

Epidemiological science

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Health solutions for the poor

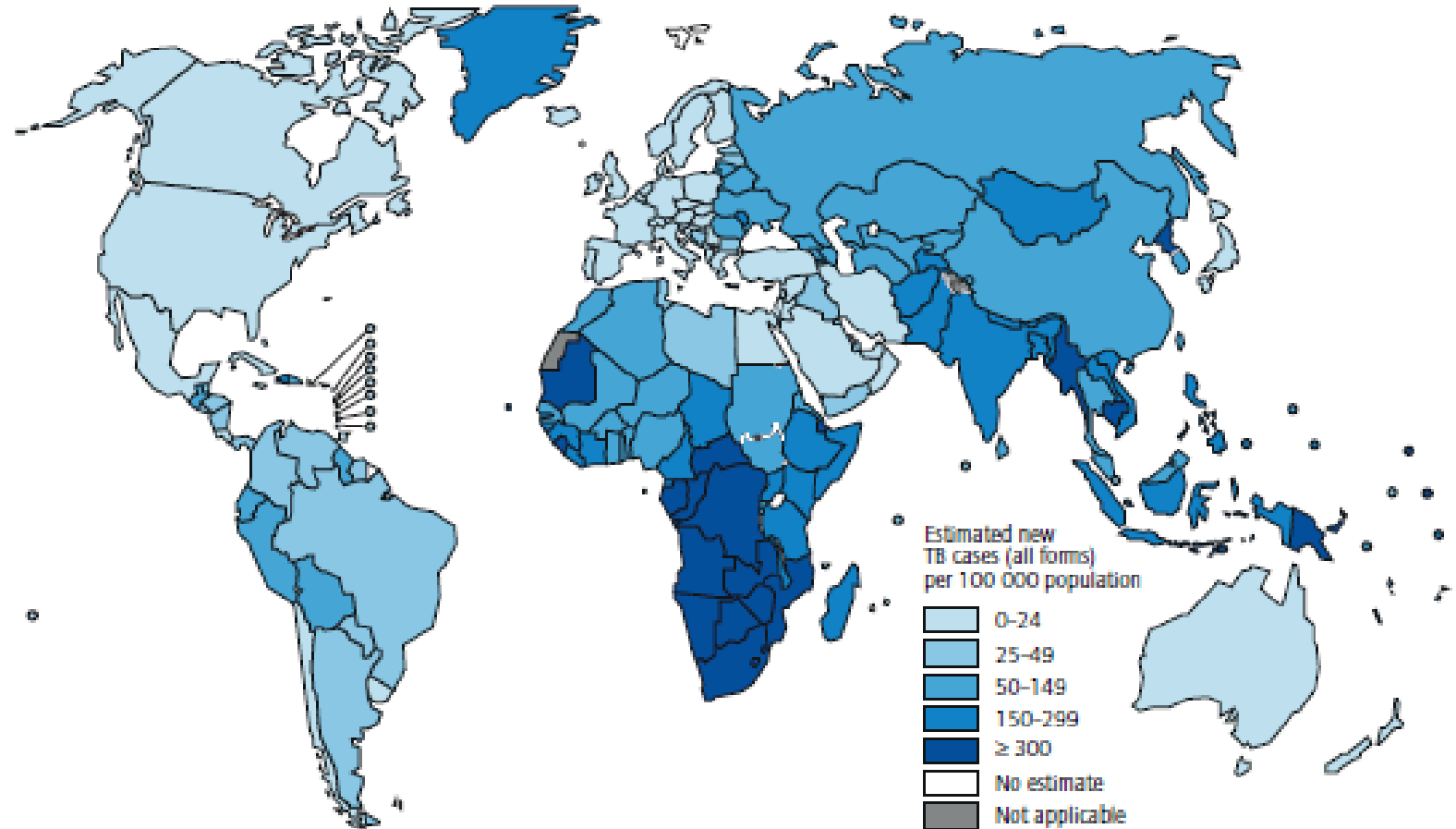


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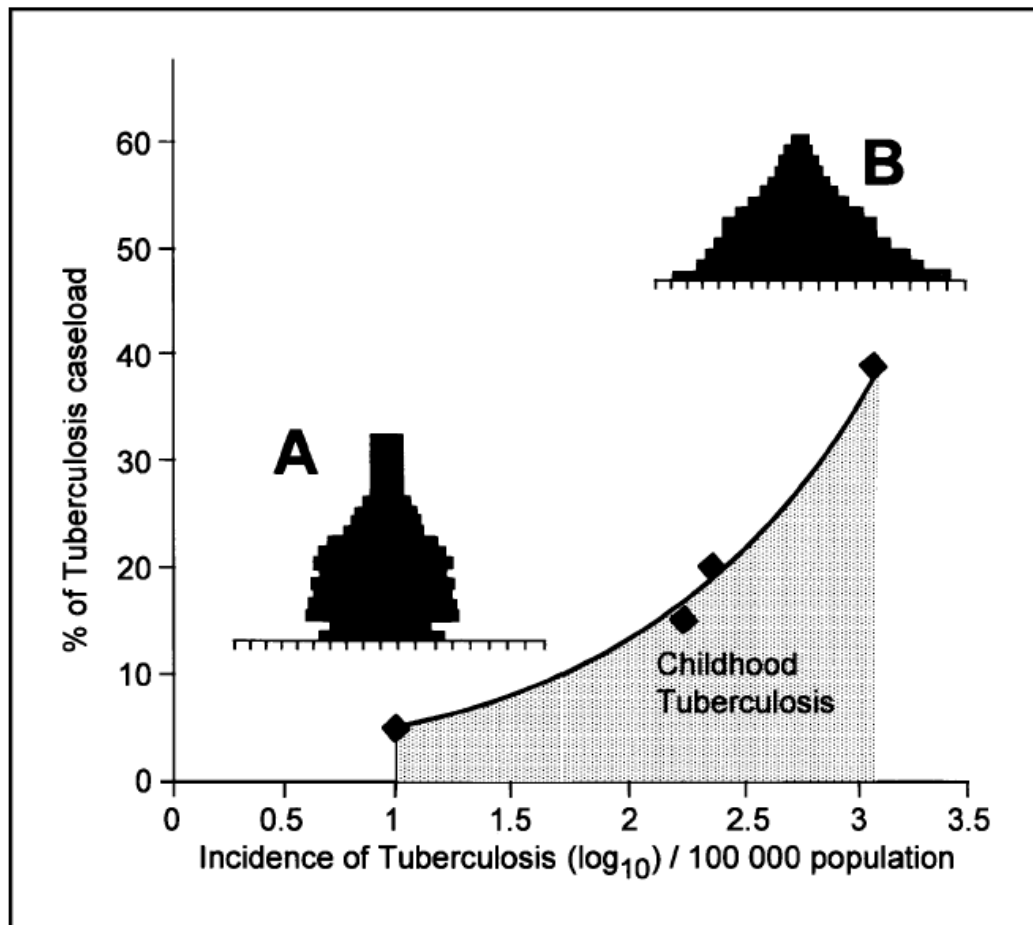
Child TB is common wherever TB is common –
but how common?



Estimated TB incidence rates, 2011



Figure 1. Percentages of the tuberculosis caseload



The percentage of the tuberculosis caseload made up by children <15 years of age in relation to the incidence of tuberculosis/100,000 population and the population pyramids typical of an (A) developed and a (B) developing community.

Reported: range 1%-40%

Important factors:

Incidence of TB

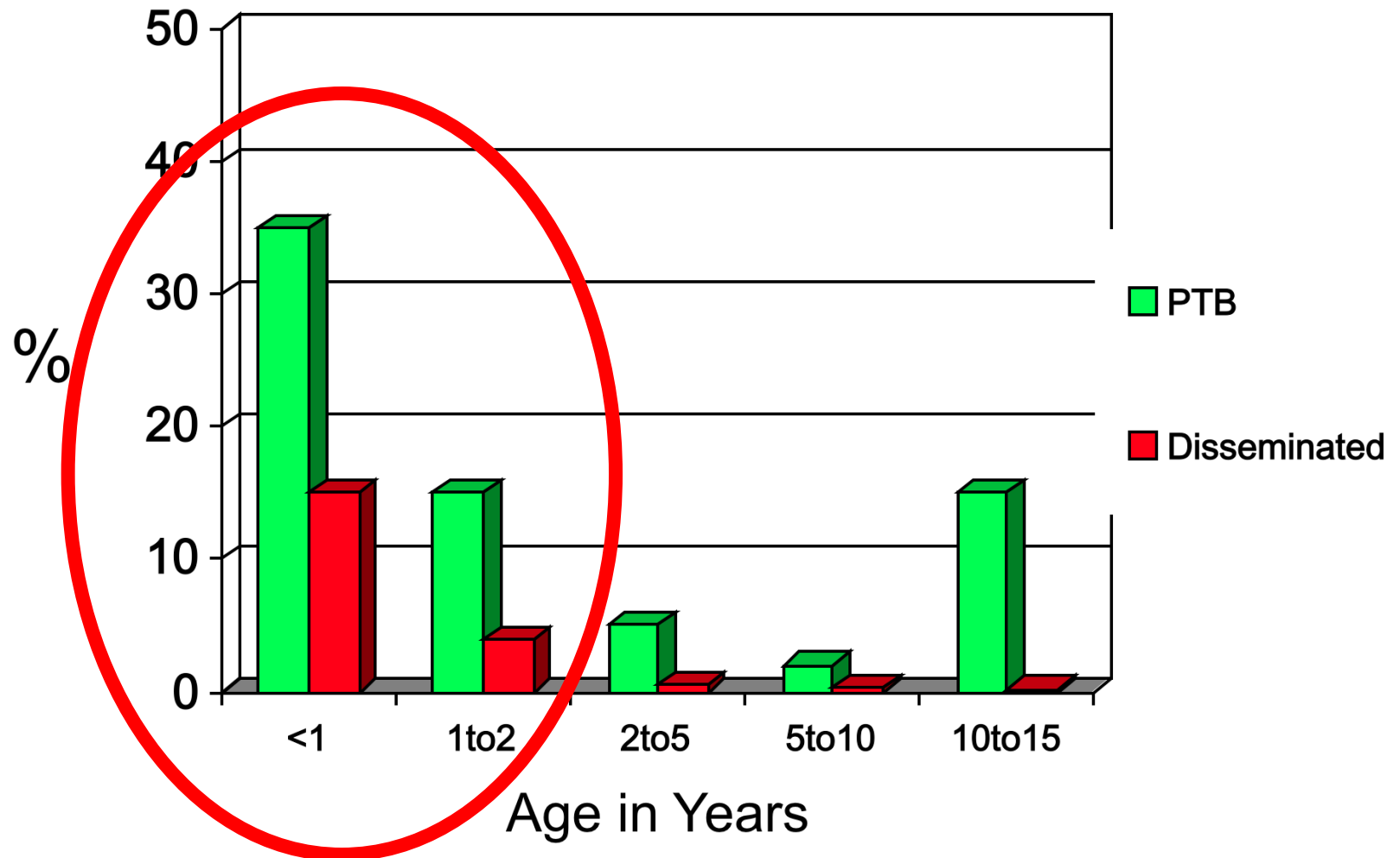
Demographics - age

Effectiveness of case-finding and management

Prevalence of risk factors in children

BCG coverage

Risk of TB disease following infection by age



Expectations in high TB endemic setting

- 0-4 years > 5-14 years
- PTB: EPTB 2:1 to 3:1
- Smear-positive disease < 10%
- The younger the child, the more likely infected by a household contact

Childhood TB caseload: Malawi 1998

Malawi NTP, 1998	numbers (proportion of childhood caseload)	proportion of total caseload
Total caseload	22,982	
Total childhood	2,739	11.9%
0-5 years	1,615 (58.9%)	7%
5-14 years	1,124 (41.1%)	4.9%
Smear-positive PTB	127 (4.6%)	1.3%
Smear-negative PTB	1,804 (65.9%)	21.3%
EPTB	808 (29.5%)	15.9%

Burden of child TB in PNG: 2005-6

Law I, et al. Poster – The Union Global Lung Health Conference 2008

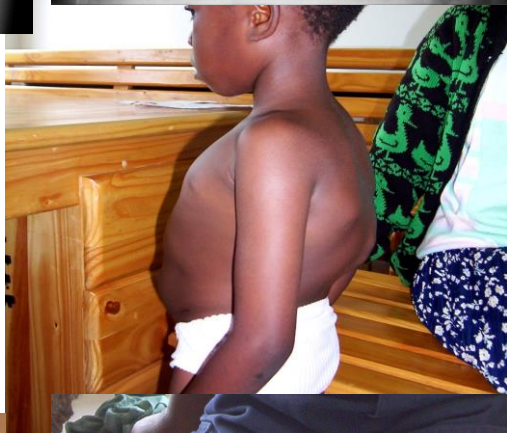
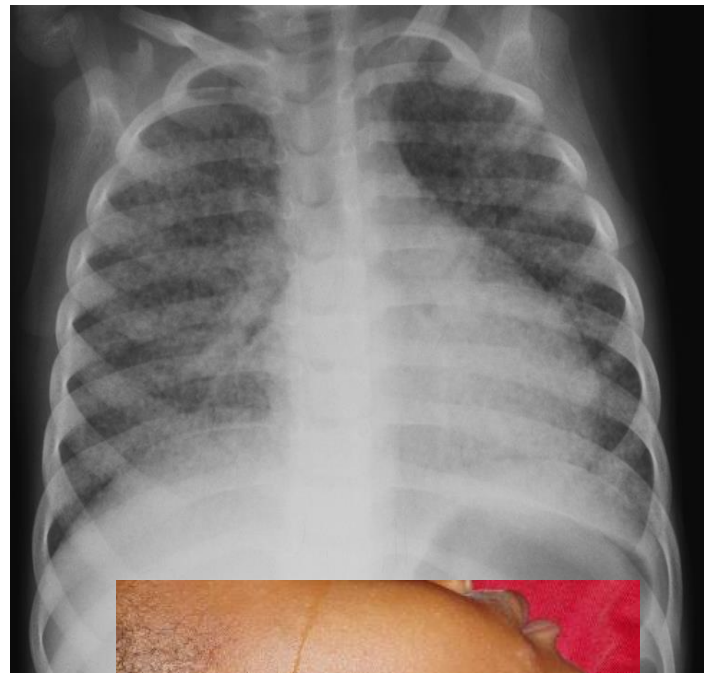
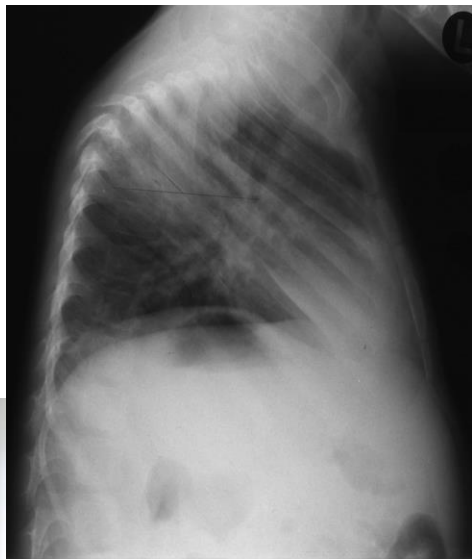
Child TB accounts for 33% of total TB case-load

Pulmonary TB	1208 (61%)
Smear positive	18
Smear negative	138
Smear not done	1052
EPTB	769 (39%)
Total	1977

Types of childhood EPTB disease

	Malawi NTP, 1998	PNG, 2005-6
EPTB cases	808	1097
Lymphadenitis	331 (41%)	342 (31%)
Pleural effusion	101 (12%)	94 (9%)
Spinal	83 (10%)	41 (4%)
Pericarditis	60 (7%)	12 (1%)
Abdominal	39 (5%)	173 (16%)
Miliary	34 (4%)	64 (6%)
Meningitis	30 (4%)	257 (23%)
Bone disease	12 (1%)	15 (1%)
Not indicated/others	118 (14.6%)	99 (9%)

EPTB represented 30% and 39% of childhood TB cases in Malawi and PNG respectively.



Revised TB recording and reporting forms and registers – version 2006



Tuberculosis Programme

Form 6

Quarterly Report on TB Case Registration in Basic Management Unit

Name of BMU: _____ Facility: _____

Patients registered during¹

_____ quarter of year _____

Name of TB Coordinator: _____ Signature: _____

Date of completion of this form: _____

Block 1: All TB cases registered²

Pulmonary sputum smear microscopy positive				New pulmonary sputum smear microscopy negative			Pulmonary sputum smear microscopy not done / not available			New extrapulmonary			Other previously treated ³	TOTAL All cases
New cases	Previously treated			0-4 yrs	5-14 yrs	≥ 15 yrs	0-4 yrs	5-14 yrs	≥ 15 yrs	0-4 yrs	5-14 yrs	≥ 15 yrs		
	Relapses	After failure	After default											

Block 2: New pulmonary sputum smear microscopy positive cases – Age group

Sex	0-4	5-14	15-24	25-34	35-44	45-54	55-64	≥ 65	Total
M									
F									

Block 3: Laboratory activity - sputum smear microscopy⁴

No. of TB suspects examined for diagnosis by sputum smear microscopy	No. of TB suspects with positive sputum smear microscopy result

Block 4: TB/HIV activities⁵

	No. patients tested for HIV before or during TB treatment ⁵	No. patients HIV positive ⁵
New sputum smear microscopy positive TB		
All TB cases		

¹ Registration period is based on date of registration of cases in the TB Register, following the start of treatment. Q1: 1 January–31 March; Q2: 1 April–30 June; Q3: 1 July–30 September; Q4: 1 October–31 December.

² Transferred in² and chronic cases are excluded. In areas routinely using culture, a separate form for unit using culture should be used.

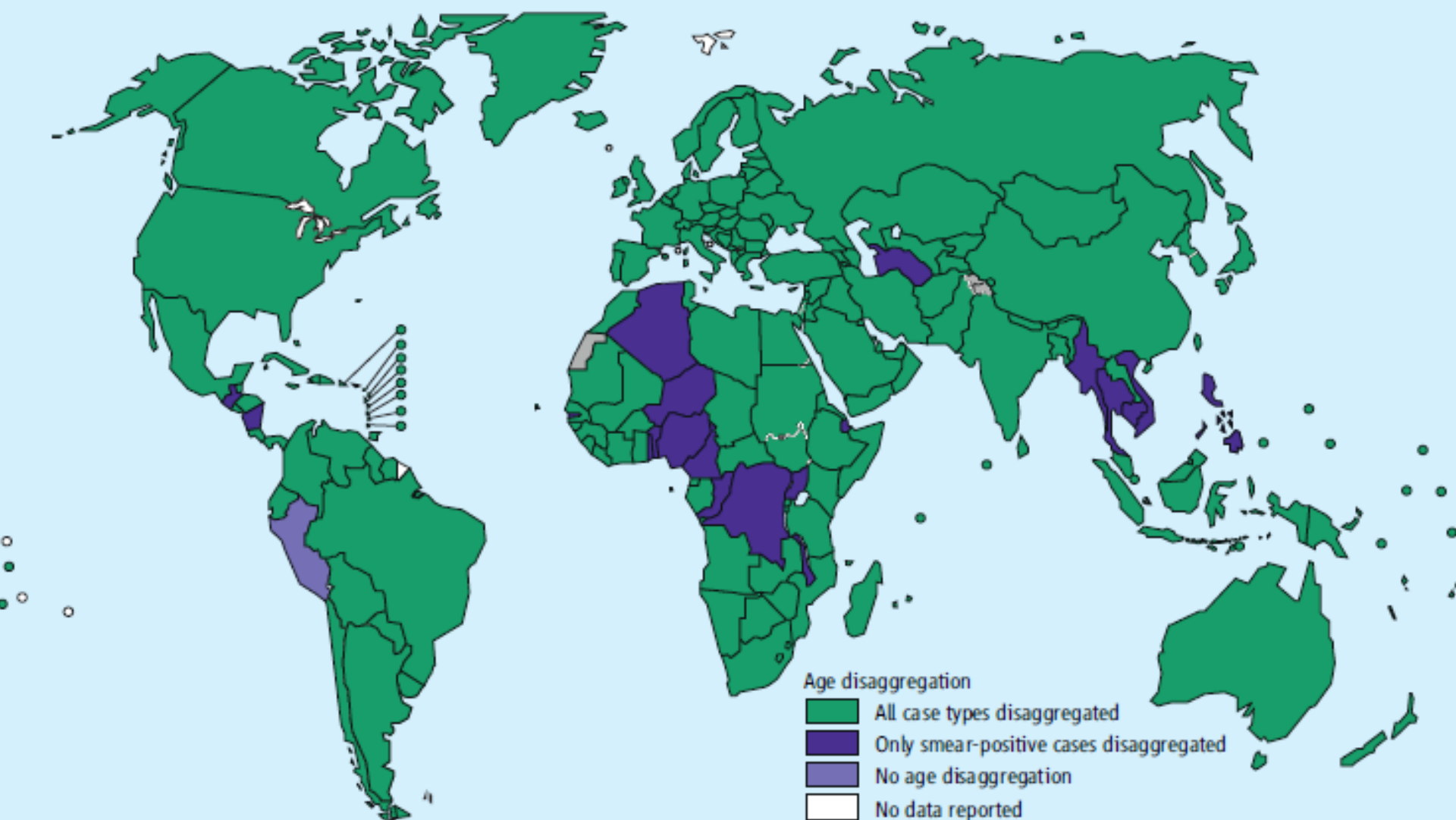
³ Other previously treated cases include pulmonary cases with unknown history of previous treatment, previously treated sputum smear microscopy negative pulmonary cases and previously treated extrapulmonary cases. Transferred in² and chronic cases are excluded.

⁴ Data collected from the TB Laboratory Register based on "Date specimen received" in the laboratory during the quarter, without including patients with examination because of follow-up.

⁵ Documented evidence of HIV tests (and results) performed in any recognized facility before TB diagnosis or during TB treatment (till end of the quarter) should be reported here.

FIGURE B2.2.3

Reporting of notification data disaggregated by age, 2012



Limitations of child TB data

Reported burden of child TB ranges from <2% to 40%

Under-recognition

Recent prevalence survey in Laos:

Culture-positive TB was 606 per 100,000

Only 78 children treated for TB in 2012 i.e. <5 per 100,000 children

Joint Monitoring Mission Report, WHO WPRO, 2013

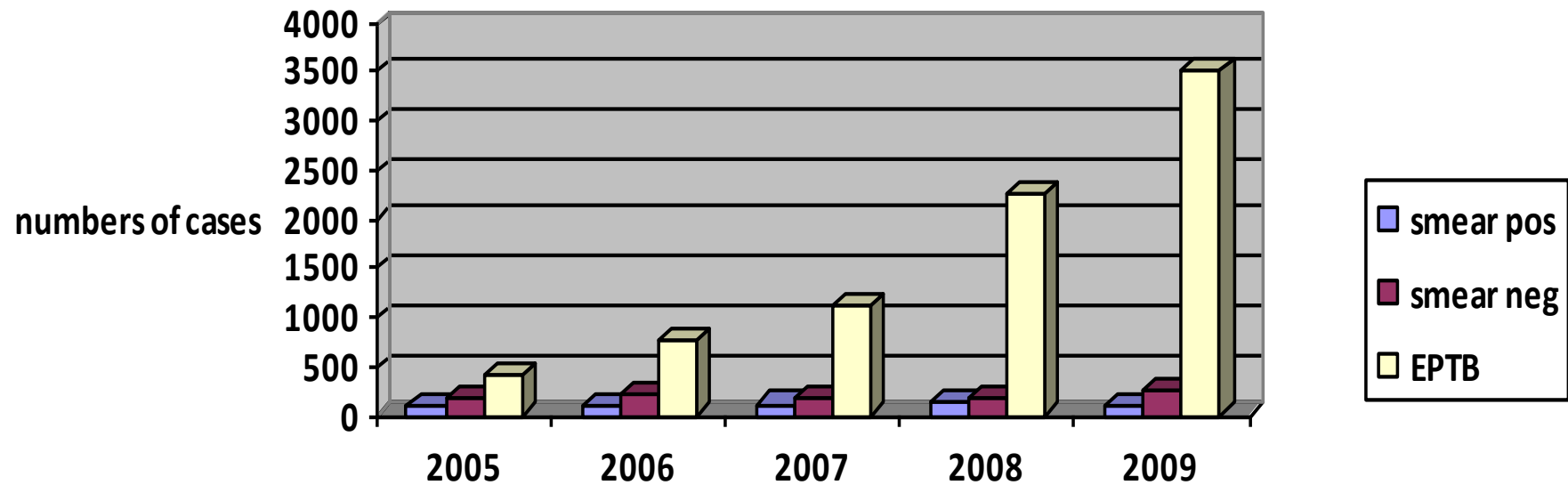
Under-reporting

Recent study from Java, Indonesia:

Only 1.6% of 4,821 TB cases in children were registered with NTP

Lestari T, et al BMC Public Health 2011

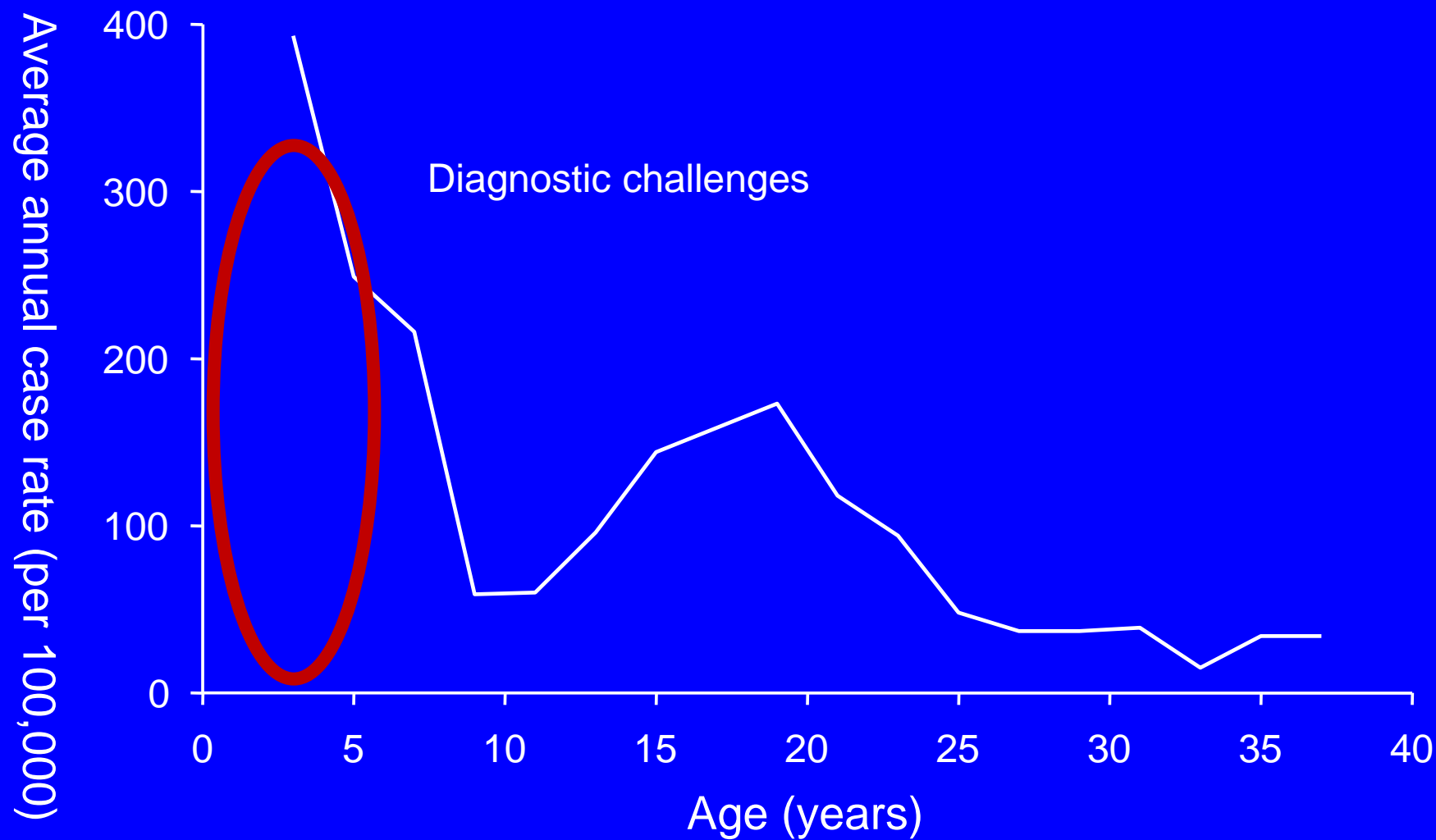
Increased attention to Child TB



Year	New PTB+ (0-14)	Primary Complex (PTB)		Hilar lymphadenopathy		TB Meningitis		Total child TB	Total TB	% Child TB
		0-4	5-14	0-4	5-14	0-4	5-14			
2008	298	3 111	20 028	1 387	2 878	64	194	27 960	128 739	22%
2009	282	8 521	13 662	4 244	5 440	175	216	32 540	134 023	24%
2010	302	9 334	12 093	4 527	5 377	370	468	32 471	137 403	24%
2011	308	10 234	14 924	5 585	6 116	256	311	37 734	143 164	26%
2012	338	13 367	17 982	4 411	4 879	163	128	42 434	147 984	29%

Child health in high TB endemic setting

- High under 5 mortality
- Young age a risk for respiratory disease, malnutrition, meningitis, HIV
- TB is a disease of poverty



Comstock GW, et al. Am J Epidemiol 1974;99:131-8

TB in context of child survival

- Severe pneumonia

Autopsy studies: TB in 9% of children dying with respiratory disease –

Bates M, et al. Curr Opin Pulm Med 2013

Clinical studies: 6% culture confirmed plus 13% clinical TB in 270 Ugandan children with acute severe pneumonia –

Nantango JM, et al BMC Pediatr 2013

- Severe malnutrition and respiratory disease

23-24% clinical TB and 4-6% microbiologically confirmed TB

De Maayer T, et al. Arch Dis Child 2011; Chisti MJ, et al 2013 - submitted

- HIV

Changing epidemiology

- Meningitis

In TB endemic settings, *M.tuberculosis* is common cause of meningitis with poor outcome –

Wolzack NK, et al. J Trop Pediatr 2012; Anga G, et al. Ann Trop Paediatr 2010

Diagnosis – well-defined symptoms

Characteristics of cough: persistent (>2 weeks), unremitting and unresponsive to antibiotics

Fatigue, reduced playfulness

Documented weight loss, failure to thrive (in preceding 3 months)

Well characterized symptoms improve diagnostic accuracy

≥ 3 years: specificity: 98.9%; PPV: 85.1%

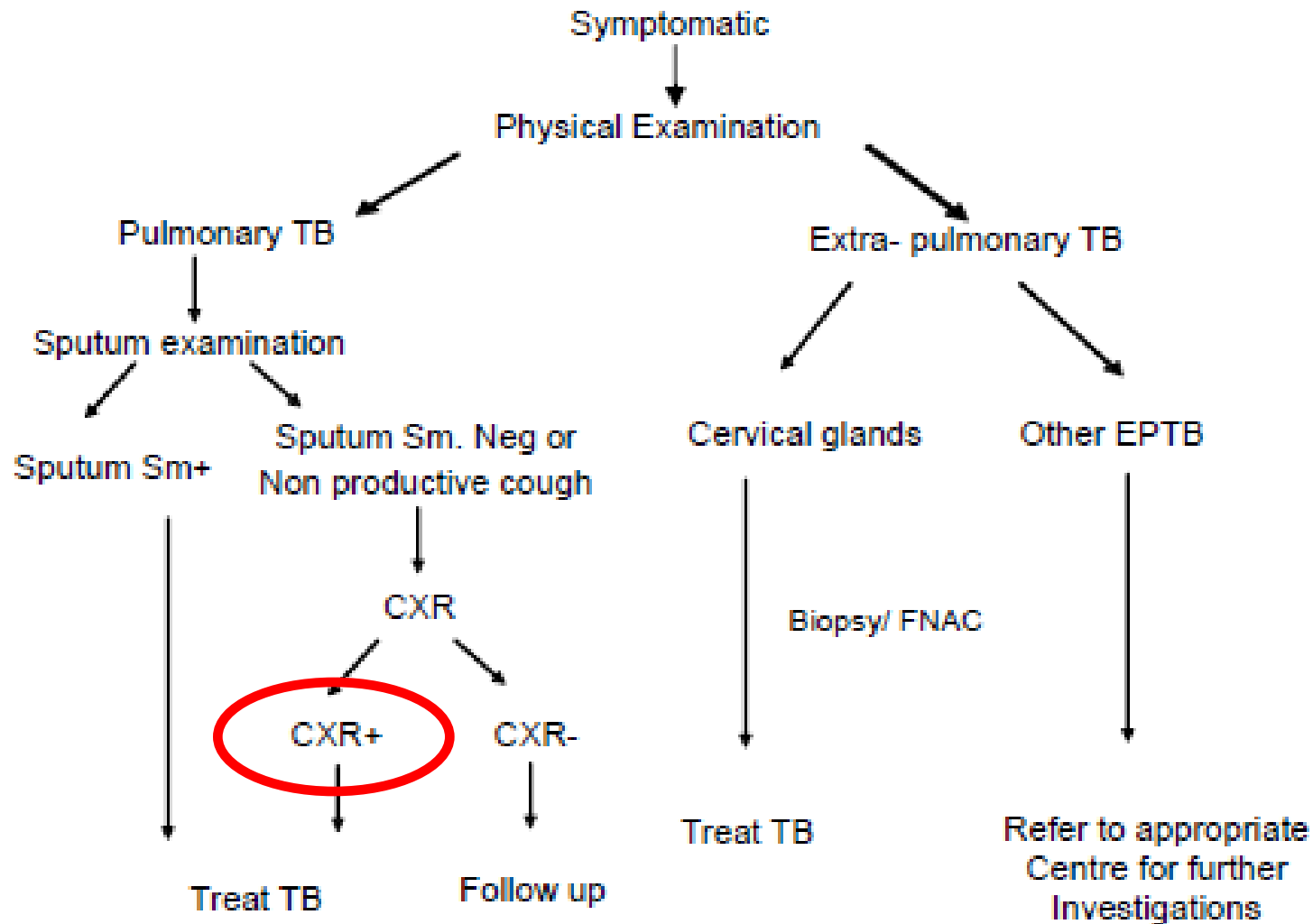
Less useful in young

< 3 years: specificity: 82.6%; PPV: 88.6%

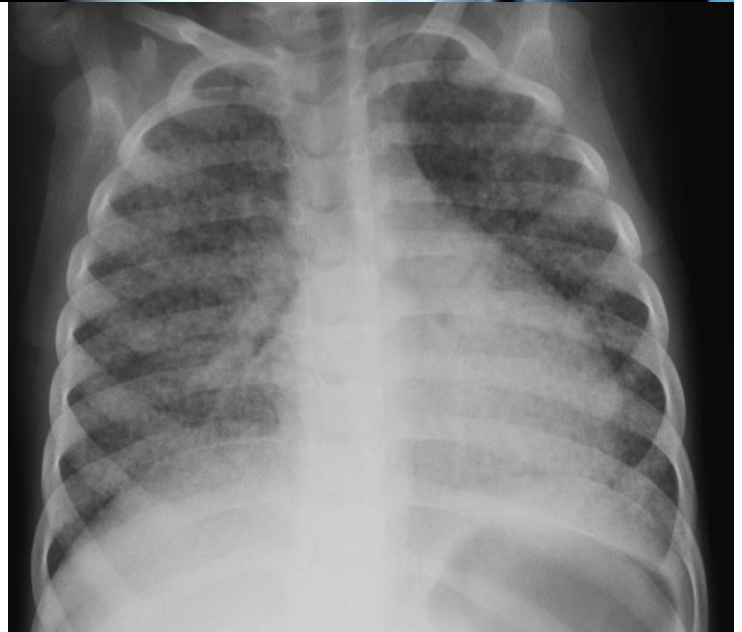
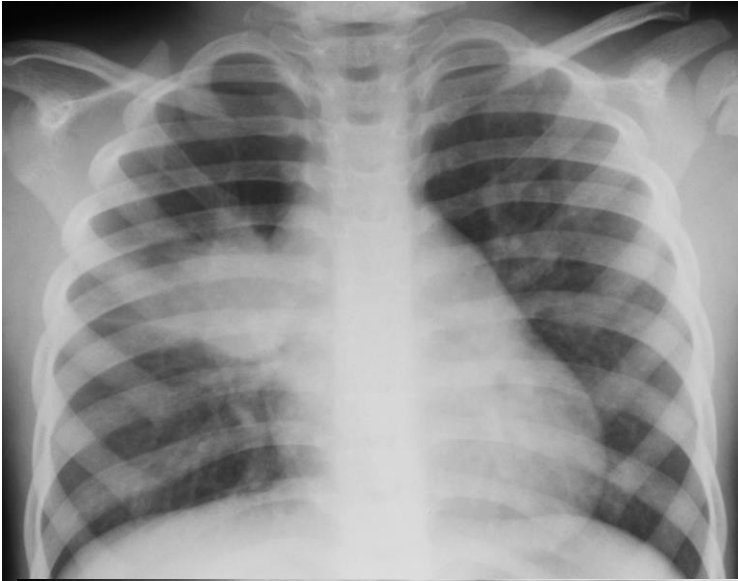
Performed poorly in HIV-infected

Assessment of a symptomatic child

8 years and older suspicious of having TB at Township and District Hospitals



CXR important tool for child TB diagnosis



Diagnostic accuracy of chest radiography in detecting mediastinal lymphadenopathy in suspected pulmonary tuberculosis

G H Swingler, G du Toit, S Andronikou, et al.

Arch Dis Child 2005 90: 1153-1156

Sensitivity = 67%

Specificity = 59%



Very low inter-observer and intra-observer agreement

Very poor agreement between reviewers on the assessment of hilar adenopathy

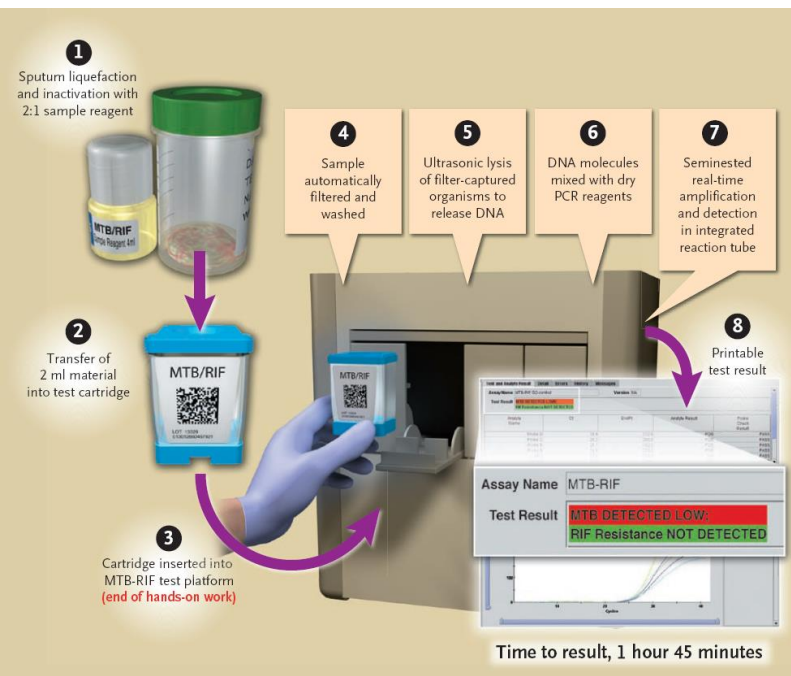
Triasih R, et al. unpublished data

	Normal		Hilar lymphadenopathy	
	kappa	95% CI	kappa	95% CI
R1 – R2	0.25	0.12 – 0.37	0.11	0.07 – 0.28
R1 – R3	0.34	0.22 – 0.45	0.25	0.06 – 0.43
R1 – R4	0.46	0.35 – 0.57	-0.03	-0.13 -0.06
R2 – R3	0.33	0.21 – 0.46	0.18	0.00 – 0.36
R2 – R4	0.33	0.21 – 0.45	-0.02	-0.13 – 0.08

Is there an easier way?

16 studies in children to date

Sensitivity 66% compared to culture
Specificity >98% compared to culture



TBXpert Project

The TBXpert Project will provide approximately 1.4 million Xpert MTB/RIF test cartridges and over 220 GeneXpert instruments for the rapid detection of TB and rifampicin resistance in 21 recipient countries in 2013-2015 (see map and list of recipient countries below). The USD25.9 million TBXpert Project is funded by UNITAID and executed by the WHO Stop TB Department and the Stop TB Partnership. To ensure country absorptive capacity and effective use of the technology, the TBXpert Project links a broad network of partners and existing initiatives for TB laboratory strengthening and innovative approaches to expand access to vulnerable populations in both the public and private sector. TBXpert Project partners include the Global Laboratory Initiative (GLI), TB REACH, the Global Drug Facility (GDF), the EXPAND-TB Project, Interactive Research and Development (IRD) and the African Society for Laboratory Medicine (ASLM).



Recipient countries:

Bangladesh, Belarus, Cambodia, Congo, Ethiopia, India, Indonesia, Kenya, Kyrgyzstan, Malawi, Mozambique, Myanmar, Nepal, Pakistan, Philippines, Republic of Moldova, Swaziland, Uganda, United Republic of Tanzania, Uzbekistan, Viet Nam

Context of case-finding

Active versus passive – early versus late disease

What can we learn from vaccine trials

young

symptoms

investigations

What do we learn from child contact studies

What could be the effect of child contact screening

Studies of child contacts in Asian countries

Study	Location	No. of child contacts	Proportion with TB infection	Proportion with TB disease
Andrew et al	India	398	39 %	5.5 %
Narain et al	India	790	24 %	NR
Kumar et al	India	142	NR	3 %*
Singh et al	India	281	34 %*	3 %*
Rathi et al	Pakistan	151	27 %	NR
Salazar et al	Philippines	153	69 %	3 %
Tornee et al	Thailand	500	47 %	NR
Nguyen et al	Lao PDR	148	31 %	NR
Okada et al	Cambodia	217	24 %*	9 %*

* Data only for < 5 years; NR: not recorded

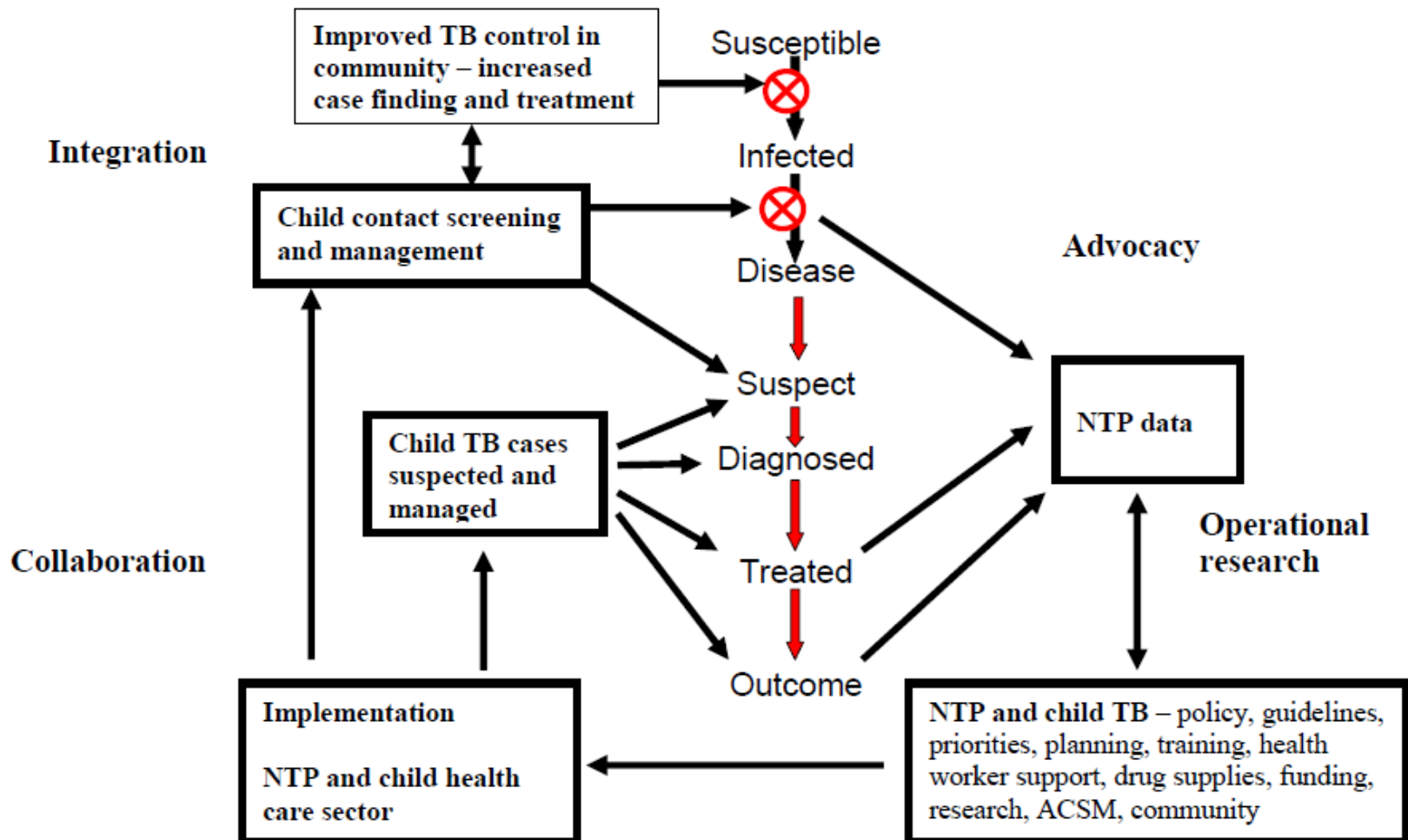
Contact investigation for active TB among child contacts in Uganda

Jaganath D, et al. Clin Infect Dis 2013 (in press)

- 761 Ugandan child household contacts with TB – half 0-5 yrs
- TB confirmed in 7% of child contacts
- More common in the young children - disease prevalence extremely high, equivalent to 16,400 per 100,000 young child contacts
- Active case-finding identified 79 children with TB that had not been diagnosed previously
- Only two (<1%) of 483 eligible children developed TB while receiving IPT

Framework for child TB and NTP

Figure. Interventions that target stages of the continuum in children from susceptibility to disease and outcome



**Global consultation on Paediatric Tuberculosis:
Disease Burden Estimation and Quantification of its Drug Market**
New York, September 25-26th

1. Strengthening surveillance: bringing the non-NTP sector into routine surveillance
2. Studies to address identified data gaps to improve estimates
3. Further data and analyses to improve estimates

Thank you