

THE GLOBAL PLAN
TO STOP TB
2006-2015



Actions for Life

TOWARDS A WORLD FREE OF TUBERCULOSIS

WHO Library Cataloguing-in-Publication Data

The global plan to stop TB, 2006-2015 / Stop TB Partnership.

1. Tuberculosis - prevention and control. 2. Tuberculosis - drug therapy. 3. Directly observed therapy. 4. Antitubercular agents - administration and dosage. 5. Strategic planning. I. Stop TB Partnership. II. World Health Organization. II. Title: The global plan to stop tuberculosis, 2006-2015.

ISBN 92 4 159399 7
(NLM classification: WF 200)

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Printed in Switzerland

Design & Layout by Blue Infinity, Geneva, Switzerland

Images supplied by Getty Images, Corbis, Image Forum and WHO Picture Library

The STOP TB Partnership is housed by the World Health Organization

Stop TB Partnership and World Health Organization. Global Plan to Stop TB 2006–2015. Geneva, World Health Organization, 2006 (WHO/HTM/STB/2006.35)

Actions for Life

TOWARDS A WORLD FREE OF TUBERCULOSIS

This document highlights ten Actions that are key to the success of the Global Plan. All are Actions for Life – all have a vital role to play as we work towards a world free of tuberculosis.



Act

This Plan is a call for action. For advocates in countries and at global level to argue the case for investing in the Plan. For all countries to fully implement the actions set out in the Plan, and to mobilize sufficient domestic and external resources to make this happen. For civil society to demand access to quality TB care and to the fruits of research and development. For community groups to support patients to come forward for diagnosis and to complete their treatment.

As Partners with a strong commitment to Stop TB, we can coordinate our actions to implement the Plan. In acting together as Partners, the sum of our efforts will be far greater than if we each acted on our own. Our actions in implementing the Plan will result in millions of lives saved.

These are actions for life - actions towards a world free of TB.

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Acknowledgements

The Partnership acknowledges with gratitude everyone who has contributed to this Global Plan:

Edugie Abebe, Olusoji Adeyi, Faruque Ahmed, Dong Il Ahn, Somsak Akksilp, Heidi Albert, Salia Alhassan, Peter Andersen, Mohamed Aziz, Susan Bacheller, Samiha Baghdadi, Louise Baker, Ripley Ballou, Subroto Banerji, Jacques Baudouy, Rachel Bauquerez, Stefano Bertozzi, Saroj Bhubaneswar, Constantin Miaka Mia Bilenge, Nils Billo, Léopold Blanc, Dan Bleed, Amy Bloom, Henry Boom, Stefaan van der Borcht, Michael Brennan, Jaap Broekmans, Karen Caines, Joanne Carter, Kenneth Castro, Richard Chaisson, Jeremiah Chakaya, Lakhbir Singh Chauhan, Lucy Chesire, Pierpaolo de Colombani, Erwin Cooreman, Brent Copp, Jane Cunningham, Michael Cynamon, Connie Davis, James Deane, Valerie Diaz, Riitta Dlodlo, Chris Dye, Mao Tan Eang, James Ebenezer, Salah Eddine-Ottmani, Saidi Egwaga, Edward Ellis, Gijs Elzinga, Sarah England, Marcos Espinal, Antonieto Evangelista, Jose Figueroa-Munoz, Katherine Floyd, Fraser Fowler, Carole Francis, Maria Freire, Uli Fruth, Barry Furr, Giuliano Gargioni, Haileyesus Getahun, Robert Gie, Philippe Glaziou, Richard Godfrey, Peter Godfrey-Faussett, Peter Gondrie, Case Gordon, Jeroen van Gorkom, Mirtha del Granado, Chris Green, Malgosia Grzemska, Juan Pablo Gutierrez, Catherine Hankins, Anthony Harries, Mark Harrington, Motoky Hayakawa, Einar Heldal, Phil Hopewell, Mehran Hosseini, Shri PK Hota, Greg Hussey, Michael Iademarco, Heather Ignatius, Wieslaw Jakubowiak, Ernesto Jaramillo, Amina Jindani, Fabienne Jouberton, Bertrand Kampoer, Tom Kanyok, Stefan Kaufmann, Dana Kissner, Kraig Klaudt, Irene Koek, Arend Kolk, Afranio Kritski, Sweetie Prem Kumar, Kitty Lambregts, Barbara Laughon, Robert Lodenkemper, Ernest Loevinsohn, Nguyen Huang Long, Wang Longde, Knut Lönnroth, Michael Luhan, Expedito Luna, Pieter van Maaren, Elizabeth Madraa, Richard Maggi, Dermot Maher, Greg Manning, Robert Matiru, Win Maung, Harriet Mayanja-Kizza, Margaret McIntyre, Ruth McNerney, Helen McShane, Anwar Mehmood, Bess Miller, Fuad Mirzavey, David Moore, Toru Mori, Michelle Munro, Nani Nair, PR Narayanan, Ed Nardell, Eva Nathanson, James Newell, Jintana Ngamvithayapong-Yanai, Wilfred Nkhoma, Vinand Nantulya, PR Narayanan, Lisa Nelson, Yasuhiro Nishijima, Paul Nunn, Austin Obi, Robert Ollar, Francis Omaswa, Gwynne Oosterbaan, Seref Ozkara, Myo Paing, Andrea Pantoja, Will Parks, Thaddeus Pennas, Mark Perkins, Diana Pope, Françoise Portaels, Luis Portal, Erik Post, Gilles Poumerol, Pilar Ramon-Pardo, Mario Raviglione, Steven Reed, Alasdair Reid, Annelies van Rie, Shalu Rozario, Giorgio Roscigno, Jean-Philippe Sac-Epee, Jerold Sadoff, Sumana Sahu, Max Salfinger, Fabio Scano, Marta Schaaf, Jerod Scholten, Harry van Schooten, Syed Karam Shah, Akihiro Seita, George Shakarishvili, Jarbas Barbosa da Silva Junior, Christine Sizemore, Peter Small, Pilar Mazzetti Soler, Paul Sommerfeld, Bertil Squire, Ger Steenbergen, Billy Stewart, John Stover, Masachi Suchi, Zerihun Tadesse, Sombat Tanprasertsuk, Roberto Tapia, Mart Tayo, Fernanda Teixeira, Arnaud Trébuq, Phyllida Travis, Bernadette Bourdin Trunz, Pervaiz Tufail, Mary Grace Tungdim, Thelma Tupasi, Melanie Vant, Francis Varaine, Andrew Vernon, Anant Vijay, Silvio Waisbord, Fraser Wares, Natalie Waugh, Diana Weil, Brian Williams, Abigail Wright, Xueqiong Wu, Abubakar Yaro, Douglas Young, Ngare Zachary, Richard Zaleskis, Matteo Zignol

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Administrative and Secretarial support

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The development of the Global Plan was coordinated by the Stop TB Partnership Secretariat, under the overall guidance of the Executive Secretary, Marcos Espinal.

Abbreviations

ACSM	Advocacy, Communications and Social Mobilization	KNCV	Koninklijke Nederlandse Centrale Vereniging ter Bestrijding van Tuberculose [Royal Netherlands Tuberculosis Foundation]
AFR	WHO African Region	LAC	Latin American countries
AIDS	acquired immunodeficiency syndrome	LTBI	latent TB infection
AMR	WHO Region of the Americas	MDG	Millennium Development Goal
ART	antiretroviral therapy	MDR-TB	multidrug-resistant TB
ARV	antiretroviral (drug)	MoH	ministry of health
BCG	Bacille Calmette-Guérin	MTEF	mid-term expenditure framework
CBO	community-based organization	NAAT	nucleic acid amplification test
CDC	Centers for Disease Control and Prevention (USA)	NAP	national AIDS programme
CPT	co-trimoxazole preventive therapy	NGO	nongovernmental organization
DALY	disability-adjusted life year	NRL	national reference laboratory
DEWG	DOTS Expansion Working Group	NTP	national TB programme
DRS	drug resistance surveillance	PAL	Practical Approach to Lung Health
DST	drug susceptibility testing	PHC	primary health care
ELISA	enzyme-linked immunosorbent assay	PLWHA	people living with HIV/AIDS
EMEs	established market economies	PMTCT	prevention of mother-to-child transmission (of HIV)
EMR	WHO Eastern Mediterranean Region	POC	point of care
EEUR	Eastern European Region (TB epidemiological region)	PPD	purified protein derivative (tuberculin)
EQA	external quality assurance	PPM	public-private mix
EUR	WHO European Region	PRSP	Poverty Reduction Strategy Paper
EPI	Expanded Programme on Immunization	PRSC	Poverty Reduction Support Credit
FIND	Foundation for Innovative New Diagnostics	PTB	pulmonary tuberculosis
G8	Group of eight countries (Canada, France, Germany, Italy, Japan, Russian Federation, United Kingdom, United States of America)	QA	quality assured
GAVI	Global Alliance for Vaccines and Immunization	R & D	research and development
GCP	good clinical practice	SCC	short-course chemotherapy
GDF	Global Drug Facility	SEAR	WHO South-East Asia Region
GFATM	Global Fund to Fight AIDS, Tuberculosis and Malaria	SRL	supranational reference laboratory
GLC	Green Light Committee	ss+	sputum smear-positive (pulmonary TB)
GLRA	German Leprosy Relief Association	ss-	sputum smear-negative (pulmonary TB)
GLP	good laboratory practice	SWAp	sector-wide approach
GMP	good manufacturing practice	TB	tuberculosis
GTZ	Deutsche Gesellschaft für Technische Zusammenarbeit [German Development Agency]	TBTCA	TB Coalition for Technical Assistance
HAART	highly active antiretroviral therapy	TDR	UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases
HBC	high-burden country	UN	United Nations
HIPC	highly indebted poor countries	UNAIDS	Joint United Nations Programme on HIV/AIDS
HIV	human immunodeficiency virus	UNDP	United Nations Development Programme
HIV+	HIV-positive	UNGASS	United Nations General Assembly Special Session
HR	human resources	UNICEF	United Nations Children's Fund
IDU	injecting drug use	VCT	voluntary counselling and testing (for HIV)
IEC	information, education, and communication	WG	working group
IND	investigational new drug applications	WGND	Working Group on New Drugs
IPT	isoniazid preventive treatment	WHO	World Health Organization
ISAC	intensified support and action countries	WPR	WHO Western Pacific Region
IUATLD	International Union Against TB and Lung Disease		

Foreword

As a cause of human suffering, death and impoverishment, TB ranks among the leading infectious diseases. The scale of the global TB epidemic demands urgent and effective action. The Stop TB Partnership was established in 2000 as a global movement to accelerate social and political action to stop the spread of TB around the world. The Partnership's goal is to eliminate TB as a public health problem and, ultimately, to secure a world free of TB. The Partnership consists of a network of over 400 committed international organizations, countries, donors from the public and private sectors, governmental and nongovernmental organizations, and individuals working together to achieve that goal.

One of the Partnership's first steps was to develop the Global Plan to Stop TB for 2001–2005. This provided a coherent agenda to rally key new partners, push forward research and development, and have a rapid impact on TB in the areas suffering most from the epidemic. This first Global Plan called for a major effort and Stop TB partners have delivered remarkable results: the number of patients treated in DOTS programmes more than doubled over 5 years, from 2 million in 2000 to well over 4 million in 2004. This rise has been driven, in part, by more ambitious programme budgets, which have also more than doubled from US\$ 400 m in 2002 to over US\$ 800 m in 2005. As a result, several high burden countries, including India and China, are close to reaching the target of 70% case detection. In addition, there has been significant progress in research and development, with a greater number than ever before of new products (diagnostics, drugs and vaccines) in the pipeline.

With much remaining to be done, the Partnership will build on the progress achieved in implementing the first Global Plan, in working towards the Partnership's ambitious but realistic targets for 2015 in this second Global Plan. The Plan sets out the actions and funding needed over the next ten years to accelerate progress in the development of new tools to Stop TB (diagnostics, drugs and vaccines) and in country-level implementation to achieve the internationally agreed targets to Stop TB. These targets comprise the TB target of the Millennium Development Goals (MDGs) and the Partnership's own targets for 2015, which are linked to the MDGs. The Plan has been developed in the context of wider MDG initiatives to reduce poverty. With its ten-year time period, this second Global Plan will support long-term regional and country planning needs.

The Stop TB Partnership is uniquely placed to promote and coordinate the comprehensive range of actions set out in this Plan. The Partnership's strength is its Partners and their track record of delivering results - the results of research and development and the results of providing effective TB care to those who need it. We are confident that all Partners will fulfil their joint commitment to maximizing their contribution to the implementation of the Plan. We urge all those involved in funding activities to Stop TB to invest in this Plan. Working together, we can Stop TB and make a dramatic difference to the lives of millions of people.



Irene KOEK
Chair
Stop TB Partnership
Coordinating Board



Ernest LOEVINSOHN
Chair Emeritus
Stop TB Partnership
Coordinating Board

Preface

Tuberculosis has been with us for too long. An epidemic that should belong to the past is still increasing globally. Despite excellent progress in expanding the DOTS strategy, the global TB incidence rate continues to grow by 1% each year. Despite the availability of affordable, effective treatment, the annual toll of 9 million new TB cases and nearly 2 million TB deaths worldwide represents an intolerable burden of human suffering, and an unacceptable barrier to socioeconomic development.

The challenges reach far into economic, societal and health infrastructure issues. The response in the Plan reflects this. TB continues to be found where there is poverty, where people are living in overcrowded and unsanitary environments, and where health is already under siege from malnutrition, co-infection with HIV, and other debilitating conditions.

Progress in TB prevention and control is integrally linked to health development overall. This recognition is a mainspring of the Plan. In the process of working towards the Millennium Development target in 2015 of having «halted ... and begun to reverse the incidence of TB», the Partnership will be contributing to a range of other important MDG goals, particularly those related to poverty reduction, gender, provision of access to affordable essential drugs in developing countries, making available the benefits of new technologies in cooperation with the private sector, and partnership.

The consensus reached on the directions for the new plan demonstrates the strength of successful partnership. That clarity of purpose, combined with a firm commitment to share responsibility for achieving the long-term goals, is an essential resource for the implementation of the Plan. It makes full use of the present evidence-based scientific tools, and sets up the research requirements and timetable for improved and affordable diagnostic tools, drugs and vaccines.

The aim is to provide access to quality diagnosis and treatment for all those in need, and ultimately, to provide safe and reliable prevention through immunization. By 2010, new drugs are envisaged that are effective against antimicrobial resistance, with shorter, more feasible treatment courses, and that are compatible with antiretroviral treatment against HIV. At the same time, simple, sensitive and rapid diagnostic tests that can be used by rural health workers should be available. The first in a series of new, safe, and effective vaccines is expected by 2015.

In the 2005 World Health Assembly resolution on sustainable financing for TB prevention and control (WHA 58.14) Member States articulated their understanding that sufficient programme financing - both domestic and external - must be maintained.

The Partnership has demonstrated its excellent work in putting together the global plan for the next decade. The powerful combination of a productive partnership and effective strategies offers a secure platform for sustainable resourcing and progress to Stop TB.



Dr LEE Jong-wook
Director-General, World Health Organization

Statements of support

As Minister of Health of the Democratic Republic of Congo, I pledge our support to the Global Partnership to Stop TB.

With 9 million cases and 2 million deaths each year, the global tuberculosis epidemic is one of the most important global humanitarian and development challenges. We recognize the Global Plan as a comprehensive assessment of the action and resources needed to meet the Stop TB Partnership's global targets for 2015. This is a critical contribution to the achievement of the Millennium Development Goals and eventually to the realization of a world free of tuberculosis.

We recall that at the 58th World Health Assembly, United Nations member states adopted a Resolution on Sustainable Financing for Tuberculosis Prevention and Control, in which they made a commitment to ensure the availability of sufficient domestic resources and of sufficient external resources to achieve the internationally agreed development goal relevant to tuberculosis control contained in the United Nations Millennium Declaration. In reaffirming this commitment, we fully support the range of measures needed to implement the Global Plan to Stop TB, 2006-2015.

We encourage all partners to join in this important endeavour to make a positive and lasting change in the global fight against tuberculosis.



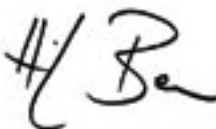
Emile BONGELI YEIKELO YA ATO
Minister of Health, Democratic Republic of Congo

The Global Plan to Stop TB for 2006-2015 clearly sets out the activities to achieve the Stop TB Partnership's global targets of halving TB prevalence and deaths by 2015. The Plan presents a convincing argument for the resources needed for actions, based on sound epidemiological analysis with robust budget justifications.

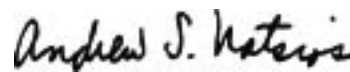
Progress towards the targets for 2015 represents a step towards the vision of a TB-free world by 2050. The Plan will serve to stimulate research and development of the new drugs, diagnostics and vaccines that will make it possible to realize this vision. Recognizing the need for long-term planning for TB control, we support the Partnership in helping to implement the Plan in line with our national policies.

One of the most significant areas in which human development can be improved is through the elimination of a preventable disease. TB is a disease of the poor. It is a disease which prevents people from escaping poverty. Investment in TB control is therefore an investment not only in alleviating human suffering from TB but also in alleviating poverty. An investment in the Global Plan to Stop TB is a sound one. We call on all nations to mobilize the resources needed to implement the Global Plan to Stop TB, as part of investments in strengthening health systems and improving health care delivery.

We are committed to Stop TB. This Plan provides the blueprint for the next decade. We support this Plan to Stop TB and call on all nations to do the same.



Hilary BENN
U.K. Secretary of State for
International Development



Andrew NATSIOS
Administrator, U.S. Agency for
International Development

Executive summary

The burden of suffering and economic loss caused by tuberculosis (TB) is an affront to our conscience. TB is a curable and preventable disease. Urgent action is necessary to scale up our efforts to Stop TB.

As a global movement to accelerate social and political action to stop the spread of TB, the Stop TB Partnership provides the platform for international organizations, countries, donors (public and private sector), governmental and nongovernmental organizations, patient organizations and individuals to contribute to a collective and concerted campaign to Stop TB. Making the most of Partners' efforts, in terms of effectiveness and efficiency, requires a plan. The Stop TB Partnership has developed a Global Plan to Stop TB that covers the period 2006–2015, building on the Partnership's first plan for 2001–2005.

Within the Partnership's strategic approaches for the next decade, the Plan sets out the activities that will make an impact on the global burden of TB. This involves reducing TB incidence – in line with the Millennium Development Goals (MDGs) – and reaching the Partnership's targets for 2015 of halving TB prevalence and deaths compared with 1990 levels. TB is a long-haul disease: the Plan represents a step towards the elimination of TB as a global public health problem by 2050, and the realization of the Partnership's vision of a TB-free world. It sets out the resources needed for actions, underpinned by sound epidemiological analysis with robust budget justifications. It supports the need for long-term planning for action at regional and country level.

The Plan provides a consensus view of what the Stop TB Partnership can achieve by 2015, provided the resources are mobilized to implement the Stop TB strategy according to the steps set out in the Plan. The Stop TB strategy encapsulates the technical approaches for TB programmes to achieve and sustain the high levels of TB case detection and cure (over 70% and 85% respectively) required to decrease the TB burden. The Plan will serve to stimulate political commitment, financial support, effective intervention, patients' involvement, community participation, and – in indicating the potential of the new tools under development to control TB (improved drugs, diagnostics and vaccines) – research and development.

The development of the Plan has relied on contributions from the Stop TB Partnership's seven working groups – on DOTS expansion; DOTS-Plus for multidrug-resistant TB; TB/HIV; new TB diagnostics; new TB drugs; new TB vaccines; and advocacy, communications and social mobilization – coordinated by the Partnership Secretariat. The Working Groups have contributed

to the two key dimensions of the Plan: (1) regional scenarios (projections of the expected impact and costs of activities oriented towards achieving the Partnership's targets for 2015 in each region), and (2) the strategic plans of the working groups and the Secretariat.

What we will achieve if we implement the Plan:

- Implementation of the Stop TB Strategy will expand equitable access for all to quality TB diagnosis and treatment.
- Over the ten years of this Plan, about 50 million people will be treated for TB under the Stop TB Strategy, including about 800 000 patients with multidrug-resistant TB (MDR-TB), and about 3 million patients who have both TB and human immunodeficiency infection (TB/HIV) will be enrolled on antiretroviral therapy (ART) (in line with UNAIDS plans for universal access).
- Some 14 million lives will be saved from 2006 to 2015.
- The first new TB drug for 40 years will be introduced in 2010, with a new short TB regimen (1–2 months) shortly after 2015.
- By 2010, diagnostic tests at the point of care will allow rapid, sensitive and inexpensive detection of active TB. By 2012, a diagnostic toolbox will accurately identify people with latent TB infection and those at high risk of progression to disease.
- By 2015 a new, safe, effective and affordable vaccine will be available with potential for a significant impact on TB control in later years.

In terms of reaching targets, full funding (US\$56 billion) and implementation of the Plan would result in:

- global achievement of the MDG «to have halted by 2015, and begun to reverse, the incidence» of TB;
- global achievement of the Partnership's 2015 targets to halve prevalence and death rates from the 1990 baseline (although achievement of the 2015 targets will most likely be later than 2015 in Eastern Europe and even later in Africa, because of the particular challenges posed by MDR-TB and HIV respectively);
- enormous progress in all regions over the period of the Plan from 2006, to 2015, with prevalence and death rates halved, or almost halved.

The total cost of the Plan – US\$56 billion – represents a threefold increase in annual investment in TB control compared with the first Global Plan. This total includes US\$9 billion for research and development and US\$47 billion for implementation of current interventions (over US\$28 billion for DOTS programmes, an additional US\$6 billion for DOTS-Plus, US\$7 billion for TB/HIV

activities, US\$3 billion for ACSM activities, and US\$3 billion for technical cooperation). Of the US\$ 47 billion for implementation of current interventions, US\$44 billion (94%) are country-level costs, representing about 80% of the Plan's total cost.

The estimated funding gap is US\$31 billion, since an estimated US\$25 billion is likely to be available based on projections of current funding trends. Full funding of the Plan will enable implementation of the Stop TB Strategy and global achievement of the Partnership's targets, as a step towards our vision of a TB-free world.

In a resolution adopted by the Fifty-eighth World Health Assembly in 2005, on «Sustainable Financing for TB Prevention and Control», all countries made a commitment to ensure the availability of sufficient domestic and external resources to achieve the MDG relevant to TB. National governments and donors must fulfil this commitment by mobilizing the funds to increase current levels of funding and fill the US\$31 billion gap.

With the will, the funds and the action, together we can Stop TB!

Résumé

La somme des souffrances et des pertes économiques causées par la tuberculose est un affront à nos consciences. Il faut agir de toute urgence pour intensifier nos efforts de lutte contre une maladie qui est curable et évitable.

En tant que mouvement mondial destiné à accélérer l'action sociale et politique pour enrayer la propagation de la tuberculose, le Partenariat «Halte à la tuberculose» permet aux organisations internationales, aux pays, aux donateurs (des secteurs public et privé), aux organisations gouvernementales et non gouvernementales, aux collectifs de patients et aux individus de participer à une campagne collective et concertée de lutte contre la maladie. Mais il est impératif de concevoir un plan pour optimiser l'efficacité et la performance des efforts déployés par chacun des partenaires. Le Partenariat «Halte à la tuberculose» a mis au point un plan mondial «Halte à la tuberculose» couvrant la période 2006–2015, et qui se fonde sur le premier plan du Partenariat pour 2001–2005.

Dans le cadre des approches stratégiques du Partenariat pour la prochaine décennie, le plan fixe les activités qui auront un effet sur le poids mondiale de la tuberculose. Il s'agit de réduire l'incidence de la maladie – conformément aux objectifs du Millénaire pour le développement (OMD) – et d'atteindre les cibles du Partenariat pour 2015, à savoir réduire de moitié la prévalence et la mortalité de la tuberculose par rapport aux chiffres de 1990. Il faut voir à long terme : le plan est une étape pour que d'ici 2050 la tuberculose ne constitue plus un problème de santé publique et pour que l'idéal du Partenariat – un monde sans tuberculose – devienne réalité. Ce plan détermine les ressources nécessaires pour combattre la maladie en se fondant sur une analyse épidémiologique sérieuse et de solides justifications budgétaires ; il met en évidence le besoin de planifier à long terme les opérations aux niveaux régional et national.

Le plan montre ce que, de l'avis général, le Partenariat «Halte à la tuberculose» peut accomplir d'ici 2015, à condition de disposer des ressources pour appliquer la stratégie «Halte à la tuberculose» suivant ses indications. La stratégie «Halte à la tuberculose» résume quels moyens techniques les programmes antituberculeux doivent utiliser pour atteindre et maintenir un niveau élevé de dépistage des cas et de guérison (plus de 70 et 85% respectivement) aux fins de réduire le poids de la morbidité. Le plan permettra de stimuler l'engagement politique, le soutien financier, les interventions efficaces, la participation des patients et de la communauté et la recherche-développement – en indiquant le potentiel que peuvent avoir de nouveaux outils de

lutte antituberculeuse en cours de conception (médicaments, diagnostics et vaccins améliorés).

L'élaboration du plan est basé sur la contribution des sept groupes de travail du Partenariat «Halte à la tuberculose» – extension de la stratégie DOTS ; initiative DOTS-Plus pour la prise en charge de la tuberculose à bacilles multirésistants (TB-MR) ; TB/VIH ; nouvelles méthodes de diagnostic de la tuberculose ; nouveaux médicaments antituberculeux ; nouveaux vaccins antituberculeux ; sensibilisation, communication et mobilisation sociale – , coordonnés par le Secrétariat du Partenariat. Ces groupes de travail ont contribué aux deux composantes clés du plan : 1) scénarios régionaux (prévisions sur l'impact escompté et les dépenses consacrées à des activités destinées à atteindre les cibles du Partenariat pour 2015 dans chaque région), et 2) plans stratégiques des groupes de travail et du Secrétariat.

Réalisations consécutives à la mise en œuvre du plan :

- L'application de la stratégie «Halte à la tuberculose» sera un progrès pour un accès universel et équitable à des diagnostics et traitements antituberculeux de qualité.
- Pendant la durée décennale du plan, quelque 50 millions de personnes seront traitées dans le cadre de la stratégie «Halte à la tuberculose», au nombre desquelles environ 800 000 patients atteints de tuberculose à bacilles multirésistants (TB-MR) et presque 3 millions de patients ayant à la fois la tuberculose et le virus de l'immunodéficience humaine (TB/VIH) recevront également un traitement antirétroviral (conformément aux plans d'accès universel de l'ONUSIDA).
- Quelque 14 millions de vies seront sauvées entre 2006 et 2015.
- Un nouvel antituberculeux – le premier depuis 40 ans – sera mis en circulation en 2010, de même qu'un nouveau schéma thérapeutique de brève durée (1–2 mois) immédiatement après 2015.
- D'ici 2010, des tests diagnostiques utilisables au niveau des centres de santé périphériques permettront de dépister la tuberculose évolutive rapidement, efficacement et à moindre frais. D'ici 2012, l'usage d'une trousse diagnostique permettra de dépister avec exactitude les personnes présentant une tuberculose latente et celles pour qui le risque d'évolution vers le stade de la maladie est élevé.
- D'ici 2015, un nouveau vaccin, sûr, efficace et abordable sera disponible : selon toute probabilité, il aura un impact considérable sur la lutte antituberculeuse à venir.

Afin d'atteindre les cibles, le financement intégral (US\$ 56 milliards) et la mise en œuvre du plan auront les effets suivants :

- Réalisation au niveau mondiale de l'objectif du Millénaire pour le développement visant, d'ici à 2015, à maîtriser l'incidence de la tuberculose et à commencer à inverser sa tendance ;
- Réalisation au niveau mondiale des cibles du Partenariat pour 2015, à savoir réduire de moitié les taux de prévalence et de mortalité par rapport à l'année 1990 (il est toutefois probable que les cibles soient atteintes après 2015 en Europe orientale, voire plus tard en Afrique, car la TB-MR et le VIH, respectivement, posent des problèmes particuliers) ;
- Sur la durée du plan, de 2006 à 2015, énormes progrès dans toutes les régions, se caractérisant par une réduction de moitié – ou presque – des taux de prévalence et de mortalité.

Par rapport au premier plan mondial, le coût total de ce nouveau plan (US\$ 56 milliards) représente une augmentation des investissements annuels de lutte antituberculeuse de l'ordre du triple. Ce total comprend US\$ 9 milliards pour la recherche-développement et US\$ 47 milliards pour la mise en œuvre des interventions actuelles (plus de US\$ 28 milliards pour les programmes DOTS, ajouté à US\$ 6 milliards pour la stratégie DOTS-plus, US\$ 7 milliards pour les activités de lutte contre la TB/VIH, US\$ 3 milliards pour les activités de sensibilisation, communication et mobilisation sociale, et US\$ 3 milliards pour la coopération technique). Sur ces US\$ 47 milliards, US\$ 44 milliards (94%) seront dépensés dans les pays, ce qui représente 80% du coût total du plan.

Des estimations montrent qu'il manquera US\$ 31 milliards ; étant donné que US\$ 25 milliards seront disponibles si les tendances de financement actuelles continuent. Grâce au financement intégral du plan, il sera possible de mettre en œuvre la stratégie «Halte à la tuberculose» et d'atteindre les cibles mondiales du Partenariat, ce qui nous rapprochera de la vision d'un monde sans tuberculose.

Dans une résolution adoptée par la Cinquante-Huitième Assemblée mondiale de la Santé en 2005, intitulée «Financement durable de la prévention et de la lutte antituberculeuses», tous les pays se sont engagés à assurer la disponibilité de ressources intérieures et extérieures suffisantes pour atteindre l'objectif du Millénaire pour le développement relatif à la tuberculose. Les gouvernements nationaux et les donateurs doivent respecter cet engagement en mobilisant des fonds pour accroître les

niveaux actuels de financement et trouver les US\$ 31 milliards manquants.

Avec de la volonté, de l'argent et l'action, nous pourrons tous ensemble faire barrage à la tuberculose!

Resumen

La carga de sufrimiento y pérdidas económicas que causa la tuberculosis pesa en nuestras conciencias. La tuberculosis es una enfermedad curable y prevenible, y hay que tomar medidas urgentes para expandir los esfuerzos realizados para detenerla. Como movimiento global para acelerar la acción social y política encaminada a detener la propagación de la tuberculosis, la alianza Alto a la Tuberculosis brinda a organizaciones internacionales, países, donantes (sector público y privado), organizaciones gubernamentales y no gubernamentales, organizaciones de pacientes e individuos una plataforma para contribuir a una campaña colectiva y concertada para detener la tuberculosis. Ahora bien, para que las actividades de los asociados rindan el máximo fruto en cuanto a eficacia y eficiencia se requiere un plan. La alianza Alto a la Tuberculosis ha desarrollado un Plan Mundial para Detener la Tuberculosis que abarca el periodo 2006-2015, basándose en el primer plan de la Alianza para 2001-2005.

Como parte de las medidas estratégicas de la Alianza para la próxima década, el plan describe las actividades que tendrán un impacto en la carga mundial de tuberculosis. Ese impacto se traducirá en una reducción de la incidencia de la enfermedad – en consonancia con los Objetivos de Desarrollo del Milenio (ODM) – y en el logro de las metas de la Alianza, fijadas para 2015, de reducir a la mitad la prevalencia de tuberculosis y la mortalidad por esa causa en comparación con los niveles de 1990. La tuberculosis es una enfermedad que hay que abordar con una perspectiva a largo plazo: el Plan representa un paso hacia la eliminación de la tuberculosis como problema de salud pública mundial para 2050, y la materialización de la visión de la Alianza de un mundo libre de esa enfermedad. En él se describen los recursos necesarios para las medidas contempladas, respaldados por un análisis epidemiológico sólido y razones presupuestarias robustas, y se subraya la necesidad de una planificación a largo plazo para la adopción de medidas a nivel regional y de país.

El Plan ofrece una perspectiva consensuada sobre lo que podría conseguir la alianza Alto a la Tuberculosis para 2015, siempre y cuando se movilicen los recursos necesarios para aplicar la estrategia Alto a la Tuberculosis en función de los pasos detallados en el Plan. Esta estrategia compendia los requisitos técnicos para que los programas de tuberculosis alcancen y mantengan los altos niveles de detección y curación de casos de la enfermedad (más del 70% y el 85%, respectivamente) requeridos para reducir la carga de tuberculosis. El Plan servirá para estimular el compromiso político, el apoyo financiero, la

eficacia de las intervenciones, la implicación de los pacientes, la participación de la comunidad y – mostrando el potencial de los nuevos instrumentos en desarrollo contra la tuberculosis (mejores medicamentos, medios diagnósticos y vacunas) – la investigación y el desarrollo.

El Plan se basa en las contribuciones de los siete grupos de trabajo de la alianza Alto a la Tuberculosis dedicados a lo siguiente: expansión del DOTS; DOTS-Plus para la tuberculosis multirresistente; tuberculosis/VIH; nuevos medios diagnósticos de la tuberculosis; nuevos medicamentos antituberculosos; nuevas vacunas contra la tuberculosis; y promoción, comunicación y movilización social – coordinados por la Secretaría de la Alianza. Los grupos de trabajo han contribuido a las dos dimensiones claves del Plan, a saber: 1) escenarios regionales (previsiones del impacto y los costos de las actividades orientadas a lograr las metas de la Alianza para 2015 en cada región), y 2) los planes estratégicos de los grupos de trabajo y de la Secretaría.

Logros previstos si implementamos el Plan:

- La implementación de la estrategia Alto a la Tuberculosis trabajará hacia la expansión del acceso equitativo para todo el mundo a medios de diagnóstico y tratamientos de calidad de la tuberculosis.
- A lo largo de los diez años de este Plan, unos 50 millones de personas recibirán tratamiento antituberculoso en el marco de la estrategia Alto a la Tuberculosis, incluidos unos 800 000 pacientes con tuberculosis multirresistente, y unos 3 millones de pacientes afectados tanto por esa enfermedad como por el virus de la inmunodeficiencia humana (TB/VIH) se beneficiarán de tratamiento antirretroviral (en consonancia con los planes del ONUSIDA para el acceso universal).
- Entre 2006 y 2015 se salvarán unos 14 millones de vidas.
- En 2010 se introducirá el primer medicamento nuevo contra la tuberculosis en 40 años, y un nuevo régimen de corta duración (1–2 meses) poco después de 2015.
- En 2010, la realización de pruebas diagnósticas en el punto de atención hará posible una detección más rápida, económica y eficaz de los casos de tuberculosis activa. En 2012, un conjunto de medios diagnósticos permitirá identificar con precisión a las personas con infección latente y a las que sufran un alto riesgo de progresión a la enfermedad.
- Para 2015 se dispondrá de una nueva vacuna segura, eficaz y asequible que podría tener gran incidencia en el control de la tuberculosis en años posteriores.

En lo relativo al logro de las metas, la financiación completa (US\$ 56 000 millones) y la aplicación del Plan tendrán como resultado:

- la consecución mundial de los ODM «haber detenido y comenzado a reducir, para el año 2015, la incidencia» de tuberculosis;
- el logro mundial de las metas de la Alianza para 2015 de reducir a la mitad la prevalencia y las tasas de mortalidad respecto a los valores de 1990 (aunque las metas fijadas para 2015 se alcanzarán probablemente con posterioridad a 2015 en Europa oriental e incluso más tarde en África, debido a los problemas particulares que plantean la tuberculosis multirresistente y el VIH, respectivamente);
- grandes progresos en todas las regiones a lo largo del periodo de 2006 a 2015 contemplado en el Plan, con una reducción a la mitad, o casi a la mitad, de la prevalencia y de las tasas de mortalidad.

El costo total del Plan – US\$ 56 000 millones – representa una triplicación de la inversión anual en control de la tuberculosis en comparación con el primer plan mundial. Ese total incluye US\$ 9000 millones para investigación y desarrollo y US\$ 47 000 millones para la aplicación de las intervenciones corrientes (más de US\$ 28 000 millones para la expansión de DOTS, otros US\$ 6000 millones para DOTS-Plus, US\$ 7000 millones para las actividades contra la coinfección TB/VIH, US\$ 3000 millones para las actividades de promoción, comunicación y movilización social, y US\$ 3000 millones para la cooperación técnica). De los US\$ 47 000 millones destinados a la aplicación de las intervenciones corrientes, US\$ 44 000 millones (94%) corresponden a costos a nivel de país, lo que representa aproximadamente un 80% del costo total del Plan.

El déficit de financiación estimado asciende a US\$ 31 000 millones, ya que US\$ 25 000 millones han sido estimados como disponibles al proyectar las tendencias de financiación actuales. La financiación íntegra del Plan permitirá aplicar la estrategia Alto a la Tuberculosis y alcanzar las metas mundiales de la Alianza, como un paso más hacia nuestro gran objetivo de un mundo libre de tuberculosis.

En una resolución adoptada por la 58ª Asamblea Mundial de la Salud en 2005, acerca de la «Financiación sostenible de la prevención y el control de la tuberculosis», todos los países se comprometieron a velar por que se aporten los recursos nacionales y externos suficientes para alcanzar los ODM relacionado con la tuberculosis. Gobiernos nacionales

y donantes deben cumplir ese compromiso movilizando los fondos necesarios para aumentar la actual financiación y enjugar el déficit de US\$ 31 000 millones.

Con voluntad, financiación y acción, unidos podemos detener la tuberculosis



Commit

We have made progress in global TB control, but much remains to be done. Building on this progress so far, the Plan sets out our commitment to implementing a new, ambitious strategy to Stop TB. We are committed to achieving our objectives in working towards the Partnership's targets for 2015 and the Millennium Development Goals.

Our commitment to successfully carrying out the Plan implies a commitment to mobilizing resources, expanding our efforts, and sustaining activities over the long term. Global TB control is a marathon, not a sprint - the targets in this Plan for 2015 are a step on the road to the long-term goal of TB elimination by 2050.

We are committed to promoting the ideals embodied in the Plan, and passing them on to the next generation.

Introduction

TB kills and blights the lives of poor people

Tuberculosis (TB) kills nearly two million people a year – 5000 every day – mainly in the poorest communities in the developing world.

It afflicts millions more. About one third of the world's population is infected with TB – that is, they have a latent TB infection that may later cause disease to develop. Nearly nine million new cases develop every year. The World Health Organization declared the disease a global emergency as long ago as 1993.

TB has a profoundly damaging economic impact on patients and their families, through spending on diagnosis and treatment, transport to get to health facilities, and time lost from work. Yet it can be cured with drugs that cost as little as US\$14–18 per patient.

The interaction of TB with human immunodeficiency virus (HIV) infection has pernicious effects. TB has become the leading cause of death among people with HIV, while infection with HIV is the most potent risk factor for a latent TB infection to convert to active TB.

As a consequence of poor treatment, strains of *Mycobacterium tuberculosis* – the bacillus that causes TB – have evolved that do not respond to treatment with the standard combination of first-line drugs. Multidrug-resistant TB has now emerged in nearly every country of the world.

In spite of the importance of TB as a global public health problem, diagnosis and treatment of TB still rely on old and imperfect technologies. New tools – diagnostic tests, drugs and vaccines – are urgently needed, particularly for use where the epidemics of HIV and multidrug-resistant TB are most severe.

A critical problem is that still not enough is being done to STOP TB.

In partnership to Stop TB

New technology has the potential to revolutionize TB control. But we can have a major impact on TB in most parts of the world today, by rapidly identifying and curing patients with active disease. This approach is at the heart of the internationally recognized strategy for TB control – the DOTS strategy – which has proven remarkably effective. Some countries in Asia and Latin America have shown the way. In other countries, TB remains a catastrophe in need of urgent measures.

“Stop TB” is a global movement to accelerate social and political action to stop the spread of TB around the world. The Stop TB Partnership was established in 2000 to realize the goal

of eliminating TB as a public health problem and, ultimately, to secure a world free of TB. It is a network of over 400 committed international organizations, countries, donors from the public and private sectors, governmental and nongovernmental organizations, and individuals working together to achieve that goal.

The Partnership's first step was to develop the Global Plan to Stop TB for 2001–2005, to provide a coherent agenda that could rally key new partners, push forward research and development, and have a rapid impact on TB in the areas suffering most from the epidemic.

Building on progress achieved, the present document – the second Global Plan to Stop TB – is intended to guide Partnership efforts in 2006–2015 to achieve the TB target of the Millennium Development Goals (MDGs), as well as the Partnership's own targets for 2015, which are linked to the MDGs. The Plan has been developed in the context of wider MDG initiatives to reduce poverty.

What can be achieved by 2015

The Partnership's Global Plan for 2006–2015 is ambitious but realistic. It is backed by sound analysis of the strategies, actions and resources needed over the next 10 years.

Provided the necessary resources are mobilized and political commitment is resolute, this is what can be achieved by 2015:

- **MDG target met:** We will have met the MDG target to have halted and begun to reverse the incidence of TB by 2015.
- **Partnership targets met:** In addition, the Partnership's own ambitious 2015 targets – to halve prevalence and death rates from the 1990 baseline – will have been met globally, with enormous progress in all regions.
- **Lives saved:** Over the 10 years of this Plan, some 14 million lives will be saved. About 50 million people will be treated for TB under a new WHO-recommended Stop TB Strategy, based on DOTS. Some 800 000 patients with multidrug-resistant TB will be treated, and more than 3 million people with both TB and HIV will start antiretroviral therapy.
- **Quality of care:** Implementation of the new Stop TB Strategy will expand access to quality diagnosis and treatment, for patients with all types of TB, for patients of all age groups, for men and women equally, and for patients from all socioeconomic strata.
- **New diagnostic tests:** By 2008, new diagnostic tests for more rapid detection of smear-negative TB will be available for use in referral laboratories. By 2010, simple, robust, affordable technologies for use at peripheral levels of the health system will enable rapid, sensitive detection of active TB at the first point of care. By 2015, we will have diagnostic

tests capable not only of identifying people with latent TB infection but also of pinpointing those who are at greatest risk of progression to active disease.

- **New drugs:** The first new TB drug for 40 years will be introduced in 2010, and by 2015 we will be on the verge of a new TB regimen that will achieve cure in 1–2 months, compared with 6–8 months now. This treatment will be effective against multidrug-resistant TB and will be compatible with antiretroviral treatment. By then, clinical trials for new treatment of latent TB infection will be under way.
- **New vaccines:** By 2015 we will have the first of a series of new, safe, effective TB vaccines available at reasonable cost, with potential for a major impact on TB control in later years.
- **Meaningful involvement of patients and communities:** Mechanisms will have been developed to involve patients and communities productively in relevant aspects of TB care and control.
- **Contribution to development:** TB control will feature strongly on the development and political agendas, and investments in TB control will have contributed to poverty reduction and health system development in poor countries. The Stop TB Partnership is committed to being an active player in collaborative efforts to strengthen health systems, and to improve the harmonization and alignment of its efforts.

The regional profiles in Part II of this plan show how the effective use of existing tools will halve prevalence and death rates by 2015 in most regions where the global TB epidemic is concentrated (the Americas, Eastern Mediterranean, South-East Asia and Western Pacific). These regions include several of the countries with the highest burden of TB, e.g. China, India and Indonesia.

Two other regions – Africa and Eastern Europe – will make similar gains over the period of the Plan (2006–2015). However, achievement of the Partnership's targets may well be later than 2015 in Eastern Europe and even later in Africa, because the targets are specified with 1990 as a baseline year. During the 1990s, failure to check HIV transmission led to a huge upsurge in TB in Africa, while the break-up of the former Soviet Union, with its attendant economic crises, meant that control over the disease slipped in Eastern Europe. From the perspective of TB control, this was a lost decade in these two regions. In August 2005, Ministers of Health in Africa declared TB an emergency in the African region – a response to an epidemic in which the annual number of new TB cases in most African countries has more than quadrupled since 1990, and which is continuing to rage across the continent, killing more than half a million people every year.

Similarly, recognizing TB in the WHO European Region as a regional emergency, in February 2005 the Regional Director

called on all Member States to ensure that TB is given the highest priority on the health and development agenda.

To achieve the targets in Africa and Eastern Europe by 2015 would require tremendous improvements in health systems, halving HIV incidence rapidly, and the early availability of new tools to increase diagnostic capacity, substantially shorten treatment, and effectively prevent TB transmission. It is unlikely that even massive additional funding or greater effort would be successful in completely overcoming the constraints by 2015. Nevertheless the plan describes an agenda for vigorous action in the next few years.

What needs to be done

The Global Plan sets out what needs to be done. It is in three parts:

- **Part I** sets out the Partnership's strategic directions for 2006–2015, based on recent achievements and the current situation.
- **Part II** summarizes planned regional activities, costs and impact for all regions with a high burden of TB, based on an ambitious but realistic scenario. It also considers what would be needed to accelerate progress towards halving prevalence and death rates in Africa and Eastern Europe.
- **Part III** summarizes the strategic plans for the Partnership's working groups and Secretariat.

The Global Plan 2006–2015 builds on the foundation for global TB control laid with the introduction of DOTS, and the accelerated action over the past five years since the inception of the Partnership. Overall it requires a further massive intensification of commitment and effort to implement in full the new Stop TB strategy based on DOTS.

It will also require funding of US\$56 billion over 10 years. More than 80% of this funding – some US\$44 billion – is for investment at the country level, while US\$12 billion is needed at global level to support technical cooperation provided by external agencies, and research and development for new drugs, vaccines and diagnostic tests. An investment of US\$56 billion will yield considerable rewards in terms of lives saved, illness, misery and poverty reduced, and the prospect of powerful new drugs, vaccines and diagnostic tests.

These achievements are within our grasp if we can rise to the considerable challenges in implementing the Plan. They would be exciting achievements in their own right. But, more than that, they are also steps on the way to the Partnership's visionary longer-term goal of eliminating TB.



Collaborate

This Plan is the embodiment of collaboration, involving the efforts of the just over 400 Partners that make up the Stop TB Partnership. Expanding this collaboration is crucial to the success of implementation of the Plan. New collaborating Partners will be drawn from within the health sector and from other sectors.

Ensuring that this collaboration is as effective and dynamic as possible is a responsibility of all Partners and of the Partnership Secretariat. Effective and dynamic collaboration requires understanding and insight into areas beyond our own special areas of interest. It requires mutual understanding of our different roles and capabilities, that are harnessed in pursuit of our common targets and goals.

The success of the Plan depends on the collaborative efforts of all Partners.

PART I

Strategic directions

1. ACHIEVEMENTS IN 2000–2005 AND CHALLENGES FOR 2006-2015

1.1 A thriving Partnership

The Stop TB Partnership has built an effective network to promote and coordinate the contributions of a wide and increasing range of stakeholders. A thriving Partnership, its global membership grew to over 400 organizations in 2005. Regional and national Stop TB partnerships are now being formed to support long-term expansion of DOTS at country level.

See Figure 1: Structure of the Stop TB Partnership

The Partnership is governed by a Partners' Forum and a Coordinating Board, supported by a strong Secretariat housed in WHO. Large, lively and successful Partners' Forum meetings were held in 2001 and 2004 to set the strategic direction and ensure consensus on priorities for action. The Partnership Coordinating Board meets every six months to provide leadership and direction, and to monitor the implementation of policies, plans and activities of the Partnership.

The Partnership has structured its seven working groups to address directly the major challenges of TB today:

- DOTS Expansion Working Group, with individual subgroups on laboratory capacity strengthening, public-private mix, childhood TB, and poverty and TB;
- Working Group on DOTS-Plus for Multidrug-resistant TB;
- TB/HIV Working Group;
- Working Group on New TB Diagnostics;

- Working Group on New TB Drugs;
- Working Group on New TB Vaccines;
- Advocacy, Communications and Social Mobilization Working Group.

One of the great strengths of the Stop TB Partnership is that it brings together the TB research community with those engaged in programme implementation. As this Plan makes clear, their effective collaboration is critical to the rapid development and deployment of sorely needed new tools.

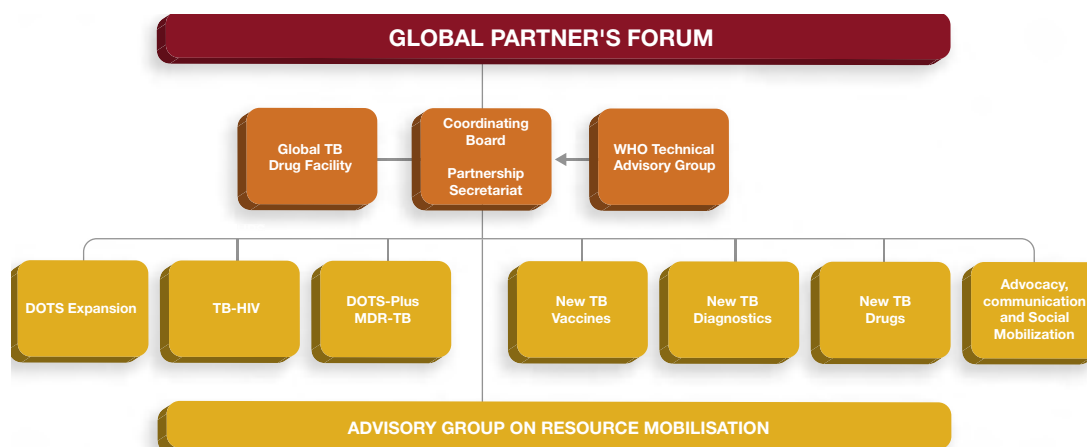
Under the Partnership's basic framework, the working groups are the primary means of coordinating activities mandated by the Board. The plans of the working groups and the Secretariat provide the basis for action, resource allocation and accountability within the Global Plan 2006–2015.

1.2 Achievements in global TB control since 2000

The Partnership will publish a full report of achievements within its first Global Plan to Stop TB 2001–2005 after the end of the plan period. The following are a few highlights to date.

Evaluation: As confirmed by an independent external evaluation in 2003, the Stop TB Partnership has established itself, in a very short period of time, as a successful public-private partnership for health.

FIGURE 1: STRUCTURE OF THE STOP TB PARTNERSHIP



Coordination and planning: The Partnership's Global Plan to Stop TB for 2001–2005 provided the first integrated plan of action for implementation and research, and identified the funding required. Most of the planned investment was for implementation of the DOTS strategy in the 22 priority countries with the largest number of TB cases (listed in Annex 2). The DOTS Expansion Working Group, in collaboration with the DOTS-Plus and TB/HIV Working Groups, coordinated implementation of the DOTS strategy and its adaptations. At country level, the 22 high-burden countries established interagency coordination committees and implemented DOTS expansion plans.

DOTS Expansion: DOTS is an internationally recognized strategy for delivering the basics of TB case-finding and cure. It is not simply a clinical approach to patients, but rather a management strategy for public health systems, including political commitment as well as case-detection through quality-assured bacteriology, short-course chemotherapy, ensuring patient adherence to treatment, adequate drug supply, and sound reporting and recording systems. The first Global Plan 2001-2005 estimated that US\$5 billion would be needed for DOTS expansion. In practice, about US\$5 billion was mobilized and spent effectively. By the end of 2003, over three-quarters of the world's population lived in countries that had officially adopted DOTS. The proportion is expected to reach over 90% by the end of 2005.

See Figure 2. Effect of the Global DOTS Expansion Plan (GDEP) on the case detection rate

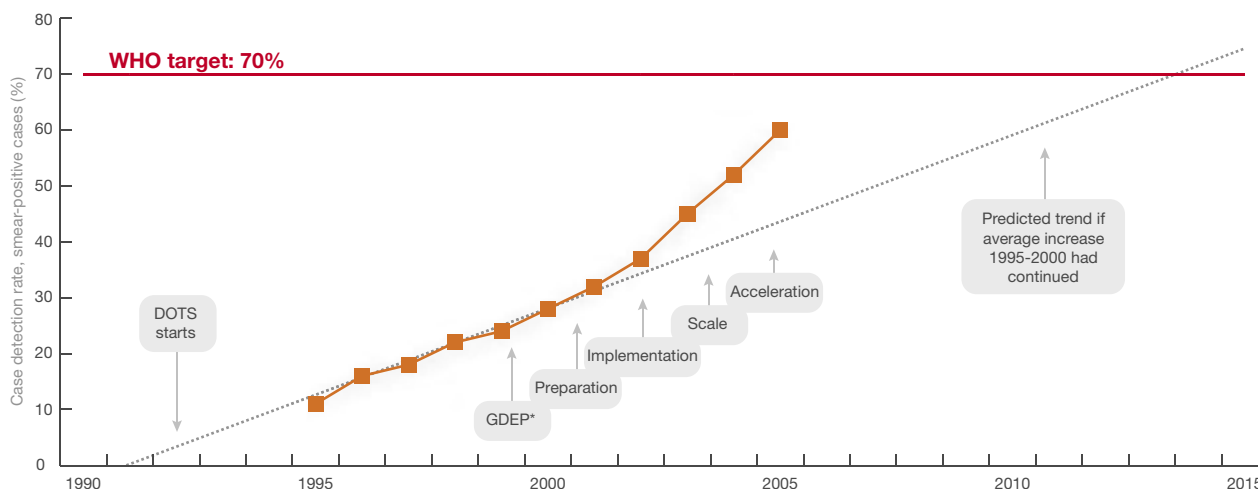
In 2000, the Partnership adopted targets for 2005 set by the World Health Assembly, of detecting 70% of new smear-positive cases, and successfully treating 85% of those detected. In the absence of HIV, achieving these targets should lead to a substantial decrease in the TB prevalence rate, and an annual decrease in the incidence rate of about 5–10%¹. This expected epidemiological impact has been demonstrated recently in, for example, Peru and the areas of China that are implementing the DOTS strategy (comprising half the country).

As illustrated in Figure 2, TB case detection under the DOTS strategy has accelerated over the past few years with implementation of the Global DOTS Expansion Plan. TB cases notified under DOTS programmes in 2003 represented 45% of estimated new smear-positive TB cases. Continuation of the upward trend would result in a case-detection rate of 60% by 2005 – short of the 70% target but a significant improvement since the launch of the first Global Plan to Stop TB, when the case-detection rate was 27%. The treatment success rate in the 2002 DOTS cohort was 82% on average, on track to achieve the 2005 target of 85% on time. However, the treatment success rate remains substantially below the average in the WHO regions of Africa (73%) and Europe (76%).

Increased technical support: With the significant influx of resources for TB control from the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM), banks and bilateral donors, new coordinated mechanisms to provide technical cooperation have been created. They focus on increasing the efficiency of support, as well as building the cadre of human resources capable of providing technical cooperation, and promoting exchange of expertise among countries with a high burden of TB. The aim is to improve technical capacity in order to make most effective use of the new funding, and so accelerate DOTS expansion towards the 2005 targets.

Drug supply: The Global Drug Facility (GDF), established by the Partnership, has provided treatment for more than 4.5 million patients, at the same time as catalysing a worldwide improvement in the quality of TB drugs, and a reduction in their cost. In addition, the Green Light Committee (GLC) promotes access to, and rational use of, second-line drugs with activity against multidrug-resistant TB. It has secured price reductions of 95% for some second-line drugs. To help prevent misuse of these drugs, the GFATM selected the GLC as its mechanism for procurement of second-line drugs and monitoring of approved projects. The GDF and the GLC are merging in a phased programme.

FIGURE 2: EFFECT OF THE GLOBAL DOTS EXPANSION PLAN ON THE CASE DETECTION RATE



Note: The 2005 value is a prediction based on current activities and trends.
* Global DOTS Expansion Plan

Multidrug-resistant TB: Multidrug-resistant TB (MDR-TB) is formally defined as resistance to isoniazid and rifampicin, the two most effective anti-TB drugs. Projects have demonstrated that management of MDR-TB is feasible and effective in resource-limited settings. As a result of additional funding for control of MDR-TB, there has been a rapid increase in the number of countries implementing DOTS-Plus. By July 2005, 36 DOTS-Plus pilot projects treating more than 10 000 patients with MDR-TB had been established in 27 countries.²

TB/HIV: The TB/HIV Working Group has published a core set of strategy and policy guidance documents to assist countries in implementing and monitoring collaborative TB/HIV activities.³ There has until now been limited collaboration between TB and HIV/AIDS control programmes, but many are beginning to adopt elements of the WHO interim policy for collaborative TB/HIV activities. By 2003, 29 of the 41 countries with the highest prevalence of TB/HIV had a national policy on TB/HIV collaboration and 16 had a national TB/HIV coordinating body.

New diagnostic tests: The creation of the Working Group on New TB Diagnostics in 2001 established a platform for focused development of new diagnostic products. Through the UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR) and the Foundation for Innovative New Diagnostics (FIND), promising technologies have been screened, and an exciting series of new product developments initiated, supported, and/or subjected to field trials. Currently there are 15 new diagnostics under development. At the same time, tools such as sample and strain banks have been developed to assist researchers.

New drugs: With support from the Working Group on New TB Drugs and the Global Alliance for TB Drug Development, there is

now a coordinated portfolio of promising new compounds, some of which have the potential to become the cornerstone drugs for TB control and even contribute to the elimination of TB in the future. There are 27 drugs in the pipeline, with research and development activity in virtually all stages of TB drug discovery and development – from early discovery projects through to clinical testing. This remarkable achievement is the result of critical collaborations between public and private partners that have leveraged the scientific and clinical knowledge of industry, the public health sector, and academic laboratories throughout the world.

New vaccines: In 2000, the Working Group on New TB Vaccines took note of the historic opportunities for development of new TB vaccines that resulted from the availability of techniques for the genetic manipulation of mycobacteria, and completion of the genome sequence of *M. tuberculosis*. By 2005, five new vaccine candidates were in phase I trials, and three more were due to start shortly. Important factors in success include major strategic investments by donors and foundations to support the Aeras Global TB Vaccine Foundation.

Advocacy and funding: The profile of TB has been raised at global level and in many countries with dedicated advocacy and communications activity to embed TB in the political agenda. Heightened political and funding support for the activities outlined in the first Global Plan to Stop TB (2000–2005) has assisted progress against TB worldwide. Expressions of support for TB control targets and for commensurate funding have been included in G8 communiqués (2000 and 2005), a World Health Assembly resolution (2005), the declaration of a TB emergency by the WHO Regional Committee for Africa, the Commission for Macroeconomics and Health (2001), and in high-level statements by Nelson Mandela, the African Union, and the

Commission for Africa. There has been substantial improvement in funding available for TB control since 2002. The Global Fund to Fight AIDS, Tuberculosis and Malaria now plays a major role in financing TB control, contributing more than one third of the budget in a number of high-burden countries.

1.3 TB today⁴

There are eight TB epidemiological regions (Figure 3)⁵. The countries in the region comprising the Established Market Economies (EME) and Central Europe have similarly high per capita income levels and low tuberculosis incidence rates. The Plan therefore focuses mainly on the other seven regions: African countries with high HIV prevalence (AFR High HIV); African countries with low HIV prevalence (AFR Low HIV); the American Region (AMR) – Latin America Countries (LAC); Eastern Europe Region (EEUR); Eastern Mediterranean Region (EMR); South-East Asia Region (SEAR); and the Western Pacific Region (WPR). It nevertheless remains important for the Established Market Economies and Central Europe to maintain and strengthen their TB control programmes.

In 2003, there were 8.8 million new cases of TB, of which 3.9 million were smear-positive; 674 000 of the patients were coinfecting with HIV. There were a total of 15.4 million cases, of which 6.9 million were smear-positive. An estimated 1.7 million people died from TB, including 229 000 people coinfecting with HIV.

See Figure 4: Estimated TB incidence rates, 2003

While the TB incidence rate is decreasing or stable in all regions except Africa, the latest available figures (2003) show that the

global incidence rate grew by 1% from 2002. This is a slower rate of growth than in previous years, but is still alarming. The continuing increase is largely due to the increasing rate in Africa, fuelled by the HIV epidemic and by the adverse social and economic situation. In Eastern Europe⁶, the incidence rate increased during the 1990s, which was a period of rapidly increasing inequity and deteriorating public health systems. It peaked around 2001 and has since fallen slightly. The rise in global incidence is slowing because the HIV epidemic in Africa is slowing.

In terms of the global distribution of the burden of TB, in 2003 the South-East Asian region notified 35% of all cases, the African region 24%, and the Western Pacific region 22%. The 22 high-burden countries account for approximately 80% of all estimated new TB cases each year. China and India alone account for 35%. India, the country with the greatest burden of TB, is also the country where the most dramatic advances are being made in DOTS expansion. Thanks to a massive recent scale-up, China expects to achieve nationwide DOTS coverage in 2005.

Although the global TB incidence rate is still slowly rising, prevalence and death rates are falling. WHO calculates that the expansion of the WHO-recommended DOTS strategy between 1990 and 2003 led to a fall in the global TB prevalence rate from 309 to 245 per 100 000 (including HIV-positive patients), including a 5% fall between 2002 and 2003.

See Figure 5: Estimated prevalence of HIV infection in TB cases, 2003

FIGURE 3: THE EIGHT TB EPIDEMIOLOGICAL REGIONS

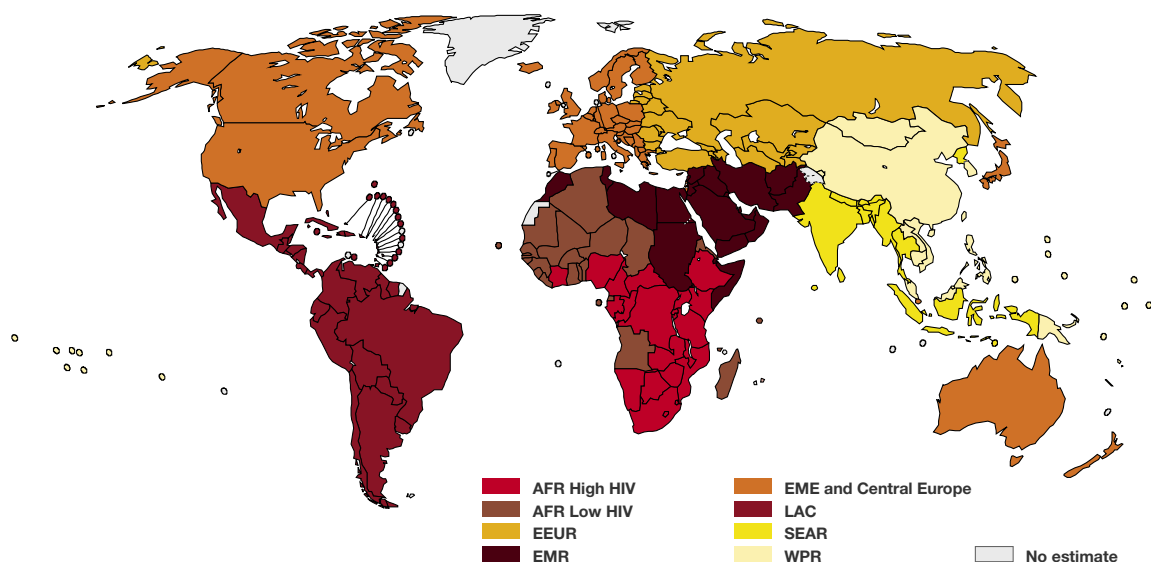
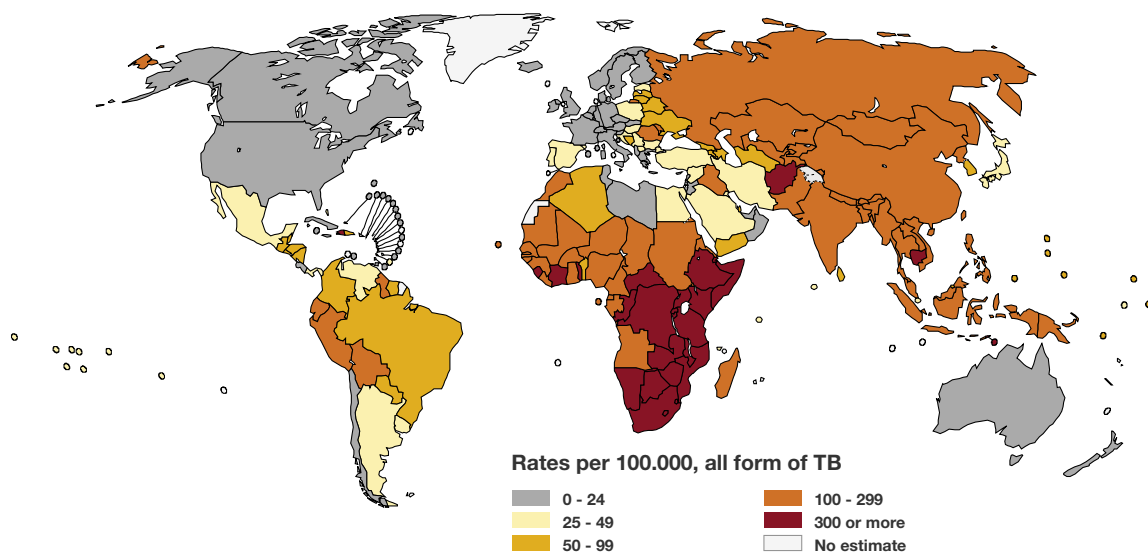
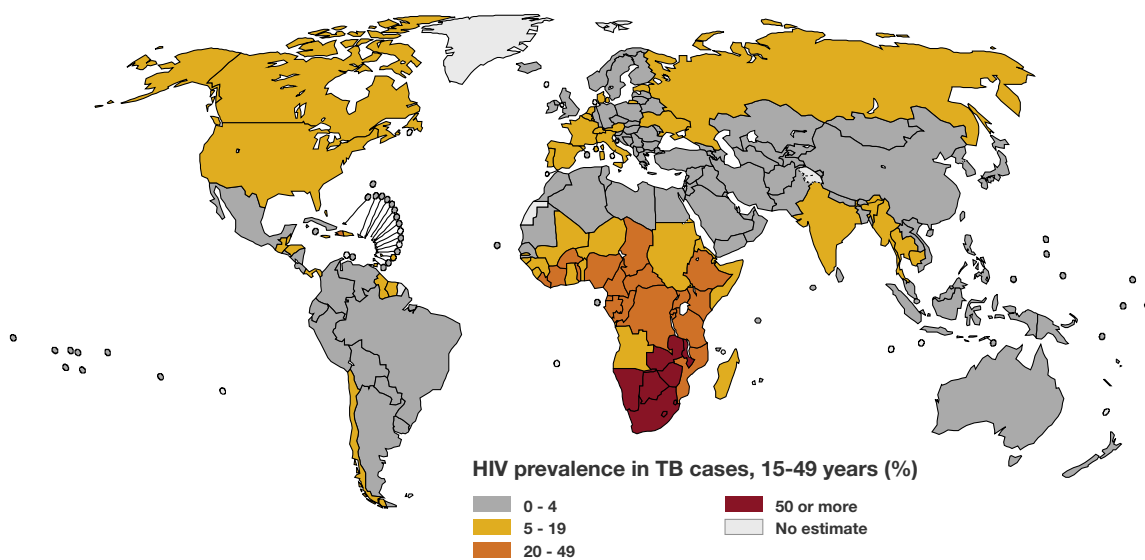


FIGURE 4: ESTIMATED TB INCIDENCE RATES, 2003**FIGURE 5:** ESTIMATED PREVALENCE OF HIV INFECTION IN TB CASES, 2003

The global death rate from TB peaked during the 1990s. Between 2002 and 2003, it fell by 2.5% overall, and by 3.5% among HIV-negative patients. If not for the strongly adverse trends in Africa, prevalence and death rates would be falling more quickly worldwide.

Several regions of the world are experiencing severe epidemics of multidrug-resistant TB that threaten TB control and translate into low cure rates. New estimates suggest that there are about half a million MDR-TB cases each year, including new and previously treated cases. The highest prevalences of MDR-TB have been observed in countries in Eastern Europe and some provinces of China. However, most regions have reported one or more countries with an MDR-TB prevalence of 5–6% among new cases. Drug resistance is also more severe in Eastern Europe than in other regions. For example, 50% of MDR-TB cases detected in these countries are resistant to all four first-line drugs, compared with only 12% in the rest of the world. While surveillance is not yet standardized, many countries in Eastern Europe also report high levels of resistance to second-line drugs.

1.4 Challenges ahead

Despite the achievements of recent years, there are still tremendous barriers to ensuring equitable access to high quality DOTS services and achieving TB control targets:

The rapid scale-up of DOTS coverage has put high demand on programme management, supervision and quality control.

In many countries, it is difficult to meet these demands because of generally weak health systems, a lack of human resources, limited funds and, ultimately, insufficient political commitment. This situation is exacerbated because governments are also rapidly scaling up interventions against other health priorities, such as HIV/AIDS and malaria. Planning and implementing DOTS programmes in settings with high rates of HIV or MDR-TB require skills and resources for interagency collaboration, programme management, supervision, monitoring and evaluation.

New tools remain urgently needed to increase the speed and precision of TB diagnosis, as well as to improve the effectiveness of treatment and reduce its duration. Progress has been impressive, but large-scale investment will continue to be necessary to make actual and potential new tools available for use.

HIV continues to present one of the greatest challenges to efforts to achieve the global TB control targets. In 2003, national TB programmes reported that few TB patients were being tested for HIV; still fewer were assessed for antiretroviral therapy (ART), and a very small fraction began ART. Even in Brazil, where ART is provided free of charge in the public sector, in 2003 only half of the notified TB patients were reported to have been tested for HIV.

Multidrug-resistant TB threatens the potential salutary impact of DOTS programmes. Although progress in widespread DOTS implementation will help prevent the further emergence of drug-resistance, expansion of effective DOTS-Plus programmes is vital to stem the contribution of drug-resistant cases to the overall TB epidemic. Too few countries have national policies for the diagnosis and treatment of MDR-TB. In some of those that do, treatment commonly fails to meet acceptable standards.

Access to good quality services is still inequitable in many settings. People in remote rural areas have serious difficulty in obtaining services unless they are highly decentralized. Poor people in general often have problems accessing services because of high direct and indirect costs. Many are caught in a disease-poverty trap, because of their high expenditure on health care. Reaching the poor with affordable, quality services is a problem not only for remote rural populations, but also for the growing population of urban poor – the slum dwellers, the homeless, and the migrants. Developing appropriate pro-poor strategies will require a broad approach involving communities, civil society, nongovernmental organizations, and all relevant health care providers.

There is still limited awareness of TB. Stigma, and poor knowledge about what types of TB services are available and effective, contribute to underuse of services and to the social costs of TB. Where quality services are available and truly accessible, it is essential to devise communication strategies to raise awareness of TB and the available treatment services, and to counter stigma. Limited awareness of TB in countries with low TB incidence is a barrier to raising donor funds for TB control in countries with high or medium TB incidence.

In most countries, large parts of the health system are still not involved in implementing DOTS. Many public and private health care providers do not use evidence-based approaches to TB diagnosis and treatment. This leads to overdiagnosis, missed or delayed diagnosis, poor treatment results, drug resistance, and wasted resources (including patients' own resources when they have to make out-of-pocket payments). In the future, the new International standards for tuberculosis care should be implemented by all health care providers involved in TB diagnosis and treatment.⁷

Sustained funding remains uncertain. Although the funding available for global TB control has increased in recent years, it will be a continuing challenge for the Partnership to help mobilize sufficient resources to reach the targets outlined in this Global Plan. Existing gaps in funding and uncertainty about future financing impede planning and implementation for both treatment and research. For example, recent data indicated that funding fell about 20% short of total needs for DOTS expansion in 2004 and 2005. A 2005 World Health Assembly resolution called for sustainable financing for TB control.⁸

2. ACHIEVING THE TARGETS: WHAT NEEDS TO BE DONE

2.1 Partnership vision, mission and targets

The Stop TB Partnership has a clear and consistent vision, mission and set of targets.

Vision

The Stop TB Partnership's vision is a TB-free world.

Mission

The Partnership's mission is:

- to ensure that every TB patient has access to effective diagnosis, treatment and cure;
- to stop transmission of TB;
- to reduce the inequitable social and economic toll of TB;
- to develop and implement new preventive, diagnostic and therapeutic tools and strategies to stop TB.

Targets

The Partnership has the following specific targets:

- **By 2005, and to be sustained or exceeded by 2015:** At least 70% of people with infectious TB will be diagnosed (i.e. under the DOTS strategy) and at least 85% of those diagnosed will be cured.
- **By 2015:** the global burden of TB disease (disease prevalence and deaths) will be reduced by 50% relative to 1990 levels. Specifically, this means reducing prevalence to 155 or fewer per 100 000 population, and reducing deaths to 14 or fewer per 100 000 per year by 2015, including people coinfecting with TB and HIV. The number of people dying from TB in 2015 should be less than 1 million.
- **By 2050:** TB will be eliminated as a global public health problem. Using the criterion for TB elimination adopted in the USA, this means that the global incidence of TB disease will be less than 1 per million population.

In addition, the Partnership is committed to meeting the Millennium Development Goal relevant to tuberculosis (goal 6, target 8) "to have halted and begun to reverse the incidence [of TB] by 2015". The interpretation of target 8 is that the incidence rate of all forms of TB should be falling by 2015.

These targets cover short-term process targets related to the implementation of DOTS as well as epidemiological impact targets for 2015, linked to the indicators for target 8 of Millennium Development Goal 6⁹. Achievement of these impact targets globally requires sustained progress in implementation. National control programmes around the world must reach at least 70% case detection and 85% treatment success, but they must also implement the wider range of activities described in this Global Plan. The results will be a major milestone on the way to achieving the Partnership's long-term target of eliminating TB as a public health problem by 2050.

2.2 Partnership strategic directions and objectives

Partnership strategic directions

To accelerate progress, the Partnership's **twin strategies** for the next 10 years will be to accelerate the development and use of better tools, and to implement a new WHO-recommended Stop TB Strategy, based on DOTS and including the International Standards for TB Care.

Results of the analytical modelling work that underpins this plan confirm that this twin track will be crucial for meeting the targets in full. They suggest, for example, that optimal use of existing tools as set out in this plan will achieve the 2015 targets in the highest burden countries, including China and India, but that new tools will be needed to meet the same targets in Africa and Eastern Europe. The introduction of effective new tools will be a prerequisite for meeting the longer-term target to eliminate TB. WHO calculates that, at the average rate of decline in TB incidence expected globally between 2010 and 2015 under this Global Plan, the incidence rate will still be about 100 times larger than the elimination target of 1 per million. We will not secure elimination without new technology, probably for mass treatment of latent infection or mass vaccination.

Tackling TB is not a sprint but a marathon, given the long cycle of the disease. Since one third of the world's population is already infected with latent TB, even if transmission could be stopped tomorrow, we would still expect some 100 million people to develop TB during their lifetime. A person infected in childhood has an appreciable chance of developing the disease in old age, when waning immunity allows TB to flare up. But our current challenge is much greater since transmission of TB is still continuing. Success will require long-term commitment and long-term, sustainable financing.

Partnership objectives

In order to achieve our mission and make our vision a reality, **the objectives** of this strategic plan are to:

- Promote wider and wiser use of existing strategies to interrupt TB transmission by:
 - increasing access to accurate diagnosis and effective treatments by accelerating DOTS implementation to achieve the global targets for TB control; and
 - increasing the availability, affordability and quality of anti-TB drugs.
- Derive strategies to address the challenges posed by emerging threats by adapting DOTS to prevent and manage multidrug-resistant TB, and to reduce the impact of HIV-related TB.
- Accelerate the elimination of TB by:
 - promoting research and development for new TB diagnostic tests, drugs and vaccines; and
 - promoting adoption of new and improved tools by ensuring appropriate use, access and affordability.

BOX 1: WHO-RECOMMENDED STOP TB STRATEGY

SIX KEY ELEMENTS

1. **Pursue quality DOTS expansion and enhancement**, improving case-finding and cure through an effective patient-centred approach to reach all patients, especially the poor.
2. **Address TB/HIV, MDR-TB and other challenges**, by scaling up TB/HIV joint activities, DOTS-Plus, and other relevant approaches.
3. **Contribute to health system strengthening** by collaborating with other health programmes and general services, for example in mobilizing the necessary human and financial resources for implementation and impact evaluation, and in sharing and applying achievements of TB control.
4. **Involve all care providers**, public, nongovernmental and private, by scaling up approaches based on a public-private mix (PPM), to ensure adherence to the International Standards of TB Care.
5. **Engage people with TB and affected communities** to demand, and contribute to, effective care. This will involve scaling up community TB care; creating demand through context-specific advocacy, communication and social mobilization; and supporting development of a patient's charter for the tuberculosis community.
6. **Enable and promote research** for the development of new drugs, diagnostics and vaccines. Research will also be needed to improve programme performance.

The Stop TB Partnership's Global Plan for 2006-2015 adopts the new WHO-recommended Stop TB Strategy (Box 1). The Stop TB Strategy provides a comprehensive and inclusive vision for global TB control, incorporating human rights imperatives and health system strengthening.

The rest of this section highlights the key approaches to be taken in pursuing the Partnership's objectives. Summaries of individual working group plans and the Partnership Secretariat plan are given in Part III.

2.3 Promoting wider and wiser use of existing strategies for TB control

Increasing access to accurate diagnosis and effective treatment through DOTS

The DOTS Expansion Working Group (DEWG) provides the focus for implementation activities, assisting countries to improve access to quality DOTS and laying the foundation for implementation activities by the DOTS-Plus and TB/HIV Working Groups. The work of these three implementation working groups is increasingly converging. Within the life of this Plan, the Partnership will review the most appropriate structure of working groups for contemporary needs. The DOTS Expansion Working Group will also pave the way for early introduction of the new tools expected to become available as a result of the efforts of

the working groups on new TB diagnostics, drugs and vaccines. The country-level activities of the Advocacy, Communication and Social Mobilization Working Group will build on the plan for DOTS Expansion.

The DOTS Expansion Working Group will continue to prioritize the 22 TB high-burden countries that together account for 80% of the global TB burden. These countries will receive an increased level of technical assistance through the DEWG, and a detailed report on them will be included in the annual WHO report on global TB control report. In addition, the designation of HBC will be used to advocate for intensified efforts and increased resources for TB control.

In 2006–2015, the DOTS Expansion Working Group will assist countries to implement the following interlinked activities:

- Achieve complete **coverage of basic DOTS** services, so that all public health units in all countries provide TB care according to the DOTS strategy by 2010. Some countries do not yet provide free treatment under DOTS for people with sputum smear-negative pulmonary TB or extrapulmonary TB, or for children with TB. In addition, all countries should work towards free provision of sputum smear microscopy and other TB diagnostic tests, and make isoniazid preventive treatment available for children.
- **Improve the quality of DOTS** by increasing the competence

and availability of human resources for undertaking DOTS tasks, and strengthening laboratory capacity for sputum smear microscopy and culture, drug management, supervision, and recording and reporting. The target is to ensure that all countries provide quality diagnosis and treatment.

- **Prioritize the needs of the poor and vulnerable.** Access to quality TB services should not be determined by type of TB, financial capacity, or social status. Given the low socioeconomic status of most people with TB, a pro-poor and equity-based approach requires that health services pay special attention to the needs of the most disadvantaged groups. This means identifying barriers and implementing measures aimed at ensuring early diagnosis and effective treatment in order to reduce the social and financial burden of the disease for patients. Specific options for addressing poverty in DOTS implementation are considered in section 3.3.
- Introduce or scale up **the public-private mix approach in DOTS**, to involve all relevant health care providers – public and private – in providing effective TB services and applying the International Standards of TB Care. Depending on the setting, this approach may include medical colleges, general hospitals, health services under insurance schemes, prison health systems,¹⁰ army health services, NGO health facilities, corporate health facilities, private specialists and general practitioners, private pharmacies, and the informal private health care sector. While there is a potential role for all providers in delivering proper TB care, national TB programmes will need to strengthen their stewardship functions, including regulation, financing, monitoring, evaluation and surveillance. Guidelines for implementing a public-private mix (PPM) approach in DOTS have recently been developed by the PPM Subgroup¹¹.
- Introduce or scale up community DOTS initiatives, to allow communities to contribute to TB control, e.g. by promoting adherence to treatment and facilitating case-finding. By 2010, all countries in Africa will have scaled up **community DOTS** initiatives and by 2015, about 1.9 billion people will live in areas with community DOTS initiatives. In countries with high HIV prevalence, there will be an overlap between TB and HIV community involvement, i.e. in case-finding and case-holding for TB treatment and antiretroviral therapy. A community contribution to TB control improves access to care, fosters a patient-centred approach to the management of TB, and has resulted in improved treatment success rates through decreased default and transfer out rates. While the type and scope of community involvement depend on location and context, many high-burden countries regard civil society as an essential partner in providing support to patients and their families. The Partnership will support the forthcoming Patients' Charter for the Tuberculosis Community (under development in tandem with the International Standards for Tuberculosis Care).
- Introduce or scale up the **Practical Approach to Lung Health (PAL)**, a comprehensive, symptom-based approach to managing patients with respiratory symptoms within the primary health care system, aimed at improving the diagnosis

of TB and the management of other chronic respiratory conditions. PAL includes standardization of clinical care procedures through the development and implementation of clinical practice guidelines, and coordination between health care levels within the district health system as well as among the various players in the health system. By 2005, PAL activities were in progress in 17 countries, and five others had requested WHO's collaboration in developing PAL.

- Introduce or scale up facilities and technical capacity for **mycobacterial culture services and drug susceptibility testing, and the incorporation of new diagnostic tools**. While high quality sputum smear microscopy is the cornerstone of DOTS, and remains the key to case detection and TB control, the strengthening of services for culture of *M. tuberculosis* and for drug susceptibility testing (DST) is necessary, especially where the prevalence of HIV or MDR-TB is high. New diagnostic tools, expected to be introduced from 2008, will gradually replace sputum smear microscopy, conventional culture and DST. Countries will then require assistance with registration of new products, formulation of new policies, purchase of equipment, training and supervision of staff, and costs.

Increasing the availability, affordability and quality of anti-TB drugs

An uninterrupted supply of high quality, affordable, first-line drugs for TB control is critical to the achievement of Partnership targets. The Global Drug Facility (GDF), which is operated by the Partnership Secretariat and which will merge with the Green Light Committee for second-line drugs, will work to **increase the availability of affordable, high quality drugs** in all countries where there is need. The GDF stimulates the development of viable markets for TB control products, other than first-line drugs. By 2010 GDF systems will be prepared for the introduction of new drugs and new diagnostic tests, as well as the harmonized supply of TB/HIV treatments.

Advocacy, communication and social mobilization

There is an urgent need for **advocacy, communications and social mobilization (ACSM)** in endemic countries, directed at rapidly building a multilevel, multisectoral social movement to eliminate TB. Achieving a high level of social commitment within health service delivery systems is particularly crucial in the context of TB. There is a need for processes that will help and empower communities to take ownership of and drive the agenda for TB elimination. Rigorous application of communication and social mobilization strategies will contribute to achieving the Partnership's targets.

The vision of the ACSM Working Group at country level is the establishment and funding of evidence-based and country-driven ACSM activities aimed at bringing about sustainable societal and behavioural change. The formulation of strong country ACSM plans needs to be supported by adequate in-country human and financial resource commitments. Additionally, the ACSM Working Group will mobilize assistance to countries in

the form of tools and franchising, training, technical advisers, opportunities for information exchange, and regular formal assessments to ensure effective ACSM programming. Specific plans will be developed to provide training opportunities and tailored needs-based inputs to individuals and public sector institutions, with the aim of rapidly strengthening in-country ACSM capacities.

Effective global advocacy is essential to place TB high on the political and development agenda in donor countries and in countries with high or medium TB incidence, foster political will, and increase financial and other resources on a sustainable basis. The ACSM Working Group will seek to achieve this by: broadening the coalition of Stop TB advocacy partners; linking TB advocacy with other global social movements, especially HIV/AIDS; fostering prominent TB champions; empowering patients and communities; and mobilizing strategically timed and focused initiatives aimed at policy-makers, legislators, funding institutions and the media.

2.4 Strategies to address the challenges posed by emerging threats

Additional strategies that build on the core foundation of the DOTS strategy are needed to address the challenges posed by MDR-TB and HIV.

Adapting DOTS to prevent and manage multidrug-resistant TB: DOTS-Plus

There are both preventive and restorative strategies to combat resistance to TB drugs – DOTS and DOTS-Plus – since DOTS alone is not sufficient to curb the TB epidemic in countries with high rates of multidrug-resistant TB and large proportions of re-treatment cases. The control of MDR-TB requires sound implementation of DOTS to prevent the development of new cases plus careful introduction of second-line drugs with adequate laboratory support to stop the amplification and circulation of resistant strains.

The priorities for the next decade are to:

- expand drug resistance surveillance (DRS);
- monitor trends and regularly update the global estimates of MDR-TB;
- strengthen capacity for quality-assured culture and drug susceptibility testing;
- dramatically scale up MDR-TB treatment according to WHO guidelines, since currently less than 2% of the total number of estimated culture-positive MDR-TB patients are treated appropriately;
- create a healthy and competitive market of quality-assured second-line drugs;
- provide technical and global coordination to accomplish the goals.

Strengthening of health systems and the health workforce to deliver sound diagnosis and treatment to all MDR-TB patients will be essential.

The vision of the Stop TB Working Group on DOTS-Plus for MDR-TB is the integration of drug resistance surveillance and the management of MDR-TB as routine components of TB control, providing access to diagnosis and treatment for all TB patients and by all health care providers, regardless of drug susceptibility patterns. This is in line with the new WHO-recommended Stop TB strategy, which encompasses all TB patients, including those with MDR-TB and HIV. As a result, all MDR-TB management measures will be implemented in collaboration with DOTS expansion and strengthening activities, and in line with the activities of the other Partnership Working Groups.

The countries with a high prevalence of MDR-TB are those of the former Soviet Union, China and India, which together account for almost three-quarters of the estimated global TB burden.

Reducing the impact of HIV-related TB

The key strategy is to reduce the global and individual burden of HIV-related TB by scaling up implementation of collaborative TB/HIV activities in countries with a high burden of TB/HIV. The severity of the TB/HIV epidemic in Africa merits particular and urgent attention. The strategic plan of the TB/HIV Working Group for 2006–2015 also reflects the Blueprint for Africa 2006–2007, a more detailed plan for intensified, short-term action, developed to accelerate progress in the region. This Blueprint for Africa was adopted by the Regional Committee for Africa, in its declaration of TB as an emergency in August 2005.

The international standards for TB/HIV collaboration have been set in WHO's Interim policy on collaborative TB/HIV activities,¹² which builds on DOTS TB programmes and HIV/AIDS programmes to provide comprehensive TB and HIV prevention, care and support services to reduce the impact of HIV-related TB. The policy sets out specific activities at country level to address the dual epidemics, including:

- establishing mechanisms for collaboration, including a coordinating body for TB/HIV activities, surveillance of HIV prevalence among TB patients, joint TB/HIV planning, and monitoring and evaluation;
- decreasing the burden of TB among people living with HIV/AIDS (PLWHA) – through intensified case-finding for earlier detection of active TB, provision of isoniazid preventive therapy (IPT) for coinfecting patients, and TB infection control in health care and congregate settings.
- decreasing the burden of HIV among TB patients – through provision of voluntary counselling and testing for people at risk of HIV, introduction of HIV prevention and co-trimoxazole preventive therapy, HIV/AIDS care and support, and introduction of antiretroviral therapy (ART).
- improving the care of people who are infected with both TB and HIV, through training and collaborative care initiatives.

Some gaps in the interim policy remain to be filled (e.g. regarding TB/HIV services for intravenous drug users), and the policy must be refined and adapted to address the needs of populations at risk on the basis of country experience and new research. Nonetheless, the priority is now to deliver, monitor and maintain its standards. Implementation of the interim policy in all high-

PART I: STRATEGIC DIRECTIONS

burden settings is therefore at the core of the TB/HIV strategic plan for 2006–2015.

The activities to be undertaken by the TB/HIV Working Group and its partners over the next 10 years to achieve the 2015 targets can be grouped in the following four broad areas:

- **to scale up implementation and expand the scope of collaborative TB/HIV activities;**
- **to develop and coordinate the research** necessary to improve the prevention, early diagnosis and rapid treatment of TB in PLWHA, and incorporate the results into global policy;
- **to increase political and resource commitment** to collaborative TB/HIV activities;
- **to contribute to strengthening health systems** to carry out TB/HIV activities.

Target countries are all those with a generalized HIV epidemic (adult HIV prevalence >1%) and large countries in which there are administrative areas with an adult HIV prevalence >1%.

2.5 Operational research

For any public health activity, operational research is necessary to determine the best ways of implementing interventions and to monitor their impact. Operational research is thus crucial in determining how to increase access to accurate diagnosis and effective treatment through the DOTS strategy, and how to adapt the DOTS strategy to address the challenges posed by drug resistance and HIV. Operational research involves the evaluation of programme operations, aimed at improved policy-making, better design and operation of health systems, and more efficient methods of service delivery. Financial and technical support is required to enhance local capacity for operational research (see Table 4). National plans for TB control should include budgeted activities for operational research as a routine part of programme activities.

2.6 Promoting development and adoption of new TB diagnostic tests, drugs and vaccines

New tools will be of critical importance in achieving the Partnership's targets, particularly in Africa and Eastern Europe, and essential to securing the Partnership's vision of eliminating TB – hence the need to invest now to reap future benefits.

New diagnostic tests

More than a century after its development, the microscopic examination of sputum is still the only widely available diagnostic tool in most developing countries for identifying TB. Unfortunately, it has a sensitivity of only 40–60% under field conditions, falling as low as 20% in the presence of HIV coinfection. Yet even this limited diagnostic test remains beyond the reach of the majority of TB patients. In resource-limited settings, drug susceptibility testing, if available, is usually

performed only after treatment has failed, which represents a missed opportunity to interrupt transmission.

One third of the population of the world has a latent infection with *M. tuberculosis*. Preventive therapy effectively reduces progression to active disease, but there is currently no way to predict which subjects are at greatest risk of progression.

The vision of the Working Group on New TB Diagnostics is the development and introduction of cost-effective and appropriate new diagnostic tools, which perform equally well in HIV-infected subjects, to:

- improve TB case detection, through increased sensitivity and specificity and improved accessibility; simple, accurate, inexpensive tests that can be performed at low levels of the health care system and that produce results on the same day are the ultimate goal;
- rapidly and inexpensively identify drug-resistant TB, permitting timely, effective treatment to reduce both individual morbidity and continuing transmission;
- reliably identify latent TB infection and determine the risk of future progression to active disease, allowing rational use of preventive therapy.

The three objectives for 2006–2015 of the Working Group on New TB Diagnostics are to:

- **address existing gaps in knowledge** that are obstructing development of new diagnostic tools;
- **develop and evaluate a portfolio of new diagnostic tools** and demonstrate their impact;
- **implement new diagnostic tools** and ensure access to them.

The greatest impact on public health in the area of TB diagnostic tests is expected to come from a highly accurate testing device that can be used in the field. The Working Group plans to promote and finance research in this area, building on advances in mycobacterial genome sequencing and expression profiling. It is anticipated that this information will facilitate the development of improved test strips suitable for use at the first point of care, and that during 2006–07 an improved test (for use on blood, serum, urine or saliva) will be developed.

New drugs

The vision of the Working Group on New TB Drugs is to have new TB regimens that will achieve cure in 1–2 months or less, rather than 6–8 months as now, will be effective against MDR-TB, will be compatible with antiretroviral therapy, and will be effective against latent TB infection. In addition, new regimens need to be affordable and easily managed in the field. This is an extremely challenging goal, but it must be met if we are to change the face of TB therapy. If progress in the basic understanding of the biology of *M. tuberculosis* continues, it is conceivable that the course of therapy could be reduced even further, to 10–12 days, before 2050, or that additional advances in therapeutic or prophylactic options may also greatly reduce TB incidence.

To achieve this vision, the Working Group has developed its strategic plan for 2006–2015 around the following areas of strategic importance:

- **basic discovery biology**, to identify and validate new targets for drugs, and to identify candidate compounds using effective screening and creative medicinal chemistry;
- **drug development**;
- **planning and execution of more effective clinical trials**, including identification of improved biomarkers and methods of assessing latent disease;
- clear and efficient **regulatory guidance**.

Eleven compounds with novel modes of action against TB are currently in clinical or advanced preclinical development. Some of these compounds, for example moxifloxacin, have been shown to reduce treatment time in animal models. The target by 2010 is the introduction of a new drug or combination of drugs that can reduce treatment duration to 3–4 months. New in vitro data suggest that compounds under development could reduce treatment duration even further. Genomic and microbiological research on novel targets supports optimism that a one-month treatment for TB is attainable and could be in clinical trials by 2015. Combining agents that attack different targets could maximize the therapeutic effectiveness of new regimens.

Only about 10% of candidate products entering the clinical pipeline advance to registration, mostly because of concerns about safety. Thus, a robust and sustained pipeline of new candidates and back-up discovery programmes is essential to success.

Affordability, adoption of, and access to new drugs, and the implementation of new regimens, are intimately linked to the manufacture and production of medicines, alone or in combination, and to the adoption of such therapies as international standards. The Working Group will therefore continue to work closely with the other working groups of the Stop TB Partnership, ministries of health, international health agencies and in-country field workers to understand their needs, in order to ensure rapid and successful introduction and adoption of the new regimens in the field. Experience has shown that the establishment of standard treatments and their subsequent implementation in the field can take years, particularly in TB control. All Stop TB Partnership working groups and the international community will need to focus on the safe, prompt and effective adoption of new tools.

New vaccines

The introduction of new, effective TB vaccines will be an essential component of any strategy to eliminate TB by 2050. Efforts to develop such vaccines are gaining substantial momentum. Scientific results from the laboratory and from early field trials have been encouraging and consistent. New TB vaccines to prevent childhood and adult forms of TB, to reduce TB in people coinfecting with HIV, and to shorten drug treatment regimens will fundamentally alter our approach to TB control.

It is probable that the next generation of vaccines will work by complementing the immune response induced by the current BCG vaccine. New vaccines could be delivered together with BCG to young children before they are exposed to *M. tuberculosis*, as a separate booster to young adults, or as an adjunct to chemotherapy. The Working Group on New TB Vaccines is promoting research on several approaches to the development of new candidate vaccines and new delivery strategies.

The overall objective of the Working Group for 2006–2015 is to have **a safe, effective, licensed vaccine available at reasonable cost by 2015**. Its objectives and workplan for 2006–2015 are to:

- **maintain and improve BCG vaccination programmes**, since it is anticipated that BCG will remain the cornerstone of TB vaccination programmes over the period covered by this Global Plan, with the next generation of new vaccines introduced as an addition to BCG vaccines, which are commonly given at birth in many countries. This requires BCG production to be sustained by a diminishing number of international suppliers.
- **expand discovery and translation research on vaccines** (“keeping the pipeline filled”);
- **facilitate preclinical development** of new vaccines;
- **build capacity at vaccine trial sites**, providing opportunities for training and capacity strengthening;
- **ensure availability of vaccine production capacity/scale-up**, requiring the development of innovative partnerships with manufacturers in developing and developed countries;
- **perform clinical trials**, and ensure that collaborators in developed and developing nations make the necessary commitment of investments.
- **provide an enabling infrastructure**.

2.7 Technical cooperation

The Stop TB Partnership provides the platform for coordinated technical support to countries, consensus on unified approaches and frameworks for monitoring and evaluation, and assistance to national TB control programmes. Consistent and focused technical cooperation to support implementation of DOTS has been a mainstay of accelerated TB control scale-up in high-burden countries over the past decade. National TB Programmes, as well as major nongovernmental providers, have benefited from guidance and assistance from a wide range of technical cooperation partners¹³ in capacity development, planning, resource mobilization, focused problem-solving, monitoring and evaluation.

The Global Fund to Fight AIDS, Tuberculosis and Malaria is now providing unprecedented levels of external financing for national TB control efforts. With this new financing mechanism, a host of new implementation challenges confront recipients and their partners. If obstacles to country implementation efforts are to be overcome, the important Global Fund financing has

BOX 2: EXAMPLES OF MECHANISMS FOR RAPID TB TECHNICAL ASSISTANCE FOR COUNTRIES

- **DOTS Expansion Working Group** – coordination of major technical partners
 - Regular shared calendar of joint and single agency missions in countries.
 - Annual meetings to coordinate activities, share best practices and address common technical challenges.
 - Annual joint missions in countries.
- **ISAC** (Intensified Support and Action Countries) – Joint initiative of Stop TB, WHO, bilateral donors, the Global Fund, and technical partners, to support managerial and technical capacity-building to increase countries' capacity to make effective use of new funds; first phase – China, India, Indonesia, Kenya, Pakistan, Romania, Russian Federation and Uganda.
- **TB CAP** (Tuberculosis Control Assistance Program) – USAID-funded consortium of eight technical assistance partners to support capacity-building, country-level programme implementation and scale-up, and advocacy in USAID-funded countries.
- **Back-up Initiative** (financed by GTZ) – support for selected countries in planning and preparing proposals to the Global Fund.
- **High-level missions** of Stop TB Partnership Board members to priority countries to help meet policy and financial challenges

to be matched by technical support. A range of mechanisms are available for coordinating the provision of rapid technical assistance.

See Box 2: Examples of mechanisms for rapid TB technical assistance for countries

Countries have benefited from the support of technical partners in preparing Global Fund grant proposals. In Round 4 (2004) of Global Fund applications, the TB grant success rate of countries that had received technical assistance was 64% compared with 40% of countries without assistance.

The crucial need now is for support for implementation. The credibility of the Global Fund, its investors, and the technical cooperation agencies rests on effective implementation at country level. However, the financing gaps for the technical partners have not yet been addressed in a consistent and adequate fashion. This amounts to an “underfunded mandate” that has ripple effects on all of the organizations' functions. The capacity of Stop TB partners to respond can no longer meet the demand from the 130 countries receiving Global Fund grants. WHO, other UN agencies and nongovernmental organizations (NGOs) – all of which are heavily dependent on voluntary contributions – are chronically under-resourced compared with the scale of assistance needed to help countries make effective use of their large grants.

The total cost to partners of providing technical assistance over the 10 years from 2006 to 2015 is estimated to be US\$2.9 billion. This sum is included in the estimates of the total cost of implementing the Global Plan.

2.8 Monitoring and evaluation

The Global Plan to Stop TB must remain relevant for all partners throughout its lifetime (2006–2015). Any ten-year plan will need to be adjusted in the light of changing circumstances. Each Working Group plan therefore sets out specific measures for monitoring and evaluation, and fruitful areas for much-needed operational research.

One of the ground-breaking elements of the DOTS strategy has been its clear methods for routine case notification, reporting, treatment cohort analysis, supervision for validation, and related performance indicators. DOTS-based recording and reporting systems are in place in over 184 countries. WHO is developing a coalition on impact measurement, with technical partners in high-burden countries, international and national agencies, and academia, in order to devise improved standard evidence-based methods of measuring the epidemiological impact of TB control measures. This will include TB prevalence surveys, household health surveys, modelling and analysis of routine data. These approaches are urgently needed to measure progress towards the MDG and Partnership impact targets.

Overall, the Partnership Secretariat has a fundamental role in monitoring and evaluation of the Partnership and the Global Plan. As a result of such monitoring and evaluation, the Secretariat will propose tactical revisions to the Global Plan that would enable faster progress towards targets.

The Partnership Secretariat will report to the Partners' Forum (at least every three years) and Coordinating Board (annually) on progress towards the achievement of the Global Plan targets. In collaboration with the working groups, the Secretariat will monitor working group inputs and measure progress towards the targets. In addition the Secretariat will facilitate a mid-term review and progress report in 2011. In 2015 it will provide a final report on the Global Plan and coordinate development of a further Global Plan for the next period.

3. KEY CROSS-CUTTING ISSUES: STRENGTHENING HEALTH SYSTEMS, TB AND POVERTY, TB IN CHILDREN, AND TB AND GENDER

3.1 Introduction

As the Partnership's working groups take forward their individual strategic plans for 2006–2015, they will work within the overall holistic vision of the Global Plan to Stop TB. To do this, the Working Groups have to work together effectively and efficiently, and to take a common approach to key cross-cutting issues. This section addresses four such issues important to the Global Plan: health system strengthening, poverty, TB in children, and TB and gender.

3.2 Strengthening health systems

The crucial need to strengthen health systems

The Global Plan for 2006–2015 has been developed at a time of increasing recognition that the achievement of most of the health-related MDGs depends on overcoming health system constraints that hinder access, equity and quality of care.

See Box 3: Core goals and functions of the health system

In planning and implementing DOTS expansion and other interventions over the past decade, countries with a high TB burden have responded to the strengths and weaknesses of their health systems. National TB Programme capacity to coordinate and guide response was strengthened, but staffing and management resources vary widely and are still seriously lacking in many countries. Innovation in many countries allowed the capacity of the public, private and community organizations engaged in service delivery to be expanded. New ways were found to overcome bottlenecks in drug supply, access to diagnosis and laboratories, use of basic information and evaluation of results. Nevertheless, it was still not possible to reach all patients in need.

The crisis in human resources for health is one of the greatest challenges in TB control and for the MDGs in general. It requires action across all levels of the health system, all programmes, partnerships and global stakeholders.

Addressing the health workforce crisis

Human resources (HR) for health are an essential component of health systems; without them, individual or public health interventions are not possible. A wide variety of workers in the health and allied fields are involved in TB control. A shortage of competent and motivated staff is one of the most important barriers to achieving the MDGs and Stop TB targets. The impact of HIV on the health workforce exacerbates the HR crisis, particularly in sub-Saharan Africa. The Global Plan recognizes that weaknesses in the workforce are complex and require concerted, comprehensive approaches to address them. National plans to pursue DOTS expansion and all the elements of the Stop TB Strategy over the next 10 years will take explicit account of the HR base in specific country settings. Furthermore, they should be integrated within larger system planning to ensure that constraints are recognized and efficient use is made of new opportunities, such as initiatives to train and finance new cadres of health staff.

The main HR issues constraining effective TB control are **insufficient quantity, quality and distribution of staff**. These problems are not specific to TB control and most require action at national level or throughout the health sector. Such action could include improvements in educational policies, financial ceilings for recruitment, and human resource planning, covering skills mix and distribution, policies to improve staff recruitment, retention and accountability, and budgets to ensure adequate remuneration. However, TB programmes should facilitate the continuing development of competence in all staff involved in TB control, and should keep accurate records of which staff have been trained and where they are.

The Global Plan envisages action on three linked platforms for health system strengthening related to TB control.

See Figure 6: Health system strengthening and TB control: advancing outcomes across three platforms

At the macro level, there is need for measures such as: advocacy and collaboration among partners to mobilize greater resources for staffing; removal of barriers to the creation of more posts; and financial reforms to allow better salaries or the use of incentives to ensure adequate distribution and increased retention of staff. At national level, the key lies in building managerial capacity for middle- to long-term HR planning, and in improving recruitment and retention policies by promoting attractive terms and conditions of service. TB programmes worldwide are using various innovative strategies to increase access to treatment, such as using staff in the private sector and in the public sector outside national TB programmes. Many of these initiatives appear to have a positive impact on the HR situation, but need to be properly evaluated. Similarly, innovative initiatives currently employed by other programmes to improve HR use could be adapted to TB control.

Wider action to strengthen health systems

The Stop TB Partnership is committed to being an active player in health system strengthening partnerships. This involves working at the global, regional and inter-regional level, where emerging alliances are promoting more concerted approaches to strengthening critical aspects of national health systems. These include global initiatives, such as the Health Metrics Network (for strengthening national information systems) and the Health Workforce Alliance.

This links with a broader discussion currently being led by the High-Level Forum on the Health MDGs about the possibility of identifying some **best practice principles** for the engagement of global health partnerships at country level. These primarily relate to alignment and harmonization,¹⁴ in the expectation that better harmonized and aligned aid from partnerships will ultimately lead to better health outcomes. While the full implications for operationalization would need to be explored once any such best practice principles are agreed, the Stop TB Partnership's Coordinating Board has already endorsed the principles of alignment and harmonization. The Stop TB Partnership will immediately work with other partnerships and agencies to achieve greater harmonization of funding streams within and beyond TB. WHO is currently creating working groups on health financing, working with private providers, and service management, designed to engage multiple partners and to promote exchange of knowledge and good practice, and more consistent action and advice in countries. Stop TB partners will contribute to these working groups.

National TB programmes and their collaborators will engage further with others to identify bottlenecks and support system-wide actions to improve stewardship and management, financing, HR development, service delivery and structures, and community engagement.

Within TB control, and through this Plan, partners will continue to scale up and further adapt innovations (including from other fields) for TB control that can strengthen systems. The strategic plans here include actions designed to improve the stewardship of TB programmes, district health systems and local services (policy guidance, strategic planning and oversight of performance), some elements of HR development, infrastructure and commodity management, service provision, financing, and vital innovations in research, technology provision, and knowledge exchange. As part of service provision, the Global Plan calls on countries to further diversify patient-friendly models of service delivery over the next 10 years to reach more of those missing care today.

The costs of pursuing actions related to health system strengthening at national level have been addressed in all the components of the Global Plan, as shown in Table 1. The costs of engagement and collaboration in global, regional and inter-regional initiatives and joint pilot innovations to strengthen health systems is estimated at approximately US\$2 million per year.

The Partnership's targets for 2015 can be reached and impact sustained, but only with country-led action in the more than

BOX 3: CORE GOALS AND FUNCTIONS OF THE HEALTH SYSTEM

Health systems in different countries have similar goals – to improve health (as equitably as possible), through systems that are responsive and financially fair. And all health systems have to carry out the same basic functions, regardless of how they are organized or which health interventions they are trying to deliver. These functions are: the development of human and other key resources; service provision; financing; and stewardship (oversight and guidance).

Source: The "Montreux challenge": making health systems work, WHO consultation, April 2005.

FIGURE 6: HEALTH SYSTEM STRENGTHENING AND TB CONTROL: ADVANCING OUTCOMES ACROSS THREE PLATFORMS

Health system strengthening related to TB control		
Partnerships and policies for health system strengthening to advance quality of, and access to, TB care and other health services, e.g. training, distribution and remuneration of human resources; financing reforms to reduce economic barriers to care; enlargement of public health infrastructure.	Innovations for TB prevention and care that are adapted or replicated to advance other health goals, e.g. use of public-private mix models of TB care for HIV treatment and maternal health; application of the Global Drug Facility approach (that links drug supply with technical assistance) to HIV and malaria treatment.	Innovations beyond TB prevention and care that are adapted or replicated for Stop TB goals, e.g. community, household or patient empowerment and communications; adaptation of efforts in HIV prevention and care and in child health for TB control objectives.

TABLE 1: COSTS OF HEALTH SYSTEM STRENGTHENING AT NATIONAL LEVEL IN THE GLOBAL PLAN TO STOP TB

Component of health system strengthening	Costs included in the Global Plan	Costs not included in the Global Plan
Human resources	Staff who work full time in TB programmes. Time of multipurpose staff who spend some of their time on TB patients (e.g. on inpatient and outpatient care for TB patients in general health care facilities, TB/HIV collaborative activities). Total time of multipurpose staff (and related total costs) assumed to increase in line with total number of patients being treated. Financial incentives where these already exist. General training related to TB and training required to implement new interventions (e.g. DOTS-Plus, TB/HIV collaborative activities). Extra staff required at national and subnational level to improve the quality of TB care and to implement new approaches (e.g. PPM, community-based care).	Increased salaries that may be necessary to improve overall recruitment and retention of health workers. New incentive schemes that can help to ensure adequate staff distribution and retention. Initial training to add to the existing stock of health workers. These cannot be estimated for TB control alone.
Engagement of non-MOH and non-state sector	Public-private mix DOTS (PPM) – all costs needed for implementation at national and subnational level.	General work required to engage the private sector that is not TB-specific. This cannot be budgeted for TB control alone.
Health information systems	Recording and reporting system for TB, TB/HIV and DOTS-Plus.	General investments required in health information systems that are not TB-specific. These cannot be budgeted for TB control alone.
Health financing	Resource mobilization efforts related to TB	Activities – e.g. resource mobilization efforts, work on financing mechanisms – that relate to the health sector as a whole. This cannot be budgeted for TB control alone.
Management capacity	TB programme management at the level existing in 2005, plus extra investments in managerial staff at national and subnational level to improve quality of TB care and to implement new approaches.	General improvements in health system management capacity, e.g. overall financial management system. This cannot be budgeted for TB control alone.
Infrastructure	Costs associated with inpatient and outpatient care provided in existing facilities (e.g. buildings, equipment). Investment in buildings and equipment that is TB-specific (e.g. renovation of clinics, purchase of microscopes). Costs to overcome poor coverage of health facilities (e.g. community-based TB care).	Building of new facilities and associated purchase of new equipment. This cannot be budgeted for TB control alone. Large investments may, however, be needed, especially in Africa.

184 countries now pursuing DOTS, implementation of the Stop TB Strategy and this Global Plan, increased resource flows, engagement within larger networks for health system strengthening, and application of poverty reduction strategies.

3.3 Addressing TB and poverty

The links between TB and poverty

The association between poverty and TB is well established. TB infection is transmitted more readily in the environmental conditions of poverty: overcrowding, inadequate ventilation and malnutrition. Improvements in socioeconomic conditions will therefore lead to reductions in tuberculosis incidence. They should also lead to improvements in access to care, its rational use, and quality of care.

See Figure 7: The link between socioeconomic development, TB and TB care

Booming population expansion, combined with poor civic planning and lack of resources for infrastructure development, has resulted in sprawling slum settlements in many urban areas, especially in the poorest countries. About 1 billion people live in urban slums and in the next 30 years the number is expected to reach 2 billion. In the poorest countries, about 80% of the urban population live in slums.¹⁵ The poor socioeconomic and environmental conditions that characterize slums facilitate transmission of most communicable diseases, including TB. The burden of TB is often greater in urban than in rural settings.

Urban areas themselves pose distinct challenges to effective TB control: challenges related to the multiplicity of public and

private health-care providers, to the complex mix of often poorly coordinated health authorities, and to the variety of patient populations with diverse characteristics and needs – slum-dwellers, migrants, drug addicts, homeless people, prison inmates and those with TB-HIV coinfection.¹⁶

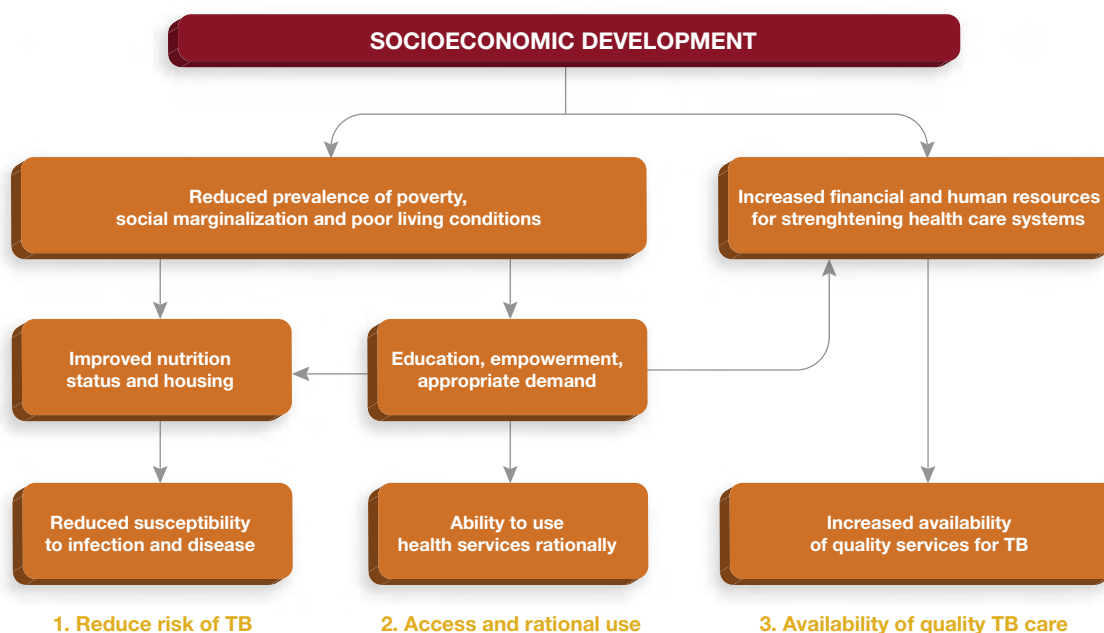
In recent years, there has been a growing recognition that TB itself reduces people's ability to work and earn a living, and that TB control therefore has the potential to reduce poverty.¹⁷ There is a need for a better understanding of this issue. The Partnership has recently commissioned a study by the World Bank of the economic impacts of TB at the household and macro level in Africa.

Concurrently there is increasing recognition that poverty means far more than economic poverty alone. It encompasses lack of opportunities (including capabilities), lack of voice and representation, and vulnerability to shocks. The Stop TB Partnership has adopted this broad conceptualization of poverty.

In 2003 the Stop TB Partnership commissioned an in-depth analysis of the evidence that TB control reduces poverty.¹⁸ The analysis was positive at the global level in that:

- the DOTS strategy's standardized, public health approach to TB treatment, by providing subsidized quality TB care, promotes better access to the poor than privately financed TB care;
- the emphasis on DOTS implementation in developing countries promotes equity in service provision at the global level.

FIGURE 7: THE LINKS BETWEEN SOCIOECONOMIC DEVELOPMENT, TB AND TB CARE



However, at the national level and below:

- Even where DOTS programmes are well established, patients with TB face substantial costs prior to TB diagnosis because care-seeking pathways are long and involve many consultations with different providers. While aggregate costs for poor people tend to be lower than those for non-poor people, costs as a proportion of income are much higher for the poor.
- Poor TB patients in developing countries are mainly dependent on daily wages or income from petty trading and have no security of income or employment. In many studies, patients were found to have borrowed money, used transfer payments (given by friends or relatives), or sold assets on account of their illness.
- There are instances where TB patients from poorer sections of society are missed or excluded from DOTS services.

Action to address TB and poverty

This analysis and related work led to the establishment of the Network for Action on TB and Poverty and the creation of the TB and Poverty Subgroup of the DOTS Expansion Working Group. In 2005 the Subgroup, together with the Network for Action on TB and Poverty and the WHO Stop TB Department, published a document, *Addressing poverty in TB control*, which outlines options for national TB programme managers to choose from in addressing poverty issues in DOTS implementation.¹⁹ This guide will be used to prioritize the needs of the poor and vulnerable in implementing all the activities of the Global Plan. As evidence and experience accumulate, these options will be revised and reformulated into formal guidelines for use at national and international levels.

Poor and vulnerable TB patients will benefit from tangible improvements as policy-makers and service providers promote this cycle of action by following the six practical steps laid out in the document (see Box 4). These practical steps are supported by the Partnership's working groups as set out in their individual strategic plans for 2006–2015. Both in overall vision and in country-level specific action, the implementation of this plan will make a substantial contribution towards achieving the MDGs for communicable diseases and poverty reduction.

3.4 Addressing TB in children

Ideally, all TB patients should receive standardized high quality care under the auspices of a national TB programme. In practice, in many countries the care provided to TB patients outside the national TB programme often falls below the standard consistent with good clinical care and good public health practice. In particular, children with TB often receive care outside national TB programmes.

The Partnership's DOTS Expansion Working Group has a Childhood TB Subgroup, which works to decrease the global burden of childhood TB mortality and morbidity, by promoting the care of children with TB as part of routine TB activities. It assists national TB programmes, technical partners, and the

Stop TB Partnership Working Groups in explicitly addressing issues related to diagnosis, treatment, and drug formulations for children with TB. There is an urgent need to improve registration of children with TB and reporting of their treatment outcomes by national TB programmes, and to use this information to ensure that all children with TB receive a high standard of care.

The strategic plans of each of the implementation working groups address the care of all patients with TB, including children. For example, the DOTS Expansion and TB/HIV Working Groups address the benefit of isoniazid preventive treatment for those at high risk of developing TB, including children under six years of age living in the same household as an adult with infectious TB, and children of any age with HIV. The Working Group on New TB Diagnostics is pursuing better diagnostic tests for use with children. To facilitate the effective treatment of children with TB, the Global Drug Facility is promoting the development of child-friendly formulations of anti-TB drugs.

3.5 Addressing TB and gender

In most countries, many more men than women have TB. The Russian Federation provides a typical example. Of almost 120 000 new TB patients registered in 2004 (excluding those in the penitentiary system), 71% (85 000) were male and 29% were female. The predominance of men among TB patients in most countries is more likely to be due to epidemiological differences between the sexes than differential access to health care.²²

However, a different picture is emerging in several countries in sub-Saharan Africa with high HIV prevalence, where the majority of notified cases are now in women. Because HIV infection rates are higher in women than in men, more TB cases are also being reported among women, especially among those aged 15–24 years.

Addressing gender-specific differences in TB epidemiology and barriers to effective care can contribute to ensuring full access to the Stop TB strategy. The Partnership is exploring what more needs to be done to mainstream gender issues in all working group activities. The Partnership recommends the following practical steps for national TB programmes to address gender issues in TB control:

1. Countries planning a population-based TB prevalence survey as a means of monitoring the national TB burden will gain important information on the sex ratio among TB cases. Differences in the sex ratio between a population-based TB prevalence survey and national TB programme reports suggest differential access to health care. Qualitative research is useful in exploring the reasons for differential access to health care.
2. Steps to address differential access to health care include:
 - developing gender-sensitive information, education and communication (IEC) programmes and activities;
 - using gender-sensitive technical training for health workers to overcome any gender-specific barriers to TB diagnosis and treatment;

BOX 4: ADDRESSING POVERTY IN TB CONTROL: SIX PRACTICAL STEPS²⁰**Step 1. Establish the profile of poor and vulnerable groups using:**

- government or other data on the prevalence and distribution of poverty and social vulnerability, and on poverty-reduction plans;
- information on which types of health care providers are used by poor and vulnerable groups;
- locally conducted surveys on the socioeconomic status of TB patients and poverty-related disparities in access to and outcomes of care;
- information on any adaptations already made in DOTS delivery to serve poor and vulnerable groups.

Step 2. Assess the barriers to accessing TB services faced by the poor and vulnerable under the following headings:

- Economic barriers: Does the organization of the TB services simplify the health care pathway? Are diagnostic and treatment services for TB well integrated into general primary care facilities? Does treatment observation require patients to make multiple visits? Which services require patients to pay?
- Geographic barriers: Identify areas where patients have to travel long distances over difficult terrain to reach TB services.
- Social and cultural barriers: Identify areas and population groups where TB services are underutilized.
- Health system barriers: Assess staff attitudes towards poor patients and investigate whether decentralization leads to strengthening of TB services at primary care level.

Step 3. Take action to overcome barriers to access. For example:

- Address economic barriers by integrating TB services within primary care provision, encourage pro-poor PPM DOTS, promote TB control in workplaces, improve the coverage of smear microscopy networks, avoid user-fees, provide free smear microscopy and other diagnostic services.
- Address geographical barriers by extending diagnostic and treatment services to remote regions, providing free transport to patients from such regions, and promoting community-based TB care.
- Address social and cultural barriers by engaging former TB patients and TB support groups to advocate for services and encourage community mobilization.
- Address health system barriers by engaging in health service decentralization to ensure capacity strengthening in less well-served areas and by establishing TB control as a district-level priority.

Step 4. Work with situations and population groups requiring special consideration, such as

- refugee communities, asylum seekers, economic migrants and displaced populations;
- pockets of deprivation in wealthier countries; ethnic minorities, homeless people;
- injecting drug users;
- prison populations.

Step 5. Harness resources for pro-poor TB services from:²¹

- available strategies to improve access to health services (such as the GFATM, Poverty Reduction Strategies);
- technologies to enhance the efficiency and effectiveness of services.

Step 6. Assess the pro-poor performance of TB control and the impact of pro-poor measures by:

- harnessing the human and other resources required for equity monitoring through alliances with partners (such as universities);
- including socioeconomic variables in routine data collection and analysis; ensuring that TB-related questions are included in district health surveys and other household surveys;
- ensuring socioeconomic questions are included in TB prevalence surveys;
- conducting periodic studies of care-seeking, diagnostic delay, and use of DOTS in health facilities, with linked socioeconomic data;
- conducting qualitative assessments among community members and TB patients about who benefits from TB services (including linked services for HIV) and who does not.



Achieve

Targets provide a spur to action and a benchmark for measuring progress. In terms of reaching targets, full funding (US\$56 billion) and implementation of the Plan would result in achievement of the Millennium Development Goal relevant to TB. It would also result in global achievement of the Partnership's 2015 targets to halve prevalence and death rates from the 1990 baseline. Achieving these targets means making enormous progress in all regions with prevalence and death rates halved, or almost halved, over the period of the Plan from 2006 to 2015.

The statistics underpinning these targets are about people. Achieving the targets means making a difference to the lives of many millions of people: to the lives of the 50 million people to be treated, and their families; to the 14 million people whose lives will be saved; to the lives of the people who in future will be spared the suffering and death caused by TB, as we develop the new diagnostics, drugs and vaccines that will pave the way for the elimination of TB by 2050.

Achieving the Partnership's targets for 2015 is a step towards the goal of TB elimination by 2050.

- ensuring that data collection and analysis take gender into consideration;
- increasing the involvement of nongovernmental health providers in TB control, and decentralizing TB care services, so that social organizations and volunteer groups (including ex-patients) who are representative of local communities can identify and address gender-specific barriers to TB diagnosis and treatment.

3. In countries with high HIV prevalence, steps to respond to the increasing proportion of women among TB patients include:

- collaboration of the national TB programme with services for women, e.g. programmes for prevention of mother-to-child transmission (PMTCT) of HIV, so that HIV-positive women can receive information about TB, periodic screening for TB, and treatment of latent TB infection;
- involvement of women's groups and organizations in TB care and prevention, e.g. by recruiting and training women, including those who are HIV-positive, to be health volunteers.

4. SUMMARY OF PLANNED ACHIEVEMENTS, RESOURCE NEEDS AND IMPACT

4.1 Planned achievements

Full implementation of the Global Plan for TB control will mean:

- **50 million people will be treated in DOTS and DOTS-Plus programmes;**
- **more than 3 million HIV-positive TB patients will be enrolled on antiretroviral therapy;**
- **advocacy, communications and social mobilization will have become an integral part of TB control;**
- **new drugs and diagnostic tests will be in use, and a new vaccine licensed.**

See Table 2: Summary of planned achievements

The Global Plan to Stop TB 2006–2015 represents a massive intensification of effort over the next decade compared with the past decade (see Table 2, which also provides the milestones for 2010). Between 2006 and 2015, 21 million smear-positive patients and nearly 30 million with smear-negative or extrapulmonary TB will be treated in DOTS programmes, compared with 12 million patients in each category from 1996 to 2005.

The annual number of people to be treated in DOTS programmes will remain roughly stable over the 10 years of the plan, at about 5 million patients per year, as improvements in case detection are offset by reductions in transmission (Figure 8a). Most of the people to be treated will be in the African, South-East Asian and Western Pacific regions (Figure 8b).

There will be a major expansion in DOTS-Plus programmes, mostly in Eastern Europe, with an acceleration over the next few years (Figures 8c and 8d). Overall, the number of people with multidrug-resistant TB treated in DOTS-Plus programmes will rise from 10 000 in the past 10 years to nearly 800 000 in the next ten.

TB/HIV collaborative activities will be massively scaled-up in line with UNAIDS plans for universal access, largely in Africa but also (for HIV testing and counselling for TB patients) in South-East Asia (Figures 8e and 8f). Some 29 million TB patients will be tested and counselled for HIV, and nearly 210 million people living with HIV (PLWHA) will be screened for TB. More than 3 million TB patients will be enrolled on antiretroviral therapy and a similar number of people living with HIV will have completed isoniazid preventive therapy.

These achievements will be secured through substantial geographic expansion of activities to improve case detection and successful treatment rates in DOTS programmes, as well as very large increases in geographic coverage of TB/HIV collaborative activities and DOTS-Plus programmes (Tables 2 and 3). These activities include:

- improvements in quality of DOTS through measures such as better staffing and supervision;
- the introduction or expansion of initiatives such as public-private mix, community-based care, PAL, and intensified TB case-finding among PLWHA;
- an increase in the number of laboratories capable of conducting bacterial culture and drug susceptibility testing.

Table 3 (page 56) sets out the planned milestones for 2010 and 2015 for the major implementation activities.

By the end of the plan period, the first of an exciting battery of new tools should have come into use, with the promise of further major breakthroughs close behind. These goals are extremely challenging, and there is inevitably an element of scientific risk and uncertainty. But new tools will be an essential component of any strategy to eliminate TB by 2050, and the current prospects offer hope.

The Working Group on New TB Drugs envisages that the first new TB drug for 40 years will be introduced in 2010. This new drug or combination of drugs will achieve cure in three to four months compared with six to eight months now. The target for 2015 is clinical testing of a rational drug combination therapy that can reduce the duration of treatment to one to two months or less. This treatment will be effective against multidrug-resistant TB and will be compatible with antiretroviral treatment for people with TB/HIV. By then, clinical trials will be under way for a new treatment of latent TB infection. All the new regimens will need to be affordable and easily managed in the field.

In addition, the Working Group on New TB Drugs expects that by 2015 an environment will have been developed that allows sustained development of new TB drugs that can ultimately be combined into novel and revolutionary TB regimens. One of the

PART I: STRATEGIC DIRECTIONS

TABLE 2: SUMMARY OF PLANNED ACHIEVEMENTS

Implementation Working Groups (a)

	2006 (b)	2010 (b)	2015 (b)	2006-2015	1996-2005
DOTS EXPANSION					
Total number of new ss+ patients treated in DOTS programmes (millions)	2.1 (3.3)	2.2 (2.8)	1.8 (2.2)	21 (27)	12 (36)*
Case detection rate (%)	65%	78%	84%	76%	32%
Total number of new ss+ patients successfully treated in DOTS programmes (millions)	1.8 (2.1)	1.9 (2.2)	1.6 (1.8)	18 (21)	9 (11)**
Treatment success rate (%)	83%	86%	87%	85%	80%
Total number of new ss-/extra-pulmonary patients treated in DOTS programmes (millions)	3.0 (4.5)	3.0 (3.9)	2.7 (3.2)	29 (39)	12 (45)*
Percentage of new ss-/extra-pulmonary patients treated in DOTS programmes	66%	78%	84%	76%	26%
DOTS-Plus					
Total number of detected MDR-TB patients treated in DOTS-Plus programmes (millions)	0.02 (0.12)	0.09 (0.14)	0.11 (0.11)	0.8 (1.3)	0.01***
Percentage of detected MDR-TB cases treated in DOTS-Plus programmes	17%	60%	100%	60%	
TB/HIV					
Total number of PLWHA attending HIV services screened for TB (millions)	11 (18)	22 (23)	26 (26)	206 (225)	NA
Percentage of PLWHA attending HIV services screened for TB (c)	61%	98%	100%	91%	
Total number of newly diagnosed and eligible PLWHA offered IPT (millions)	1.2 (30)	2.6 (35)	3.1 (40)	24 (354)	NA
Percentage of PLWHA offered IPT	4%	8%	8%	7%	
Total number of TB patients in DOTS programmes HIV tested and counselled (millions)	1.6 (3.4)	3.1 (3.8)	2.9 (3.4)	27 (36)	NA
Percentage of TB patients treated in DOTS programmes HIV tested and counselled	47%	81%	85%	74%	
Total number of TB patients (HIV positive and eligible) in DOTS programmes enrolled on ART (millions)	0.2 (0.5)	0.3 (0.6)	0.4 (0.6)	3.2 (5.6)	NA
Percentage of TB patients (HIV positive and eligible) in DOTS programmes enrolled on ART	44%	57%	57%	57%	
Advocacy, Communications and Social Mobilization					
	Intensive capacity building to implement ACSM activities in 6 priority countries with GFATM funding.	15 countries implementing ACS, generating quantitative and qualitative data on ACS contribution to TB control.	All high-burden countries implementing ACS initiatives.	ACS is a standard component of the international strategy for TB control.	NA

New Tools Working Groups

	by 2006	by 2010	by 2015
Vaccines			
	5 candidates in phase I trials.	9 candidates in phase II trials; at least 2 vaccines in phase IIb or 'Proof of Concept' trials by 2008; beginning of phase III trials.	4 phase III efficacy trials carried out. One safe, effective, licensed vaccine available by 2015.
Drugs			
	27 new compounds in the TB pipeline.	1-2 new drugs registered for TB indication; treatment shortened to 3-4 months.	7 new drugs registered for TB indication; regimen revolutionized: clinical testing of drugs that can shorten treatment to 1-2 months.
Diagnostics			
	Rapid culture for case detection and DST in demonstration phase.	Point of care, rapid culture, improved microscopy, Phage detection (+DST) and simplified NAAT introduced.	Predictive test for LTBI in demonstration phase.

(a) The percentages are not always exactly the numerator divided by the denominator due to rounding errors.

(b) Numbers in parentheses indicate the denominator. For DOTS Expansion it is new TB cases.

For DOTS-Plus it is the total number of detected MDR-TB cases.

For PLWHA screened for TB it is total number of PLWHA attending HIV services. For PLWHA offered IPT it is all PLWHA.

For TB patients HIV tested and counselled it is TB patients treated under DOTS covered by TB/HIV activities. For TB patients enrolled on ART it is TB/HIV positive patients known to be eligible for ART.

(c) HIV services include testing and counselling and HIV treatment and care services

* Numerator is based on notification data and assumes values for 2004 and 2005 as for 2003.

** Denominator is based on either total notifications or total cases that are registered for DOTS treatment. Since total registered cases are sometimes lower than total notifications, the denominator (11 million) is lower than total notifications (12 million).

*** Refers to number of patients approved by GLC from 2000-2004.

NA: data not available but likely to be very low.

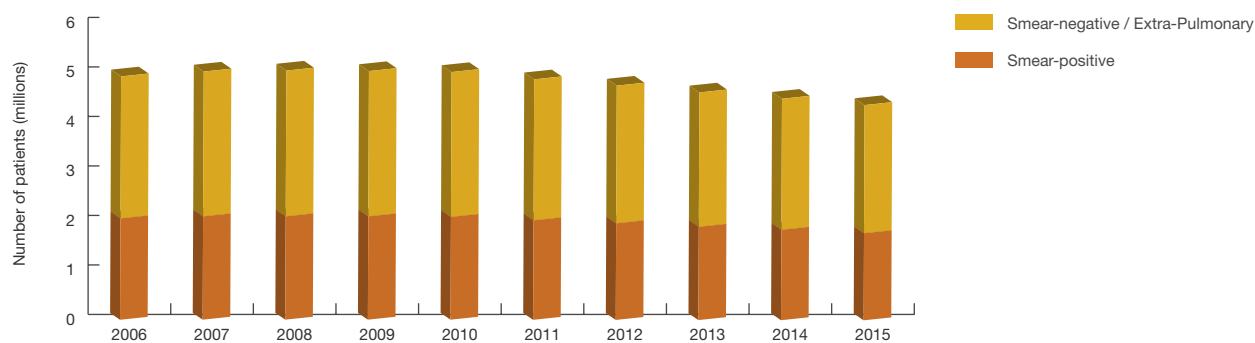
DST: Drug susceptibility testing.

NAAT: Nucleic acid amplification test.

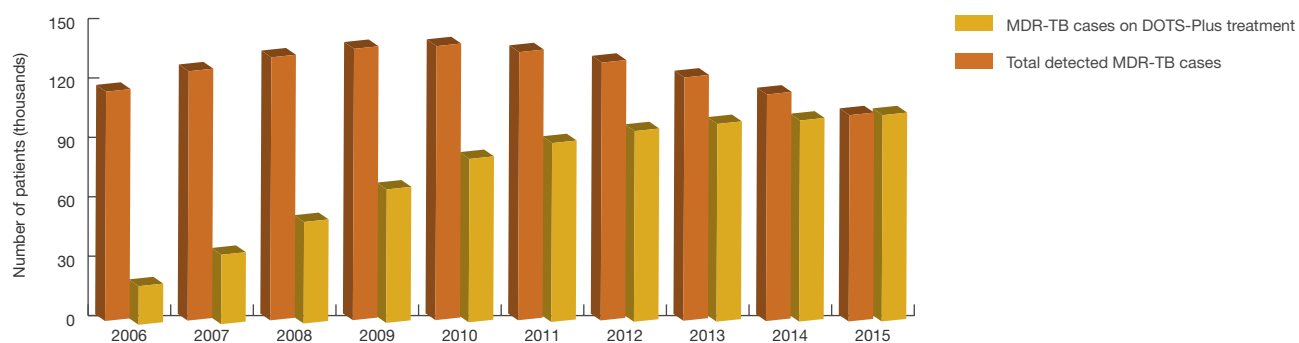
LTBI: latent tuberculosis infection.

FIGURE 8: PLANNED ACHIEVEMENTS BY DOTS EXPANSION, DOTS-PLUS AND TB/HIV WORKING GROUPS, 2006–2015

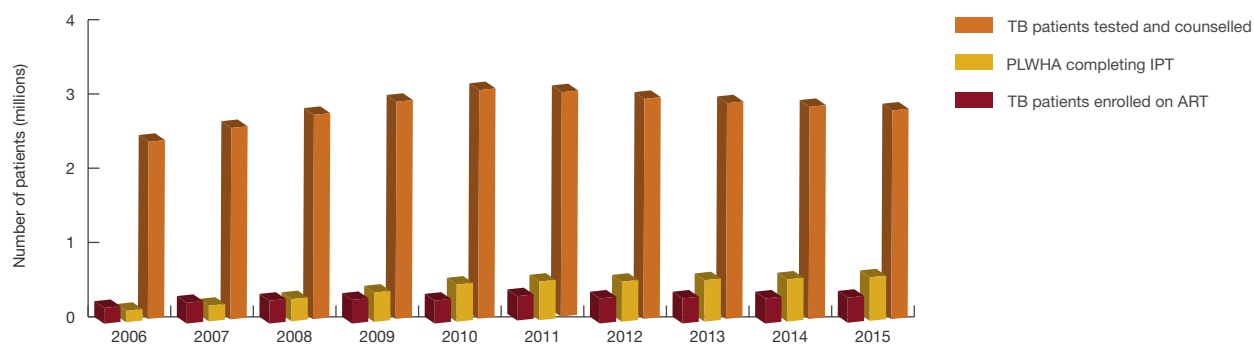
a. All TB cases to be treated in DOTS programmes, all regions, 2006-2015

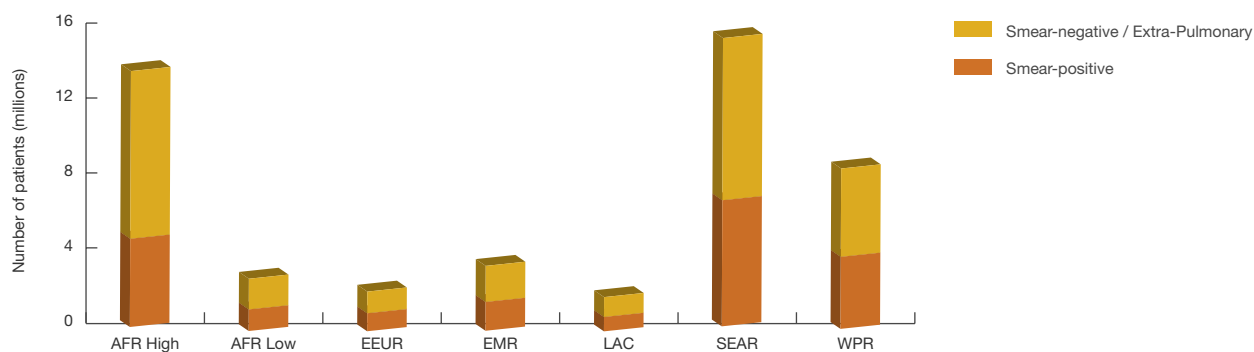
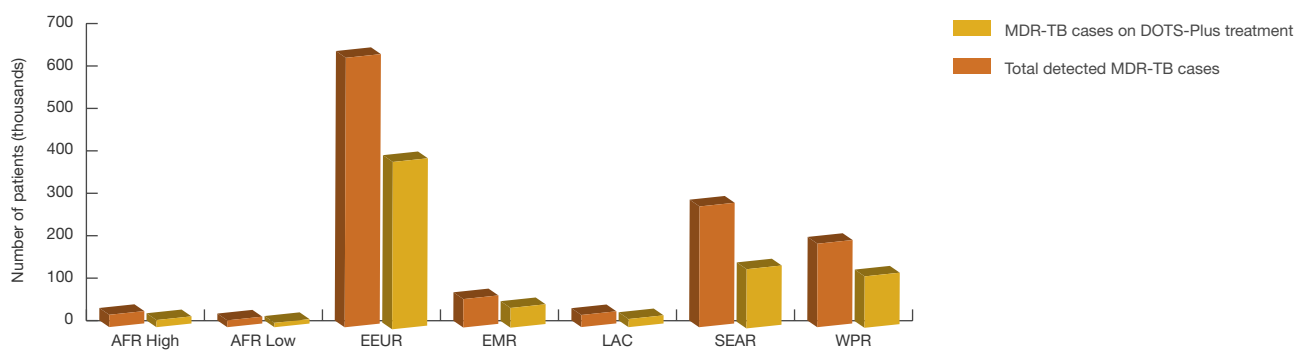
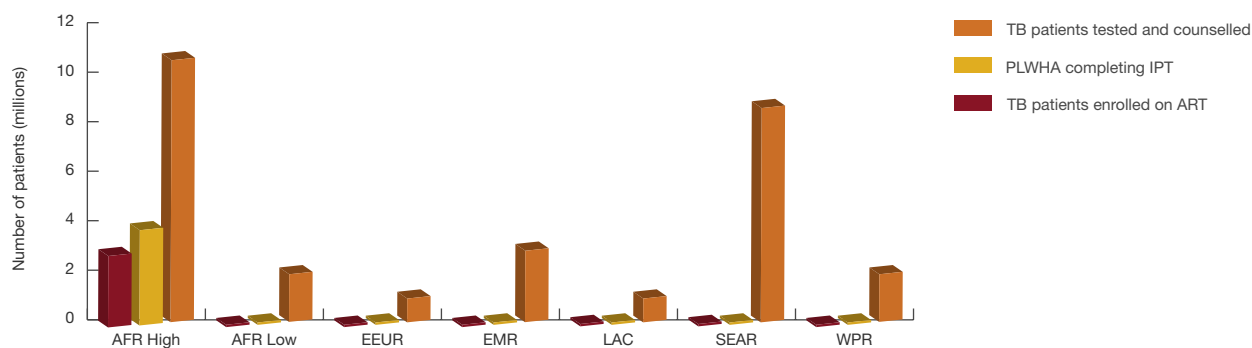


c. MDR-TB cases detected and MDR-TB cases in DOTS-Plus programmes, all regions, 2006-2015



e. TB/HIV patients tested and counselled, enrolled on ART, and PLWHA completing IPT, all regions, 2006-2015



b. All TB cases to be treated in DOTS programmes by region, 2006-2015**d. MDR-TB cases detected and MDR-TB cases in DOTS-Plus programmes by region, 2006-2015****f. TB/HIV patients tested and counselled, enrolled on ART, and PLWHA completing IPT by region, 2006-2015**



Invest

Implementing the Plan requires an investment by many partners - an investment in time and effort. The Plan also requires many Partners to invest financial resources. The total cost of realizing the Plan is \$56 billion over ten years. Past experience indicates that a financial investment to Stop TB is a good investment - one that yields results.

All countries have made a commitment to ensure the availability of sufficient domestic and external resources to achieve the Millennium Development Goal relevant to TB. An investment of \$56 billion over the next ten years will result in 50 million TB patients treated, 14 million lives saved, and the development of the new diagnostics, drugs and vaccines that can revolutionize global TB control.

Investing in the Plan brings better TB control, healthier communities and less poverty.

TABLE 3: MAJOR IMPLEMENTATION ACTIVITIES

	2005	2010	2015
DOTS coverage	All 22 high-burden countries covered except Brazil and Russian Federation	Full DOTS coverage	
DOTS quality improvement	Considerable investments and achievements, especially in SEAR and WPR	Completed in all priority countries in Africa, AMR, EMR and E EUR	Completed in all countries
Public-Private Mix DOTS	Pilot-tested in most high-burden countries, limited scale-up in a few high-burden countries and other countries	Scale-up completed in key countries, and started in most high-burden countries and other priority countries	Scale up completed. 3.8 billion people covered*
Community DOTS	Widely used in a number of countries, mainly in AFR, SEAR and WPR	Full scale-up completed to cover whole population in Africa and most other high-burden countries/ priority countries.	Scale-up completed in all relevant areas, covering 1.9 billion people*
Practical Approach to Lung Health	In progress in 17 countries	Scale-up started in selected countries, predominantly in EMR, E EUR and AMR	Scale-up completed in all relevant areas, covering 2 billion people*
Culture and Drug Susceptibility Testing	Widely used in E EUR but quality improvement needed. Very limited in other regions	At least 50% of the population in all regions live in areas with culture and DST services	Scale-up completed covering more than 5 billion people*
DOTS-Plus	35 GLC-approved DOTS-Plus projects in 29 countries. Revised DOTS-Plus guidelines. Reform of DOTS-Plus WG and GLC to meet future challenges.	DRS data from 130 countries, including those with high prevalence of MDR TB. Quality-assured 2nd line drugs produced in high-burden countries. Quality-assured culture/ DST in 92% of E European TB cases and 60% of re-treatment cases in other regions.	Revision of MDR estimates based on representative DRS data from 90% of settings. Culture and DST for all re-treatment cases worldwide and all cases in E Europe. All detected MDR cases treated with quality-assured drugs.
TB/HIV collaborative activities	Many countries in all regions with high prevalence of HIV-related TB scaling up collaborative TB/HIV activities	Full scale-up completed in countries with highest prevalence of HIV-related TB	Full scale-up in all relevant settings (i.e. where adult HIV prevalence >1% in general population or >5% among TB patients)

* The populations covered refer to the number of people living in areas where the approaches have been implemented.

PART I: STRATEGIC DIRECTIONS

lessons learnt since the introduction of the existing anti-TB drugs is that continued worldwide commitment, research and vigilance to ensure a constant pipeline of new antimicrobials is required to eliminate tuberculosis within the twenty-first century.

The Working Group on New TB Diagnostics plans to introduce by 2008 an easy-to-use diagnostic technology for referral laboratories, with an accuracy similar to that of culture but capable of providing results in a few hours or days instead of weeks. By 2010 new tests will be available for detection of active TB at the first point of care, e.g. for use by rural health workers. Such tests will be more sensitive, simpler and as affordable as smear microscopy. They will involve either an instrument-free device requiring minimal training or a hand-held, simplified instrument that requires minor training. By 2015 we will have a rapid diagnostic procedure capable not only of identifying people with latent infection (whether HIV-positive or not) but also discriminating those at greatest risk of progression to active disease.

The development of new vaccines is particularly challenging but potentially most rewarding. The timetable for vaccine development is driven by the availability of suitable candidates and the need for extensive clinical trials to establish their safety and confirm their efficacy in human populations. The Working Group on New TB Vaccines expects that a new, safe, effective vaccine – the first of a series – will be licensed and available at reasonable cost by 2015.

4.2 Resource needs and financing

The total cost of the Global Plan for 2006–2015 is estimated as US\$56.1 billion.

- **80% (US\$44.3 billion) is for country-level activities, especially in Africa.**
- **A large part of the cost (US\$28.9 billion) is for DOTS programmes.**
- **DOTS-Plus and TB/HIV activities will cost about US\$5.8 and US\$6.7 billion respectively.**
- **Research and development of new tools requires US\$9 billion.**

Resource needs

Table 4 provides a summary of total costs and funding gaps from 2006 to 2015 by Working Groups. Figure 9 provides the distribution of costs in different ways, as explained below.

The total cost of the Global Plan for the ten-year period is US\$56.2 billion, of which US\$25.3 billion is currently estimated as available, leaving a funding gap of US\$30.8 billion (Figure 9a). The Working Groups have each planned for a two- to sevenfold increase in annual investments compared with the first Global Plan. Overall the plan involves a threefold increase in annual investment in TB control compared with the first Global Plan to Stop TB.

The majority of the cost is for investment in DOTS programmes (US\$28.9 billion), followed by TB/HIV activities (US\$6.7 billion) and DOTS-Plus (US\$5.8 billion) (Figure 9b). The total cost of research and development is US\$9 billion, most of which is for drugs and vaccines.

More than 80% of the total cost is for investment at the country level (US\$44.3 billion), while US\$11.9 billion is needed at global level to support research and development (US\$9 billion) and technical cooperation by international agencies (US\$2.9 billion) (Figure 9c). Over 40% of country-level investments are needed in Africa (US\$19.4 billion), followed by Eastern Europe with a total need of US\$9.2 billion; other regions each need between US\$2 billion and US\$6 billion (Figure 9d).

Figure 10 shows the distribution of costs from 2006–2015. The total costs per year increase steadily over time, from US\$4.2 billion in 2006 to US\$6.5 billion in 2015.

Figure 11 shows total country needs by region from 2006–2015. Of the US\$44.3 billion needed for investment at country level, the biggest regional cost increases over the plan period are in Africa and Eastern Europe, with costs in other regions remaining fairly stable.

Figure 12 shows total country needs by region and activity. In all regions, DOTS Expansion accounts for the largest share of costs, although TB/HIV is important in Africa and DOTS-Plus is important in Eastern Europe.

Financing and resource mobilization

Figure 13 shows the distribution of total country needs by region and activity. The funding needed for implementation is estimated at US\$22.5 billion, out of a total need of US\$47.2 billion (Table 4 and Figure 13a, b). The shortfall in available funding increases from US\$1.4 billion in 2006 to US\$3.1 billion in 2015. There are two major reasons for this increase in the funding gap. The first is that the estimates of available funding are based on the assumption that domestic and donor funding (excluding GFATM) will be sustained at 2005 and 2004 levels, respectively (see also footnote to Table 4). At the same time, the Plan includes large investments in new interventions, in line with the new Stop TB Strategy (Figure 13a). These include new approaches to DOTS implementation (e.g. PPM, PAL) as well as much more widespread implementation of DOTS-Plus, TB/HIV and ACSM-related interventions. The Plan also includes much more investment in technical cooperation, which is needed to support this substantial increase in both the number and scale of interventions. These additional large investments will require increased funding commitments from both governments of high-burden countries and donors. Given the existing distribution of funding for TB control and the size of the funding gap, it is likely that a large proportion of this gap will need to be financed by the governments of high-burden countries themselves (donor funding would need to increase about eight times to fill the gap for implementation whereas domestic funding would need to double to fill this gap).

TABLE 4: TOTAL COSTS AND FUNDING GAPS 2006–2015 BY WORKING GROUP (US\$ BILLIONS)

Second Global Plan to Stop TB, ten-year period, 2006-2015				First Global Plan, five-year period, 2001-2005
	Costs	Available Funding*	Funding Gap	Costs
IMPLEMENTATION WORKING GROUPS				
DOTS EXPANSION Country Needs	28.9	<p>Gap US\$22.5 billion, 51%</p> <p>Domestic funding US\$ 19.2 billion, 43%</p> <p>Other Donor Sources US\$ 1.7 billion, 4%</p> <p>GFATM US\$ 0.9 billion, 2%</p>	6.0	
DOTS-PLUS Country Needs	5.8		1.1	
TB/HIV Country Needs	6.7		0.6	
ACSM Country Needs	2.9		0.0	
International Agencies (technical cooperation)**	2.9	0.7	2.2	0.3
Total Implementation WG	47.2	22.5	24.7	8.0
NEW TOOLS WORKING GROUPS				
Research & Development				
VACCINES***	3.6	2.1	1.5	0.4
DRUGS	4.8	0.6	4.2	0.3
DIAGNOSTICS	0.5	0.1	0.4	0.2
Total New Tools	9.0	2.8	6.1	0.9
TOTAL NEEDS GLOBAL PLAN	56.1	25.3	30.8	9.1

* Domestic funding assumes government commitments in 2005 are sustained and increase in line with inflation; GFATM commitments are based on results of Rounds 1 to 5 (these cover 2006-2011); other donor funding assumes commitments reported in 2004 are sustained and increase in line with inflation.

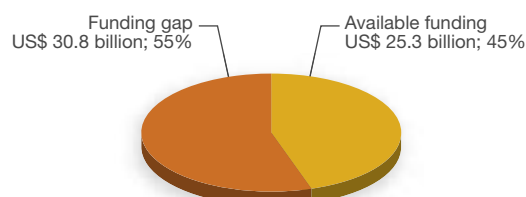
** Technical cooperation includes strategic and technical support, capacity building, monitoring and evaluation, operational research and policy development, and WG operations.

*** Includes costs for maintenance of the current BCG vaccination programme.

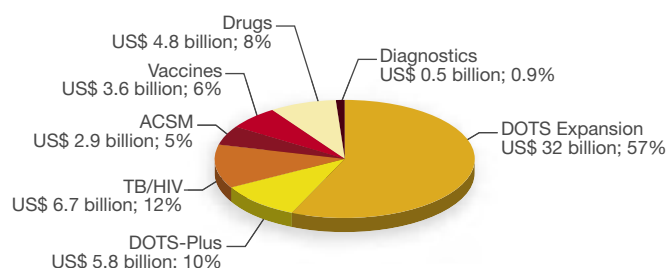
N.B. Column totals may not add up exactly due to rounding.

FIGURE 9: DISTRIBUTION OF TOTAL COSTS OF THE GLOBAL PLAN, 2006–2015**a. Total needs, available funding and funding gap, 2006-2015**

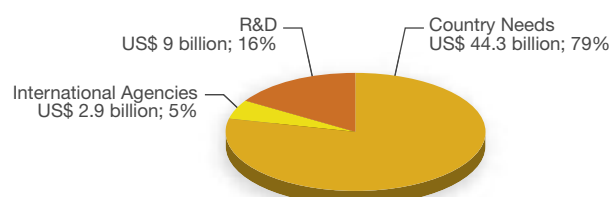
Total needs: US\$ 56.1 billion

**b. Total needs by WG area of responsibility*, 2006-2015**

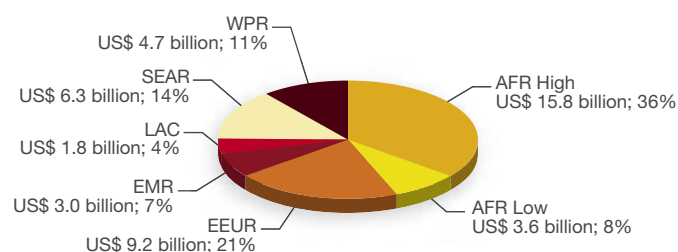
Total needs: US\$ 56.1 billion

**c. Total needs for countries, R&D and international agencies, 2006-2015**

Total needs: US\$ 56.1 billion

**d. Total country needs for implementation by region, 2006-2015**

Total needs: US\$ 44.3 billion



* The cost for international agencies (technical cooperation) for DOTS Expansion, DOTS-Plus, TB/HIV and ACSM Working Groups is included under DOTS Expansion.

FIGURE 10: TOTAL COSTS FOR IMPLEMENTATION AND NEW TOOLS, 2006–2015

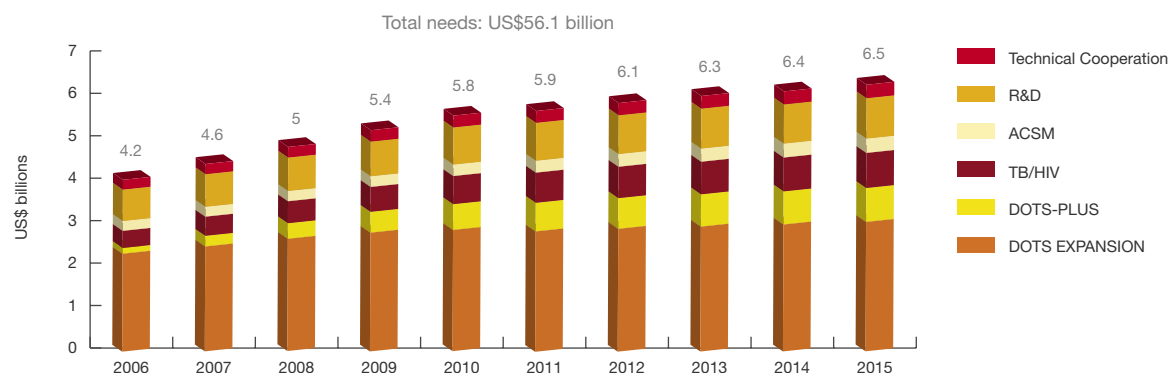


FIGURE 11: TOTAL COUNTRY NEEDS BY REGION, 2006–2015

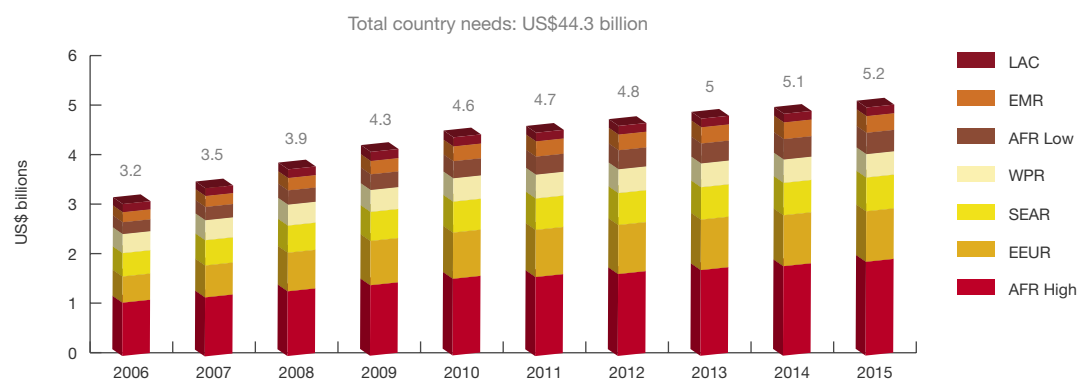


FIGURE 12: TOTAL COUNTRY NEEDS FOR IMPLEMENTATION BY REGION

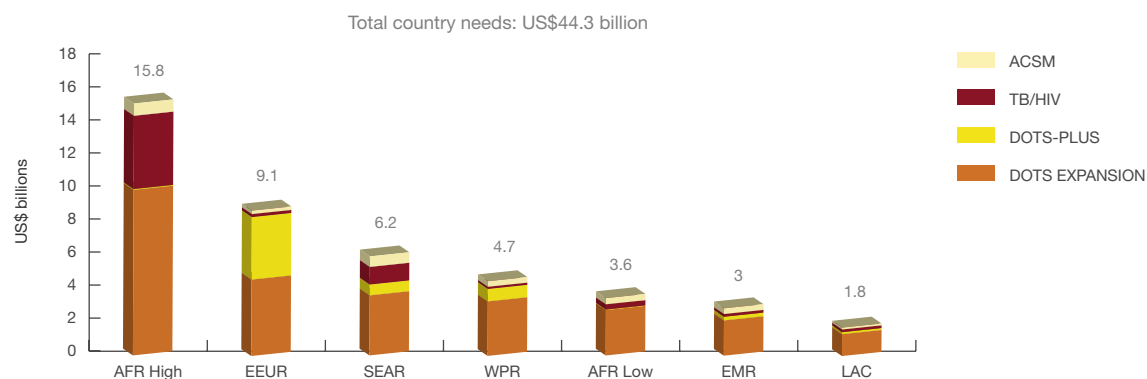
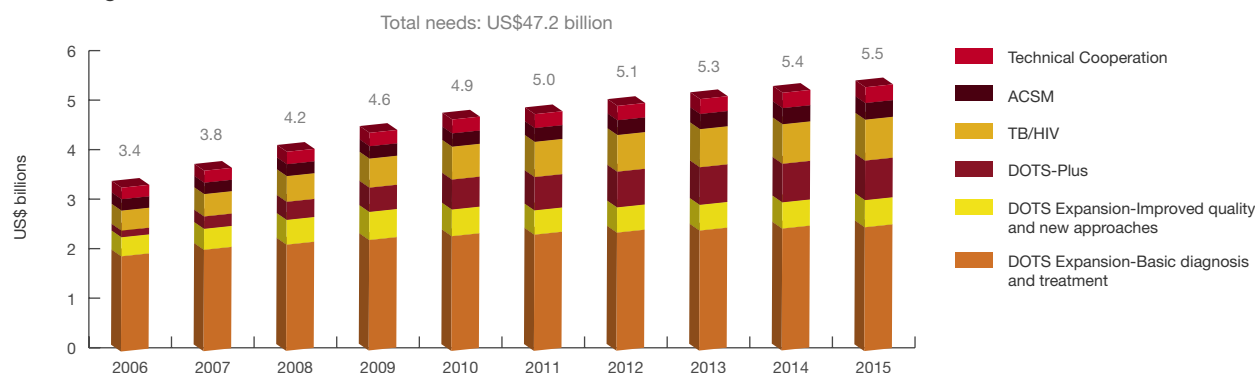
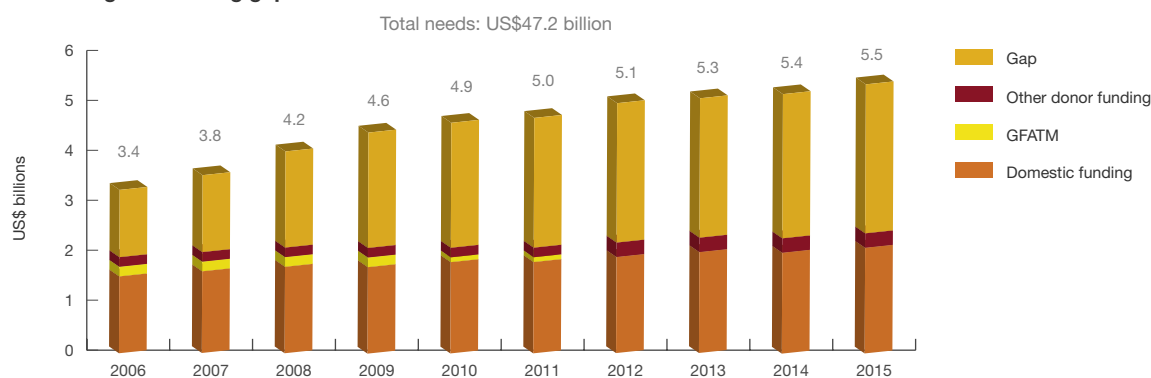
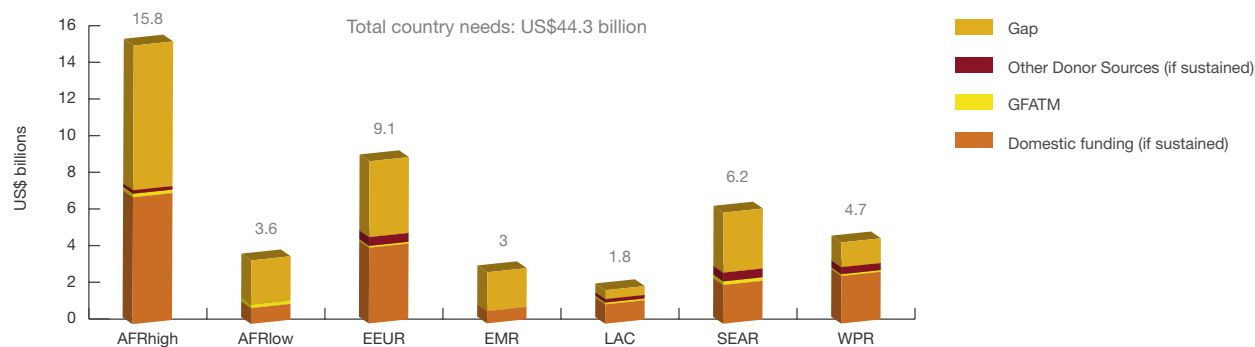


FIGURE 13: TOTAL COUNTRY NEEDS, AVAILABLE FUNDING AND FUNDING GAPS FOR IMPLEMENTATION, 2006–2015**a. Funding needs****b. Funding and funding gaps****c. Funding and funding gaps by region***

* Since technical cooperation is not estimated at regional level, the total gap represented here is US\$ 22.5 billion rather than US\$ 24.7 billion.

To mobilize the level of financial support required to implement the Global Plan for 2006–2015 (US\$56.1 billion over 10 years), the profile of TB on international and national development agendas must be greatly enhanced and political commitment strengthened at all levels. The Partnership will achieve these goals through: intensified and strategically focused advocacy at all levels; coalition building to engage a broader range of partners; strengthened partnership building, particularly with new donors; and mobilization of civil society by empowering patient activists and communities. Since the largest gap in funding needs for country-level implementation is in Africa, a particular focus on this region is necessary (figure 13 c).

Currently budgets for TB control are channelled through diverse routes. In 2005 over half of the finance for TB in the 22 high-burden countries was from government budgets, including some external funding through direct support by donors of poverty reduction strategies. The remaining TB control funds came from loans, grants (including for specific TB projects) and the GFATM. In many countries, private spending on TB also accounts for a considerable proportion of the total. Governments and donors also fund programmes aimed at strengthening the broader health sector, including increasing the size and retention of the health workforce.

To scale up funding to meet the objectives of this Plan, it will be necessary to work through, and to coordinate better, this same range of funding instruments. Current levels of public health spending in most low-income countries fall far short of the minimum needed to deliver universal access to services. In Abuja in 2000, African governments committed themselves to increase funding for health from an average of 8% to 15% of their budgets. However, most are far from reaching that target. Countries can be supported to mobilize additional domestic resources for health but additional external finances are needed to help close the gap.

Donor countries have committed themselves to increasing their assistance to development. If used effectively, such new resources can lead to greatly expanded access to essential health services, including TB diagnosis and treatment. However, the diversity of funding instruments carries a risk of duplication, gaps, and lack of coherence in channelling finance to where it can be used effectively. The Stop TB Partnership, working from the resource needs identified in this Plan, will support the analysis of the relative needs and effectiveness of different funding channels (e.g. health sector support through government budgets or the GFATM), to help ensure that resources are used to greatest impact.

4.3 Impact of the Global Plan

Full implementation of the second Global Plan for TB Control will mean:

- **14 million lives will be saved in the 10 years 2006–2015;**
- **the MDG target for TB – to have halted and begun to reverse the incidence of TB by 2015 – will be achieved**
- **the Partnership's own ambitious targets for 2015 – to halve prevalence and death rates from the 1990 baseline – will be met globally.**

On the basis of this ambitious but realistic scenario, the global targets for 2015 will be achieved and a total of 14 million lives will be saved during the Plan period, mostly in the South-East Asian, Western Pacific and African regions (Figure 14). Almost 30 million TB cases will be prevented, mostly in the South-East Asian and the Western Pacific regions. The number of new cases of TB will fall from about 8 million in 2005 to fewer than 6 million in 2015.

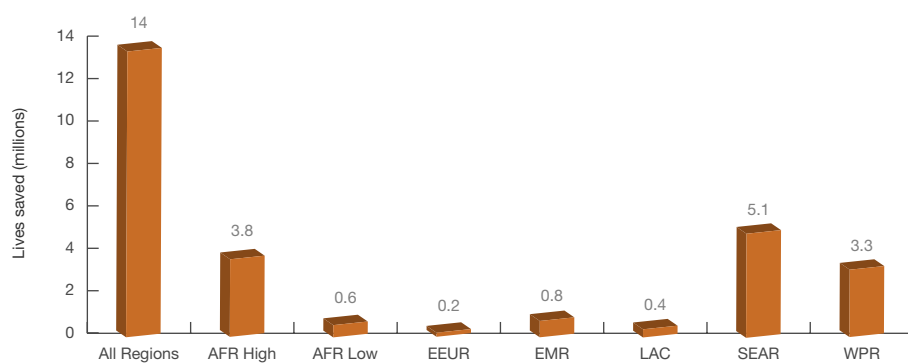
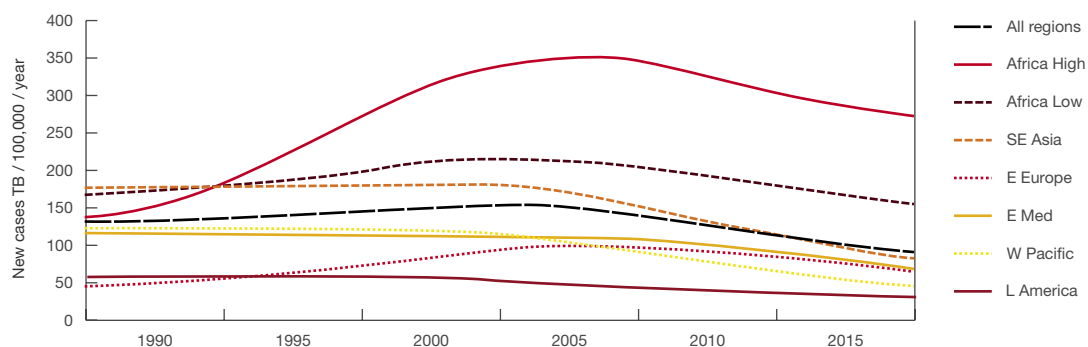
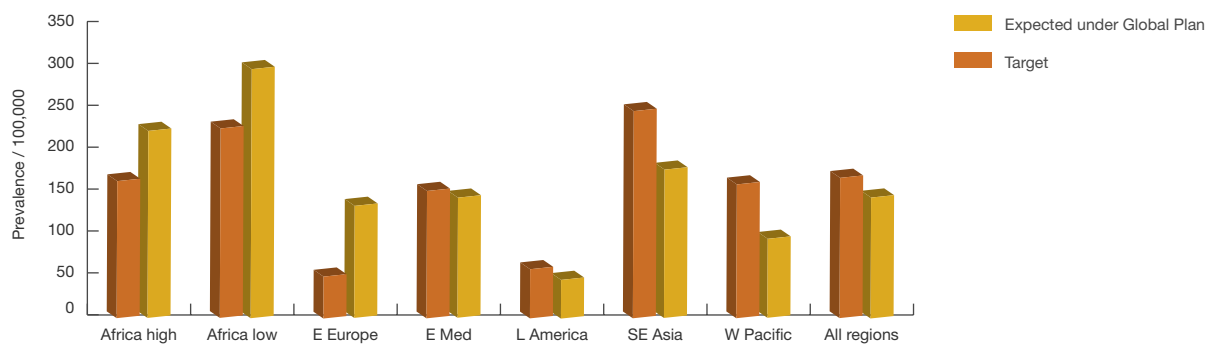
See Figure 15. Projected rates of TB incidence, prevalence and deaths, assuming full implementation of the Global Plan in seven regions of the world

Globally and in all regions, TB incidence rates will fall by 2015, thus meeting the MDG target relevant to TB (figure 15a). In most of the regions where the global TB epidemic is concentrated (Latin America, Eastern Mediterranean, South-East Asia and Western Pacific), prevalence and death rates will have reached or exceeded the Partnership's targets for 2015 (to halve prevalence and death rates from the 1990 baseline) (figure 15 b, c). The gains made in the two other regions (Eastern Europe and Africa) over the period of the Plan (2006–2015) will be similar to progress in other regions, despite their formidable challenges. However, achievement of the Partnership's targets may well be later than 2015 in Eastern Europe and even later in Africa, because the targets are expressed with 1990 as a baseline year and the 1990s saw huge upsurges of TB in both regions.

To achieve the targets in Africa and Eastern Europe by 2015 would require tremendous improvements in health systems in general, an early 50% reduction in HIV incidence, and the very rapid availability of new tools. It is unlikely that even massive additional funding or even greater effort would be successful in completely overcoming the constraints by 2015, though all efforts must be made to halve prevalence and deaths as swiftly as possible. The different regional needs and results are considered in more detail in Part II.

Cost-effectiveness

Combining projected costs and projected impact, the Global Plan will cost about US\$150 per disability adjusted life year (DALY)²³ gained – or less than US\$1 per day of life saved. TB control in the South-East Asian and Western Pacific regions is particularly cost-effective, at about US\$60–70 per DALY gained. By contrast, the cost per DALY is markedly higher in Eastern Europe, because of the extensive reliance on relatively expensive hospitalization during normal TB treatment and because of the

FIGURE 14: NUMBER OF LIVES EXPECTED TO BE SAVED UNDER THE GLOBAL PLAN, 2006-2015**FIGURE 15:** PROJECTED RATES OF CHANGES IN TB INCIDENCE, PREVALENCE AND DEATHS, ASSUMING FULL IMPLEMENTATION OF THE GLOBAL PLAN IN SEVEN REGIONS OF THE WORLD**a. TB incidence rate by region, 2006-2015****b. Prevalence in 2015 in comparison with targets**

c. Death rates in 2015 in comparison with targets

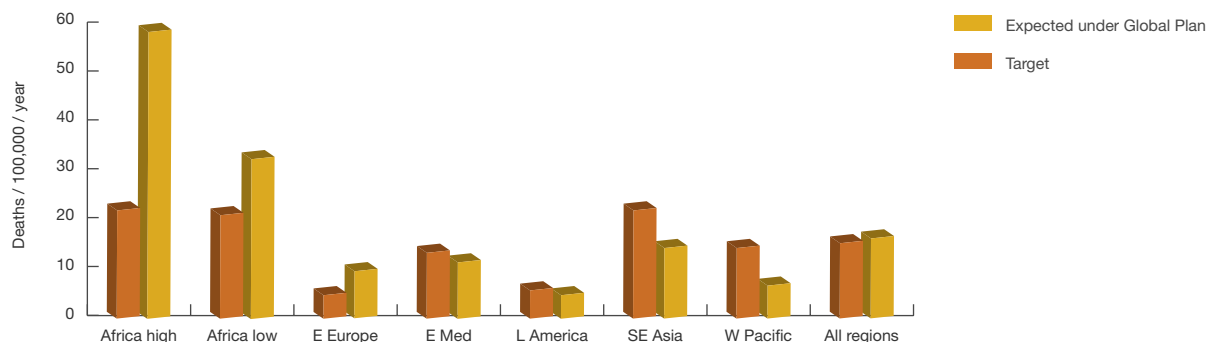
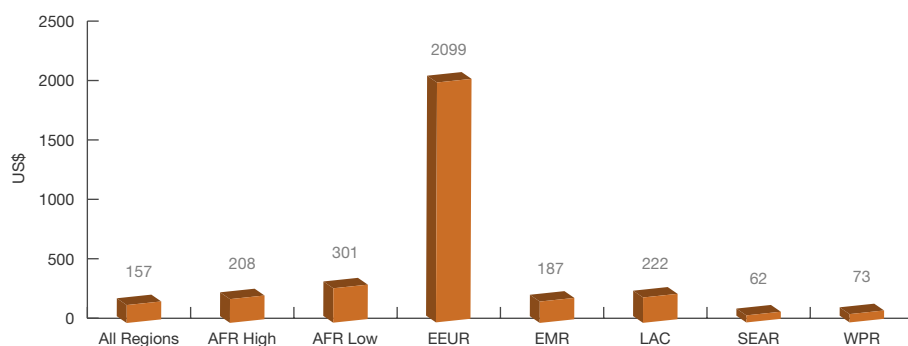


FIGURE 16: COST-EFFECTIVENESS OF GLOBAL PLAN

Cost per DALY gained by region 2006-2015



much higher costs associated with treating MDR-TB.

See Figure 16: Cost-effectiveness of Global Plan

New tools

The above projections are based on optimal use of existing drugs, diagnostics, and vaccines. They do not, at this stage, incorporate assumptions about the impact of new tools introduced within the Plan period.

Modelling work commissioned by the UN Millennium Project²⁴ confirmed the large potential gains from rapid scale-up of DOTS, but suggested that the impact of DOTS could be substantially increased if new tools were available. For example, by reducing the likelihood of default and failure, shorter drug regimens could bring down annual incidence and mortality by around 40% by

2030. Simplified regimens combined with new diagnostic tests could facilitate broader case detection in DOTS programmes, which would magnify these benefits significantly. Further modelling work is currently being undertaken by the Working Group on New TB Diagnostics.

It is difficult to predict the exact effects of new vaccines because we do not know their mode of action and efficacy. However, the impact of new vaccines can be simulated by introducing vaccine-related parameters into existing epidemiological models of the TB pandemic, and making guesses about the unknowns. Doing so suggests that the introduction between 2014 and 2018 of a new vaccine that can be given to everybody could reduce TB incidence in Africa and South-East Asia by over 20% during the first 10 years of use and up to 40% by 2050.

5. CONCLUSION

Tuberculosis ranks among the top three infectious diseases as a cause of disease burden. The unprecedented scale of the TB epidemic and the human rights approach to TB demand urgent and effective action now.

This Global Plan to Stop TB sets out what needs to be done over the 10 years from 2006 to 2015 and what can be achieved. The strategies are clear. The plans are detailed. The potential outcomes, given adequate support, are exciting.

The scale of the challenge should not be underestimated. Nevertheless, rigorous analysis indicates that globally it will be possible to meet the UN Millennium Development Goal target to “have halted by 2015, and begun to reverse the incidence of TB”, and the Partnership’s own demanding targets for 2015 to halve prevalence and death rates from the 1990 baseline. In the process, the Partnership will also contribute to achieving a range of other MDGs, particularly those related to poverty reduction, gender, partnership, providing access to affordable essential drugs in developing countries, and making available the benefits of new technologies in cooperation with the private sector.

Plans for implementation of TB control during the period are ambitious, realistic and shaped to individual country needs. In those countries – in Asia, Latin America and parts of the Eastern Mediterranean – where success is already being built, the need is to consolidate that success, sustain progress and lay the foundation for eventual elimination of TB. Long-term investment and commitment are essential.

In Africa and Eastern Europe, where success remains elusive because of HIV or multidrug-resistant TB and wider societal and health system issues, emergency action is critical. As in other regions, the constraints cannot be overcome by the Stop TB Partnership alone, however effective. Collaboration with HIV programmes is essential. More generally, to reach the targets and bridge the unacceptable gaps between regions, the Stop TB Partnership will engage with other partners in the African and Eastern European regions and with the international financial institutions to seek increased political commitment and to address health system, infrastructure and economic barriers to the full-scale implementation of core strategies to address TB, TB/HIV and multidrug-resistant TB.

The success of this ambitious Global Plan to Stop TB will rest on the ability of advocacy efforts to mobilize the unprecedented levels of political will and financial resources that are needed to reverse the epidemic. The Stop TB Partnership aims to ensure that TB control remains a critical priority for governments and the general public worldwide. It will catalyse TB advocacy and communication, and promote the Partnership as an effective mechanism for innovation and progress. It will also foster change and debate in favour of enhanced TB control through engagement with wider health sector strengthening and financing reform agendas along with other social and economic development issues.

In its quest for a TB-free world by 2050, the Partnership will seek to ensure the full and active contribution of all its partners to TB control and poverty reduction. It will support national and regional partnerships to strengthen TB control at local level. These partnerships will become self-sustaining, independently operating entities answerable to their own constituent partners under the umbrella of the Global Stop TB Partnership and the Global Plan to Stop TB.

Implementation of the plan, at the cost of US\$56 billion, will save some 14 million lives over the next 10 years, using only existing tools. But it will also be the precursor for future gains. Because TB dynamics are slow, implementation activities from 2006 to 2015 will yield benefits later as well as those shown here as occurring within the period of the Plan. Even more dramatically, the investment in new drugs, new diagnostic tests and new vaccines will begin to pay rich dividends beyond 2015. The real prize will be the elimination of TB.

PART II

Global and regional scenarios for TB control 2006–2015

6. STRATEGIC DIRECTIONS, GLOBAL AND REGIONAL SCENARIOS AND WORKING GROUP PLANS

Part I of this Global Plan set out the strategic directions to reach the Stop TB Partnership's global targets for TB control for 2015, which are linked to the MDGs. Part II describes ambitious but realistic scenarios for the impact and costs of planned activities for the regions with a high burden of TB, while Part III summarizes the specific strategic plans of the seven working groups and the Partnership secretariat for the period 2006–2015.

6.1 The analytical process that underpins the Global Plan

The Stop TB Partnership has been conscious that the working group plans must be based on sound epidemiological analysis and robust budget justifications in order to provide a powerful argument for resource mobilization. The development of each working group's strategic plan and of the overall Global Plan has therefore been informed by an analysis of the expected impact, with the accompanying costs, of the planned scale-up of activities oriented towards achieving the targets for 2015. The analysis has required close interaction between representatives of all the Partnership's working groups, WHO Regional Offices and the team assessing the epidemiological impact and costs of the currently available and new tools.

Scenarios for implementation for 2006–2015 have been developed globally and for seven of the eight TB epidemiological regions:²⁵ Africa, high HIV prevalence, and Africa, low HIV prevalence, which are presented together; American region (AMR) – Latin American countries (LAC); Eastern European Region (EEUR); Eastern Mediterranean Region (EMR); South-East Asian Region (SEAR); and Western Pacific Region (WPR).

The Established Market Economies (EME) and Central Europe are considered together as one epidemiological region in section 9. However, because they have similarly high per capita income rates and low tuberculosis incidence rates, detailed implementation scenarios have not been developed.

In developing the scenarios, assumptions have been made about the pace of scale-up and the coverage of different activities. Estimates have been made of TB case detection and treatment outcomes over the next 10 years, as well of TB prevalence, incidence and death rates in relation to the 2015 targets. The scenarios also include estimated costs of country implementation as well as external technical support. Full details of the methodology can be found at <http://www.stoptb.org/GlobalPlan>.

These regional scenarios are not implementation plans, though the methodology offers an approach that can be applied at country level. The next step will be to develop detailed regional and country implementation plans (integrating DOTS Expansion, DOTS-Plus and TB/HIV actions), based on the respective strategic plans. But the regional scenarios are indicative of what



Treat

Access to quality diagnosis and treatment is a human right for all who have TB. Over the ten years of the Plan, about 50 million people will be treated for TB under the Stop TB Strategy. Treatment benefits the individual with TB and the community. Since TB is spread from person to person, protecting the community from TB depends on ensuring effective treatment of individuals with the disease.

At the heart of the Plan is an approach that links innovation with implementation. As new diagnostics and drugs become available, their implementation will enable patients to be treated more quickly and more effectively. Progress in vaccine development raises the prospect of a new, safe and effective vaccine being available by 2015. This will make prevention a key ally of treatment.

Treatment of TB saves lives and protects our communities.

could be achieved, with ambitious but realistic assumptions. They try to predict what could happen if TB control activities go well, while taking into account general barriers that are difficult to overcome during the ten-year time-span of the Global Plan, or that lie outside the domain of TB control, such as severe health systems constraints.

The current epidemiological modelling does not include any assumptions about poverty reduction and its impact on the TB epidemic. If there are considerable socioeconomic improvements as a result of action to achieve other MDG targets, the prospects of reaching the TB control targets earlier – in Africa and Eastern Europe, for example – will be much better. Similarly, if new preventive, diagnostic or treatment tools become available, they could have dramatic effects on the TB epidemic.

6.2 The global scenario for meeting the MDG target and the Partnership's 2015 targets

As described in Part I, under this ambitious but realistic scenario, all regions will see incidence, prevalence and death rate trends go down rapidly over the next 10 years as a result of the various planned TB control activities.

The MDG target to “have halted and begun to reverse the incidence of TB by 2015” will be met in all regions.

In addition, the Partnership's own challenging 2015 targets – to halve prevalence and death rates from the 1990 baseline – will be met globally, with potentially enormous progress in all regions.

6.3 Halving TB prevalence and death rates in individual regions

The scenarios generated in the planning process showed that the Partnership's targets of halving prevalence and death rates could be achieved by 2015 in most regions where the TB epidemic is concentrated. However, the scenarios showed that these targets would not be achieved by 2015 in Africa and Eastern Europe. The profiles in section 7 include details of the scenario for all TB epidemiological regions, while section 8 considers what further measures would be needed to achieve the targets on time in Africa and Eastern Europe.

7. REGIONAL PROFILES: AN AMBITIOUS BUT REALISTIC SCENARIO

Each regional profile is set out in the following format:

- achievements;
- challenges;
- priority activities;
- expected effects and costs;
- chart showing planned scale-up of activities;
- table of milestones related to implementation of DOTS expansion, DOTS-Plus and TB/HIV activities;
- set of six graphs showing estimated impact and costs of planned activities:
 - (i) case detection rate (new sputum smear-positive cases),
 - (ii) number of cases treated under DOTS and DOTS-Plus,
 - (iii) incidence (all forms of TB),
 - (iv) prevalence (all forms of TB),
 - (v) mortality (all forms of TB),
 - (vi) costs per year of DOTS expansion, DOTS-Plus and TB/HIV activities.

The graphs of expected incidence, prevalence and mortality show three different scenarios:

- 1) No DOTS. This assumes that the strategy was never introduced in any region, so treatment would continue as it was pre-DOTS, with variable rates of case detection and typically lower rates of cure. This gives a baseline against which to compare acquired and future gains.
- 2) Sustained DOTS. Case detection and treatment success rates increase until 2005, and then remain steady until 2015.
- 3) Full implementation of the Global Plan.

7.1 African Region: summary of planned activities, impact and costs

Within the African Region there are two distinct epidemiological subregions in terms of TB and HIV burden. The high HIV prevalence subregion (AFR high) includes countries with an estimated adult HIV prevalence rate equal to or greater than 4%; the remaining countries constitute the low HIV prevalence subregion (AFR low).²⁶ The following section summarizes achievements to date, challenges, priority activities, and expected effects and costs for the African region, and highlights key differences between AFR high and AFR low. Summary tables and figures are presented separately for the two subregions.

Achievements to date

There has been good progress in DOTS expansion in the African Region in recent years. Nine of the world's 22 TB high-burden countries are in Africa, and all nine (Democratic Republic of Congo, Ethiopia, Kenya, Mozambique, Nigeria, South Africa, Uganda, United Republic of Tanzania and Zimbabwe) have a DOTS programme. Only five of the 46 countries in the region have not adopted DOTS as the national strategy for TB control, though some core elements of the strategy have not been adequately implemented in a few countries. Case detection increased steadily from 23% to 48% between 1995 and 2003, and is expected to reach 55% in 2005. Though short of the 70% target, this is a significant achievement given the severe health systems constraints in the region.

All nine TB high-burden countries in the African region fall in the AFR high subregion, and face particular challenges related to the HIV epidemic. Many countries with high HIV prevalence have established pilot projects for collaborative TB/HIV activities (e.g. Democratic Republic of Congo, Ethiopia, Rwanda, United Republic of Tanzania) or are already scaling up TB/HIV activities nationally (e.g. Kenya, Malawi, and South Africa).

Several countries have taken up community-based DOTS, and are now at various stages of programme implementation. Coverage of drug resistance surveillance is increasing. Kenya has a DOTS-Plus pilot approved by the Green Light Committee for DOTS-Plus. South Africa is one of the few high-burden countries in which the national TB programme provides treatment for multidrug-resistant TB (MDR-TB) cases. The programme, however, has not been endorsed by the Green Light Committee.

Challenges

Despite these achievements, TB control in the region faces severe challenges, of which the greatest is perhaps the impact of HIV on increasing TB incidence. However, a range of additional factors contributes to the uncontrolled epidemic, including widespread poverty and very weak health systems. Major constraints on the delivery of quality care include: inadequate infrastructure, poor access to health facilities, insufficient staffing and human resource development, insufficient and substandard laboratory services, and limited links between national TB programmes and HIV programmes, as well as with other public and private health care providers.

The treatment success rate has remained more or less unchanged since 1998 at just above 70%, considerably short of the 85% target. This low rate is due not only to the high rates of death among people living with HIV/AIDS but also to high rates of treatment interruption and transfer. Efforts are needed specifically to improve treatment and care for HIV-positive TB patients, generally to improve case management, referral and transfer mechanisms, and defaulter tracing, and to improve TB diagnosis (that will also help improve the case detection rate).

Drug resistance surveillance data are limited and few trends are available from the African Region. This is of particular concern given that little information is available about MDR-TB in high HIV-prevalence settings.

Priority activities 2006–2015

Ministers of Health from 46 Member States of the Africa Region unanimously declared TB an emergency in the Region in August 2005. The declaration urged countries to develop and implement, with immediate effect, emergency strategies and plans to control the worsening of the epidemic. This declaration of emergency will be crucial in accelerating the implementation of priority activities and in garnering the necessary commitments from all stakeholders, both nationally and internationally.

The first priority is to move from basic geographical coverage of DOTS, to improved quality and access. Quality improvements require intensified efforts to strengthen laboratory services, treatment management, and supervision. This, in turn, requires that the root problems of the human resource crisis and weak health systems are addressed (see Section 3.2). Advocacy for higher and sustained political commitment at national and international level will be key. Tackling the human resource crisis goes far beyond TB control alone, and will require the implementation of human resource development strategies in the public health sector, e.g. more attractive career and salary structures, and improved training, as well as the establishment of partnerships with communities and all health care providers, in order to tap all available human.

Implementation of collaborative TB/HIV activities is another priority in the region, in particular in the high HIV prevalence countries. TB/HIV collaborative activities will have begun in all high HIV prevalence countries by 2007, with full coverage by 2010.

Access will be improved by further decentralizing services. For the majority of the population living in rural areas, establishing and scaling up community-based DOTS will improve access to quality care, particularly for the most disadvantaged, and will also address some gender-related barriers to access (see Section 3.5). Through social mobilization, communities participate in treatment support and contribute to identifying TB suspects and referring them for diagnosis. The public-private mix DOTS (PPM DOTS) approach will be relevant mainly in urban settings, where it will contribute to making DOTS services available to vulnerable urban populations, such as slum dwellers and migrants. It will also facilitate links between large central hospitals and public health facilities in the cities. The Practical Approach to Lung

Health (PAL) will be introduced gradually in settings with sound DOTS programmes in place.

Rapid introduction and scale-up of culture services, especially new rapid culture methods, is particularly important to improve diagnosis of sputum smear-negative and extrapulmonary TB among people living with HIV/AIDS. Drug resistance surveillance will be expanded and the relationship between HIV and MDR-TB will be monitored. Diagnosis and treatment of MDR-TB will be pilot tested and scaled up, and will focus on previously treated patients.

Better coordination between TB programmes, anti-poverty initiatives and health system strengthening is needed to ensure that TB treatment is accessible to all socioeconomic groups (but most importantly to the poor), and to women and men equally. Debt relief for highly indebted poor countries (HIPC) could contribute to ensuring universal access to quality TB care by freeing up domestic resources. However, the Poverty Reduction Strategy Papers (PRSP), Medium Term Expenditure Frameworks (MTEF), Poverty Reduction Support Credits (PRSCs) and other broad planning mechanisms, such as Sector-Wide Approaches (SWAps), hold the potential for addressing constraints and placing financing for TB in a sustainable and flexible long-term strategic plan, with multisectoral involvement. The establishment of National Stop TB Partnerships will be encouraged to forge multisectoral involvement and coordination.

Expected effects and costs

Successful implementation of the activities described above is expected to increase case detection to over 70% by 2010 and over 80% by 2015. Treatment success rate should reach the target of 85% by 2010 and be sustained at this level. If this proves to be the case, it is predicted that the MDG target, to have halted and begun to reverse the incidence of TB by 2015, will be met. However, achievement of the Partnership's other TB targets for 2015 – to halve prevalence and death rate – will be reached later in the African region. An important reason is that the targets were set with 1990 levels as baseline. Since there was a dramatic increase in TB incidence, prevalence and death rates between 1990 and 2005, the time remaining until 2015 is almost certainly too short to revert to 1990 levels.

For AFR high, it is estimated that about 14 million people will be treated in DOTS programmes and 18 000 in DOTS-Plus. In addition, 2.6 million TB patients will be enrolled on antiretroviral therapy (ART). The combined effect of all interventions will be to prevent about 3.8 millions deaths, in comparison with a situation in which no DOTS programmes are implemented, or about 1.9 millions deaths, in comparison with a situation in which TB control efforts are sustained at 2005 levels.

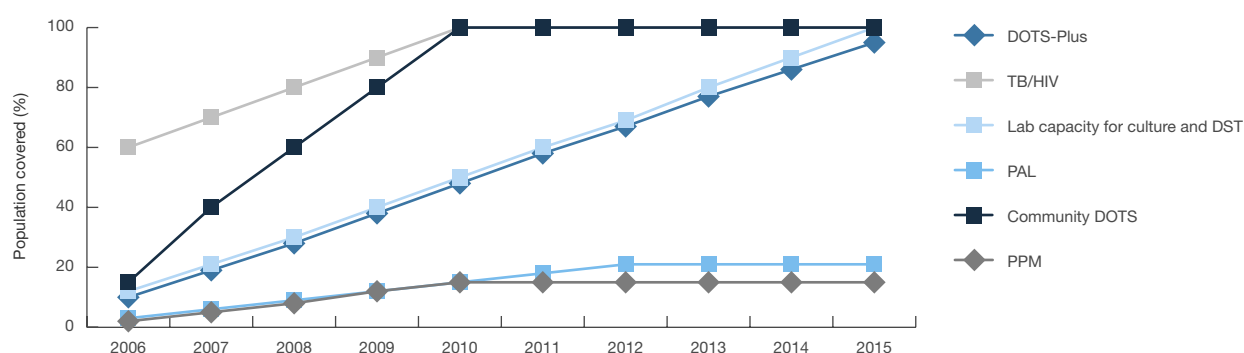
For AFR low, it is estimated that about 2.9 million people will be treated in DOTS programmes and 11 000 in DOTS-Plus. In addition, almost 140 000 TB patients will be enrolled on ART. The combined effect of all interventions will be to prevent about 600 000 deaths, in comparison with a situation in which no DOTS programmes are implemented, and about 160 000 deaths,

in comparison with a situation in which TB control efforts are sustained at 2005 levels.

The estimated total cost of DOTS Expansion, DOTS-Plus and TB/HIV control activities in the African region from 2006 to 2015 is US\$18.3 billion, of which US\$15.1 billion is needed for countries with high HIV prevalence and US\$ 3.2billion for countries with low HIV prevalence.

TABLE 5: COST OF PLANNED TB CONTROL ACTIVITIES AFRICAN REGION 2006–2015

Planned activities	High HIV countries US\$ millions	Low HIV countries US\$ millions	Total US\$ millions
DOTS expansion and quality	10,419 (69%)	2,859 (89%)	13,278 (72%)
DOTS-Plus	45 (1%)	26 (1%)	71 (1%)
TB/HIV collaborative activities	4,605 (30%)	334 (11%)	4,940 (27%)
TOTAL	15,070 (100%)	3,219 (100%)	18,289 (100%)

SUMMARY CHARTS FOR AFRICAN COUNTRIES WITH HIGH HIV PREVALENCE**FIGURE 17: PLANNED SCALE UP OF ACTIVITIES 2006–2015****African countries with high HIV prevalence**

N.B. Population coverage is the percentage of the population that lives in an area where the activity is implemented. For TB/HIV collaborative activities, the percentage refers to the proportion of the eligible population, i.e. the population living in areas with an HIV prevalence above 1%. For DOTS-Plus, it is the percentage of detected MDR-TB cases that are enrolled in DOTS-Plus programmes.

TABLE 6: MILESTONES RELATED TO IMPLEMENTATION OF DOTS EXPANSION, DOTS-PLUS AND TB/HIV ACTIVITIES (a)

African countries with high HIV prevalence	2006 (b)	2010 (b)	2015 (b)
DOTS EXPANSION			
DOTS coverage	100%	100%	100%
Total number of new ss+ patients treated in DOTS programmes (thousands)	437 (673)	504 (650)	524 (629)
Case detection rate new ss+ (%)	65%	77%	83%
Treatment success rate new ss+ (%)	75%	85%	86%
Total number of new ss-/extra-pulmonary patients treated in DOTS programmes (thousands)	833 (1249)	952 (1188)	990 (1162)
Percentage of new ss-/extra-pulmonary patients treated in DOTS programmes	67%	80%	85%
DOTS-Plus			
Total number of detected MDR-TB patients treated in DOTS-Plus programmes (thousands)	0.2 (2.3)	1.5 (3.1)	3.3 (3.3)
Percentage of detected MDR-TB cases treated in DOTS-Plus programmes	10%	50%	100%
MDR-TB treatment success rate (%)	71%	73%	75%
Percentage of culture positive cases that are re-treatment cases	15%	12%	10%
TB/HIV			
Total number of PLWHA attending HIV services screened for TB (millions) (c)	9.9 (16)	18 (18)	21 (21)
Percentage of PLWHA attending HIV services screened for TB (d)	63%	100%	100%
Total number of newly diagnosed and eligible PLWHA offered IPT (millions)	1.0 (24)	2.1 (28)	2.4 (30)
Percentage of PLWHA offered IPT	4%	8%	8%
Total number of TB patients in DOTS programmes HIV tested and counselled (millions)	0.6 (1.3)	1.2 (1.5)	1.3 (1.5)
Percentage of TB patients treated in DOTS programmes HIV tested and counselled	51%	85%	85%
Total number of TB patients (HIV positive and eligible) in DOTS programmes enrolled on ART (millions)	0.2 (0.4)	0.3 (0.5)	0.3 (0.5)
Percentage of TB patients (HIV positive and eligible) in DOTS programmes enrolled on ART	45%	55%	59%

(a) The percentages are not always exactly the numerator divided by the denominator due to rounding errors.

(b) Numbers in parentheses indicate the denominator. For DOTS Expansion it is new TB cases.

For DOTS-Plus it is the total number of detected MDR-TB cases.

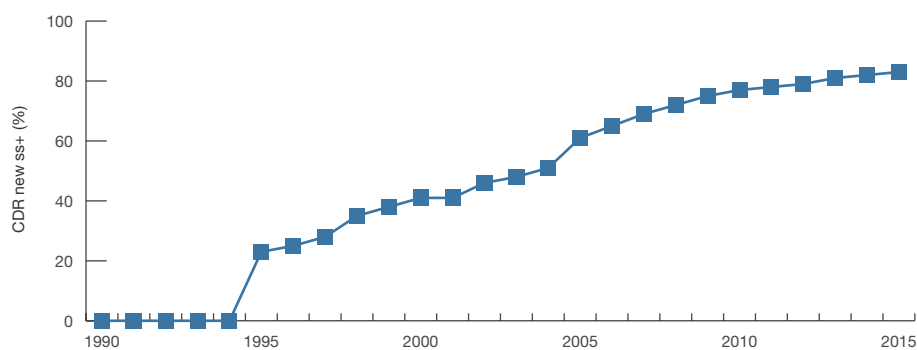
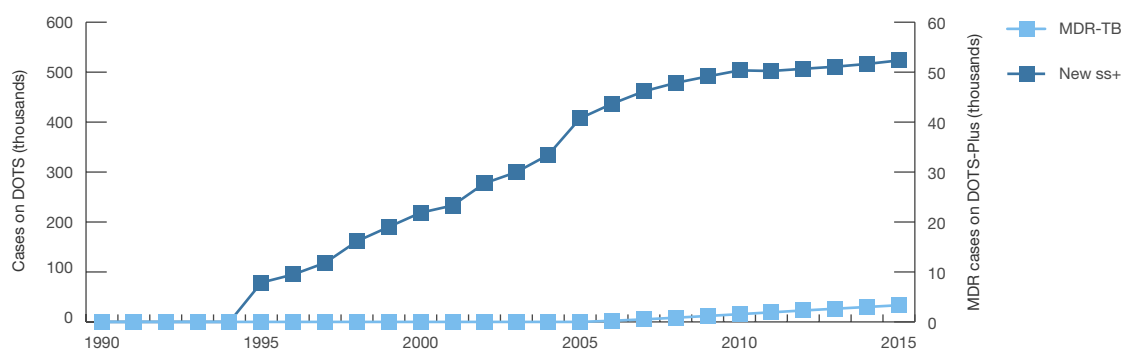
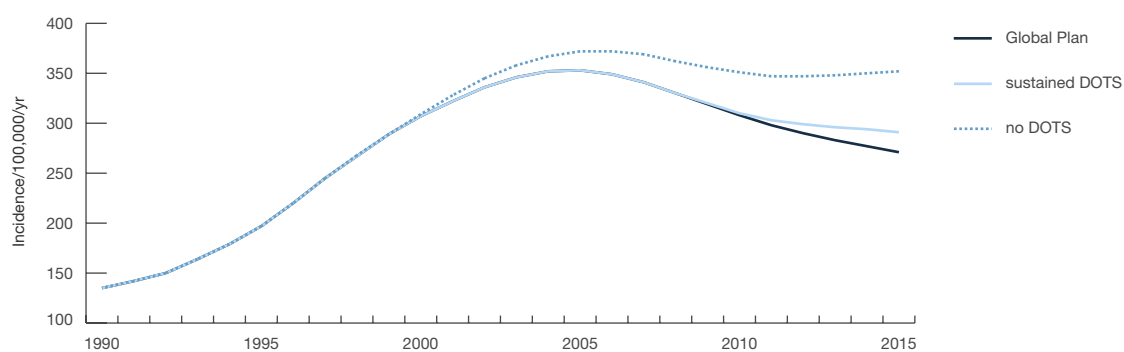
For PLWHA screened for TB it is the total number of PLWHA attending HIV services. For PLWHA offered IPT it is the total number of PLWHA.

For TB patients HIV tested and counselled it is the total number of TB patients treated under DOTS in areas covered by TB/HIV collaborative activities.

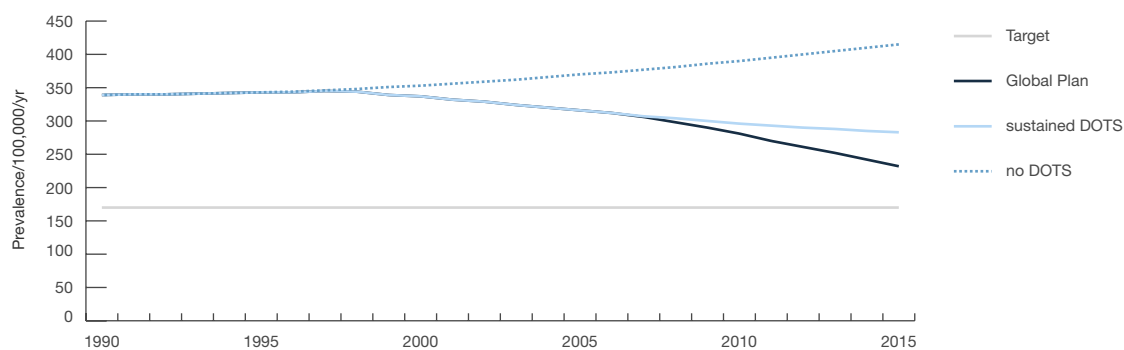
For TB patients enrolled on ART it is the total number of HIV positive TB patients in DOTS programmes that are eligible for ART in areas covered by TB/HIV collaborative activities.

(c) Please note that unlike for other Regions, for AFR high HIV prevalence the numbers for TB/HIV activities are presented in millions as opposed to thousands.

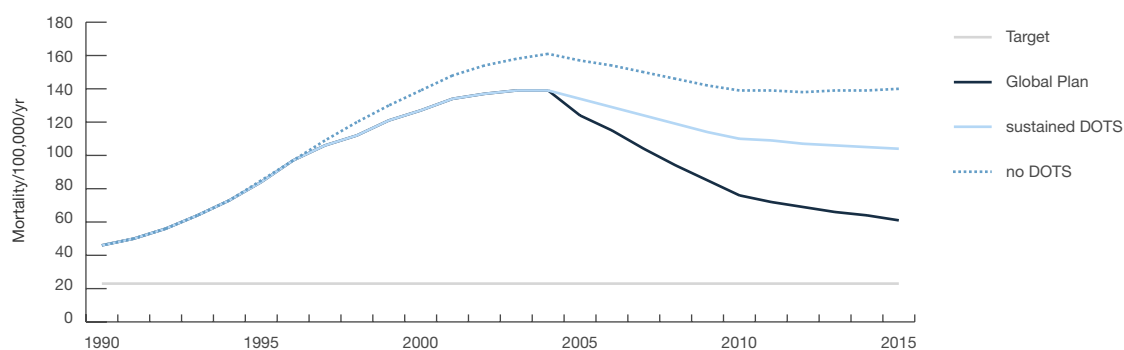
(d) HIV services include testing and counselling and HIV treatment and care services

FIGURE 18: ESTIMATED IMPACT AND COSTS OF PLANNED INTENSIFIED ACTIVITIES 2006–2015**African countries with high HIV prevalence: Case detection rate, new ss+ cases****African countries with high HIV prevalence: Number of cases treated under DOTS/DOTS-Plus****African countries with high HIV prevalence: Incidence**

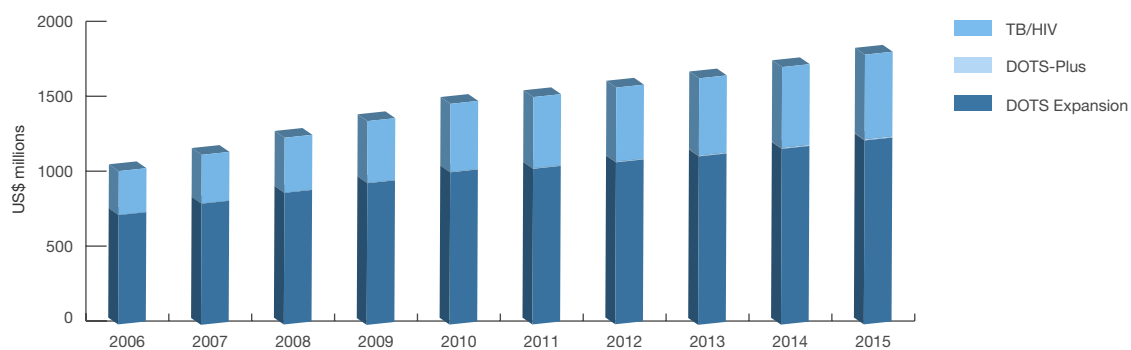
African countries with high HIV prevalence: Prevalence



African countries with high HIV prevalence: Mortality



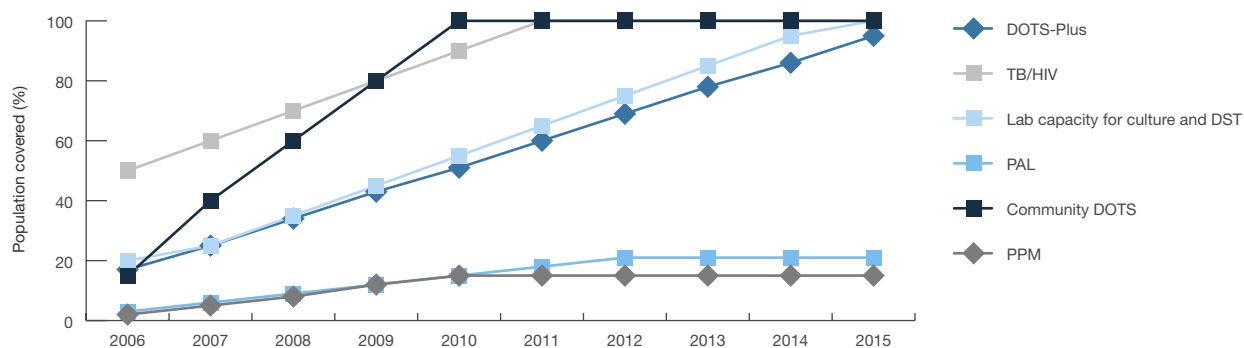
African countries with high HIV prevalence: Total costs



SUMMARY CHARTS FOR AFRICAN COUNTRIES WITH LOW HIV PREVALENCE

FIGURE 19: PLANNED SCALE UP OF ACTIVITIES 2006-2015

African countries with low HIV prevalence



N.B. Population coverage is the percentage of the population that lives in an area where the activity is implemented. For TB/HIV collaborative activities the percentage refers to the proportion of the eligible population, i.e. the population living in areas with an HIV prevalence above 1%. For DOTS-Plus, it is the percentage of detected MDR-TB cases that are enrolled in DOTS-Plus programmes.

TABLE 7: MILESTONES RELATED TO IMPLEMENTATION OF DOTS EXPANSION, DOTS-PLUS AND TB/HIV ACTIVITIES (a)

African countries with low HIV prevalence	2006 (b)	2010 (b)	2015 (b)
DOTS EXPANSION			
DOTS coverage	100%	100%	100%
Total number of new ss+ patients treated in DOTS programmes (thousands)	107 (169)	126 (177)	127 (159)
Case detection rate new ss+ (%)	60%	71%	80%
Treatment success rate new ss+ (%)	77%	85%	86%
Total number of new ss-/extra-pulmonary patients treated in DOTS programmes (thousands)	147 (241)	175 (243)	181 (226)
Percentage of new ss-/extra-pulmonary patients treated in DOTS programmes	61%	72%	80%
DOTS-Plus			
Total number of detected MDR-TB patients treated in DOTS-Plus programmes (thousands)	0.2 (0.9)	0.9 (1.7)	2.1 (2.1)
Percentage of detected MDR-TB cases treated in DOTS-Plus programmes	17%	54%	100%
MDR-TB treatment success rate (%)	71%	73%	75%
Percentage of culture positive cases that are re-treatment cases	10%	8%	6%
TB/HIV			
Total number of PLWHA attending HIV services screened for TB (thousands)	693 (1,316)	1,522 (1,671)	2,095 (2,095)
Percentage of PLWHA attending HIV services screened for TB (c)	53%	91%	100%
Total number of newly diagnosed and eligible PLWHA offered IPT (thousands)	63 (2,734)	162 (3,271)	197 (4,116)
Percentage of PLWHA offered IPT	2%	5%	5%
Total number of TB patients in DOTS programmes HIV tested and counselled (thousands)	89 (210)	191 (250)	217 (255)
Percentage of TB patients treated in DOTS programmes HIV tested and counselled	43%	77%	85%
Total number of TB patients (HIV positive and eligible) in DOTS programmes enrolled on ART (thousands)	8 (17)	14 (24)	18 (31)
Percentage of TB patients (HIV positive and eligible) in DOTS programmes enrolled on ART	44%	55%	60%

(a) The percentages are not always exactly the numerator divided by the denominator due to rounding errors.

(b) Numbers in parentheses indicate the denominator. For DOTS Expansion it is new TB cases.

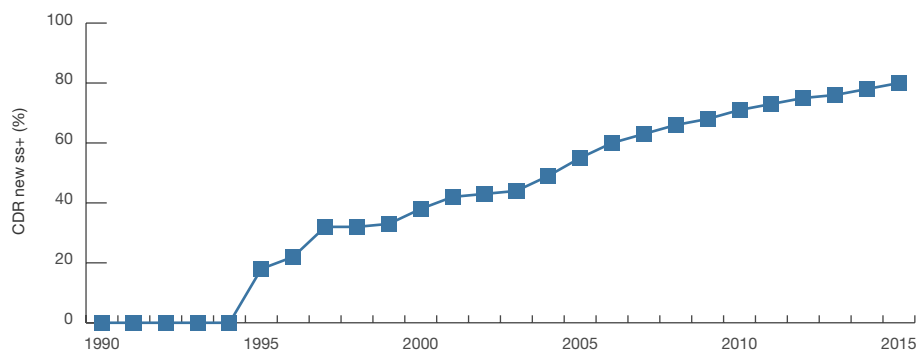
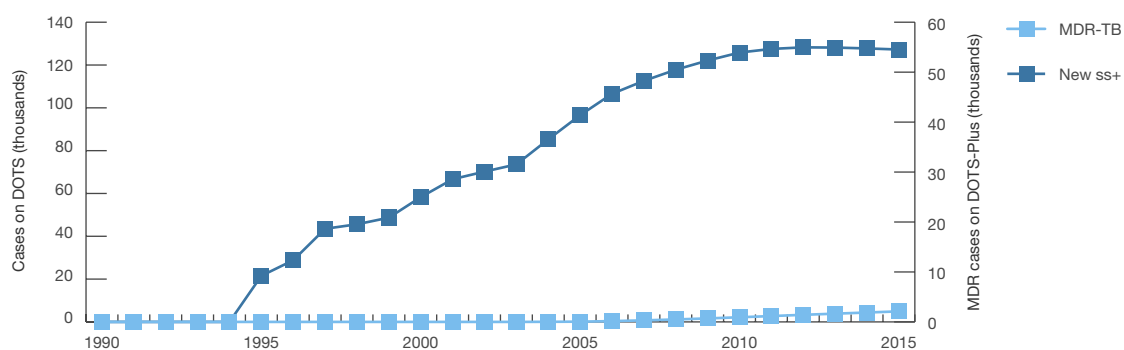
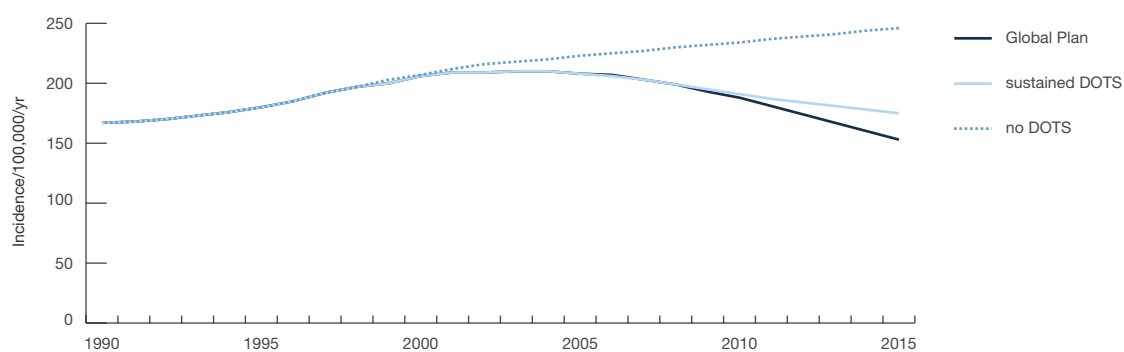
For DOTS-Plus it is the total number of detected MDR-TB cases.

For PLWHA screened for TB it is the total number of PLWHA attending HIV services. For PLWHA offered IPT it is the total number of PLWHA.

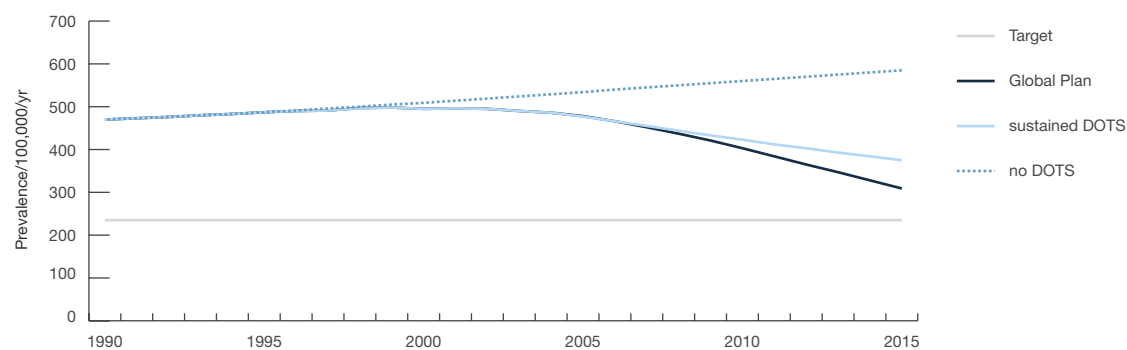
For TB patients HIV tested and counselled it is the total number of TB patients treated under DOTS in areas covered by TB/HIV collaborative activities.

For TB patients enrolled on ART it is the total number of HIV positive TB patients in DOTS programmes that are eligible for ART in areas covered by TB/HIV collaborative activities.

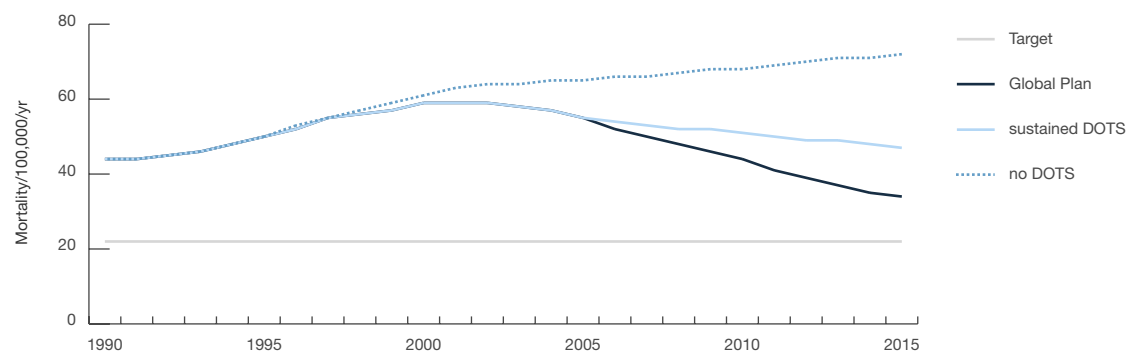
(c) HIV services include testing and counselling and HIV treatment and care services.

FIGURE 20: ESTIMATED IMPACT AND COSTS OF PLANNED INTENSIFIED ACTIVITIES 2006–2015**African countries with low HIV prevalence: Case detection rate, new ss+ cases****African countries with low HIV prevalence: Number of cases treated under DOTS/DOTS-Plus****African countries with low HIV prevalence: Incidence**

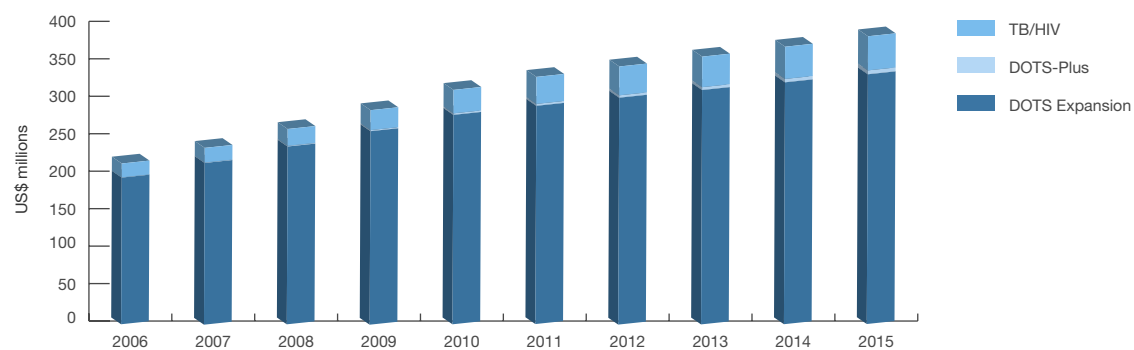
African countries with low HIV prevalence: Prevalence



African countries with low HIV prevalence: Mortality



African countries with low HIV prevalence: Total costs



7.2 American Region (Latin American countries): summary of planned activities, impact and costs

Achievements

Major progress has been made in TB control in the American region. A number of countries in the region have had excellent TB control programmes following DOTS principles for some time (such as Chile, Cuba, and Uruguay), and since 2003 the DOTS strategy has been implemented in 33 countries, giving an estimated regional DOTS coverage of 78%. The case detection rate under DOTS reached 50% in 2003 and is predicted to increase to 67% in 2005. The treatment success rate for new smear-positive cases in DOTS areas has increased from 77% (1994 cohort) to 81% (2002 cohort) and is expected to reach the 2005 target of 85% in the 2005 cohort.

TB prevalence and incidence are already decreasing. From 1994 to 2003, the incidence of TB in the WHO Region of the Americas showed a downward trend of 1.6% per year for all forms, and 2.6% per year for smear-positive cases. This downward trend is essentially attributed to fewer cases in Brazil, Chile, Costa Rica, Cuba and Peru. Data from drug resistance surveys are available for most countries in the region, as a result of existing laboratory networks and the commitment of national TB programmes to monitor the emergence of drug resistance. Nine countries have already implemented DOTS-Plus pilot projects and several others are planning to introduce sound MDR-TB management schemes.

Challenges

Although the region is on track to reach the Partnership's 2015 targets linked to the MDGs, it should be emphasized that current achievements essentially reflect results in countries with successful long-standing national TB programmes, which have shown sustained improvement against their indicators (such as Brazil, Chile, Costa Rica, El Salvador and Peru). Reaching the MDG target will depend mainly on progress over the next 10 years in low- and middle-income countries with a high TB burden,²⁷ and on ensuring that TB services reach the poorest and marginalized groups of society in all countries in the region.

Furthermore, some countries where DOTS needs to be strengthened have recently implemented health sector reforms, or are subject to political or social instability, impoverishment, or rapid spread of HIV/AIDS. All these pose challenges, and technical assistance will need to be tailored to the epidemiological, social, operational, and developmental situation of the health system and the national TB programme in each country.

Priority activities 2006–2015

Regional efforts will focus on countries with weak health systems, a high degree of poverty, a high TB burden, high MDR-TB or high HIV/AIDS prevalence. A regional TB control plan for 2006–2015 has been developed with the involvement of a range of partners and regional experts. It aims to strengthen DOTS implementation and to improve the quality of TB care by following the Stop TB strategy. This includes fostering TB/HIV

and MDR-TB management at primary care level and promoting community participation, particularly in those countries and for those minority groups where poor access to health care remains a significant barrier to adequate implementation of DOTS. The plan includes: further improvements in the quality of diagnostic and treatment services; implementing the Practical Approach to Lung Health in countries with a low TB burden (Chile, Costa Rica, El Salvador, Uruguay and Venezuela), as well as in countries requiring intensified case-finding (Bolivia and Peru); and expansion of public-private mix for DOTS (PPM DOTS) initiatives, with a focus on urban areas.

Collaborative TB/HIV activities will be scaled up in countries with a generalized HIV epidemic (the Dominican Republic, Guatemala, Guyana, Haiti and Honduras), Brazil and the English-speaking Caribbean. HIV testing for all TB patients, accompanied by the provision of ART for all those found HIV-positive, will be promoted in settings with a high TB/HIV burden. All other countries in the region will implement surveillance of HIV among TB patients.

The regional laboratory network will be consolidated further to help strengthen country laboratory networks and support drug-resistance monitoring in all countries. Implementation of the DOTS-Plus strategy will be scaled up widely, with the aim of making DOTS-Plus available to at least 90% of all diagnosed MDR-TB patients by 2015. By the end of 2015, it is expected that drug susceptibility testing will be provided for 20% of targeted new TB cases and 100% of previously treated TB cases.

The regional plan also involves the development of human resources and implementation of advocacy and communication strategies for tuberculosis control, in order to stimulate greater government commitment, and enhance community participation and social mobilization. In-country capacity-building for operational research is high on the region's agenda. The WHO regional office will continue working with partners to identify resources to support the consolidation, analysis and dissemination of the results of current operational research projects, as well as to encourage new projects, particularly in key areas such as TB/HIV diagnosis and case management, monitoring the impact of PPM DOTS initiatives, reducing default rates, identifying risk factors for relapses, and outcomes of MDR-TB treatment in some countries.

Expected effects and costs

Given successful implementation of planned activities, case detection is expected to increase to 86% by 2010 and 91% by 2015. Treatment success rate is expected to reach 87% in 2010 and remain at this level until 2015. Provided that this is achieved, a continued decline in incidence, prevalence and death rate is expected and the region will meet the Partnership's targets for 2015.

During the period of the Plan, it is estimated that about 2 million patients in the region will be treated in DOTS programmes and 20 000 in DOTS-Plus. In addition, 33 000 TB patients will be enrolled on ART. The combined effect of all interventions will

prevent about 406 000 deaths, in comparison with a situation in which no DOTS programmes are implemented, and about 28 000 deaths, in comparison with a situation in which TB control efforts are sustained at 2005 levels only.

The total estimated cost of DOTS Expansion, DOTS-Plus and TB/HIV control activities in the American region for 2006–2015 is about US\$1.7 billion.

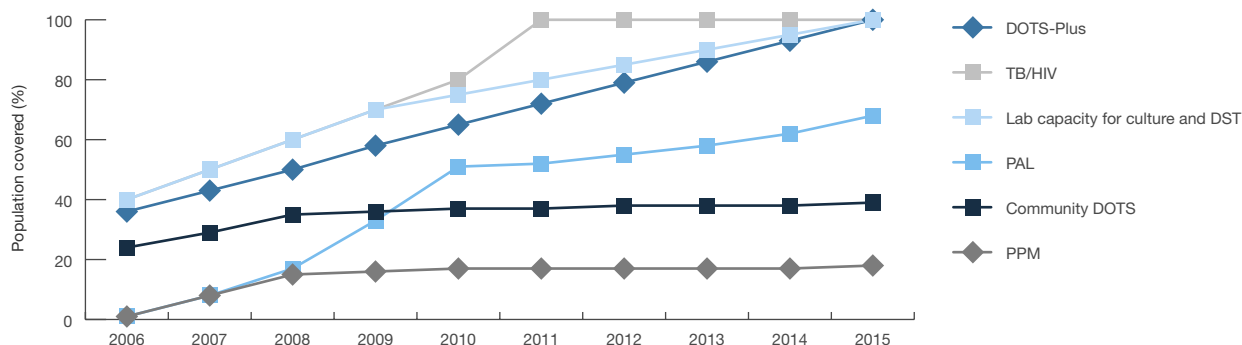
TABLE 8: COST OF PLANNED TB CONTROL ACTIVITIES, AMERICAN REGION (LATIN AMERICAN COUNTRIES) 2006–2015

Planned activities	US\$ millions
DOTS expansion and quality	1,383 (83%)
DOTS-Plus	121 (7%)
TB/HIV collaborative activities	166 (10%)
TOTAL	1,670 (100%)

SUMMARY CHARTS FOR AMERICAN REGION (LATIN AMERICAN COUNTRIES)

FIGURE 21: PLANNED SCALE UP OF ACTIVITIES 2006-2015

American Region (Latin American countries)



N.B. Population coverage is the percentage of the population that lives in an area where the activity is implemented. For TB/HIV collaborative activities the percentage refers to the proportion of the eligible population, i.e. the population living in areas with an HIV prevalence above 1%. For DOTS-Plus, it is the percentage of detected MDR-TB cases that are enrolled in DOTS-Plus programmes.

TABLE 9: MILESTONES RELATED TO IMPLEMENTATION OF DOTS EXPANSION, DOTS-PLUS AND TB/HIV ACTIVITIES (a)

American Region (Latin American countries)	2006 (b)	2010 (b)	2015 (b)
DOTS EXPANSION			
DOTS coverage	71%	100%	100%
Total number of new ss+ patients treated in DOTS programmes (thousands)	87 (123)	88 (104)	71 (80)
Case detection rate new ss+ (%)	71%	85%	90%
Treatment success rate new ss+ (%)	85%	85%	87%
Total number of new ss-/extra-pulmonary patients treated in DOTS programmes (thousands)	114 (159)	117 (136)	97 (108)
Percentage of new ss-/extra-pulmonary patients treated in DOTS programmes	72%	86%	90%
DOTS-Plus			
Total number of detected MDR-TB patients treated in DOTS-Plus programmes (thousands)	1.1 (3.0)	2.0 (3.1)	2.6 (2.6)
Percentage of detected MDR-TB cases treated in DOTS-Plus programmes	36%	65%	100%
MDR-TB treatment success rate (%)	71%	73%	75%
Percentage of culture positive cases that are re-treatment cases	16%	13%	10%
TB/HIV			
Total number of PLWHA attending HIV services screened for TB (thousands)	178 (408)	621 (760)	957 (957)
Percentage of PLWHA attending HIV services screened for TB (c)	44%	82%	100%
Total number of newly diagnosed and eligible PLWHA offered IPT (thousands)	22 (1,011)	58 (1,304)	65 (1,657)
Percentage of PLWHA offered IPT	2%	4%	4%
Total number of TB patients in DOTS programmes HIV tested and counselled (thousands)	41 (121)	119 (174)	122 (143)
Percentage of TB patients treated in DOTS programmes HIV tested and counselled	34%	68%	85%
Total number of TB patients (HIV positive and eligible) in DOTS programmes enrolled on ART (thousands)	1.3 (5.4)	4.0 (10)	4.2 (12)
Percentage of TB patients (HIV positive and eligible) in DOTS programmes enrolled on ART	24%	33%	33%

(a) The percentages are not always exactly the numerator divided by the denominator due to rounding errors.

(b) Numbers in parentheses indicate the denominator. For DOTS Expansion it is new TB cases.

For DOTS-Plus it is the total number of detected MDR-TB cases.

For PLWHA screened for TB it is the total number of PLWHA attending HIV services. For PLWHA offered IPT it is the total number of PLWHA.

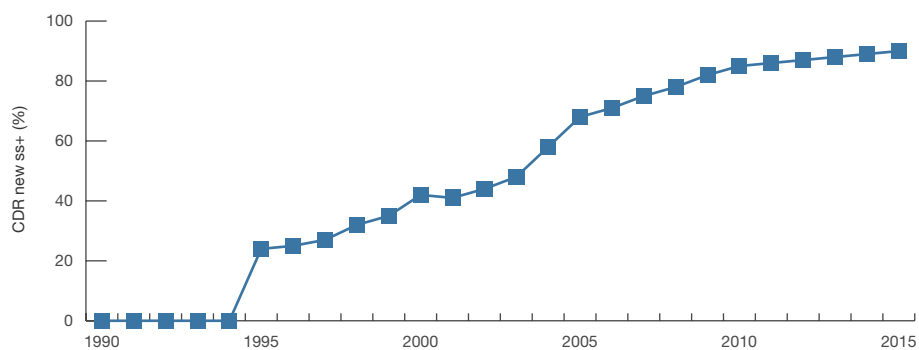
For TB patients HIV tested and counselled it is the total number of TB patients treated under DOTS in areas covered by TB/HIV collaborative activities.

For TB patients enrolled on ART it is the total number of HIV positive TB patients in DOTS programmes that are eligible for ART in areas covered by TB/HIV collaborative activities.

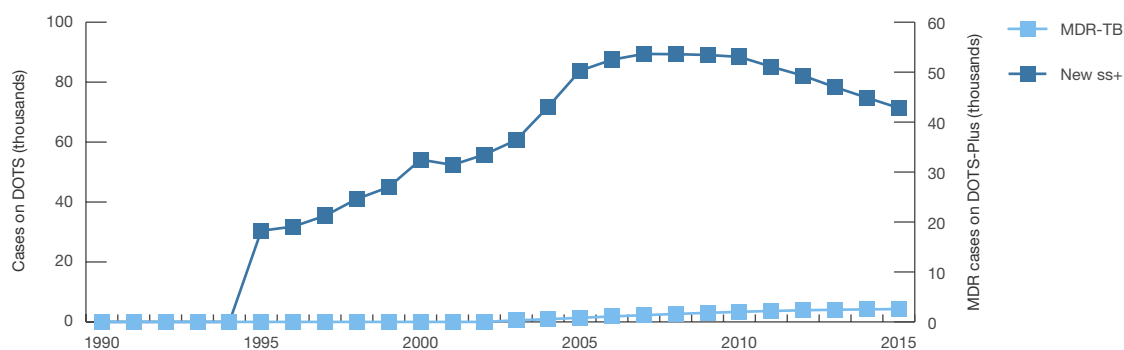
(c) HIV services include testing and counselling and HIV treatment and care services.

FIGURE 22: ESTIMATED IMPACT AND COSTS OF PLANNED INTENSIFIED ACTIVITIES 2006–2015

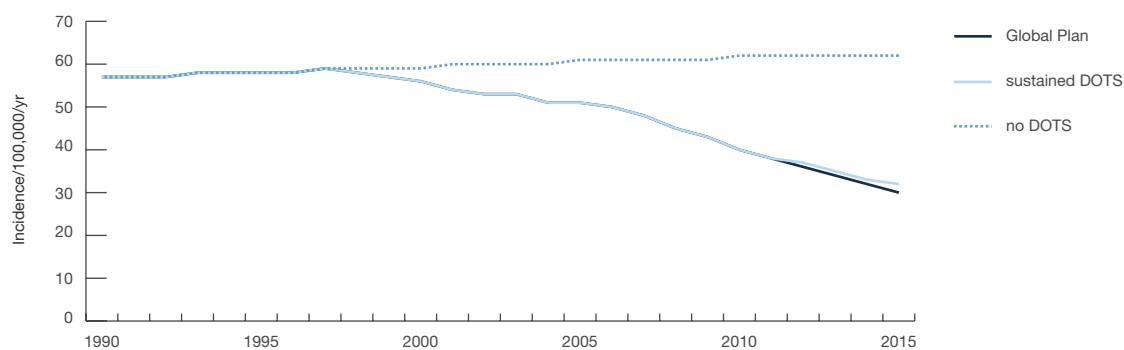
American Region (Latin American countries): Case detection rate, new ss+ cases

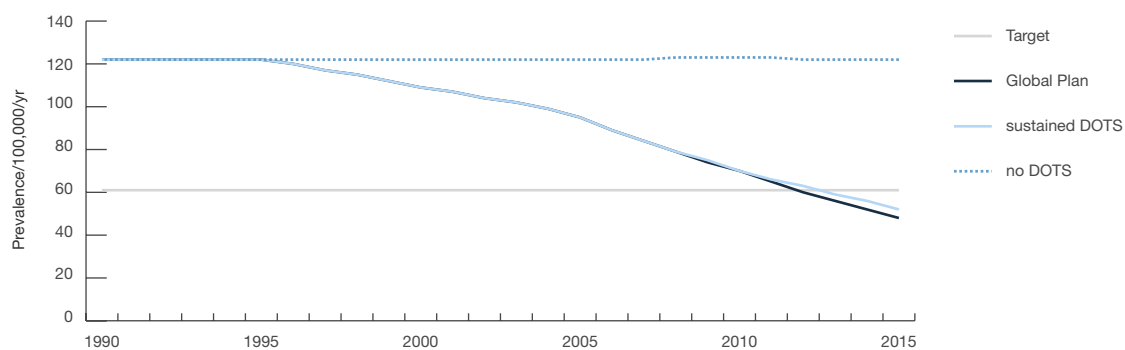
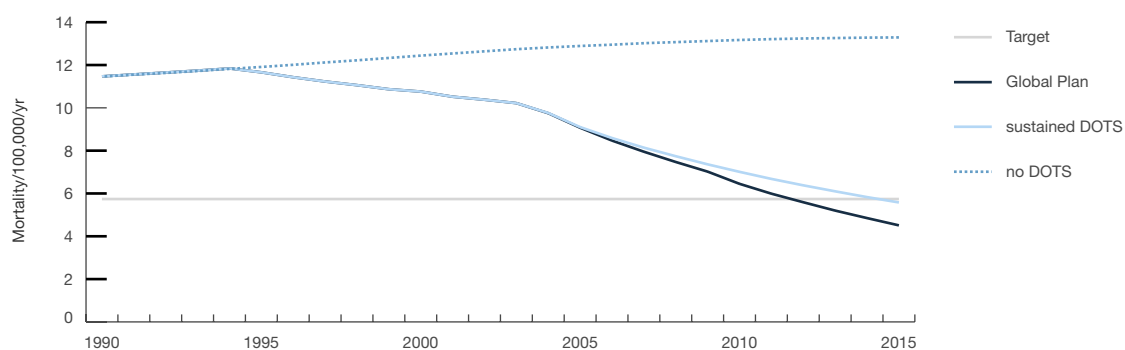
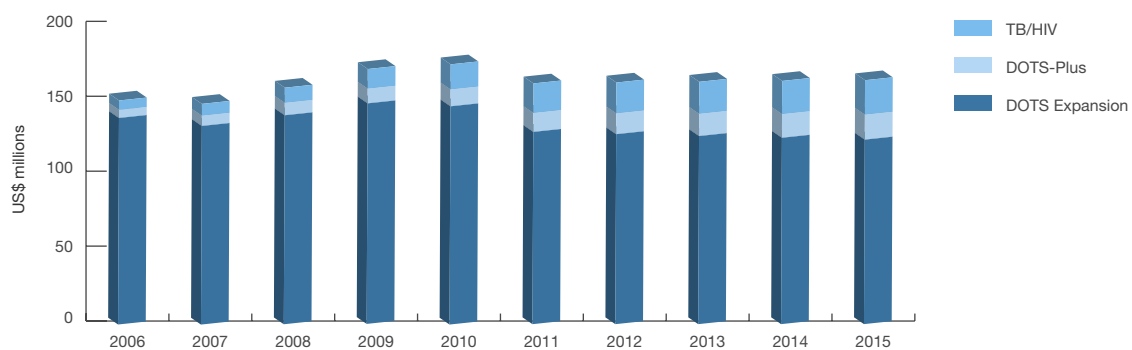


American Region (Latin American countries): Number of cases treated under DOTS/DOTS-Plus



American Region (Latin American countries): Incidence



American Region (Latin American countries): Prevalence**American Region (Latin American countries): Mortality****American Region (Latin American countries): Total costs**

7.3 Eastern Mediterranean Region: summary of planned activities, impact and costs

Achievements

The DOTS strategy was introduced in the Eastern Mediterranean Region in the mid-1990s. Almost all countries in the Region have since expanded DOTS services throughout the network of health facilities of Ministries of Health, achieving 100% population coverage as well as high treatment success rates. In 2005, the regional DOTS coverage was close to 90% and the regional average treatment success rate 84%. There are many middle-income countries in the Region with a well developed public health care infrastructure. Political commitment to TB control is generally good. Most countries have thus laid the foundation for effective TB control. In other words, they have completed the first stage in the development of TB control, which is to achieve basic DOTS coverage and good treatment outcome within the existing programmes.

Encouragingly, a few countries, such as Morocco and Tunisia, have already achieved the 2005 global targets of detecting at least 70% of new smear-positive cases and treating successfully at least 85% of these cases. TB incidence has started to decline in these countries.

There is increasing awareness in the Region of the impact of HIV on TB. Initial steps have been taken to establish HIV surveillance among TB patients and to implement collaborative TB/HIV activities where appropriate. DOTS-Plus pilot projects have been implemented in Egypt, Jordan, Lebanon, Syrian Arab Republic and Tunisia, and the Practical Approach to Lung Health (PAL) strategy has been initiated in Jordan, Morocco, Syrian Arab Republic and Tunisia.

Challenges

Geographical expansion of DOTS is incomplete in countries with complex emergencies because of poor health infrastructure or an unsafe environment, namely Afghanistan, Iraq, Somalia and Sudan (South and Darfur). The other countries in the Region are now in the second stage in the development of TB control – the stage of further improving quality and access. They are struggling with low case detection: the regional case detection rate is expected to be only 45% by the end of 2005. Case detection in the Region's two high-burden countries – Pakistan and Afghanistan – is still very low at 17% and 18%, respectively. This low case detection is due to many factors. Key components of DOTS, particularly case-finding and surveillance, are not always of high quality. In many countries of the Region, the private health care sector is booming but is not yet involved in DOTS. In addition, important segments of the public health care sector, such as social security health services or army health services, are not yet involved.

Coverage of drug resistance surveillance is low but is being expanded. The impact of HIV on TB is becoming increasingly important in countries with a generalized HIV epidemic (e.g. Djibouti, Somalia, Sudan) and in those where injecting drug use

is an important cause of HIV infection (e.g. the Islamic Republic of Iran). The challenge will be to implement collaborative TB/HIV activities to address HIV-related TB in settings where health systems are weak and health service delivery is complicated by civil conflict.

Priority activities 2006–2015

The first priority is to improve further the quality of key basic components of DOTS, such as laboratory diagnosis, surveillance and drug management, and to develop and sustain adequate human resources to deliver quality DOTS. Public-private mix for DOTS will be scaled up widely. The involvement of the NGO sector will continue to be essential in areas with complex emergencies.

In order to facilitate implementation of DOTS-Plus, culture and drug susceptibility testing services will be scaled up. It is expected that by 2015 DST will be provided for 100% of previously treated TB patients. DOTS-Plus will be expanded in a stepwise approach to reach 100% coverage by 2015. Scaling up culture services will also improve the diagnosis of smear-negative TB cases, which is particularly important for areas with high HIV prevalence.

To further improve quality across different health sectors, and help boost case detection, PAL will be implemented widely in the region. Community DOTS will be scaled up in selected rural areas. Surveillance is important to assess and monitor the burden of HIV infection in TB patients. Collaborative TB/HIV activities need to be implemented and strengthened in settings with a high HIV burden.

Operational research activities will continue to be promoted in order to solve problems identified through the TB surveillance and TB control information system. Countries in the Eastern Mediterranean Region will be supported in adapting, developing and implementing special strategies to control TB, especially in poor settings and in big cities. In order to realize sustainable political, technical and financial support to TB control, Stop TB Partnerships will be developed at regional and national levels, and strategic approaches for communication, advocacy and social mobilization will be adapted and implemented.

Expected effects and costs

Successful implementation of the activities described above is expected to increase case detection rapidly to 73% by 2010 and 80% by 2015. Treatment success rate will increase from 84% to 87% in 2010 and be sustained at this level. TB incidence, prevalence and death rate are already falling in the Region. Planned activities are predicted to boost the decline further and the 2015 Partnership targets, linked to the MDG target, will be met in the Eastern Mediterranean Region.

During the period of the plan (2006–2015), it is estimated that 3.6 million people will be treated in DOTS programmes and 48 000 in DOTS-Plus. In addition, 36 000 TB patients will be enrolled on antiretroviral therapy. The combined effect of all interventions will be to prevent about 798 000 deaths, in comparison with a

PART II: GLOBAL AND REGIONAL SCENARIOS FOR TB CONTROL 2006–2015

situation in which no DOTS programmes are implemented, or about 196 000 deaths in comparison with a situation in which TB control efforts are sustained at 2005 levels.

The total estimated cost of DOTS expansion, DOTS-Plus and TB/HIV control activities in the Eastern Mediterranean Region from 2006 to 2015 is US\$2.6 billion.

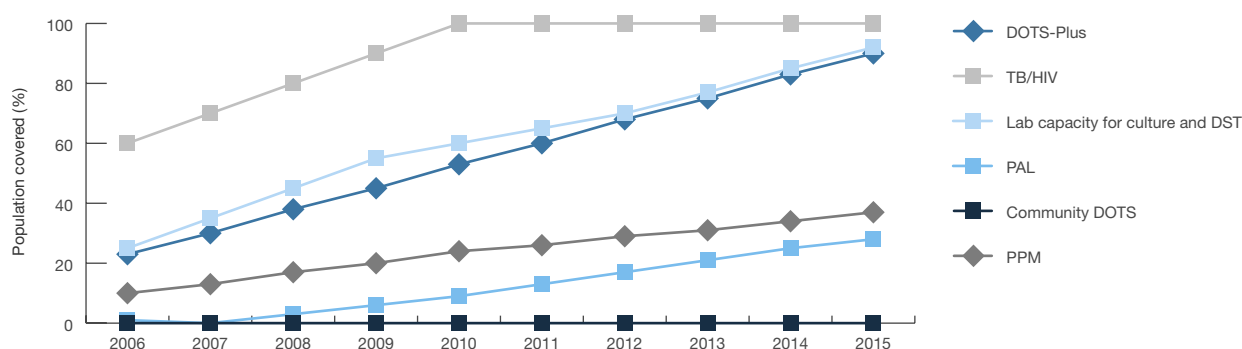
**TABLE 10: COST OF PLANNED TB CONTROL ACTIVITIES
EASTERN MEDITERRANEAN REGION 2006–2015**

Planned activities	US\$ millions
DOTS expansion and quality	2,221 (85%)
DOTS-Plus	226 (9%)
TB/HIV collaborative activities	175 (7%)
TOTAL	2,622 (100%)

SUMMARY CHARTS FOR EASTERN MEDITERRANEAN REGION

FIGURE 23: PLANNED SCALE UP OF ACTIVITIES 2006-2015

Eastern Mediterranean Region



N.B. Population coverage is the percentage of the population that lives in an area where the activity is implemented. For TB/HIV collaborative activities the percentage refers to the proportion of the eligible population, i.e. the population living in areas with an HIV prevalence above 1%. For DOTS-Plus, it is the percentage of detected MDR-TB cases that are enrolled in DOTS-Plus programmes.

TABLE 11: MILESTONES RELATED TO IMPLEMENTATION OF DOTS EXPANSION, DOTS-PLUS AND TB/HIV ACTIVITIES (a)

Eastern Mediterranean Region	2006 (b)	2010 (b)	2015 (b)
DOTS EXPANSION			
DOTS coverage	100%	100%	100%
Total number of new ss+ patients treated in DOTS programmes (thousands)	133 (267)	180 (247)	154 (194)
Case detection rate new ss+ (%)	50%	73%	80%
Treatment success rate new ss+ (%)	85%	85%	87%
Total number of new ss-/extra-pulmonary patients treated in DOTS programmes (thousands)	166 (331)	224 (309)	193 (244)
Percentage of new ss-/extra-pulmonary patients treated in DOTS programmes	50%	73%	79%
DOTS-Plus			
Total number of detected MDR-TB patients treated in DOTS-Plus programmes (thousands)	0.7 (3.0)	4.3 (7.4)	9.2 (9.2)
Percentage of detected MDR-TB cases treated in DOTS-Plus programmes	25%	58%	100%
MDR-TB treatment success rate (%)	71%	73%	75%
Percentage of culture positive cases that are re-treatment cases	13%	12%	10%
TB/HIV			
Total number of PLWHA attending HIV services screened for TB (thousands)	98 (159)	241 (241)	323 (323)
Percentage of PLWHA attending HIV services screened for TB (c)	62%	100%	100%
Total number of newly diagnosed and eligible PLWHA offered IPT (thousands)	6.2 (254)	6.8 (390)	6.9 (526)
Percentage of PLWHA offered IPT	2%	2%	1%
Total number of TB patients in DOTS programmes HIV tested and counselled (thousands)	152 (299)	344 (404)	296 (348)
Percentage of TB patients treated in DOTS programmes HIV tested and counselled	51%	85%	85%
Total number of TB patients (HIV positive and eligible) in DOTS programmes enrolled on ART (thousands)	1.5 (3.4)	3.6 (6.6)	4.3 (8.2)
Percentage of TB patients (HIV positive and eligible) in DOTS programmes enrolled on ART	46%	57%	62%

(a) The percentages are not always exactly the numerator divided by the denominator due to rounding errors.

(b) Numbers in parentheses indicate the denominator. For DOTS Expansion it is new TB cases.

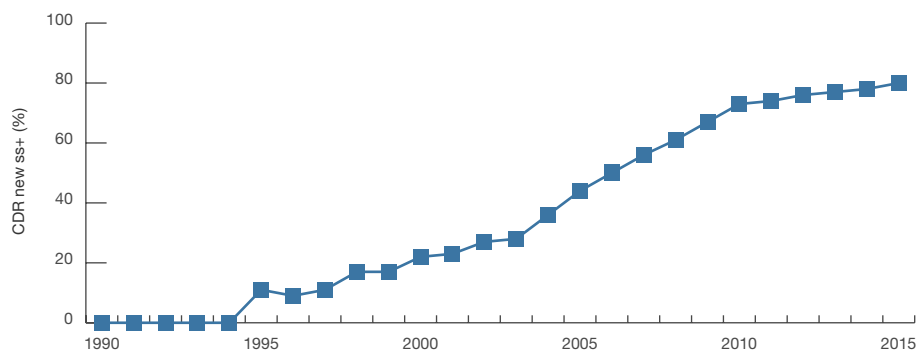
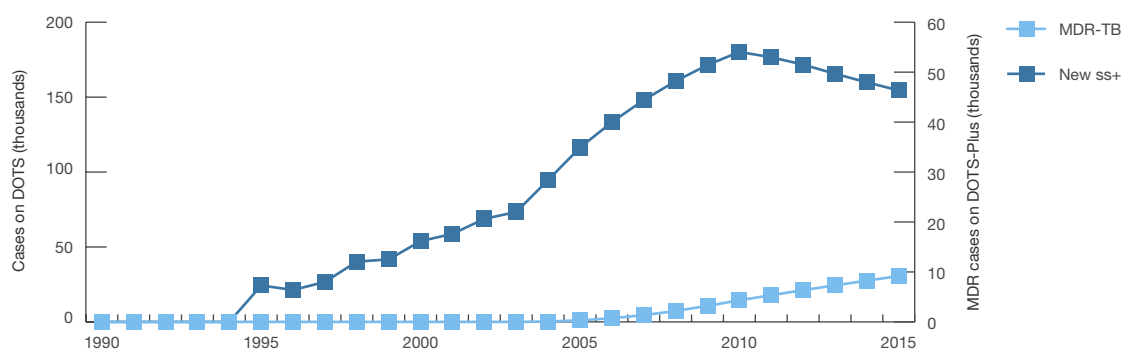
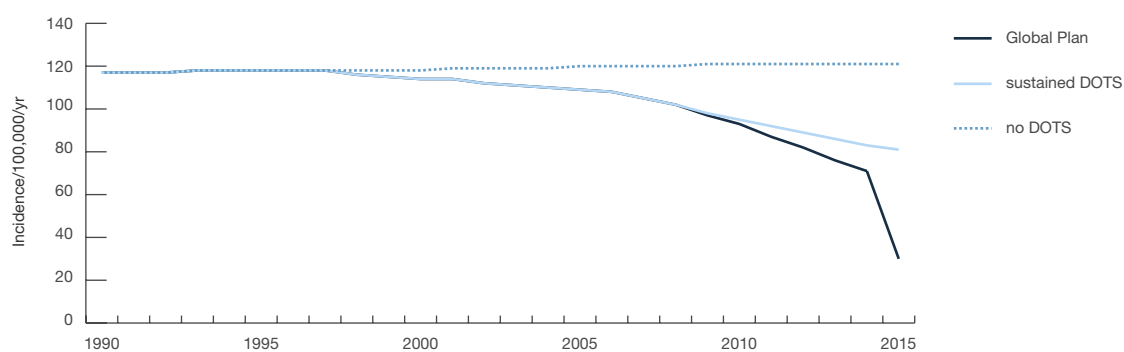
For DOTS-Plus it is the total number of detected MDR-TB cases.

For PLWHA screened for TB it is the total number of PLWHA attending HIV services. For PLWHA offered IPT it is the total number of PLWHA.

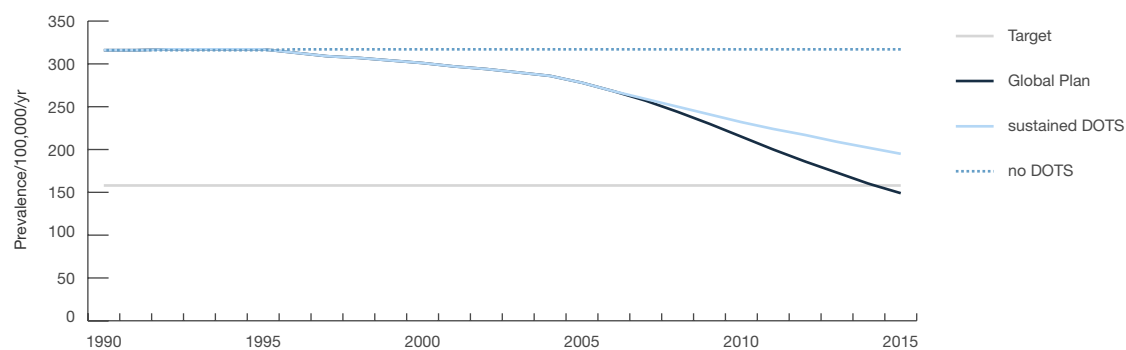
For TB patients HIV tested and counselled it is the total number of TB patients treated under DOTS in areas covered by TB/HIV collaborative activities.

For TB patients enrolled on ART it is the total number of HIV positive TB patients in DOTS programmes that are eligible for ART in areas covered by TB/HIV collaborative activities.

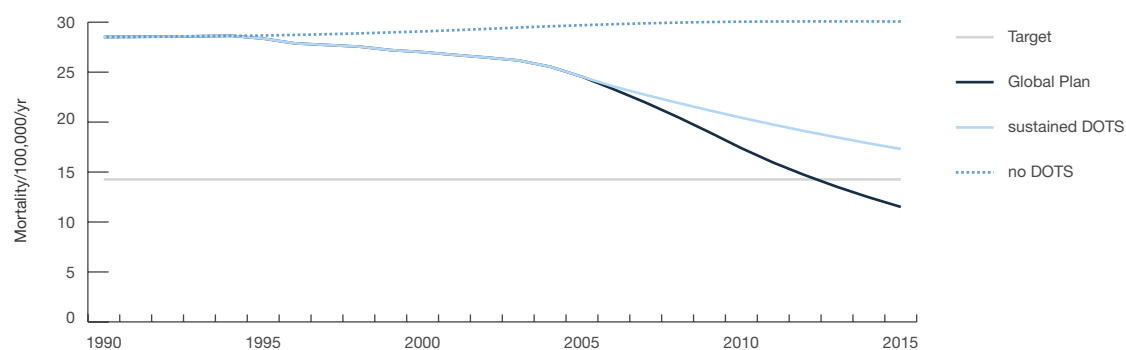
(c) HIV services include testing and counselling and HIV treatment and care services.

FIGURE 24: ESTIMATED IMPACT AND COSTS OF PLANNED INTENSIFIED ACTIVITIES 2006–2015**Eastern Mediterranean Region: Case detection rate, new ss+ cases****Eastern Mediterranean Region: Number of cases treated under DOTS/DOTS-Plus****Eastern Mediterranean Region: Incidence**

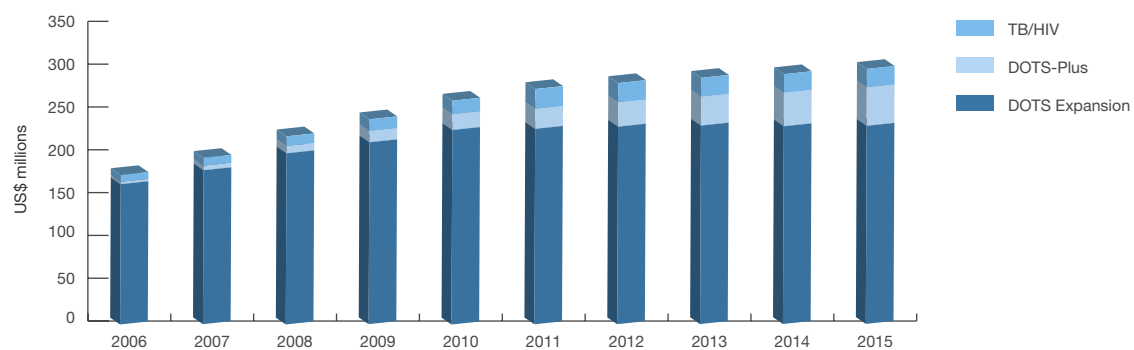
Eastern Mediterranean Region: Prevalence



Eastern Mediterranean Region: Mortality



Eastern Mediterranean Region: Total costs



7.4 Eastern European Region: summary of planned activities, impact and costs

Achievements

The rapid increase in case notification rates in the Eastern European Region after the collapse of the Soviet Union – reaching nearly 15% per year – appears to have been halted. Case notification rates peaked in 2001, since when they have started slowly to decline. DOTS coverage increased from 30% in 2000 to 39% in 2003 and is expected to reach 46% in 2005. The case detection rate was only 22% in 2003 but is expected to reach 40% in 2005. However, this progress has to be seen against a 2005 global target of 70%. The treatment success rate in DOTS programmes reached 76% in the 2002 cohort, with a target of 85% for 2005. Improved treatment success rates can be attributed to improved implementation of DOTS, sometimes as a result of the introduction of incentives and enablers targeting socially vulnerable TB patients and health workers involved in TB control. Special risk groups – minorities, refugees and asylum seekers – have been targeted in some places, but the interventions are limited to the project areas, in spite of the good results achieved.

With assistance from the Green Light Committee and several partners, sound MDR-TB control based on WHO recommendations has been implemented countrywide in Estonia and Latvia, and pilot-testing has started in Azerbaijan and Georgia (in prison projects), Kyrgyzstan, the Republic of Moldova, Romania, the Russian Federation and Uzbekistan. A number of countries are planning to set up pilot projects and scale up DOTS-Plus, with funding mainly from the GFATM. Pilot projects of collaborative TB/HIV activities to address HIV-related TB have commenced or are planned in most of the countries with a high burden of TB/HIV coinfection.

Challenges

The Eastern European Region has the lowest level of DOTS coverage and DOTS case detection of all regions. The regional treatment success rate is second-lowest, only slightly higher than that in the high HIV prevalence African Region. The expansion of high quality TB diagnostic and treatment services in the Eastern European Region is severely limited by lack of political will, weak public health infrastructure (particularly a lack of laboratory capacity to perform high quality bacteriological investigations), the vertical organization of TB control programmes, limited involvement of important health care providers, and, perhaps most importantly, inadequately trained human resources.

The majority of TB patients in the Region belong to socially vulnerable groups, such as the homeless, the unemployed, migrants, alcohol-dependent people, and ex-prisoners. With measures to alleviate poverty and improve living standards in these countries, public health efforts to control TB will have only limited impact.

The wide extent of drug resistance (including MDR-TB) in Eastern Europe represents a critical challenge to TB control, as reflected in low treatment success rates. MDR-TB patients managed outside DOTS-Plus projects are treated according to

the availability of drugs and the ability of patients to purchase drugs, with a high risk of inadequate treatment and continuing amplification of drug resistance. Three reports on global anti-TB drug resistance surveillance have confirmed the serious scale and spread of drug resistance in Eastern Europe, especially in the former Soviet Union countries. In addition, drug resistance patterns are more severe than in other regions, with TB strains often resistant to all first-line drugs and also to some second-line drugs.

Prisons in the former Soviet Union have been highlighted as a breeding ground for TB, and especially MDR-TB, which spreads easily as a result of overcrowding, inadequate ventilation, malnutrition and poor hygiene. The incidence of TB is approximately 50 times higher, and the mortality rate approximately 28 times higher, among prisoners than among the civilian population in these countries. Drug shortages and weak laboratory services resulting in late diagnosis and inadequate treatment have led to a high burden of MDR-TB in the penal system. In addition, TB control in prisons is poorly integrated with civilian TB control programmes.

HIV has spread rapidly in the Eastern European Region since the late 1990s, particularly among intravenous drug users. An estimated 50–90% of HIV infections in Eastern Europe and Central Asia are caused by injecting drug use. The lack of coordination between TB and HIV/AIDS control programmes in these countries and the absence of a clear strategy to address HIV in intravenous drug users – in conjunction with the general constraints in TB control described above – are likely to result in a large epidemic of HIV-related TB among intravenous drug users in the Region, with the worrying possibility of overlap between HIV and MDR-TB.

Priority activities 2006–2015

Mobilizing political support is crucial to implement the priority activities. An important priority is to complete DOTS coverage, while increasing the involvement of all relevant health care providers, especially the public primary health care sector, in identifying suspects, and carrying out primary diagnosis and follow-up treatment of TB patients. Special attention is needed to link prison health services (and other non-Ministry of Health services) with national TB programmes. Incentive schemes need to be scaled up. The current role of the private sector in TB care should be studied and the potential for collaboration explored. The quality of training activities to develop and sustain a competent workforce for TB control must be assured.

It is essential to improve the laboratory network to meet international standards and provide reliable services for diagnosing TB and MDR-TB. Drug resistance surveillance will be expanded. Quality-assured culture and drug susceptibility testing should be available to cover 90% of all TB cases in 2010 and 100% in 2015 respectively. A massive effort is needed to scale-up DOTS-Plus implementation beyond the pilot phase and as an integrated component of TB control services. Population coverage of DOTS-Plus should expand to 70% in 2010 and 100% in 2015.

Coordination for TB/HIV should be launched in countries to establish surveillance of HIV among TB patients and to implement collaborative TB/HIV activities, especially targeted at injecting drug users. All the countries with a high burden of HIV-related TB will be implementing collaborative TB/HIV activities, including HIV surveillance among TB patients, by 2010.

Expected effects and costs

Through intensified efforts, DOTS is expected to reach 100% population coverage by 2010. Case detection is expected to increase to 72% in 2010 and then accelerate to 97% in 2015. The treatment success rate is expected to reach 85% by 2010.

About 2.2 million people will be treated in DOTS programmes from 2006 to 2015, and more than 410 000 in DOTS-Plus. In addition, about 31 000 TB patients will be enrolled on antiretroviral therapy. The combined effect of all interventions will be to prevent about 218 000 deaths, in comparison with a situation in which no DOTS programmes are implemented, or about 155 000 deaths in comparison with a situation in which TB control efforts are sustained at 2005 levels. With the implementation of sound TB control, it is also expected that the estimated proportion of re-treatment cases will decrease from 42% in 2005 to 18% in 2015.

The MDG target to have halted and begun to reverse the incidence of TB by 2015 will be met. The Partnership's additional 2015 targets to halve prevalence and death rates from the 1990 baseline will be achieved later than 2015 in Eastern Europe. This is because of the rapid increase in these parameters during the 1990s, and the additional serious constraints described above. The estimated total cost of DOTS expansion, DOTS-Plus and TB/HIV control activities in the Eastern European region from 2006 to 2015 is US\$8.9 billion.

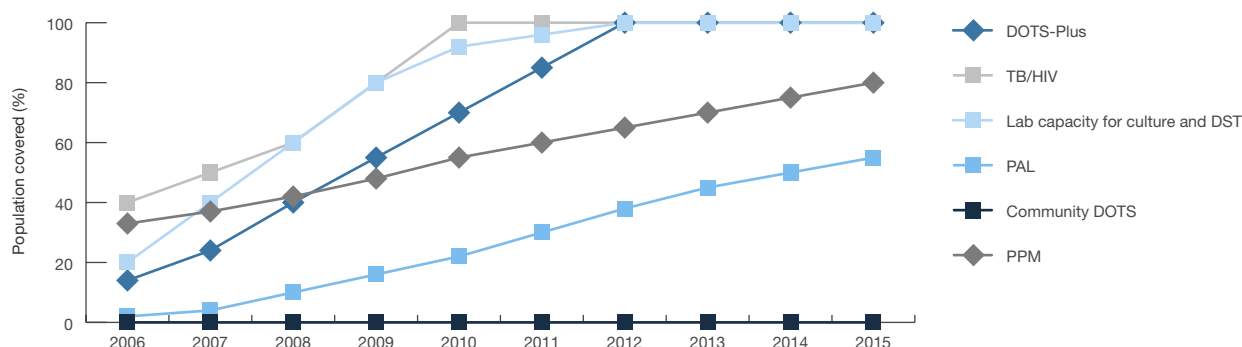
TABLE 12: COST OF PLANNED TB CONTROL ACTIVITIES, EASTERN EUROPEAN REGION 2006–2015

Planned activities	US\$ millions
DOTS expansion and quality	4,809 (54%)
DOTS-Plus	3,928 (44%)
TB/HIV collaborative activities	186 (2%)
TOTAL	8,923 (100%)

SUMMARY CHARTS FOR EASTERN EUROPEAN REGION

FIGURE 25: PLANNED SCALE UP OF ACTIVITIES 2006–2015

Eastern European Region



N.B. Population coverage is the percentage of the population that lives in an area where the activity is implemented. For TB/HIV collaborative activities the percentage refers to the proportion of the eligible population, i.e. the population living in areas with an HIV prevalence above 1%. For DOTS-Plus, it is the percentage of detected MDR-TB cases that are enrolled in DOTS-Plus programmes.

TABLE 13: MILESTONES RELATED TO IMPLEMENTATION OF DOTS EXPANSION, DOTS-PLUS AND TB/HIV ACTIVITIES (a)

Eastern European Region	2006 (b)	2010 (b)	2015 (b)
DOTS EXPANSION			
DOTS coverage	56%	100%	100%
Total number of new ss+ patients treated in DOTS programmes (thousands)	73 (158)	110 (151)	111 (113)
Case detection rate new ss+ (%)	46%	73%	98%
Treatment success rate new ss+ (%)	77%	85%	85%
Total number of new ss-/extra-pulmonary patients treated in DOTS programmes (thousands)	88 (198)	108 (194)	137 (149)
Percentage of new ss-/extra-pulmonary patients treated in DOTS programmes	44%	56%	92%
DOTS-Plus			
Total number of detected MDR-TB patients treated in DOTS-Plus programmes (thousands)	14 (78)	50 (71)	45 (45)
Percentage of detected MDR-TB cases treated in DOTS-Plus programmes	18%	70%	100%
MDR-TB treatment success rate (%)	73%	76%	80%
Percentage of culture positive cases that are re-treatment cases	39%	30%	18%
TB/HIV			
Total number of PLWHA attending HIV services screened for TB (thousands)	82 (171)	745 (745)	1,143 (1,143)
Percentage of PLWHA attending HIV services screened for TB (c)	48%	100%	100%
Total number of newly diagnosed and eligible PLWHA offered IPT (thousands)	21 (714)	141 (1,582)	203 (2,468)
Percentage of PLWHA offered IPT	3%	9%	8%
Total number of TB patients in DOTS programmes HIV tested and counselled (thousands)	18 (54)	111 (131)	126 (149)
Percentage of TB patients treated in DOTS programmes HIV tested and counselled	34%	85%	85%
Total number of TB patients (HIV positive and eligible) in DOTS programmes enrolled on ART (thousands)	0.5 (1.1)	3.1 (5.3)	5.1 (9.2)
Percentage of TB patients (HIV positive and eligible) in DOTS programmes enrolled on ART	45%	57%	59%

(a) The percentages are not always exactly the numerator divided by the denominator due to rounding errors.

(b) Numbers in parentheses indicate the denominator. For DOTS Expansion it is new TB cases.

For DOTS-Plus it is the total number of detected MDR-TB cases.

For PLWHA screened for TB it is the total number of PLWHA attending HIV services. For PLWHA offered IPT it is the total number of PLWHA.

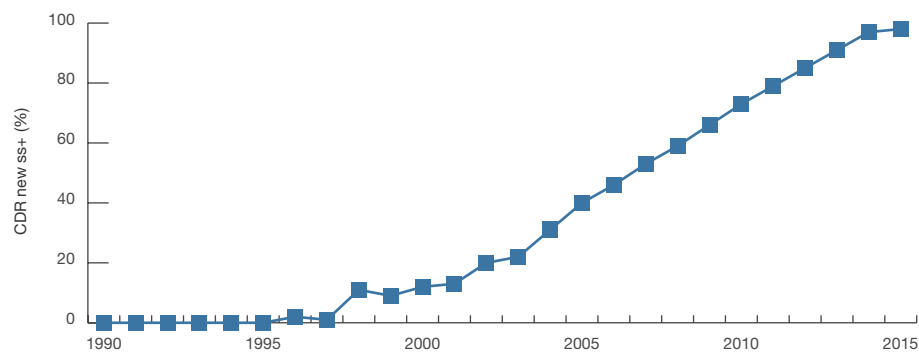
For TB patients HIV tested and counselled it is the total number of TB patients treated under DOTS in areas covered by TB/HIV collaborative activities.

For TB patients enrolled on ART it is the total number of HIV positive TB patients in DOTS programmes that are eligible for ART in areas covered by TB/HIV collaborative activities.

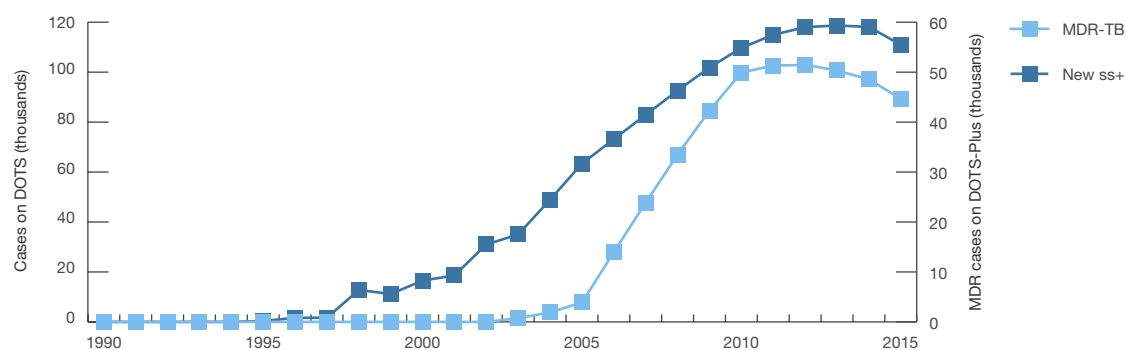
(c) HIV services include testing and counselling and HIV treatment and care services.

FIGURE 26: ESTIMATED IMPACT AND COSTS OF PLANNED INTENSIFIED ACTIVITIES 2006–2015

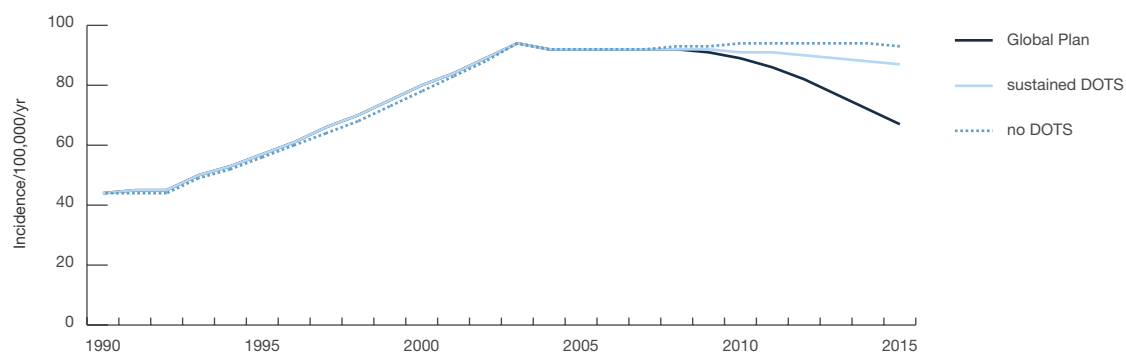
Eastern European Region: Case detection rate, new ss+ cases

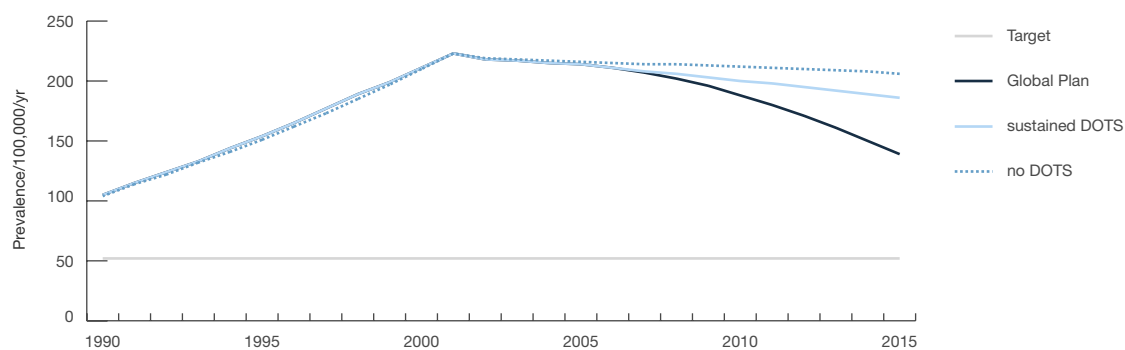
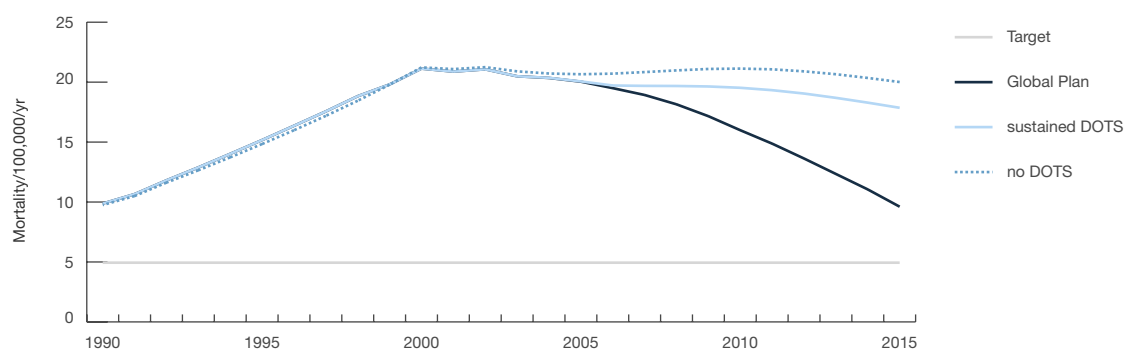
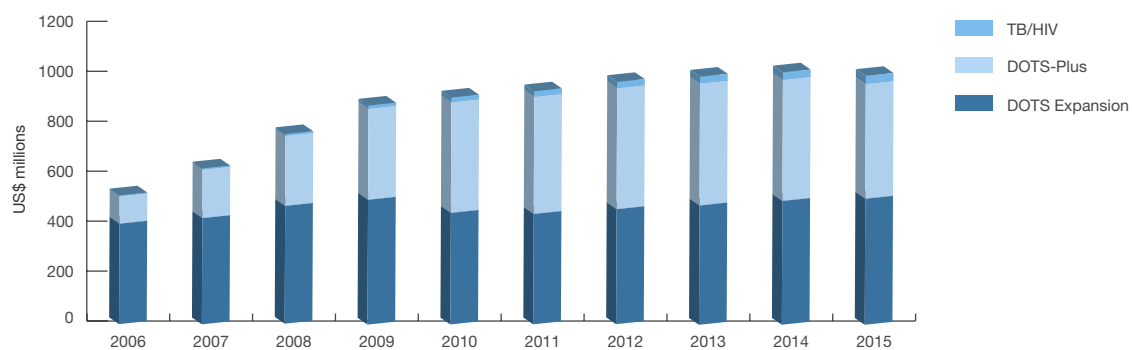


Eastern European Region: Number of cases treated under DOTS/DOTS-Plus



Eastern European Region: Incidence



Eastern European Region: Prevalence**Eastern European Region: Mortality****Eastern European Region: Total costs**

7.5 South-East Asian Region: summary of planned activities, impact and costs

Achievements

DOTS expanded rapidly in the South-East Asian Region over the period of the Partnership's first Global Plan (2001–2005), and 100% geographical coverage was achieved in 2005. All the Region's TB high-burden countries (Bangladesh, India, Indonesia, Myanmar and Thailand) have made impressive progress in improving coverage and quality. Case detection increased from a mere 18% in 2000 to 45% in 2003 and is expected to reach about 65% by the end of 2005, against the World Health Assembly and Stop TB Partnership's 2005 target of 70%. The treatment success rate in the region is already 85.3%, meeting the 2005 target of 85%. This progress has been made possible through strong political commitment and large investments in improved infrastructure, reliable drug supply, increased staffing, improved laboratory services, and intensified training and supervision.

Increasingly, TB programmes in the Region have reached out to a wide range of public and private health care providers in order to increase access to quality services. Community involvement is already a prominent feature in several TB programmes in the Region. NGOs with roots in the local community are playing leading roles in several places. Community volunteers are widely used to supervise treatment.

The WHO's Regional Strategic Plan on HIV/TB recommends key strategies and interventions for reducing HIV/TB-associated morbidity and mortality through enhanced collaboration between national TB and AIDS programmes. Thailand has established comprehensive joint TB/HIV services throughout the country. India, Indonesia, and Myanmar have established formal collaboration between their national TB programmes and national AIDS programmes and have identified collaborative TB/HIV interventions and activities, while three countries (India, Myanmar and Thailand) are planning to carry out HIV surveillance among TB patients.

DOTS-Plus pilot projects are being implemented in India and Nepal. India has a national plan for drug resistance surveillance as well as a plan for pilot-testing and implementing DOTS-Plus. Currently, the capacity for culture and drug susceptibility testing is very limited in the Region, though Bangladesh, Indonesia and Myanmar are also planning to scale up quality-assured culture, DST and DOTS-Plus with resources from the GFATM.

Challenges

Over the Plan period of 2006–2015, strong political commitment needs to be maintained and the current level of funding increased in order to continue to improve access to quality TB services. With an estimated 35% of cases still not being reached through existing DOTS services, significant and sustained efforts will be needed to continue the current positive trends. Most countries in the Region have a very diversified health care system, with a number of public and private health care providers still not linked to the DOTS programmes. A major challenge for the future is to

involve a critical mass of these providers in extending quality-assured DOTS services in both urban and rural areas.

The South-East Asian Region is the Region second-hardest hit by the HIV-epidemic, after sub-Saharan Africa. More than 6 million people were estimated to be living with HIV in December 2004. The extent of the epidemic of TB/HIV coinfection in the Region will depend on the future course of the HIV epidemic, as well as on efforts to control TB. Estimated HIV prevalence among TB patients ranges from 0.1% in Bangladesh, through 4.6% in India, to 8.7% in Thailand. Data from a region of Thailand with low HIV prevalence illustrate that the uptake of HIV counselling and testing is low among TB patients, a challenge that will need to be addressed as HIV counselling and testing facilities become more readily accessible.

Coverage of drug resistance surveillance is low in the Region, mainly because of limited data from Bangladesh, India and Indonesia, making it difficult to assess the regional MDR-TB situation. Available data show that, while the levels of MDR-TB among previously untreated cases may be below 3%, the large numbers of TB cases translate into a significant burden of MDR-TB in South-East Asia. It is estimated that 25% of all MDR-TB cases worldwide are in India alone. Most national TB programmes in the Region do not at present diagnose and treat MDR-TB patients, though many other public and private providers do, using second-line drugs, which are widely available.

Priority activities 2006–2015

First and foremost, attention will need to be focused on sustaining commitment and resources for TB control, particularly sustaining adequate human resource capabilities to deliver quality DOTS services. Second, to increase the reach of DOTS, scaling up the participation of other sectors – particularly the large and vibrant private sector in the Region – will be critical. Expanding the public-private mix for DOTS will be especially important in the rapidly growing urban areas, where TB control struggles to cope with a complex range of health providers as well as a diverse mix of TB patients, including slum-dwellers and migrants.

Community outreach activities, as well as education, information and communications campaigns empowering communities to develop their own strategies, will be important if quality services are to be provided for the poor and the marginalized in remote rural and cross-border areas, and among displaced communities. Decentralizing services and involving all health and social workers at the grass-roots level should help reduce barriers to access for women and children.

The Region also needs to focus on the growing problem of drug resistance. Improving the quality of DOTS services made available by all health care providers will halt and reverse the development of drug resistance. DST should be scaled up to cover 20% of new TB patients and 100% of previously treated TB patients in 2015. DOTS-Plus population coverage should expand to 50% by 2010 and 100% by 2015.

Surveillance of HIV among TB patients needs to be established in countries with a high burden of HIV-related TB. Collaborative TB/HIV activities will be expanded to all populations with a high burden of HIV-related TB by the end of 2009. PAL initiatives will be scaled up, with a main focus on urban areas.

Expected effects and costs

Through the intensified efforts outlined above, case detection is expected to increase to 79% by 2010 and 84% by 2015. Treatment success rate is already at the 2005 target level of 85% and is expected to increase to between 85%-90% by 2010 and then remain at this level (noting that 87% is used as the treatment success rate in the scenario calculations). As a consequence, the expected decline in incidence, prevalence and death rates would mean that the Partnership's targets would be met ahead of the target date of 2015 in the South-East Asian Region.

The projected rapid decline in incidence and new cases under the scenario shown in the figures is based on the assumption that all countries and particularly the five high-burden countries in the Region will continue to maintain or surpass the 70% case detection and 85% treatment success rates. These rates of decline will also depend on how effectively initiatives such as DOTS-Plus, PPM-DOTS and interventions for TB-HIV among others, are implemented to counterbalance the effect of HIV and the emergence of MDR-TB in countries in the Region.

During the period of the Plan (2006–2015), it is estimated that at least 16 million people will be treated in DOTS programmes and more than 145 000 in DOTS-Plus. In addition, 306 000 TB patients will be enrolled on antiretroviral therapy. The combined effect of all interventions will be to prevent about 5 million deaths, in comparison with a situation in which no DOTS programmes are implemented, or about 460 000 deaths in comparison with a situation in which TB control efforts are sustained at 2005 levels. With the implementation of sound TB control, the estimated proportion of re-treatment cases should decrease from 25% in 2005 to 12% in 2015.

The total estimated cost of DOTS expansion, DOTS-Plus and TB/HIV control activities in the South-East Asian region from 2006 to 2015 is US\$5.5 billion.

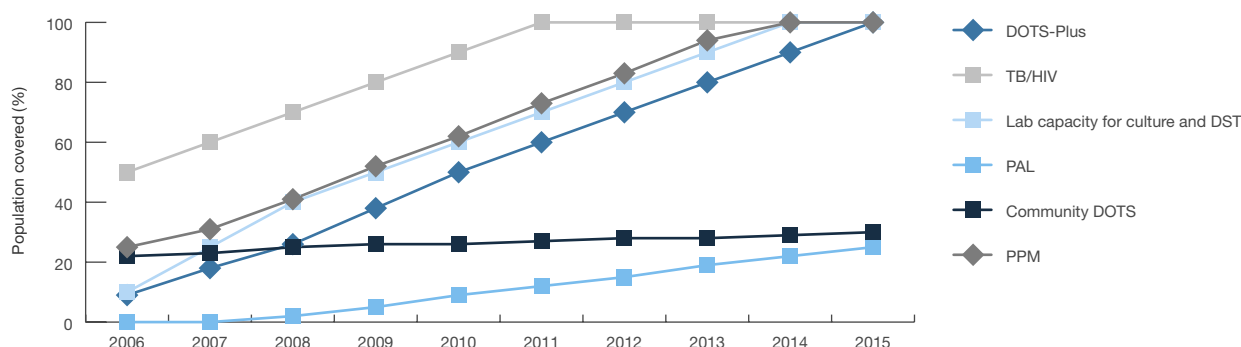
TABLE 14: COST OF PLANNED TB CONTROL ACTIVITIES, SOUTH-EAST ASIAN REGION 2006–2015

Planned activities	US\$ millions
DOTS expansion and quality	3,778 (68%)
DOTS-Plus	678 (12%)
TB/HIV collaborative activities	1,112 (20%)
TOTAL	5,569 (100%)

SUMMARY CHARTS FOR SOUTH-EAST ASIAN REGION

FIGURE 27: PLANNED SCALE UP OF ACTIVITIES 2006-2015

South-East Asian Region



N.B. Population coverage is the percentage of the population that lives in an area where the activity is implemented. For TB/HIV collaborative activities the percentage refers to the proportion of the eligible population, i.e. the population living in areas with an HIV prevalence above 1%. For DOTS-Plus, it is the percentage of detected MDR-TB cases that are enrolled in DOTS-Plus programmes.

TABLE 15: MILESTONES RELATED TO IMPLEMENTATION OF DOTS EXPANSION, DOTS-PLUS AND TB/HIV ACTIVITIES (a)

South-East Asian Region	2006 (b)	2010 (b)	2015 (b)
DOTS EXPANSION			
DOTS coverage	100%	100%	100%
Total number of new ss+ patients treated in DOTS programmes (thousands)	790 (1178)	742 (939)	562 (668)
Case detection rate new ss+ (%)	67%	79%	84%
Treatment success rate new ss+ (%)	85%	87%	87%
Total number of new ss-/extra-pulmonary patients treated in DOTS programmes (thousands)	1,012 (1,507)	953 (1,209)	737 (880)
Percentage of new ss-/extra-pulmonary patients treated in DOTS programmes	67%	79%	84%
DOTS-Plus			
Total number of detected MDR-TB patients treated in DOTS-Plus programmes (thousands)	2.0 (22)	14 (34)	26 (26)
Percentage of detected MDR-TB cases treated in DOTS-Plus programmes	9%	43%	100%
MDR-TB treatment success rate (%)	71%	73%	75%
Percentage of culture positive cases that are re-treatment cases	24%	19%	12%
TB/HIV			
Total number of PLWHA attending HIV services screened for TB (thousands)	307 (550)	692 (749)	877 (877)
Percentage of PLWHA attending HIV services screened for TB (c)	56%	92%	100%
Total number of newly diagnosed and eligible PLWHA offered IPT (thousands)	59 (1,049)	157 (1,244)	199 (1,421)
Percentage of PLWHA offered IPT	6%	13%	14%
Total number of TB patients in DOTS programmes HIV tested and counselled (thousands)	528 (1,243)	895 (1,170)	762 (896)
Percentage of TB patients treated in DOTS programmes HIV tested and counselled	43%	77%	85%
Total number of TB patients (HIV positive and eligible) in DOTS programmes enrolled on ART (thousands)	21 (47)	31 (51)	33 (55)
Percentage of TB patients (HIV positive and eligible) in DOTS programmes enrolled on ART	45%	55%	59%

(a) The percentages are not always exactly the numerator divided by the denominator due to rounding errors.

(b) Numbers in parentheses indicate the denominator. For DOTS Expansion it is new TB cases.

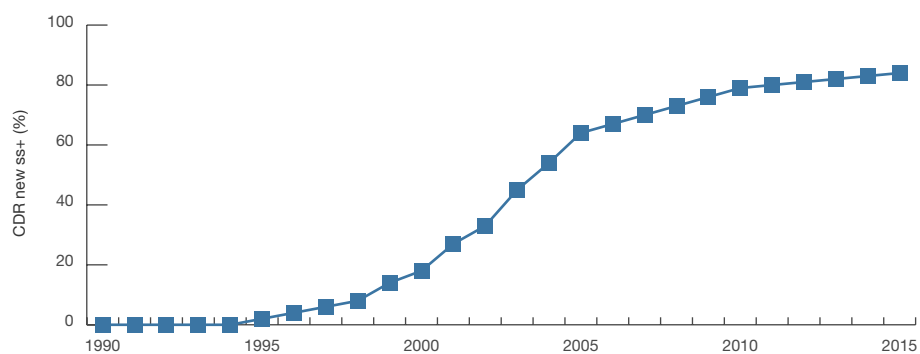
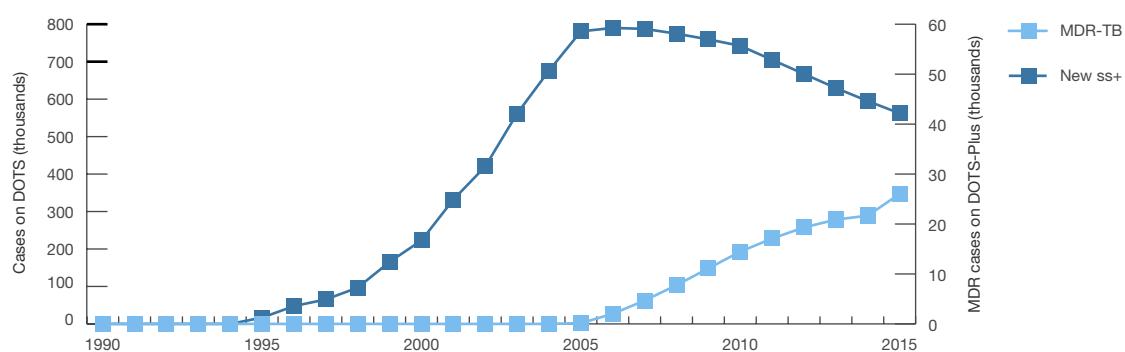
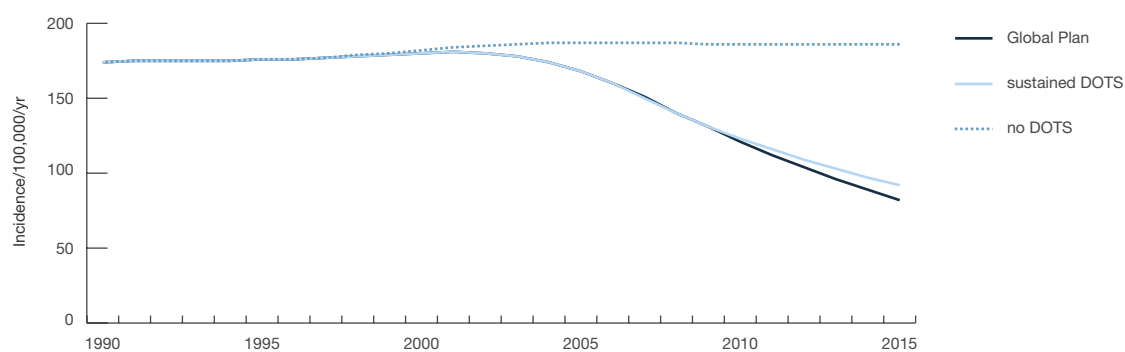
For DOTS-Plus it is the total number of detected MDR-TB cases.

For PLWHA screened for TB it is the total number of PLWHA attending HIV services. For PLWHA offered IPT it is the total number of PLWHA.

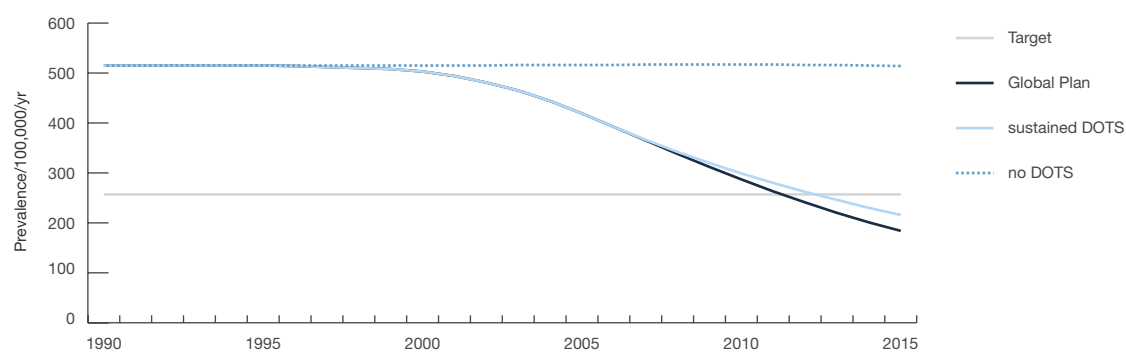
For TB patients HIV tested and counselled it is the total number of TB patients treated under DOTS in areas covered by TB/HIV collaborative activities.

For TB patients enrolled on ART it is the total number of HIV positive TB patients in DOTS programmes that are eligible for ART in areas covered by TB/HIV collaborative activities.

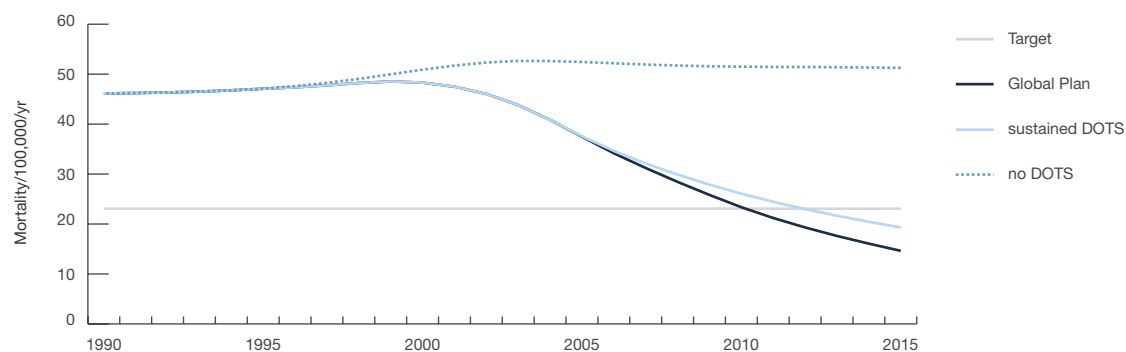
(c) HIV services include testing and counselling and HIV treatment and care services.

FIGURE 28: ESTIMATED IMPACT AND COSTS OF PLANNED INTENSIFIED ACTIVITIES 2006–2015**South-East Asian Region: Case detection rate, new ss+ cases****South-East Asian Region: Number of cases treated under DOTS/DOTS-Plus****South-East Asian Region: Incidence**

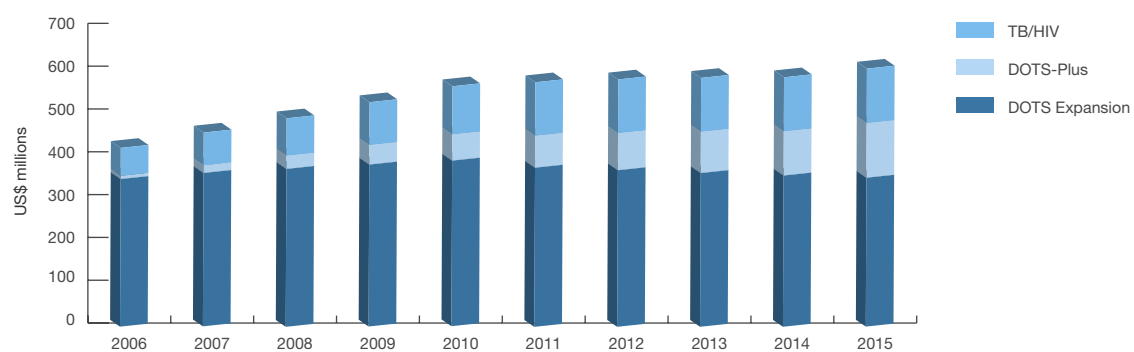
South-East Asian Region: Prevalence



South-East Asian Region: Mortality



South-East Asian Region: Total costs



7.6 Western Pacific Region: summary of planned activities, impact and costs

Achievements

In the Western Pacific Region, DOTS coverage and case detection have increased steadily from 58% and 44%, respectively, in 1998 to 90% and 52% in 2003. Preliminary data show continued progress in 2004 and early 2005, which makes it likely that the Region will reach the 2005 targets for DOTS coverage and case detection (70%). The treatment success rate has exceeded the 2005 target of 85% for several years. The implementation of the regional strategy to Stop TB in the Western Pacific has been critical to achieving this progress. Large investments have been made to ensure focused technical support, capacity strengthening, effective coordination, information exchange, advocacy, monitoring and supervision, strengthened partnerships and mobilization of resources for TB control.

Four TB high-burden countries—Cambodia, China, the Philippines and Viet Nam – together account for 95% of the estimated TB cases in the region. Viet Nam has a high-performing programme that has reached the 2005 TB targets for several years, although this success has not yet resulted in a decline in TB incidence. China has made huge progress in recent years because of strong political commitment and increased local and external funding. As a result, DOTS coverage has rapidly increased and the quality of DOTS improved. Recently a large-scale initiative has been launched to involve China's huge hospital sector in DOTS implementation and to improve disease notification. This initiative has led to a rapid increase in case detection. The Philippines has continuously improved programme performance since 2001 and is scaling up public-private mix for DOTS to further boost case detection and improve TB case management in the private sector. DOTS-Plus is being expanded in the country with support from the GFATM. Cambodia has improved DOTS quality and access in parallel with strengthening general primary health care services.

Collaboration between HIV and TB programmes has been established in Cambodia and pilots have been set up in Viet Nam. In China a national framework to address TB/HIV has been outlined. In addition to the existing DOTS-Plus project in the Philippines, national plans for pilot-testing and scaling up DOTS-Plus have been developed in China, Mongolia and Viet Nam.

The Region has invested in the development of a strong laboratory network. With support from supranational reference laboratories in Australia, Hong Kong SAR, Japan and the Republic of Korea, an extensive programme of quality assurance of laboratory services and drug resistance surveillance has been established throughout the Region.

Challenges

Recent successes need to be maintained through sustained levels of political commitment and funding. The rapid expansion of services has put pressure on programme management and

quality control. Full attention is needed to secure and sustain high quality DOTS services. The large number and diversity of health care providers in the region who are not yet involved in DOTS present a major challenge.

The impact of the HIV epidemic on TB control in parts of the region and among certain populations (such as injecting drug users) will need to be closely monitored and addressed. China is reporting high MDR-TB prevalence and it is estimated that more than 30% of the global MDR-TB cases are in China. MDR-TB patients are currently treated outside the national TB programme on an individual basis and have to pay for services. Second-line drugs are produced in the country and are widely available.

Priority actions 2006–2015

First and foremost, intensified efforts are needed to further strengthen laboratory services, supervision and central programme management throughout the Region. For this, it is essential to increase and sustain human resources and strengthen their capacity to implement TB control. Another priority is to complete the scale-up of PPM DOTS, with a special focus on public and private hospitals in China and the Philippines by 2010 and in selected parts of Cambodia and Viet Nam by 2015.

Implementation of DOTS-Plus will be very important in several countries in the Region, including China, Mongolia, the Philippines and Viet Nam. Quality-assured culture and drug susceptibility testing should be available to cover 100% of new and previously treated TB cases by 2015. Population coverage of DOTS-Plus should expand to more than 50% in 2010 and 100% in 2015.

Collaborative TB-HIV activities will be pilot-tested in China and scaled up in Cambodia and Viet Nam. HIV surveillance among TB patients will be established across the region, with 100% regional coverage by 2010. Community DOTS initiatives will be an important part of the strategy for rural areas in some countries. The Practical Approach to Lung Health will be pilot-tested and scaled up in selected countries by 2015.

Expected effects and costs

With successful implementation of the intensified efforts described above, case detection is expected to increase further to 80% in 2010 and then be sustained at this level. The treatment success rate is already above the Partnership's target of 85%. The current downward trends in TB incidence, prevalence and death rate are predicted to continue, ensuring that the Partnership's 2015 targets linked to the MDGs will be exceeded by a significant margin.

About 9 million people with TB will be treated under DOTS from 2006 to 2015, and 126 000 people will be treated under DOTS-Plus. Almost 12 000 HIV-positive TB patients will receive antiretroviral therapy. The combined effect of all interventions will be to prevent about 3 million deaths, in comparison with a situation in which no DOTS programmes are implemented, or about 99 000 deaths in comparison with a situation in

which TB control efforts are sustained at 2005 levels. With the implementation of sound TB control, it is expected that the estimated proportion of re-treatment cases will decrease from 32% in 2005 to 15% in 2015.

The estimated total cost of all planned TB control activities in the Western Pacific Region from 2006 to 2015 is US\$4.3 billion.

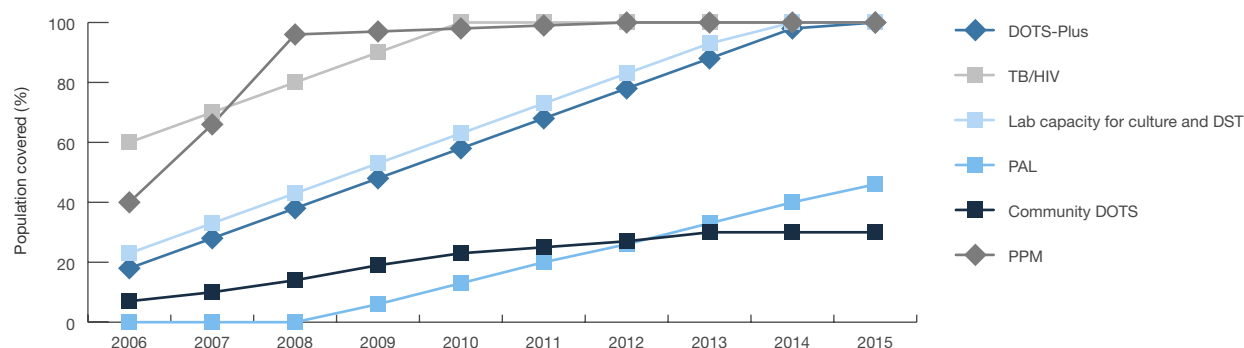
TABLE 16: COST OF PLANNED TB CONTROL ACTIVITIES, WESTERN PACIFIC REGION 2006–2015

Planned activities	US\$ millions
DOTS expansion and quality	3,434 (79%)
DOTS-Plus	782 (18%)
TB/HIV collaborative activities	137 (3%)
TOTAL	4,353 (100%)

SUMMARY CHARTS FOR WESTERN PACIFIC REGION

FIGURE 29: PLANNED SCALE UP OF ACTIVITIES 2006-2015

Western Pacific Region



N.B. Population coverage is the percentage of the population that lives in an area where the activity is implemented. For TB/HIV collaborative activities the percentage refers to the proportion of the eligible population, i.e. the population living in areas with an HIV prevalence above 1%. For DOTS-Plus, it is the percentage of detected MDR-TB cases that are enrolled in DOTS-Plus programmes.

TABLE 17: MILESTONES RELATED TO IMPLEMENTATION OF DOTS EXPANSION, DOTS-PLUS AND TB/HIV ACTIVITIES (a)

Western Pacific Region	2006 (b)	2010 (b)	2015 (b)
DOTS EXPANSION			
DOTS coverage	100%	100%	100%
Total number of new ss+ patients treated in DOTS programmes (thousands)	504 (692)	412 (514)	284 (349)
Case detection rate new ss+ (%)	73%	80%	81%
Treatment success rate new ss+ (%)	87%	87%	87%
Total number of new ss-/extra-pulmonary patients treated in DOTS programmes (thousands)	624 (856)	516 (641)	357 (439)
Percentage of new ss-/extra-pulmonary patients treated in DOTS programmes	73%	80%	81%
DOTS-Plus			
Total number of detected MDR-TB patients treated in DOTS-Plus programmes (thousands)	2.1 (12)	13 (23)	20 (20)
Percentage of detected MDR-TB cases treated in DOTS-Plus programmes	17%	54%	100%
MDR-TB treatment success rate (%)	71%	73%	75%
Percentage of culture positive cases that are re-treatment cases	30%	23%	15%
TB/HIV			
Total number of PLWHA attending HIV services screened for TB (thousands)	17 (25)	51 (51)	67 (67)
Percentage of PLWHA attending HIV services screened for TB (c)	66%	100%	100%
Total number of newly diagnosed and eligible PLWHA offered IPT (thousands)	3.6 (185)	15 (301)	21 (380)
Percentage of PLWHA offered IPT	2%	5%	6%
Total number of TB patients in DOTS programmes HIV tested and counselled (thousands)	115 (225)	157 (185)	108 (127)
Percentage of TB patients treated in DOTS programmes HIV tested and counselled	51%	85%	85%
Total number of TB patients (HIV positive and eligible) in DOTS programmes enrolled on ART (thousands)	0.7 (2.4)	1.3 (3.2)	1.3 (2.9)
Percentage of TB patients (HIV positive and eligible) in DOTS programmes enrolled on ART	31%	39%	40%

(a) The percentages are not always exactly the numerator divided by the denominator due to rounding errors.

(b) Numbers in parentheses indicate the denominator. For DOTS Expansion it is new TB cases.

For DOTS-Plus it is the total number of detected MDR-TB cases.

For PLWHA screened for TB it is the total number of PLWHA attending HIV services. For PLWHA offered IPT it is the total number of PLWHA.

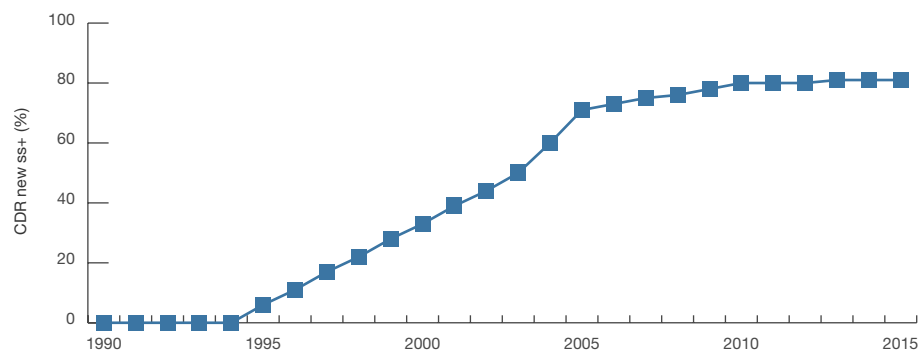
For TB patients HIV tested and counselled it is the total number of TB patients treated under DOTS in areas covered by TB/HIV collaborative activities.

For TB patients enrolled on ART it is the total number of HIV positive TB patients in DOTS programmes that are eligible for ART in areas covered by TB/HIV collaborative activities.

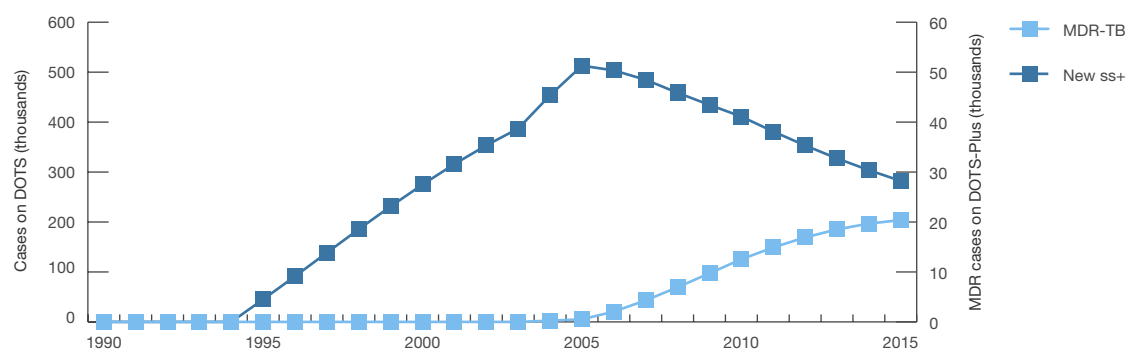
(c) HIV services include testing and counselling and HIV treatment and care services.

FIGURE 30: ESTIMATED IMPACT AND COSTS OF PLANNED INTENSIFIED ACTIVITIES 2006–2015

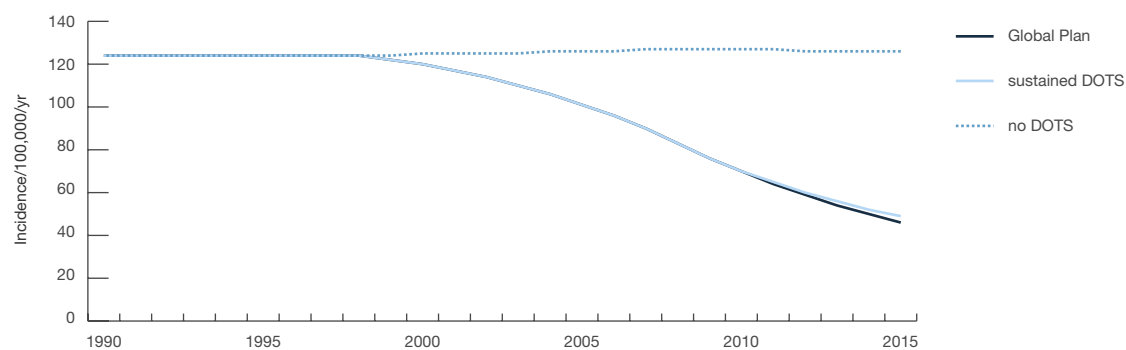
Western Pacific Region: Case detection rate, new ss+ cases



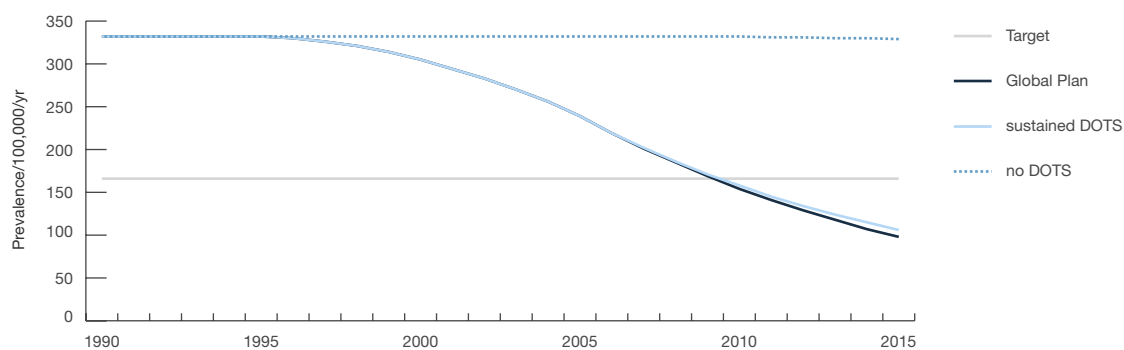
Western Pacific Region: Number of cases treated under DOTS/DOTS-Plus



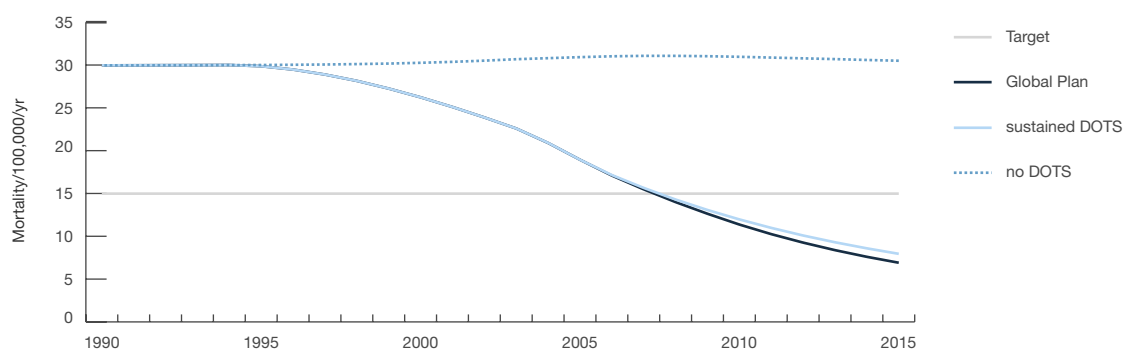
Western Pacific Region: Incidence



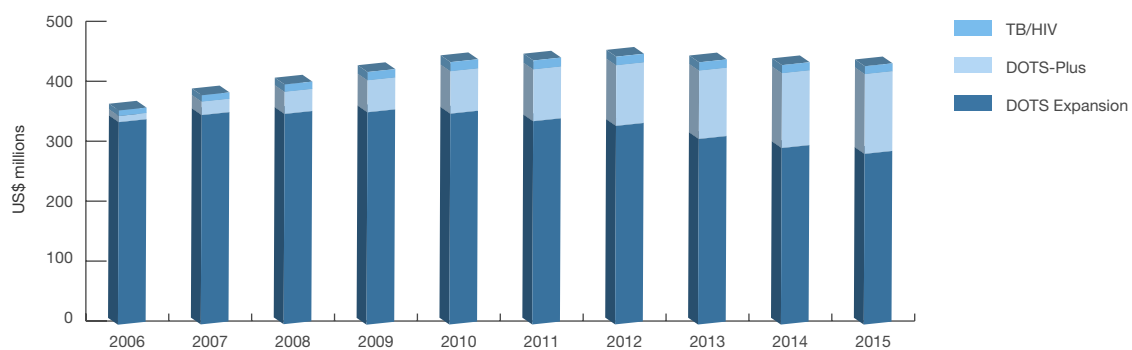
Western Pacific Region: Prevalence



Western Pacific Region: Mortality



Western Pacific Region: Total costs



8. HALVING TB PREVALENCE AND DEATH RATES IN AFRICA AND EASTERN EUROPE

The ambitious but realistic scenarios described, while holding out the prospect of significant progress, are not sufficient to achieve the Partnership's 2015 targets on time in Africa and Eastern Europe. The question thus arises as to what extra measures would be necessary to achieve the targets of halving prevalence and death rates in these two regions by 2015 (compared to the baseline values in 1990). To respond to this, additional scenarios have been developed. The analysis of what would be required to meet the targets in these regions indicated a range of actions, of which the scale, timing and feasibility vary considerably.

In most regions, the projected proportional reductions in prevalence and death rates are similar (see figure 15b, c). The notable exception is Africa where, on account of the impact of HIV on TB case fatality, achieving the target of halving the death rate is much more difficult than halving prevalence. As an illustration of the further actions needed to achieve the 2015 targets in Africa and Eastern Europe, Table 18 shows what must be done to halve the death rate, with an assessment of feasibility.

The analysis that underpins the development of these additional scenarios sheds light on the serious constraints in Eastern Europe and Africa. Overcoming these constraints would require massive improvements in general health systems, a reduction of 50% in HIV incidence, and the rapid availability of powerful new tools to increase diagnostic capacity, substantially shorten treatment duration, and effectively prevent TB. It is unlikely that even massive additional funding or even greater effort would be successful in completely overcoming the constraints. Nevertheless, all efforts must be made to achieve the Partnership's targets as quickly as possible in these two regions. Thus, there is no excuse not to invest massively.

It should be remembered that the targets for 2015 are specified relative to 1990 as the baseline year. The epidemiological situation in both Eastern Europe and Africa deteriorated greatly during the 1990s, making achievement of the targets in these two regions problematic. Nevertheless, even with high rates of HIV and drug resistance, the improvements that can be achieved over the Plan period (2006–2015) in Africa and Eastern Europe are similar to what can be achieved in other regions. Since the focus of the Plan is on what will happen over the next 10 years, rather than on what has happened since 1990, it is important to identify the progress that could be made for each region within that period. In Africa and Eastern Europe, much of the progress necessary to reach the 2015 targets will depend on the implementation over the coming decade of the full array of interventions that are part of the Global Strategy to Stop TB. In contrast, in the other regions much of the progress necessary to reach the 2015 targets was made over the past decade, and further progress mainly represents consolidation of these achievements.

See Table 18: Further actions needed to achieve the 2015 target for deaths in Africa and Eastern Europe

9. ESTABLISHED MARKET ECONOMIES (EME) AND CENTRAL EUROPE

The Established Market Economies (EME) and Central Europe are combined together here as one epidemiological region because they have similarly high per capita incomes and low TB incidence rates. Since the main focus of this Global Plan is on the countries with high TB incidence, and the combined estimated incident cases in the EME and Central Europe represented only 1.7% of the global total in 2003, this regional profile does not include a detailed set of projections. Many of the countries in the EME and Central Europe have developed national plans for TB control. The strategic approach relevant in these countries includes a focus on settings (e.g. metropolitan areas) and risk groups (e.g. immigrants) with a TB incidence above the national average. Such plans include the national plan for the USA, developed by the Federal TB Task Force in 2004 (based on the recommendations made by the Institute of Medicine in its report in 2000²⁸) and the national plan for England, published in 2004.²⁹

The effective application of chemotherapy in the latter half of the twentieth century further accelerated the already declining TB case notifications in industrialized countries. From the mid-1980s onwards, however, several countries saw a slow-down in the decline, while others saw the trend reversed, with case notifications increasing for the first time in many years. For example, in the United States of America, after 30 years of steady decline, TB incidence increased regularly between 1985 and 1992.³⁰ Factors responsible for this reversal included increased poverty among marginalized groups in inner city areas, immigration from countries with high TB prevalence, the impact of HIV, and most importantly the failure to maintain the necessary public health infrastructure (as in the case of New York City), under the mistaken belief that tuberculosis was a problem of the past.³¹ The consequences of this failure to maintain the necessary public health infrastructure serve as a sharp reminder to countries of the importance of maintaining commitment to TB control. The commitment to ensuring universal access to quality TB diagnosis and treatment implies particular efforts to reach those groups at increased risk of TB, including the poor, the homeless and immigrants (whether legal or illegal).

Many countries in Europe, including Denmark, the Netherlands, Sweden and the United Kingdom, reported a slow-down in the decline, or even a steady rise, in TB cases.³² The high proportion of cases in the foreign-born (e.g. 24% in France, 51% in the Netherlands, 54% in Sweden, 68% in Switzerland) pointed to immigration as the main cause of this change in trend.³³ Annual case rates in foreign-born populations often exceed 50 per 100 000 and may even exceed 100 per 100 000 (e.g. in the Netherlands), in contrast to rates in native-born populations of usually less than 15 per 100 000. In many countries, tuberculosis has declined steadily among the native-born, while rising among the foreign-born.

See Figure 31. The number of TB cases in sixteen European countries among native-born and foreign-born.

TABLE 18: FURTHER ACTIONS NEEDED TO ACHIEVE THE 2015 TARGET FOR DEATHS IN AFRICA AND EASTERN EUROPE

Action (under additional scenarios)	Assessment of feasibility
AFRICA	
ART much more rapidly available, e.g. as proposed by WHO/UNAIDS, in line with the «3 by 5» initiative.	Since the «3 by 5» initiative will probably not achieve its target by 2005, it appears unlikely that ART access for TB patients can be made much more rapidly available.
Very high rates of case detection and treatment success from 2006–2015 under DOTS, with 90% case detection for HIV-negative TB cases (both smear-positive and smear-negative) and 85% treatment success.	Very unlikely – the infrastructure and human resources in Africa are inadequate to allow these levels of case detection and treatment success, although the situation could be different if improved diagnostics and treatment regimens became widely available (towards 2010), and if investments now resulted in improvements in infrastructure and human resources (from 2010 onwards).
Preventive therapy: 20% of people coinfecting with MTB and HIV treated annually so that they do not develop active TB. This could be achieved with isoniazid (IPT), ART, or some combination of IPT and ART (or with some other drug yet to be discovered).	Very unlikely – the infrastructure and human resources in Africa are inadequate to deliver these levels of preventive therapy, although the situation could be different if improved diagnostics for latent TB infection and preventive therapy became widely available (towards 2010).
HIV incidence rate cut to half the value forecast by UNAIDS in 2005, and held at that level from 2006 to 2015.	Extremely unlikely – the infrastructure and human resources in Africa are inadequate to deliver the measures available to control HIV transmission quickly enough and on a sufficiently large scale to result in this unprecedented rate of decline in HIV incidence.
Vaccination from 2006 onwards, annually protecting 20% of uninfected people from ever acquiring TB infection (with the assumption that the vaccine does not protect people who are already HIV-positive).	Extremely unlikely – the Working Group on Vaccines estimates that new vaccines will be available in 2015.
EASTERN EUROPE	
Extreme DOTS (90% case detection with 85% treatment success in 2006–2015).	Very unlikely that these levels could be reached so quickly, even though experience of rapid, large-scale DOTS implementation in China and India indicates that strong political support in large countries with reasonable health infrastructure, adequate funding and strong financial management can result in high levels of case detection and treatment success. Improved drugs and diagnostics could help reach these levels.
More rapid expansion of DOTS-Plus: 90% case detection for MDR-TB patients, as for DOTS; MDR-TB among culture-positive cases falls from 10% to 5% by 2010; the ratio of previously treated cases to new cases falls to 10% by 2010; 70% of MDR-TB patients are on DOTS-Plus from 2006 onwards, rising to 100% by 2015; 85% treatment success among MDR-TB patients under DOTS-Plus from 2006 to 2015; 100% DST for culture-positive patients 2006–15.	Very unlikely, largely because of the lack of political will, financial management capacity and laboratory infrastructure, and the lack of experience of large-scale and rapid scale-up of DOTS-Plus.

The foreign-born now account for a large proportion of tuberculosis cases in the Established Market Economies, as shown for example by many countries in Europe.³⁴

See Figure 32. *Contribution of the foreign-born to tuberculosis in countries in Europe in 2002.*

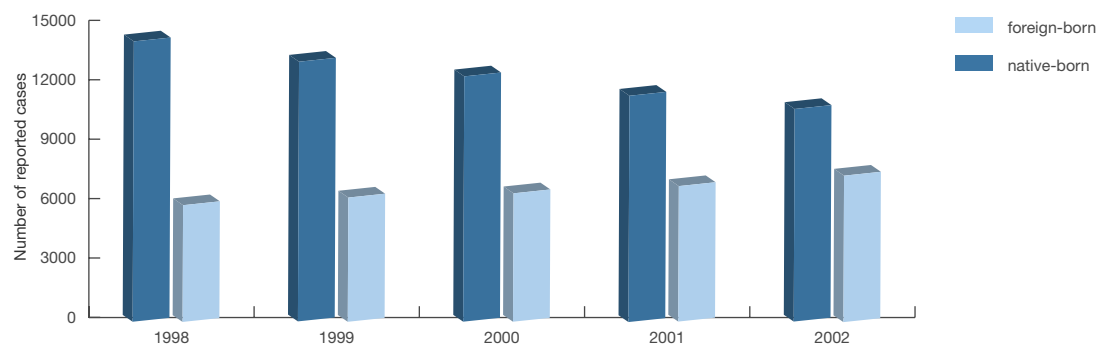
The impact of HIV on TB in Western Europe has been largely limited to certain countries (e.g. Portugal, Spain) and cities (e.g. Amsterdam, Paris).³⁵ In most countries in Western Europe, the proportion of AIDS cases diagnosed with TB is low. The two notable exceptions are Portugal and Spain,³⁶ where the overlap between the population infected with HIV and the population infected with *M. tuberculosis* is greater than in the other countries of western Europe. TB incidence rates in Japan are still high at about 40 per 100 000, but are declining.³⁷ In other industrialized countries, including Australia, Canada and New Zealand, rates have levelled off over the past few years below 10 per 100 000. The proportion of foreign-born among TB patients is about 70% in Australia and Canada.

Investment in TB control in the countries in the EME and Central Europe involves investment in both domestic and international TB control. One implication of the high proportion of cases in the foreign-born in most industrialized countries is that TB control in these settings depends on TB control globally. Industrialized

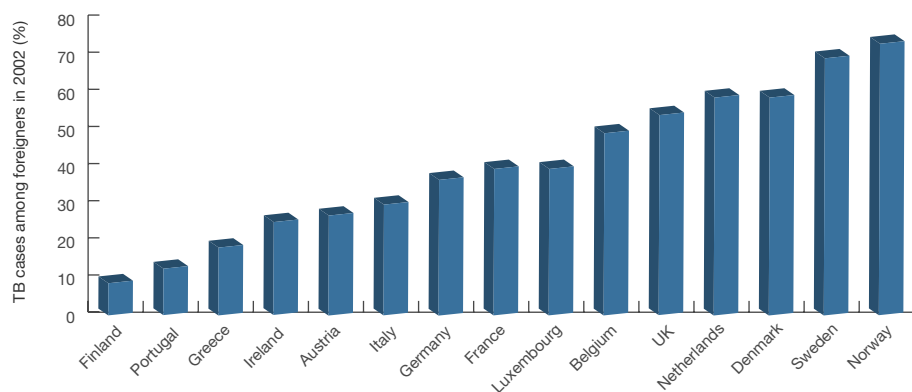
countries need to invest in tuberculosis control in countries with high TB incidence, not only to contribute to alleviating human suffering and poverty, but also to reduce the tuberculosis risk, including risk of multidrug-resistance,³⁸ that the foreign-born bring with them when they migrate from the countries with high tuberculosis incidence. This investment in TB control in high-incidence countries may bring economic benefits by reducing TB among migrants and therefore also the costs of TB-related morbidity and mortality. For example, an economic analysis showed that a US\$35 million investment in TB control in Mexico by the USA would result in net discounted savings of US\$108 million in the USA over a 20-year period, through decreased costs associated with TB among Mexican migrants to the USA.³⁹

FIGURE 31: THE NUMBER OF TB CASES IN SIXTEEN EUROPEAN COUNTRIES AMONG NATIVE-BORN AND FOREIGN-BORN.

TB decline in West Europeans, but steady in immigrants



Sixteen countries: Austria, Belgium, Czech Republic, Denmark, Finland, Greece, Hungary, Ireland, Netherlands, Slovakia, Slovenia, Sweden, UK, Iceland, Norway, Switzerland

FIGURE 32: CONTRIBUTION OF THE FOREIGN-BORN TO TUBERCULOSIS IN COUNTRIES IN EUROPE IN 2002.**Foreign-born make a large and growing contribution to TB in Europe**

PART III

Partnership action to achieve the goals

10. SUMMARY STRATEGIC PLANS 2006–2015 OF THE PARTNERSHIP WORKING GROUPS AND SECRETARIAT

10.1 Introduction

The Stop TB Working Groups, together with the Secretariat, will be responsible for the Partnership action required to achieve the Partnership's goals for 2015 and lay the foundation for eliminating TB by 2050.

Part III of the Global Plan to Stop TB provides summaries of the strategic plans for 2006–2015 for each Working Group and for the Stop TB Partnership Secretariat. The full strategic plans are available at <http://www.stoptb.org/GlobalPlan>.

The seven working groups of the Stop TB partnership were established to ensure that effective action to combat TB takes place in a planned, coordinated and efficient manner. Working groups are organized around specific areas of activity:

- DOTS expansion;
- DOTS-Plus for multidrug-resistant TB;
- TB/HIV;
- new TB diagnostics;
- new TB drugs;
- new TB vaccines;
- advocacy, communications and social mobilization.

Each working group has the following functions:

- to map activities in its specific area, including activities by different partners, policy and research developments, opportunities for further action, and resource needs;
- to assist countries to plan, implement, and monitor coordinated action;
- to report to the Stop TB Partnership Coordinating Board and the Partners' Forum on the progress, constraints and assistance required; and
- to coordinate with other partners, working groups, or committees to ensure synergy of activities.



Reach

TB represents a global threat to health. Full implementation of the Plan will expand the reach of quality TB care towards all patients, wherever they live and irrespective of their gender, age, socio-economic group or type of TB.

To ensure all TB patients have access to quality care, the Stop TB Partnership will reach out to a wide range of Partners. In reaching out to all those who have a role to play to Stop TB, we reach out to the communities blighted by TB, touching millions of lives.

The Partnership's aim is for quality TB care and the benefits of research and development to reach everybody in need.

10.2 Implementation Working Group plans

The activities of the Stop TB Partnership's three implementation working groups reflect the implementation of the Stop TB strategy. The aim of the DOTS Expansion Working Group is to assist countries in improving access to high quality DOTS, a key pillar of the Stop TB strategy. This provides a core foundation for the additional elements of the Stop TB strategy regarding multidrug-resistant TB (Working Group on DOTS-Plus for Multidrug-resistant TB) and HIV-related TB (TB/HIV Working Group). The DEWG plan therefore provides the starting-point for the DOTS-Plus and TB/HIV plans, which are supplementary and complementary to the DEWG plan.

The activities of the three implementation working groups provide the foundation for the efforts of the Advocacy, Communications and Social Mobilization Working Group to strengthen strategic communication and social mobilization for improved TB control in countries. The plans of the three implementation working groups will also pave the way for effective implementation of the new tools expected to become available through the working groups on new diagnostics, new drugs and new vaccines.

In each of the Partnership's implementation working groups, country-level implementation will be guided by the Partnership's mission to ensure that every TB patient has access to effective diagnosis, treatment and cure, and in particular the recognition that service delivery must take account of the needs of the poor and vulnerable. There is no universal, "one-size-fits-all" solution to the problems that poor TB patients face across the world in accessing high-quality TB services. Each country needs to understand who the poor and vulnerable are, investigate the barriers they face in accessing services, take action to overcome these barriers, harness the resources required to sustain these actions and monitor progress towards equity targets (see Box 5, p. X). Similarly, country-level implementation will need to be guided by epidemiological analysis of other risk groups.

Steps to ensure TB infection control in health care and congregate settings are crucial in interrupting the chain of transmission in settings where people (especially those living with HIV) may be at increased risk of TB, including sometimes multidrug-resistant TB. The TB infection control measures promoted by the three implementation working groups include those recommended for health care settings⁴⁰ and prisons.⁴¹

10.2.1 DOTS Expansion Working Group: summary strategic plan, 2006–2015

The DEWG strategic plan sets out the Working Group's contribution to meeting the Partnership's 2015 global targets for TB control, linked to the MDGs. It will also help in the achievement of Millennium Development Goal 1: To eradicate extreme poverty and hunger. The DEWG strategic plan acknowledges the profound importance of poverty alleviation and socioeconomic development for long-term control of the TB epidemic, while focusing on mechanisms to implement effectively quality TB diagnosis and treatment for all, particularly the poor, in line with the DOTS strategy.

Strategic vision for global TB control and DOTS

More than a decade of DOTS in countries with diverse characteristics has offered two distinct lessons: DOTS is indeed essential for TB control, but the original five elements of DOTS alone are not enough to control TB globally. The DOTS strategy is now at the heart of the Stop TB strategy, conveying a clear message about its pro-poor and patient-centred approach. The Stop TB strategy reflects the Partnership's mission to ensure that every TB patient has access to effective diagnosis, treatment and cure. As we progress from meeting the 2005 global targets to achieving those for 2015, all members of the Stop TB Partnership need to articulate a comprehensive and inclusive vision for global TB control, including the following essential elements of the Stop TB strategy:

1. **Pursuing quality DOTS expansion and enhancement, through:**
 - (i) Political commitment, with long-term planning, adequate human resources, expanded and sustainable financing, to reach the targets set by the World Health Assembly and the Stop TB Partnership.
 - (ii) Case detection through quality-assured bacteriological testing (microscopy, culture, DST) and strengthening of the laboratory network to facilitate detection of sputum smear-positive, sputum smear-negative, drug-resistant and MDR-TB cases.
 - (iii) Standardized treatment, under proper case management conditions, including directly observed treatment to reduce the risk of acquiring drug resistance, and support of patients to increase adherence to treatment and chance of cure.
 - (iv) An effective and regular drug supply system, with improved drug management capacity.
 - (v) An efficient monitoring system for programme supervision and evaluation, including measurement of impact.
2. **Addressing TB/HIV, MDR-TB and other special challenges**, by scaling up TB/HIV joint activities, DOTS Plus, and other relevant approaches.
3. **Contributing to health system strengthening**, by collaborating with other health programmes and general services in, for example, mobilizing the human and financial resources needed for implementation and impact evaluation, and by sharing and applying achievements of TB control.

4. **Involving all care providers**, public, nongovernmental and private, by scaling up approaches based on a public-private mix, to ensure adherence to the International Standards for TB Care, with a focus on health providers used by the poor.
5. **Engaging people with TB and affected communities**, by scaling up community TB care and providing opportunities for meaningful involvement of patients and communities in increasing awareness, demanding high-quality services, supervising treatment, and reducing stigma.
6. **Enabling and promoting research** to improve programme performance and to develop new drugs, diagnostics and vaccines.

Broadening the scope of DOTS expansion

DOTS expansion is more than simply expanding the geographical coverage of DOTS. It implies ensuring equitable access to quality TB diagnosis and treatment for all patients, i.e. for patients with all types of TB, patients of all age groups and from all socioeconomic strata, and men and women equally.

This will necessitate expanding quality TB diagnosis and treatment to all parts of the health sector and beyond, i.e. ensuring that all health care providers use the International Standards for TB Care, and expanding the involvement of patients and communities in TB control.

The DEWG will also assist countries to expand use of existing and new technologies. This includes existing, but underutilized, technologies, such as culture and drug susceptibility testing and isoniazid preventive treatment, as well as new diagnostic and treatment tools that will become available in the future.

Objectives for DOTS expansion 2006–2015

The DEWG and its partners will continue to assist countries to work towards two main outcome objectives.

Outcome objective 1: To achieve and sustain performance beyond the "70/85" targets.

In order to achieve and sustain performance beyond the targets of 70% case detection 85% successful treatment, continued efforts are needed to improve the quality of DOTS, through improvement of programme management, supervision, and laboratory services for sputum smear microscopy, and strengthening of human resources. However, in most countries this will not be enough. Meaningful and effective involvement of all relevant partners, including patients and communities, is essential to reach patients who are treated outside DOTS programmes, as well as those who are currently not diagnosed or not treated. The PPM DOTS, community DOTS, TB/HIV and PAL approaches can help increase case detection and should be applied more widely. To achieve and sustain performance beyond the 70/85 targets, all partners need to be involved in DOTS implementation.

Outcome objective 2: To ensure equitable access to quality TB care for all people with TB, especially the poor and marginalized.

DOTS expansion starts with the achievement of the "70/85"

targets and ends with all people with TB having access to quality TB services. Neither the type of TB, nor financial capacity, nor social status should determine access to quality TB services. "All people with TB" includes people of all ages and everyone with extrapulmonary disease or pulmonary sputum smear-negative disease. It also includes people with TB/HIV coinfection and people with multidrug-resistant TB. Given the poor socioeconomic status of most people with TB, a pro-poor and equity-based approach requires that health services pay special attention to the needs of the most disadvantaged groups. Improving access to quality services also means reducing the harmful effects of poor medical practice. The key strategies are to make sure that all health care providers adopt the International Standards of TB Care, and to educate patients to use available services in a rational way and to advocate for high-quality care.

Main activities for DOTS expansion in countries

To achieve these two objectives, the partners of the DEWG will assist countries in implementing the following seven interlinked activities. Detailed regional and country implementation plans for DOTS expansion are being developed, based on the DEWG strategic plan. Country planning, setting of local targets, and implementation require local situational analysis to determine local challenges, barriers and opportunities.

1. Complete DOTS coverage.

Global target: All public health basic management units in all countries will provide TB care according to the DOTS strategy by 2010.

Basic coverage of DOTS within public health structures will soon be complete in the 22 high-burden countries, but some countries do not yet provide free treatment under DOTS to patients with sputum smear-negative pulmonary TB or extrapulmonary TB, or to children with TB. In addition, all countries should work towards free provision of sputum smear microscopy and other TB diagnostic tests. Finally, isoniazid preventive treatment for children needs to be implemented in countries that have not yet done so; this process will be facilitated by the work of the Childhood TB Subgroup of the DEWG.

2. Improve quality of DOTS.

Global target: All countries will provide quality diagnosis and treatment and achieve at least 85% treatment success rate by 2015.

The core element of improved quality is improved human resource capacity for undertaking the tasks needed in DOTS, including sputum smear microscopy, drug management, case management, supervision, recording and reporting, and laboratory diagnosis. Plans to improve DOTS quality should be tailored to national and local conditions, while taking into account general health systems challenges and competing needs within the health services. Increased political commitment and increased financing of DOTS are essential in most countries.

3. Public-private mix DOTS.

Global target: All countries will have developed guidelines, by 2010, for the involvement of relevant public and private health care providers in DOTS, and will have implemented them by

2015. By 2015 about 3.8 billion people will live in areas with PPM DOTS initiatives.

PPM DOTS is a comprehensive approach involving all relevant health care providers in DOTS, ensuring that they apply the International Standard of TB care and provide TB care free of charge or at very low cost to patients. PPM DOTS has been shown to increase case detection and cure rates, while reducing the financial burden on poor patients. The PPM DOTS approach is particularly relevant in settings where large numbers of public and private health care providers are not yet involved in DOTS. While there is a potential role for all providers in delivering DOTS services, the PPM DOTS approach emphasizes that the national TB programme should retain and strengthen its stewardship functions, including regulation, financing, monitoring, evaluation and surveillance. The PPM DOTS Subgroup of DEWG will continue to assist countries in developing national policies and operational guidelines to scale up and evaluate PPM DOTS initiatives, and will stimulate further research on PPM DOTS.

4. Community DOTS.

Global target: All countries in Africa will have scaled up community DOTS initiatives by 2010. By 2015, about 1.9 billion people globally will live in areas with community DOTS initiatives.

There is an acute need to further decentralize the provision of TB services beyond health facilities, in order to increase geographical access and to foster people's participation in supporting patients. Community DOTS has been shown to result in improved treatment success rates through decreased default and transfer out rates. A subsequent impact on case detection rates, related both to improved awareness and better access to care, has also been reported. Furthermore, community DOTS reduces treatment costs for patients, NTPs and society.

5. Practical Approach to Lung health.

Global target: PAL will be introduced in 20% of developing countries by 2010 and in 50% by 2015. Approximately 2 billion people will live in areas with PAL initiatives by 2015.

PAL is a primary health care (PHC) strategy for the integrated management of respiratory conditions in patients aged five years and over. It aims to improve: (i) the quality of care for every respiratory patient, and (ii) the efficiency of PHC services in treating respiratory conditions, with a focus on TB, acute respiratory infections and chronic respiratory diseases.

6. Culture services, drug susceptibility testing and new diagnostic tests.

Global target 1: All countries will have developed capacity by 2015 to perform culture and DST according to national policies.

Global target 2: From 2010 new diagnostic tools will be introduced gradually and are expected to cover at least 50% of the eligible population by 2015.

The Subgroup on Laboratory Capacity Strengthening will continue to assist countries in improving performance of TB laboratories to provide reliable diagnostic services to NTPs.

Since high-quality sputum smear microscopy is the cornerstone of DOTS and remains the highest priority for case detection and TB control, the primary focus will be on improving performance of sputum smear microscopy, including ensuring external quality assurance (EQA). Strengthening of services for culture of *M. tuberculosis* and for DST is necessary, especially in high HIV and MDR-TB prevalence settings. The introduction and progressive scale-up of culture and DST will depend on the local epidemiological situation.

The DEWG and its Subgroup on Laboratory Capacity Strengthening will assist countries in introducing new diagnostic tools in routine NTP operations, as they become available from 2010 and gradually replace sputum smear microscopy, conventional culture and DST. The Subgroup will also support the development of operational research capacity and of prioritised research agenda.

7. Prioritize the needs of the poor and vulnerable.

Global target 1: By 2010 all countries will have developed capacity to monitor the extent to which DOTS reaches and serves the poor and vulnerable.

Global target 2: By 2010 all countries will have developed key strategies for improving access to DOTS for the poor and vulnerable.

Global target 3: By 2015 all countries will have developed the capacity to demonstrate and monitor the contribution made by DOTS to poverty alleviation.

The TB and Poverty Subgroup of the DEWG has outlined options for NTP managers to choose from in addressing poverty issues in DOTS implementation. The Subgroup will stimulate operational research to improve access to DOTS and, as experience and evidence accumulates, these options will be revised and reformulated into formal guidelines for use at national and international levels.

Support to countries

In order to assist countries in implementing the activities outlined above, the partners of the DEWG and its subgroups (Childhood TB Subgroup, Subgroup on Laboratory Capacity Strengthening, PPM DOTS Subgroup and TB and Poverty Subgroup) will focus on the following three main areas:

- Country support: both strategic and technical support to countries; and capacity-building at global and regional levels.
- Monitoring of DOTS expansion and MDG indicators, covering (1) monitoring of progress towards targets; (2) monitoring of implementation of national plans, and (3) financial monitoring, including tracking of financial flows and estimation of sources and expenditure areas within NTP budgets.
- Operational research and policy development.

The DEWG will continue to prioritize high-burden countries. Currently, DEWG is targeting 22 high-burden countries that together make up 80% of the global TB burden. In the coming 10 years, the classification of high-burden countries may change according to changing TB epidemiology as well as changing needs for technical support.

Case detection and treatment outcome

A central assumption to the estimated impact on case detection and treatment outcome is that the different activities are synergistic and dependent on each other. If all the proposed activities are implemented according to the scenario, it is expected that the case detection target will be reached in all regions by 2010, and that case detection will be 80% or above in all regions by 2015. Treatment success rate is expected to reach 85% or more in all regions at the latest by 2010 and to be sustained from then onwards.

Impact on TB burden

Under the present scenario, incidence, prevalence and death rate trends will go down rapidly over the next 10 years in all regions, as a result of the various TB control activities of the DEWG in conjunction with those of the DOTS-Plus and TB/HIV Working Groups. The MDG target – to have halted, and begun to reverse by 2015 the spread (incidence) of TB – will be met in all regions.

Key risk factors

Key risk factors for not achieving the objectives of the Working Group include:

- Deteriorating health systems: Many TB programmes today struggle to implement quality services in the context of health workforce crises, continuous low levels of public funding for health care, weak government stewardship, and on occasion collapsed health service networks. The DEWG has identified a range of mechanisms through which DOTS expansion strengthens health systems, as well as how health systems development creates better conditions for TB control.
- Devolution of TB control responsibilities from the public sector: The risk that the role of the government sector is played down as a result of a new focus on the involvement of private sector and civil society should be seriously addressed. The DEWG and the Stop TB Partnership need to advocate strongly for increased resources to strengthen the public sector as a core condition for involving other sectors.
- Dilution of the focus of TB control: As DOTS evolves, there is a risk that the focus on its essential components will be lost. The key to success is to continue to stress the need for high quality in basic DOTS functions, while raising the additional resources needed to implement new approaches.
- Loss of broad support from the public health community, if the TB control community pays too little attention to the impact of poverty on the TB epidemic. The messages need to be clear that long-term TB control depends on economic development, and that DOTS expansion contributes to breaking the disease-poverty circle, both directly (by reducing health care costs to patients), and indirectly (by improving productivity through reducing death and disability).
- Failure to mobilize the domestic and external resources needed for full implementation of the DEWG strategic plan.

See Table 19: Budget requirements for the DOTS Expansion Working Group: 2006–2015 (US\$ MILLIONS)

TABLE 19: BUDGET REQUIREMENTS FOR THE DOTS EXPANSION WORKING GROUP: 2006–2015 (US\$ MILLIONS)

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	ALL YEARS	% TOTAL
COUNTRY NEEDS												
ALL REGIONS	2,404	2,568	2,751	2,906	2,967	2,952	3,013	3,057	3,113	3,173	28,904	92%
AFR- HIGH	759	841	913	983	1,056	1,080	1,123	1,169	1,219	1,276	10,419	33%
AFR LOW	203	224	247	268	291	303	315	325	336	347	2,859	9%
EEUR	418	442	490	520	465	460	479	497	515	525	4,809	15%
EMR	170	187	208	221	236	237	240	241	240	240	2,221	7%
LAC	143	138	145	153	151	133	132	131	129	128	1,383	4%
SEAR	359	373	383	393	402	386	380	373	367	362	3,778	12%
WPR	351	363	365	368	366	353	344	322	306	296	3,434	11%
INTERNATIONAL AGENCY NEEDS												
TECHNICAL COOPERATION*	219	226	232	239	246	254	261	269	277	286	2,510	8%
WG OPERATIONAL NEEDS												
	1	1	1	1	1	1	1	1	1	1	11	0.04%
TOTAL	2,624	2,794	2,985	3,147	3,214	3,207	3,276	3,327	3,392	3,460	31,426	

* Some aspects of technical cooperation will be undertaken jointly for DOTS Expansion, TB/HIV and DOTS-Plus. Since it is difficult to identify what share of these costs applies to each WG, the total is shown here.

10.2.2 Working Group on DOTS-Plus for MDR-TB: summary strategic plan, 2006–2015

DOTS-Plus was launched in 1999 to manage multidrug-resistant TB (MDR-TB) with second-line drugs in resource-limited settings. The Stop TB Partnership's Working Group on DOTS-Plus for MDR-TB was established in 2000. It is now clear that DOTS-Plus is an effective, feasible and cost-effective intervention, and the main challenges today are to expand drug-resistance surveillance (DRS) and monitor drug resistance trends worldwide, and to scale-up implementation of DOTS-Plus beyond the pilot phase as an integrated component of DOTS.

Strategic vision for 2006–2015

The vision of the Working Group on DOTS-Plus for MDR-TB is to integrate drug resistance surveillance and the management of MDR-TB as routine components of TB control, providing access to diagnosis and treatment for all TB patients and covering all health care providers. This is in line with the comprehensive approach to global TB control expressed in the new Stop TB Strategy, encompassing all TB patients including those with MDR-TB and TB/HIV. As a result, all MDR-TB management measures will be implemented in collaboration with the DEWG and will be in line with the activities of the other Stop TB working groups.

Current threat of multidrug-resistant tuberculosis

Along with HIV/AIDS, MDR-TB is the most important threat to TB control. Countries with a high MDR-TB prevalence generally have a history of poor TB control. There are both preventive and restorative strategies to combat resistance – DOTS and DOTS-Plus.

The major barrier to treatment of MDR-TB is the high cost of second-line drugs, which are at least 300 times more expensive than first-line drugs, on the basis of Green Light Committee prices, and between 1000 and 3000 times more expensive in terms of market prices. Additional barriers include the requirement for a sophisticated laboratory to conduct culture and drug susceptibility testing, severe side-effects associated with second-line drugs, and fear of development of resistance to second-line drugs. Consequently, most national TB programmes, other than those in the established market economies and the former Soviet Union, choose to focus on prevention of drug resistance to the exclusion of diagnosis and treatment of MDR-TB. This means that MDR-TB sufferers are left with little or no hope of recovery and that MDR-TB continues to spread.

At the same time, in many countries – including China and India which account for 35% of the global TB caseload – private practitioners and public providers not linked to the NTP diagnose and treat MDR-TB patients. Their treatment practices often fail to meet acceptable standards. The misuse of second-line drugs could lead to the creation of TB strains resistant to all known anti-TB drugs. The control of MDR-TB requires sound implementation of DOTS to prevent the development of new cases, and careful introduction of second-line drugs

with adequate laboratory support to stop the amplification and circulation of resistant strains.

Priorities and objectives

In May 2005, the World Health Assembly resolution on “Sustainable Financing for TB Prevention and Control” encouraged all Member States “to ensure that all tuberculosis patients have access to the universal standard of care” and requested the Director-General of WHO “to implement and strengthen strategies for the effective control of, and management of persons with, drug-resistant TB”.

Currently, less than 2% of the estimated number of culture-positive MDR-TB patients are treated according to WHO recommendations. With the planned expansion of DOTS-Plus, it is envisaged that by 2015, 56% of culture-positive MDR-TB patients will be detected and treated. During the 10-year period of the Global Plan, a cumulative 23% of all culture-positive MDR-TB patients will be treated under DOTS-Plus.

It is estimated that, during the Plan period, 778 000 MDR-TB cases will be treated according to WHO guidelines, 53% of them in the Eastern European Region, 19% in the South-East Asian Region, and 16% in the Western Pacific Region (Figure 33). Of these, 75% or 587 000 will be treated successfully. With the implementation of DOTS and DOTS-Plus, it is expected that the estimated global proportion of re-treatment cases will decrease from 20% in 2005 to 11% in 2015. Most importantly, it is expected that the number of MDR-TB cases will be reduced from an estimated 533 000 in 2005 to 193 000 in 2015, mainly as a result of reduction in incidence and in proportion of re-treatment cases and as a combined effect of all TB control interventions. With the expansion of DOTS-Plus, it is expected that 142 000 deaths from MDR-TB will be averted between 2006 and 2015 (Tables 7 and 8).

See Figure 33: Number of MDR-TB patients to be treated per year under DOTS-Plus by region, 2006–2015

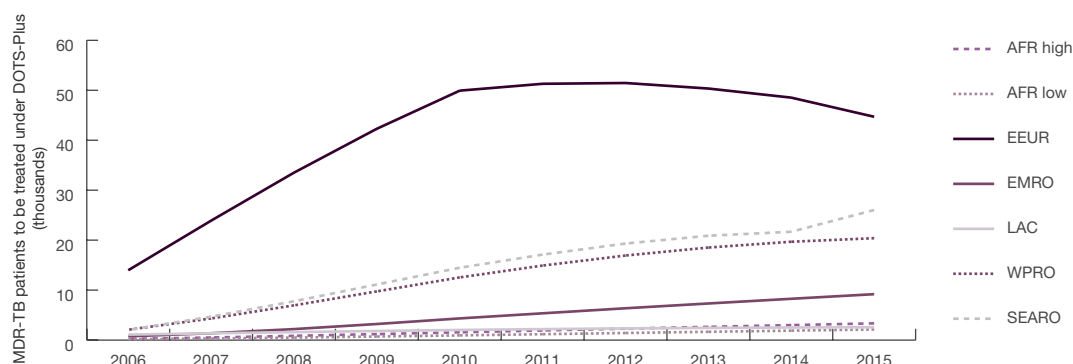
To achieve these goals, the priorities for the next decade are to:

- expand drug resistance surveillance;
- monitor trends and regularly update the global MDR-TB estimates;
- strengthen capacity to perform quality-assured culture and drug susceptibility testing;
- scale up MDR-TB treatment according to WHO guidelines;
- create a healthy and competitive market of quality-assured second-line drugs;
- provide technical and global coordination to accomplish the goals.

Strengthening of health systems and the health workforce to deliver sound diagnostic and treatment services to all MDR-TB patients will be essential to underpin these priorities.

The Green Light Committee mechanism needs to be reformed to meet the increasing demand for quality-assured second-line drugs and technical assistance. One possibility would be to decentralize the functions of reviewing and monitoring DOTS-Plus implementation to WHO regional level. In addition, the GLC

FIGURE 33: NUMBER OF MDR-TB PATIENTS TO BE TREATED PER YEAR UNDER DOTS-PLUS BY REGION, 2006–2015



should converge with the Global TB Drug Facility to ensure a reliable and experienced “bundling” mechanism for anti-TB drugs.

The Working Group has five specific objectives for 2015:

Objective 1: By 2015, representative and reliable data should be available on the global magnitude of MDR-TB, trends in high MDR-TB prevalence countries, and the relationship between MDR-TB and HIV/AIDS.

Milestones: Drug resistance data should be ready for publication in 2010 for 130 countries with either a high TB burden, expected high MDR-TB prevalence, or high HIV prevalence, with half reporting trend data with three or more data points. Revised estimates of the global MDR-TB burden will be published. In 2015, data should be available for 90% of settings, with 70% of settings reporting trend data with three or more data points.

Objective 2: By 2015, all regions should carry out DST for all previously treated TB patients. In the Eastern European Region, DST should also be done for all new TB patients, while in the Latin American, South-East Asian and Western Pacific Regions, DST should be done for 20% of new TB patients, focused on people at increased risk of MDR-TB.

Milestones: By 2010, all countries with a national reference laboratory (NRL) should be performing quality-assured culture and DST, and collaborating with a supranational reference laboratory (SRL). DST will have expanded to cover 92% of all new and previously treated cases in Eastern Europe. All other regions will be providing DST for approximately 60% of targeted previously treated patients, and the Latin American, South-East Asian and Western Pacific Regions will also provide DST for at least 10% of targeted new cases.

Objective 3: By 2015, all detected MDR-TB patients should be treated with quality-assured second-line drugs in line with WHO guidelines (17% of the estimated culture-positive MDR-TB cases in 2010 and 56% in 2015).

Objective 4: By 2015, the price of second-line drugs will have been further reduced, and quality-assured second-line drugs will be produced by manufacturers based in countries with a high burden of MDR-TB.

Milestone: By 2010, quality-assured production of second-line drugs will have been established in several countries with a high MDR-TB burden, including China, India, the Russian Federation and South Africa.

Objective 5: Provide technical direction and strategic planning for the management and coordination of global MDR-TB surveillance and control, in close collaboration with other Stop TB Working Groups including those on new drugs and diagnostics.

Milestones: By 2006, the structure and functions of the Stop TB Working Group on DOTS-Plus for MDR-TB and its subgroups, including the GLC, will be reviewed and adapted to the new challenge of scaling up the diagnosis and treatment of MDR-TB, reaching beyond the initial phase of pilot-testing MDR-TB management. Drug resistance surveillance will be included in the Working Group. By 2008, all WHO regions will have regional GLC mechanisms reviewing applications and ensuring that DOTS-Plus is monitored regularly as part of routine TB control missions. By 2015, all regions and countries will include DRS and MDR-TB management in regular TB courses and workshops.

Monitoring and evaluation

The global MDR-TB situation is monitored by the WHO/IUATLD global DRS project, and data are published every three years. In addition, MDR-TB estimates have been published and are updated regularly. DOTS-Plus programme performance is currently monitored by WHO and the Green Light Committee. Information will become available on second-line drug use in public and private sectors from an inventory conducted in 2005.

The SRL network was started in conjunction with the WHO/IUATLD global DRS project, and is composed of twenty-three TB laboratories conducting annual proficiency testing. This

PART III: PARTNERSHIP ACTION TO ACHIEVE THE GOALS

network is also responsible for the quality assurance of DST in NRLs worldwide.

A DOTS-Plus recording and reporting system has recently been developed, to allow managers at different levels of NTPs to monitor overall DOTS-Plus programme performance. In the future, elements of this system will also be included in the DOTS recording and reporting system at district level.

As the DOTS strategy evolves to include all TB patients, MDR-TB notifications and treatment outcomes should become part of the annual WHO report (Global tuberculosis control: surveillance, planning and financing).

Monitoring of progress in MDR-TB control will also be undertaken in collaboration with partners and WHO regional and country staff during routine technical missions.

Finally, annual or semi-annual meetings of the Working Group on DOTS-Plus for MDR-TB will take place to review the progress made in global DRS and MDR-TB control, and to give strategic direction for future activities. The Working Group will also monitor funding and expenditure on the global coordination of DOTS-Plus scale-up during the Plan period.

Key risk factors

The Working Group has identified four major areas of risk which it will seek to address.

- A deterioration in the global MDR-TB situation and continued misuse of second-line drugs.

Unless DOTS-Plus is promoted and scaled up by all health care providers involved in diagnosing and treating MDR-TB (including private practitioners), there is a risk that TB strains resistant to all known anti-TB drugs will emerge and start to circulate. In addition, the potential joint impact of HIV and MDR-TB in resource-limited settings cannot be overstated and requires urgent attention.

Poor quality drugs may favour the emergence of additional drug resistance. Manufacturers of second-line drugs must be mobilized to apply to the WHO prequalification system for second-line drugs, especially as some countries may not be interested in purchasing drugs from the GLC (mainly countries producing second-line drugs). In order to ensure the use of quality-assured drugs, WHO and its partners should advocate for NTPs and funding agencies to purchase drugs from companies on the WHO list of prequalified manufacturers.

- A lack of well functioning laboratory networks providing culture and drug susceptibility testing.

Currently, one of the biggest obstacles to monitoring drug resistance and implementing DOTS-Plus programmes is the lack of well functioning culture and DST laboratories. A massive influx of both technical and financial resources is required to scale up laboratory services, in order to expand DRS and DOTS-Plus globally. The first priority is to have a well equipped, safe, and highly performing central laboratory; services can then be

expanded as needed, while maintaining quality. Improvement in laboratory networks would include both the optimal use of existing tools and the development and implementation of new technology. Both the Working Group on New TB Diagnostics and the DEWG laboratory-strengthening subgroup have budgeted for scale-up within the Global Plan.

- Lack of political will.

Lack of national policies on MDR-TB control and of leadership to engage all health care providers present threats to the global MDR-TB situation. Future success will depend on the political commitment and stability of countries, and the commitment of the donor community and technical agencies to scale-up and strengthen DOTS-Plus programmes.

Political commitment is key for any DOTS-Plus programme and must translate into financial and human resources. At country level, financial resources are needed for all aspects of DOTS-Plus implementation. The GFATM now plays a major role in the financing of MDR-TB control, contributing to almost half the current GLC-approved projects. Strengthening the workforce to deliver sound MDR-TB control services is a priority for the next decade, and countries need to have clear plans for human resource development and the financial resources to realize them.

- Lack of global coordination.

At global level, a smooth scale-up of DRS and DOTS-Plus requires resources for monitoring the global MDR-TB epidemic and DOTS-Plus programme performance, as well as continued policy development and dissemination of guidelines. Human resources are needed to provide technical assistance to countries for planning, monitoring, expanding and evaluating DOTS-Plus.

See Table 20: Expected achievements and costs of DOTS-Plus, 2006–2015, by region.

See Table 21: Scale-up of DST and DOTS-Plus by region

Budget requirements for the Working Group on DOTS-Plus for MDR-TB: 2006–2015

The funding needed for DOTS-Plus implementation at country level for the 10-year period of the Global Plan, 2006–2015, is US\$5.8 billion. More than 60% of the funds (US\$3.9 billion) are needed for the Eastern European Region.

See Table 22: Budget requirements for the Working Group on DOTS-Plus for MDR-TB: 2006–2015 (US\$ MILLIONS)

TABLE 20: EXPECTED ACHIEVEMENTS AND COSTS OF DOTS-PLUS, 2006–2015, BY REGION.

	Estimated number of culture-positive MDR-TB cases (thousands)	Number of patients treated under DOTS-Plus (thousands)	Number of patients successfully treated (thousands)	Deaths averted (thousands)	Cost per patient treated under DOTS-Plus (US\$)	Total costs (million US\$)
Africa – high HIV/AIDS	147	18	13	3	2,273	38
Africa – low HIV/AIDS	58	11	8	2	1,979	20
Eastern Europe	858	410	315	72	8,196	3,450
Eastern Mediterranean	407	48	36	6	3,897	180
Latin America	72	20	15	3	5,189	103
South-East Asia	1,021	145	107	31	3,908	545
Western Pacific	809	126	93	25	5,197	644
TOTAL	3,372	778	587	142	-	4,980

TABLE 21: SCALE-UP OF DST AND DOTS-PLUS BY REGION

	DST coverage of new cases (%)			DST coverage of previously treated cases (%)			DOTS-Plus coverage among detected MDR-TB patients (%)		
	2005	2010	2015	2005	2010	2015	2005	2010	2015
Africa – high HIV/AIDS	0	0	0	0	60	100	0	50	100
Africa – low HIV/AIDS	0	0	0	21	60	100	8	54	100
Eastern Europe	83	92	100	83	92	100	5	70	100
Eastern Mediterranean	0	0	0	21	60	100	17	58	100
Latin America	12	16	20	42	71	100	29	65	100
South-East Asia	3	12	20	18	59	100	1	43	100
Western Pacific	0	10	20	10	55	100	8	54	100

TABLE 22: BUDGET REQUIREMENTS FOR THE WORKING GROUP ON DOTS-PLUS FOR MDR-TB: 2006–2015 (US\$ MILLIONS)

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	ALL YEARS	% TOTAL
COUNTRY NEEDS												
ALL REGIONS	142	258	383	510	634	700	752	788	811	828	5,806	100%
AFR- HIGH	1	1	2	3	4	5	6	7	8	9	45	1%
AFR LOW	0	1	1	2	2	3	3	4	5	5	26	0.4%
EEUR	114	202	291	379	461	487	504	508	504	478	3,928	68%
EMR	3	5	9	14	19	24	30	35	41	47	226	4%
LAC	6	7	9	10	12	13	14	16	16	17	121	2%
SEAR	8	19	32	47	64	77	90	100	107	133	678	12%
WPR	11	23	38	55	73	90	105	118	130	138	782	13%
INTERNATIONAL AGENCY NEEDS												
TECHNICAL COOPERATION*	-	-	-	-	-	-	-	-	-	-	-	-
WG OPERATIONAL NEEDS												
	1	1	1	1	1	1	1	1	1	1	11	0.2%
TOTAL	143	259	384	511	635	701	753	789	812	829	5,817	

* Some aspects of technical cooperation will be undertaken jointly for DOTS Expansion, TB/HIV and DOTS-Plus. Since it is difficult to identify what share of these costs applies to each working group, the total is shown in the budget for DOTS Expansion. Annual total cost ranges from US\$220 million to US\$280 million.

10.2.3 TB/HIV Working Group: summary strategic plan, 2006–15

The creation of the Stop TB Partnership's TB/HIV Working Group in 2000 initiated a more collaborative approach to the prevention and care of HIV-related TB, which builds on existing DOTS programmes and comprehensive HIV/AIDS prevention and care.

Strategic vision: 2006–2015

The strategic vision of the TB/HIV Working Group for 2006–2015 is to reduce the global burden of HIV-related TB through effective collaboration between TB and HIV programmes and communities, and evidence-based collaborative TB/HIV activities, to achieve the global targets for 2015, including the MDG and Stop TB Partnership targets for TB and HIV. The vision is rooted in the new WHO Stop TB Strategy.

The **mission** of the TB/HIV Working Group is to develop an effective, evidence-based policy to reduce the impact of HIV-related TB and to promote, monitor and evaluate the global implementation and impact of this policy.

The Working Group's **goal** is to understand and address the epidemic of HIV-related TB by:

- promoting and supporting research to establish a comprehensive evidence-based global policy on collaborative TB/HIV activities;
- building effective collaboration between TB and HIV/AIDS programmes and communities and engaging all health providers in implementing TB/HIV activities in countries and communities with a high burden of HIV-related TB.

TB/HIV activities are not a substitute for well-functioning DOTS-based TB programmes and comprehensive HIV/AIDS prevention and care programmes. Instead they aim to build on existing programmes, exploiting the synergies and commonalities between them to deliver comprehensive, high-quality, accessible, patient-centred prevention, care and support services to people affected by TB and HIV – two diseases that often occur in the same community or the same patient.

Objectives

Guidelines have been developed for TB/HIV collaboration,⁴² building on DOTS TB programmes and HIV/AIDS programmes to provide comprehensive TB and HIV prevention, care and support services to reduce the impact of HIV-related TB. While the TB/HIV policy still needs to be refined and some gaps remain to be filled (e.g. TB/HIV services for injecting drug users), the priority is now to deliver, monitor and maintain these standards in the context of the overall Stop TB Strategy and the goal of universal access to HIV treatment and care by 2010 endorsed by the G8 in 2005.

Urgent implementation of the TB/HIV policy in all settings with a high HIV burden is at the core of the TB/HIV strategic plan for 2006–2015, together with expansion of the evidence base through country experience and new research, in order to

refine and adapt the policy and address the needs of at-risk populations. The plan considers what is needed to overcome general health service constraints to the adoption of new policy and the provision of universal access to TB/HIV services. The declaration, by the WHO Regional Committee for Africa, of TB as an emergency in Africa and the severity of the TB/HIV epidemic in Africa merit urgent attention. The plan also reflects the Blueprint for Africa 2006–2007, a more detailed, intensified, short-term action plan developed to accelerate progress in the Region.

The TB/HIV Working Group strategic plan sets out the activities that need to be undertaken by the Working Group and its partners over the next 10 years to achieve the 2015 targets, under four objectives.

Objective 1: Scale up and expand collaborative TB/HIV activities

1.1 Scale up implementation of the TB/HIV policy.⁴³

Ambitious rates of scale-up of TB/HIV activities are needed to achieve universal access to HIV treatment and care by 2010, and to reach Partnership targets for 2015, linked to the MDGs. TB control will need to be fully coordinated with the HIV community and general health services. In most settings, TB treatment services are decentralized to the health facility level, whereas few countries have as yet decentralized ART to health facility level, making this an urgent priority. The TB/HIV Working Group must foster decentralization of comprehensive HIV care to facility level. Where possible, TB/HIV services should be delivered at community level to increase accessibility.

1.2 Expand the scope of existing global policy to increase accessibility and acceptability of collaborative TB/HIV activities. The TB/HIV policy will be finalized and refined using country experience and new evidence. It will be adapted to ensure that TB/HIV services are appropriate, accessible, acceptable and affordable to populations not specifically covered in existing policy, including women, children, mobile or remote populations, the poor, intravenous drug users and prisoners. Collaboration will need to be expanded to include other services, e.g. maternal and child health, harm reduction, and prison services, in order to respond to the needs of these populations, and increase TB and HIV case-finding through targeted screening and contact tracing. Tools to identify, measure and reduce stigma should be developed.

1.3 Address immediate gaps and bottlenecks in the implementation of TB/HIV services.

Policies and guidelines on antiretroviral treatment of HIV-infected people with TB are urgently required. Diagnostic algorithms are needed for more rapid identification of people with smear-negative or extrapulmonary TB, which are more common in those with HIV. Generic training materials (see objective 4.3 below) should be made available for countries and technical assistance should be available, if needed, to help countries translate policy guidance into specific implementation plans.

1.4 Improve quality improvement through surveillance, monitoring and evaluation

The Working Group should take the lead in global coordination of collaborative TB/HIV activities and in demonstrating the impact of TB/HIV activities. This will require effective monitoring and evaluation systems to provide reliable and regular information on the progress and impact of national level TB/HIV activities. This information must feed into TB and HIV planning cycles at all levels, turning results into best practices, improvement in programme quality, and strong advocacy messages to support investment in TB/HIV activities. Monitoring and evaluation should demonstrate whether services are accessible and responding to the needs of the poor, women and marginalized groups.

Objective 2: Develop and coordinate implementation of research to improve the prevention, early diagnosis and rapid treatment of TB in PLWHA and incorporate results into global policy.

2.1 Continually refine the prioritized research agenda for collaborative TB/HIV activities and support operational research on TB/HIV at country level.

There is an urgent need for more TB/HIV research to strengthen the evidence base for prevention, diagnosis and management of TB/HIV. The Working Group will play a key role in pursuing the global TB/HIV research agenda. This will require close collaboration with TB and HIV policy-makers, affected communities and researchers, to direct the research agenda and mobilize the necessary resources. The agenda must cover basic science research, research into new tools (in collaboration with the new tools working groups of the Partnership), and operational research. Innovative ways of coordinating delivery of TB/HIV services need to be explored, e.g. “one-stop shops” for both TB and HIV services, and integration of service delivery at district level.

2.2 Translate research findings into global policy and practice.

One of the most important roles of the Working Group will be to manage the process of disseminating research findings and translating them into global policy and practice. A continuous cycle, in which policy-makers and policy-users inform research priorities, and research informs policy, must be maintained. Close collaboration with the Partnership’s new tools working groups will be necessary to facilitate testing of new drugs, diagnostics and vaccines as they become available and ensure their rapid application.

Objective 3: Increase political and resource commitment to collaborative TB/HIV activities.

3.1 Mobilize technical, financial, and human resources

National policy-makers, health professionals and affected communities, including PLWHA, need to be encouraged to take the lead in TB/HIV activities, to define country priorities and allocate available national financial resources for comprehensive TB and HIV prevention and care, supplemented as necessary by external funds. The TB/HIV Working Group will work with the other working groups to help countries to mobilize additional resources for TB/HIV control from bilateral and multilateral donors, as well as nongovernmental organizations, and other

international and philanthropic funding initiatives. Donors must be encouraged to allow TB- or HIV-specific funding to be used for TB/HIV activities.

3.2 Advocacy and communication

International advocacy and communication efforts need to be directed at placing TB and TB/HIV near the top of the health and development agendas, alongside HIV/AIDS. Grassroots TB and HIV activists can work together to considerably enhance impact. Messages should be sustained, directed and tailored to specific audiences. This community mobilization approach needs to be adapted to increase political commitment to TB/HIV activities. These objectives will be implemented in collaboration with the ACSM Working Group.

Objective 4: Contribute to strengthening health systems to deliver collaborative TB/HIV activities.

4.1 Strengthen DOTS-based TB control and comprehensive HIV/AIDS prevention, care and support.

Diagnosis and treatment of TB under DOTS and HIV prevention are the most effective interventions to reduce the impact of HIV-related TB. The TB community needs to work more closely with the HIV community to advocate at community, district, and country level, as well as internationally, for comprehensive TB and HIV prevention, care and support. The WHO Department of HIV/AIDS and UNAIDS are planning for universal access to HIV/AIDS prevention, care and treatment by 2010, and the TB community must become a major partner in this ambitious plan.

4.2 Develop a multisectoral approach to collaborative TB/HIV activities with strong programme planning, management and sustainable financing.

Many of the broader determinants influencing TB and HIV are outside the direct influence of the health sector, but could be effectively addressed through a collaborative approach. The multisectoral approach to HIV/AIDS prevention and care, adopted by UNAIDS and UNICEF, should be adapted to include TB and TB/HIV on the agendas of the major sectors that have an influence on health, e.g. economy, education, employment, and justice. Ministries of health should work with other line ministries (e.g. defence, prisons, and police), national NGO networks and professional associations to promote their engagement in policy formulation, planning and implementation of national TB control activities.

4.3 Human resource capacity development.

Of all the health system constraints limiting TB and HIV control, the most acute is the health workforce crisis. A collaborative approach to human resource capacity development will benefit both programmes. A joint TB and HIV programme approach to TB/HIV training should be adopted, and coordinated with other disease-specific programmes, such as the WHO Integrated Management of Adult and Adolescent Illness. In the short term, externally funded international and national staff will be required to assist national programmes in scaling up activities. The major technical agencies in TB/HIV, such as the Centers for Disease Control and Prevention (CDC), Damien Foundation, the

German Leprosy Relief Association (GLRA), IUATLD, the Royal Netherlands Tuberculosis Foundation (KNCV) and WHO, can provide technical assistance to plan, implement, monitor and evaluate TB/HIV activities. Experience shows that initial training must be followed by on-the-job supervision if it is to be fully utilized.

4.4 Engage all health care providers in collaborative TB/HIV activities.

Many health care providers outside the traditional public health system are providing care for TB and HIV, and could be engaged in providing comprehensive, high-quality TB/HIV prevention and care services in line with national programmes. The Public Private Mix DOTS Subgroup has pioneered the principles of involving health providers outside the public health system in TB control and this model will be adapted to include collaborative TB/HIV activities and HIV/AIDS prevention and care.

4.5 Engage people with TB and HIV and affected communities in planning, delivering, monitoring and evaluating collaborative TB/HIV activities.

People and communities affected by TB and HIV should be empowered to play a central role in planning, delivering, monitoring and evaluating TB/HIV activities. Resources must be identified to support community activism and involvement in TB/HIV. In low-resource settings, especially where human resource capacity is limited, communities and groups, such as faith-based organizations and PLWHA groups, can play an important role in delivering TB/HIV activities, provided that adequate training and supportive supervision are provided in partnership with the formal health sector to ensure quality care that responds to individual and community needs.

4.6 Strengthen laboratory capacity for collaborative TB/HIV activities

Overall laboratory capacity, infrastructure and quality need to be greatly improved to assist in the diagnosis and management of HIV-related TB, especially smear-negative, extrapulmonary and multidrug resistant TB, and TB in children. The speed and reliability of TB diagnosis must be improved, as well as the capacity of TB laboratories to diagnose and stage HIV infection, and monitor effects and side-effects of dual TB and HIV treatment.

Key risk factors

The key risk factors for not achieving the objectives of the Working Group include the following:

- The HIV epidemic continues to spread. The TB community must advocate for all efforts to mitigate the impact of HIV/AIDS and to promote HIV prevention and treatment as a vital component of TB control strategy.
- Poverty and inequality increase. Unless the level of absolute poverty can be reduced, it will be difficult to reduce the incidence of TB and HIV.
- Weak health systems. Weak capacity to deliver TB/HIV control strategies in low-income countries will be among the greatest constraints to achieving the 2015 targets.
- Lack of commitment to TB/HIV collaboration. TB and HIV

programmes and communities must be committed to, and agree on, the principles and methods. Political commitment is key to allocation of human and financial resources.

- Lack of global coordination. Inadequate funding for the Working Group will mean that it is unable to direct new research, refine policy, provide technical assistance to countries, and undertake monitoring and evaluation.

Monitoring and evaluation

A guide to monitoring and evaluating collaborative TB/HIV activities defines core indicators.⁴⁴ Existing globally recommended data collection tools for TB and HIV/AIDS are being adapted to capture additional TB/HIV data. TB/HIV activities are now included in the global TB reporting system and should be included in the global AIDS reporting frameworks. The impact of TB/HIV activities will be measured in terms of existing impact indicators, such as TB mortality, TB incidence, and HIV incidence.

See Table 23: Collaborative TB/HIV activities defined in the TB/HIV policy

See Table 24: Budget requirements for the TB/HIV Working Group: 2006-2015 (US\$ MILLIONS)

TABLE 23: COLLABORATIVE TB/HIV ACTIVITIES DEFINED IN THE TB/HIV POLICY

Activity	Description	Steps that may be required
ESTABLISH THE MECHANISMS FOR COLLABORATION		
Set up a coordinating body for TB/HIV activities effective at all levels	Representative body to plan, coordinate and implement collaborative TB/HIV activities, advocate for resources, build capacity and involve all stakeholders.	National-level working group, with representatives of national TB programme, national AIDS control programme (NAP), Global Fund, private sector, major partners, to meet at least quarterly District level committee - may include district TB coordinator, district medical officer, district AIDS control officer, community representatives, local NGOs.
Surveillance of HIV prevalence among TB patients	Establishing the burden of HIV disease among TB patients, to understand the overlap between the two diseases and assist in rational planning of services.	Assessment of HIV epidemic status, TB situation and available resources and expertise, to identify the best surveillance method, e.g. special periodic surveys, sentinel surveys, or data from routine HIV testing of TB patients.
Joint TB/HIV planning	Develop joint plans, to include resource mobilization, standard operating procedures, capacity-building and training, advocacy, communication and social mobilization, community involvement and research.	NTP and NAP to develop and implement a joint plan for collaborative TB/HIV activities or to incorporate TB/HIV activities into their respective NTP and NAP plans.
Monitoring and evaluation	Adapt TB and HIV monitoring and evaluation systems to capture information on collaborative TB/HIV activities.	Revise TB and HIV recording and reporting forms and registers to be able to capture information on collaborative TB/HIV activities. Train staff in revised recording and reporting. Joint analysis of results.
DECREASE THE BURDEN OF TUBERCULOSIS IN PEOPLE LIVING WITH HIV/AIDS		
Intensified tuberculosis case-finding	Regular screening of PLWHA for active TB in all HIV care and support settings and HIV testing settings.	NAP to liaise with NTP for protocol development, training of staff, ensuring access to TB diagnostic services for those found to have TB symptoms on screening.
Isoniazid preventive therapy	Preventing active TB disease by giving treatment for latent TB infection to PLWHA who do not have active TB.	NAP to liaise with NTP for protocol development, training of staff, drug supplies, follow-up, adherence support.
TB infection control in health care and congregate settings	PLWHA are at high risk of developing active TB after exposure. Every effort must be made to reduce exposure in institutional settings where HIV prevalence is high e.g. medical clinics, hospitals, prisons.	NTP and NAP to establish infection control policy and monitor implementation of policy in all high HIV prevalence settings; will require liaison with other sectors, e.g. industry, prisons.
DECREASE THE BURDEN OF HIV/AIDS IN TUBERCULOSIS PATIENTS		
HIV testing and counselling	Where HIV epidemic is generalized all TB patients should be encouraged to have HIV counselling and testing, ideally within the TB service.	Requires political commitment, NTP to liaise with NAP on developing policy and guidelines, training, accessing test kits, confidential counselling space in clinics, referral mechanism, and transport or incentives if testing not available on site.
HIV prevention	Appropriate HIV prevention advice and methods should be made available to TB patients where HIV prevalence is high.	NTP to liaise with NAP to develop IEC materials, train staff, provide condoms, safe injection practice, needle exchange, methadone replacement, as appropriate.
Co-trimoxazole preventive therapy	Co-trimoxazole preventive therapy reduces mortality and morbidity among HIV-positive TB patients	Requires staff training, drug supplies, adherence support, IEC materials.
HIV/AIDS care and support	HIV-positive TB patients must be able to access comprehensive HIV care and support, ideally within the TB service	NTP to coordinate with NAP to provide training, ensure access to treatment for opportunistic infections, referral mechanisms, and transport or incentives if care and support not available on site.
Antiretroviral therapy	NTP can be an important entry point for ART as a high proportion of HIV-positive TB patients are eligible for ART	NTP to liaise with NAP on protocols, training, access to drugs, ensuring that ART and TB treatment regimens are compatible, recording and reporting, adherence support, IEC materials.

TABLE 24: BUDGET REQUIREMENTS FOR THE TB/HIV WORKING GROUP: 2006-2015 (US\$ MILLIONS)

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	ALL YEARS	% TOTAL
COUNTRY NEEDS												
ALL REGIONS	418	470	536	615	689	742	768	795	825	858	6,716	100%
AFR- HIGH	304	337	380	428	471	493	512	534	559	586	4,605	68%
AFR LOW	19	20	23	28	32	37	40	42	45	47	334	5%
EEUR	3	4	7	13	19	23	26	28	31	33	186	3%
EMR	8	9	12	14	16	24	23	23	22	22	175	3%
LAC	6	8	10	14	17	20	21	22	23	24	166	2%
SEAR	68	79	91	104	117	130	130	131	131	132	1,112	17%
WPR	9	11	13	14	16	16	15	15	14	14	137	2%
INTERNATIONAL AGENCY NEEDS												
TECHNICAL COOPERATION*	-	-	-	-	-	-	-	-	-	-	-	-
WG OPERATIONAL NEEDS												
	1	1	1	1	1	1	1	1	1	1	11	0.2%
TOTAL	419	471	537	616	690	744	769	796	826	859	6,727	

* Some aspects of technical cooperation will be undertaken jointly for DOTS Expansion, TB/HIV and DOTS-Plus. Since it is difficult to identify what share of these costs applies to each working group, the total is shown in the budget for DOTS Expansion. Annual total cost ranges from US\$220 millions to US\$280 millions

10.3 New Tools Working Group plans

Introduction

New tools to control TB are critical to achieving the Partnership's goal of reversing the TB epidemic and eventually eradicating the disease by 2050. In areas of high HIV/AIDS prevalence and rising drug resistance, the TB epidemic is overwhelming current drugs and diagnostics. Furthermore, we cannot hope to achieve the long-term vision of TB elimination without effective new vaccines to drain the reservoir of latent infection. Together, the three working groups on new tools are working to meet these challenges and provide better technologies for preventing TB, and speeding the process of diagnosis and treatment, especially in Africa and Eastern Europe, where TB/HIV and MDR-TB make TB control tremendously difficult.

Cross-cutting issues

There are many cross-cutting issues and synergies in the development and application of new tools.

A primary shared interest is in basic research to address fundamental gaps in the science and understanding of the biology and pathogenesis of *Mycobacterium tuberculosis*. Current investment in basic tuberculosis research is inadequate to sustain the pipeline of discovery. The Stop TB Partnership is united in advocating for increased investment in fundamental scientific research on tuberculosis to fortify the foundations of knowledge that will lead to future major advancements in the field.

The establishment of the clinical trials platform for the evaluation and demonstration of new tools in national TB control programmes is essential. Additionally, new technologies should be applied synergistically to secure a cumulative epidemiological impact as well as more effective and simplified management of TB control.

Addressing poverty is another key cross-cutting issue. The new tools working groups recognize the need to develop new technologies that will be affordable in developing countries, where the bulk of the TB burden lies. Creative intellectual property mechanisms that protect the public health sector and enhance access to new technologies by underprivileged patients are being implemented.

Expectations for 2006–2015 and beyond

Currently there are 15 diagnostics, 27 drugs, and 12 vaccine candidates in the research and development pipeline. By 2006, the first new diagnostics for culture and sensitivity testing, with a shorter response time, will be introduced; by 2010, new rapid diagnostics that are more sensitive than microscopy will be available for use at clinic level. The first new drug for TB will be launched by 2010, and by 2015, we will be on the verge of an entirely new regimen of novel chemical entities that will shorten treatment to one to two months. Starting in 2015, new-generation TB vaccines will be available. New diagnostics, drugs and vaccines to fight latent disease will be available between 2012 and 2018 to help us move towards the eventual elimination of TB.

Synergy with implementation working groups and Secretariat

The new tools working groups are engaged in active discussions and collaboration with the implementation working groups to evaluate and demonstrate new technologies in national TB control programmes. The Working Group on New TB Diagnostics and the DOTS Expansion Working Group are already collaborating in demonstration projects for new technologies.

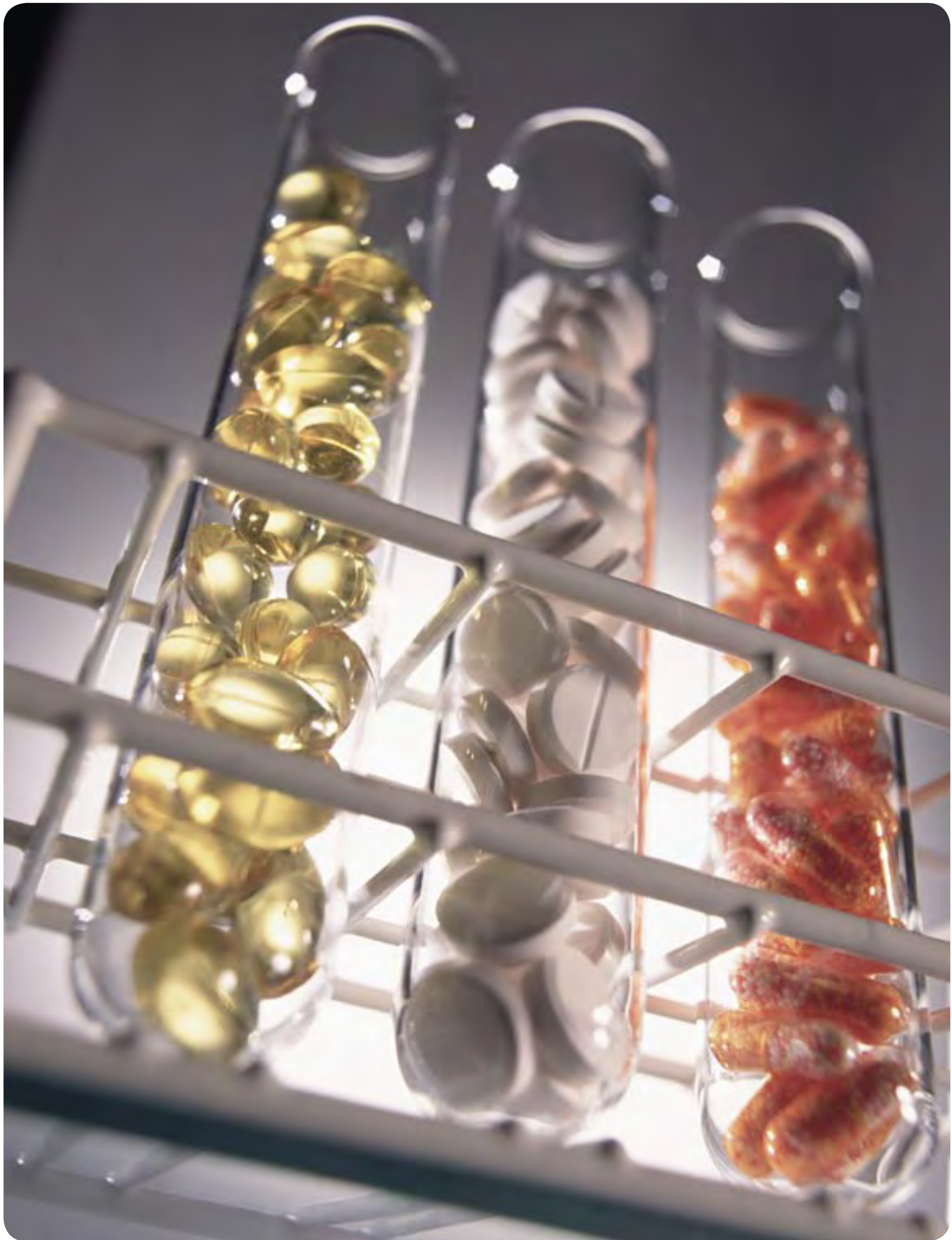
With regulatory approval of new tools expected in the next five years, a plan for incorporating these new technologies into current TB control, or "retooling", is urgently needed. Historically, significant time lags between the creation of new tools and their adoption in the field have delayed patients' access to the best technologies to fight TB. The Partnership Secretariat and all seven working groups will develop a concrete plan to address:

1. the prompt approval of new tools for adoption by WHO and in countries;
2. purchasing mechanisms; and
3. the training of health care workers and national TB programmes who will use and administer these new tools in the field.

New mechanisms will ensure smooth and rapid transition of new research and development tools directly to the field. Additionally, a budget will be allocated to ensure that these activities can be carried out and new technologies can be promptly adopted.

As new technologies and tools for TB control come on-line, the Partnership's Global Drug Facility plans to integrate their delivery into the overall package it offers. The GDF will need to negotiate concessional pricing of new technologies, and sustain the reputation of the Partnership and Secretariat for supporting the provision of high-quality, low-cost TB control interventions. Between 2008 and 2011, GDF systems will be prepared for the introduction of new drugs and new diagnostics, and possibly TB/HIV treatments packaged together. In a parallel effort, the Working Group on New TB Vaccines will initiate collaboration with the Global Alliance for Vaccines and Immunization (GAVI), the newly established International Financing Facility for Immunization and the Expanded Programme on Immunization (EPI) to develop plans and mechanisms for swift introduction of new-generation vaccines as they become available (approximately 2013).

The Stop TB Partnership Secretariat will encourage and support the development of new procedures in order to improve the collaboration between the groups, and will facilitate progress towards the common goal of TB control.



Innovate

The Plan has a two-track approach to Stop TB: maximizing the benefit of applying the existing tools for TB control, while at the same time developing the new tools (diagnostics, drugs and vaccines) that are so urgently needed. Innovation is key to both these approaches. The Plan encompasses innovative methods of expanding access to quality TB care. The Plan also encompasses the innovation of research and development in making available the new, improved tools to Stop TB.

Until recently, TB as a global health issue suffered from a lack of investment in the development of innovative tools to Stop TB. Full funding of the Plan will transform this situation, as new diagnostics, drugs and vaccines become increasingly available. The dramatic breakthrough to eliminate TB by 2050 depends on these innovative tools.

Innovation is the key to progress, through maximizing the benefit from existing tools and promoting the development of new tools to Stop TB.

10.3.1 Working Group on New TB Diagnostics: summary strategic plan, 2006–2015

The Working Group on New TB Diagnostics was established in 2001 with the aim of coordinating and facilitating the development of a toolbox of widely accessible diagnostic tests to augment control of the global TB epidemic. Over the coming decade the Working Group plans to bring through a portfolio of such diagnostic tests, with implementation level ranging from the district level laboratory to first point of care (POC).

Strategic vision: 2006–2015

More than a century after its original development, the microscopic examination of sputum is still the only widely available diagnostic tool for identifying TB in most developing countries. Unfortunately, the test has a sensitivity of only 40–60% under field conditions, falling as low as 20% in the presence of HIV coinfection. Yet even this unremarkable diagnostic test remains beyond the reach of the majority of TB patients.

In resource-limited settings drug susceptibility testing, if available, is usually performed only after treatment failure, missing an opportunity to interrupt transmission. In contrast the standard of care in industrialized nations is universal susceptibility testing. One third of the population of the world has a latently infection with *M. tuberculosis*. Preventive therapy effectively reduces progression to active disease, but there is currently no way to predict which subjects are at greatest risk of progression, with most to gain from such therapy.

These three issues dominate the current strategic direction of the Working Group on New TB Diagnostics.

The vision of the Working Group is to develop and introduce cost-effective and appropriate new diagnostic tools that are accessible to patients and will contribute towards improved control of the global TB epidemic and improve the quality of patient care.

The ideal toolbox would contain diagnostic technologies that perform equally well in HIV-infected subjects, to

1. improve TB case detection, through high sensitivity and specificity and improved accessibility – simple, accurate, inexpensive products that produce results on the same day, and can be applied at low levels of care, are the ultimate goal;
2. rapidly and inexpensively identify drug-resistant TB, allowing timely effective treatment to reduce both individual morbidity and transmission;
3. reliably identify latent TB infection and define the risk of future progression to active disease, allowing rational use of preventive therapy in appropriate subjects.

See Objectives on opposite page

Activities

Discovery biology and basic technology

The greatest impact on public health in the TB diagnostics area is expected from a highly accurate and field-usable testing device. The most prominent barrier to the development of suitable antigen or antibody assays is the lack of suitable targets. In existing serological tests, sensitivity is relatively high

only in patients with smear-positive disease, and much lower in children, patients with extrapulmonary or smear-negative disease, or HIV coinfection, thus offering little additional benefit over sputum smear. During 2005, the Working Group, in collaboration with TDR, will complete an assessment of a wide range of commercially available rapid serological tests.

In 2005–2006 FIND will select more promising antigen combinations, on the basis of available research data and expert knowledge and opinion. The Working Group plans to foster and finance additional research in this area, building on advances in mycobacterial genome sequencing and expression profiling. It is anticipated that this information will facilitate the development of subsequent generations of improved test strips suitable for use at point of care, and that during 2006–07 an improved POC test (for blood, serum, urine or saliva) will be developed.

Research on predictive markers for the conversion of latent infection into active disease is still in its infancy. The Working Group estimates that basic research at academic sites will be needed for at least three more years before product development can be initiated. The market for such products will be broad, thus a reasonable drive for resource allocation in competent research centres can be assumed, which will be monitored and supported by the Working Group.

Nucleic acid amplification tests (NAAT) show promise for rapid and reliable detection of *M. tuberculosis* in sputum and other samples. The key challenge for harnessing the benefit from these technologies in the public health sector of developing countries is discovering highly integrated, user-friendly solutions that are affordable. During 2005–06 FIND will assess the technical feasibility of several candidate system concepts with a view to selecting development partners for a highly integrated NAAT product for use at the first referral level (district laboratory) or at the peripheral level (currently microscopy centre) by 2008.

Product development

The Working Group will support product development both directly, through product-specific development partnerships, and indirectly, through the creation of a stimulating and enabling framework.

The direct measures will include financial and logistic support for a portfolio of projects that respond to the specific needs of the different levels of the public health system in high-burden countries (first referral level or district laboratory, peripheral laboratory or microscopy site, and point of care or rural health post). Different products will be needed for case detection, diagnosis of MDR-TB, and latent infection. The essential targets for product introduction at the different levels of the health system are outlined in Figure 34.

See Figure 34: Targets for introduction of tests, leading to sustainable adoption, 2006–2015

The indirect measures, comprising an enabling infrastructure, are: (1) the release in 2005 of the first comprehensive market report with special emphasis on the public health markets in developing countries; (2) the detailed identification and description of customer requirements – these customer requirements are specific for the different segments of the public health system and serve as a basis for more detailed product

OBJECTIVE 1: Address existing gaps in knowledge that are obstructing development of new diagnostic tools

TARGETS	INDICATORS (APPLY TO ALL 3 TARGETS)
<ul style="list-style-type: none"> • Sensitive early detection of active disease Discovery science to identify new markers (also in HIV-infected subjects) with improved discriminative power for active disease (may be antigenic, immunological, proteomic or other) Validation of candidate targets in suitable screening format (e.g. enzyme-linked immunosorbent assay (ELISA)) with patient samples from target populations Exploration and further refinement of understanding of transmission dynamics and natural history to inform mathematical modelling of potential impact of new diagnostic tools • Identification of latent TB infection at risk of progression Discovery science to identify new markers (also in HIV-infected subjects) with improved discriminative power for predicting future progression to active disease (may be antigenic, immunological, proteomic or other) Evaluation of predictive value, in identifying subjects at risk of progression, of next generation of existing tools for detection of latent TB infection • Simple, rapid identification of drug resistance Discovery science to identify novel markers of drug resistance for first- and second-line drugs in cultured isolates Discovery science to improve detection of drug resistance direct from patient samples Validation of marker candidates in suitable screening format with patient samples from target populations 	<ul style="list-style-type: none"> • Number of studies received and financed through "requests for applications" • Number of agencies having announced related funding opportunities • Number of related peer-reviewed publications • Number of new promising technologies reported • Number of new diagnostic reagents/targets identified • Number of new promising technologies identified through landscape-mapping • Number of requests for reference material received by sample and strain banks • Number of publications associated with use of sample and strain banks • Number of target validation studies performed under the auspices of the Working Group on New TB Diagnostics • Number of new targets with contractually assured affordable and sustainable product access

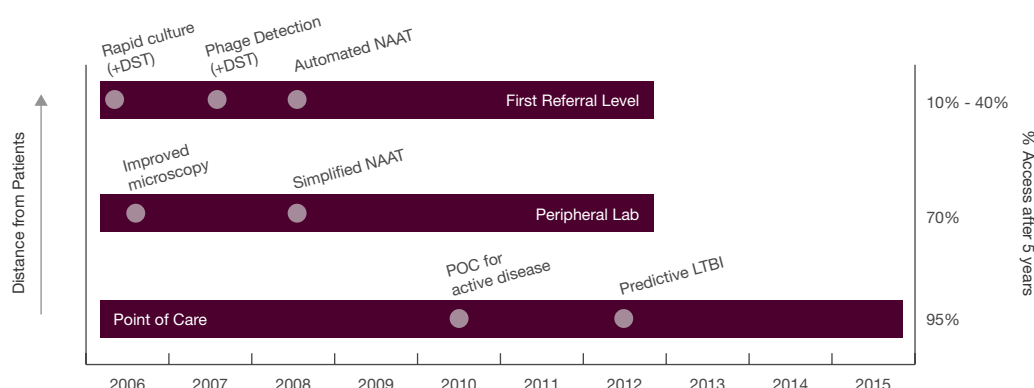
OBJECTIVE 2: Development and evaluation of a portfolio of new diagnostic tools and demonstration of impact

TARGETS	INDICATORS (APPLY TO ALL 3 TARGETS)
<ul style="list-style-type: none"> • Sensitive, early detection of active disease Conceptualization and development initiation of simple rapid-format tests for TB in sputum, serum, saliva or urine based on improved targets Introduction of at least one product for use in district laboratories by 2007 Introduction of at least one product for use in peripheral laboratories by 2008 Introduction of at least one POC product for health centres by 2010 • Identification of latent TB infection at risk of progression Conceptualization and development initiation of test for risk of disease progression in a suitable platform based on best candidates Introduction of at least one product for point of care use by 2012 • Simple, rapid identification of drug resistance Conceptualization and development initiation of tests for drug resistance requiring equal or less infrastructure and training than current technologies Introduction of at least one product at first referral level by 2006 and at peripheral laboratory by 2008 <p>For all three targets:</p> <ul style="list-style-type: none"> • Inclusion of related goals in research funding calls by major funding agencies • Public sector product development agreements with industry • Coordinated evaluation and demonstration projects 	<ul style="list-style-type: none"> • Number of agencies announcing relevant funding opportunities • Defined customer requirements and product specifications • Number of product development agreements with industrial partners • Number of successfully completed development and technical evaluations according to product specifications • Number of clinical evaluation and demonstration sites developed and authorized • Number of evaluation projects initiated • Number of evaluation projects completed • Number of peer-reviewed publications reporting results from evaluation projects • Agreement on empiric design of demonstration studies with selected NTPs • Number of demonstration studies initiated and completed • Number of peer-reviewed publications reporting results from demonstration studies • Number of new targets with contractually assured affordable and sustainable product access

OBJECTIVE 3: Implementation of new diagnostic tools and ensuring access

TARGETS	INDICATORS
<ul style="list-style-type: none"> • Definitive predictions of impact from the use of improved diagnostics on TB detection rate and transmission • Operational studies to demonstrate epidemiological and economic impact of new tools in high-burden settings • Accelerated registration of products with proven utility • National and international policy changes reflecting impact of new diagnostics • Creation of demand through communication to stakeholders (NTPs, MOH, technical and funding agencies.) • Ensured access to proven technologies through inclusion in GDF or other procurement mechanisms 	<ul style="list-style-type: none"> • Completion of mathematical model defining impact and cost-effectiveness • Number of countries with streamlined regulatory procedures for TB diagnostics • Number of market analysis updates • Number of new diagnostic tools included in TB policy recommendations of international technical agencies • Number of new diagnostic tools included in national TB policy recommendations • Number of NTPs using new diagnostic tools at district level • Number of NTPs using new diagnostic tools at local level • Number of NTPs using new diagnostic tools at point of care

FIGURE 34: TARGETS FOR INTRODUCTION OF TESTS, LEADING TO SUSTAINABLE ADOPTION, 2006–2015



specifications; (3) further expansion and maintenance of the sample and strain bank to support product development with selected partners and in other qualifying centres; (4) laboratory strengthening for clinical trials; (5) development of diagnostic trial design and monitoring tools; (6) generation of an inventory of clinical trial sites; (7) collation of information on regulatory and procurement policy.

Evaluation

All products sponsored by or developed under the auspices of the Working Group and FIND will undergo detailed technical evaluation, facilitated by the availability of well characterized clinical samples and strains from the TB sample and strain banks, and field studies performed in well established and qualified research sites in high-burden countries.

Demonstration

Products that successfully complete the development process and technical evaluation studies will subsequently be tested and further characterized in demonstration studies. The first such studies, which are already under way, involve a rapid culture method for case detection and detection of drug resistance that is already in widespread use in the developed world, and offers significantly higher sensitivity than smear microscopy. Optimizing the translation of these technologies into improved TB control and patient care is the focus of the demonstration projects under way in several African countries with high HIV/TB coinfection rates, and in Eastern Europe for the management of MDR-TB. Other demonstration projects will be initiated in the near future to evaluate improved microscopy.

Regulatory issues

In recent years the Working Group has undertaken a comprehensive survey of the regulatory situation for TB diagnostics in high-burden countries, identified local stakeholders and gained insights into likely future trends in the regulatory environment. The Working Group will contribute to the harmonization of regulatory requirements by assembling a team of representatives from all affected stakeholders (regulatory bodies, manufacturers

and public health agencies) and supporting studies that create confidence in a harmonized approach.

Monitoring and evaluation

Progress towards the overall goals of producing new diagnostic tools, as envisaged above, will be reviewed against the targets and timelines described at annual meetings of the Working Group. Dedicated secretariat staff will continuously monitor progress and highlight bottlenecks and problems at the annual meetings of the Working Group, or to appropriate individuals or subgroups.

Key risk factors

- **Insufficient financial investment and delayed investment**
Adequate investment early on is required to fund discovery and early-stage technologies. Product-specific development agreements require financial commitments covering the entire planning phase of the project (until introduction) – otherwise attractive financial terms for the public health market cannot be achieved.
- **Technologies fail**
Technologies can fail during the discovery phase or development phase, or during evaluation or demonstration studies, although the risk of failure decreases as projects reach later phases. To offset the risk of failure, the breadth of the development portfolio is risk-balanced comprising multiple options at each level.
- **Inadequate laboratory strengthening**
Many of the new diagnostic technologies require improved laboratory capacity and development of laboratory infrastructure, which will vary according to the technology to be implemented. Collaboration with the DOTS Expansion Subgroup on Laboratory Strengthening will ensure the timely and appropriate strengthening of laboratory services to meet the requirements for implementation of new diagnostics.

- Inadequate access to new products

The introduction of improved diagnostic tools based on positive outcomes in evaluation and demonstration studies does not necessarily guarantee broad access and use. Potential constraints include high product or infrastructure costs, regulatory hurdles, lack of local or NTP "buy-in", and unreliable distribution and product support systems. The Working Group on New TB Diagnostics has developed a range of approaches to overcome these constraints, including contractually agreed affordable product pricing in development partnerships, regulatory harmonization activities, early involvement of local stakeholders in demonstration projects, and drawing on the experience of the Global Drug Facility.

- Interrupted product supply

The Working Group plans to make significant investments in discovery, product development studies and supporting activities, the return for which must be a reliable and uninterrupted supply of high-quality product. This, in turn, depends on careful selection of development partners and manufacturers. To address the risk that manufacturers and suppliers might change their business focus, sell out, default or collapse, the Working Group, through FIND, has developed an intellectual property strategy that ensures access to the know-how built into all sponsored products, through a royalty-free licence scheme that allows the transfer of the manufacturing process to more appropriate business partners if necessary.

prequalification of manufacturers, market analysis updates, regulatory harmonization, Working Group operations).

This amounts to a total budget need of US\$516 million. The estimated total financing available among all stakeholders is US\$80 million, some of which may be shared costs with industry. The funding gap is therefore estimated at US\$436 million.

See Table 25: Research and development costs for specific technologies

Modelling the predicted impact of novel diagnostics for detection of active TB

It is expected that new diagnostics will improve TB control by improving the accuracy of detection of active TB cases in all patient groups, with tools that are widely accessible logistically, financially and technologically. A mathematical model is being developed to test this hypothesis, and to generate predictions of the potential impact on TB epidemiology. The model will be used to investigate the potential impact of a range of tools, with varying sensitivity for detection of smear-positive and smear-negative disease, and will take into account the predicted reach (or penetration) of each tool (e.g. district laboratory, local microscopy unit, POC) as well as performance compared with existing tools in both HIV-infected and uninfected subjects. The interaction between these predicted impacts and the anticipated epidemiological effects of the measures described in the strategic plans of the implementation working groups (on DOTS expansion, TB/HIV, and DOTS-Plus for Multidrug-resistant TB) will also be investigated.

Budget requirements for the Working Group on New TB Diagnostics: 2006–2015

The funding required to support basic science and the development, evaluation, and demonstration of the proposed tests is US\$497 million. An additional US\$19 million is required for enabling and supporting infrastructure (reference material banks, clinical trial training, laboratory strengthening,

TABLE 25: RESEARCH AND DEVELOPMENT COSTS FOR SPECIFIC TECHNOLOGIES FOR NEW TB DIAGNOSTICS, 2006–2015 (US\$ MILLIONS)

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	All years	% total
Early-Stage Diagnostic Development and Research	24	24	25	24	23	21	20	18	14	14	206	40%
Discovery Science (to include POC, Phage, predictive LTBi)	8.6	8.8	9.1	8.7	8.2	7.7	7.1	6.5	5.0	5.2	75	14%
Development (to include above plus simplified and automated NAAT, rapid culture and improved microscopy)	15	16	16	15	14	13	12	11	9	9	131	25%
Clinical Trials	35	36	37	35	33	31	29	26	20	21	303	59%
Clinical trial training and laboratory strengthening	0.4	0.4	0.4	0.4	0.4	0.3	0.3	0.3	0.2	0.2	3	0.7%
Reference material banks	0.4	0.4	0.4	0.4	0.4	0.3	0.3	0.3	0.2	0.2	3	0.7%
Pre-qualification of manufacturers	0.5	0.5	0.6	0.5	0.5	0.5	0.4	0.4	0.3	0.3	5	0.9%
Market analysis updates	0.0	0.2	0.2	0.2	0.0	0.0	0.0	0.0	0.0	0.0	1	0.1%
Evaluation projects (all tools listed above)	9.2	9.5	9.8	9.3	8.8	8.2	7.6	7.0	5.4	5.6	80	16%
Demonstration projects (all tools listed above)	24.2	24.9	25.7	24.4	23.1	21.6	20.0	18.3	14.1	14.6	211	41%
Regulatory Approval and Registration	0.2	0.2	0.2	0.2	0.2	0.0	0.0	0.0	0.0	0.0	1	0.2%
Regulatory harmonization	0.2	0.2	0.2	0.2	0.2	0.0	0.0	0.0	0.0	0.0	1	0.2%
WG Operations	0.5	0.5	0.5	0.5	0.6	0.6	0.6	0.6	0.6	0.7	6	1%
Meetings, Secretariat, Coordination	0.3	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.4	0.4	3	0.7%
Advocacy	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.3	0.3	2	0.4%
TOTAL	59	61	63	60	56	53	49	45	35	36	516	

10.3.2 Working Group on New TB Drugs: summary strategic plan, 2006–2015

The Working Group on New TB Drugs was established in 2000. Its goal is the development of new, affordable TB drugs. In 2005, for the first time in 40 years, there is a coordinated portfolio of promising new compounds, some of which have the potential to become the cornerstone drugs of TB control and even contribute to future elimination of TB.

Strategic vision: 2006–2015

The Working Group on New TB Drugs (WGND) envisages an environment by 2015 that will allow for the sustained development of new TB drugs that can ultimately be combined into completely novel and revolutionary TB regimens. Continued worldwide commitment, research and vigilance to ensure a consistent pipeline of new antimicrobials is required to eliminate tuberculosis within the twenty-first century.

TB control has long been hindered by the lengthy (6–8 months) and complex treatment required by current drugs, and is further complicated by the disease's deadly interaction with HIV/AIDS and the rise of multidrug resistance. The WGND's vision is to have new TB regimens that will achieve cure in 1–2 months or less, will be effective against MDR-TB, will be compatible with antiretroviral treatments, and will be effective against latent TB infection. In addition, new regimens must be affordable and easily managed in the field. It is conceivable, should continued progress be made in the basic understanding of the biology of *M. tuberculosis*, that the course of therapy could be reduced even further, to 10–12 days before 2050, or that additional advances in therapeutic or prophylactic options not currently available may greatly reduce TB incidence.

To achieve this vision, the WGND has identified the following areas of strategic importance:

- (a) basic discovery biology to identify and validate new targets and identify candidate compounds using effective screens and creative medicinal chemistry;
- (b) active and sustained drug development efforts;
- (c) planning and execution of more effective clinical trials, including identification of improved biomarkers and methods of assessing latent disease; and
- (d) clear and efficient regulatory guidance.

Objectives

Discovery biology and chemistry

Objective 1: Identify and validate drug targets for persistent bacilli and latent disease.

Objective 2: Ascertain mechanisms of action of drugs in the global portfolio to generate complementary or even synergistic combinations effective against *M. tuberculosis*.

The objective of the WGND is to identify and validate drug targets for both persistent bacilli and latent disease by 2015 or earlier. This will require a concerted international effort to develop a comprehensive understanding of the basic biology of

persistence and latency, so that new agents in development can effectively and rapidly eliminate these organism phenotypes.

A second objective is to understand fully the mode of action of all compounds under development. This objective is important to devise novel and enhanced molecules for specific drug targets, with maximum bactericidal and sterilizing activity. The WGND further recognizes that there is a unique opportunity to produce a new generation of TB drugs with maximum therapeutic impact, through rational combinations of these compounds. *M. tuberculosis* is an unusual pathogen in that there is no horizontal exchange of drug resistance (e.g. through plasmids). Therefore, the introduction of multiple novel drugs in fixed combinations would not only treat existing drug-resistant strains but, if properly managed, could eliminate the potential for future resistance. Specifically, the target by 2015 is to ascertain the mechanisms of action of the drugs in the global portfolio in order to generate complementary or even synergistic combinations effective against mycobacteria.

Recognizing the promise of multiple approaches to drug discovery, the WGND pursues a balanced approach to drug development, encompassing identification and screening of new targets, medicinal chemistry, combinatorial chemistry, and exploration of natural products.

Drug development

Objective 3: Develop a sustainable portfolio of new drug candidates that meet the drug profile criteria.

Objective 4: Develop animal models that can be used to predict the activity and side-effects of compounds, and validated surrogate markers that are broadly adopted by TB drug developers.

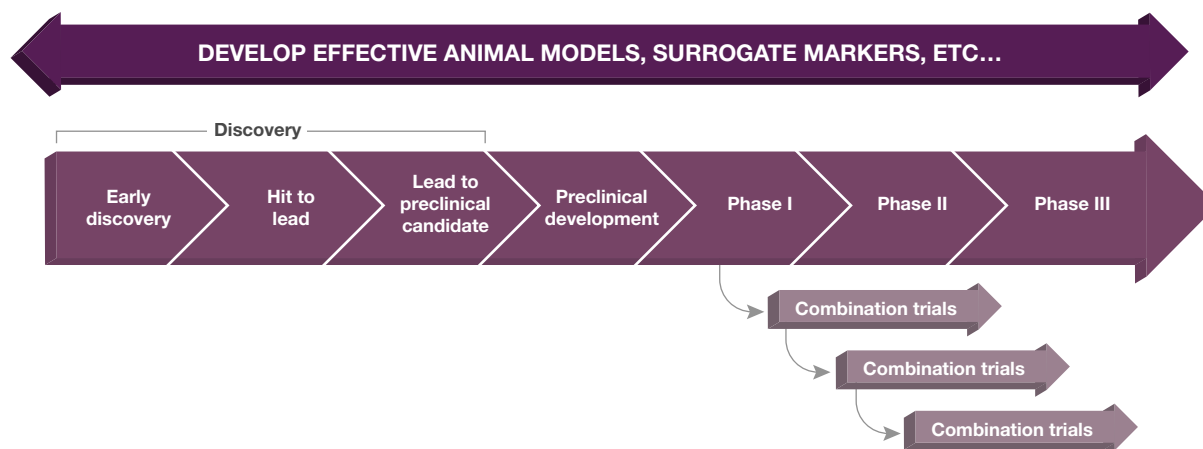
The objective by 2015 is to have a sustainable portfolio of new drug candidates under development that meet the drug profile criteria required for a duration of therapy of 1–2 months. There are 11 compounds with novel modes of action for TB that are currently in or approaching clinical development. Some of these compounds, e.g. moxifloxacin, have been shown to reduce treatment time in animal models. The target, by 2010, is the introduction of a new drug or combination of drugs that can reduce time of treatment to 3–4 months.

New in vitro data suggest that compounds currently under development could reduce treatment duration even further. The target for 2015 is the clinical testing of a rational drug combination therapy that can reduce the required time of treatment to 1–2 months or less.

Figure 35 outlines the drug development process from discovery to registration, including the proposed concurrent testing of multiple rational drug combinations.

Successful drug development is predicated on preclinical and clinical testing, careful monitoring, and strong portfolio management. If a compound is to fail in development, it is preferable that it does so early. Animal models that can predict

FIGURE 35: TB DRUG DEVELOPMENT PIPELINE



compound activity and side-effects as well as validated surrogate markers that are broadly adopted by TB drug developers are urgently required.

Planning and execution of clinical trials

Objective 5: Build clinical trial sites and initiate and conduct clinical trials that meet regulatory requirements and the highest ethical standards. Develop biomarkers, surrogate end-points, and testing programmes to speed future clinical development programmes.

The objective is the timely initiation and conduct of clinical trials according to appropriate regulatory requirements and the highest ethical standards. This demands clinical trial sites that meet the standards of Good Clinical Practice (GCP) and Good Manufacturing Practice (GMP). Trained personnel, sound infrastructure and appropriate procedures for patient recruitment, adherence and retention are also needed.

Proof of cure in TB requires lengthy clinical trials. Thus, biomarkers and surrogate end-points must be developed as part of a translational research strategy to speed future clinical development programmes. Testing programmes that allow more rapid and precise dose selection and optimization of complementary drug combinations are also needed.

Regulatory approval and registration

Objective 6: Establish harmonized regulatory guidelines, including fast-track approval for TB drug developers.

There has been a hiatus in TB drug development of over 40 years, and there are no TB-specific regulatory guidelines for drug development. Therefore, as compounds enter into clinical development, it is imperative that harmonized regulatory guidelines, including fast-track approval, become available for TB drug developers worldwide. This will require open and active dialogue during the next decade among drug development groups, regulatory agencies and external experts to define and

agree on novel trial approaches and registration criteria for TB drugs.

Activities

Discovery biology and chemistry

Many promising discovery activities are in progress in 2005, coordinated by Working Group partners, and are likely to produce several new lead candidates by 2015. The Novartis Institute for Tropical Diseases, TB Alliance, and National Institute of Allergy and Infectious Disease (NIAID) are collaborating on work on nitroimidazole analogues. GlaxoSmithKline and the TB Alliance are assessing candidates in the classes of pleuromutilins, isocitrate lyase inhibitors, and InhA inhibitors. AstraZeneca Pharmaceuticals, the Gates Grand Challenge awardees, investigators at St George's Hospital Medical School, and university researchers supported by the US National Institutes of Health are exploring the nature of the *M. tuberculosis* proteosome in persistence, and developing assays and strategies to attack slowly replicating mycobacteria.

The Tuberculosis Structural Biology Consortium and individual investigators continue to decipher the large *M. tuberculosis* genomic sequence and crystallize *M. tuberculosis* proteins to obtain a better understanding of potential targets and hence design inhibitors. The Institute for Tuberculosis Research, University of Illinois, and the TB Alliance are exploring the biology and chemistry of newer macrolide antibiotics.

Several discovery programmes are testing natural products from plants and ocean sources, performing combinatorial and focused chemistry around known antitubercular agents, synthesizing analogues to attack novel targets (such as methyl transferase and complex lipid transporters), and screening new libraries of proven antibiotics (quinolones, oxazolidinones, quinolines, etc.). NIAID TB drug development contractors (www.taacf.org) provide services to screen new chemical entities from laboratories throughout the world and to assess and compare candidates in animal model efficacy tests.

PART III: PARTNERSHIP ACTION TO ACHIEVE THE GOALS

Key milestones in discovery include factors such as: identification of compounds with drug-like qualities (solubility, medicinal chemistry, metabolic stability); development of structure–activity relationships for a specific target; achievement of selectivity for the target; completion of cell-based toxicity assessments; identification of molecular mode of action; and demonstration of efficacy in an appropriate animal model of disease. The WGND will support meetings and other activities to inform partners about global activities and progress towards increasing the number of preclinical candidates entering development.

Drug development

Eleven compounds are currently in clinical or advanced preclinical development by several sponsors. The key milestones for discovery-stage compounds will be achieved when lead compounds meet sponsor criteria set for advancement of leads into advanced preclinical development. Most of the decisions about proceeding or not are driven by the development plan, and are based on how the new drug will be used clinically. Thus, criteria for a drug to be added to existing regimens with daily dosing for many months may be different from those for a drug that is intended for prophylaxis with intermittent dosing. Animal safety tests, pharmacokinetic and pharmacodynamic characterizations, spectrum of microbial activity including against resistant TB strains, chemical synthesis routes, and cost factor into the decision to enter a candidate compound into animal safety studies under good laboratory practice (GLP). These tests are lengthy, expensive and require large amounts of purified compound. The formal reports are included in submissions to regulatory agencies for investigational new drug applications (IND). An IND submission is a critical milestone, as it indicates that objective data generated by a GLP-certified laboratory have supported the sponsor's decision to proceed. A second critical milestone is approval by regulatory agencies for entry into phase I human safety trials. This is followed by initiation of phase II and III trials, leading to a new drug application (NDA). If the compiled data from all these studies are convincing to the regulatory agencies, a new drug or new indication will be registered and launched.

The failure of drug candidates to complete the research and development process is a significant risk for sponsors, both in terms of time and funds. Only roughly 10% of candidates that enter the clinical pipeline advance to registration, mostly because of safety concerns. Thus, a robust and sustained pipeline of new candidates and back-up discovery programmes is essential to success. As new drug entities arise as candidates, the WGND will assist in fostering early communication among partners to allow modelling to begin of drug compatibility and complementarities in efficacy. The Working Group will serve as a platform for interaction among partners to increase efficiency and decrease risk for the process as a whole.

Planning and execution of clinical trials

Clinical trials of tuberculosis drugs are being conducted around the world in sites sponsored by organizations such as the National Institute of Pharmaceutical Education and Research (NIPER), CDC's Tuberculosis Trials Consortium (TBTC), the

European and Developing Countries Clinical Trials Partnership (EDCTP), the South African Medical Research Council (MRC), the International Union against Tuberculosis and Lung Disease (IUATLD), the National Institute of Allergy and Infectious Diseases (NIAID), and the NIAID/Case Western Reserve University-funded Tuberculosis Research Unit (TBRU), among others. These sites have previously carried out successful trials of existing drugs in a variety of combinations.

However, the need for clinical trial sites that meet registration-standard regulatory criteria is increasing dramatically, as the new compounds under development in the global TB pipeline reach preclinical milestones.

Because no centralized roster of qualified sites exists, clinical trial sites are being assessed individually and independently by individual sponsors of compounds in the pipeline. Bilateral agreements, as is customary and appropriate, are being established between the sponsors and principal investigators at each site. It is expected that trials will commence as each site, or group of sites, is prepared for the proposed trial and is not withdrawn by regulatory agencies.

This process is time-consuming and leads to redundancies. Therefore, the WGND will seek to streamline the clinical trial process by carrying out a mapping exercise to identify registration-standard qualified sites worldwide. It is expected that this mapping will be based on information provided by members of the Working Group and will be finished by late 2006.

The WGND will establish a roster of clinical trial site, which will outline the capabilities of each site, including all the regulatory assurances. The roster will be placed in a database that will be made public via the Internet at a readily available website, such as the Stop TB Partnership site.

The information gathered for the clinical trial site roster will also help in assessment of the capacity of each site and identification of existing gaps, whether in human resources, ability to recruit patients, infrastructure needs, or other areas. This assessment will identify what is needed to ensure viable, ethical and competent sites. This activity will be continuous.

Regulatory approval and registration

Starting in 2006, and throughout the term of this strategic plan, as appropriate, the WGND will cosponsor meetings with regulatory agencies in developed and endemic countries, with the first objective being the establishment of regulatory guidelines to allow registration of a new compound for the treatment of TB by 2010. Additional meetings and symposia sponsored or cosponsored by the WGND to discuss, validate and help establish surrogate markers will take place yearly in conjunction with other international fora such as the IUATLD conference in Paris or the Gordon TB Research Conference.

Monitoring and evaluation

An important function of the WGND will be to map progress among the partners and other bodies that may start activities in TB drug development. A database of projects, compounds, and clinical trials will be established to reflect the current status worldwide.

Careful monitoring and evaluation of a large number of clinical trials will be expensive. Modest initiatives to expand capacity are under way at WHO/TDR, but are unlikely to satisfy the demand created by the initiation of multiple regulatory-quality TB clinical trials. Development of international monitoring standards and increased global monitoring ability are needed to ensure that promising agents are not impeded in their progress towards registration and utilization.

Key risk factors

Only one in 10 new, first-in-human drug candidates achieve registration. The portfolio must therefore be robust with a continual pipeline of candidates entering clinical evaluation.

With the highest-burden countries experiencing emergencies in relation to HIV/AIDS and TB concomitantly, the paradigm of clinical evaluation of new drugs is becoming more and more complex. Expanded capacity for human pharmacokinetic and drug interaction studies will be necessary to ensure that an adequate human clinical database is available for each compound in a timely manner appropriate to these latter phases of development.

Clinical sites for testing new drugs exist, but the projected level of activity suggests that they will be under severe pressure.

New regimens may not be made available to the patients (e.g. because of delay in the establishment of standard treatments and their subsequent implementation in the field). All working groups and the international community will need to focus on the safe, prompt and effective adoption of new tools.

Budget requirements for the Working Group on New TB Drugs: 2006–2015

The financial realities of TB drug development require that the philanthropic and public sectors participate financially with industry to assume some of the risks involved in candidate drug development. The momentum achieved in the past five years has been possible only because of the financial commitment of public and private entities. To implement the WGND's vision, substantial additional resources and political commitment will be needed over the next 10 years.

One of the most significant expenses in drug development involves the financing of large-scale clinical trials. These are costly both because of the large numbers of people necessary and because of the long duration of follow-up (currently up to 2 years) required to determine rates of relapse. A significant expansion of global capacity in TB clinical trials will be needed to move a large number of promising compounds and regimens rapidly through phase II and III trials. Much of this expansion

will take place primarily in the developing world, where this effort will de facto contribute to the development of individual technical skills and the strengthening of programme expertise in planning and evaluation. This is a domain in which the public and philanthropic sectors can make substantial contributions. The WGND will facilitate the activities needed for strategic planning and providing resources in advance of clinical trials. Substantial capital investment is necessary for successful new TB regimens to become available to the world. The total funding necessary is US\$4800 million; the funding available amounts to US\$620 million, leaving a total funding gap of US\$ 4180 million.

See Table 26: Budget requirements for the Working Group on New TB drugs, 2006–2015

TABLE 26: BUDGET REQUIREMENTS FOR THE WORKING GROUP ON NEW TB DRUGS, 2006–2015 (US\$ MILLIONS)

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	All years	% total
Early-Stage Drug Development and Research	211	217	224	231	237	245	252	260	267	275	2,419	50%
Basic Research	5.0	5.2	5.3	5.5	5.6	5.8	6.0	6.1	6.3	6.5	57	1%
Lead Optimization	195	201	207	213	219	226	233	240	247	254	2,235	47%
Preclinical	11	11	12	12	12	13	13	14	14	14	126	3%
Clinical Trials	207	213	220	226	233	240	247	255	262	270	2,373	49%
Phase I	7.0	7.2	7.4	7.6	7.9	8.1	8.4	8.6	8.9	9.1	80	2%
Phase II	50	52	53	55	56	58	60	61	63	65	573	12%
Phase III	150	155	159	164	169	174	179	184	190	196	1,720	36%
Regulatory Approval and Registration	0	1	0	1	0	1	0	1	0	1	6	0.1%
Registration	0.0	1.0	0.0	1.1	0.0	1.2	0.0	1.2	0.0	1.3	6	0.1%
WG Operations	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	2	0.04%
TOTAL	418	432	444	458	471	486	499	516	530	547	4,800	

10.3.3 Working Group on New TB Vaccines: summary strategic plan, 2006–2015

The Working Group on Vaccine Development was established in 2000. Its aim is to foster and coordinate collaborative efforts to develop novel vaccination approaches that are effective in reducing TB disease.

Strategic vision

Development of new vaccines to protect against tuberculosis is gaining substantial momentum. Encouraging and consistent scientific results from the laboratory and from early field trials indicate that introduction of new effective TB vaccines will be an essential component of any strategy to eliminate tuberculosis by 2050. New TB vaccines to prevent childhood and adult forms of tuberculosis, to reduce tuberculosis in persons coinfecting with HIV, and to shorten drug treatment regimens will fundamentally alter our approach to TB control.

It is probable that the next generation of vaccines will work by complementing the immune response induced by the current BCG vaccine. New vaccines could be delivered together with BCG at an early age before exposure to *M. tuberculosis* has occurred, as a separate booster to young adults, or as an adjunct to chemotherapy. The Working Group is promoting research and development on several approaches to the development of new candidate vaccines and new delivery strategies. The timetable for vaccine development is driven by the availability of suitable candidates and the need for extensive clinical trials to establish their safety and confirm their efficacy in human populations. It is anticipated that a new vaccine will be available by 2015.

It is difficult to predict the exact contributions to TB control that such a new vaccine will have. However, the impact of new vaccines can be simulated by introducing vaccine-related parameters into existing epidemiological models of the TB pandemic. One such simulation suggests that introducing a new vaccine between 2014 and 2018 that can be given to everybody could reduce TB incidence in Africa and South-East Asia by over 20% during the first 10 years of use and up to 40% by 2050.⁴⁵

The strategic vision of the Working Group is that improved vaccines and vaccination strategies will make a crucial contribution to achieving the Stop TB Partnership's target for 2050 of reducing the global incidence of TB disease to less than 1 case per million population.

Achievements to date

In 2000, the Working Group took note of the historic opportunities for development of new TB vaccines that resulted from the availability of techniques for the genetic manipulation of mycobacteria, and completion of the genome sequence of *M. tuberculosis*. These advances facilitated production of new vaccine candidates in the form of live recombinant mycobacteria or mycobacterial genes, expressed in a variety of immunogenic forms. In parallel, advances were being made in our understanding of the cellular and molecular mechanisms underlying protective immunity, in humans as well as in experimental laboratory

animals. In the first Global Plan, the Working Group objective was to have five promising vaccine candidates in phase I trials in 2005. With four candidates in phase I trials in 2005 and three more lined up to follow by early 2006, this objective can be considered as largely achieved.

Important factors included major strategic investments by the European Community and the US National Institutes of Health. These donors established consortia of vaccine researchers and centralized facilities for preclinical evaluation, which have allowed comparative testing and selection of optimal candidates for progression to clinical trials. In addition, progress towards clinical trials has been promoted by major awards from the Bill and Melinda Gates Foundation to support the Aeras Global TB Vaccine Foundation and its predecessor, the Sequella Global TB Foundation.

Objectives

The overall objective of the Working Group for 2006–15 is to have **a safe, effective, licensed vaccine available at reasonable cost by 2015.**

Objective 1: Maintain and improve BCG vaccination programmes

It is anticipated that BCG will remain the cornerstone of TB vaccination programmes over the period covered by the Global Plan, with the next generation of new vaccines introduced as an addition to BCG vaccine, which is commonly given at birth in many countries. Important issues include sustaining BCG production by a diminishing number of international suppliers, analysis of possible variations in vaccine efficacy as a result of genetic changes in BCG substrains, and establishment of a rational system for deciding when and how different substrains should be used.

Objective 2: Discovery and translation research ("keeping the pipeline filled")

There is a need to expand discovery and translational research on vaccines. Progress with current clinical candidates does not signal an end of discovery research, but rather provides opportunities to link fundamental research to human studies. It is likely that experience gained as current candidates move through clinical trials will contribute to development of new candidates in an iterative process of refinement. In parallel, there is a well recognized need for further research in immunology to support development of evaluation criteria for vaccines in phase II/IIb trials and for the identification of correlates of immunity in phase III trials. The Working Group anticipates that scientists from high-burden countries will make a growing contribution in this area, particularly in the areas of epidemiology and human immune assay development.

Objective 3: Facilitate preclinical development

There is a need to identify and assist in the development of facilities for production of pilot lots of vaccine candidates suitable for human trials, and to ensure that these candidates are subject to appropriate tests to confirm biological potency and lack of toxicity in experimental systems.

Objective 4: Build capacity at vaccine trial sites

Carrying out vaccine trials requires local expertise as well as baseline data for the populations that will participate. Prerequisites include baseline epidemiological information, development of community interaction programmes, development of protocols that comply with legal and ethical requirements, coordination with national regulatory authorities, local proficiency in immunological assays and diagnostic procedures, and infrastructure for vaccine delivery. These activities provide important opportunities for training and capacity strengthening, and require interaction with other working groups in the Stop TB Partnership.

Objective 5: Ensure availability of vaccine production capacity/scale-up

The potential to scale up production of experimental vaccines to a level suitable for widespread distribution in multicentre, multinational studies is an essential factor in the selection of candidates for clinical trials. Also, it is anticipated that a new licensed vaccine would be made available at a cost that is affordable to resource-poor countries. It is likely that demands will exceed the capacity of existing vaccine production facilities and investment will be needed in one or more dedicated GMP-quality production facilities. This activity will require the establishment of innovative partnerships with manufacturers in developing and developed countries.

Objective 6: Perform clinical trials

Evaluation of vaccine candidates requires a series of clinical trials of increasing size, complexity and cost, to progressively evaluate safety, immunogenicity and, finally, efficacy. Ensuring investments by collaborators in developed and developing nations is a major challenge for the Partnership at this juncture.

- Phase I trials include initial assessment of safety, typically in groups of about 30 healthy adults.
- Phase II trials require expanded safety studies with larger groups, testing different vaccine doses and delivery protocols, and including specific target populations (people previously exposed to *M. tuberculosis*, those coinfecting with HIV, adolescents, children and infants, etc.). Measurement of immunogenicity in phase II trials provides key data for deciding on future development.
- Phase IIB trials necessitate a further expansion from phase II, to test whether the candidate meets performance criteria set for entry into full-scale phase III efficacy trials.
- Phase III trials, which are substantially larger and require extensive resources, test the efficacy of the vaccine. Decision criteria for moving into phase III trials include: the availability of a suitable clinical site to access target populations; a facility for “scaled-up” manufacturing of reproducible vaccine lots; a clinical development plan that ensures that successful trials will produce data that can be used in licensing applications; potential to develop correlates of immunity (or surrogates) from the trial; a country willing to license the vaccine; a regulatory process to license the vaccine; and discussion with local TB care programmes to facilitate integration with TB drugs and diagnostics for trials. In order to ensure the availability of sufficient numbers of trial participants and geographically representative trial

results, multiple phase III trials sites in different parts of the world will be needed.

- Phase IV trials are post-licensing studies, using in-country infrastructure to monitor safety and determine the effectiveness of the vaccine through epidemiological studies.

Objective 7: Provide an enabling infrastructure

The Working Group will act as a focal point for discussion of vaccine development issues, serving as an honest and impartial broker among different stakeholder communities, and facilitating the development of consensus protocols and criteria for vaccine assessment. Specific initiatives include preparation of a scientific blueprint, assessment of the economic impact of vaccines with different performance characteristics, facilitation of international regulatory harmonization for TB vaccines, identification of standard reagents and protocols to produce comparable preclinical and clinical data, identification of facilities for timely vaccine production, and preparation for accelerated access to licensed vaccines for high-burden countries. The Working Group also serves as a centralized mechanism for integrating these activities with the development of vaccines for other diseases

Targets and indicators

In the overall workplan for 2006–2015, the first target is that at least 20 vaccine candidates will have entered phase I clinical trials by 2015. It is anticipated that multiple candidates will progress through clinical trials in parallel and that unsuccessful candidates will be continually replaced by new entrants.

It is anticipated that phase II trials of the first candidates will be well under way in 2006. Initial phase II trials will take approximately 3 years, with an expected reduction to 2 years following development and refinement of trial protocols and immunological assays. The second target is that nine candidates will be evaluated in phase II trials. Furthermore, by 2008 there will be at least two vaccines in phase IIB or “proof of concept” trials, which will provide some early indication of efficacy and therefore significantly reduce the risk of failure in phase III.

The first phase III trials could begin as early as 2010. They will test the ability of vaccine candidates to act as pre-exposure vaccines and will take 4 years to complete. Post-infection trial protocols will be available from 2011 and are expected to take 3 years to complete. The third target for the Global Plan is to carry out a total of four phase III efficacy trials.

Approximately two years will be required to complete licensing procedures and to begin to distribute a successful vaccine. The final target is to have a safe, effective, licensed vaccine available at reasonable cost by 2015.

See Figure 36: Timelines for TB vaccine development 2006–2015

Monitoring and evaluation

Progress towards the overall goal of producing an effective vaccine by 2015 will be reviewed against the targets and timelines set out above at annual meetings of the Working Group. Dedicated secretariat staff will monitor progress on a continuous basis and highlight bottlenecks and problems at the annual meeting of the full Working Group, or to appropriate individuals or subgroups. The development of international monitoring standards and increased global monitoring ability are needed to ensure that promising agents are not impeded in their progress towards registration and use.

Risks and challenges

Scientific challenges.

The major factor that could prevent achievement of the 2015 target relates to the scientific uncertainty about protective immunity to TB, and our current lack of experience with new TB vaccines in human populations. In spite of recent advances in our understanding of host responses to *M. tuberculosis* infection and TB disease, we may nevertheless be unable to identify vaccine candidates that provide consistent protection against TB. The dual strategy of maintaining support for relevant activities in vaccine discovery research while maximizing the number of candidates introduced into clinical trials provides the optimal means of increasing our chances of developing an effective vaccine.

Additionally, we may identify a promising preclinical candidate that confers enhanced immune response but displays unacceptable adverse events, for example, exacerbating other underlying disease symptoms. We may be able to develop a vaccine that is effective in immunocompetent individuals, but that fails at a population level in areas with high rates of HIV coinfection. It is conceivable that a successful vaccine could promote selection of strains of *M. tuberculosis* with altered pathogenicity that allows them to escape from vaccine control.

Financial uncertainties.

Vaccine development is expensive. Despite impressive commitments by the public sector and philanthropic organizations, a funding gap remains of at least 60% of the total required to achieve the objectives of the TB vaccine development plan on time.

The problem largely lies in insufficient commercial investment in TB vaccine development. As with the development of many new vaccines and drugs against diseases of poverty, this is related to the small size of the market for these innovative, but expensive, products. Diverse mechanisms have been put in place or are being considered to overcome this, including direct research funding and provision of disease burden information.

However, experts agree that such “push” initiatives, valuable as they are, are not enough and that “pull” efforts are needed to create a market in developing countries, in order to achieve the same level of involvement of the pharmaceutical industry that is typically observed for diseases prevalent in affluent countries. Mechanisms that ensure market take-up of new products are also essential and advanced purchasing agreements may be advantageous in this regard. Such advance market commitments are unlikely to materialize for TB vaccines alone, but rather as part of a comprehensive package to provide new tools against a whole range of major communicable diseases, including HIV and malaria.

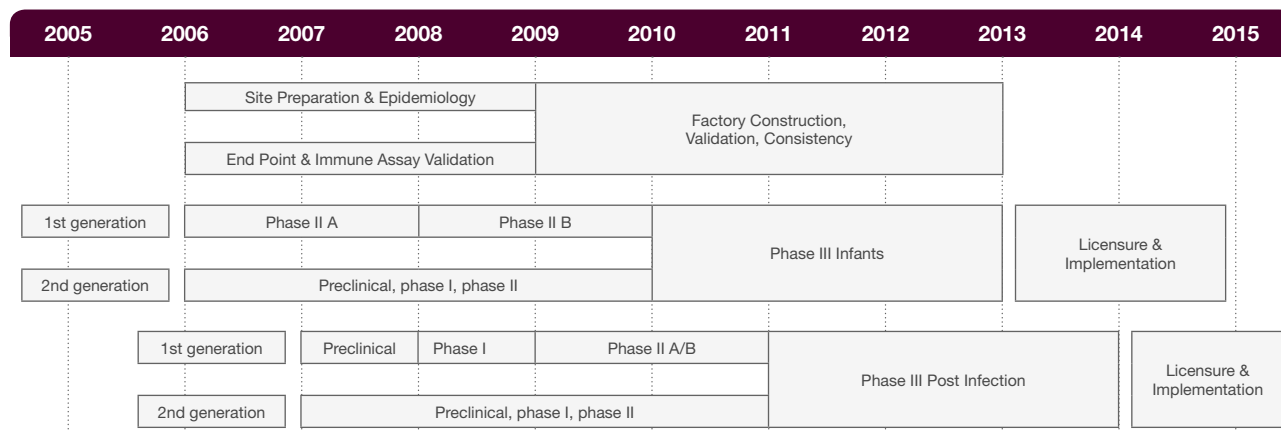
A prime objective for the TB community must therefore be to advocate to ensure that development of tools against TB is part of any initiative to create an enlarged market for innovative new pharmaceuticals for developing countries.

Budget requirements for the Working Group on New TB Vaccines: 2006–2015

See Table 27: Working Group budget, 2006–2015 (US\$millions)

The total funding necessary is US\$3,641 million; the funding available is US\$2,065 million, leaving a total funding gap of US\$1,576 million.

FIGURE 36: TIMELINES FOR TB VACCINE DEVELOPMENT 2006–2015



PART III: PARTNERSHIP ACTION TO ACHIEVE THE GOALS

TABLE 27: BUDGET REQUIREMENTS FOR THE WORKING GROUP ON NEW TB VACCINES, 2006-2015 (US\$ MILLIONS)

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	All years	% total
PROGRAMME NEEDS (a)	130	134	138	142	146	151	155	160	165	170	1,490	41%
Objective 1: Maintain and improve BCG programmes Estimated cost of US\$0.10 per dose with an annual production of 400 million doses per year, plus US\$0.90 per dose distribution costs for an annual cohort of 100 million children.	130	134	138	142	146	151	155	160	165	170	1,490	41%
RESEARCH NEEDS (a)	155	163	168	184	230	237	244	252	221	228	2,082	57%
Objective 2: Discovery and translation research («keeping the pipeline filled») ¹⁹	120	124	127	131	135	139	143	148	152	157	1,376	38%
Objective 3: Facilitate preclinical development Preclinical development (including toxicology, safety, regulatory, IP) estimated at US\$725 000 per candidate (20 candidates)	5	5	5								15	0.4%
Objective 4: Build capacity at vaccine trial sites Estimated as 10% of total trial costs for phase I and II trials	3	4	4	4	0	0	0	0	0	0	16	0.4%
Objective 5: Ensure availability of vaccine production capacity/ scale-up Phase I lots (US\$5 million); phase II/III lots (US\$76.5 million); manufacturing facility (US\$100 million).	12	15	16	33	34	35	36	37	0	0	217	6%
Objective 6: Perform clinical trials and prepare access to new vaccines Phase I: 20 candidates/6 permutations/30 subjects – US\$45 million. Phase II: 9 candidates/6 permutations/300 subjects – US\$100 million. Phase II: 4 trials/40 000 subjects – US\$240 million.	15	15	15	16	61	63	65	67	69	71	457	13%
WORKING GROUP OPERATIONS (a)	6	6	6	7	7	7	7	7	8	8	69	2%
Objective 7: Providing an enabling infrastructure Critical items include staff and communications (US\$225 000 per year); economic analysis and blueprint (US\$850 000 per year), meetings (US\$100 000 per year), consultancy (US\$45 000 per year), scientific outreach activities (US\$50 000 per year).	6	6	6	7	7	7	7	7	8	8	69	2%
TOTAL	291	303	312	333	383	395	407	419	393	405	3,641	

(a) Unit costs in column 1 are in 2006 prices. Total budgets after 2006 do not exactly correspond to these unit prices since they have been adjusted for inflation.



Advocate

Everybody involved in creating, developing and delivering the Plan must act as an advocate to ensure that TB features prominently on the global political and health agenda. People with TB and communities affected by TB who are empowered to speak out will be potent advocates for change. «Business as usual» is not enough.

The Plan provides a sound argument for the resources needed for action, and is therefore a powerful tool for advocates. Sustained advocacy will help persuade national governments and donors to fulfil their commitment to Stop TB by investing in the Plan.

Each of us can speak out and help mobilize support for the Plan to Stop TB.

10.4 Advocacy, Communication and Social Mobilization Working Group: summary strategic plan, 2006–2015

Introduction

A significant scaling-up of advocacy, communication and social mobilization for TB will be needed to achieve the global targets for TB control. In 2005, the Advocacy, Communication and Social Mobilization Working Group (ACSM WG) was established to mobilize political, social and financial resources, to sustain and expand the global movement to eliminate TB, and to foster the development of more effective ACSM programming at country level in support of TB control. It succeeded an earlier Partnership Task Force on Advocacy and Communications. This is a summary of the Working Group's strategic plan for 2006 to 2015. The full plan is available at <http://www.stoptb.org/GlobalPlan>.

Strategic vision 2006–2015

The success of the Partnership's Global Plan to Stop TB for 2006–2015 will rest on the ability of ACSM efforts to generate political, social, and behavioural change at all levels. There is an urgent need to expand ACSM in donor and endemic countries, directed at rapidly building and financing a multilevel, multisectoral social movement to reverse the TB epidemic and achieve the Millennium Development Goals and the Stop TB Partnership's targets. While the Working Group's principal focus in this summary plan is on developing ACSM strategies in support of existing global TB targets, the ACSM Working Group's strategic vision is to achieve TB-free communities by:

- (1) Global advocacy: creating the political accountability and social pressure required to shape policy agendas and mobilize US\$56 billion from 2006 to 2015 for TB control and new tool development; and
- (2) Country-level ACSM: establishing and funding evidence-based and innovative country- and community-driven ACSM activities to effect sustainable societal and behavioural change at the national, subnational and individual level, aimed at ensuring access to treatment and care for all, particularly the poor, vulnerable and hard-to-reach populations.

Objectives

The Working Group will focus on building ACSM capacity at all levels so that appropriate, effective strategies can be developed, prioritized, implemented and sustained, to achieve the Working Group's vision and advance the Global Plan's targets. The following objectives are intended to further the Working Group's vision, and support and enhance both the new WHO Stop TB Strategy and the aims of the Stop TB Partnership's other working groups:

- (1) Help to mobilize the financial resources required to fund fully the Global Plan for 2006–2015 for DOTS expansion, DOTS-Plus for MDR-TB, new tool development, and TB/HIV efforts.
- (2) Encourage a higher profile of TB on national, regional, and international policy agendas.

- (3) Increase political and social support for TB control policies recommended by WHO, including the International Standard of Care and Patients Charter.
- (4) Engage policy-makers, international, regional and national-level stakeholders, the media, the private sector, patients, communities and others to secure greater political support for TB control, including through the development and promotion of national partnerships.
- (5) Build the capacity of national TB programmes and partnerships, and other key actors to develop and implement multisectoral, participatory, sustainable ACSM plans, supported by adequate in-country human and financial resources, to improve case detection and treatment outcomes, empower affected communities, and combat stigma and discrimination.
- (6) Build the capacity of civil society and affected communities in donor and endemic countries to advocate for universal access to treatment and mobilize collective action in the fight against TB.
- (7) Promote exchange of information between the Working Groups and the sharing of ACSM-related lessons and experiences to ensure maximum impact, encourage participation and facilitate collaboration.
- (8) Build ACSM indicators and monitoring and evaluation mechanisms into institutional monitoring and evaluation systems.

Targets and milestones

Global advocacy

- By 2010, civil society TB advocacy organizations or coalitions will be functioning in 20 donor countries and 40 endemic countries.
- By 2015, the ACSM Working Group will have helped to mobilize US\$56 billion for the control of TB and the development of new tools in accordance with the Partnership's Global Plan in order to achieve the Millennium Development Goals and meet the Stop TB Partnership's targets.

Country-level ACSM

- By 2015, multisectoral, participatory ACSM methodology will be a fully developed component of the WHO Stop TB Strategy.
- By 2015, all priority countries will be implementing effective and participatory ACSM initiatives.
 - By 2008, at least 10 endemic countries will have developed and will be implementing multisectoral, participatory ACSM initiatives and generating qualitative and quantitative data on the contribution of ACSM to TB control.
 - By 2010, at least 20 priority countries will be implementing multisectoral, participatory ACSM initiatives, and monitoring and evaluating their outcomes.

Activities and implementation

The ACSM Working Group will liaise with the Stop TB Partnership's implementation and new tools working groups, national TB programmes, civil society, patients and affected communities to bring about sustainable political, behavioural and social changes to advance the Working Group's vision. The ACSM Working Group views global advocacy efforts and ACSM at country level as elements of the same systems approach, although each requires distinct skills and orientation. The components of advocacy, communication and social mobilization reinforce each other and must be integrated into the broader technical effort to control TB. It should be stressed that successful ACSM strategies and activities are situational and opportunistic, depending as they do on ever-changing global, national, political and social contexts. Even so, a number of "good practices" have emerged from previous ACSM efforts for TB and these are embodied in the ACSM Working Group's strategic plan.

The Working Group will focus on the following main areas of work:

- advocacy activities at the global, regional and national level;
- communication activities at the national and subnational level;
- cross-cutting activities, as outlined below.

Advocacy activities at the global, regional and national level

These activities will aim to command the attention of key policy-makers, international and regional organizations (e.g. World Bank, NEPAD, African Union, European Union and multinational corporations), international NGOs, the private sector and media, to generate political support and mobilize resources for TB control.

- Mainstream TB into larger health and development initiatives. TB advocacy efforts will be linked to future G8 Summits, key UN processes such as the 2005 General Assembly High Level Meeting on HIV/AIDS, the global movement related to achieving the Millennium Development Goals, and other initiatives and important gatherings at the global, regional and country level. Activities will include encouraging HIV/AIDS groups to incorporate TB into their agendas.
- Strategic mapping of resource streams. Identifying key funding streams for TB control and development of new tools, mobilizing allies and initiating specific activities to influence relevant decision-makers is critical in order to secure financial commitments.
- Foster champions. Building support and awareness among policy-makers within and outside the health sector, and among other community leaders and icons, is critical to expanding and sustaining political commitment. Champions at all levels will be identified, educated and supported to advocate strategically and effectively for increased funding for TB control.

These advocacy activities will be enabled by civil society advocacy organizations or coalitions, as well as by national TB programmes and partnerships at country level. Global and national partners, specifically NGOs or coalitions with a proven track record in mobilizing financial and political support for health or social development issues, will assist in building advocacy capacity in donor and endemic countries and capacity to implement TB control in endemic countries. Capacity-building for civil society advocacy will need to be rolled out, in a sustainable manner, starting with at least four donor countries and eight endemic countries per year (Figure 37). By 2010, civil society TB advocacy organizations or coalitions will be functioning in 20 donor countries and 40 endemic countries.

Communication activities at the national and subnational level

In endemic countries these activities will aim to eliminate stigma and discrimination and to improve case detection and treatment.

- Develop ACSM guidelines and handbooks to improve knowledge exchange and promote good practices for ACSM at country level. These documents will include assessment and problem-solving tools to enable national TB programmes, civil society and other stakeholders to develop comprehensive, country-driven ACSM strategies in support of TB control. Materials will include examples of country experiences and tools related to communications programming, patient and community involvement in TB programme design, ACSM human resource development, strategic planning, operational research, monitoring and evaluation.
- Create a technical assistance framework to assist countries and civil society organizations with ACSM planning, activities, monitoring and evaluation. This framework will be designed to help NTPs and other key partners implement intensive, sustainable and detailed ACSM strategies. The framework will also include assistance to endemic countries to help develop Global Fund proposals to resource these activities on an ongoing basis.
- Develop, adapt and promote clear policy messages. Prototype ACSM messages, materials, images and strategies are essential to brand, market, and align global, national and local ACSM activities. For example, the Universal Standard of TB Care, the Patients' Charter and the Stop TB Strategy will be used as effective tools to improve the quality of TB services.

Capacity-building for ACSM at country level will be rooted in national TB programmes and the Stop TB Partnership model, to help countries and other key partners develop and implement country-driven ACSM plans that include funding for needs assessments, national and subnational communication coordinators or focal points, district-level ACSM activities, distribution of IEC materials, and monitoring and evaluation.

Capacity-building will need to be rolled out in a sustainable manner, starting with five endemic countries each year for a total of 20 countries by 2010. These countries will require

intensive technical assistance to address high levels of stigma, TB/HIV coinfection, and other behavioural and societal barriers to treatment-seeking and treatment-providing behaviour. International, regional and national partners with experience in developing country-level capacity in communication and social mobilization might include media resource and communication programming centres, social marketing organizations, advertising firms, NGOs, community-based organizations (CBOs), patient and community associations, and health promotion/communication departments within ministries of health.

Important cross-cutting activities

- Strengthen the participation of TB patients and communities in every aspect of TB control. Global, regional, national and local TB organizations have a special responsibility to broaden their decision-making constituency to include current and former patients. Empowering patients and affected communities will increase the feasibility and appropriateness of planned activities and contribute to improving programme efficacy.
- Use the influence of the media. Increased media visibility is critical for building awareness and facilitating policy dialogue, providing a strong profile and voice for affected communities, and for resource and social mobilization. The media are also an important channel for messages aimed at effecting behavioural and societal change. Activities to generate media interest will include preparing a global and regional media strategy, educating and engaging the media, organizing media events around key opportunities, producing press-friendly materials, etc.
- Establish and support national TB partnerships. National TB partnerships can provide the basis for building larger TB ACSM coalitions and, in endemic countries, improve coordination of ACSM efforts designed to improve health-seeking and health-providing behaviour, build health literacy, and encourage patient-centred care
- Enhancing web and electronic information and knowledge-sharing. This includes increasing information exchange (including between the working groups), discussion and transparency; coordinating the participation of new and existing partners; facilitating long-distance learning; and encouraging cross-fertilization of ideas.
- Investing in operational research. Commissioned studies and operational research are needed to document good practices and constantly improve ACSM methodology, particularly at country level.

ACSM Working Group secretariat support for the organization of international, regional and national meetings, information-sharing, and coordination of technical assistance will also be required.

ACSM impact

Impact of ACSM on global resource mobilization

The Working Group estimates that an annual investment of US\$0.5–2 million a year in advocacy activities is required to generate US\$100 million in funding for TB control. To mobilize the US\$5.5 billion of annual financial support needed for this

Global Plan, 0.5% per dollar will be required for advocacy activities. A further investment of 5–15% for ACSM activities in national TB programme budgets should also be encouraged (see <http://www.stoptb.org/GlobalPlan> for more information). This is consistent with the estimated US\$5 million that Stop TB partners are currently spending per year on advocacy, and which mobilizes an estimated US\$300 million in external aid flows for endemic countries, technical agencies, and the GDF.

Impact of ACSM in countries on case detection and treatment outcomes

The ACSM WG strategic plan at country level draws on recent evaluations in other public health communication fields to suggest that ACSM for TB should help to maintain current case detection and cure rates in most countries. In situations where DOTS services are assured, well planned and fully resourced, communication and social mobilization interventions should increase case detection and treatment outcome by as much as 5–10%, although accounting for all confounding variables will be difficult.

Few studies have assessed the cost of communication activities for TB in relation to their impact. Additional research is needed to define and evaluate the causal relationship between communication activities and increased service usage and treatment success. However, an analysis of ACSM components in TB proposals submitted to the fifth round of the GFATM strongly suggests that ACSM budget for country level activities can be extrapolated for the Global Plan to Stop TB.

Monitoring and evaluation

The Working Group will coordinate monitoring and evaluation efforts to measure the outcomes of global, regional and national ACSM efforts and their contributions to TB control. Existing information and data collection systems, methods, and indicators will be used to generate and evaluate various data. The Working Group will also develop a core set of indicators for inclusion in existing formal data collection systems and a participatory process for measuring the impact and cost-effectiveness of ACSM activities at all levels. At the global level, the Working Group will commission reviews to analyse progress towards building ACSM capacity and the achievement of the Global Plan to Stop TB. At the country level, ACSM should be included as a component of all national TB programme reviews. Working Group meetings and other meetings of international, regional and national-level stakeholders will be held to track progress, disseminate evidence on good practices and lessons learned, and modify the ACSM strategy and activities when necessary.

Budget requirements for 2006–2015

The budget required to accomplish the Working Group's goals over the period 2006–2015 is estimated at US\$3.2 billion. Details are given in Table 28. It is assumed that funding for the coordination of global and regional strategic planning, technical assistance and evaluation will come from donations to the Stop TB Partnership Secretariat from bilateral donors. The bulk of funding for country-level ACSM activities will come from the GFATM and bilateral sources in the short term and increasingly

from national government allocations in the longer term. Partners at country level should also contribute by committing realistic proportions of their budgets to ACSM activities.

See Table 28: Budget requirements for the ACSM Working Group: 2006–2015 (US\$ MILLIONS)

FIGURE 37: ROLLOUT OF ACSM CAPACITY-BUILDING ACTIVITIES IN DONOR AND ENDEMIC COUNTRIES

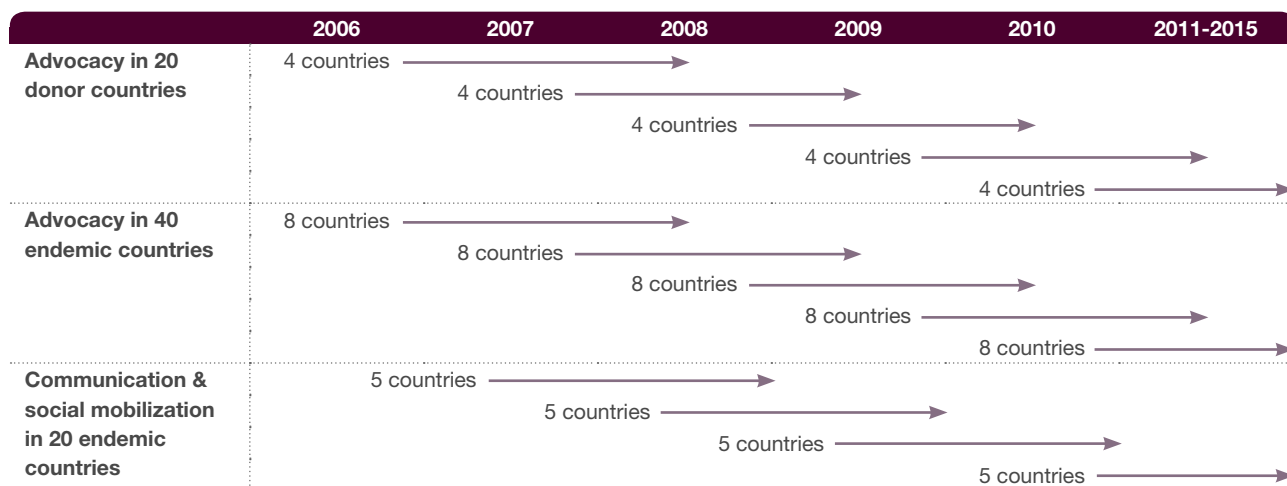


TABLE 28: BUDGET REQUIREMENTS FOR THE ACSM WORKING GROUP: 2006–2015 (US\$ MILLIONS)

COUNTRY NEEDS	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	All years	%Total
All regions	242	236	249	257	282	295	308	323	337	353	2,882	90%
AFRO-high	61	63	66	69	74	78	82	86	91	95	767	24%
AFRO-low	30	31	33	35	37	39	42	44	46	49	386	12%
EEUR	19	20	21	21	22	23	23	24	25	26	224	7%
EMR	33	31	32	33	34	36	38	40	42	44	365	11%
LAC	10	11	11	12	12	13	13	14	14	15	124	4%
SEAR	57	57	59	61	64	67	70	73	76	79	663	21%
WPR	30	23	26	26	38	39	41	42	44	45	353	11%

INTERNATIONAL AGENCY NEEDS	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	All years	%Total
Technical assistance	2	2	3	4	3	2	2	2	3	3	27	1%
Strategic and technical support	0.8	0.8	1.3	1.7	1.4	0.9	1.0	1.0	1.0	1.0	11	0%
Capacity building	1.2	1.2	1.9	2.6	2.0	1.4	1.4	1.5	1.5	1.6	16	1%

Monitoring and Evaluation	3	3	3	3	4	4	4	4	4	4	37	1%
Impact	0.5	0.5	1.1	1.1	1.1	1.2	1.2	1.2	1.3	1.3	10	0.3%
Planning/implementation	2.0	2.1	2.1	2.2	2.3	2.3	2.4	2.5	2.5	2.6	23	0.7%
Financial monitoring	0.2	0.2	0.2	0.2	0.2	0.3	0.5	0.5	0.5	0.5	3.4	0.01%

Operational Research and Policy Development	5	5	5	5	6	5	5	5	4	4	49	2%
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Working Group and subgroup meetings	1	1	1	2	2	2	2	2	3	3	20	0.6%
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Global Advocacy	11	13	15	18	21	22	23	23	24	25	194	6%
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TOTAL NEEDS	263	260	278	291	318	330	345	360	374	391	3,208	
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10.5 Stop TB Partnership Secretariat: summary strategic plan, 2006–2015

Introduction

The Secretariat aims to ensure that, by enabling partners to work together, the Partnership has greater positive impact on global TB control than if individual partners worked alone.

Strategic vision

The Secretariat's strategic vision is that the full and active contribution of all partners to TB control and poverty reduction will lead to a TB-free world by 2050. Its mission is to empower partners in sustained action, to create synergies and to catalyse innovation, in order to achieve the Partnership's 2015 TB targets linked to the MDGs.

The Secretariat is a facilitator and broker for partners, a stimulator of innovation, a communicator on progress and an ambassador for Stop TB. It is not a programme manager, a funding agency or a policy-maker. The Secretariat is housed in the World Health Organization.

Objectives

The Secretariat has eight specific objectives for 2006–2015:

Objective 1: Promote accountability, flexibility and coordination in the management of partnership resources.

Objective 2: Stimulate the mobilization of the resources needed to permit the implementation of the Global Plan to Stop TB (2006–2015).

Objective 3: Ensure the effective functioning, growth, dynamism and catalysing effect of the GDF in global TB control.

Objective 4: Facilitate relationships between and with existing partners and strengthen our coalition by reaching out to new or potential partners.

Objective 5: Build skills, resources and capacity at regional and national level to enable successful partnerships to be developed.

Objective 6: Place TB on the global development agenda, while at the same time mainstreaming pro-poor approaches into TB control.

Objective 7: Take TB beyond the existing reach and scope of traditional disease control programmes by catalysing new opportunities and promoting the aims and objectives of the Global Plan to Stop TB (2006–2015).

Objective 8: Monitor and evaluate the impact of the Secretariat and Partnership in delivery of the Global Plan to Stop TB (2006–2015).

Activities

Secretariat activities to secure these objectives fall into four core areas of work.

Financial resources (objectives 1 and 2)

Targets to 2015:

- To strengthen the Secretariat's reputation for accountable, flexible and well-coordinated management of resources.
- To mobilize the resources needed to enable the Partnership to fully implement the Global Plan to Stop TB (2006–2015).

Accountability and financial management

A Secretariat that can rise to the challenge of brokering a growing pool of resources requires strong management skills. In particular, development of the Partnership Trust Fund to secure the funding requirement for all core areas of Secretariat activity will be fundamental. By 2015, the Fund should reach a cumulative US\$500 million. Secretariat success will be built on streamlining and standardizing operating procedures within the Secretariat and across the Partnership structure, including working groups, in order to match available resources to the requirements of working groups, national TB control programmes and partnerships. The Secretariat will use innovative interactive technological approaches to facilitate its coordination and management function.

Resource mobilization

The Secretariat is not a funding agency. However, to ensure full implementation of the Global Plan to Stop TB, the Secretariat will aim to help the Partnership mobilize a growing share of the resources required: by influencing donor policy, using innovative approaches and securing a solid reputation based on the quality of the Secretariat's performance. The milestones for the Partnership are to secure 10% of Global Plan funding requirements by 2007, 25% by 2009, 50% by 2011 and 100% by 2015.

A long-range resource action plan will ensure consistent and effective donor engagement. In addition to nurturing existing donors, the Secretariat will aim to realize 10% of its income from new donors by 2011. It will develop constructive relations with the private sector, securing a public/private funding ratio for Secretariat activities of 80/20 by 2015. The Secretariat will stimulate the mobilization of sufficient financial resources to ensure the implementation of Secretariat functions, provide seed funding for national partnerships, provide catalytic financial support to the working groups, and support the effective evolution of special initiatives such as the GDF.

The Secretariat will grow the pool of available funding for technical assistance, at the same time as brokering technical advice on proposals and resource mobilization to countries and partners, as required – notably in support of interaction with international financial mechanisms (such as GFATM). It will establish a tracking and early warning system to inform partners of funding opportunities.

Access to TB drugs (objective 3)

Targets to 2015:

- The GDF will provide a cumulative total of 25 million patient treatments through both grant and direct procurement service lines.
- Support for access to quality affordable anti-TB drugs will be provided in all countries where there is need.
- The GDF will stimulate the development of viable markets for TB control products, other than first-line anti-TB drugs.

The Global Drug Facility

Drug supply is a critical partnership resource underpinning the assumptions of the Global Plan to Stop TB (2006–2015). An important part of the Secretariat's strategic vision is therefore the evolution of the GDF to ensure access to quality, affordable anti-TB drugs in all countries where there is need. By 2007, the supply of anti-TB drugs through the GDF will meet the biennial target of patient treatments to be delivered globally, as identified by the DOTS Expansion Working Group.

Though the focus of the GDF within the Secretariat will remain the provision of first-line TB treatment, the GDF will expand the range of products available in its catalogue, to introduce diagnostic kits, paediatric anti-TB drugs, single anti-TB drug formulations for patients experiencing side-effects with currently available fixed-dose combination formulations, and second-line anti-TB drugs (following the merger by 2007 with the Green Light Committee – currently the supply mechanism for second line anti-TB drugs). Moreover, in view of the close relationship between TB and HIV infection, the GDF will be prepared for the harmonized supply of TB/HIV preventive therapies by 2007 and possible TB/HIV treatment therapies by 2009.

Beyond this, the GDF will become more actively involved in the process of supporting the development and diversification of competition in national and global anti-TB drug markets. It will facilitate the prequalification process for anti-TB drugs and rapidly scale up its direct procurement service (in which the development and impact of the GFATM will be a major determining factor). The longer-term aim is to support self-sufficiency in drug management at national and regional level through the implementation of the GDF's Sustaining the Gains Strategy and the establishment of a technical assistance service line to broker support from partners for countries in need. The strengthening of the GDF at regional level, to be completed by 2007, will facilitate the process.

As new technologies and tools for TB control come on-line towards the middle of the timeframe for this strategic plan, the GDF plans to incorporate them into the overall package of services it offers. The GDF will need to negotiate concessional pricing for new technologies and tools, as well as promoting quality assurance of the same, thereby sustaining the reputation of the Partnership and Secretariat for supporting the provision of quality, low-cost TB control interventions. By 2011, GDF systems will be prepared for the introduction of new drugs and new diagnostics. By 2015, plans and service lines for new vaccines will be fully developed.

Partnership and external relations (objectives 4, 5 and 6)

Targets to 2015:

- An increased number and proportion of TB stakeholders will become active partners in Stop TB.
- Skills and resources will be available at regional and national levels to develop successful Stop TB partnerships.
- TB will be further mainstreamed into global and national development agendas.

- Pro-poor approaches will be mainstreamed into TB control.
- A unique brand for Stop TB will be accepted and promoted by all partners.

Partnership and governance

The Secretariat believes that dynamic global, regional and local partnerships can offer huge advantages for stakeholders in TB control. To maximize the benefit from proactive rather than passive involvement of partners, the Secretariat will actively engage and coordinate with working groups, non-traditional partners and NGOs, and will strengthen the constituency of patient-TB experts.

The Secretariat will support national and regional partnerships to strengthen TB control at local level. These partnerships will become self-sustaining, independently operating entities answerable to their own constituent partners under the umbrella of the Global Stop TB Partnership and the Global Plan to Stop TB (2006–2015). Drawing on Secretariat seed funding and technical support, 10 national partnerships will be established by 2011 and an additional 12 by 2015. The Secretariat will monitor and evaluate the effectiveness of partnerships to guide future development.

The Stop TB Partnership governance structure is well established and commands broad support. However, given the ambitious targets of the Global Plan, the Secretariat will need to maximize the strategic output of governance mechanisms designed to coordinate the partnership effectively. The Secretariat will organize at least three Partners' Forum meetings during 2006–2015. It will also continue to organize meetings of the Coordinating Board at least twice a year, and of other executive bodies as required, to ensure that the mandate of partners is implemented.

External relations: advocacy and country communication

The Secretariat aims to ensure that TB control remains a critical priority for governments and the general public worldwide. It will catalyse TB advocacy, communication and social mobilization activities at all levels, and promote the Stop TB Partnership as an effective mechanism for innovation and progress. The Secretariat will enhance the influence of the Stop TB movement, to engage eminent champions and to acquire new donors and non-traditional partners worldwide. As such, the Secretariat will promote the working groups and the Global Drug Facility, and be an ambassador for a unique Stop TB "brand".

The Secretariat will support the Advocacy, Communication and Social Mobilization Working Group in promoting the Global Plan as a living document, and strengthen linkages between advocacy, resource mobilization efforts and the mainstreaming of TB into development and political agendas. The Partnership Secretariat team currently acts as the secretariat of the ACSM Working Group, but this function may be transferred to a partner agency by 2009.

Catalysing change and monitoring progress (objectives 7 and 8)

Targets to 2015:

- TB control will reach beyond traditional disease control and will feature in wider health and socioeconomic development agendas.
- The Secretariat will be capable of supporting the retooling of partners, who require assistance, in preparation for the introduction of new products and new technologies.
- Progress against the milestones, targets and impact of the Global Plan and working group activities will be evaluated and documented

Catalysing change and innovation

The Global Plan to Stop TB (2006–2015) must remain relevant for all partners throughout its lifetime. The challenge for the Stop TB Partnership Secretariat is to facilitate for partners a stream of new, added value products and services that enable partners to deliver against the Global Plan targets. Delivery of this objective will keep TB control, the Partnership and the Secretariat dynamic and at the cutting edge, able to respond rapidly to social, political or epidemiological change.

By ensuring a flow of information about new policy direction and initiatives, and by initiating debate among partners on coordinated responses beyond TB, the Secretariat will ensure that TB stakeholders are fully engaged and have an influential voice to catalyse change. The Secretariat also aims to identify ever wider circles of influence for the Stop TB Partnership beyond the current health agenda.

In particular, the Secretariat will catalyse change and debate in favour of enhanced TB control, through engagement with wider health sector strengthening and financing reform agendas, along with other social and economic development issues (such as poverty reduction, equity, gender, education, human rights, etc.). By 2007, TB will be further mainstreamed into the health systems strengthening agenda at global level and in important regional debates on development issues. A gender perspective and a human-rights-based approach will be integrated into all key Secretariat activity areas, including advocacy and communications, resource mobilization, partnership-building and technical assistance. By 2009, the Secretariat will facilitate a guide on the mainstreaming of human-rights-based approaches in TB programming. By 2011, it will secure strategic alliances to promote human rights, equity and gender awareness in global TB programming and Secretariat activities.

The Secretariat will support the working groups in the promotion of patient-friendly new technologies and will identify opportunities and resources to enable innovative projects to be nurtured. By 2009, it will develop a network to broker technical assistance to retool the Secretariat and key partners and countries for the introduction of new technologies. By 2015, the Secretariat will have the skill set necessary to support the implementation of the next Global Plan to Stop TB.

Monitoring and evaluation

The Secretariat has a fundamental role in monitoring and evaluating the Partnership and the Global Plan to Stop TB (2006–2015). The Partnership Secretariat will report to the Partner's Forum (at least every 3 years) and Coordinating Board (annually) on progress towards the achievement of the Global Plan targets. In coordination and collaboration with the working groups, the Secretariat will monitor and oversee working group inputs and measure progress against the targets of the Global Plan. The Secretariat will provide a progress report at each Partners' Forum. In addition, in 2011 the Secretariat will facilitate a mid-term review and progress report. In 2015 it will provide a final report on the Global Plan to Stop TB (2006–2015) and facilitate development of a further Global Plan for the next period. The purpose of this monitoring and evaluation activity is to enable the Secretariat to propose tactical revisions that could add value and enable partners to implement innovative solutions to better deliver against the Global Plan targets.

Risk factors

The Secretariat will seek to mitigate to the greatest degree possible the following potential risks to the successful implementation of the strategy outlined in this plan.

- A shift of donor emphasis to other diseases or sectors, as a result of an unfavourable global political context for TB control, leads to insufficient resource mobilization.
- The strategic direction adopted by the GFATM, or its future impact or reputation, affects the flow of global funds, with adverse consequences for the GDF.
- A lack of accountability, passive engagement of partners, or the failure of independent national or regional partnerships undermines the reputation of the global Partnership to Stop TB.
- Secretariat staffing levels are unstable or insufficient for required tasks.
- Partners and stakeholders are resistant to the Secretariat adopting and supporting new ideas and working methods.

Budget requirements for the Partnership Secretariat: 2006–2015

In order to carry out the activities outlined in this strategic plan, it is estimated that the Secretariat will require US\$519 million over the duration of the Global Plan.

Most of this sum – some 87% – will support the activities of the Global Drug Facility, which will require funding of approximately US\$450 million over the 10 years of the plan. The balance of US\$69 million (13%) will be required for Secretariat support for all other activities outlined above, including seed funding of innovative projects and brokering of support for partners. Table 29 provides a breakdown of budget requirements.

TABLE 29: BUDGET REQUIREMENTS FOR THE PARTNERSHIP SECRETARIAT, 2006–2015

SECRETARIAT ACTIVITIES	Estimated total budget requirements 2006–2015 (US\$)
Accountability and financial management	7,000,000
Resource mobilization	8,000,000
The Global Drug Facility – drug procurement	425,000,000
The Global Drug Facility – drug markets and management	25,000,000
Partnership strengthening activities	13,000,000
Governance	5,000,000
Advocacy	10,000,000
Country communication	8,750,000
Working group coordination	5,000,000
Change and innovation	6,500,000
Monitoring and evaluation	6,000,000
TOTAL	519,250,000



Hope

The revitalization of global efforts to Stop TB since the early 1990s has restored a sense of hope. In the past, a sense of hopelessness pervaded efforts to control many diseases of poverty, including TB. There was an acceptance that TB will always be with us. The substantial progress made against TB brings hope to all Partners as the work begins to implement the Plan.

Where poverty stalks the globe, communities have suffered the losses due to TB from generation to generation. The actions set out in the Plan to Stop TB will provide hope. Hope for the millions of people suffering and dying from TB. Hope for future generations that our actions will spare them from the ravages of this disease.

This hope is embodied in the Plan's actions for life - actions towards a world free of TB.

Glossary

antiretroviral therapy

Drugs for the treatment of HIV infection.

AFR high

Epidemiological region of high HIV prevalence countries in Africa.

AFR low

Epidemiological region of low HIV prevalence countries in Africa.

default

Patient stopping treatment before completion.

disability-adjusted life year (DALY)

A health gap measure that combines the time lived with disability and the time lost due to premature mortality.

DOTS strategy

The WHO-recommended strategy for TB control (based on case-finding and cure and comprising five key elements) that forms the precursor to, and basis of, the Stop TB strategy.

DOTS-Plus

The adaptation of the DOTS strategy to respond to multidrug-resistant TB.

drug susceptibility testing

Determining in a culture of *Mycobacterium tuberculosis* the anti-TB drugs that are effective against that particular sample.

extrapulmonary TB

TB affecting a part of the body other than the lungs.

Global Drug Facility

A mechanism established as an initiative of the Stop TB Partnership to expand access to, and availability of, high-quality TB drugs to facilitate global DOTS expansion.

Global Fund to Fight AIDS, Tuberculosis and Malaria

An international health financing agency that supports interventions against these three diseases.

Green Light Committee

A committee established under the Working Group on DOTS-Plus for MDR-TB, which reviews applications from potential DOTS-Plus pilot projects to determine their compliance with guidelines for access to concessionally priced second-line anti-TB drugs.

Highly Indebted Poor Countries (HIPC) initiative

An initiative launched in 1996 by the World Bank and the International Monetary Fund, which created a framework for all creditors to provide debt relief to the world's poorest and most heavily indebted countries.

HIV-negative

Describes a person in whom a blood test has shown the absence of antibodies against HIV.

HIV-positive

Describes a person in whom a blood test has shown the presence of antibodies against HIV.

HIV-related TB

TB occurring in somebody infected with HIV.

HIV status

The state of being HIV-positive or HIV-negative.

HIV test

A blood test for antibodies against HIV.

incidence

The number of new cases of a disease arising in a given period in a specified population.

International Standards for TB Care

A widely accepted level of care that all practitioners should follow in dealing with patients with TB or with symptoms and signs suggestive of TB.

latent TB infection

The presence in the body of tuberculosis bacilli that are dormant (usually in the lung) and not causing harm, but that may become active and cause disease.

Mid-Term Expenditure Framework (MTEF)

A multi-year public expenditure planning exercise, which is used to set out the future budget requirements for existing services, and to assess the resource implications of future policy changes and any new programmes.

Millennium Development Goals (MDGs)

Time-bound and quantified targets for addressing various dimensions of development, adopted by world leaders at the United Nations Millennium Summit in 2000.

multidrug-resistant TB

TB resistant to isoniazid and rifampicin (the two most effective anti-TB drugs).

mycobacterial culture

Growth of mycobacteria in special medium in the laboratory.

Mycobacterium tuberculosis

The microorganism (a bacillus) that causes tuberculosis.

Poverty Reduction Strategies

The major instrument for national planning in low- and some middle-income countries.

Poverty Reduction Strategy Paper (PRSP)

A document that describes a country's macroeconomic, structural and social policies and programmes to promote growth and reduce poverty, as well as associated external financing needs and major sources of financing. It is required for debt relief through the Heavily Indebted Poor Countries (HIPC) initiative.

Poverty Reduction Support Credit (PRSC)

A mechanism that provides support for the implementation of a country's poverty reduction strategy and the associated programme of social, structural, institutional, and policy reforms.

Practical Approach to Lung Health (PAL)

A comprehensive, symptom-based approach to the management of patients with respiratory symptoms within the primary health care system.

prevalence

The number of cases of a disease in a defined population at a specified point of time.

preventive treatment

Treatment aimed at preventing disease, e.g. isoniazid for the prevention of TB.

public-private mix (PPM) DOTS

A comprehensive approach to involve all relevant health care providers (public and private) in providing effective TB services.

pulmonary TB

TB affecting the lungs.

Sector-Wide Approach (SWAp)

A process in which funding for a sector (whether internal or from donors) supports a single policy and expenditure programme, under government leadership, and adopting common approaches across the sector.

sputum smear-negative

Absence of TB bacilli on sputum microscopy.

sputum smear-positive

Presence of TB bacilli on sputum microscopy.

Stop TB strategy

The new WHO-recommended strategy for TB control elaborated in 2006 that encompasses and goes beyond the DOTS strategy.

TB/HIV

The interaction between the epidemics of TB and HIV (sometimes refers to TB patients who also have HIV infection).

TB Epidemiological Regions

This annex lists the countries and territories in each of the eight TB epidemiological regions: (1) Africa, high HIV prevalence (AFR High); (2) Africa, low HIV prevalence (AFR Low); (3) American Region (AMR) – Latin American countries (LAC); (4) Eastern European Region (EEUR); (5) Eastern Mediterranean Region (EMR); (6) the Established Market Economies (EME) and Central Europe (CEUR); (7) South-East Asian Region (SEAR); and (8) Western Pacific Region (WPR).

1) Africa, High HIV Prevalence (AFR High)

- Botswana
- Burundi
- Cameroon
- Central African Republic
- Congo
- Côte d'Ivoire
- Democratic Republic of Congo
- Ethiopia
- Gabon
- Kenya
- Malawi
- Mozambique
- Namibia
- Nigeria
- Lesotho
- Rwanda
- South Africa
- Swaziland
- Uganda
- United Republic of Tanzania
- Zambia
- Zimbabwe

2) Africa, Low HIV Prevalence (AFR Low)

- Algeria
- Angola
- Benin
- Burkina Faso
- Cape Verde
- Chad
- Comoros
- Equatorial Guinea
- Eritrea
- Gambia
- Ghana
- Guinea
- Guinea-Bissau
- Liberia
- Madagascar
- Mali
- Mauritania
- Mauritius
- Niger
- Sao Tome & Principe
- Senegal
- Seychelles
- Sierra Leone
- Togo

3) American region (AMR) – Latin American countries (LAC)

- Anguilla
- Antigua & Barbuda
- Argentina
- Bahamas
- Barbados
- Belize
- Bermuda
- Bolivia
- Brazil
- British Virgin Islands
- Cayman Islands
- Chile
- Colombia
- Costa Rica
- Cuba
- Dominica
- Dominican Republic
- Ecuador
- El Salvador
- Grenada
- Guatemala
- Guyana
- Haiti
- Honduras
- Jamaica
- Mexico
- Montserrat
- Netherlands Antilles
- Nicaragua
- Panama
- Paraguay
- Peru
- Puerto Rico
- Saint Kitts and Nevis
- Saint Lucia
- St Vincent and the Grenadines
- Suriname
- Trinidad and Tobago
- Turks & Caicos Islands
- Uruguay
- US Virgin Islands
- Venezuela

4) Eastern Europe (EEUR)

- Armenia
- Azerbaijan
- Belarus
- Bulgaria
- Estonia
- Georgia
- Kazakhstan
- Kyrgyzstan
- Latvia
- Lithuania
- Republic of Moldova
- Romania
- Russian Federation
- Tajikistan
- Turkey
- Turkmenistan
- Ukraine
- Uzbekistan

5) Eastern Mediterranean (EMR)

- Afghanistan
- Bahrain
- Djibouti
- Egypt
- Islamic Republic of Iran
- Iraq
- Jordan
- Kuwait
- Lebanon
- Libyan Arab Jamahiriya
- Morocco
- Oman
- Pakistan
- Qatar
- Saudi Arabia
- Somalia
- Sudan
- Syrian Arab Republic
- Tunisia
- United Arab Emirates
- West Bank & Gaza Strip
- Yemen

6) Established Market Economies (EME)

- | | | | | |
|------------------|-----------|--------------|---------------|------------------|
| • Andorra | • Denmark | • Ireland | • Monaco | • Singapore |
| • Australia | • Finland | • Israel | • Netherlands | • Spain |
| • Austria | • France | • Italy | • New Zealand | • Sweden |
| • Belgium | • Germany | • Japan | • Norway | • Switzerland |
| • Canada | • Greece | • Luxembourg | • Portugal | • United Kingdom |
| • Czech Republic | • Iceland | • Malta | • San Marino | • USA |

and Central Europe (CEUR)

- | | | | | |
|-----------------------------|-----------|----------------------------|------------|-----------------------------------|
| • Albania | • Croatia | • Poland | • Slovakia | • The Former |
| • Bosnia and
Herzegovina | • Cyprus | • Serbia and
Montenegro | • Slovenia | Yugoslav Republic of
Macedonia |
| | • Hungary | | | |

7) South-East Asia (SEAR)

- | | | |
|--|-------------|---------------|
| • Bangladesh | • India | • Nepal |
| • Bhutan | • Indonesia | • Sri Lanka |
| • Democratic People's
Republic of Korea | • Maldives | • Thailand |
| | • Myanmar | • Timor-Leste |

8) Western Pacific (WPR)

- | | | | | |
|---------------------------|---------------------------------------|-------------------------------|---------------------|------------------------------|
| • American Samoa | • Fiji | • Micronesia | • Papua New Guinea | • Vanuatu |
| • Brunei Darussalam | • French Polynesia | • Mongolia | • Philippines | • Viet Nam |
| • Cambodia | • Guam | • Nauru | • Republic of Korea | • Wallis & Futuna
Islands |
| • China | • Kiribati | • New Caledonia | • Samoa | |
| • China, Hong Kong
SAR | • Lao People's
Democratic Republic | • Niue | • Solomon Islands | |
| • China, Macao SAR | • Malaysia | • Northern Mariana
Islands | • Tokelau | |
| • Cook Islands | • Marshall Islands | • Palau | • Tonga | |
| | | | • Tuvalu | |

The 22 TB high-burden countries, 2005

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|---------------|-----------------------------------|--------------|----------------------------------|------------|
| • Afghanistan | • Democratic Republic
of Congo | • Kenya | • Philippines | • Thailand |
| • Bangladesh | • Ethiopia | • Mozambique | • Russian Federation | • Uganda |
| • Brazil | • India | • Myanmar | • South Africa | • Viet Nam |
| • Cambodia | • Indonesia | • Nigeria | • United Republic of
Tanzania | • Zimbabwe |
| • China | | • Pakistan | | |

End notes

¹ The prevalence of a disease is the number of cases in a defined population at a specified point in time, while its incidence is the number of new cases arising in a given period in the population. The prevalence rate and the incidence rate are often expressed as the number of cases per 100 000 population.

² Azerbaijan, Bolivia, Costa Rica, El Salvador, Egypt, Estonia, Georgia, Haiti, Honduras, India, Jordan, Kenya, Kyrgyzstan, Latvia, Lebanon, Malawi, Mexico, Moldova, Nepal, Nicaragua, Peru, Philippines, Romania, the Russian Federation, Syrian Arab Republic, Tunisia and Uzbekistan.

³ Interim policy on collaborative TB/HIV activities; Strategic framework to decrease the burden of TB/HIV; Guidelines for implementing collaborative TB and HIV programme activities; Guidelines for HIV surveillance among TB patients; and A guide to monitoring and evaluation for collaborative TB/HIV activities (all available from www.who.int/tb/publications/2005/en/)

⁴ Latest available data (mostly relating to 2003) and findings are taken from the WHO report, Global tuberculosis control: surveillance, planning, financing. WHO Report 2005. Geneva, World Health Organization, 2005 (WHO/HTM/TB/2005.349). The Stop TB Partnership is indebted to its authors and WHO.

⁵ Annex 2 lists the countries in each of these regions.

⁶ The countries included in the WHO definition of Eastern Europe are Armenia, Azerbaijan, Belarus, Bulgaria, Estonia, Georgia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Republic of Moldova, Romania, Russian Federation, Tajikistan, Turkey, Turkmenistan, Ukraine, Uzbekistan.

⁷ The International standards for tuberculosis care describe a widely accepted level of care that all practitioners, public and private, should apply in dealing with patients with tuberculosis or with symptoms and signs suggestive of tuberculosis: a diagnosis should be established promptly and accurately; standardized treatment regimens of proven efficacy should be used together with appropriate treatment support and supervision; the response to treatment should be monitored; and the essential public health responsibilities must be carried out. Prompt, accurate diagnosis and effective treatment are not only essential for good patient care; they are the cornerstone of TB control. Substandard care will result in poor patient outcomes, continued infectiousness with transmission of the infection to family and other community members, and, perhaps, generation of drug resistance.

⁸ World Health Organization. Fifty-eighth World Health Assembly. Resolution WHA 58.14. Geneva, Switzerland: World Health Organization; 2005.

⁹ Millennium Development Goal 6, Target 8 – to have halted and begun to reverse the incidence of malaria and other major diseases – has two indicators for TB: Indicator 23: Prevalence and death rates associated with tuberculosis and Indicator 24: Proportion of tuberculosis cases detected and cured under DOTS (internationally recommended TB control strategy).

¹⁰ WHO and International Committee of the Red Cross. TB control in prisons: a manual for programme directors. Geneva, WHO 2000 (WHO/CDS/TB/ 2000.281).

¹¹ Engaging all health care providers to improve access, equity and quality of TB care – guidelines on implementing public-private mix for DOTS. WHO/HTM/TB/2006.360. Geneva, WHO, 2005.

¹² Interim policy on collaborative TB/HIV activities. Geneva, WHO, 2005 (www.who.int/tb/publications/tbhiv_interim_policy/en/index.html).

¹³ The WHO report, Global tuberculosis control (2005), indicates the key technical cooperation partners in the high-burden countries.

¹⁴ Alignment refers to efforts to bring the policies, procedures, systems and cycles of donors (including global health partnerships like the Stop TB Partnership) into line with those of the country being supported, and harmonization refers to efforts to streamline and coordinate approaches among donors.

¹⁵ UN-Habitat. The challenge of slums: global report on human settlements. Nairobi, United Nations Human Settlements Programme (UN-Habitat), 2003.

- ¹⁶ Lönnroth K, Zignol M, Uplekar M. Controlling TB in large metropolitan settings. In: Raviglione M, Lambregts van Weezenbeek K, eds. *Tuberculosis: a comprehensive international approach*. (in press).
- ¹⁷ Hanson CL. *Tuberculosis, poverty and inequity: a review of the literature and discussion of issues*, Geneva, Stop TB Partnership, World Health Organization, 2002.
- ¹⁸ Nhlema B et al. *A systematic analysis of TB and poverty*. Geneva, Stop TB Partnership, World Health Organization, 2003.
- ¹⁹ *Addressing poverty in TB control. Options for national TB control programmes*. Geneva, WHO, 2005 (WHO/HTM/TB/2005.352).
- ²⁰ *Addressing poverty in TB control. Options for national TB control programmes*. Geneva, WHO, 2005 (WHO/HTM/TB/2005.352).
- ²¹ This work will also be promoted within the Advocacy, Communications and Social Mobilization Working Group.
- ²² Borgdorff MW, Nagelkerke NJD, Dye C, Nunn P. 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): 123-132.
- ²³ The DALY is a measure of burden of disease that extends the concept of potential years of life lost due to premature death to include equivalent years of healthy life lost as a result of poor health or disability. The DALY combines in one measure the time lived with disability and the time lost due to premature mortality. One DALY can be thought of as one lost year of healthy life.
- ²⁴ Salomon J, Getz W. Prospects for advancing tuberculosis control efforts through novel therapies. In: UN Millennium Project Task Force on HIV/AIDS, Malaria, TB, and Access to Essential Medicines, *Investing in strategies to reverse the global incidence of TB*. London, Earthscan, 2005.
- ²⁵ Annex 2 lists the countries and territories in each of these eight TB epidemiological regions.
- ²⁶ High HIV prevalence countries in AFR: 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.
- ²⁷ WHO classifies countries in the region as having a high TB burden when the estimated TB incidence is greater than 50 per 100 000 population. Brazil and Peru together notify approximately 50% of cases in the region.
- ²⁸ Institute of Medicine. *Ending neglect: the elimination of tuberculosis in the United States*. National Academy Press, Washington DC, 2000.
- ²⁹ Department of Health. *Stopping tuberculosis in England*. London, Department of Health Publications, 2004.
- ³⁰ Cantwell MF, Snider DE Jr, Cauthen GM, Onorato IM. Epidemiology of tuberculosis in the United States, 1985 through 1992. *Journal of the American Medical Association*, 1994, 272: 535-539.
- ³¹ Frieden TR, Fujiwara PL, Washko RM, Hamburg MA. Tuberculosis in New York City: turning the tide. *New England Journal of Medicine*, 1995, 333: 229-33.
- ³² Raviglione MC et al. Secular trends of tuberculosis in Western Europe. *Bulletin of the World Health Organization*, 1993, 71: 297-306.
- ³³ Rieder HL et al. Tuberculosis control in Europe and international migration. Report of European Task Force. *European Respiratory Journal*, 1994, 7: 1545-1553.
- ³⁴ EuroTB. *Surveillance of tuberculosis in Europe . Report on tuberculosis cases notified in 2002*, Saint-Maurice, France. December 2004.
- ³⁵ Raviglione MC et al. Tuberculosis - Western Europe, 1974-1991. *Morbidity and Mortality Weekly Report*, 1993, 42:628-31.
- ³⁶ European Centre for the Epidemiological Monitoring of AIDS. *HIV/AIDS Surveillance in Europe: Quarterly Report, No. 46*, 30 June 1995.

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- ³⁸ Granich R, Oh P, Lewis B, Porco TC, Flood J. Multidrug-resistance among persons with tuberculosis in California, 1994-2003. *Journal of the American Medical Association*, 2005, 293: 2732-9.
- ³⁹ Schwartzman K et al. Domestic returns from investment in the control of tuberculosis in other countries. *New England Journal of Medicine*, 2005, 353: 32-44.
- ⁴⁰ WHO. Guidelines for the prevention of tuberculosis in health care facilities in resource-limited settings. Geneva, 1999 (WHO/TB/99.269); and WHO. Guidelines for the programmatic management of drug-resistant tuberculosis, Geneva (in press).
- ⁴¹ WHO and International Committee of the Red Cross. TB control in prisons: a manual for programme directors. Geneva, 2000 (WHO/CDS/TB/ 2000.281).
- ⁴² Interim policy on collaborative TB/HIV activities. Geneva, WHO (www.who.int/tb/publications/tbhiv_interim_policy/en/index.html).
- ⁴³ Interim policy on collaborative TB/HIV activities. Geneva, WHO (www.who.int/tb/publications/tbhiv_interim_policy/en/index.html).
- ⁴⁴ World Health Organization. A guide to monitoring and evaluation for collaborative TB/HIV activities. Geneva, World Health Organization 2004 (WHO/HTM/TB/2004.342 and WHO/HIV/2004.09)
- ⁴⁵ Assumptions in the simulation: 5 years needed to reach 80% final coverage; 80% efficacy in immunocompetent individuals and 40% efficacy in HIV-positive individuals; duration of immunity 10 years; MDR and HIV prevalence stable at current values.

