The 2004 International Conference on Improving Use of Medicines highlighted the urgent need to develop strategies to improve adherence to antiretroviral treatment (ART) (www.icium.org). Accepted wisdom is that if the ART adherence rate is less than 90–95%, treatment can fail, and the virus may become resistant. A review of adherence studies for chronic illnesses found that achieving adherence rates above 80% is difficult, even in resource-rich countries. Therefore, the ability to accurately monitor adherence rates for ART and immediately address problems is crucial.

Although many countries are scaling-up ART programmes, no one has developed any practical approaches to monitor treatment adherence programatically. The International Network for the Rational Use of Drugs Initiative on Adherence to Antiretroviral Therapy (INRUD–IAA) is taking on the challenge. INRUD, comprising 25 member groups, was established in 1989 to design, test and disseminate effective strategies to improve the way medicines are prescribed, dispensed and used, especially in resource-poor countries.

In 2006, national AIDS control programmes and INRUD groups carried out surveys in Ethiopia, Kenya, Rwanda, Uganda and the United Republic of Tanzania to assess how ART programmes were tracking patient adherence and treatment defaulting. Findings showed that programmes defined treatment adherence and patient defaulting differently – the surveys identified 14 different definitions of defaulting, ranging from missing an appointment by one day to six months. As a result, reliable comparisons were impossible. Yet, although data collection and measurement were haphazard, clinics and pharmacies were recording much useful information.

Developing indicators through collaboration

Representatives from the INRUD groups and AIDS control programmes that had coordinated the survey and technical staff from Management Sciences for Health, WHO’s Department of Technical Cooperation for Essential Drugs and Traditional Medicine, the Karolinska Institutet, and Harvard Medical School gathered in Entebbe in April 2006 to discuss the survey findings. The participants agreed on the need to standardize definitions of adherence and defaulting and define practical measurement methods. Standard indicators could help identify patients at risk, monitor facility and programme performance, and track changes. A measurement methodology would need to be practical, affordable and reproducible in any setting and provide reliable results.

Participants drafted core indicators to measure treatment adherence and defaulting. They also suggested complementary indicators to address causes of good and bad adherence.

The set of core indicators and their data sources are:

- Self-reported doses of antiretroviral (ARV) medicine missed over a recent period (interviews or clinical records).
- Number of days that ARV medicines were dispensed over the last six months or a year (pharmacy records).
- Patient attendance at appointments and the number of...
days until reappearance following a missed appointment (clinic appointment logs).

- Pill counts at each patient's clinic visit compared to their expected pill consumption (clinical or pharmacy records).

**Self report-based adherence measures**

A clinician or pharmacist can easily collect data for this indicator by asking patients whether they have missed any doses of pills in a number of days, and if so, how many. Using clinical records to measure this indicator is possible only if the question has been asked consistently and recorded routinely. In practice, clinicians or pharmacists may have asked patients about their adherence but not recorded the answer. Also, the recall period may have ranged from their adherence yesterday to that since the last clinic visit.

Three indicators could be measured using self-reporting:

- Percentage of patients with full adherence to ART (i.e., no doses missed in the recall period, which is 3 days in the INRUD–IAA methodology).

- Percentage of ARV doses patients took during the recall period.

- Percentage of patients with more than 95% adherence to ARV treatment (i.e., missed no more than 1 dose in 20, which for periods shorter than 3 days, is equivalent to full adherence).

**Dispensing-based adherence measures**

Pharmacy dispensing records are useful to measure longer-term adherence patterns. By counting the number of days that medication is dispensed over a period, three other adherence indicators can be calculated: long-term adherence in ARV use, the achievement of long-term adherence targets, and the rate of discontinuing ARVs. Typically, this methodology is based on abstracting computer databases, such as those from health insurance companies. The INRUD–IAA project tested the feasibility of sampling written records.

The dispensing-based adherence measures are defined as:

- Average percentage of days a sample of patients received ARVs for a defined period, such as 6 months (180 days) (e.g., patients at a facility receive ARVs an average of 162/180 days – or 90% of days).

- Percentage of sampled patients who received ARVs for a target percentage of days in a defined period (e.g., 90% of patients receive ARVs for at least the 95% target over 6 months – 171/180 days).
Percentage of patients who experienced a gap in ARV availability of more than 30 days in a row during a defined period.

Using dispensing data may overestimate true adherence – the patient may have received the medicine, but did not consume it correctly. However, if the patient never received the medicine, then they cannot adhere to treatment; for example, if the patient was dispensed medicine for 145 out of 184 treatment days, then the patient’s maximum adherence rate could only be 79%.

Pill count-based adherence measures

Pill counts are used by some ART programmes to compare a patient’s actual and expected consumption since the pharmacy last dispensed the medicine. If records include pill counts, the data can be used to calculate the pill count adherence measures.

Patient attendance-based defaulting measures

A missed appointment should trigger programme action to reach out to patients at risk of defaulting on their treatment; however, because the patient may have had extra days of medicine, attendance failure within three days of an appointment can also be a trigger point. Finally, the programme’s failure to re-establish contact with patients within 30 days of a missed appointment indicates the level of treatment defaulting.

The three performance indicators related to defaulting could be:

- Percentage of patients who do not appear for their appointments on the scheduled day.
- Percentage of patients who miss their original appointment, but come within 3 days of the missed appointment.
- Percentage of patients who miss their appointment and who do not reappear at the clinic within 30 days of the missed appointment.

Complementary indicators

Complementary indicators can help identify why patients have problems adhering to treatment; for example, staff with high average workloads may not have the time to adequately counsel patients. Data for these indicators can be collected at the same time as data for the core indicators.

Complementary indicators and their data sources include:

- Average staff workloads (for example, patients per hour);
- Percentage availability and stock-outs of key ART-related medicines (interviews and record review).
- Percentage of prescribed medicines that were dispensed;
- Percentage of patients who know how to take their medicine;
- Percentage of medicines properly packaged and labelled;
- Clinical or functional status, such as whether they are able to carry out normal activity (patient exit interviews).
- Age; gender; tuberculosis status;
- WHO disease stage at initiation of ARVs;
- CD4 count or viral load at treatment initiation and in the last 6 months (clinical or pharmacy records).

Field testing methods

Ethiopia, Kenya, Rwanda and Uganda tested the feasibility and reliability of collecting the adherence indicators between October 2006 and June 2007. The results of the surveys are published elsewhere.

The sampling strategy included 20 health facilities with at least 100 patients on ARVs chosen randomly in each country. Data collectors were practicing pharmacists, doctors, or senior-level students. Teams of three, four or five data collectors surveyed a
single facility in one day and entered the day’s data in the evening.

In each facility, data collectors randomly sampled medical and pharmacy records and interviewed 30 patients as they exited the clinic. In the first two field tests (Kenya and Rwanda), data collectors selected two retrospective cohorts each comprising 100 patient records. The first cohort included patients who had attended the clinic during the month one year before (Kenya) or six months before (Rwanda). Data collectors examined the pharmacy records to see how many days of medicine had been dispensed over the period. The second cohort was used to track patients from the previous three months to see when and if they showed up for their next appointment. 

Results and discussion

Self-reported adherence in exit interviews

Interviewers carried out 1,631 interviews in the four countries, averaging 20 per facility. Some facilities in each country were surveyed on days with few patient appointments. Therefore, confirming the number of patients expected on the day of the survey is very important in planning. In nearly all facilities, most patients claimed full adherence over the last 3 days – however, some did not. These individuals are most at risk of poor adherence, which is best captured by this indicator:

- Percentage of patients who claimed full adherence to ART over the last 3 days.

Consistently using a standard question to assess individual patients’ recent adherence can rapidly identify patients who need counselling. On a larger scale, this information can help a programme manager focus on facilities having problems maintaining high levels of treatment adherence.

Dispensing-based adherence measures

In almost all facilities it was possible to assess the number of days of ART dispensed over the last 6 months. More than 6,500 records showed that it was possible to calculate:

- Percentage of days that a sample of patients received medicines over the last six months.

- Percentage of patients with gaps in treatment of more than 30 days over the last six months.

Monitoring data on long-term adherence could be a useful tool to identify patients with adherence problems. Aggregate data would help a programme manager identify facilities with problems in drug supply, dispensing, or patient adherence in addition to highlighting facilities that are performing well. The data would also be useful for monitoring facility performance over time. Clinics with computerized dispensing systems would find this monitoring particularly easy.

Defaulting

Almost all facilities recorded the dates of attendance and next appointment, so that calculating the two attendance indicators was nearly always possible:

- Percentage of patients who arrived on or before the day of their next appointment.

- Percentage of patients who arrived within 3 days of their appointment.

A standard approach for identifying patients who miss appointments can help programmes develop community outreach systems.
addition, the information would allow a programme manager to help facilities with a patient attendance problem identify causes and appropriate interventions.

Usefulness of pill counts and self-report in clinic notes

Overall, only 15% of 6,551 patient records included a pill count; therefore, calculating adherence measures based on pill counts in medical and pharmacy records does not appear to be widely applicable.

More records included a self-report adherence measure (45% overall), although this measure was infrequently recorded in Rwanda (10%). However, the methods used to derive these self-report measures varied, which makes comparisons problematic. In Ethiopia, for example, the method of recording self-reported adherence was to use a “G” to indicate better than 95% adherence (good) or an “F” (fair) or a “P” (poor) for less than 95%. Of the 83% of records that included a self-report measure, 96% were rated “good.”

Conclusion

The INRUD–IAA field tests examined four categories of indicators for adherence to antiretroviral medicines and treatment defaulting: 1) self-reported adherence from exit interviews, 2) days supplied by medicine, 3) patient attendance, and 4) pill counts and self-reports in clinic records. The first three methods offer feasible approaches to standardizing measures of adherence and defaulting in low-resource settings. Pill counts are used too infrequently; whereas, self-reports in clinic records appear more promising. However, the consistency of the data-gathering methods needs to be assessed.

The four field tests provided excellent evidence that these indicators can be measured in resource-poor settings. Managers will be able to examine the causes of poor performance in certain facilities and work with them to make improvements – for example, by promoting both community involvement and individual patient ownership and responsibility, which proved successful in a South African township. Facilities that are doing well can also share lessons on how to achieve exceptional performance. However, only by monitoring adherence and defaulting can we know where and what kind of interventions are needed.

The INRUD–IAA has now validated these core adherence indicators against clinical outcomes so they can identify facilities needing attention. It is developing a manual with supporting software that describes the recommended indicators, data collection methodology, and analyses, similar to WHO’s How to investigate drug use in health facilities. WHO will also publish this adherence indicator package when it has been field tested. Finally, the participating countries are using qualitative methods to investigate the reasons for good and poor adherence at both patient and facility level as a step towards developing appropriate strategies for improvement.

References

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