

Family-Centered Approach: Framework for Managing Children Exposed to DR-TB

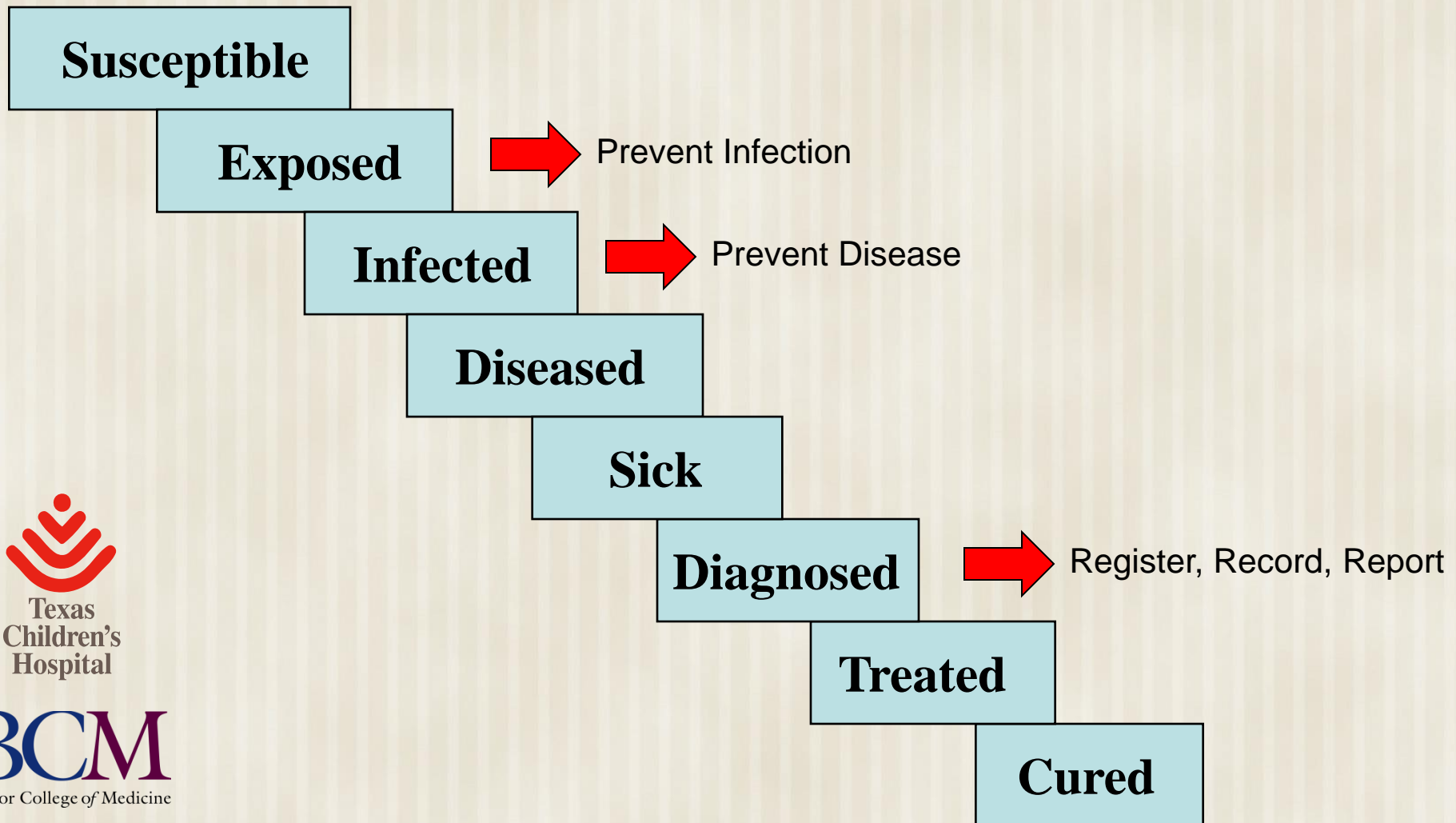
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TRANSITIONS IN TUBERCULOSIS



Katherine HK Hsu, M.D.

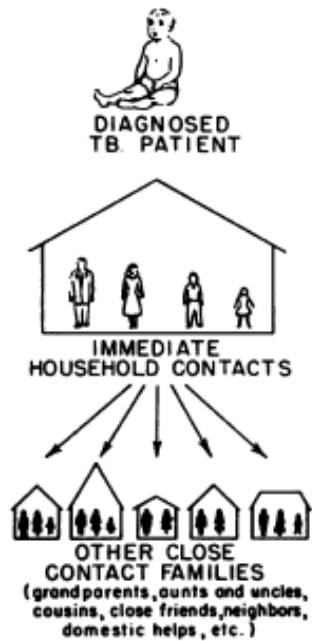


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SCHEME OF APPROACH



AGENCIES CO-OPERATING IN SCHEME

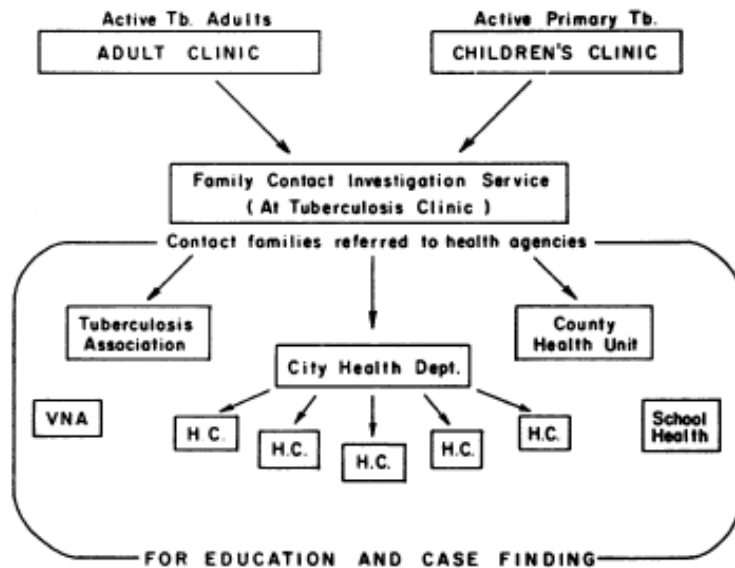


Figure 1—The Scheme for Tuberculosis Contact Investigation

Hsu KHK: Contact investigation: A practical approach to tuberculosis eradication. *AJPH* 53;1751, 1963.



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The findings of a study of 205 family groups for tuberculosis and tuberculosis contacts are reported. These show that tuberculosis exists in “pools” involving large numbers of cases. Public health efforts should be directed to these pools of infection, and contact investigation has proved very efficient in finding pools. Intensive contact investigation will permit wide chemoprophylaxis amid children and young adults.

What Does Family Centered Contact Tracing Do?



- Identifies recently exposed and infected children
 - 1) Opportunity to prevent establishment of infection
 - 2) Prevent infection from progressing to disease
 - 3) Detect early disease – easier to treat & cure
 - 4) Prevent dissemination, hospitalization

- Only opportunity to determine drug susceptibility for:
 - 1) 50% to 70% of children with disease
 - 2) 100% of children with infection



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Some Results from Contact Tracing Studies

Jaganath et al. Clin Infect Dis 2013 epub

- Study of 761 childhood household contacts of TB cases in Uganda
- ~ half of the contacts were children < 5 years of age
- Patients followed for 2 years
- 10% prevalence of TB disease among the children [71% were culture positive] – 16,400 per 100,000!!!
- No cases of disseminated disease [? Effect of early intervention]
- 483/490 [99%] children started on INH did not develop disease
- 2 TB cases while on IPT, one case after completion
- BCG was protective, esp. among children < 5 years of age
- Characteristics of index case not a/w disease in contacts



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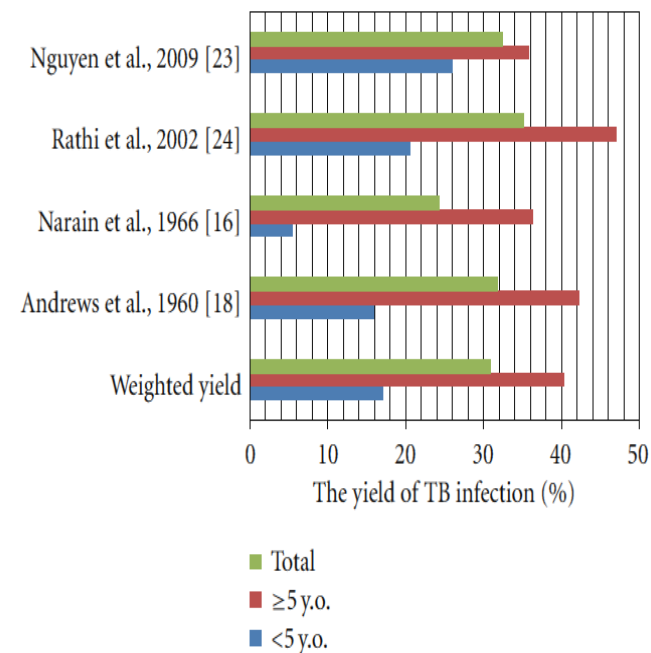
Some Results from Contact Tracing Studies

Triasih et al. J Trop Med 2012 DOI:10.1055/2012/301808

TABLE 2: The yields of household contact investigation among child contacts.

Author	Country	Number of source case	Number of child contacts	Yield (%) for TB infection			Yield (%) for TB disease		
				<5 yo	5–15 yo	<15 yo	<5 yo	5–15 yo	<15 yo
Andrews et al. [18]	India	191	398	16.2	53.6	38.8	→ 9.2	3	5.5
Narain et al. [16]	India	75	790	5.5	36.5	24.4	NR	NR	NR
Kumar et al. [17]	India	50	142	NR	NR	NR	→ 3.2	NR	NR
Singh et al. [15]	India	200	281	33.8	NR	NR	→ 3.2	NR	NR
Rathi et al. [24]	Pakistan	77	151	7.8	21.8	29.6	NR	NR	NR
Salazar-Vergara et al. [25]	Philippines	62	153	51.2	76.9	69.2	NR	NR	→ 3.3
Tornee et al. [19]	Thailand	325	480	NR	NR	47.8	NR	NR	NR
Tornee et al. [20]	Thailand	342	500	NR	NR	47.1	NR	NR	NR
Iskandar et al. [22]	Indonesia	54	61	10	NR	NR	→ 16.4	NR	NR
Nguyen et al. [23]	Lao	72	148	26	35.7	31.1	NR	NR	NR
Okada et al. [21]	Cambodia	164	217	24	NR	NR	→ 8.7	NR	NR

NR: not reported.



Tuberculosis and latent tuberculosis infection in close contacts of people with pulmonary tuberculosis in low-income and middle-income countries: a systematic review and meta-analysis

Lancet Infect Dis 2008;

8: 359–68

Janina Morrison, Madhukar Pai, Philip C Hopewell

	Total studies (n)	Pooled yield (95% CI)	Heterogeneity		References
			p	I ²	
Active tuberculosis					
Child contacts					
<5 years	13	8.5% (7.4–9.7%)	<0.001	88.8%	18,21,22,31,37–39, 41,45,46,50,59,60
5–14 years	6	6.0% (4.7–7.5%)	0.064	43.5%	18,31,38,39,45,59
<15 years	8	7.0% (6.0–8.0%)	<0.001	88.3%	17,18,31,33,38,39,45,59
Adult contacts (>15 years)	9	6.5% (5.7–7.4%)	<0.001	70.1%	16–18,31,33,38,39,41,45
LTBI					
Child contacts					
<5 years	14	30.4% (28.6–32.3%)	<0.001	94.4%	17,18,21,22,31,39,43,45, 53,54,56,57,59,60
5–14 years	7	47.9% (45.5–50.4%)	<0.001	96.0%	17,31,39,43,53,56,59
<15 years	10	40.4% (38.7–42.2%)	<0.001	97.8%	16,17,31,39,44,48,53,56, 58,59
Adult contacts (>15 years)	7	64.6% (62.9–66.2%)	<0.001	98.7%	17,18,31,39,43,48,53

Table 6: Pooled data for all active tuberculosis and LTBI among household contacts, by age



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Opportunities for chemoprophylaxis in children with culture-confirmed tuberculosis

K. DU PREEZ*, A. C. HESSELING*, A. M. MANDALAKAS*[‡], B. J. MARAIS[§] & H. S. SCHAAF*[†]

Annals of Tropical Paediatrics (2011) 31, 301–310

TABLE 2. TB disease spectrum in children with documented exposure stratified by age, HIV status and those who did not receive chemoprophylaxis.

Type of tuberculosis	All child contacts <i>n</i> =333 (%)	<5 yrs <i>n</i> =237 (%)	HIV-infected <i>n</i> =68 (%)
Pulmonary TB only	156 (46.8)	123 (51.9)	41 (60.3)
Extra-pulmonary TB only	30 (9.0)	19 (8.0)	0 (0)
Pulmonary & extra-pulmonary TB	147 (44.1)	95 (40.1)	27 (39.7)
Disseminated TB (included above)	73 (21.9)	58 (24.5)	16 (23.5)
Missed opportunities for chemoprophylaxis*			
Type of tuberculosis	<5 yrs <i>n</i> =146 (%)	HIV-infected ≥5 yrs <i>n</i> =10 (%)	
Pulmonary TB only	75 (51.4)	6 (60.0)	
Extra-pulmonary TB only	13 (8.9)	0 (0)	
Pulmonary & extra-pulmonary TB	58 (39.7)	4 (40.0)	
Disseminated TB (included above)	37 (25.3)	2 (20.0)	

* Children <5 yrs of age or HIV-infected with documented TB exposure who did not receive chemoprophylaxis as per local guidelines at the time of the study. Types of extra-pulmonary TB included meningitis, miliary, peripheral lymph nodes, pleural effusion, pericardial effusion, abdominal and mastoiditis.



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Tuberculosis burden in households of patients with multidrug-resistant and extensively drug-resistant tuberculosis: a retrospective cohort study

Lancet 2011; 377: 147-52

Mercedes C Becerra, Sasha C Appleton, Molly F Franke, Katiuska Chalco, Fernando Arteaga, Jaime Bayona, Megan Murray, Sidney S Atwood, Carole D Mitnick

	Overall			Index XDR			Index MDR			Adjusted hazard ratio (95% CI)*
	Incidence rate per 100 000 person-years*	Cases	Person-years	Incidence rate per 100 000 person-years*	Cases	Person-years	Incidence rate per 100 000 person-years*	Cases	Person-years	
Year 1	3165	140	4423	4252	13	306	3084	127	4117	1.24 (0.57-2.66)
Year 2	1092	47	4303	2714	8	295	973	39	4008	2.44 (1.09-5.46)
Year 3	764	30	3927	1816	5	275	685	25	3651	2.67 (0.99-7.20)
Year 4	1112	25	2247	2734	5	183	969	20	2065	2.81 (0.89-8.83)
Overall (years 1-4)	1624	242	14 900	2928	31	1059	1524	211	13 841	1.88 (1.10-3.21)

*Adjusted for household clustering.

Table 3: Incidence of active tuberculosis in household contacts during 4-year follow-up period

Risk factors for infection and disease in child contacts of multidrug-resistant tuberculosis: a cross-sectional study

Seddon *et al. BMC Infectious Diseases* 2013, **13**:392
<http://www.biomedcentral.com/1471-2334/13/392>

James A Seddon^{1,2*}, Anneke C Hesselning¹, Peter Godfrey-Faussett², Katherine Fielding³ and H Simon Schaaf^{1,4}

Abstract

Background: Young children exposed to *Mycobacterium tuberculosis* have a high risk of disease progression following infection. This study aimed to determine risk factors for *M. tuberculosis* infection and disease in children following exposure to adults with multidrug-resistant (MDR) tuberculosis (TB).

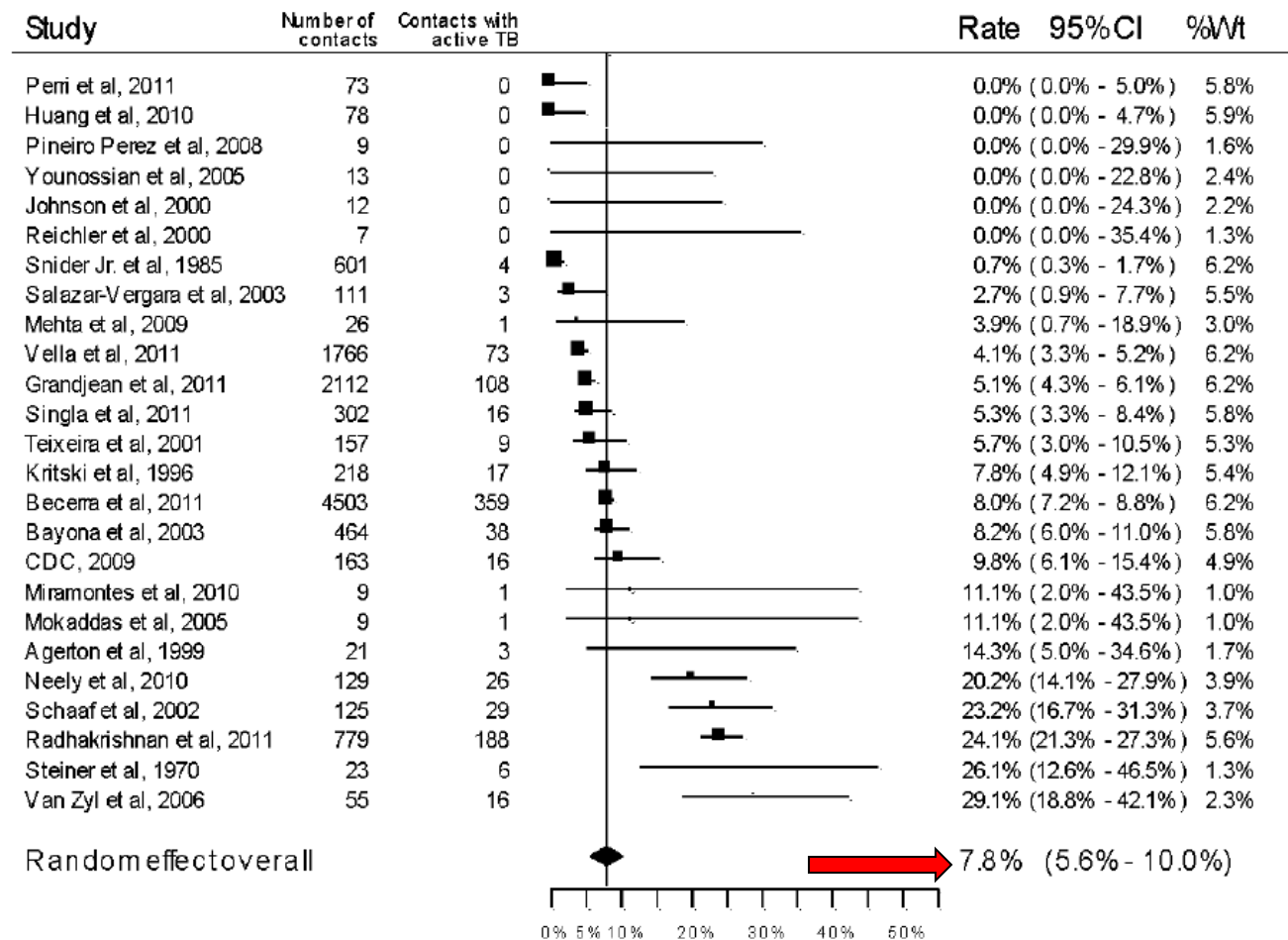
Methods: Cross-sectional study; all children aged < 5 years, routinely referred per local guidelines to the provincial specialist MDR-TB clinic, Western Cape Province, South Africa, following identification as contacts of adult MDR-TB source cases, were eligible for enrolment from May 2010 through April 2011. Demographic, clinical and social characteristics were collected. All children underwent HIV and tuberculin skin testing.

Results: Of 228 children enrolled (median age: 30 months), 102 (44.7%) were classified as infected. Of these, 15 (14.7%) had TB disease at enrolment. Of 217 children tested for HIV, 8 (3.7%) were positive. In adjusted analysis, child's age (AOR: 1.43; 95% CI: 1.13-1.91; $p = 0.002$) and previous TB treatment history (AOR: 2.51; 95% CI: 1.22-5.17; $p = 0.01$) were independent risk factors for infection. Increasing age of the MDR-TB source case (AOR: 0.67; 95% CI: 0.45-1.00; $p = 0.05$) was protective and source case alcohol use (AOR: 2.59; 95% CI: 1.29-5.22; $p = 0.007$) was associated with increased odds of infection in adjusted analysis. Decreasing age of the child ($p = 0.01$) and positive HIV status (AOR: 25.3; 95% CI: 1.63-393; $p = 0.01$) were associated with prevalent TB disease.

Conclusion: A high proportion of children exposed to MDR-TB are infected or diseased. Early contact tracing might provide opportunities to prevent the progression to TB disease in children identified as having been exposed to MDR-TB.

Keywords: Pediatric, Infection, Disease, Drug-resistant, Tuberculosis, Children

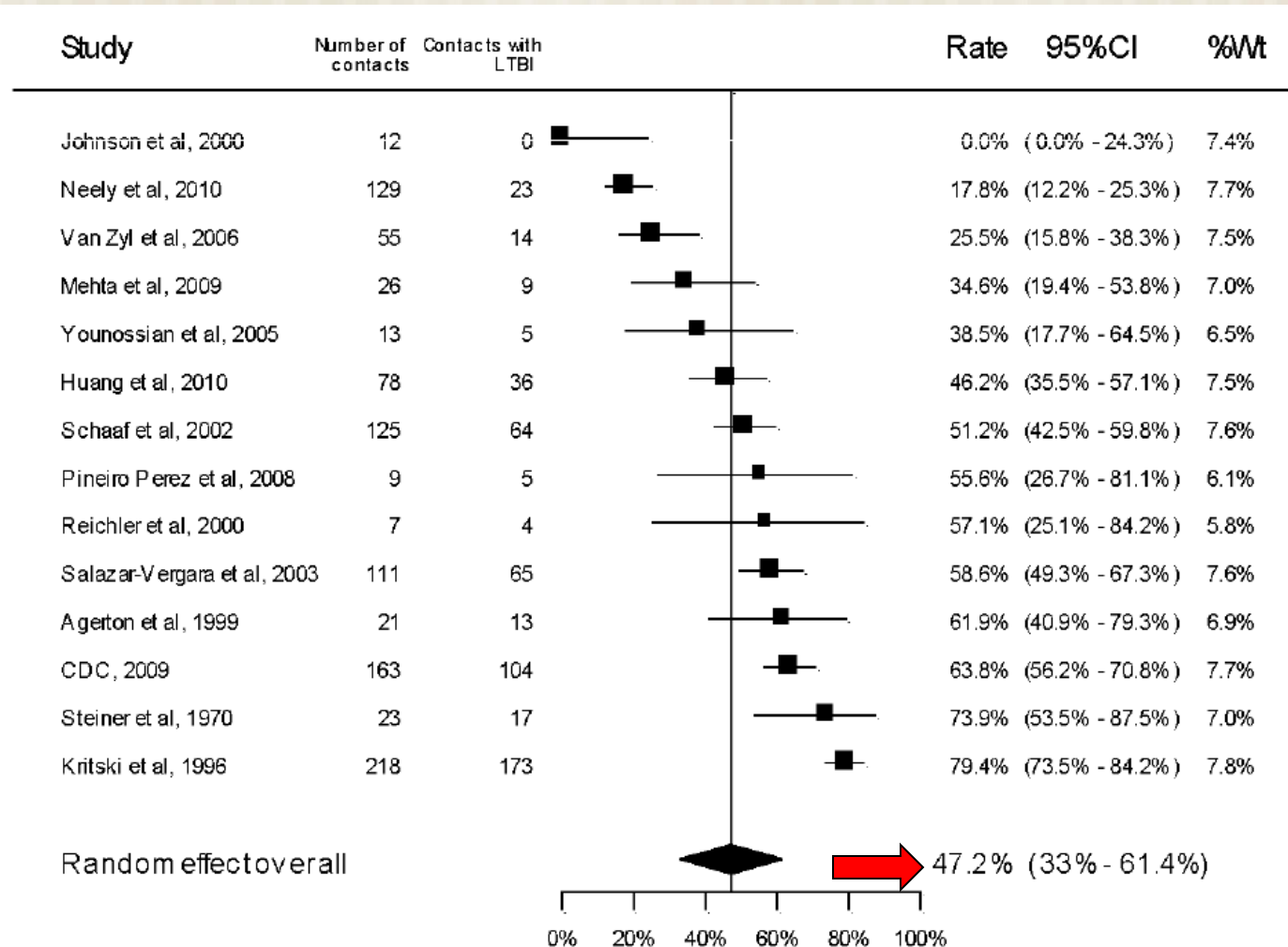
Shah et al. Yield of contact investigations in households of DR-TB patients: systematic review and meta-analysis. *CID* 2013 epub ahead of print



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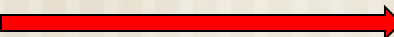
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ASSOCIATE INVESTIGATION [“Reverse Contact Tracing”]

- Identification and evaluation of close contacts of children and adolescents with LTBI or TB disease
- can be considered a form of targeted testing
 - Index Case  Source Case
 - yield of finding cases of tuberculosis may be low
 - yield of finding LTBI is 30% to 40% in the U.S.
 - *effective only if index child with LTBI was tested because of risk*





ASSOCIATE INVESTIGATIONS FOR CHILDREN WITH LTBI

Location	Year	# of associates	# (%) positive TST	TB cases
San Francisco	1986	831	330 (40)	3
NYC	1993-5	659	210 (32)	0
NYC	1996-8	668	198 (30)	3
San Diego	2001-2	713	292 (41)	0
Ft. Worth	1999-01	87	31 (35)	2

Why is treating latent tuberculosis infection an essential part of getting to zero?



- Many infections are not “latent” but are “active”
- Vulnerable patients progress rapidly to life-threatening forms of TB: young children, immunocompromised persons, elderly
- In some cases, can treat TB infection before the person becomes immunocompromised
- Prevention of future cases = less transmission in the future to vulnerable persons
- BCG vaccine prevents many but not all cases of life-threatening TB in children and adults
- Treating MDR-TB infection may be safer and more effective than treating MDR-TB disease 
- Contact investigation: the most “bang” for the “buck” – high risk, high rate, motivation to treat, drug susceptibilities known, DOT and DOPT 



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Why Family-Centered Contact Tracing Is Important For MDR-TB



- Benefit for the individual – accurate diagnosis and appropriate treatment
- Benefit for the family -
 1. access to DOT and other support services;
 2. support each other in treatment;
 3. psychologic effect of preventing disease in loved ones;
 4. empowerment over the disease
- Benefit for society – prevent future disease
- Benefit for NTP – accurate case-finding, prevention, cost-containment



Graham and Triasih. More evidence to support screening of child contacts of tuberculosis cases: If not now, then when?

Clin Infect Dis 2013

Will
Power



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“We already have the policy, the evidence and the tools we need to implement [contact tracing]; even the political will is beginning to emerge. It will not be easy, but this recent study [in Uganda] further highlights the consequences and missed opportunities of continued neglect.”