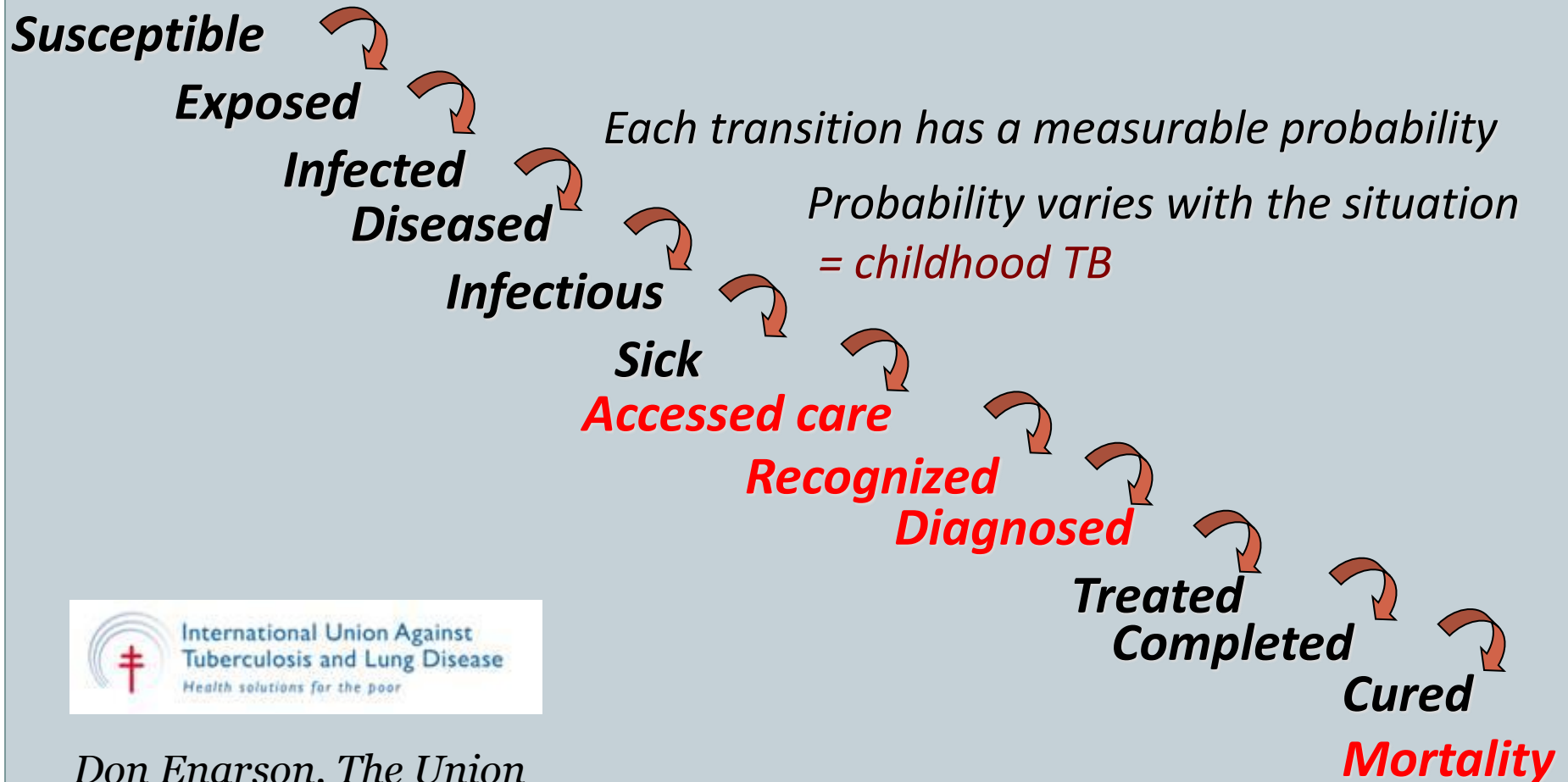


The implementation science for measuring the TB burden in children



**ANNEKE C. HESSELING
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SOUTH AFRICA
31 OCTOBER 2013**

Key transitions in TB transmission



Don Enarson, The Union

Key transitions in estimating TB burden in children



1. Evidence
2. Policy
3. Practice/implementation
4. Evaluation

Mediated by political will



Estimated total cases in children	490 000
Childhood cases notified	327 000
TB deaths in children	64 000 >200 deaths per day

Notification data disaggregated by age

(Data from a suburban setting in Cape Town, 2007 - 2009)



Courtesy, Florian Marx

Notification data disaggregated by age (Data from a country in Central Asia, 2009)



Courtesy, Florian Marx

Improvement of childhood TB burden estimates



1. “Low hanging fruit” – incremental changes – 2 examples
2. Paradigm shifts?
3. Future work, estimates and modeling (not addressed)

Incremental changes



A. Improved recording and reporting of hospital cases



1. Extrapolate case load
2. Severe disease (sentinel events)
3. TB mortality
4. High risk populations (HIV-infected, pneumonia, malnutrition)
5. DR-TB

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 of child TB registered with NTP

INCOMPLETE REGISTRATION OF HOSPITAL CHILD TB CASES: SOUTH AFRICA



	Not registered n=101 (37.8%)	Registered n=166 (62.2%)	p-value
Clinical factors			
Disseminated TB	29 (28.7)	27 (16.3)	0.015*
Miliary TB	12 (11.9)	16 (9.6)	0.562
TB Meningitis	22 (21.8)	13 (7.8)	0.001*
Deaths prior to referral	10 (9.9)	0 (0.0)	<0.001*
Type of consultation			
Outpatient	16 (15.9)	41 (24.7)	0.087
Inpatient	85 (84.2)	125 (75.3)	
Admission (days)	16 (5, 29)	3 (9, 20)	0.052

Recording and reporting of DR-TB

- Proportion childhood TB in EDR.web: **4.4%**
- ⑩ etr.net: 17% childhood TB
- ⑩ Most EDR.web entries correct
- ⑩ Internal inconsistencies
- ⑩ Deleted entries

Children treated for DR-TB = 77

- BHCD = 57
- TCH/clinic = 20

EDR.web extract 2012

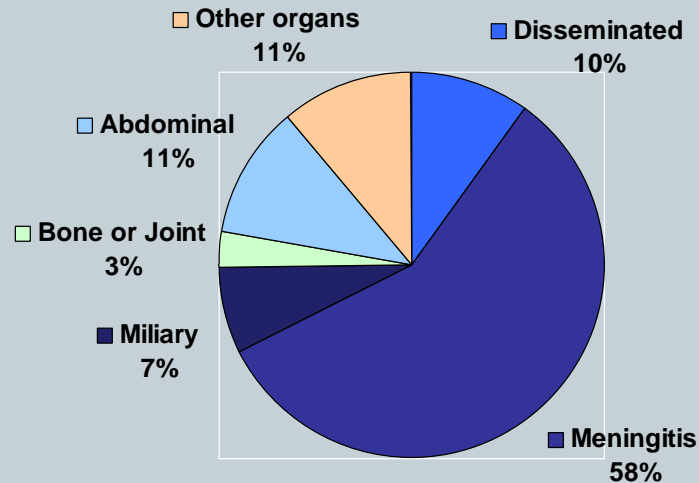
- Total = 1861
- All children = 81 (4.4%)
- Children in BHCD drainage area = 63

Children with DR-TB not in EDR.web = 28 (36%)

Children entered in EDR.web not identified in cohort = 14

Positive matches between clinical cohort & EDR.web extract = **49 (64%)**

Severe child TB cases identified in hospitals; Western Cape Province, South Africa (2005-2011)



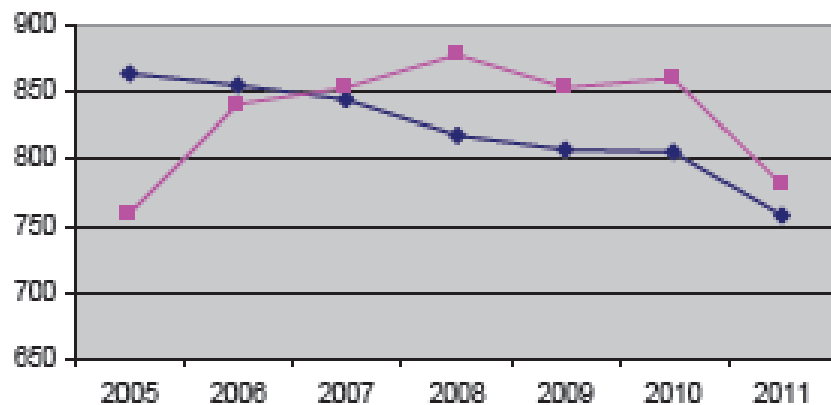
223
Severe TB
cases
identified in
hospitals

179
Hospital
folders
found

26
Registered
in ETR.net
(11.6%)

84
Primary
care record
(47%)

95
No primary
care record
(53%)



◆ TB incidence / 100,000 population
 ■ TB incidence <5-years / 100,000 pop <5-years

E. Maritz, E. Mendel, P. Naidoo

LINKING HOSPITAL TO COMMUNITY CARE (Q1,2_, 2012



	Total n=197 (%)	Bact + n=74 (%)	Bact – n=123 (%)
HIV ¹			
HIV-exposed	63 (39)	18 (31)	45 (44)
HIV status			
Infected	45 (23)	12 (16)	33 (26)
Non-infected	139 (70)	56 (76)	83 (67)
Not tested	13 (7)	6 (8)	7 (6)
HIV diagnosed at current admission	11 (24)	4 (33)	7 (21)
TB contact history ²			
TB contact	107 (57)	36 (51)	71 (60)
Parental source case	45 (24)	13 (19)	32 (27)

LINKING HOSPITAL TO COMMUNITY CARE



	Total n=197	Bact + n=74 (%)	Bact – n=123 (%)
Disease classification			
Pulmonary TB only	112 (57)	34 (46)	78 (63)
Extra-pulmonary TB only	44 (22)	10 (13)	34 (28)
Both PTB and EPTB	41 (21)	30 (41)	11 (9)
Discharge referral facilities			
Community TB clinics	133 (68)	44 (59)	89 (72)
TB Hospitals	42 (21)	18 (24)	24 (20)
Secondary Hospitals	7 (4)	3 (4)	4 (3)
Medium Term Care facilities	4 (2)	0 (0)	4 (3)
Other	6 (3)	4 (5)	2 (2)
Died in hospital	5 (3)	5 (7)	0 (0)
TB referral letter completed	107/133 (81)	34/44 (77)	73/89 (82)

HOSPITAL LINK INTERVENTION



Matching data (etr.net)	Pre- intervention Jul 2007- Jun 2009 n=267 (%)	Post- intervention Jan – May 2012 n=162 (%)
Community PHC referrals only	125/183 (68)	87/106 (82)
Death prior to discharge	0/10 (0)	5/5 (100%)

Corrected provincial TB notification rate: >20% higher

Results of 4 DR surveys



Characteristics	2003-05	2005-07	2007-09	2009-2011
All cult+ cases	323 (%)	291 (%)	294 (%)	340 (%)
Med age (yrs)	2.5	2.75	2.1	2.4
Boys	173 (53.6)	154 (52.9)	156 (53.1)	177 (52.1)
Prev TB Rx	59 (18.3)	65 (22.3)	50 (17.0)	59 (17.4)
HIV test done*	243 (75.2)	174 (59.8)	217 (73.8)	288 (84.7)
HIV-infected*	64 (26.3)	49 (28.2)	63 (29.0)	63 (21.9)

****As percentage of tests done**

Significant differences:

*HIV tests done (2005-2007 to 2009-2011): $p < 0.0001$; Trend for decrease in HIV infection from high to low: $p = 0.07$

Results of 4 DR surveys



DST results	2003-05	2005-07	2007-09	2009-2011
All cult+ cases	323 (%)	291 (%)	294 (%)	340 (%)
DST done*	320 (99.1)	285 (97.9)	292 (99.3)	340 (100)
Any DR	41 (12.8)	43 (15.1)	45 (15.4)	49 (14.4)
INH mono-R	22 (6.9)	22 (7.7)	15 (5.1)	19 (5.6)
RMP mono-R**	0	2 (0.7)	4 (1.4)	6 (1.8)
MDR	19 (5.9)	19 (6.7)	26 (8.9)	24 (7.1)

*Further percentages based on number of DST results**Significant differences: RMR increase from 1st to 4th period: $p = 0.03$ (Fisher exact 2-tailed)

All paediatric treated TB cases: >600 per annum

RESEARCH ARTICLE

Open Access

High incidence of pulmonary tuberculosis in children admitted with severe pneumonia in Uganda

Josephine M Nantongo¹, Eric Wobudeya^{2,4*}, Ezekiel Mupere¹, Moses Joloba³, Willy Ssengooba³, Harriet N Kisembo⁵, Irene R Lubega^{1,4} and Philippa M Musoke^{1,4}

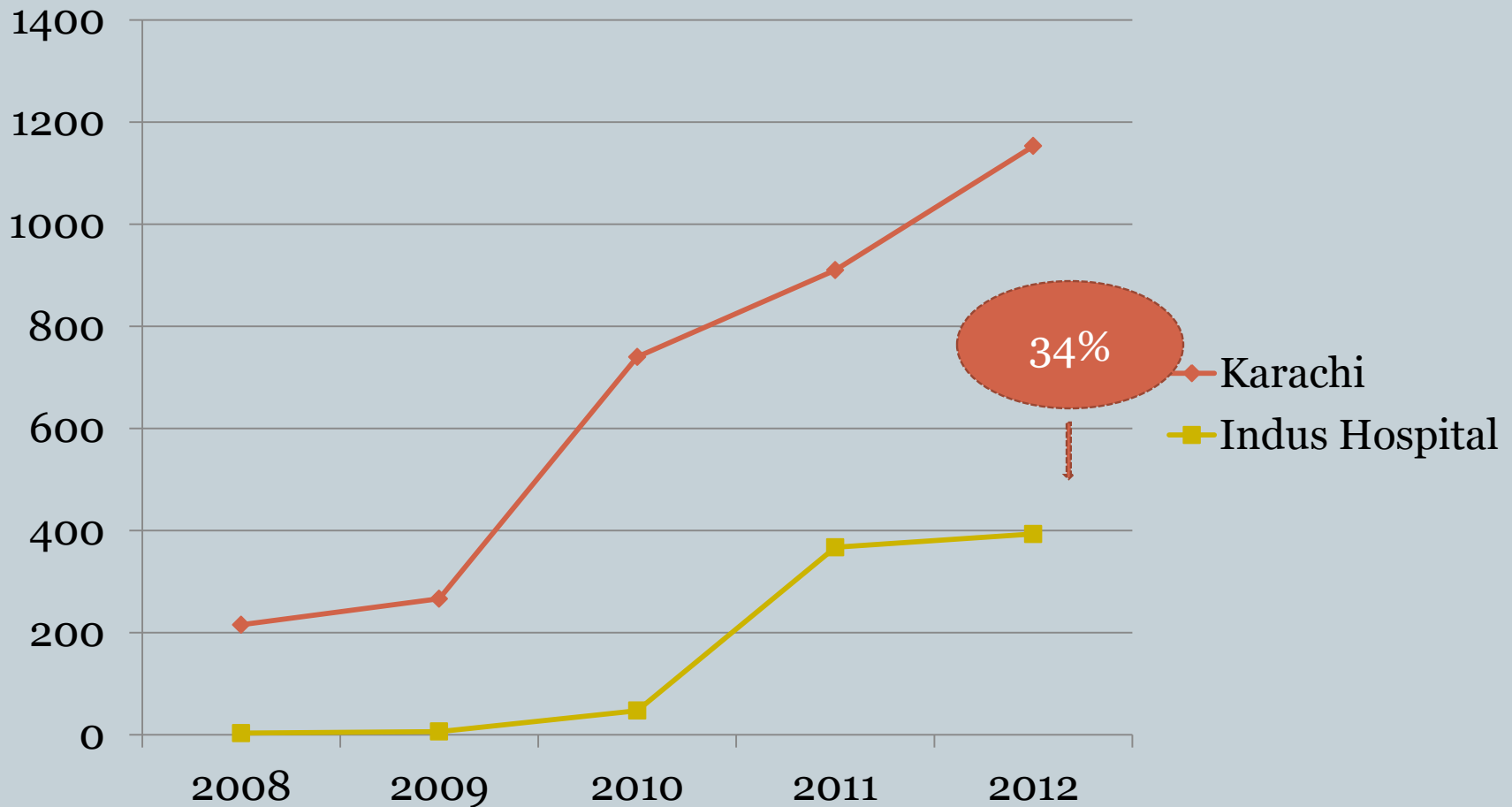
Results: Of the 270 children with severe pneumonia who were recruited over a 5-month period in 2011, the incidence ratio of pulmonary TB in children admitted with severe pneumonia was 18.9% (95% CI 14.6 – 23.9). The proportion of culture confirmed PTB was 6.3% (95% CI 3.8 – 9.7). Age group under 1 year and 1 to 5 years (OR 2.8 (95% CI 1.7 – 7.4) and OR 2.4 (95% CI 1.05 – 5.9) respectively) were more likely to be associated with pulmonary TB compared to those children over 5 years of age. A history of TB smear positive contact was associated with pulmonary TB (OR 3.0 (95% CI 1.3–6.5)).

Recording and reporting of hospital data



- Implementation: each health care facility: diagnose, treat but also record and report
- Hospital treatment register
- Hospital deaths recorded
- Ongoing surveillance of culture+ and “sentinel” cases
- HIV management
- DR-TB
- Value of “notification” ?
- Link hospital to community care

PPM: contribution of a private hospital towards child TB case reporting, Pakistan



Courtesy, Farhana Amanullah



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	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Female	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

15-20 year olds?

GDF treatment since 2001



- 19, 886, 158 FLD
- 1,4 million paediatric treatments and prophylaxis
- 55, 880 SLD
- In 2011: paediatric FLDs procured: \$3,928,781
- No paediatric TB guideline = no drugs
- Requires recording and reporting by age bands

B. Contact management



The overall yield for all TB (bacteriologically confirmed and clinically diagnosed) was 4.5% (95% CI 4.3-4.8, I(2)=95.5%) of contacts investigated; for cases with bacteriological confirmation the yield was 2.3% (95% CI 2.1-2.5, I(2)=96.6%).

Latent tuberculosis infection was found in 51.4% of contacts investigated.

“Contact investigation merits serious consideration as a means to improve early case detection and decrease transmission of *M tuberculosis* in high-incidence areas”.

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



- 761 children from 351 households
- 79 TB cases
- 10% prevalent TB
- 71% bacteriologically confirmed

Evidence that informs the rationale for screening of children who are close contacts of a case of tuberculosis and for providing preventive therapy for this high-risk group has been available for >50 years [1, 2]. The policy is almost universally accepted, being included in global and almost all national tuberculosis control program guidelines [3]. However, in practice it is rarely implemented except in low-tuberculosis-burden, resource-rich settings [4]. Contact screening has 2 main roles. One is to identify at-risk contacts such as young or human immunodeficiency virus (HIV)–infected children who require preventive therapy. The other is to identify contacts of any age who have tuberculosis, that is, active, case finding.

GAPS IN IPT IMPLEMENTATION



- **India:** Poor uptake of screening (14%), and poor uptake of IPT initiation (19%) (*Rekha, et al. IJTLD, 2009*)
- **Laos:** Poor uptake of IPT (0/148), and poor knowledge of infectiousness amongst TB patients (*Nguyen, et al. BMC Infect Dis, 2009*)
- **Malawi:** only 9% of TB-exposed children were screened for TB and initiated on IPT (*Claessens, et al. IJTLD, 2002*) AND despite education of TB patients about the benefits and importance of contact screening, only 8% attended the hospital-based clinic (*Nyirenda, et al. IJTLD, 2006*)
- **Botswana:** 1/3 of community screened contacts who were symptomatic, did not attend the clinic for further investigations (*Ghandi et al. IJTLD, 2011*)

BARRIERS TO IPT DELIVERY



- Knowledge, understanding and perception amongst TB patients and NTP staff
- Treatment side-effects
- Transport and cost difficulties
- Lack of management / monitoring structure and tools, indicators
- **Political will**

*Hill, et al. Plos Medicine,
2011*

CHILD ISONIAZID PREVENTIVE THERAPY REGISTER

Adult		Child									
¹ Date dd / mm / yyyy	Adult case TB register nu ####/ yy or "N/A"	Name and Surname	Gender & Age		² Physical Address & contact telephone number	HIV status Pos/ Neg/ Not done	³ Return date dd / mm / yyyy	⁴ Number of pills issued	Number of pills returned	If IPT stopped, give reason ⁵	
		Surname	M	F			Initial visit (leave open)		N/A (leave open)		
		Name						1			
								2			
								3			
								4			
								5			

Using TB contact management as quantification of paediatric disease burden



- Quantify number at-risk children (community, facility) – **indirect estimate of childhood TB burden**
- Estimate number infected and diseased (who should be attending)
- Document who attended and TB prevention offered
- Quantify missing cases
- Earlier diagnosis and less severe disease

“Contact investigation study (TB-and neighbouring households): children with a documented TB source case less likely to have severe disease than those without (21% vs. 44%; OR: 0.34, 95%CI: 0.12; 1.01, $p=0.025$)”

B. Paradigm shift



- Address fragmentation in health services for children - standalone TB program
- Childhood TB included in all child and maternal health services
- Inclusion child TB indicators including contact management
- Integrated TB reporting systems accessible to facilities
- Linkage to households and TB source cases

South Africa

| High TB burden | High HIV burden | High MDR-TB burden |



New cases	Smear-positive	Smear-negative/ unknown/ not done	Extrapulmonary
M:F ratio	1.3	1.1	1.0
Age < 15	2 677	33 601	2 327

Need for paediatric indicators

More suggestions



- TB electronic data linked to all health data (PMTCT, HIV, EPI, clinic visits, hospital admissions)
- Integrated health information systems?
- Birth and death registration data linked
- All TB drugs dispensed (including IPT) logged
- Incentives to families to access child TB care
- Broaden scope of IPT delivery beyond TB program

Recording and reporting of routine data



- Indicator-driven
- Ongoing evaluation
- Political will

TST surveys



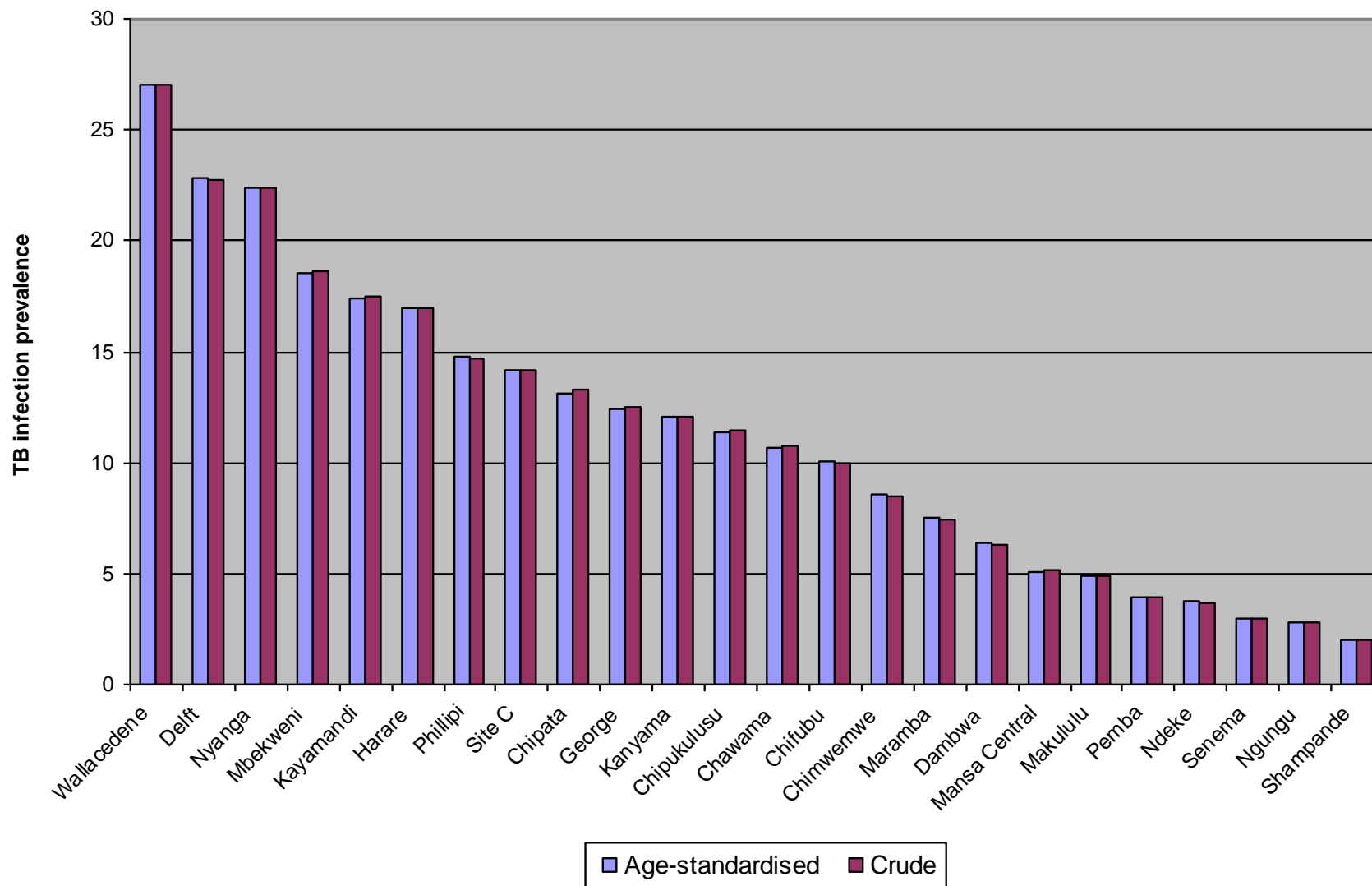
“Validation” of findings from adult prevalence surveys

Annual risks of tuberculous infection in The Netherlands from 1910 to 1969, derived from the findings of tuberculin surveys, with possible alternative risks for the period 1933 to 1947

Year	Annual risk of tuberculous infection (%)	Possible alternative risk* (%)	Year	Annual risk of tuberculous infection (%)	Possible alternative risk* (%)
1910	11.31		1940	2.08	1.72
11	10.74		41	1.82	1.70
12	10.20		42	1.58	1.72
13	9.68		43	1.38	1.78
14	9.18		44	1.20	1.90
1915	8.72		1945	1.05	2.10
16	8.27		46	0.92	1.45
17	7.85		47	0.80	1.00
18	7.44		48	0.70	
19	7.06		49	0.61	
1920	6.69		1950	0.53	
21	6.35		51	0.46	
22	6.02		52	0.40	
23	5.71		53	0.35	
24	5.41		54	0.30	
1925	5.13		1955	0.265	
26	4.86		56	0.231	
27	4.61		57	0.202	
28	4.37		58	0.176	
29	4.14		59	0.153	
1930	3.92		1960	0.133	
31	3.72		61	0.116	
32	3.52		62	0.101	
33	3.34	3.09	63	0.088	
34	3.16	2.72	64	0.077	
1935	2.99	2.42	1965	0.067	
36	2.84	2.18	66	0.058	
37	2.69	2.00	67	0.051	
38	2.55	1.87	68	0.044	
39	2.41	1.78	69	0.038	

Age standardised prevalence of *M.tb* infection in children (Mantoux test done n=25 048, read n= 22 563)

Comparison of crude Vs indirect age-standardised TB infection prevalence measures (TST \geq 15mm) by
ZAMSTAR community







ARTI*

- Zambia: 2.8%
- South Africa: 4.2%

Incidence rate of TB infection in Zambia vs. South African communities was 1.2/100 pyrs compared to 4.5/100 pyrs.

Prevalence surveys: targeted inclusion children



- Adolescents
- TST surveys
- Hospital audits including sentinel cases
- Selected high risk populations:
 1. HIV-infected children
 2. Acute pneumonia
 3. PEM
- Contact management audits
- Link child contact management to adult cases detected in prevalence surveys

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