4. TREATMENT AND CARE FOR PEOPLE LIVING WITH HIV

Key findings

- More than 4 million [3 700 000–4 360 000] adults and children were receiving antiretroviral therapy in low- and middle-income countries at the end of 2008; over one million more people than at the end of 2007. This represents a 36% increase in one year, and a 10-fold increase in 5 years. The greatest increase in the number of people receiving treatment in 2008 was in sub-Saharan Africa, the region with the greatest need.

- Despite progress, antiretroviral therapy coverage in low- and middle-income countries stood at 42% [40–47%] of the 9.5 million [8 600 000–10 000 000] people in need at the end of 2008, up from 33% [30–36%] at the end of 2007.

- Around 275,700 children under 15 years of age were receiving antiretroviral therapy in low- and middle-income countries at the end of 2008, up from 198 000 at the end of 2007. Antiretroviral therapy coverage for children was 38% [31–47%]. Disaggregated data by sex suggest that adult women are slightly advantaged as compared to adult men in accessing antiretroviral therapy in low- and middle-income countries overall.

- More countries provided national programme data on patient retention on antiretroviral therapy. The data showed that most patient attrition occurred during the first year of treatment. Patient retention tended to stabilize thereafter. Retention in sub-Saharan Africa was estimated at 75% at 12 months following initiation, and at 67% at 24 months, consistent with data obtained from cohort studies. However, many people living with HIV continue to be diagnosed late, preventing the timely initiation of antiretroviral therapy when its impact on survival would be greatest.

- Implementation of various elements of the WHO global strategy for prevention and assessment of HIV drug resistance continued to expand during 2008. Data from 9 countries which conducted surveys in geographical areas where antiretroviral therapy was first provided in the country suggest that transmitted resistance to all drugs and drug classes was below 5%.

- The vast majority of adults on treatment in low- and middle-income countries are receiving first-line antiretroviral drug regimens, and only 2% are receiving second-line regimens. Data also suggest that the majority of national HIV programmes are following WHO-recommended treatment guidelines.

- The weighted average median price of the four combinations most widely used in first-line treatment was US$ 143 per person per year in low-income countries, US$ 162 per person per year in lower-middle income countries and US$ 161 per year in upper middle-income countries. The prices of most first-line regimens decreased by between 30–68% from 2004 to 2008 in low- and middle-income countries. Second-line regimens continue to be more expensive.

- More countries are providing data on collaborative interventions to address the dual epidemic of HIV and TB, although further efforts are needed to enable comprehensive global analysis. Around 16% of notified TB patients knew their HIV status in reporting low- and middle-income countries in 2007, with evidence of scale-up in many high-burden countries. Antiretroviral therapy coverage among people living with HIV and TB remains low. Implementation of the “3 Is” – intensified TB case finding among HIV patients, isoniazid preventive therapy and TB infection control - shows some evidence of progress, but data are incomplete and political commitment remains insufficient to accelerate scale-up.
Since 2003, the international momentum generated by the “3 by 5” initiative has continued to support efforts to scale up access to antiretroviral therapy for people living with HIV in low- and middle-income countries. With a public health approach to treatment characterized by simplified and standardized clinical decision-making, drug regimens and systems to monitor the outcomes of people receiving antiretroviral therapy, resource-limited countries have been able to make antiretroviral therapy available to an increasing number of those in need, reaching over 4 million people by the end of 2008 and showing evidence of retaining people on treatment and improved health outcomes.

Nevertheless, current global access to treatment services falls far short of need, raising questions regarding the sustainability of these programmes in the coming years, especially given the current global economic downturn. Further, as the number of people enrolled in treatment programmes continues to grow, several challenges are emerging. People are being diagnosed at a late stage of disease progression, resulting in delayed access to treatment and high rates of mortality in the early months after initiation, and the prices of second-line drug regimens continue to be high. Treatment services are often inequitably distributed between urban and rural areas or unavailable to some population groups such as injecting drug users or in some settings such as prisons. Expanded access to HIV testing and counselling must accompany the scaling up of treatment programmes, and continued high-quality services and improved patient monitoring systems are needed to increase retention.

The dual epidemic of TB and HIV also continues to be a major factor in morbidity and mortality among people living with HIV, especially in sub-Saharan Africa, undermining efforts to prevent and control HIV. Evidence indicates progress in scaling up collaborative interventions and improvement in the capacity of national HIV programmes to report on progress, but efforts need to be redoubled to achieve universal access to HIV testing, treatment and care, as well as intensified TB case-finding, isoniazid preventive therapy and TB infection control (the “three I’s”).

Further, coinfection with viral hepatitis, especially hepatitis B and hepatitis C, is an increasing challenge in countries with concentrated HIV epidemics, especially among people who inject drugs. Underlying viral hepatitis is becoming a major cause of death among people with HIV and hepatitis coinfection who are being treated with anti-HIV drugs. Malignancies other than classic AIDS-associated Kaposi’s sarcoma, non-Hodgkin lymphomas and cervical cancer are also emerging as causes of morbidity and mortality in settings where people are surviving longer with access to antiretroviral therapy. Similar to HIV/TB coinfection, an integrated package of collaborative activities is needed to diagnose, treat and prevent these conditions in affected populations.

### 4.1. Antiretroviral therapy

#### 4.1.1. Global, regional and country progress in access to antiretroviral therapy

When the “3 by 5” initiative was launched in 2003, an estimated 400 000 people were receiving antiretroviral therapy in low- and middle-income countries (1). Since then, political commitment and efforts by multiple stakeholders have resulted in a massive increase in the number of people receiving antiretroviral therapy.

At the end of 2008, WHO, UNICEF and UNAIDS estimate that 4 030 000 people [3 700 000–4 360 000] were receiving antiretroviral therapy, more than 1 million more people than at the end of 2007 (Table 4.1). This represents a 36% increase in 1 year and a 10-fold increase in 5 years (Fig. 4.1). It is important to note that this figure of 1 million more people receiving antiretroviral therapy at the end of 2008 is lower than the exact number of people who initiated antiretroviral therapy during the year due to attrition from treatment programmes (see Section 4.1.5 and Box 4.4). The total number of people who initiated antiretroviral therapy during 2008 was not reported by countries.

The greatest increase in the number of people receiving treatment in 2008 was in sub-Saharan Africa, the region with the greatest need. About 2 925 000 [2 690 000–3 160 000] people were receiving antiretroviral therapy at the end of 2008 in this region versus 2 100 000 [1 905 000–2 295 000] people in 2007. This represents a regional increase of 39% in 1 year and a 30-fold increase since the end of 2003.

Progress was substantially higher in Eastern and Southern Africa, with 2 395 000 [2 205 000–2 585 000] people receiving antiretroviral therapy at the end of 2008, representing a 43% increase in one year, than in Western and Central Africa (530 000 people receiving antiretroviral therapy, a 26% increase). Of the 20 low- and middle-income countries with the highest number of people on antiretroviral therapy at the end of 2008 (representing 83% of the total), 15 are in sub-Saharan Africa, of which 12 in Eastern and Southern Africa (Table 4.2).

About 445 000 [405 000–485 000] people were receiving antiretroviral therapy in Latin America and the Caribbean in December 2008. The percentage increase in the number of people receiving treatment (14%) is lower than in other regions. Since many large countries in this subregion have already reached high levels of coverage, their capacity to generate large increases within one year is more limited.
Table 4.1. Estimated number of adults and children (combined) receiving antiretroviral therapy and needing antiretroviral therapy and percentage coverage in low- and middle-income countries by region, December 2003 to December 2008

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Sub-Saharan Africa</td>
<td>2 955 000 [2 690 000–3 160 000]</td>
<td>6 300 000 [5 470 000–7 000 000]</td>
<td>45% [44–48%]</td>
<td>6 200 000 [5 300 000–7 200 000]</td>
<td>5 100 000 [4 200 000–7 000 000]</td>
<td>31% [28–38%]</td>
<td>100 000 [75 000–125 000]</td>
</tr>
<tr>
<td>Eastern and Southern Africa</td>
<td>2 395 000 [2 205 000–2 585 000]</td>
<td>6 300 000 [5 470 000–7 000 000]</td>
<td>46% [45–48%]</td>
<td>1 600 000 [1 500 000–1 700 000]</td>
<td>4 200 000 [3 300 000–5 200 000]</td>
<td>33% [30–39%]</td>
<td>75 000 [56 000–94 000]</td>
</tr>
<tr>
<td>Western and Central Africa</td>
<td>530 000 [485 000–575 000]</td>
<td>1 300 000 [1 200 000–1 400 000]</td>
<td>43% [38–48%]</td>
<td>420 000 [360 000–480 000]</td>
<td>1 100 000 [950 000–1 200 000]</td>
<td>29% [22–37%]</td>
<td>25 000 [19 000–31 000]</td>
</tr>
<tr>
<td>Latin America and the Caribbean</td>
<td>445 000 [405 000–485 000]</td>
<td>820 000 [750 000–870 000]</td>
<td>54% [51–58%]</td>
<td>390 000 [350 000–430 000]</td>
<td>770 000 [700 000–820 000]</td>
<td>50% [47–55%]</td>
<td>210 000 [180 000–240 000]</td>
</tr>
<tr>
<td>East, South and South-East Asia</td>
<td>565 000 [520 000–610 000]</td>
<td>1 500 000 [1 300 000–1 700 000]</td>
<td>37% [33–41%]</td>
<td>420 000 [375 000–465 000]</td>
<td>1 500 000 [1 200 000–1 800 000]</td>
<td>29% [23–37%]</td>
<td>70 000 [52 000–88 000]</td>
</tr>
<tr>
<td>Europe and Central Asia</td>
<td>85 000 [80 000–90 000]</td>
<td>135 000 [120 000–150 000]</td>
<td>29% [27–31%]</td>
<td>54 000 [50 000–58 000]</td>
<td>340 000 [320 000–410 000]</td>
<td>16% [13–19%]</td>
<td>15 000 [11 000–19 000]</td>
</tr>
<tr>
<td>North Africa and the Middle East</td>
<td>10 000 [9 000–11 000]</td>
<td>68 000 [52 000–84 000]</td>
<td>14% [12–16%]</td>
<td>7 000 [6 000–8 000]</td>
<td>63 000 [48 000–78 000]</td>
<td>11% [8–14%]</td>
<td>1 000 [750–1 250]</td>
</tr>
<tr>
<td>Total</td>
<td>4 030 000 [3 700 000–4 360 000]</td>
<td>9 500 000 [8 600 000–10 400 000]</td>
<td>42% [39–45%]</td>
<td>2 970 000 [2 700 000–3 260 000]</td>
<td>9 000 000 [8 200 000–9 900 000]</td>
<td>33% [30–36%]</td>
<td>400 000 [300 000–500 000]</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 for Annex 1. See Box 4.2 on estimating treatment need for an interpretation of the data on antiretroviral therapy need and coverage in 2007 and 2008.

b The coverage estimate is based on the unrounded estimated numbers of people receiving and needing antiretroviral therapy.

Fig. 4.1. Number of people receiving antiretroviral therapy in low- and middle-income countries, by region, 2002–2008
than in other regions. In the Caribbean subregion, 33% more people were receiving treatment at the end of 2008 than at the end of 2007.

In Europe and Central Asia, 85 000 [80 000–90 000] people were receiving antiretroviral therapy at the end of 2008 versus 54 000 [51 000–57 000] people at the end of 2007. Between 2007 and 2008, 57% more people started receiving antiretroviral therapy in this region. Europe and Central Asia had the highest percentage regional increase worldwide, although the antiretroviral therapy need in this region is not as high as that in other regions.

In East, South and South-East Asia, 565 000 [520 000–610 000] people were receiving antiretroviral therapy at the end of 2008. This represents a regional increase of 35% in one year and an 8-fold increase over the 70 000 [52 000–88 000] people receiving treatment at the end of 2003.

In North Africa and the Middle East, 10 000 [9000–11 000] people had access to antiretroviral therapy in 2008 versus 7000 [6000–8000] in 2007, a 43% increase.

More high-income countries reported data on the number of people receiving antiretroviral therapy in 2008 than in 2007. However, recent data are not available from some of these countries, including countries in North America where no data from the United States of America have been reported since 2003. The number of people receiving antiretroviral therapy in high-income countries is estimated to be at least

<table>
<thead>
<tr>
<th>Country</th>
<th>Geographical region</th>
<th>Number or people receiving antiretroviral therapy in December 2007</th>
<th>Number or people receiving antiretroviral therapy in December 2008</th>
<th>Percentage of total, 2008</th>
<th>% increase 2007–2008</th>
</tr>
</thead>
<tbody>
<tr>
<td>South Africa</td>
<td>Sub-Saharan Africa</td>
<td>458 951</td>
<td>700 500</td>
<td>17%</td>
<td>53%</td>
</tr>
<tr>
<td>Kenya</td>
<td>Sub-Saharan Africa</td>
<td>177 000</td>
<td>242 881</td>
<td>6%</td>
<td>32%</td>
</tr>
<tr>
<td>Nigeria</td>
<td>Sub-Saharan Africa</td>
<td>197 694</td>
<td>238 659</td>
<td>6%</td>
<td>21%</td>
</tr>
<tr>
<td>India</td>
<td>East, South and South-East Asia</td>
<td>158 020</td>
<td>234 581</td>
<td>6%</td>
<td>48%</td>
</tr>
<tr>
<td>Zambia</td>
<td>Sub-Saharan Africa</td>
<td>151 199</td>
<td>225 634</td>
<td>6%</td>
<td>49%</td>
</tr>
<tr>
<td>Brazil</td>
<td>Latin America and the Caribbean</td>
<td>181 000</td>
<td>190 101</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>Thailand</td>
<td>East, South and South-East Asia</td>
<td>152 974</td>
<td>179 557</td>
<td>4%</td>
<td>17%</td>
</tr>
<tr>
<td>Uganda</td>
<td>Sub-Saharan Africa</td>
<td>115 348</td>
<td>164 341</td>
<td>4%</td>
<td>42%</td>
</tr>
<tr>
<td>United Republic of Tanzania</td>
<td>Sub-Saharan Africa</td>
<td>135 696</td>
<td>154 468</td>
<td>4%</td>
<td>14%</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>Sub-Saharan Africa</td>
<td>97 692</td>
<td>147 804</td>
<td>4%</td>
<td>47%</td>
</tr>
<tr>
<td>Malawi</td>
<td>Sub-Saharan Africa</td>
<td>100 649</td>
<td>146 657</td>
<td>4%</td>
<td>46%</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>Sub-Saharan Africa</td>
<td>90 212</td>
<td>132 379</td>
<td>3%</td>
<td>47%</td>
</tr>
<tr>
<td>Mozambique</td>
<td>Sub-Saharan Africa</td>
<td>89 592</td>
<td>128 330</td>
<td>3%</td>
<td>43%</td>
</tr>
<tr>
<td>Botswana</td>
<td>Sub-Saharan Africa</td>
<td>92 932</td>
<td>117 045</td>
<td>3%</td>
<td>26%</td>
</tr>
<tr>
<td>Rwanda</td>
<td>Sub-Saharan Africa</td>
<td>48 569</td>
<td>63 149</td>
<td>2%</td>
<td>30%</td>
</tr>
<tr>
<td>Cameroon</td>
<td>Sub-Saharan Africa</td>
<td>45 817</td>
<td>59 960</td>
<td>1%</td>
<td>33%</td>
</tr>
<tr>
<td>Namibia</td>
<td>Sub-Saharan Africa</td>
<td>52 316</td>
<td>59 331</td>
<td>1%</td>
<td>12%</td>
</tr>
<tr>
<td>Mexico</td>
<td>Latin America and the Caribbean</td>
<td>43 051</td>
<td>55 000</td>
<td>1%</td>
<td>28%</td>
</tr>
<tr>
<td>Russian Federation</td>
<td>Europe and Central Asia</td>
<td>31 094</td>
<td>54 900</td>
<td>1%</td>
<td>77%</td>
</tr>
<tr>
<td>Côte d’Ivoire</td>
<td>Sub-Saharan Africa</td>
<td>38 221</td>
<td>51 833</td>
<td>1%</td>
<td>36%</td>
</tr>
</tbody>
</table>

* This figure differs from the one published in the 2008 progress report (2), as the reported data were cumulative and not the number currently receiving antiretroviral therapy at the end of 2007.

**Table 4.2. Twenty low- and middle-income countries with the highest number of people receiving antiretroviral therapy in December 2008, progress between 2007 and 2008 in these countries and their representative share of the total number of people receiving antiretroviral therapy in low- and middle-income countries in 2008**

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**Box 4.1. The Global Fund to Fight AIDS, Tuberculosis and Malaria and the United States President’s Emergency Plan for AIDS Relief, the two largest funders of antiretroviral therapy programmes in low- and middle-income countries**

The two major international sources of funding for antiretroviral therapy programmes in low- and middle-income countries are the Global Fund to Fight AIDS, Tuberculosis and Malaria and the United States President’s Emergency Plan for AIDS Relief. At the end of 2008, Global Fund-supported programmes provided treatment to 2.0 million people (3), and programmes financed by the Emergency Plan supported antiretroviral therapy for 2.1 million people (4). However, about 1.15 million people were receiving treatment through programmes jointly financed by the two initiatives; hence, together they supported programmes that provided treatment to almost 2.95 million people at the end of 2008.
695 500 (Table 4.3). Worldwide, the total number of people accessing antiretroviral therapy in both low- and middle-income countries and high-income countries at the end of 2008 is estimated to be more than 4.7 million.

**Table 4.3. Estimated number of people receiving antiretroviral therapy in high-income countries at the end of 2008**

<table>
<thead>
<tr>
<th>Region</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Europe</td>
<td>302 000</td>
</tr>
<tr>
<td>Asia, Oceania and Middle</td>
<td>11 500</td>
</tr>
<tr>
<td>North America and the Caribbean</td>
<td>300 000</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>695 500</strong></td>
</tr>
</tbody>
</table>

4.1.2. **Antiretroviral therapy coverage in low- and middle-income countries**

Coverage of antiretroviral therapy in low- and middle-income countries reached 42% [40–47%] of the 9.5 million [8.7 million – 10.0 million] people in need at the end of 2008 (Box 4.2 explains recent revisions in estimates of treatment need). In 2007, coverage was 33% [30–36%].

In sub-Saharan Africa, antiretroviral therapy coverage was 44% [41–48%] in 2008 compared with 33% [30–36%] in 2007. Differences in coverage among subregions are increasing: 48% [45–53%] of those in need had access to antiretroviral therapy in Eastern and Southern Africa versus 30% [28–34%] in Western and Central Africa. Sub-Saharan Africa represents 70% of the estimated treatment need in low- and middle-income countries and 73% of the total number of people receiving treatment at the end of 2008.

Regional coverage in Latin America and the Caribbean was 54% [51-60%] in 2008 versus 50% [47-55%] in 2007. In Latin America, coverage was 55% [52–60%], the highest coverage for any group of low- and middle-income countries. Coverage in the Caribbean was 51% [46–59%]. Latin America and the Caribbean represents only 8% of the estimated treatment need in low- and middle-income countries but 11% of the total number of people receiving treatment at the end of 2008.

In Europe and Central Asia, antiretroviral therapy coverage was 23% [19-27%] at the end of 2008, up from 16% [13–19%] in 2007. This region represents 4% of the estimated global total treatment need and about 2% of those reported to be receiving treatment.

Antiretroviral therapy coverage in East, South and South-East Asia was 37% [31-47%] in 2008 versus 29% [23-37%] in 2007. This region represents 16% of the estimated treatment need in low- and middle-income countries and 14% of the total number of people receiving treatment at the end of 2008.

Coverage in North Africa and the Middle East increased from 11% [8-14%] in 2007 to 14% [11-19%] in 2008.

---

**Box 4.2. Estimating antiretroviral therapy need and coverage among adults**

Antiretroviral therapy coverage measures the proportion of people needing antiretroviral therapy who 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 needing antiretroviral therapy) is generated using a standardized statistical modelling approach. Estimating the number of people who need antiretroviral therapy raises some definition and measurement issues, which in turn influence estimates of coverage.

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. The national HIV estimates are used as a basis to calculate the number of people in need. This includes all people who meet treatment initiation criteria, whether or not these people know their HIV status and their eligibility for antiretroviral therapy.

Treatment needs are estimated using a software package called Spectrum. This takes into consideration the national epidemiological data and some key assumptions that include the adult prevalence over time, the average survival of people living with HIV with and without antiretroviral therapy and the average time between seroconversion and eligibility for antiretroviral therapy. In addition, the number of people receiving treatment is taken into account to generate estimates of treatment need.

**Definition of eligibility for antiretroviral therapy**

Currently, WHO recommends that adults living with HIV in resource-limited settings should start antiretroviral therapy when the infection has been confirmed and there are signs of clinical advanced disease (HIV disease stage IV, regardless of CD4 cell count; and stage III with CD4 cell count below 350 cells per mm3) or laboratory evidence of severe immunosuppression (CD4 cell count below 200 per mm3 irrespective of disease stage).
4.1.3. Access to antiretroviral therapy among women and children

About 275 700 children younger than 15 years of age were receiving antiretroviral therapy at the end of 2008, up from 198 000 at the end of 2007, or a 39% increase in 1 year (Chapter 5 analyses treatment of children in detail). Overall, children represent 6.8% of people receiving antiretroviral therapy, with regional differences varying from 3.5% in Latin America to 8.1% in Eastern and Southern Africa.

Among 730 000 [580 000–880 000] children in need overall in low- and middle-income countries, 38% [31–47%] had access to treatment versus 43% for adults [39–46%]. In Latin America and the Caribbean, East, South and South-East Asia and Europe and Central Asia, coverage for children is higher than for adults (Table 4.4).

Disaggregated data by sex on the number of adults (<15 years) receiving antiretroviral therapy is available from 90 low- and middle-income countries, representing...
Table 4.4. Number of adults and children younger than 15 years receiving antiretroviral therapy and estimated antiretroviral therapy need and coverage among adults and children in low- and middle-income countries by region, December 2008

<table>
<thead>
<tr>
<th>Geographical region</th>
<th>Reported number of adults (15 years) receiving antiretroviral therapy, December 2008</th>
<th>Estimated number of adults needing antiretroviral therapy, 2008 (range)</th>
<th>Antiretroviral therapy coverage among adults, December 2008 (range)</th>
<th>Reported number of children (0-14 years) receiving antiretroviral therapy, December 2008</th>
<th>Estimated number of children needing antiretroviral therapy, 2008 (range)</th>
<th>Antiretroviral therapy coverage among children, December 2008 (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sub-Saharan Africa</td>
<td>2.700 000 [2.600 000–2.800 000]</td>
<td>6.100 000 [5.700 000–6.500 000]</td>
<td>44% [41–47%]</td>
<td>224 000 [200 000–250 000]</td>
<td>640 000 [500 000–700 000]</td>
<td>35% [29–41%]</td>
</tr>
<tr>
<td>Eastern and Southern Africa</td>
<td>2.000 000 [1.900 000–2.100 000]</td>
<td>4.500 000 [4.200 000–4.900 000]</td>
<td>49% [45–52%]</td>
<td>195 100 [170 000–220 000]</td>
<td>440 000 [340 000–540 000]</td>
<td>44% [36–57%]</td>
</tr>
<tr>
<td>Western and Central Africa</td>
<td>500 000 [450 000–550 000]</td>
<td>1.600 000 [1.400 000–1.700 000]</td>
<td>32% [29–35%]</td>
<td>29 800 [25 000–35 000]</td>
<td>200 000 [140 000–260 000]</td>
<td>15% [11–22%]</td>
</tr>
<tr>
<td>Latin America and the Caribbean</td>
<td>429 000 [400 000–450 000]</td>
<td>800 000 [730 000–850 000]</td>
<td>54% [51–59%]</td>
<td>16 100 [11 000–21 000]</td>
<td>21 000 [18 000–25 000]</td>
<td>76% [65–89%]</td>
</tr>
<tr>
<td>Latin America</td>
<td>399 000 [370 000–420 000]</td>
<td>730 000 [660 000–770 000]</td>
<td>54% [51–59%]</td>
<td>11 700 [8 000–15 000]</td>
<td>17 000 [14 000–20 000]</td>
<td>82% [70–95%]</td>
</tr>
<tr>
<td>Caribbean</td>
<td>36 000 [30 000–40 000]</td>
<td>70 000 [63 000–79 000]</td>
<td>53% [46–57%]</td>
<td>2 500 [2 000–3 000]</td>
<td>4 600 [3 400–5 800]</td>
<td>55% [43–72%]</td>
</tr>
<tr>
<td>East, South and South-East Asia</td>
<td>537 000 [500 000–570 000]</td>
<td>1 500 000 [1 200 000–1 800 000]</td>
<td>36% [30–44%]</td>
<td>30 000 [25 000–35 000]</td>
<td>58 000 [41 000–73 000]</td>
<td>52% [38–73%]</td>
</tr>
<tr>
<td>Europe and Central Asia</td>
<td>80 000 [70 000–90 000]</td>
<td>370 000 [330 000–410 000]</td>
<td>22% [18–26%]</td>
<td>4 200 [3 700–4 700]</td>
<td>4 900 [4 300–5 500]</td>
<td>85% [75–95%]</td>
</tr>
<tr>
<td>North Africa and the Middle East</td>
<td>9 400 [8 000–10 000]</td>
<td>63 000 [49 000–81 000]</td>
<td>15% [11–19%]</td>
<td>4 000 [3 500–4 500]</td>
<td>6 700 [5 400–8 100]</td>
<td>6% [4–14%]</td>
</tr>
<tr>
<td>Total</td>
<td>3 755 000 [3 600 000–3 900 000]</td>
<td>8 800 000 [8 100 000–9 500 000]</td>
<td>43% [39–46%]</td>
<td>275 700 [250 000–300 000]</td>
<td>730 000 [580 000–880 000]</td>
<td>38% [33–42%]</td>
</tr>
</tbody>
</table>

Note: some numbers do not add up due to rounding.

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

b The coverage estimate is based on the unrounded estimated numbers of people receiving and needing antiretroviral therapy.

80% of the 3.76 million adults receiving treatment in 2008. The data show that, in low- and middle-income countries overall, adult women are slightly advantaged compared with adult men in accessing antiretroviral therapy. About 45% of women in need and 37% of men in need received antiretroviral therapy at the end of 2008. About 60% of the adults receiving antiretroviral therapy among the reporting countries are women, while they represent 55% of the people in need.

These overall figures hide regional differences. In sub-Saharan Africa, women are advantaged compared with men: in 35 countries with disaggregated data, 64% of adults receiving antiretroviral therapy were women while they represent 60% of adults in need. On the other hand, men are advantaged in North Africa and the Middle East (eight countries): 48% and 55%. In the three other regions, access to antiretroviral therapy is equitable between men and women: in Latin America and the Caribbean (9 countries reporting disaggregated data), 33% of people receiving antiretroviral therapy were women while they represent 33% of people in need; in East, South and South-East Asia (18 countries), both figures were 39%; in Europe and Central Asia (19 countries) the figures were 43% and 42% respectively. See Annex 2 for country-specific data on people receiving antiretroviral therapy by age and sex.

4.1.4. Availability of antiretroviral therapy

The number and distribution of health facilities providing antiretroviral therapy are key indicators of the scale-up of a national treatment programme and increased access to treatment services. In 2008, 115 low- and middle-income countries reported 12 400 health facilities providing antiretroviral therapy. Of these facilities, 74% were in the public sector and 11% in the private sector (15% were unspecified).

Eighty-one countries provided data for both 2007 and 2008. In these countries, the reported number of health facilities providing antiretroviral therapy increased from 6820 to 9200, or a 35% increase in 1 year. The number of facilities providing antiretroviral therapy increased from 6820 to 9200, or a 35% increase in 1 year.
Box 4.3. Decentralizing antiretroviral therapy services in Cameroon (12)

Cameroon launched its national antiretroviral therapy programme in 2001 by providing services at the main tertiary-level reference hospitals. The programme was subsequently decentralized to district hospitals in 2005. Antiretroviral therapy was made available free of charge in the public sector in 2007, and by June 2008, treatment services were available in 106 of 174 districts, with 5238 people receiving antiretroviral therapy.

Between September 2006 and April 2007, France’s Agence nationale de recherche sur le sida et les hépatites virales conducted an evaluation in 27 hospitals offering antiretroviral therapy with the objective of documenting the experience of service decentralization to district hospitals and its impact on the effectiveness of treatment and the quality of life of the people receiving antiretroviral therapy.

The evaluation found that 71% of the people receiving antiretroviral therapy were women, and about three fourths were living below the poverty line. People enrolled in district hospitals had a more precarious social situation than those in reference hospitals, with lower levels of education and income. Following an HIV diagnosis, people in district hospitals initiated antiretroviral therapy earlier than people in reference hospitals and at slightly higher CD4 counts. People in district hospitals adhered to treatment better than those in reference hospitals. People followed in district hospitals and reference hospitals had similar immune restoration at six months and similar quality of life.

This evaluation also documented the structural factors associated with treatment interruption for more than two days. Besides the stock-out of drugs at treatment sites, the absence of clinicians, the consequent shifting of tasks to paramedical staff and the lack of psychosocial support by professional social workers were associated with more frequent treatment interruptions and lower quality of life. The study, which was conducted before antiretroviral therapy became free of charge in the public sector, also showed that 20% of people could not buy their antiretroviral drugs in the previous month, leading to treatment interruption. Making antiretroviral therapy available free of charge is a major step in increasing the reach of the national treatment programme in Cameroon.

In addition, progress between 2005 and 2008 can be assessed in 47 countries that reported these data for all four years. The number of health facilities providing antiretroviral therapy in these countries nearly doubled during this period, from 4700 to 9360. Progress was especially significant in the 26 sub-Saharan African countries reporting comparable data, increasing by 264% from 1440 health facilities providing antiretroviral therapy in 2005 to 5240 in 2008.

The average number of people receiving antiretroviral therapy per health facility decreased from 300 in 2007 to 250 in 2008. Health facilities in sub-Saharan Africa continue to treat more people per site than in the rest of the world (370 people per health facility providing antiretroviral therapy in sub-Saharan Africa versus 60 in Europe and Central Asia, 140 in East, South and South-East Asia, 80 in North Africa and the Middle East, and 180 in Latin America and the Caribbean).

Improving access to treatment for hard-to-reach populations, including those who are located far from urban centres, is critical if countries are to reach universal access to treatment services. Data need to be disaggregated further to assess equity in service availability for people living in rural areas and for marginalized or hard-to-reach populations (Box 4.3). Evidence from such countries as Malawi suggests that such services are being gradually decentralized. Models of decentralized care, including the WHO Integrated Management of Adolescent and Adult Illness (IMAI) model, have been developed to ensure that the quality of services is maintained as treatment sites expand and decentralize (11).

4.1.5. Outcomes and impacts of scaling up antiretroviral therapy

Outcomes at the programme level: retention on antiretroviral therapy

Antiretroviral therapy is a life-long intervention. The long-term outcomes and effects of treatment programmes need to be determined to monitor and improve programme performance and to build and sustain political commitment to programme efforts. Annual documentation of the percentage of adults and children with HIV who continue to receive treatment after initiating antiretroviral therapy1 is useful for programmes, as it helps in understanding how effective they are at retaining people on antiretroviral therapy over time (Box 4.4).

Countries have substantially improved the monitoring and reporting of retention data. Data collected by WHO, UNICEF and UNAIDS show that, in 2008, 59% of reporting low- and middle-income countries provided information on the retention of people receiving antiretroviral therapy at 12 months following treatment initiation. An increasing number

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1 United Nations General Assembly Special Session on HIV/AIDS (UNGASS) indicator 24 on the percentage of adults and children with HIV known to be receiving treatment at 12 months after initiation of antiretroviral therapy, and yearly thereafter.
Box 4.4. Challenges in monitoring HIV treatment cohorts

Antiretroviral therapy is a life-long intervention that requires careful monitoring and follow-up. With treatment being rapidly scaled up since 2003, cohort monitoring – following up people as they continue receiving antiretroviral therapy over time – has become critical for successful programme management and generating evidence on the outcomes of antiretroviral therapy and patient retention, or the proportion of people who continue antiretroviral therapy among those who ever started. Although efforts have been made in this direction, the existence of highly heterogeneous monitoring systems and the use of non-standardized definitions across programmes create additional hurdles for accurately measuring the success of programmes.

Attrition from an antiretroviral therapy programme - or the number of people in a cohort who discontinue treatment - is classified in three underlying causes: treatment stop, death and lost to follow-up (Fig. 4.2).

Treatment stop refers to a health care decision to interrupt antiretroviral therapy. It can be permanent or temporary, such as in case of severe toxicity. A systematic literature review of cohorts in sub-Saharan Africa estimated that less than 5% of attrition in cohort studies falls in this category (13).

Death is the main outcome used to estimate the survival of people who start treatment. In many low- and middle-income countries, where vital registration systems are weak and most people die at home, health information systems incompletely capture deaths. When a person who started antiretroviral therapy dies and the information is not reported to the clinic, the person is considered as being lost to follow-up and reported as such in cohort monitoring.

A person is considered as being lost to follow-up when he or she does not come back to the treatment facility for a refill of antiretroviral drugs until the end of the reporting period. The definition of lost to follow-up varies considerably in the literature, ranging from a missed appointment to numerous months of absence.

In fact, “lost to follow-up” covers people in many different circumstances. Some may have died, and others may have moved - on their own or by referral from their original clinics - to another site, where they continue to receive treatment. A meta-analysis of 17 studies from sub-Saharan Africa tracking outcomes among 6420 people lost to follow-up found that 34% were not traceable due to registration problems, 29% had died and 37% were alive. Among the last group, many people, ranging from 12% to 54% depending on the study, had actually transferred to another clinic (14).

People receiving antiretroviral therapy who transfer from one clinic to another is increasing with the scaling up and the decentralization of services. A study in Malawi tracing 805 people transferred found that 737 (92%) of them could be found in their new clinic and were continuing to receive antiretroviral therapy (15). Nevertheless, as people remain on treatment, albeit at a different clinic, the transfer seems to remain mostly an issue of monitoring and proper recording rather than attrition.

In addition to definitional issues, recent evidence indicates that the quality of the data collected at the clinical level can also vary substantially among programmes. In Malawi, researchers performing supervision and data control in 89 facilities estimated that routine reports undercounted the number of people receiving antiretroviral therapy by 5% and the number of people receiving first-line antiretroviral drug regimens by 12% (16). In Mali, the opposite was found: a data quality control study undertaken for the Global Fund estimated that routine reports overcounted the number of people receiving antiretroviral therapy by 7% (17).
of countries also reported data on retention over longer time frames, with one in every four countries providing retention data at 48 months. In 2007, only two countries in sub-Saharan Africa reported retention rates at 24 months and none at 48 months.

Of 61 low- and middle-income countries reporting data, 30 (49%) exhibited patient retention rates of over 80%, 10 (16%) of which exceeded 90% retention at 12 months. In total, despite regional variation, 51 (84%) countries reported retention rates at 12 months greater than 70% (Fig. 4.3). Table 4.5 shows regional trends after aggregating data reported by individual countries. Among countries in sub-Saharan Africa, patient retention on antiretroviral therapy was estimated to be 75% at 12 months (22 countries reporting) and 67% at 24 months (13 countries reporting) (Table 4.5 and Fig. 4.5).

Aggregate retention rates across reporting countries did not differ by sex or by age. Twenty-five countries reported

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**Table 4.5. Retention on antiretroviral therapy at 12, 24, 36 and 48 months – estimates from aggregated country reports, low- and middle-income countries by region, 2008**

<table>
<thead>
<tr>
<th></th>
<th>East, South and South-East Asia</th>
<th>Europe and Central Asia</th>
<th>Latin America and the Caribbean</th>
<th>North Africa and the Middle East</th>
<th>Sub-Saharan Africa</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of countries reporting</td>
<td>13</td>
<td>10</td>
<td>12</td>
<td>4</td>
<td>22</td>
<td>61</td>
</tr>
<tr>
<td>Percentage of people receiving antiretroviral therapy</td>
<td>80.2</td>
<td>74.1</td>
<td>85.5</td>
<td>89.6</td>
<td>75.2</td>
<td>79.5</td>
</tr>
<tr>
<td>Number of people receiving antiretroviral therapy (numerator)</td>
<td>43 392</td>
<td>897</td>
<td>83 031</td>
<td>784</td>
<td>108 318</td>
<td>236 422</td>
</tr>
<tr>
<td>Number of people assessed for outcomes (denominator)</td>
<td>54 116</td>
<td>1 211</td>
<td>97 168</td>
<td>875</td>
<td>144 038</td>
<td>297 408</td>
</tr>
<tr>
<td>24 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of countries reporting</td>
<td>7</td>
<td>9</td>
<td>10</td>
<td>3</td>
<td>13</td>
<td>42</td>
</tr>
<tr>
<td>Percentage of people receiving antiretroviral therapy</td>
<td>68.7</td>
<td>63.4</td>
<td>78.6</td>
<td>92.3</td>
<td>66.8</td>
<td>74.8</td>
</tr>
<tr>
<td>Number of people receiving antiretroviral therapy (numerator)</td>
<td>3 403</td>
<td>453</td>
<td>68 496</td>
<td>197</td>
<td>26 067</td>
<td>99 016</td>
</tr>
<tr>
<td>Number of people assessed for outcomes (denominator)</td>
<td>4 952</td>
<td>714</td>
<td>87 097</td>
<td>647</td>
<td>39 017</td>
<td>132 427</td>
</tr>
<tr>
<td>36 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of countries reporting</td>
<td>4</td>
<td>7</td>
<td>6</td>
<td>3</td>
<td>10</td>
<td>30</td>
</tr>
<tr>
<td>Percentage of people receiving antiretroviral therapy</td>
<td>66.7</td>
<td>63.4</td>
<td>77.0</td>
<td>86.8</td>
<td>65.6</td>
<td>73.8</td>
</tr>
<tr>
<td>Number of people receiving antiretroviral therapy (numerator)</td>
<td>1 304</td>
<td>286</td>
<td>28 827</td>
<td>105</td>
<td>8 221</td>
<td>38 823</td>
</tr>
<tr>
<td>Number of people assessed for outcomes (denominator)</td>
<td>1 956</td>
<td>453</td>
<td>37 412</td>
<td>190</td>
<td>12 523</td>
<td>52 572</td>
</tr>
<tr>
<td>48 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of countries reporting</td>
<td>4</td>
<td>4</td>
<td>6</td>
<td>3</td>
<td>5</td>
<td>22</td>
</tr>
<tr>
<td>Percentage of people receiving antiretroviral therapy</td>
<td>55.4</td>
<td>66.8</td>
<td>74.5</td>
<td>78.4</td>
<td>67.2</td>
<td>73.1</td>
</tr>
<tr>
<td>Number of people receiving antiretroviral therapy (numerator)</td>
<td>416</td>
<td>175</td>
<td>15 857</td>
<td>156</td>
<td>1 999</td>
<td>18 603</td>
</tr>
<tr>
<td>Number of people assessed for outcomes (denominator)</td>
<td>751</td>
<td>262</td>
<td>21 278</td>
<td>199</td>
<td>2 973</td>
<td>25 463</td>
</tr>
</tbody>
</table>
disaggregated retention rates at 12 months by sex and 21 countries by age. The retention rate was estimated at 77.3% (6960 of 9001) among men; 76.8% (7186 of 9351) among women; 77.9% (959 of 1231) among children younger than 15 years old; and 78.3% (16 896 of 21 585) among adults and adolescents.

The availability of comparable programme data from high-income countries is limited, although some cohort studies have documented retention in care. A study among 2619 military veterans in the United States who started to receive antiretroviral therapy and were followed up to 2002 (18) showed that at least 36% missed one quarterly visit or more during the first year on antiretroviral therapy, which was associated with worse survival on treatment. This study concluded that retention on care remained an issue even in high-resource settings.

The data on retention reported by national programmes are consistent with those obtained from cohort studies. A review of results from 33 cohorts comprising 74 289 people who started antiretroviral therapy in 13 countries in sub-Saharan Africa estimated the proportion of people continuing on antiretroviral therapy to be 80% at 6 months, 75% at 12 months and 62% at 24 months. “Lost to follow-up” accounted for 56% of attrition and death for 40% (13). Retention rates in the cohorts differed vastly depending on whether services were supported by the public sector, nongovernmental organizations, the private sector or workplaces, on whether any fees for service were charged (free of charge or full or partial user charge) and on the period of enrolment (most were enrolled between 2001 and 2004).

Several programmes have published outcomes based on longer follow-up from routine monitoring data that include baseline characteristics. Botswana’s national treatment programme published data on 633 people starting antiretroviral therapy in 2002. At baseline, the median CD4 count was 67 cells per mm3, and 85% were at WHO clinical stages 3 or 4. At five years, survival was estimated at 79% and the probability of being lost to follow-up was 22%; thus, about 57% were on antiretroviral therapy after 5 years (19). The Province of Cape Town, South Africa published results

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Box 4.5. Methodological issues in measuring the percentage of adults and children with HIV known to be receiving treatment 12 months after initiating antiretroviral therapy

**Definitions**

Estimates of retention in treatment programmes, or the percentage of adults and children with HIV who are known to be receiving antiretroviral therapy 12 months after initiation, should be generated for each calendar year to document annual progress. Retention rates are calculated as follows:

\[
\frac{\text{Number of people alive and still on antiretroviral therapy at 12 months}}{\text{Number of people started on antiretroviral therapy in the preceding calendar year}}
\]

For example, in 2008, the denominator must comprise everyone who started receiving antiretroviral therapy during 2007 (or the most recent local calendar year in use). The numerator should include everyone who started receiving antiretroviral therapy in 2007 and was still alive and on treatment after 12 months — thus, people who died before 12 months, stopped treatment and did not restart before 12 months or were lost to follow-up before 12 months should not be included in the numerator. A similar approach should be used to estimate retention at 24, 36 and 48 months and at subsequent 12-month intervals. All treatment facilities should produce this indicator and the results should be aggregated to produce national figures.

**Major constraints in generating and interpreting data**

The quality of the information produced depends on the cohort monitoring system in place at treatment facilities and on how well it can capture attrition (see Box 4.4). Challenges exist in measuring both sides of the equation. For the denominator, some countries may produce this indicator by selecting only a sample of treatment facilities, which may therefore not reflect a true national picture. Others may generate a cumulative indicator, adding together everyone ever started on antiretroviral therapy and not only those who started during the most recent year, thereby underestimating the current rate of retention, as overall programme performance may have improved over the years.

Determining the numerator can also be complex because it is not always clear how the monitoring systems record people who are no longer being seen in the facility. Some countries may exclude people who die from their calculations, keeping those no longer being seen, resulting in an overestimation of the actual retention on antiretroviral therapy. Incomplete records of transfers between facilities may also underestimate retention.

These issues highlight the difficulties programme managers and researchers face when producing and analysing data on retention in treatment programmes. Nevertheless, interpretation depends largely on the methods employed by local managers (see Box 4.12 on three interlinked patient monitoring systems).
based on monitoring data compiled from all of its treatment sites and including 12,587 adults and 1,709 children. Among adults, 23% started treatment with a CD4 count lower than 50 cells per mm$^3$. The proportions retained on treatment at four years were 76% among adults and 82% at three years among children (20). Thailand’s national treatment programme published data on the outcomes of 58,008 people who started antiretroviral therapy between 2000 and 2005. At baseline, the median CD4 count was 41 cells per mm$^3$ and 51% had AIDS. Survival at five years was estimated at 78%; in addition, 9% were lost to follow-up and 1% permanently stopped treatment (21).

The data also show that late access to antiretroviral therapy remains the most important threat to survival, a challenge that can only be resolved by dramatically expanding earlier access to HIV diagnosis and screening for treatment eligibility.

The data on short- and mid-term retention on antiretroviral therapy reported by low- and middle-income countries confirm the effectiveness of treatment programmes and the substantial gains in terms of survival and averted mortality due to antiretroviral therapy. This result is especially remarkable given the advanced stage of disease Box 4.6. Scaling up antiretroviral therapy in Papua New Guinea from 2004 to 2008

Since the first HIV case was reported in 1987, the HIV epidemic in Papua New Guinea has been growing rapidly. The epidemic was characterized as being generalized in 2004, and by the end of 2008, the adult HIV prevalence was estimated at 0.95%, with more than 36,000 adults and children living with HIV.

In 2004, Papua New Guinea established a national antiretroviral therapy programme, beginning with two pilot treatment sites in collaboration with development partners including WHO, AusAID and the Asian Development Bank. In 2005, Papua New Guinea began scaling up antiretroviral therapy provision with financial support from the Global Fund, which enabled commodities such as antiretroviral drugs and HIV test kits to be procured, human resources to be recruited and trained and treatment sites and laboratory services to be improved. The number of treatment sites increased to 52 by the end of 2008, with 5,195 people receiving antiretroviral therapy. About 500 health workers were trained in service delivery using the WHO model of Integrated Management of and Adolescent Adult Illness (IMAI). The training model and materials, treatment guidelines and patient monitoring tools were reviewed in collaboration with WHO and other development partners. The expansion of antiretroviral therapy has been accompanied by efforts to expand HIV testing and counselling and improve laboratory infrastructure, which facilitated the identification of people and their enrolment in treatment services. In addition, eight CD4 machines were made available for laboratory monitoring as well as the use of dried blood spots to improve HIV diagnosis among children.

To reinforce the monitoring of people receiving antiretroviral therapy, support service delivery and measure outcomes, computerized national and site-specific databases were established and health care workers were trained and mentored to use these databases. This mechanism is also used to monitor early warning indicators of HIV drug resistance. National retention rates of people receiving antiretroviral therapy were high and comparable with other countries in the region (Fig. 4.4).

The successful scaling up of treatment services has not been without challenges. Papua New Guinea has rugged topography with limited communication infrastructure. The capital city is not linked by road to most provinces, and air transport remains the main way of accessing most provinces and districts, where 87% of the population resides according to a 2006 census. The country established a vertical drug supply mechanism to allow uninterrupted drug supplies, and contracted a company to supply drugs to treatment sites from the capital. Nevertheless, the treatment programme continues to face delays in the delivery of HIV test results and access to treatment services, especially in remote areas. Insufficient treatment facilities for children, frequent breakdowns of laboratory equipment due to electrical power fluctuations, inadequate use of data to inform programme implementation and persistent stigma and discrimination all hamper the provision of services in the country.

**Fig. 4.4.** 12-month retention of people receiving antiretroviral therapy in selected treatment sites, Papua New Guinea, 2008

<table>
<thead>
<tr>
<th>Site</th>
<th>Retention Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anua Moriri</td>
<td>76%</td>
</tr>
<tr>
<td>Michaels</td>
<td>89%</td>
</tr>
<tr>
<td>Heduru</td>
<td>87%</td>
</tr>
<tr>
<td>Tininga</td>
<td>77%</td>
</tr>
<tr>
<td>National</td>
<td>83%</td>
</tr>
</tbody>
</table>

{$n$ = number of people receiving antiretroviral therapy.}
at which most people enrol in treatment programmes. Indeed, the baseline CD4 count has been shown to be the most important predictor of survival (22) and of immune reconstitution (23). People initiating therapy at higher CD4 levels tend to achieve comparably greater CD4 cell counts and tend to do so more rapidly (23). In low- and middle-income countries, the median survival without antiretroviral therapy of people with clinical AIDS is estimated to be less than 1 year, and that for people with a CD4 count below 200 cells per mm$^3$ is estimated to be 2.1 years (24). Considering that treatment is often initiated well below this CD4 threshold, the importance of these results should not be underestimated.

The data also confirm that most attrition from treatment – or the number of people starting antiretroviral therapy who discontinue it – occurred within the first year after initiation of therapy and tended to decline or to stabilize after 12 months (Fig. 4.5). These trends corroborate the view that most attrition in the first year following initiation of treatment seems to be due to high mortality rates related to late access to antiretroviral therapy. Regional differences in retention rates also reflect a difference in the stage at which antiretroviral therapy was initiated.

Various cohort studies in low- and middle-income countries have shown that most deaths among people receiving antiretroviral therapy occur in the early months following treatment initiation and that mortality declines substantially thereafter (20,22,23). Evidence suggests that early high mortality rates probably depend not only on the care delivered by programmes but more fundamentally on the stage of disease at the time of enrolment in the programme and the quality of preceding health care (25).

Even in high-income countries, many people start treatment at a disease stage more advanced than if HIV had been diagnosed earlier. In studies from high-income countries, among people first diagnosed with HIV, the proportion with severe disease – defined by clinical AIDS conditions or by CD4 counts below 200 CD4 cells per mm$^3$ – varied from 24% to 45% (26).

Unfortunately, many national programmes provide access to antiretroviral therapy when HIV is at a severe disease stage, mostly due to late access to HIV diagnosis and screening for antiretroviral therapy. Data from national programmes on baseline characteristics at the start of antiretroviral therapy are limited, and available data are mostly derived from cohort studies, which may not always be representative of a country or a region. The ART-LINC Collaboration$^1$ of 17

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$^1$ 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 France’s Agence nationale de recherche 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.
coHORTS IN LOW- AND MIDDLE-INCOME COUNTRIES HAS PRODUCED DATA ON THE BASELINE CD4 COUNT OF 36,715 ADULTS INITIATING ANTIRETROVIRAL THERAPY BETWEEN 2001 AND 2006. PEOPLE ARE INCREASINGLY STARTING TREATMENT EARLIER IN LOW- AND MIDDLE-INCOME COUNTRIES, WITH MORE STARTING THERAPY AT HIGHER CD4 LEVELS THAN BEFORE (FIG. 4.6), HIGHLIGHTING REGIONAL DIFFERENCES. PEOPLE IN SUB-SAHARAN AFRICA TENDED TO GAIN ACCESS TO ANTIRETROVIRAL THERAPY AT A MORE SEVERE STAGE OF DISEASE THAN PEOPLE IN OTHER REGIONS (27). AN ANALYSIS OF COHORT-LEVEL AGGREGATED INDICATORS IN EIGHT COUNTRIES IN SUB-SAHARAN AFRICA SUPPORTED BY THE UNITED STATES PRESIDENT’S EMERGENCY PLAN FOR AIDS RELIEF SHOWED THAT THE MEDIAN CD4 COUNT WHEN TREATMENT WAS INITIATED INCREASED FROM 115 CELLS/MM³ IN 2005 TO 140 IN 2008 (28).

DATA FROM PROGRAMME MONITORING IN CAPE TOWN PROVINCE, SOUTH AFRICA SHOW THAT THE SEVERITY OF ILLNESS AMONG PEOPLE STARTING ANTIRETROVIRAL THERAPY DECREASED OVER TIME AS BASELINE CD4 COUNT INCREASED: INDEED, WHILE THE PROPORTION OF ADULTS STARTING ANTIRETROVIRAL THERAPY BELOW 50 CD4 CELLS PER MM³ DECREASED FROM 51.3% IN 2001 TO 21.5% IN 2005, MORTALITY DURING THE FIRST SIX MONTHS OF ANTIRETROVIRAL THERAPY ALMOST HALVED OVER THE SAME PERIOD: FROM 12.7% TO 6.6% (20).

LATE DIAGNOSIS DUE TO LACK OF KNOWLEDGE OF HIV STATUS REMAINS AN ISSUE TO BE RECKONED AND DEALT WITH, AS IT CONTINUES TO PREVENT THE INITIATION OF ANTIRETROVIRAL THERAPY WHEN ITS EFFECT ON SURVIVAL WOULD BE GREATEST.1 DATA ALSO SUGGEST THAT DELAYS IN INITIATING ANTIRETROVIRAL THERAPY FOLLOWING HIV DIAGNOSIS, INCLUDING FOR PEOPLE WITH LOW CD4 COUNTS, COULD CONTRIBUTE TO EARLY MORTALITY. A PROSPECTIVE ANALYSIS OF 896 PEOPLE ENROLLED IN HIV CARE IN DURBAN, SOUTH AFRICA (30) SHOWED THAT THEY ARE OFTEN SEVERELY IMMUNOSUPPRESSED AT HIV DIAGNOSIS (64% OF THOSE TESTED HAD CD4 COUNT <200 PER MM³), AND ONLY HALF OF THOSE ELIGIBLE STARTED ANTIRETROVIRAL THERAPY WITHIN 12 MONTHS. COUNTRIES MUST REDOUBLE EFFORTS TO MAKE ADAPTATE TESTING AND COUNSELLING AVAILABLE TO EVERYONE AND ENSURE IMMEDIATE REFERRAL TO HIV CARE SERVICES FOR REGULAR SCREENING FOR TREATMENT ELIGIBILITY, FOLLOW-UP AND TIMELY INITIATION OF TREATMENT IN CASE OF NEED. CONTINUED EFFORTS ARE ALSO NEEDED TO ADDRESS ISSUES RELATED TO STIGMA, DISCRIMINATION AND MENTAL BARRIERS SUCH AS FEELINGS OF FEAR, DENIAL OR SHAME.

SEVERAL ADDITIONAL FACTORS RELATED TO THE QUALITY OF HEALTH SERVICES AND TO DIFFERENCES IN GENERAL POPULATION HEALTH ACROSS SITES, PROGRAMMES AND REGIONS ARE ALSO LIKELY TO AFFECT MORTALITY. FOR INSTANCE, STRONG SUPPLY MANAGEMENT SYSTEMS ARE ESSENTIAL TO ENSURE UNINTERRUPTED LIFE-LONG ACCESS TO ANTIRETROVIRAL THERAPY (SEE CHAPTER 6). IN COUNTRIES REPORTING A STOCK-OUT OF ANTIRETROVIRAL DRUGS DURING 2008, THIS PROGRAMMATIC BOTTLENECK MAY HAVE CONTRIBUTED TO ATTRITION.

Even when antiretroviral drugs are distributed free of charge, fees for service and user charges paid for biological monitoring and other services appear to be related to lower retention (22,31). A systematic review of 33 cohorts in low- and middle-income countries showed that programmes that required no payment had higher retention rates (13). In a fee-for-service HIV clinic in Uganda, the probability of remaining alive and in care at four years was estimated to be 35% (32).

The quality of services and adherence support provided must also be considered. Facilities with long delays, insufficient staff and deficient infrastructure are unlikely to retain people on treatment and increase survival adequately in the long term. The geographical location of treatment sites can also increase barriers to treatment – both directly, such as through increased costs associated with transport and food, and indirectly, in terms of time spent on travel and waiting in queues (33).

Further, improving HIV care and diagnosis and treatment of opportunistic infections, strengthening HIV/TB activities with the three I’s for HIV/TB (see section 4.2) and ensuring access to co-trimoxazole prophylaxis remain key to improving the survival of people receiving antiretroviral therapy and the performance of programmes. The Development of Antiretroviral Therapy in Africa (DART) study included 3316 people starting antiretroviral therapy in Uganda and Zimbabwe and showed that co-trimoxazole prophylaxis reduced mortality by half in the first 12 weeks of antiretroviral therapy (Box 4.7) (34).

The added value to survival of laboratory monitoring is unclear. The DART clinical trial, which compared laboratory and clinical monitoring with clinically driven monitoring,
Box 4.7. Development of Antiretroviral Therapy in Africa (DART) trial

The DART clinical trial compared two approaches to monitoring people receiving antiretroviral therapy (35,37). Conducted in Uganda and Zimbabwe, the study included 3316 adults initiating antiretroviral therapy for the first time and allocated them randomly to two groups: the first group received laboratory and clinical monitoring and the second clinically driven monitoring. In the laboratory and clinical monitoring group, full blood count, biochemistry and CD4 count were systematically monitored every 12 weeks; in the clinically driven monitoring group, the results of full blood count and biochemistry were returned when requested by health care personnel, but the results of CD4 count were not returned.

Sixty-five per cent of the study participants were women. At baseline, the median CD4 count was 86 cells per mm³, and 33% of participants had a CD4 count of less than 50 cells per mm³. The participants were followed up until December 2008, with a median follow-up period of 4.9 years. Overall, 7% of the participants were reported as being lost to follow-up, with a similar rate in the groups.

The trial showed no differences in disease progression and survival between groups during the first two years of antiretroviral therapy and a small but statistically significant benefit in the laboratory and clinical monitoring group only from the third year onwards related to a later switch to second-line regimens in the clinically driven monitoring group compared with the laboratory and clinical monitoring group. Survival at five years was estimated to be 90% in the laboratory and clinical monitoring group versus 87% in the clinically driven monitoring group. The authors compare this to a historical cohort (Entebbe cohort) from the period before the introduction of antiretroviral therapy, which estimated survival at five years to be 8%. At the end of the study period, 78% of the participants in the laboratory and clinical monitoring group and 81% in the clinically driven monitoring group remained on the first-line regimen. The groups had similar immune restoration. In participants remaining on a first-line regimen, the median CD4 count was 356 cells per mm³ at the end of the trial. There were few and nonsignificant differences between the groups in the rate of detection of adverse events.

In a separate cost-effectiveness analysis, the incremental cost-effectiveness ratio for using laboratory and clinical monitoring versus clinically driven monitoring was estimated to be US$ 9016 per year of life gained. The authors concluded that antiretroviral therapy can be delivered safely without laboratory monitoring in sub-Saharan Africa, questioning the need for routine CD4 monitoring over and above routine clinical monitoring, particularly from the second year of antiretroviral therapy.

showed no differences in disease progression and survival during two years and a small but statistically significant benefit in the group with laboratory and clinical monitoring only from the third year of antiretroviral therapy (35). A simulation model found modest benefit of viral load and CD4 versus clinical monitoring for people starting treatment with stavudine (d4T), lamivudine (3TC) and nevirapine (NVP) (36).

Impacts of antiretroviral therapy on mortality at the population level

The absence or the delay in generating vital statistics explains most of the current difficulty in assessing how antiretroviral therapy affects mortality at the population level. Many low- and middle-income countries have weak vital or civil registration systems, especially countries with a high HIV burden, creating difficulty in measuring HIV-attributable mortality. Even when these systems exist, they are usually not exhaustive and the cause of death is misreported or underreported. The use of data from these systems also suffers from delays in reporting. Surveys sometimes use verbal autopsies to retrospectively assess HIV-attributable mortality in a population; however, this approach often lacks baseline data for assessing how access to antiretroviral therapy affects HIV-related mortality.

Direct population assessments are still rare (Box 4.8). In Addis-Ababa, Ethiopia, surveillance of burials was conducted as a substitute for deficient vital registration systems. For HIV-attributable deaths, lay reports of cause of death were ascertained by verbal autopsy in a sample of cases. From 2001 to 2007, this study estimated that HIV-attributable deaths in adults were reduced by half over the five years, and the decline, which was reported in both sexes, accelerated after a policy to provide free antiretroviral therapy was introduced in 2005 (38). Demographic surveillance linked with verbal autopsy among 32 000 people in northern Malawi from 2002 to 2006 also demonstrated the rapid effect of scaling up antiretroviral therapy. Before antiretroviral therapy, 65% of deaths among adults were attributed to HIV. Eight months after a treatment clinic opened, the overall mortality among adults in this population declined by 10%, with the greatest decline (35%) along the main road where the mortality was highest (39).

In four countries in sub-Saharan Africa, the mortality in five large treatment programmes was compared with the mortality in the general population. Mortality in the first three months after starting antiretroviral therapy was 130 times higher than in the general population and declined to 4 times higher during the second year of antiretroviral therapy. The excess mortality was correlated with the disease stage at the start of therapy and, for the people starting at WHO stages 1 or 2 and with a CD4 count exceeding 200 cells per mm³, the mortality after one year of treatment was almost the same as that among the general population. The authors
suggest that much of the excess mortality in this cohort receiving antiretroviral therapy could have been prevented by initiating treatment earlier (40).

The UNAIDS/WHO Reference Group on Estimates, Modelling and Projections also develops estimates of mortality. These estimates are derived by statistical modelling using data from surveillance and programme monitoring with the software packages Estimation and Projection Package (EPP) and Spectrum (67). Based on this modelling, the estimated global annual number of AIDS deaths declined from 2.2 million [1.9 million – 2.6 million] in 2005 to 2.0 million [1.8 million – 2.3 million] in 2007 (42). Other data sources also indicate declining rates of HIV-related mortality. In an evaluation of outcomes in 12 countries supported by the United States President’s Emergency Plan for AIDS Relief, deaths from HIV or AIDS were estimated to have declined by an average of 6.3% per year over the period of scale up supported by the United States President’s Emergency Plan for AIDS Relief versus a 14.1% mean annual increase before. HIV-related deaths had declined by 10.5% (95% confidence interval: -16.6 to -4.4) in countries supported by the United States President’s Emergency Plan for AIDS Relief compared with other countries (43). In Botswana, the national programme reported that the annual number of adult AIDS-related deaths was estimated to have halved from a peak exceeding 15,500 in 2003 to 7,400 in 2008 with 80% treatment coverage (44). Continued research and improved mortality registration systems are needed to better assess how antiretroviral therapy affects mortality at the population level.

4.1.6. Prevention and assessment of HIV drug resistance

As access to antiretroviral therapy continues to expand, the emergence of HIV drug resistance is inevitable due to the high rates of replication and mutation of HIV and the sustained, life-long need for treatment. To support the optimal functioning of treatment programmes and maintain the effectiveness of first- and second-line antiretroviral drug regimens, WHO recommends that countries develop and implement national and regional strategies to prevent and assess the emergence of HIV drug resistance using a public health approach. The key elements of the strategy include establishing national HIV drug resistance working groups and implementation plans; routine monitoring “early warning” programme indicators at (selected) representative treatment sites; conducting surveys to assess the prevention, emergence and transmission of drug resistance; supporting the adherence of people receiving antiretroviral therapy and continuity of drug supplies at antiretroviral therapy sites; providing quality-assured laboratory testing for surveillance of HIV drug resistance; and producing regular reports with recommendations for public health action (45).

At the global level, HIVResNet, an international network of experts, countries and institutions working together to support and evaluate efforts to prevent and assess drug resistance, advises on implementing the WHO strategy. Implementation of various elements of the WHO strategy continued to expand during 2008 and into 2009. By mid-2009, WHO and HIVResNet partners had provided technical assistance to 53 countries, up from 25 at the end of 2007. To plan and implement the WHO strategy, 28 new countries developed national HIV drug resistance strategies and established terms of reference for national drug resistance working groups (Fig. 4.8).

WHO HIVResNet also coordinates a global network of accredited laboratories that perform quality-assured genotyping for HIV drug resistance surveillance and monitoring at the country level (46). As of June 2009, 24 laboratories had been accredited worldwide, up from 7 at the end of 2007. This was accompanied by the provision of training to laboratory technicians and efforts to increase technology transfer and knowledge sharing between laboratories with different capacities.
Fig. 4.8. Countries implementing at least one element of the WHO Global Strategy for the Prevention and Assessment of HIV Drug Resistance and locations of HIV drug resistance testing laboratories, February 2009

Table 4.6. Surveys of transmitted HIV drug resistance

<table>
<thead>
<tr>
<th>Country</th>
<th>Area</th>
<th>Period</th>
<th>Site type</th>
<th>Predominant HIV-1 subtypes</th>
<th>Transmitted resistance classification (all antiretroviral drug classes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethiopia (49)</td>
<td>Addis Ababa</td>
<td>Apr-Aug 2005</td>
<td>Antenatal care</td>
<td>C</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>India (50)</td>
<td>Mumbai</td>
<td>2007</td>
<td>Voluntary counselling and testing</td>
<td>C</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>Malawi (51)</td>
<td>Lilongwe</td>
<td>Nov-Dec 2006</td>
<td>Prevention of mother-to-child transmission</td>
<td>C</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>South Africa (52)</td>
<td>Gauteng Province</td>
<td>Oct 2002</td>
<td>Antenatal care</td>
<td>C</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>South Africa (52)</td>
<td>Gauteng Province</td>
<td>Oct 2004</td>
<td>Antenatal care</td>
<td>C</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>South Africa (52)</td>
<td>KwaZulu-Natal</td>
<td>2005</td>
<td>Antenatal care</td>
<td>C</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>South Africa (52)</td>
<td>Gauteng Province</td>
<td>2006</td>
<td>Antenatal care</td>
<td>C</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>South Africa (52)</td>
<td>KwaZulu-Natal</td>
<td>2006</td>
<td>Antenatal care</td>
<td>C</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>South Africa (52)</td>
<td>Western Cape</td>
<td>2006</td>
<td>Antenatal care</td>
<td>C</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>South Africa (52)</td>
<td>Gauteng Province</td>
<td>2007</td>
<td>Antenatal care</td>
<td>C</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>South Africa (52)</td>
<td>KwaZulu-Natal</td>
<td>2007</td>
<td>Antenatal care</td>
<td>C</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>Swaziland (53)</td>
<td>Manzini-Mbabane Corridor</td>
<td>Jul-Aug 2006</td>
<td>Antenatal care</td>
<td>C</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>Thailand (54)</td>
<td>Bangkok</td>
<td>Jul-2005-Apr 2006</td>
<td>Blood donation</td>
<td>CRF01-AE</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>Thailand (54)</td>
<td>Bangkok</td>
<td>Jul-Dec 2005</td>
<td>Voluntary counselling and testing</td>
<td>CRF01-AE</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>United Republic of Tanzania (55)</td>
<td>Dar Es Salaam</td>
<td>Nov 2005-Feb 2006</td>
<td>Antenatal care</td>
<td>A, C</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>Viet Nam (56)</td>
<td>Hanoi</td>
<td>Feb-Jun 2006</td>
<td>Voluntary counselling and testing</td>
<td>CRF01-AE, CRF05-01B</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>Uganda (57)</td>
<td>Kampala</td>
<td>2006</td>
<td>Antenatal care</td>
<td>A, D, C</td>
<td>&lt;5%</td>
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</tbody>
</table>
Early warning indicators are programme-based quality assurance indicators for antiretroviral therapy programmes. Strengthening specific aspects of first-line antiretroviral therapy programme delivery will minimize preventable HIV drug resistance and prolong the efficacy of the more affordable first-line regimens. Fourteen countries had piloted the monitoring of early warning indicators in antiretroviral therapy sites as of mid-2009. Seven countries had begun to implement surveys to monitor the prevention of HIV drug resistance and associated factors in sentinel antiretroviral therapy sites using the WHO protocol; eight additional countries are developing protocols or have submitted protocols for review. Through mid-2009, 25 countries had completed or were in the process of implementing HIV drug resistance threshold surveys to evaluate transmitted drug resistance with technical support from WHO and partners. Nine countries reported data from surveys performed in geographical areas where antiretroviral therapy was first provided in the country (47–55). All surveys reported less than 5% transmitted resistance to all drugs and drug classes in these areas (Table 4.6).

4.1.7. Antiretroviral drug regimens
In 2009, the WHO AIDS Medicines and Diagnostics Service (56) conducted the third annual survey on the distribution and composition of first- and second-line antiretroviral therapy regimens used in low- and middle-income countries. A standardized questionnaire was sent to 43 countries with the highest number of people receiving antiretroviral therapy as of December 2008. Thirty-six countries reported 2,634,000 people receiving antiretroviral therapy, or 65% of the estimated 4 million people receiving antiretroviral therapy in low- and middle-income countries as of December 2008. In these 36 countries, 93% of the people receiving antiretroviral therapy were adults (2,450,000) and 7% were children (184,000).

The first key finding was that, among adults, the vast majority (2,400,000) were receiving first-line regimens. Information on specific first-line regimens was available for 98% of the adults; 99% were receiving first-line regimens in accordance with 2006 WHO treatment guidelines (8). A majority (45%) of adults (Fig. 4.9) used stavudine (d4T) + lamivudine (3TC) + nevirapine (NVP), followed by zidovudine (AZT) + 3TC + efavirenz (EFV) (18%), AZT + 3TC + NVP (17%), d4T + 3TC + EFV (11%) and tenofovir (TDF)-based regimens (8%). These included TDF + emtricitabine (FTC) + NVP (3%), TDF + FTC + EFV (3%), TDF + 3TC + NVP (1%) and TDF + 3TC + EFV (1%). In total, 67% of adults receiving first-line antiretroviral therapy were receiving NVP as the non-nucleoside component versus 32% receiving EFV.

1 The 36 responding countries included Angola, Benin, Botswana, Burkina Faso, Burundi, Cambodia, Cameroon, Chad, China, Côte d’Ivoire, Democratic Republic of the Congo, Djibouti, Ethiopia, Ghana, Guyana, India, Islamic Republic of Iran, Kenya, Lesotho, Liberia, Malawi, Mali, Mozambique, Namibia, Nigeria, Pakistan, Rwanda, Senegal, Sudan, Swaziland, Togo, Uganda, Ukraine, United Republic of Tanzania, Zambia and Zimbabwe.

Fig. 4.9. Main first-line antiretroviral regimens used among 2.4 million adults in 36 low- and middle-income countries, December 2008

* TDF-based regimens: TDF + FTC + NVP (3%), TDF + FTC + EFV (3%), TDF + 3TC + NVP (1%) and TDF + 3TC + EFV (1%).
Only 2% of adults (51,000) among the study population were receiving second-line regimens. Information on specific regimens used was available for 50,000 people and showed that 81% were receiving regimens recommended by the 2006 WHO treatment guidelines (8). Ritonavir-boosted lopinavir (LPV/r) was the predominant protease inhibitor used by 93% of adults receiving second-line treatment. Other protease inhibitors used were indinavir with a ritonavir boost (1%) and saquinavir with a ritonavir boost (1%). A majority of adults used TDF + FTC + LPV/r or TDF + 3TC + LPV/r (35%), AZT + FTC + TDF + LPV/r or AZT + 3TC + TDF + LPV/r (17%), abacavir (ABC) + didanosine (ddI) + LPV/r (15%), AZT + 3TC + LPV/r (8%) and AZT + ddI + LPV/r (5%) (Fig. 4.10).

The vast majority of children (97%) from responding countries were receiving first-line regimens (178,000), with information on specific regimens available for 99% of them. About 173,000 were receiving first-line regimens recommended by the WHO treatment guidelines (8). The most commonly used regimen was d4T + 3TC + NVP (41%), followed by AZT + 3TC + NVP (37%), AZT + 3TC + EFV (12%) and d4T + 3TC + EFV (7%) (Fig. 4.11). The distribution between regimens containing AZT (51%) and d4T (48%) is almost equal. In total, 79% of children receiving first-line antiretroviral therapy were receiving NVP as the non-nucleoside component versus 19% receiving EFV.
Three per cent of children in the study population (around 6000) were receiving a second-line regimen. Information on specific regimens was available for 98% of them. The most common regimen was ABC + d4T + LPV/r (28%) followed by ABC + ddI + LPV/r (23%), d4T + 3TC + ddI (11%), d4T + 3TC + LPV/r (8%), 3TC + ddI + LPV/r (7%) and AZT + 3TC + LPV/r (6%) (Fig. 4.12). LPV/r was the predominant protease inhibitor and used by 83% children receiving second-line therapy. The remaining 17% of children received a second-line regimen without a protease inhibitor, which is recommended as the backbone of second-line regimens in WHO guidelines. (8)

With 1 million more people receiving antiretroviral therapy in December 2008 than 12 months earlier, the market for antiretroviral drugs continues to expand rapidly in low- and middle-income countries. Uptake of most individual antiretroviral drugs increased in 2008 for first- and second-line regimens among both adults and children. However, the proportion of adults receiving second-line regimens remained low in 2008, amounting to not more than 2% of adults on antiretroviral therapy in the responding countries. The two preceding surveys conducted by the WHO AIDS Medicines and Diagnostics Service found similar results in 2007 (3%) and 2006 (4%). There could be numerous explanations for these trends, including the continued effectiveness of most first-line regimens; the limited capacity of countries to accurately diagnose treatment failure, resulting in low rates of switching to second-line regimens; or the limited availability of second-line drugs, due in part to high costs.

Table 4.7 summarizes key findings in antiretroviral drug use trends among adults, including for individual antiretroviral drugs, from 2006 to 2008. Preliminary analysis of 2008 data confirms some of the trends observed in 2007. In 2008, the data show a net increase in the use of TDF, with 8% of adults receiving TDF in first-line regimens and 56% of adults receiving it in second-line regimens versus 1.5% and 14% in 2007 and <1% and 4% in 2006 respectively. The data also show a decrease in the use of d4T, with 56% of adults receiving a d4T-containing first-line regimen in 2008, 63% in 2007 and 69% in 2006. The use of AZT increased from 24% in 2007 and 25% in 2006 to 35% of adults receiving a first-line regimen in 2008.

An increase in the use of second-line drugs and of AZT and TDF in first-line and second-line regimens implies a rise in the cost of drugs for HIV programmes in low- and medium-income countries (see section 4.1.6 for data on drug prices). This represents a major challenge for country programmes, national authorities and the international development community, who will need to raise additional resources to sustain and expand treatment access.

<table>
<thead>
<tr>
<th>Table 4.7. Trends in antiretroviral drug use in low- and middle-income countries reporting to WHO, 2006–2008</th>
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</thead>
<tbody>
<tr>
<td>Major parameters</td>
</tr>
<tr>
<td>Proportion of people receiving first-line therapy</td>
</tr>
<tr>
<td>Proportion of people receiving second-line therapy</td>
</tr>
<tr>
<td>Use of d4T in first-line regimens</td>
</tr>
<tr>
<td>Use of AZT in first-line regimens</td>
</tr>
<tr>
<td>Use of TDF in first-line regimens</td>
</tr>
<tr>
<td>Use of TDF in second-line regimens</td>
</tr>
</tbody>
</table>

Source: Renaud-Thery et al. (57) and Towards universal access: scaling up priority HIV/AIDS interventions in the health sector. Progress report 2008 (2).
Finally, the survey results provide evidence of evolution in treatment guidelines at the country level. Of 36 responding countries, 16 countries reported being in the process of revising treatment protocols for adults and 19 countries in the process of revising treatment protocols for children. The most frequently reported changes in adult treatment guidelines were the introduction of TDF (nine countries), a change from d4T as the preferred first-line option (seven countries) and an increase in the CD4 threshold for treatment initiation to below 250 cells per mm$^2$ (two countries) or below 350 cells per mm$^2$ (four countries). For guidelines for treating children, the major reported change was the introduction of antiretroviral therapy as soon as HIV infection is confirmed in infants, regardless of CD4 count (four countries), as WHO recommended in June 2008 (58).

The 2006, 2007 and 2008 surveys also confirmed that most national HIV programmes are following WHO-recommended treatment guidelines (8): 99% and 81% of people on first- and second-line antiretroviral drug regimens, respectively. These recommendations will be revised in 2009 (Box 4.9), with a review of evidence on the optimal time to initiate treatment and the choice of drugs. WHO will continue to report on evolving trends in the use of antiretroviral drug regimens.

Box 4.9. When to start: revising the WHO antiretroviral therapy guidelines for adults and adolescents

Current WHO guidelines on antiretroviral therapy for HIV infection in adults and adolescents (8) recommend that, in resource-limited settings, adults living with HIV should start antiretroviral therapy when the infection has been confirmed and there are signs of advanced or severe clinical disease or where laboratory testing confirms severe or advanced immunosuppression. However, the ideal starting-point for treatment among asymptomatic people with CD4 cell counts above this level has not been established. These guidelines take a public health approach to scaling up antiretroviral therapy based on standardized regimens and monitoring and simplified management of people receiving antiretroviral therapy (8).

The question of the optimal time to initiate antiretroviral therapy has gained importance in recent scientific discussion, as data from observational studies conducted in high-income countries suggest that initiating antiretroviral therapy earlier can reduce the occurrence of non-AIDS events, including cancer and cardiovascular, renal and hepatic complications. Some studies suggest that treatment initiation should be considered among people with CD4 values of less than 350 cells per mm$^3$ or even higher thresholds in some situations (59–63). Such emerging evidence is important to inform future revisions of international treatment guidelines along with assessing the feasibility and acceptability of any changes in recommendations.

At the population level, recommendations on when to initiate antiretroviral therapy need to consider several factors. The recent evidence on the benefits of early initiation is based on observational cohorts from high-income countries and cannot be assumed to be directly applicable to people living with HIV in all settings. Mortality rates and the range of morbidity differ between high-income and resource-limited settings. The available range of antiretroviral drugs, their cost-effectiveness and the options for treatment monitoring and support may also be more limited in low- and middle-income countries. The toxicity profile of the preferred first-line regimens and the local burden of AIDS and non-AIDS events in the epidemic will influence decisions on the optimal time to start antiretroviral therapy. Data from cohorts in low-income countries have also shown that treatment initiation is occurring later in the course of disease as compared with high-income settings, mainly due to late diagnosis of HIV infection, and treatment is frequently initiated based on clinical status alone because of poor access to laboratory facilities. Various randomized clinical trials currently underway will generate further, more definitive evidence on the optimal time for initiating treatment.

In late 2009, WHO will lead an expert consultative process to review new evidence: grade its quality in terms of the study design, relevance of outcomes and consistency of results; and revise its recommendations as appropriate. It will not only consider the latest evidence on the threshold for initiating treatment but also the toxicity of preferred first-line treatment regimens, the choice of drugs for second-line treatment when first-line therapy fails and recommendations on the use of viral load and CD4 in monitoring treatment outcomes in resource-limited settings. It will consider issues related to antiretroviral therapy for people living with HIV and TB or viral hepatitis and specific considerations for childbearing women and injecting drug users.

For national programmes, any increase in the threshold of treatment initiation will also affect the overall numbers of people needing antiretroviral therapy and the resources required to achieve universal access goals. A preliminary model suggests that initiating treatment at a threshold CD4 cell count of less than 275 cells per mm$^3$ could increase treatment need by about 50%, and a threshold of less than 350 cells per mm$^3$ could double treatment need compared with current parameters. If estimates of treatment need increase, current measurements of treatment coverage will decline.
4.1.8. 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 106 low- and middle-income countries since January 2007 (64).

The data show that the prices of most first-line regimens decreased by 30–68% from 2004 to 2008 and by 10–40% from 2006 to 2008, contributing greatly to the wider availability of treatment. However, prices remain high in most countries in Europe and Central Asia, East, South and South-East Asia and Latin America. The average prices paid for second-line regimens continue to be high in both low- and middle-income countries in all regions (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 countries¹

The median price paid for first-line treatment (prequalified by WHO or approved or tentatively approved by the United States Food and Drug Administration) in low-income countries in 2008 ranged from US$ 88 per person per year for the fixed-dose combination of 3TC + NVP + d4T (the most widely used combination) to US$ 261 for the fixed-dose combination EFV + [3TC + AZT] (Fig. 4.13). The weighted average median price of the four combinations most widely used in first-line treatment (representing 91% of the prescribed first-line treatments in low-income countries) was US$ 143 per person per year in 2008, 16% lower than the price in 2007. The decline in drug prices between 2004 and 2008 (48%) can be attributed to the sustained scaling up of treatment programmes, growing transaction volumes and predictability of demand, competition between a growing number of products prequalified by WHO and favourable pricing policies by pharmaceutical companies.

The prices of formulations for children (weighing 10 kg or more) declined even more rapidly, from US$ 436 per person per year in 2004 to US$ 105 in 2008 for the most common used formulation of 3TC + NVP + AZT. This decrease in prices can similarly be attributed to an increasing market share of formulations for children, the successful negotiations between the William J. Clinton Foundation and major generic manufacturers and the development of fixed-dose combination formulations for children.

Prices of first-line regimens in lower-middle-income countries²

The average prices paid for first-line regimens declined significantly in lower-middle-income countries and approached those paid in low-income countries. The

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¹ Countries with a gross national income per capita of US$ 935 or less.
² Countries with a gross national income per capita between US$ 936 and US$ 3705.

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Fig. 4.13. Median annual cost (in US dollars) of first-line antiretroviral drug regimens in low-income countries by year, 2004–2008
median prices in 2008 ranged from US$ 100 per person per year for the least expensive regimen of 3TC + NVP + d4T to US$ 293 per person per year for the most expensive regimen of EFV + [3TC + AZT] (Fig. 4.14). In the same year, the weighted median price of the four most widely used combinations in first-line treatment was US$ 162 per person per year, a decrease of 22% from the 2007 price.

The formulations for children (weighing 10 kg or more) declined more substantially in price, from US$ 235 per person per year in 2004 to US$ 105 in 2008 for the most commonly used formulation of 3TC + NVP + AZT.

Prices of first-line regimens in upper-middle-income countries

The average prices paid for first-line regimens also declined significantly in upper-middle-income countries and approached those paid in low- and lower-middle income countries. The median prices in 2008 ranged from US$ 110 per person per year for the least expensive regimen of 3TC + NVP + d4T to US$ 289 per person per year for the most expensive regimen of EFV + [3TC + AZT] (Fig. 4.15). In the same year, the weighted average median price of the four most widely used combinations in first-line treatment was US$ 161 per person per year. The formulations for children

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1 Countries with a gross national income per capita between US$ 3706 and US$ 11 455.
(weighing 10 kg or more) declined in price from US$ 785 per person per year in 2004 to US$ 221 for the most commonly used formulation of 3TC + NVP + AZT in 2008.

Second-line regimens in low- and middle-income countries
The average prices paid for second-line regimens also declined but continue to be significantly more expensive than first-line regimens in low-income, lower-middle-income and upper-middle-income countries. In 2008, the median cost of a regimen of three single doses of ABC, ddI and LPV/r, the most expensive commonly used second-line regimen, was US$ 1105 per person per year in low-income countries, US$ 2192 in lower-middle-income countries and US$ 2634 in upper-middle-income countries. The median cost of FTC + TDF + LPV/r, the most commonly used second-line regimen, was US$ 819 per person per year in low-income countries, US$ 1479 in lower-middle-income countries and US$ 1677 in upper-middle-income countries. The actual prices paid for second-line regimens vary significantly between countries.

The decline in the prices of second-line drugs between 2004 and 2008 can be attributed to the prequalification of generic alternatives of ABC, LPV/r and TDF, the scaling up of treatment programmes and new pricing policies by pharmaceutical companies, which increased competition between WHO-prequalified products. As the number of people who need access to second-line regimens continues to grow, addressing the high cost of second-line regimens will become increasingly important to ensure the most cost-effective use of available resources.

4.2. Prevention, care and management of HIV/TB coinfection

The problem of HIV-related TB remains a serious challenge for the health sector response to HIV. Recent data show that, of the 9.27 million incident TB cases worldwide in 2007, an estimated 1.37 million were among people living with HIV (Box 4.11). About 456 000 people living with HIV died from TB in 2007, 23% of the estimated 2 million HIV-related deaths in that year. The revised estimates of TB cases among people living with HIV also suggest that the risk for acquiring TB is 20 to 37 times greater among people living with HIV than in the general population, depending on the prevalence of HIV in the population. In some countries in sub-Saharan Africa, up to 80% of people with TB are also living with HIV.

Data on drug-resistant forms of TB show that, of the 9.27 million incident TB cases in 2007, an estimated 0.5 million involved cases of multidrug-resistant TB. The region of Europe and Central Asia is especially severely affected. Of the 27 countries that account for 85% of multidrug-resistant TB cases globally, 15 are in the WHO European Region. In addition, 55 countries and territories reported at least one case of extensively drug-resistant TB in 2007. People living with HIV have a higher risk of drug-resistant forms of TB due to difficulty and delays in diagnosis, lack of access to antiretroviral therapy and complications of concomitant TB treatment and antiretroviral therapy, poor implementation of isoniazid preventive therapy and inadequate TB infection control measures, with increased mortality and greatly reduced survival time (65–67).

Collaborative activities between national TB and HIV programmes are essential to prevent, diagnose and treat TB among people living with HIV. The activities include establishing mechanisms for collaboration (such as coordinating bodies, joint planning, surveillance and monitoring and evaluation); decreasing the burden of HIV among people with TB (with HIV testing and counselling, Box 4.10. Pharmacovigilance

The rapid scaling up of antiretroviral therapy needs to be accompanied by the development of sound pharmacovigilance practice to track adverse events, ensure consistent reporting and support patient safety and clinical management. In 2008, WHO launched a project to improve the safety of antiretroviral drugs in low- and middle-income countries. The project, funded by the Bill & Melinda Gates Foundation, aims to develop and harmonize definitions and tools for pharmacovigilance of antiretroviral drugs, support priority countries, formulate a research agenda and improve the sharing and dissemination of information. The pharmacovigilance efforts rely upon partnership with other related WHO programmes (such as those for essential medicines, maternal health, malaria and tropical diseases research), research groups and regulatory authorities within countries, and nongovernmental organizations.

The project will help guide the development of treatment recommendations and better identify the laboratory and diagnosis infrastructures needed for improving antiretroviral therapy management. By improving and harmonizing the detection and reporting of adverse events and toxicity, it will also contribute to generating better knowledge of adverse events associated with antiretroviral drug; these are currently widely underreported and their importance remains unknown in low- and middle-income countries.

1 This section draws largely from Global tuberculosis control 2009 – epidemiology, strategy, financing which reported 2007 data (68). Additional references are cited where relevant.
Estimated HIV prevalence in new TB cases, 2007

- 0–4%
- 5–19%
- 20–49%
- ≥50%
- Data not available

Fig. 4.16. Estimated HIV prevalence (%) among people newly infected with TB, 2007

Joint mechanisms for collaboration
Progress in developing policies and collaborative mechanisms was analysed among 63 priority countries that collectively account for 99% of the estimated TB cases among people living with HIV worldwide. Among these countries, the number of countries with a coordinating body for collaborative HIV/TB activities increased from 35 in 2005 to 44 in 2007 (representing 70% of the total estimated TB cases among people living with HIV accounted for by reporting countries), and the number of countries with joint plans increased from 34 to 42 over the same time period. Forty-six countries (88% of total estimated TB cases among people living with HIV accounted for by reporting countries) conducted HIV surveillance among people with TB in 2007 versus 28 countries in 2005.

Box 4.11. Revised estimates of the number of people with TB among those living with HIV
The estimated numbers of TB cases and deaths among people living with HIV in 2007 are approximately double those published in previous years. These revised estimates do not reflect an increase in the number of incident TB cases but upwardly revise the estimated proportion of people with incident TB who are living with HIV. These estimates are based on more extensive data on the prevalence of HIV among people with TB that became available during 2007, both from programme data and surveillance reports. The expansion of provider-initiated HIV testing and counselling provided reliable data on the prevalence of HIV among people with TB in 49 countries in 2007 versus only 13 countries in 2006. In addition, country-specific measurements of the prevalence of HIV among people with TB were also available from an additional 15 countries through surveys or sentinel surveillance. Such direct measurement from these 64 countries enabled the numbers of people living with HIV who had TB and died from TB in 2007 to be more accurately estimated.

The data were also used to recalculate previous estimates of the numbers of cases and deaths to analyse trends. Better coverage of HIV surveillance among people with TB and improved monitoring of national HIV programmes will enable these data to be improved further in the future.

Box 4.11. Revised estimates of the number of people with TB among those living with HIV

The estimated numbers of TB cases and deaths among people living with HIV in 2007 are approximately double those published in previous years. These revised estimates do not reflect an increase in the number of incident TB cases but upwardly revise the estimated proportion of people with incident TB who are living with HIV. These estimates are based on more extensive data on the prevalence of HIV among people with TB that became available during 2007, both from programme data and surveillance reports. The expansion of provider-initiated HIV testing and counselling provided reliable data on the prevalence of HIV among people with TB in 49 countries in 2007 versus only 13 countries in 2006. In addition, country-specific measurements of the prevalence of HIV among people with TB were also available from an additional 15 countries through surveys or sentinel surveillance. Such direct measurement from these 64 countries enabled the numbers of people living with HIV who had TB and died from TB in 2007 to be more accurately estimated.

The data were also used to recalculate previous estimates of the numbers of cases and deaths to analyse trends. Better coverage of HIV surveillance among people with TB and improved monitoring of national HIV programmes will enable these data to be improved further in the future.

1 These refer to 41 countries that were identified as priorities at the global level in 2002 and that account for 97% of the estimated people living with HIV and TB globally, plus additional 22 countries identified by UNAIDS as having a generalized HIV epidemic.
Reducing the burden of HIV among people with TB and their communities

HIV counselling and testing serves as a gateway for access to HIV and TB prevention, treatment and care and is recommended for everyone presenting with signs and symptoms of TB and people with confirmed TB. There has been substantial progress in expanding HIV testing and counselling for people with TB in recent years. The number of countries with a policy for HIV testing and counselling of people with TB among the 63 HIV/TB priority countries accounting for 99% of the global HIV/TB burden increased from 38 in 2005 to 52 in 2007 (covering 96% of estimated TB cases living with HIV).

Data on programme coverage are analysed for all reporting countries. Almost 1 million people with TB (16% of notified TB cases) knew their HIV status across 135 reporting countries in 2007 versus about 700 000 people in 112 countries in 2006 and 22 000 people in 9 countries in 2002. In sub-Saharan Africa, nearly 492 000 people with TB knew their HIV status in 2007, representing 37% of known people with TB and an increase of about 10 times since 2004 (Fig. 4.17). Among the countries with high prevalence of HIV among people with TB in this region, Kenya, Lesotho, Malawi, Rwanda and Swaziland achieved high rates of HIV testing in 2007. In Kenya, for instance, 79% of notified TB cases were tested for HIV in 2007 versus 60% in 2006.

The number of people with TB with known HIV status also increased in other regions. In India, more than 80 000 people with TB have been tested for HIV.

Antiretroviral therapy is a high-priority life-saving intervention for people living with HIV. Studies and modelling efforts suggest that early initiation of antiretroviral therapy for people living with HIV who develop TB may lead to reduced mortality and incidence of TB (69–73).

Fig. 4.17. Rates of HIV testing among people with TB in countries in sub-Saharan Africa, 2004–2007
The number of people living with HIV and TB who received antiretroviral therapy across all reporting countries increased from about 67 000 in 69 reporting countries in 2006 to about 90 000 in 73 reporting countries in 2007 and to 125 000 people in 77 reporting countries in 2008. Of these, 105 000 people were in sub-Saharan Africa, 12 000 in East, South and South-East Asia, 7000 in Latin America and the Caribbean, 1000 in Europe and Central Asia and 150 in North Africa and the Middle East. This represents 16% of the estimated people living with HIV and TB in reporting countries receiving antiretroviral therapy, which is much lower than the overall estimated global antiretroviral therapy coverage. Given the increasing evidence of access to testing for people with TB, the clear benefits of antiretroviral therapy for people with TB and better links between TB and HIV services, this gap may reflect the weaknesses of reporting access to care among people with HIV and TB by settings providing HIV services. It may also reflect the difficulties in managing antiretroviral therapy among people with TB.

Co-trimoxazole has been proven to reduce morbidity and mortality among people living with HIV and TB. Provision of co-trimoxazole preventive therapy also increased in the past years. The total number of people living with HIV and TB who were treated with co-trimoxazole preventive therapy in all reporting countries increased by 38% from 145 000 in 2006 (55 countries) to nearly 200 000 in 2007 (60 countries). However, these data also suggest that HIV testing alone may not guarantee access to other HIV prevention, treatment and care services.

Reducing the burden of TB among people with HIV

In 2008, a WHO-convened expert consultation recognized the limited implementation of interventions to decrease the burden of TB among people living with HIV and re-emphasized the importance of three priority public health actions to prevent and treat TB among them – the three ‘I’s for HIV/TB of isoniazid preventive treatment, intensified case-finding and infection control for TB (74). Available data show that countries are making efforts to scale up each of these interventions and to report on progress; however, many countries have not begun to implement the three ‘I’s (Box 4.12).

Intensified case-finding for TB is a vital first step in providing access to necessary health services to those in need. Information on TB control policies shows that among the 63 priority countries accounting for 99% of the global HIV/TB burden, 52 countries had policies for intensified TB case-finding among people with HIV in 2007, up from 44 in 2006 and 24 in 2005.

A comparison of countries reporting data in 2007 and 2008 provides evidence of substantial improvements in rates of reporting. Thirty-seven countries (with 29% of the estimated global HIV/TB burden) reported 322 000 people living with HIV screened for TB in 2008 versus 38 000 in 30 countries (2% of the global HIV/TB burden) in 2007. Nine

1 Data reported by countries to WHO, UNICEF and UNAIDS in response to the annual reporting form for monitoring the health sector response to HIV/AIDS, 2008 and 2009.

Box 4.12. Supporting implementation and monitoring of the three I’s for HIV/TB

The WHO strategy for Integrated Management of Adolescent and Adult Illness (IMAI) and the related tools support an integrated approach to primary health care and strengthening health systems based on both clinical and management and logistical input to strengthen the district health system or district network.

Since 2006, the integrated package of tools has been expanded further to include integrated services for preventing the mother-to-child transmission of HIV (with antiretroviral therapy delivered through antenatal sites) and HIV/TB interventions (75). The HIV/TB co-management and TB infection control clinical module has been developed for primary care providers at health centres and at district hospital outpatient clinics. These primary care tools operationalize updated normative guidance for HIV service providers to accelerate the implementation of the three ‘I’s. These tools help health workers to recommend HIV testing and counselling to people with TB and those suspected of having TB, provide evidence-based training on when to suspect TB disease among people living with HIV, assess people living with HIV for TB during initial visits and each follow-up visit, co-manage TB and HIV and implement basic TB infection control measures in their health facilities. Of the 35 countries using the IMAI approach, 11 countries (representing 30% of the global estimated HIV-related TB cases) have already adapted the HIV/TB modules.

Three interlinked patient monitoring systems for HIV care/ART, MCH/PMTCT (including malaria prevention during pregnancy), and HIV/TB (76) being developed jointly by WHO, UNICEF, UNAIDS, the United States Centres for Disease Control and Prevention and other partners thus supports the monitoring of TB preventive therapy, TB screening and TB and antiretroviral therapy co-treatment within HIV services. The revised HIV care and antiretroviral therapy monitoring tools also allocate space for recording TB screening among people living with HIV. These interlinked tools are critical to ensure improved monitoring of the interventions through a comprehensive approach, especially in countries with high mortality from TB among people with HIV, including those on antiretroviral therapy.
countries reporting data for both 2007 and 2008 show an increase of around 30% in intensified case-finding. However, 7 of the 10 countries containing 68% of global estimated HIV-related TB cases did not report data on screening for TB among people living with HIV in 2008. Thus, although more countries are reporting this information, current reporting rates remain inadequate to analyse the global coverage of intensified case-finding for TB in 2008.

WHO policy also recommends isoniazid preventive therapy for people living with HIV. Information on national policies shows that the number of countries with policies related to providing isoniazid preventive therapy increased marginally from 24 countries in 2005 to 29 countries in 2007 among the 63 priority countries. This indicates that many countries continue to lack commitment and efforts to scale up this key intervention.

Country data on the provision of isoniazid preventive therapy to people living with HIV also show improvements in reporting and provide some evidence of progress. Comparing data reported in 2007 and 2008, the reported number of people with HIV receiving isoniazid preventive therapy increased about 11-fold from 5000 in 2007 (25 countries representing 3% of the global HIV/TB burden) to 62 000 people in 2008 (18 countries representing 18% of the global HIV/TB burden). Within six countries that reported providing isoniazid preventive therapy in both 2007 and 2008, the number of people living with HIV who received isoniazid preventive therapy increased from 2000 to 3100. However, once again, of the 10 countries with the highest estimated HIV-related TB burden, 8 did not provide data on this indicator in 2008, creating difficulty in assessing the global situation at the end of the year.

TB infection control measures are equally important in settings providing health services, particularly to people with HIV, but this critical TB prevention intervention is often overlooked. The large expansion of HIV services in areas with high TB prevalence has often created conditions for hospital-related TB transmission among vulnerable patients, their families and health care workers. Several serious TB outbreaks have been reported in health care settings among people living with HIV and the health workforce (77–82). Among the 63 priority countries, 34 reported having a policy for infection control in 2007, up from 20 in 2005 and 31 in 2006. Although more countries are reporting infection control policies in health care settings, opportunities exist for improved implementation as part of HIV and TB prevention, treatment and care.

Box 4.13. Improving monitoring and evaluation systems for HIV/TB interventions

National TB programmes (interventions to reduce the burden of HIV among people with TB) and national HIV programmes (interventions to reduce the burden of TB among people living with HIV) generate data on progress in scaling up collaborative HIV/TB interventions. International partners such as WHO collect these data annually to monitor and report on progress in achieving global TB and HIV targets. Although all these data suggest year-on-year improvements in reporting, they also shed light on some limitations in current reporting systems and issues to be addressed in the coming years.

The data on implementing the three I’s for HIV/TB for reducing the burden of TB among people with HIV need to be interpreted with caution. Despite visible improvement in country-level monitoring and reporting efforts during the past two years, most countries still do not have the capacity for timely and quality reporting at the national level. Although the reported numbers of people living with HIV receiving TB screening and receiving isoniazid preventive therapy are increasing, assessing the exact proportion those in need who are receiving these services is difficult due to the weaknesses in reporting.

In addition to the incompleteness of reporting, the analysis of country reports also highlights discrepancies between data on the three I’s reported to WHO via national TB programmes versus via national HIV programmes. In 2007, more countries provided data via national TB programmes than via HIV programmes for the same indicators related to collaborative HIV/TB interventions. For instance, in 2007, 84 countries reported data to WHO on TB screening of people living with HIV, representing 65% of the global estimated number of people living with HIV and TB. Of these 84 countries, 54 reported results through national TB programmes, 15 through national HIV programmes and 17 through both.

These differences in reporting rates underscore the urgent need to build capacity in national HIV programmes and create synergy with the long-established national TB programmes. WHO’s TB programme has been collecting these data from national HIV programmes via the national TB programmes since 2002, and WHO’s HIV programme began collecting these data directly from national HIV programmes in 2006 in response to international commitments to monitor and report on progress towards universal access to HIV prevention, treatment and care. The international community is supporting country efforts to strengthen WHO-recommended integrated monitoring and reporting systems for HIV/TB programmes and promote greater harmonization of data generating and reporting in the future.
To conclude, more people living with HIV have TB than previously estimated, and TB remains a leading cause of death and a life-threatening disease among people living with HIV. Although clear, evidence-based strategies to prevent, diagnose and treat TB have been widely articulated and agreed, the implementation of many of these interventions continues to lag behind at the country level. In some of the countries with the highest burdens of HIV-related TB, the lack of political commitment and investment in collaborative TB/HIV interventions are undermining the effects of HIV programmes.

Some progress has been made in recent years, yet the data show that access to essential interventions to decrease the burden of HIV-related TB coinfection remains far from the goal of universal access. Urgent political commitment and capacity-building are required to increase access to HIV testing, treatment and care for people with TB and to scale up the three I’s for HIV/TB for people living with HIV.

The data also draw attention to the urgent need to strengthen integrated monitoring and evaluation systems to assess the progress and outcomes of collaborative HIV/TB interventions. With weak programme monitoring and low reporting rates, global analysis of progress cannot fully reflect country efforts, even where access to interventions may be expanding. Greater investment in joint indicators and integrated monitoring tools are urgently needed to ensure access to vital HIV/TB services in the coming years (Box 4.13).
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