Paediatric TB: disease burden estimation and the opportunities it creates to strengthening surveillance

Workshop 04

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GLOBAL TB
PROGRAMME

World Health Organization

Overview

- The WHO Global Task Force on TB Impact Measurement
  - Who are we?
  - What is our mandate and area of work?
- Background to estimates of disease burden for paediatric TB
- Epidemiological estimates of disease burden for paediatric TB: current rationale, strengths, limitations, next steps
  - Incidence
  - Mortality
  - Prevalence
- Opportunities to strengthening surveillance

WHO Global Task Force on TB Impact Measurement

www.who.int/tb/advisory_bodies/impact_measurement_taskforce

National TB Programmes of many countries
& key technical and funding agencies

International Union Against Tuberculosis and Lung Disease

Bill & Melinda Gates foundation

CDC Centers for Disease Control and Prevention

ecdc European Centre for Disease Prevention and Control

London School of Hygiene & Tropical Medicine

KNCV Tuberculosis Foundation To eliminate TB

The Global Fund To Fight AIDS, Tuberculosis and Malaria

Harvard

USAID From the American People

Task Force mandate (2006–2015)

- **To produce robust, rigorous, widely-endorsed assessment of whether 2015 targets are achieved at global level, regional and country levels**

- **To regularly report on progress towards impact targets in years leading up to 2015**

- **To strengthen national capacity in monitoring and evaluation of TB control**

2015 targets for global TB control

UN Millennium Development Goals

- Halt and reverse incidence (MDG 6, Target 6.c)

Stop TB Partnership

- Halve prevalence and mortality rates compared with baseline of 1990

3 strategic areas of work

(defined December 2007, 2nd Task Force meeting)

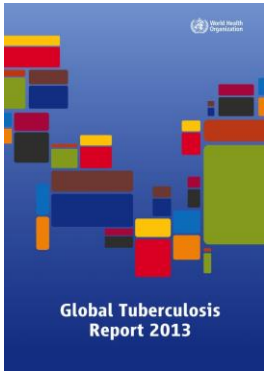
1. **National TB prevalence surveys in 22 (+) global focus countries**

2. **Strengthening surveillance of TB cases and deaths in all countries**

3. **Periodic review and revision of methods used to translate surveillance and survey data into estimates of disease burden**

What do we offer to countries?

Regional and country workshops
moving away from expert knowledge
promoting direct measurement



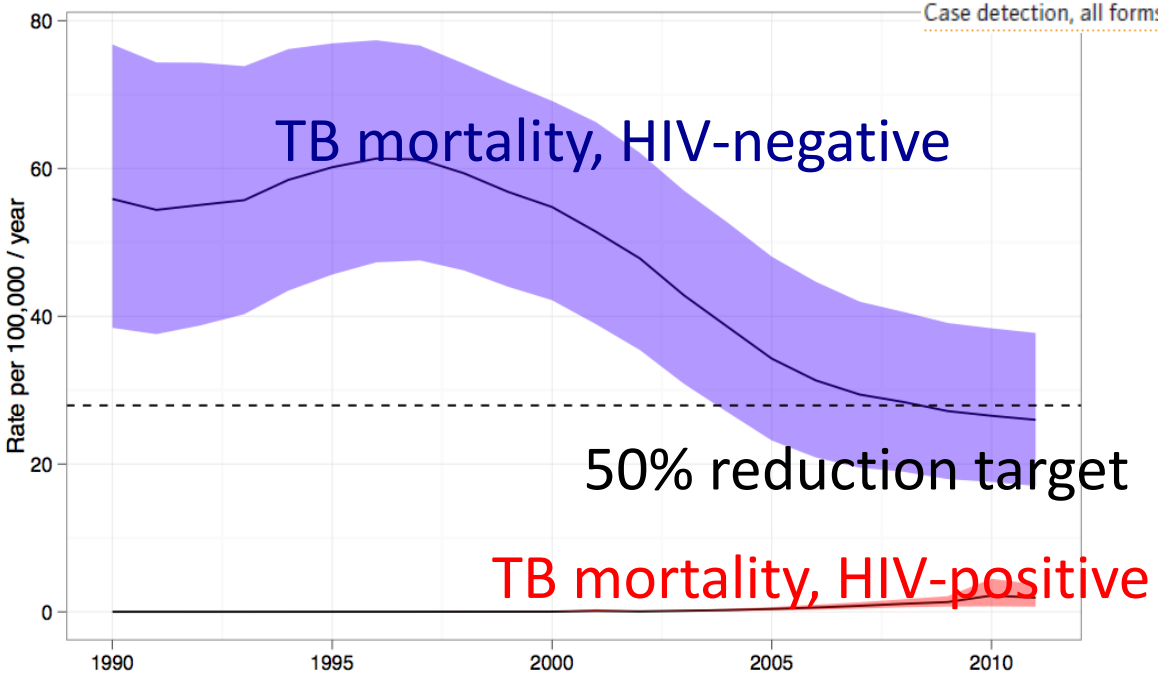
INDONESIA

HIGH TB BURDEN | HIGH HIV BURDEN | HIGH MDR-TB BURDEN

Estimates of TB burden[a] 2011

	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	65 (29–120)	27 (12–48)
Prevalence (includes HIV+TB)	680 (310–1 200)	281 (130–489)
Incidence (includes HIV+TB)	450 (370–540)	187 (155–222)
Incidence (HIV+TB)	15 (11–20)	6.2 (4.4–8.3)
Case detection, all forms (%)	70 (59–85)	

Quantify the burden of TB



Monitor effectiveness of control programs by quantifying trends

Why are paediatric disease burden estimates important?

- How big of a problem paediatric TB really is?
- Are interventions aiming to have an impact on disease burden working?
- Competing health priorities; appropriate investment and funding allocation
- Addressing neglect of paediatric TB
- Evidence-based advocacy

Background to paediatric disease burden estimates

- What makes the estimates problematic?
  - Lack of gold-standard, point-of-care, diagnostic tool
  - Scarcity of robust, nationwide data
  - Neglect of recording and reporting of "non-infectious" TB cases among children

- What will improve estimates?
  - Global momentum for childhood TB

- WHO-led effort in collaboration with the Childhood TB Subgroup (*since March 2011*)
  - First set of estimates in 2012, updated in 2013
  - Collaboration with TB Alliance, STEP TB (since January 2013)

WHO TB data collection system

- TB case notifications collected online on an annual basis

TABLE 1.1

Reporting of data in the 2013 round of global TB data collection

WHO REGION OR SET OF COUNTRIES	COUNTRIES AND TERRITORIES	
	NUMBER	NUMBER THAT REPORTED DATA
African Region	46	45
Eastern Mediterranean Region	23	23
European Region[a]	54	42
Region of the Americas	46	46
South-East Asia Region	11	11
Western Pacific Region	36	30
High-burden countries (HBCs)[b]	22	22
World	**216**	**197**

[a] Countries that did not report by the deadlines were mostly low-incidence countries in Western Europe.

- Disaggregated by
  - new/retreated status;
  - TB case type: SP, SN, EP;
  - age & sex.

2.16 New pulmonary smear-negative/smear-unknown/smear-not done TB cases by age and sex, 2009 calendar year (number of patients)

Time-changes in the distribution of cases by age and sex are analyzed by WHO to understand trends in disease burden and gaps in the performance of TB surveillance

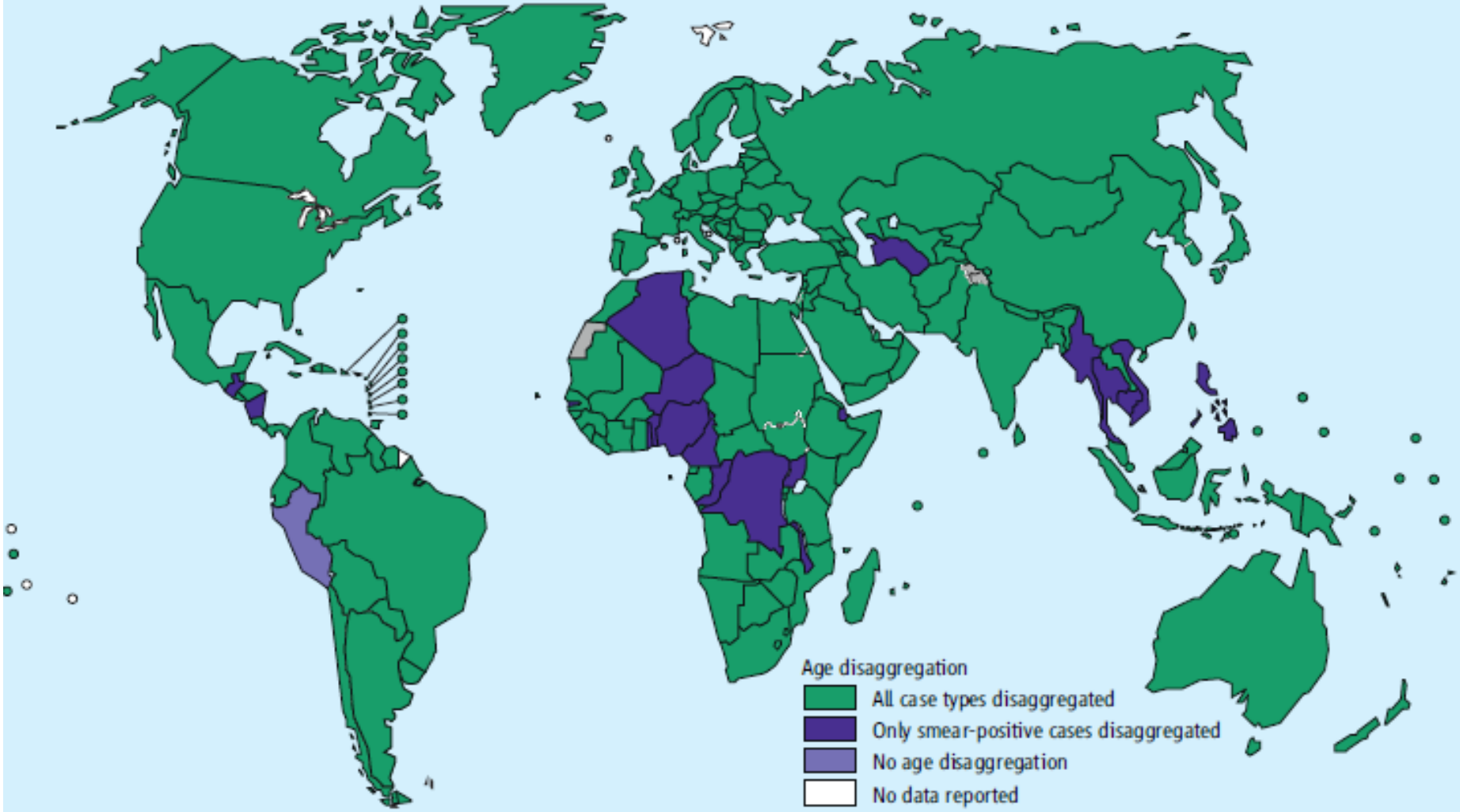
If you have data by age and sex that do not fit this framework (e.g., different age groups), please provide the data that you do have in the "Remarks" section.

	0-4	5-14	0-14	15-24	25-34	35-44	45-54	55-64	65+	Unknown
Male										
Female										

Incidence *data source* (2012)

FIGURE B2.2.3

Reporting of notification data disaggregated by age, 2012



Incidence *estimation* (2012)

TABLE B2.2.3

New TB case notifications in 2012, by case type and age disaggregation

	SMEAR-POSITIVE	SMEAR-NEGATIVE[a]	EXTRA-PULMONARY
Total notifications	2 568 789	1 935 971	817 462
Countries disaggregating by age	2 551 136	1 597 530	678 953
Countries not disaggregating by age	17 653	338 441	138 509
(% total notifications disaggregated)	(99%)	(83%)	(83%)
Number of countries that reported notifications disaggregated by age (number of HBCs)[b]	204 (22)	184 (14)	184 (14)
Total childhood notifications from countries disaggregating by age	46 488	163 477	91 308
Total estimated childhood notifications among all countries	349 000		

[a] This includes reported cases for whom smear results were unknown or not done.
[b] An additional nine countries reported zero TB cases for 2012 and three countries had not reported data to WHO by July 2013.

Estimated notifications:

349 000

Global Case Detection Rate:

66% (64%-69%)

Estimated incidence:

530 000 (510 000 – 550 000)

6% of total 8.6 million incident cases are children

Incidence
strengths, limitations

Strengths

- Making use of a global, annually available data source: TB notifications

Limitations

- Assumed gap between notifications and real incidence is the same for children as for adults
- No adjustment made for misdiagnosis. Each notified case is assumed to be true case of TB
- Assume 0 paediatric cases among case type unknown and retreatments

Incidence
next steps

Short-term

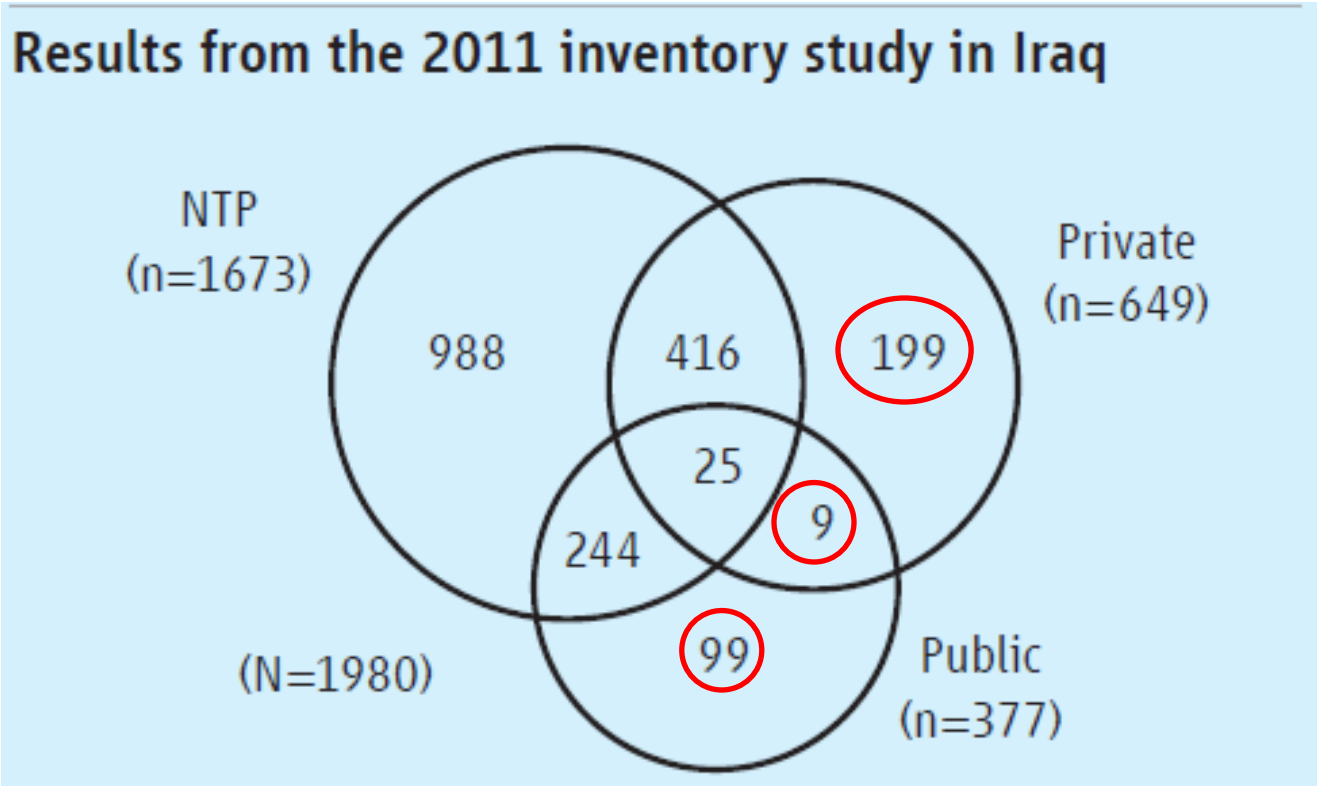
- Complementary mathematical modelling work
  - novel approach to estimating incidence
  - disaggregation by HIV status
- Generation of new, nationwide data (particularly on informing the gap between notifications and real incidence)

Longer-term

- Promote the use of case-based electronic recording and reporting and strengthening links outside the NTP network e.g. paediatricians (*getting to the under-reported*)
- TB integration in MCH programmes (*getting to the under-diagnosed*)

Quantifying the level of under-reporting

nationwide inventory studies



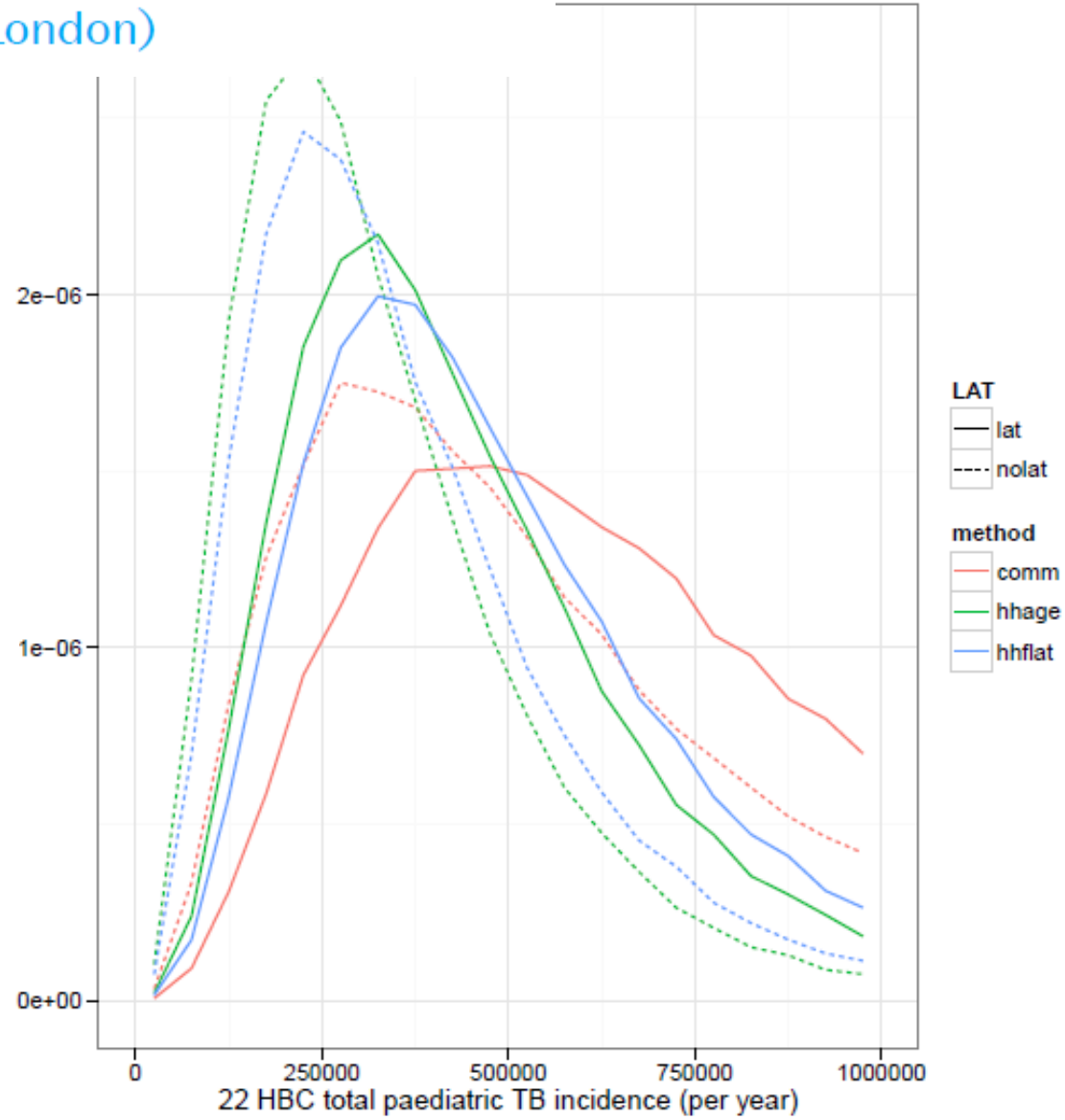
Under-reporting: (199+99+9)/1980 = 16%

An estimated **additional** cases 473 (394 – 565)

A modelling approach to estimating the burden of paediatric TB

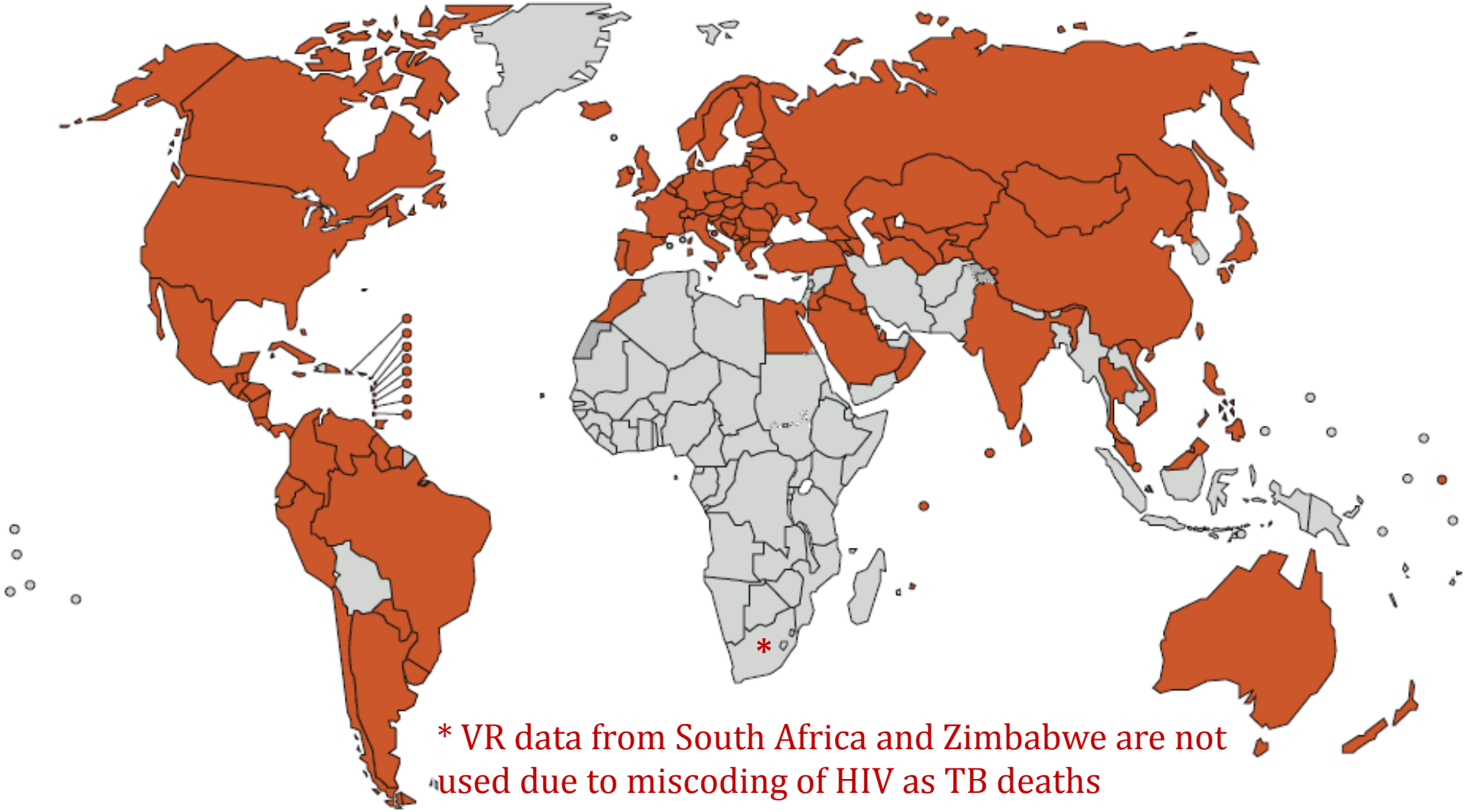
Pete Dodd (University of Sheffield)
& James Seddon (Imperial College London)

Ongoing **complementary analytical work** to increase our understanding and **build a richer, more consistent picture**



Mortality *data source* (2012)

Countries (in orange) for which TB mortality is estimated using measurements from vital registration (n=121) systems and/or mortality surveys (n=2, India and Viet Nam)



* VR data from South Africa and Zimbabwe are not used due to miscoding of HIV as TB deaths

Mortality *estimation* (2012)

- Underlying cause of death is TB (excludes TB deaths among PLHIV)
  - ICD-10: codes A15-A19
  - ICD-9: codes 010-018
- Adjust reported d deaths from VR: $d_a = \frac{d}{c(1-g)}$

  where c denotes system coverage and g proportion of ill-defined causes
- *For countries with VR data*: use adjusted reported paediatric TB deaths d_a
- *For countries without VR data*: use an ecological statistical model to predict the ratio of paediatric to adult adjusted TB deaths

74 000 (59 000 – 90 000) TB deaths (HIV-negative)

8% of total 940 000 TB deaths (HIV-negative)

Mortality
strengths, limitations

Strengths

- **National** vital registration systems with standard coding of cause of death, reporting data to WHO **annually**

Limitations

- All countries used in model are middle to high income
- Uncertainty of estimates is not fully propagated
- Possible under-estimation due to miscoding of TB deaths (e.g. pneumonia, malnutrition, HIV/AIDS)
- The only available VR data from Africa, that from South Africa and Zimbabwe, are not used due to the miscoding of HIV as TB deaths

Mortality
next steps

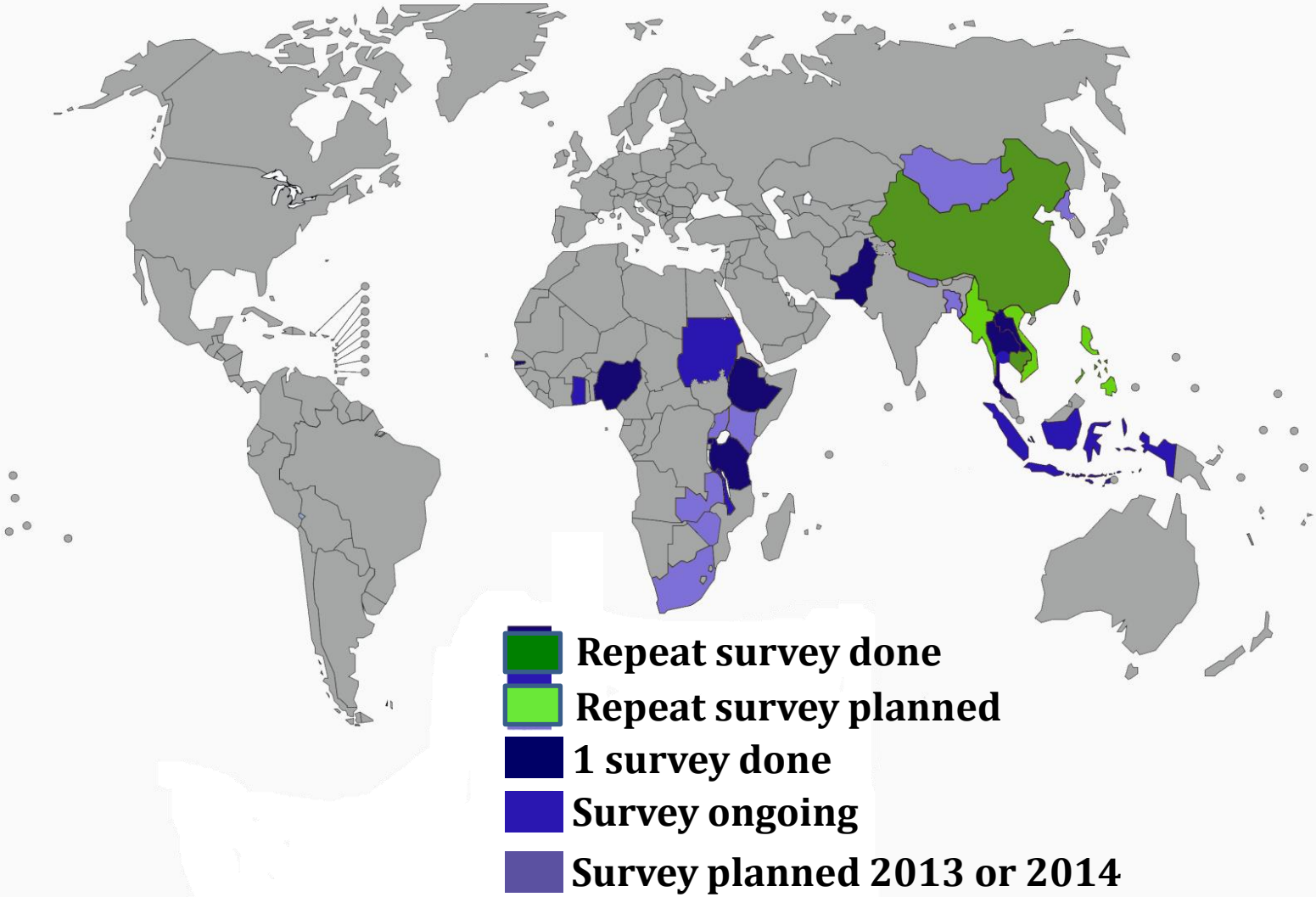
- Additional analytical work
  - Further develop the ecological model
  - Mathematical modelling (e.g. TB deaths in HIV co-infected children)
- Collaboration with CHERG*: investigate options to quantify the miscoding of TB deaths in VR systems (e.g. due to pneumonia, malnutrition, HIV/AIDS)
- Investigate options for "correcting" VR data from South Africa and Zimbabwe
- Advocate for the development of and investment in VR systems
  - Allows for a direct measurement of mortality: level of & time trends
  - Serving many health programmes, not only TB
  - Interest from funding agencies: Global Fund investment in VR, part of HIS strengthening grants (e.g. Indonesia)

* UNICEF & WHO's Child Health Epidemiology Reference Group

National TB prevalence surveys (15+ years)

overview of global progress

12 completed 2008-2012, an additional 17 to be completed 2014-17

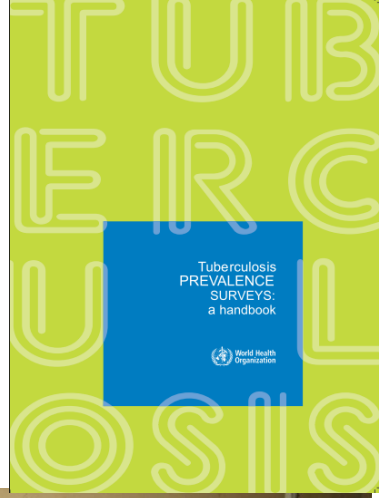


Field operations

(100-200 participants/day

5-7 days/cluster)

Census collection



Group instructions to participants

Reception and interview screening

Chest X-ray screening

Chest X-ray reading

Sputum specimen collection for those screened positive

Result for all and exit

National prevalence surveys that included children in the past

NATIONAL SURVEYS*	Age group	Participants N (%[1])	S+[2] cases N (%[1])	S+[2] rate per 100,000	B+[3] cases N (%[1])	B+[3] rate per 100,000
China 1990	0 -14	401,997 (28)	30 (2)	7	51 (2)	13
China 2000**	0 -14	89,295 (24)	6 (1)	7	11 (2)	12
Cambodia 2002**	10 -14	4,591 (21)	3 (4)	65	4 (1)	87
Philippines 1997	10–19	4,989 (31)	6 (9)	120	18 (10)	361
Philippines 2007	10–19	6,728 (29)	1 (2)	15	11 (7)	163
Republic of Korea 1990	5-19	16,468 (34)	2 (3)	12	5 (4)	30
Republic of Korea 1995	5-19	19,005 (29)	1 (2)	5	2 (1)	11

* Pulmonary TB with CXR screening; ** Additional symptoms screening;
[1] Over total survey population; [2] Smear-positive; [3] Bacteriologically-confirmed (smear and/or culture positive)

Survey's in the 2000's

- Heterogeneous age groups, difficult to pool
- 20-29% of the sample size to detect 1-4% S+ and 2-7% B+ cases

Why not include children in prevalence surveys?

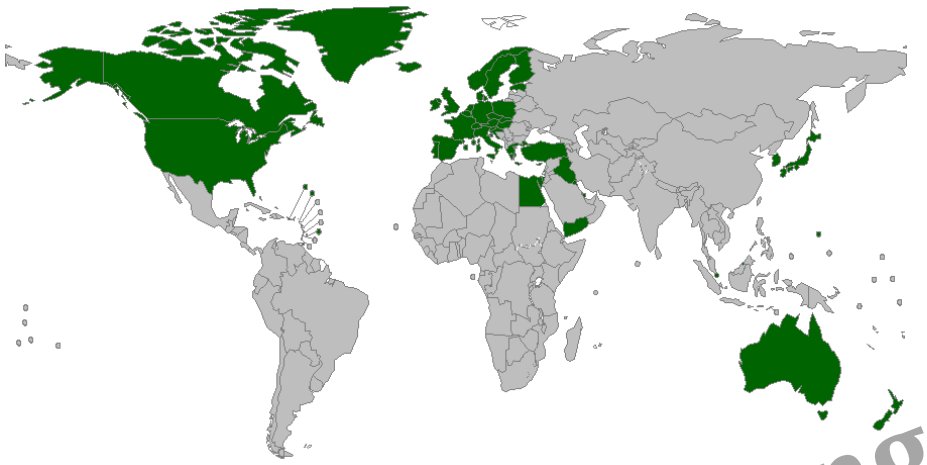
Item	*Current design*	*Adding children*
Prevalence estimate	Bacteriologically-confirmed TB among 15+ in the general population	- A more accurate estimate among the total population - Still imprecise estimate of prevalence among children
Sample size	Typically about 50,000-70,000	- 20% increase if 10+ included - 60-100% increase if 0-14 included
Screening algorithm	CXR and symptoms	- CXR problematic in children - No reliable test for tuberculous infection
Confirmation of TB	Sputum smear microscopy and culture (with supporting CXR evidence)	- Invasive and uncomfortable diagnostic procedures - Referral hospital for follow-up diagnosis and treatment required
Budget	- USD 1-2 million in Asia - USD 2-4 million in Africa	- Prolonged cluster operations - Inclusion of pediatrician - Larger sample size - Additional equipment - Referral hospital incidentals and transportation

Prevalence
next steps

- Data source does not exist at global level
- With current tools the WHO Global Task Force on TB Impact Measurement does not recommend the inclusion of children in nationwide prevalence surveys of pulmonary TB
- No disease burden estimate of paediatric TB prevalence is currently produced
- Global sentinel sites for stand-alone prevalence surveys among children?
- Is there room for contact tracing studies instead?
- Deterministic model to estimate prevalence

Current status of direct measurement

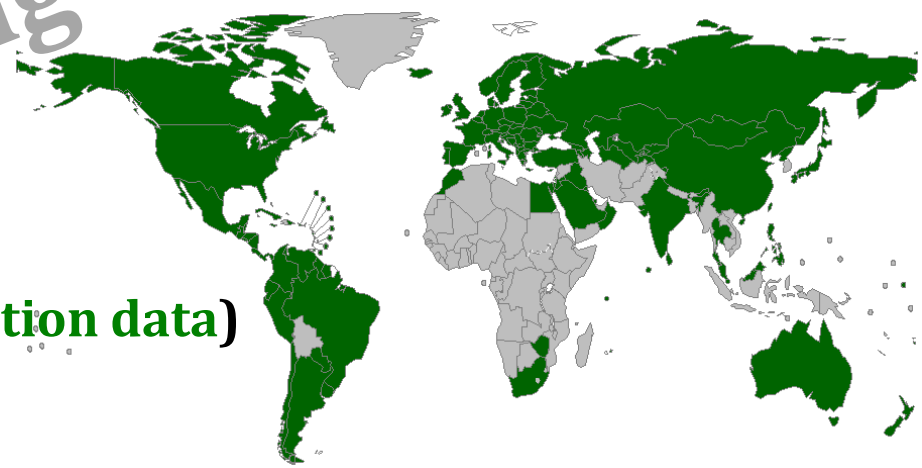
TB incidence and mortality



Incidence

(notification data)

Clearly a long way to go



Mortality

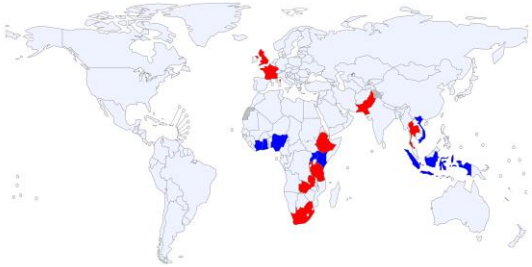
(vital registration data)

Opportunities to identifying strengths & gaps in national TB surveillance systems

- **Checklist of standards & benchmarks**
  - **To assess a national surveillance system's ability to accurately measure TB cases and deaths**
  - **To identify gaps that need to be addressed**

- **Completed with accompanying user guide & ready for roll-out January 2013**
  - **10 standards to assess if notification and VR data provide direct measure of TB incidence and mortality**
  - **3 supplementary standards: *HIV-related TB, drug-resistant TB and TB in children***
  - **Benchmarks for each standard to allow assessment of whether standard is met or not**

- **Now being rolled out**
  - **7 countries to date, 8 planned**
    - **GF high burden/impact countries prioritized**
    - **Linked to "impact analyses", programme reviews**
    - **M&E investment plans to close surveillance gaps**



The Global Fund
To Fight AIDS, Tuberculosis and Malaria

Strategy for measurement of impact, TERG* 2012

1. **Invest in routine information systems and surveys**

2. **Link to/build on programme or "mini" reviews**
   - Strengthen epi/impact analysis component of reviews
   - Invest based on results of epi/impact analyses and systematic assessments of routine surveillance
   - M&E investment plans

3. **Epi/impact analyses essential part of developing concept note in new funding model**

Funding allocation based on directly measurable (as opposed to estimated) indicators

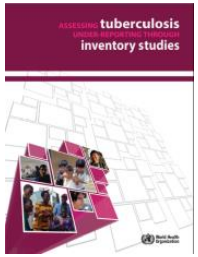
* Global Fund's Technical Evaluation Reference Group

Investment plan to strengthen surveillance, Indonesia (total budget US 1 million excl. VR)

Activity
Vital registration (VR): maintaining and scaling up the nationally-representative sample VR system
Inventory study to measure the level of underreporting
Capacity building for data management and statistical analysis – through attending courses and extra staffing at the central level
Implementation of the *Service Availability and Readiness Assessment Tool* and health facility data quality assessment
Assessment of the Integrated Tuberculosis Information System (SITT) Phase 2 in 2014
Implementing mandatory notification policy
Analysis of available mortality data
Drug resistance survey or sentinel surveillance
Nationally representative survey of HIV prevalence among TB patients
Corrective actions required to compile all the reports from Papua

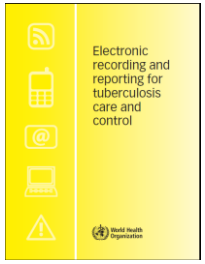
Available relevant guidance to countries

Guide on inventory studies to measure TB under-reporting (2012)



Among all health providers including paediatricians

Electronic recording and reporting guide (2011)



Case-based information allows NTPs to perform "know-your-epidemic" type of analyses including age of ALL cases

Global Consultation on Paediatric Tuberculosis: Disease Burden Estimation and Quantification of Its Drug Market

25-26 September, 2013

Hosted by the Speeding Treatments to End Paediatric Tuberculosis (STEP-TB) Project
Sponsored by USAID and UNITAID

Objectives

1. To review available data and highlight gaps
2. To review analytical methods and epidemiological indicators
3. To define and prioritise specific actions that can be taken by TB Alliance, WHO, and other participating organizations
4. To catalyse efforts to strengthen routine surveillance and promote consensus in disease burden estimation

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- Global TB Programme
- Stop TB Partnership Secretariat
- TB Alliance
- UNITAID
- DfID
- USAID
- TB CARE

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