



Global Tuberculosis Control

*A short update to
the 2009 report*



World Health
Organization

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A SHORT UPDATE TO THE 2009 REPORT



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Abbreviations

ACSM	advocacy, communication and social mobilization	HIV	human immunodeficiency virus
AFR	WHO African Region	ICD-10	International Statistical Classification of Diseases
AIDS	acquired immunodeficiency syndrome	IPT	isoniazid preventive therapy
AMR	WHO Region of the Americas	IRR	incidence rate ratio
ARI	annual risk of infection	ISTC	International Standards for Tuberculosis Care
ART	antiretroviral therapy	MDG	Millennium Development Goal
CBC	community-based TB care	MDR-TB	multidrug-resistant tuberculosis (resistance to, at least, isoniazid and rifampicin)
CFR	case fatality rate	NGO	nongovernmental organization
CPT	co-trimoxazole preventive therapy	NTP	national tuberculosis control programme or equivalent
DOT	directly observed treatment	PAL	Practical Approach to Lung Health
DOTS	the basic package that underpins the Stop TB Strategy	PPM	Public-Private Mix
DRS	drug resistance surveillance or survey	SEAR	WHO South-East Asia Region
DST	drug susceptibility testing	TB	tuberculosis
ECDC	European Centre for Disease Prevention and Control	UNAIDS	Joint United Nations Programme on HIV/AIDS
EMR	WHO Eastern Mediterranean Region	UNITAID	international facility for the purchase of diagnostics and drugs for diagnosis and treatment of HIV/AIDS, malaria and TB
EU	European Union	USAID	United States Agency for International Development
EUR	WHO European Region	VR	vital registration
FIND	Foundation for Innovative New Diagnostics	WHA	World Health Assembly
GDF	Global TB Drug Facility	WHO	World Health Organization
GLC	Green Light Committee	WPR	WHO Western Pacific Region
GLI	Global Laboratory Initiative	XDR-TB	TB caused by MDR strains that are also resistant to a fluoroquinolone and, at least, one second-line injectable agent (amikacin, kanamycin and/or capreomycin)
Global Fund	The Global Fund to fight AIDS, Tuberculosis and Malaria		
Global Plan	Global Plan to Stop TB, 2006-2015		
GNI	gross national income		
HBC	high-burden country of which there are 22 that account for approximately 80% of all new TB cases arising each year		

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Summary

This report is a short update to the WHO report on global tuberculosis (TB) control that was published in March 2009, based on data collected from July to September 2009. It is designed to fill an 18-month gap between the full reports of 2009 (in March) and 2010 (in October), following changes to the production cycle of the report in 2009 that have been made to ensure that future reports in the series¹ contain more up-to-date data.

The report includes the latest (2008) estimates of the global burden of TB (incidence, prevalence and mortality). It also includes an assessment of progress in implementing the Stop TB Strategy and the Global Plan to Stop TB, which in combination have set out what needs to be done to achieve the 2015 global targets for TB control. These targets are that incidence should be falling by 2015 (MDG Target 6.c) and that prevalence and mortality rates should be halved by 2015 compared with their level in 1990. The latest data (up to 2010) on financing for TB control are presented, and progress towards the 2015 targets at global and regional level is analysed. The report also features updates about the work of the Global Laboratory Initiative and the WHO Global Task Force on TB Impact Measurement, and highlights achievements in TB control during the period 1995–2008 as well as the success of a new initiative in 2009 in which global TB data collection went online.

In 2008, there were an estimated 8.9–9.9 million incident cases of TB, 9.6–13.3 million prevalent cases of TB, 1.1–1.7 million deaths from TB among HIV-negative people and an additional 0.45–0.62 million TB deaths among HIV-positive people (classified as HIV deaths in the International Statistical Classification of Diseases), with best estimates of 9.4 million, 11.1 million, 1.3 million and 0.52 million, respectively.

The number of notified cases of TB in 2008 was 5.7 million, equivalent to 55–67% of all incident cases, with a best estimate of 61% (10% less than the Global Plan milestone of a case detection rate of 71% in 2008). Among patients in the 2007 cohort, 86% were successfully treated; this is the first time that the target of 85% (first set in 1991) has been exceeded at global level. Progress in implementation of interventions to reduce the burden of TB in HIV-positive people has continued; in 2008, 22% of TB patients knew their HIV status (up from 20% in 2007) including 45% of patients in the African Region; 0.3 million people were enrolled on co-

trimoxazole preventive therapy; and 0.1 million people were enrolled on antiretroviral therapy. Almost 30 000 cases of multidrug-resistant TB (MDR-TB) were notified in 2008; this is 11% of the total number of cases of MDR-TB estimated to exist among cases notified in 2008. Diagnosis and treatment of MDR-TB need to be rapidly expanded.

Funding for TB control has increased since 2002, and is expected to reach US\$ 4.1 billion in 2010. Funding gaps remain, however; compared with the Global Plan, funding gaps amount to at least US\$ 2.1 billion in 2010.

Globally, incidence rates peaked at 143 (range, 136–151) cases per 100 000 population in 2004. The world as a whole is on track to achieve MDG Target 6.c, as are eight of nine epidemiological subregions (the exception being African countries with a low prevalence of HIV). Six epidemiological subregions (Central Europe, Eastern Europe, the Eastern Mediterranean, high-income countries, Latin America and the Western Pacific) appear to have achieved the Stop TB Partnership target of halving the 1990 prevalence rate and four (Central Europe, high-income countries, Latin America and the Western Pacific) appear to have achieved the Stop TB Partnership target of halving the 1990 mortality rate, in advance of the target year of 2015. Prevalence and mortality rates are falling in all other regions with the exception of African countries with a low prevalence of HIV, although reaching the global target appears impossible in the African Region. Globally, the gulf between prevalence and mortality rates in 2008 and the target levels in African countries make it unlikely that 1990 prevalence and death rates will be halved by 2015 for the world as a whole.

Reductions in disease burden achieved to date follow fourteen years of intensive efforts at global, regional and country levels to implement the DOTS strategy (1995–2005) and its successor, the Stop TB Strategy (2006–). Between 1995 and 2008, a cumulative total of 36 million TB patients were successfully treated in DOTS programmes, and up to 6 million deaths were averted. To consolidate the major progress in global TB control achieved in recent years, intensified efforts to plan, finance and implement the range of interventions and approaches included in the Stop TB Strategy, according to the targets established in the Global Plan to Stop TB, are needed.

¹ The 2009 report was the 13th annual report in a series that started in 1997.

Introduction

The World Health Organization (WHO) has published an annual report on global tuberculosis (TB) control every year since 1997. The main purpose of the report is to provide a comprehensive and up-to-date assessment of the TB epidemic and progress in controlling the disease at global, regional and country levels in the context of global targets set for 2015. The 2009 report (the 13th in the series) was published, as in all previous years, on 24 March – World TB Day.

Despite its advantages, a major limitation of publishing the report on World TB Day is that much of the most important data are from two years prior to the year that the report is published. For example, with a production cycle of approximately nine months (from the date of the original request to countries for reporting of data to the date of publication, with data validation, review, analysis, writing, layout and printing in between), the 2009 report included case notifications as well as estimates of disease burden (incidence, prevalence and mortality) from 2007. The latest year for which most of the data on implementation of the Stop TB Strategy were available was also 2007.

To make the report more up-to-date, with an emphasis on data from the most recent complete calendar year, a decision to change the production cycle was taken by WHO in mid-

2009. From 2010 onwards, annual reports will be published around October.

Publishing a report in October 2010 that includes data from 2009 requires two rounds of global TB data collection between the 2009 and 2010 reports. The 2009 round of data collection was conducted, as in previous years, from July to September. The next round of data collection (the 2010 round) will occur much earlier, around March/April 2010.¹

This short update to the 2009 WHO report on global TB control is designed to fill the 18-month gap between the major reports of March 2009 and October 2010. The main part of the report presents the latest data on the global TB epidemic and progress in TB control, up to and including data compiled in 2009. The following topics are covered (in the order in which they appear):

- Methods;
- The global burden of TB (incidence, prevalence and mortality) in 2008;
- Global targets for reducing the burden of TB, set for 2015;
- The WHO Stop TB Strategy and the Global Plan to Stop TB, which in combination set out what needs to be done to achieve the 2015 targets;

BOX 1

What's new in this report?

This report contains more up-to-date data than any report on global TB control previously published by WHO, with all of the key results based on data collected in 2009. The report is published only two months after completing the 2009 round of global TB data collection, in which data were reported by 198 countries and territories representing >99% of the world's population and global TB cases.

Estimates of the burden of TB (incidence, prevalence and mortality) have been improved following 18 months of work by an expert group convened by the WHO Global Task Force on TB Impact Measurement as well as increased availability of data. The number of countries with direct measurements of HIV infection in TB patients has risen to 103 (up from 64 in the 2008 round of data collection), and TB mortality is now based on direct measurements from vital registration systems for 89 countries (compared with three for which such direct measurements were used in previous reports). Estimates have also been updated using in-depth analyses and country consultations conducted during a series of regional workshops and country missions in 2009. All estimates are provided with uncertainty intervals; this will become routine practice in all future reports. Estimates of the number of TB cases occurring among women are also included.

The report focuses on progress towards achieving the targets that have been set for 2015 within the context of the Millennium Development Goals and the Global Plan to Stop TB. Compared with previous reports, assessment of whether the target of a 70% case detection rate has been achieved is given much less attention. This reflects the fact that the target year (2005) has now passed, that there are difficulties in measuring this indicator, and increasing emphasis on achieving universal access to health care.

Besides reporting of data collected in 2009, the report also highlights achievements in TB control during the period 1995–2008, features updates about the work of the Global Laboratory Initiative and the WHO Global Task Force on TB Impact Measurement, and describes the success of a new initiative in 2009 in which global TB data collection went online.

¹ The exact timing will be defined after further consultations with those involved in reporting data.

- Progress in implementing the Stop TB Strategy and the Global Plan to Stop TB. Particular attention is given to analysis of case notifications, treatment outcomes, case detection rates, the role of public-private mix (PPM) initiatives in engaging all health-care providers in TB control, implementation of collaborative TB/HIV activities and the management of multi-drug resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB);
- Financing for TB control;
- Progress towards the 2015 targets for reducing the burden of TB. This section provides an up-to-date assessment

of progress towards achieving the targets for reductions in incidence, prevalence and mortality;

- Improving measurement of the burden of TB. This section summarizes the current status of the work of the WHO Global Task Force on TB Impact Measurement;
- Conclusions.

The report update also contains an annex that explains the methods used to produce estimates of disease burden. This annex has been included following important updates to the methods used to produce such estimates in 2009 (**BOX 1**).

1. Methods

For the 2009 round of data collection, data collection forms were updated from those used in 2008. Efforts were made to shorten the forms and to simplify the data being requested wherever possible. Two versions of the data collection form were developed (a long form and a short form). The short form was adapted for use in high-income countries (that is, countries with a gross national income per capita \geq US\$ 11 906 in 2008, as defined by the World Bank) and/or low-incidence countries (defined as countries with an incidence rate <20 cases per 100 000 population or <10 cases in total). In consultation with WHO regional offices, some countries that met the criteria for receiving the short form were instead requested to complete the long form. This included countries that had in previous years provided the more detailed financial data requested on the long form, and island states in the Western Pacific Region.

Both forms requested data on the following topics: case notifications and treatment outcomes, including breakdowns by age, sex and HIV status; an overview of services for the diagnosis and treatment of TB; laboratory diagnostic services; human resource development; drug management; monitoring and evaluation, including impact measurement; collaborative TB/HIV activities; management of drug-resistant-TB; TB control in vulnerable populations and high-risk groups; health systems strengthening and the integration of TB control in primary health care; TB infection control; the Practical Approach to Lung Health (PAL); PPM; advocacy, communication and social mobilization (ACSM); operational research; adoption and use of new technologies; the budgets of national TB control programmes (NTPs) in 2008 and 2009; utilization of general health services (hospitalization and outpatient visits) during treatment; and NTP expenditures in 2008.

For the first time in 2009, a web-based online system (<http://www.stoptb.org/tme>) was used to report and validate data in all regions except the European Region (**BOX 2**).¹ This new system was developed in mid-2009 and, despite initial concerns about how many countries would be willing to report data in this new way, proved to be a great

success. Feedback was universally positive, and 198 countries and territories (out of a total of 204 from which data were requested) representing $>99\%$ of the world's population and global TB cases reported data online. This included all countries in the African Region (46/46), the Eastern Mediterranean Region (22/22), the South-East Asia Region (11/11) and the Region of the Americas (36/36). The only missing reports were from Niue, Palau and Wallis and Futuna Islands (in the Western Pacific Region) and Austria, Monaco and San Marino (in the European Region). Following the deadline for reporting of data, all reports were carefully reviewed using a system of in-built validation checks (also available to country-based staff reporting data), with any follow-up queries returned to respondents online.

All data collected online in 2009 were imported to a master database that holds the TB-related data that have been compiled by WHO since 1995. Data from the two online systems used in the European Region² were uploaded to the master database separately. For the purposes of this report, all data in the global and European online systems as of 10 November 2009 were imported to the master database and used, together with historical data reported in previous years, to produce analyses and related tables and figures. Country respondents continue to have the option of updating or adding data to the online system, which will be used for analyses conducted for the 2010 report.

Three additional points should be highlighted:

- NTPs sometimes provide WHO with updated information for previous years, for incorporation in the global TB database. As a result, the data presented in this report may differ from those published in previous reports;
- Assessment of progress in implementing PPM initiatives and global efforts to strengthen laboratory services and

¹ The European Region already has its own system for online reporting of data.

² One system for countries of the European Union, managed by the European Centre for Disease Control and Prevention (ECDC); the other for all European countries, managed by the WHO Regional Office for the European Region.

BOX 2**Global TB data collection goes online in 2009**

In July 2009, WHO launched a new web-based system for collecting global TB data (<http://www.stoptb.org/tme>) to coincide with the distribution of the 2009 TB data collection forms. The new system allows representatives of NTPs as well as staff in WHO regional and country offices to complete the annual TB data collection forms online, replacing the previous system of recording data in spreadsheets and returning them to WHO by e-mail.

The new system has the following advantages:

- It provides a secure and easy approach for reporting of data;
- Data are automatically saved and stored in the global TB database, which also contains data collected in previous years;
- The task of reporting data can be shared among various colleagues;
- There is no need to complete the report at one time; users can log on and edit parts of the report as often as necessary before the deadline for reporting of data;
- Data are checked as they are being entered (real-time validation);
- Users have access to a report that highlights any inconsistencies among different sections of a report and any inconsistencies with data provided in previous years;
- Data entry screens are tailored for use by each country, and are available in English, French and Spanish;
- Users have access to summary tables showing real-time progress in reporting at regional and country levels;
- All changes are logged to ensure documentation of changes to data;
- There is no need to submit a paper form or an Excel spreadsheet.

Passwords were issued to NTP representatives as well as to WHO staff at global, regional and country levels. All those using the system were able to assess progress in completing reports and had a common platform for reviewing data and resolving queries.

The system was a great success: 198 reports were submitted online, and feedback from users was universally positive. In 2010, the system will be further developed, for example to allow easy downloading of data and the generation of country profiles.

impact measurement, both of which are featured in this report, draw on information from key informants as well as the WHO TB data collection form;

- The annual data collection form and database system used by WHO are designed for collecting aggregated national data. They are not recommended for collection of data within countries.¹

The **ANNEX** provides details about the methods used to produce estimates of disease burden. A fuller explanation of the methods used to compile and analyse other data is provided in the 2009 report on global TB control.² Summaries of data by region and country (comparable to the data included in Annexes 2 and 3 of the 2009 WHO report on global TB control) will be published on the web in early 2010.

2. The global burden of TB

2.1 Incidence

In 2008, there were an estimated 9.4 (range, 8.9–9.9 million) million incident cases (equivalent to 139 cases per 100 000 population) of TB globally (**TABLE 1, FIGURE 1**). This is an increase from the 9.3 million TB cases estimated to have occurred in 2007, as slow reductions in incidence rates per capita continue to be outweighed by increases in population. Estimates of the number of cases broken down by age and sex are being prepared by an expert group³ as part of an update to the Global Burden of Disease study,⁴ due to be published in 2010. Provisional analyses indicate that women account for an estimated 3.6 million cases (range, 3.4–3.8 million).

Most of the estimated number of cases in 2008 occurred in Asia (55%) and Africa (30%),⁵ with small proportions of cases in the Eastern Mediterranean Region (7%), the European Region (5%) and the Region of the Americas (3%). The 22 high-burden countries (HBCs, defined as the countries that rank first to 22nd in terms of absolute numbers of cases

and which have received particular attention at the global level since 2000) shown in **TABLE 1** account for 80% of all estimated cases worldwide. The five countries that rank first to fifth in terms of total numbers of incident cases in 2008 are India (1.6–2.4 million), China (1.0–1.6 million), South Africa (0.38–0.57 million), Nigeria (0.37–0.55 million) and Indonesia (0.34–0.52 million). India and China alone account for an estimated 35% of TB cases worldwide.

¹ WHO recommendations for recording and reporting within countries are described at: http://www.who.int/tb/dots/r_and_r_forms/en/index.html

² *Global tuberculosis control: epidemiology, strategy, financing. WHO report 2009*. Geneva, World Health Organization, 2009 (WHO/HTM/TB/2009.411).

³ This expert group is convened by the WHO Global Task Force on TB Impact Measurement. See also section 8 of this report.

⁴ This study will be an update to Lopez, A.D. et al. *Global burden of disease and risk factors*. New York, Oxford University Press and The World Bank, 2006.

⁵ Asia here means the WHO regions of South-East Asia and the Western Pacific. Africa means the WHO African Region.

TABLE 1
Estimated epidemiological burden of TB, 2008

	POPULATION	MORTALITY ^a			PREVALENCE			INCIDENCE			TB/HIV (%) ^b		
		BEST	LOW	HIGH	BEST	LOW	HIGH	BEST	LOW	HIGH	BEST	LOW	HIGH
Afghanistan ^c	27 208 324	9 201	3 923	17 964	73 621	41 568	117 413	51 456	41 165	61 748	-	-	-
Bangladesh	160 000 128	79 252	31 463	152 003	659 586	418 373	982 401	359 671	287 737	431 606	0.1	0.1	0.1
Brazil	191 971 504	7 284	2 714	15 249	55 694	12 407	112 628	89 210	73 395	107 052	21	17	25
Cambodia	14 562 008	11 449	4 792	22 262	99 007	58 019	154 174	71 382	57 106	85 658	15	12	18
China	1 337 411 200	160 086	64 683	329 249	1 175 048	408 980	2 203 167	1 301 322	1 041 057	1 561 586	1.7	0.2	2.7
DR Congo	64 256 636	49 417	19 701	94 920	423 350	267 368	631 855	245 162	196 130	294 195	8	6.4	9.6
Ethiopia	80 713 432	51 532	20 831	99 280	455 430	281 164	688 741	297 337	237 870	356 805	17	15	19
India	1 181 411 968	276 512	119 082	553 196	2 186 402	1 044 202	3 739 672	1 982 628	1 586 103	2 379 154	6.7	5.5	7.9
Indonesia	227 345 088	62 246	26 826	124 570	483 512	229 832	828 415	429 730	343 784	515 677	2.8	2.2	3.6
Kenya	38 765 312	7 365	2 653	16 092	71 340	17 436	143 440	127 014	101 611	152 417	45	36	54
Mozambique	22 382 532	8 155	3 050	16 805	105 097	64 989	159 949	94 045	75 236	112 854	60	48	72
Myanmar	49 563 020	28 219	12 181	55 967	230 921	117 941	385 034	200 060	160 048	240 072	11	8.8	13
Nigeria	151 212 256	94 826	33 833	181 508	922 575	625 992	1 299 190	457 675	366 140	549 210	27	22	33
Pakistan ^c	176 952 128	69 482	29 910	136 428	555 237	304 242	897 731	409 392	327 513	491 270	1.3	0.9	1.8
Philippines	90 348 440	46 996	19 943	91 576	378 098	217 088	597 488	257 317	205 853	308 780	0.3	0.2	0.3
Russian Federation	141 394 304	20 888	10 233	36 654	97 644	21 259	195 563	150 898	128 263	181 077	6	4.8	7.2
South Africa	49 667 628	19 349	8 257	39 064	301 079	142 051	514 650	476 732	381 386	572 079	71	70	73
Thailand	67 386 384	12 890	5 557	25 404	110 129	59 410	178 829	92 087	73 669	110 504	17	14	20
Uganda	31 656 864	8 526	3 217	17 516	108 524	66 744	165 870	98 356	78 685	118 027	59	47	71
UR Tanzania	42 483 924	5 447	2 601	9 395	54 956	36 198	77 478	80 653	75 613	86 414	47	38	56
Viet Nam	87 095 920	29 981	12 254	62 097	244 559	121 713	419 052	174 593	143 782	238 468	3.7	3.0	4.5
Zimbabwe	12 462 879	6 761	2 666	13 030	98 482	62 614	146 929	94 940	75 952	113 928	68	66	71
High-burden countries	4 246 251 879	1 065 865	878 777	1 515 671	8 890 291	7 611 821	11 596 165	7 541 660	7 076 649	8 124 477	14	13	16
AFR	804 865 016	385 055	323 496	554 236	3 809 650	3 429 910	4 473 415	2 828 485	2 685 695	3 009 670	38	34	41
AMR	919 896 357	29 135	24 186	41 611	221 354	181 300	345 426	281 682	264 584	302 394	13	12	16
EMR	584 354 906	115 137	78 633	195 852	929 166	702 873	1 342 886	674 585	601 842	764 917	2.2	1.8	2.7
EUR	889 169 869	55 688	44 905	76 173	322 310	250 661	539 714	425 038	398 508	457 822	5.6	4.8	6.4
SEAR	1 760 485 706	477 701	321 234	804 372	3 805 588	2 745 818	5 884 647	3 213 236	2 841 409	3 663 645	5.7	4.5	7.2
WPR	1 788 176 627	261 770	170 216	466 350	2 007 681	1 336 179	3 623 886	1 946 012	1 706 148	2 241 112	2.3	1.3	4.2
Global	6 746 948 481	1 324 487	1 090 085	1 667 321	11 095 750	9 607 465	13 307 187	9 369 038	8 877 248	9 923 728	15	13	16

^a Mortality excluding HIV, according to ICD-10.

^b Percentage of incident TB cases that are HIV-positive.

^c Estimates are provisional, pending further analyses and data collection in 2010.

- Indicates data not available.

Of the 9.4 million incident cases in 2008, an estimated 1.2–1.6 million (13–16%) were HIV-positive, with a best estimate of 1.4 million (15%) (TABLE 1, FIGURE 2). Of these HIV-positive cases, 78% were in the African Region and 13% were in the South-East Asia Region.

2.2 Prevalence

There were an estimated 11.1 million (range, 9.6–13.3 million) prevalent cases of TB in 2008 (TABLE 1),¹ equivalent to 164 cases per 100 000 population.

2.3 Mortality

In 2008, an estimated 1.3 million (range, 1.1–1.7 million) deaths, including 0.5 million (range, 0.45–0.62 million) deaths among women, occurred among HIV-negative incident cases of TB. This is equivalent to 20 deaths per 100 000 population (TABLE 1). There were an estimated 0.5 million deaths among incident TB cases who were HIV-positive (data

not shown); these deaths are classified as HIV deaths in the 10th revision of the International Statistical Classification of Diseases (ICD-10). The number of TB deaths per 100 000 population among HIV-negative people plus the estimated TB deaths among HIV-positive people equates to a best estimate of 28 deaths per 100 000 population.

2.4 MDR-TB and XDR-TB

There were an estimated 0.5 million cases of MDR-TB in 2007.² There are 27 countries (15 in the European Region)

¹ This figure is considerably lower than the estimate previously published for 2007. This reflects changes to methods used to estimate the number of prevalent cases of TB – see ANNEX.

² See *Global tuberculosis control: epidemiology, strategy, financing. WHO report 2009*. Geneva, World Health Organization, 2009 (WHO/HTM/TB/2009.411). Figures have not been updated for 2008 in this report because the methods used to produce estimates of MDR-TB are being refined. Updated estimates will be published in a report on drug-resistant TB that is due to be published by WHO in March 2010.

FIGURE 1
Estimated TB incidence rates, 2008

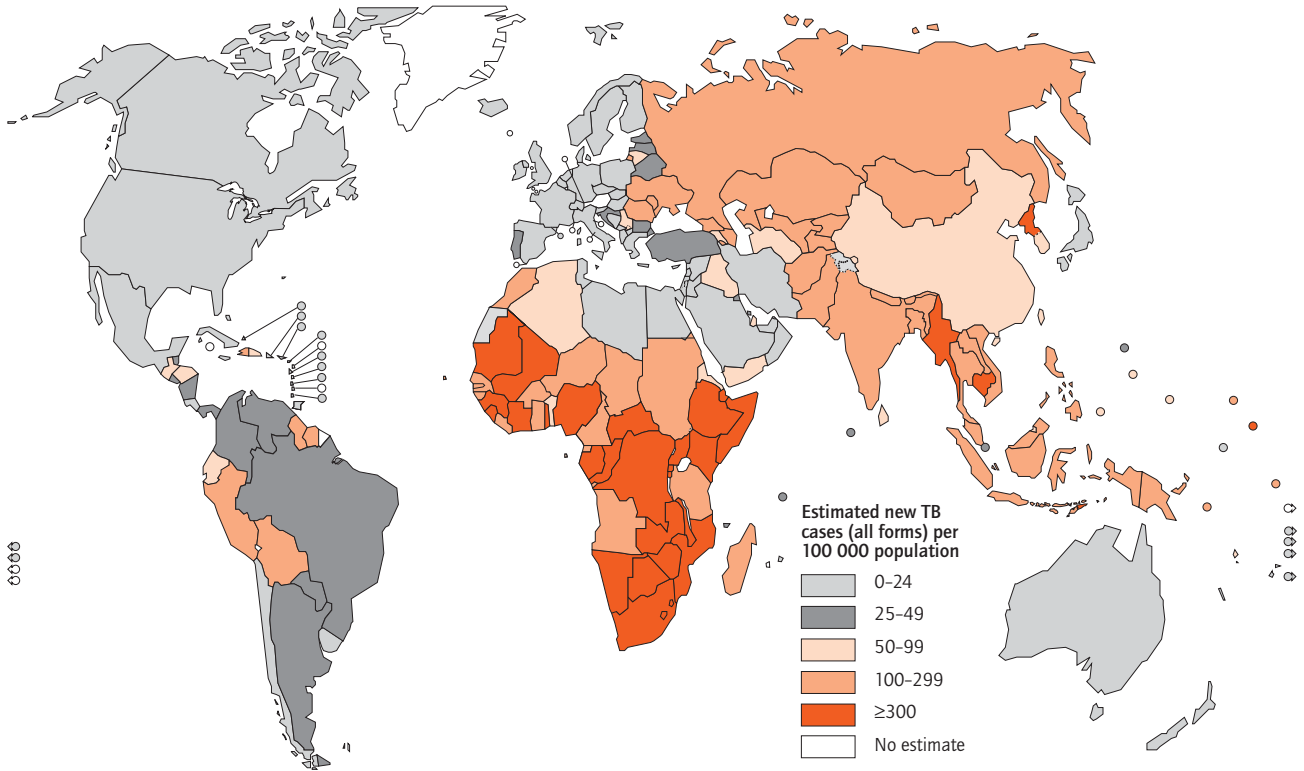
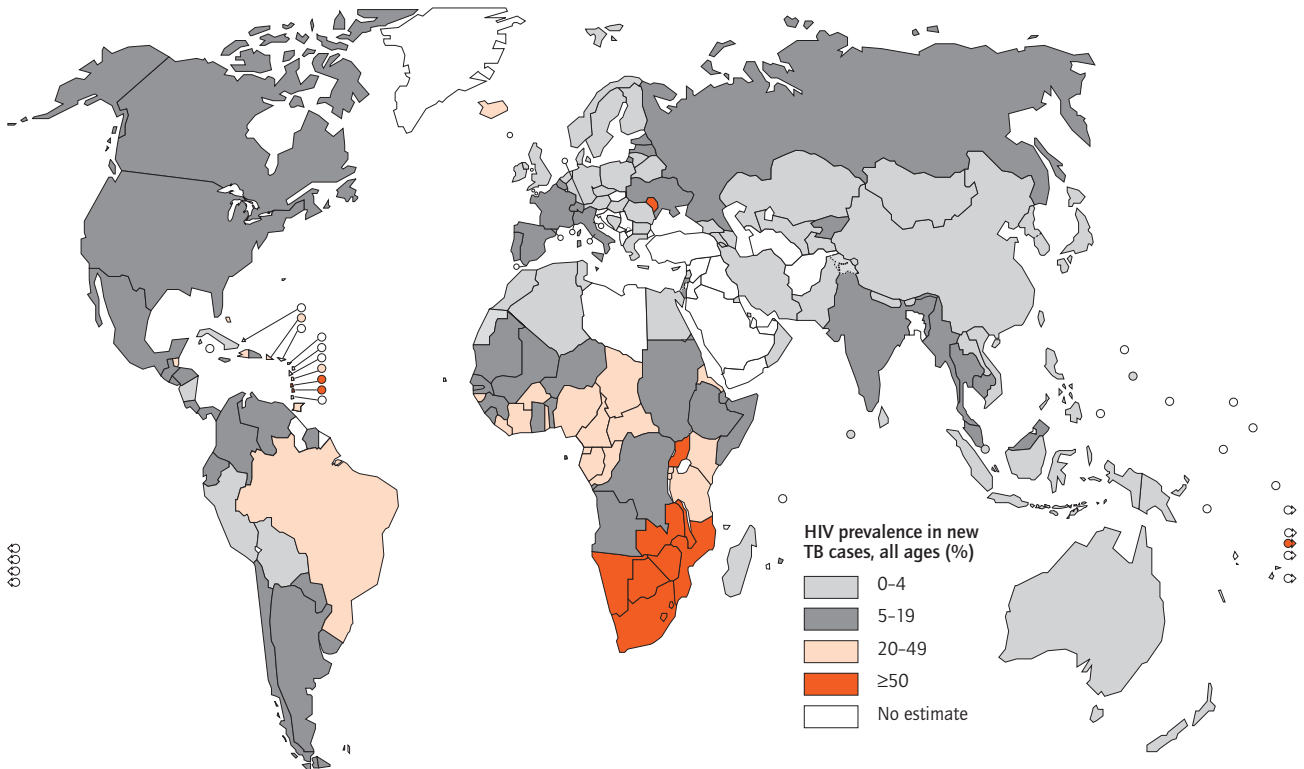


FIGURE 2
Estimated HIV prevalence in new TB cases, 2008



that account for 85% of all such cases; these countries have been termed the 27 high MDR-TB burden countries (see also SECTION 5.5). The countries that ranked first to fifth in terms of total numbers of MDR-TB cases in 2007 were

India (131 000), China (112 000), the Russian Federation (43 000), South Africa (16 000) and Bangladesh (15 000). By November 2009, 57 countries and territories had reported at least one case of XDR-TB.

3. Global targets for reductions in disease burden

Global targets for reducing the burden of disease attributed to TB are summarized in TABLE 2. Achieving the targets set for 2015 is the main focus of national and international efforts in TB control. These targets are (i) to halt and reverse

the incidence of TB by 2015 (MDG Target 6.c) and (ii) to halve TB prevalence and death rates by 2015, compared with their levels in 1990.

■ TABLE 2
Goals, targets and indicators for TB control

HEALTH IN THE MILLENNIUM DEVELOPMENT GOALS SET FOR 2015	
Goal 6: Combat HIV/AIDS, malaria and other diseases	
Target 6.c:	Halt and begin to reverse the incidence of malaria and other major diseases
Indicator 6.9:	Incidence, prevalence and death rates associated with TB
Indicator 6.10:	Proportion of TB cases detected and cured under DOTS
Stop TB Partnership targets set for 2015 and 2050	
By 2015:	The global burden of TB (per capita prevalence and death rates) will be reduced by 50% relative to 1990 levels.
By 2050:	The global incidence of active TB will be less than 1 case per million population per year.

4. The Stop TB Strategy and the Global Plan to Stop TB

The Stop TB Strategy¹ is the approach recommended by WHO to reduce the burden of TB in line with global targets set for 2015. The strategy is summarized in TABLE 3. The six major components of the strategy are: (i) pursue high-quality DOTS expansion and enhancement; (ii) address TB/HIV, MDR-TB, and the needs of poor and vulnerable populations; (iii) contribute to health system strengthening based on primary health care; (iv) engage all care providers; (v) empower people with TB, and communities through partnership; and (vi) enable and promote research.

The Stop TB Partnership's Global Plan to Stop TB, 2006–2015 (hereafter the Global Plan) sets out the scale at which the interventions included in the Stop TB Strategy need to be implemented to achieve the 2015 targets.² The major targets

(which can be defined as input, output and outcome targets) in the Global Plan include:

- Detection of 84% of infectious cases globally by 2015;
- A treatment success rate among smear-positive cases of 87% by 2015;
- HIV testing of 85% of TB patients by 2010, with this level sustained in subsequent years;
- Enrolment of 95% of HIV-positive TB patients on cotrimoxazole preventive therapy (CPT) by 2010, with this level sustained in subsequent years;
- Enrolment of 320 000 HIV-positive TB patients on antiretroviral treatment (ART) by 2010, equivalent to 80% of the TB patients estimated to be in need of such treatment at the time the Global Plan was developed;
- Diagnosis and treatment of 80% of the estimated number of smear-positive and/or culture-positive cases of MDR-TB by 2015, in programmes following international guidelines for the management of drug-resistant TB. The number of

¹ *The Stop TB Strategy: building on and enhancing DOTS to meet the TB-related Millennium Development Goals*. Geneva, World Health Organization, 2006 (WHO/HTM/TB/2006.368).

² *The Global Plan to Stop TB, 2006–2015: actions for life towards a world free of tuberculosis*. Geneva, World Health Organization, 2006 (WHO/HTM/STB/2006.35).

TABLE 3
The Stop TB Strategy at a glance

THE STOP TB STRATEGY	
VISION	A TB-free world
GOAL	To dramatically reduce the global burden of TB by 2015 in line with the Millennium Development Goals and the Stop TB Partnership targets
OBJECTIVES	<ul style="list-style-type: none"> • Achieve universal access to quality diagnosis and patient-centred treatment • Reduce the human suffering and socioeconomic burden associated with TB • Protect vulnerable populations from TB, TB/HIV and drug-resistant TB • Support development of new tools and enable their timely and effective use • Protect and promote human rights in TB prevention, care and control
TARGETS	<ul style="list-style-type: none"> • MDG 6, Target 6.c: Halt and begin to reverse the incidence of TB by 2015 • Targets linked to the MDGs and endorsed by Stop TB Partnership: <ul style="list-style-type: none"> – 2015: reduce prevalence of and deaths due to TB by 50% – 2050: eliminate TB as a public health problem
COMPONENTS	
1. Pursue high-quality DOTS expansion and enhancement	<ul style="list-style-type: none"> a. Secure political commitment, with adequate and sustained financing b. Ensure early case detection, and diagnosis through quality-assured bacteriology c. Provide standardized treatment with supervision, and patient support d. Ensure effective drug supply and management e. Monitor and evaluate performance and impact
2. Address TB/HIV, MDR-TB, and the needs of poor and vulnerable populations	<ul style="list-style-type: none"> a. Scale-up collaborative TB/HIV activities b. Scale-up prevention and management of multidrug-resistant TB (MDR-TB) c. Address the needs of TB contacts, and of poor and vulnerable populations
3. Contribute to health system strengthening based on primary health care	<ul style="list-style-type: none"> a. Help improve health policies, human resource development, financing, supplies, service delivery, and information b. Strengthen infection control in health services, other congregate settings and households c. Upgrade laboratory networks, and implement the Practical Approach to Lung Health (PAL) d. Adapt successful approaches from other fields and sectors, and foster action on the social determinants of health
4. Engage all care providers	<ul style="list-style-type: none"> a. Involve all public, voluntary, corporate and private providers through Public-Private Mix (PPM) approaches b. Promote use of the International Standards for Tuberculosis Care (ISTC)
5. Empower people with TB, and communities through partnership	<ul style="list-style-type: none"> a. Pursue advocacy, communication and social mobilization b. Foster community participation in TB care, prevention and health promotion c. Promote use of the Patients' Charter for Tuberculosis Care
6. Enable and promote research	<ul style="list-style-type: none"> a. Conduct programme-based operational research b. Advocate for and participate in research to develop new diagnostics, drugs and vaccines

patients to be treated in 2015 has been estimated by the MDR-TB working group of the Stop TB Partnership as around 357 000 cases in the 27 high MDR-TB burden countries;

- Mobilization of between US\$ 3 billion and US\$ 9 billion per year, increasing over time, to finance implementation of the Stop TB Strategy, plus at least US\$ 1 billion per year

for research and development related to new drugs, new diagnostics and new vaccines.

The next section presents the latest data on progress made in implementing the Stop TB Strategy, where appropriate in the context of targets set in the Global Plan.

Achievements in TB control, 1995–2008

WHO developed the DOTS strategy as the internationally recommended approach to TB control in the mid-1990s. DOTS is also the foundation of the Stop TB Strategy, which was launched by WHO in 2006 to guide TB control efforts during the period 2006–2015. The start of WHO efforts to systematically monitor progress in TB control on an annual basis in 1995 coincided with global promotion and expansion of the DOTS strategy.

The data that have been compiled 1995–2009 allow an assessment of the achievements of TB control between 1995 and 2008. During this period, 36 million patients have been successfully treated in DOTS programmes. This has averted millions of deaths – at least 2 million but possibly as many as 6 million,¹ compared with what would have occurred had DOTS not been implemented.²

Globally, incidence rates appear to have peaked, at 143 (range, 136–151) cases per 100 000 population in 2004. This means that the world is on track to achieve MDG Target 6.c, as are eight of nine epidemiological subregions (the exception being African countries with a low prevalence of HIV). Six epidemiological subregions (Central Europe, Eastern Europe, the Eastern Mediterranean, high-income countries, Latin America and the Western Pacific) appear to have achieved the Stop TB Partnership target of halving the 1990 prevalence rate and four (Central Europe, high-income countries, Latin America and the Western Pacific) appear to have achieved the Stop TB Partnership target of halving the 1990 mortality rate, in advance of the target year of 2015. Prevalence rates are also falling globally and in all other regions with the exception of African countries with a low prevalence of HIV.

¹ Excluding deaths averted among HIV-positive people, which are classified as HIV rather than TB deaths.

² Defined as a case notification rate maintained at the 1995 level.

5. Progress in implementing the Stop TB Strategy and the Global Plan to Stop TB

5.1 Case notifications

In 2008, 5.7 million cases of TB (new cases and relapse cases) were notified to NTPs, including 2.7 million new smear-positive cases, 2.0 million new smear-negative pulmonary cases (or cases for which smear status was unknown) and 0.8 million new cases of extrapulmonary TB (TABLE 4).¹

Among pulmonary cases, 57% of total notifications were smear-positive. Among the 22 HBCs, the percentage of notifications that were smear-positive was much lower in the Russian Federation (31%), Zimbabwe (33%), Kenya (44%) and Ethiopia (45%), while a comparatively high proportion were smear-positive in the Democratic Republic of the Congo (86%), Bangladesh (83%), Viet Nam (74%) and Cambodia (72%).

5.2 Treatment outcomes

Globally, the rate of treatment success for new smear-positive cases treated in the 2007 cohort was 86% (TABLE 5). This is the first time that the treatment success rate has exceeded the global target of 85%, which was set by the World Health Assembly (WHA) in 1991. Three regions – the Eastern Mediterranean (88%), Western Pacific (92%), and South-East Asia (88%) regions – exceeded the target, as did 53 countries. The treatment success rate was 79% in the African

Region, 82% in the Region of the Americas and 67% in the European Region (where death and failure rates are comparatively high). Between 2006 and 2007, treatment success rates were maintained or improved in all regions with the exception of the European Region.

Among the 22 HBCs, the 85% target was met or exceeded in 13 countries, including in Afghanistan for the first time. Encouragingly, the rate of treatment success was also 85% in Kenya and 88% in the United Republic of Tanzania, showing that countries in which there is a high prevalence of HIV among TB cases are able to achieve this target.

5.3 Case detection rates and the role of PPM in engaging all care providers

The case detection rate (calculated as the number of notified cases of TB in one year divided by the number of estimated incident cases of TB in the same year, and expressed as a percentage) has been a much-used indicator of progress in TB control for more than a decade. The considerable attention given to the case detection rate was in line with the two principal global targets (case detection and treatment success rates) set for TB control during the period 1991 to 2005. The targets of reaching a 70% case detection rate and an 85% treatment success rate by 2000 were set in 1991 by the WHA, with the target year subsequently reset to 2005.

This report update, as well as future reports on global TB control, will gradually place less emphasis on the case detection rate. There are several good reasons for doing this:

- The target year of 2005 has now passed;

¹ No distinction is made between DOTS and non-DOTS programmes. This is because by 2007, virtually all (more than 99%) notified cases were reported to WHO as treated in DOTS programmes. In 2009, the WHO data collection form made no distinction between notifications in DOTS and non-DOTS programmes.

TABLE 4
Case notifications, 2008

	NEW AND RELAPSE	NEW CASES			RE-TREAT EXCL. RELAPSE	OTHER ^a	PERCENT PULMONARY CASES SMEAR POSITIVE
		SMEAR-POSITIVE	SMEAR-NEGATIVE/ UNKNOWN	NEW.EP			
Afghanistan	28 301	13 136	7 903	6 127	0	0	62
Bangladesh	151 062	106 373	22 192	18 359	2 853	0	83
Brazil	73 395	37 697	22 665	10 122	8 263	0	62
Cambodia	38 927	19 860	7 847	10 678	893	0	72
China	975 821	462 596	431 115	35 546	58 378	0	52
DR Congo	104 426	69 477	11 498	19 450	3 789	-	86
Ethiopia	141 157	40 794	49 372	48 794	752	-	45
India	1 332 267	615 977	390 356	219 946	185 071	0	61
Indonesia	296 514	166 376	116 850	9 673	1 815	-	59
Kenya	99 941	36 811	46 115	16 881	10 310	0	44
Mozambique	39 261	18 824	14 117	5 012	474	0	57
Myanmar	124 037	41 248	44 034	34 447	4 701	-	48
Nigeria	85 674	46 026	34 211	3 026	4 637	0	57
Pakistan	245 635	100 102	106 207	34 386	3 043	-	49
Philippines	139 603	85 025	49 916	2 085	6 289	0	63
Russian Federation	128 263	33 949	75 775	3 769	86 642	0	31
South Africa	343 855	138 803	132 972	48 251	40 641	4 386	51
Thailand	55 252	28 788	16 933	7 815	2 240	-	63
Uganda	42 178	22 766	13 190	4 710	1 665	0	63
UR Tanzania	60 490	24 171	21 935	12 784	2 874	-	52
Viet Nam	97 772	53 484	19 056	18 610	912	0	74
Zimbabwe	36 650	9 830	19 956	5 931	2 698	0	33
High burden countries	4 640 481	2 172 113	1 654 215	576 402	428 940	4 386	57
AFR	1 329 581	595 184	446 859	232 864	82 374	4 607	57
AMR	218 249	119 862	51 818	33 218	13 193	232	70
EMR	392 633	166 558	137 780	77 247	5 393	18	55
EUR	336 443	104 916	157 185	42 692	109 655	8 225	40
SEAR	2 078 238	1 007 382	635 427	310 700	209 433	132	61
WPR	1 363 479	661 923	549 225	88 551	71 613	3 839	55
Global	5 718 623	2 655 825	1 978 294	785 272	491 661	17 053	57

^a Cases not included elsewhere in the table.

- Indicates data not available.

- The Global Plan established targets well in excess of 70% for most of the period 2006–2015;
- There is increasing emphasis on achieving universal access to health care, which implies detecting and treating well in excess of 70% of cases;
- There are difficulties with estimating incidence in absolute terms – the value required for the denominator in the calculation of the case detection rate (see ANNEX for further details on estimating the incidence of TB);¹ and
- There has been a major shift towards focusing on impact targets i.e. the 2015 targets for reducing the burden of disease (TABLE 2).

The best estimate of the case detection rate of new smear-positive cases in 2008 was 62% (range 56–68%) (TABLE 6), which is 9% less than the milestone of 71% that was set in

the Global Plan. The highest rates of case detection in 2008 are estimated to be in the European Region and the Region of the Americas, followed by the Western Pacific Region, with the lowest rate estimated for the African Region. Among the HBCs, the highest rates of case detection in 2008 are estimated to be in Indonesia, Brazil, China, the Russian Federation and the United Republic of Tanzania, with the lowest rate (24%, range 20–30%) in Zimbabwe. Of note is the case detection rate estimated for Viet Nam, which at 62% (range, 45–75%) is considerably lower than estimates published in previous years, following new evidence from a nationwide survey of the prevalence of TB disease completed in 2007 combined with an in-depth analysis of surveillance data in early 2009.

The case detection rate for all forms of TB (TABLE 7) is estimated at 61% in 2008 (range 55–67%). Among regions, the European and Western Pacific regions and the Region of the Americas have the highest rates of case detection; the African Region has the lowest. There is considerable variation among HBCs, although, as for detection of smear-

¹ It is more feasible to estimate trends in TB incidence than its absolute level. For example, trends can be estimated using time-series of TB notification data, provided that the effect of changes in case-finding efforts and determinants of changes in TB incidence can be distinguished.

TABLE 5
Treatment success rates among new smear-positive cases (%), 1994–2007 cohorts

	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
Afghanistan	-	-	45	33	86	85	84	87	86	89	90	84	87
Bangladesh	71	63	73	77	79	81	83	84	85	90	91	92	92
Brazil	17	20	27	40	78	71	55	80	77	76	76	73	-
Cambodia	91	94	91	95	93	91	92	92	93	91	93	93	94
China	93	94	95	95	95	93	95	92	93	94	94	94	94
DR Congo	74	48	64	70	69	78	77	78	83	85	85	86	87
Ethiopia	61	71	72	74	74	80	76	76	70	79	78	84	84
India	25	21	18	27	21	34	54	60	76	82	86	86	87
Indonesia	91	81	54	58	50	87	86	86	87	90	91	91	91
Kenya	75	77	65	77	79	80	80	79	80	80	82	85	85
Mozambique	39	55	65	-	71	75	78	78	76	77	79	83	79
Myanmar	67	79	82	82	81	82	81	81	81	84	84	84	85
Nigeria	49	32	73	73	75	79	79	79	78	73	75	76	82
Pakistan	70	-	67	23	70	74	77	78	79	82	83	88	91
Philippines	60	35	78	71	87	88	88	88	88	87	89	88	89
Russian Federation	65	57	67	68	65	68	67	67	61	60	58	58	58
South Africa	58	61	68	72	57	63	61	68	67	69	71	74	74
Thailand	64	78	58	68	77	69	75	74	73	74	75	77	83
Uganda	44	33	40	62	61	63	56	60	68	70	73	70	75
UR Tanzania	73	76	77	76	78	78	81	80	81	81	82	85	88
Viet Nam	89	89	85	92	92	92	93	92	92	93	92	93	92
Zimbabwe	53	32	69	70	73	69	71	67	66	54	68	60	78
High burden countries	53	50	56	62	60	67	72	75	81	84	86	87	88
AFR	60	56	64	70	68	71	70	73	73	74	76	75	79
AMR	50	51	58	67	79	76	69	81	80	79	78	75	82
EMR	79	66	73	57	79	81	82	84	82	83	83	86	88
EUR	67	58	72	63	75	75	72	74	75	69	71	69	67
SEAR	33	31	29	40	34	50	63	68	79	84	87	87	88
WPR	80	72	91	92	91	90	91	90	91	92	92	92	92
Global	57	54	60	64	64	69	73	76	80	83	85	84	86

- Indicates data not available.

positive cases, the highest estimated rates of case detection in 2008 were in Brazil, China and the Russian Federation as well as India, Indonesia, Kenya and South Africa.

Despite difficulties with estimating the case detection rate, efforts to increase the percentage of TB cases that are diagnosed and treated according to international guidelines is clearly of major importance. In many countries, one of the best ways to do this is for NTPs to establish collaboration with the full range of health-care providers through PPM initiatives.¹

PPM initiatives are being scaled up in many countries but, as in previous rounds of global TB data collection, the contribution of different care providers to case notifications is hard to quantify. In 2008, only a handful of HBCs reported data on the source of referral or place of treatment of TB patients. This reflects the fact that most NTPs are not yet recording data on the source of referral and the place of treatment of TB patients on a routine basis.² In the absence of such

data, **BOX 4** provides examples of what can be achieved through PPM, using data from Bangladesh, Kenya and the Philippines.

Overall, rates of case detection have stagnated since 2006, and renewed efforts to increase case-finding are needed to keep pace with Global Plan milestones (**FIGURE 3**). The gap between estimated case detection rates in practice and the milestones included in the Global Plan is biggest in the African Region. A gap is opening up in the Western Pacific Region, where case detection rates have remained stable since 2005. The case detection rate has been increasing in the Eastern Mediterranean and South-East Asia regions, and this rate of progress needs to be maintained to keep pace

¹ *Global tuberculosis control: epidemiology, strategy, financing. WHO report 2009*. Geneva, World Health Organization, 2009 (WHO/HTM/TB/2009.411). See Chapter 2, in which a case study of PPM in Pakistan was featured.

² WHO recommends that the source of referral and the place of treatment should be routinely recorded and reported.

TABLE 6
Case detection rate for new smear-positive cases (%), 1995–2008^a

	1995			2000			2005			2008		
	BEST	LOW	HIGH	BEST	LOW	HIGH	BEST	LOW	HIGH	BEST	LOW	HIGH
Afghanistan ^b	–	–	–	18	15	22	51	43	64	61	51	76
Bangladesh	15	12	18	25	21	31	51	42	64	61	51	76
Brazil	71	59	88	70	58	87	79	65	93	75	63	91
Cambodia	35	30	44	44	37	55	61	51	76	56	47	70
China	20	17	25	31	26	39	73	61	91	72	60	90
DR Congo	46	38	57	49	40	61	62	52	78	66	55	83
Ethiopia	16	13	20	33	27	41	30	25	38	32	27	40
India	37	28	43	45	34	51	60	46	69	70	53	80
Indonesia	18	15	23	28	23	35	79	66	99	80	67	100
Kenya	53	44	66	53	44	66	65	54	81	68	57	85
Mozambique	59	49	74	45	38	56	44	37	55	47	39	59
Myanmar	10	8	13	19	16	24	39	32	48	43	35	53
Nigeria	11	9	13	12	10	15	18	15	22	24	20	29
Pakistan ^b	2	2	3	2	2	3	30	25	38	58	49	73
Philippines	76	63	95	53	44	66	64	54	80	67	56	84
Russian Federation	77	64	96	49	41	62	68	57	83	73	61	86
South Africa	41	34	52	69	57	86	66	55	83	68	57	85
Thailand	51	42	64	43	36	54	68	57	85	64	54	81
Uganda	48	40	60	49	40	61	45	38	57	54	45	68
UR Tanzania	69	58	80	70	61	79	71	66	77	70	65	75
Viet Nam	51	37	62	67	49	81	66	48	80	62	45	75
Zimbabwe	38	31	47	39	33	49	30	25	37	24	20	30
High-burden countries	31	29	34	38	35	40	58	54	62	63	59	68
AFR	36	30	44	39	33	49	44	37	55	47	39	58
AMR	68	56	84	71	59	88	75	63	91	78	65	93
EMR	20	17	25	24	20	30	42	35	52	59	49	73
EUR	70	59	86	60	51	74	66	56	80	78	66	94
SEAR	29	23	35	39	31	46	60	48	72	68	54	81
WPR	33	27	41	39	33	49	70	58	88	70	58	87
Global	35	31	39	40	36	45	57	52	63	62	56	68

^a Estimates for all years are recalculated as new information becomes available and techniques are refined, so they may differ from those published previously.

^b Estimates are provisional, pending further analyses and data collection in 2010.

– Indicates data not available.

with the Global Plan. The European Region is the only region where current estimates of the case detection rate exceed Global Plan milestones.

5.4 Collaborative TB/HIV activities

Collaborative TB/HIV activities are essential to ensure that HIV-positive TB patients are identified and treated appropriately, and to prevent TB in HIV-positive people.¹ These activities include establishing mechanisms for collaboration between TB and HIV programmes; infection control in health-care and congregate settings; HIV testing of TB patients and – for those TB patients infected with HIV – CPT and ART; and intensified TB case-finding among people living with HIV followed by isoniazid preventive therapy (IPT) for those without active TB. HIV testing of TB patients, provision of CPT and

referral for ART are typically the responsibility of NTPs, while national HIV programmes are typically responsible for intensified case-finding among HIV-positive people and provision of IPT to those without active TB.

Further progress in implementation of collaborative TB/HIV activities was made in 2008, consolidating achievements documented in previous reports. Almost 1.4 million TB patients knew their HIV status in 2008 (22% of notified cases), up from 1.2 million in 2007 (FIGURE 4). The highest rates of HIV testing were reported in the European Region, the Region of the Americas and the African Region, where 79%, 49% and 45% of TB patients knew their HIV status, respectively (TABLE 8). There were 50 countries in which at least 75% of TB patients knew their HIV status, including 11 African countries (FIGURE 5). Of the TB patients who were known to be HIV-positive, around two-thirds or just over 0.2 million were enrolled on CPT and around one-third or 0.1 million were enrolled on ART (FIGURE 6); these numbers are about one-third of the milestones of 0.6 million and 0.3 mil-

¹ *Interim policy on collaborative TB/HIV activities*. Geneva, World Health Organization, 2004 (WHO/HTM/TB/2004.330; WHO/HTM/HIV/2004.1).

TABLE 7
Case detection rate for all cases (%), 1995–2008^a

	1995			2000			2005			2008		
	BEST	LOW	HIGH	BEST	LOW	HIGH	BEST	LOW	HIGH	BEST	LOW	HIGH
Afghanistan ^b	–	–	–	18	15	23	47	39	59	55	46	69
Bangladesh	20	16	25	24	20	30	36	30	45	42	35	52
Brazil	79	66	99	74	62	93	84	70	100	82	69	100
Cambodia	23	19	29	28	23	35	51	42	63	55	45	68
China	38	32	48	34	28	43	68	57	85	75	62	94
DR Congo	40	33	50	35	29	43	40	33	50	43	35	53
Ethiopia	20	17	25	42	35	52	42	35	52	47	40	59
India	34	28	43	64	53	80	61	51	76	67	56	84
Indonesia	10	8	12	22	18	27	61	51	77	69	57	86
Kenya	46	38	57	50	42	63	71	59	88	79	66	98
Mozambique	43	36	54	31	26	38	35	29	44	42	35	52
Myanmar	10	9	13	16	14	20	55	46	69	62	52	78
Nigeria	6	5	8	8	6	10	14	11	17	19	16	23
Pakistan ^b	4	4	5	3	3	4	37	31	46	60	50	75
Philippines	47	39	59	47	39	59	53	44	67	54	45	68
Russian Federation	53	44	67	77	64	97	82	68	100	85	71	100
South Africa	56	47	70	59	49	73	61	51	76	72	60	90
Thailand	55	46	69	40	33	50	64	54	80	60	50	75
Uganda	38	32	47	37	30	46	39	32	48	43	36	54
UR Tanzania	59	50	68	67	59	76	74	68	79	75	70	80
Viet Nam	37	27	45	56	41	68	56	41	68	56	41	68
Zimbabwe	55	46	69	60	50	75	49	41	61	39	32	48
High-burden countries	33	30	35	42	39	45	55	51	59	62	57	65
AFR	38	32	47	38	31	47	42	35	53	47	39	58
AMR	68	57	84	70	59	87	75	63	91	77	65	92
EMR	21	18	26	25	21	30	46	39	57	60	50	75
EUR	62	53	77	76	64	93	80	67	96	79	66	95
SEAR	28	23	35	49	41	62	58	48	72	65	54	81
WPR	42	35	52	40	33	50	65	54	81	70	58	87
Global	37	34	41	45	41	49	56	50	61	61	55	67

^a Estimates for all years are recalculated as new information becomes available and techniques are refined, so they may differ from those published previously.

^b Estimates are provisional, pending further analyses and data collection in 2010.

– Indicates data not available.

lion that were set in the Global Plan for 2009, respectively.

Although the numbers remain a small fraction of the number of people who know that they are HIV-positive and a smaller fraction still of the estimated total number of HIV-positive people worldwide, screening for TB among HIV-positive people and provision of IPT to those without active TB more than doubled between 2007 and 2008. The number of HIV-positive people screened for TB increased from 0.6 million to 1.4 million, and the number of people who were provided with IPT grew from under 30 000 in 2007 to around 50 000 in 2008 (FIGURE 7).

5.5 MDR-TB and XDR-TB

Globally, just under 30 000 cases of MDR-TB were notified to WHO in 2008, mostly by European countries and South Africa (FIGURE 8, TABLE 9). This was 11% of the estimated number of cases of MDR-TB among all notified cases of pulmonary TB in 2008 (TABLE 9). The number of notified cases reported to WHO was slightly lower than in 2007, but coun-

try reports suggest that numbers will be higher in 2009 and 2010, including in the three countries where the estimated number of cases is highest: China, India and the Russian Federation (FIGURE 8, TABLE 9).

Among notified cases, an increasing share is being enrolled on treatment in projects or programmes approved by the Green Light Committee (GLC), and are thus known to be receiving treatment according to international guidelines. The number reached around 6 000 in 2008, and is expected to rise to almost 29 000 in 2010. This remains a small fraction of the estimated number of cases, and much more rapid expansion of diagnosis and treatment – within and outside projects and programmes approved by the GLC – is needed to approach the targets included in the MDR-TB component of the Global Plan (FIGURE 9).

National data on treatment outcomes among cohorts of at least 100 patients are currently limited to six countries: Brazil, Kazakhstan, Latvia, Peru, Romania and Turkey (FIGURE 10). Rates of treatment success are variable, rang-

FIGURE 3
Case detection rates 1995–2008 (grey) compared with Global Plan targets/milestones (red), globally and in seven sub-regions

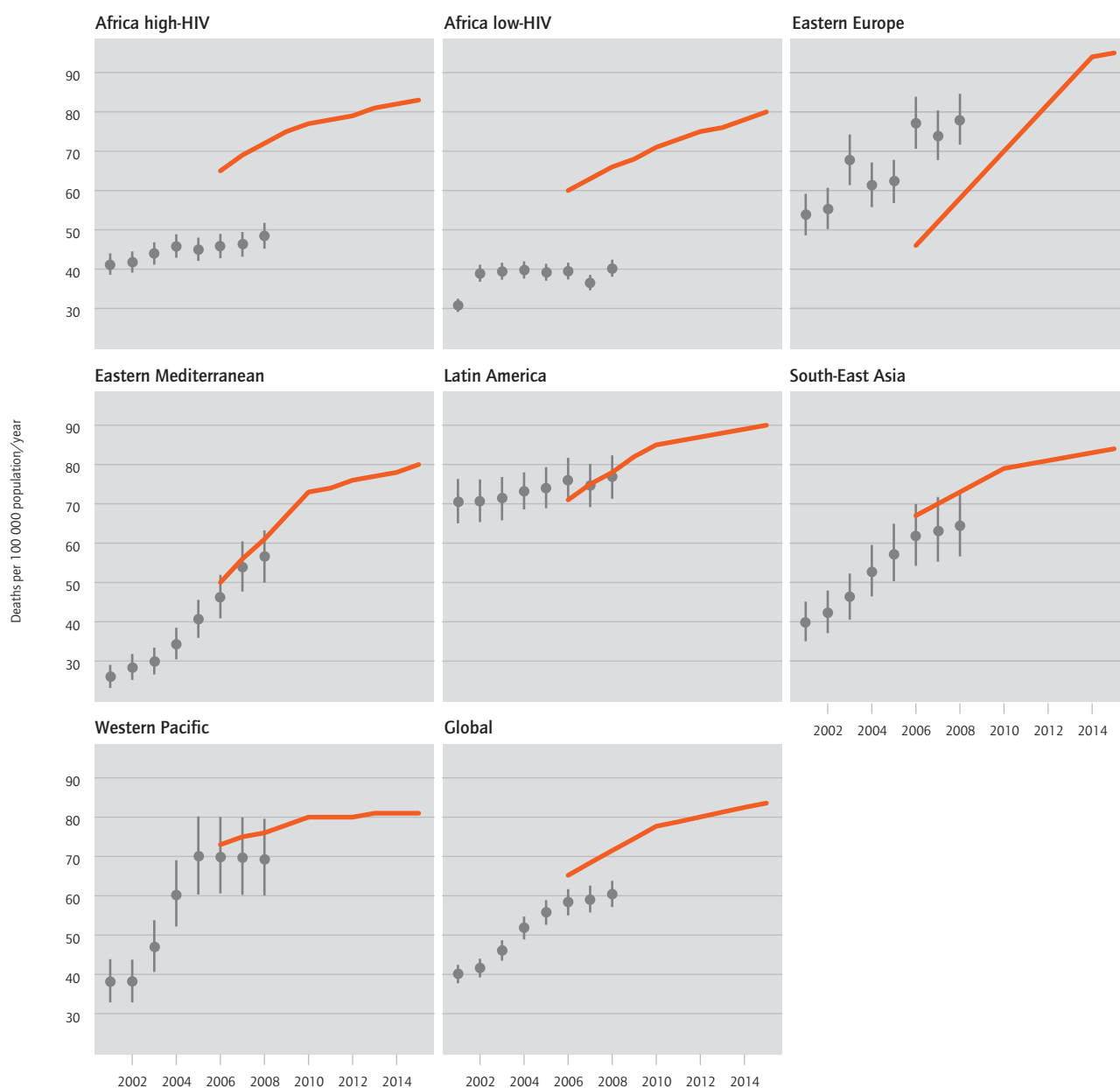


TABLE 8
HIV testing and treatment in TB patients, by WHO region, 2008

	NUMBER OF TB PATIENTS WITH KNOWN HIV STATUS (THOUSANDS)	% OF NOTIFIED TB PATIENTS TESTED FOR HIV	% OF TESTED TB PATIENTS HIV-POSITIVE	% OF ESTIMATED HIV-POSITIVE TB CASES ^a IDENTIFIED BY TESTING	% OF IDENTIFIED HIV-POSITIVE TB PATIENTS STARTED ON CPT	% OF IDENTIFIED HIV-POSITIVE TB PATIENTS STARTED ON ART	REGIONAL DISTRIBUTION OF ESTIMATED HIV-POSITIVE TB CASES (%)	NUMBER OF HIV-POSITIVE PEOPLE SCREENED FOR TB (THOUSANDS)	NUMBER OF HIV-POSITIVE PEOPLE PROVIDED IPT (THOUSANDS)
AFR	636	45	46	27	73	30	78	729	26
AMR	113	49	15	45	36	67	2.7	48	12
EMR	22	5.4	4.1	5.8	39	55	1.1	12	0.7
EUR	357	79	3.3	48	61	29	1.7	205	9.2
SEA	94	4.1	18	9.3	54	35	13	300	0.2
WPR	152	11	7.0	24	55	28	3.1	90	0.7
Global	1374	22	26	25	71	32	100	1384	48

^a Includes estimated HIV-positive TB cases in countries which did not provide information on testing.

BOX 4**Public-Private Mix (PPM): diverse approaches, distinct achievements****Bangladesh – PPM in rural areas¹**

The Damien Foundation Bangladesh has involved semi-qualified, private “gram dakter” (“village doctors”) in TB control in rural areas with a total population of around 30 million. Over several years, more than 18 000 village doctors have been trained to refer suspected TB cases for free diagnosis and to provide directly observed treatment (DOT) free-of-charge to patients living in their vicinity. The source of referral and the place where DOT is provided are recorded as part of the standardized TB recording and reporting system, which enables the contribution of village doctors to case notification and treatment outcomes to be quantified. Each year, about 15–20% of all notified cases of smear-positive TB cases are referred by village doctors. In 2007, more than 60% of the 24 000 cases that were notified received DOT from village doctors and the treatment success rate among patients supervised by the village doctors was around 90%. Village doctors are also involved in supervising the outpatient treatment of patients with MDR-TB. Involvement of village doctors in TB control is a national policy in Bangladesh.

Kenya – PPM in urban areas²

The Kenya Association for Prevention of Tuberculosis Lung Disease has involved private chest physicians in Nairobi in TB control since 1997, through a collaboration that started with a pharmaceutical company providing anti-TB drugs at subsidized costs. Support to private hospitals and chest physicians (including anti-TB drugs) is now provided by the NTP. The private sector accounts for around 10% of the TB cases notified in Nairobi. PPM activities have been expanded to other cities as well, where there is considerable scope for effective engagement of practicing nurses, clinical officers, pharmacies and private laboratories. Efforts also extend to collaborative TB/HIV activities.

The Philippines – PPM nationwide³

PPM in the Philippines is known as PPMD (Public-Private Mix for DOTS). PPMD was adopted as a national strategy to increase case detection and improve access to DOTS services in poor urban areas in 2003. Since then, a close collaboration between the NTP and the Philippines Coalition Against Tuberculosis (PhilCAT) has produced impressive results. By the end of 2008, there were 220 PPMD units operating across the country (of which 170 were supported through Global Fund grants); more than 5000 private physicians had been trained as referring physicians; and 48 500 TB cases had been managed by PPMD units. In 2008, case notifications increased by 18% in areas where PPMD was implemented. Treatment success rates among patients managed in PPMD units have been in the range 85–90%. Financial incentives that are part of a TB-DOTS outpatient package provided by the Philippines Health Insurance Organization offer the prospect of making PPMD financially sustainable, even when grants from the Global Fund end.

¹ Personal communication, Dr Hamid Salim, Damien Foundation Bangladesh, 2009.

² Chakaya J, Uplekar M, Mansoor J et al. Public-private mix for control of tuberculosis and TB-HIV in Nairobi, Kenya: outcomes, opportunities and obstacles. *Int J Tuberc Lung Dis*, 2008. 12(11); 1274–8.

³ Department of Health. Philippines and World Health Organization. Joint tuberculosis programme review: Philippines, 2009.

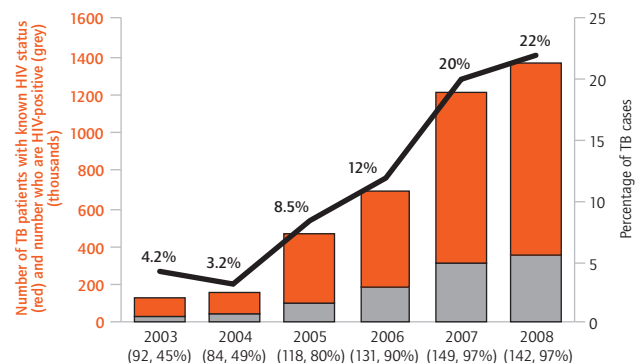
ing from below 40% to above 80%, with lower cure rates and higher death rates among retreatment cases.

One of the most important constraints to rapid expansion of diagnosis and treatment for MDR-TB is laboratory capacity. Without greater capacity to diagnose MDR-TB, the number of cases diagnosed and treated will continue to remain low. In 2008, diagnostic testing for drug susceptibility, or DST, among new cases of TB was almost entirely confined to the European Region and the Region of the Americas (FIGURE 11). Among retreatment cases, DST was done for 17% of cases in the Region of the Americas and for 13% in the European Region, with figures of less than 10% in all other regions.

Recent efforts to strengthen laboratory services, under the umbrella of the Global Laboratory Initiative, are highlighted in BOX 5.

FIGURE 4

HIV testing for TB patients, 2003–2008. Number (bars) and percentage (line) of notified new and re-treatment TB cases for which the HIV status (HIV-positive in grey) was recorded in the TB register. The numbers under each bar show the number of countries reporting data,^a followed by the percentage of total estimated HIV-positive TB cases accounted for by reporting countries.



^a Data are only shown for countries for which data were reported on both the number of cases for whom HIV status was known and the number of cases that were HIV-positive.

FIGURE 5
HIV testing for TB patients, 2008

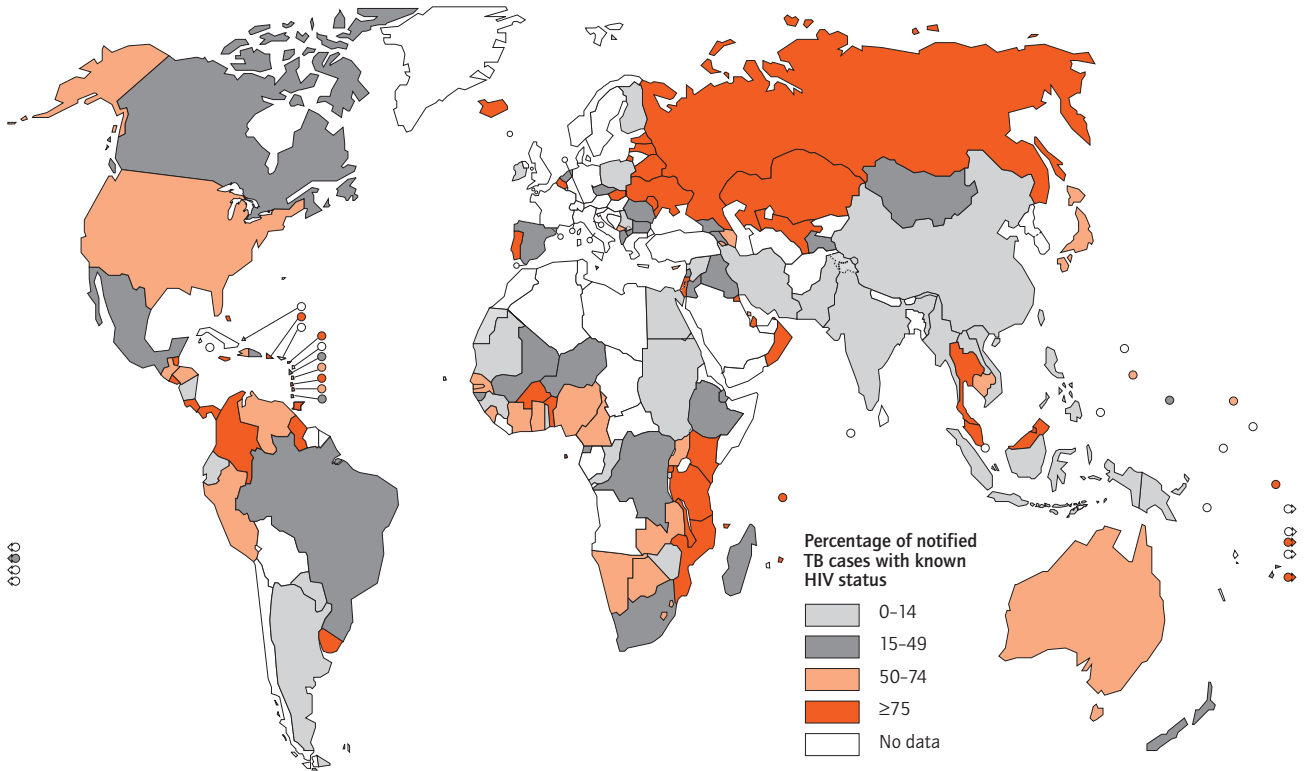


FIGURE 6

Co-trimoxazole preventive therapy and antiretroviral therapy for HIV-positive TB patients, 2003–2008. Numbers (bars) and percentages (above bars) of estimated HIV-positive people started on CPT (red) and ART (grey). The numbers under each bar show the number of countries reporting data, followed by the percentage of total estimated HIV-positive TB cases accounted for by reporting countries.

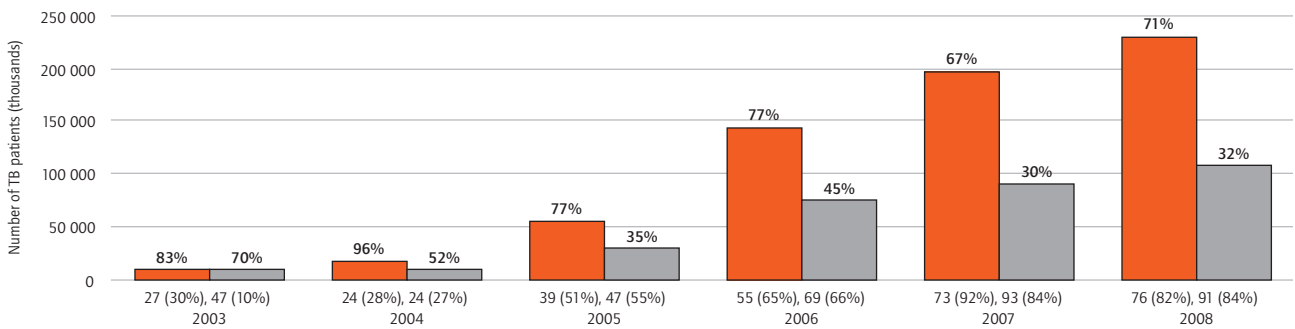
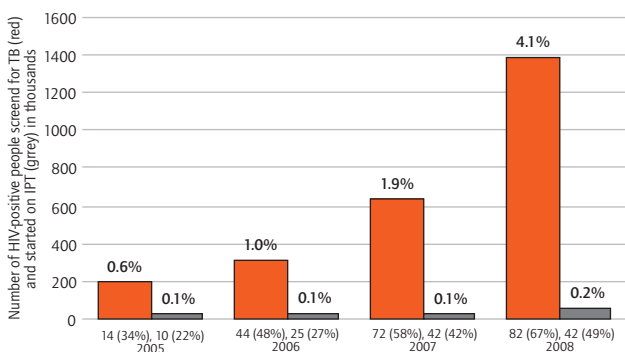


FIGURE 7

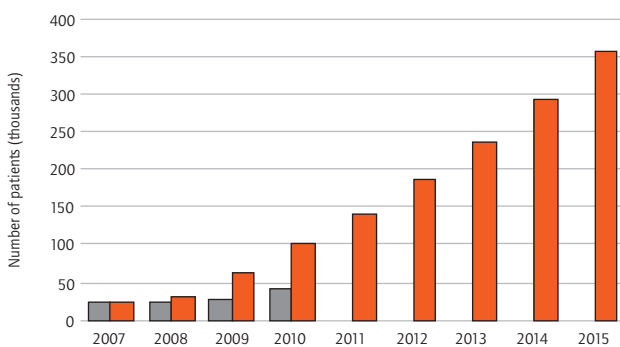
Intensified TB case-finding and IPT provision among HIV-positive people. Numbers (bars) and percentages (above bars) of estimated HIV-positive people screened for TB (red) and started on IPT^a (grey). Numbers under bars show the number of countries reporting data followed by the percentage of total estimated HIV-positive people accounted for by reporting countries.



^a Percentages for IPT figures are calculated using the estimated number of HIV-positive people without active TB.

FIGURE 9

Notified cases of MDR-TB (2007-2008) and projected numbers of patients to be enrolled on treatment (2009-2010) in the 27 high MDR-TB burden countries (grey) compared with targets/milestones included in the Global Plan^a (red). Numbers are for smear and/or culture-positive cases of MDR-TB



^a The targets/milestones for scaling-up treatment of MDR-TB in the Global Plan are based on updated projections produced in March 2009, in preparation for a ministerial meeting on MDR/XDR-TB held in Beijing, China in April 2009.

FIGURE 8

Notified cases of MDR-TB (2005-2008) and projected numbers of patients to be enrolled on treatment (2009-2010). The numbers under each bar show the number of countries reporting data.

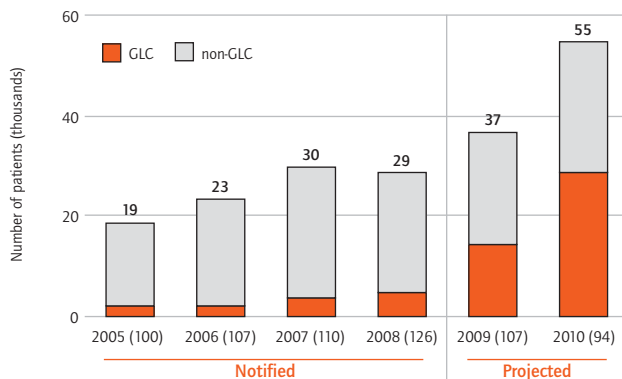
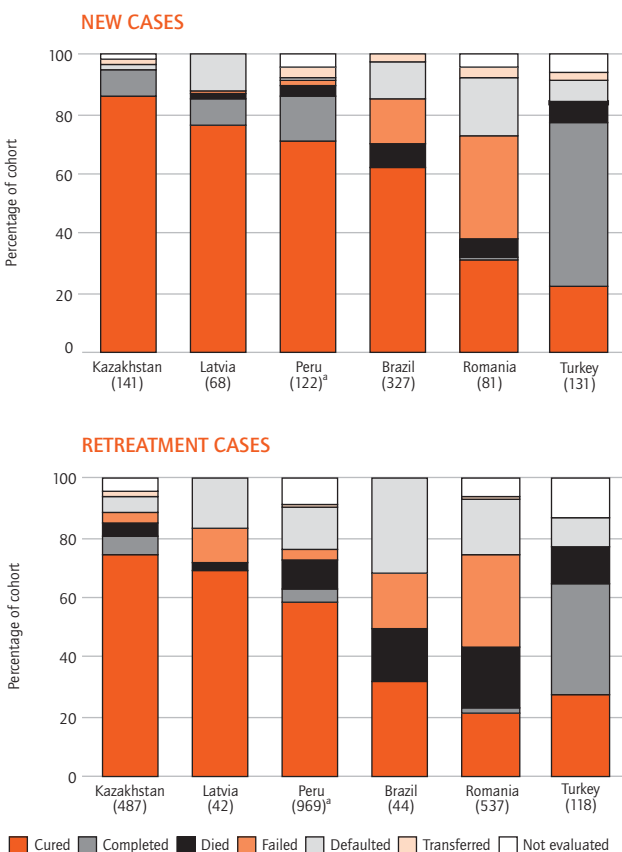


FIGURE 10

Treatment outcomes for patients with MDR-TB in six countries, 2006 cohort. The total number of patients in each cohort is shown under each bar. Only countries reporting outcomes for >100 MDR-TB cases and for both new and retreatment patients shown. Countries ranked by proportion cured among new cases.



^a Data from 2005.

TABLE 9

Number of cases of MDR-TB estimated, notified and expected to be treated, 27 high MDR-TB burden countries and WHO regions

		ESTIMATED % OF ALL TB CASES WITH MDR-TB	TOTAL NUMBER OF ESTIMATED CASES OF MDR-TB IN 2007 ^a	ESTIMATED CASES OF MDR-TB AMONG NOTIFIED CASES OF PULMONARY TB ^b (A)	NOTIFIED CASES OF MDR-TB (B)	NOTIFIED CASES OF MDR-TB AS % OF ESTIMATED CASES OF MDR-TB AMONG ALL NOTIFIED CASES OF PULMONARY TB (B/A) ^c	EXPECTED NUMBER OF CASES OF MDR-TB TO BE TREATED	
							2009	2010
1	Armenia	17	486	284	128	45	60	120
2	Azerbaijan	36	3 916	2 928	-	-	-	-
3	Bangladesh	4.0	14 506	4 868	147	3	205	-
4	Belarus	16	1 101	465	-	-	-	-
5	Bulgaria	12	371	240	32	13	50	55
6	China	7.5	112 348	67 835	-	-	837	3 291
7	DR Congo	2.8	7 336	2 247	128	5.7	254	252
8	Estonia	20	123	72	74	103	80	80
9	Ethiopia	1.9	5 979	1 557	130	8.3	45	200
10	Georgia	13	728	556	481	87	340	270
11	India	5.4	130 526	63 592	308	0.5	1 420	8 000
12	Indonesia	2.3	12 209	5 909	446	7.5	100	400
13	Kazakhstan	32	11 102	7 432	4 390	59	4 115	5 408
14	Kyrgyzstan	17	1 290	858	189	22	350	220
15	Latvia	14	202	119	129	108	120	135
16	Lithuania	17	464	303	113	37	-	-
17	Myanmar	4.7	4 181	3 983	508	13	75	125
18	Nigeria	2.4	11 700	1 851	23	1.2	80	325
19	Pakistan	4.3	13 218	8 290	40	0.5	-	450
20	Philippines	4.6	12 125	5 950	929	16	864	1 494
21	Republic of Moldova	29	2 231	1 399	1 048	75	560	540
22	Russian Federation	21	42 969	40 094	6 960	17	8 383	12 000
23	South Africa	2.8	15 914	8 506	6 219	73	5 662	6 071
24	Tajikistan	23	4 688	1 262	-	-	-	-
25	Ukraine	19	9 835	5 793	-	-	1 100	1 940
26	Uzbekistan	24	9 450	3 668	155	4.2	720	1 010
27	Viet Nam	4.0	6 468	2 877	-	-	350	500
High MDR-TB burden countries		5.7	435 470	242 938	22 577	9.3	25 770	42 886
	AFR	2.4	75 657	25 432	7 736	30	8 364	10 587
	AMR	3.2	10 214	5 632	2 209	39	3 546	3 198
	EMR	3.8	23 049	10 940	547	5	702	1 060
	EUR	17	92 554	63 288	15 199	24	17 049	23 173
	SEAR	4.8	173 660	84 640	1 864	2.2	4 521	11 196
	WPR	6.3	135 411	76 835	1 198	1.6	2 326	5 627
Global		4.9	510 545	266 768	28 753	11	36 508	54 841

^a Estimates of cases of MDR-TB from 2007 reproduced (see Global TB Report – March 2009).

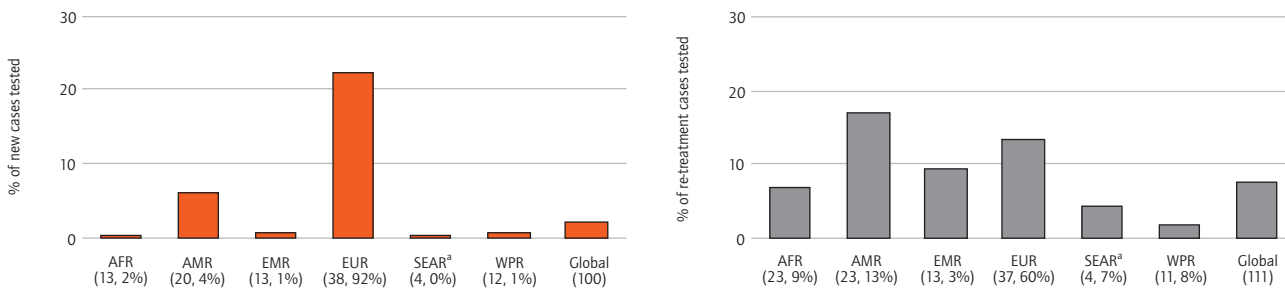
^b Total numbers of notified cases of pulmonary TB are multiplied by 0.9 to estimate the number of cases that would be culture-positive if tested.

^c Percentages may exceed 100% as a result of conservative estimates of MDR-TB and/or notification of cases of MDR-TB from a previous year.

- Indicates data not available.

FIGURE 11

Diagnostic DST for new and re-treatment cases, by WHO region, 2008. The numbers under each bar show the number of countries reporting data, followed by the percentage of cases of MDR-TB reported worldwide accounted for by countries in each region.



^a Data from India excluded as <0.1% of notified cases were tested.

BOX 5

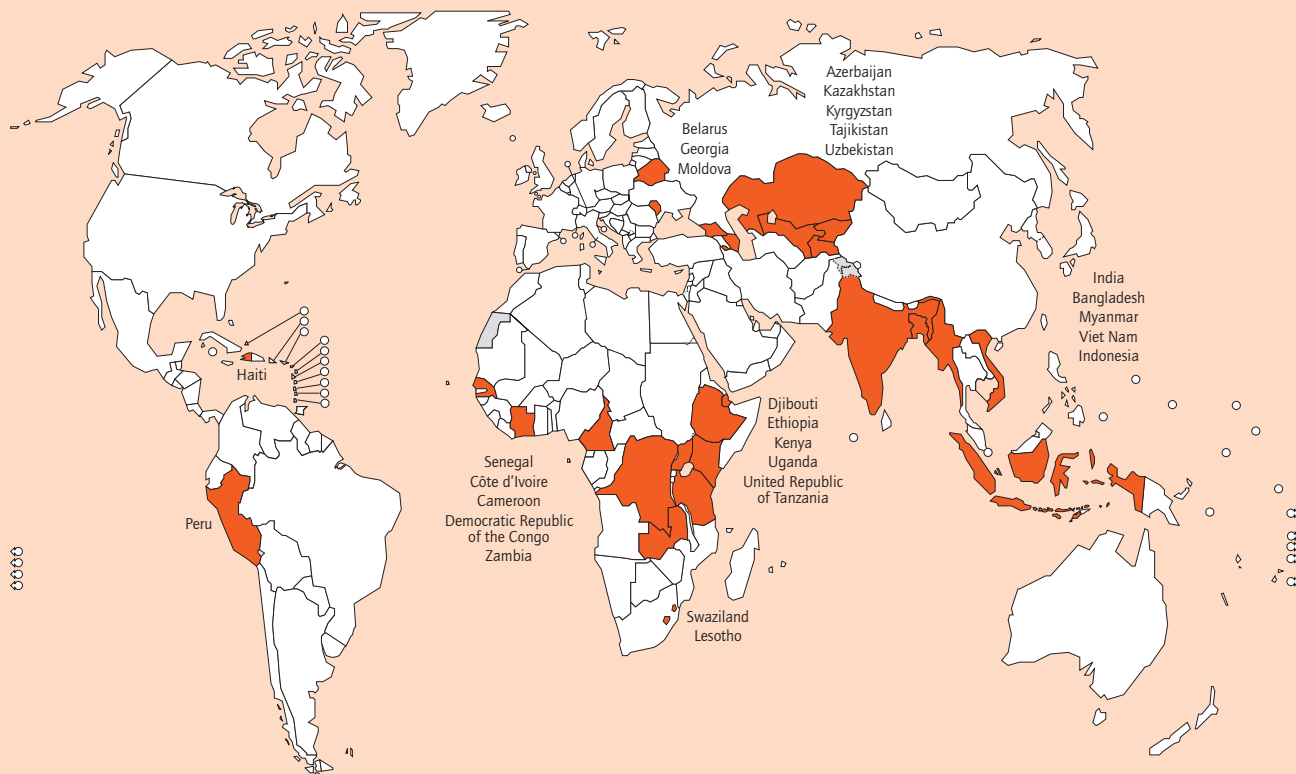
EXPAND-TB: Expanding Access to New Diagnostics for patients at risk of multidrug resistant tuberculosis (MDR-TB)

To address the massive need to scale up laboratory services with the capability to test for drug-resistant TB, a network of international partners has combined to form the Global Laboratory Initiative (GLI). The GLI is working with NTPs, non-governmental organizations, technical and financial partners, and WHO offices at country and regional levels to strengthen laboratory services and to encourage the adoption of new diagnostic tools once these have been endorsed by WHO. The secretariat of the GLI is hosted by the Stop TB Department of WHO.

In 2008, UNITAID approved a project called EXPAND-TB, which will support the procurement and use of new TB diagnostic tools in low and lower-middle income countries between 2009 and 2013. Project partners include WHO-GLI, the Foundation for Innovative New Diagnostics (FIND) and the Stop TB Partnership's Global Drug Facility (GDF). EXPAND-TB aims to narrow the diagnostic gap affecting control of MDR-TB by accelerating access to new diagnostic technologies within appropriate laboratory services, accompanied by the necessary transfer of technology while also ensuring that new tools are properly integrated within TB control programmes.

EXPAND-TB requires extensive complementary resources to strengthen laboratory infrastructure and services in recipient countries. Building on the foundation of UNITAID support, the project is seeking to mobilize resources from other partners to support the upgrading and modernization of national TB reference laboratories, training in good laboratory practice, bio-safety, new diagnostic methods, and technical assistance.

EXPAND-TB currently covers 27 countries (see map).



6. Financing for TB control

6.1 High-burden countries

The funding available for TB control in the 22 HBCs has increased each year since 2002, and is expected to reach US\$ 2.6 billion in 2010 (FIGURE 12, FIGURE 13, FIGURE 14). Most of this funding has been used to support DOTS implementation, although the share for MDR-TB (mostly accounted for by funding in the Russian Federation and South Africa) has increased since 2007 (FIGURE 12). The relatively small amount of funding reported for collaborative TB/HIV activities reflects the fact that funding for most of these interventions is channelled through national HIV programmes and nongovernmental organizations (NGOs) rather than via NTPs. National governments are the largest source of funding (FIGURE 13): for example, they account for 84% of total expected funding in 2010. Financing from the Global Fund has become increasingly important since 2004, reaching just over US\$ 200 million in 2010. Other donor funding is expected to amount to just under US\$ 100 million in 2010. In absolute terms, 68% of the funding expected in 2010 is accounted for by just two countries: the Russian Federation and South Africa (FIGURE 14).¹

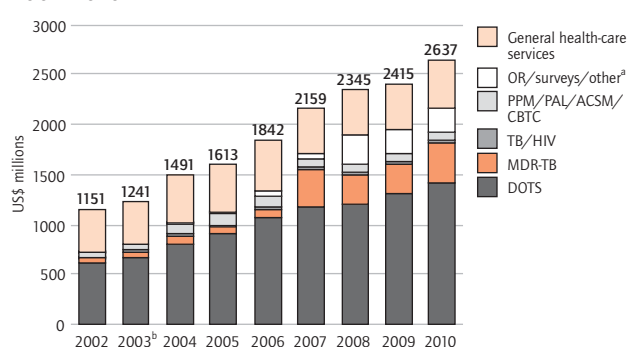
Although increases in funding have continued in 2009 and 2010 despite a global financial crisis, NTPs continue to report funding gaps (FIGURE 15). The funding gaps reported since 2007 have been much larger than those reported during 2002–2006, as NTPs expand the range of interventions being planned in line with the Stop TB Strategy. Funding gaps are not only for interventions such as treatment of MDR-TB and collaborative TB/HIV activities, however; some countries continue to report funding gaps for first-line anti-TB drugs as well. The funding gap reported for 2010 is US\$ 0.5 billion.

Trends in funding for the 22 HBCs as a whole conceal important variations among countries (TABLE 10, FIGURE 16, FIGURE 17). Both NTP budgets and funding of NTPs have been increasing in most countries; however, there are exceptions where funding has fluctuated markedly, both up and down (for example in Bangladesh, Myanmar, Viet Nam, and Zimbabwe) and where funding is expected to be lower in 2010 compared with 2009 (for example in Brazil and Pakistan) (FIGURE 16). Funding has been closest to keeping pace with increases in NTP budgets in Brazil, China, India, the Philippines and the Russian Federation; in contrast, funding gaps have persisted in most African countries as well as Afghanistan, Myanmar and Pakistan. In 2010, the Russian Federation, Thailand, Brazil and China will rely primarily on domestic funding (including loans),² but in other HBCs

¹ Financial data were not reported for South Africa in 2009. Data and estimates for South Africa in this section are based on adjustments to data reported in 2006 and 2007.

² The same is likely to be true for South Africa, based on data reported in previous years, but financial data were not reported to WHO in 2009 pending completion of a costing study commissioned by the Department of Health.

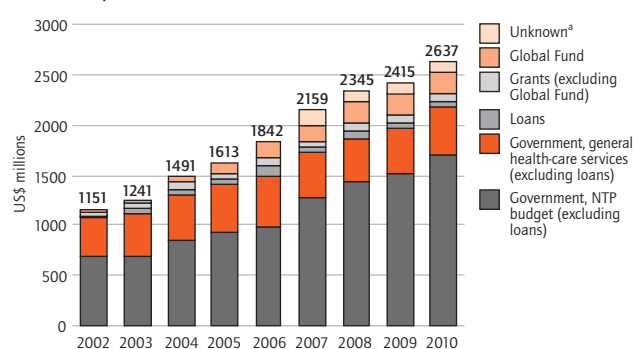
■ FIGURE 12
Funding for TB control by line item, high-burden countries, 2002–2010



^a Category "OR/surveys/other" shown only from 2006 onwards, following changes in data requested by WHO.

^b Funding for the Russian Federation 2002–2003 was not reported by line item. The breakdown in these two years is estimated based on the breakdown in 2004.

■ FIGURE 13
Funding for TB control by source of funding, high-burden countries, 2002–2010



^a Unknown source applies only to a portion of the budget for MDR-hospitals in South Africa.

around 40% or more of available funding is from grants from external donors. Afghanistan and the Democratic Republic of the Congo are particularly dependent on donor funding.

There is also considerable variation in the cost per patient treated under DOTS (FIGURE 18). This ranges from under US\$ 100 (in Bangladesh, India, Myanmar and Pakistan) to around US\$ 1000 (in Brazil and South Africa) to over US\$ 5000 (in the Russian Federation; the main outlier). These differences are partly linked to income levels (for example, Brazil and South Africa are upper-middle income countries where prices for inputs such as NTP staff and hospital care are higher than in low-income countries), but are also linked to the extent to which hospitalization is relied upon during treatment. This is the major reason for particularly high costs in the Russian Federation, where an extensive network of TB hospitals and sanatoria is used to treat TB patients. Costs in African countries also tend to be higher than those in Asian countries, even among countries with similar income levels.

FIGURE 14
Funding for TB control by country, high-burden countries, 2002–2010

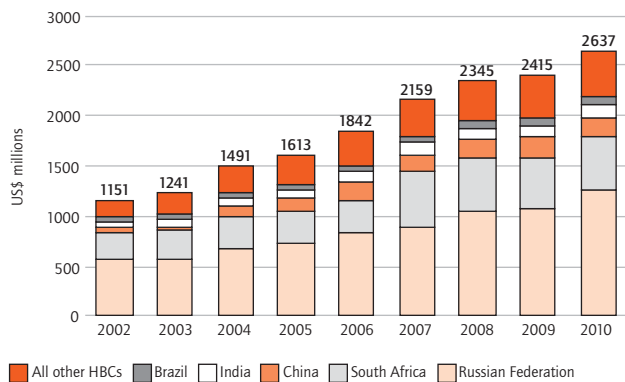


FIGURE 15
Funding gaps reported by NTPs, high-burden countries, 2002–2010

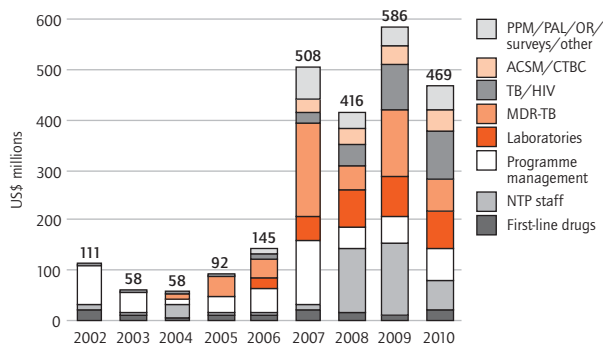


FIGURE 16
NTP budgets and available funding, 22 high-burden countries, 2002–2010

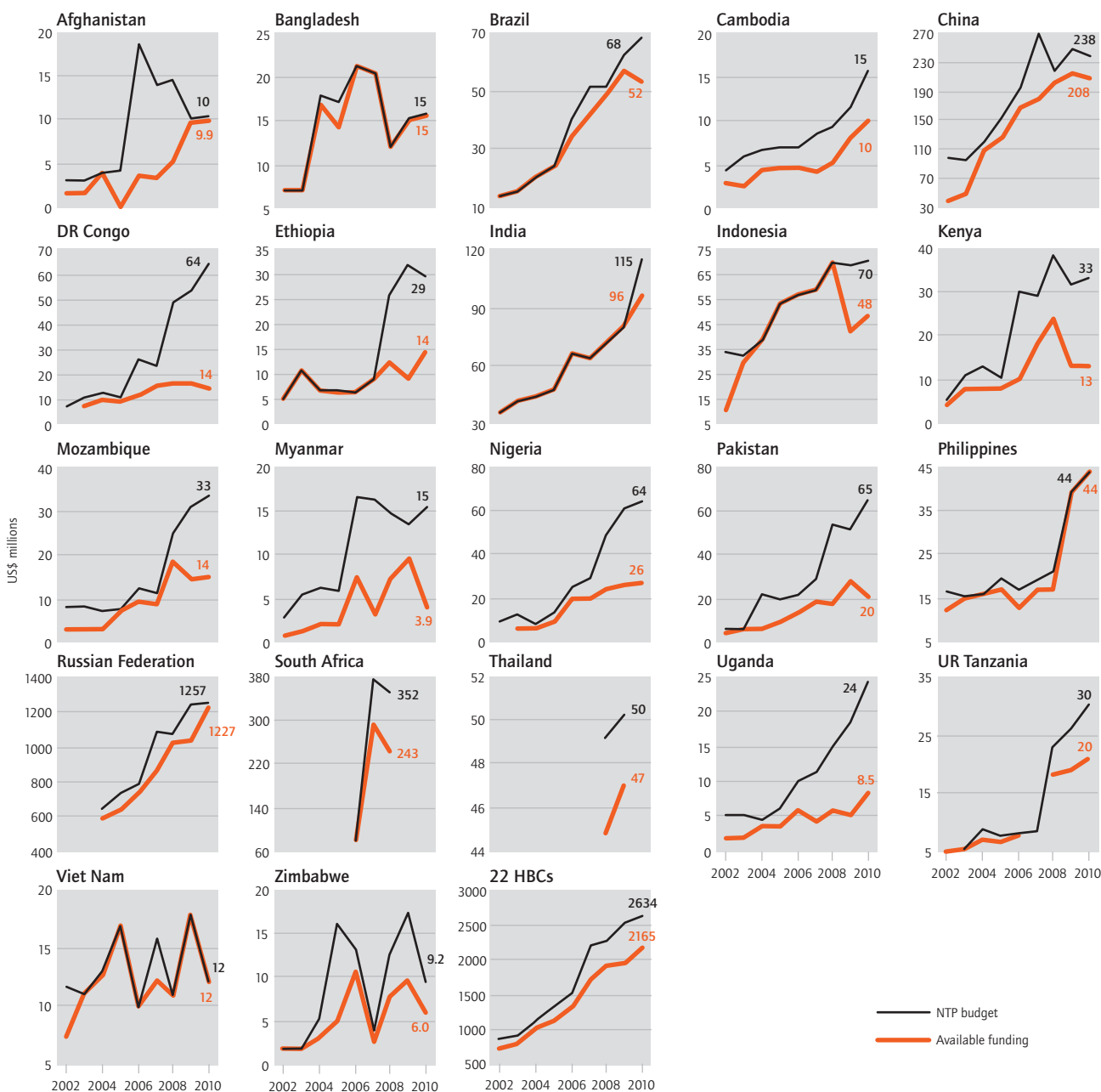


TABLE 10

NTP budgets, available funding, cost of utilization of general health-care services and total TB control costs, high-burden countries, 2010 (US\$ millions)

	NTP BUDGET	AVAILABLE FUNDING				FUNDING GAP	COST OF UTILIZATION OF GENERAL HEALTH-CARE SERVICES	TOTAL TB CONTROL COSTS ^a
		GOVERNMENT (EXCLUDING LOANS)	LOANS	GRANTS (EXCLUDING GLOBAL FUND)	GLOBAL FUND			
Afghanistan	10	0.2	0	5.5	4.2	0.3	1.2	12
Bangladesh	16	5.1	1.1	0.0	9.5	0.1	1.7	18
Brazil	68	45	0	2.3	4.8	16	31	99
Cambodia	16	1.2	0	3.2	5.7	5.8	2.9	19
China	239	179	0	0.8	28	30	0	239
DR Congo	65	1.6	0	3.7	9.4	50	1.2	66
Ethiopia	30	1.7	0	2.3	11	15	16	46
India	115	9.5	39	19	29	19	23	138
Indonesia	71	19	0	7.9	22	22	11	82
Kenya	33	1.8	1.0	5.8	4.3	20	5.1	38
Mozambique	34	2.6	0	8.7	3.5	19	6.4	40
Myanmar	16	0.5	0	3.3	0	12	2.0	18
Nigeria	64	3.7	0	11	13	38	23	87
Pakistan	65	9.7	0	3.2	7.9	45	3.7	69
Philippines	44	24	0	0	21	0.0	18	62
Russian Federation	1 258	1213	0	1.4	12	31	33	1 291
South Africa ^b	363	-	-	-	-	-	273	636
Thailand	52	48	0	0	0.8	3.3	1.2	53
Uganda	24	0.5	1.5	4.1	2.4	16	0.5	25
UR Tanzania	30	7.1	0	8.1	5.6	9.5	0.6	31
Viet Nam	12	6.4	0	1.2	4.4	0	13	25
Zimbabwe	9.2	0.4	0	0.3	5.3	3.2	5.2	14
High-burden countries	2 634	1 580	43	92	203	354	472	3 106

^a Calculated as NTP budget plus cost of utilization of general health-care services.

^b Numbers for South Africa estimated based on data reported in 2007.

FIGURE 17

Sources of funding for TB control, 21 high-burden countries, 2010^a

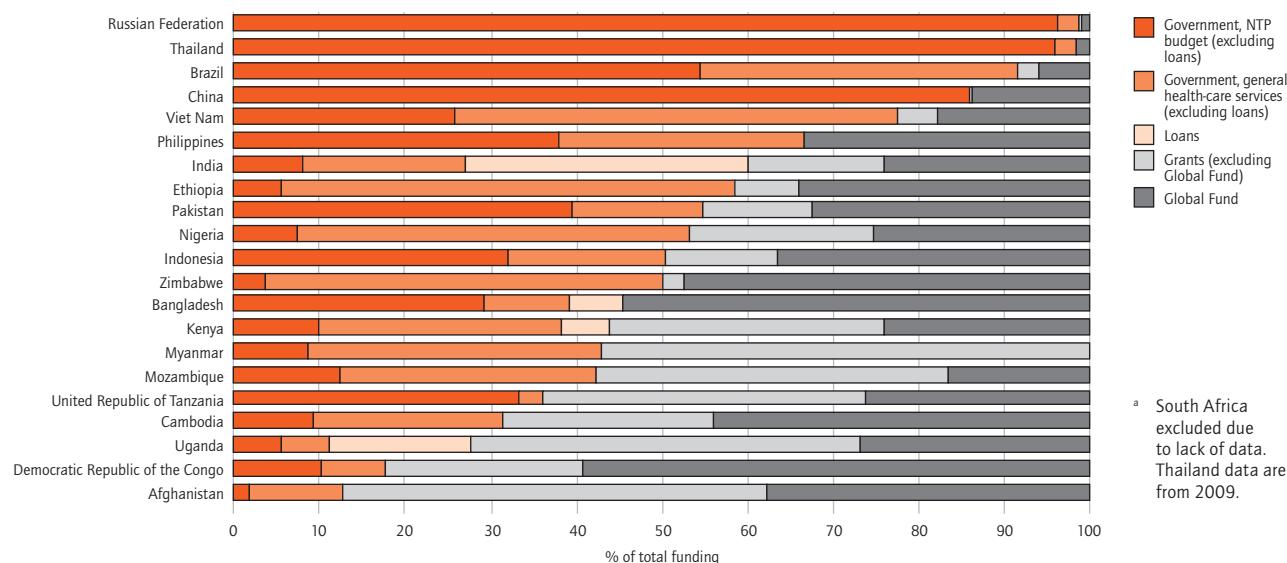
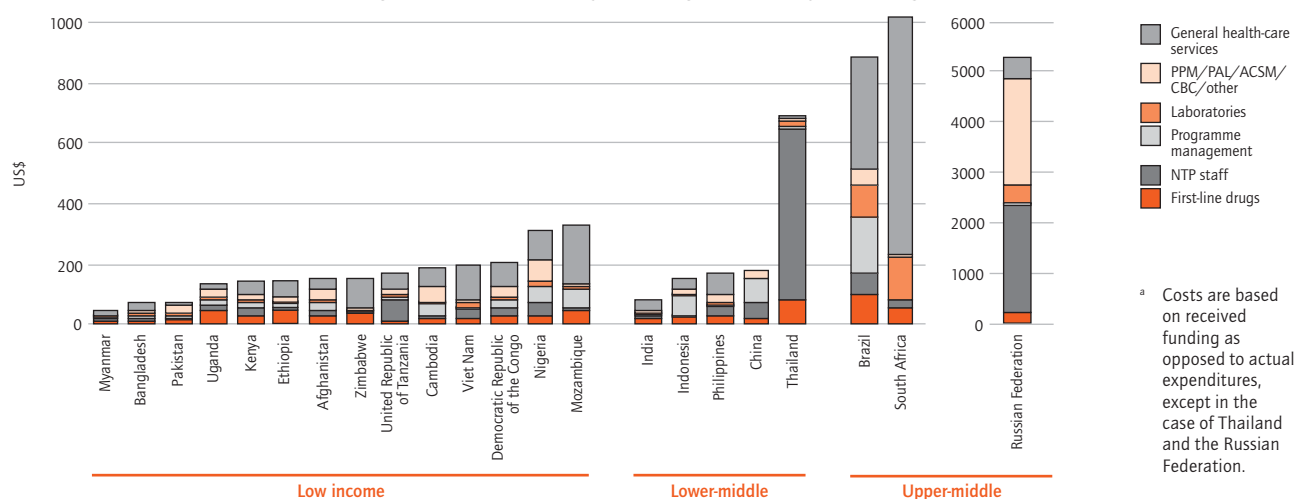


FIGURE 18
Costs per DOTS patient treated, 22 high-burden countries by income group, three-year average, 2006–2008^a



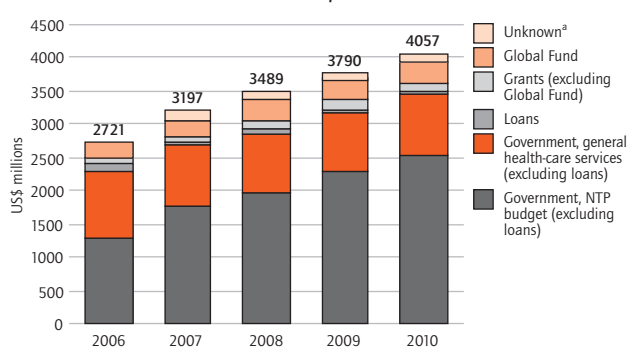
^a Costs are based on received funding as opposed to actual expenditures, except in the case of Thailand and the Russian Federation.

6.2 High-burden countries and other countries

Besides the 22 HBCs, there are 96 other countries that have reported financial data to WHO since 2006, and which allow assessment of trends in funding for TB control. These 118 countries account for 94% of the total number of TB cases globally. In these 118 countries, funding for TB control has grown from US\$ 2.7 billion in 2006 to US\$ 4.1 billion in 2010 (FIGURE 19). As in HBCs, the largest share of funding is from national governments (86%), followed by the Global Fund (US\$ 350 million, or 9% of total funding) and then by grants from donors besides the Global Fund (US\$ 112 million, or 3%). The source of funding was unknown for the remaining 2%. Most of the available funding is in the European Region (US\$ 1.9 billion, mostly in the Russian Federation), followed by the African Region (US\$ 0.5 billion) and the Western Pacific Region (US\$ 0.3 billion). The funding gaps identified by these 112 countries amount to US\$ 0.8 billion in 2010.

A comparison of the funding available in the countries that reported financial data with the funding requirements set out in the Global Plan is provided, by region and for the period 2006–2010, in FIGURE 20.¹ Overall, funding falls short of Global Plan requirements in all regions with the exception of the European Region. Outside the European Region, exceptions for which the funding reported to be available is higher than funding requirements estimated in the Global Plan are diagnosis and treatment for MDR-TB in the African Region and the Region of the Americas. Overall, the gap between the funding reported by these countries in 2010 and the funding requirements for these countries according to the Global Plan is US\$ 2.1 billion. Most of the extra funding required according to the Global Plan is for MDR-TB diagnosis and treatment in the European, South-East Asia and Western Pacific regions, and for DOTS and collaborative TB/HIV activities in the African Region.

FIGURE 19
Funding for TB control by source of funding, 22 high-burden countries and 96 other countries, 2006–2010



^a Unknown source applies to South Africa.

¹ This analysis is for the 22 HBCs and a subset of 76 other countries that were among the 171 countries considered in the Global Plan.

7. Progress towards global targets for reductions in disease burden

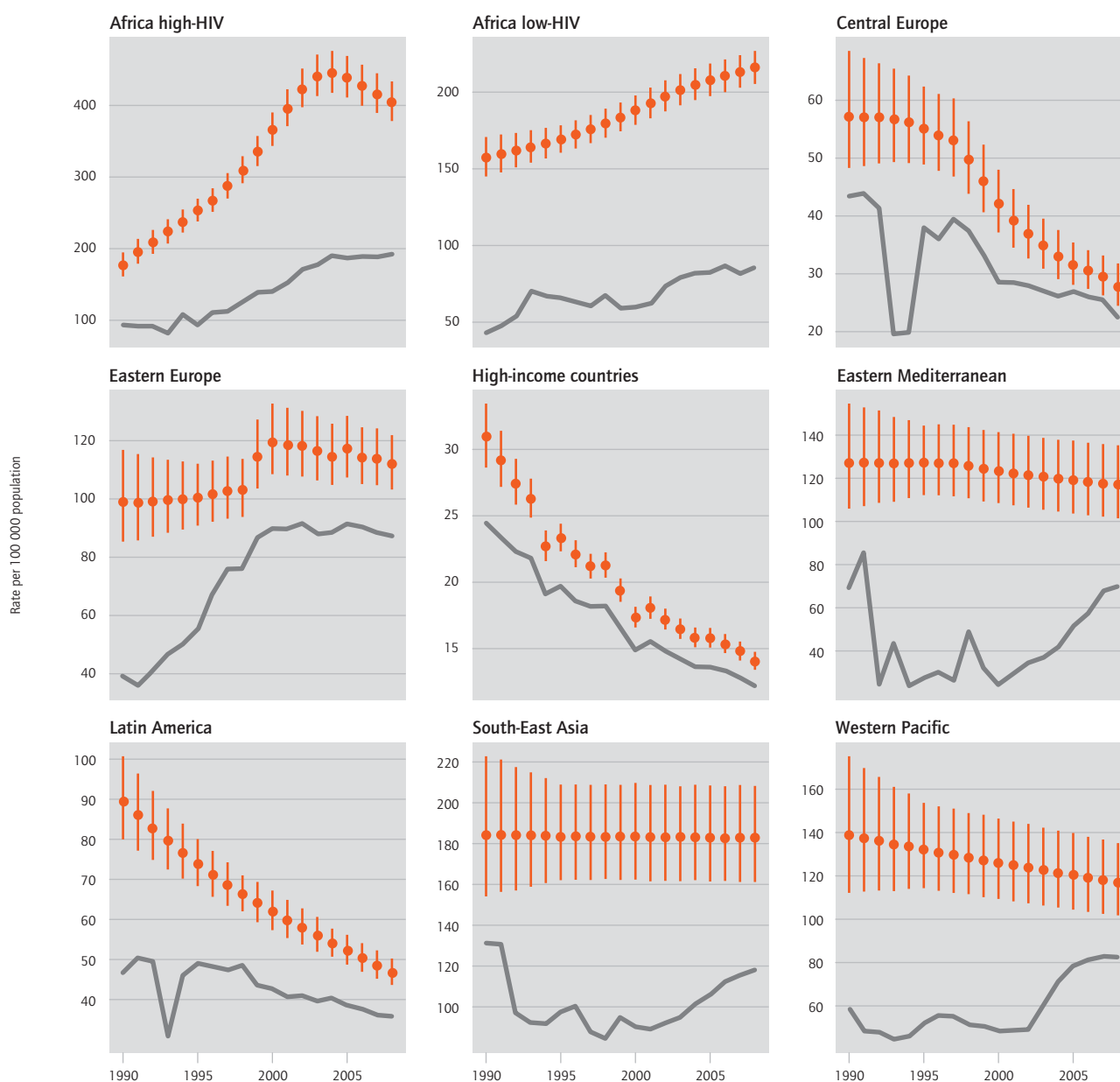
Progress towards achieving the impact targets set for 2015 – to halt and reverse the incidence of TB by 2015, and to halve prevalence and mortality rates compared with a baseline of 1990 – is illustrated at regional level in **FIGURE 21**, **FIGURE 22** and **FIGURE 23**, and at global level in **FIGURE 24**.

Incidence rates are declining in all nine epidemiological subregions¹ with the exception of African countries with a low prevalence of HIV (**FIGURE 21**). The rate of decline varies, from less than 1% per year in the South-East Asia Region

to around 4% per year in Latin America as well as African countries with a high prevalence of HIV; in the latter, the TB epidemic appears to have reversed in 2004 following many years of increasing TB incidence rates associated with the HIV epidemic. Globally, incidence rates peaked at 143 (range, 136–151) cases per 100 000 population in 2004. Provided the downward trend is sustained, the world as a whole is on track to achieve MDG Target 6.c.

■ **FIGURE 21**

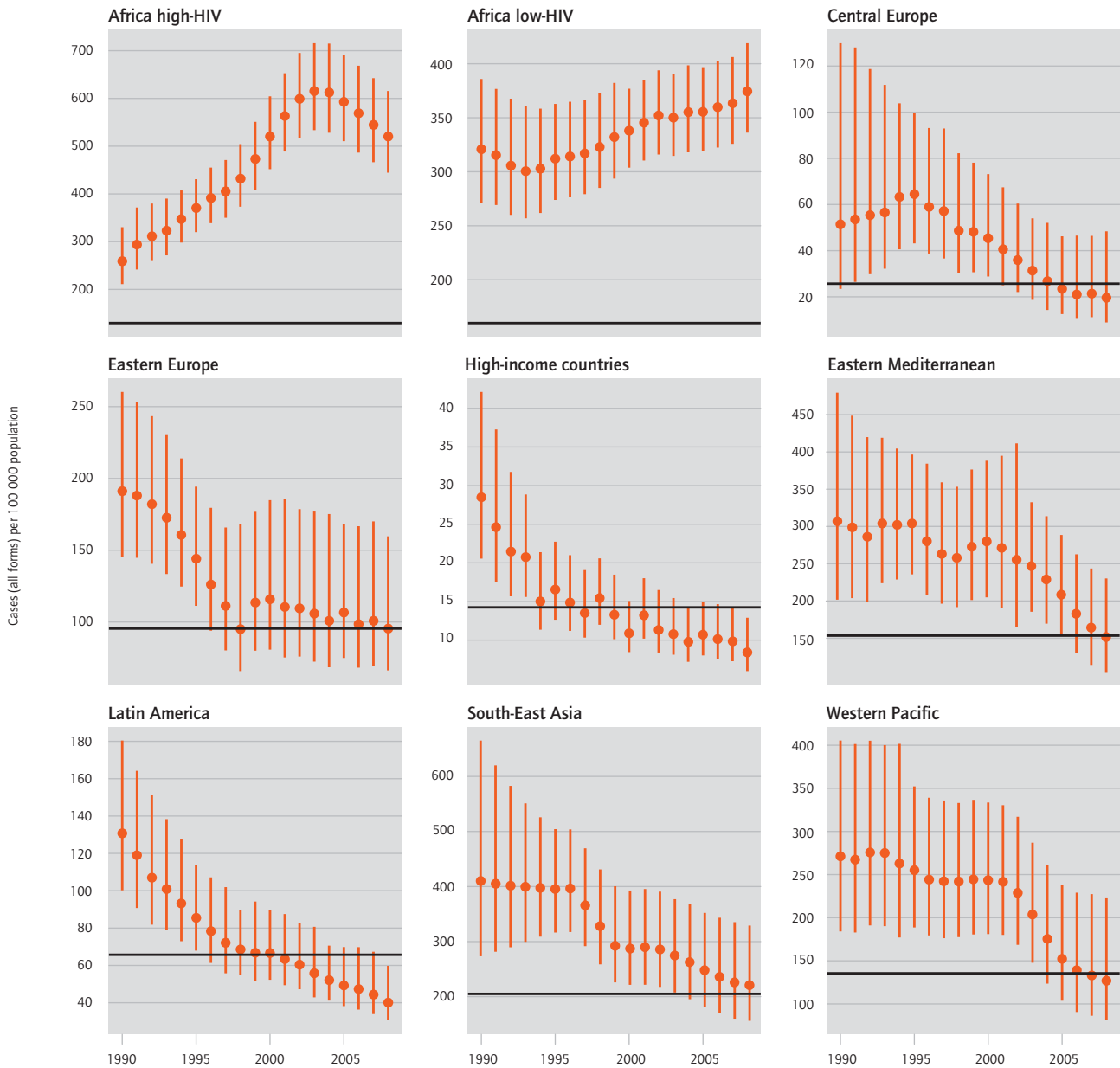
Trends in estimated incidence rates (red) and notification rates (grey) in nine subregions, 1990–2008



¹ For definition of the countries included in each subregion, please refer to **ANNEX**.

■ FIGURE 22

Progress towards achieving the target of halving prevalence rates by 2015 compared with the level of 1990 in nine subregions



Black line shows the target level of a 50% reduction in prevalence by 2015, compared with 1990.

Prevalence rates are falling in six of nine epidemiological subregions, increasing in African countries with low HIV prevalence and approximately stable in Central and Eastern European countries (FIGURE 22). Six of the nine subregions (Central Europe, Eastern Europe, the Eastern Mediterranean, high-income countries, Latin America and the Western Pacific) appear to have achieved the target of halving the 1990 prevalence rate already, well in advance of the target year of 2015. The South-East Asia region was close to the target level in 2008, and achieving the target appears feasible by 2015. Achievement of the target appears impossible in African countries.

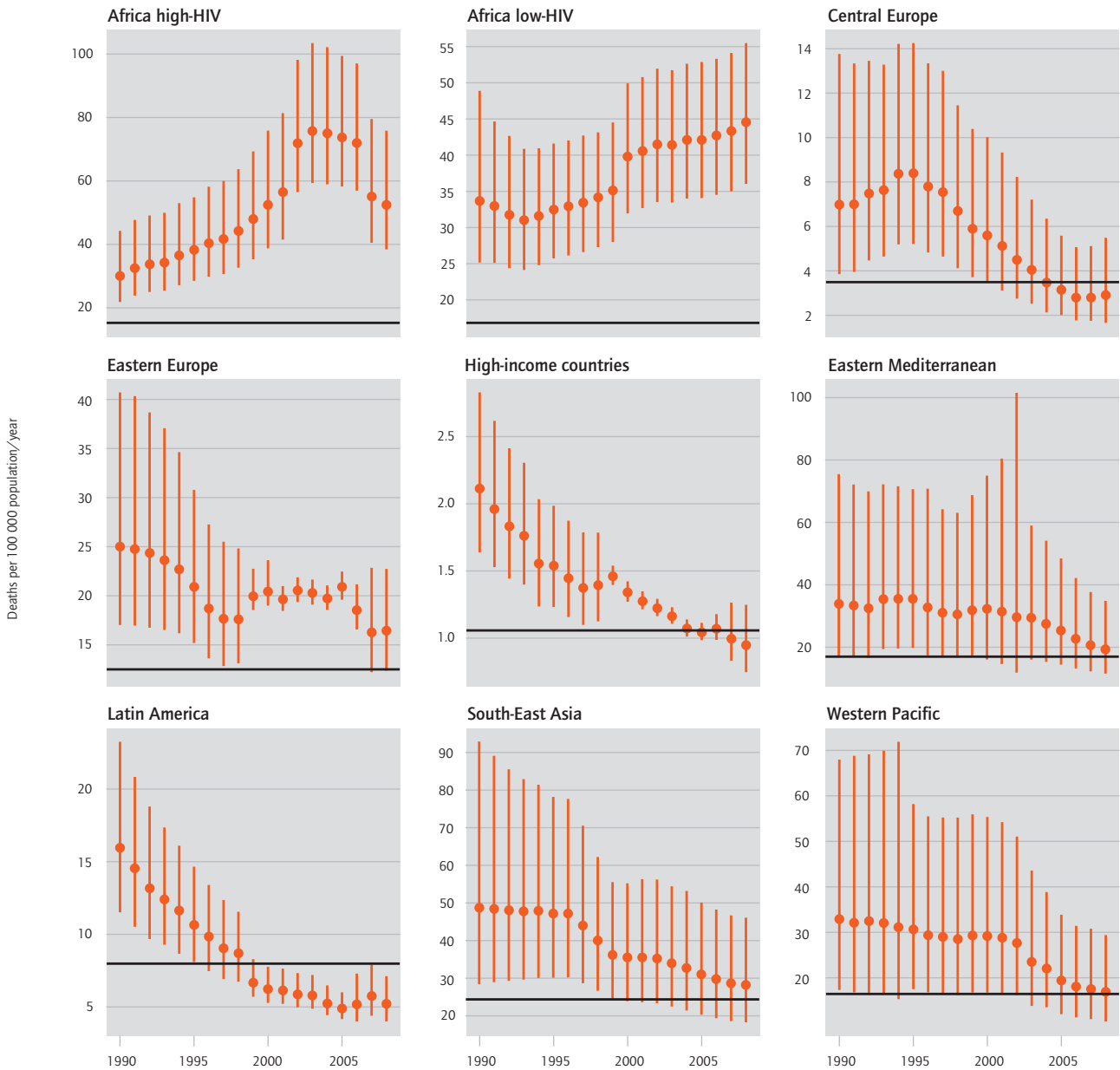
Mortality rates (excluding TB deaths in HIV-positive people) have been falling in four of nine epidemiological

subregions since 1990 (Central Europe, high-income countries, Latin America and the Western Pacific), falling since around 2003 in three regions (African countries with a high prevalence of HIV, Eastern Europe and South-East Asia), and increasing since the mid-1990s in African countries with a low prevalence of HIV (FIGURE 22). Four of the nine subregions (Central Europe, high-income countries, Latin America and the Western Pacific) appear to have achieved the target of halving the 1990 mortality rate already, well in advance of the target year of 2015. Achievement of the target in Eastern Europe, the Eastern Mediterranean and South-East Asia appears feasible. Achievement of the target appears impossible in African countries.

Globally, the gulf between prevalence and mortality rates

FIGURE 23

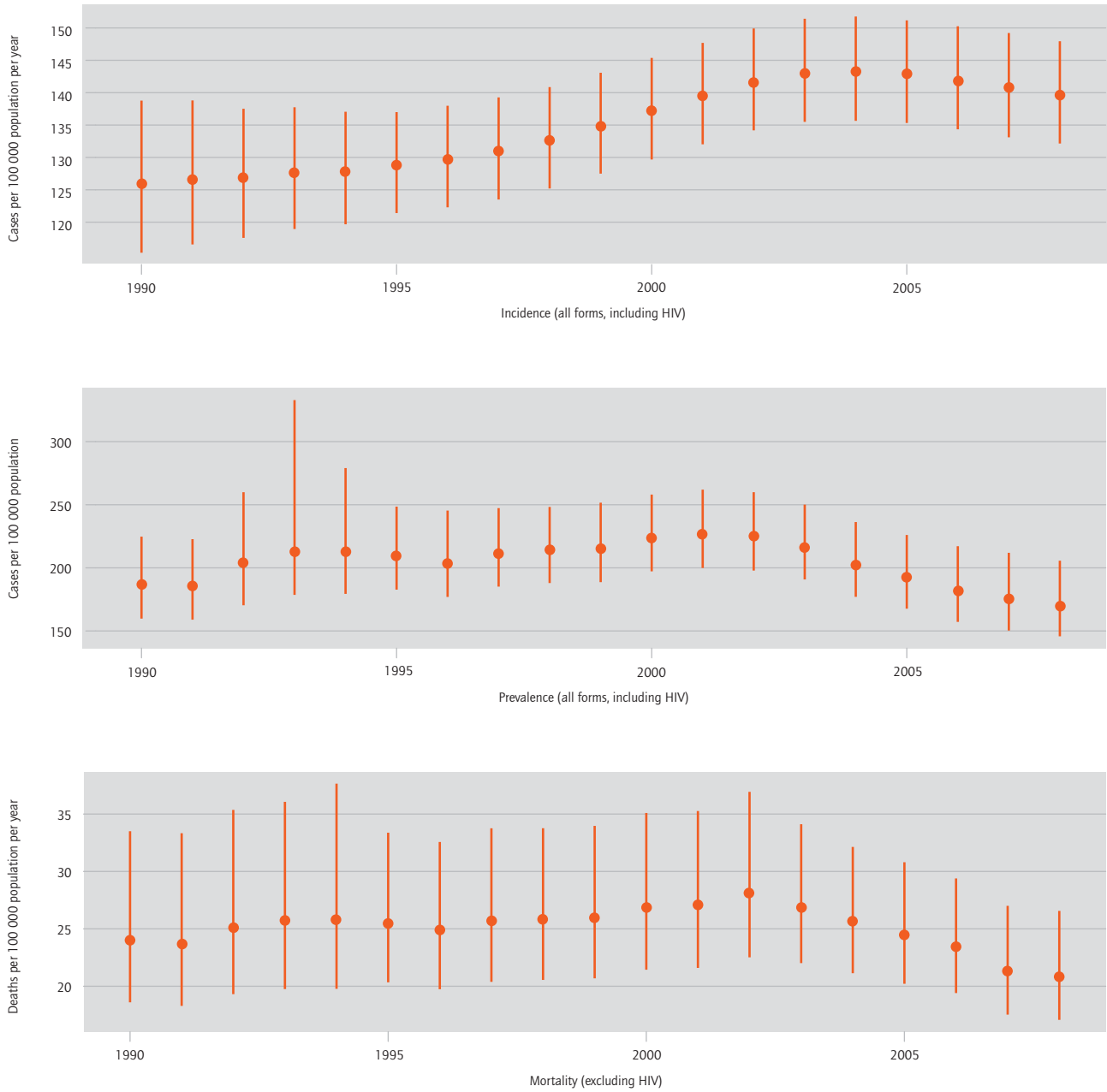
Progress towards achieving the target of halving mortality rates by 2015 compared with the level of 1990 in nine subregions. Comparatively less uncertainty is attached to data points when most of the underlying aggregated data is composed of measurements from Vital Registration.



in 2008 and achieving the targets in African countries makes it unlikely that 1990 prevalence and death rates will be halved by 2015 for the world as a whole (FIGURE 24).

FIGURE 24

Global rates of TB incidence, prevalence and mortality, including in people with HIV, 1990–2008



8. Improving measurement of the global burden of TB

Estimates of TB incidence, prevalence and mortality and their trend (presented in **TABLE 1** and in **FIGURES 21-24**) are based on the best available data and analytical methods. Methods were updated in 2009 following 18 months of work by an expert group convened under the umbrella of the WHO Global Task Force on TB Impact Measurement.¹ Improvements to methods include systematic documentation of expert opinion and how this has been used in estimates of disease burden, simplification of models,² updates to parameter values based on the results of systematic reviews, much greater use of mortality data from vital registration systems (89 countries instead of the three from which estimates were derived up to 2008) and systematic documentation of uncertainty (hence the uncertainty intervals shown on the estimates of disease burden in this report).

Despite this progress, estimates of disease burden could be substantially improved in the period up to 2015 (and beyond) with better surveillance systems, more extensive and in-depth analysis of available surveillance and programmatic data, and additional survey data. For example, with the

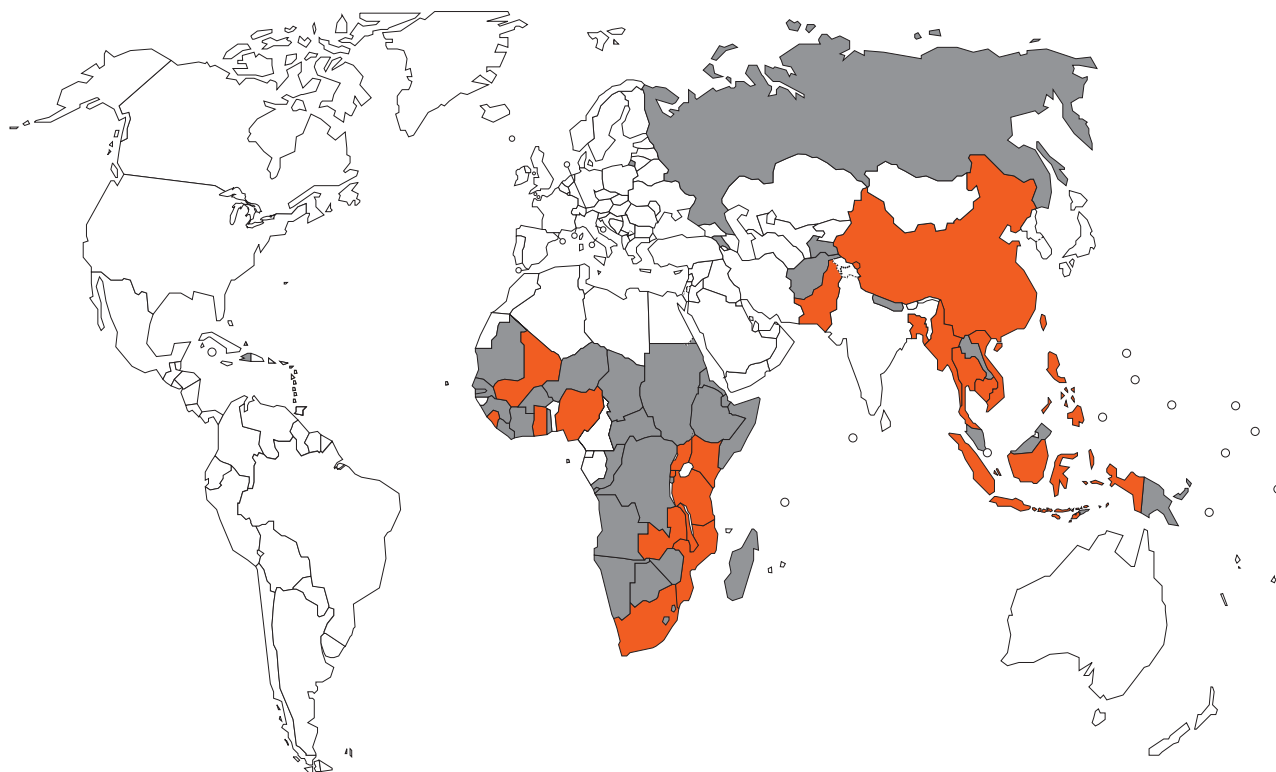
exception of Eritrea in 2005, the last nationwide and population-based surveys of the prevalence of TB disease in the African Region were undertaken between 1957 and 1961; only around 10% of TB-attributable deaths (in HIV-negative people) are recorded in vital registration systems and reported to WHO; and most notification systems are recording only around 50–70% of estimated cases.

Besides its work on reviewing and updating the methods used to produce estimates of disease burden, the WHO Global Task Force on TB Impact Measurement is thus pursuing two other major strategic tracks of work:

- Surveys of the prevalence of TB disease in 21 global focus countries (**FIGURE 25**), carried out according to WHO guidelines and related Task Force recommendations;
- Strengthening of surveillance systems and use of surveillance data from notification and vital registration systems. The Task Force has defined a conceptual framework for this work (**FIGURE 26**) and related tools to implement it in practice.

■ FIGURE 25

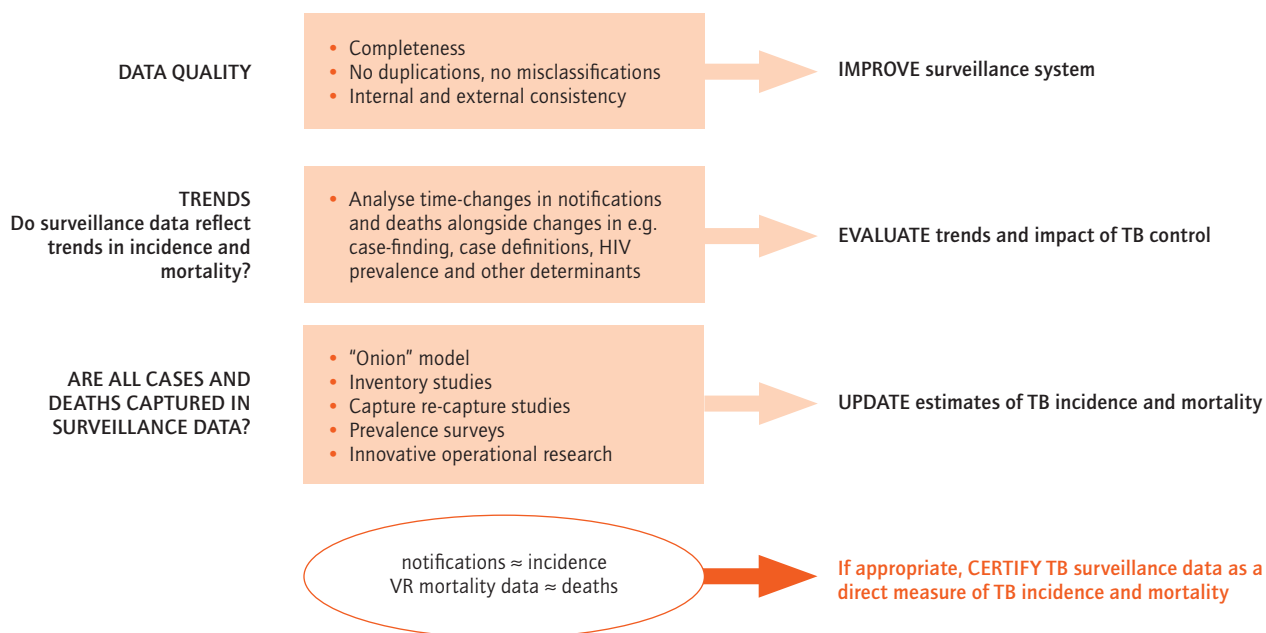
The 21 global focus countries where a national survey of the prevalence of TB disease is recommended in the period 2008–2015 (red), and extended list of countries meeting the criteria (grey) for implementing such surveys



¹ For further details, see the Task Force website at http://www.who.int/tb/advisory_bodies/impact_measurement_taskforce/en/index.html. The review is also the basis for the TB component of the forthcoming update to the Global Burden of Disease, due for publication in 2010.

² For example, some parameter values are now estimated only at global level or for regions, rather than for each country individually.

■ **FIGURE 26**
 Framework for assessment of TB surveillance data (notification and vital registration data)



As of November 2009, all of the countries in the South-East Asia and Western Pacific regions where prevalence surveys are recommended (Bangladesh, Cambodia, China, Indonesia, Myanmar, the Philippines, Thailand and Viet Nam) are on track with survey implementation. Bangladesh, the Philippines and Viet Nam have completed surveys, with subsequent surveys planned close to 2015; Cambodia and China will implement surveys in 2010, following surveys already conducted in 2002 in Cambodia and in 1990 and 2000 in China; a survey is currently under way in Myanmar and in preparation in Thailand; and in Indonesia, a follow-up to the 2004 survey is expected around 2012. In the Eastern Mediterranean Region, Pakistan has secured full funding for a survey but security concerns may preclude implementation.

The greatest challenge in terms of implementation of prevalence surveys is in the African Region. Nonetheless, considerable progress was made during 2009, with five countries now in a strong position to start surveys in 2010 (Ethiopia, Nigeria, Rwanda, South Africa and Zambia); the United Republic of Tanzania also appears in a relatively strong position to implement a survey, with all X-ray equipment already procured. Preparations are relatively advanced in Ghana, Kenya, Malawi, Mali and Uganda, but funding gaps remain a major bottleneck.

In 2009, substantial progress has been made with the

analysis of surveillance and programmatic data, linked to recommendations for how surveillance systems need to be strengthened towards the ultimate goal of measuring cases and deaths directly from notification and vital registration data. Regional workshops to apply the Task Force framework (FIGURE 26) for systematic assessment of surveillance data were held for countries in the Eastern Mediterranean, European and South-East Asia regions and the Region of the Americas, covering a total of 59 countries. Similar work was also undertaken through country missions to the Philippines, the United Republic of Tanzania and Viet Nam. An important conclusion from workshops and country missions was that there is an urgent need to introduce electronic recording and reporting systems, without which it is difficult or impossible to adequately assess many aspects of data quality, and that more widespread adoption of updated recommendations on recording and reporting is required (for example, to ensure availability of data disaggregated by HIV status and source of referral). In 2010, workshops are planned for countries in the African and Western Pacific regions.

Besides improving estimates of disease burden, better data and better analysis of these data should be of great value in identifying where and why cases are not being detected and, in turn, defining which components of the Stop TB Strategy need to be introduced or scaled-up to improve TB control.

9. Conclusions

The global burden of TB is falling slowly. If current trends are sustained, the world as a whole will have achieved the MDG target of halting and reversing the incidence of TB in 2004, well in advance of 2015. Six epidemiological subregions appear to have achieved the Stop TB Partnership target of halving the 1990 prevalence rate and four appear to have achieved the Stop TB Partnership target of halving the 1990 mortality rate, in advance of the target year of 2015. Prevalence and mortality rates are falling in all other regions with the exception of African countries with a low prevalence of HIV, although reaching the global target will be difficult in the South-East Asia Region and it appears impossible in the African Region.

Reductions in disease burden achieved to date follow fourteen years of intensive efforts at global, regional and country levels to implement the DOTS strategy (1995–2005) and its successor, the Stop TB Strategy (2006–). Between 1995 and 2008, a cumulative total of 36 million TB patients were successfully treated in DOTS programmes, and up to 6 million

deaths were averted. The treatment success rate achieved in DOTS cohorts worldwide exceeded the global target of 85% for the first time in 2007, reaching 86%.

Although increasing numbers of TB cases have access to high-quality treatment for TB as well as access to related interventions such as ART, much more remains to be done. More than one-third of incident TB cases are not reported as treated in DOTS programmes, around 90% of patients with MDR-TB are not being diagnosed and treated according to international guidelines, the majority of HIV-positive TB cases do not know their HIV status and most of the HIV-positive TB patients who do know their HIV status are not yet accessing ART. Funding gaps remain large, despite increases in funding since 2002.

To consolidate the major progress in global TB control achieved in recent years, intensified efforts to plan, finance and implement the range of interventions and approaches included in the Stop TB Strategy, according to the targets established in the Global Plan to Stop TB, are needed.

Methods used to estimate the burden of TB

1. General approach

The World Health Organization (WHO) produces estimates of the burden of TB (incidence, prevalence and mortality) annually using information gathered through surveillance systems (case notifications and death registrations), special studies (including surveys of the prevalence of disease and in-depth analyses of surveillance data), expert opinion and consultations with countries. Two recent publications provide up-to-date guidance about how TB incidence, prevalence and mortality should be measured,^{1,2} based on the work of the WHO Global Task Force on TB Impact Measurement (hereafter the Task Force).³ The methods used to estimate the burden of disease were updated in 2009 following 18 months of work by an expert group convened under the umbrella of the Task Force. Improvements to methods include systematic documentation of expert opinion and how this has been used to produce estimates of disease burden, simplification of models,⁴ updates to parameter values based on the results of systematic reviews, much greater use of mortality data from vital registration systems (89 countries instead of the three from which estimates were derived up to 2008) and systematic documentation of uncertainty (hence the uncertainty intervals shown on all of the estimates of disease burden in this report).

2. Definitions and data sources

2.1 Definition of incidence, prevalence and mortality

Incidence is defined as the number of new and relapse cases of TB (all forms) occurring in a year. Relapse cases are defined as people who have been previously treated for TB and for whom there was bacteriological confirmation of cure and/or documentation that treatment was completed. Relapse cases may be true relapses or a subsequent episode of TB caused by reinfection.

Prevalence is defined as the number of TB cases (all forms) at a given point in time. Estimates of disease burden assume that notified cases are removed from the pool of prevalent cases after a mean duration of three months (by which time most treated cases are culture-negative and would not be identified as confirmed TB cases according to standard case definitions recommended for surveys of the prevalence of TB disease⁵).

Mortality is defined as the number of deaths caused by TB, excluding deaths in HIV-positive TB cases, according to the definitions used in the 10th revision of the International Clas-

sification of Diseases (ICD-10). Estimates of deaths due to TB in HIV-positive cases are presented separately from estimates of deaths due to TB in HIV-negative cases.

2.2 Definition of regions

Regional analyses are generally undertaken for the six WHO regions (that is, the African Region, the Region of the Americas, the Eastern Mediterranean Region, the European Region, the South-East Asia Region and the Western Pacific Region). For analyses of epidemiological trends at the regional level, the African Region is divided into countries with low and high rates of HIV infection (with "high" defined as an infection rate of $\geq 4\%$ in adults aged 15–49 years in 2004, as estimated by UNAIDS⁶). Central and eastern Europe (that is, countries of the former Soviet states plus Bulgaria and Romania) are also distinguished. Countries in western Europe are analysed together with other high-income countries in a category defined as Established Market Economies (EME).⁷ The countries within each of the resulting nine epidemiological groups or regions are listed in **TABLE A1.1**.

2.3 Population estimates

Where population sizes are needed to calculate TB indicators, the latest revision of estimates provided,⁸ by the United Nations Population Division (UNPD) is used.⁹ The UNPD estimates sometimes differ from those made by countries.

2.4 Sources of data on TB mortality

The best sources of data about deaths from TB (excluding those among HIV-positive people) are vital registration (VR) systems in which causes of death are coded according to the

¹ Dye C. et al. Measuring tuberculosis burden, trends and the impact of control programmes. *Lancet Infectious Diseases* (published online 16 January 2008; <http://infection.thelancet.com>).

² TB Impact Measurement: WHO policy and recommendations for how to assess the epidemiological burden of TB and the impact of TB control. Geneva, World Health Organization, 2009 [in press].

³ For further details, see the Task Force web site at http://www.who.int/tb/advisory_bodies/impact_measurement_taskforce/en/index.html. The review is also the basis for the TB component of the forthcoming update to the Global Burden of Disease Project (<http://www.globalburden.org/>), due for publication in 2010.

⁴ For example, some parameter values are now estimated only at global level or for regions, rather than for each country individually.

⁵ WHO, editor. Assessing tuberculosis prevalence through population-based surveys. Manila. World Health Organization, 2007.

⁶ <http://www.unaids.org/en/KnowledgeCentre/HIVData/default.asp>; accessed 12 November 2009.

⁷ As defined by the World Bank. High-income countries are those with a per capita gross national income of US\$ 11 906 or more in 2008.

⁸ <http://esa.un.org/unpp/> (accessed 12 November 2009).

⁹ *World population prospects – the 2008 revision*. New York, United Nations Population Division, 2007.

TABLE A.1
Nine epidemiological groups of countries and territories

Africa high-HIV	Botswana, Burundi, Cameroon, Central African Republic, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Ethiopia, Gabon, Kenya, Lesotho, Malawi, Mozambique, Namibia, Nigeria, Rwanda, South Africa, Swaziland, Uganda, United Republic of Tanzania, Zambia, Zimbabwe
Africa low-HIV	Algeria, Angola, Benin, Burkina Faso, Cape Verde, Chad, Comoros, Djibouti, Eritrea, Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Madagascar, Mali, Mauritania, Mauritius, Niger, Sao Tome and Principe, Senegal, Seychelles, Sierra Leone, Somalia, Sudan, Togo
Central Europe	Albania, Bosnia and Herzegovina, Montenegro, Poland, Serbia, The former Yugoslav Republic of Macedonia, Turkey
Eastern Europe	Armenia, Azerbaijan, Belarus, Bulgaria, Georgia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Republic of Moldova, Romania, Russian Federation, Tajikistan, Turkmenistan, Ukraine, Uzbekistan
High-income countries	Andorra, Antigua and Barbuda, Australia, Austria, Bahamas, Bahrain, Barbados, Belgium, Bermuda, Brunei Darussalam, Canada, Cayman Islands, China, Hong Kong SAR, China, Macao SAR, Croatia, Cyprus, Czech Republic, Denmark, Equatorial Guinea, Estonia, Finland, France, French Polynesia, Germany, Greece, Guam, Hungary, Iceland, Ireland, Israel, Italy, Japan, Kuwait, Luxembourg, Malta, Monaco, Netherlands, Netherlands Antilles, New Caledonia, New Zealand, Northern Mariana Islands, Norway, Oman, Portugal, Puerto Rico, Qatar, Republic of Korea, San Marino, Saudi Arabia, Singapore, Slovakia, Slovenia, Spain, Sweden, Switzerland, Trinidad and Tobago, United Arab Emirates, United Kingdom of Great Britain and Northern Ireland, United States of America, US Virgin Islands
Eastern Mediterranean	Afghanistan, Egypt, Iran (Islamic Republic of), Iraq, Jordan, Lebanon, Libyan Arab Jamahiriya, Morocco, Pakistan, Syrian Arab Republic, Tunisia, West Bank and Gaza Strip, Yemen
Latin America	Anguilla, Argentina, Belize, Bolivia (Plurinational State of), Brazil, British Virgin Islands, Chile, Colombia, Costa Rica, Cuba, Dominica, Dominican Republic, Ecuador, El Salvador, Grenada, Guatemala, Guyana, Haiti, Honduras, Jamaica, Mexico, Montserrat, Nicaragua, Panama, Paraguay, Peru, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, Suriname, Turks and Caicos Islands, Uruguay, Venezuela (Bolivarian Republic of)
South-East Asia	Bangladesh, Bhutan, Democratic People's Republic of Korea, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand, Timor-Leste
Western Pacific	American Samoa, Cambodia, China, Cook Islands, Fiji, Kiribati, Lao People's Democratic Republic, Malaysia, Marshall Islands, Micronesia (Federated States of), Mongolia, Nauru, Niue, Palau, Papua New Guinea, Philippines, Samoa, Solomon Islands, Tokelau, Tonga, Tuvalu, Vanuatu, Viet Nam, Wallis and Futuna Islands

ICD-10. Deaths from TB in HIV-positive people are coded under HIV-associated codes.

Data from VR systems are reported to WHO by Member States and territories every year. National data on TB mortality that met the following two criteria were selected for inclusion in the Global TB database as direct measurements of TB mortality (excluding HIV):

1. The VR system included more than 70% of registered deaths; and
2. Less than 20% of causes of deaths were ill-defined.

Time-series of VR measurements that met both criteria were available for 89 countries.

2.5 Sources of data on TB prevalence

The best way to measure the prevalence of TB is through national population-based surveys of TB disease.^{1,2} Data from such surveys are available for an increasing number of countries. It should be noted, however, that measurements of prevalence are typically confined to the adult population. Furthermore, prevalence surveys exclude extrapulmonary TB as well as smear-negative and culture-negative TB.

¹ Glaziou P et al. Tuberculosis prevalence surveys: rationale and cost. *International Journal of Tuberculosis and Lung Disease*, 2008, 12(9):1003–1008.

² WHO (ed.). *Assessing tuberculosis prevalence through population-based surveys*. Manila, World Health Organization, 2007.

2.6 Sources of data on TB incidence

No country has ever undertaken a nationwide survey of TB incidence due to the large sample sizes required and associated major logistic and financial challenges. No direct measurements of the incidence of TB are therefore available. Theoretically, data from TB information systems that are linked to health systems of high coverage and performance may capture all (or almost all) incident cases of TB. However, as yet no standard and widely-endorsed criteria and benchmarks for classifying TB surveillance systems are available (the Task Force is working on the development of such standards).

In the absence of direct measurements, estimates of TB incidence rely on expert opinion or are derived indirectly from high-quality measurements of prevalence (from surveys of the prevalence of TB disease), from high-quality measurements of mortality (from vital registration) and from special studies using capture-recapture modelling approaches.

The main sources of data used to update the 1990–2008 time series of TB incidence were:

1. Notification data for new and relapse cases;
2. Expert opinion about the coverage of the TB surveillance system, documented during four regional workshops held in 2009 in the Region of the Americas, the Eastern Mediterranean Region, the European Region and the South-East Asia Region. Expert opinion was elicited after in-depth analysis of notification data (including data

from subnational administrative levels) and programmatic data reflecting efforts in TB control (for example, data on infrastructure, staffing, the performance of services and funding). In addition, data on access to health care from Demographic and Health Surveys and the overall performance of health systems (using indicators such as the infant mortality rate) were used to substantiate opinion on the proportion of cases with no or very limited access to health care. To facilitate the documentation of expert opinion, an "onion" framework¹ was used in which different layers represent distinct populations of TB cases that are not captured by national TB information systems (for example, cases with no access to health care and cases with access to private health-care services but not reported to national TB control programmes [NTPs]). Surveillance data were assessed using a three-step process. This started with a systematic assessment of data quality, including an assessment of the over-dispersion of count data, followed by exploration of potential factors driving time-changes in case notifications and then by assessment of the likely number of TB cases that are not notified. These methods are documented in a workbook available on the web site of the Task Force;²

3. Measurements of prevalence from surveys of the prevalence of TB disease;
4. Measurements of TB mortality from VR systems;
5. Measurements from capture-recapture studies³ in which at least three sources of information were used (thus allowing adjustment for between-source dependencies using log-linear models); and
6. Previously published time-series of the incidence of TB. These were used for countries from the two WHO regions that were not covered by regional workshops and country visits in 2009 (the African and Western Pacific regions). The one exception was Viet Nam (in the Western Pacific Region), for which data from a recent survey of the prevalence of TB disease as well as an in-depth analysis of surveillance data were available.

3. Estimates of TB incidence, 1990–2008

3.1 From estimates of the proportion of cases detected

In countries participating in regional workshops, incidence was estimated according to the following equation:

$$\text{incidence} = \frac{\text{case notifications}}{\text{proportion of cases detected}} \quad 1$$

The proportion of cases detected, with uncertainty bounds, was estimated for three years (1997, 2003 and 2008) following in-depth analysis of national and subnational data. Incidence curves were built based on those estimates, and smoothed using a cubic splines smoother function available in the core statistics package of the R statistical environment.⁴ If insufficient data were available to determine the factors leading to time-changes in case notifications, incidence was assumed to follow a flat trend going through the best estimate of incidence.

In countries in the EME group, the level of TB incidence was assumed to be distributed between notification rates for combined new and relapse cases (lower uncertainty bound, noted l), and 1.3 times the notification rate (upper uncertainty bound, noted u). The country-specific and year-specific distribution of incidence was assumed to follow a log-normal distribution with standard error on the log-scale

$$\log(\sigma) = \frac{1}{4} \log\left(\frac{u}{l}\right) \text{ where } u = 1.3l.$$

The log expected value of incidence was set at

$$\log(\mu) = \frac{1}{2} \log(lu).$$

In the absence of country-specific data on the quality and coverage of TB surveillance systems, it was assumed that TB surveillance systems from countries in the EME group performed similarly well, although the model does allow for stochastic fluctuations. Updates for countries in the EME group will commence in 2010, through systematic assessments of the performance of surveillance systems, under the umbrella of special projects conducted in collaboration with partners such as the European Centre for Disease Prevention and Control and the UK Health Protection Agency.

3.2 From empirical measurements of disease prevalence

In countries where surveys of the prevalence of TB disease have been conducted, the case detection ratio (ratio of notification over incidence) c is computed according to the following equation:⁵

$$c = \frac{N}{\frac{N}{P} + \frac{1}{d}} \quad 2$$

where N denotes notifications, P denotes prevalence and d denotes the duration of disease in non-notified cases. Durations d are assumed to follow an exponential distribution with rate $r=1/d$, where r is not dependent on the time from onset of disease. In undiagnosed and untreated TB, r is the sum of TB death rates and spontaneous cure rates. In treated but not notified TB cases, r is the sum of TB death rates in treated TB and the cure rate.

The duration of disease cannot be directly measured.

¹ http://www.who.int/tb/advisory_bodies/impact_measurement_taskforce/en/index.html (accessed 17 November 2009).

² http://www.who.int/tb/advisory_bodies/impact_measurement_taskforce/en/index.html (accessed 17 November 2009).

³ Chao A et al. The applications of capture-recapture models to epidemiological data. *Statistics in Medicine*, 2001, 20(20):3123–3157.

⁴ R Development Core Team. *R: a language and environment for statistical computing*. Vienna, Austria, R Foundation for Statistical Computing, 2009 (<http://www.R-project.org>).

⁵ Borgdorff MW. New measurable indicator for tuberculosis case detection. *Emerging Infectious Diseases*, 2004, 10(9):1523–1528.

For example, measurements of the duration of symptoms in prevalent TB cases that are detected during a prevalence survey are systematically biased towards lower values, as active case-finding truncates the natural history of undiagnosed disease. Measurements of the duration of disease in notified cases ignore the duration of non-notified and untreated cases.

Literature reviews commissioned by the Task Force provide estimates of the duration of disease in untreated TB cases from the pre-chemotherapy era (that is, prior to 1940). The best estimate of the duration of disease (for smear-positive and smear-negative cases combined) in HIV-negative individuals is about three years, corresponding to a case fatality rate (CFR) of 0.34. There are few data on the duration of disease in HIV-infected individuals, and a disease duration ratio of 0.31 (0.18–0.53) in HIV-positive people as compared with HIV-negative people was used.^{1,2}

When measurements from two prevalence surveys were available, trends in TB incidence were derived by fitting a log-linear model to indirect estimates of TB incidence. When three or more prevalence measurements were available, the incidence time-series was completed using cubic spline interpolation. If only one prevalence survey measurement was available, time-trends were assessed using in-depth analysis of surveillance data, as described above.

In this report, the prevalence to incidence method was used in only one country (Viet Nam), following a meeting in early 2009 in which consensus was reached among WHO and national experts. Similar updates to time-series of TB incidence are planned in other countries (mostly in the Western Pacific Region) in 2010.

3.3 From measurements of mortality

In three countries (Brazil, Mexico and South Africa), incidence was estimated in early 2009 from TB mortality, using the following equation:

$$\text{incidence} = \frac{\text{deaths}}{\text{proportion of incident cases that die}} \quad 3$$

Previously published time-series of incidence for those three countries were extended to 2008, using methods described in SECTION 3.4 below.

3.4 From previously published time-series of incidence (to be phased out)

In all remaining countries, previously published time-series of TB incidence were extended by fitting a log-linear model to the estimates for 2005–2007, to predict a value for 2008. Most countries in this group will be re-assessed in 2010. Since previously published time-series of incidence did not document uncertainty ranges, lower and upper uncertainty bounds (u and l in our notation) were arbitrarily set at $\pm 20\%$ of the best estimate.

Incidence estimates are no longer derived from surveys of the prevalence of TB infection as measured in tuberculin

surveys. The Task Force has deemed the methods for deriving incidence from the prevalence of infection to be too unreliable. It is also doubtful whether trends in infection measured through repeat tuberculin surveys provide a reliable estimate of trends in TB incidence.

3.5 Disaggregation of estimated incident cases

Aggregated estimates of TB incidence for 2008 were distributed among 16 age and sex groups by generating multinomially distributed random number vectors and computing multinomial probabilities based on observed counts in notified cases of smear-positive TB. A similar approach was used to generate estimates of TB incidence disaggregated by smear status.

The obvious limitation of this approach is the assumption that case detection ratios are the same among all categories of case. However, there were insufficient data available to generate vectors of probabilities adjusted for varying case detection ratios among age and sex groups, and between smear-positive and smear-negative cases. It is generally thought that TB is underreported in younger age groups compared with other age groups; however, some countries are known to over-report children with a positive tuberculin reaction (but no other sign of active TB disease) as cases of TB. Furthermore, the frequency of smear-positive TB in children is less than in adults, which means that estimates tend to be biased towards low values. Greater efforts are needed to strengthen surveillance systems so that they capture more reliable data on TB in children.

To disaggregate cases by sex, the assumption of a constant case detection ratio is more robust. It is supported by comparisons of ratios of notification rates to prevalence rates that have been directly measured in surveys of the prevalence of TB disease. These show no clear evidence of systematic differences in case detection rates between men and women.³

4. Estimates of the prevalence of HIV among incident cases of TB, 1990–2008

The prevalence of HIV infection among incident cases of TB was directly estimated from country-specific and empirical data wherever possible. For the estimates published in this report, data were available for 103 countries from national surveys (42 countries), sentinel surveillance systems (20 countries) or provider-initiated testing (41 countries). Data from provider-initiated testing were used in countries where the coverage of testing was 50% or more of new and relapse cases of TB.

¹ Williams B, Maher D. Tuberculosis fuelled by HIV: putting out the flames. *American Journal of Respiratory and Critical Care Medicine*, 2007, 175: 6–8.

² Wood R et al. Undiagnosed tuberculosis in a community with high HIV prevalence: implications for tuberculosis control. *American Journal of Respiratory and Critical Care Medicine*, 2007, 175: 87–93.

³ Borgdorff MW et al. Gender and tuberculosis: a comparison of prevalence surveys with notification data to explore sex differences in case detection. *International Journal of Tuberculosis and Lung Disease*, 2000, 4(2):123–32.

For countries where surveillance data were not available or where the percentage of TB patients being tested was below 50%, the prevalence of HIV was estimated indirectly according to equation 4 (for details, see the **APPENDIX**), where t is HIV prevalence among incident TB cases, h is HIV prevalence in the general population (from the latest time-series provided by UNAIDS) and ρ is the incidence rate ratio (IRR) (that is, the incidence rate of TB in HIV-positive people divided by the incidence rate of TB in HIV-negative people).¹

$$t = \frac{h\rho}{1 + h(\rho - 1)} \quad 4$$

To estimate ρ from empirical data, equation 4 was rearranged as follows:

$$\rho = \frac{t(1 - h)}{h(1 - t)} \quad 5$$

Using data from countries where HIV prevalence in the general population has been estimated by UNAIDS as an independent variable, a linear model of logit-transformed t was fitted using logit-transformed h (see **FIGURE A.1**) according to the following equation, written in matrix notation,

$$H - T = X\hat{\theta} \quad 6$$

where H is a vector of $\text{logit}(h)$, T is a vector of $\text{logit}(t)$, X is an $n \times 2$ matrix corresponding to n (t, h) data points, and two columns in which the first column holds 1s, and the second column holds an indicator variable g that equals 1 if the level of HIV in the general population exceeds 1% and is otherwise zero. The vector θ holds two estimated model parameters, the intercept and the coefficient for g . The two incidence rate ratios ρ given two levels of g are then obtained from:

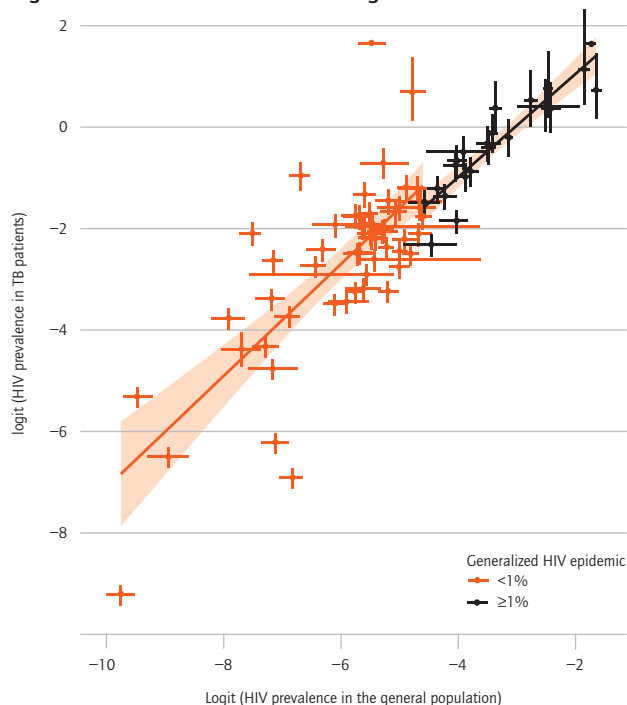
$$\rho_g = e^{\sum \theta} \quad 7$$

Models were run using Monte Carlo simulations in which h was drawn randomly from a log-linear distribution with a standard error computed as described in **SECTION 3.1**, with low and high uncertainty bounds as provided by UNAIDS. Quantiles of interest for the IRR were then extracted to summarize the distributions of IRR in low and high HIV-prevalence settings.

The estimated IRR for countries with a high prevalence of HIV was 20.4 (95% confidence interval 18.7–22.3) and 27.6 (26.2–29) in settings with a low prevalence of HIV. The predicted IRRs were used to calculate the prevalence of HIV in TB cases for the years 1990–2006, using equation 4, by drawing IRR values at random from a distribution assumed to be normal in Monte Carlo simulations.

The time series of HIV in TB cases was then constructed by using the empirical estimate of the IRR in 2008 (when measures for t and h were available), or by using the predicted IRR, under the assumption that the IRR did not change over time.

FIGURE A.1 HIV prevalence in newly notified TB cases against HIV prevalence in the general population, after logit transformation. Countries with a generalized HIV epidemic (defined here as a prevalence of HIV in the general population $\geq 1\%$) are depicted in blue and other countries are shown in red. Horizontal and vertical segments represent 95% confidence intervals of HIV estimates in the general population and measurements of HIV among TB cases, respectively. A linear regression model was fitted to the logit-transformed data.



Three important limitations of these methods are:

- The assumption that the IRR is time-independent. This is likely to result in increasingly biased estimates (towards high values) of the burden of HIV in TB the further back in time the estimates go.
- There is no specific accounting for the protective effect of ART on the incidence of TB. Since measurements are taken in populations with various levels of access to ART, the 2008 empirically measured IRRs do incorporate the effect of ART to some extent. However, estimates prior to 2008 are likely to be biased, since in these years the coverage of ART was lower. Here, the bias is towards lower values.
- Measurements of t used to estimate the IRR were assumed to be known with no error. In several countries, reports of HIV infection in TB cases include HIV test results obtained during the course of or towards the end of TB treatment. Rates of coinfection are therefore among survivors with a lower probability of HIV infection. As the coverage or provider-initiated testing increases towards 100% of new and relapse TB cases, the quality of such measurements will improve.

¹ Data on HIV prevalence in the general population are unpublished data provided to WHO by UNAIDS.

5. Estimates of TB mortality rates, 1990–2008

Mortality measurements from VR systems in 89 countries that met the criteria defined in SECTION 2.4 were adjusted to account for incomplete coverage. This was done by assuming that the distribution of causes of deaths in non-coded deaths was similar to that in coded deaths. In addition, 50% of the deaths with ill-defined causes were proportionately redistributed among known TB causes, with the assumption that there was a lower likelihood that an ill-defined death was an actual TB death. Errors in measurements (misclassifications) and assumptions (redistributions) were assumed to be log-normally distributed with a standard deviation on the log scale

$$\sigma = \frac{0.05 \mu}{v + s/2}$$

where μ is the mortality measurement, v the coverage of the VR system and s is the rate of ill-defined codes. In other words, the standard deviation was arbitrarily inflated in proportion to VR coverage and ill-defined causes of death.

The number of deaths from TB is estimated by multiplying the incidence of TB in each year by the estimated CFR. Separate CFRs were used for four categories of case: notified or not, and infected with HIV or not. Furthermore, separate CFR distributions were used for non-notified cases in countries in the EME group to account for the comparatively lower likelihood that cases remain untreated, and for notified cases in eastern Europe to account for the higher burden of multidrug-resistant TB (MDR-TB) and associated higher CFRs.

A Bayesian approach was used to generate time-series of TB mortality. First, prior distributions of CFRs were used to generate mortality time-series for the 89 countries where mortality measurements from VR systems were available and where those measurements met the quality criteria described in SECTION 2.4. Parameter distributions for CFRs were then adjusted globally in an iterative process, to maximize the median posterior mortalities going through uncertainty bands of VR measurements of mortality, in a process where the outcome to be predicted was constrained within a plausible range of values.

Limitations of this method include:

- The use of global distributions of CFRs and the assumption that posterior CFRs for countries with VR measurements apply to other countries. Countries with VR measurements are likely to be different from countries where no VR mortality measurements are available. It is hoped that strengthened efforts to measure TB mortality directly, either through VR systems or from interim systems such as sample VR combined with well-designed autopsy studies will improve our understanding of CFRs.
- Aggregated mortality estimates were distributed among 16 age and sex groups by generating multinomially distributed random number vectors, and then computing multinomial probabilities based on observed counts in notified cases of smear-positive TB. The obvious limitations here are that CFRs are constant across case categories, and

that the distribution of deaths in age and sex groups mirrors the distribution of cases of new smear-positive TB. Insufficient data were available to adjust vectors of probabilities to account for varying CFRs. In-depth analysis of age-specific mortality rates will be carried out in 2010 to improve our understanding of the variation in case fatality among age groups.

6. Estimates of TB prevalence rates, 1990–2008

Entries into the pool of prevalent cases come from incidence multiplied by the size of the susceptible population. Exits from the pool occur as a result of death, self-cure in undiagnosed cases, cure from non-notified treatments, and notification. In our model, notified cases are removed from the pool of prevalent cases. Distributions of the duration of disease are used for non-notified cases (the group of non-notified cases include undiagnosed cases and cases that are diagnosed and treated but not notified to NTPs). The distributions used are described in SECTION 3.2.

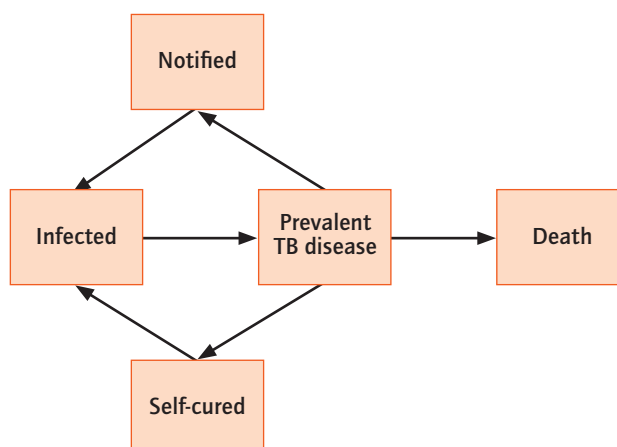
Our model ensures full consistency in the estimation of TB incidence from the prevalence of TB and estimation of the prevalence of TB from TB incidence. However, the model specification is based on some assumptions that may be violated in reality. In particular, the time-independence of the rate of removal from the pool of prevalent cases is unlikely to hold in practice; however, this assumption has been made in almost all publications of dynamic models of TB, since the country-specific data necessary to appropriately model time-dependencies are generally not available. The model is described in FIGURE A.2.

Equation 2 can be rearranged as follows:

$$P = \frac{Nd}{c} (1 - c) \quad 8$$

Prevalence numbers were inflated by assuming a delay of three months when moving to the compartment of notified cases, with bounds of two and four months.

■ FIGURE A.2
Model of TB case detection. The arrows depict rates of cases moving from one compartment to the other.



7. Estimation of uncertainty

There are many potential sources of uncertainty associated with estimates of TB incidence, prevalence and mortality, as well as estimates of the burden of HIV-associated TB and MDR-TB. These include uncertainties in input data, in parameter values, in extrapolations used to impute missing data, and in the model used.

We used fixed population values from the UNPD. Although these values have uncertainty attached to them, we did not account for it.

Notification data are of uneven quality. Cases may be underreported (missing quarterly reports from remote administrative areas are not uncommon), misclassified (in particular, misclassification of relapse cases in the category of new cases is common), or over-reported as a result of duplicated entries in TB information systems. The latter two issues can only be addressed efficiently in countries with case-based nationwide TB databases that include patient identifiers. Sudden changes in notifications over time are often the result of errors or inconsistencies in reporting, but may sometimes reflect abrupt changes in TB epidemiology (for example, resulting from a rapid influx of migrants from countries with a high-burden of TB, or from rapid improvement in case-finding efforts). Missing national aggregates of new and relapse cases were imputed by cubic spline interpolation; however, notification trajectories were not automatically smoothed over time, to avoid introducing systematic errors in countries where time-changes are reflecting true changes in the epidemiology of TB. Attempts to obtain corrections for historical data are made every year, but only rarely do countries provide

appropriate data corrections. It is therefore generally unclear when bumps in notifications are most likely reflecting reporting errors. Future regional workshops will include a systematic effort to correct for such data deficiencies using expert opinion, for those cases where corrections appear necessary.

Model parameter values are described in **TABLE A.2**.

The model used the following sequence: (1) incidence estimation, (2) estimation of IRRs for TB/HIV, (3) estimation of HIV prevalence among incident cases, (4) estimation of mortality, (5) estimation of prevalence, and (6) distribution of incident cases and deaths among age and sex groups. By design, some steps were independent from each other (e.g. step 4 may be done before or after step 5).

The general approach to uncertainty analyses was to draw values from specified distributions for every parameter (except for notifications and population values) in Monte Carlo simulations, with the number of simulation runs set so that they were sufficient to ensure stability in the outcome distributions. The same random number generator seed was used for every country, and errors were assumed to be time-dependent within countries (thus generating autocorrelation in time-series). Regional parameters were used in some instances (for example, for CFRs).

Summaries of quantities of interest were obtained by extracting the 2.5, 50 and 97.5 centiles of posterior distributions.

Regional and global aggregated summaries for incidence, prevalence and mortality were obtained by aggregating country-specific distributions.

TABLE A.2
Model parameter estimates

MODEL PARAMETER	DISTRIBUTION	DISTRIBUTION PARAMETERS*
Incidence Established Market Economies	Log-normal	$\log(\sigma) = \frac{1}{4} \log\left(\frac{u}{l}\right)$ $\log(\mu) = \frac{1}{2} \log(lu)$
HIV prevalence (general population)	Log-normal	$\log(\sigma) = \frac{1}{4} \log\left(\frac{u}{l}\right)$
HIV prevalence (incident TB)	Log-normal	$\log(\sigma) = \frac{1}{4} \log\left(\frac{u}{l}\right)$
Duration non-notified HIV-negative	Triangular	Mode=3; l=2; u=4
Duration ratio HIV-negative/HIV-positive	Log-normal	$\mu = e^{0.31}$ $\sigma = e^{0.2}$
Case fatality rate non-notified HIV-negative	Triangular	Mode=0.3; l=0.05; u=0.7
Case fatality rate non-notified HIV-negative, group of Established Market Economies	Triangular	Mode=0.07; c=0.02; u=0.2
Case fatality rate notified HIV-negative	Triangular	Mode=0.05; l=0.01; u=0.12
Case fatality rate notified HIV-negative, Eastern European Group	Triangular	Mode=0.1; l=0.04; u=0.2
Case fatality rate non-notified HIV-positive	Triangular	Mode=0.4; l=0.2; u=0.9
Case fatality rate non-notified HIV-positive, group of Established Market Economies	Triangular	Mode=0.2; l=0.1; u=0.5
Case fatality rate notified HIV-positive	Triangular	Mode=0.25; l=0.1; u=0.5
Case fatality rate notified HIV-positive, group of Established Market Economies	Triangular	Mode=0.15; l=0.05; u=0.3

* u and l denote upper and lower uncertainty bounds

Appendix: Deriving the prevalence of HIV in incident TB from the prevalence of HIV in the general population

The following notation is used in this appendix:

N denotes the population size during one year; I denotes incident TB cases occurring over one year; subscript + indicates HIV-infected; subscript - indicates HIV-negative. Therefore, I_+/N_+ is the incidence of TB in HIV-positive adults and I_-/N_- is the incidence of TB in HIV-negative adults.

The incidence rate ratio ρ (the ratio of incidence of TB in HIV-positive adults to the incidence of TB in HIV-negative adults) is defined as follows:

$$\rho = \frac{I_+/N_+}{I_-/N_-}$$

we can rearrange to get:

$$\rho I_-/N_- = I_+/N_+$$

then

$$\rho I_-/I_+ = N_-/N_+$$

to the top of the left hand side we add and subtract I^+ , to the right hand side we add and subtract N^+

$$\rho \frac{I_- + I_+ - I_+}{I_+} = \frac{N_- + N_+ - N_+}{N_+}$$

since $I_- + I_+ = I$, and $N_- + N_+ = N$ we can simplify as follows:

$$\rho \left(\frac{I}{I_+} - 1 \right) = \frac{N}{N_+} - 1$$

multiplying out the LHS,

$$\frac{\rho I}{I_+} - \rho = \frac{N}{N_+} - 1,$$

then dividing through by ρ :

$$\frac{I}{I_+} = \left(\frac{N}{N_+} - 1 + \rho \right) / \rho$$

inverting both sides:

$$t = \frac{\rho}{\left(\frac{1}{h} - 1 + \rho \right)} = \frac{h\rho}{1 + h(\rho - 1)}$$

where $h = N_+/N$ denotes HIV prevalence in adults and $t = I_+/I$ denotes HIV prevalence in new adult TB cases.

The World Health Organization monitors
the global tuberculosis epidemic in support
of national TB control programmes.

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