

Scale up: meeting targets in global tuberculosis control

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Despite great progress, global targets for tuberculosis case detection and cure might not be reached by 2005. In particular, there is a serious case-detection gap between estimated annual incident cases and those reported under the strategy for tuberculosis control branded as DOTS. Delays in reaching targets result in lack of effect on incidence of disease, which is of particular concern in regions where incidence is increasing—eg, sub-Saharan Africa and the former Soviet Union. Four key actions will speed up progress towards reaching global targets: 1) equipping national tuberculosis programmes to have a stewardship role in engaging all health providers in implementing the DOTS strategy; 2) establishing the feasibility of national certification systems of DOTS coverage; 3) promoting community action to contribute to patient care and to voice demand for the DOTS strategy; and 4) increasing support to sub-Saharan Africa for implementation of a strategy of expanded scope to counter HIV-1-fuelled tuberculosis.

Despite great progress during the past decade in the adoption and implementation of the strategy for tuberculosis control branded as DOTS, the global targets of detecting at least 70% of all estimated infectious cases and curing at least 85% of those might not be reached by 2005. Here, we provide the background to this situation by first outlining the principles of tuberculosis control that underpin the DOTS strategy and the formulation of the global targets. We then briefly review global progress over the past 5 years towards reaching the targets, and global trends in disease epidemiology. Consideration of the specific constraints identified in the highest-burden countries and of the main overall constraints to scaling up implementation of the DOTS strategy leads to key proposals for overcoming these constraints and for speeding up progress towards meeting the global control targets for tuberculosis.

Background

Principles of tuberculosis control

Although new and improved drugs, methods of diagnosis, and vaccines will be developed eventually, which could greatly decrease the global burden of tuberculosis, until then control of the disease is based on interruption of its transmission through the rapid identification and cure of infectious cases. The five elements of the DOTS strategy represent the policy package for delivering the essential basics of tuberculosis case finding and cure (panel).¹

Formulation of global control targets

In 1991, all countries adopted a World Health Assembly (WHA) resolution, setting two tuberculosis control targets for the year 2000—to detect at least 70% of all new infectious cases and to cure at least 85% of those detected.² These targets were based on the observation that, in the absence of control measures (case finding and chemotherapy), each infectious case causes on average about 20 new infections, out of which two new cases will

arise (one infectious and one non-infectious).^{3,4} The reproduction number—ie, the number of new cases that arise from a single infectious case—is therefore one for infectious cases, and the tuberculosis epidemic is in a steady state. Achievement of an 85% cure rate and a 70% case-detection rate would reduce both the prevalence of infectious cases and the number of infected contacts by about 40%.³ Since the assumption is that in the absence of control measures the prevalence of sputum smear-positive cases is twice the incidence of sputum smear-positive TB cases,³ achievement of these targets will reduce the incidence of infectious cases by 20%. The choice of these global targets in 1991 indicated the need to achieve a great epidemiological effect by reaching targets that field experience had shown were feasible in countries in which incidence of tuberculosis was high.

Mathematical modelling is useful to analyse the expected effect on incidence of disease in relation to varying cure and case-detection rates.⁵ Figure 1 shows the expected annual rate of decline in tuberculosis incidence for different cure rates and case-detection rates in a population with a stable annual incidence of disease of about 100 in 100 000 per year (in the absence of effective control measures). Typically, without implementation of the DOTS strategy, case detection is about 70% or more, with an average cure rate of only 50%—eg, in parts of southeast Asia and Latin America. As national tuberculosis programmes scale up implementation of the DOTS strategy, the cure rate increases with a consequent decline in incidence. Reaching the 70% case detection and 85% cure rate targets leads to an expected decline in annual incidence of 6–7% per year.

Five elements of DOTS strategy for tuberculosis control

- Sustained government commitment to control
- Diagnosis based on quality-assured sputum-smear microscopy mainly among symptomatic patients presenting to health services
- Standardised short-course chemotherapy for all cases under proper case-management conditions, including direct observation of treatment
- Uninterrupted supply of quality-assured drugs
- A standard recording and reporting system, enabling programme monitoring by systematic assessment of treatment outcomes of all patients registered

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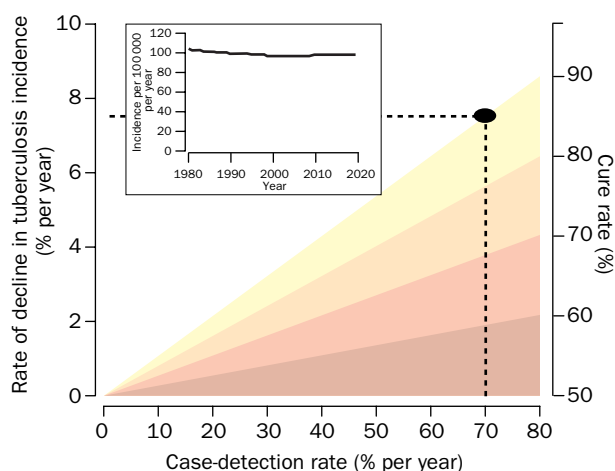


Figure 1: Rate of decline in tuberculosis incidence when modelled against changes in case-detection and cure rate
Inset shows annual incidence rate per 100 000 of baseline population before implementation of DOTS strategy. Dashed line indicates expected annual rate of decline in incidence if WHO targets for case-detection and cure rates are met.

The national programme in Peru, for example, achieved these targets during the 1990s, and now boasts a more than 90% case-detection rate, a 93% cure rate, and an average annual rate of decline in tuberculosis incidence of 6.5% per year.⁶

Monitoring of implementation of DOTS strategy

WHO coordinates a global tuberculosis monitoring and assessment project in which countries report annual progress in implementation of the DOTS strategy.⁷ The main indicators of progress are population coverage by the DOTS strategy, and cure and case-detection rates.⁸ Measurement of population coverage by the DOTS strategy is not easy. Countries report DOTS coverage as the proportion of the population that lives in administrative areas with access, in principle, to tuberculosis care consistent with the DOTS strategy. However, in practice, the proportion of the population with access to the DOTS strategy is less than this administrative measure, on account of several possible barriers—geographic, financial, and cultural—to access within the administrative area. The cure rate is reported by each country on the basis of a cohort analysis of treatment outcomes of registered patients. Since practice varies considerably between countries in documenting negative sputum smears on completion of treatment, for practical purposes we consider the treatment success rate (cure + treatment completion) as a proxy for cure rate.⁸ The formula for calculation of the case-detection rate in each country is: annual new sputum smear-positive pulmonary tuberculosis reported under DOTS divided by the estimated annual new sputum smear-positive pulmonary tuberculosis incidence for a particular country.⁸ The numerator is derived annually from country reports of registered cases⁸ and the denominator is an estimate based on various inputs, including surveys of prevalence of tuberculosis infection and disease, vital registration data, and independent assessments of quality of surveillance systems.^{9,10}

Global progress from 1998–2003

That the year 2000 targets would not be met on time became apparent as early as 1998. This realisation served to galvanise international activities. WHO convened an ad-hoc committee to review barriers to progress and make

recommendations to strengthen implementation of the DOTS strategy and accelerate its effect.¹¹ Most of the recommendations have materialised, including the establishment of a global alliance named the Stop TB Partnership,¹² the creation of a Global Drug Facility, providing quality drugs against tuberculosis to countries in need,¹³ a Ministerial Conference in Amsterdam in 2000 to call for renewed political commitment,¹⁴ and a strategic focus on the 22 highest-burden countries, responsible for 80% of estimated global tuberculosis incidence. In 2000, the World Health Assembly postponed the date for achievement of targets until 2005.¹⁵

WHO published the Global DOTS Expansion Plan (GDEP)¹⁶ in 2001. The plan is based on two factors: the preparation in each country of a mid-term (at least 5 years) DOTS expansion plan, and the establishment of a mechanism for interagency co-ordination to ensure that all relevant partners contribute to the implementation of the national plan.¹⁶ In 2001, the Stop TB Partnership launched the Global Plan to Stop TB (GPSTB),¹⁷ setting out the comprehensive range of implementation and research activities needed to reach the WHO targets by 2005. Further work¹⁸ has clarified the financial resources necessary. However, the 2003 global report on tuberculosis,⁸ reporting information from 2000–01, suggests that WHO targets might not be met even by 2005. Estimated global incidence in 2000 was 8.2 million cases,⁹ the global case detection rate under DOTS was about half (30%) the geographic DOTS strategy coverage (60%), and the average global cure rate was about 84%. The two main concerns are that, first, the case-detection rate is low, and second, the 85% treatment success target might be reached globally but not in sub-Saharan Africa largely because of the HIV-1 epidemic.

Trends in disease incidence

The absence of a global decline in tuberculosis incidence is largely due to its increased incidence in sub-Saharan Africa and in the former Soviet Union (figure 2).⁸ Apart from these two regions, annual incidence is declining slowly (0.5–1% per year). Reduction of tuberculosis in the developing world to rates similar to those in industrialised countries will take decades unless methods change.¹⁹ The greater the delay in achieving the global targets for tuberculosis control, the greater the burden of illness and death in the meantime. We must, therefore, ascertain and understand the determinants of the global case-detection gap under the DOTS strategy, and analyse the relation between incidence of disease and changes in case-detection and cure rate in sub-Saharan Africa and in the former Soviet Union.

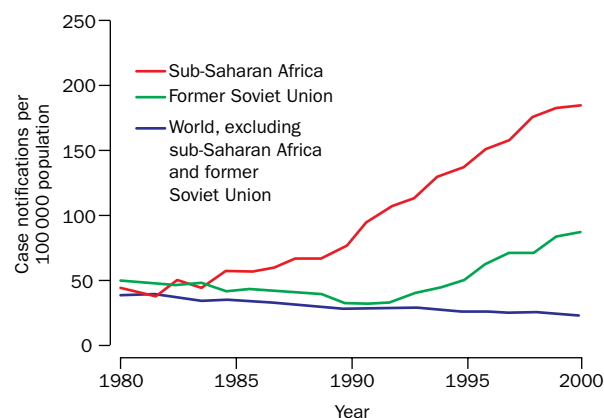


Figure 2: Tuberculosis notification rates per 100 000 population

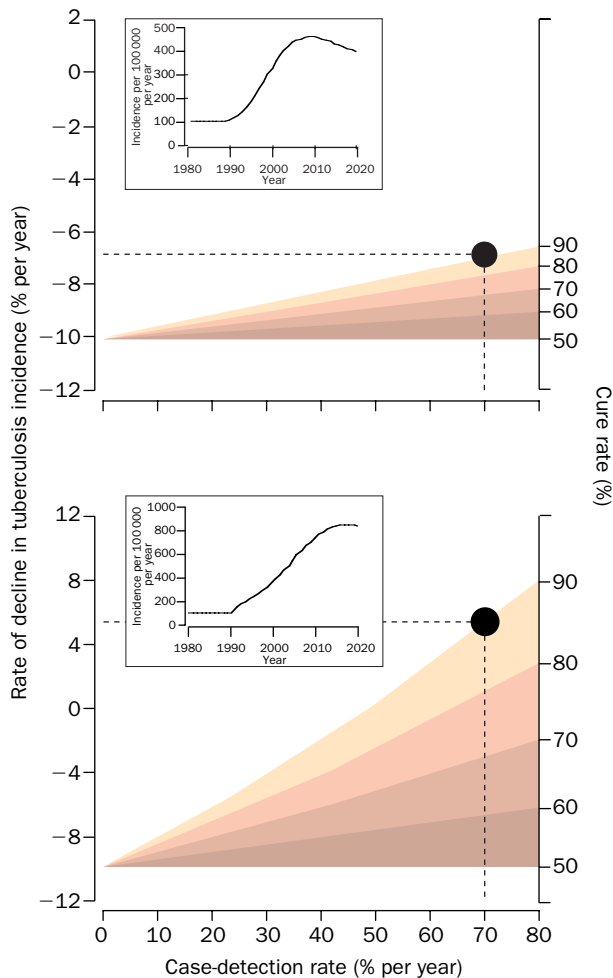


Figure 3: **Relation between case-detection and cure rates, and rate of decline in tuberculosis in populations with high HIV-1 prevalence (upper) and in those with an increased breakdown to disease after infection (lower)**

Insets show annual incidence rate per 100 000 of baseline population before implementation of DOTS strategy. Dashed line indicates expected annual rate of decline in incidence if WHO targets for case-detection and cure rates are met.

Case-detection gap

The globally estimated case-detection rate under the DOTS strategy lags well behind geographic DOTS strategy coverage. Linear extrapolation implies that, with 100% geographic coverage, only half of all new infectious cases would be detected under the DOTS strategy. A similar comparison of geographic coverage versus case detection under the DOTS strategy per country reveals that full geographic DOTS strategy coverage is paralleled by achievement of the 70% case-detection target in only a few settings.²⁰ Up to the end of the 1990s, national tuberculosis programmes have concentrated on implementing the DOTS strategy through government health facilities, in the expectation that increased availability of high-quality diagnostic methods and care through government health facilities would result in increased case detection. The case-detection gap under the DOTS strategy, however, suggests that the 70% target might not be reachable by merely expanding access to care under the DOTS strategy through governmental services.

The discrepancy between geographic DOTS coverage and rate of case detection would be easily explained if the country-by-country estimates of the denominator were

systematically and substantially too high. However, different estimation exercises (albeit with similar methods) undertaken over the past decade have produced quite consistent results.^{9,10,21–23} Furthermore, some countries do reach case-detection rates of 70% or more under the DOTS strategy, lending support to the validity of these estimates or, at least, the absence of a systematic error.⁸

Since there is no clear evidence of gross overestimation of the denominator, new estimates based on yet-to-be-defined methods will probably not greatly change the overall picture. Thus, the likely reason for the low case-detection rate is that the numerator remains much lower than expected—ie, many infectious patients do not have access to health facilities where tuberculosis care (diagnosis and treatment) consistent with the DOTS strategy is available. This view is confirmed qualitatively by observations²⁴ that in countries with full geographic DOTS strategy coverage, patients often receive care from health providers who are not linked to the national tuberculosis programmes and whose diagnosis and treatment practices are not consistent with the DOTS strategy—eg, private doctors, clinicians working in health facilities in different branches of the public-health system, and those working for employer health services. Many cases therefore remain unregistered and inadequately treated.

Sub-Saharan Africa and former Soviet Union

Nine of the 22 highest-burden countries are in two areas of the world where tuberculosis incidence is rising rapidly (figure 2); eight are in sub-Saharan Africa, and the ninth, Russia, is at the heart of the former Soviet Union. Figure 3 shows the results of modelling the annual rate of decline in tuberculosis incidence expected for different cure and case-detection rates in populations with a high HIV-1 prevalence and in those with a high rate of breakdown to disease after infection.

In high HIV-1-prevalence populations—eg, many countries in eastern and southern Africa—tuberculosis incidence is increasing at 10% per year (figure 3) without full implementation of the DOTS strategy. During the phase of rapidly increasing tuberculosis incidence driven by HIV-1, achieving the targets of 70% case detection and 85% cure rate will only slow down the rate of tuberculosis increase to 7% per year. The results of modelling indicate that measures to fully implement the DOTS strategy—ie, improving its quality of delivery and engaging all health providers—will not alone reverse the HIV-1-driven increase in tuberculosis in sub-Saharan Africa. As the HIV-1 epidemic continues to rise in this region,²⁵ incidence of tuberculosis will also continue to rise. A strategy of expanded scope is necessary to counter the HIV-1-driven tuberculosis epidemic, consisting of measures aimed directly against tuberculosis (full implementation of the DOTS strategy with intensified case-finding and preventive treatment) and measures against HIV-1 (and therefore indirectly against tuberculosis), including prevention of HIV-1 transmission and provision of antiretrovirals.²⁶

The assumption in the former Soviet Union is that the 10% yearly increase in tuberculosis incidence rate is a consequence of increased susceptibility to infection and to increased breakdown to disease after infection. The model predicts that attaining the targets of 70% case detection and 85% cure rate will result in a trend reversal from a 10% increase to a 4% decrease in tuberculosis incidence. This trend is expected because when the case reproduction number is higher than under stable conditions (figure 1), the effect of DOTS is greater. Measures to fully implement the DOTS strategy should result in achievement of the targets.

Country	Cumulative tuberculosis incidence, 2001 (%) ¹¹	DOTS coverage, 2001 (%) ¹¹	Case-detection rate under DOTS, 2001 (%) ¹¹	Success rate under DOTS, 2000 (%) ¹¹	HIV-1 prevalence in individuals aged 15–49 years (%) ²⁹	Main identified constraints and corresponding challenges in overcoming them*
India	21.5	45	n.a.	84	0.8	1,2
China	38.7	68	20	95	0.1	2,3,4
Indonesia	45.6	98	21	87	0.1	2,5,6
Bangladesh	49.5	95	28	83	<0.1	4,6,7
Nigeria	52.9	55	20	79	5.8	1,2,5,8
South Africa	56.1	77	85	66	20.1	5,8
Pakistan	59.1	24	10	74	0.1	2,4
Philippines	61.9	95	57	88	<0.1	2,5
Russian Federation	64.3	15	31	68	0.9	1,3,4,9
Ethiopia	66.6	70	42	80	6.4	4,7,8
Kenya	68.8	100	47	80	15.0	4,8
Democratic Republic of the Congo	70.8	70	61	78	4.9	4,7
Vietnam	72.5	99.8	84	92	0.3	2,7
Tanzania	74	100	47	78	7.8	4,7,8
Brazil	75.3	32	78	84	0.7	3,5
Thailand	76.3				1.8	5,6
Zimbabwe	77.3	100	47	69	33.7	1,4,8
Cambodia	78.3	100	41	91	2.7	5,7
Uganda	79.3	100	52	63	5.0	4,7,8
Burma	80.2	78	60	82	n.a.	1,4,7
Afghanistan	81		n.a.		n.a.	4,7

Data presented by managers of national tuberculosis programmes in the 22 countries at the third DEWG meeting, held in Montreal, Canada, in October, 2002.

*Constraints (challenges in overcoming them): 1=insufficient funding (how to convince governments of developing countries and development partners to mobilise more funds for tuberculosis control); 2=lack of involvement of full range of health-care providers in delivery of DOTS strategy (how to equip national programmes for stewardship of control activities, involving full range of health providers); 3=insufficient political commitment (how to advocate and lobby for improved political commitment); 4=inadequate human resource capacity (how to develop increased human resource capacity); 5=inadequate quality of implementation of the DOTS strategy (how to provide technical assistance for improved quality of implementation of DOTS strategy); 6=aligning tuberculosis control with health-system reforms (how to maximise opportunities and minimise threats for control, arising from health-system reforms); 7=poor primary care infrastructure (how to develop and strengthen primary-care infrastructure); 8=tuberculosis epidemic exacerbated by HIV-1 (how to improve collaboration between tuberculosis and HIV programmes in tackling HIV-related disease); 9=high prevalence of multi-drug-resistant tuberculosis (how to extend the provision of better management of multi-drug-resistant disease).

Factors preventing full implementation of DOTS strategy in 22 high-burden countries, and ways to overcome these constraints

Constraints to progress in implementing DOTS Constraints in highest-burden countries

In 1998, the ad-hoc committee set up by WHO recommended a particular focus on the 22 countries that bear 80% of the tuberculosis burden.¹¹ The DOTS Expansion Working Group (DEWG) has, since then, identified the specific constraints, and challenges in overcoming them, in each of these countries as a preliminary step to finding solutions (table).⁸

Overall constraints

Progress towards reaching the global targets for tuberculosis control through the DOTS strategy depends on closing the case-detection gap and maintaining or improving cure rate (depending on the region). Looking at the country-specific constraints in the table from a broader perspective, we have identified three main constraints.

Quality of delivery of care

The provision of technical assistance to the national tuberculosis programmes through a network of agencies coordinated by the DEWG provides a system of programme quality control. Common difficulties noted during programme reviews include under-recognition of suspected cases of tuberculosis, underdiagnosis of disease, and under-reporting of cases (WHO, unpublished country reports). For example, even a reputable programme noted that up to 14% of smear-positive cases detected in laboratories were not registered for treatment.²⁷ Until now, delivery of care consistent with the DOTS strategy has largely been through government health facilities. Constant attention to quality control is necessary as delivery of care expands beyond government health facilities to other health providers.

Access to DOTS strategy

The patient and health-system factors that limit access to care in those areas that have adopted the DOTS strategy

vary nationally and internationally. Health-system factors include lack of human resources, limited laboratory capacity, inconvenient opening hours and location of health facilities, and limited awareness of tuberculosis among some health workers. Patient factors include limited tuberculosis awareness, inability to afford costs related to diagnosis and treatment, and cultural constraints to health-care access.

Non-adoption of DOTS strategy

For various reasons, some patients obtain care from health providers whose delivery of tuberculosis care is not consistent with the DOTS strategy. First, some countries have not adopted the DOTS strategy, and most have not achieved full geographic DOTS-strategy coverage.⁸ Second, not all care provision through government health facilities is linked to the national tuberculosis programme and follows its standards. Dependent on the setting, this situation is true for different branches of health facilities under the Ministry of Health,²⁸ or for other government health facilities not under the Ministry of Health—eg, urban administrations,²⁹ social-security schemes, prisons,³⁰ and army health facilities. Third, many non-government health providers are often not linked to the national tuberculosis programme—eg, private practitioners,²⁴ academic institutions, non-governmental organisation (NGO) services, and traditional healers.

The standard of care is generally lower among health providers not delivering care consistent with the DOTS strategy. Such providers cannot generally guarantee the following three elements of the DOTS strategy: diagnosis based on quality-assured sputum-smear microscopy; standardised short-course chemotherapy under proper case-management conditions (including direct observation of treatment); and recording and reporting of cases and their treatment results.

Scaling up implementation of DOTS strategy

With slow progress in global implementation of the DOTS strategy, WHO targets are probably not within reach by 2005. Implementation of the DOTS strategy therefore needs to be urgently scaled up while we wait for new and improved methods (drugs, diagnostics, and vaccines) to deal with tuberculosis. This need is particularly great in regions where disease incidence is increasing—namely, in the former Soviet Union and in sub-Saharan Africa.

Government and non-government contributions are essential to overcome the general and country-specific constraints to scaling up implementation of the DOTS strategy. We propose four key approaches to overcome the difficulties of poor quality, inadequate access, and non-adoption of the DOTS strategy, and thereby to improve global case-detection and cure rates.

Engagement of health-care providers

Governments have the general responsibility for stewardship of health activities that involve all health providers. With respect to tuberculosis control, national tuberculosis programmes within individual countries should be equipped a) to coordinate involvement of the full range of health providers in delivering care under the DOTS strategy to ensure full access and to close the case-detection gap, and b) to ensure quality control (of the technical components of diagnosis, treatment, and monitoring) and a high cure rate. Overall, government stewardship involves the proper organisation, management, distribution, and location of health facilities, and stewardship offered by the national tuberculosis programme involves a specialised managerial and monitoring system and an integrated care-delivery approach.³¹ Governments should consider reform of legislative and regulatory frameworks in support of the engagement of the full range of health providers in sustained and high-quality implementation of the DOTS strategy.³²

There is increasing experience of engaging different health providers under stewardship of national tuberculosis programmes: government services, whether Ministry of Health (nationally and locally administrated) services or not—eg, social-security schemes, prisons, military—and non-government services—eg, NGOs, community groups,³³ private practitioners,³⁴ and employers.³⁵ In practice, all health providers should either refer patients to public-health facilities that deliver tuberculosis care under the DOTS strategy, or that deliver care consistent with the DOTS strategy in collaboration with the national tuberculosis programme. To engage the full range of health providers, many countries will need to undertake legislative and policy reform and invest in developing human-resource capacity (for strengthened stewardship and service delivery). The coordinated provision of technical assistance to national programmes through the DEWG provides the opportunity to scale up the contribution of all health-care providers and to ensure full implementation of the DOTS strategy.

Certification of DOTS strategy coverage

Since national tuberculosis programmes are responsible both for implementation of the DOTS strategy and for the effectively subjective assessment (in the absence of formal assessment criteria) of geographic DOTS strategy coverage, overestimation of the latter is not surprising. Such overestimation contributes to the case-detection gap. Methods used to assess DOTS strategy coverage need to go beyond geographic coverage by public-health services towards a more accurate indication of population access to care. One approach is to establish the feasibility of a certification

system for the full range of health providers who deliver tuberculosis care consistent with the DOTS strategy. Certification would involve assessment by the national tuberculosis programmes of population access and quality of care delivery (using standard treatment outcomes), with validation as part of the technical assistance coordinated by the DEWG to enhance objectivity. Pilot studies of this approach are necessary.

Promotion of community action

Communities have played an important part in tuberculosis control in developed countries.³⁶ They are also essential to demand and deliver care under the DOTS strategy in developing countries. Two key roles include supporting patients in adhering to and completing treatment,³⁷ and voicing demand for quality care under the DOTS strategy. There is a particular need for expansion of community contribution to care in sub-Saharan Africa, where results of pilot projects³³ in several different settings have shown this aim to be feasible, effective, affordable, and cost-effective in maintaining a satisfactory cure rate. Local NGOs are crucial to mobilise people and organise action.³³ In collaboration with financial and technical partners, national tuberculosis programmes should intensify efforts to scale up community contribution to care consistent with the DOTS strategy.

Various social mobilisation techniques can support advocacy initiatives by NGOs and patient groups, which can help articulate demand for high quality care delivered through full implementation of the DOTS strategy. The Stop TB Partnership should support and help to develop these initiatives. Advocacy should not only be aimed at care providers but also at local and higher administrative and political authorities. Local NGOs are well placed to plan and implement initiatives for overcoming barriers to access to care, which are designed to match the local need—eg, through incentive and enabler schemes to promote case-holding.

Intensified efforts for sub-Saharan Africa

Implementation of the strategy of expanded scope to control HIV-1-related tuberculosis depends on sustained and intensified efforts, backed by increased external support because of the severity of the epidemics of tuberculosis and HIV-1 and their overlap, the slowness of change in sexual behaviour to control HIV-1 transmission,³⁸ the scale of the challenge to make antiretroviral drugs widely available, and the limited absorption capacity of health systems. On account of the latter, the increasing resources becoming available³⁹—eg, from the Global Fund to fight AIDS, Tuberculosis, and Malaria, and from the World Bank—should help to strengthen health infrastructure, especially primary care, to be able to deliver commodities, eg, antiretrovirals.

The same public-health principles underpin the DOTS strategy for tuberculosis control and strategies for control of other communicable diseases. Thus, investment in implementing the DOTS strategy can serve to strengthen general health systems, as well as providing a model for making antiretroviral drugs widely available.⁴⁰

Conclusion

A full year remains before 2005, the global target date for achieving 70% case detection and 85% cure rate. The Stop TB Partnership provides the mechanism for international partners and the governments of high-incidence countries to speed up progress in implementation of the DOTS strategy. Achievement of this aim depends on intensified action to fully engage all health providers in implemen-

tation of the DOTS strategy and to mobilise communities for advocacy and patient support. Development and implementation of the proposed certification mechanism for delivery of care consistent with the DOTS strategy will result in better assessment of the case-detection gap.

The four key approaches outlined should help most regions to make great progress towards achieving the global targets. Tuberculosis incidence is declining worldwide, except in the former Soviet Union and in sub-Saharan Africa. To turn the rising trend of incidence in these regions depends on rapid scale-up of implementation of the DOTS strategy and, in sub-Saharan Africa, full implementation of measures to control HIV-1 transmission and treat HIV-1 infection and HIV-1-related diseases. Since overall achievement of 70% case detection and 85% cure rate globally will be a hollow victory unless each individual region also achieves the targets, sub-Saharan Africa needs a specific focus of international attention.

With two slightly different estimation methods, both the GDEP¹⁶ and the GPSTB¹⁷ estimated that a total of US\$6 billion would be needed over the 5 years from 2000 to 2005 to achieve the 2005 global targets. The governments of the highest-burden countries are expected to cover an estimated 69% of the loss. Thus, the global financial gap stands at about US\$300 million annually. Closing this financial gap and systematically applying the four approaches outlined, are paramount to achieve the 2005 targets and, subsequently, to decrease the global burden of tuberculosis.

Contributors

G Elzinga and M Raviglione conceived the paper. All authors contributed to analysis of problems and generation of proposed solutions, and to preparation of the report.

Conflict of interest statement

None declared.

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