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Editorial

Monitoring treatment outcomes in patients with chronic disease: lessons from tuberculosis and HIV/AIDS care and treatment programmes

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There are two types of chronic disease. First, there is the chronic disease that can be cured after a period of several months or several years, tuberculosis being the classical prototype with drug-sensitive disease requiring 6 months of antituberculosis treatment and drug-resistant disease requiring treatment for up to 2 years. In tuberculosis, although cure is defined programmatically and is based on patients completing treatment with negative bacteriology [1], many patients may be left chronically disabled with residual symptomatic lung damage. Second, there is the chronic disease that cannot be cured and requires lifelong indefinite treatment, examples being HIV/AIDS and non-communicable diseases such as diabetes mellitus, chronic obstructive airways disease and cardiovascular disease.

Ever since the 'DOTS TB Strategy Framework' was launched in 1994 [2], tuberculosis control programmes all over the world have monitored, recorded and reported on the treatment outcomes of patients registered for treatment. At the district, provincial and national level, the reporting is done quarterly – there is the 'quarterly cohort report of case finding' recording all patients registered within a specific geographic area, stratified by type and category of disease, and 12 months later there is the 'quarterly cohort report of treatment outcomes' recording what has happened to each of these patients according to well-established, standardised definitions (Table 1) [1]. For each patient, the outcomes are mutually exclusive with the convention that the first reported outcome takes precedence – for example, if a patient is classified as failure and then dies 2 days later, the reported outcome is 'failure'. The recording and reporting of these outcomes is of crucial importance programmatically because it provides a way to assess performance at local and national levels. It also helps to assess impact of co-morbid disease such as HIV/AIDS which in the 1980s and 1990s resulted in increasing TB case fatality in affected countries [3]. Each year, these data are collated into 12-month cohort reports at the country level and sent to the Global TB Programme of the World Health Organization to feature in the Global Tuberculosis Report [4].

Chronic disease, communicable or non-communicable, that requires lifelong treatment has to be reported differently as patients cannot be cured. For example, in patients with HIV/AIDS, treatment is for life with first-line, second-line or third-line antiretroviral treatment (ART). In Malawi, health workers at ART facilities record and report site-specific data, and these are then collated into national data. The two essential pieces of information are how many new patients are being initiated and registered for ART each quarter and how many cumulatively are retained alive and on therapy, stratified by type of ART regimen. For the treatment outcome parameter, the process is as follows. New registrations are added quarterly to all previous registrations, giving the total number of patients ever registered on ART. At the end of each quarter, each patient has his/her outcome status censored – who is alive and on ART, dead, lost to

Table 1 Standardised treatment outcomes in patients with smear-positive tuberculosis

Outcome	Definition	Comment
Cure	Patient who is smear snegative in the last month of treatment and on at least one previous occasion	Each patient has one mutually exclusive treatment outcome given at the end of the treatment regimen – which is 6 months for those with new presumed drug-susceptible disease.
Treatment completed*	Patient who has completed treatment but who does not meet the criteria to be classified as a cure or a failure	Dates of adverse outcomes such as died or lost to follow-up are useful but not essential to record at the programme level
Treatment failure	Patient who is sputum smear positive at 5 months or later during treatment†	Once a patient is cured or has completed treatment, he/she no longer has tuberculosis
Died	Patient who dies for any reason during the course of treatment	
Lost to follow-up (defaulted)	Patient whose treatment was interrupted for two consecutive months or more	
Transfer out	Patient who has been transferred to another recording and reporting unit and for whom the treatment outcome is not known	

*Treatment success is defined as the sum of patients cured and those who have completed treatment.
†Also a patient who was initially smear-negative before starting treatment and became smear-positive after completing the initial phase of treatment.
Adapted from reference [1].

follow-up, stopped ART on their own volition or transferred out (Table 2) [5]. Each outcome, as in the case with tuberculosis, is mutually exclusive. However, for an individual patient, the outcome can change from one quarter to another – a patient may stop treatment because of unacceptable side effects only to restart 6 months later because of disease progression. The date of any adverse outcome (died, stopped, lost to follow-up) is recorded as this enables group cohort survival analysis to be carried out. Of those alive and on ART, patients are further stratified by what ART regimen they are taking, and other parameters may be added such as medication adherence or side effects.

Treatment outcomes for those on ART provide strategic information of crucial importance. The end of every quarter allows a snapshot of the programme at both local clinic and national levels. For example, by 31 December 2013, 672 142 patients had ever been registered for ART in Malawi of whom 472 865 were alive and retained in care with precise numbers known for loss to follow-up, death and those who had stopped therapy [6]. These quarterly data collected over a decade allow the country to review the progressive scale-up of those alive and on ART and see where these patients are being treated (hospital, urban health centre, rural health centre, private clinic): reliable patient data at all levels are necessary for forecasting drug and commodity procurement, human

Table 2 Standardised treatment outcomes in HIV-infected patients on antiretroviral therapy (ART)

Outcome	Definition	Comment
Alive and on treatment	Patient who has attended an ART clinic at least once in the quarter (i.e. 3 months)	Patients alive and on treatment are further stratified by type of ART regimen and other parameters
Died	Patient who dies for any reason while on or off treatment	Each patient has one mutually exclusive treatment outcome given at the end of each quarter – patients can change outcomes from one quarter to the next
Lost-to-follow-up (defaulted)	Patient who has not returned to the clinic and is *not* known to have transferred out, stopped ART or died. This outcome applies at 2 months after the patient is expected to have run out of antiretroviral drugs	Recording the date of each adverse outcome is essential at the programme level to do group cohort survival analysis
Stopped ART	Patient who was last known to be alive and is known to have stopped taking ART regardless of reason and length of time	For national reports, transfers between clinics are removed from the cumulative registered denominator to avoid double counting of patients
Transfer out	Patient who has been transferred to another recording and reporting unit	

ART, antiretroviral therapy.
Adapted from reference [5].

resource needs and the logistics required to keep the programme on track. Treatment outcome data also allow performance to be tracked over time; for example, is the program improving each quarter with lowering its early death rates and are the most recent cohorts doing better than the earlier cohorts registered 5–10 years ago?

A similar cohort analysis approach has been used for monitoring outcomes and obtaining strategic clinic and programmatic information for patients with chronic non-communicable disease such as diabetes mellitus and hypertension, and this in turn allows performance to be assessed and potentially improved [7, 8].

Patients who transfer from one registration facility to another require special mention. For example, in national tuberculosis programmes throughout the world, patients who transfer out from their original registration facility then transfer in to the new facility to continue treatment. Their status in the new facility is recorded as 'transfer in', but they are not included in the new facility's cohort. The new facility, however, has to follow up the patient and report to the original registration facility on the patient's outcome. If the outcome is cured, failed or died, for example, this is recorded and reported in the original TB patient register. If, however, the outcome is not known and the patient has been lost to follow-up, then this information is passed to the original registration facility and the patient is recorded as 'transferred out' (Table 1). The original registration facility thus takes on the responsibility for its full cohort of patients and reports accordingly on treatment outcomes.

This is different in the ART programme. When a patient transfers from one registration facility to another, the new facility registers the patient as a 'transfer in' and takes responsibility for the long-term follow-up of this patient, reporting on the treatment outcomes each quarter. This approach works well for each ART facility, but becomes problematic when the facility data are collated for national reporting as those transferred out and transferred in are double counted. In the national reports, therefore, patients who transfer between facilities are therefore counted and removed from the denominator of patients ever registered at facilities around the country, and it is from this amended denominator that quarterly treatment outcomes are ascertained.

Most tuberculosis and HIV/AIDS programmes in low-resource settings use paper-based treatment cards and patient registers. For tuberculosis programmes, paper-based systems remain an adequate monitoring tool – the cohorts of patients are not huge, they remain similar in size from one quarter to the next, and patients close out on treatment 6–9 months after registration. The monitoring and reporting tasks are manageable, although WHO has called on national TB programmes to implement electronic recording and reporting which can allow for real-time and potentially better patient care monitoring [9]. Chronic lifelong disease is completely different. Every quarter, the treatment cards of all patients who have ever been registered in a facility have to be assessed to see who is alive, dead, lost to follow-up and stopped treatment, and with the current human resource shortages throughout most of Africa, this growing burden of work is neither manageable nor sustainable, especially as numbers continue to increase. Many facilities in a country like Malawi have several thousand patients registered for ART, and wading through paper systems to monitor and count treatment outcomes takes time and detracts from patient care. In this situation, electronic medical record systems have to be the solution, even in low-resource settings. In Malawi, for example, the need for this was appreciated 10 years ago, and a simple, inexpensive, real-time, point-of-care, touch screen electronic system for monitoring ART was developed and scaled up [10]. By 31 December 2013, more than 393 000 HIV-infected patients had been registered on ART at 46 government clinics in the country using the electronic medical record system described above.

The same approach to monitoring treatment outcomes through electronic medical record systems has been used for patients with diabetes mellitus and hypertension in Malawi and Jordan at the health facility level and is working well [7, 8, 11]. Valuable strategic information is being collected and, as described earlier, is being used to evaluate facility-based programme outcomes, clinic performance and cohort survival over time. As the world community begins to negotiate and formulate the sustainable development goals (SDG) for the post-2015 era, convincing arguments are being made for having a concise, measurable and attainable target for the one health goal (SDG3) focused on reductions in premature mortality from communicable (tuberculosis, HIV/AIDS and malaria) and chronic non-communicable diseases [12]. While we continue to push for the currently non-existent vital registration systems of births, deaths and causes of death in many low- and middle-income countries to provide the necessary metrics, a proper tracking of treatment outcomes for chronic disease will be an additional critical component to measure progress over the next 15 years.

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