

Discussion

Progress towards the Millennium Development Goals

Within the framework of the United Nations MDGs, TB control is guided by five principal indicators, two that quantify DOTS implementation (case detection, treatment success) and three that could measure the impact of DOTS on the epidemic (incidence, prevalence, mortality). The MDG framework is a stimulus to think beyond the 2005 targets for DOTS implementation, and to consider the benefits of TB control up to and beyond 2015. Long-term thinking underpins sustainable TB control, and is vital for planning the trajectory towards TB elimination.

This is the first in this series of annual reports to evaluate changes in incidence, prevalence and deaths from 1990, the MDG reference year, through to 2003. Based primarily on trends in case notifications, the TB incidence rate was, by 2003, falling or stable in seven out of the nine regions of the world defined in Figure 6. Incidence rates in eastern Europe (mostly countries of the former Soviet Union) and Africa (countries with low and high HIV rates) increased during the 1990s, but appear to have peaked in Europe around 2001, and have since fallen. There is no persuasive method of predicting when peak incidence rates will be reached, and at what levels, in Africa, but the rates of increase slowed markedly during the 1990s.

Because these adverse regional effects are diminishing, the rate of increase in global incidence is also slowing, after growing most rapidly in the mid 1990s. The global incidence rate reached 140 per 100 000 population in 2003 (8.8 million new cases, including those who are HIV-positive), but was still increasing at 1.0% annually. This assessment is, however, dependent on the assumptions we have made about trends in HBCs. For example, the series of case notifications for India suggest that the incidence rate is falling, but the preferred assumption, until further evidence be-

comes available, is that incidence is stable (this is conservative with respect to case detection and the impact of DOTS). If the incidence rate is actually falling in India at 2.4% per year, as indicated by case notifications in 1992–2003, then the global incidence rate would also be falling, albeit slowly.

The trend in global TB incidence has been little affected, so far, by DOTS programmes. Chemotherapy is more likely to have reduced TB prevalence and deaths, but neither of these indicators is measured routinely in HBCs. The calculations presented here, which are derived from estimates of incidence, duration and case fatality, suggest that the global prevalence rate fell from 309 to 245 per 100 000 between 1990 and 2003 (including HIV-positive TB patients), and was falling at 5% per year in 2003. The TB death rate (including deaths among HIV-positive TB patients) was also falling in 2003, but more slowly at 2.5% per year. Prevalence and deaths, like incidence, have been rising in Africa, and most steeply in African countries with the highest rates of HIV infection. In our assessment, incidence, prevalence and death rates are falling or stable in five out of the six WHO regions, and in seven of the nine regions of the world shown in Figure 6.

Treatment success in the 2002 cohort was reported to be 82% of 1.4 million registered cases, close to the 85% target, but no higher than in the previous two annual cohorts. The overall rate of treatment success is strongly influenced by data from the three countries that have the largest numbers of new cases annually – China, India and Indonesia. All three submitted data indicating that the 85% target had been exceeded in 2002. These are impressive results, achieved while treating hundreds of thousands of patients, but success rates reported to be higher than 90% (e.g. China) need to be kept under review.

Of greater concern are the low cure

rates in the European Region and the African Region in 2002. The European Region reported the highest rate of treatment failure, probably linked to the high levels of drug resistance in countries of the former Soviet Union. It also reported the second highest death rate on treatment, which is likely to be associated both with drug resistance and with the high proportion of elderly patients in Western Europe. The African Region reported the highest death rates in TB patients, undoubtedly associated with HIV coinfection. But the success rate of African DOTS programmes was also low because they lost 19% of patients through default, transfer between treatment centres or by failing to record any outcome of treatment (patients “not evaluated”). Such losses to follow-up were also high in the Region of the Americas, Eastern Mediterranean Region and European Region.

The target for treatment success under DOTS refers only to new smear-positive cases, but information about patients presenting for re-treatment, including the outcomes of treatment for these patients, is also indicative of programme performance. The WHO data collection form for the 2002 cohort asked DOTS programmes to distinguish between re-treatment after relapse, default and failure, both for cases reported in 2003 and for patients undergoing re-treatment during 2002. Although it is probable that the case definitions (Table 2) are not strictly observed (and many re-treated patients were not classified in data submitted to WHO), some of the findings deserve comment. First, the comparative success of treatment for different classes of patients was consistent with expectations: lower on average for re-treated than for new cases; and among re-treated patients, higher for relapses, intermediate for defaulters and lowest for failures. Moreover, patients who defaulted during their first course of treatment tended to default from a second or subsequent course of treatment.

Third, the regional distribution of adverse re-treatment outcomes resembled the pattern observed for new cases: African countries reported high death rates and many patients were lost to follow-up; European countries reported high rates of death and treatment failure. The accuracy of reporting needs to be verified, but these data should help to identify TB patients who, for example, are less likely to comply with treatment (persistent defaulters) and those who are more likely to be infected with HIV (especially in Africa), or who are carrying drug-resistant bacilli (especially in eastern Europe).

Although DOTS programmes have diagnosed and treated more than 17 million cases since 1995, the global DOTS case detection rate was still only 45% in 2003, well below the 70% target. However, the detection rate increased by 8% between 2002 and 2003, faster than at any time since recording began in 1995. If detection continues to increase at this rate, the estimated global case detection rate will be approximately 60% by 2005.

While the acceleration in case-finding during 2003 exceeded expectations, most of the additional patients (63%) were reported by just two countries: China and India. If this pace of expansion is to be maintained or accelerated, other HBCs must contribute more. Approximately 1.8 million smear-positive cases were notified by DOTS programmes in 2003. According to our estimates, another 1.4 million new patients, undetected by DOTS programmes in 2003, were living in just eight HBCs, including China and India. Together, these 3.2 million patients account for more than 70% of new cases arising in 2003. Therefore, intensive case-finding in these countries would contribute greatly to meeting the global target of 70% case detection.

In some regions of the world, large numbers of patients are reported from outside DOTS areas. The 70% target could be reached in the Region of the Americas by ensuring that more than 43 000 smear-positive patients currently reported by non-DOTS programmes are diagnosed and treated under DOTS, the majority in Brazil. In

the European Region, the Russian Federation reported more than 100 000 patients from the 75% of the country not yet covered by DOTS, 23 000 of which were new smear-positive patients. China and India reported an additional 70 000 new smear-positive patients from non-DOTS areas in 2003.

By contrast, DOTS programmes in other HBCs including Bangladesh, Ethiopia, Indonesia, Nigeria and Pakistan will have to recruit patients that are not yet seen and reported by public health surveillance systems. These unreported patients undoubtedly exist because they are found, for example, during population-based prevalence surveys. Some never receive TB treatment; some are treated in public and private clinics and hospitals that are not linked to ministries of health. To ensure that these patients have access to DOTS services, TB control programmes will need to embark on new activities and establish new collaborations, many of which will be specific to the structure of local health services.

Considering both of the targets for DOTS implementation, Viet Nam was still the only member of the current group of HBCs to have reached 70% case detection and 85% treatment success by 2003. However, Cambodia, Myanmar and the Philippines were all close to achieving the targets. Although these Asian countries have different problems to solve, they should, with China and India, be able to meet the targets by 2005.

Smear-positive patients are the focus of the DOTS strategy, but many DOTS programmes also routinely treat smear-negative patients, with pulmonary or extrapulmonary disease. For the countries that report smear-negative patients, the numbers may be less accurate than for smear-positive disease because diagnosis is more difficult. In this context, the remarkable differences between regions in the proportions of patients reported with extrapulmonary disease need further investigation. The exceptionally high extrapulmonary case-load in the Eastern Mediterranean Region (20–30%) might be due to over-diagnosis, but it might also be a real and unex-

plained epidemiological phenomenon.

The establishment of the MDGs presents a challenge, not just for the implementation of DOTS and other means of TB control, but also for the measurement of epidemiological impact. Ideally, all countries would count new cases and deaths via a comprehensive routine system of surveillance and vital registration, and estimate the prevalence of disease and infection by population-based surveys. In reality, countries will have to select some methods of measurement in preference to others. Some guidance on the advantages and disadvantages of different epidemiological measurements is given in Table 21.

Planning and DOTS implementation

All HBCs have a strategic plan for DOTS expansion and, during 2005, many will begin a new planning cycle for the next five years. However, the transition from planning to implementation, and then to the improvement of coverage, case detection and treatment success has been slower than anticipated in several countries. The success of some NTPs in raising funds for TB control (and particularly from the GFATM) has not been followed by productive spending.

Among the obstacles to DOTS expansion, five are of overriding importance: shortages of trained staff, lack of political commitment, weak laboratory services, and the inadequate management of MDR-TB and of TB in people infected with HIV.

The acute shortage of adequately trained staff affects the distribution and quality of services. This workforce crisis is felt particularly in the under-performance of central management, and through failings in the laboratory network. To remedy the problem, the HBCs need, at the very least, strong and clear policies for recruiting, retaining and motivating staff. One way to secure political commitment to solve this and other problems is by strengthening national and international partnerships. A consistent message about the importance of TB control, delivered from various constituencies, is a basis for effective advocacy and communication.

TABLE 21

Advantages and disadvantages of various epidemiological measurements for TB control

Text in blue refers to attributes of the indicator; regular text refers to attributes of the measurement technique.

MEASURE	ADVANTAGES	DISADVANTAGES
Prevalence of infection	Risk of infection changes relatively quickly in response to control (but prevalence, from which risk is calculated, changes slowly).	Measures infection, not disease burden; not an MDG indicator.
From tuberculin surveys	Relatively cheap and logistically straightforward.	Results often hard to interpret where infection rates are low and where BCG coverage is high or where exposure to environmental mycobacteria is high; measures average risk of infection over past 5–10 years; Styblo 1:50 rule for indirectly estimating disease incidence may not be applicable under chemotherapy, or where HIV infection rates are high.
Prevalence of disease	Component due to duration of illness changes relatively quickly in response to control; MDG indicator.	Component due to incidence changes slowly in response to control.
From population-based surveys	Accurate measure of bacteriologically confirmed disease; should change quickly in response to control; surveys useful where routine surveillance data are poor, and are a platform for related investigations e.g. of interactions between patients and health system.	Costly; logistically complex (especially with radiography), therefore cannot be measured annually; does not easily lead to an estimate of TB incidence (denominator of WHO case detection rate), because duration is hard to assess.
Incidence of disease	Direct measure of denominator of WHO case detection rate; MDG indicator.	Changes slowly following reductions in transmission.
From case notifications	Direct measure of incidence; absolute incidence can be assessed from routine case reports where case detection judged to be high; trends can be judged from series of routine case reports, if measured consistently; every country now has a surveillance system, reporting annually or sub-annually.	Case detection mostly low in high-burden countries (underestimates incidence), and may vary through time (inaccurate trends).
From consecutive prevalence surveys	Direct measure of incidence.	Costly; logistically complex; requires ≥ 2 surveys with carefully judged survey interval and follow-up of individual patients.
TB mortality	Direct measure of TB burden accounting for a high proportion of DALYs; case fatality falls quickly in a new control programme; MDG indicator.	Component due to incidence changes slowly in response to control; hard to reduce case fatality further in low-burden countries.
From observations on patient cohorts	Direct observation of number of patients dying.	Deaths observed are those in cohort only, not in the population at large, and not beyond the period of cohort follow-up; deaths among defaulters and transfers usually unknown; TB not always the cause of death for patients on TB treatment.
From product of incidence and case-fatality rate	Simple and widely applicable.	Relies on accurate measures of incidence (above) and case fatality; case fatality measurable in observed DOTS cohorts, but not among patients treated elsewhere or untreated. Approximate at best.
From vital (death) registrations (VR)	Direct measure of TB deaths and trends; can be reported annually or sub-annually.	VR does not yet exist in many high-burden countries (notably in Africa and Asia); typically underestimates TB deaths; sensitivity and specificity untested.
From verbal autopsy (VA)	Review of registered deaths can improve accuracy of cause of death statistics.	Sensitivity and specificity of VA not fully evaluated; where no death registration system exists, laborious to compile deaths from a rare disease, and requires large sample sizes.

Besides the staff shortages, many laboratories participating in DOTS programmes have insufficient equipment and supplies, and limited procedures for quality assurance. All these essential elements need to be in place before laboratories take on the larger tasks of culturing *M.*

tuberculosis and testing for drug sensitivity, as will be required to integrate DOTS-Plus projects within DOTS programmes. To help improve capacity in HBCs, the DEWG has established a subgroup concerned with laboratory strengthening.

In addition to the deficiencies in

laboratories, the lack of national policies on MDR-TB management, the widespread availability of drugs of uncertain quality and the large numbers of MDR-TB patients treated outside the NTP together suggest that the treatment of drug-resistant TB is often inadequate. The high propor-

tions of re-treatment cases reported by NTPs are also a signal that drug-resistant forms of TB could be common in some populations where no surveys have yet been done. There are several remedies. WHO is in the process of expanding drug resistance surveillance and DOTS-Plus components within the context of regular TB control programmes. WHO is also working to establish a long-term competitive market for quality-assured drugs by leading a project to pre-qualify second-line drugs worldwide. GFATM grants are also being used to stimulate demand for drugs from reliable manufacturers. The Fund has selected the GLC as the mechanism for second-line drug procurement, and for monitoring approved projects.

The management of drug-resistant TB will be aided by a better understanding of the scale and distribution of the problem. Surveillance of drug resistance must be expanded to the five HBCs for which no data are yet available,⁸ and to other countries suspected to have high prevalence rates of MDR-TB. Information about new TB patients will be supplemented by data on patients presenting for re-treatment, including the systematic notification of all categories of re-treatment cases, the reporting of treatment outcomes and representative drug resistance surveys.

During 2003, very few TB patients had access to VCT and to ART. The numbers that actually have access to these services are probably somewhat higher than reported, but cannot be accurately known until TB/HIV monitoring systems are substantially improved. HIV/AIDS programme staff are increasingly aware of the fact that people infected with HIV are at high risk of developing active TB, while their counterparts in TB control programmes are seeing the impact of HIV on TB case-load, and on death rates in cohorts of TB patients on treatment. There has, until now, been little collaboration between TB and HIV/AIDS control programmes, but many such programmes are beginning to adopt elements of the WHO interim policy on collaborative TB/HIV activities.¹⁵ Even with the imperfect data presented in this report, it is clear that

much closer collaborations of this kind are needed to develop and improve access to prevention, treatment and support services, for both TB and HIV/AIDS patients.

Notwithstanding these weaknesses, this report has also identified a series of positive developments in DOTS implementation. The contributions to TB control of NGOs and community groups are clear expressions of the growing commitment of civil society. The work of these groups puts patients at the centre of the DOTS strategy, and improves access to TB services in remote areas and among disadvantaged and marginalized populations. NGOs are increasingly recognized as essential members of national partnerships for TB control. This recognition is helping not only to coordinate routine activities but also to develop a collaborative approach to solving the problems faced by NTPs. Some African countries are planning to involve community groups in collaborative TB/HIV activities. PPM projects are showing a measurable impact on case detection in several Asian countries, and may prove to be a mechanism for expanding TB control services in African cities.

With the significant influx of resources for TB control (from the GFATM, banks and bilaterals), especially to HBCs, some additional, catalytic funding is needed to ensure that NTPs have the technical capacity to make the best use of the new grants and loans. To satisfy this need, Stop TB partners launched a new initiative in 2003 – ISAC – an extraordinary effort to push towards the 2005 targets in selected countries, including China, India and Indonesia. The technical work under way aims to facilitate the access of patients to DOTS services, for example by expanding the geographical coverage of DOTS, by involving a greater diversity of public and private health-care providers, by strengthening in-country advocacy and social mobilization, and through partnership building and collaborative TB/HIV activities.

Financing DOTS expansion

There has been a big increase in NTP budgets and a big improvement in the

funding available for TB control since 2002, with particularly large increases between 2003 and 2004. The total reported NTP budgets for the 22 HBCs in 2005 are US\$ 741 million, of which US\$ 622 million is available and US\$ 119 million is a funding gap. The total estimated costs of TB control³² are projected to be US\$ 1.3 billion, of which US\$ 1.2 billion is already available. With the exception of large additional government contributions in China, Indonesia and the Russian Federation, almost all of the extra funding for TB control since 2002 is from GFATM grants. The GFATM now plays a major role in the financing of TB control, contributing more than one third of the budget in several HBCs, and over half in a few.

As usual, the summary statistics conceal important variations among countries. Our analyses suggest that in 2005, the HBCs fall into four categories. In the first are four countries (India, Myanmar, the Philippines and Viet Nam) that have budgets consistent with reaching the 2005 targets, and which are likely to have minimal or no funding shortfall. India has continued to expand rapidly with fully-funded budgets over the period 2002–2004, which, in 2003, provided more than enough money for planned activities. The Indian Revised National TB Control Programme has also maintained a constant budget per patient treated during the rapid expansion of DOTS. In the second are four countries that are close to being in this group, but which need to make up funding shortfalls (China, Cambodia), or where it is unclear how many more cases will actually be detected and successfully treated as a result of the substantial additional funds now available (Bangladesh, Indonesia). China stands out as having developed much larger budgets for 2004 and 2005 compared with previous years, for mobilizing a substantial increase in domestic and external financing to fund these budgets and for being the first HBC to secure full disbursement of a

³² i.e. NTP budgets plus the cost of hospitalization and outpatient clinic visits of TB patients that are usually not included in NTP budgets.

two-year GFATM grant. In the third group are five countries that report no, or negligible, funding gaps for 2005, but whose plans are not sufficient to reach the targets for case detection (e.g. Ethiopia) or there are doubts about whether existing plans will ensure achievement of the treatment success target (e.g. South Africa). The nine countries in the final group need special attention because they report large funding gaps and, in addition, do not expect to treat enough patients to reach the case detection target (eight countries) and/or there are doubts about whether they can reach the treatment success target. Among these nine countries, Nigeria and Zimbabwe are the only low-income HBCs not to have secured GFATM funding to date. Pakistan's funding shortfall is a consequence, in large part, of planning for accelerated DOTS expansion in 2005.

The funding gap of US\$ 119 million identified by all NTPs for 2005 is higher than reported in 2003 and 2004, but may still be an underestimate. The budget gap is the difference between the funds needed to carry out planned activities and the funds actually available. If the activities planned by NTPs for 2005 are a realistic assessment of what can be achieved, the budget gaps reported are arguably an accurate reflection of the funding gap. However, the activities required to meet the 2005 case detection target are greater than planned in 12 countries, and while Brazil and South Africa may already detect more than 70% of all TB cases it is unclear whether they are budgeting sufficient resources to reach the target for treatment success. In this sense, the funding gaps are underestimates, although Brazil and South Africa are relatively wealthy middle-income countries that should be able to find any necessary resources from domestic budgets (Brazil has already increased its NTP budget by 50% since 2002). Apart from the question of whether NTPs are budgeting enough to meet targets, further reasons why the NTP budgets and associated funding gaps could be considered too low are the generally limited budgets for collaborative TB/HIV activities, especially in African

countries, and the typically small or non-existent budgets for second-line drugs to treat MDR-TB patients (the Russian Federation is a notable exception).

For NTPs to carry out their activities as planned, they must actually receive the funds promised or anticipated. The establishment of the GFATM has not so far caused a decline in grant funding from other sources, and the Fund is thus apparently providing additional money. Nevertheless, its central financing role in several countries, and its smaller but nonetheless important contribution in others, means that the rate at which funds are made available in countries is of considerable importance. If these funds are not received by the NTP, gaps will replace expected GFATM contributions. This is a concern for some countries, where delays in receiving expected disbursements are already evident. The most important example is Mozambique, which had not received funds by the end of 2004, even though its proposal was approved in January 2003. Removing the obstacles to disbursement should be a priority, particularly in countries where GFATM grants contribute a large share of planned budgets.

For those countries that have secured large additional grants or loans, the key question now is whether the NTP can spend the money effectively. In 2003, expenditures were lower than the funding available, and in that year the total amount of money available was much lower than in 2004 or 2005. The most obvious need is for additional staff, particularly those with general and financial management skills. This need has already been recognized in several countries, and additional funds have been sought through the ISAC initiative. For example, China's ISAC proposal includes a budget to support the recruitment of new staff at provincial level. Bangladesh has also identified a need for additional staff at central level, following its successful application to the GFATM.

When countries succeed in mobilizing additional funds, the new money must be translated into better programme performance. For most coun-

tries it is too early to say whether or not this is happening, because the biggest budgetary and funding increases have mostly been in 2004. However, it is striking that India's TB control programme is both relatively low cost and very effective. As data become available for more years, it will be possible to assess the relative cost-effectiveness of TB control in the 22 HBCs, and the reasons for variation among countries.

Some HBCs still have difficulties in providing financial data. South Africa has not yet been able to complete the financial section of the WHO data collection form. A major part of the explanation is that budgeting for TB control is decentralized in South Africa. Decentralization has also affected the completeness of data available for Afghanistan and Thailand. Most NTPs find it more difficult to provide data on expenditures than budgets. Similarly, expenditures are not yet available on the GFATM web site, although the Fund does provide an impressive volume of data on budgets, grant agreements and disbursements. Efforts to follow up data were intensified in the African Region in 2004, and resulted in major improvements in the quantity and quality of data collected. Similar efforts are now needed in other regions, both for the HBCs and other countries.

In summary, financing for global TB control has improved since 2002, dramatically in some countries. Some HBCs now have sufficient funds, but must show that they can spend them effectively; some have no apparent shortfall, but should verify that their budgets are sufficient to meet targets; some have an obvious funding gap, and must focus on raising the money needed to improve programme performance.