



TOWARDS
ZERO
DEATHS

Module 4

PREVENTION OF CHILDHOOD TB



International Union
Against Tuberculosis
and Lung Disease



World Health
Organization

Available approaches to prevent TB in children



Improved case-finding and management	Early identification and effective treatment of infectious TB cases will reduce the burden of child TB

Available approaches to prevent TB in children



Improved case-finding and management	Early identification and effective treatment of infectious TB cases will reduce the burden of child TB
BCG	Neonatal BCG immunisation is used widely but efficacy is variable The main proven benefit of neonatal BCG is protection against severe disseminated forms of TB in children

Effectiveness of BCG is variable



- BCG more protective against disseminated TB and TBM than pulmonary TB
- BCG has a role in prevention of leprosy
- BCG effectiveness to protect from TB also depends on:
 - BCG strain used
 - Age it is given
 - Region

BCG protects against disseminated TB in children



	Publication date	Efficacy (% , 95% CI)		Publication date	Efficacy (% , 95% CI)
Tuberculous meningitis			Miliary tuberculosis		
Buenos Aires, Argentina	1988	98% (70 to 100)	Buenos Aires, Argentina	1988	78% (28 to 93)
Bahia, Brazil	1991	91% (78 to 97)	Yangon, Burma	1987	80% (45 to 92)
São Paulo, Brazil	1990/93	87% (72 to 94)	Papua New Guinea*	1980	70% (0 to 91)
São Paulo, Brazil	1990/93	92% (65 to 98)	Djakarta, Indonesia	1983	75% (5 to 94)
Belo Horizonte, Brazil	1988	81% (47 to 93)	Summary efficacy		77% (58 to 87)
Belo Horizonte, Brazil	1988	65% (17 to 86)			
Yangon, Burma	1987	52% (13 to 73)			
Nagpur, India	1996	87% (70 to 94)			
Chennai, India	1996	77% (63 to 86)			
Delhi, India	1996	64% (30 to 81)			
Delhi, India	1989	84% (69 to 97)			
Lucknow, India	1999	47% (-6 to 74)			
Papua New Guinea*	1980	58% (-36 to 87)			
Delhi, India	1993	56% (-49 to 87)			
Summary efficacy		73% (67 to 79)			

**Summary Efficacy
Miliary Tuberculosis 77%**

**Summary Efficacy
Tuberculous Meningitis 73%**

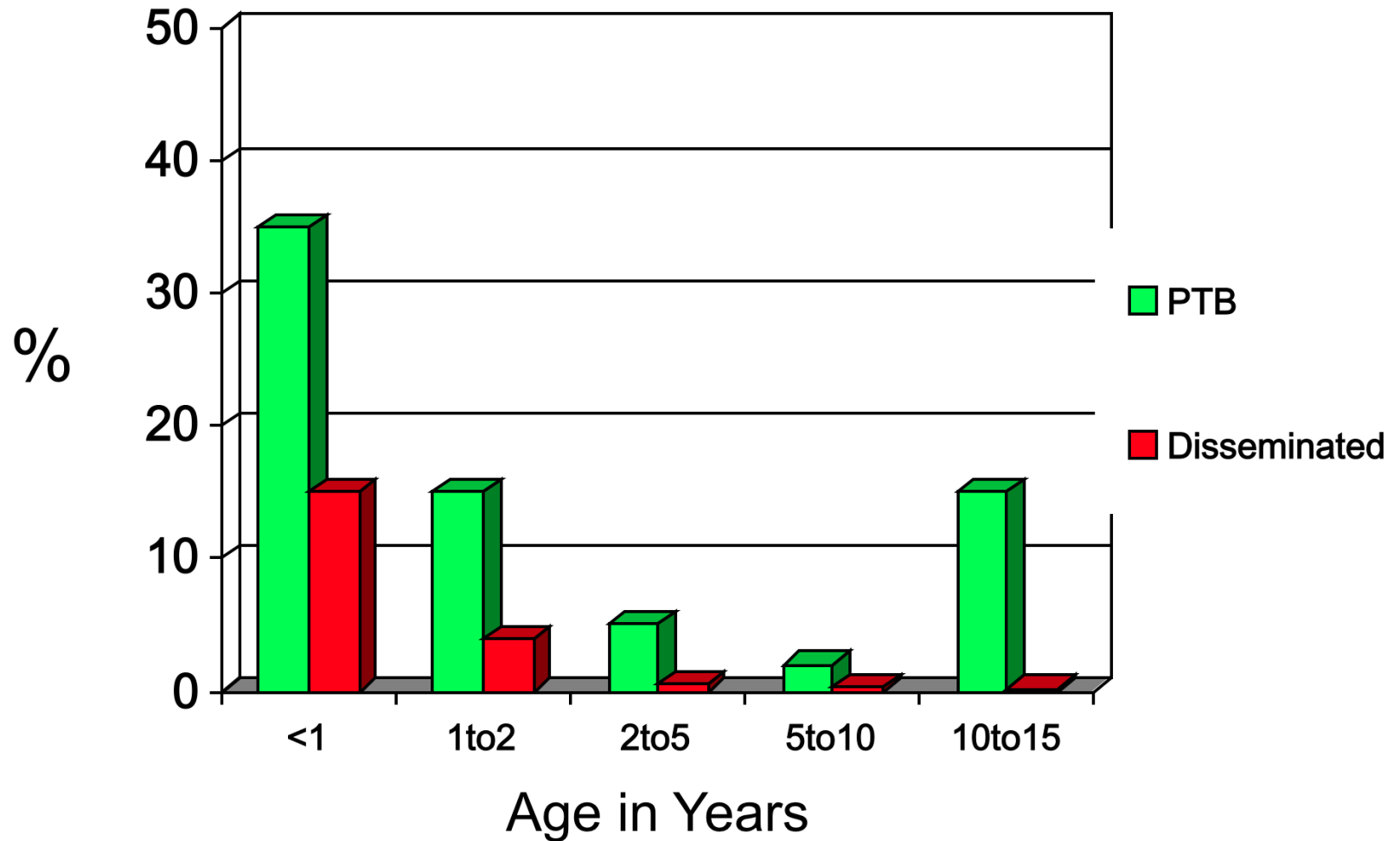
Trunz, et al. Lancet 2006

Available approaches to prevent TB in children



Improved case-finding and management	Early identification and effective treatment of infectious TB cases will reduce the burden of child TB
BCG	Neonatal BCG immunisation is used widely but efficacy is variable The main proven benefit of neonatal BCG is protection against severe disseminated forms of TB in children
Contact screening and management	This has huge potential to reduce the burden of TB in children Focus is on individuals infected with TB that have greatest likelihood of developing active TB disease following infection – this includes infants, young children and HIV-infected children of any age Widely recommended but uptake by families and implementation by NTP are poor

Risk of TB disease following infection by age



Studies of child contacts in African communities



- One-third to two-thirds of child household contacts of TB cases have evidence of TB infection i.e. TST positive
- Incidence of TB disease among household contacts is very high – reported as >1,000 cases/100,000 population
- Likelihood of infection is related to closeness/proximity of contact to and sputum smear positivity of index case
- Risk of infection greatest when the index case is the child's carer e.g. mother, grandmother
- HIV-infected children are at increased risk of exposure to TB

Kenyon TA et al, *Int J Tuberc Lung Dis* 2002; Sinfield R, et al *Ann Trop Paediatr* 2006;

Jackson-Sillah D, et al *Trans R Soc Trop Med Hyg* 2007; Morrison J, et al *Lancet Infect Dis* 2008

Studies of child contacts in Asian countries



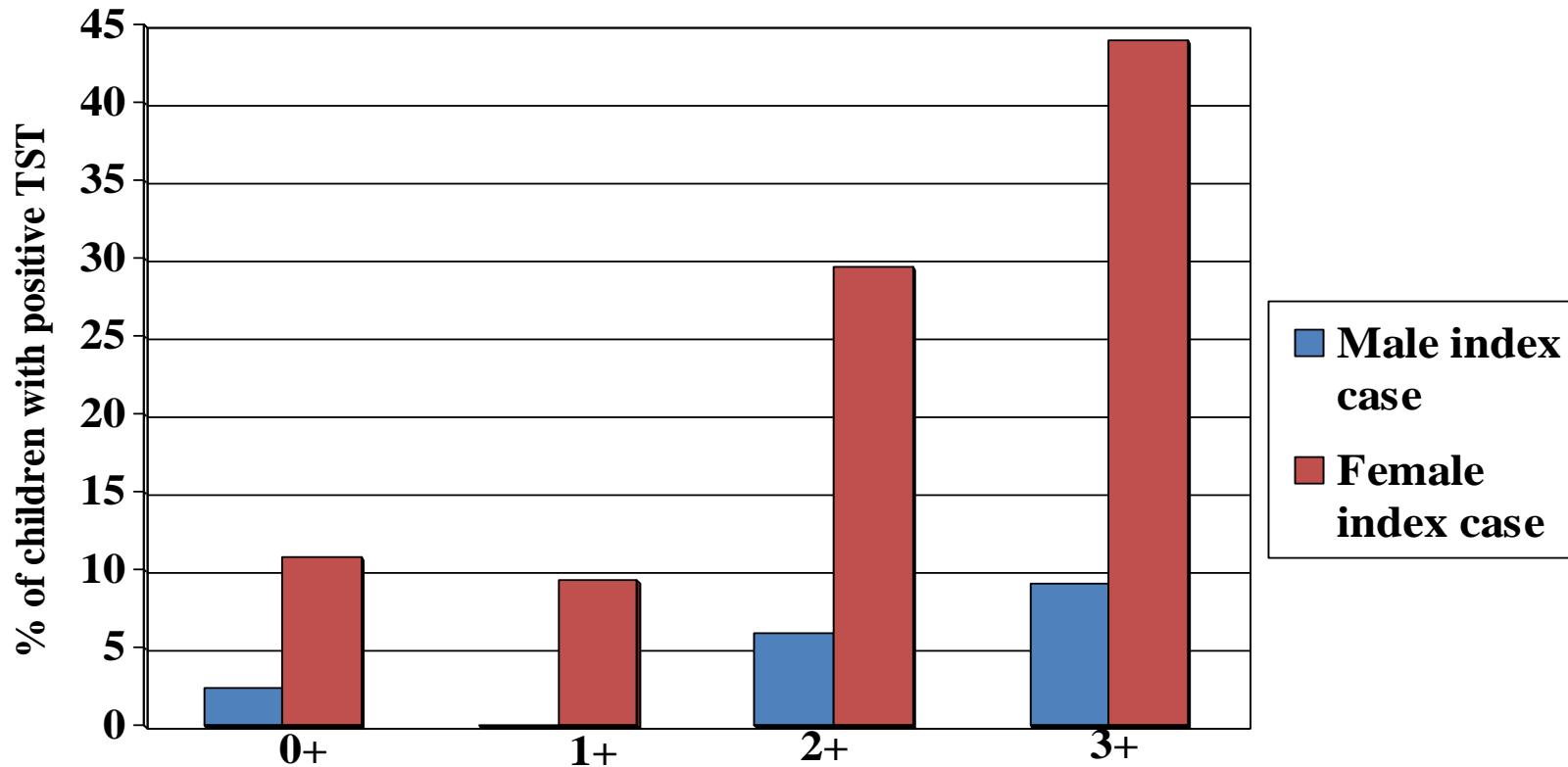
Study	Location	No. of child contacts	Proportion with TB infection	Proportion with TB disease
Andrew et al	India	398	39 %	5.5 %
Narain et al	India	790	24 %	NR
Kumar et al	India	142	NR	3 %*
Singh et al	India	281	34 %*	3 %*
Rathi et al	Pakistan	151	27 %	NR
Salazar et al	Philippines	153	69 %	3 %
Tornee et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

From Triasih R et al, J Trop Med 2012

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

Proportion of children with TB infection (positive TST) by degree of smear positivity of the source case

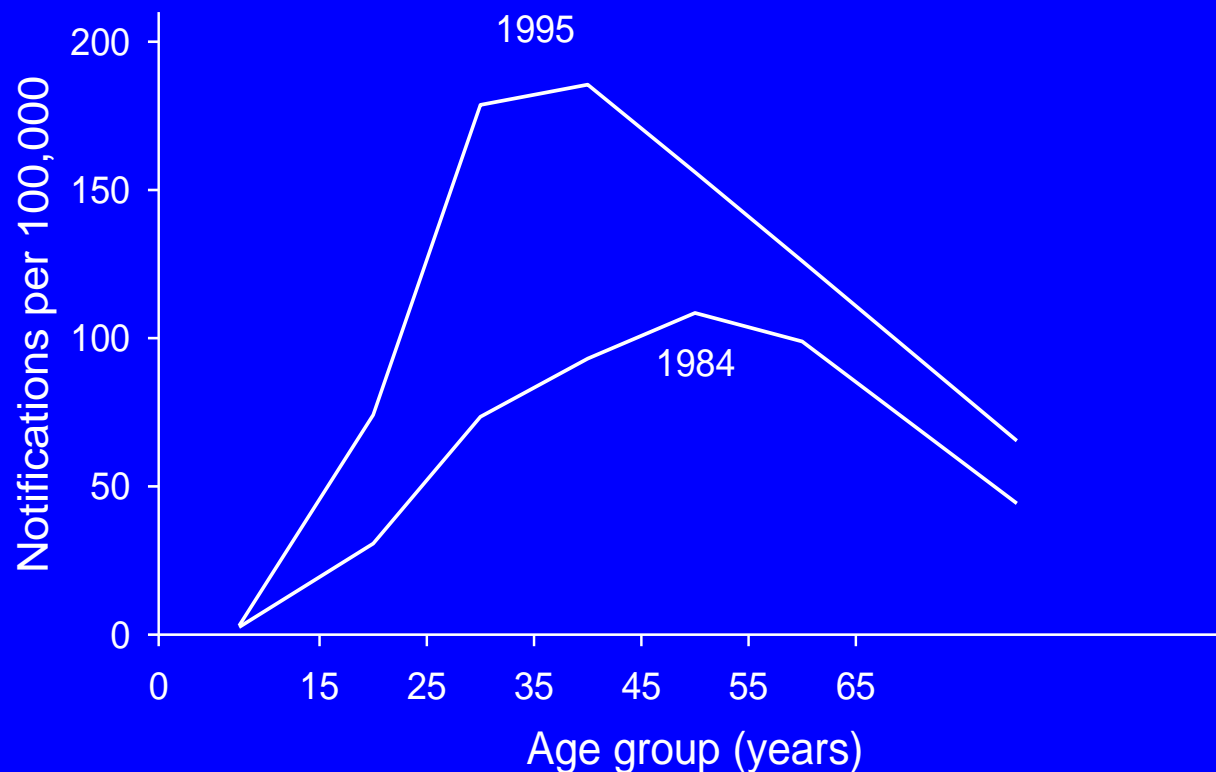
Kenyon TA et al, Int J Tuberc Lung Dis 2002



Increased risk of TB exposure among young children in HIV-endemic countries



Notification Rates of Sputum Smear-Positive Tuberculosis, by Age, Tanzania Mainland, 1984 and 1995



Tanzania NTLN / IUATLD. Progress Report 1996; No. 36

More evidence to support screening of child contacts of TB cases: if not now, then when?

Graham SM, Triasih R. Clin Infect Dis 2013



- Evidence that informs the rationale for screening child TB contacts available for over 50 years
- Policy universally accepted but rarely implemented
- Contact screening has two main roles:
 - to identify at-risk contacts such as young or HIV-infected children that require preventive therapy
 - to identify contacts of any age that have tuberculosis i.e. active case-finding.

Why is child contact screening important? Prevent child morbidity and mortality



- The prevalence of TB infection is high among child contacts

Triasih R et al, J Trop Med 2012

- Child household TB contacts had significant increase risk of all-cause mortality compared to children living in non-TB households in same community

- If mother had TB, 8-fold increase: MRR 7.82 (95% CI 2.1-30)

AF Gomes et al, Thorax 2011

- Missed opportunities for IPT were common (71%) in at-risk children that later presented with confirmed TB disease

- 81% were <3 years of age, 25% had disseminated TB and 5% died

- TB source case was the mother or father in 74/156 (47.4%) children

K Du Preez et al, Ann Trop Paediatr 2011

Why is contact screening important?

Increased case-finding



- The prevalence of TB infection and disease is high among contacts

J Morrison, et al. Lancet Infect Dis 2008

- All TB cases 4.5% (95% CI 4.3-4.8)
- Confirmed cases 2.3% (95% CI 2.1-2.5)
- Latent TB infection 51.4% (95% CI 50.6-52.2)

- TB prevalence significantly higher by active case finding in household contacts (1735/100,000) than with passive case finding (191/100,000)

R Zachariah et al, Int J Tuberc Lung Dis 2003

- Incidence of TB disease among contacts was 603 per 100,000 (95% CI 370-830)

PC Hill et al, PLoS ONE 2008

and in same community, prevalence of TB cases was 1518 per 100,000 among 2174 contacts of 317 adults with smear-positive PTB

D Jackson-Sillah et al, Trans R Soc Trop Med Hyg 2007

Contact investigation for active TB among child contacts in Uganda

Jaganath D, et al. Clin Infect Dis 2013



- 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



Early evidence from USA

- 420 children with positive TST in RCT
- IPT (5mg/kg) versus placebo
- TB meningitis: 1 child in IPT versus 6 children in placebo group
- EPTB: 6 children in IPT versus 25 in placebo group

Lincoln EM, et al. Pediatrics 1960

- Observational study of 2,494 children received IPT
- 15, 943 person years of observation
- No child < 5 years developed TB
- No reactivation during adolescence

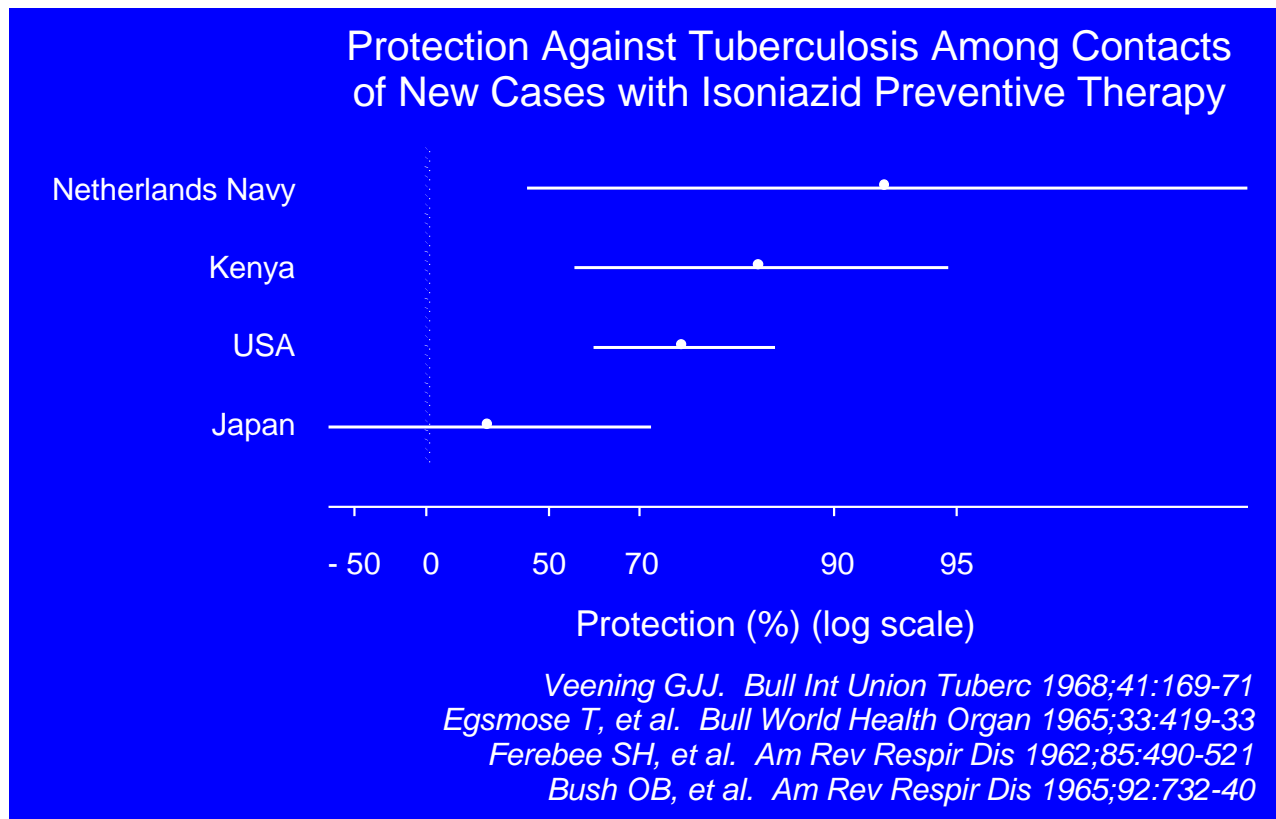
Hsu K, JAMA 1984

IPT reduces the risk of TB disease by around 60% among infected contacts of all ages

Smeijja MJ et al, Cochrane Databse Syst Rev 2000



Large observational studies suggest that the efficacy may be higher (80-90%) in child contacts



Policy Forum

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

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Tropical Medicine and International Health

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Review

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

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Symptom-based screening is also recommended in the WHO guidance

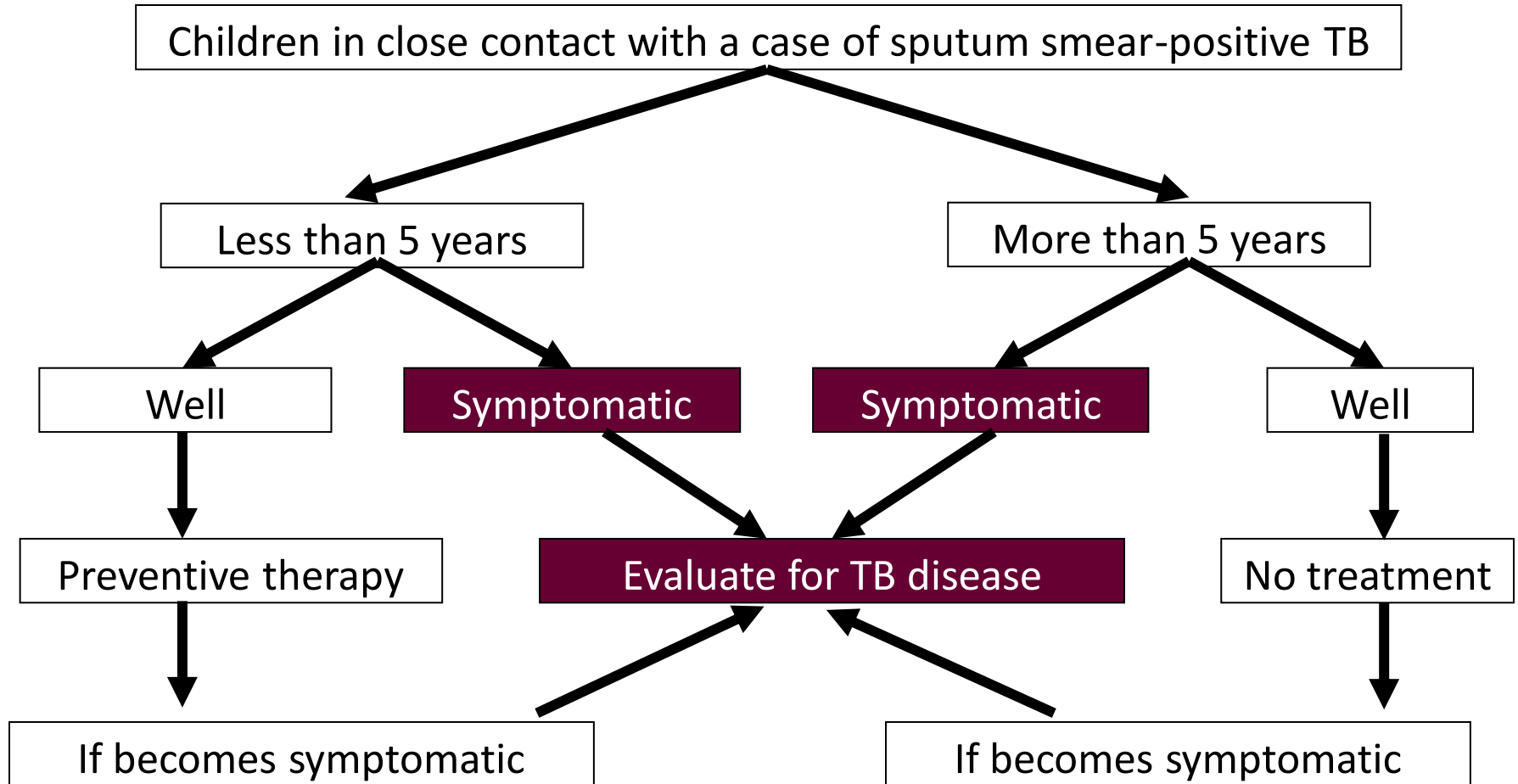


WHO/HTM/TB/2006.371
WHO/FCH/CAH/2006.7

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



WHO symptom based screening



Note that contact screening has two important roles

- 1. Active case-finding**
- 2. Preventive therapy for at-risk contacts without TB**

Management of child contacts



- **Decentralise:** symptom-based screening provides opportunity to undertake an integrated family-based approach in the community around the source case receiving DOT rather than requiring referral to health facility for all cases
- **Adherence:** to IPT for 6 months is a major challenge
- **Enhanced case-finding:** Note that symptom-based screening also aims to identify symptomatic contacts of any age for investigation for possible TB disease

Management of child contacts



List close contacts

- What is the age of the contact?
- Is the contact HIV-infected?
- Does the contact have any symptoms suggestive of TB?

Checklist of main symptoms

- Persistent cough for more than 2 weeks
- Weight loss or failure to gain weight
- Persistent fever for more than 1 week and/or night sweats
- Fatigue, reduced playfulness, less active

Management of child contacts



Criteria for contacts to receive IPT

- No active TB disease – no symptoms suggestive of TB

AND

- At high risk of disease following TB exposure
 - < 5 years
 - HIV-infected

Management of contacts	Response	Action
Symptomatic Sputum smear positive	TB treatment	Register
Symptomatic Sputum smear-negative or not available	Refer for further assessment	Fill referral form for patient to take Fill referral register which stays at health facility
Asymptomatic and high risk	IPT	IPT register
Asymptomatic and not high risk	No treatment	Advise to return if symptoms develop

Sample IPT register



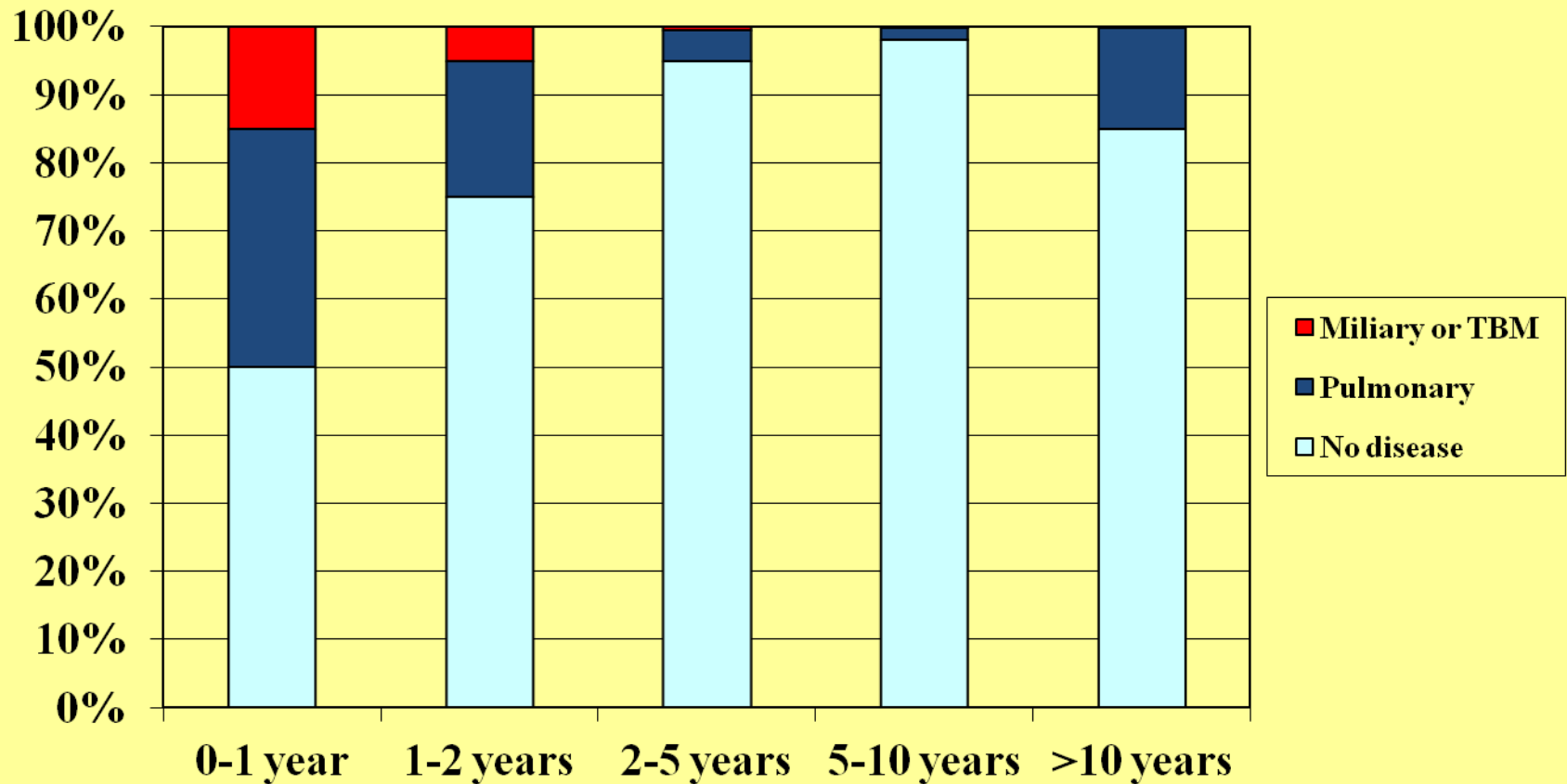
Isoniazid Preventive Treatment Register

PHC centre/Hospital TB control Unit:

Year:

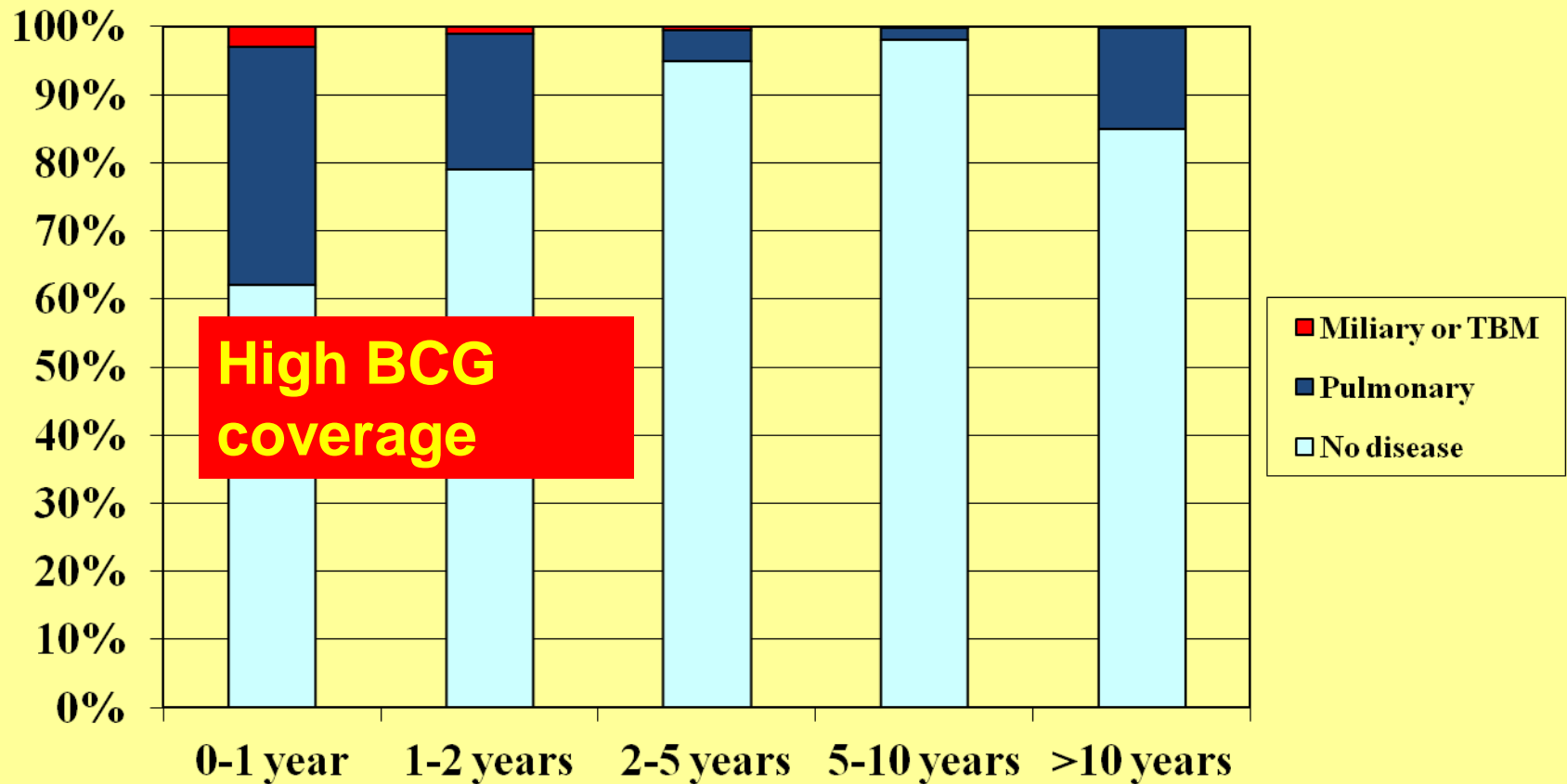
No.	Name of TB contact treated with IPT	Age	Sex	HIV-infected (Y/N)	IPT started on (date)	IPT completed (Y/N)

Average age specific risk for disease development following primary infection (pre-BCG)

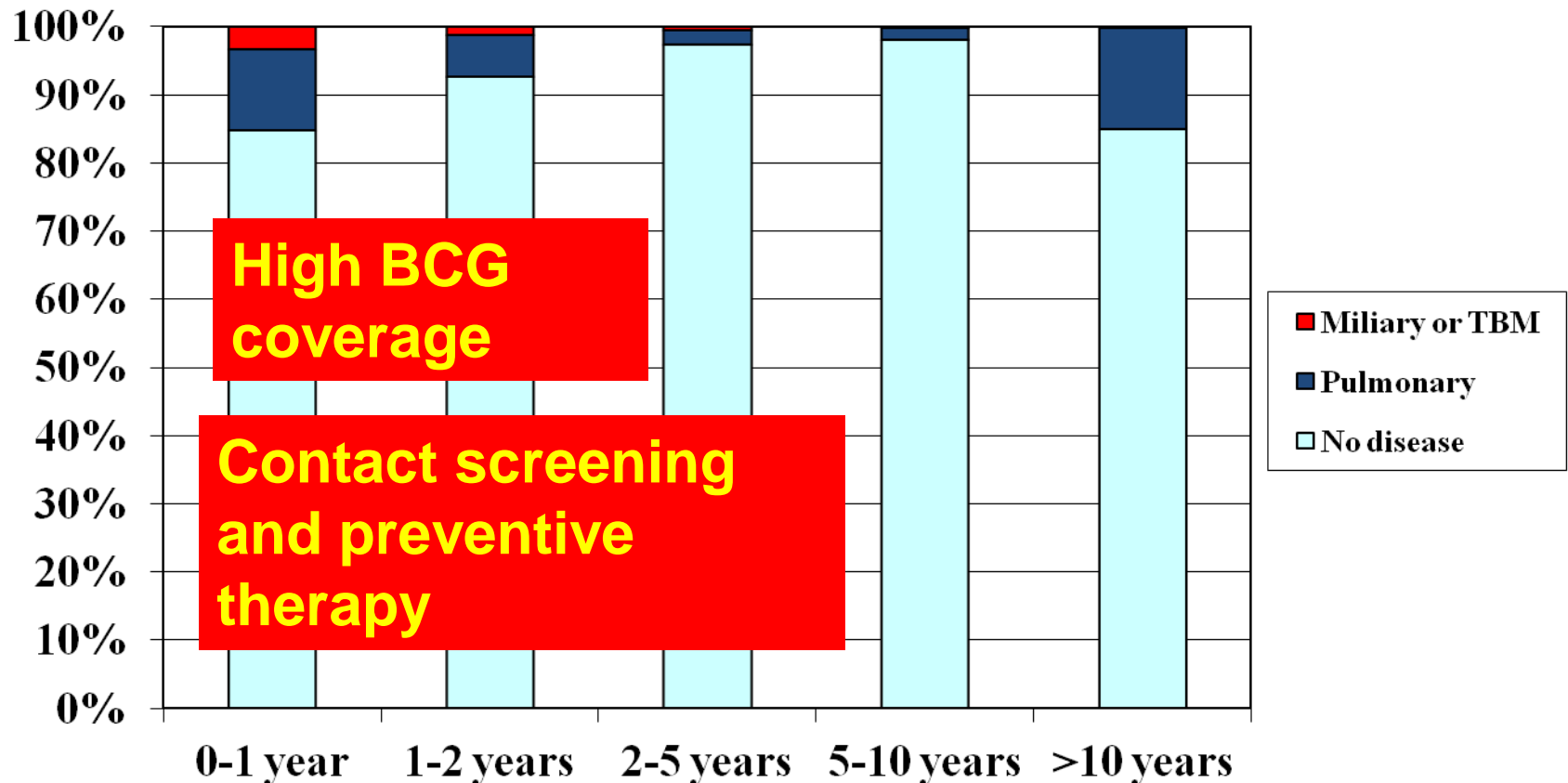


Adapted from Marais B, et al. Int J Tuberc Lung Dis 2004

Average age specific risk for disease development following primary infection with BCG



Average age specific risk for disease development following primary infection: BCG and IPT



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Infection control	Lack of awareness of risk for children attending health facilities with carers – TB wards; TB clinics; HIV clinics

Summary of prevention



- The main effectiveness of neonatal BCG is prevention of severe, disseminated disease in infants and young children
- Child contact screening and management has huge potential to reduce the burden of child TB
- Child contact screening and management can be instituted at the peripheral facility level on the basis of symptom-based screening
- Community-based child contact screening and management is a means of case-finding suspected TB cases of any age
- IPT must be given for at least 6 months to be effective and a major challenge for effectiveness of IPT is adherence and follow-up is critical
- Contact screening and management has huge potential for operational research