Use of a Comprehensive HIV Care Cascade for Evaluating HIV Program Performance: Findings From 4 Sub-Saharan African Countries

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Abstract

Background—The traditional HIV treatment cascade has been noted to have limitations. A proposed comprehensive HIV care cascade that uses cohort methodology offers additional information as it accounts for all patients. Using data from 4 countries, we compare patient outcomes using both approaches.

Methods—Data from 390,603 HIV-infected adults (>15 years) enrolled at 217 facilities in Kenya, Mozambique, Rwanda, and Tanzania from 2005 to 2011 were included. Outcomes of all patients at 3, 6, and 12 months after enrollment were categorized as optimal, suboptimal, or poor. Optimal outcomes included retention in care, antiretroviral therapy (ART) initiation, and documented transfer. Suboptimal outcomes included retention in care without ART initiation among eligible patients or those without eligibility data. Poor outcomes included loss to follow-up and death.

Results—The comprehensive HIV care cascade demonstrated that at 3, 6 and 12 months, 58%, 51%, and 49% of patients had optimal outcomes; 22%, 12%, and 7% had suboptimal outcomes, and 20%, 37% and 44% had poor outcomes. Of all patients enrolled in care, 56% were retained in care at 12 months after enrollment. In comparison, the traditional HIV treatment cascade found 89% of patients enrolled in HIV care were assessed for ART eligibility, of whom 48% were...
determined to be ART-eligible with 70% initiating ART, and 78% of those initiated on ART retained at 12 months.

Conclusions—The comprehensive HIV care cascade follows outcomes of all patients, including pre-ART patients, who enroll in HIV care over time and uses quality of care parameters for categorizing outcomes. The comprehensive HIV care cascade provides complementary information to that of the traditional HIV treatment cascade and is a valuable tool for monitoring HIV program performance.

Keywords
HIV; retention; antiretroviral; HIV care cascade

INTRODUCTION
Scale-up of adult HIV care and treatment has been substantial with over 13 million adults receiving antiretroviral therapy (ART) by the end of 2014. The HIV treatment cascade is a tool that has been adapted by HIV programs to evaluate the quality of such activities by measuring the proportion of patients achieving essential steps in the HIV continuum of care that are necessary to maximize individual health and population prevention benefits of ART. The HIV treatment cascade’s ultimate end point is viral load suppression or retention after ART initiation in settings where viral load measurement is not available. However, the HIV treatment cascade does not follow outcomes of patients ineligible for ART, referred to as pre-ART patients. Thus, in many resource-limited settings where national and international guidelines currently do not recommend universal treatment, the traditional HIV treatment cascade does not provide a comprehensive assessment of all patient outcomes.

We propose an alternative approach, which we term the “comprehensive HIV care cascade,” that can be used to provide additional complementary information to that of the traditional HIV treatment cascade on HIV program performance. The comprehensive HIV care cascade uses cohort methodology to account for all patients who enroll in HIV programs over time irrespective of ART eligibility and uses quality-of-care categories (optimal, suboptimal, and poor) for grouping patient outcomes. This approach builds further on approaches aiming to capture outcomes for the subset of pre-ART patients. We posit that the comprehensive HIV care cascade could be an important tool that complements the traditional HIV treatment cascade to evaluate HIV program performance, at the health facility, across health facilities, or at regional or country levels.

The objectives of this analysis were (1) to use the comprehensive HIV care cascade to evaluate patient outcomes across ICAP-supported HIV programs using data from adults newly enrolling in HIV care in 4 sub-Saharan African countries and (2) to compare outcomes using the comprehensive HIV care cascade to those measured using the traditional HIV treatment cascade using these data.
METHODS

Study Population

The study population includes data from HIV-infected adults aged 15 years or older who enrolled in HIV care at 217 HIV facilities in Kenya, Mozambique, Rwanda, and Tanzania from January 2005 to June 2011. Follow-up data were included through June 2012. Enrollment in HIV care was defined as completing at least 1 visit where clinical parameters (ie, height, weight, CD4+ cell count, or WHO stage) were recorded. Pre-ART patients were defined as individuals who were not on ART, including those with known ART ineligibility, unknown ART eligibility, or known ART eligibility but who were not initiated on treatment. The recommended package of pre-ART care included a provider assessment of a patient’s medical history and clinical examination and involved WHO staging, CD4+ count testing, screening for tuberculosis and sexually transmitted infections, and counseling regarding partner and family HIV testing and prevention interventions. ART patients were defined as those on ART. All facilities received technical support from ICAP at Columbia University through funding from the President’s Emergency Plan for AIDS Relief (PEPFAR). Health facilities included in this analysis participated in the Identifying Optimal Models Study, which used routinely collected patient- and facility-level data to measure patient and program outcomes. Patient information routinely collected during each clinic visit was documented by health care providers on national patient forms and subsequently entered by trained data clerks into a patient-level database. Data quality assessments were conducted quarterly to check for completeness and accuracy comparing paper records to data in electronic databases. Deidentified versions of electronic databases were compiled semiannually and shared with study investigators.

Traditional HIV Treatment Cascade Approach

In this analysis, the traditional HIV treatment cascade was adapted to use data routinely available for patients in sub-Saharan Africa and included the following steps: (1) number enrolled in HIV care, (2) number assessed for ART eligibility, (3) number determined ART eligible as per national guidelines, (4) number initiated on ART, and (5) number retained at 12 months after ART initiation. Outcomes for pre-ART patients, time frames for achievement of each step (except the final step), and reasons for attrition between steps are commonly not included in this approach.

Comprehensive HIV Care Cascade Approach

In the comprehensive HIV care cascade, outcomes for all patient enrolled in HIV care were assessed at 3, 6, and 12 months after enrollment and classified into the following mutually exclusive categories of optimal, suboptimal, and poor outcomes.

- “Optimal outcomes” included retained in pre-ART care with known ART ineligibility, initiated ART by the end of the given time point, retained on ART, or documented transfer.
- “Suboptimal outcomes” included retained in pre-ART care with known ART eligibility and retained in pre-ART care with undocumented or
indeterminate eligibility (e.g., no available CD4+ count and/or WHO stage results to assess eligibility).

- “Poor outcomes” included loss to follow-up (LTF) or death, occurring either before or after ART initiation. Because ART initiation was assessed as the proportion initiating within 3 months, outcomes after ART initiation (death and LTF) were only assessed at the 6- and 12-month time points.

Assessment for ART eligibility was based on presence of documented CD4+ count and/or WHO clinical stage, and ART eligibility was determined based on prevailing national guidelines that largely reflected WHO recommendations at that point in time. For patients enrolling in care between 2005 and 2009, WHO 2006 guidelines were used.11 For patients enrolling between 2010 and 2011, 2010 WHO guidelines were used (see Table, Supplemental Digital Content, http://links.lww.com/QAI/A710).12Follow-up schedule for ART patients involved visits every 1–3 months and for pre-ART patients every 6–12 months as per country guidelines.

For the assessment at 3 months, patients were categorized into those initiating ART within 3 months of enrollment and those who had not yet initiated ART at 3 months. Those not yet initiating ART at 3 months were further categorized into being retained in pre-ART care, documented transfer out, LTF, and recorded death before ART initiation. At 6 and 12 months, additional categories were added to reflect outcomes after ART initiation, including retained on ART, LTF, and death after ART initiation.

Patients were categorized as retained in care if they were known to be alive and attending clinic with documented visits in the medical record. LTF was defined as no clinic visit for 6 months for ART patients and 12 months for pre-ART patients with no subsequent visit or documented transfer or death. Patients who met the definition of LTF were assigned date of LTF 15 days after their last recorded visit. Death and transfers were determined from medical records. Patients with documented transfer were censored at their recorded date of transfer.

**Statistical Analysis**

For the traditional HIV treatment cascade, the proportion of patients achieving each step in the cascade was calculated as a conditional proportion (with the number achieving the previous step as the denominator). Retention on ART 12 months after ART initiation was estimated using Kaplan–Meier survival analytic techniques, with patients transferring out censored at their recorded transfer date. In the comprehensive HIV care cascade, at each time point in follow-up, patients were categorized into the mutually exclusive categories described above. Tests for differences in achievement of steps in the treatment and comprehensive cascade between countries were performed using χ² tests.

**Ethical Considerations**

The Identifying Optimal Models Study was approved by each country’s ethics committee. The study was designated non-human subjects research by the Institutional Review Board at Columbia University Medical Center; the Center for Global Health at the US Centers for
Disease Control and Prevention determined the study to not involve engagement in human subject research.

RESULTS

Patient and Facility Characteristics

From January 2005 through June 2011, a total of 390,603 patients were newly enrolled in HIV care at 217 health facilities in Kenya, Mozambique, Rwanda, and Tanzania (Table 1). Most patients (52%) were enrolled in Mozambique, with 26% in Kenya, 14% in Tanzania, and 8% in Rwanda. Sixty-seven percent of patients were female, and the median age was 33 years (Interquartile range, IQR, 27–71). Median CD4+ count at enrollment in HIV care was 270 cells per microliter (IQR, 122–473), ranging from 218 cells per microliter (IQR, 89–414) in Kenya to 395 cells per microliter (215–613) in Rwanda. At enrollment in care, 20% had a CD4+ count ≤200 cells per microliter and 34% of patients had a WHO Stage III/VI. Documentation of CD4+ count or WHO staging at enrollment was missing for 193,270 (50%) and 98,873 (25%) of patients, respectively, with 58,474 (15%) of patients missing both enrollment CD4+ count and WHO staging. The proportion of patients missing both CD4+ count and a WHO Stage at enrollment ranged from 4.1% in Rwanda to 20.4% in Mozambique. The proportion missing both measures decreased over time across the entire cohort from 27% in 2005 to 10% in 2011. The median number of patients per facility was 5037 in Mozambique as compared with 474 in Kenya, 437 in Rwanda, and 458 in Tanzania. Of all facilities, 56% were primary-level care facilities and 48% were located in rural areas.

Outcomes Based on the Traditional HIV Treatment Cascade

Of the 390,603 patients enrolled in HIV care, 345,839 (89%) were assessed for ART eligibility at any point during their follow-up period (Fig. 1). Of those assessed for ART eligibility, 167,523 (48%) were eligible for ART per national guidelines and 117,525 (70%) of the latter initiated treatment. Of patients who initiated ART, 91,211 (78%) were retained at 12 months after ART initiation. This approach does not report outcomes for 273,078 patients (70% of all patients enrolled in care), which includes 44,764 patients (11% of all patients) who were not assessed for ART eligibility, 178,316 patients (46% of all patients) who were ART ineligible, and 49,998 patients (13% of all patients) who were ART eligible but did not initiate treatment.

Outcomes Based on the Comprehensive HIV Care Cascade

Using the comprehensive HIV care cascade approach, outcomes for all 390,603 patients enrolled in care were determined at 3, 6, and 12 months after enrollment in care.

Optimal Outcomes

Of the 390,603 patients enrolled in HIV care, 58%, 51%, and 49% achieved optimal outcomes at 3, 6, and 12 months after enrollment in care, respectively (Fig. 2A). Among the 227,134 patients (58% of all patients) who achieved optimal outcomes at 3 months, 118,698 (30%) were ART-ineligible patients who were retained in pre-ART care, 102,839 (26%) were patients initiating ART, and 5597 (1%) were patients who transferred care to another facility (Fig. 2B, Table S1, Supplemental Digital Content, http://
Among the 190,122 (49%) patients who achieved optimal outcomes at 12 months, 64,833 (17%) were ART-ineligible patients who were retained in pre-ART care, 19,039 (5%) were patients initiating ART, 86,300 (22%) were patients retained on ART, and 19,950 (5%) were patients who transferred.

Suboptimal Outcomes

The proportion of all patients enrolled in HIV care with suboptimal outcomes decreased from 22% at 3 months to 7% at 12 months after enrollment in HIV care. At 3 months, 50,352 patients with suboptimal outcomes (13% of the entire cohort) were ART eligible but had not yet initiated ART despite being retained in care and 33,911 (9%) were retained in care but had undocumented/indeterminate ART eligibility status (Fig. 2B, Table S1, Supplemental Digital Content, http://links.lww.com/QAI/A710). At 12 months, 18,376 (5%) patients were ART eligible but had not initiated ART and 10,149 (3%) were retained but had undocumented/indeterminate ART eligibility status.

Poor Outcomes

The proportion of patients with poor outcomes increased over time with 20% at 3 months, 37% at 6 months, and 44% at 12 months after enrollment. Most patients categorized with poor outcomes were pre-ART patients who were LTF, and the proportion of these patients increased over time from 74,226 (19%) of all enrolled patients at 3 months to 136,118 (35%) at 12 months. The proportion of patients with documented death was similar among pre-ART patients at 3, 6, and 12 months (1.3%, 1.6%, and 1.8%, respectively) and among ART patients at 6 and 12 months (1.1% and 1.6%, respectively) (Fig. 2B, see Table S1, Supplemental Digital Content, http://links.lww.com/QAI/A710).

Outcomes by Country Using Both Approaches

Examining outcomes by country using the HIV treatment cascade (Fig. 3), between 85% and 98% of patients who enrolled in care were assessed for ART eligibility ($\chi^2$, $P \leq 0.0001$ for difference between countries) and 67%–85% of ART-eligible patients initiated ART ($P \leq 0.0001$), with the largest proportion initiating ART in facilities in Rwanda. Retention among ART patients at 12 months after ART initiation ranged between 75% and 90% across countries, with the highest retention observed in Rwanda ($P \leq 0.0001$).

Using the comprehensive HIV care cascade, more striking differences emerge by country. Optimal outcomes differed substantially at 12 months by country ranging from 41% to 83% (Kenya 52%, Mozambique 41%, Rwanda 83%, and Tanzania 51%, $P \leq 0.0001$ for difference across countries) (Fig. 4). The smallest decrease in optimal outcomes over the 12-month period from enrollment was in Rwanda (4%) and the largest in Mozambique (12%). At 12 months, Rwanda had a high proportion (83%) of patients with optimal outcomes, with 3% with suboptimal outcomes and 14% with poor outcomes—the majority of the latter involved pre-ART patients who were lost to follow-up.
DISCUSSION

The comprehensive HIV care cascade is a valuable tool for monitoring HIV program performance as it provides additional and complementary information to that available in the traditional HIV treatment cascade approach. The key feature of the comprehensive HIV care cascade is inclusion of outcomes for all patients—both pre-ART and ART. In addition, the latter approach stratifies outcomes into 3 categories that reflect programmatic quality, that is, optimal, suboptimal, and poor outcomes, as well as measures these outcomes at specific time points from the date of enrollment in HIV care. Use of the traditional HIV treatment cascade approach to evaluate HIV program performance would not account for outcomes among 273,078 of the 390,603 patients (70%) enrolled in care who did not initiate ART.

The proposed comprehensive HIV care cascade demonstrated that nearly half (49%) of all patients enrolled in HIV care had optimal outcomes, and 56% of all patients were retained in care at 12 months after enrollment. In comparison, the traditional HIV treatment cascade demonstrated that 78% of all patients who initiated ART were retained in care at 12 months after initiation, a proportion comparable with that noted in other studies.13,14 The latter outcome, which may appear at first glance more favorable, is because of its focus on a subset of patients enrolled in care—those who initiate ART. Several studies have shown that pre-ART patients are at higher risk for LTF and death,15–18 and thus, it becomes critical to account for pre-ART patient outcomes to minimize poor outcomes for all patients enrolled in care.

An additional strength of the comprehensive HIV care cascade approach is that it accounts for patient outcomes over time using categories that reflect the quality of programs. In this analysis, optimal outcomes among pre-ART patients decreased over time, whereas poor outcomes (mainly LTFs) increased over time. Interestingly at 3 months follow-up, a similar proportion of pre-ART and ART patients (30% and 26%, respectively) had optimal outcomes, but by 12 months, 35% of all patients enrolled in care were pre-ART patients who were lost to follow-up—the largest subset of the entire cohort. This underscores the importance of designing retention interventions to be implemented early after enrollment in care for patients not eligible for ART at that point in time.

Patients with suboptimal outcomes offer a ready opportunity for interventions that could have favorable impact on program performance as these patients are still retained in care but may not have received appropriate medical care. For example, over time, the proportion of patients with undocumented ART eligibility assessment decreased, which could be further improved. HIV programs can prioritize initiating ART among eligible patients who have yet to start treatment. Delays in treatment initiation for ART-eligible patients have been shown to be associated with increase in mortality19 and a reduced likelihood of restoring CD4+ counts.20 Identifying and addressing the reasons for failure to initiate ART among eligible patients could potentially shift a substantial number of individuals from suboptimal to optimal outcome category. Appropriate interventions may include providing additional provider training on the importance of prompt ART initiation, counseling reluctant patients regarding the importance of ART for their health and well-being, and addressing their concerns about potential side effects associated with ART use.
LTF was the main reason for poor outcomes in this cohort of patients, with greater LTF among pre-ART patients as compared with ART patients. However, it is important to note that patients categorized as LTF may represent a diverse group that includes those who have died or transferred to another health facility, but without documentation of either of these outcomes in their medical records, as well as those that have disengaged from care. Our findings demonstrate that HIV programs need to introduce interventions to reduce the high rates of LTF, particularly among pre-ART patients as indicated above. Retaining such individuals in care is critical so that they can be regularly monitored for their own health, for determination of ART eligibility, and to provide them with other interventions such as regular screening for tuberculosis, provision of co-trimoxazole and isoniazid prophylaxes, as appropriate, risk reduction counseling, and other supportive services.

The comprehensive HIV care cascade also provides a more nuanced assessment of program performance across countries allowing for south-to-south learning and focused quality improvement activities. A stark difference was noted across countries in terms of proportion of patients with optimal outcomes, ranging from 41% to 83% based on findings from the analyses per the comprehensive HIV care cascade, largely because of differences in outcomes for pre-ART patients. The magnitude of difference would not have been appreciated if assessment was solely based on the use of the traditional HIV treatment cascade, which reported between 75% and 90% of patients initiated on ART retained at 12 months after ART initiation across the 4 countries. One reason for the larger differences noted between countries in outcomes when using the comprehensive HIV care cascade is that a much smaller proportion (35%) of patients enrolled in HIV care in Rwanda were ART eligible as compared with Kenya (46%), Mozambique (52%), and Tanzania (53%). As studies have demonstrated superior retention for patients on ART as compared with pre-ART, the focus on retention of patients on ART can mask substantial differences in overall program performance. Another potential explanation for the differences noted across countries may be patient age as fewer younger patients (15–24 years) were enrolled in care in Rwanda compared with Mozambique. Studies have reported lower retention rates in younger individuals. Finally, the larger number of patients followed by a health facility has been associated with inferior retention rates. In our study, the median number of patients per facility in Mozambique was significantly higher as compared with facilities in the other 3 countries, which may have contributed to higher LTF in that country. It is possible that countries may have provided different pre-ART packages of care; some more attractive to patients. Regardless of the reason(s), the high proportion of patients with optimal outcomes observed from the data from Rwanda is consistent with findings from other studies.

It is also important to note that the comprehensive HIV care cascade remains relevant as guidelines change and ART eligibility expands. For example, many countries are adopting the WHO 2013 guidelines, which recommend ART initiation for persons with CD4+ count <500 cells per microliter. In these settings, the proportion of pre-ART patients are likely to decrease over time; however, the recommended categories, that is, optimal, suboptimal, and poor outcomes, remain relevant and important in accounting for outcomes for all patients enrolled in care. Similarly, if treatment is expanded to include all HIV-infected patients, some patients will continue to be eligible for treatment but not initiated (a suboptimal outcome), or eligible for treatment but died before treatment start (a poor outcome). Also,
for countries where viral load monitoring becomes available, the comprehensive HIV care cascade can be adapted to include viral load suppression as the most distal outcome of interest.

The analysis has several strengths. The study includes a large cohort of adult patients enrolled in HIV care from sub-Saharan Africa from various types of health facilities and from diverse countries. The study used programmatic data allowing for generalizability of the findings. A limitation of the analysis is the issue of missing data, particularly of CD4+ count and WHO staging for ART eligibility determination, which is implicit in using routinely collected program data often using paper-based medical records. However, it is important to note that the comprehensive HIV care cascade includes outcomes for all patients including those with missing data.

CONCLUSIONS

In conclusion, the comprehensive HIV care cascade we describe offers additional and complementary information to the traditional HIV treatment cascade for assessing HIV program quality. The comprehensive approach accounts for all patients enrolled in HIV care irrespective of ART eligibility and/or treatment status, uses specific time frames from enrollment for measuring outcomes, and uses quality of care parameters for categorizing outcomes. Such an approach can be a better differentiator between programs with pre-ART patients regarding overall performance and can serve as a monitoring tool to identify gaps in service models and offer opportunities for specific interventions to improve outcomes. This approach has the potential to enhance quality and enable achievement of the full potential of the global HIV program scale-up.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References


FIGURE 1.
HIV treatment cascade (N = 390,603 adults at 217 facilities in Kenya, Mozambique, Rwanda, and Tanzania from January 2005 to June 2011).
FIGURE 2.
A, Comprehensive HIV care cascade with outcome categories, and (B) comprehensive HIV care cascade with subgroups within outcome categories (N = 390,603 adults at 217 facilities in Kenya, Mozambique, Rwanda, and Tanzania from January 2005 to June 2011).
FIGURE 3.
HIV treatment cascade by country program (N = 390,603 adults at 217 facilities in Kenya, Mozambique, Rwanda, and Tanzania from January 2005 to June 2011).
FIGURE 4.
Comprehensive HIV care cascade by county program (Kenya N = 101,938 patients at 85 facilities, Mozambique N = 201,503 patients at 34 facilities, Rwanda N = 32,105 patients at 41 facilities, and Tanzania N = 55,057 patients at 57 facilities).
TABLE 1

Patient and Facility Characteristics

<table>
<thead>
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<th></th>
<th>Overall</th>
<th>Kenya</th>
<th>Mozambique</th>
<th>Rwanda</th>
<th>Tanzania</th>
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<tr>
<td></td>
<td>N (%)</td>
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<td>Total</td>
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<td>101,938</td>
<td>201,503</td>
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<td>70,307</td>
<td>134,695</td>
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<td>Age, yrs</td>
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<td>Median (IQR)</td>
<td>33 (27.0–41.0)</td>
<td>35.0 (28.5–42.5)</td>
<td>31.0 (25.0–40.0)</td>
<td>34.1 (27.7–41.7)</td>
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<td>15–24</td>
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<td>42,769 (77.7)</td>
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<td>17,414 (8.6)</td>
<td>2890 (9.0)</td>
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<td>Median (IQR)</td>
<td>270 (122–473)</td>
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<td>266 (125–457)</td>
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<td>≤50</td>
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<td>102,771 (51.0)</td>
<td>4539 (14.1)</td>
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<td>WHO stage at enrollment</td>
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<td>4856 (15.1)</td>
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<td>70,700 (18.1)</td>
<td>18,461 (18.1)</td>
<td>35,081 (17.4)</td>
<td>5026 (15.7)</td>
<td>12,132 (22.0)</td>
</tr>
</tbody>
</table>
Overall | Kenya | Mozambique | Rwanda | Tanzania
--- | --- | --- | --- | ---
2010 | 67,155 (17.2) | 17,060 (16.7) | 34,448 (17.1) | 4090 (12.7) | 11,557 (21.0)
2011 | 21,860 (5.6) | 4557 (4.5) | 12,142 (6.0) | 36 (0.1) | 5125 (9.3)

Facility-level characteristics

<table>
<thead>
<tr>
<th>Facility type</th>
<th>Overall</th>
<th>Kenya</th>
<th>Mozambique</th>
<th>Rwanda</th>
<th>Tanzania</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. facilities</td>
<td>217 (100)</td>
<td>85 (39.2)</td>
<td>34 (15.7)</td>
<td>41 (18.9)</td>
<td>57 (26.0)</td>
</tr>
<tr>
<td>Facility type</td>
<td>Primary</td>
<td>Secondary/tertiary</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. facilities</td>
<td>122 (56.2)</td>
<td>95 (43.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Facility location</td>
<td>Urban</td>
<td>Semiurban</td>
<td>Rural</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. facilities</td>
<td>40 (18.4)</td>
<td>72 (33.2)</td>
<td>105 (48.4)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>