Tuberculosis prevention: An under prioritized YET critical intervention to reduce child tuberculosis morbidity and mortality

Moorine Penninah Sekadde Childhood TB focal point, NTP Uganda

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Context

- Underestimation of the burden of TB disease among children due to poor diagnostics and non-specific presentations.
- Only 45% of the global estimated 1M children with TB were notified in 2017
- Majority are at risk of preventable TB related complications and death.
- Only 23% of the global estimated 1.3 M eligible under five contacts were initiated on TB preventive therapy in 2017

Urgent need to strengthen LTBI treatment among eligible childhood TB contacts

TB preventive treatment for people living with HIV and children under 5 years of age who were household contacts of a bacteriologically confirmed pulmonary TB case, high TB or TB/HIV burden countries, 2017

	TREATMENT PEOPLE LIVING WITH HIV	PEOPLE LIVING WITH HIV NEWLY ENROLLED IN CARE STARTED ON TB PREVENTIVE		ESTIMATED NUMBER OF CHILD CONTACTS UNDER 5 YEARS OF AGE ELIGIBLE FOR TB PREVENTIVE TREATMENT ³		CHILDREN UNDER 5 YEARS OF AGE STARTED ON TB PREVENTIVE TREATMENT		
							COVERAGE® (%)	
	NEWLY ENROLLED IN CARE	NUMBER	COVERAGE (%)	B/SY ESTIMATE	UNCERTAINTY INTERVAL	NUMBER	BEST ESTIMATE	UNCERTAINTY INTERVAL
Angola	22 137	2 842	13	24 800	(22 600-27 000)			
Bangladesh				54 400	(49 500-59 200)	11 394	/21 \	(19-23)
Botswana				781	(711–850)	556	/ **	
Brazil				2 860	(1 850-3 860)			
Cambodia	3 582	754	21	5 540	(5 040-6 030)	2 410	44	(40-48)
Cameroon				10 300	(9 400-11 200)	89	0.86	(0.79-0.95)
Central African Republic	8 180	0	0	3 500	(3 190-3 810)			
Chad				4 520	(4 110-4 920)			
China				10 400	(6 710-14 000)			
Congo	1 380	272	•	2 410	(2 190-2 620)	98	4.1	(3.7-4.5)
DPR Korea				9 450	(8 610-10 300)	11 984	**	
DR Congo				84 400	(76 900-92 000)	13 045	15	(14-17)
Eswatini	23 271	232	1.0	1 200	(1 090-1 300)	89	7.4	(6.8-8.2)
Ethiopia	39 126	17 801	45	27 500	(25 100-30 000)	2 964	11	(9.9-12)
Ghana				3 710	(3 380-4 040)			
Guinea-Bissau				2 060	(1 880-2 250)	394	19	(18–21)
India	173 174	18 162	10	344 000	(314 000-375 000)	38 745	11	(10-12)
Indonesia	49 215	7 681	16	71 500	(65 200-77 900))-77 900) 6 080		
Kenya	155 377	136 495	*	24 900	(22 700-27 100)	6 521	26	(24-29)
Lesotho				1 760	(1 610-1 920)			
Liberia				2 300	(2 100-2 510)	133	5.8	(5.3-6.3)
Malawi	168 972			4 530	(4 130-4 940)	3 068	**	
Mozambique	1 480 908	170 022	•	21 000	(19 100-22 800)	26 087	>100	
Myanmar	37 402	6 531	17	15 900	(14 500-17 300)	337	2.1	(1.9-2.3)
Namibia	21 213	3 143	15	3 150	(2 860-3 430)	1 069	34	(31–37)
Nigeria	232 822	91 873	39	52 500	(47 800-57 200)	10 258	**	
Pakistan				107 000	(97 100-116 000)			
Papua New Guinea	3 788	590	16	2 430	(2 210-2 640)			
Philippines	6 755	3 817	57	55 200	(50 200-60 100)	6 473	**	
Russian Federation	16 868	16 368	97	1 690	(1 100-2 290)	10 096	**	
Sierra Leone	23 693	5 323	22	7 690	(7 010-8 380)			
South Africa	710 083	375 650	53	40 800	(37 200-44 500)	32 104	79	(72-86)
Thailand				5 510	(5 020-6 000)	278	5.0	(4.6-5.5)
Uganda				20 700	(18 900-22 500)	1 734	8.4	(7.7-9.2)
UR Tanzania				21 000	(19 100–22 800)	7 303	35	(32–38)
VietNam	14 509	4 552	31	15 600	(14 200–17 000)	4 128	26	(24-29)
Zambia	234 586	42 961	18	10 600	(9 670–11 600)	404	3.8	(3.5-4.2)
Zimbabwe	164 963	17 618	**	7 610	(6 930-8 290)	1 789	24	(22-26)

More than enough evidence to support TB preventive Therapy !!!

The impact of isoniazid preventive therapy and antiretroviral therapy on tuberculosis in children infected with HIV in a high tuberculosis incidence setting

L J Frigati, ¹ K Kranzer, ² M F Cotton, ³ H S Schaaf, ³ C J Lombard, ⁴ H J Zar¹

Background Tuberculosis (TB) is a major cause of morbidity and mortality among children infected with HIV. Strategies to prevent TB in children include isoniazid preventive therapy (IPT) and antiretroviral therapy (ART). IPT and ART have been reported to reduce TB incidence in adults but there are few studies in children.

Objective To investigate the combined effect of IPT and ART on TB risk in children infected with HIV.

Key messages

What is the key question?

► Does isoniazid preventive therapy (IPT) reduce tuberculosis (TB) in HIV-infected children on

What is the bottom line?

Latent tuberculosis infection

> Updated and guidelines for programmatic

Ayieko et al. BMC Infectious Diseases 2014, 14:91 http://www.biomedcentral.com/1471-2334/14/91

RESEARCH ARTICLE

Efficacy of isoniazid prophylactic therapy in prevention of tuberculosis in children:

James Ayieko^{1,4*}, Lisa Abuogi², Brett Simchowitz^{3,4}, Elizabeth A Bukusi¹, Allan H Smith⁴ and Arthur Reingold⁴

Background: Children are highly susceptible to tuberculosis; thus, there is need for safe and effective preventive interventions. Our objective was to evaluate the efficacy of isoniazid in prevention of tuberculosis morbidity and mortality in children aged 15 years or younger by performing a meta-analysis of randomized controlled trials. To our knowledge, this is the first meta-analysis evaluating efficacy of isoniazid prophylaxis in prevention of tuberculosis

BM



END TB

World Health Organization

Research

Research

Effect of isoniazid prophylaxis on mortality and incidence of tuberculosis in children with HIV: randomised controlled trial Heather J Zar, Mark F Cotton, Stanzi Strauss, Janine Karpakis, Gregory Hussey, H Simon Schaaf, Helena Rabie, Carl J

Lombard

Objectives To investigate the impact of isoniazid prophylaxis on mortality and incidence of tuberculosis in children with HIV. Design Two centre prospective double blind placebo controlled

urat. Participants Children aged ≥8 weeks with HIV. ratusipanus Chiunen ageu <0 weeks whit fits. Interventions Isoniazid or placebo given with co-trimoxazole either daily or three times a week.

Prevention of tuberculosis in children with HIV through prophylaxis with isoniazid may be effective in reducing mortality in areas with a high prevalence of tuberculosis. In studies of adults with HIV, prophylaxis with isoniazid significantly reduced the incidence of unberculosis and produced a favourable trend in membracine of innertonosis and produced a avourance term in mortality in those with a positive result on a tuberculin skin test. The effect of such prophylaxis in children, however, is unknown.

Impact of isoniazid preventive therapy **Open** on mortality among children less than 5 years old following exposure to tuberculosis at home in Guinea-Bissau: a prospective cohort study

> Victor Francisco Gomes. 1,2 Andreas Andersen, 1,2 Grethe Lemvik, 1,3 Christian Wejse, 1,3 Ines Oliveira, 1,2 Fina J Vieira, 4 Luis José Carlos, 5 Cesaltina da Silva Vieira, 4 Peter Aaby, 1,2 Per Gustafson⁶

Effect of household TB contact management

Potential effect of household contact management on childhood tuberculosis: a mathematical modelling study

Peter J Dodd, Courtney M Yuen, Mercedes C Becerra, Paul Revill, Helen E Jenkins, James A Seddon

Summary

Background Tuberculosis is recognised as a major cause of morbidity and mortality in children, with most cases in children going undiagnosed and resulting in poor outcomes. Household contact management, which aims to identify children with active tuberculosis and to provide preventive therapy for those with HIV or those younger than 5 years, has long been recommended but has very poor coverage globally. New guidelines include widespread provision of preventive therapy to children with a positive tuberculin skin test (TST) who are older than 5 years.

Methods In this mathematical modelling study, we provide the first global and national estimates of the impact of moving from zero to full coverage of household contact management (with and without preventive therapy for TST-positive children older than 5 years). We assembled data on tuberculosis notifications, household structure, household contact co-prevalence of tuberculosis disease and infection, the efficacy of preventive therapy, and the natural history of childhood tuberculosis. We used a model to estimate households visited, children screened, and treatment courses given for active and latent tuberculosis. We calculated the numbers of tuberculosis cases, deaths, and life-years lost because of tuberculosis for each intervention scenario and country.

Findings We estimated that full implementation of household contact management would prevent 159 500 (75% uncertainty interval [UI] 147 000–170 900) cases of tuberculosis and 108 400 (75% UI 98 800–116 700) deaths in children younger than 15 years (representing the loss of 7 30 5 000 [75% UI 6 663 000–7 87 4 000] life-years). We estimated that preventing one child death from tuberculosis would require visiting 48 households, screening 77 children, giving 48 preventive therapy courses, and giving two tuberculosis treatments versus no household contact management.

Highlights

- Full implementation of household contact management in children < 15 years would prevent:-
- √ 159 500 case (75% UI 147 000— 170 900) cases of TB
- ✓ 108 400 (75% UI 98 800–116 700) deaths due to TB

Examples of Implementing TB preventive Therapy under routine national TB programs

A. Evaluations of current programmatic practice						
Study	Setting	Study population	Methods	Findings		
Osman, 2013	14 primary health care facilities in Cape Town	< 5 year old household contacts	Retrospective review of electronic data records	 33.3% of 1179 records of infectious adult TB cases had no documentation of contacts Of the 525 contacts aged <5 years who were documented, less than half were screened for TB 141 (27%) contacts initiated IPT Only 18 (13%) completed IPT 		
Van Wyk, 2011	Primary community clinics in Cape Town	< 5 year old household contacts	Record review of routinely collected program data	 46% (310) of the TB case clinical charts did not have contacts documented 4 of the 149 under five contacts were screened Only 1% (2) were initiated on IPT 2 of the 56 under five contacts of non-infectious cases were screened and 1 was started on IPT contrary to recommendations 		
Claessens, 2002	44 districts hospitals in Malawi	< 5 year old household contacts	Cross sectional study by the Malawi NTP	 Only 21% of 659 smear positive patients had been informed about the need to screen their children for TB Only 9% of the 365 children were screened for TB 22 (6%) of children received IPT 		

Examples of Implementing TB preventive Therapy under routine national TB programs

B. Successful Programmatic Interventions						
Study	Setting	Study population	Methods	Findings		
Adjobimey, (2016)	Benin NTP Clinics	< 5 year old household contacts of smear positive TB	Integrating the contact management program under the NTP	 496 under 5 year old household contacts were initiated on 6 months IPT with an initiation rate of= 99.6%; 		
			Patients were asked to bring their under-five contacts to TB treatment visits and a phone call or home visit for missed appointments was made	The IPT completion rate was 86.1% with adherence based on clinic attendance		
Van Soelen, 2013	Urban clinic setting in Cape Town	< 5 year old household contacts	Introduction of an IPT register in the clinic	 More child contacts per adult case were identified (0.7 (54 children) vs. 0.3 (24 children)) as compared to pre-register An increase in the number of children started on IPT (54 vs. 4) was observed 37% of those who started, completed therapy compared to no information during pre-register period 		

Care giver related factors

- 1.Lack of awareness
- 2. Attitude giving medicines to a well child
- 3. Concern for undesired effects
- 4. Transport costs
- 5. Patient transfers
- 6. Relocation
- 7. Lack of convenient appointment times
- 8. Duration of therapy

Health provider related factors

- 1. Limited health worker confidence
- 2. Unclear eligibility criteria
- 3. Fear of long-term isoniazid resistance
- 4. Concern over availability of the supplies
- 5. Sub optimal implantation of active contact investigation

GAPS IN TB
CONTACT
MANAGEMENT
POLICY AND
IMPLEMENTATION

Health system related factors

- 1. Lack of standardized of policy guidelines 2. Lack of a sensitive TB screening tool
- 3. Varying eligibility for non-HIV infected individuals (different WHO eligibility criteria for low and high TB endemic settings)
- 4. Lack of standardized management tools (including reporting) for TPT
- 5. Sub optimal implementation of contact tracing
- 5. Need for accreditation of health facilities in some countries
- 6. Cost
- 7. Lack of program indicators on IPT
- 8.
- 9. Interrupted supplies
- 10. Fragmentation of monitoring and evaluation systems among multiple service providers
- 11. Large, unregulated private health sector

Opportunities for Improving TB contact Management

Service delivery

TB Contact investigation
Child survival programs (IMCI,
ICCM)

Monitoring and evaluation tools

Health work force

Effective training and mentorship strategies

Information

Guidelines

Monitoring and evaluation tools

Community engagement (ENGAGE-TB)

E-HMIS

Medical products, vaccines, and technologies

Shorter TB preventive regimen
Child friendly formulations
Rapid TB diagnostics — Xpert
E-Health Information System

Financing

Country specific budgets

Bilateral and Multilateral agencies

Global Fund

(Medicines, Diagnostics, Catastrophic costs)

Leadership and Governance

Country specific multisector plans

Child and Adolescent TB Road map 2018

END Strategy

Commitment from the UN HLM

HEALTH SYSTEM FRAMEWORK: BUILDING BLOCKS

UNTIL NO CHILD DIES OF TB!!!!!!