage for antiretroviral therapy. This sex disparity is particularly pronounced in generalized epidemics, which may be related to the fact that many HIV-positive women have two portals of entry for treatment—HIV treatment programmes and programmes to prevent mother-to-child transmission. Seven countries have equal coverage for men and women, while in two countries—Belize and Chile—men have much higher coverage than women. Additional research is needed to explore the reasons why women generally receive more coverage than men and to identify more effective strategies for increasing universal access to treatment.

Antiretroviral drugs are being successfully administered in some of the world’s most challenging settings. In conflict-affected areas of the Democratic Republic of Congo, for example, an HIV treatment programme by Médecins sans Frontières has achieved treatment adherence rates comparable with those reported in non-conflict settings.

Expanding treatment access: a collective endeavour

The rapid growth in antiretroviral therapy coverage represents one of the great success stories in recent global health history. Less than ten years ago, even as antiretroviral drugs were contributing to sharp declines in HIV-related morbidity and mortality in high-income countries, it was widely assumed that these life-preserving medications would remain unaffordable and thus unavailable in low-income countries, perhaps for decades.

In the case of HIV, alleviating the stark disparities in health-care access that typify global health practice has required the leadership and coordination of diverse stakeholders at global, regional, and national levels. In response to the WHO/UNAIDS “3 by 5” initiative, national governments embraced the push to expand HIV treatment access, establishing ambitious targets and making extensive efforts to build national capacity and address obstacles to scale-up. Civil society has mobilized in support of universal treatment access, with particular leadership provided by people living with HIV. At the global level, the Political Declaration on HIV/AIDS, adopted at the UN General Assembly’s High Level Meeting on HIV/AIDS in 2006, pledged to move towards universal access to HIV prevention, treatment, care, and support by 2010—a goal that has obtained the strong support of key global and regional bodies, ranging from the G8 industrialized countries to the African Union and the Caribbean Community and Common Market.

Leading donors have helped finance the expansion of access to treatment. PEPFAR aims to reach 2.5 million people with treatment by 2012. As of December 2007, the Global Fund was supporting the delivery of antiretroviral drugs to 1.4 million people, which represents an increase of 88% from the previous year (Global Fund, 2008). UNITAID—a relatively new international mechanism for purchasing drugs that is funded by airline taxes—is playing a major role in scaling up paediatric treatment programmes and services to prevent mother-to-child transmission.

Many private companies are also helping to expand HIV treatment access (Global Business Coalition on HIV/AIDS, 2007). In Botswana, the mining company Debswana entered into a formal partnership with the national government to accelerate treatment scale-up, by covering the delivery of antiretroviral drugs to its HIV-positive workers (UNGASS, 2008a).

Ten medium-to-large companies are among the

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1 Launched in December 2003, the “3 by 5” initiative proposed a massive scale-up of antiretroviral therapy, sufficient to ensure that 3 million people would be on antiretroviral drugs by the end of 2005. Although the goal of 3 million people on treatment was not reached until two years after the 2005 deadline, “3 by 5” was critical in catalysing unprecedented action to expand treatment access in resource-limited settings.
members of the Suriname Business Coalition Against HIV, which recently implemented a strategic action plan on HIV to increase business involvement in the HIV response (UNGASS, 2008b). However, substantial additional efforts are required to fully engage industry in treatment scale-up, because both government and nongovernmental informants in only 9% of countries with generalized epidemics say that workplace HIV treatment services or treatment referral systems through the workplace have been implemented in all districts in need (UNGASS Country Progress Reports, 2008).

Numerous faith-based organizations are also playing a part in expanding treatment access, providing as much as 40% of all HIV-related health services in some countries (WHO, 2007f). With financial assistance from bodies such as the Global Fund, the Churches Health Association of Zambia will provide antiretroviral drugs to 17 000 individuals by the end of 2008 and is updating more than 100 church health facilities to implement Directly Observed Therapy, Short-course (DOTS) for tuberculosis. According to recent surveys, programmes supported by the Anglican Church were delivering antiretroviral drugs to 10 000 individuals in the United Republic of Tanzania (Anglican United Nations Office, 2007), and Catholic religious orders were supporting delivery of the drugs to more than 90 000 people worldwide (International Union of Superiors General, 2008).

People living with HIV have mobilized in countries throughout the world to support accelerated treatment scale-up and to promote treatment success. In Kenya, a national network of post-test clubs helps newly diagnosed individuals in understanding HIV and becoming active partners in their own health care. After meeting with representatives from 20 pharmaceutical companies, Ashar Alo, a leading network of people living with HIV in Bangladesh, forged an agreement to obtain lower prices for antiretroviral drugs and to establish a drug contribution
Research to improve treatment options

Although available antiretroviral drug regimens markedly improve the health and longevity of HIV-positive patients, a number of uncertainties remain with respect to the medical management of HIV disease. Research continues in an effort to identify the most effective regimens for individuals who have not previously received therapy (Eron et al., 2006; MacArthur et al., 2006; Lazzarin et al., 2007; Delfraissy et al., 2008). Whether to intervene with antiretroviral drugs during acute HIV infection also continues to be a topic of debate, as well as the focus of continuing clinical research (Fidler et al., 2008; Panel on Antiretroviral Guidelines, 2008). Also essential is research to develop new therapeutic options that are simpler to take, less toxic, and more affordable.

A priority that is the subject of urgent research efforts and will continue to grow in importance is the development of optimally effective treatment regimens for individuals in whom one or more antiretroviral drug combinations have failed (Abgrail et al., 2006; Clotet et al., 2007). Researchers are also working to develop new classes of antiretroviral drugs. These include compounds that inhibit the virus from entering cells (Este & Telenti, 2007) or that interfere with the integrase enzyme that plays a role in HIV replication (Grinsztejn et al, 2007).

In addition, extensive research is continuing into the potential for genetic testing to offer eventually the possibility of more precise tailoring of antiretroviral drug regimens to individual patients. Already, in clinical settings where it is available, HLA-B5701 screening permits clinicians to identify hypersensitivity to abacavir and thereby avoid potentially fatal drug toxicities (Phillips & Malial, 2008).

Introducing and adapting HIV treatment

The process for bringing antiretroviral therapy to scale in resource-limited settings is well characterized (WHO, 2006a). Countries are advised to develop national treatment plans with clear targets, to promote provider-initiated HIV testing and counselling to increase treatment uptake, and to undertake efforts to strengthen health and regulatory systems. All countries report having in place a policy or strategy to promote comprehensive HIV treatment, care, and support. Most (85%) countries with generalized epidemics, and 52% of countries with concentrated epidemics, report having developed national estimates and projected future needs of the number of individuals requiring antiretroviral therapy (UNGASS Country Progress Reports, 2008).

WHO recommends national use and consolidated purchase of standardized antiretroviral drug regimens consisting of fixed-dose combinations. Preferred first-line regimens include two nucleoside reverse transcriptase inhibitors (NRTIs) and one non-nucleoside reverse transcriptase inhibitor (NNRTI). For second-line regimens, preference is given to a combination of two NRTIs (at least one of which is new) and a protease inhibitor boosted with ritonavir (WHO, 2006a).
Most national HIV treatment guidelines are in accord with WHO recommendations on first-line regimens and on routine clinical monitoring (Beck et al., 2006). However, civil society surveys in 16 low- and middle-income countries found that many clinical settings were prescribing regimens that were inconsistent with global treatment guidelines (International Treatment Preparedness Coalition, 2007), highlighting the need for follow-up to ensure adherence to national standards.

The best time to initiate antiretroviral therapy remains a subject of debate. WHO advises clinicians working in settings where CD4 testing is available to consider initiating treatment when a patient’s CD4 count falls below 350 cells per mm³ and to initiate treatment in all patients under 200 CD4 cells per mm³. Where CD4 testing is unavailable, WHO recommends that antiretroviral therapy be started when patients exhibit clinical signs of advanced or severe immune suppression (WHO, 2006a). The United States Department of Health and Human Services recommends initiation of antiretroviral therapy in patients who have experienced an AIDS-defining opportunistic illness or have a CD4 count less than 350 cells per mm³ (Panel on Antiretroviral Guidelines, 2008).

**Treatment and care for children**

Without treatment, approximately half of children with perinatal HIV infection will die by age two (Newell et al., 2004; Marston et al., 2005). Extensive experience in high-income countries has shown that antiretroviral drugs can reduce illness and death in children and adolescents living with HIV (Patel et al., 2008). In Western Europe in 2006, for example, only 10 children infected via mother-to-child transmission died of AIDS (EuroHIV, 2007).

When made accessible in resource-poor settings, treatment for children has proved highly effective. Studies of the effectiveness of antiretroviral treatment have found two-year survival rates exceeding 80% in various settings, including Côte d’Ivoire, Haiti, Malawi, and Zambia (Fassinou et al., 2004; Rouet et al., 2006; Bolton-Moore et al., 2007; Bong et al., 2007; George et al., 2007). Other studies have found survival probability at 12 months ranging from 87% (O’Brien et al., 2006) to more than 95% in settings in sub-Saharan Africa and Asia (Puthanakit et al., 2005; Janssens et al., 2007; Reddi et al., 2007; Arrivé et al., 2008).

Although use of antiretroviral drugs to treat children has increased in recent years in sub-Saharan Africa, children living with HIV are about one third as likely to receive antiretroviral therapy as adults living with HIV as a whole (Prendergast et al., 2007).

According to national governments, paediatric HIV treatment is available in all districts in need in 44% of countries with a concentrated

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**Redoubling national efforts to achieve universal treatment access in Ethiopia**

Ethiopia’s initial effort in 2004–2006 to bring antiretroviral therapy to scale reached 65% of its target of 100 000. In November 2006, the Government launched a two-year Millennium AIDS Campaign to generate swifter expansion of treatment access. The campaign relies on decentralization of the response, clear performance targets, coordinated planning, broad-based communications, and improved integration of HIV treatment into health-care settings. In its first seven months the campaign reached almost 1 million people with HIV testing, counselling, and services; it also initiated antiretroviral therapy for more than 31 000 patients (Ethiopia Federal Ministry of Health, 2007).
epidemic and in 36% of countries with a generalized epidemic. Nongovernmental informants suggest that access is in reality even more scarce, affirming the widespread availability of paediatric treatment in only 31% of countries with a concentrated epidemic and 9% of countries with a generalized epidemic (UNGASS Country Progress Reports, 2008).

Several factors threaten treatment access for HIV-infected children. For example, prompt diagnosis of HIV infection in infants is critical, but is often difficult to achieve. HIV-exposed children usually have maternal HIV antibodies in their first months of life, even when they themselves are uninfected; therefore, traditional HIV antibody testing (Enzyme-Linked ImmunoSorbent Assay, or ELISA, or rapid testing) does not reliably detect actual HIV infection in the first 6−18 months. Virological tests—including HIV DNA polymerase chain reaction (PCR), real-time HIV RNA PCR, or use of an ultrasensitive p24 antigen test—are thus required to make an accurate and timely diagnosis. However, access to such technologies is frequently limited and highly variable in resource-limited settings (De Baets et al., 2005; Prendergast et al., 2007). The cost and complexity of these test methods have declined in recent years, making it more feasible to implement such assays in resource-limited settings (WHO, 2006b). Testing of dried blood spots derived from the infant’s heelstick avoids difficulties associated with phlebotomy in infants and permits centralization of laboratory capacity (WHO, 2006c). The use of dried blood spots offers the potential to greatly increase early diagnosis and timely treatment of HIV in young children. According to a study in South Africa, use of available, affordable strategies to improve diagnosis of HIV-exposed infants could significantly improve the odds that HIV-infected children will survive (Sherman, Matsebula & Jones 2005).

Clinicians are exploring various strategies to increase treatment uptake for children living with HIV. For example, child health cards that document an infant’s status following the child’s participation in a programme to prevent mother-to-child transmission enable health workers to respond appropriately at the child’s first postnatal visit for immunizations. Just as provider-initiated testing and counselling is helping in the scale-up of services to prevent mother−to−child transmission and HIV treatment generally, this approach is now being used in certain settings where children living with HIV are likely to be found such as paediatric wards in high-prevalence countries.

Available antiretroviral drugs were initially developed for adults; most standard fixed-dose combinations are inappropriate for children. To help clinicians to identify the appropriate dosing of antiretroviral drugs for children, WHO developed updated, user-friendly paediatric dosing tables. In collaboration with the Clinton Foundation, UNITAID has negotiated a 40% decline in the prices of paediatric antiretroviral drugs and, as of December 2007, was supporting HIV diagnostics and treatment for 102 000 children worldwide (UNITAID, 2008).

Monitoring treatment success

In the absence of viral load measurements in resource-limited settings, clinicians are advised to use clinical or immunological monitoring, or both, to decide when to initiate therapy, assess treatment success, and decide when to change from first-line to second-line regimens. Because antiretroviral drugs do not eradicate the virus but rather maintain viral replication at low levels (see Palmer et al., 2008), treatment must be continued without interruption. Antiretroviral treatment failure, as measured by increasing viral load, tends to occur rather slowly in clinical settings, especially now that therapeutic regimens and techniques for clinical management of antiretroviral drug administration have improved (Phillips et al., 2007). Studies in the United Kingdom indicate that nearly 11% of patients will die within five years of extensive failure of the three primary classes of antiretroviral medications (Phillips et al., 2007).
The prevalence of HIV drug resistance has grown over time in high-income countries and in Brazil, where antiretroviral drugs have been in use for longer than anywhere else (Weinstock et al., 2004; Barreto et al., 2006). In the low- and lower-middle-income countries where antiretroviral drugs were introduced more recently, much lower rates of resistance prevail, but these may increase as people on therapy live longer.

A high level of treatment adherence is needed to avoid or delay the emergence of drug resistance, which is closely associated with treatment failure (Panel on Antiretroviral Guidelines, 2008). A growing body of data associates treatment interruptions—including those guided by CD4 count—with viral rebound, poorer clinical outcomes, and diminished quality of life (Strategies for Management of Antiretroviral Therapy Study Group, 2006; Burman et al., 2008; UK Collaborative HIV Cohort Study, 2008). Efforts to promote treatment adherence have been helped by the simplification of antiretroviral drug regimens in recent years, including the development of once-daily dosing (Johnson et al., 2006; Niel Malan, 2008).

Although strong treatment adherence can be achieved in resource-limited settings and in various vulnerable populations (see Mills et al., 2006), many people living with HIV find it difficult to adhere to antiretroviral drug regimens. In a clinic setting in Johannesburg, nearly one in six patients who started on treatment dropped out of care over a 15-month period (Dalal et al., 2008). Factors that may contribute

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**Monitoring for side-effects**

Up to half of patients on antiretroviral therapy may experience adverse effects of the medications (Fellay et al., 2001). Common side-effects vary depending on the drug regimen, but can include hypersensitivity, lactic acidosis, increases in blood lipids, bleeding events, anaemia, neuropathy, lipodystrophy, and pancreatitis (NIH, 2008). While most side-effects diminish over time, some can be life-threatening, underscoring the importance of careful patient monitoring (NIH, 2008).

As a leading HIV clinician has advised, “The success of [antiretrovirals] comes at a price” (Lange, 2006). That price is paid by the person taking the drugs. The unpleasant, often painful, and potentially disfiguring side-effects sometimes associated with the drugs may have a significant negative impact on quality of life and on an individual’s ability or willingness to adhere to the prescribed regimen.

Management of side-effects constitutes an essential component of antiretroviral drug administration. After more than a decade of clinical experience in administration of antiretroviral drugs, more is known about the side-effect profiles of different antiretroviral drugs. Improvements in the evidence base have made it easier for clinicians to prescribe regimens with a greater likelihood of long-term treatment success and to refine regimens when side-effects emerge. However, management of side-effects can be more difficult in resource-limited settings, where drug substitution may not always be feasible due to limited access to the full array of antiretroviral drugs licensed for use in high-income countries.
to non-adherence are numerous and may vary, depending on the population and setting. Factors include social and economic factors (e.g. poverty, unstable housing, and inadequate transportation to distant treatment centres), and non-HIV-related health conditions (e.g. active chemical dependence or mental illness) (Hicks et al., 2007; Tegger et al., 2008). Ensuring strong treatment adherence for children can be especially difficult due to the shortage of appropriate paediatric formulations, the unpalatability of some paediatric antiretroviral drugs, and the dependence on a caregiver for delivery of the medication.

Although antiretroviral treatment adherence has been the focus of numerous clinical trials, optimal strategies for measuring and improving treatment adherence have yet to be characterized (Panel on Antiretroviral Guidelines, 2008). Patient education, counselling, and use of reminders have shown promise as strategies to support treatment adherence (Wang et al., 2007; Wang & Wu, 2007; Aspeling & van Wyk, 2008).

In rural Uganda, more than 95% of patients were at least 95% adherent (based on pill count) following exposure to various adherence interventions including group education, personal adherence planning, medication companions, and weekly home delivery of the drugs (Weidle et al., 2006). Peer-based programmes that provide continuing aid in adhering to treatment have proven to be effective; for example, in the West Java Province of Indonesia, the programme Pantura Plus Karawang trains and supports volunteers in rural and urban areas to provide adherence assistance to individuals on antiretroviral therapy.

**Non-antiretroviral components of comprehensive HIV treatment and care**

The medical management of HIV involves much more than treatment of the underlying HIV infection. HIV-related immune suppression increases the risk of a broad range of debilitating, potentially life-threatening conditions;
therefore, the prevention and treatment of such opportunistic illnesses are central to effective HIV treatment and care. People living with HIV also frequently have other health conditions not directly tied to their HIV infection, and these may be more severe in the presence of HIV, or may complicate antiretroviral therapy. Maximizing the success of HIV treatment also requires attention to nutrition, mental health, and social and economic factors, such as access to transport. Only by ensuring that people living with HIV are actively engaged in their own medical care will clinicians be able to provide prompt and effective treatment for the range of conditions to which HIV-positive people are potentially vulnerable.

**Tuberculosis**

While the world has rightly focused extraordinary attention on bringing antiretroviral therapy to scale, much less effort has been directed towards an enterprise that could yield comparable reductions in HIV-related morbidity and mortality—timely prevention, diagnosis, and treatment of tuberculosis in people living with HIV.

Tuberculosis remains the most common opportunistic infection for people living with HIV, including those on antiretroviral therapy, and a leading cause of death for people living with HIV in low- and middle-income countries (Egger, 2007). The synergistic relationship between HIV and tuberculosis is illustrated in Figure 5.6, which demonstrates how declines in HIV prevalence in Zimbabwe drove a subsequent drop in tuberculosis cases. Because of the synergistic impact between HIV and tuberculosis, Africa is now experiencing what tuberculosis experts are calling the worst tuberculosis epidemic since the advent of antibiotics (Chaisson, 2008).

An estimated 22% of tuberculosis cases in Africa occur in people living with HIV; in some coun-

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**FIGURE 5.7** Percentage of incident tuberculosis cases in people living with HIV receiving both antiretroviral and anti-tuberculosis medications, 2007

![Graph showing percentage of countries reporting incident tuberculosis cases](chart)

Note: No data from North America

Source: UNGASS data provided by countries, 2008.
tries in the region, this figure is as high as 70% (WHO, 2008a). Up to half of children living with HIV in South Africa are coinfected with tuberculosis (Prendergast et al., 2007). While tuberculosis incidence has declined globally in recent years, the number of cases continues to increase in areas heavily affected by HIV or drug-resistant tuberculosis, such as Africa and Eastern Europe (WHO, 2008a).

**Diagnosing and treating active tuberculosis.**
Tuberculosis is particularly difficult to diagnose in people living with HIV, both with sputum microscopy and clinically (Hopewell et al., 2006; Chaisson & Martinson, 2008). More sensitive diagnostic tools could reduce tuberculosis-related mortality in people living with HIV by 20% (Dowdy et al., 2006), but such technologies are rarely available in resource-limited settings (Chaisson & Martinson, 2008).

Treatment of tuberculosis in individuals living with HIV follows the same basic approach as for patients not infected with HIV. However, despite the existence of affordable, well-understood treatments for tuberculosis, only 32% of tuberculosis cases in people living with HIV received both antiretroviral and anti-tuberculosis drugs (Figure 5.7) (UNGASS data provided by countries, 2008). As measured by the number of patients needing co-treatment, the greatest unmet need for dual HIV and tuberculosis treatment is in sub-Saharan Africa (Figure 5.8). In comparison to tuberculosis patients without HIV infection, tuberculosis patients who are living with HIV have lower treatment success rates, primarily due to an increased risk of death (Figure 5.9) (UNGASS data provided by countries, 2008; WHO, 2008a).

It is recommended that HIV-positive patients routinely receive co-trimoxazole, which can result in a 40% reduction in mortality (WHO,
In 2006, 78% of HIV-positive tuberculosis patients received co-trimoxazole prophylaxis (WHO, 2008a).

Potential drug−drug interactions, as well as difficulties associated with adhering to multiple regimens, may complicate the simultaneous treatment of tuberculosis and HIV (Hopewell et al., 2006). In 2007, WHO issued a new module for comanagement of tuberculosis and HIV under its Integrated Management of Adolescent and Adult Illness initiative (WHO, 2007b). Careful and continuing education is essential to help patients on HIV and tuberculosis treatment to take a large number of pills appropriately and to adhere to medication changes required by standard co-treatment regimens.

Regardless of HIV status, careful adherence to tuberculosis regimens is essential to avoid the emergence of drug-resistance, which causes treatment failure and can be transmitted to others. People living with HIV have been shown to be twice as likely to have multidrug resistant tuberculosis (MDR−TB) as people who do not have HIV infection (WHO, 2008c). In a rural area of KwaZulu Natal Province in South Africa, an outbreak of extensively drug resistant tuberculosis (XDR−TB), i.e. tuberculosis that is resistant to both first- and second-line anti-tuberculosis drugs, was associated with extremely high mortality among people living with HIV (Gandhi et al., 2006).

**Preventing active tuberculosis in people living with HIV.** It is recommended that all people living with HIV be screened regularly for active tuberculosis. In the absence of evidence of active disease, individuals should be considered for treatment of latent tuberculosis infection with a 6−9-month course of preventive therapy.
(WHO, 2004). According to national governments, only 42% of countries with generalized epidemics have implemented routine tuberculosis screening for HIV-positive patients, and only 27% provide tuberculosis preventive therapy in districts in need for people living with HIV; nongovernmental informants indicate that these two services are widely available in only 24% of countries with generalized epidemics (NCPI data reported from countries, 2008). A WHO survey of 41 countries with moderate-to-high burden of HIV and tuberculosis found that, although 51% of countries had national policies for the provision of preventive tuberculosis therapy to HIV-positive individuals with latent tuberculosis infection, only 15% of countries had implemented the policy at a national scale. Globally, only 27 000 HIV-positive people in low- and middle-income countries were started on isoniazid preventive therapy in 2006, and nearly all of these were in a single country—Botswana (WHO, 2008a).

**Preventing further transmission.** Health-care settings serve as a potentially important venue for the transmission of tuberculosis—and more worryingly, XDR-TB—to people living with HIV. Mathematical modelling indicates that implementation of available infection control practices in health-care settings could prevent almost half of all XDR-TB cases in South Africa (Basu et al., 2007). According to national reports, more than 60% of countries with generalized epidemics have yet to implement proper infection control procedures to prevent tuberculosis transmission in high-prevalence settings, such as HIV care clinics (UNGASS Country Progress Reports, 2008).

**Systemic challenges to address HIV/tuberculosis coinfection.** Institutional weaknesses are combining to impede the ability of countries to address the synergistic threat posed by HIV/tuberculosis coinfection. In particular, efforts to reduce tuberculosis-related morbidity and mortality among people living with HIV are undermined by the failure to integrate HIV and tuberculosis service delivery at national and subnational levels, resulting in missed opportunities to deliver optimal prevention, diagnosis, and treatment services.

While financing for tuberculosis control efforts in high-burden countries has more than doubled since 2002, many heavily affected countries have not adequately budgeted for activities to reduce the burden of HIV-related tuberculosis. Health-system barriers, such as inadequate drug supplies and laboratory capacity, remain a constraint to effective management of in people living with HIV (WHO, 2007d).

Of the 63 countries that collectively account for 97% of estimated HIV-positive tuberculosis cases worldwide, 63% have established national plans for integrated delivery of HIV and tuberculosis care. However, many such plans have not been translated into effective delivery systems. Although the Global Plan to Stop TB, 2006–2015 established a global target of testing 1.6 million tuberculosis patients annually for HIV, approximately 700 000 tuberculosis patients were tested for HIV in 2006 (WHO, 2008a) (Figure 5.10).

**Technological challenges to improving tuberculosis outcomes in people living with HIV.** No new class of tuberculosis drugs has been approved in more than 40 years, and the principal diagnostic test is more than 100 years old. Greatly increased investment in research for new tools to prevent, diagnose, and treat tuberculosis in people living with HIV is needed.

**Other HIV-related illnesses**

In addition to tuberculosis, individuals living with HIV may be vulnerable to a host of opportunistic illnesses such as *Pneumocystis carinii* pneumonia, cytomegalovirus retinitis, various oral diseases and complications, changes in bone mass and increased risk of bone disease, and cervical cancer. Antiretroviral therapy is often critical to effective management of opportunistic infections because the recovery of immune function usually significantly reduces the risk of suffering an opportunistic illness (Heiden et al.,
In addition, clinical interventions focus on the opportunistic condition itself, necessitating continuing patient monitoring, accurate diagnostic tools, timely prophylaxis, and targeted treatment.

Access to medications and other health services required for the management of HIV-related opportunistic conditions is often sharply limited in many resource-limited settings. A total of 70% of countries surveyed by WHO cited erratic supplies and frequent stockouts as barriers to national scaling up of co-trimoxazole prophylaxis, which is used in the treatment of tuberculosis and other HIV-related opportunistic infections (Vittoria, 2008).

Hepatitis B is endemic in many countries with high HIV prevalence and is especially concentrated among children. In a study in Côte d’Ivoire, 12% of children living with HIV were coinfected with hepatitis B (Rouet et al., 2008). Adults coinfected with HIV and hepatitis B progress to chronic hepatitis B infection five times faster than adults without HIV infection. Antiretroviral drugs are often difficult to tolerate for individuals coinfected with HIV and hepatitis B, necessitating close and continuing patient monitoring (Hoffman, 2007). Studies have also noted a potential increased risk for antiretroviral drug resistance in children coinfected with HIV and hepatitis B (Rouet et al., 2008). There is no cure for hepatitis B, although the disease can be suppressed with prolonged, sometimes indefinite, therapy. Unfortunately, of the seven drugs currently used to treat chronic hepatitis B infection in high-income countries, only one is widely available in Africa and Asia (Hoffman, 2007).

**Treatment needs of injecting drug users**

Although it is entirely feasible to obtain excellent medical outcomes through antiretroviral therapy in HIV-positive individuals with chemical dependency, substance addiction may have an important impact on therapeutic approaches. Alcohol consumption, for example, may exacerbate side-effects of the drugs (NIH, 2008), and patients with chemical dependence may find it hard to adhere to prescribed regimens.
Substitution treatment with methadone or buprenorphine is effective for the treatment of opioid dependence. WHO added methadone to the list of essential medications in 2005. However, a major barrier to the successful treatment of HIV-positive people with opioid dependence is the shortage or complete absence of substitution treatment in many parts of the world—the result of government policies that prohibit such services (see Chapter 4). Unmet need for substitution treatment for chemical dependence is especially great in China, India, and the Russian Federation (WHO, 2008b). According to reports by nongovernmental informants, many countries—in Eastern Europe and Central Asia, South and South-East Asia, and North America—have laws, regulations or policies that impede use of HIV services by injecting drug users (UNGASS Country Progress Reports, 2008) (Figure 5.11).

Coinfection with one or more forms of hepatitis is common among people living with HIV in many parts of the world. Studies in the United States suggest that 50%–90% of HIV-positive injecting drug users are also infected with hepatitis C (Centers for Disease Control and Prevention, 2005). HIV infection significantly increases the risk of death from liver disease in individuals infected with hepatitis C (Smit et al., 2008). Although it is possible to achieve excellent clinical outcomes for individuals coinfected with HIV and hepatitis C, simultaneous medical management of both conditions can be complex due to potential drug interactions and toxicities, and uncertainties about the best therapeutic approaches (Sulkowski & Benhamou, 2007).

**Diseases of ageing**

In settings where antiretroviral drugs have been in widespread use since the mid-1990s, treatment has radically altered the natural course of HIV infection, expanding the spectrum of health problems presented by individuals living with HIV and altering the most common causes of death among HIV-positive people (Smit et al., 2006). In particular, chronic illnesses and co-morbidities cause an increasingly large...
percentage of deaths among people living with HIV in settings where antiretroviral drugs have been used widely for more than a decade. Between 1995 and 2006, the percentage of non-HIV-related deaths among people living with HIV in New York City increased from 8% to 32%, with cardiovascular conditions and non-AIDS-defining cancers accounting for nearly half of all deaths (New York City Department of Health and Mental Hygiene, 2007). In Norway, while the risk of HIV-related death has declined 80% in the era of combination antiretroviral therapy, the mortality rate for individuals living with HIV is still four times higher than in the general population (2007).

As people living with HIV in low- and middle-income countries live longer as a result of increased access to antiretroviral drugs, it is likely that the range and prevalence of HIV-related opportunistic infections will also evolve. For example, based on experience in high-income countries, where the drugs have been widely available since the mid-1990s, various non-AIDS-defining cancers may become increasingly important complications of HIV infection (Grulich et al., 2007; Dhir et al., 2008).

**Mental health**

As a life-threatening and highly stigmatized illness, HIV infection inevitably has effects on mental health. It is estimated that nearly half of all people living with HIV worldwide will suffer at some point from clinical depression (Miller, 2006). In addition to its psychosocial consequences, HIV infection can have important biological effects on mental health functioning, resulting in cognitive impairment and dementia (Freeman et al., 2005).

Integrating mental health services into antiretroviral treatment programmes is critical to effective care and treatment. On average, patients with a mood, anxiety, or substance abuse disorder have a less robust virological response to antiretroviral therapy than individuals without such a condition (Pence et al., 2007). Depression has also been associated with reduced nutritional intake among people living with HIV (Isaac et al., 2008).

Proven counselling, social support, and psychotherapeutic strategies exist to address the mental health needs of people living with HIV (Catalan et al., 2005). National governments in countries with generalized epidemics report that psychosocial support services are available in all districts in need in 52% of countries, although nongovernmental informants say this is the case in only 27% of such countries (UNGASS Country Progress Reports, 2008.) Professional mental health services are seldom available in low- and middle-income countries. While mental disorders account for more than 11% of the total burden of disease in low- and middle-income countries, many countries invest less than 1% of their health budget in mental health services (Patel, 2007). Expanding mental health capacity in settings where antiretroviral drugs are being administered is an important priority in the push towards universal treatment access.

**Nutrition and HIV treatment and care**

Nutritional status is one of the best predictors of HIV-related mortality. As HIV disease progresses, nutritional status often declines. HIV infection increases protein, micronutrient, and energy requirements in both adults and children (WHO, 2003; Friis, 2005). At the same time, HIV-related symptoms such as lack of appetite, mouth sores, or nutrient malabsorption may decrease nutritional intake. Lack of access to adequate food is a particular challenge for people who initiate antiretroviral therapy, and has been shown to inhibit uptake of treatment.

HIV exacerbates already severe nutritional deficiencies that are common in many countries that have been heavily affected by the epidemic. Among least-developed countries generally, 35% of the population suffers from inadequate nutrition (UNDP, 2007). Micronutrient deficiencies are one of the most common forms of poor nutrition in low-income countries, and may further compromise the immune systems of
people living with HIV, diminishing the body’s ability to fight infection (Food and Nutrition Technical Assistance, 2004a; Jones et al., 2006).

In the case of HIV-positive children, poor nutrition accelerates HIV disease progression and increases the risk of death in the early years of life (Walzer et al., 2006). In sub-Saharan Africa and other countries affected by HIV, nutritional deficiencies are common among children (Bryce et al., 2008). It is particularly important to monitor the nutritional intake of breastfed children born to HIV-positive mothers during weaning, this transition often results in underfeeding and a consequent increased risk of mortality or stunting (Becquet et al., 2006).

Timely nutritional support for people living with HIV may help extend the asymptomatic period of relative health for people living with HIV, or, where severe immune deterioration has already occurred, it may reduce the risk of death. (For a summary of available evidence on the impact of nutritional support on health outcomes for people living with HIV, see Gillespie & Kadiyala, 2005) Proven strategies for improving the nutritional status of individuals living with HIV include food rations in food-insecure areas, micronutrient supplementation, and therapeutic foods to address the effects of moderate or severe malnutrition (Gillespie & Kadiyala, 2005). Nutritional care for people living with HIV is available in all districts in only 11% of countries with generalized epidemics, according to nongovernmental reports, although government reports say such services are widely available in 23% of countries (UNGASS Country Progress Reports, 2008).

Nutritional monitoring, along with appropriate and timely intervention, is a critical component of antiretroviral management. At the most basic level, when patients are hungry or undernourished, they find it difficult, sometimes impossible, to adhere to complex regimens (Marston & DeCock, 2004). Depending on the regimen prescribed, taking antiretroviral drugs can require dietary restrictions; some drugs are best taken on an empty stomach, while metabolism of others is optimized when taken at or near mealtime (Food and Nutrition Technical Assistance, 2004b). As with any drug, antiretroviral medicines are likely to be most effective when taken by people who are well nourished. In addition, certain common side-effects of the drugs, such as nausea or loss of appetite, may result in reduced nutritional intake.

A recent operational research project by the World Food Programme and the Centre for Infectious Disease Research in Zambia found that patients on antiretroviral therapy who received focused nutritional support experienced better rates of treatment adherence.

**Improving access to treatment and care services**

Although there has been major progress, treatment scale-up has not kept pace with actual needs. In diverse regions, the quest to bring life-preserving HIV therapies to those who need them has encountered a range of obstacles. To achieve universal access, effective strategies are required to overcome these impediments.

**Limited knowledge of HIV serostatus**

Affordable technologies exist to diagnose HIV infection, including rapid tests that avoid the need for individuals to return to testing sites to receive their test results. Although diagnosing HIV is fairly straightforward in adults—except soon after exposure to the virus, when more sophisticated technologies are needed to make a definitive diagnosis—it is more complicated in young children, as described above.

Timely diagnosis of HIV infection is critical to effective medical management of HIV infection. Individuals diagnosed late in the course of infection respond less well to antiretroviral therapy and are at increased risk of illness and death (Girardi, Sabin & Monforte, 2007). A study of people in New York City found that individuals with an opportunistic illness at the time of their AIDS diagnosis were three times more likely to die within three years than those with fewer than 200
Palliative care in national HIV responses

An issue of emerging importance in the push towards universal access is the role of palliative care as an integral component of national HIV responses. Palliative care includes psychosocial support, access to pain and symptom control, and other measures to address the physical, mental, and spiritual dimensions of coping with HIV and related conditions.

Existing palliative care programmes are under enormous pressure to meet growing demands. For example, in the Motheo District of the Free State, South Africa, there are an estimated 44 000 maternal orphans, 7736 of whom are living with HIV. More than 25 000 children under the age of 10 are thought to be malnourished. The district’s one palliative care programme is equipped to serve 1300 children, a fraction of those in need of support (Dippenaar & Marston, 2008).

Legal and regulatory barriers to accessing cheap and simple pain control medication are a major impediment to comprehensive palliative care services. The International Narcotics Control Board has recognized that most countries have low consumption of opioid-based medicines and that seven high-income countries that account for only 12% of the world’s population (Austria, Australia, Canada, France, Germany, the United Kingdom and the United States) consume 84% of medical morphine. The Board has urged governments to critically examine and revise the ways they assess domestic needs for opiates (International Narcotics Control Board, 1989).

CD4 cells per mm$^3$ but no history of an opportunistic infection (New York City Department of Health and Mental Hygiene, 2005).

Many people living with HIV are diagnosed with the virus only after extensive immune deterioration has occurred. For example, in Brazil—despite more than a decade of experience with publicly provided antiretroviral drugs—almost half of people with HIV are diagnosed with infection at the same time they are diagnosed with AIDS (Agence France Presse, 2008). Large population-based surveys in low- and middle-income countries have only recently begun collecting information on respondents’ HIV testing history, precluding an analysis of testing trends. Even more recently, serological testing has been incorporated into these surveys, permitting an analysis of both HIV status and testing history. In the 16 countries where this analysis has been possible, most respondents who have tested HIV-positive had never received an HIV test (MEASURE DHS, 2008). In almost 40% of countries with generalized epidemics, governments report that HIV counselling and testing services have not been implemented in all districts in need. Nongovernmental sources report that HIV counselling and testing services are not widely available in 70% of countries (UNGASS Country Progress Reports, 2008). HIV testing and counseling services for tuberculosis patients are not yet universally available: in countries with a generalized epidemic, 46% of government reports indicate these services to be available in all districts in need, but only 27% of nongovernmental reports (UNGASS Country Progress Reports, 2008).

The challenge of ensuring widespread and timely knowledge of HIV serostatus is not unique to
low- and middle-income countries. It is estimated that 25% of all HIV-positive people in the United States have yet to be diagnosed (Centers for Disease Control and Prevention, 2002). In New York City, a global financial capital, one in four people who tested HIV-positive received an AIDS diagnosis within one month of their positive test (New York City Department of Health and Mental Hygiene, 2007).

As Chapter 2 describes, the severe stigma attached to HIV in many countries discourages many people from learning their HIV serostatus (Weiser et al., 2006). Yet there is growing evidence that concerted national action to promote testing and tackle HIV stigma can significantly increase testing rates. For example, many countries are implementing provider-initiated HIV testing and counselling in health-care settings (UNAIDS & WHO, 2007), as well as using rapid testing technology, mobile vans, and other outreach methods to increase knowledge of HIV serostatus. In Botswana, the number of people using testing services more than doubled in the year after implementation of provider-initiated testing and counselling (Steen et al., 2007). Social and behavioural science research suggests that the magnitude and nature of services linked to testing are often key determinants of use (Obermeyer & Osborn, 2007).

A national campaign promoting knowledge of HIV serostatus in Malawi culminated in the second ‘National HIV Testing and Counseling Week’ in July 2007. The 186,631 people tested that week significantly exceeded the campaign’s target of 130,000, with more than 80% of these individuals never having been tested previously. The campaign resulted in the diagnosis of HIV infection in 15,667 people, including 6.1% of males tested, 9.7% of non-pregnant females, and 11.3% of pregnant women (Malawi National AIDS Commission, 2007). Likewise, Ethiopia achieved an eight-fold increase in use of HIV testing and counselling services, identifying more than 108,000 new HIV infections, or 6% of all people tested (Ethiopia Federal Ministry of Health, 2007).

As African traditional medicine is often the primary, and sometimes the only, accessible health-care option in some parts of sub-Saharan Africa, involvement of traditional healers in the HIV response is critical. In the KwaZulu Natal Province of South Africa, efforts have focused on building the capacity of traditional healers to discuss HIV and sexuality with those who seek care.

Economic obstacles

Individuals often confront economic impediments to using antiretroviral drugs in the form of user fees, co-payments or other out-of-pocket costs borne by affected households. Most countries (92%, according to nongovernmental reports) have policies providing for free antiretroviral drugs (UNGASS Country Progress Reports, 2008.) However, civil society surveys in 17 countries found that many patients that receive free drugs must cover the sometimes considerable costs of diagnostic tests or treatments for opportunistic infections (International Treatment Preparedness Coalition, 2007). (see Figure 5.12) In recognition of the potential access barriers posed by out-of-pocket costs, the Government of Cameroon began making HIV treatment free in 2007, an approach pursued by numerous other countries.

Treatment may sometimes be much more easily accessible in urban areas than in rural settings. Limited access to transportation can significantly limit treatment access for HIV-positive people in rural areas. Even when a local clinic is able to provide antiretroviral drugs, HIV-positive rural dwellers must sometimes travel hours to obtain CD4 or viral load tests (International Treatment Preparedness Coalition, 2007). In 2008, Indian Railways announced a 50% discount on train fares for HIV-positive individuals travelling to receive HIV treatment.
Ensuring equal access

In addition to increasing the overall number of people receiving antiretroviral drugs, focused efforts are required to ensure that all people needing treatment have equal access. Civil society surveys confirm that many people living with HIV, especially those from marginalized groups, often face considerable obstacles to accessing HIV treatment (Human Rights Watch, 2007a; International Treatment Preparedness Coalition, 2007). Nongovernmental respondents report that 74% of countries have policies in place to ensure equal access to HIV prevention, treatment, care, and support for most-at-risk populations; however, they also report that 63% of countries have laws, regulations, or policies that impede service access for such groups (UNGASS Country Progress Reports 2008). For example, several countries stipulate that young people living with HIV must obtain parental consent before receiving antiretroviral drugs. According to the civil society “shadow” report on national progress in the Russian Federation, a national registry of drug users often results in discrimination in service access for HIV-positive people whose names appear on the registry.

Sustaining HIV treatment and care

While considerable progress has been achieved in expanding access to antiretroviral therapy, an exceptional, decades-long collective effort will be needed to sustain access to lifelong HIV treatment. The number of people needing treatment will continue to grow as the HIV disease process advances to advance in the estimated 30 million HIV-positive people worldwide who have never been on treatment. Moreover, per-patient treatment costs are likely to increase over time, as patients on standard fixed-dose combinations move to more costly second- and third-line drugs.

The challenge of sustaining treatment advances is vividly illustrated by the experience of Brazil. The leader of global efforts to expand treatment access, Brazil began offering antiretroviral treatment through its public health system in 1996, then expanded access rapidly while achieving a nearly five-fold reduction in the cost of the medications between 1997 and 2004. Yet recently, budget outlays for HIV treatment have significantly risen (Nunn et al., 2007). It is estimated that the cost of providing the drugs in Brazil in 2008 will be US$ 525 million—more than double the amount spent in 2004 (UNAIDS, 2007b).

To ensure that recent improvements in treatment access are sustained over the long run, focused efforts will be required to address key factors that might jeopardize treatment access in future years.

Human resources

Acute shortages of health-care professionals impede treatment scale-up in many of the countries heavily affected by the epidemic. Home to more than two thirds of all people living with
CHAPTER 5

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Global resolve to strengthen health systems in resource-limited settings

Expanding and sustaining treatment access in resource-limited settings will require the creation of strong and durable human capacity to administer antiretroviral therapy. This priority has attracted a broad array of capacity-building efforts. One such initiative led by WHO focuses on ways to “treat, train, and retain” health workers (Samb et al., 2007).

Donors are placing greater emphasis on strengthening health systems to support HIV treatment scale-up. In 2007, PEPFAR spent US$ 638 million to build capacity in public and private health sectors (PEPFAR, 2008). In November 2007, the Global Fund announced that 20% of funding for its 2008 round of competitive grantmaking would focus on system strengthening measures, such as upgrading infrastructure, strengthening supply chain systems, and reinforcing human resources (Global Fund, 2007b).

The epidemic itself is undermining the capacity of health-care systems to meet the challenge posed by the push towards universal access. While the actual number of health-care workers infected with HIV may appear relatively modest in a given country, these infections can have a major impact on the national HIV response, as a modest number of clinicians are often responsible for delivering antiretroviral drugs, even in high-prevalence countries. The critical need to preserve essential human capacity in

HIV, sub-Saharan Africa has only 3% of the world’s health workers and accounts for less than 1% of global health spending (WHO, 2006d). While, for example, 347 physicians are available for every 100,000 people in Norway, there are only two for every 100,000 people in Malawi or the United Republic of Tanzania (UNDP, 2007). Numerous factors contribute to the human resource crisis in health-care systems, including the weakness of national medical education and training programmes, limited implementation of national human resource management policies, and the well-documented “brain drain” of health professionals who migrate from low-paying jobs in their home countries to more remunerative work in high-income or neighbouring countries (Moore & Morrison, 2007; Arah, Ogbu & Okeke, 2008).

The epidemic itself is undermining the capacity of health-care systems to meet the challenge posed by the push towards universal access. While the actual number of health-care workers infected with HIV may appear relatively modest in a given country, these infections can have a major impact on the national HIV response, as a modest number of clinicians are often responsible for delivering antiretroviral drugs, even in high-prevalence countries. The critical need to preserve essential human capacity in
health sectors has prompted some countries to introduce special HIV prevention and treatment services for health workers. For example, in Malawi, more than 1000 health-care workers were receiving antiretroviral drugs in June 2006. The Government of Malawi estimates that improved antiretroviral therapy access saves the lives of 250 health-care workers, generating productivity savings roughly equal to the amount of human resources required to deliver antiretroviral drugs on a national scale (Makombe et al., 2007). Identification of human resource constraints as an impediment to implementation of a Global Fund grant in Malawi prompted the Global Fund to approve allocation of US$ 40 million to support the country’s emergency human resource strategy, which has also attracted significant financing from the United Kingdom Department for International Development.

Personnel shortages also impede the functioning of systems that are vital to treatment access. For example, national regulatory authorities are often extremely weak in low- and middle-income countries (Gray, 2004). As a result, many newer and second-line antiretroviral drugs remain unregistered in some high-prevalence countries (International Treatment Preparedness Coalition, 2007). A number of strategies have been proposed to reduce the drug registration bottleneck in low- and middle-income countries, including targeted capacity-building in national regulatory authorities, greater regional collaboration in drug registration, and increased assistance to low-income countries from regulators in high-income countries (Gray, 2004).

Supply management problems may also interfere with the delivery of antiretroviral drugs. Civil society surveys in 17 countries found that antiretroviral drug stockouts (i.e. no stock available) were reported in diverse clinical settings in different regions in 2007 (International Treatment Preparedness Coalition, 2007). While stockouts are a common problem for many health conditions in resource-limited countries, functioning back-up systems are needed to prevent interruption of HIV treatment.

Improving diagnostic capacity

Although a public health approach makes it possible to administer antiretroviral drugs in the absence of sophisticated diagnostic techniques that are standard in high-income settings, improved diagnostic capacity in resource-limited settings will help clinicians to maximize the impact and durability of antiretroviral therapy. The need for virological testing to diagnose HIV in perinatally exposed children has particular implications for local laboratory capacity. Experience indicates the feasibility of implementing CD4 and viral-load testing in resource-limited settings, and the scaling up
Task shifting to increase health system capacity

One of several strategies to address acute health-care worker shortages, task shifting involves the redistribution of clinical tasks within the health team from more to less specialized health workers—for example, from specialist physicians to general practitioners, from physicians to nurses, and from nurses to trained members of the community. Task shifting increases the efficiency of health-care delivery, expands the human resource pool, and facilitates more rapid scale-up of treatment programmes (WHO, 2007e).

Task shifting has emerged in recent years as a major topic of discussion in HIV circles as a result of treatment scale-up, but the approach is common in many resource-limited settings. Non-physician clinicians are prevalent in 25 of 47 African countries surveyed, outnumbering physicians in nine countries (WHO, UNAIDS & PEPFAR, 2008). More than three decades experience with use of community workers for DOTS tuberculosis therapy underscores the capability of such workers to deliver many primary care services (Samb et al., 2007). Although the emphasis on task shifting for antiretroviral therapy scale-up may give rise to concerns about the possibility of second-class care in resource-limited settings, the reality is that task shifting has become common in clinical settings in high-income countries, with increased and satisfactory use of physician’s assistants and nurse practitioners (Wilson et al., 2005).

To expedite treatment scale-up and expand human resources, several countries with high HIV prevalence have supplemented the longstanding informal use of non-physicians with more systematic efforts to promote task shifting as a component of their national HIV strategies. These efforts are yielding promising results. In Mozambique, after training medical officers to prescribe antiretroviral drugs in 85% of the country’s clinical sites, the number of sites administering the drugs increased more than three-fold in eight months, while treatment coverage increased from 9.4% to 16.4% (Gimbel et al., 2007). Programmes using a nurse-centred approach to HIV service delivery in Haiti and Rwanda report low loss to follow-up, high treatment success rates, and levels of mortality that are comparable with those in more traditional antiretroviral programmes (WHO, UNAIDS & PEPFAR, 2008).

To help guide efforts to extend human resources for HIV, WHO, UNAIDS, and the PEPFAR initiative collaboratively developed detailed guidelines for task shifting; these guidelines address quality-assurance mechanisms and other pertinent issues. Task shifting is not a panacea for infrastructure weaknesses that inhibit treatment scale-up, but instead is one of many approaches that should be pursued, such as increased remuneration for health-care workers in resource-limited settings and improved medical education and training.

of such assays is an important health priority (WHO, 2007a).

Several methods exist for measuring CD4 counts including a new, simple, low-cost assay that may be especially well-suited to small facilities that lack extensive laboratory capacity (Srithanaviboonchai et al., 2008). The Clinton Foundation has negotiated price reductions of up to 80% from the leading makers of technologies for CD4 and viral-load testing.

Ensuring the affordability of antiretroviral drugs

In many countries heavily affected by HIV—including Kenya, Malawi, Nigeria, and Zambia—annual per capita spending on health care of any kind is less than US$ 100 (PPP)
(UNDP, 2007). In settings where health resources are so limited, many medications are deemed too expensive for routine use in resource-limited settings (Steinbrook, 2007). Historically, this has been particularly true for new, patented medications developed by pharmaceutical companies in high-income countries.

As in many other arenas, the HIV response has helped forge new ways of improving access to essential medications in low- and middle-income countries. Due to activist pressure, the emergence of competition from generic manufacturers, and direct negotiations with pharmaceutical companies by UNAIDS and other partners, prices for the leading antiretroviral drugs have fallen sharply during the last ten years. What has emerged is a pricing regime that has long been advocated by global health experts but seldom put into practice; that is, “tiered” pricing, whereby companies charge different prices depending on a country’s ability to pay. The new approach to drug pricing has freed up substantial resources for health services in low- and middle-income countries. For example, it is estimated that Brazil saved approximately US$ 1 billion between 2001 and 2005 as a result of its domestic generic manufacture of eight antiretroviral drugs and its negotiation of price reductions from manufacturers (Nunn et al., 2007). National governments in 94% of countries with generalized epidemics, as well as in 61% of countries with concentrated epidemics, report having national policies for using generic drugs or parallel importation of medications to promote antiretroviral access (UNGASS Country Progress Reports 2008).

Prices have been reduced under the adoption of international trade rules that provide for flexible application of intellectual property provisions with respect to medications needed to address serious public health problems. Under prevailing rules, countries may issue compulsory licenses for patented medications where access is necessary to protect public health.

In addition, the existence of a flourishing generic pharmaceutical industry in countries such as Brazil, India, South Africa, and Thailand has exerted a downward pressure on prices and increased the range of affordable options for national treatment programmes. India, the largest supplier of medications to low- and middle-income countries, exports two thirds of the drugs it manufactures (Steinbrook, 2007).

The existing global intellectual property framework has not precluded the emergence of controversies and uncertainties. In 2007, for example, a public dispute arose between Thailand and Abbott Laboratories after the country announced plans to issue a compulsory license for the noncommercial use of the company’s lopinavir-ritonavir antiretroviral drug. This decision by Thailand followed the government’s unsuccessful negotiations with Abbott to agree on an affordable price for the medication. In addition, since 2005, India has been issuing patents, as required by the World Trade Organization. Whether this change might ultimately drive prices upward by impeding the ability of India’s generics industry to produce key antiretroviral drugs is a source of concern.

Despite the pricing breakthroughs of recent years, further declines in the cost of purchasing antiretroviral drugs are needed to accelerate treatment scale-up. This is especially true with regard to second- and third-line antiretroviral drugs, which typically cost significantly more than first-line drugs in low- and middle-income countries. Although only 4% of patients on antiretroviral therapy in 23 countries surveyed by WHO were on second-line regimens in 2006 (WHO, 2007a), the need for second-line therapies will grow over time. An estimated 3% of patients on first-line antiretroviral drugs—or approximately 180 000 individuals in 2008—will need to switch to second-line regimens each year (WHO, 2006b). Following negotiations with leading manufacturers of generic medications, in May 2007 the Clinton Foundation and UNITAID announced steep price reductions on 16 different formulations of eight second-line antiretroviral drugs. WHO has issued guidance to countries on criteria to use in selecting second-
line regimens for use in national treatment guidelines (WHO, 2007a).

While major progress has been achieved, daunting challenges lie ahead if the world is to move towards universal access. Yet experience during this decade underscores that such challenges can be overcome. As Chapter 7 explains, sustaining the long-term response will demand strong political commitment, even greater resources, expanded national capacity, and the active involvement of all stakeholders, especially people living with HIV.

Evidence for action

Are the right actions being taken?

- All countries have a national policy or strategy to promote comprehensive HIV treatment, care, and support.
- Nearly all (85%) countries with generalized epidemics and 52% with concentrated epidemics report having reliable estimates and having projected future needs of the number of individuals requiring antiretroviral therapy.
- National governments in 92% of low- and middle-income countries report that current policies provide for delivery of antiretroviral drugs free of charge.

Are the right actions being undertaken in the right manner?

- Globally, women are receiving higher coverage of antiretroviral therapy than men, although children have sharply lower coverage of antiretroviral drugs than adults and adolescents in generalized epidemic countries where burden is highest.
- Nongovernmental informants report that many countries (40%), including most in Eastern Europe and Central Asia, South and South-East Asia, and North America, have laws, regulations or policies that impede access to HIV-related services among injecting drug users.
- HIV and tuberculosis treatment services have not been effectively integrated in most countries in which there are large numbers of individuals with co-infection with HIV and tuberculosis. National governments indicate that only 42% of countries with generalized epidemics have implemented routine tuberculosis screening for HIV-positive patients, and only 27% provide tuberculosis preventive therapy in all districts in need; nongovernment responses indicate that these two services are widely available in only 24% of countries with generalized epidemics.

Have these actions been sufficiently scaled up to make a difference?

- By the end of 2007, antiretroviral drugs reached 3 million people in low- and middle-income countries, representing 31% of estimated global need and a 45% improvement over 2006.
- AIDS deaths have started to decline, in part as a result of improved treatment access. Expanded antiretroviral access is also improving quality of life for people living with HIV.
- Only 32% of incident tuberculosis cases in people living with HIV received dual treatment for their HIV and tuberculosis in 2007.