2. TREATMENT AND CARE FOR PEOPLE LIVING WITH HIV

Key findings

- About 950 000 more people were receiving antiretroviral therapy at the end of 2007 compared with the end of 2006, reaching nearly 3 million people living with HIV receiving antiretroviral therapy.

- The greatest increase in the number of people receiving treatment was in sub-Saharan Africa.

- Despite these unprecedented gains, global coverage of antiretroviral therapy in low- and middle-income countries remains low (31% of the need).

- Treatment programmes are facing challenges related to high mortality in the early months of treatment and low rates of retention.

- Access to antiretroviral therapy among women is higher than or equal to access among men.

- About 97% of adults and children on therapy in low- and middle-income countries are receiving first-line antiretroviral drug regimens.

- The average price of second-line regimens remains high in low- and middle-income countries.

- Access to co-trimoxazole prophylaxis and antiretroviral therapy for people living with HIV/TB is falling short because many people with TB do not know their HIV status.
2.1 Antiretroviral therapy

Recent years have seen an unprecedented momentum to expand access to antiretroviral therapy in low- and middle-income countries and to reduce morbidity and mortality among people living with HIV. Countries are using simplified and standardized approaches to initiate, deliver and monitor treatment and are able to purchase antiretroviral drugs at increasingly lower prices. However, the number of people receiving antiretroviral therapy continues to fall short of the need, and new challenges are emerging as treatment is scaled up.

### Table 2.1. Estimated number of people receiving antiretroviral therapy, people needing antiretroviral therapy and percentage coverage in low- and middle-income countries according to region, December 2003 to December 2007

<table>
<thead>
<tr>
<th>Geographical region</th>
<th>Estimated number of people receiving antiretroviral therapy, December 2007 (range)</th>
<th>Estimated number of people needing antiretroviral therapy, December 2007 (range)</th>
<th>Antiretroviral therapy coverage, December 2007 (range)</th>
<th>Estimated number of people receiving antiretroviral therapy, December 2006 (range)</th>
<th>Estimated number of people needing antiretroviral therapy, December 2006 (range)</th>
<th>Antiretroviral therapy coverage, December 2006 (range)</th>
<th>Estimated number of people receiving antiretroviral therapy, December 2005 (range)</th>
<th>Estimated number of people needing antiretroviral therapy, December 2005 (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sub-Saharan Africa</td>
<td>2 120 000 ([1 925 000–2 315 000])</td>
<td>7 000 000 ([6 250 000–7 900 000])</td>
<td>30% ([27%–34%])</td>
<td>1 375 000 ([1 280 000–1 470 000])</td>
<td>6 700 000 ([5 900 000–7 600 000])</td>
<td>21% ([18%–23%])</td>
<td>100 000 ([75 000–125 000])</td>
<td></td>
</tr>
<tr>
<td>Eastern and southern Africa</td>
<td>1 690 000 ([1 560 000–1 820 000])</td>
<td>5 300 000 ([4 720 000–6 000 000])</td>
<td>32% ([28%–36%])</td>
<td>1 115 000 ([1 000 000–1 180 000])</td>
<td>5 100 000 ([4 400 000–5 700 000])</td>
<td>22% ([20%–25%])</td>
<td>75 000 ([56 000–94 000])</td>
<td></td>
</tr>
<tr>
<td>West and central Africa</td>
<td>430 000 ([370 000–490 000])</td>
<td>1 700 000 ([1 400 000–2 100 000])</td>
<td>25% ([20%–31%])</td>
<td>260 000 ([230 000–290 000])</td>
<td>1 600 000 ([1 400 000–2 100 000])</td>
<td>16% ([12%–19%])</td>
<td>25 000 ([19 000–31 000])</td>
<td></td>
</tr>
<tr>
<td>Latin America and the Caribbean</td>
<td>390 000 ([350 000–430 000])</td>
<td>630 000 ([550 000–770 000])</td>
<td>62% ([51%–70%])</td>
<td>345 000 ([305 000–385 000])</td>
<td>600 000 ([510 000–740 000])</td>
<td>58% ([47%–63%])</td>
<td>210 000 ([160 000–240 000])</td>
<td></td>
</tr>
<tr>
<td>Latin America</td>
<td>360 000 ([320 000–400 000])</td>
<td>560 000 ([490 000–700 000])</td>
<td>64% ([51%–73%])</td>
<td>325 000 ([290 000–365 000])</td>
<td>530 000 ([400 000–650 000])</td>
<td>81% ([49%–72%])</td>
<td>208 000 ([108 000–250 000])</td>
<td></td>
</tr>
<tr>
<td>The Caribbean</td>
<td>30 000 ([25 000–35 000])</td>
<td>70 000 ([60 000–80 000])</td>
<td>43% ([38%–50%])</td>
<td>20 000 ([15 000–25 000])</td>
<td>65 000 ([50 000–75 000])</td>
<td>31% ([27%–40%])</td>
<td>4 000 ([3 000–5 000])</td>
<td></td>
</tr>
<tr>
<td>East, South and South-East Asia</td>
<td>420 000 ([375 000–465 000])</td>
<td>1 700 000 ([1 300 000–2 100 000])</td>
<td>25% ([20%–32%])</td>
<td>280 000 ([225 000–335 000])</td>
<td>1 600 000 ([1 220 000–2 060 000])</td>
<td>18% ([14%–23%])</td>
<td>70 000 ([52 000–88 000])</td>
<td></td>
</tr>
<tr>
<td>Europe and Central Asia</td>
<td>54 000 ([51 000–57 000])</td>
<td>320 000 ([240 000–400 000])</td>
<td>17% ([12%–22%])</td>
<td>35 000 ([23 000–37 000])</td>
<td>260 000 ([180 000–380 000])</td>
<td>13% ([9%–19%])</td>
<td>15 000 ([11 000–19 000])</td>
<td></td>
</tr>
<tr>
<td>North Africa and the Middle East</td>
<td>7 000 ([6 000–8 000])</td>
<td>100 000 ([70 000–135 000])</td>
<td>7% ([5%–10%])</td>
<td>5 000 ([4 000–6 000])</td>
<td>97 000 ([60 000–130 000])</td>
<td>5% ([4%–8%])</td>
<td>1 000 ([750–1 250])</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>2 990 000 ([2 700 000–3 280 000])</td>
<td>9 700 000 ([8 700 000–11 000 000])</td>
<td>31% ([27%–34%])</td>
<td>2 040 000 ([1 850 000–2 230 000])</td>
<td>9 300 000 ([8 200 000–10 600 000])</td>
<td>22% ([19%–25%])</td>
<td>400 000 ([300 000–500 000])</td>
<td></td>
</tr>
</tbody>
</table>

**Note:** Some numbers do not add up due to rounding.

a. For an explanation of the methods used, see explanatory notes to Annex 1.

b. Data on children – when available – are included.

c. The coverage estimate is based on the estimated numbers of people receiving and needing antiretroviral therapy.
Close to 3 million people [2,990,000 people; range 2,700,000 – 3,280,000] were receiving antiretroviral therapy at the end of 2007. This represents a 7.5-fold increase in four years.

The year 2007 also saw an unprecedented annual increase in the number of people receiving antiretroviral therapy. About 950,000 more people were receiving antiretroviral therapy at the end of 2007 compared with the end of 2006, versus a corresponding increase of 750,000 in 2006 (2). This represents an average monthly increase of 79,000 more people receiving antiretroviral therapy in 2007.

However, global coverage of antiretroviral therapy is still limited, reaching 31% [27–34%] of the 9.7 million [8.7 million–11.0 million] people in need at the end of 2007. In comparison, these percentages were 5% [4–6%] in 2003, 8% [7–10%] in 2004, 15% [13–17%] in 2005 and 22% [19–25%] in 2006. Box 2.1 explains recent revisions in estimates of treatment need.

Box 2.1. Estimating antiretroviral therapy need and coverage

Antiretroviral therapy coverage measures the proportion of people who need antiretroviral therapy that have access to it. The numerator (the number of people receiving antiretroviral therapy) is derived from national programme reporting systems, aggregated from health facilities or other service delivery sites. The denominator (the total number of people who need antiretroviral therapy) is generated using a standardized statistical modelling approach (3). Estimating the number of people who need antiretroviral therapy raises some definition and measurement issues, which in turn influence estimates of coverage.

To estimate the number of people who need antiretroviral therapy in a country, WHO and UNAIDS use statistical modelling methods that include all people who meet treatment initiation criteria, whether or not these people know their HIV status and their eligibility for antiretroviral therapy. Hence the number of people who need antiretroviral therapy in a country includes:

- the people currently receiving antiretroviral therapy;
- the people who know they are HIV-positive and are eligible for antiretroviral therapy but do not have access to it;
- the people who do not know their HIV status but meet criteria for initiating treatment.

A comprehensive estimate of the number of people who need treatment should include all three categories of people mentioned above.

Estimation methods
Based on the recommendations of the UNAIDS Reference Group on Estimates, Modelling and Projections, UNAIDS and WHO have developed modelling methods and tools to generate country estimates of the magnitude of the epidemic and key impact indicators, including mortality (3). Treatment needs are estimated using a statistical software package called Spectrum (4). The tool takes into consideration epidemiological surveillance data and key assumptions (including adult prevalence over time, average survival of people living with HIV with and without antiretroviral therapy and average time between seroconversion and eligibility for antiretroviral therapy) to generate estimates of treatment need. The estimation methods are regularly updated using new epidemiological and research data and improved methods.

Some countries have developed their own method for estimating treatment need, which could differ from the estimates derived using UNAIDS/WHO methods. For example, some countries do not include the third category of people mentioned above (the people who do not know their HIV status but meet criteria for initiating treatment) in their estimates of treatment need, which incompletely represents the progress that needs to be made to achieve universal access.

To analyse and compare antiretroviral therapy coverage across countries, this report uses standardized estimates of treatment need derived using UNAIDS/WHO methods. The software is used to generate ranges around estimates for antiretroviral therapy need. Depending on the quality of surveillance data, the ranges can be very large in some countries. The point estimate is used to calculate coverage.

Annex 1 reports alternative estimates of needs based on individual country methods.

New parameters in estimation methods in 2007
The global, regional and country estimates of treatment need published in this report cannot be compared with the 2006 estimates published in 2007 due to new parameters in the estimation model. In 2006, the UNAIDS Reference Group on Estimates, Modelling and Projections recommended changes in various parameters in the estimation method based on new evidence. Specifically, the Reference Group recommended that the net survival time from seroconversion to death in the absence of antiretroviral therapy be increased from 9 years to 11 years, with the time from seroconversion to antiretroviral therapy eligibility revised to 8 (instead of 7) years and the time from antiretroviral therapy eligibility to death revised to 3 (instead of 2) years. These revised parameters,
together with an increasing number of people receiving antiretroviral therapy, has resulted in a substantial increase in the estimates of the total number of people who need antiretroviral therapy. In 2007, 9.7 million [8.7 million–11.0 million] people are estimated to need antiretroviral therapy. When the revised parameters are applied retrospectively to the previous year, 9.3 million [8.2 million–10.6 million] people are estimated to have needed antiretroviral therapy in 2006, instead of 7.1 million as published last year. Based on these new estimates, global coverage in 2006 was 22% [19–25%] instead of 28% [24–34%] as previously published.

In the years to come, the estimation of treatment need will continue to evolve due to changes in treatment guidelines, estimation methods and trends in the epidemic, rendering comparisons of coverage difficult.

**Changes in treatment guidelines**

WHO guidelines currently recommend: prescribing antiretroviral therapy to everyone with a clinical condition indicative of WHO clinical stage 4 irrespective of CD4 cell count; prescribing antiretroviral therapy to everyone with a CD4 cell count under 200 cells per mm3 irrespective of the clinical stage; and considering prescribing antiretroviral therapy when the CD4 cell count is below 350 cells per mm3 and the person has clinical stage 3 disease (5). Future changes in such recommendations would influence the estimates of treatment need.

**The expanding epidemic**

Despite prevention efforts, 2.5 million [1.8 million–4.1 million] people were infected in 2007, and this number was above 3.0 million in the late 1990s and early 2000s. With an average period of eight years between HIV infection and treatment eligibility, between 2.5 million and 3.0 million additional people will therefore newly need treatment each year in the coming years. This total must be added to the increasing number of people who are currently receiving treatment or are eligible based on WHO guidelines.

The greatest increase in the number of people receiving treatment in 2007 was in sub-Saharan Africa (Fig. 2.1 and 2.2). About 2 120 000 [1 925 000–2 315 000] people were receiving antiretroviral therapy at the end of 2007 in sub-Saharan Africa versus 1 375 000 [1 280 000–1 470 000] people in 2006. This represents an increase of 54% in one year in this region. Regional antiretroviral therapy coverage was 30% [27–34%] in 2007 versus 21% [18–23%] in 2006 and just 2% in 2003. Coverage is higher in eastern and southern Africa (32% [28–36%]) than in west and central Africa (25% [20–31%]). Sub-Saharan Africa represents 71% of the estimated total treatment need in low- and middle-income countries and 72% of the total number of people receiving treatment at the end of 2007.

In East, South and South-East Asia, an estimated 420 000 [375 000–465 000] people were receiving antiretroviral therapy at the end of 2007. Regional antiretroviral therapy coverage was 25% [20–32%] in 2007 versus 18% [14–23%] in 2006. This represents an increase of 51% in the number of people receiving antiretroviral therapy in one year in this region and a 6-fold increase over the 70 000 [52 000–88 000] people receiving treatment at the end of 2003. East, South and South-East Asia represents around 18% of the estimated total treatment need in low- and middle-income countries and 14% of the total number of people receiving treatment at the end of 2007.

About 390 000 [350 000–430 000] people were receiving antiretroviral therapy in Latin America and the Caribbean in December 2007, representing coverage of around 62% [51–70%] in this region versus 58% [47–68%] in 2006. The number of people receiving treatment in this region increased slightly in one year (13%). However, many countries in the region have already reached a high level of coverage, which limits their capacity to generate a large increase within one year. Latin America and the Caribbean represents only 6.5% of the estimated total treatment need in low- and middle-income countries but 13% of the total number of people receiving treatment at the end of 2007.

In Europe and Central Asia, 54 000 people [51 000–57 000] people were receiving antiretroviral therapy at the end of 2007 versus only 15 000 people at the end of 2003. Between 2006 and 2007, about 54% more people received antiretroviral therapy. Regional antiretroviral therapy coverage was 17% [12–22%] at the end of 2007. Europe and Central Asia represent 3% of the estimated total treatment need in low- and middle-income countries and about 2% of those reported to be receiving treatment.

North Africa and the Middle East has the lowest regional coverage: 7% [5–10%] versus 5% [4–8%] in 2006. An estimated 7000 [6000–8000] people were receiving treatment at the end of 2007, while 100 000 [70 000–135 000] people were in need. Progress in this region depends largely on scale-up in Sudan, which accounts for 87% of treatment need but has only 1% coverage.
Fig. 2.1. Antiretroviral therapy coverage in sub-Saharan Africa, 2003–2007

Fig. 2.2. Number of people receiving antiretroviral therapy in low- and middle-income countries, 2002–2007
At the end of 2007, 46 low- and middle-income countries were providing antiretroviral therapy to at least 31% of the people in need (the global average for low- and middle-income countries, including adults and children). Eleven countries achieved coverage of 50–75% of the people in need and eight countries achieved a coverage level of at least 75% of the people in need (Table 2.2).

Fifteen countries accounted for 75% of the 3 million people receiving treatment in low- and middle-income countries in 2007 (Fig. 2.3). Some of these countries substantially increased the number of people receiving treatment in 2007 as compared with 2006, with rates of increase exceeding 100% in three countries (Mozambique, Nigeria and the United Republic of Tanzania). Despite this progress, treatment in many of these countries remains well below the estimated need. Coverage exceeded 50% in 4 of these 15 countries (Botswana, Brazil, Namibia and Thailand), while in Ethiopia, Mozambique, Nigeria, South Africa and Zimbabwe, coverage was below the global average for low- and middle-income countries (below 31%, including adults and children).

In addition to the 3 million people receiving antiretroviral therapy in low- and middle-income countries at the end of 2007, an estimated minimum of 600 000 people were receiving antiretroviral therapy in high-income countries. However, obtaining an accurate estimate of this figure is difficult as many high-income countries do not collect and report this information systematically.

The Global Fund to Fight AIDS, Tuberculosis and Malaria and the United States President’s Emergency Plan for AIDS Relief are major sources of funding for antiretroviral therapy programmes in low- and middle-income countries. The Global Fund estimates that its funding supported the provision of treatment to 1 448 000 people at the end of 2007. Programmes financed by the United States President’s Emergency Plan for AIDS Relief are estimated to have supported the provision of treatment to 1 445 500 people. As about 910 000 people were receiving treatment through programmes jointly financed by the two initiatives, they were together supporting the provision of treatment to almost 2 million people at the end of 2007.

2.1.2 Expanding the availability of antiretroviral therapy

The number of sites delivering antiretroviral therapy is an important variable in assessing progress in scale-up and indicates the volume of people receiving antiretroviral therapy per site across regions. In 2007, globally, about 10 000 sites provided antiretroviral therapy in 119 reporting countries. This is more than twice the 4000 sites providing antiretroviral therapy in 2005. Of the 10 000 sites, about 4200 were in sub-Saharan Africa. The global average number of people who received antiretroviral therapy per site was about 300, but the number of people per site was higher in sub-Saharan Africa, with approximately 455 people per site. Although these figures are based on aggregate data and do not represent

### Table 2.2. Estimated antiretroviral therapy coverage of at least 31% in low- and middle-income countries, December 2007

<table>
<thead>
<tr>
<th>Countries with 31–50% antiretroviral therapy coverage (n = 27)</th>
<th>Countries with 50–75% antiretroviral therapy coverage (n = 11)</th>
<th>Countries with 75% or more antiretroviral therapy coverage (n = 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belize</td>
<td>Malawi</td>
<td>Argentina</td>
</tr>
<tr>
<td>Benin</td>
<td>Malaysia</td>
<td>Cambodia</td>
</tr>
<tr>
<td>Burkina Faso</td>
<td>Mali</td>
<td>El Salvador</td>
</tr>
<tr>
<td>Colombia</td>
<td>Morocco</td>
<td>Mexico</td>
</tr>
<tr>
<td>Dominican Republic</td>
<td>Papua New Guinea</td>
<td>Moldova</td>
</tr>
<tr>
<td>Ecuador</td>
<td>Peru</td>
<td>Panama</td>
</tr>
<tr>
<td>Equatorial Guinea</td>
<td>Philippines</td>
<td>Romania</td>
</tr>
<tr>
<td>Gabon</td>
<td>Poland</td>
<td>Rwanda</td>
</tr>
<tr>
<td>Guatemala</td>
<td>Suriname</td>
<td>Senegal</td>
</tr>
<tr>
<td>Guyana</td>
<td>Swaziland</td>
<td>Thailand</td>
</tr>
<tr>
<td>Haiti</td>
<td>Uganda</td>
<td>Uruguay</td>
</tr>
<tr>
<td>Honduras</td>
<td>United Republic of Tanzania</td>
<td></td>
</tr>
<tr>
<td>Jamaica</td>
<td>Zambia</td>
<td></td>
</tr>
<tr>
<td>Kenya</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a The overall antiretroviral therapy coverage for low- and middle-income countries is 31%.
b Countries with an estimated antiretroviral therapy need of less than 1000 people. The data for these countries should be interpreted cautiously.

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1 Data reported to WHO in response to the annual questionnaire for monitoring the health sector response to HIV/AIDS, 2007.
Box 2.2. The public health approach to scaling up antiretroviral therapy

The public health approach addresses the health needs of a population based on the principles of simplification, standardization, decentralization, equity and participation by the people receiving antiretroviral therapy and the community (6).

The main components of the public health approach to scaling up antiretroviral therapy are:

- standardizing regimens and simplifying formularies
- simplifying clinical decision-making and standardizing treatment monitoring
- standardizing management of toxicity and drug–drug interaction
- monitoring HIV drug resistance at the population level.

Implementing a public health approach to scaling up antiretroviral therapy requires:

- decentralized, integrated delivery of care
- task-shifting and specialized support
- antiretroviral therapy free of charge at the point of service delivery
- strengthened procurement and supply management
- tracking progress.

The diversity of the sites delivering antiretroviral therapy in Africa, they do underscore ongoing challenges to both the health care workforce and health systems in delivering adequate care and treatment.

Efforts to scale up access to antiretroviral therapy have reinforced the need for a comprehensive public health approach at the district, national and international levels (Box 2.2).

Access to antiretroviral therapy for rural populations has been of rising concern, especially in low-income countries with generalized epidemics. Many rural populations live at great distances from the urban tertiary care sites that have been the focus of most antiretroviral therapy rollout to date.
Increasing evidence indicates that decentralizing the delivery of HIV services and providing community support can facilitate the scaling up of antiretroviral therapy, even in the most resource-limited settings (Box 2.3). In South Africa, a programme delivering antiretroviral drugs through community health clinics in a rural area of KwaZulu-Natal resulted in meeting the needs of more than 60% of the people who need antiretroviral therapy after 24 months of programme initiation in a geographically dispersed rural population (7). In another rural area of South Africa, delivering antiretroviral therapy through primary health care sites, using adherence counsellors to provide a broad range of services and integrating HIV services into other components of clinical care resulted in faster enrolment of individuals, better retention of individuals on treatment and 95% treatment coverage (8).

In Ethiopia, the Ministry of Health began decentralizing the delivery of antiretroviral therapy to health centres in 2006, when hospital enrolment was insufficient to keep pace with treatment need. Clinical teams in health centres were trained using the WHO Integrated Management of Adolescent and Adult Illness (IMAI) training tools for service delivery (9). Currently, 210 health centres provide HIV care and antiretroviral therapy to 16,572 individuals, comprising 18% of the national total of 90,212 currently receiving antiretroviral therapy in Ethiopia (10).

### Box 2.3. Providing antiretroviral therapy in a conflict setting: the example of Uganda

The Acholi, Lango and Karamoja subregions of Uganda have been facing civil conflict for the past 20 years, resulting in a breakdown of health infrastructure and a large internally displaced population living in camps. The HIV prevalence in these regions is high; the results of recent surveys have indicated that the HIV prevalence in Acholi and Lango is 8.3% versus the national average of 6.3% (11).

Since 2004, the Ministry of Health, local government institutions, international donors, United Nations agencies and nongovernmental organizations have implemented a joint programme for scaling up the delivery of health services among internally displaced populations in affected areas. The programme includes increasing access to HIV testing and counselling, condoms, HIV care and treatment and social support to vulnerable populations in camps for internally displaced people. As a result of these efforts, the coverage of antiretroviral therapy in Acholi and Lango increased from 1228 people receiving treatment in 5 sites in 2004 to 9994 people in 35 sites at the end of 2007. In Karamoja, the number of people receiving antiretroviral therapy increased from 33 in 2004 to 456 in 2007. However, national estimates indicate that the total number of people currently receiving antiretroviral therapy represents only 39% of the people in need in these two subregions.

Strong collaboration among implementing partners, involvement of local representatives and regular supervision and monitoring have been key factors in scaling up services in the affected areas. The shortage of health workers was addressed by using the IMAI approach with support from WHO to train clinical teams, facilitate task-shifting towards health workers with less training and involve people living with HIV as “expert patients” to provide adherence counselling and support.

However, service delivery in these subregions continues to face several challenges, including inadequate infrastructure, high rates of attrition among health workers, frequent stock-outs of drugs and commodities and the difficulty of sustaining access to treatment for internally displaced populations as they begin returning to their original homes as peace negotiations conclude.

2 Ethiopia’s health network model consists of primary community health posts, health centres and district or zonal hospitals.
Fig. 2.4 presents the pattern in selected countries with at least 5000 people receiving antiretroviral therapy. In most countries, women comprise a higher proportion of the people receiving treatment than would be expected based on the percentage of people needing antiretroviral therapy who are women. Annex 2 provides country-level disaggregated data.

**Fig. 2.4. Women as a percentage of all people receiving antiretroviral therapy versus women as a percentage of all people needing treatment, selected low- and middle-income countries, 2007**

- **Percentage of people on treatment who are female**
- **Percentage of people in need of treatment who are female**

**Sub-Saharan Africa**
- Burkina Faso
- Burundi
- Senegal
- Namibia
- Lesotho
- Togo
- Kenya
- Cameroon
- Côte d’Ivoire
- Mali
- United Republic of Tanzania
- South Africa
- Chad
- Uganda
- Swaziland
- Rwanda
- Zimbabwe
- Nigeria
- Mozambique
- Botswana
- Malawi
- Central African Republic
- Guinea
- Zambia
- Ethiopia
- Gabon
- Democratic Republic of the Congo

**Latin America and the Caribbean**
- Haiti
- El Salvador
- Argentina
- Brazil
- Chile

**Asia**
- Cambodia
- China
- Myanmar
- India
- Viet Nam

**Europe**
- Romania
- Ukraine

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**Footnotes:**

- Based on the antiretroviral therapy needs among women as a proportion of the total needs among both sexes in 2007. The values are sorted in descending order of the percentage of people receiving antiretroviral therapy who are women within each region. This figure includes only countries with treatment data available by sex for at least 5000 people. Annex 2 provides more country-specific data.
- Treatment data by sex are based on partial data sets and/or are not based on the most recent national-level data. See Annex 2 for further details.
- The estimated need for antiretroviral therapy is currently under review and will be adjusted, as appropriate, based on new data collected during 2008.
The ART-LINC Collaboration\(^3\) recently conducted a comprehensive, multi-site analysis to compare the number of women on antiretroviral therapy with the HIV prevalence among women in low- and middle-income countries in Africa, Asia and Latin America. This study also found that women were not disadvantaged in access to antiretroviral therapy compared with men. The study, which included 33,164 individuals (19,989 women and 13,175 men) participating in 29 centres in 13 countries, suggested that more attention be paid to ensuring that men living with HIV start treatment earlier in the course of the disease (13).

Although the overall ratio of women to men receiving antiretroviral therapy is in accordance with the distribution of HIV infection by sex, in some countries pregnant women living with HIV have poor access to antiretroviral therapy for their own health (for more details, see subsection 5.4.2).

Recent data also reveal that an increasing number of children are benefiting from treatment programmes. Section 5 presents detailed information on equity in access to treatment for pregnant women and children.

Concerns have also been raised regarding equity in access to antiretroviral therapy for populations at high risk of HIV infection, including injecting drug users, men who have sex with men, sex workers and prisoners. Data on the coverage of antiretroviral therapy among these populations are extremely limited. The most comprehensive data on the coverage of antiretroviral therapy among population groups most at risk are available for injecting drug users in the WHO European Region (Box 2.4). The data suggest that, despite recent efforts, the coverage of antiretroviral therapy among these populations remains low.

In addition, socioeconomic status can play an important role in determining access to priority care and treatment interventions and overall health outcomes (Box 2.5). Conclusive evidence indicates that abolishing user fees at the point of service delivery leads to increased uptake of and adherence to antiretroviral therapy (16).

In 2007, of 76 reporting low- and middle-income countries, 72 had a policy for providing antiretroviral therapy free of charge in the public sector.\(^4\) However, data on the implementation of these policies at the country level are limited. Seventy countries also reported having policies for providing co-trimoxazole free of charge in the public sector. A smaller number of countries reported having a policy for providing laboratory monitoring free of charge. As the cost of laboratory monitoring is relatively high, this could represent a barrier for accessing antiretroviral therapy services in low-income settings. Countries in eastern Europe provide a good example, as both HIV treatment and laboratory monitoring are provided free of charge in the public sector.

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**Box 2.4. Antiretroviral therapy coverage among injecting drug users in Europe**

Injecting drug use accounts for the overwhelming majority of HIV cases in Eastern Europe and Central Asia and contributes significantly to older HIV epidemics in many countries in western Europe (14).

Access to antiretroviral therapy for injecting drug users in Europe is increasing. In 2002, among 27 countries reporting in the WHO European Region, injecting drug users accounted for 46% of reported HIV cases, yet only 10% of those receiving antiretroviral therapy were injecting drug users. By 2006, among 38 reporting countries, injecting drug users represented 59% of reported HIV cases and 30% of all people receiving antiretroviral therapy (15).

However, regional variation within Europe is considerable. Antiretroviral therapy coverage is high in western Europe, where injecting drug users represented 29% of reported HIV cases and 30% of people receiving antiretroviral therapy in 2006. In eastern Europe, countries such as Ukraine have made substantial progress in scaling up the provision of antiretroviral therapy among injecting drug users in recent years. However overall, coverage of antiretroviral therapy is inequitable. In 2006, more than 70% of reported HIV cases were among injecting drug users, but they represented 39% of people receiving antiretroviral therapy.

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\(^3\) The Antiretroviral Therapy in Low-Income Countries (ART-LINC) Collaboration is a network of clinics in Africa, South America and Asia. It was established to examine outcomes for people living with HIV treated in resource-limited settings and to compare experiences across settings. It is supported by the French Agence Nationale de Recherches sur le SIDA et les Hépatites Virales, the European and Developing Countries Clinical Trials Partnership, the United States National Institutes of Health and the United States Agency for International Development.

\(^4\) Data reported to WHO in response to the annual questionnaire for monitoring the health sector response to HIV/AIDS, 2007.
Box 2.5. Socioeconomic determinants of access to antiretroviral therapy in Malawi

A WHO study of the socioeconomic determinants of access to antiretroviral therapy in Malawi (17) found that, nationally, 66% of the people accessing antiretroviral therapy services did this at the secondary level of care (in district hospitals) versus only 8.5% at the primary level (in community clinics and health centres). This means that accessing treatment requires incurring not only direct costs such as transport and food but also opportunity costs in terms of time spent on travel and waiting in queues. Exit interviews conducted in a sample of 947 people being treated at facilities in the Lilongwe and Rumphi districts found that the median travel time to the treatment facility was 60 minutes for the entire sample. Travel time to treatment facilities varied across income levels. The poorest 20% travel a longer distance and incur higher transport costs to reach a treatment facility. Fig. 2.5 shows the average time taken to reach an antiretroviral therapy facility according to socioeconomic group.

The study also found that the average waiting time at the treatment facility for men and women was similar (mean waiting time of 126 minutes for men and 128 minutes for women). People visiting mission hospitals and government health centres had shorter waiting times than people visiting private not-for-profit facilities.

![Fig. 2.5. Determinants of travel time to an antiretroviral therapy facility in Malawi, 2007](image)

Q1–Q5: income quintiles; JCE: Junior Certificate Examination; MSCE: Malawi School Certificate Examination.
2.1.4 Impact and outcomes of scaling up antiretroviral therapy

Since 2002, the expanded provision of antiretroviral therapy in low- and middle-income countries has resulted in an estimated gain of 3.2 million [2.9 million to 3.6 million] life-years, including 2 million [1.9 million to 2.3 million] in sub-Saharan Africa.

Survival and improved clinical outcomes

Improvements in survival time and clinical outcomes have been demonstrated in a growing number of cohorts in low- and middle-income countries (18–21). A recent meta-analysis of data from the ART-LINC Collaboration (22) tracked CD4 cell counts among adolescents and adults in low- and middle-income countries up to five years (beginning with treatment initiation). The study found that the median CD4 count rose from 108 cells per µl at the time of treatment initiation to 442 cells per µl at five years following initiation among those remaining on antiretroviral therapy for five years. The cohort of almost 20,000 individuals, of whom 60% were women, demonstrates that strong and sustained CD4 cell recovery can be achieved over extended periods of time in resource-limited settings. The effect of antiretroviral therapy on reducing mortality and morbidity in low- and middle-income countries is even more significant when supplemented by co-trimoxazole prophylaxis. A recent study demonstrated a 95% reduction in mortality among people receiving both antiretroviral therapy and co-trimoxazole prophylaxis compared with untreated people (23).

Levels of adherence, a key variable in determining clinical efficacy, appear to be comparable among population groups being treated in both high-income and low- and middle-income settings. A meta-analysis of studies from sub-Saharan Africa found that adherence rates were similar to or exceeded those from North American and European population groups. This is consistent with findings from Brazil, one of the first countries outside the Organisation for Economic Co-operation and Development to implement a universal access programme for antiretroviral therapy (24,25). However, these findings should be interpreted with caution because the results of studies conducted as part of research projects and in well-resourced settings may not be able to be replicated outside such settings. Many people continue to face difficulty in adhering to treatment. This is related to both structural factors (such as the cost of treatment, distance to health facilities or stigma) as well as individual factors (such as the side effects of drugs and comorbidity).

Although the evidence indicates substantial improvements in clinical outcomes and their impact at the population level, some trends raise concern. Recent evidence (26) indicates that many people die after an HIV-positive diagnosis and before they can access antiretroviral therapy. Further, despite significant gains in survival time since treatment began to be scaled up, people in low- and middle-income countries still have higher mortality in the first six months of treatment than people in high-income countries (27). This suggests that late diagnosis, late initiation of therapy, undiagnosed comorbidity and differential access to health care contribute to unequal treatment outcomes.

Retention is also emerging as a critical issue in antiretroviral therapy programmes. A recent study from the ART-LINC Collaboration (28) reviewed retention data for 5491 people being treated in 15 programmes in Africa, Asia and Latin America. Researchers found that early loss to follow-up in antiretroviral therapy programmes was becoming increasingly common in the context of treatment scale-up and was associated with fee-for-service programmes and more advanced immunodeficiency at baseline. The study suggests that the infrastructure and number of staff required to document and trace the people lost to follow-up are becoming increasingly inadequate due to the pressure on public health programmes to start the maximum number of new people on antiretroviral therapy as part of efforts to scale up treatment. Another recent review of treatment programmes in sub-Saharan Africa (29) found that retention averaged 75% after one year and 62% after two years, although the retention rates varied widely among programmes. The issue of retention will be a significant challenge as the pace of scale-up increases.

Impact of treatment on prevention

In addition to clinical outcomes, evidence indicates that antiretroviral therapy programmes can be implemented in a way that emphasizes HIV prevention. Studies (30,31) have found that sexually active people receiving antiretroviral therapy may be more likely to practice protected sex and use contraceptives. Mounting evidence, including several studies of serodiscordant couples, also shows that effective viral suppression combined with appropriate behavioural prevention support (such as the use of condoms) reduces HIV transmission (32,33). Although additional evidence is required on the extent to which scaling up antiretroviral therapy affects the incidence and prevalence of HIV at the population level, scientific studies to date indicate that antiretroviral therapy should be considered part of a comprehensive and integrated approach to HIV prevention and that cost-effectiveness analysis of prevention programmes in low- and middle-income countries should include antiretroviral therapy.

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5 Based on available evidence, the UNAIDS Reference Group on Estimates, Modeling and Projections assumes that the death rate among people receiving antiretroviral therapy in low- and middle-income countries is 15% in the first year of treatment and 5% in the following years.
6 Both these studies were based mostly on clinic-based cohorts. Hence they may classify people who have been formally or informally transferred to another clinic as lost to follow-up and may underestimate retention.
Socioeconomic benefits
Socioeconomic determinants are known to play a part in both access to antiretroviral therapy and in the effects of scaling up antiretroviral therapy at the population level. Recent studies confirming increases in labour force participation among individuals receiving antiretroviral therapy (34) have demonstrated that investing in HIV prevention and treatment can have broader social and economic effects in high-burden countries. A recent study of tea plantation workers in Kenya (35) found that those living with HIV who were receiving antiretroviral therapy worked at least twice as many days in a month as they would have in the absence of treatment.

2.1.5 Prevention and assessment of HIV drug resistance

As larger numbers of people receive treatment, preventing and assessing HIV drug resistance become increasingly important.

The WHO HIVResNet is a global network of individuals, institutions and countries working in HIV drug resistance that supports WHO in developing and implementing a public health approach to preventing and assessing HIV drug resistance. With the support of HIVResNet, WHO has developed a comprehensive strategy for minimizing the emergence and transmission of HIV drug resistance at the population level (Box 2.6). The purpose of the strategy is to prolong and maximize the quality of life of people living with HIV by supporting optimal antiretroviral therapy programme functioning, maintaining the effectiveness of standard first- and second-line antiretroviral regimens used in low- and middle-income countries and potentially reducing HIV transmission.

In 2007, the WHO Global Strategy for Prevention and Assessment of HIV Drug Resistance also received support from national governments including Canada, Italy, Spain and the United States of America as well as additional support to specific countries from other partners.

During 2006–2007, 25 countries received technical assistance from WHO and its HIVResNet partners for developing and implementing national HIV drug resistance plans. All 25 countries implemented one or more elements of their national HIV drug resistance strategies.

Box 2.6. Strategy for prevention and assessment of HIV drug resistance

The HIV drug resistance strategy provides country-level guidance for the following activities:

- formation of a national HIV drug resistance working group to develop and implement a national plan for preventing and assessing HIV drug resistance in coordination with the national strategy for HIV prevention and care;
- monitoring the extent to which antiretroviral therapy sites are functioning to prevent HIV drug resistance through site-level early warning indicators for HIV drug resistance;
- conducting surveys to assess the prevention and emergence of HIV drug resistance during antiretroviral therapy and the transmission of HIV drug resistance;
- accrediting laboratories for HIV drug resistance genotypic testing at the national, regional and global levels to form the WHO HIVResNet laboratory network;
- implementing the WHO HIV drug resistance database; and
- producing an annual report with evidence-based recommendations for public health action to prevent HIV drug resistance at the antiretroviral therapy site level and the national antiretroviral therapy programme level.

Source: Bennett et al. (36)
The WHO Global HIV Drug Resistance Laboratory Network was formed to provide quality-assured laboratory results for HIV drug resistance surveillance and monitoring. As of August 2007, 28 laboratories were assessed for accreditation and 7 were accredited. Two additional laboratories were in the process of being assessed (Fig. 2.6).

Seven countries have reported results (37–44) from the surveillance of transmitted HIV drug resistance in geographical areas where antiretroviral therapy was first used within the country (Table 2.3). All reported less than 5% transmitted resistance to all antiretroviral drugs and drug classes.

### 2.1.6 Antiretroviral drug regimens

WHO treatment guidelines reflect the principles of the public health approach. They focus on maximizing survival at the population level through standardized treatment regimens and simplified formularies, delivered to individuals through simplified clinical decision-making and standardized treatment monitoring (5). Guidelines issued by WHO evolve based on scientific evidence and clinical management experience in resource-limited settings.

As treatment continues to be scaled up, establishing the principles and criteria by which priorities among antiretroviral drug options are set is becoming increasingly urgent, especially for the growing number of individuals who require second-line therapy (Box 2.7).

**Distribution and use of antiretroviral drug regimens**

In 2007, WHO conducted the second annual survey on the distribution and composition of first- and second-line antiretroviral therapy regimens used in low- and middle-income countries (46,47). Surveys were sent to national AIDS programmes in 41 countries in March 2007. The selected countries include the 40 countries with the highest number of people receiving antiretroviral therapy as of December 2006 as well as Guyana (to include all 15 focus countries of the United States President’s Emergency Plan for AIDS Relief). Thirty countries responded, representing 63% of the estimated 2 million people receiving antiretroviral therapy in resource-limited countries as of December 2006. Ninety-three per cent of the people receiving antiretroviral therapy in the 30 responding countries were adults and 7% were children.

The vast majority of adults (97%) were receiving first-line regimens. Information on specific regimens was available...
Table 2.3. Surveys of transmitted HIV drug resistance in seven countries: characteristics and summary results

<table>
<thead>
<tr>
<th>Country</th>
<th>Area and time period</th>
<th>Site type</th>
<th>Percentage participation (of the people eligible)</th>
<th>Predominant HIV-1 subtype(s)</th>
<th>Transmitted resistance classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethiopia (37)</td>
<td>Addis Ababa, April–August 2005</td>
<td>Antenatal care</td>
<td>100%</td>
<td>C</td>
<td>&lt;5% (all classes)</td>
</tr>
<tr>
<td>Malawi (38)</td>
<td>Lilongwe, October–December 2006</td>
<td>Prevention of mother-to-child transmission</td>
<td>100%</td>
<td>C</td>
<td>&lt;5% (all classes)</td>
</tr>
<tr>
<td>South Africa (39)</td>
<td>Gauteng Province, October 2004</td>
<td>Antenatal care</td>
<td>100%</td>
<td>C</td>
<td>&lt;5% (all classes)</td>
</tr>
<tr>
<td>South Africa (39)</td>
<td>Gauteng Province, October 2004</td>
<td>Antenatal care</td>
<td>100%</td>
<td>C</td>
<td>&lt;5% (all classes)</td>
</tr>
<tr>
<td>Swaziland (40)</td>
<td>Manzini-Mbani corridor, July–August 2006</td>
<td>Antenatal care</td>
<td>100%</td>
<td>C</td>
<td>&lt;5% (all classes)</td>
</tr>
<tr>
<td>Thailand (41)</td>
<td>Bangkok, July 2005 –April 2006</td>
<td>Blood donation site</td>
<td>100%</td>
<td>CRF01-AE</td>
<td>&lt;5% (all classes)</td>
</tr>
<tr>
<td>Thailand (41)</td>
<td>Bangkok, July–December 2005</td>
<td>Voluntary counselling and testing sites</td>
<td>100%</td>
<td>CRF01-AE</td>
<td>&lt;5% (all classes)</td>
</tr>
<tr>
<td>United Republic of Tanzania (42)</td>
<td>Dar Es Salaam, November 2005 – February 2006</td>
<td>Antenatal care</td>
<td>100%</td>
<td>A1, C</td>
<td>&lt;5% (all classes)</td>
</tr>
<tr>
<td>Viet Nam (43)</td>
<td>Hanoi, February–June 2006</td>
<td>Voluntary counselling and testing sites</td>
<td>99%</td>
<td>CRF01-AE</td>
<td>&lt;5% (all classes)</td>
</tr>
</tbody>
</table>

HIV drug resistance threshold surveys to assess transmitted HIV drug resistance are performed in one or more cities or health planning areas of a country where antiretroviral therapy has been available for the longest period of time – that is, where transmission of drug resistant strains would be most likely to be seen initially. Separate surveys may be performed in different subgroups of interest in each area. The transmitted resistance to relevant drug classes and drugs is classified as <5%, 5–15% or >15% based on a small number of specimens collected from eligible individuals who are consecutively initially. Separate surveys may be performed in different subgroups of interest in each area. The transmitted resistance to relevant drug classes and drugs is classified as <5%, 5–15% or >15% based on a small number of specimens collected from eligible individuals who are consecutively diagnosed with HIV (44).

Box 2.7. Simplifying current options for second-line antiretroviral therapy

As low-income countries rapidly expand their HIV treatment programmes, they are increasingly faced with the need to make second-line regimens available. In response to requests from national programme managers and regulatory agencies for additional operational guidance in this area, WHO convened a working group of experts and implementing partners in 2007 to advise on selecting, setting priorities for and planning for second-line antiretroviral medicines recommended in the current WHO treatment guidelines (5).

The meeting developed guidance (45) on simplified options for second-line regimens for low- and middle-income countries based on the limited options of most formularies. Six major domains were considered while developing recommendations regarding second-line regimens: efficacy, simplicity, toxicity, population coverage, low potential cost and compatibility for children.

The following second-line regimens were ranked as the highest priorities among the second-line options WHO recommended in its 2006 guidelines (5).

1. For people who initiated antiretroviral therapy with thymidine-based analogues (first-line regimens containing zidovudine or stavudine), the second-line regimens should preferably comprise tenofovir + lamivudine, tenofovir + emtricitabine or abacavir + didanosine as the nucleoside background component associated with either of the following ritonavir-boosted protease inhibitor options: lopinavir + ritonavir or atazanavir + ritonavir.

2. For people who initiated antiretroviral therapy with non-thymidine-based analogues (first-line regimens containing tenofovir or abacavir), the second-line regimens should preferably comprise zidovudine + lamivudine associated with either of the following ritonavir-boosted protease inhibitor options: lopinavir + ritonavir or atazanavir + ritonavir.

This priority-setting is not a revision of the WHO treatment guidelines published in 2006 (5). The other antiretroviral drug options presented in the WHO treatment guidelines are still valid for clinical use.
for 91% of these people. Almost 90% were receiving first-line regimens in accordance with WHO 2006 treatment guidelines (5). Fig. 2.7 presents the composition of the most common adult first-line regimens.

Three percent of adults among the study population were on second-line regimens. Information on specific regimens used was available for 72% of this population. The most common adult second-line regimens included abacavir + didanosine + ritonavir-boosted lopinavir (15%), zidovudine + didanosine + ritonavir-boosted lopinavir (14%), zidovudine + lamivudine + ritonavir-boosted lopinavir (7%), tenofovir + lamivudine + ritonavir-boosted lopinavir (7%), tenofovir + emtricitabine + ritonavir-boosted lopinavir (4%) and stavudine + lamivudine + ritonavir-boosted lopinavir (3%). About 60% of adults on second-line regimens were on regimens that were in accordance with the 2006 WHO treatment guidelines (5), a substantially lower percentage compared with first-line regimens.

The vast majority of children (97%) from responding countries were on first-line regimens, with information on specific regimens available for 94% of children. About 91% of children were receiving first-line regimens in accordance with 2006 WHO treatment guidelines (5). Fig. 2.8 presents the distribution and composition of first-line regimens among children.

Three percent of children among the study population were receiving a second-line regimen. Only 21 countries provided information on specific regimens available for 94% of children. The most common second-line regimens included zidovudine + lamivudine + ritonavir-boosted lopinavir (24%), didanosine + abacavir + ritonavir-boosted lopinavir (12%), stavudine + didanosine + ritonavir-boosted lopinavir (8%) and stavudine + lamivudine + ritonavir-boosted lopinavir (7%). A subset of the data was analyzed from the 21 countries that completed both 2006 and 2007 surveys to compare the distribution in the 2007 survey with the data collected in 2006. The results for this subset showed that the proportion of adults receiving antiretroviral therapy who are treated with second-line regimens continues to be low and is not increasing. Four per cent of adults receiving antiretroviral therapy were on second-line regimens in 2006 versus 3% in 2007. This is slightly lower than the original forecasts, which anticipated an annual switch rate of 5%. This result cannot be clearly interpreted. Possible interpretations include demand-driven factors (such as a limited need for second-line regimens because many people have recently initiated antiretroviral therapy) or supply-driven factors (such as a lack of available options to construct a viable second-line regimen).

Pharmacovigilance

Although about 3 million people are currently estimated to be receiving antiretroviral therapy in low- and middle-income countries globally, the scaling up of treatment has not been matched by a proportionate development in pharmacovigilance practice in low- and middle-income countries. Drug toxicity can severely affect people’s health and safety and undermine their adherence to antiretroviral therapy, not only increasing morbidity and mortality but also leading to the emergence of secondary drug resistance.

The current knowledge of the side effects and adverse events of antiretroviral therapy is based on data collected primarily in high-income countries from populations whose demographics, genetic background, nutritional status and comorbidity may vary substantially from those of the populations in low- and middle-income countries. Of the 80 000 reports of adverse reactions to antiretroviral medicines included in the WHO global Individual Case Safety Reports (ICSR) database at the WHO Collaborating Centre for International Drug Monitoring Programme in Uppsala, Sweden, only 6000 came from low- and middle-income countries, substantially compromising the identification and optimal management of drug adverse events (48).
Fig. 2.7. First-line antiretroviral drug regimens used among adults in 30 low- and middle-income countries, 2007

Fig. 2.8. First-line antiretroviral drug regimens used among children in 30 low- and middle-income countries, 2007

d4T: stavudine; 3TC: lamivudine; NVP: nevirapine; AZT: zidovudine; EFV: efavirenz; TDF: tenofovir.
WHO has developed a strategy to improve the mapping of adverse events, ensure consistent reporting and ultimately improve patient safety and clinical management (Box 2.8).

Prequalification and quality assurance of antiretroviral products
WHO’s Prequalification Programme conducts evaluation and inspection activities and builds national capacity for manufacturing and monitoring high-quality medicines. WHO began reviewing HIV antiretroviral medicines for this programme in 2001. At present, the list of prequalified medicinal products includes 178 formulations of antiretroviral medicines, of which 56 originate from innovator companies and 122 from generic companies. In 2007, WHO prequalified 13 new formulations of antiretroviral medicines, received 23 dossier submissions and began delivering technical assistance (such as on formulations of antiretroviral medicines for children) at the country level.

In 2005–2006, WHO conducted a quality assurance survey of antiretroviral medicines in Cameroon, the Democratic Republic of the Congo, Kenya, Nigeria, Uganda, United Republic of Tanzania and Zambia (49). Of the 395 samples tested, none had quality deficiencies that would pose a risk to the people taking them. The results of this and future surveys on drug quality are key to ensuring that the pace of scaling up treatment does not compromise the quality of the medicines available.

2.1.7 Antiretroviral drug prices
The Global Price Reporting Mechanism (GPRM) for antiretroviral drugs, established in 2004, provides information on the transaction prices of antiretroviral drugs purchased in low- and middle-income countries (50).

In low- and middle-income countries, the prices of most first-line medicines decreased by 30–64% from 2004 to 2007 and by 10–40% from 2006 to 2007. This has contributed greatly to the wider availability of treatment. However, prices remain high in most countries in eastern Europe and Latin America.

The average prices paid for second-line regimens remain high in both low- and middle-income countries (with some exceptions in certain low-income countries), where few or no prequalified generic alternatives are available.

Prices of first-line regimens in low-income countries
The median price paid for first-line treatment (prequalified by WHO) in low-income countries in 2007 ranged from US$ 92 per person per year for the fixed-dose combination of stavudine + lamivudine + nevirapine (the most widely used combination) to US$ 294 for the fixed-dose combination zidovudine + lamivudine plus etavirenz (Fig. 2.9). The weighted average median price of the four combinations most widely used in first-line treatment (representing 86% of the prescribed first-line treatments in low-income countries) was US$ 170 per person per year in 2007.8

The decline in drug prices between 2004 and 2007 can be attributed to the scaling up of treatment programmes, increased competition between a growing number of products prequalified by WHO, new pricing policies by pharmaceutical companies and successful negotiations between the William J. Clinton Foundation and major generic manufacturers.9

Box 2.8. WHO strategy for strengthening pharmacovigilance
To respond to the need to strengthen pharmacovigilance and improve treatment monitoring in resource-limited settings, WHO has developed a plan for:
- coordinating and standardizing approaches to pharmacovigilance for antiretroviral medicines;
- supporting national authorities in investing in identifying and managing pharmacovigilance for antiretroviral medicines;
- conducting, coordinating and supporting focused studies on adverse event and drug–drug interactions linked to antiretroviral medicines;
- supporting regional and global data collection through improved spontaneous and active reporting of adverse events linked to antiretroviral medicines; and
- analysing data and disseminating information on pharmacovigilance.

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8 The weighted average price is calculated by assigning to the price of each combination a weight that equals the proportion that the combination represents in the global volume of first-line regimens in low-income (and, respectively, middle-income) countries.
9 In 2008, WHO published an addendum (51) to the 2006 guidelines on antiretroviral therapy in adults and adolescents (5), indicating that lowering the stavudine dosage to 30 mg twice daily for all adults and adolescents, regardless of body weight, resulted in less toxicity and clinical outcomes comparable to the higher dosage. Previously, dosing for people >60 kg was recommended at 40 mg twice daily; and dosing for people <60 kg was recommended at 30 mg twice daily. The reduced dosage has also contributed to the reduction in the cost of first-line regimens that include stavudine.
**Prices of first-line regimens in middle-income countries**

The average prices paid for first-line regimens have declined significantly in middle-income countries and are now closer to those paid in low-income countries (Fig. 2.10). The median prices in 2007 ranged from US$ 91 per person per year for the least expensive regimen of stavudine + lamivudine + nevirapine to US$ 357 per person per year for the most expensive regimen of zidovudine + lamivudine + efavirenz. In the same year, the weighted median price of the four most widely used combinations in first-line treatment was US$ 188 per person per year.

**Fig. 2.9.** Median price (United States dollars) of first-line antiretroviral drug regimens in low-income countries, 2004–2007

![Graph showing median treatment cost per person per year for various regimens in low-income countries from 2004 to 2007.](image)

**Fig. 2.10.** Median price (United States dollars) of first-line antiretroviral drug regimens in middle-income countries, 2004–2007

![Graph showing median treatment cost per person per year for various regimens in middle-income countries from 2004 to 2007.](image)
Fig. 2.11. Median price (United States dollars) of second-line antiretroviral drug regimens in low-income countries, 2004–2007

<table>
<thead>
<tr>
<th>Drug Regimen</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZT (300 mg) + 3TC (150 mg) + LPV/r (200/50 mg)</td>
<td>791</td>
<td>799</td>
<td>621</td>
<td></td>
</tr>
<tr>
<td>TDF (300 mg) + 3TC (150 mg) + LPV/r (200/50 mg)</td>
<td>943</td>
<td>919</td>
<td>779</td>
<td>741</td>
</tr>
<tr>
<td>AZT (300 mg) + ddI (400 mg) + LPV/r (200/50 mg)</td>
<td>956</td>
<td>977</td>
<td>y3</td>
<td>y4</td>
</tr>
<tr>
<td>ABC (300 mg) + ddl (400 mg) + LPV/r (200/50 mg)</td>
<td>1893</td>
<td>1893</td>
<td>919</td>
<td>919</td>
</tr>
</tbody>
</table>

AZT: zidovudine; 3TC: lamivudine; LPV/r: ritonavir-boosted lopinavir; TDF: tenofovir; ddI: didanosine; ABC: abacavir.

Fig. 2.12. Median price (United States dollars) of second-line antiretroviral drug regimens in middle-income countries, 2004–2007

<table>
<thead>
<tr>
<th>Drug Regimen</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZT (300 mg) + 3TC (150 mg) + LPV/r (200/50 mg)</td>
<td>6/46</td>
<td>4842</td>
<td>1666</td>
<td>1221</td>
</tr>
<tr>
<td>TDF (300 mg) + 3TC (150 mg) + LPV/r (200/50 mg)</td>
<td>6999</td>
<td>4916</td>
<td>1893</td>
<td>1395</td>
</tr>
<tr>
<td>AZT (300 mg) + ddI (400 mg) + LPV/r (200/50 mg)</td>
<td>6527</td>
<td>6722</td>
<td>3622</td>
<td>3009</td>
</tr>
<tr>
<td>ABC (300 mg) + ddl (400 mg) + LPV/r (200/50 mg)</td>
<td>7273</td>
<td>6464</td>
<td>3429</td>
<td>3309</td>
</tr>
</tbody>
</table>

AZT: zidovudine; 3TC: lamivudine; LPV/r: ritonavir-boosted lopinavir; TDF: tenofovir; ddI: didanosine; ABC: abacavir.
Second-line regimens in low- and middle-income countries

Second-line regimens are still significantly more expensive than first-line regimens in low- and middle-income countries. In 2007, the median cost of a regimen of didanosine + abacavir + ritonavir-boosted lopinavir, the most commonly used second-line regimen (Fig. 2.11 and 2.12), was US$1214 in low-income countries and US$3306 in middle-income countries. The median cost of tenofovir + lamivudine + ritonavir-boosted lopinavir is US$747 per person per year in low-income countries and US$1355 per person per year in middle-income countries. The actual prices paid for second-line regimens vary significantly between countries. For example, South Africa pays an average price of US$1600 per person per year for didanosine + abacavir + ritonavir-boosted lopinavir, whereas El Salvador paid US$3448 per person per year for the same regimen in 2007.

As the absolute numbers of people who need access to second-line regimens continue to grow, addressing the high cost of second-line regimens will become increasingly important to ensure the most cost-effective use of available resources (Box 2.9).

2.1.8 Laboratory services

The public health approach to scaling up access to antiretroviral therapy recommends that antiretroviral therapy can be initiated with the use of WHO clinical staging in the absence of laboratory capacity to measure CD4 cell count (52) and that people receiving antiretroviral therapy can be monitored clinically in terms of toxicity (so that antiretroviral drugs can be substituted) and treatment failure (so that second-line antiretroviral therapy can be initiated).

A recent modelling study (53) provides support for these simple recommendations, which will enable the decentralized management of antiretroviral therapy. The study predicted that, at five years, the survival for people in Africa started on a standard antiretroviral therapy regimen (stavudine + lamivudine + nevirapine) would be 83% for people monitored for viral load, 82% for people monitored for CD4 count and 82% for clinical monitoring using WHO staging alone. The corresponding figures over a 20-year period were 67%, 64% and 64%, respectively. The study also indicated that using viral load monitoring is not a cost-effective strategy for resource-limited settings.

Box 2.9. Using market information to lower drug prices: the example of Morocco

Morocco, a middle-income country with a concentrated HIV epidemic, has been paying high prices for antiretroviral drugs compared with other middle-income countries. Since antiretroviral drugs were introduced to the country in 1998, Morocco has introduced a number of measures to bring down their cost, including negotiating prices with pharmaceutical companies; reducing import tariffs and introducing generic combinations. In 2005, Morocco signed an agreement with the Clinton Foundation HIV/AIDS Initiative to obtain lower prices for antiretroviral drugs. With these efforts, the average price for first-line treatment fell from US$1300 per person per month in 1998 to US$48 per person per month in 2007. However, this price was still relatively high compared with other middle-income countries that have a comparable number of people who need treatment.

During 2007, the Ministry of Health worked with national stakeholders and international organizations, including WHO and UNAIDS, to review current antiretroviral drug prices, determine additional options for price reductions and develop an action plan on drug pricing.

Data from the WHO Global Price Reporting Mechanism were used to compare the antiretroviral drug prices in Morocco between 2003 and 2007 with the prices in other middle-income countries. In many cases, even 2007 prices in Morocco were more than 30% higher than the median prices paid in middle-income countries.

The group also undertook a review of patent status, recommended measures to facilitate the registration of generic products and held discussions with suppliers based on a comparison of prices in comparable countries. National treatment experts reviewed the list of individual and fixed-dose combinations being used in the country and selected a smaller number of cost-effective products that could be procured in large quantities while maintaining optimal treatment outcomes.

As a result of these efforts, the price per person per year for first-line antiretroviral drugs decreased by 23–57% from 2004 to 2007.
Efforts to strengthen laboratory capacity remain important for measuring CD4 counts (especially to guide when antiretroviral therapy can optimally be initiated) and for viral load to assess adherence and to review initial responses to antiretroviral therapy. However, access to laboratory services, as part of general strengthening of the health system or as a specific focus of antiretroviral therapy programmes, must not be scaled up at the expense of continuing to expand access to antiretroviral therapy.

In 2007, of the 74 low- and middle-income countries that reported data on the use of CD4 monitoring for providing antiretroviral therapy, most reported using CD4 monitoring in all or some of their treatment facilities, either on site or through referral. Only two countries reported that they were providing antiretroviral therapy without any CD4 monitoring. Of the 5856 facilities providing antiretroviral therapy in these 74 countries, 4850 facilities (78%) were using CD4 monitoring on site or through referral. Countries in the WHO Region of the Americas reported a higher proportion of facilities using CD4 monitoring (95%) than other WHO regions, where the proportion was 69–80%. However, even where CD4 monitoring is available, countries may face challenges such as difficulty in servicing and maintaining the equipment, insufficient capacity to meet the demand for testing and delays in returning results in time to the clinician and the person being monitored to immediately inform treatment decisions. Countries in eastern Europe report using both CD4 and viral load monitoring to initiate antiretroviral therapy and monitor outcomes.

2.2 Care and management of HIV/TB co-infection and other types of comorbidity

Managing the broad range of opportunistic infections and comorbidity related to HIV requires an integrated health sector response. Appropriate prevention and treatment of opportunistic infections and comorbidity can substantially reduce morbidity and mortality among people living with HIV. The health sector also needs to ensure that people living with HIV have access to appropriate nutritional and psychosocial support, palliative care and end-of-life care.

TB remains among the leading causes of HIV-related morbidity and mortality. Whether a person with HIV is receiving antiretroviral therapy or not, HIV-associated TB is both preventable and curable.

2.2.1 Responding to the dual epidemic of HIV and TB

About one third of the world’s population is infected with Mycobacterium tuberculosis, the bacterium that causes TB. Although the bacterium usually remains latent, people with intact immune systems have a lifetime risk of developing active disease of about 5–10%. This risk of developing TB increases dramatically among people living with HIV to around 10% per year.

Recent reports continue to highlight the major public health threat posed by the dual epidemics of HIV and TB. TB is now the most frequent life-threatening opportunistic disease among people living with HIV, including those receiving antiretroviral therapy, and is a leading cause of death. The emergence of ever more dangerous strains of multidrug-resistant TB strains, including extensively drug-resistant TB, represents a critical threat to global health and security.

Since 1990, TB incidence has increased dramatically in HIV-endemic regions. In sub-Saharan Africa, TB cases have increased between two-fold and six-fold, resulting in enormous demands on health services and increased mortality.

10 Data reported to WHO in response to the annual questionnaire for monitoring the health sector response to HIV/AIDS, 2007.
11 Section 2.2.1 draws largely from Global tuberculosis control 2008 – surveillance, planning, financing (54). Additional relevant references are cited in this section.
Globally, 700,000 people living with HIV had TB in 2006. About 12% of deaths among people living with HIV globally are due to TB. Sub-Saharan Africa accounts for 85% of the people with both TB and HIV, with a disproportionately heavy burden in some countries (Fig. 2.13). South Africa, for example, has 0.7% of the world’s population but accounts for 28% of the world’s people with both HIV and TB and 33% of the cases in sub-Saharan Africa. Cohorts of people receiving antiretroviral therapy reveal high rates of TB among people initiating treatment, particularly in the first 6 months.

The dual epidemic of HIV and TB has considerable effects outside sub-Saharan Africa. TB incidence rates are high in many countries in Europe. Factors such as the high incidence of TB in many countries; the high level of multidrug-resistant TB; the appearance of extensive drug-resistant TB; the TB outbreaks in the growing pool of people living with HIV and the large population in prisons; and increasing population mobility make TB a regional emergency and call for effective region-wide control. Injecting drug use is a major driver of the HIV epidemic in many countries in Europe, and the concomitant risk of developing TB presents further complexity for HIV and TB case detection and management (including avoiding services and poor treatment adherence).

**Fig. 2.13.** Estimated HIV prevalence (%) among people newly infected with TB, 2006
**Emergence of drug-resistant TB**

Most cases of TB can be cured with a drug regimen of 6–8 months. However, the recent emergence of multidrug-resistant TB and extensively drug-resistant TB poses a significant public health threat, especially for countries with high HIV prevalence (Box 2.10).12

**WHO-recommended interventions to prevent and address HIV/TB**

Collaborative HIV/TB activities are essential to decrease the burden of TB among people living with HIV and the burden of HIV among people with TB and should be priorities for both HIV and TB control programmes. WHO has identified key HIV/TB collaborative activities (Box 2.11) for TB and HIV programmes to define and set priorities for implementing a joint response to the dual epidemic.

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**Box 2.10. Increasing rates of multidrug-resistant TB and extensively drug-resistant TB**

In February 2008, WHO released a report indicating that multidrug-resistant TB had reached the highest rates ever recorded (56). The report was based on information collected on 90 000 people with TB in 81 countries between 2002 and 2006.

Almost half a million of the total of 9 million new cases of TB are multidrug-resistant TB. The highest prevalence rates of multidrug-resistant TB were reported in Azerbaijan, Moldova, the Russian Federation, Ukraine and Uzbekistan. Ukraine, for example, reported that the level of multidrug-resistant TB among people living with HIV was almost twice that of people with TB but without HIV. In sub-Saharan Africa, the region with both the highest rates of TB and HIV in the world, data were available for only six countries. This creates difficulty in assessing the true burden of co-infection.

The report also indicated that extensively drug-resistant TB, which is virtually untreatable, has been recorded in 45 countries and that HIV infection is strongly linked to multidrug-resistant TB. Recent data on extensively drug-resistant TB among people living with HIV in sub-Saharan Africa suggest a mortality rate of over 95%. Urgent action is needed to control extensively drug-resistant TB, including an increased focus on new approaches to preventing, diagnosing and treating TB. These include, but are not limited to, increased implementation of the “three Is” for people living with HIV: intensified case-finding for TB, isoniazid preventive therapy to prevent TB and infection control for TB. These interventions are intimately linked with screening for TB, a necessary part of the decision-making process for TB infection control, preventive therapy and diagnosis.

An estimated US$ 4.8 billion is needed for overall TB control in low- and middle-income countries in 2008, with US$ 1 billion required for multidrug-resistant TB and extensively drug-resistant TB alone.

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12 Multidrug-resistant TB occurs when the 1st bacteria are resistant to at least isoniazid and rifampicin, the two most powerful anti-TB drugs. Extensively drug-resistant TB is TB that is resistant to any fluoroquinolone and at least one of three injectable second-line drugs (capreomycin, kanamycin and amikacin) in addition to isoniazid and rifampicin.
Box 2.11. Recommended HIV/TB collaborative activities

WHO recommends the following collaborative HIV/TB activities for national HIV and TB programmes (57).

Establish mechanisms for collaboration
- Set up a coordinating body for HIV/TB activities effective at all levels
- Conduct surveillance of HIV prevalence among people with TB
- Carry out joint HIV/TB planning
- Conduct monitoring and evaluation

Decrease the burden of TB among people living with HIV
- Establish intensified TB case-finding
- Introduce isoniazid preventive therapy
- Ensure TB infection control in health care and congregate settings

Decrease the burden of HIV among people with TB
- Provide HIV testing and counselling
- Introduce HIV prevention methods
- Introduce co-trimoxazole preventive therapy
- Ensure HIV care and support
- Introduce antiretroviral therapy

Fig. 2.14. Mechanisms for collaboration and policies for collaborative HIV/TB activities among 63 priority countries, 2005–2006

Box 2.12. Scaling up co-trimoxazole prophylaxis and isoniazid preventive therapy

In 2007, WHO conducted a global survey to assess progress in developing and implementing policy recommendations on providing co-trimoxazole prophylaxis and isoniazid preventive therapy. The survey collected data on national policies on co-trimoxazole prophylaxis and isoniazid preventive therapy in HIV infection, their current level of implementation at various facilities and barriers to developing or implementing these policies. A self-administered questionnaire was addressed to WHO offices in 69 countries representing 98% of the global HIV/TB burden and 97% of the global HIV burden. Forty-one countries responded to the survey. The 41 responding countries represented 85% of the global HIV/TB burden and 82% of the global HIV burden.

Co-trimoxazole prophylaxis
Of the 41 respondent countries, 38 (93%) had developed national policy on providing co-trimoxazole prophylaxis to people living with HIV. However, only 25 countries (61%) had implemented the policy at the national scale (Fig. 2.16). In 24 of these 25 countries (96%), more than 80% of facilities providing antiretroviral therapy were also providing co-trimoxazole prophylaxis. However, TB care services provided little co-trimoxazole prophylaxis. Further, facilities providing services to children living with HIV and HIV-exposed infants provided little co-trimoxazole prophylaxis.

Overall, most countries included in the survey had made progress with developing policy on co-trimoxazole prophylaxis. However, many countries faced challenges in scaling up implementation. Erratic supply and stock-outs of co-trimoxazole at health care facilities were reported to be the major obstacle to scaling up co-trimoxazole prophylaxis policy at the national level in 70% of the countries that provided this information. Other barriers to national scaling up of the co-trimoxazole prophylaxis policy included insufficient training and supervision of health care workers, lack of human resources, lack of systems to monitor the provision of co-trimoxazole prophylaxis, insufficient advocacy on the benefits of co-trimoxazole prophylaxis, lack of integration of HIV/TB services and fear of stigma.

Greater advocacy on the benefits of co-trimoxazole prophylaxis and assistance to the countries to improve their drug management system can help countries in scaling up this intervention. The Global Fund to Fight AIDS, Tuberculosis and Malaria and other international funding agencies should consider including instructions on the importance of co-trimoxazole procurement and monitoring the scaling up of co-trimoxazole prophylaxis in their guidance for funding proposals.

Isoniazid preventive therapy
Of the 41 respondent countries, 21 (51%) had developed a national policy on providing isoniazid preventive therapy to people living with HIV. However only 15% (6 of 41 countries) had implemented the policy at the national scale (Fig. 2.16). Even in countries that had developed national policy on isoniazid preventive therapy, little isoniazid preventive therapy was provided in all facilities providing HIV and TB care.

Similarly, the development and implementation of isoniazid preventive therapy at the national level remains suboptimal in most of these countries. Difficulty in ruling out active TB, poor intensified TB case-finding, difficulty in diagnosing latent TB and concerns regarding adherence and the development of mono-resistance to isoniazid were the main reasons provided for not developing and implementing a national policy on isoniazid preventive therapy. Other reasons included a lack of consensus among policy-makers and experts and uncertainty regarding the long-term benefits of isoniazid preventive therapy. Countries that had developed policy on isoniazid preventive therapy faced similar challenges to achieve national scale-up.

Strong advocacy, dissemination of the strong evidence-based information regarding the benefits and feasibility of isoniazid preventive therapy and issuing updated normative guidelines for the implementation of isoniazid preventive therapy as an essential component of HIV care can assist countries in adopting and implementing isoniazid preventive therapy guidelines on a large scale. A recent WHO expert consultation on the “three Is” recommended the urgent development of co-packaged and/or co-formulated co-trimoxazole and isoniazid to address issues regarding logistics, adherence and integration of services.
Global coverage of collaborative HIV/TB activities

Decreasing the burden of HIV among people with TB

Countries have made progress in both HIV and TB prevention programmes in recent years. Remarkable progress has been made in implementing interventions designed for people living with TB, particularly HIV testing, the provision of co-trimoxazole and access to antiretroviral therapy.

However, despite the expansion in HIV testing and counselling of people with TB in recent years, overall coverage still remains insufficient (54). Almost 700 000 people with TB were tested for HIV in 2006 in 112 reporting countries, up from 470 000 in 2005 and 22 000 in 2002. The total number of people with TB tested for HIV in 2006 represents 12% of notified TB cases globally and 22% of notified TB cases in sub-Saharan Africa. On average, half the people with TB who are tested for HIV are found to be HIV-positive. Not testing the remaining 78% of people with TB in sub-Saharan Africa therefore represents a potentially huge missed opportunity for prevention, care and treatment for people living with TB and HIV.

Noteworthy increases in HIV testing and counselling of people with TB have been reported in some countries in sub-Saharan Africa with a high HIV/TB burden (Fig. 2.15). The percentage of notified TB cases that were tested for HIV quadrupled from 7.5% to 35% among 11 countries in sub-Saharan Africa that reported data for all years 2002–2006 and accounted for more than 50% of the world’s HIV-positive people with TB. The highest testing rates were achieved in Rwanda (76%), Malawi (64%) and Kenya (60%). Progress in HIV testing and counselling of people with TB has also been significant in some countries in Asia. In Malaysia, 69% of people with TB had an HIV test recorded in the TB registers between January and September 2007.13

Fig. 2.15. Number and percentage of notified TB cases who were tested for HIV in the 64 countries that reported data for each year from 2004 to 2006

![Graph showing number and percentage of notified TB cases who were tested for HIV from 2004 to 2006](13)

The numbers above the bars are the percentage of people with notified TB who were tested for HIV.

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13 Data reported to WHO in response to the annual questionnaire for monitoring the health sector response to HIV/AIDS, 2007.
In addition to scaling up HIV testing and counselling as a routine activity, countries also need to implement comprehensive and effective prevention approaches for people living with HIV and TB to address difficult issues such as partner testing, family planning, discordant couple counselling and HIV and TB case-finding among family members. Several countries have initiated these activities, and activities such as partner testing for people living with HIV and TB are expected to become the standard of care in areas with higher HIV prevalence.

There has also been considerable progress in providing co-trimoxazole prophylaxis and antiretroviral therapy to people living with HIV and TB. The number of people living with HIV and TB treated with co-trimoxazole prophylaxis reached 147,000 in 2006, which represents 78% of the people living with HIV and TB that were identified through testing and 2.5 times higher than the 58,000 people treated with co-trimoxazole prophylaxis in 2005. A larger number of people living with HIV and TB could receive co-trimoxazole prophylaxis if more countries were to emulate the high rates of HIV testing in such countries as Kenya, Malawi and Rwanda.

Globally, about 67,000 people living with HIV and TB began antiretroviral therapy in 2006. This is more than twice the 29,000 people living with HIV and TB reported to have enrolled in antiretroviral therapy programmes in 2005 and seven times the number reported in 2004 (98,000 people living with HIV and TB). Overall, 41% of diagnosed people living with HIV and TB could receive co-trimoxazole prophylaxis if more countries were to emulate the high rates of HIV testing in such countries as Kenya, Malawi and Rwanda.

Decreasing the burden of TB among people living with HIV

Expanding the prevention and treatment of TB among people living with HIV is an urgent priority for both HIV and TB programmes. There are several key public health interventions for preventing and treating TB including the “three Is”: isoniazid preventive treatment, intensified case-finding for active TB and TB infection control (Box 2.13).

Despite the significant progress made in targeting people living with TB, the implementation of interventions to reduce the impact of TB among people living with HIV is far below the targets set in 2006 in the Global Plan to Stop TB 2006–2015 (62).

Intensified case-finding or screening for TB among people living with HIV remains low. Only about 314,200 people living with HIV were reported to be screened for TB in 2006, which represents a tiny fraction of the global target of screening 11 million people living with HIV by 2015.

The recent outbreak of extensively drug-resistant TB in Tugela Ferry, South Africa, with nearly 100% mortality among people living with HIV, has re-emphasized the serious need for improved TB infection control, especially in settings providing services to people living with HIV. Although some countries have recognized the need to scale up TB infection control, progress in implementing infection control interventions has been very slow. WHO will update its current guidelines on preventing TB infection in health care facilities in resource-limited settings (59,60) in the second half of 2008.

**Box 2.13. The “three Is”: priority and linked public health interventions for people living with HIV**

**Intensified case-finding**

HIV services are using several screening approaches to intensify their TB case-finding efforts. Screening people living with HIV for TB is a vital first step in TB infection control and in deciding whether to place someone on isoniazid preventive therapy or TB treatment.

**Infection control for TB**

TB infection control measures are essential to prevent the spread of *Mycobacterium tuberculosis* to vulnerable people, health care workers and the community. WHO issued TB infection control guidelines for resource-limited settings in 1999 (59) including an addendum in 2006 (60). Appropriate infection control measures (for example, developing a TB infection control plan, “fast-tracking” coughing patients, assuring rapid TB diagnosis, improving ventilation, etc.) should be implemented and reviewed periodically to minimize the transmission risk.

**Isoniazid preventive therapy**

TB preventive therapy is safe and effective for people living with HIV in a setting with high TB prevalence. It reduces the risk of developing active TB in the short term by 60% of what it would have been without such treatment (61). Although antiretroviral therapy for the people who are eligible significantly reduces the risk of developing TB, isoniazid preventive therapy has significant added value for people living with HIV in areas with high TB prevalence. Integrating isoniazid preventive therapy into routinely provided HIV care services is therefore a high priority and should contribute to other efforts to reduce the impact of TB on people living with HIV.
Provision of isoniazid preventive therapy to people living with HIV also remains extremely low. About 27 000 people living with HIV but without active TB were started on isoniazid preventive therapy in 2006. This represents only 0.1% of the 33 million people estimated to be infected with HIV worldwide. Seventy per cent of those started on isoniazid preventive therapy in 2006 were in Botswana.

Although guidelines do exist, national programmes need additional operational guidance on how to scale up comprehensive TB prevention activities within HIV clinical settings. WHO convened an expert consultation on the “three Is” in April 2008 with key stakeholders including government, expert, donor, and civil society representatives. The participants discussed key challenges to implementation and developed recommendations regarding specific actions to increase implementation. WHO will continue to work with countries to develop guidance for national programmes to scale up access to these vital interventions for people living with HIV.

2.2.2 HIV and viral hepatitis

Of the more than 30 million people living with HIV worldwide, about 3 million people are estimated to be chronically infected with hepatitis B virus and around 4–5 million people are estimated to be coinfected with hepatitis C virus (63).

Rates of hepatitis B virus infection are high in the endemic countries of Asia and Africa, where infection occurs perinatally or early in life. The prevalence of hepatitis B virus infection is also high among men who have sex with men in high-income countries as a result of sexual transmission of hepatitis B virus. More than half the men who have sex with men in these countries have evidence of past hepatitis B virus infection, and 5–10% have chronic hepatitis B virus infection.

The prevalence of chronic hepatitis C virus infection among people living with HIV in western Europe and the United States is estimated to be 25–30%. Coinfection rates average over 40% in eastern Europe, with rates as high as 70–95% estimated for Estonia, the Russian Federation and Ukraine. Hepatitis C virus transmission is ongoing among men who have sex with men in the United States of America (64).

Because both hepatitis B virus and hepatitis C virus are efficiently transmitted by sharing contaminated needles and other injecting equipment (such as water and solution), HIV, hepatitis B virus and hepatitis C virus coinfection are common among injecting drug users. The prevalence of hepatitis C virus among injecting drug users living with HIV has been estimated at 72–95% in some countries (63).

An effective vaccine exists for hepatitis B virus. It needs to be used more widely to protect the people at risk of hepatitis B virus, including injecting drug users, infants, men who have sex with men, sex workers and health care workers who risk nosocomial infection from needle-stick injuries. There is no vaccine for hepatitis C virus, but harm reduction measures effectively protect against HIV, hepatitis B virus and hepatitis C virus.

Several antiretroviral drugs, including lamivudine and tenofovir, are highly effective against chronic hepatitis B virus infection. Operational research studies are being undertaken to identify the best way to manage HIV and hepatitis B virus co-therapy and to avoid the emergence of drug resistance to hepatitis B virus.

Access to treatment for hepatitis B virus and hepatitis C virus is limited in most countries, especially among injecting drug users and people in drug treatment programmes, in part due to the high cost of treatment. Recent evidence (65) indicates that treatment adherence among current and former injecting drug users is comparable to that of non-users. However, in many countries, injecting drug users continue to be explicitly excluded from treatment due to fears of drug–drug interactions and the possibility of reinfection regardless of their clinical indication, their willingness to receive treatment and the proven efficacy of treating hepatitis B virus and hepatitis C virus infection in this population.

As antiretroviral therapy becomes more widely available and individuals live longer, the patterns of comorbidity and mortality among people living with HIV are changing. Chronic liver disease, a major complication of chronic infection with hepatitis B virus and hepatitis C virus, now causes significant morbidity and mortality among people living with HIV (66,67). HIV accelerates the disease progression of both hepatitis B virus and hepatitis C virus, and reactivating both infections can complicate immune reconstitution inflammatory syndrome. There is therefore a pressing need to better assess the magnitude of disease associated with hepatitis B virus and hepatitis C virus among people living with HIV and to ensure that appropriate treatment is available for coinfected individuals. Underlying chronic liver disease can also increase significantly the toxicity of some antiretroviral drugs.

2.2.3 HIV and other comorbidity

The global scaling up of antiretroviral therapy has increased the survival rates of people living with HIV in resource-limited settings. However, it has also been associated with the emergence of other types of comorbidity apparently associated with the persistence of HIV infection among them.
Several clinical studies have examined changes in mortality patterns among people living with HIV in the era of highly active antiretroviral therapy. Studies from both high-income and low- and middle-income countries (68,69) are finding that non-AIDS-defining comorbidity diseases – such as diabetes mellitus, cancer, cardiovascular disease, liver disease and other non AIDS-defining comorbidity – are rapidly replacing AIDS-defining illnesses as more likely causes of death among people living with HIV than in the general population.

The incidence of HIV-associated malignancies continues to increase in resource-limited settings where antiretroviral therapy is not yet widely available. Kaposi’s sarcoma is now the most frequently reported malignancy in many countries in sub-Saharan Africa. In some areas, Kaposi’s sarcoma is more common among men than all other types of cancer combined. In contrast, in the United States, Europe and Australia, the incidence of Kaposi’s sarcoma among people living with HIV has declined by at least 70% since 1997, when highly active antiretroviral therapy became widely available (70). The long-term risk of AIDS- and non-AIDS-defining cancer among people on antiretroviral therapy is uncertain. However an increased risk of AIDS- and non-AIDS-defining cancer has been identified in some observational cohorts in Europe, particularly among people with prolonged immunosuppression (71,72).

WHO will work with partners in coming years to address these emerging issues. Planned actions include establishing a global database linked with international cancer registry and research protocols, simplified treatment protocols and links with prevention and palliative care for people living with HIV who have cancer.
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