

Papers

Achieving the millennium development goals for health

Cost effectiveness analysis of strategies for tuberculosis control in developing countries

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This article is part of a series examining the cost effectiveness of strategies to achieve the millennium development goals for health

Abstract

Objective To assess the costs and health effects of tuberculosis control interventions in Africa and South East Asia in the context of the millennium development goals.

Design Cost effectiveness analysis based on an epidemiological model.

Setting Analyses undertaken for two regions classified by WHO according to their epidemiological grouping—Afr-E, countries in sub-Saharan Africa with very high adult and high child mortality, and Sear-D, countries in South East Asia with high adult and high child mortality.

Data sources Published studies, costing databases, expert opinion.

Main outcome measures Costs per disability adjusted life year (DALY) averted in 2000 international dollars (\$Int).

Results Treatment of new cases of smear-positive tuberculosis in DOTS programmes cost \$Int6-8 per DALY averted in Afr-E and \$Int7 per DALY averted in Sear-D at coverage levels of 50-95%. In Afr-E, adding treatment of smear-negative and extra-pulmonary cases at a coverage level of 95% cost \$Int95 per DALY averted; the addition of DOTS-Plus treatment for multidrug resistant cases cost \$Int123. In Sear-D, these costs were \$Int52 and \$Int226, respectively. The full combination of interventions could reduce prevalence and mortality by over 50% in Sear-D between 1990 and 2010, and by almost 50% between 2000 and 2010 in Afr-E.

Conclusions DOTS treatment of new smear-positive cases is the first priority in tuberculosis control, including in countries with high HIV prevalence. DOTS treatment of smear-negative and extra-pulmonary cases and DOTS-Plus treatment of multidrug resistant cases are also highly cost effective. To achieve the millennium development goal for tuberculosis control, substantial extra investment is needed to increase case finding and implement interventions on a wider scale.

Introduction

Every year almost nine million people contract tuberculosis, and almost two million die from the disease.¹ In many parts of the world it is reappearing in almost epidemic proportions, mainly because of coinfection with HIV/AIDS and increasing multidrug resistance.^{1 2} In developing countries, tuberculosis is second only to HIV/AIDS as the most common cause of adult death and is one of the top public health problems almost everywhere. For this reason, the United Nations millennium development goals

Box 1: Goals, targets, and indicators for tuberculosis control

Millennium development goal 6: Combat HIV/AIDS, malaria, and other diseases

Target 8: Have halted by 2015 and begun to reverse the incidence of malaria and other major diseases

Indicator 23: Prevalence and death rates associated with tuberculosis

Indicator 24: Proportion of tuberculosis cases detected and cured under DOTS (the internationally recommended tuberculosis control strategy)

Stop TB Partnership targets

By 2005: At least 70% of people with infectious tuberculosis will be diagnosed (that is, under the DOTS strategy), and at least 85% cured

By 2015: The global burden of tuberculosis (prevalence and death rates) will be reduced by half compared with 1990 levels. This means reducing prevalence to $\leq 150/100\ 000$ and deaths to $\leq 15/100\ 000$ /year by 2015 (including cases coinfecting with HIV). The number of people dying from tuberculosis in 2015 should be < 1 million, including those coinfecting with HIV

By 2050: The global incidence of tuberculosis disease will be < 1 case/million population/year (the criterion for tuberculosis "elimination" adopted in the United States)

include targets and indicators related to tuberculosis control, which have been adopted and extended by the international Stop TB Partnership. The targets include reversing tuberculosis incidence by 2015, halving tuberculosis prevalence and mortality by 2015 (compared with 1990), and diagnosing 70% of new smear-positive cases and curing 85% of these cases by 2015 (see box 1).³

For many countries, the targets will not be achieved at current rates of progress.⁴ This is despite the existence of effective interventions to diagnose and cure tuberculosis, and thus to decrease transmission. A key question, therefore, is whether the correct mix of interventions is currently being used, and what strategies should be scaled up if current international efforts to raise extra funds for health care are successful. Cost and cost effectiveness analyses can provide valuable inputs to these decisions by identifying the most efficient ways of deliver-



Further details of the methods used appear on bmj.com

Box 2: Definitions of types of tuberculosis and recommended control strategies

Types of tuberculosis

Pulmonary tuberculosis—Commonest form of tuberculosis (about 70-90% of all cases), which affects the lungs

Smear-positive pulmonary tuberculosis—The most infectious cases can be diagnosed bacteriologically by means of sputum smear microscopy (about 60% of all pulmonary cases)

Smear-negative pulmonary tuberculosis—Diagnosed on the basis of clinical signs and symptoms, a chest x ray, and failure to respond to a standard course of antibiotics

Extra-pulmonary tuberculosis—Tuberculosis that occurs outside the lungs

Drug susceptible tuberculosis—Tuberculosis bacteria susceptible to standard antituberculosis drugs

Multidrug resistant tuberculosis—Resistance to at least rifampicin and isoniazid, the two most effective first line antituberculosis drugs

Recommended tuberculosis control strategies

DOTS—Internationally recommended tuberculosis control strategy, developed in the mid-1990s and has been implemented in 182 countries. It has five essential components: political commitment, diagnosis by sputum smear microscopy, short course treatment with standard first line drug regimens, a reliable drug supply, and a recording and reporting system that allows assessment of individual patient outcomes and overall programme performance

DOTS-Plus—Strategy for management of cases with multidrug resistant tuberculosis, developed by the World Health Organization and partner agencies from 1999. It is based on the same principles as the DOTS strategy but includes use of sputum cultures and drug susceptibility tests for diagnosis, and use of second line as well as first line drugs

Stop TB strategy—Developed by WHO during 2005, designed to guide tuberculosis control efforts during 2006 to 2015. It builds on the DOTS and DOTS-Plus strategies and has six major components: pursuing expansion and enhancement of DOTS; addressing tuberculosis and HIV coinfection, multidrug resistant tuberculosis, and other special challenges; helping to strengthen healthcare systems; engaging all healthcare providers; empowering patients and communities; and promoting research. The strategy underpins the second “Global Plan to Stop TB,” which also covers the period 2006-15

ing diagnosis and treatment services at different levels of resource availability.

The main interventions recommended to control tuberculosis are short course treatment with first line drugs for drug-susceptible tuberculosis (smear-positive pulmonary, smear-negative pulmonary, and extra-pulmonary) within the framework of the DOTS strategy, and treatment of cases with multidrug resistant tuberculosis with longer and more complex drug regimens that include second line as well as first line drugs within the framework of the DOTS-Plus strategy (see box 2 for definitions).

To date, most economic studies of tuberculosis interventions in developing countries have evaluated short course treatment for drug susceptible, smear-positive pulmonary tuberculosis,⁵⁻⁷ since these cases are the most infectious and therefore of greatest concern from a public health perspective. Most of these studies are from Africa,⁸ although Asia has the highest burden of tuberculosis. Two studies in Africa have also reported the cost effectiveness of treating smear-negative cases.^{9 10} There is one published study, from Peru, of treatment for multidrug resistant tuberculosis with first line and second line drugs.¹¹

Table 1 Levels of tuberculosis control globally and in the two regions Afr-E and Sear-D in 2003 and target levels

Indicator	Global	Afr-E	Sear-D
Cases diagnosed in DOTS programmes (%):			
2003	45	56	47
2015 target	≥70	≥70	≥70
Cure rates in DOTS programmes (%):			
2003	82	72	86
2015 target	≥85	≥85	≥85
No of cases treated in DOTS-Plus programmes in 2003			
	<10 000	Very small	Very small
Tuberculosis incidence (per 100 000):			
1990	121	156	177
2003	140	443	178
2015 target	<121	<156	<177
Tuberculosis prevalence (per 100 000):			
1990	309	318	532
2003	245	590	307
2015 target	154	159	266
Tuberculosis mortality (per 100 000):			
1990	28	45	47
2003	28	96	35
2015 target	14	22	23

Most of these studies did not assess the impact of interventions on transmission, and most used indicators of effectiveness that are specific to tuberculosis control. This prevents the cost effectiveness of tuberculosis control being compared with that of interventions for other diseases. Moreover, interventions have generally been considered individually and not in combination with complementary control strategies—for example, the cost effectiveness of providing simultaneous treatment for new smear-positive and new smear-negative and extra-pulmonary cases has not been evaluated even though in practice they are usually undertaken at the same time.

Five years after the adoption of the millennium declaration, an up to date assessment of the cost effectiveness of tuberculosis control strategies is needed. In this paper we address the question of what are the costs and effects of treatment of new smear-positive cases and of new smear-negative and extra-pulmonary cases in DOTS programmes, and of DOTS-Plus treatment for multidrug resistant cases that have not responded to first line treatments, both singly and in combination. Our analysis includes assessment of the impact of interventions on transmission, a generic measure of effectiveness, and covers Asia as well as Africa.

Methods

General approach

In common with the other papers in this series,¹²⁻¹⁷ we evaluated interventions for two particular regions classified by the World Health Organization according to their epidemiological characteristics: Afr-E, which includes countries in sub-Saharan Africa with very high adult and high child mortality, and Sear-D, which includes countries in South East Asia with high adult and high child mortality.¹⁸ Table 1 shows the existing levels of tuberculosis control globally and for these two regions.

Interventions run for the 10 years 2000-9, and we included all benefits accruing during the period 2000-100. We evaluated the three standard levels of geographical coverage—50%, 80%, and 95%—which in this case mean the percentage of eligible cases living in areas where treatment is available. We assessed costs from a societal perspective, and used a population model to translate disease-specific results into a generic measure of health

effects. Details of the standardised analytical approach are available in Evans et al.¹⁸

Interventions

Because the technologies available to tackle tuberculosis are well known, we restricted our analysis to four interventions:

Minimal DOTS—Treatment in DOTS programmes for new smear-positive cases only. We assume that the percentage of cases diagnosed and treated in areas covered by DOTS increases linearly from year 2000 levels to the WHO target of 70% in 2009 and that the cure rate is at the WHO target level of 85% from 2000 to 2009. In areas not covered by DOTS, we assume that no cases are treated. In all areas, no cases are treated from 2010 onwards.

Full DOTS—As for minimal DOTS plus treatment of smear-negative and extra-pulmonary cases in DOTS programmes. We assume that the percentage of cases diagnosed and cured is the same as for smear-positive cases. We did not consider the treatment of smear-negative and extra-pulmonary cases separately because in practice it would not be introduced in the absence of treatment for the more infectious smear-positive cases.

Minimal DOTS plus resistant cases—As for minimal DOTS plus treatment of multidrug resistant cases in DOTS-Plus programmes with an 18 month regimen that includes first and second line drugs. We assume that patients are tested for multidrug resistance after failing treatment with the short course of first line drugs. Treatment of multidrug resistant tuberculosis must be combined with the basic strategy because multidrug resistance does not exist without initial treatment. We assume the cure rate to vary from 48% (baseline analysis) to 70% (sensitivity analysis).¹¹

Full combination—As for full DOTS plus DOTS-Plus treatment for multidrug resistant tuberculosis as defined above.

The maximum scale at which we considered each intervention is much greater than the level of tuberculosis control efforts in 2003 (table 1).

Estimating health effects

We estimated health effects in three steps. Firstly, we calibrated a published tuberculosis-HIV model^{19 20} to produce tuberculosis incidence, prevalence, and mortality for each region that matched those observed between 1950 and 2000. We applied parameters similar to those that were specified in the original paper.¹⁹ Our regional population estimates, including background mortality, were based on WHO estimates.²¹ Regional estimates of HIV/AIDS incidence, prevalence, and mortality for the period were based on internal projections by UNAIDS (the Joint UN Programme on HIV/AIDS). Full details of the model and parameters are available in the appendix on bmj.com.

Secondly, we used the calibrated tuberculosis-HIV model to project incidence, prevalence, and mortality for the period 2000–100 for the base case of no interventions, and then for each of the intervention scenarios.

Thirdly, we used the population model PopMod²² to combine the projected incidence, prevalence, and mortality data with the standard health state valuations²³ to estimate the population impact of the different interventions in terms of healthy years lived.¹⁸ We ran the model for the length of time necessary for all people affected by the interventions to have died. The difference between the healthy years lived in each intervention scenario and the no-intervention scenario is the health gain of the intervention, or the number of disability adjusted life years (DALYs) averted.

Estimating costs

We based our estimates of the resources required—diagnostic tests, drug use, health centre visits for supervision and monitoring, and hospitalisation—for each intervention on WHO treatment protocols and expert opinion of actual practice. We based drug costs on the latest WHO negotiated prices, with a mark-up for international and local transportation costs.^{24 25} Unit costs of health centre visits and hospital inpatient days were taken from Adam et al,²⁶ while those for laboratory tests and x rays were based on the best available international cost information included in WHO's costing database. We combined unit costs with patterns of resource use to estimate the cost per patient treated. We then calculated total patient costs as the cost per patient treated multiplied by the number of patients treated (calculated as the annual incidence of disease from the model multiplied by the relevant coverage level and then by the percentage of cases diagnosed and treated in the areas covered).

We estimated the costs of running the programmes (that is, costs above the individual patient level, such as managerial staff) using a standardised approach.¹⁸ All costs are reported in international dollars (\$Int) for the year 2000, and the conversion from \$Int to US\$ is explained elsewhere.¹⁸ Details of all cost calculations are found in the appendix on bmj.com.

Results

The tuberculosis model replicated the strong increase in the incidence of infectious disease in Afr-E from around 1990, with an annual growth rate of about 10% between 1990 and 2000. In Sear-D, the tuberculosis model estimates an annual decline in incidence of 1% in the same period.

Intervention effects

Tables 2 and 3 show the health effects, costs, and cost effectiveness of the different interventions in Afr-E and Sear-D. When only smear-positive cases are treated in DOTS programmes and the geographical coverage level is 95%, an average of 0.62 million are treated in Afr-E and 1.38 million in Sear-D each year. The annual cost averages \$Int366m in Afr-E and \$Int536m in Sear-D. The total number of DALYs averted per year averages 44.8 million in Afr-E and 76.6 million in Sear-D. Adding treatment of smear-negative and extra-pulmonary cases or of multidrug resistance cases increases costs considerably but increases the DALYs averted only slightly. Increasing the coverage level from 50% to 95% roughly doubles both costs and effects for each of the four interventions considered.

In both regions, treating only smear-positive cases is the most cost effective intervention, with an average cost per DALY averted of \leq \$Int8 at all coverage levels. The next most cost effective intervention in both regions is treatment for both smear-positive and smear-negative and extra-pulmonary cases at a coverage level of 95%, at a cost per DALY averted of \$Int95 in Afr-E and \$Int52 in Sear-D. This is followed by implementing the full combination of interventions, including treatment for multidrug resistant tuberculosis, at a cost per DALY averted of \$Int123 in Afr-E and \$Int226 in Sear-D.

The figure shows the order in which interventions should be introduced according to their cost effectiveness for Afr-E (that is, the expansion path). Treating only smear-positive cases at a coverage level of 50% would be introduced first. With more resources, coverage would be expanded to 80% and then to 95%. With yet more resources, treatment of smear-negative and extra-pulmonary cases would be introduced, followed by the addition

Table 2 Annual numbers of patients treated, total costs in international dollars (\$Int), total effects, and average and incremental cost effectiveness for various tuberculosis control interventions in the Afr-E region

Intervention*	Coverage level	No of patients treated (millions)			Yearly costs (\$Int millions)	Yearly DALYs averted (millions)	Cost per DALY averted (\$Int)	
		New smear-positive cases	New smear-negative and extra-pulmonary cases	Multidrug resistant cases			Average	Incremental†
Minimal DOTS	50%	0.33	NA	NA	146.3	23.6	6.2	6.2
	80%	0.52	NA	NA	262.6	37.7	7.0	8.2
	95%	0.62	NA	NA	366.3	44.8	8.2	14.7
Full DOTS	50%	0.32	0.27	NA	242.4	24.9	9.7	NA
	80%	0.52	0.43	NA	439.6	39.9	11.0	NA
	95%	0.62	0.51	NA	612.2	47.4	12.9	94.5
Minimal DOTS plus resistant cases	50%	0.32	NA	0.01	184.1	24.1	7.6	NA
	80%	0.51	NA	0.02	343.4	38.6	8.9	NA
	95%	0.61	NA	0.03	495.9	45.9	10.8	NA
Full combination	50%	0.32	0.27	0.01	279.1	25.5	11.0	NA
	80%	0.51	0.43	0.02	518.6	40.8	12.7	NA
	95%	0.61	0.51	0.03	739.4	48.4	15.3	123.2

Values are averages over the 10 year evaluation period. Costs are given in international dollars (a hypothetical unit of currency that has the same purchasing power that the US\$ has in the United States at a given point in time) and can be converted in US\$ for a reference country in a region. For example, cost estimates in Afr-E in \$Int should be divided by 4.5 to obtain US\$ cost estimates for Kenya. Details of this approach are discussed elsewhere.¹⁸

NA=Not applicable.

*See methods section for details of interventions.

†Incremental costs per DALY averted measure the increase in cost divided by the increase in effects when a new intervention is added to an existing intervention. Values are not shown for interventions that are dominated (more costly but less effective than others).

of treatment for multidrug resistant cases. The expansion path is similar in Sear-D.

In Sear-D, our model suggests that implementing the full combination of interventions could reduce tuberculosis prevalence and mortality by 71% and 64% respectively between 1990 and 2010. In Afr-E prevalence and mortality increase substantially between 1990 and 2000, because of the HIV epidemic, but could fall by 50% and 40% respectively between 2000 and 2010.

Sensitivity and uncertainty analyses

We undertook various sensitivity analyses, and table 4 shows the results for Afr-E. Changes to the parameters that were most uncertain, such as cure rate of standardised second line treatment of multidrug resistant cases, had little impact on our cost per DALY averted results. Similar results applied for Sear-D (data not shown).

Discussion

Since the early 1990s, short course drug treatment for new smear-positive cases of tuberculosis has been promoted as one of the most cost effective healthcare interventions available, based on a study in three low income African countries in the late 1980s that reported a cost per DALY averted of US\$1-3.⁵ Our updated analysis, covering countries with some of the highest rates of tuberculosis infection in sub-Saharan Africa and South East Asia, supports this result, with the cost per DALY averted at around \$Int8 (<US\$2) in both regions. The addition of the other interventions that we considered—treatment of smear-negative and extra-pulmonary cases in DOTS programmes and treatment of multidrug resistant cases in DOTS-Plus programmes—is also highly cost effective compared with commonly used benchmarks.¹⁷

Table 3 Annual numbers of patients treated, total costs in international dollars (\$Int), total effects, and average and incremental cost effectiveness for various tuberculosis control interventions in the Sear-D region

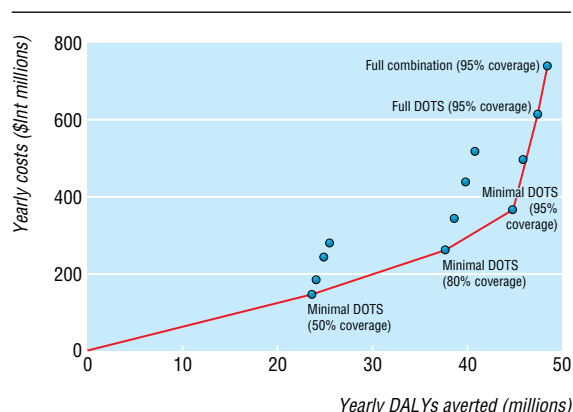
Intervention*	Coverage level	No of patients treated (millions)			Yearly costs (\$Int millions)	Yearly DALYs averted (millions)	Cost per DALY averted (\$Int)	
		New smear-positive cases	New smear-negative and extra-pulmonary cases	Multidrug resistant cases			Average	Incremental†
Minimal DOTS	50%	0.73	NA	NA	293.1	40.3	7.3	NA
	80%	1.16	NA	NA	442.6	64.5	6.9	6.9
	95%	1.38	NA	NA	536.4	76.6	7.0	7.8
Full DOTS	50%	0.72	0.25	NA	473.7	43.9	10.8	NA
	80%	1.15	0.40	NA	731.7	70.2	10.4	NA
	95%	1.37	0.47	NA	883.4	83.4	10.6	51.6
Minimal DOTS plus resistant cases	50%	0.72	NA	0.10	500.4	41.3	12.1	NA
	80%	1.15	NA	0.16	773.4	66.0	11.7	NA
	95%	1.36	NA	0.18	932.6	78.4	11.9	NA
Full combination	50%	0.71	0.25	0.10	677.4	44.8	15.1	NA
	80%	1.14	0.39	0.15	1056.7	71.6	14.7	NA
	95%	1.35	0.47	0.18	1272.7	85.1	15.0	226.4

Values are averages over the 10 year evaluation period. Costs are given in international dollars (a hypothetical unit of currency that has the same purchasing power that the US\$ has in the United States at a given point in time) and can be converted in US\$ for a reference country in a region. For example, cost estimates in Sear-D in \$Int should be divided by 5.2 to obtain US\$ cost estimates for India. Details of this approach are discussed elsewhere.¹⁸

NA=Not applicable.

*See methods section for details of interventions.

†Incremental costs per DALY averted measure the increase in cost divided by the increase in effects when a new intervention is added to an existing intervention. Values are not shown for interventions that are dominated (more costly but less effective than others).



Expansion path for tuberculosis interventions in Afr-E region according to average and incremental cost effectiveness. (See methods for description of interventions)

Limitations of study

Our study has several limitations. Some of these are related to the general methodological approach to cost effectiveness analysis, and are discussed in more detail elsewhere in this series.¹⁸ Others are more specific to tuberculosis control.

In the absence of better data, we assumed that key model parameters such as tuberculosis transmission rates are the same across regions. Studies of the transmissibility of multidrug resistant tuberculosis have produced variable results, and our assumption that multidrug resistant tuberculosis and drug susceptible tuberculosis are equally transmissible contrasts with the more conservative range of assumptions considered in an earlier study.¹¹

Evidence about the costs of increasing the percentage of tuberculosis cases that are treated in DOTS programmes

remains limited, and, despite building in extra costs to allow for this, we may have underestimated them. The only published cost data for DOTS-Plus programmes are from Peru.

Our study results may not be directly generalisable to other settings because of differences in regional epidemiological and economic profiles. However, the results of studies for other regions that used similar methods show similar results.²⁷

The strengths of our study include the use of a tuberculosis model that has been published and widely applied,²⁰ consideration of combinations of interventions, inclusion of transmission in the analysis, use of a generic measure of effectiveness, and testing of important assumptions through sensitivity analyses.

Implications of results

Our results have three major policy implications. Firstly, they reinforce the principle that treatment of smear-positive cases in DOTS programmes must be the basis of any tuberculosis control strategy, as has become standard practice in almost all control programmes.

Secondly, they show that there is a strong economic case for treating smear-negative and extra-pulmonary cases in DOTS programmes and for treating multidrug resistant cases in DOTS-Plus programmes, as set out in WHO's new "Stop TB" strategy and the second global plan for tuberculosis control (see box 2).

Finally, our study shows that substantial scaling up of all three interventions is needed in the next 10 years if the millennium development goal and related targets for tuberculosis control are to be reached. In particular, the case detection rate must be improved so that many more tuberculosis cases are diagnosed and successfully treated, in line with existing targets. Improving the case detection rate will mean ensuring that people who currently have access to treatment facilities are covered and that coverage is expanded to people who do not currently have

Table 4 Results of sensitivity analysis on costs per DALY averted for Afr-E region at 95% coverage level

Change in parameter	Intervention*	Total costs (\$Int millions)	DALYs averted (millions)	Cost per DALY averted (\$Int)†	
				Average	Incremental†
Linear increase in case detection rate over 10 years from current rate to 60% (instead of 70%)	Minimal DOTS	356.3	41.8	8.5	15.3
	Full DOTS	590.2	44.2	13.3	NA
	Minimal DOTS plus resistant cases	483.3	42.8	11.3	NA
	Full combination	715.0	45.2	15.8	103.5
Immediate increase in case detection rate from current rate to 70% (instead of linear increase over 10 years)	Minimal DOTS	387.1	49.8	7.8	14.0
	Full DOTS	656.8	52.5	12.5	NA
	Minimal DOTS plus resistant cases	522.5	50.9	10.3	NA
	Full combination	789.4	53.6	14.7	105.1
Cure rate for first line treatment 75% (instead of 85%)	Minimal DOTS	383.6	35.2	10.9	19.6
	Full DOTS	645.8	37.3	17.3	NA
	Minimal DOTS plus resistant cases	587.5	37.1	15.8	NA
	Full combination	845.6	39.1	21.6	118.1
Incidence of tuberculosis in year 2000 20% higher compared with base case analysis	Minimal DOTS	398.9	29.2	13.7	24.6
	Full DOTS	678.4	35.1	19.3	NA
	Minimal DOTS plus resistant cases	547.9	33.0	16.6	39.0
	Full combination	824.3	35.8	23.0	98.2
Unit cost of outpatient visit \$Int14.36 (instead of \$Int7.18)	Minimal DOTS	517.8	44.8	11.6	43.4
	Full DOTS	843.8	47.4	17.8	NA
	Minimal DOTS plus resistant cases	717.5	45.9	15.6	NA
	Full combination	1040.3	48.4	21.5	143.7
Cure rate for second line treatment of resistant cases 70% (instead of 48%)	Minimal DOTS plus resistant cases	495.3	46.1	10.7	NA
	Full combination	738.5	48.6	15.2	87.8
Proportion of failed treatment cases that are multidrug resistant 29% (instead of 58%)	Minimal DOTS plus resistant cases	496.6	45.6	10.9	NA
	Full combination	740.5	48.2	15.4	105.8

Costs are given in international dollars (\$Int), described in detail elsewhere.¹⁸

*See methods section for details of interventions.

†For minimal DOTS intervention in comparison with the intervention at 80% coverage.

NA=Not applicable. Intervention is dominated by other, more cost effective, options.

What is already known on this topic

Studies have shown that DOTS treatment of new cases of smear-positive tuberculosis to be a cost effective intervention in Africa, but data for other regions of the world or for treating smear-negative and extra-pulmonary cases and multidrug resistant tuberculosis are scarce

Most studies have not considered the impact of interventions on transmission or interactions among interventions and have used measures of effectiveness that do not allow comparisons with other health interventions

What this study adds

This comprehensive and standardised analysis of different interventions in Africa and South East Asia accounts for both transmission and interactions among interventions

Treatment of smear-positive, smear-negative, and extra-pulmonary cases in DOTS programmes and treatment of multidrug resistant cases in DOTS-Plus programmes are cost effective in both regions

These results provide a strong case for substantial investment to improve case finding and to implement these interventions on a much wider scale

access. Such scaling up would bring the millennium development goal and related Stop TB Partnership targets within reach in South East Asia and achieve major progress towards these targets in Africa.

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- 1 World Health Organization. *Global tuberculosis control—surveillance, planning, financing WHO report 2005*. Geneva: WHO, 2005.
- 2 World Health Organization. *Anti-tuberculosis drug resistance in the world report No 3, 2004*. Geneva: WHO, 2005. (www.who.int/gtb/publications/drugresistance/2004/index.htm.)
- 3 United Nations. *United Nations millennium declaration General Assembly resolution A/RES/55/2*. New York: UN, 2000.
- 4 Dye C, Watt CJ, Bleed DM, Hosseini SM, Ravighione MC. Evolution of tuberculosis control and prospects for reducing tuberculosis incidence, prevalence, and deaths globally. *JAMA* 2005;293:2767-75.
- 5 Murray CJ, DeJonghe E, Chum HJ, Nyangulu DS, Salomao A, Styblo K. Cost effectiveness of chemotherapy for pulmonary tuberculosis in three sub-Saharan African countries. *Lancet* 1991;338:1305-8.
- 6 Floyd K. Costs and effectiveness—the impact of economic studies on TB control. *Tuberculosis (Edinb)* 2003;83:187-200.

- 7 Borgdorff MW, Floyd K, Broekmans JF. Interventions to reduce tuberculosis mortality and transmission in low- and middle-income countries. *Bull World Health Organ* 2002;80:217-27.
- 8 Maher D, Mikulencak M. *What is DOTS? A guide to understanding the WHO-recommended TB control strategy known as DOTS*. Geneva: World Health Organization, 1999.
- 9 Nganda B, Wang'ombe J, Floyd K, Kangangi J. Cost and cost-effectiveness of increased community and primary care facility involvement in tuberculosis care in Machakos District, Kenya. *Int J Tuberc Lung Dis* 2003;7:S14-20.
- 10 Floyd K, Skeva J, Nyirenda T, Gausi F, Salaniponi F. Cost and cost-effectiveness of increased community and primary care facility involvement in tuberculosis care in Lilongwe District, Malawi. *Int J Tuberc Lung Dis* 2003;7:S29-37.
- 11 Suárez PG, Floyd K, Portocarrero J, Alarcon E, Rapiti E, Ramos G, et al. Feasibility and cost-effectiveness of standardized second-line drug treatment for chronic tuberculosis patients: a national cohort study in Peru. *Lancet* 2002;359:1980-9.
- 12 Evans DB, Adam T, Tan-Torres Edejer T, Lim SS, Cassels A, Evans TG, et al. Achieving the millennium development goals for health: Time to reassess strategies for improving health in developing countries? *BMJ* 2005;331:1133-6.
- 13 Adam T, Lim SS, Mehta S, Bhutta ZA, Fogstad H, Mathai M, et al. Achieving the millennium development goals for health: Cost effectiveness analysis of strategies for maternal and neonatal health in developing countries. *BMJ* 2005;331:1107-10.
- 14 Tan-Torres Edejer T, Aikins M, Black R, Wolfson L, Hutubessy R, Evans DB. Achieving the millennium development goals for health: Cost effectiveness analysis of strategies for child health in developing countries. *BMJ* 2005 Nov 10; epub ahead of print (doi:10.1136/bmj.38652.550278.7C).
- 15 Morel CM, Lauer JA, Evans DB. Achieving the millennium development goals for health: Cost effectiveness analysis of strategies to combat malaria in developing countries. *BMJ* 2005 Nov 10; epub ahead of print (doi:10.1136/bmj.38639.702384.AE).
- 16 Hogan DR, Baltussen R, Hayashi C, Lauer JA, Salomon JA. Achieving the millennium development goals for health: Cost effectiveness analysis of strategies to combat HIV/AIDS in developing countries. *BMJ* 2005 Nov 10; epub ahead of print (doi:10.1136/bmj.38643.368692.68).
- 17 Evans DB, Lim SS, Adam T, Tan-Torres Edejer T, for the WHO-CHOICE MDG Team. Achieving the millennium development goals for health: evaluation of current strategies and future priorities for improving health in developing countries. *BMJ* 2005 Nov 10; epub ahead of print (doi:10.1136/bmj.38658.675243.94).
- 18 Evans DB, Tan-Torres Edejer T, Adam T, Lim SS, for the WHO-CHOICE MDG Team. Achieving the millennium development goals for health: Methods to assess the costs and health effects of interventions for improving health in developing countries. *BMJ* 2005;331:1137-40.
- 19 Stover J. *TB-HIV spreadsheet model. A model for illustrating the effects of the HIV epidemic on tuberculosis*. Washington, DC: Futures Group International, POLICY project, 1998.
- 20 Dye C, Garnett GP, Sleeman K, Williams BG. Prospects for worldwide tuberculosis control under the WHO DOTS strategy. *Lancet* 1998;352:1886-91.
- 21 World Health Organization. Population, death rates, and reproductive rates for the 14 GBD subregions. www3.who.int/whosis/menu.cfm?path=evidence,cea,cea_epi,cea_epi_demographic (accessed 1 Nov 2005).
- 22 Lauer JA, Murray CJL, Roehrich K, Wirth H. PopMod: a longitudinal four-state population model with two disease states and comorbidity. *Cost Eff Resour Alloc* 2003;1:6.
- 23 Murray CJL, Lopez AD, eds. *The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries and risk factors in 1990 and projected to 2020*. Cambridge, MA: Harvard University Press for the World Health Organization and World Bank, 1996.
- 24 Johns B, Baltussen R, Adam T, Hutubessy RCW. Programme costs in the economic evaluation of health interventions. *Cost Eff Resour Alloc* 2003;1:1.
- 25 Johns B, Baltussen R. Accounting for the costs of scaling up health interventions. *Health Econ* 2004;13:1117-24.
- 26 Adam T, Evans DB, Murray CJL. Econometric estimation of country-specific hospital costs. *Cost Eff Resour Alloc* 2003;1:3.
- 27 World Health Organization. WHO-CHOICE (choosing interventions that are cost effective) project. www.who.int/choice. (Accepted 12 October 2005)

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