T8.4: Prospects for tuberculosis control in sub-Saharan Africa

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Abstract:

The UN Millennium Development Goals (MDGs) for TB control are: (a) to detect, by 2005, 70% of new sputum smear-positive TB cases, and to successfully treat 85% of these; (b) by 2015, to ensure that TB incidence is falling, and to halve 1990 prevalence and death rates. The Global Plan to Stop TB, costing around US$56 billion over the period 2006–15, is a package of interventions designed to meet the MDGs globally. The plan is based on combination chemotherapy for active TB (the DOTS strategy), but includes other measures such as the management of TB linked to HIV/AIDS and the development of new technology. The implementation of the plan in Africa, at a cost of US$20 billion, should ensure that TB incidence will be falling by 2015. However, the targets for halving prevalence and death rates are very unlikely to be met in Africa under any conceivable set of circumstances. To make a bigger impact in Africa will require an intense and sustained attack on TB using methods that go well beyond conventional drug treatment, including large-scale isoniazid preventive therapy, widespread antiretroviral therapy, the reduction of HIV incidence, and the rapid introduction of new diagnostics, drugs and vaccines.

Contents

Introduction

Objective To evaluate the prospects for reaching five targets for TB control in Africa, as specified by the United Nations Millennium Development Goals (MDGs). These are: by 2005, to detect 70% of new sputum smear-positive TB cases, and successfully treat 85% of these; by 2015, to reduce TB incidence, and to halve 1990 prevalence and death rates.

Data sources and methods TB case notifications (1980–2003) from DOTS and non-DOTS programmes; cohort treatment outcomes (1994–2002) reported annually to the WHO by up to 200 countries; TB death registrations; prevalence surveys of infection and disease; mathematical and statistical modelling to evaluate trends and to forecast the impact of control measures, especially through DOTS (the internationally recognised TB control strategy based on chemotherapy) and its extensions, but also including new tools (diagnostics, drugs, vaccines).

Data synthesis and analysis The TB incidence rate was increasing globally at about 1% annually in 2003, but more quickly in regions of sub-Saharan Africa with either low (<4% in adults 15–49 years) or high rates (≥ 4%) of HIV infection. Case detection rates by DOTS programmes in Africa increased from an estimated 24% in 1995 to 50% in 2003, well short of the 70% target. In 2003, reported treatment success was 82% globally, but much lower in African countries with high and low HIV infection rates (71% and 74%, respectively). With the aggressive implementation of DOTS, plus appropriate elaborations for the management of drug-resistant TB and TB linked to HIV/AIDS, target rates of case detection and cure could be reached in every region of the world. TB incidence rates should be falling by 2015, and prevalence and death rates could be halved globally. The cost of implementing the full package worldwide would be around US$56 billion over the period 2006–2015, of which US$20 billion would be spent in Africa. The implementation of this package of measures in Africa should ensure that TB incidence will be falling by 2015. However, the targets for halving prevalence and death rates are very unlikely to be met in Africa under any conceivable set of circumstances. To make a bigger impact than is possible with DOTS needs a wider range of interventions including: large-scale isoniazid preventive therapy, antiretroviral therapy, the reduction of HIV incidence, and the rapid introduction of new diagnostics, drugs and vaccines. These extra measures would require a sharp increase in the budget for TB control in Africa.

Conclusions National TB control programmes must continue to strengthen and expand the DOTS strategy in sub-Saharan Africa. DOTS and its extensions will not be sufficient to meet the MDGs, but should nonetheless have a substantial impact on the African epidemic. TB control in Africa has to be done in partnership with other health programmes because success depends on the improvement of health staffing and infrastructure, and more specifically on progress in the prevention and treatment of HIV/AIDS.

During the early 1990s, the essential methods for TB diagnosis and treatment became part of the DOTS strategy, which has become the internationally recommended approach to TB control.(WHO 2002a, 2002b) The term DOTS was at first an acronym referring to directly observed treatment (DOT) and short-course chemotherapy, but has become the term used to describe a broader, public health strategy with five principal elements: political commitment; case detection by sputum smear microscopy mostly among self-referring symptomatic patients; standard short-course chemotherapy with supportive patient management, including DOT; a system to ensure regular drug supplies; and a standard recording and reporting system, including the evaluation of treatment outcomes. Standard short-course regimens can cure over 90% of new drug-susceptible TB cases, and high cure rates are a prerequisite for expanding case finding. At 70% case detection, 85% cure and in the absence of HIV infection, the TB prevalence rate is expected to fall substantially (Styblo and Bumgarner 1991) and incidence rate should fall at around 5–10% per year (Dye et al. 1998; Borgdorff et al. 2002).

Since 2000, the United Nations Millennium Development Goals (MDGs; Table 1) have provided a framework for evaluating both implementation and impact, under target 8 (among 18), which is to ‘have halted by 2015 and begun to reverse the incidence of malaria and other major diseases’ (United Nations Statistics Division 2004). The objective is expressed in terms of incidence, but the MDGs also specify that epidemiological impact should be measured in terms of the reduction in TB prevalence and deaths. The target for these two indicators, based on a resolution passed at the 2000 Okinawa (Japan) summit of G8 industrialised nations, and subsequently adopted by the Stop TB Partnership, is to halve TB prevalence and death rates between 1990 and 2015. Regarding the implementation of DOTS, the WHO's World Health Assembly set two targets: to detect 70% of all new sputum smear-positive cases arising each year (i.e. a 70% case detection rate), and to successfully treat 85% of these cases (Barnum 1986; WHO 1991; Jamison et al. 1993; World Bank 1993; de Jonghe et al. 1994). Although these are global targets, they have been adopted as regional targets (e.g. for the WHO African Region) and as national targets by individual countries.

Although the DOTS strategy is now regarded as fundamental to TB control, sub-Saharan Africa will require more than DOTS to meet the targets set by the MDGs, especially because of the powerful link between HIV/AIDS and TB in this region. A more inclusive approach to control will embrace methods for preventing both TB and HIV infection, and for stopping the progression from infection to active disease among people who are infected with both *Mycobacterium tuberculosis* and HIV. Stepping up the control effort also requires new technology: better diagnostics, drugs and vaccines.

In this analysis of progress and prospects for TB control in Africa, we begin by re-evaluating the scale and direction of the TB epidemic, and by summarising the progress made in DOTS implementation up to the end of 2003. This forms the background for an evaluation of whether DOTS has reduced, and will continue to reduce, TB incidence, prevalence and deaths in sub-Saharan Africa. With the evidence at hand, we comment on the prospects for reaching the MDGs through DOTS expansion alone, through the implementation of a more comprehensive strategy, and through the introduction of new technology. The analysis presented in this paper is based on a recently published review of TB epidemiology and control (Dye et al. 2005), and on work carried out for the second Global Plan to Stop TB (2006–2015), done under the auspices of the Stop TB Partnership and to be published early in 2006.

Table 1: MDGs for TB control

- Goal 6 (of 8)
  - Target 8 (of 18): ‘to have halted and begun to reverse incidence’
    - *Indicator 24 (target year 2005)*

      Implementation of DOTS (smear-positive cases)

      Case detection 70%

      Treatment success 85%

    - *Indicator 23 (target year 2015, baseline 1990)*

      Epidemiological impact (any method of control; all forms of TB)

      Prevalence 50% of ≈ 300/100,000

      Deaths 50% of ≈ 30/100,000 (<1 million deaths)

Methods

Case notifications, case detection and treatment outcomes

Case definitions and the classification of treatment outcomes used by WHO are fully described elsewhere.(WHO, International Union against Tuberculosis and Lung Disease et al. 2001; WHO 2005) Here, we distinguish between the incidence (new cases arising annually) and prevalence (cases existing at one point in time) of latent infection with *Mycobacterium tuberculosis* and active TB disease, and between numbers of cases and rates per 100,000 population. The WHO has compiled TB case notifications, from DOTS and non-DOTS programmes, for up to 200 countries and territories for 1980–2003. Since 1994, we have also received the results of treatment for patients registered in DOTS cohorts between 1994 and 2002. The principal measure of case detection for each country is the number of patients with new smear-positive sputum samples reported by the DOTS programme in one year divided by the estimated annual incidence of smear-positive cases. TB incidence rates are rarely measured directly, so incidence is estimated from population-based surveys of the prevalence of *M. tuberculosis* infection or TB disease, or from independent assessments, often qualitative, of the performance of surveillance systems. Errors on the point estimates of incidence for high-burden countries typically range from –20% to +40% (Dye et al. 1999). Some low estimates of case detection are supported by independent research showing why patients are not detected by DOTS programmes (China Tuberculosis Control Collaboration 2004).

In making estimates of incidence, the WHO assumes that human TB caused by mycobacteria other than *M. tuberculosis* (often referred to as MOTT) is rare. However, the contribution made by *M. bovis* and other mycobacterial species, especially in patients who are also infected with HIV (Ayele et al. 2004; Karakousis et al. 2004), is not accurately known.

In general, estimates of incidence, and therefore case detection, should be considered approximate.

Treatment success under DOTS is defined as the percentage of smear-positive patients registered in an annual cohort that are cured (negative sputum smear at the end of treatment), plus the percentage who complete treatment. The other defined outcomes of treatment are: died, defaulted, failed (positive sputum smear at the end of treatment), transferred (outcome unknown after transfer to another treatment centre), or not evaluated (no outcome reported). To obtain high rates of treatment success, DOTS programmes must achieve high standards clinically, and they must provide comprehensive reports on patients in their care. By and large, DOTS programmes follow recommended procedures for evaluating treatment outcomes, though this does not exclude the possibility that cure rates are overestimated in some settings (underestimation is less likely given that health workers are responding to performance targets). Cure rates outside DOTS programmes are poorly known because recording and reporting often does not follow standard procedures.

Estimating TB burden and trends, 1990–2003

For this analysis, the WHO African Region is divided into two sub-regions comprising those countries with high HIV infection rates (≥ 4% in adults 15–49 years in 2003) and those with low rates of HIV infection (<4%). The countries in each region are shown in Figure 1 and listed in full elsewhere (WHO 2005). ‘Africa – high HIV’ consists of 22 countries mostly in eastern and southern Africa; ‘Africa – low HIV’ consists of 27 countries mostly in west and central Africa. Where reporting from a country has been consistent through time (without large variations from year to year), and is unlikely to have been influenced by changes in case detection effort, we take the trend in notifications to represent the true trend in incidence. Most notified cases of TB are assumed to be *M. tuberculosis*, but some may be due to other mycobacterial species, such as *M. bovis*. Though these are usually not identified specifically, they are not necessarily excluded from case notifications.

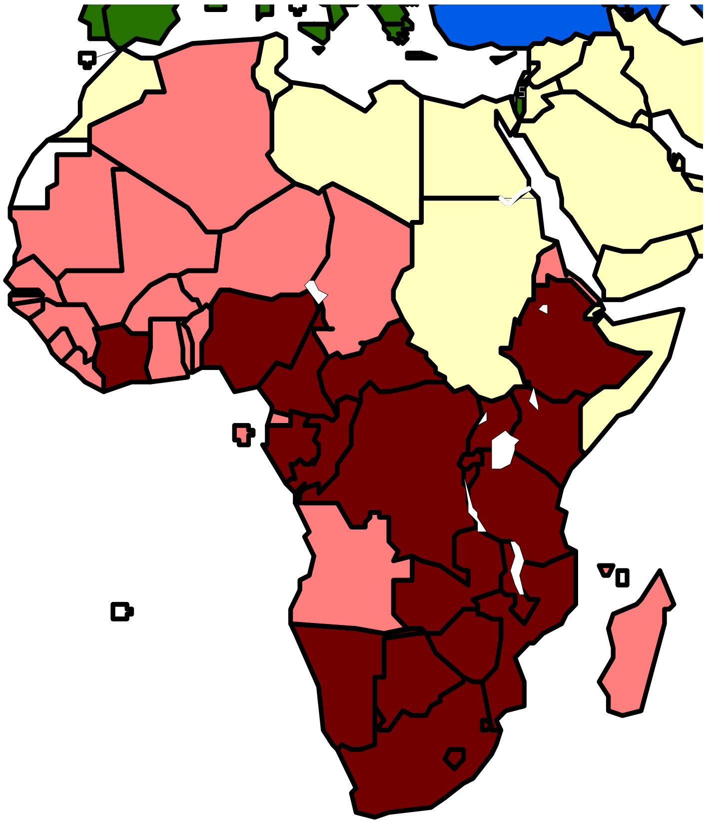

Figure 1: The WHO African Region (red) is divided into two sub-regions comprising those countries with high HIV infection rates (dark, ≥ 4% in adults 15–49 years in 2003) and those with low rates of HIV infection (light, <4%).

Countries that do not provide reliable case notifications are assumed to follow the trend for their own epidemiological regions, here for each of the two regions in Africa. The number of cases notified divided by the estimated proportion of cases detected gives the total incidence rate for any country in any year, and hence the time series of estimated incidence rates for 1990–2003.

Because TB prevalence and death rates are rarely measured directly (e.g. by population-based surveys), they are usually calculated indirectly. TB prevalence is the product of incidence and duration, and the TB mortality rate is the product of incidence and case fatality (Dye et al. 1999; Corbett et al. 2003). Estimates of duration and case fatality are made with greater or less precision according to the source of data. Estimates of case fatality are most reliable for patients treated under DOTS (WHO 2005), or for those who are not treated at all (data from natural history studies in the pre-chemotherapy era (Styblo 1991; Rieder 1999). The data are least reliable for patients treated with various drug regimens that are not recommended by the WHO. This applies mainly to patients who are treated outside DOTS programmes; estimates of the numbers of such patients, by country, are given elsewhere (Dye et al. 1999; Corbett et al. 2003).

The duration of illness is typically shorter for patients treated under DOTS than for patients who are treated elsewhere or untreated, so the average duration of illness falls as the proportion of patients treated under DOTS increases (higher case detection rate). DOTS programmes are therefore associated with lower prevalence rates. By the same mechanism, the geographical expansion of DOTS reduces both the case fatality rate and the TB mortality rate in the whole population.

The uncertainties associated with these methods are discussed more fully elsewhere (Dye et al. 1999; Corbett et al. 2003; WHO 2005).

Forecasting TB trends, 2003–2015

Two approaches were used to define trends in incidence, prevalence and deaths – statistical and mathematical modelling. The statistical approach is a curve-fitting exercise that uses data on case notifications collected up to 2003 (WHO 2005) to forecast incidence rates to 2015, assuming that TB control has no additional impact on the TB epidemic. Two methods of fitting were used, based on the case notification series for each region of Africa: (1) incidence rate changing exponentially (1.5% per year for African countries with low rates of HIV infection); (2) increase in incidence rate slowing exponentially (–10% per year for African countries with high rates of HIV infection).

If these fits to the notification data were used to forecast trends in the TB epidemic, they would give a pessimistic view of changes in incidence because they neglect any impact of control on transmission. To allow for the effects of transmission, we used the compartmental mathematical model depicted in Figure 2, which is based on models used in several previously published studies (Dye et al. 1998; Dye and Williams 2000; Currie et al. 2003; Williams et al. 2005; Currie et al. in press). The model has been extended beyond the basic framework shown in Figure 2 to allow for the more rapid transition rates seen among people who are co-infected with *M. tuberculosis* and HIV; see, for example (Currie et al. 2003). The underlying HIV epidemic that has such a profound effect on TB is as described and forecast by UNAIDS (personal communication).

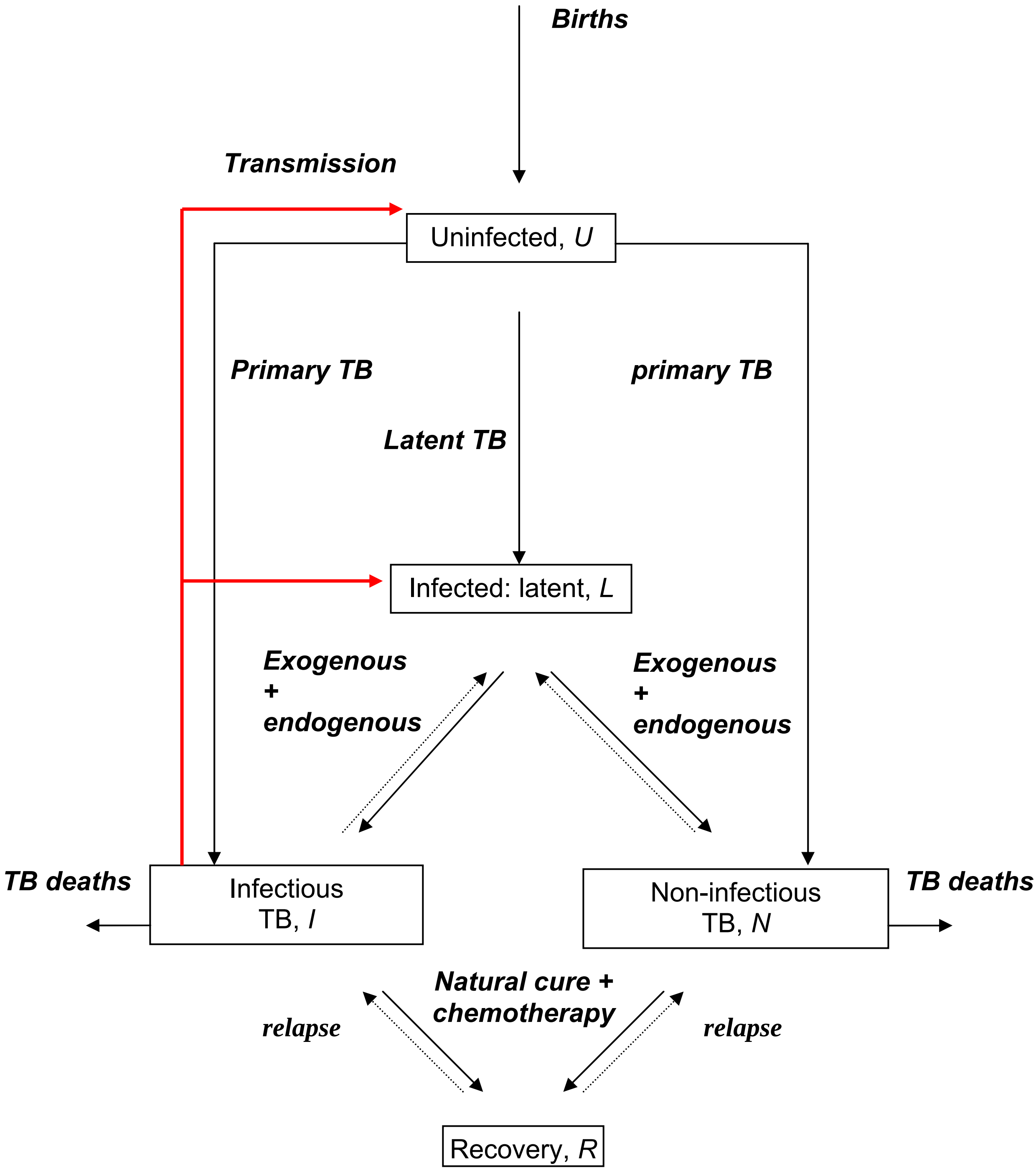

Figure 2: Basic mathematical model of TB transmission used to investigate the impact of various control strategies. A more complex model, based on the scheme above, has been developed to investigate the management of drug-resistant TB and of TB associated with HIV/AIDS, including control methods that go beyond short-course chemotherapy administered under the DOTS strategy. The various extensions to the basic model depicted here are described elsewhere (Dye et al. 1998; Dye and Williams 2000; Currie et al. 2003; Williams et al. 2005; Currie et al. in press).

Results

Dynamics of the African TB epidemic

Although the incidence rates of TB have been increasing most quickly in eastern and southern African countries with the highest rates of HIV infection, there is evidence that the rate of increase is slowing (Figure 3). The trajectories of the TB epidemics in these countries will depend on the dynamics of HIV infection; however, if the trend from 1990 to 2003 persists, the estimated TB incidence rate will exceed 500 per 100,000 by 2015 (≈ 3.3 million new cases). In other parts of Africa that have lower rates of HIV infection, the rate of increase in TB has been much slower (1–2% per year), but the case notifications give no indication of when or at what level TB incidence will reach its peak.

Figure 3 also shows, for contrast, the global trend in incidence rate, which was increasing most quickly at 1.5% per year in 1995, but has since been decelerating (WHO 2005). If the trends suggested by the case notifications are correct, and if these trends persist, the global incidence rate will reach about 150 per 100,000 in 2015, generating more than 10 million new cases worldwide in that year. TB epidemics in parts of the world outside Africa are either stable or in decline. The upward trajectory of the African epidemic is the principal reason why TB incidence is rising globally.

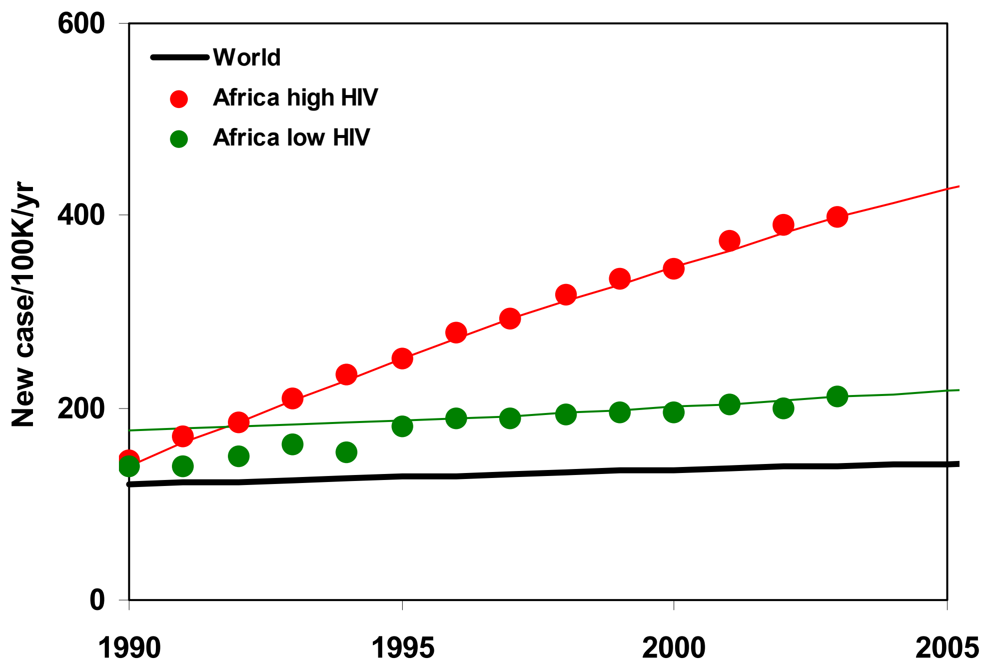

Figure 3: Trajectories of the TB epidemic for two sub-regions of Africa, and for the whole world. The countries in each region are listed in full elsewhere (WHO 2005). Points mark trends in incidence rates, derived from case notifications up to 2003. Fitted lines for Africa – low HIV (green) are based on the more stable (and probably more reliable) incidence rates estimated from 1995 onwards.

The DOTS strategy in Africa

The case detection rate by DOTS programmes in Africa was estimated to be 24% in 1995, rising to 50% in 2003, well below the 70% target. Treatment success was 59% in the 1994 cohort of sputum smear-positive patients and 73% in the 2002 cohort (438,000 patients). The reported treatment success was far below the 85% target in 2002 because 7% of patients died and 19% were lost to follow-up (defaulted, transferred to other treatment centres, or not evaluated). In addition, 13% of patients completed treatment without evidence of smear conversion. It is therefore not certain that these patients were cured. These poor results are almost certainly linked to the high rates of HIV infection in Africa (Table 2 separates treatment results for the sub-regions with low and high rates of HIV infection), but these data also point to deficiencies in the management of national TB control programmes.

Table 2: Adverse outcomes of treatment, and overall treatment success, for TB patients registered in DOTS cohorts in 2002, for two sub-regions of sub-Saharan Africa and for the world. Data are the percentages of smear-positive patients with different outcomes, among all those registered for treatment (WHO 2005). Shaded cells identify relatively important reasons for low treatment success in the two parts of Africa.

Region	Died	Failed	Defaulted	Transferred	Not Evaluated	Treatment success
Africa – high HIV	**8.0**	1.0	**9.7**	**6.8**	3.5	71.1
Africa – low HIV	3.8	3.1	**14.4**	3.6	0.7	74.4
World	4.8	1.6	6.7	3.4	1.4	82.0

Epidemiological impact of DOTS

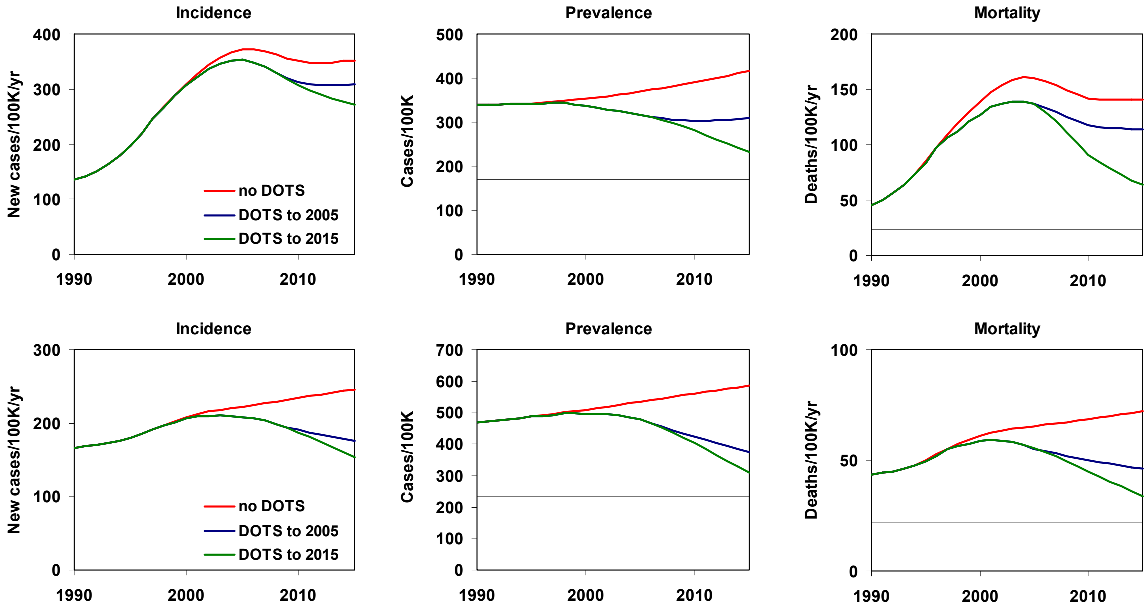

Figure 4: Expected epidemiological impact of the DOTS strategy on TB incidence, prevalence and deaths. Calculations assume that DOTS has never been implemented (red), that case detection and cure rates will improve up to 2005 and then hold steady until 2015 (blue), or that case detection and cure rates will improve up to 2015. Series refer to African countries with high (upper panel) or low (lower panel) rates of HIV infection. Horizontal lines mark MDG targets for 2015; the target death rate is about 20 per 100,000 population per year in both sub-regions.

Most of the impact DOTS had on transmission up to 2003 is reflected in the trends in incidence rates (Figure 3). To investigate what will happen beyond 2003, we explore three different scenarios, as developed for the second Global Plan to Stop TB:

Scenario 1: No DOTS. We assume that the DOTS strategy was never introduced into Africa. This gives a baseline against which to compare gains that have already been made, and which might be made in future.

Scenario 2: DOTS to 2005. Case detection and cure rates improve up to 2005, and then hold steady until 2015. The values of case detection and cure for 2005, based on data collected up to 2003, are 55% and 72% for Africa – high HIV, and 55% and 75% for Africa – low HIV.

Scenario 3: DOTS to 2015. In this more ambitious scenario, case detection and cure rates improve up to 2015. The values of case detection and cure at 2015 are 69% and 86% for Africa – high HIV, and 75% and 86% for Africa – low HIV, i.e. close to or exceeding target levels for both sub-regions. To reach such high rates of case detection and cure requires various additions to the basic DOTS strategy in Africa, including community-based care and the screening of HIV-infected people for active TB. The joint management of TB and HIV/AIDS also allows for the provision of isoniazid preventive therapy

(IPT) to reduce the risk of progressing to active TB among persons who are co-infected. It further assumes that antiretroviral therapy (ART) will be available to improve survival and healthy life expectancy among HIV-positive TB patients.

These different scenarios for DOTS implementation generate the changes in incidence, prevalence and deaths shown in Figure 4. Although HIV has driven TB incidence rates upwards, full implementation of DOTS under Scenario 3 is expected to force incidence downwards by 2015, as required by the MDGs. However, these calculations also show that MDG targets for reducing TB prevalence and (especially) deaths are very unlikely to be met by 2015, even under Scenario 3. At the average rate of decline in mortality observed between 2010 and 2015, the MDG target would not be met until around 2030. If the rate of decline in mortality slows, as it has elsewhere, the target will be reached later than 2030. Africa therefore requires a more intensive set of interventions to meet the MDGs, as described in the next section.

Beyond DOTS: how to reach the MDGs in Africa

African countries with high rates of HIV infection

Scenario 3 postulates rates of case detection and cure that are well above current levels in Africa, and which therefore already set demanding targets for DOTS implementation. Nonetheless, we proceed here by asking what more would need to be done, in theory, to reach target MDGs death rates (approximately 20 per 100,000 population per year) in the two sub-regions of Africa by 2015. The implication for Africa – high HIV is that, over the next decade, TB mortality rate must be reduced by 13% annually. This has been achieved on a smaller scale, even with a high proportion of TB patients infected with HIV, but it is not likely to be possible in Africa.

The interventions are as follows, building on Scenario 3 (Figure 5, dark-blue line), each one added in turn to the combination, with the cumulative impact shown by the sequence of lines running from top to bottom in Figure 5. The purpose is to show what is needed for TB control in Africa from a biomedical standpoint, and to consider how far we can go beyond the probable (Scenario 3) towards the impossible:

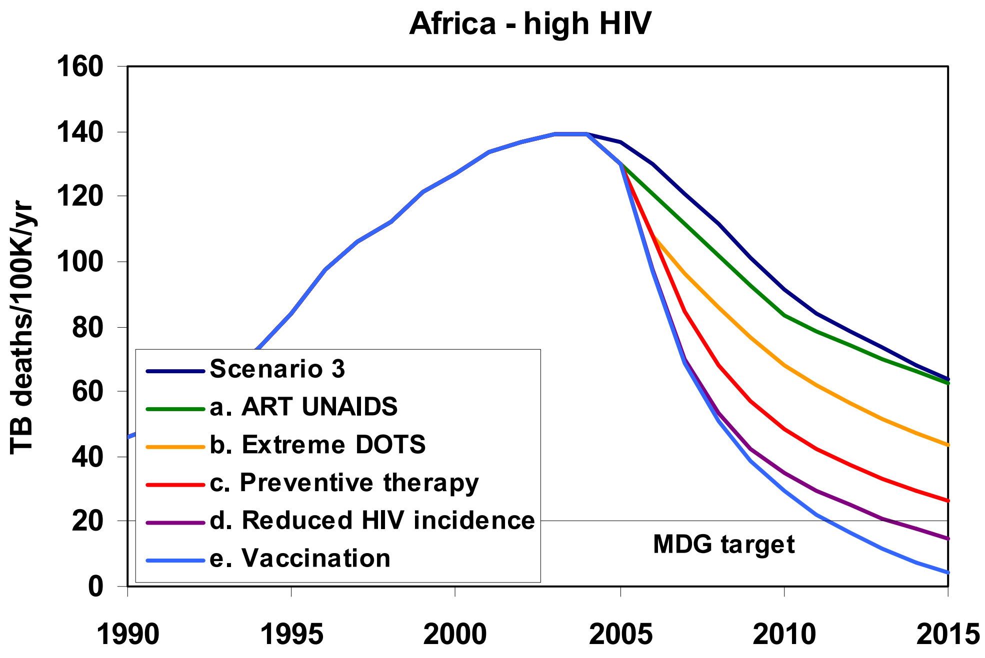

Figure 5: Combinations of interventions, going beyond Scenario 3 for DOTS implementation, that will reach the MDGs in African countries most affected by HIV.

a More rapid distribution of ART, as proposed by UNAIDS (ART UNAIDS, green line). Compared with OR, ART is made available to more TB patients sooner, in line with the '3by5' initiative (3 million HIV/AIDS patients on ART by 2005). This reduces TB deaths sooner, but the death rate by 2015 is about the same as in Scenario 3. This scenario has no effect on the number of people to be offered IPT, or the number of TB patients discovered through intensive case finding.

b Extreme DOTS (90% case detection for HIV-negative TB cases, both smear-positive and smear-negative, 85% treatment success, 2006–2015, orange line). Although these high rates of case detection and cure might be achieved before 2015, they could not be reached within the space of a year or two, as has been assumed in these calculations. Moreover, such high rates of case detection and cure would probably require: (i) new diagnostics and drugs; and/or (ii) intensive case finding via annual population-based screening for TB. The latter has never been done on a large scale in Africa.

c Preventive therapy (20% of people co-infected with *M. tuberculosis* and HIV are treated annually so that they will never develop active TB, red line). In principle, this might be achieved with IPT, ART, some combination of IPT and ART, or with some other drug yet to be discovered. To have 20% of co-infected people completing preventive therapy each year would require an IPT campaign of unprecedented dimensions in Africa. To keep costs down, it would also require a new diagnostic tool to accurately identify people who are co-infected with *M. tuberculosis* and HIV (IPT need not be given to people who are infected with HIV only). In practice, neither the WHO nor UNAIDS are proposing (so far) that ART could or should be used to reduce TB incidence.

d HIV incidence rate cut to half the value forecast by UNAIDS in 2005, and held at that level from 2006–2015 (purple line). Although there are clear and highly efficacious mechanisms for preventing HIV infection (condoms, abstinence, prophylactic drugs etc), few people believe they will be rapidly adopted across Africa.

e Vaccination annually protects 20% of uninfected people from ever acquiring TB infection (light-blue line). We assume that the vaccine does not protect people who are already HIV-positive. No such vaccine yet exists (BCG typically has low efficacy against pulmonary TB in highly endemic countries). A vaccine might ultimately have the effect depicted in Figure 2, but this will not happen before 2010, and is unlikely to happen before 2015.

The feasibility of each of these interventions is therefore in doubt, and yet, to have the required impact, all would be needed in combination.

Although it is hard to see how the MDGs, strictly defined, could be met in the region of Africa most affected by HIV, it is important to realise that Scenario 3 alone is expected to cut the TB death rate by about half between 2005 and 2015. Notwithstanding high rates of HIV infection, these interventions are therefore highly effective. Africa's problem in meeting the MDGs arises in large part because the baseline year is set at 1990, which is shortly after the point at which TB epidemics were at a minimum in the second half of the 20th century.

African countries with lower rates of HIV infection

Because the HIV epidemic elsewhere in Africa has had less of an impact on TB, the same set of interventions would bring the TB death rate closer to the target level by 2015 (Figure 6). Under Scenario 3, the target death rate would not be met until around 2025. Notice, however, that the death rate would be significantly reduced, by about 40%, between 2005 and 2015.

Figure 6 also underscores the importance of strengthening and expanding DOTS. Although the various interventions are not strictly comparable (they have different modes of action, are introduced to different levels and in a specific sequence), DOTS is the most effective single intervention (as we have repeatedly found in modelling studies). But it remains questionable (as it was for Africa – high HIV) whether the high rates of case detection and cure required by extreme DOTS could be achieved within a year or two, and maintained until 2015.

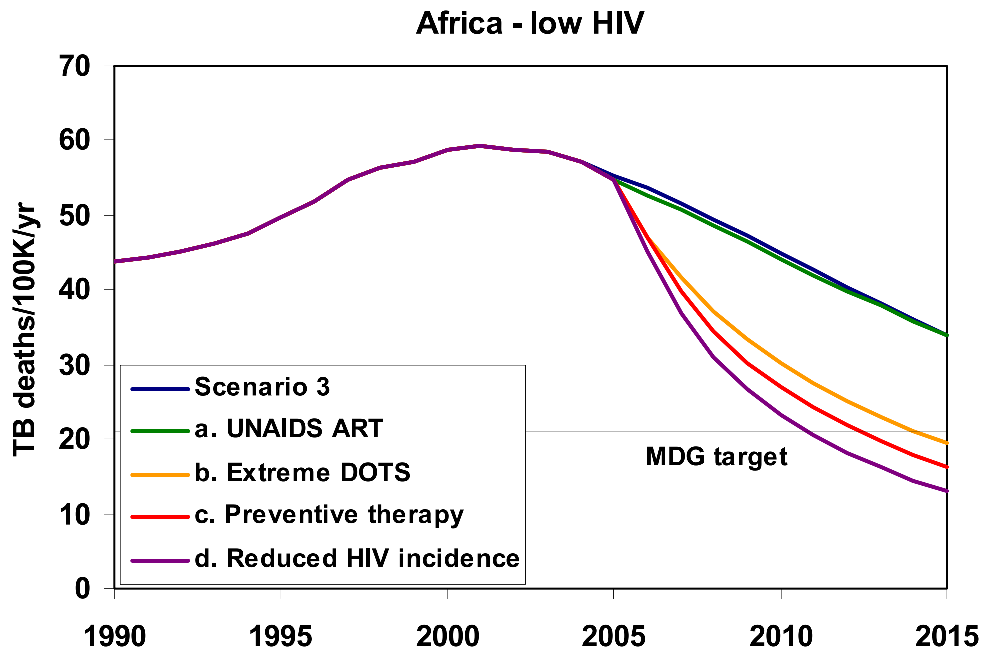

Figure 6: Combinations of interventions, going beyond Scenario 3 for DOTS implementation, that will reach the MDGs in African countries with lower rates of HIV infection.

Cost of TB control in Africa

An extensive costing exercise carried out for development of the Global Plan suggests that Scenario 3 for DOTS implementation would cost US$3.6 billion in Africa – lonsive control measures have rarely been implemented in practice, or because the tools needed do not yet cost. However, rough and speculative calculations give totals of US$10.3 billion in Africa – low HIV and US$40.1 billion in Africa – high HIV over the period 2006–2015.

The cost of implementing Scenario 3 globally is estimated at US$56 billion over the period 2006–2015. Adding (a)–(d) in Africa could double this total over 10 years.

Conclusion

Although the incidence rate of TB was still rising in Africa in 2003, it is expected to be falling again by 2015, satisfying the MDGs target. DOTS programmes should hasten the downturn, especially if they can markedly improve the rates of case detection and treatment success as proposed under Scenario 3. The much bigger challenge in Africa is to halve 1990 prevalence and (especially) death rates by 2015. To approach that goal will require, at the very least, stronger DOTS programmes, but probably much more. We estimate that the cost of controlling TB in Africa over the period 2006–2015 would be about US$20 billion under Scenario 3. This includes the package of measures based on DOTS that could feasibly be implemented but which would not reach the MDGs. To reach the MDG targets would require, in theory, a far more ambitious set of interventions that would be practically impossible to implement and very much more costly.

Although Africa will not reach the MDGs for TB control, it is important to realise that the DOTS strategy, with various elaborations to manage HIV-related TB and drug resistance, can have a substantial epidemiological impact. Under Scenario 3, the death rate, for example, is expected to fall by about half between 2005 and 2015. Thus, failure to meet targets in Africa reflects, in large part, the unfortunate choice of 1990 as the baseline year for the MDGs. It is not entirely due to high rates of HIV infection and poor health services, though these are also important factors.

In some places where DOTS has already been implemented, the basic tools are plainly inadequate. For TB patients who are HIV-positive, the risk of death during and following treatment is much higher than for patients who are not infected with HIV. Some improvements to DOTS could be instituted immediately. TB patients and suspects should be tested for HIV infection, and offered cotrimoxazole and antiretroviral drugs, in appropriate combination with anti-TB drugs (Harries et al. 2001; Williams and Dye 2003; WHO 2004). There should be active search for TB cases among HIV-infected people (Zachariah, Spielmann et al. 2003). Those who do not have active TB should be offered isoniazid preventive treatment (Aisu et al. 1995; Johnson et al. 2001; Quigley et al. 2001; Churchyard et al. 2003; Currie et al. 2004; Dye and Floyd in press). On top of this, TB control programmes must work in partnership with HIV/AIDS control programmes to assess the benefits of reducing HIV incidence. Most difficult of all perhaps, DOTS programmes must participate in the expansion of health services to serve populations where no professional healthcare is yet available. For example, half of the population of Ethiopia currently has no access to health services, and therefore no access to TB diagnosis and treatment.

Beyond the process of strengthening current procedures, it is not difficult to imagine new technology that would improve the efficacy and effectiveness of TB control. The first new tools to reach field application will probably be diagnostics (Foundation for Innovative New Diagnostics (FIND), www.finddiagnostics.org). A sensitive and specific test for active TB that is cheap and simple to use at the first point of contact between patients and health services would be a major advance in diagnosis. Mycobacterial culture detects a higher proportion of active TB patients than sputum smear microscopy, and is a prerequisite for screening for drug resistance. However, present culture methods are slow, taking 4–6 weeks to obtain a result. Technology based on phage amplification and nucleic acid amplification can establish whether cultures are positive in days or hours, but this technology needs to be packaged for use in developing countries (Woods 2001; Albert et al. 2002, 2004). The tuberculin skin test is being superseded in many developed countries by more specific methods for detecting infection (Doherty et al. 2002; Pai et al. 2004). A test that can predict who will progress from latent to active disease, as yet hypothetical, would greatly increase the feasibility of treating latent infection.

A new drug could improve cure rates by shortening the duration of treatment to 2–3 months so as to improve compliance, by increasing the cure rate among patients carrying bacilli resistant to present drugs, or perhaps by reducing the relapse rate among patients co-infected with HIV (Global Alliance for TB Drug Development, www.tballiance.org). The ultimate tool may be a vaccine that can prevent TB, even among people who are already infected (Lietman and Blower 2000) (AREAS Global TB Vaccine Foundation, www.aeras.org).

All forecasts of health trends are surrounded by uncertainties, and there are numerous weaknesses in the data on which our calculations are based. For example, TB incidence is estimated by various indirect methods because incidence is rarely measured directly in longitudinal field surveys. Similarly, TB death statistics would ideally come from reliable vital registration systems, but most African countries do not systematically or accurately record deaths by cause. In addition, the assessment of regional trends in incidence requires judgements about the reliability of case notifications reported by individual countries. With these and other doubts about the accuracy of data and forecasts, regional plans for TB control must include procedures for improving the reliability of data.

Although this paper focuses on tuberculosis, the process of controlling TB cannot be carried out in isolation. TB control must be seen as contributing to the wider development agenda set out by the MDGs (poverty reduction, gender equality, partnership development, AIDS control etc). Reciprocally, effective TB control requires, especially in Africa, the strengthening of health staffing and infrastructure, and immediate action on HIV prevention (not just AIDS treatment). The eight MDGs and associated interventions are not a disconnected list, and maximum gains will be made when all the proposed interventions are put in place together.

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