

TB-HIV Thailand/Asian Perspective

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Thailand

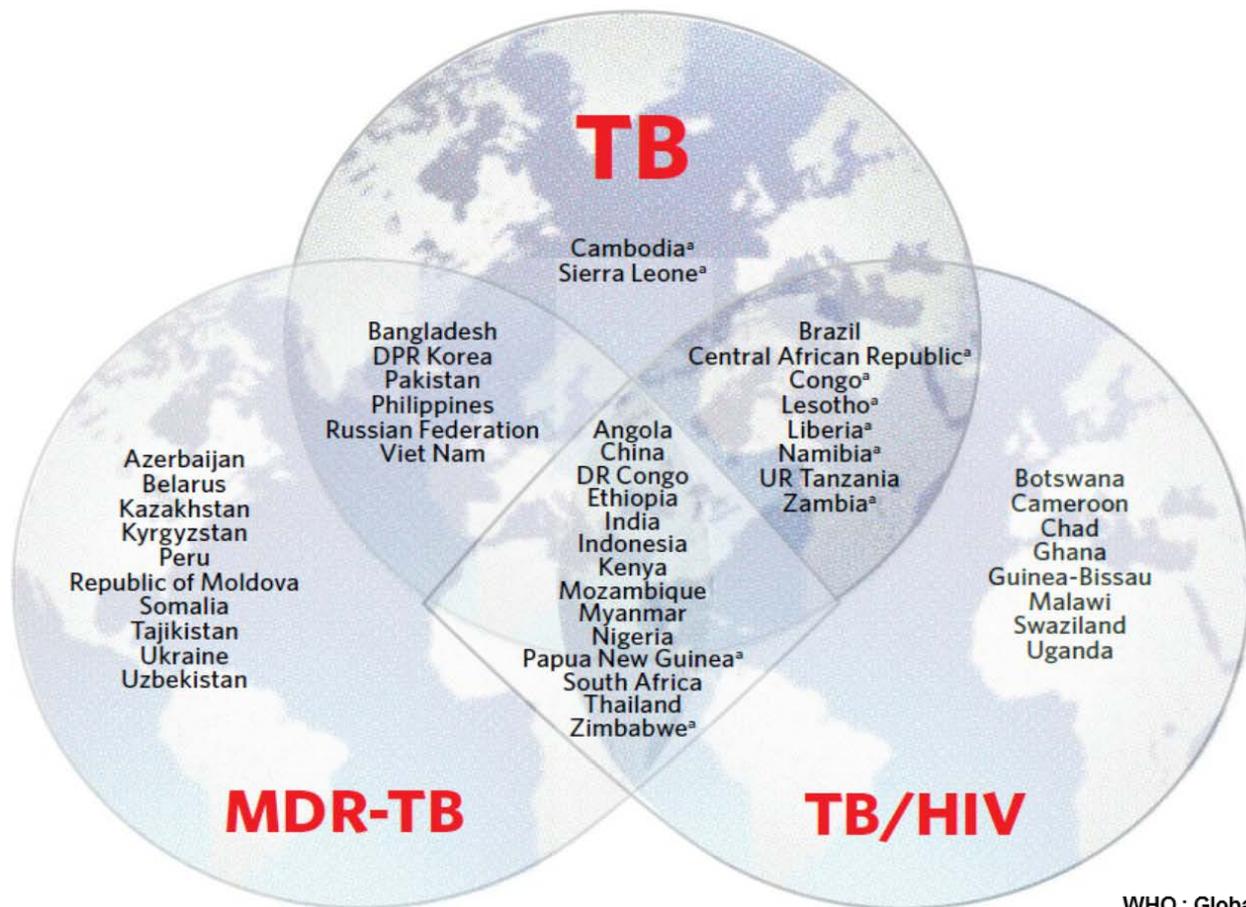
Bangkok | 10-12 April



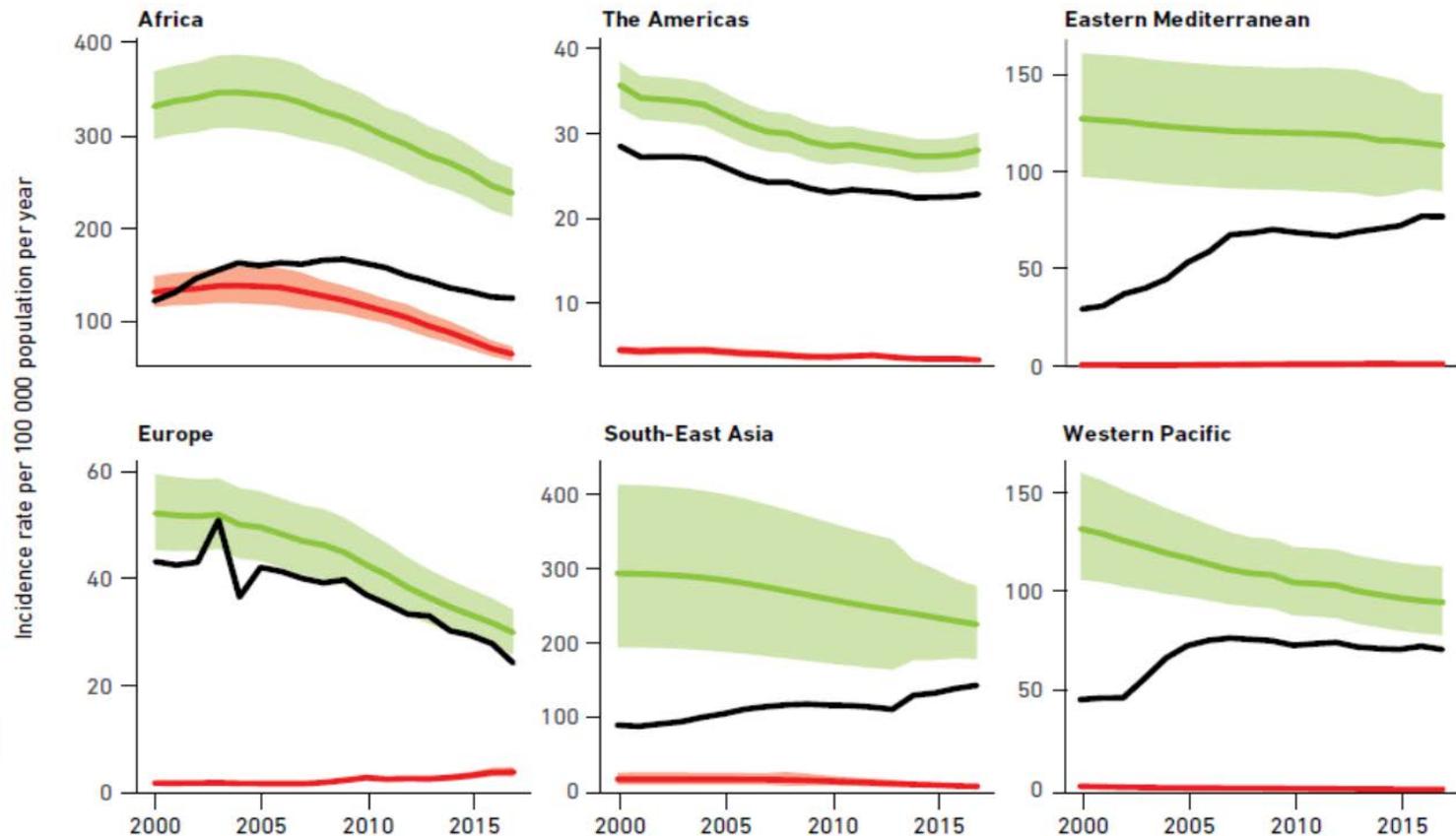
Tuberculosis Situation in Asia 2018

	POPULATION	HIV-NEGATIVE TB MORTALITY		HIV-POSITIVE TB MORTALITY ^b		TOTAL TB INCIDENCE		HIV-POSITIVE TB INCIDENCE	
		BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL
High TB burden countries	4 760 000	1 110	1 030–1 190	247	214–282	8 720	7 680–9 810	766	680–857
Africa	1 050 000	413	348–485	252	219–287	2 480	2 210–2 760	663	585–747
The Americas	1 010 000	18	17–19	6.0	5.3–6.7	282	262–302	30	28–33
Eastern Mediterranean	682 000	89	75–104	3.0	1.8–4.5	771	611–950	9.8	6.0–15
Europe	920 000	24	23–25	5.0	3.8–6.4	273	236–313	33	26–42
South-East Asia	1 970 000	638	598–679	28	22–36	4 440	3 530–5 450	152	117–191
Western Pacific	1 900 000	92	85–100	5.0	3.8–6.4	1 800	1 490–2 130	31	24–40
GLOBAL	7 520 000	1 270	1 190–1 360	300	266–335	10 000	9 000–11 100	920	832–1 010

Countries in the three TB high-burden country lists that will be used by WHO during the period 2016-2021 and their areas of overlap



Regional trends in estimated TB incidence rates by WHO region, 2000–2017. Total TB incidence rates are shown in **green** and incidence rates of HIV-positive TB are shown in **red**. Shaded areas represent uncertainty intervals. The **black** lines show notifications of new and relapse cases for comparison with estimates of the total incidence rate.



Country profile of TB/HIV

Country	China	India	Indonesia
Population	1410 M	1340 M	264 M
Incidence of TB (No.cases)	889,000	2,740,000	842,000
No. notification	778,390	1,908,371	446,732
GAP	110,610	831,629	395,268
Incidence of TB/HIV (no.cases)	12,000	86,000	36,000
No. notification	4,246	36,440	7,729
GAP	7,754	49,560	28,271
% of TB with HIV testing	55%	64%	29%
% of HIV positive	1.3%	3.1%	4.3%
% on ARV treatment	-	79%	29%

Country profile of TB/HIV

Country	Myanmar	Thailand
Population	53 M	69 M
Incidence of TB (No.cases)	191,000	108,000
No. notification	132,025	82,008
GAP	58,975	25,992
Incidence of TB/HIV (no.cases)	17,000	11,000
No. notification	10,164	7,130
GAP	6,836	3,870
% of TB with HIV testing	90%	82%
% of HIV positive	8.7%	11%
% on ARV treatment	63%	64%

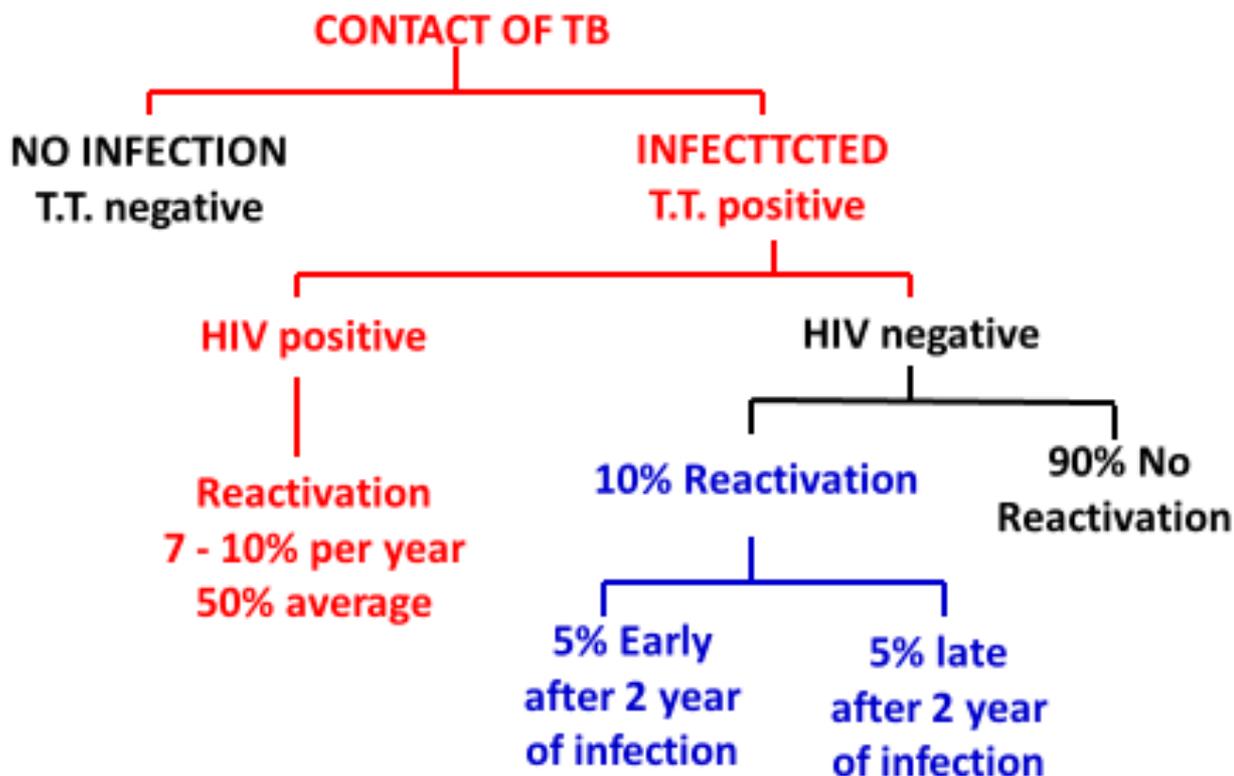
Mortality of TB/HIV in Asia

Country	No.cases	Mortality (per 100,000 population)
China	1,800	0.13
India	11,000	0.79
Indonesia	9,400	3.6
Myanmar	4,200	9.2
Thailand	2,900	4.2

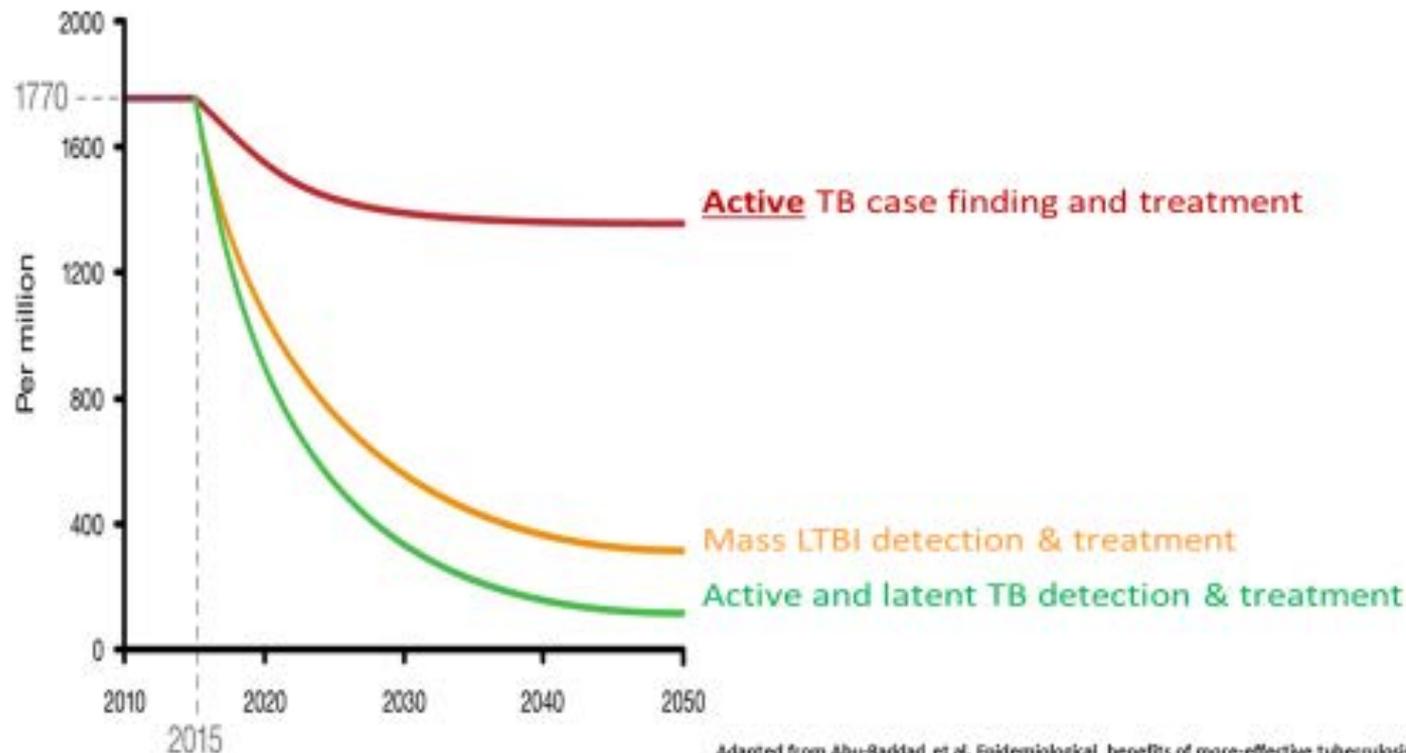
Tuberculosis Treatment in TB/HIV patient in Asia (2017)

Country	Success rate
China	51%
India	75%
Indonesia	64%
Myanmar	73%
Thailand	72%

NATURAL HISTORY OF TB AND EFFECT OF HIV INFECTION



Epidemiological Benefits of more-effective tuberculosis vaccines, drugs, and diagnostics



Adapted from Abu-Raddad et al. Epidemiological benefits of more-effective tuberculosis vaccines, drugs, and diagnostics. PNAS. 2009; 106: 13980-5.

Guidelines on the management of latent tuberculosis infection

THE
END TB
STRATEGY



World Health
Organization

Latent tuberculosis infection

Updated and
consolidated
guidelines for
programmatic
management

THE
END TB
STRATEGY



World Health
Organization

2.1 Adults and adolescents living with HIV

Adults and adolescents living with HIV, with unknown or a positive tuberculin skin test (TST) and are unlikely to have active TB should receive preventive treatment of TB as part of a comprehensive package of HIV care. Treatment should be given to these individuals irrespective of the degree of immunosuppression and also to those on antiretroviral treatment (ART), those who have previously been treated for TB and pregnant women. (*Strong recommendation, high-quality evidence. Existing recommendation*)

Source of existing recommendation: Guidelines for intensified tuberculosis case-finding and isoniazid preventive therapy for people living with HIV in resource-constrained settings. Geneva; World Health Organization; 2011 (http://apps.who.int/iris/bitstream/10665/44472/1/9789241500708_eng.pdf).

Treatment of latent tuberculosis infection in HIV infected persons (Review)

Comparison 2. Isoniazid vs placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Incidence of active TB (confirmed, probable or possible)	8	4136	Risk Ratio (M-H, Fixed, 95% CI)	0.67 [0.51, 0.87]
1.1 PPD+	4	1311	Risk Ratio (M-H, Fixed, 95% CI)	0.36 [0.22, 0.61]
1.2 PPD-	7	2490	Risk Ratio (M-H, Fixed, 95% CI)	0.86 [0.59, 1.26]
1.3 PPD unknown	2	335	Risk Ratio (M-H, Fixed, 95% CI)	0.86 [0.48, 1.52]
2 Incidence of confirmed TB	4	2063	Risk Ratio (M-H, Fixed, 95% CI)	0.72 [0.47, 1.11]
2.1 PPD+	1	112	Risk Ratio (M-H, Fixed, 95% CI)	0.13 [0.01, 2.32]

Treatment of latent tuberculosis infection in HIV infected persons (Review)

Comparison 1. Any TB drug vs placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Incidence of active TB (confirmed, probable or possible)	9	5762	Risk Ratio (M-H, Fixed, 95% CI)	0.68 [0.54, 0.85]
1.1 PPD+	4	2378	Risk Ratio (M-H, Fixed, 95% CI)	0.38 [0.25, 0.57]
1.2 PPD-	8	2920	Risk Ratio (M-H, Fixed, 95% CI)	0.89 [0.64, 1.24]
1.3 PPD unknown	2	464	Risk Ratio (M-H, Fixed, 95% CI)	0.81 [0.49, 1.34]
2 Incidence of confirmed TB	4	2573	Risk Ratio (M-H, Fixed, 95% CI)	0.73 [0.49, 1.08]
2.1 PPD+	1	161	Risk Ratio (M-H, Fixed, 95% CI)	0.30 [0.06, 1.57]
2.2 PPD-	3	1353	Risk Ratio (M-H, Fixed, 95% CI)	0.74 [0.38, 1.45]
2.3 PPD unknown	2	1059	Risk Ratio (M-H, Fixed, 95% CI)	0.79 [0.47, 1.32]
3 Incidence of death (all cause)	9	5762	Risk Ratio (M-H, Fixed, 95% CI)	0.94 [0.85, 1.05]
3.1 PPD+	4	2378	Risk Ratio (M-H, Fixed, 95% CI)	0.80 [0.63, 1.02]
3.2 PPD-	8	2920	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.89, 1.14]
3.3 PPD unknown	2	464	Risk Ratio (M-H, Fixed, 95% CI)	0.84 [0.58, 1.24]
4 Incidence of AIDS	2	355	Risk Ratio (M-H, Fixed, 95% CI)	0.88 [0.60, 1.28]
4.1 PPD+	1	63	Risk Ratio (M-H, Fixed, 95% CI)	0.36 [0.15, 0.85]
4.2 PPD-	2	292	Risk Ratio (M-H, Fixed, 95% CI)	1.10 [0.72, 1.69]
4.3 PPD unknown	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Incidence of adverse events leading to stopping treatment	8	5525	Risk Ratio (M-H, Fixed, 95% CI)	2.55 [1.70, 3.85]

Table 2 Recommended dosages of drugs for the treatment of LTBI

Drug regimen	Dose per kg body weight	Maximum dose
Isoniazid alone, daily for 6 or 9 months	Adults, 5 mg Children, 10 mg (range, 7-15 mg)	300 mg
Daily rifampicin alone for 3-4 months	Adults, 10 mg Children, 15 mg (range, 10-20 mg)	600 mg
Daily isoniazid plus rifampicin for 3-4 months	Isoniazid: Adults, 5 mg Children, 10 mg (range, 7-15 mg) Rifampicin Adults, 10 mg Children, 15 mg (range, 10-20 mg)	Isoniazid, 300 mg Rifampicin, 600 mg
Weekly rifapentine plus isoniazid for 3 months (12 doses)	Individuals aged ≥ 12 years: Isoniazid: 15 mg Individuals aged 2-11 years: isoniazid: 25 mg Rifapentine: 10.0-14.0 kg = 300 mg 14.1-25.0 kg = 450 mg 25.1-32.0 kg = 600 mg 32.1-50.0 kg = 750 mg > 50 kg = 900 mg	Isoniazid, 900 mg Rifapentine, 900 mg

Latent Tuberculosis Infection Treatment in HIV seropositive in Asia

Country	LTBI with Isoniazid 2016
China	-
India	10 %
Indonesia	16 %
Myanmar	17 %
Thailand	-

Three months of weekly rifapentine and isoniazid for treatment of *Mycobacterium tuberculosis* infection in HIV-coinfected persons (TBTC Study 26/ACTG 5259)*

Table 1. Characteristics of the modified intention-to-treat (MITT) study population.

Characteristic	3HP, N=206, n (%)	9H, N=193, n (%)	P value
Median age-years (IQR) ^a	36 (30–44)	36 (29–44)	0.85
Median CD4 ⁺ lymphocyte count – baseline (IQR) ^b	495 (389–675)	538 (418–729)	0.09
ART reported ^c	67 (33)	58 (30)	0.67
Male sex	146 (71)	131 (68)	0.59

Table 2. Tuberculosis cases and event rates by treatment arm.

Treatment arm	N	No. of TB cases	TB rate per 100 p-y	Cumulative TB rate (%)	Difference in cumulative TB rate ^a	Upper bound of the 95% CI (%)
Modified intention to treat population						
9H	193	6	1.25	3.50	–2.49	0.60
3HP	206	2	0.39	1.01		
Per protocol population						
9H	123	2	0.63	1.81	–1.25	1.47
3HP	183	1	0.21	0.56		

3HP, 3 months of weekly rifapentine plus isoniazid under direct observation; 9H, 9 months of daily isoniazid, self-administered.

^aThe difference is the rate for 3HP minus the rate for 9H.

**Three months of weekly rifapentine and isoniazid for
treatment of *Mycobacterium tuberculosis*
infection in HIV-coinfected persons** (TBTC Study 26/ACTG 5259)*

Table 3. Safety and tolerability of the study regimens.

Characteristic	3HP, N = 207, n (%)	9H, N = 186, n (%)	P value	% Difference (95% CI) ^a
Treatment completion (MITT)	183/206 (89)	123/193 (64)	<0.001	25.0 (17.0, 33.0)
Discontinuation because of adverse drug reaction	7 (3)	8 (4)	0.79	-1.0 (-4.7, 2.9)
Grade 3 toxicity	14 (7)	18 (10)	0.36	-3.0 (-8.4, 2.5)
Grade 4 toxicity	4 (2)	10 (5)	0.10	-3.0 (-7.2, 0.3)
Grade 5 (death)	6 (3)	5 (3)	1.00	0.2 (-3.0, 3.5)
Discontinuation due to hepatotoxicity ^b	2 (1)	8 (4)	0.05	-3.0 (-6.5, -0.1)
Flu-like/systemic drug reaction	2 (1)	0 (0)	0.50	1.0 (-0.4, 2.3)

Among participants who received at least 1 dose of study medications, except as noted. Percentages are in parentheses. 3HP, 3 months of weekly rifapentine plus isoniazid under direct observation; 9H, 9 months of daily isoniazid, self-administered.

^a95% CI for the difference in proportions using the Wilson Score Interval method.

^bNeither of the two persons in the 3HP arm and three of the eight persons in the 9H arm had underlying hepatitis C virus infection.

Impacts of 12-dose regimen for latent tuberculosis infection

Treatment completion rate and cost-effectiveness in Taiwan

Table 6

The medication and labor costs of 3HP and 9H regimens.

		3HP			9H		
		n	n (once a week)	Cost/patients	n	n (day)	Cost/patients
Medication costs							
Isoniazid	US\$ 0.03	9	12	3.24	3	270	24.3
Rifapentine	US\$ 3	6	12	216	—	—	
Total				219.24			24.3
Labor costs	US\$ 3.5 per hour		12	42		198	693
Medication costs and Labor costs				261.24			717.3

Table 7

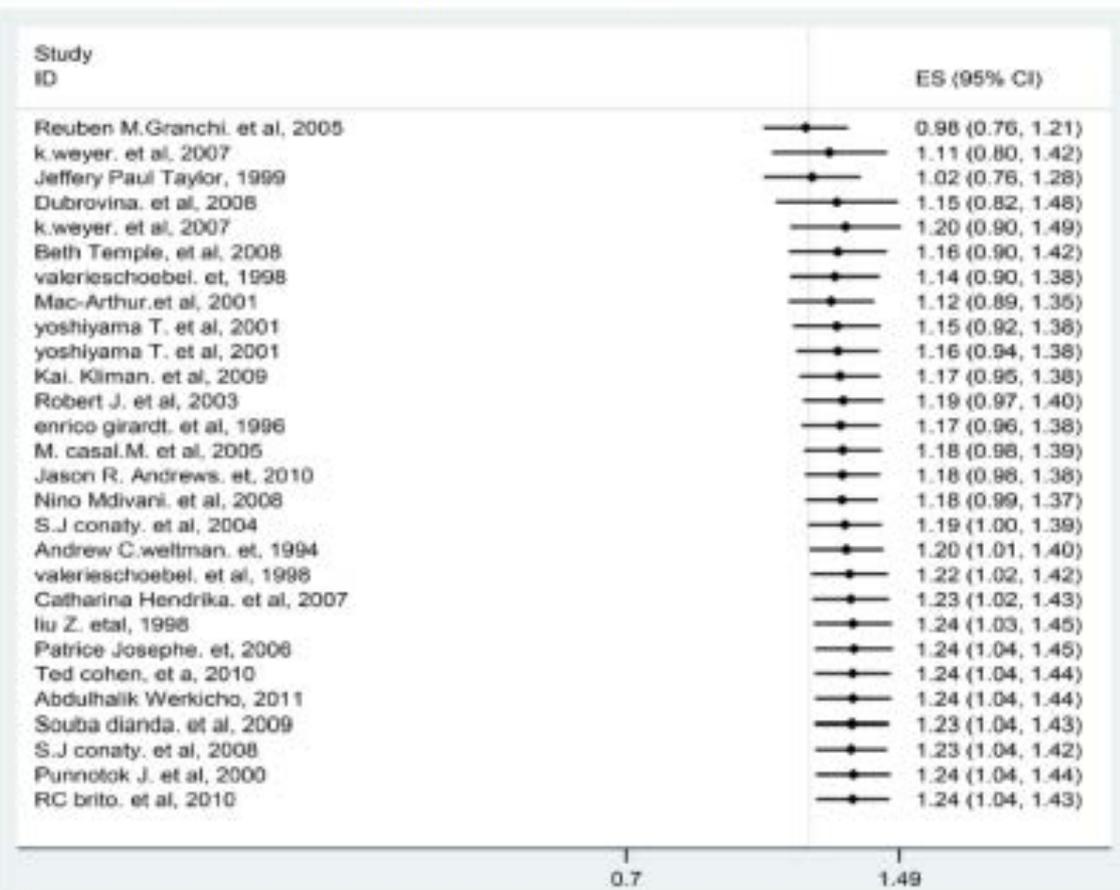
The cost-effectiveness ratio to avoided 1 case of tuberculosis in 3HP group and 9H group.

	3HP N=98	9H N=515
Cases estimated to become active TB	5	26
Cases actual become active TB	0	2
Cost for one TB case avoided (1 TB case avoided when 20 LTBI cases treated)	\$261.24 per case	\$717.3*(515/24)
	Total \$5225	Total \$15392

Concern of Clinician for Treatment of LTBI in HIV seropositive patient

- Adverse drug events such as hepatitis especially in adult HIV seropositive patients who received anti-retrovirus treatment.**
- Primary drug resistant of INH is high in Asia.**
- Duration of LTBI treatment is too long 6-9 months.**
- Non-adherence of LTBI treatment in HIV seropositive patient will amplify INH resistant in general population.**

Association between HIV/AIDS and Multi-Drug Resistance Tuberculosis: A Systematic Review and Meta-Analysis



Association between HIV/AIDS and Multi-Drug
Resistance Tuberculosis: A Systematic Review and Meta-
Analysis

Table 1. Summary of the 24 observational studies assessing the association between HIV/AIDS and multi-drug resistance tuberculosis included in the meta-analysis.

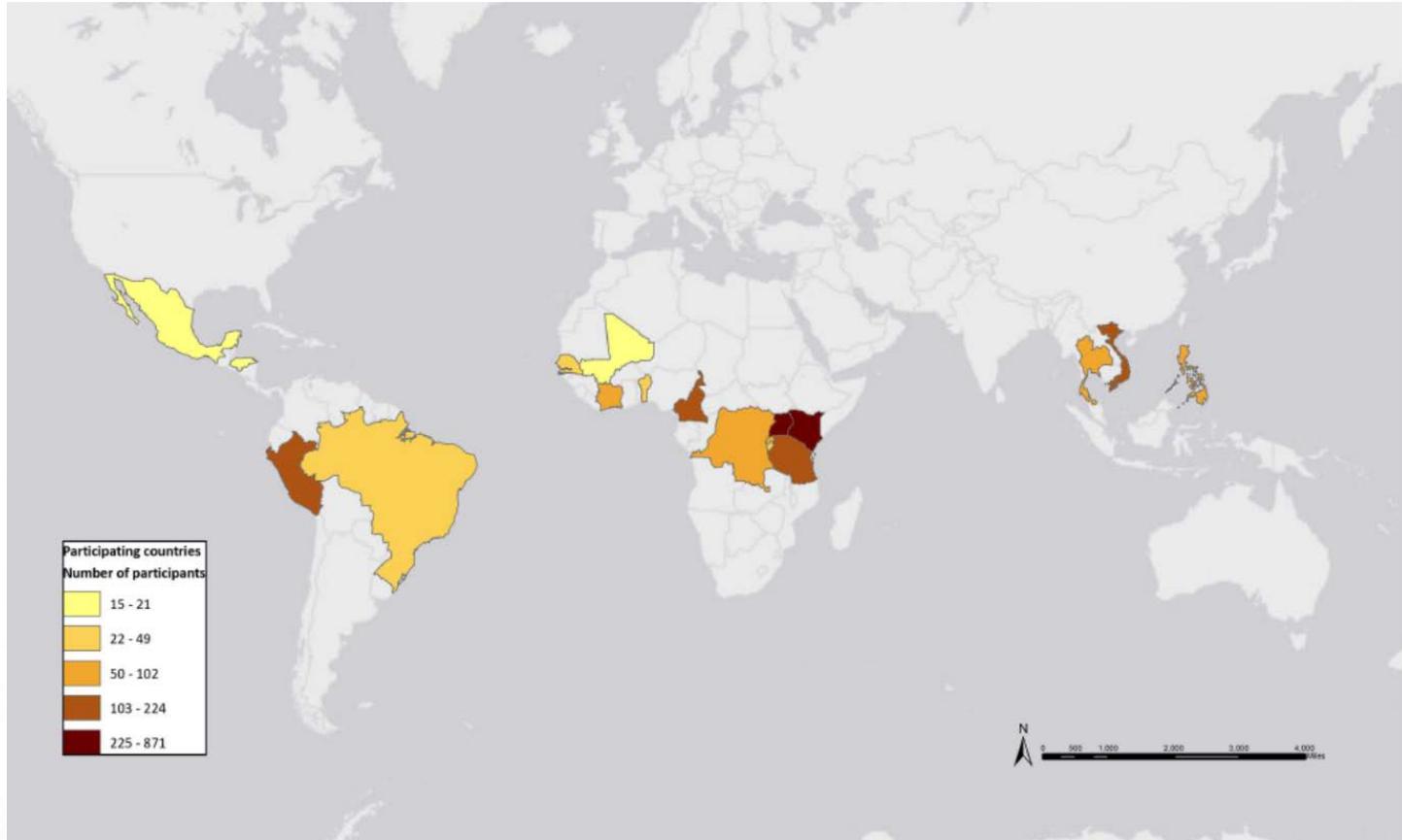
First author, year, country	Design	Sample size	MDR-type	Number HIV+	MDR-TB HIV+	Number HIV-	MDR-TB HIV-	AOR	CI
Dubrovina. et al, 2008 (Ukraine)	Cross-sectional ^a	1540	Any	307	31.6%	1143	23.8%	1.7	1.3–2.3
Valerieschoeel et al, 1998 (France)	Case-control ^a	1334	Primary	893	1.2%	5864	0.3%	3.3	1.5–7.3
		4	secondary	107	11.2%	868	6.6%	1	0.5–2.0
Robert M.Granchi. et al, 2005 (California)	Cross-sectional ^a	2871	Any	2031	4%	2736	1.4%		0.78–1.23
		2				2		0.98	
Patrice Josephe. et al, 2006 (Haiti)	Cross-sectional ^a	330	primary	115	10%	166	3%	3.2	1.1–8.9
Andrew C.weltman. et al, 1994(newyork city)	Case-control ^a	172	any	78	26.9%	25	4%	2.7	1.1–6.8
Nino Mdivani. et al, 2008 (Georgia)	cross-sectional ^a	996	any	5	40%	227	28.6%	1.4*	0.47–4.17
Catharina Hendrika. tal,2007(Netherlands)	Cross-sectional ^a	7090	primary	308	1.6%	646	0.6%	2.78	1.09–7.1
Kliiman K. 2009 (Estonia)	Cross sectional ^a	1163	any	54	16.7%	914	18.8%	1.57	0.80–3.11
SJ conaty. et al,2004 (England Wales)	Case-control ^b	9541	Primary	274	3.6%	7936	1%	2.5	1.2–5.20
			secondary	19	21.4%	611	8.2%	2.8	0.6–11.9
k.weyer. et al, 2007 (s/Africa)	Cross-sectional ^b	5866	any	2700	3.4%	1939	2.9%	1.3	1.0–1.70
			Secondary	501	7.9%	418	5.7%	1.46	1.04–2.07

Tuberculosis and HIV co-infection in Vietnam

Comparison of tuberculosis patients with and without HIV co-infection in Vietnam (2011–2014)

	All n (%)	HIV uninfected n (%)	HIV co-infected n (%)	HIV status unknown n (%)	OR (95% CI)*
All TB					
Pulmonary TB sm+	59 435 (58.2)	38 581 (60.4)	2 245 (50.4)	18 609 (55.0)	0.7 (0.6 - 0.7)
Pulmonary TB sm-	21 288 (20.8)	12 659 (19.8)	931 (20.9)	7 698 (22.7)	1.1 (1.0 - 1.2)
Extra-pulmonary TB	21 459 (21.0)	12 628 (19.8)	1 276 (28.7)	7 555 (22.3)	1.6 (1.5 - 1.7)
Total (N)	102 182	63 868	4 452	33 862	
Pulmonary TB sm+					
New	50 582 (85.1)	32 827 (85.1)	1 773 (79)	15 982 (85.9)	0.7 (0.6 - 0.7)
Retreatment after recurrence	7 090 (11.9)	4 630 (12.0)	343 (15.3)	2 117 (11.4)	1.3 (1.2 - 1.5)
Retreatment after treatment failure	573 (1.0)	394 (1.0)	37 (1.6)	142 (0.8)	1.6 (1.2 - 2.3)
Retreatment after treatment interruption	453 (0.8)	264 (0.7)	34 (1.5)	155 (0.8)	2.2 (1.6 - 3.2)
Other AFB(+)	737 (1.2)	466 (1.2)	58 (2.6)	213 (1.1)	2.2 (1.6 - 2.9)
Total (N)	59 435	38 581	2 245	18 609	
MDR-TB					
New	53 (5.0)	30 (4.0)	6 (15.0)	17 (9.3)	4.2 (1.6 - 10.8)
Failure Cat 1	172 (17.8)	139 (18.7)	6 (15.0)	27 (14.8)	0.8 (0.3 - 1.9)
Failure Cat 2	382 (39.6)	318 (42.8)	13 (32.5)	51 (28.0)	0.6 (0.3 - 1.3)
TB recurrence	298 (30.9)	212 (28.5)	12 (30.0)	74 (40.7)	1.1 (0.5 - 2.2)
Default	22 (2.3)	16 (2.2)	2 (5.0)	4 (2.2)	2.4 (0.5-10.8)
Other	38 (3.9)	28 (3.8)	1 (2.5)	9 (4.9)	0.7 (0.1 - 4.9)
Total (N)	965	743	40	182	

Low implementation of Xpert MTB/RIF among HIV/TB co-infected adults in the International epidemiologic Databases to Evaluate AIDS (IeDEA) program



Low implementation of Xpert MTB/RIF among HIV/TB co-infected adults in the International epidemiologic Databases to Evaluate AIDS (IeDEA) program

Table 3. TB testing utilization and outcomes among 2722 adult patients.

	n (%)
TB test utilization (n = 2722)	
Received at least one TB test	2070 (76%)
Received no TB test	650 (24%)
Missing	2 (<1%)
Type of TB test performed (n = 2555)*	
AFB smear	2025 (79%)
Culture	333 (13%)
Xpert	118 (5%)
Other NAAT	79 (3%)
Among TB tested (n = 2070), TB test results	
At least 1 positive result	931 (45%)
Negative	1139 (55%)

Low implementation of Xpert MTB/RIF among HIV/TB co-infected adults in the International epidemiologic Databases to Evaluate AIDS (IeDEA) program

Table 2. Xpert availability at participating sites.

Xpert availability	Participating Sites * (n = 30)	Patient Xpert receipt+ (n = 2722)
In this clinic	4 (13%)	28/754 (4%)
In the same health facility (but not at this clinic)	6 (20%)	44/326 (13%)
Only offsite (at distance)	9 (30%)	35/1153 (3%)
Not available	10 (33%)	11/453 (2%)
Availability unknown	1 (3%)	0/36 (0%)

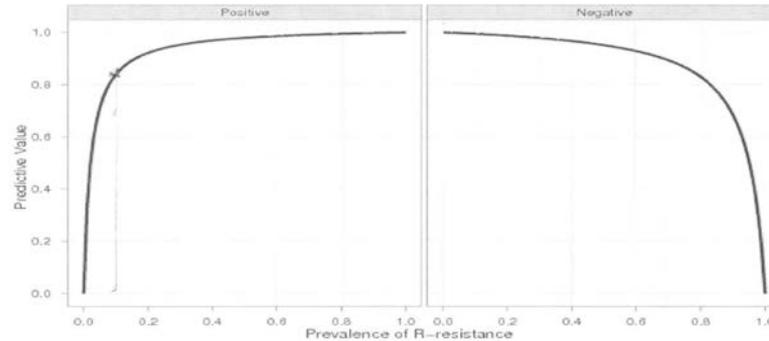
Low implementation of Xpert MTB/RIF among HIV/TB co-infected adults in the International epidemiologic Databases to Evaluate AIDS (IeDEA) program

Table 4. Xpert MTB/RIF utilization and outcomes among 2722 adult patients.

	n (%)
Xpert utilization (n = 2722)	
Not done	2602 (96%)
Done	118 (4%)
Missing	2 (<1%)
Among Xpert test done (n = 118), Xpert results	
Positive	76 (64%)
Negative	42 (36%)
Among Xpert test positives (n = 76), Rifampicin resistance	
No	64 (84%)
Yes	10 (13%)
Missing	2 (2%)

D- Predictive values of Xpert MTB/RIF for the diagnosis of MDR-TB

Xpert MTB/RIF sensitivity and specificity for the diagnosis of Rifampicin resistance are assumed equal to 0.95 and 0.98, respectively [5].



Predictive values of Xpert MTB/RIF for the diagnosis of MDR-TB depend on Xpert MTB/RIF's sensitivity and specificity to diagnose Rif-resistance, the prevalence of rifampicine resistance and the conditional probability of INH-resistance given Rifampicin resistance:

$$\Pr(H^+, R^+ | Xp^+, \mu) = \Pr(R^+ | Xp^+, \rho) \cdot \Pr(H^+ | R^+) \quad (1)$$

where μ indicates the prevalence of MDR-TB (resistance to H and R are denoted H^+ and R^+ , respectively), and $\Pr(R^+ | Xp^+, \rho)$ denotes the predictive value of a Positive Xpert MTB/RIF test (positive for R-resistance) given prevalence of R-resistance ρ .

Figures 1 and 2 below show the predictive values of Xpert MTB/RIF for the diagnosis of TB as determined from the Global Drug Resistance project over the period 1994–2010, which includes 445 country-year data points for Drug Resistance (DR) in new cases and 383 country-year data points for DR in retreatment cases. Positive predictive values of Xpert MTB/RIF to diagnose MDR-TB increase with the prevalence of MDR-TB, and therefore, are relatively higher in cases re-registered for a treatment change. Among

TB/HIV in Asia

- **More than 100,000 TB/HIV patients in Asia did not get diagnosis and access to both TB and HIV care.**
- **Under utilization of Xpert MTB/RIF for diagnosis of TB in TB/HIV patients.**
- **Low coverage of HIV infection screening in TB patients**
- **Isoniazid preventive therapy in HIV seropositive patient is not a priority in NTP program.**
- **Mortality rate of TB/HIV patients is rather high some countries in Asia.**
- **Multidrug resistant in TB/HIV patients is higher than general population.**
- **ARV treatment rate in TB/HIV is low.**

TB Clinic

HIV Clinic

Same group of Health Care Staffs

Laboratory

Laboratory