

Child TB subgroup update

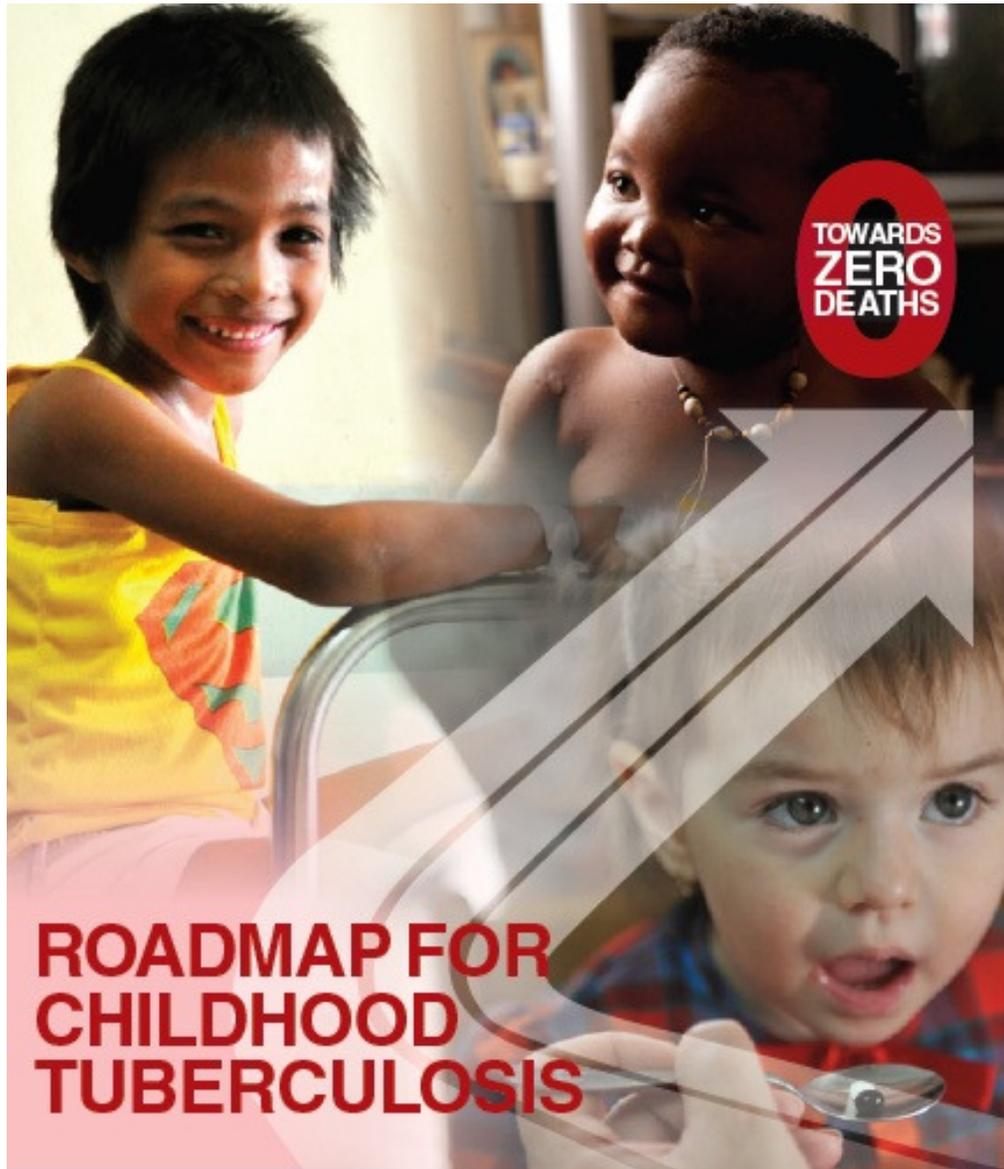
2015



Update

- Membership now over 200
- New members of core group in 2015
 - Betina Mendez Alcântara Gabardo, Chair, Child TB Advisory Committee of the Americas
 - Anna Scardigli, The Global Fund
 - Valérie Schwoebel, The Union
 - Keri Lijinsky, USAID, Bureau for Africa
 - Ya Diul Mukadi, Senior TB Advisor, USAID Global Health Bureau
 - Eleanor (Ellie) Click, CDC USA
 - Pervaiz Tufail, Civil Society

 - *Anne Detjen*, UNICEF
- Core group conference calls in 2015: March 10, July 14, Oct 6
- Future chair – elect at annual subgroup meeting in 2016



TOWARDS
ZERO
DEATHS

ROADMAP FOR CHILDHOOD TUBERCULOSIS



Increasing recognition that TB is an increasingly important cause of morbidity and mortality in infants and young children globally

Viewpoint

Importance of tuberculosis control to address child survival



Stephen M Graham, Charalambos Sismanidis, Heather J Menzies, Ben J Marais, Anne K Detjen, Robert E Black

Tuberculosis commonly affects young children (<5 years) in countries that have high rates of child mortality.¹ The global public health focus to control tuberculosis has traditionally aimed to reduce transmission through early

death and not contributory causes to WHO, vital registration data cannot be used to estimate the number of tuberculosis deaths in people living with HIV. Further, vital registration data are available for only 3% of global

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[http://dx.doi.org/10.1016/S0140-6736\(14\)60420-7](http://dx.doi.org/10.1016/S0140-6736(14)60420-7)

“ There are many contributions which the pediatrician can make to a TB control program.

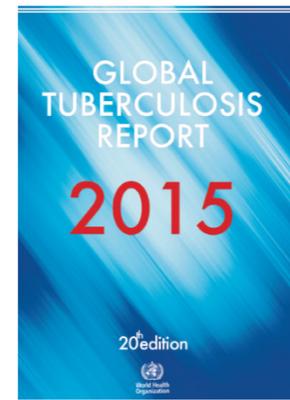
First the negativism about tuberculosis so prevalent in pediatrics must be overcome...”

Edith Lincoln, 1961

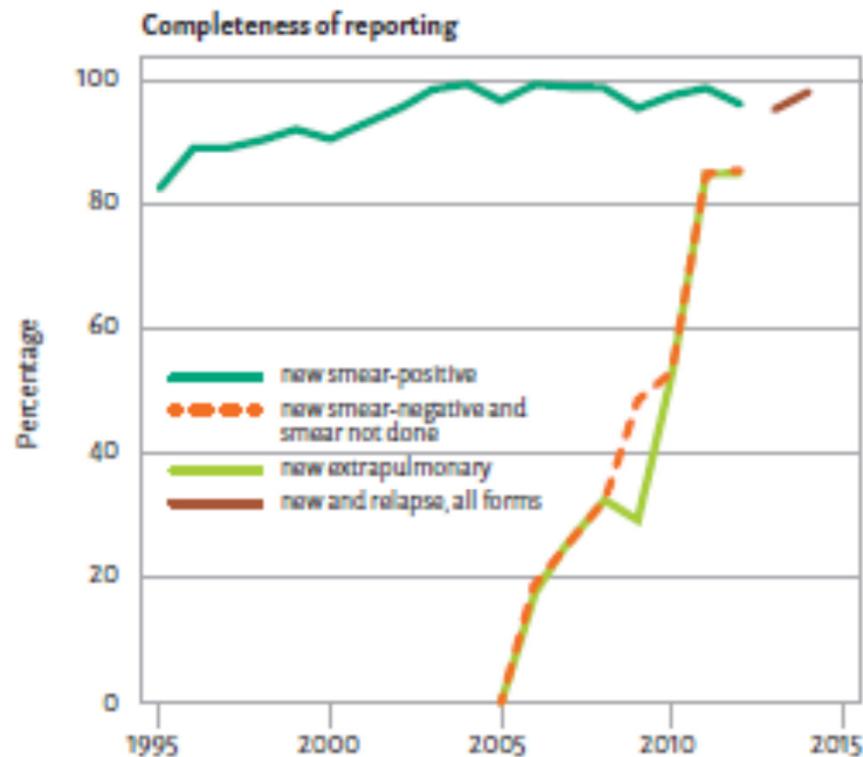
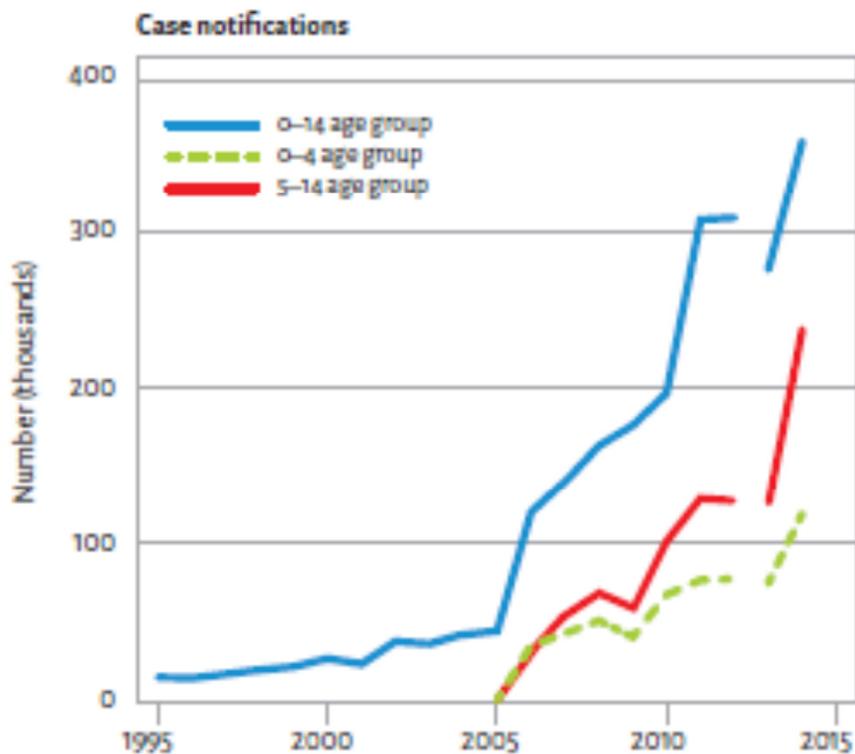


FIGURE 1. Edith Lincoln at the commencement of her studies

“Know your epidemic”

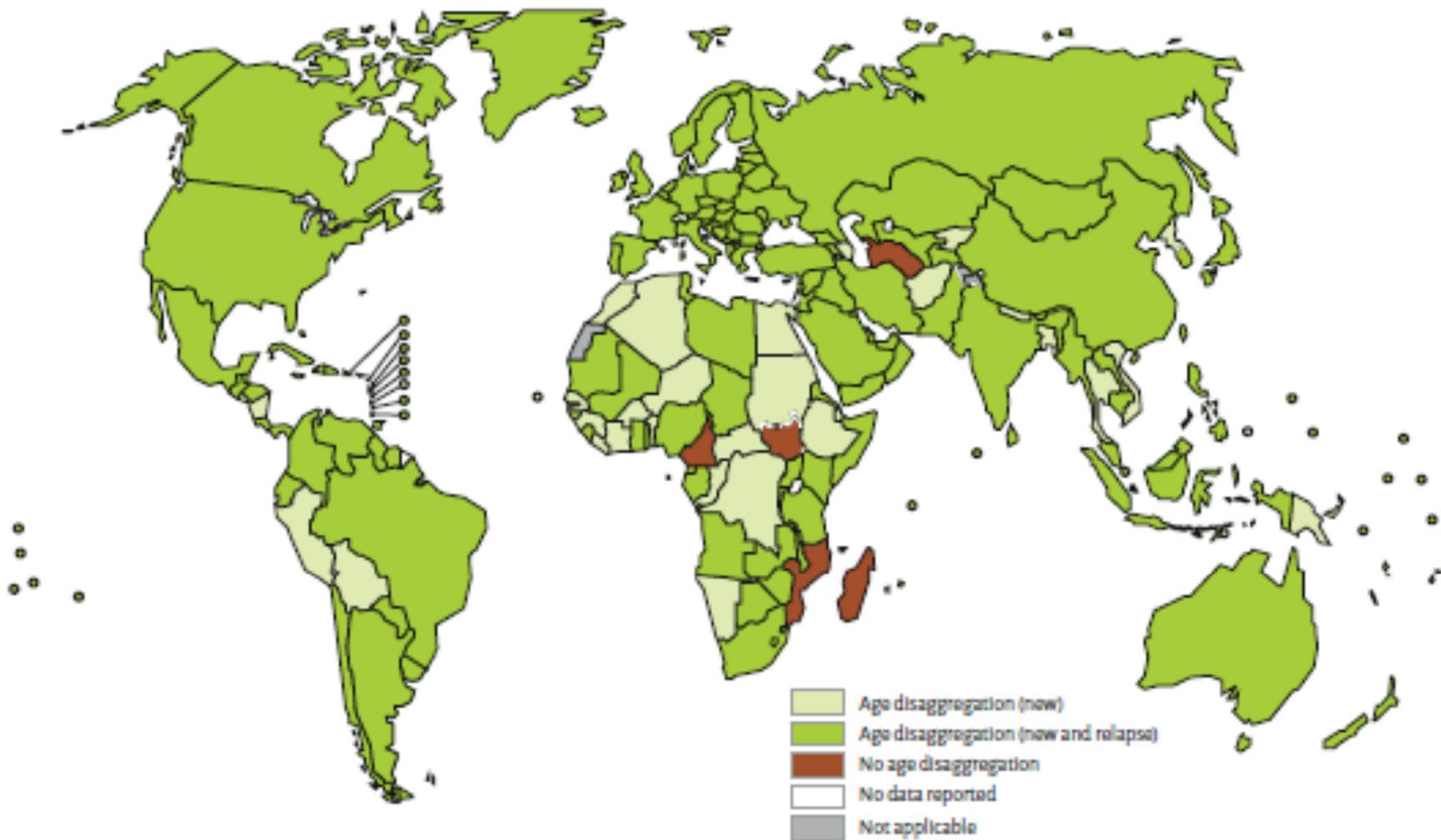


Global progress in reporting of TB cases among children, 1995–2014.³ Left panel: Number of notifications of cases among children reported to WHO. Right panel: Percentage of case notifications reported to WHO that are age-disaggregated.

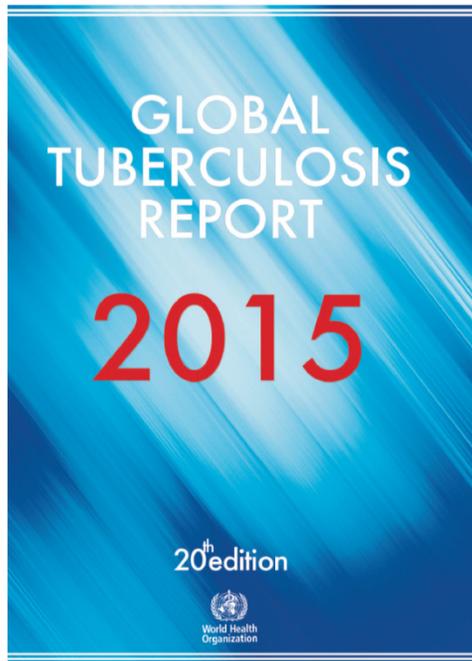


“Know your epidemic”

Reporting of new and relapse TB case notifications disaggregated by age, 2014



“Know your epidemic”



TB in children (0-14 yrs)
358,521 reported in 2014
- 30% higher than for 2013

Best estimates:

1,000,000 cases (UI: 900,000-1,100,000) or 10.4% of total caseload
140,000 deaths (cf.80,000 estimated for HIV uninfected in 2013)

Box 2.5 Estimating TB incidence among children: challenges, progress to date and next steps

It is well recognized that estimating the incidence of TB in children is difficult and that published estimates vary.^{a,b} There are at least four major reasons for this:

- 1. TB in children is rarely bacteriologically confirmed.** Direct examination of sputum smears and tuberculin skin testing both suffer from very poor diagnostic performance. TB in children is thus a condition that is usually clinically diagnosed based on a combination of signs and symptoms that are not specific to TB. Case definitions are inconsistent among countries and within countries over time (as a result of changes in medical practice).
- 2. Paediatricians who diagnose TB do not always report cases to public health authorities.** Childhood TB is not usually a public health priority and effective linkages between NTPs and the hospitals and clinics where children are usually diagnosed are lacking. Reporting of cases is therefore often incomplete and not supported by a legal framework.
- 3. TB cases among children are less likely to be diagnosed in countries with a high burden of TB compared with adults.** Sick children may be evaluated in facilities with little to no capacity to diagnose childhood TB, and diagnostic challenges (the low specificity of clinical signs and symptoms) translate into low access to quality diagnosis and care services.
- 4. Different methods have been used to produce estimates.** These include a dynamic model and statistical approaches.

The estimates included in this report are based on combining results from a dynamic model,^c a statistical approach based on a recent study,^d and methods previously used by WHO^e in a statistical ensemble model.⁶ Estimates from the dynamic model and statistical approaches using the most updated data for 2014 were found to be similar. This has contributed to a more robust combined estimate compared with those produced using the dynamic model or statistical approaches on their own. In turn, this means that the uncertainty interval from the ensemble approach

is narrower than those of estimates produced from each approach used on its own. Nonetheless, the uncertainty interval relative to the best estimate is about twice as large as the relative uncertainty of the overall TB incidence estimate for all ages.

The lack of overlap between the estimate of childhood TB incidence in this report and the one published in the 2014 edition^b illustrates the difficulties in producing such estimates (explained above) and limitations in the documentation of uncertainty. The estimates in this report use an updated methodological approach recommended by the WHO Global Task Force on TB Impact Measurement (**Box 2.1, Box 2.2**). However, even using this approach does not allow all sources of uncertainty, such as uncertainty due to model specification, to be fully quantified in practice.

The variability and lack of stability in recently published estimates of TB incidence among children is concerning. Addressing this challenge requires much greater commitment from national public health authorities to the definition and application of consistent case definitions, to ensuring reporting of cases based on a legal framework and ensuring that children who are close contacts of people with TB are thoroughly investigated using up-to-date national recommendations.

^a JA Seddon and D Shingadia. Epidemiology and disease burden of tuberculosis in children: a global perspective. *Infect Drug Resist*, 7:153–65, null 2014.

^b World Health Organization. *Global tuberculosis report 2014*. World Health Organization, Geneva; 2014. (WHO/HTM/TB/2014.08). See particularly **Box 2.5 in Chapter 2**.

^c PJ Dodd, E Gardiner, R Coghlan, and JA Seddon. Burden of childhood tuberculosis in 22 high-burden countries: a mathematical modelling study. *Lancet Glob Health* 2014; 2:e453–9.

^d HE Jenkins, AW Tolman, CM Yuen et al. Incidence of multidrug-resistant tuberculosis disease in children: systematic review and global estimates. *Lancet*, 2014; 383:1572–9.

^e For details, see the **online technical appendix** to this report at www.who.int/tb/data.

ROADMAP FOR CHILDHOOD TUBERCULOSIS



THE END TB STRATEGY



World Health
Organization

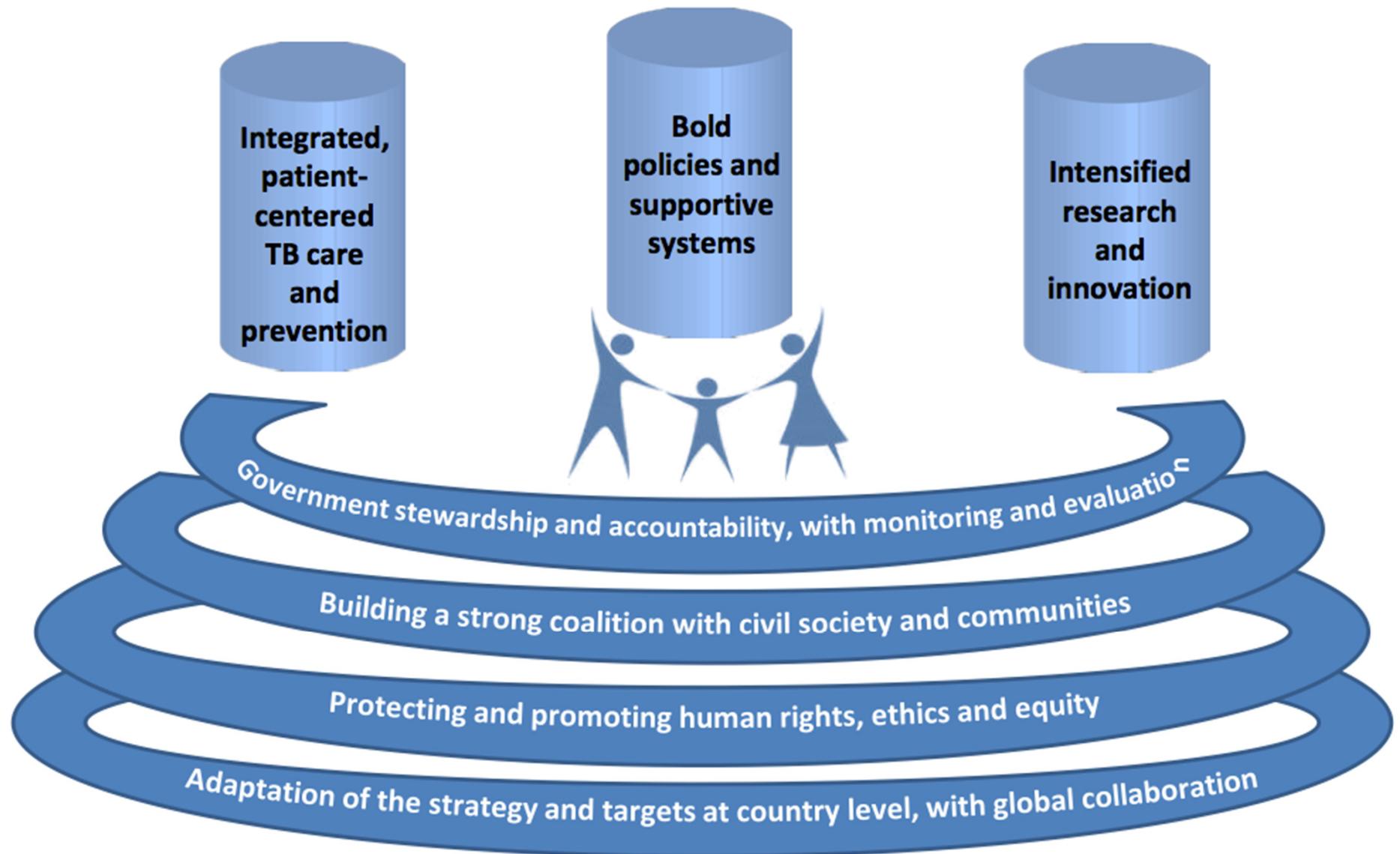
*Global strategy and targets for
tuberculosis prevention, care
and control after 2015*



VISION	A world free of tuberculosis – zero deaths, disease and suffering due to tuberculosis			
GOAL	End the global tuberculosis epidemic			
INDICATORS	MILESTONES		TARGETS	
	2020	2025	SDG 2030*	END TB 2035
Reduction in number of TB deaths compared with 2015 (%)	35%	75%	90%	95%
Reduction in TB incidence rate compared with 2015 (%)	20% (<85/100 000)	50% (<55/100 000)	80% (<20/100 000)	90% (<10/100 000)
TB-affected families facing catastrophic costs due to TB (%)	Zero	Zero	Zero	Zero

Proposed post-2015 Global TB Strategy

Pillars and principles



People-centred TB care



Community

Engagement & Partnership



Family



Social protection



Risk group
BCG & LTBI

Social determinant



Patient



Infected and become sick

Treatment and care



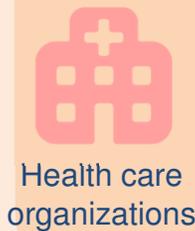
Community health workers



Health Workers



Community health workers



Health care organizations

Health system capacity



Laboratory network

Treatment and care for all

Governance and stewardship



Global Plan to Stop TB 2016-2020

Included End TB goals for 2025.....

- 90% or more of children who have been exposed to TB receive preventive therapy
- 90% or more of people in close contact with all people diagnosed with TB should be evaluated for TB

FRAMEWORK TOWARDS

TB ELIMINATION

IN LOW-INCIDENCE COUNTRIES



World Health
Organization

2014

WHO LTBI taskforce

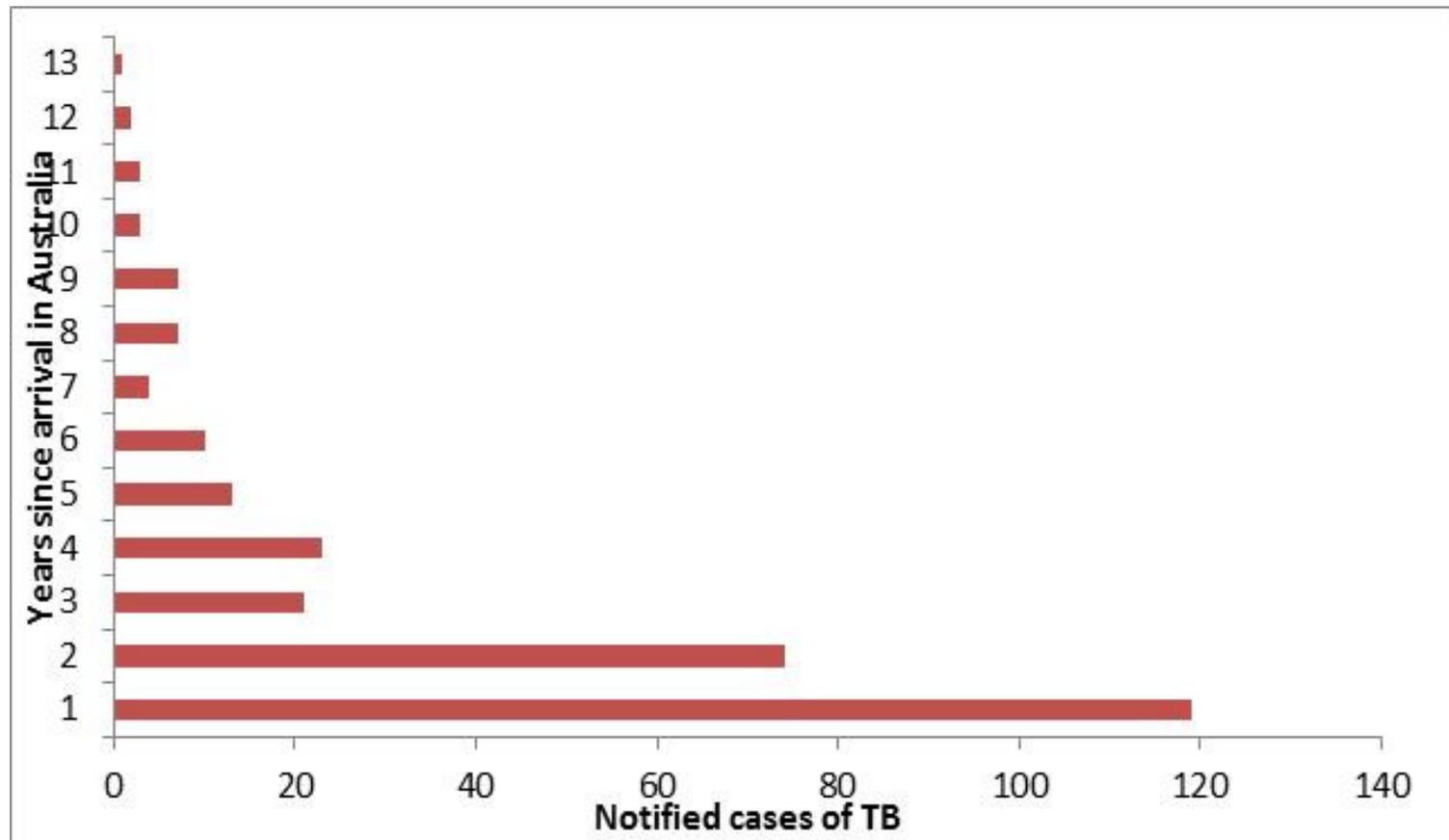
Current estimates: one-third of global population infected i.e. > 2 billion with 10% lifetime risk of TB disease

Established 2015 with aim to raise the profile of programmatic management of LTBI particularly in low incidence countries, including monitoring and evaluation of implemented activities, as well as promoting research.

The purpose of the Task Force is to:

- Analyse bottlenecks, identify innovative approaches and unblock barriers for implementation of the guidelines at global and national level.
- Develop a framework to monitor and evaluate the implementation of LTBI management, including standardised indicators.
- Promote research on LTBI by identifying knowledge gaps, and define priorities in both fundamental and operational research.
- Contribute to the process for the re-estimation of the global burden of LTBI.

Notified cases in Australia (2003-2012) in overseas-born children by years since arrival



Note that in USA, recently introduced enhanced pre-migration screening for LTBI followed by CXR (if positive) in children (2-14 years) examined in countries where WHO TB incidence is ≥ 20 per 100,000 population per year.

Job aides

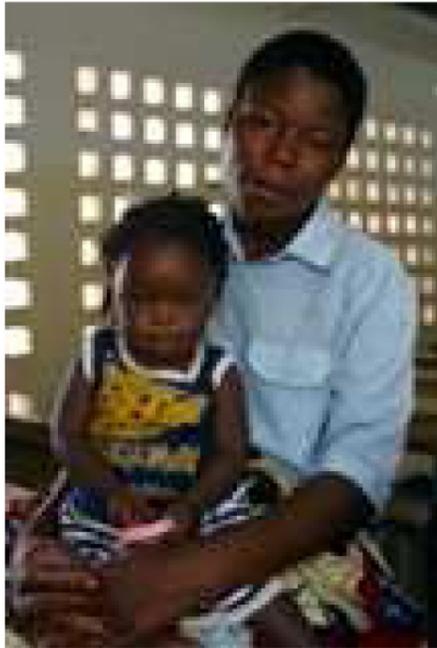
Desk-guide for diagnosis and management of TB in children



Management of Multidrug-Resistant Tuberculosis in Children: A Field Guide



Desk-guide for diagnosis and management of TB in children



Guide de diagnostic et de prise en charge de la tuberculose chez l'enfant



Technical assistance

- Sri Lanka
- Pakistan NTP review
- Bangladesh
- Nepal
- India – JMM
- China – ToT
- Viet Nam
- The Philippines

Regional TB meetings – child TB with NTP

- Childhood TB consultation for the African region, April 20-21, Johannesburg
- Eastern Mediterranean NTP Manager's meeting, Sept 6-8, Cairo
- Regional Meeting on child TB in the Americas, October 21-22, Brasilia
- South-East Asian Regional NTP meeting, October 26-30, Colombo
- Regional consultation on child TB in European Region, November 11-15, Copenhagen
- Western Pacific Regional NTP manager's meeting – postponed to Q1, 2016



Contents lists available at [ScienceDirect](#)

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journal homepage: www.elsevier.com/locate/ijid



Regional initiatives to address the challenges of tuberculosis in children: perspectives from the Asia-Pacific region

Stephen M. Graham^{a,b,c,*}, Malgorzata Grzemska^d, Annemieke Brands^d, Huong Nguyen^e, James Amini^f, Rina Triasih^g, Khurshid Talukder^h, Shakil Ahmedⁱ, Farhana Amanullah^j, Blessina Kumar^k, Pervaiz Tufail^l, Anne Detjen^a, Ben Marais^m, Cornelia Hennigⁿ, Tauhid Islamⁿ



Childhood TB Meeting for the African Region

Southern Sun O.R Tambo Hotel,
Johannesburg, South Africa,
20-21th April 2015



Framework for addressing Childhood tuberculosis

in the African Region

for National TB Programmes

Activities

- WHO consultation on research for TB – Stockholm, Nov 2014
- World TB Day 2015 – launch of e-learning course
- Ethics meeting, May 2015, Switzerland
- STAG TB, June 2015, Geneva – session on child TB
- Global Health Practitioner Conference, Washington, October

- KNCV – child benchmarking tool developed
- NIH new diagnostics - SOPs
- TAG's annual pipeline report
- Advisory Panel for Global TB Alliance, NY

STEP-TB project

launch of new dispersible FDCs for treatment of children with drug-susceptible TB 1st December

manufacturer identified – 15 USD per course

WHO collaborating with TB Alliance and UNICEF

IJTLD supplement issue December 2015

Lunchtime symposium today!



RESEARCH ARTICLE

Understanding Market Size and Reporting Gaps for Paediatric TB in Indonesia, Nigeria and Pakistan: Supporting Improved Treatment of Childhood TB in the Advent of New Medicines

Renia Coghlan¹*, Elizabeth Gardiner², Farhana Amanullah³, Chikwe Ihekweazu⁴, Rina Triasih⁵, Malgorzata Grzemska⁶, Charalambos Sismanidis⁶



Example of a weight band table when using the “new” FDC being developed

Weight bands	Numbers of tablets		
	Intensive Phase		Continuation Phase
	RHZ	E	RH
	75/50/150	100	75/50
4-7kg	1	1	1
8-11kg	2	2	2
12-15kg	3	3	3
16-24 kg	4	4	4
25 kg+	Go to adult dosages and preparations		

Tracking Investments in Pediatric TB R & D

- TAG started tracking *pediatric* TB R&D spending in 2010
- Actual pediatric TB R&D spending is tracked against the \$200 million target for 2011–2015 published in the *Roadmap for Childhood Tuberculosis*
- The *Global Plan to End TB* includes some pediatric TB R&D funding targets for 2016–2020

2015 Report Findings

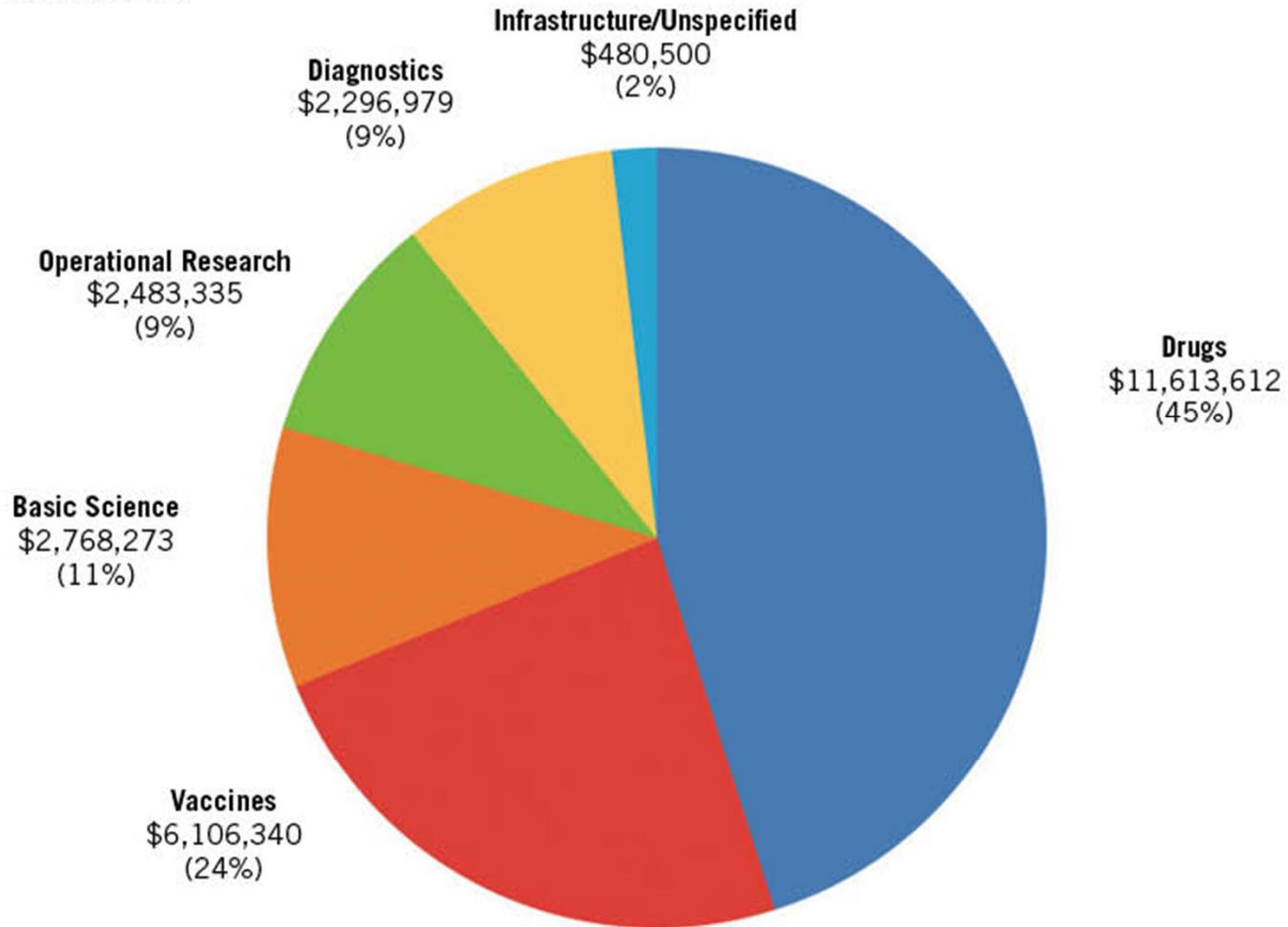
- 20 funders reported pediatric TB R&D spending
- In 2014, funders gave **\$25.7 million** to research related to pediatric TB



*The full report is available here: <http://www.treatmentactiongroup.org/tbrd2015>

FIGURE 12

Pediatric TB R&D Funding by Research Category, 2014
Total: \$25,749,039



Cf. 25.3 million in 2013

Research

- New (and old) diagnostics
- Epidemiology in at-risk groups
- Preventive therapy – DS and DR
- Shorter treatment regimens
- Second line and new drugs – PK and safety

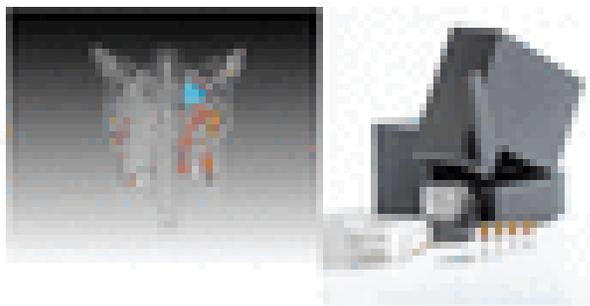
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AIDS

hrvma

Clinical Infectious Diseases

Advances in Tuberculosis
Research: A Blueprint for
Opportunities



A Supplement to Clinical Infectious Diseases

OXFORD
UNIVERSITY PRESS
oxfordjournals.org

A Blueprint to Address Research Gaps in the Development of Biomarkers for Pediatric Tuberculosis

Mark Patrick Nicol,^{1,a} Devasena Gnanashanmugam,^{2,a} Renee Browning,² Eleanor S. Click,³ Luis E. Cuevas,⁴ Anne Detjen,⁵ Steve M. Graham,^{5,6,7} Michael Levin,⁸ Mamodikoe Makhene,² Payam Nahid,⁹ Carlos M. Perez-Velez,¹⁰ Klaus Reither,¹¹ Rinn Song,^{12,13} Hans M. L. Spiegel,¹⁴ Carol Worrell,² Heather J. Zar,¹⁵ and Gerhard Walzl¹⁶

Clinical Case Definitions for Classification of Intrathoracic Tuberculosis in Children: An Update

Stephen M. Graham,^{1,2,3} Luis E. Cuevas,⁴ Patrick Jean-Philippe,⁵ Renee Browning,⁶ Martina Casenghi,⁷ Anne K. Detjen,² Devasena Gnanashanmugam,⁸ Anneke C. Hesselink,⁹ Beate Kampmann,^{10,11} Anna Mandalakas,¹¹ Ben J. Marais,¹² Marco Schito,¹³ Hans M. L. Spiegel,¹⁴ Jeffrey R. Starke,¹¹ Carol Worrell,^{12,13} and Heather J. Zar¹⁶

Recent Developments and Future Opportunities in the Treatment of Tuberculosis in Children

James A. Seddon,^{1,2} Lindsay McKenna,³ Tejshri Shah,² and Beate Kampmann^{1,2,4}

Reference standards and SOPs

The Union

International Union Against
Tuberculosis and Lung Disease
Health solutions for the poor



Childhood TB Learning Portal

COURSES

RESOURCES

COMMUNITY

HELP

[Register/Sign In](#)



Welcome to the Childhood TB Learning Portal. We support the development of knowledge, skills and networks for those involved in the prevention, diagnosis and management of children with TB. You can complete free, online courses, explore additional resources and join a community of peers dedicated to beating childhood TB.

Childhood TB for Healthcare Workers: an Online Course



Childhood TB for Healthcare Workers: An Online Course

- Launched in 2015 by The Union in collaboration with the World Health Organization
- Available in English and French
- Additional languages being considered
- Course covers how to diagnose, treat, and prevent childhood TB, including how to perform contact screening
- Designed for healthcare workers at the primary and secondary levels of the healthcare system



USAID
FROM THE AMERICAN PEOPLE

TB CARE I



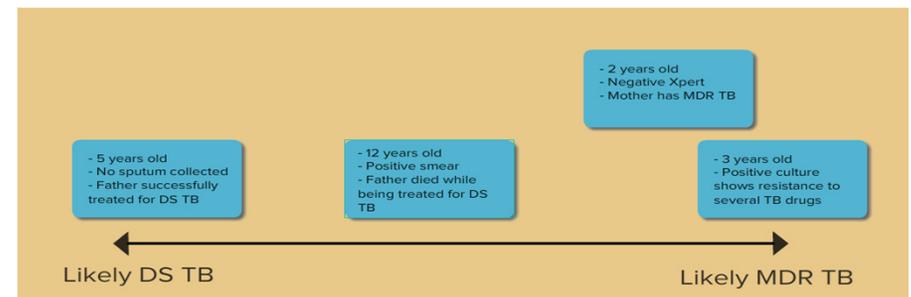
**World Health
Organization**

To come in 2016/17: Facilitator guide for online training

- Goal: to apply concepts learned in the online course to one's work setting in order to improve the care of children with TB
- Provides information necessary to lead a facilitated session
- Can be adapted to different practice locations
- Organized by module and follows format of the online course

Childhood MDR-TB for Healthcare Workers: An Online Course

- Similar process and format as *Childhood TB for Healthcare Workers: An Online Course*
- Designed for more specialized audience
- Goal is to link healthcare workers with existing resources and evidence to gain confidence to treat children with MDR-TB
- 5 modules
 1. Introduction
 2. Diagnosis
 3. Treatment
 4. Programme Management
 5. Comprehensive Review





**CENTER FOR GLOBAL
HEALTH DELIVERY-DUBAI**
HARVARD MEDICAL SCHOOL

POLICY BRIEF

**Post-Exposure Management of
Multidrug-Resistant Tuberculosis Contacts:
Evidence-Based Recommendations**



Thanks to you all



**Global Consultation on Childhood TB for High Burden Countries
in the Eastern Mediterranean, South East Asia,
and Western Pacific Regions**

Jakarta, Indonesia, 29 September - 1 October 2014

