Child TB subgroup annual meeting

2016

Stop TB Partnership

World Health Organization

Objectives

To share national and regional experiences in scaling up the response to childhood TB and to discuss next steps to move the agenda forward.

To discuss how to operationalize the End TB Strategy with a focus on childhood TB.

To give an update on the activities of the working group since the last annual meeting in Cape Town, South Africa.

Child TB subgroup of Stop TB Partnership formed 2003

WHO Guidance for NTPs on the management of TB in children 2006

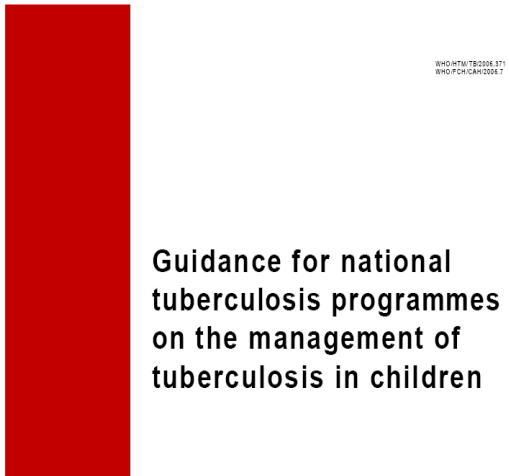
International Child TB Meeting, Stockholm, 2011

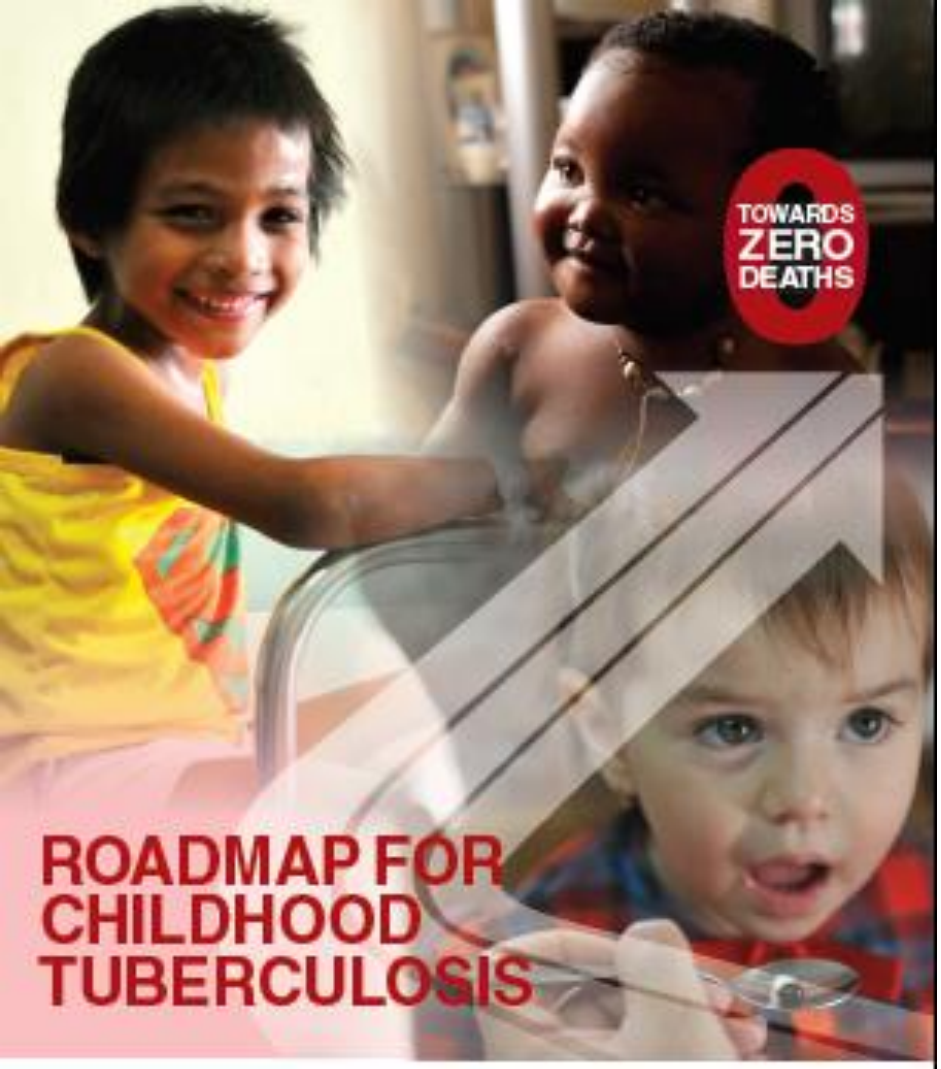
First estimates of child TB in Global TB Report 2012

Roadmap for Childhood TB 2013

WHO Guidance for NTPs on the management of TB in children 2014

End TB Strategy (and SDGs) 2015





ROADMAP FOR CHILDHOOD TUBERCULOSIS

World Health Organization · CDC · unicef · International Union Against Tuberculosis and Lung Disease · TAG Treatment Action Group · Stop TB Partnership · USAID

ROADMAP FOR CHILDHOOD TUBERCULOSIS

TOWARDS ZERO DEATHS

- Include the needs of children and adolescents in research, policy development and clinical practices
- Collect and report better data, including data on prevention
- Develop training and reference materials for health care workers
- Foster local expertise and leadership
- Do not miss critical opportunities for intervention
- Engage key stakeholders
- Develop integrated family-centred and community-centred strategies
- Address research gaps
- Meet funding needs for childhood TB
- Form coalitions and partnerships to improve tools for diagnosis and treatment

The End TB Strategy: 3 pillars and 4 Principles

SDG health goal 3 and its 13 targets by 2030

3.1 Reduce Maternal mortality

3.2 Reduce child and neonatal mortality

3.3 **End the epidemics of AIDS, tuberculosis,** malaria & neglected tropical diseases and combat hepatitis, water-borne and other communicable diseases

3.4 Reduce mortality due to NCD and improve mental health

3.5 Strengthen Prevention and treatment of substance abuse (narcotics, alcohol)

3.6 Reduce Mortality due to road traffic injuries

3.7 Universal access to sexual and reproductive health-care services

3.8 Achieve universal health coverage

3.9 Reduce deaths and illness due to pollution and contamination

3.a Strengthen implementation FCTC (tobacco)

3.b Access to affordable essential medicines and technologies

3.c Increased health financing and health workforce in developing countries

3.d Enhance capacity for early warning, risk reduction and management of national and global health risks

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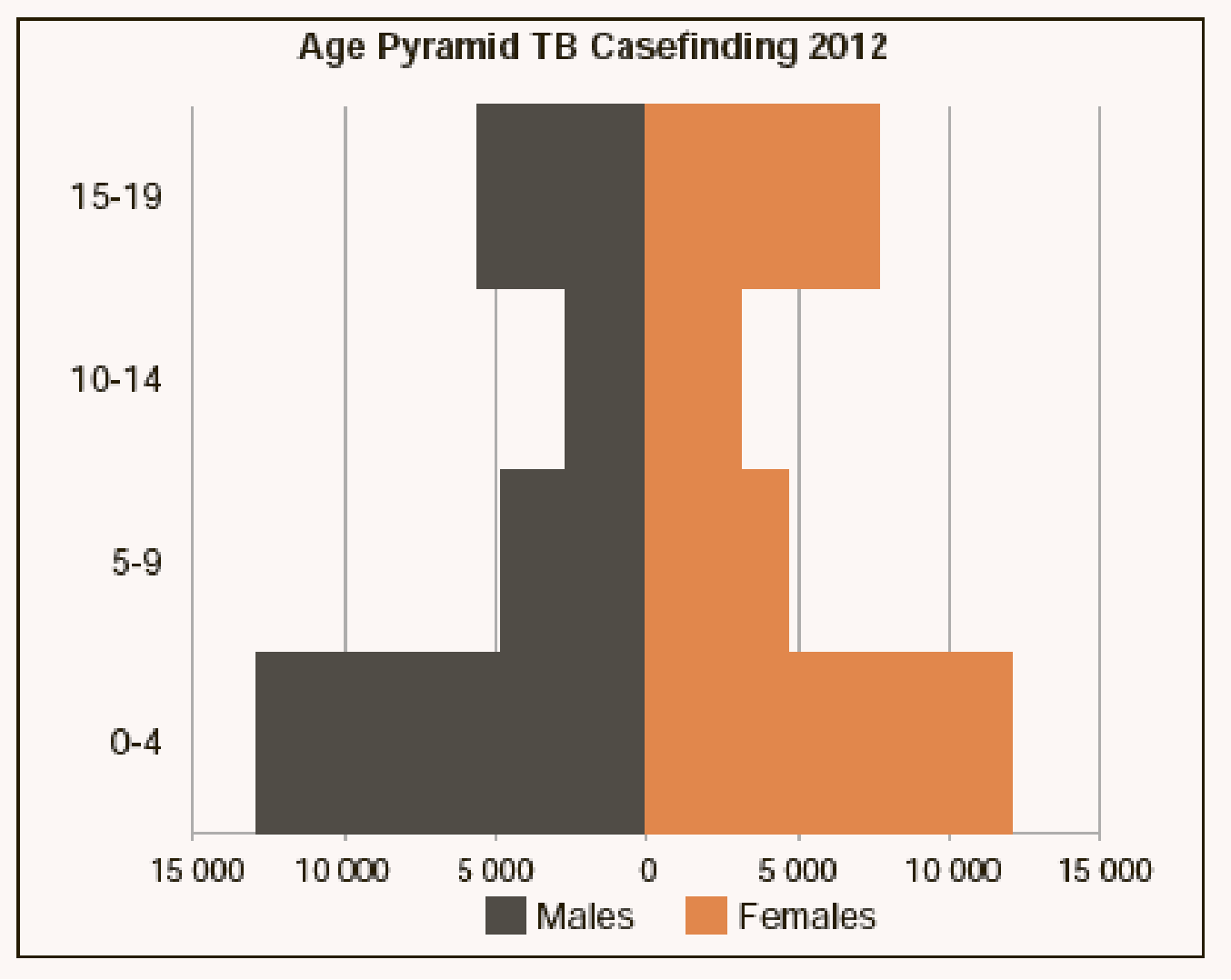
TB in adolescents



Smith J, Moyo S, Day C. South African Health Review 2013/14

“Know your epidemic”

TB in children (0-14 yrs)

Around 1,000,000 cases or 10% of total caseload
M:F ratio: 1.1-0.9
40% in SE Asia and 31% in Africa

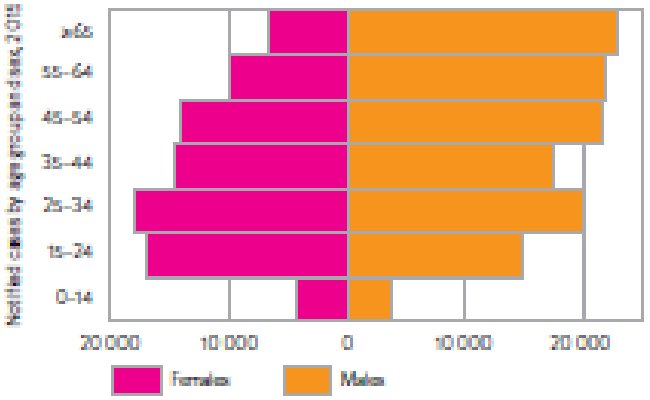
169,000 deaths in HIV-uninfected
41,000 deaths in HIV-infected

Increasing case notifications to 6.3% of notified cases globally

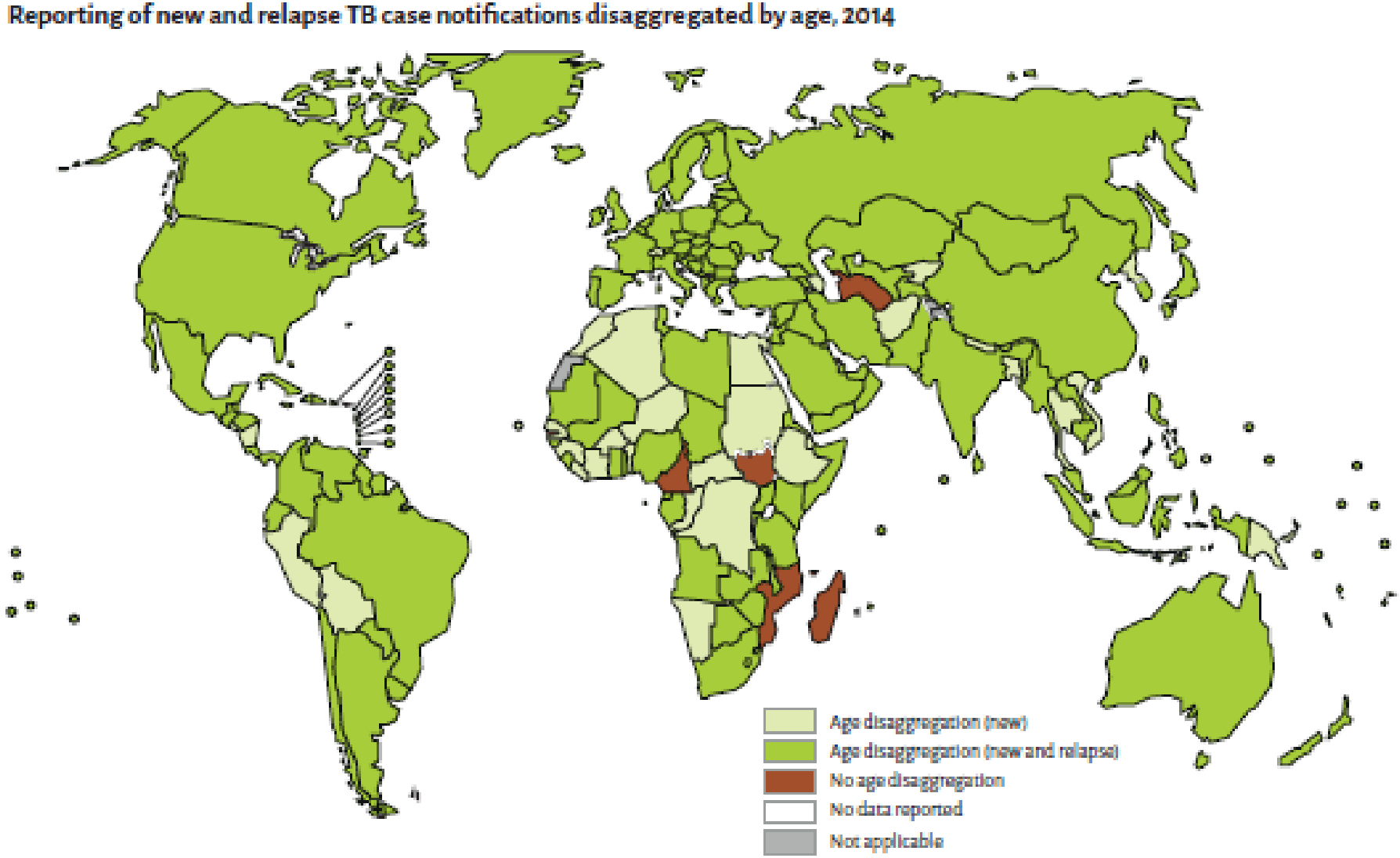
Country specific data

Estimated TB incidence by age and sex (thousands),[a] 2015

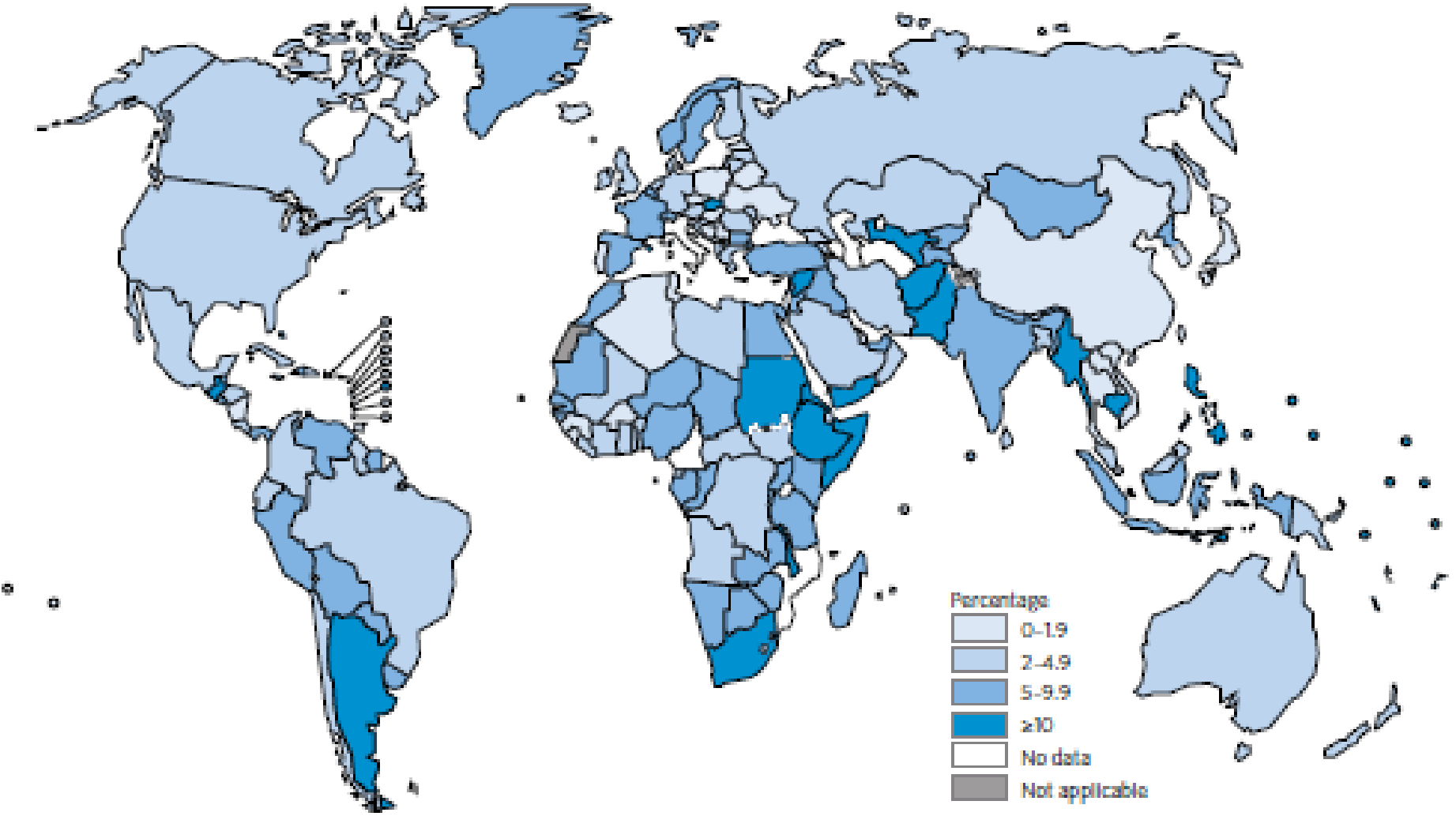
	0–14 years	>14 years	Total
Females	20 (9.9–31)	131 (62–200)	151 (72–231)
Males	17 (9.8–24)	194 (134–254)	211 (143–278)
Total	37 (23–51)	325 (247–403)	362 (234–517)



Reporting disaggregated by age



Proportion of new and relapse TB that were children in 2015



The burden of MDR TB

It is estimated that 25,000 children developed MDR TB in 2014 although the vast majority (>95%) were not detected and treated

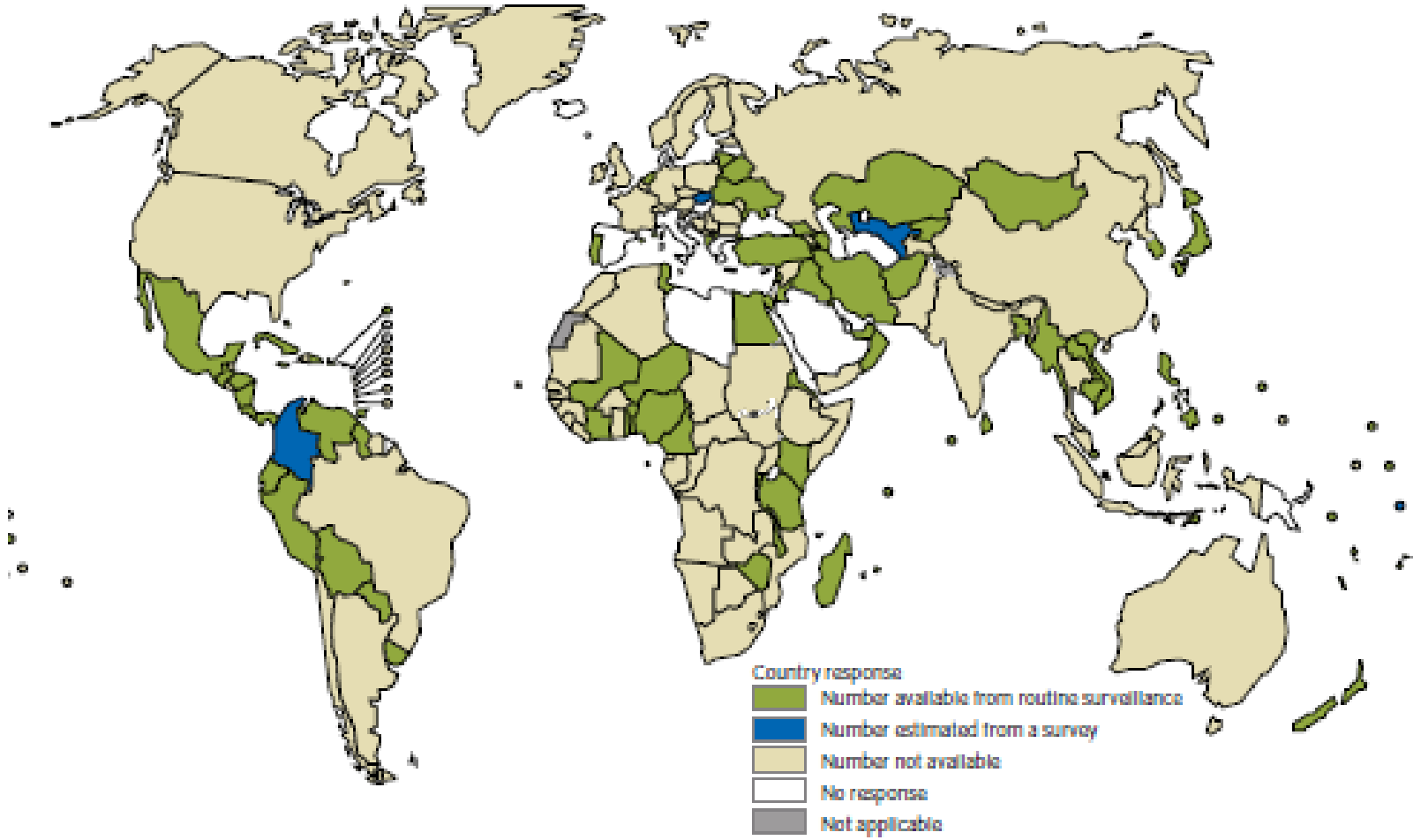
Shorter course regimens and towards no injectables
New drugs (DLM/BDQ) for children

Preventive therapy for MDR TB contacts a major current issue
- RCTs commenced in 2016
- Observational evidence accumulates

- Dodd PJ, Sismanidis C, Seddon JA. Global burden of drug-resistant tuberculosis in children: a mathematical modelling study. *Lancet Infect. Dis* 2016
- Seddon JA, Fred D, Amanullah F *et al.* Post-exposure management of multidrug-resistant tuberculosis contacts: evidence-based recommendations. Policy brief no. 1. Dubai, United Arab Emirates: Harvard Medical School Center for Global Health Delivery, Dubai, 2015.
- Harausz E, Garcia-Prats AJ, Seddon J *et al. AJRCCM 2016*

Prevention of TB in children	
Improved case-finding and management	Early identification and effective treatment of infectious TB and MDR TB cases will reduce the burden of child TB and MDR TB
BCG	The main benefit of neonatal BCG is protection against severe disseminated forms of TB in children Recent global shortages: in 2015, 163 countries with >90% coverage in 102 countries
Contact screening and management	Opportunity for active case detection of TB in contacts of all ages Focus of LTBI management is on individuals infected with TB that have greatest likelihood of developing active TB disease following infection – this includes young children and HIV-infected children of any age Widely recommended but uptake by families and implementation by NTP are poor
Infection control	Lack of awareness of risk for children attending health facilities with carers – TB wards; TB clinics; HIV clinics

Available data on numbers of eligible child contacts that were started on preventive therapy in 2015



Only 9 of 30 high burden countries reported data

Afghanistan and Bangladesh reported the largest number: around 10,000

WHO African region reported 28% of total

Global Plan to End TB 2016-2020

Includes 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

A "top ten" indicator for monitoring implementation of the End TB Strategy

90% or more of children aged <5 years who are household contacts of TB cases started on treatment for LTBI

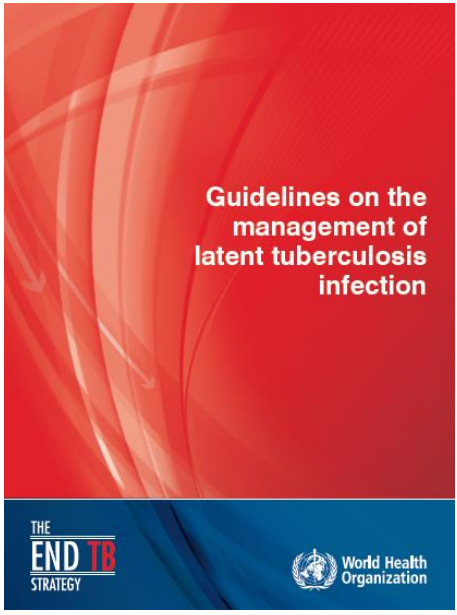
LTBI management

87,000 children started on “preventive treatment” or 7% of estimated 1.2 million young child household contacts of bacteriologically confirmed TB cases in 2015

Recommendations for high TB burden setting
- TB incidence rate ≥100 per 100,000 population

Strong recommendations for at-risk populations:
•People living with HIV
•Children under 5 years of age who are household contacts of pulmonary TB cases

Global and national indicators
•Proportion of children who are household contacts who have completed evaluation for TB
•Proportion of those eligible for prevention that have started treatment
•Proportion that have completed



Numbers for LTBI management in children

Estimates in 2014: 2.4 million young children (<5 years) and 5.1 million older children (5-14 years) living in households of patients with TB

Of these, around 240,000 (10%) young children and 420,000 (8%) older children will have TB

Of the remaining 2.16 million young child contacts and 4.68 million older child contacts without TB, it was estimated that 848,453 (or 39%) and 2,660,885 (or 57%) were infected.

Therefore, the global target of 90% or more of exposed children translates to:

- at least 6.2 million child contacts of all ages treated with preventive therapy if screening did not include testing for LTBI
- around 2 million if preventive therapy was limited to young child contacts.

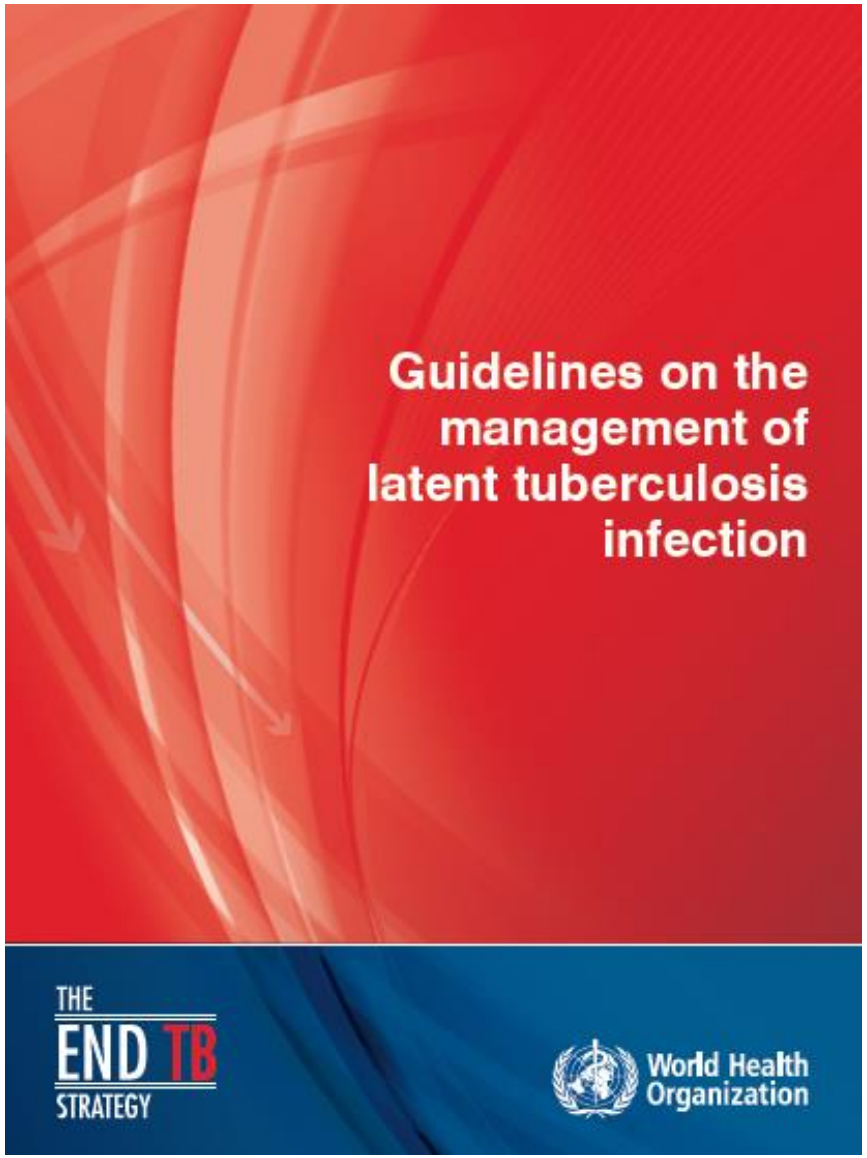
Yuen CM, Jenkins HE, Chang R, Mpunga J, Becerra MC. *Public Health Action* 6(2), 83-96 (2016).

Detection of LTBI

- Current major shortages of tuberculin solution
- A novel skin test C-Tb developed at Statens Serum Institut, Copenhagen uses specific *M.tuberculosis* antigens (ESAT-6 and CFP-10) with cut-point of 5 mm induration established
- C-Tb is more specific that TST as not affected by prior BCG
- When evaluated in patients with active TB, sensitivity lower than for TST and reduced in PLHIV with marked immunosuppression as measured by CD4 count (as for TST)
- Compared to IGRA, C-Tb does not require a laboratory and is likely to be low-cost

Aggerbeck H, Giemza R, Joshi P *et al. PLoS One* 8, e64215 (2013).

Hoff ST, Peter JG, Theron G *et al. Eur. Resp. J.* 47, 919-928 (2016).



Treatment options recommended for LTBI include:

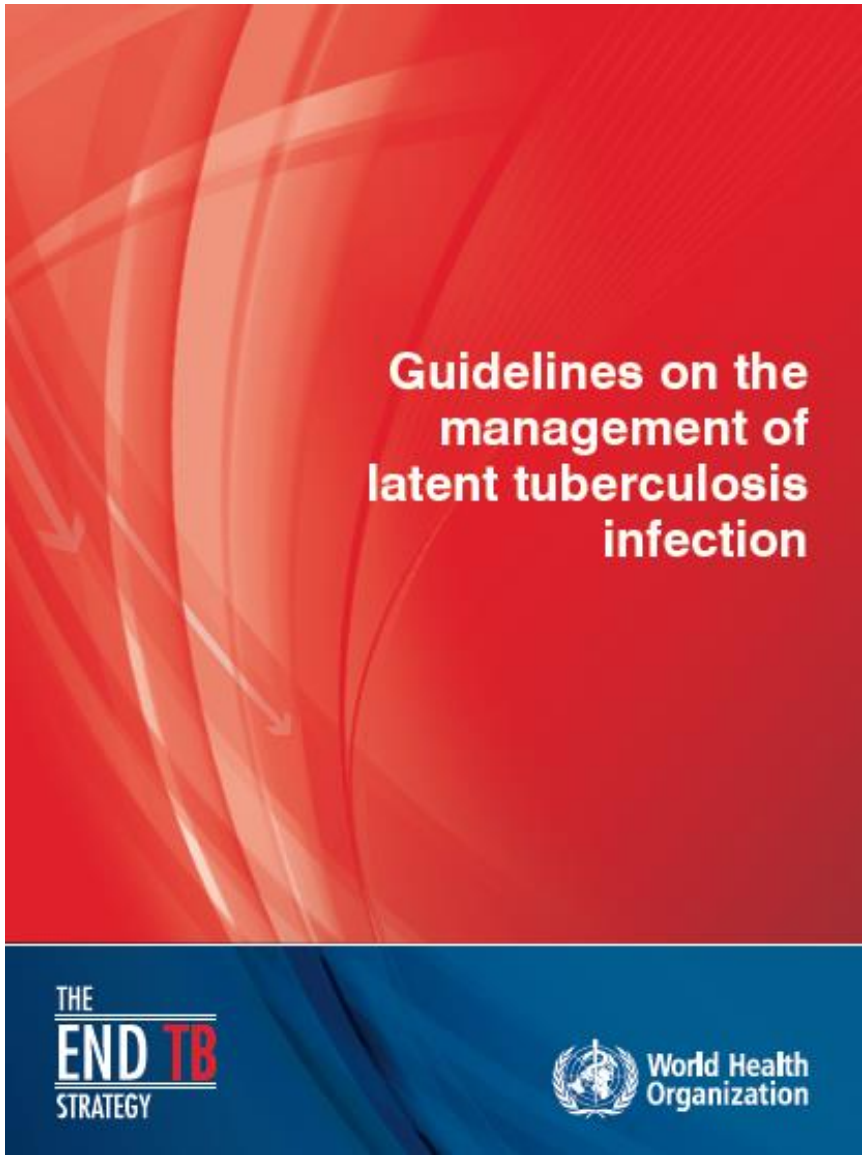
6H, or

9H, or

3HP weekly rifapentine plus isoniazid, or

3RH

(Strong recommendation, moderate to high quality of evidence).



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OPEN ACCESS Freely available online

PLoS MEDICINE

Policy Forum

Closing the Policy-Practice Gap in the Management of Child Contacts of Tuberculosis Cases in Developing Countries

Philip C. Hill[1]*, Merrin E. Rutherford[1], Rick Audas[2], Reinout van Crevel[3], Stephen M. Graham[4,5]

1 Centre for International Health, Department of Preventive and Social Medicine, University of Otago School of Medicine, Dunedin, New Zealand, **2** Department of Preventive and Social Medicine, University of Otago School of Medicine, Dunedin, New Zealand, **3** Department of Medicine, Radboud University Njimegen Medical Centre, Njimegen, The Netherlands, **4** Centre for International Child Health, Department of Paediatrics, University of Melbourne, Melbourne, Australia, **5** International Union Against Tuberculosis and Lung Disease, Paris, France

Tropical Medicine and International Health doi:10.1111/j.1365-3156.2012.03053.x

VOLUME 17 NO 10 PP 1264–1273 OCTOBER 2012

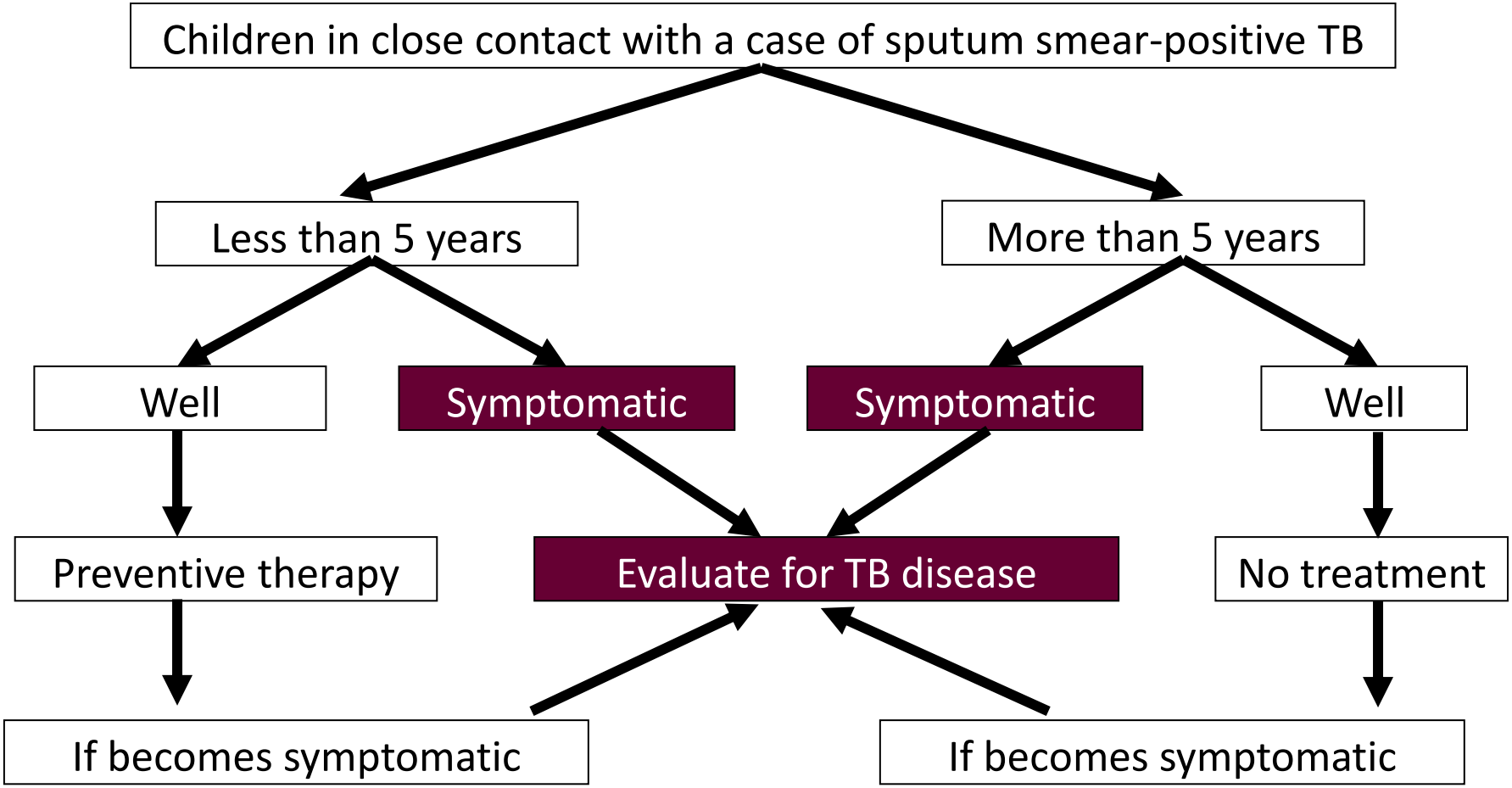
Review

Preventive therapy in children exposed to *Mycobacterium tuberculosis*: problems and solutions

Merrin E. Rutherford[1], Philip C. Hill[1], Rina Triasih[2], Rebecca Sinfield[3], Reinout van Crevel[4] and Stephen M. Graham[5]

1 *Centre for International Health, Department of Preventive and Social Medicine, University of Otago, Dunedin, New Zealand*
2 *Department of Pediatrics, Faculty of Medicine, Gadjah Mada University, Yogyakarta, Indonesia*
3 *Mersey Deanery, Liverpool, UK*
4 *Department of Medicine, Radboud University Medical Centre, Nijmegen, The Netherlands*
5 *Centre for International Child Health, University of Melbourne, Department of Paediatrics and Murdoch Children's Research Institute, Royal Children's Hospital, Melbourne, Vic., Australia*

WHO symptom based screening



Need for M & E tools for contact management

- Numbers screened
- Numbers (%) diagnosed with TB
- Numbers (%) eligible for preventive therapy
- Numbers (%) received preventive therapy
- Numbers (%) completed preventive therapy

Sample Contact Screening Register

No.	Date of contact screen	Name of index case	Name of contact	Age	Sex		Symptom screen 1.Well 2.Symptomatic		HIV status 1.Positive 2.Negative 3.Unknown			Management 1.IPT 2.TB treatment 3.Nil 4.Did not seek care				Date and sign when complete
					M	F	1	2	1	2	3	1	2	3	4	

Sample IPT register

Isoniazid Preventive Treatment Register

PHC centre/Hospital TB control Unit: Year:

No.	Name	Age	Sex (M/F)	HIV-infected (Y/N/U)	IPT started (date)	Monthly follow-up Insert weight and tick if collected IPT						Outcome 1.Complete IPT 2.Did not complete 3.Treated for TB
						1	2	3	4	5	6	

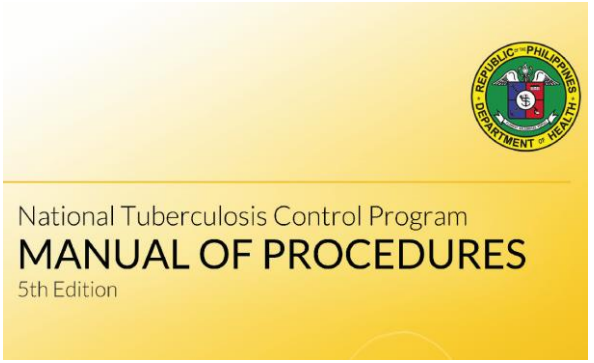
Introduction of the new FDCs in 2016

- Rifampicin 75 mg + Isoniazid 50 mg + Pyrazinamide 150 mg (two-month intensive phase)
- Rifampicin 75 mg + Isoniazid 50 mg (four-month continuation phase)

- Product attributes: Correct, WHO-recommended doses, Dispersible in liquid, Palatable fruit flavors
- The average treatment costs is $15.54 through the Global Drug Facility (GDF)
- First introduced in Kenya and PNG
- UNITAID funding to scale-up

Table No. 14 - Drug Administration According to Kg Body Weight for Children

Body Weight (Kgs.)	Isoniazid (200mg/5ml)	Rifampicin (200mg/5ml)	Pyrazinamide (250mg/5ml)	Ethambutol (400mg/tab)	Streptomycin* (1g/2ml)
	10mg/kg	15mg/kg	30mg/kg	20mg/kg	30mg/kg
	ml	ml	ml	Tablet	ml
2.1-3	0.75	1.00	1.75	1/8*	0.18
3.1-4	1.00	1.50	2.50	1/4*	0.24
4.1-5	1.25	2.00	3.00		0.3
5.1-6	1.50	2.25	3.50		0.36
6.1-7	1.75	2.50	4.25		0.42
7.1-8	2.00	3.00	4.75	1/2	0.48
8.1-9	2.25	3.50	5.50		0.54
9.1-10	2.50	3.75	6.00		0.6
10.1-11	2.75	4.00	6.50		0.66
11.1-12	3.00	4.50	7.25		0.72
12.1-13	3.25	5.00	7.75	3/4	0.78
13.1-14	3.50	5.25	8.50		0.84
14.1-15	3.75	5.50	9.00		0.9
15.1-16	4.00	6.00	9.50		0.96
16.1-17	4.25	6.50	10.25		1.02
17.1-18	4.50	6.75	10.75		1.08
18.1-19	4.75	7.00	11.50	1	1.14
19.1-20	5.00	7.50	12.00		1.20
20.1-21	5.25	8.00	12.50		1.26
21.1-22	5.50	8.25	13.25		1.32
22.1-23	5.75	8.50	13.75		1.38
23.1-24	6.00	9.00	14.50		1.44
24.1-25	6.25	9.50	15.00	1+1/4	1.5
25.1-26	6.50	9.75	15.50		1.56
26.1-27	6.75	10.00	16.00		1.62
27.1-28	7.00	10.50	16.75		1.68
28.1-29	7.25	11.00	17.50	1+1/2	1.74
29.1-30	7.50	11.25	18.00		1.8



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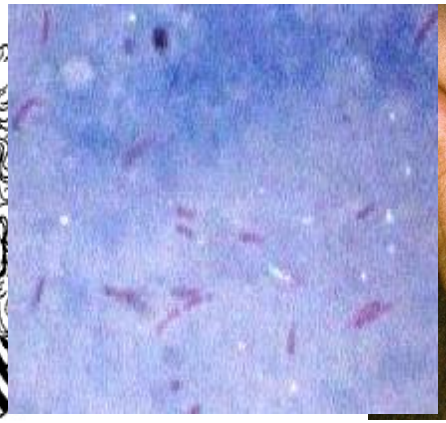
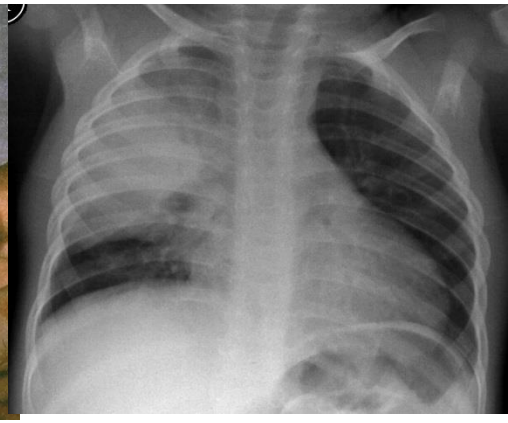
3.1-4	1.00	1.50	2.50		0.24

	Numbers of tablets		
	Intensive Phase		Continuation Phase
	RHZ	E	RH
Weight bands	**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 For example: 2 RHZE 150/75/400/275		

24.1-25	6.25	9.50	15.00		1.5
25.1-26	6.50	9.75	15.50	1+1/4	1.56
26.1-27	6.75	10.00	16.00		1.62
27.1-28	7.00	10.50	16.75		1.68
28.1-29	7.25	11.00	17.50	1+1/2	1.74
29.1-30	7.50	11.25	18.00		1.8

Rapid development of diagnostics





History

High negative predictive value but poor specificity

Bacteriology

1882

Very low sensitivity

Tuberculin Skin Test

1890

Indicates infection with limitations of sensitivity and specificity

Chest X-ray

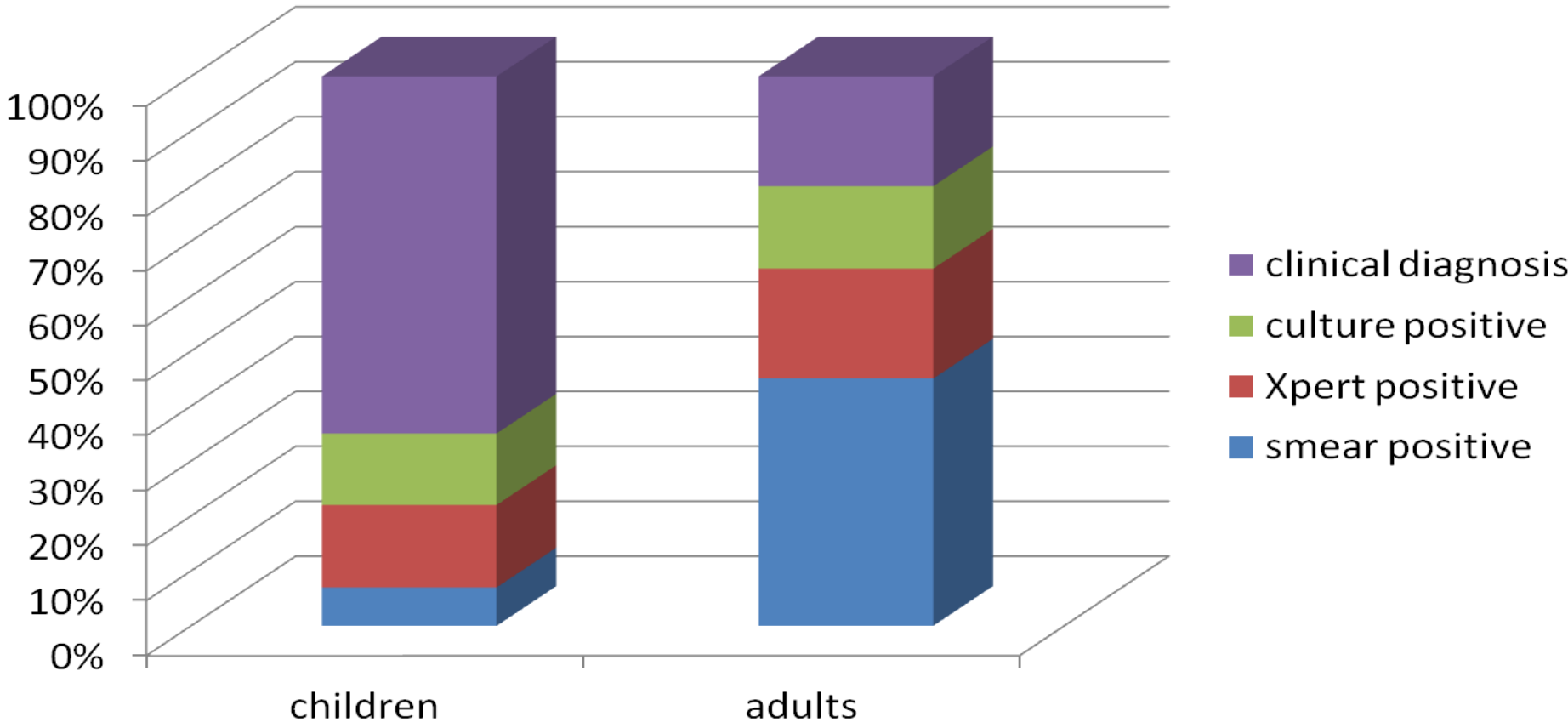
1896

Low specificity

Clinical challenges are the diagnostic challenges

- Young age
- Acute severe pneumonia
- HIV-infected
- Malnourished
- MDR TB

Diagnostic yield from Xpert for pulmonary TB comparing children to adults



Xpert cannot be used to rule out TB

Xpert needs research on implementation to inform optimal usage in children

Experience of Xpert yield for presumptive TB in children in programmatic conditions

- Diagnostic yield twice as high as smear microscopy in Indian children with presumptive TB
- 12970 presumptive with 1,107 (8.5%) TB diagnosed
- Of these, 143 (13%) with Rif resistance

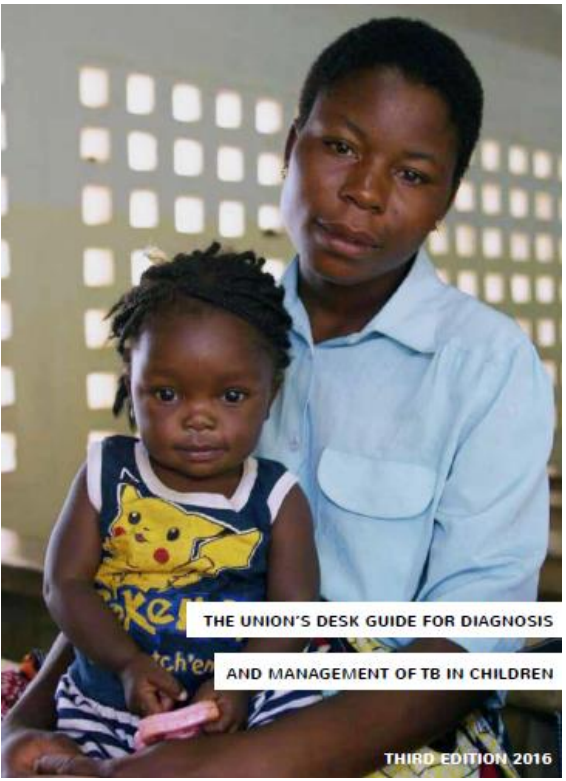
Combined data: Raizada N, et al. PLoS ONE 2014 and 2016

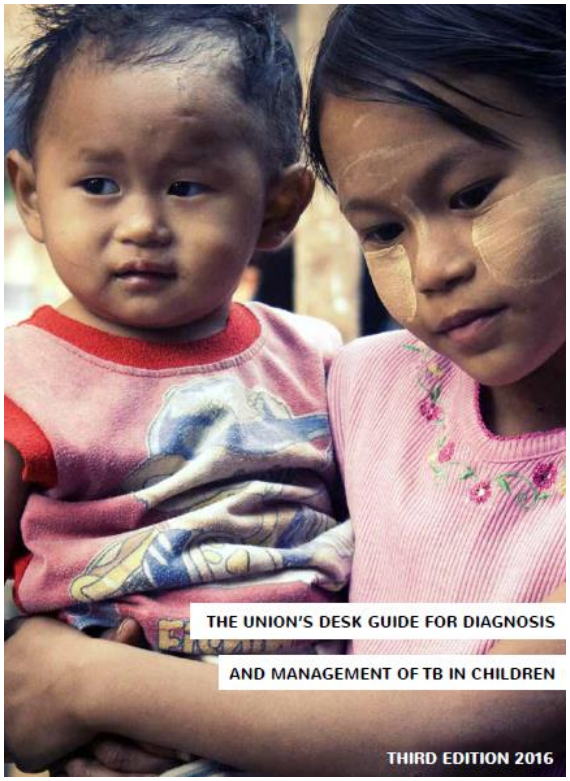
- Similar yield from induced sputum (5%), gastric lavage (6%) and CSF (7%) – higher yield (36%) from FNA

Raizada N, et al. PLoS ONE 2016

- Lower sensitivity (42%) from Xpert in outpatients versus inpatients and from presumptive cases from contact screening Togun T, et al. IJTLD 2015; Detjen AK, et al Lancet Resp Med 2015

Job aides


THE UNION'S DESK GUIDE FOR DIAGNOSIS
AND MANAGEMENT OF TB IN CHILDREN
THIRD EDITION 2016


THE UNION'S DESK GUIDE FOR DIAGNOSIS
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THIRD EDITION 2016


Management of Multidrug-Resistant Tuberculosis in Children: A Field Guide
Photo: Justin Jay
Sentinel Project
Second Edition: March, 2015

Resources


Desk-guide for diagnosis and management of TB in children
WHO treatme
guidelines for
resistant tub
2016 update
THE END TB STRATEGY
World Health Organization
The Union
International Union Against Tuberculosis and Lung Disease
Health solutions for the poor
COURSES
RESOURCES
COMMUNITY
HELP
>>HOME >COURSES
Register/Sign In
Childhood TB Portal
TOWARDS ZERO
CHILDHO
TRAININ
TOOLKIT
World Health Organization
Sentinel Project
on pediatric drug resistant tuberculosis
Join in here:
Your email address
Country
SUBSCRIBE
HOME
ABOUT
RESOURCES
UPDATES
STORIES
About the Sentinel Project on Pediatric Drug-Resistant Tuberculosis
Pediatric drug-resistant tuberculosis is both a preventable and curable disease. Every child who dies with drug-resistant tuberculosis is a sentinel for both ongoing transmission and inadequate treatment delivery systems.
The Sentinel Project on Pediatric Drug-Resistant Tuberculosis is a global partnership of researchers, caregivers, and advocates who share a vision of a world where no child dies from this curable and preventable disease. We are collaborating to raise the visibility of this vulnerable population of children, and to share evidence and resources that can increase children's access to prompt and effective treatment.
Site Map
Mailing Address: 641 Huntington Ave, Boston MA 02115 USA
Contact us: sentinel_project@hms.harvard.edu

Update

- Membership increased by around 30% to 284 members
- New members of core group in 2016
  - Mandy Slutsker, WHO Civil Society Task Force
  - High burden country/regional representation: WPRO – Telly How stepped down and replaced by Dr Sally Gatchalian (Philippines Pediatric Infectious Disease Society)

- Core group conference calls in 2016: February 23, July 19
- Core group F2F meeting: Oct 27

- New chair elected for 2017

Technical assistance and training

- Sri Lanka
- Nepal
- Viet Nam
- The Philippines
- Kenya
- Indonesia
- Myanmar
- PNG

TB meetings and conferences

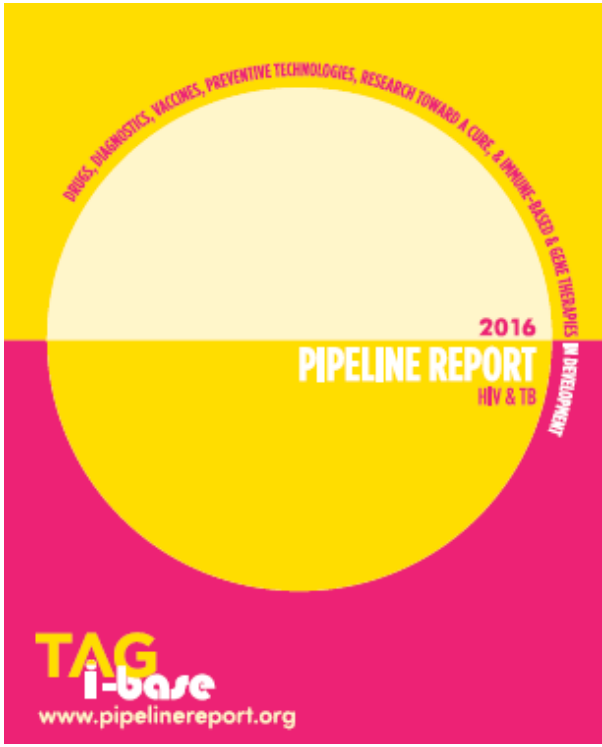
- Annual WHO STAG TB meeting, Geneva
- NTP managers meeting, Geneva
- Pan African Thoracic Society meeting, Nairobi
- Annual PhilCAT Convention, Manila
- The Union European, Bratislava
- PNG Paediatric Society, Port Moresby
- Western Pacific Regional NTP manager's meeting, Manila
- IMCI meeting, Geneva
- Unicef meeting in collaboration with WHO and TB Alliance, New York.
- A 3-day interactive seminar on 'Where is TB in Maternal and Child Health' held on the MSH LeaderNet platform
- American Society of Tropical Medicine and Hygiene annual meeting, Atlanta
- Union World conference on Lung Health, Liverpool

Contribution to TB guidelines

- NTP guidelines updated
- WHO consolidated guidelines on LTBI management
- WHO MDR TB guidelines
- WHO new drugs in children
- WHO Chest radiography in TB detection
- NIH SOPs for diagnostics

Research

- New (and old) diagnostics including biomarkers
- New (and old) preventive therapy – DS and DR
- Shorter treatment regimens
- Shorter LTBI management regimens
- Second line and new drugs – PK and safety
- Implementation research



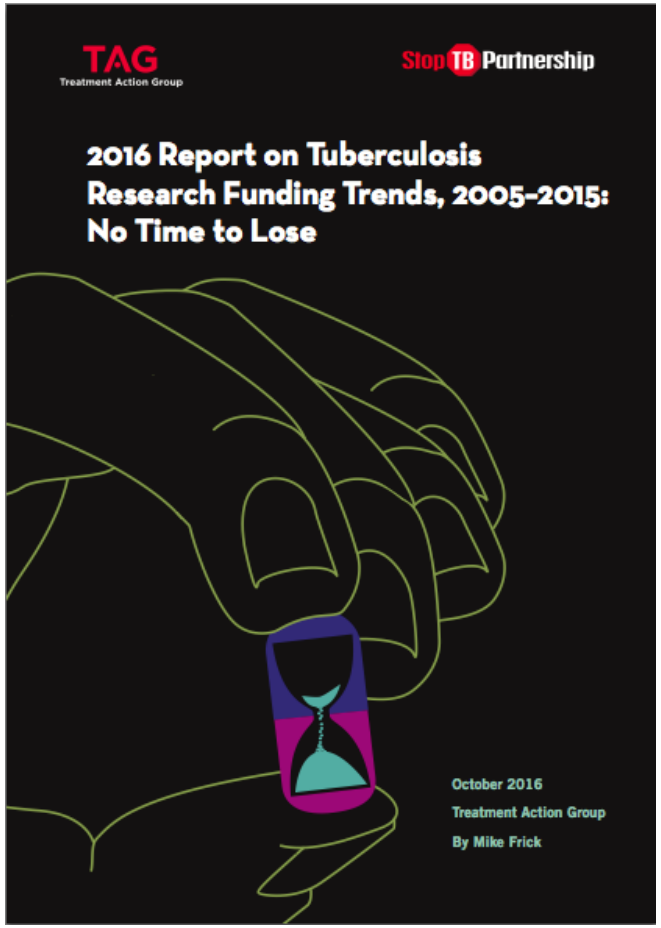
The full report is available here: http://www.pipelinereport.org

2016 TB R&D Resource Tracking Report

TAG started tracking *pediatric* TB R&D spending in 2010

The *Global Plan to End TB* includes some pediatric TB R&D funding targets: currently at about 50% of $200M targeted for 2011-2015 in Childhood TB Roadmap

2011-2015 pediatric TB R&D investments make up about 3% of total TB R&D spending and most is on drug development (60%)



2016 TB R&D Resource Tracking Report Findings

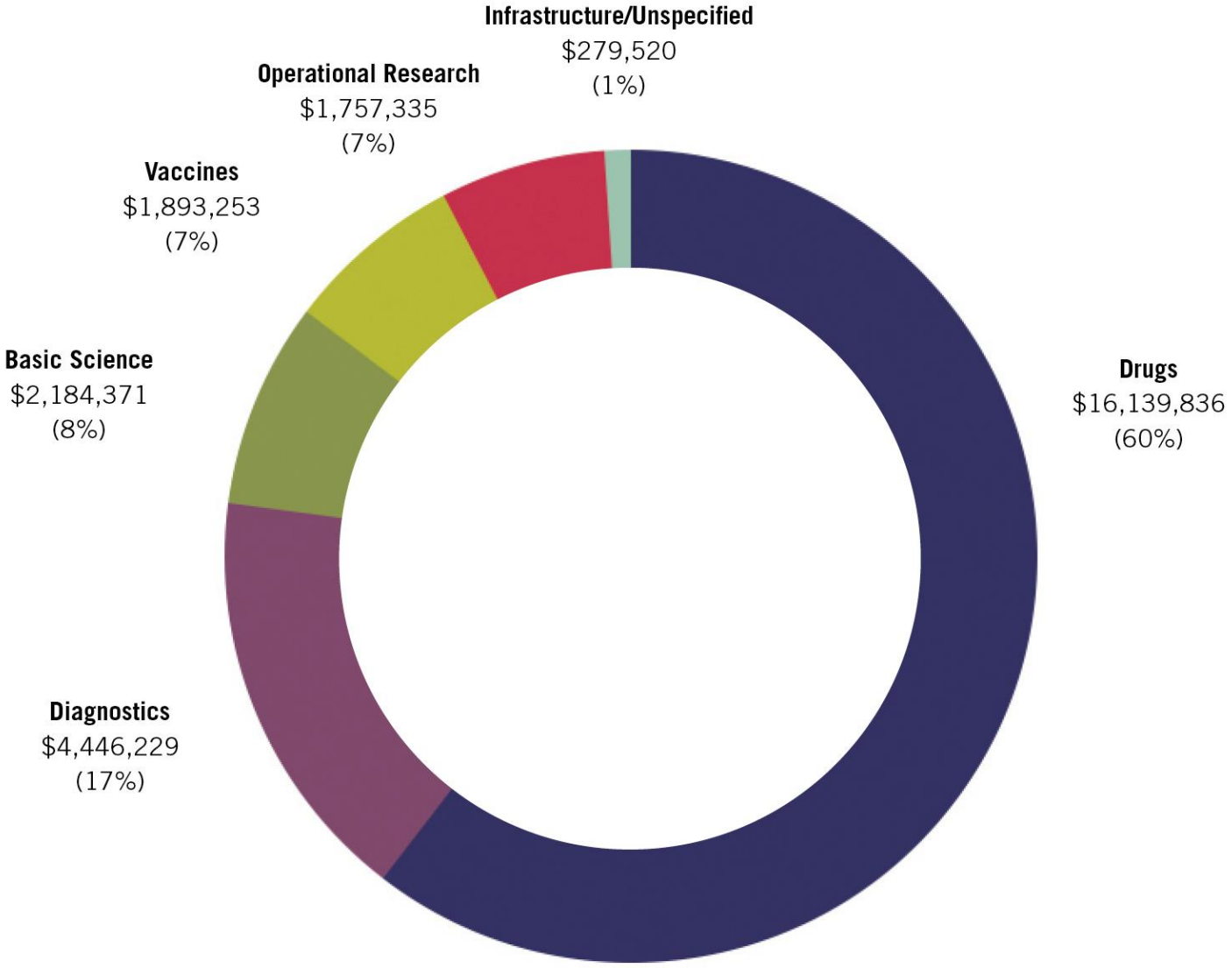
In 2015, $26.7M invested in pediatric TB R&D

- 60% drugs
- 17% diagnostics
- 8% basic science
- 7% vaccines
- 7% operational research

TB R&D Resource Tracking Report available:
http://www.treatmentactiongroup.org/tbrd2016

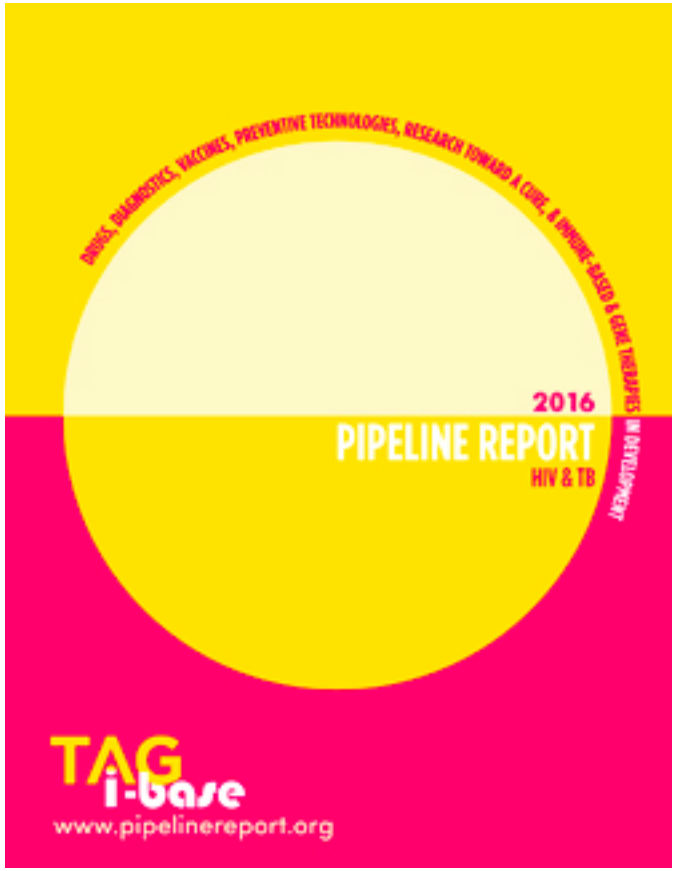
Pediatric TB R&D Funding by Research Category, 2015

Total: $26,700,543



2016 Pipeline Report

- Tracks pipeline for pediatric TB treatment studies and formulation development
- And now also includes special section tracking pediatric TB diagnostics research
- Includes recommendations for researchers, regulators, policy makers, and donors to help fill critical knowledge gaps, expedite development, and facilitate access



Pipeline Report available from: http://www.pipelinereport.org.

Acknowledgements

- WHO Global TB Programme
  - Malgosia Grzemska
  - Annemieke Brands
- Core members of Child TB sub-group
- NTP managers and Regional WHO TB programmes
- TB Alliance
- USAID