

Algorithmic Approaches to Child TB Management in Resource-limited Settings

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Stockholm declaration



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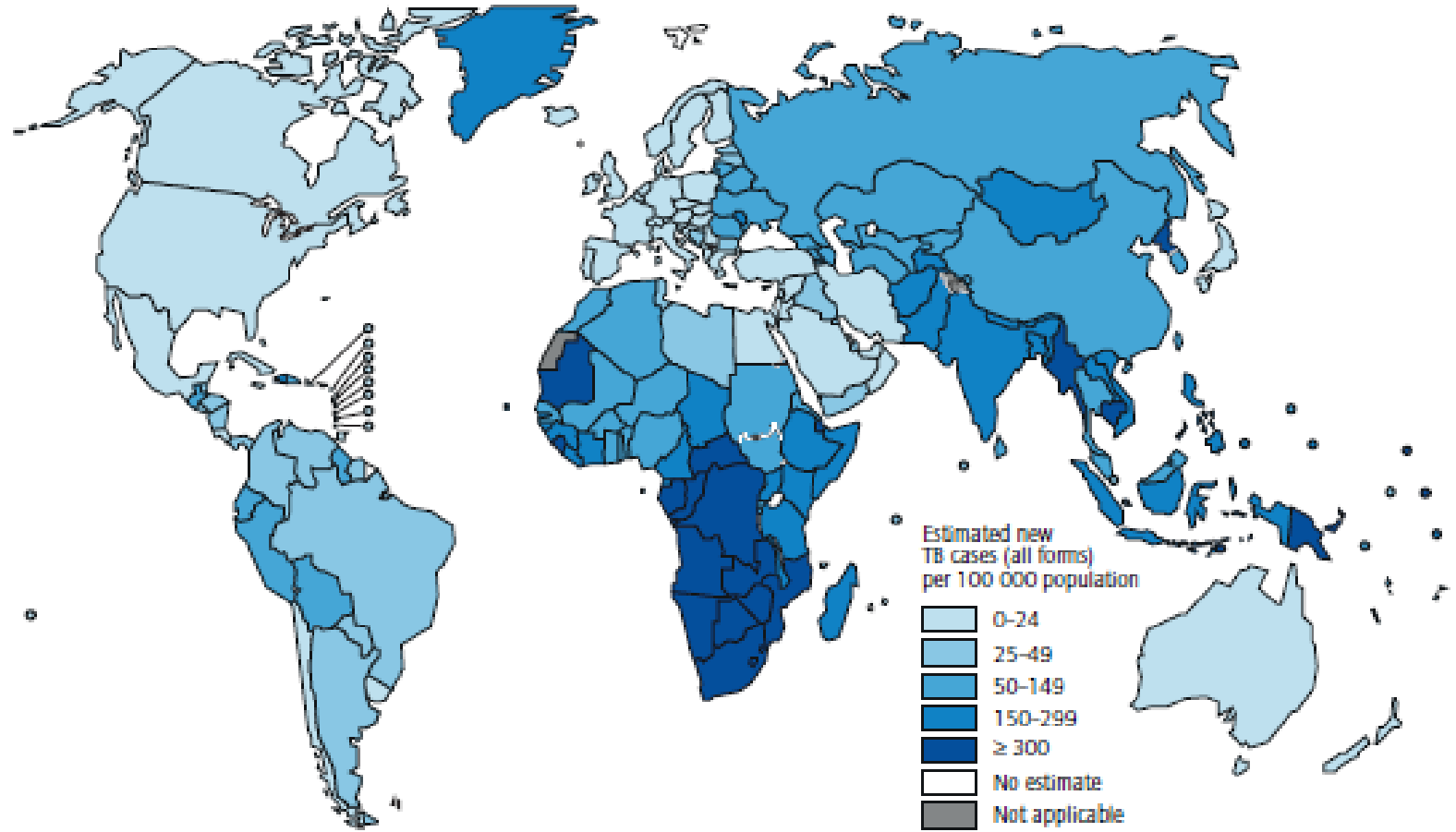
CALL TO ACTION for CHILDHOOD TB

[Read the Call in French](#), [Read the Call in Russian](#)

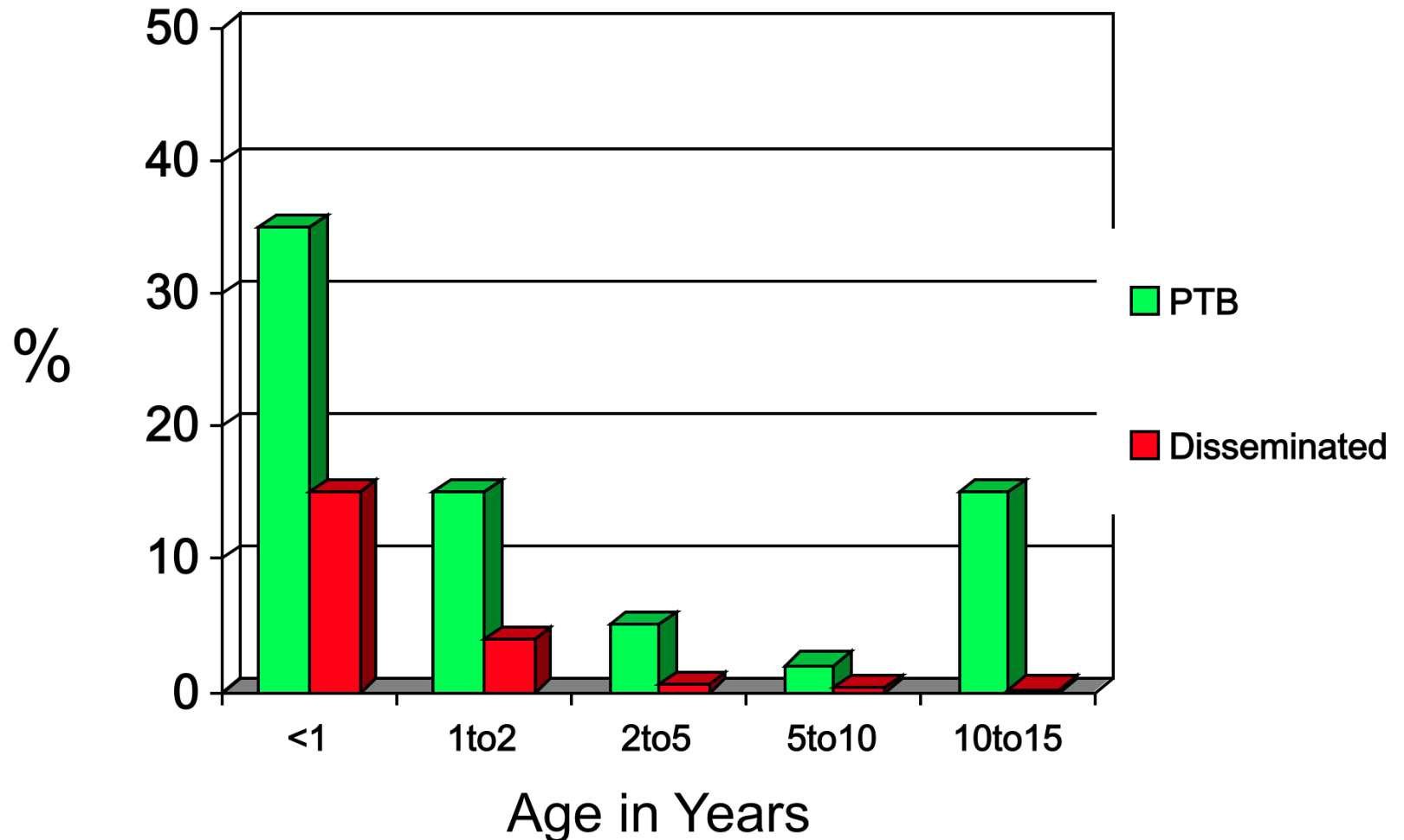
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We, participants gathered at the 'International Childhood Tuberculosis Meeting' held March 17-18, 2011 in Stockholm, Sweden recognize that:

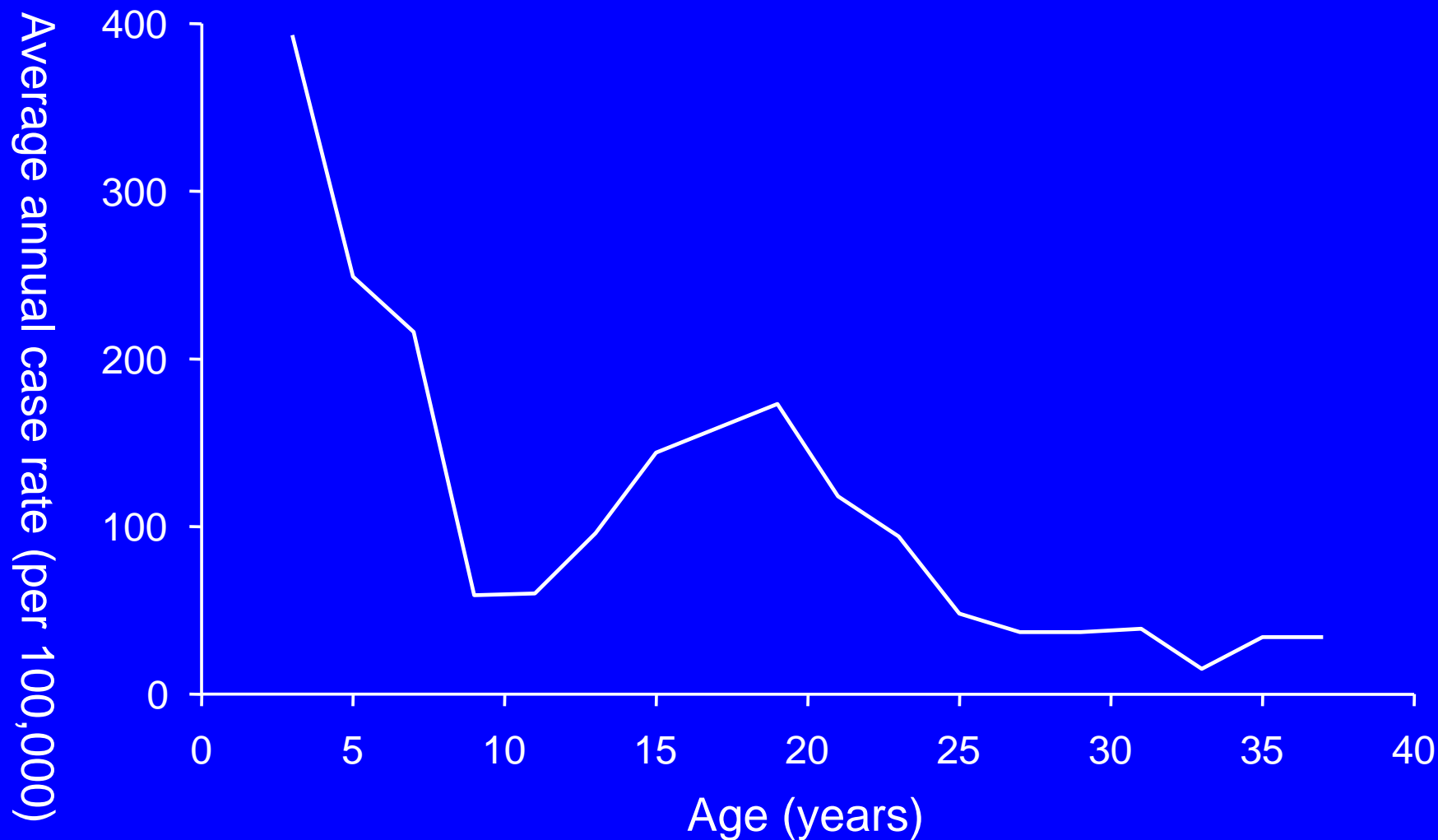
Estimated TB incidence rates, 2011



Risk of TB disease following infection by age

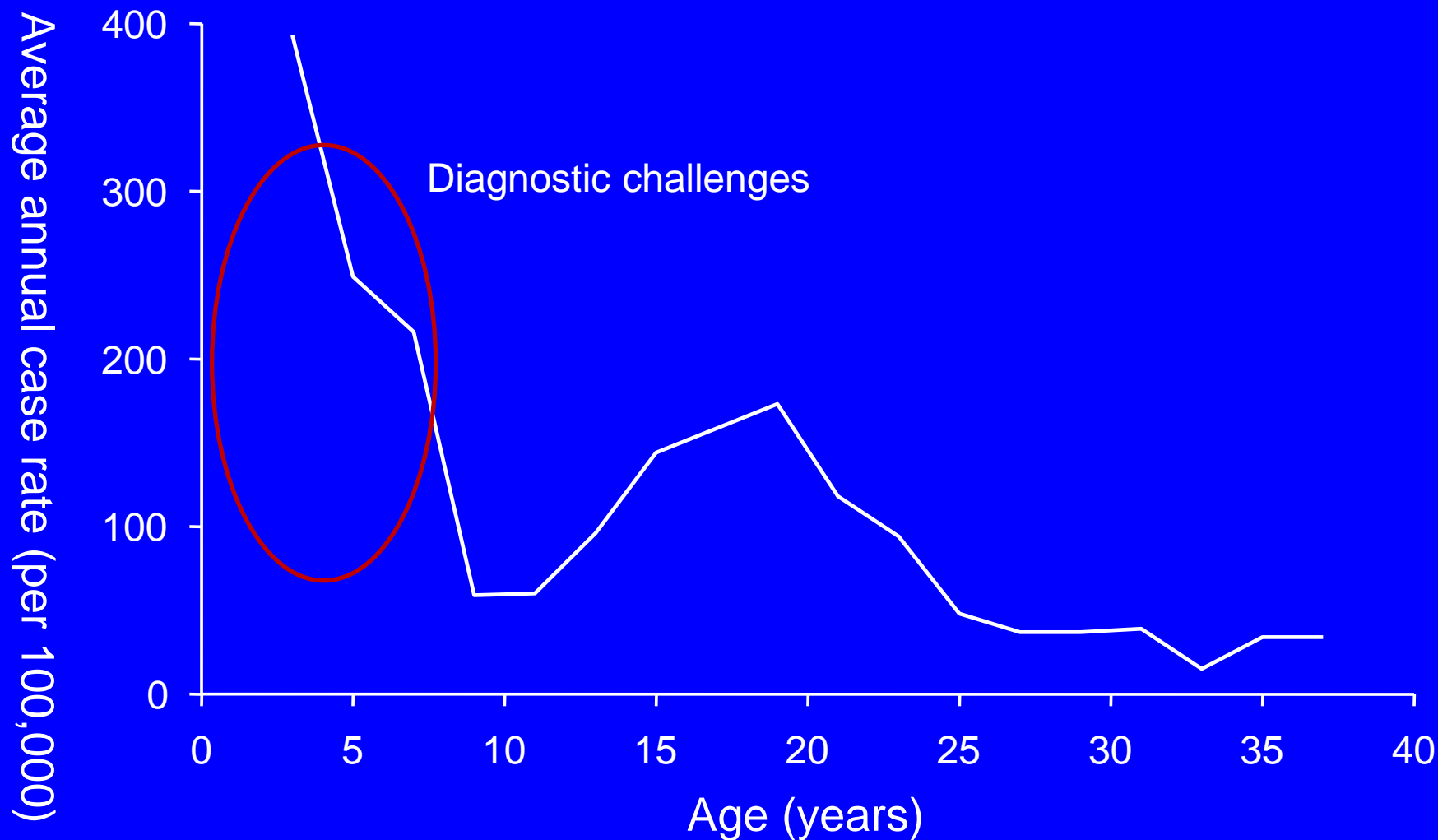


Incidence by age when TB was first diagnosed



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

Incidence by age when TB was first diagnosed



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

Child TB caseload in Malawi in 1998

Harries AD et al. Int J Tuberc Lung Dis 2002

Malawi NTP, 1998	numbers (proportion of childhood caseload)	proportion of total caseload
Total caseload	22,982	
Total childhood	2,739	11.9%
0-4 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%)

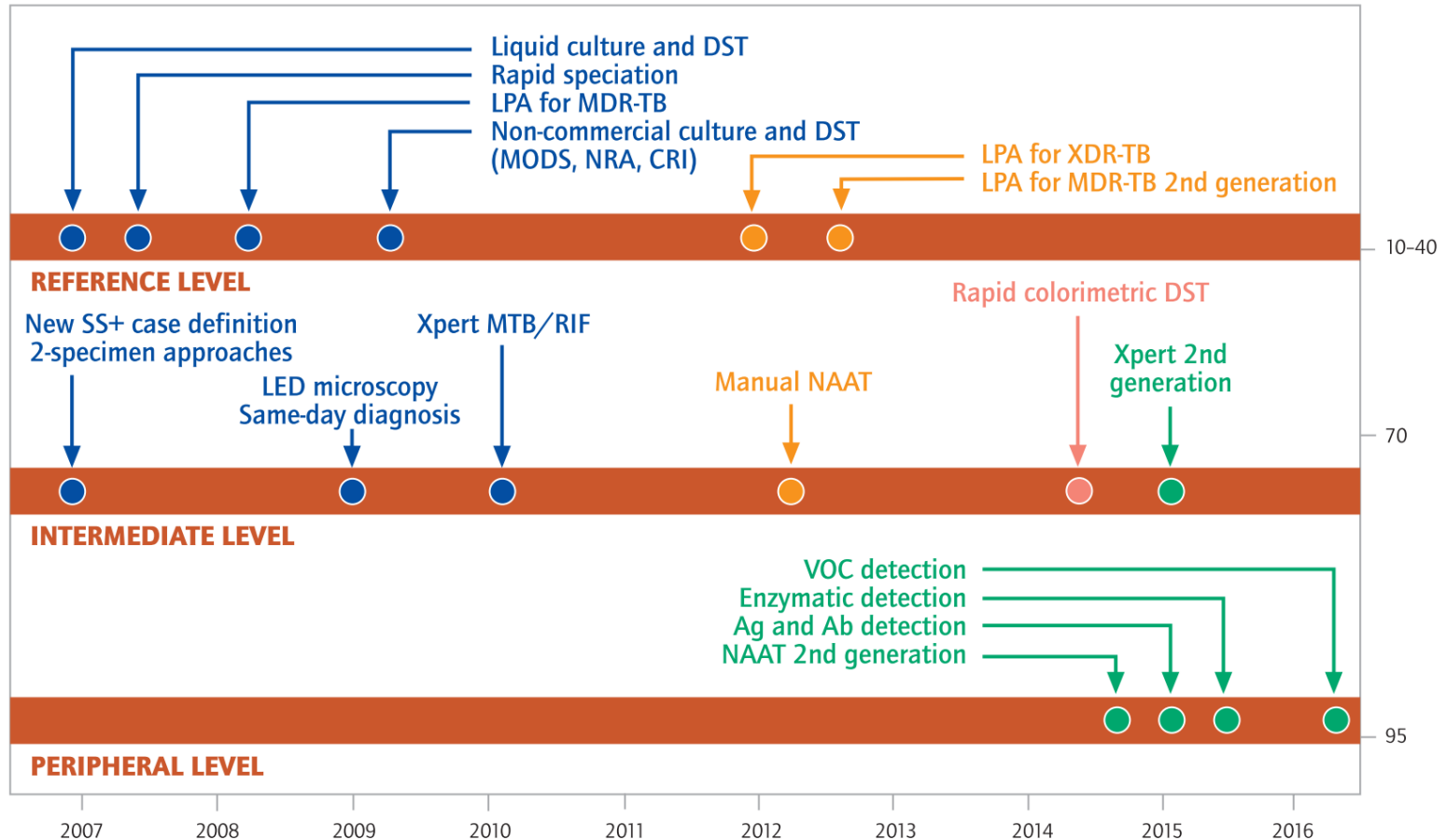
EPTB represented 30% and 39% of childhood TB cases in Malawi and PNG respectively.

Clinical management challenges

“Diagnosis is difficult”



New diagnostics pipeline



■ Technologies or methods endorsed by WHO
■ Technologies commercialized, not yet endorsed by WHO
■ Technologies at feasibility stage
■ Technologies at early stages of development

Access after 5 years (%)

Distance from patients

Test	Publications		Performance in children
	Adults	Children	
Fine needle aspiration	> 6000	140	Potentially good. Most promising when combined with culture or NAAT
Fluorescence Microscopy (FM)	299	1	No data for LED-FM
LED-FM	33	0	
MODS	31	2	More sensitive than LJ. Duplicate GA for MODS was the best diagnostic test in one study
BACTEC 960	49	0	Anecdotic data suggest performance in children's sputum similar to adults
Fully automated BACTEC	13	0	
Line Probe assays	113	1	
LAMP	13	0	
Automated NAAT (Xpert)	32	4	

BOX 2.2

The burden of TB disease among children

For many years, the prevention, diagnosis and treatment of TB among children have been relatively neglected. Greatest attention has been given to the detection and treatment of infectious cases, most of

which occur in adults. The 2006 includes case-finding as children and prevention household as newly detect of TB in children (defined a progress, robust data on of WHO report on global TB c burden of TB disease amor cases and 64 000 deaths , difficult to estimate the bu used to produce this first s to improve them are discus

Challenges in assessing deaths among children

There is no easy-to-use and children. Most children hav diagnose with sputum sme especially younger children,

Diagnosis is usually made using a combination of clinical (as opposed to laboratory) criteria and a non-specific test for tuberculous infection, but there is no universally applied diagnostic algorithm.

The definitive diagnosis of extrapulmonary TB requires specialized

similar results). WHO does not request age-disaggregated data for relapse cases or those reported as of unknown treatment history; the number of children in these categories was assumed to be zero.

“best estimates” of 490 000 cases of TB in children per year

= 6% of the global burden

assumptions that

- **the ratio of notified to incident cases at global level in 2011 was the same as for adults**
- **the reported cases are true cases**

Estimates of TB mortality in children in 2011 – methods and results

Mortality data disaggregated by age from VR systems that have been reported to WHO were analysed. TB death rates per 100 000

Global Tuberculosis Report 2012

Child TB data and NTP

Indonesia 2010 data: 296,272 total cases
28,312 child TB cases or 9.6%

WHO Global TB Report, 2011

Marked variation between provinces: 1.5% to 17%

More common in 5-14 years

In some provinces, sputum smear positive 25-30% of child TB cases

Contact screening minimal

TB Prevalence in Lao PDR: Age ≥ 15 years

Smear Positive cases:

263 per 100,000 (95%CI 189-339)

Culture Positive cases:

606 per 100,000 (95%CI 458-753)

78 cases of total child TB in 2012

< 5 per 100,000 child population

Smear-positive or lymph node disease

RESEARCH ARTICLE

Open Access

High caseload of childhood tuberculosis in hospitals on Java Island, Indonesia: a cross sectional study

Trisasi Lestari^{1*}, Ari Probandari², Anna-Karin Hurtig³ and Adi Utarini¹

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

Burden of child TB in Java 2005

TB cases	Inpatient	Outpatient	Overall
Total TB cases	5,877	15,694	21,571
Child TB cases	N=648	N=4173	N=4821
% of total burden	11%	27%	22%
< 5 years	56%	53%	53%
Smear positive disease	16%	8%	9%
EPTB	15%	6%	8%
Non-teaching hospital	73%	76%	75%
Private health facility	8%	7%	7%

Diagnosis is central

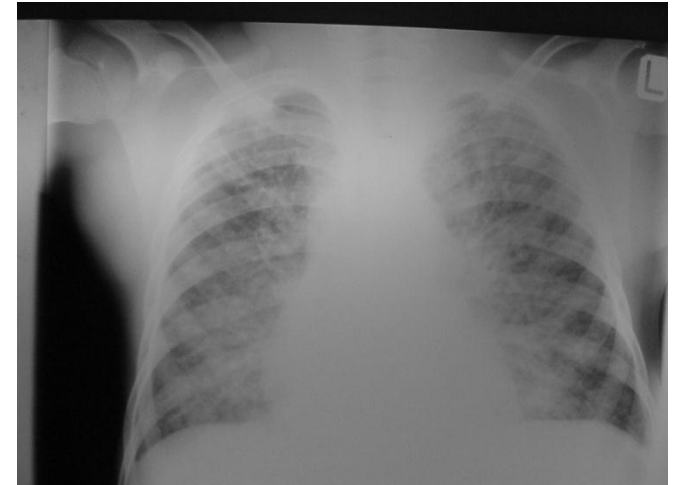
Diagnosis is critical

Diagnosis is (usually) clinical

Diagnosis can be challenging

Clinical challenges are the diagnostic challenges

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



Recommended approach to diagnose TB in children

WHO Guidance for NTP on management of TB in children 2006

1. Careful history

includes history of TB contact
symptoms suggestive of TB

2. Clinical examination

includes growth assessment

3. Tuberculin skin test

4. Bacteriological confirmation whenever possible

5. Investigations relevant for suspected PTB or suspected EPTB

6. HIV testing

Recommended approach to diagnose TB in children

1. Careful history

includes history of TB contact
symptoms suggestive of TB

Note that TST and culture are often unavailable. Neither is required for a decision to treat for TB in most cases.

2. Clinical examination

includes growth assessment

CXR is an important tool for diagnosis of TB in children

3. Tuberculin skin test

Sputum should be collected for smear microscopy if available

4. Bacteriological confirmation whenever possible

as in older children

5. Investigations relevant for suspected PTB or suspected EPTB

6. HIV testing routine

SYMPOSIUM ON PEDIATRIC TUBERCULOSIS

The Use of Diagnostic Systems for Tuberculosis in Children

Stephen M. Graham

Table 2 The Keith Edwards (Papua New Guinea) TB score [22]

Feature	0	1	2	3	4	Score
Duration of illness (in weeks)	<2	2–4		>4		
Nutrition status (% of wt for age)	>80	60–80		<60		
Family history of TB	None	Family history of TB, but not sputum-positive		Family member with sputum-positive TB		
Significant Mantoux (..... mm)				Positive		
Lymph nodes: large, painless, firm; sinus in neck/axilla				Yes		
Night sweats or unexplained fever for >2 wks			Yes			
Angle deformity of spine					Yes	
Malnutrition not improving after 4 wks of treatment				Yes		
Joint swelling, firm, non-fluid, non-traumatic				Yes		
Unexplained ascites				Yes		
Coma for >48 h (with or without convulsions)				Yes		
				TOTAL ^a		

^aA total score of 7 or more indicates a high likelihood of TB

Structured approaches for the screening and diagnosis of childhood tuberculosis in a high prevalence region of South Africa

Mark Hatherill,^a Monique Hanslo,^a Tony Hawkrigde,^b Francesca Little,^c Lesley Workman,^a Hassan Mahomed,^a Michele Tameris,^a Sizulu Moyo,^a Hennie Geldenhuys,^a Willem Hanekom,^a Lawrence Geiter^d & Gregory Hussey^a

Bull World Health Organ 2010;88:312–320 | doi:10.2471/BLT.09.062893

Fig. 1. Frequency of cases classified as tuberculosis with various scoring systems, with hierarchical and numerical outcomes condensed to a binary “tuberculosis/not tuberculosis” output, South Africa, 2001–2006

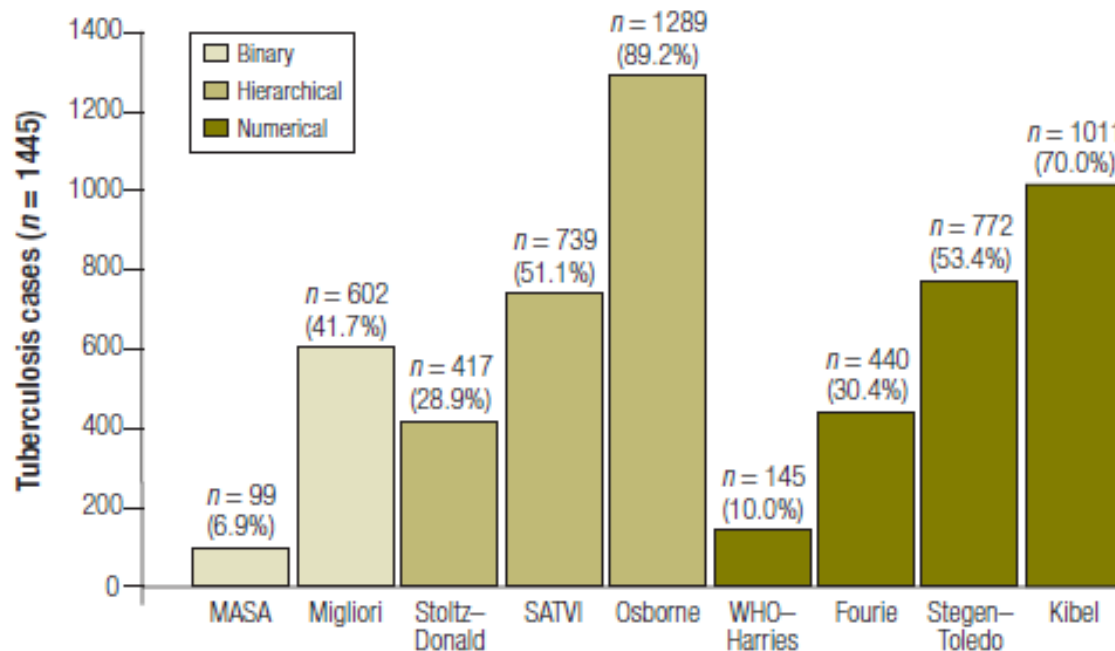


Table 3 Score system for diagnosis of pulmonary tuberculosis in children. Ministry of Health, Brazil (27,28)

Clinical manifestations	Score
Fever or cough, lost energy, sputum, weight loss, night sweats >2 weeks	+15
No symptoms or symptoms <2 weeks	0
Respiratory infection improving with or without antibiotic therapy for common bacteria	-10
Thoracic X-ray	
Enlarged hilum or miliary pattern	+15
Exudate or patch shadow (with or without cavitation) unaltered >2 weeks or worse with antibiotic therapy for common bacteria	+15
Exudate or patch shadow (with or without cavitation) <2 weeks	+5
Normal	-5
Contact with tuberculous adult	
Close, <2 years	+10
None or occasional	0
BCG vaccination and Tuberculin test	
BCG 2 years or no BCG (≥ 10 mm)	+15
BCG <2 years (≥ 15 mm)	+15
BCG yes/no (5 mm to 9 mm)	+5
BCG yes/no (≤ 5 mm)	0
Nutritional status	
Severe malnutrition (grade III)	+5
Eutrophic or no severe malnutrition	0

Score interpretation: ≥ 40 : PTB very likely; 30–35: possible PTB; ≤ 25 : PTB unlikely

Cut-off of ≥ 40 :
sensitivity of 52%
specificity of 98%

Scores were lower in
HIV-infected children

Child TB diagnosis in Malawian hospitals

Weismuller MM, Graham SM et al. Int J Tuberc Lung Dis 2002

	Number (%) of patients	Number (%) in each type of hospital		
		<u>Central</u>	<u>District</u>	<u>Mission</u>
All childhood TB	150	36	74	40
<u>PTB:</u>	98	21	51	26
CXR	93 (95)	20 (95)	49 (96)	24 (92)
tuberculin test	6 (6)	4 (19)	1 (2)	1 (4)
sputum submission	6 (6)	0	5 (10)	1 (4)
gastric aspirate	2 (2)	0	0	2 (8)
HIV serology	6 (6)	1 (5)	3 (6)	2 (8)

Structured approaches for the screening and diagnosis of childhood tuberculosis in a high prevalence region of South Africa

Mark Hatherill,^a Monique Hanslo,^a Tony Hawkridge,^b Francesca Little,^c Lesley Workman,^a Hassan Mahomed,^a Michele Tameris,^a Sizulu Moyo,^a Hennie Geldenhuys,^a Willem Hanekom,^a Lawrence Geiter^d & Gregory Hussey^a

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Table 1. Results of chest radiograph assessment by three independent paediatric reviewers, grouped by certainty of tuberculosis diagnosis, South Africa, 2001–2006

Diagnostic certainty ^a	Reviewer 1		Reviewer 2		Reviewer 3		Final classification	
	No.	%	No.	%	No.	%	No.	%
Highly likely to have tuberculosis	16	1.1	29	2.0	171	11.8		
Likely to have tuberculosis	20	1.4	38	2.6	323	22.4		
Suspected of having tuberculosis	124	8.6	145	10.0	242	16.7		
Positive	160	11.1	212	14.6	736	50.9	271	18.8
Inconclusive	45	3.1	35	2.4	82	5.7		
Abnormal but not tuberculosis	102	7.1	139	9.6	312	21.6		
Normal	1038	71.8	778	53.9	59	4.1		
Negative	1185	82.0	952	65.9	453	31.4	1174	81.2
Not read	100	6.9	281	19.5	256	17.7		
Total	1445	100	1445	100	1445	100	1445	100

Desk-guide for diagnosis and management of TB in children



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

Diagnosis of PTB

Typical symptoms

- ❖ Cough especially if persistent and not improving
- ❖ Weight loss or failure to gain weight
- ❖ Fever and/or night sweats
- ❖ Fatigue, reduced playfulness, less active

Especially if symptoms persist (>2 weeks) without improvement following other appropriate therapies (e.g. broad-spectrum antibiotics for cough; anti-malarial treatment for fever; or nutritional rehabilitation for malnutrition)

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

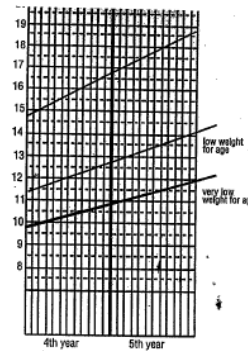
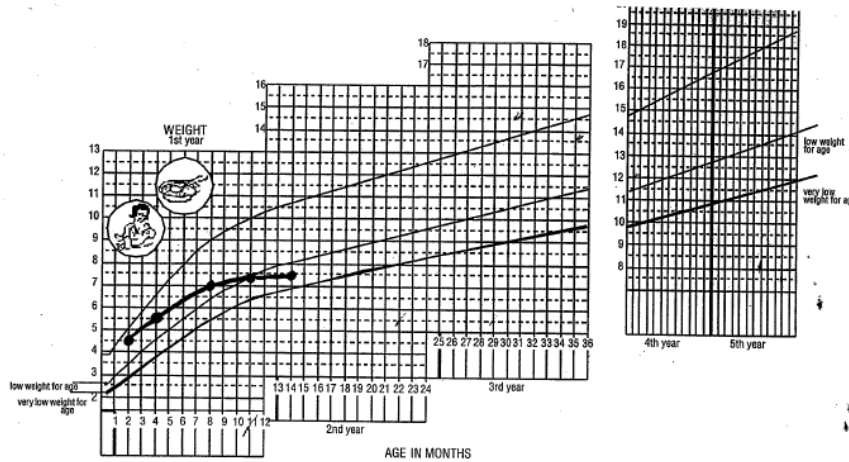
History of contact

note the following.....

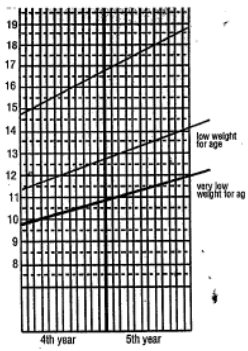
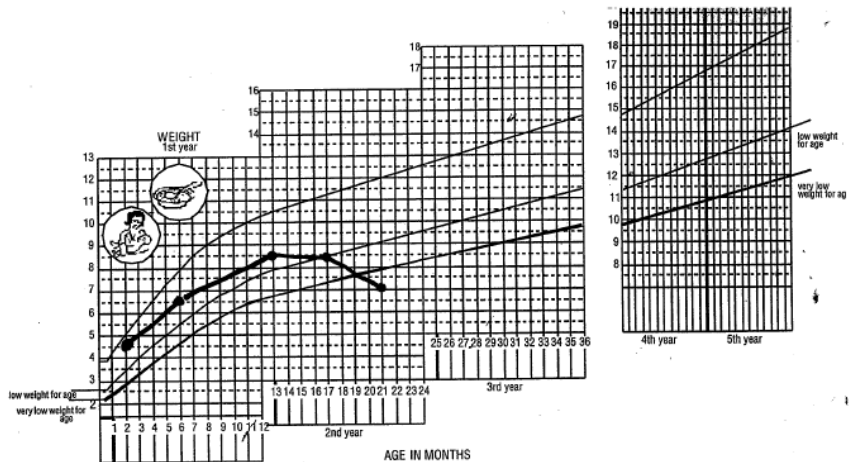
- ❖ Closeness of contact
- ❖ Sputum smear result of index case (if known)
- ❖ Timing of contact
 - children usually develop TB within 2 years after exposure and most (90%) within the first year

- ❖ If no source case is identified, always ask about anyone in household with cough – if so, request assessment of that person for possible TB

Check weight, record weight and compare to previous weights

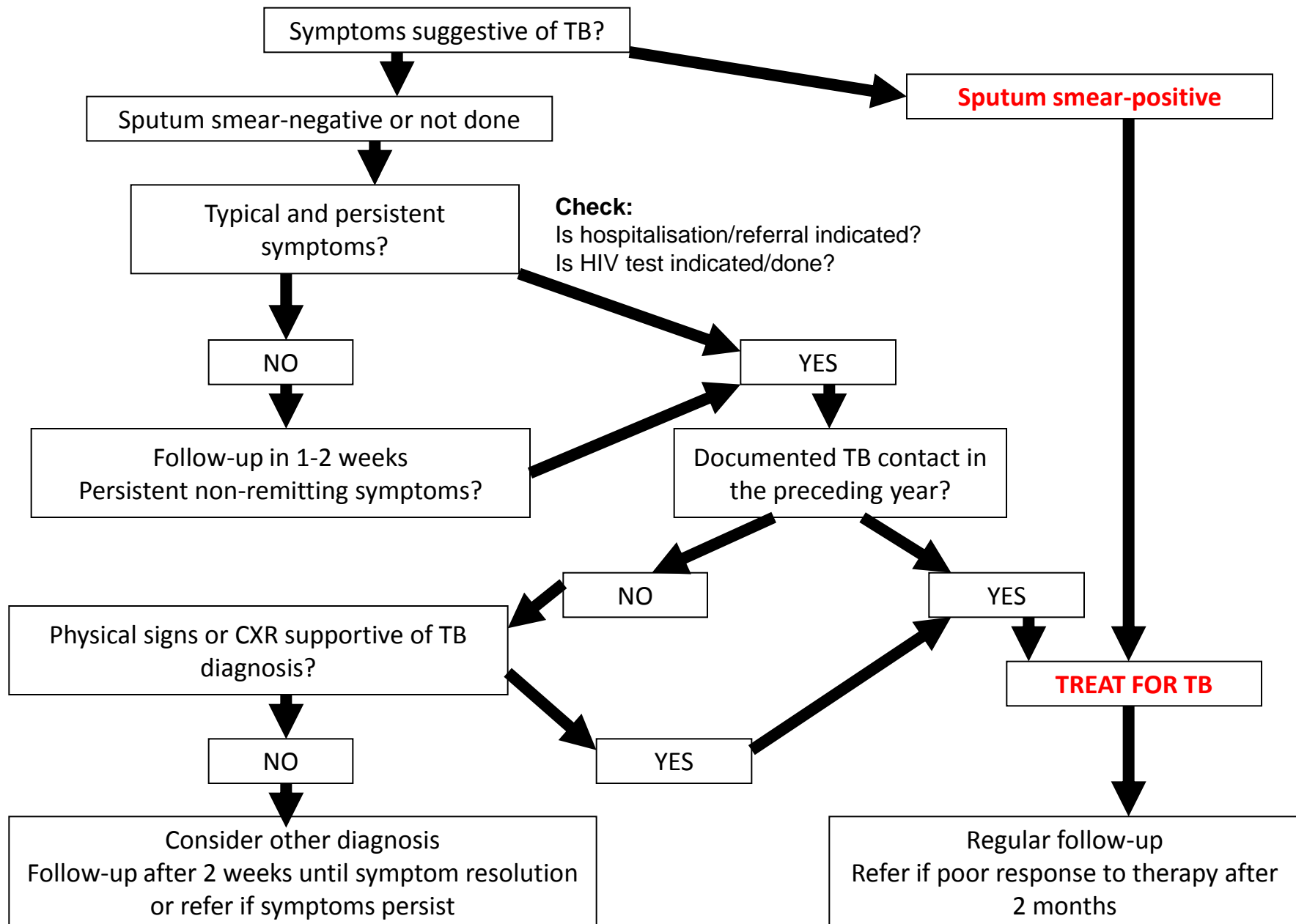


Growth faltering or failure to thrive



Weight loss

Guidance for the diagnosis of children who present with symptoms



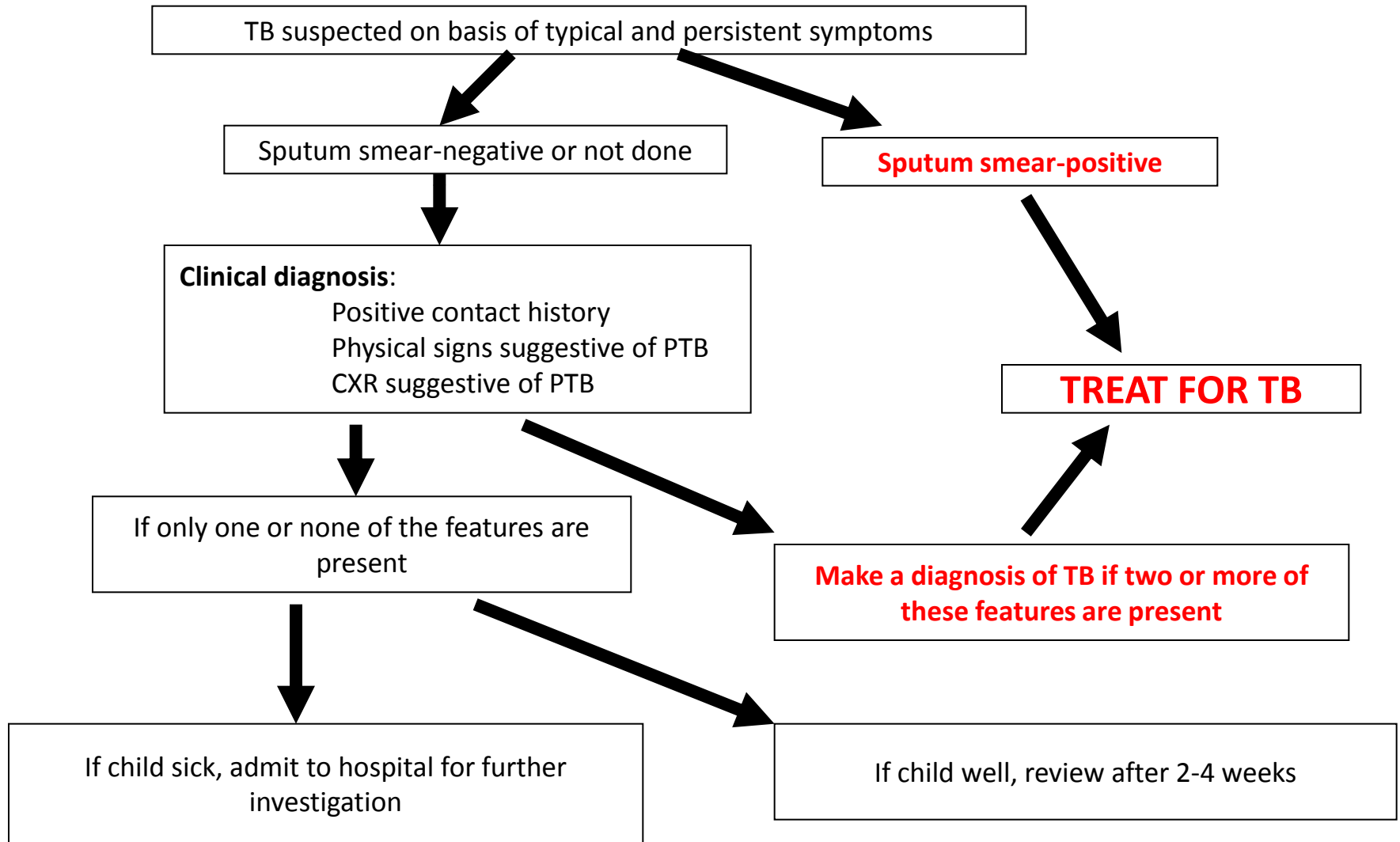
HIV and TB in children

HIV infection status should be established in all children with suspected TB

HIV test is extremely useful and important because:

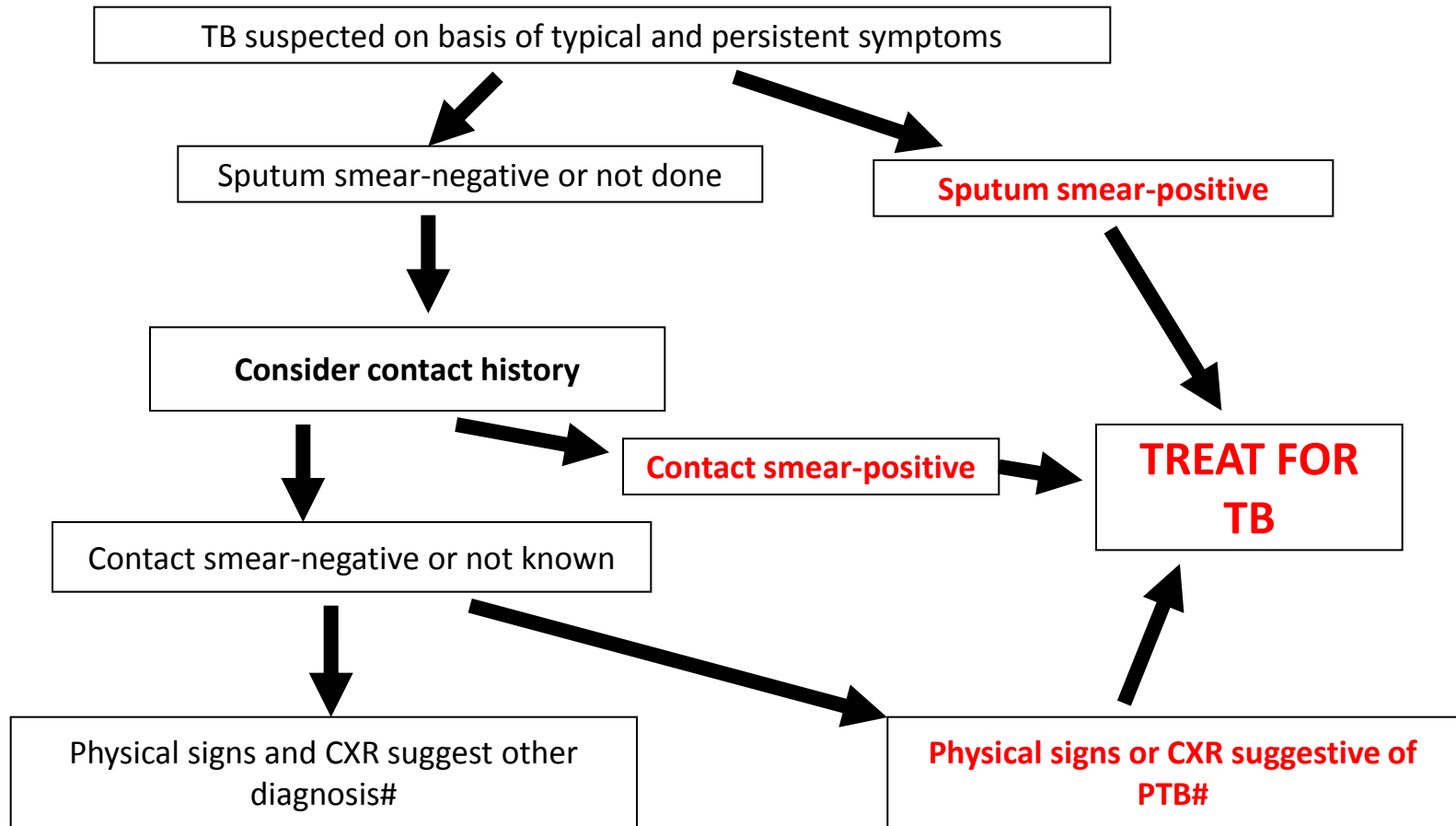
1. Exclusion of HIV reduces the diagnostic possibilities
2. Need for HIV-related care in addition to management of TB

Approach to TB diagnosis in HIV-uninfected child



Decision for further outpatient review or inpatient management or referral will clearly depend on clinical state and available levels of care.

Approach to TB diagnosis in HIV-infected child



It can be difficult to clearly define what is “suggestive of PTB” on clinical or radiological findings in HIV-infected children because of clinical overlap between PTB and other forms of HIV-related lung disease: note further slides with Table and CXRs.

CXR abnormalities of PTB in HIV-infected children are mainly similar to those in HIV-uninfected children.

Clinical approach to TB diagnosis

Note that clinical assessment should include decision for hospitalisation or referral depending on severity of clinical signs or need for other appropriate management

INDICATIONS REQUIRING HOSPITALIZATION/REFERRAL

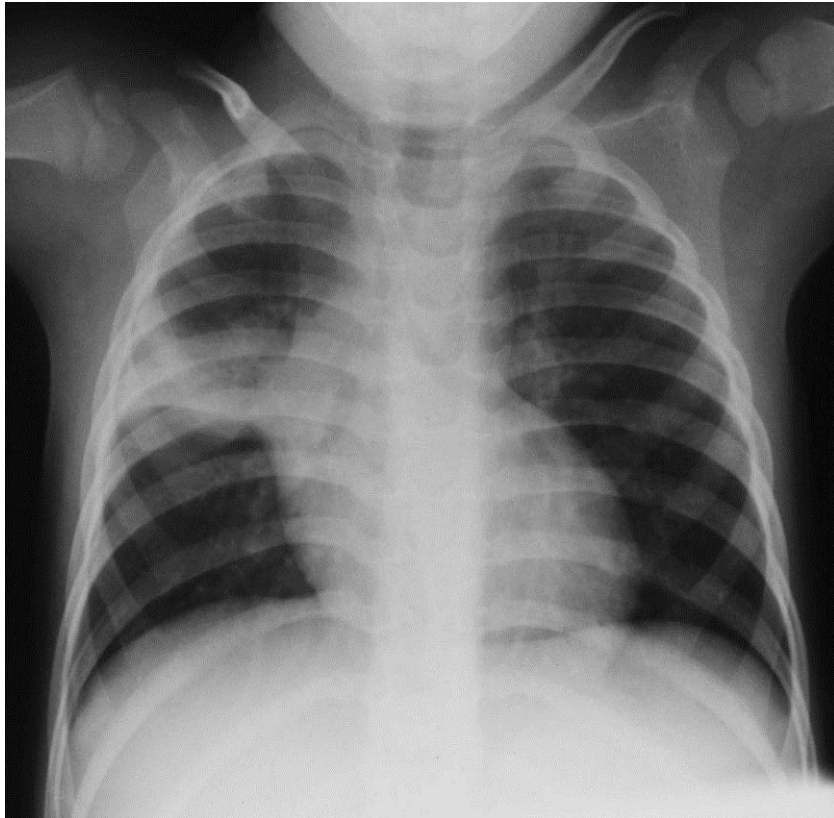
- Severe forms of PTB and EPTB for further investigation and initial management
- Severe malnutrition for nutritional rehabilitation
- Signs of severe pneumonia (i.e. chest in-drawing) or respiratory distress
- Other co-morbidities e.g. severe anaemia

Referral should also be considered if

- Diagnostic uncertainty requiring further investigation at referral level
- Necessary for HIV-related care e.g. to commence ART

Diagnostic atlas of intrathoracic tuberculosis in children:
a guide for low-income countries 2003.

Robert Gie, IUATLD



Freely available on-line

<http://www.theunion.org/index.php/en/component/flexicontent/items/item/110-diagnostic-atlas-of-intrathoracic-tuberculosis-in-children>

Checklist: the symptomatic child with suspected TB

1. Are the symptoms persistent and typical of TB?
2. Is there a positive contact history?
3. Check growth chart and record weight
4. Is the child HIV infected?
5. Is hospitalization or referral indicated?

If the child is not so sick that hospitalization or immediate referral is required, then follow-up is an important tool to determine persistence of symptoms or poor weight gain.

Clinical approach to diagnosis of EPTB

Extrapulmonary TB is common in children and presentation varies with age.

Symptoms vary depending on site of disease and characteristically are persistent, progressive and may be associated with weight loss or poor weight gain.

Clinical assessment in all cases should consider:

History of contact

Sputum for smear microscopy

HIV test

Diagnosis of TB adenitis

TB adenitis is most common in cervical region. Lymph node enlargement is painless and asymmetrical, often multiple, discreet or matted.

Nodes are typically large (>2 x 2 cm) i.e. visibly enlarged not just palpable.

Lymph node enlargement is persistent (>1 month) and not responsive to other treatment such as antibiotics.

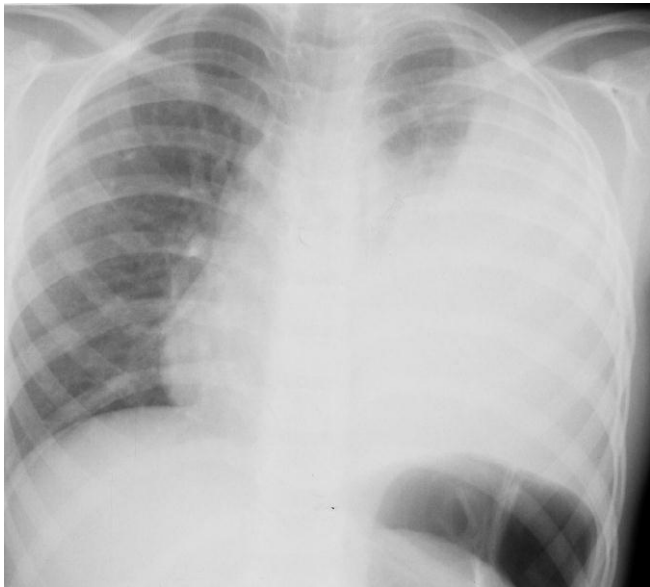
Sinus and discharge may develop.

Usual age is 2-10 years.

May or may not be associated with other symptoms of TB.

TST (if available) usually strongly reactive.





TB pleural effusion is common and tends to occur in school-aged children.

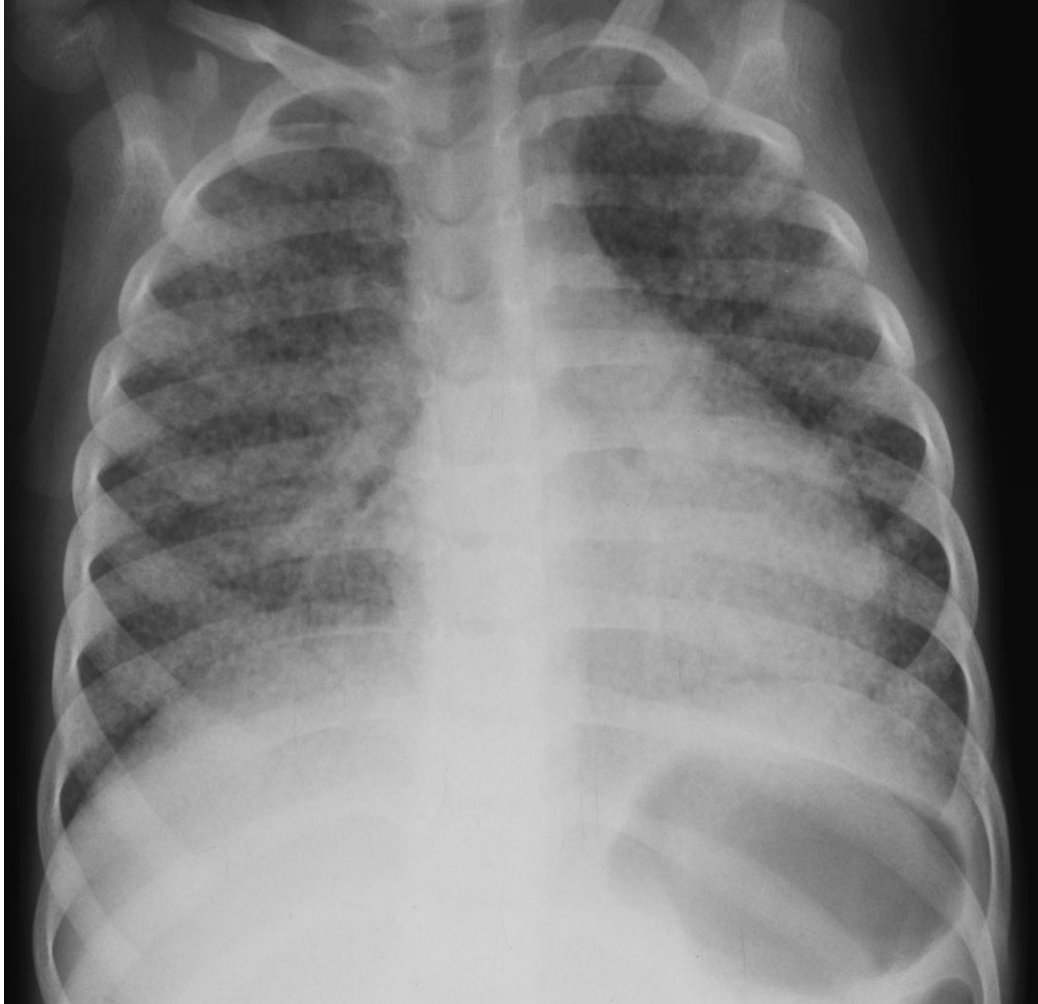
Pleural tap safe and very useful as may need to differentiate TB from suppurative empyema

Other less common sites for effusion, usually painless, include peritoneal and pericardial spaces, also usually in school-aged children.

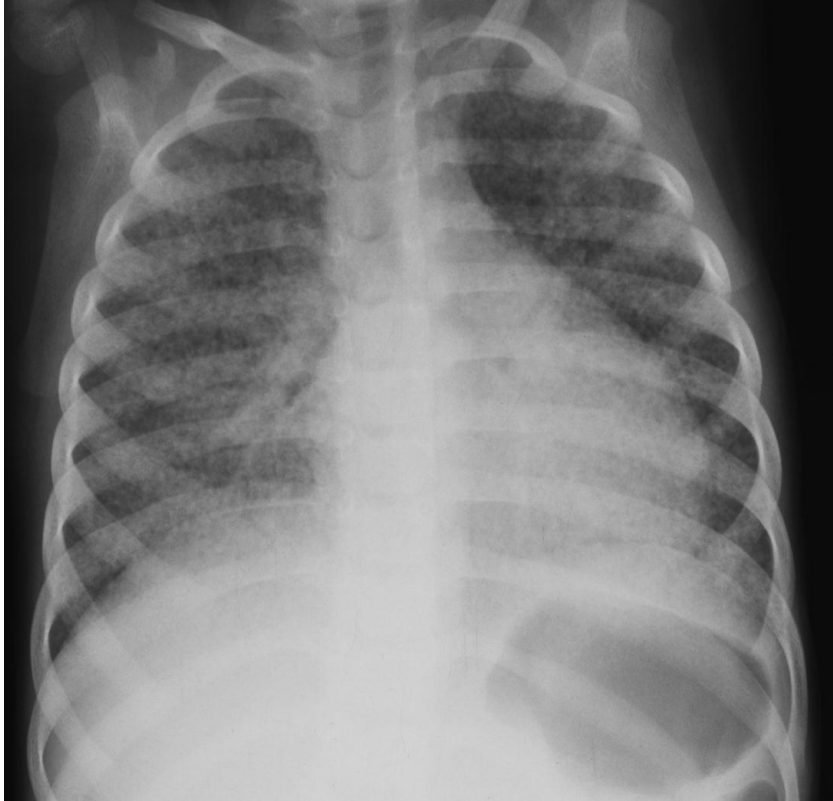
Ultrasound and tap of effusion for microscopy and protein is very useful.



This CXR shows the classical bilateral diffuse micronodular pattern consistent with miliary TB.



Miliary TB can be difficult to differentiate in HIV-infected children from the diffuse reticulonodular pattern of LIP.



Osteoarticular TB is not uncommon in children, again in school-aged group.

Spinal TB causes destruction of vertebral bodies leading to typical spinal deformity and possibly paralysis.

Hips and knees are the other typical site, usually mono-articular with painless effusion. Joint tap helpful to distinguish from septic arthritis.



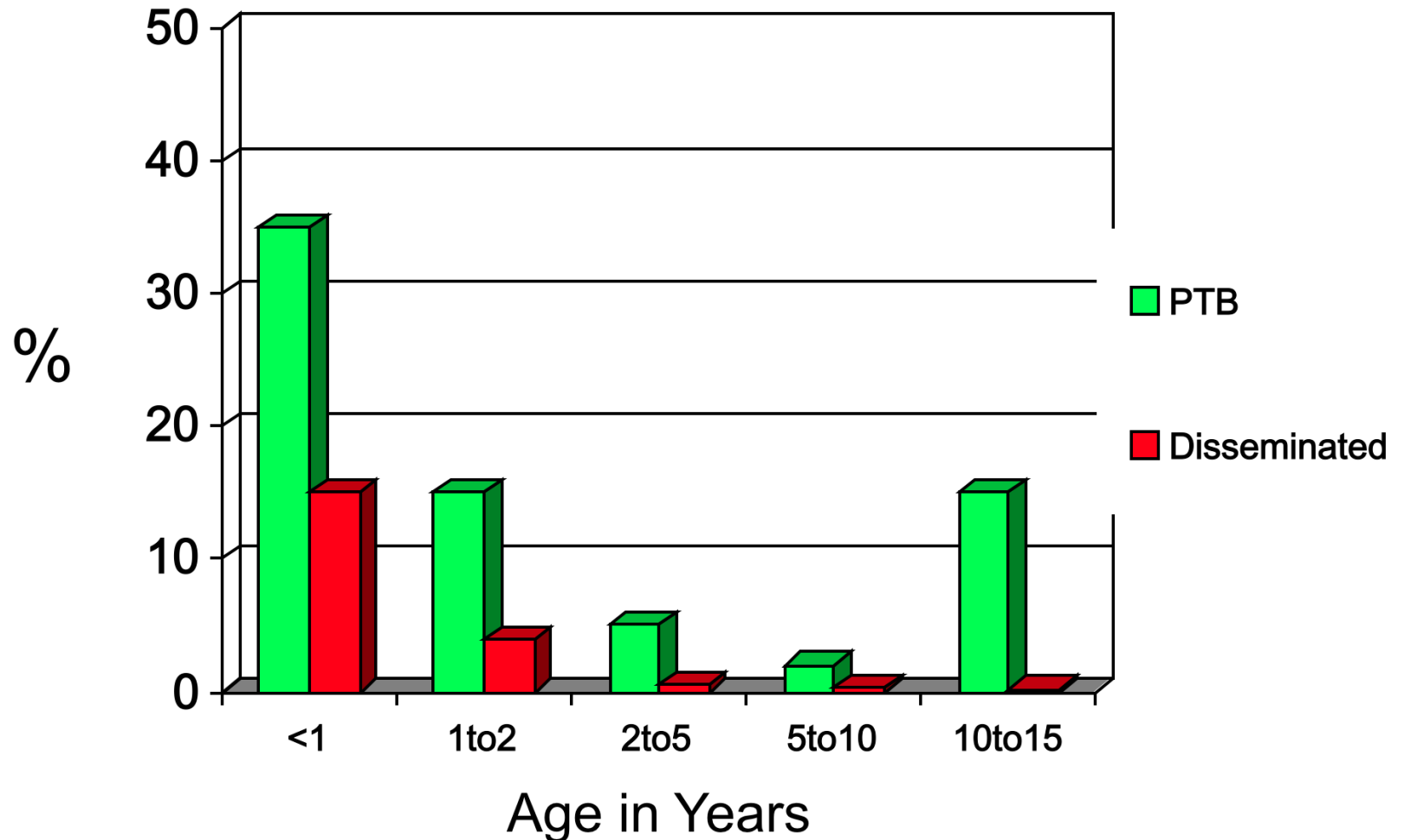
Child TB data and NTP

All children diagnosed with TB should be registered with NTP

Important information includes age, TB type, HIV status and treatment outcome – as for all cases with TB

These data are important for M&E as well as informing training activities, drug procurement, strategic plans etc

Risk of TB disease following infection by age



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 %*

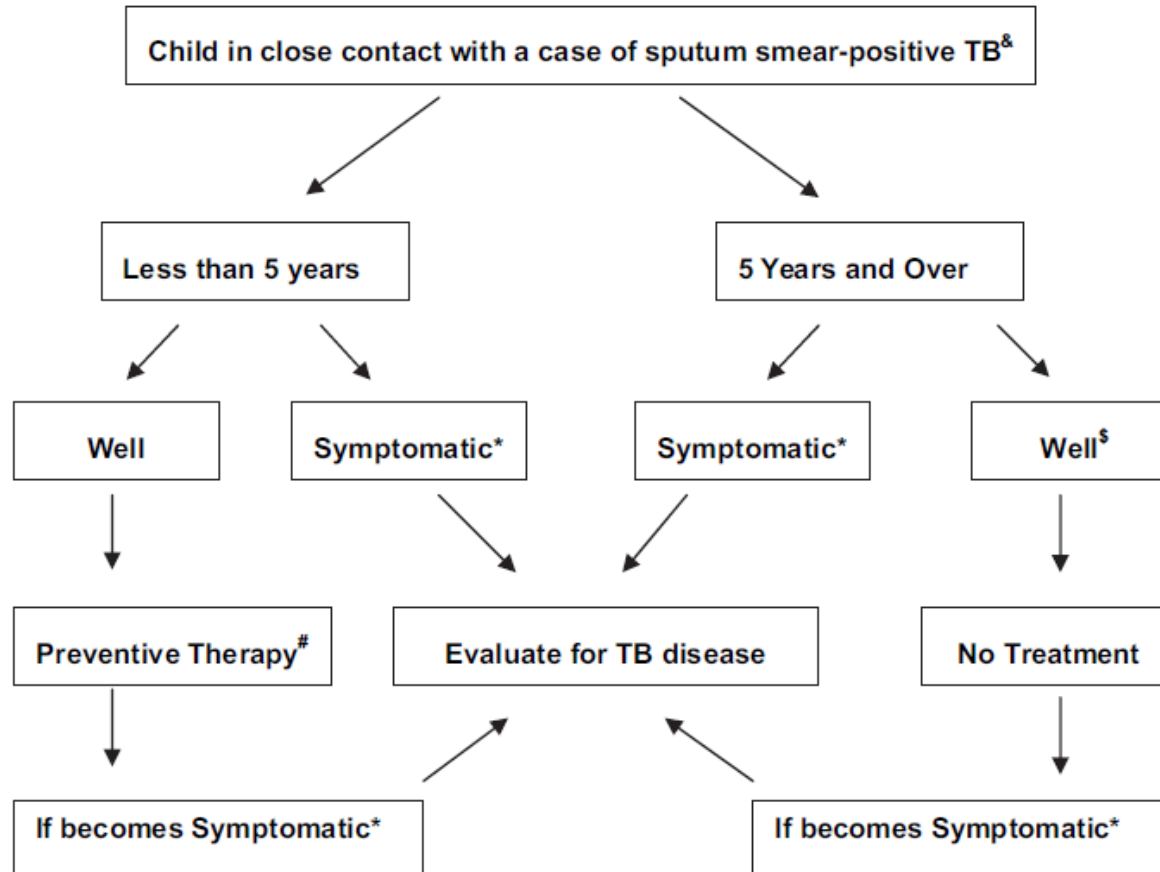
* Data only for < 5 years; NR: not recorded

Symptom-based screening of child contacts is recommended by WHO

WHO/HTM/TB/2006.371
WHO/FCH/CAH/2006.7

**Guidance for national
tuberculosis programmes
on the management of
tuberculosis in children**





[&] Also consider if the mother or primary caregiver has sputum smear-negative pulmonary TB

^{*} Symptomatic: If TB is suspected, refer to local guidelines on diagnosis of childhood TB

[#] Isoniazid 10/mg/kg daily for 6 months

[§] Unless the child is HIV-infected (in which case isoniazid 10/mg/kg daily for 6 months is indicated)

Thank you



EVERYONE

TELLS ME TO MOVE ON

NO ONE TELLS ME HOW