

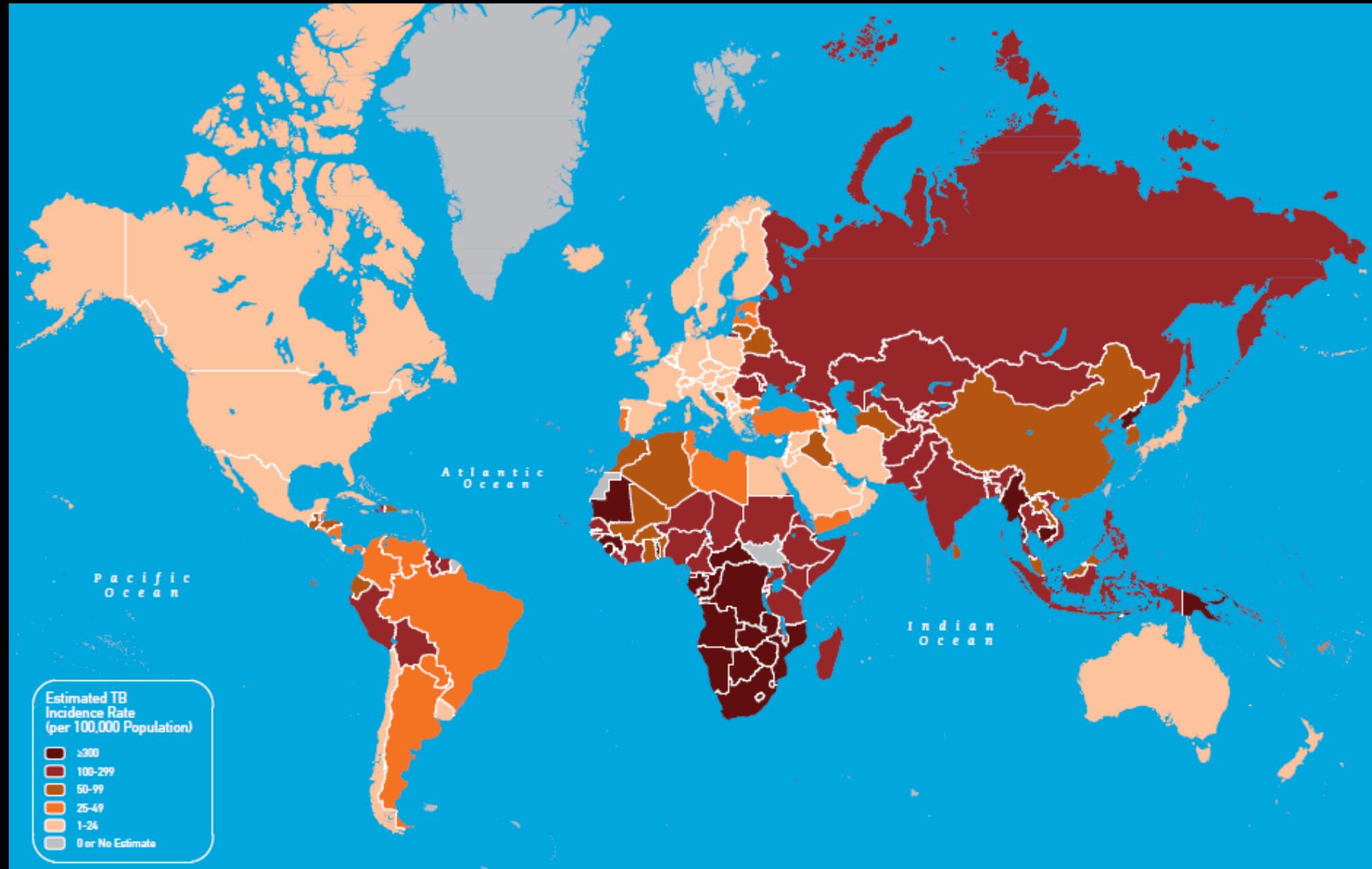
Childhood TB: emerging from the shadows

Tania Thomas, MD, MPH

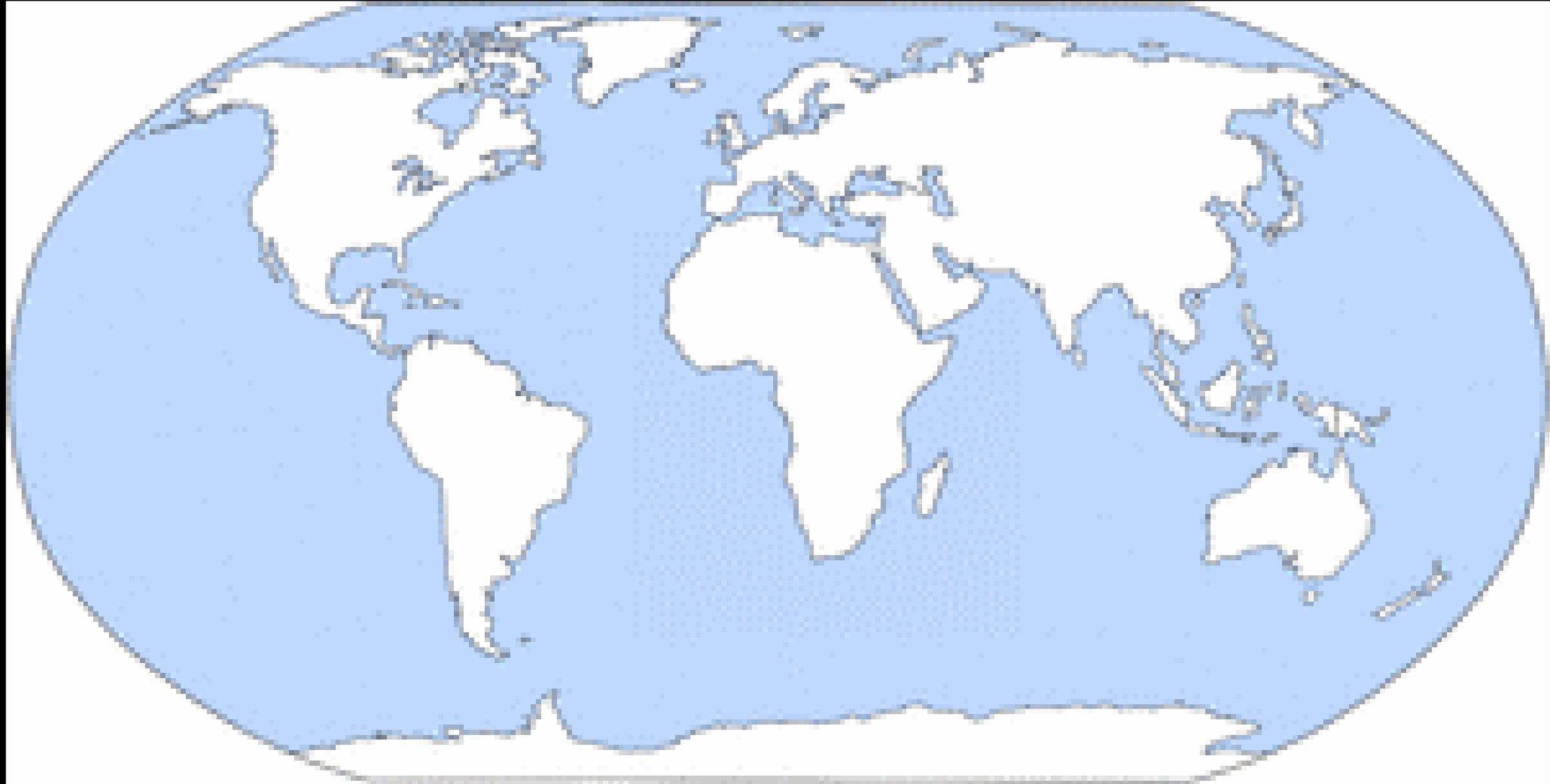
Infectious Diseases & International Health,

University of Virginia

Estimated global incidence of TB, 2010



Estimates of childhood TB?



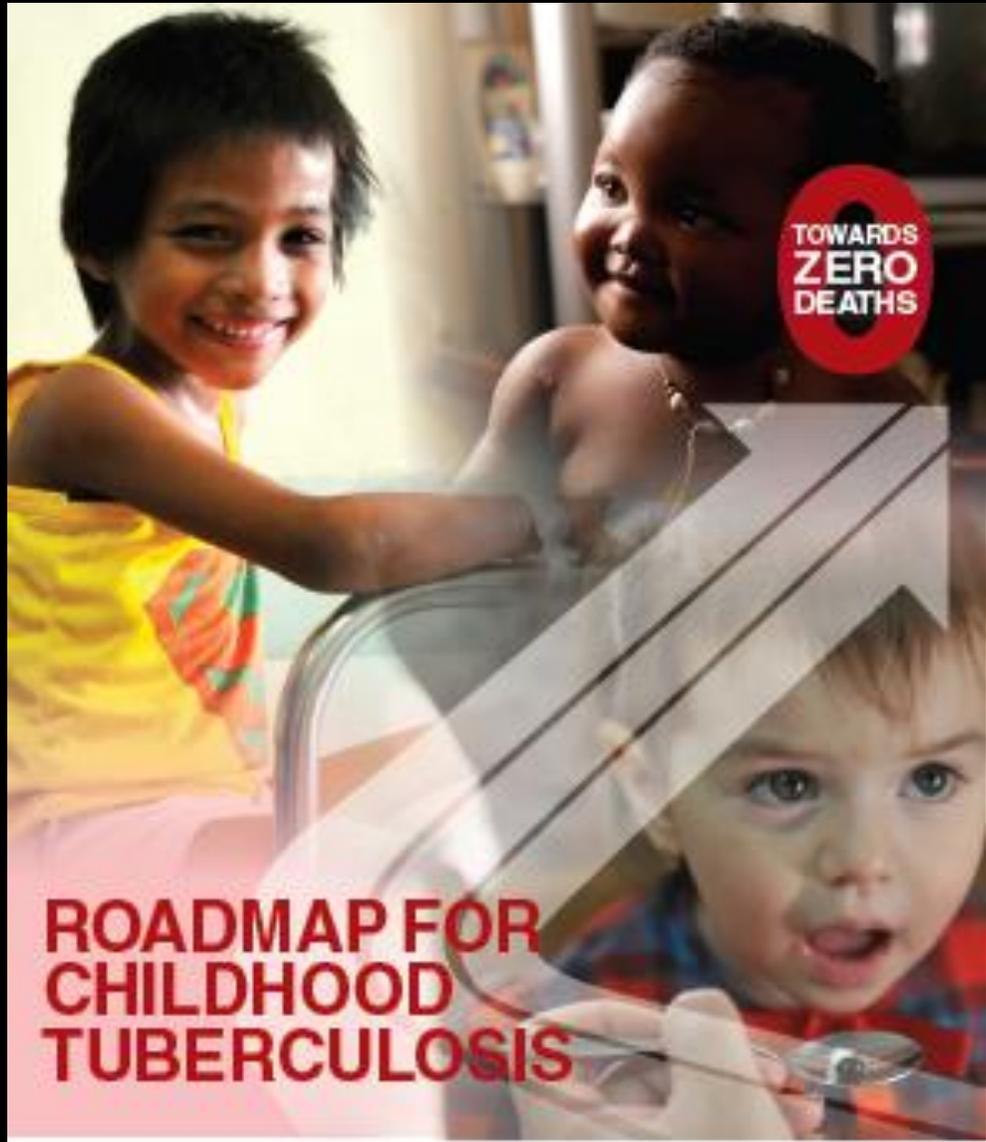
Childhood TB: a neglected epidemic

- Scope is not fully known
 - >500,000 cases annually worldwide.
 - 74,000 deaths*
 - In the US: 0.8 cases/100,000 population (2012)
- Challenges in confirming the diagnosis
 - Inability to produce sputum easily
 - Low bacillary burden
 - Microbiologic means of diagnosis don't work as well in children
 - ~2% are AFB-smear positive
 - Overall, ~30-40% confirmed by microbiologic methods
- Less important from a public health standpoint
- Reliance upon the BCG vaccine

* Excluding HIV/TB deaths

TIPPING
POINT





TOWARDS
ZERO
DEATHS

ROADMAP FOR CHILDHOOD TUBERCULOSIS

 World Health Organization
  CDC
  unicef
  International Union Against Tuberculosis and Lung Disease

 TAG Treatment Action Group
  Stop TB Partnership
  USAID



TIMELINE: KEY ACTIONS TO ADDRESS CHILDHOOD TB

Short term by 2015

Increased action in countries to prioritize childhood TB and implement activities such as contact investigation and IPT to detect and manage TB in children, in line with international standards

High profile of childhood TB at the global and national levels

Capacity building of health workers scaled up at all levels to detect and manage children with TB

Antenatal screening for TB, in tandem with HIV – detect, treat or prevent TB in mothers

Advocacy for research on new diagnostics, drugs and vaccines for childhood TB

Improved recording and reporting of data on childhood TB

Medium term by 2020

Improved prevention, detection, diagnosis and management of TB in children

Integrated approaches implemented across the health system to address TB in children and pregnant women

Inclusion of children in trials of new diagnostics and drugs

Development of new diagnostics suitable for children

Long term by 2025

Test for latent TB with ability to predict disease progression in children

Point of care test with good accuracy for childhood TB

Shorter, child-friendly regimens for both infection and disease

Vaccines to prevent infection and disease in children and adults



Additional tools?

Diagnosis

Relationship Between Tuberculin Skin Test (TST) Size and Interferon Gamma Release Assay (IGRA) Result: When Should Clinicians Obtain IGRAs in Children With Positive TSTs?

Andrea T. Cruz, MD, MPH¹ and Jeffrey R. Starke, MD¹

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Prevention

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Twice-weekly therapy for children with tuberculosis infection or exposure

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- 1383 children <18 years of age treated biweekly for exposure or LTBI
- Safe: 3% experienced side effects
- Effective: 98% efficacy
- Good completion rates: 99% of exposed, 96% of infected children

Rifapentine Pharmacokinetics and Tolerability in Children and Adults Treated Once Weekly With Rifapentine and Isoniazid for Latent Tuberculosis Infection

Marc Weiner,^{1,2,a} Radojka M. Savic,^{3,a} William R. Mac Kenzie,⁴ Diane Wing,¹ Charles A. Peloquin,⁵ Melissa Engle,¹ Erin Bliven,⁴ Thomas J. Prihoda,⁶ Jonathan A. L. Gelfond,⁷ Nigel A. Scott,⁴ Susan M. Abdel-Rahman,⁸ Gregory L. Kearns,⁸ William J. Burman,⁹ Timothy R. Sterling,¹⁰ and M. Elsa Villarino⁴; for the Tuberculosis Trials Consortium PREVENT TB Pharmacokinetic Group

- 80 children (ages 2-11 years)
- Dose for children 2-fold higher compared to adults
- Achieved 1.3-fold higher drug-level concentration
- Well tolerated
- Associated with successful treatment outcomes

Table 1. Rifapentine Dosing for Children With Latent Tuberculosis Infection in the Present Study^a

Weight (kg)	Rifapentine Dose (mg)	Rifapentine Dose (mg/kg)	Age of Study Patients, y (mean ± standard deviation)
10–14	300	21–30	2.6 ± 0.8
>14–25	450	18–32	4.5 ± 1.6
>25–32	600	19–24	7.4 ± 2.2
>32–50	750	15–23	9.7 ± 2.4
>50	900	≤18	38.8 ± 12.9

^aN = 80 children. Same dosing guideline was used for children in the PREVENT TB trial.

Management of Drug resistant TB

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

Caring for Children with Drug-Resistant Tuberculosis Practice-based Recommendations

James A. Seddon^{1,2}, Jennifer J. Furin³, Marianne Gale⁴, Hernan Del Castillo Barrientos^{5,6}, Rocío M. Hurtado^{7,8,9}, Farhana Amanullah¹⁰, Nathan Ford¹¹, Jeffrey R. Starke¹², and H. Simon Schaaf^{1,13}; on behalf of the Sentinel Project on Pediatric Drug-Resistant Tuberculosis



MDR-TB Weight-Based Dosing Chart for Children

Target Dose	Group 1: Oral first-line anti-TB drugs		Group 2:	Group 3: Fluoroquinolones			Group 4: Oral bacteriostatis agents		Group 5:		Target Dose	
	Ethambutol (15-25 mg/kg)	Pyrazinamide (30-40 mg/kg)	Injectable anti-TB drugs (Injectable)	Levofloxacin (15-20 mg/kg)	Moxifloxacin (7.5-10 mg/kg)	Ofloxacin (15-20 mg/kg)	Cycloserine/ Terizidone (15-20 mg/kg)	PAS (150-200 mg/kg)	Protonamide Ethionamide (15-20 mg/kg)	Anti-TB drugs with unclear efficacy of	Isoniazid High Dose (15-20 mg/kg)	



What's on the horizon?



Vaccine Development

CANDIDATE	STAGE OF DEVELOPMENT
Crucell Ad35/MVA85A	Phase 1
M72 + AS01E	Phase 2b
H4/AERAS-404 + IC31	Phase 2 (adolescents)
ID93 + GLA-SE	Phase 1
MVA85A/AERAS-485	Phase 2b (infants): safe, not effective
H56/AERAS-456 + IC31	Phase 2
Crucell Ad35/AERAS-402	Phase 1 (infants)
DAR-901	Phase 1

The logo for AERAS, featuring a stylized blue triangle icon to the left of the word "AERAS" in a serif font.

Additional treatment options





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