



Report on **Tuberculosis**



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**Report of the Scientific Working Group
meeting on Tuberculosis**

Geneva, 3–6 October, 2005

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Contents

Executive summary	1
1. Background and objectives	5
2. Social, economic and behavioural research	13
3. Epidemiology of tuberculosis	17
4. Case-finding and access to care	20
5. Diagnosis of tuberculosis	23
6. Drugs for tuberculosis (including immunomodulators)	29
7. Clinical management of tuberculosis	32
8. Vaccine development	36
9. Implementation research	42
10. Cross-cutting issues	45
11. Research support	49
12. Major initiatives and partnerships	52
13. Research gaps and research priorities for TDR	56
 Annex 1	
AGENDA: Scientific Working Group on Tuberculosis	63
 Annex 2	
LIST OF PARTICIPANTS: Scientific Working Group on Tuberculosis	67
 Annex 3	
WORKING PAPERS: Scientific Working Group on Tuberculosis	73
Working paper 1. <i>Latent tuberculosis infection: burden and control</i>	74
Working paper 2. <i>Tuberculosis and HIV: operational challenges facing collaboration and integration</i>	83
Working paper 3. <i>New drug development for tuberculosis: opportunities and challenges for research</i>	92
Appendix: Stop TB Partnership Working Group on New TB Drugs: membership as of September 2005	98
Working paper 4. <i>Tuberculosis deaths among populations with high HIV prevalence</i>	100
Working paper 5. <i>The current state of development of new vaccines for tuberculosis: criticisms and suggestions</i>	109

Executive summary

Tuberculosis is a major global health problem, responsible for more than 4500 deaths each day. A decade of intensified efforts at tuberculosis (TB) control has reduced global incidence except in Africa, where the disease continues to rise, driven by the HIV pandemic and poverty. However, unprecedented efforts to address deficiencies in TB control – including developing new drugs, new diagnostics, new vaccines, and new strategies to implement proven interventions – bring hope of tangible progress in TB control. Led by the Stop TB Partnership, the global community of TB public health officials, clinicians and researchers is poised to achieve within ten years the Millennium Development Goal target for tuberculosis, which aims to halt and begin to reverse the incidence of TB by 2015. These efforts strive towards eliminating tuberculosis as a global health problem by mid-century.

This report reflects the consensus of the Scientific Working Group on Tuberculosis, convened in Geneva in October 2005; it provides guidance to the UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR) and partners involved in TB research and control. The proposed research agenda accommodates the public health concerns expressed in the Stop TB Partnership's Second Global Plan to Stop TB (2006–2015), and aims to work towards the unified objective of addressing the growing epidemic and meeting the ambitious, though realistic, targets for 2015. The challenges are many, but the time is ripe for action and for moving forwards in TB research.

Success requires invigorated control efforts, improved collaboration, and a special commitment to reach people living in poverty. A prerequisite to this success is to generate new knowledge, new strategies and new tools derived from research on tuberculosis. There are two general areas in which research should be applied in order for TB control targets to be achieved: research on programme implementation and development of new tools.

Research on implementation

Research on programme implementation is essential. Up to 60% of TB cases can be detected with smear microscopy, and nearly all can be cured with six months of treatment using existing regimens. However, the current shortfall in case detection suggests that we do not know how to optimize case detection.

Case detection and access to care

How can case detection be improved? Answers to this question will only derive from better understanding of the social and behavioural forces limiting case detection and from evaluations of new case detection strategies. Key factors to study are the barriers to accessing care, including transportation, user fees, hunger, work, gender discrimination and health system

infrastructure. Research on the factors limiting case detection at sites where TB screening occurs, including schools, workplaces, health and other centres providing HIV testing and care, and hospitals, will be necessary to identify appropriate outreach strategies. Operational research and tests of alternative design for detecting those with TB symptoms, and ensuring diagnosis and rapid entry into care, will be necessary to optimize case finding.

Diagnostics

To what extent can we optimize existing diagnostic methods – sputum smear microscopy, culture, and drug sensitivity testing – to increase identification of sputum smear-positive cases? Research on sputum concentration methods and fluorescence microscopy is essential to establish the optimal protocol for sputum-based diagnosis. In addition, improved mycobacterial culture systems need evaluating for their impact on case detection, including relating cost and performance to diagnostic yield. The role of drug sensitivity testing needs to be further examined. Finally, and perhaps most importantly, current diagnostic algorithms – which include both laboratory and empiric components (such as the use of empiric antibiotic trials to exclude TB) – need to be rigorously evaluated and improved.

Treatment

How can treatment outcomes be optimized with current drugs? Treatment adherence support strategies (such as directly-observed therapy and patient support systems) need to be assessed and optimized. The role of immunomodulatory drugs needs to be carefully assessed, with meta-analysis of existing data, and new trials are needed to assess the benefit of immunomodulators in conditions where benefit might accrue. Finally, the effect of treating HIV in patients co-infected with TB needs to be addressed. Ongoing studies should help identify optimum approaches for treatment of co-infected patients, but alternative co-infection treatment strategies need to be evaluated for improving clinical outcomes. Such clinical research would benefit from exploration of strategies to improve and integrate HIV care and TB treatment at national, district and health centre levels, as a means of overcoming infrastructural and manpower constraints and improving clinical outcomes – in keeping with HIV/TB policies. Social science research has a unique role to play in identifying the reasons for the successes and failures of current TB treatment and prevention efforts.

Development of new tools

The existing arsenal of diagnostic tests, anti-mycobacterial drugs, and bacille Calmette-Guérin (BCG) vaccine, is inadequate. New tools for TB diagnosis, treatment, and prevention are essential if long-term TB control targets are to be met.

New diagnostics

With at least 5 million cases of active TB unnotified each year, extra-pulmonary disease, paediatric TB and multidrug-resistant TB pose significant diagnostic challenges which are not addressed by sputum-smear microscopy. Diagnostics should be driven by the reality of the health system infrastructure; well-engineered, simple tests are needed at the point-of-care, at district hospital laboratories, and at central laboratories. The Stop TB Partnership Working Group on Diagnostics has articulated a focused research agenda for new diagnostics, including the detection of extra-pulmonary and paediatric TB infection and other forms of sputum smear-negative disease; the success of this programme will depend upon simple, sensitive and specific technology for diagnosis in the field, and appropriate funding.

New drugs

Short-course chemotherapy for TB consists of adhering tightly to six months of treatment with drugs with suboptimal toxicity profiles, but in patients co-infected with HIV these drugs are challenged by interactions with antiretroviral drugs used to treat advanced HIV disease. A simple regimen for simultaneous treatment does not yet exist. Strategic treatment goals include: developing a short and simple TB treatment regimen; developing improved treatment for multidrug-resistant (MDR)-TB; and identifying and developing drugs that can be safely co-administered with antiretroviral drugs in patients with TB/HIV co-infection. Such drugs will substantially improve treatment outcomes, simplify programme implementation, and accelerate TB control efforts. The TB Alliance has a comprehensive strategy and timeline to evaluate the promising pipeline of drugs and develop a better regimen within the next decade.

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