

Kingdom of Cambodia

Nation Religion King

Ministry of Health

Report

**National HIV Seroprevalence Survey
Amongst TB Patients in Cambodia, 2005**

National Center for Tuberculosis and Leprosy Control (CENAT)



Ministry of Health



**National Center for
Tuberculosis and Leprosy Control**

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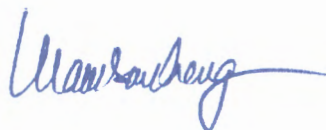
The second National HIV Sero-prevalence Survey Amongst TB Patients in Cambodia was conducted in January 2005 by the National TB Program (NTP). It is the result of excellent collaborative efforts among the major partners and staff of the National Tuberculosis Control Program .

Since information from research activities become more and more important for NTP, the findings of the survey will be of great significance for the management of TB/HIV, particularly in planning, monitoring and evaluation. In addition, the findings will assist the NTP in gearing its efforts towards contribution to reaching the Millennium Development Goals by 2015.

The successful completion of this survey also highlights the great commitment of the Ministry of Health of the Kingdom of Cambodia, the National Centre for Tuberculosis and Leprosy Control (CENAT) and various partners concerned to jointly combat the disease in the kingdom.

Phnom Penh, 06 March, 2006

Secretary of State for Health



Dr. Mam Bun Heng

Acknowledgements

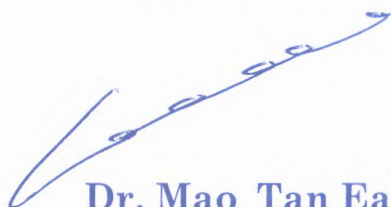
On behalf of the National TB Control Program we would like to express our deep thanks and appreciation to all organizations and individuals for their contributions in making this survey successful.

We would like to profoundly thank CENAT/JICA TB control Project, JATA/RIT, Japanese Foundation for AIDS Prevention and WHO for their technical and financial supports for the survey.

We sincerely hope the survey results will be of great use in bringing a brighter future to those who suffer from Tuberculosis.

Phnom Penh, ០៣ March, 2006

National Center for TB and Leprosy Control
Director

A handwritten signature in blue ink, consisting of a series of loops and a long horizontal stroke, positioned above the printed name.

Dr. Mao Tan Eang

Executive Summary

HIV epidemic in South East Asia which started in late 1980's left negative impact on TB epidemic of Cambodia. The Cambodia National Center for Tuberculosis and Leprosy Control (CENAT) has started TB/HIV surveillance since 2003.

The TB/HIV surveillance 2003 enrolled all TB patients registered in NTP in January, 2003. In total, 2,240 were enrolled in the analysis. The surveillance 2003 showed HIV prevalence among all TB patients and new smear-positive pulmonary TB were 11.8 % and 8.2 %, respectively. The surveillance was conducted again in January, 2005 in order to monitor the trend of HIV epidemic and its impact among TB patients.

The unlinked anonymous HIV testing was applied. Particle agglutination assay and immunochromatography were simultaneously used for HIV testing. All data was entered into a computerized database and analyzed using STATA8.

2,668 patients were contacted in total. 23 were excluded, of which 4 were due to missing the data collection forms and 19 were due to not being obtained serum from. Of 2,645, 13 were not confirmed as TB. Finally, 2,632 patients were analyzed in the surveillance.

Overall HIV sero-prevalence among all TB patients was 9.9%. Among smear-positive pulmonary TB with/without extra-pulmonary TB cases, overall HIV sero-prevalence declined from 11.4% to 5.2%. Among smear-negative pulmonary TB and/or extra-pulmonary TB cases, an overall number of the cases taken for the survey in 2005 was 46% bigger than that of 2003, but the HIV sero-prevalence remained same, 18.5%. The risk factors on HIV sero-prevalence were analyzed by logistic regression model. These were Thai border area, Coastal area, Phnom Penh, all age groups except more than 65, non-Cambodian, not-new treatment category, and smear-negative pulmonary TB and/or extra-pulmonary TB.

It is inferred that decline of the HIV sero-prevalence among smear-positive pulmonary TB cases was due to decline of HIV epidemic and improvement of case detection by DOTS expansion in NTP. To the contrary, the increase of HIV-positive smear-negative pulmonary and/or extra-pulmonary TB suggested that the HIV epidemic worsened morbidity and mortality of TB patients. Based on such a precedent case of Chiang Rai, Thailand, it is estimated that HIV epidemic will continue to effect on TB epidemic and increase TB patients for next several years in Cambodia. Against TB/HIV dual epidemic, there are urgent needs of further interventions.

I. INTRODUCTION

HIV epidemic in South East Asia which started in late 1980's hit Cambodia (National Center for HIV/AIDS, Dermatology and STD [NCHAD], Ministry of Health, Cambodia, 2004) and also left negative impact on tuberculosis (TB) epidemic of Cambodia, which has been known as one of the high TB epidemic countries in the world (World Health Organization [WHO], 2003). The Cambodia National Center for Tuberculosis and Leprosy Control (CENAT) has started HIV seroprevalence surveillance among TB patients (TB/HIV surveillance) since 2003 funded and technically assisted by WHO and Japan International Cooperation Agency (JICA) in order to measure the HIV epidemic impact on TB epidemic and monitor the trend of HIV epidemic by cross-sectional population surveillance using National Tuberculosis Program (NTP) network expanded in the whole country.

The TB/HIV surveillance 2003 enrolled all TB patients registered in NTP in January, 2003 regardless of whether they knew their HIV sero-status or not. Anonymous HIV testing was applied to those who consented to the surveillance. 2,295 patients were contacted and 2,244 who were confirmed TB diagnosis and obtained serum were enrolled in the analysis.

The TB/HIV surveillance 2003 showed interesting results; HIV prevalence among all TB patients and new smear positive pulmonary TB were 11.8 % and 8.5 %, respectively . These results were much higher than those previously obtained from the HIV sentinel surveillance conducted by NCHADS which reported HIV prevalence among TB patients as 6.0% in 2001 and 8.4% in 2002 (NCHAD, Cambodia, 2004).

Moreover, the TB/HIV surveillance 2003 revealed several risk factors which associated to HIV epidemic such as resident areas (Thai border area, the coastal area and Phnom Penh), sexually active age groups (25 to 34 and year 35 to 44), smear negative pulmonary TB and extra pulmonary TB: It was astonishing that in Phnom Penh, the HIV prevalence rates among all TB patients and new smear-positive pulmonary TB were as high as 34.3 % .

The TB/HIV surveillance was conducted again in January, 2005 following the same protocol of the surveillance 2003 in order to monitor the trend of HIV epidemic among TB patients by comparing the results to those in 2003. It was also expected to gain the whole picture of HIV epidemic in Cambodia and to investigate the associations of the risk factors which previously identified in 2003. The result would be useful to plan interventions for both TB control and HIV control in the country.

II. METHODOLOGY

1. Sampling Size and Sampling Procedure

Based on the statistics of first half of 2003, and supposing that there was no seasonal change in the numbers of recruited TB patients, the estimated number of all forms of TB cases registered in NTP was 27,656, annually. If the true HIV prevalence were 13.8% and it measured 11.8% as an error in the confidence of 99% (2% difference as an acceptable error), 1842 samples would be adequate.

All eligible TB patients diagnosed during the study period would be enrolled as a representative sample (consecutive sampling), however, the enough sample size would be applied in order to allow international comparison among new smear-positive pulmonary TB. Therefore, we have decided to over-recruit by 15% or 2,167 samples. It was estimated that average monthly number of the TB patient was 2,305 ($27,656 / 12 = 2,305$). Therefore, one month would be enough to fulfill the necessary sample size as an inclusion period of this surveillance.

2. Study Population

This surveillance was cross-sectional population study. All TB patients who were diagnosed as TB and newly registered to NTP in January 2005 were all contacted as eligible persons regardless of whether they knew their HIV sero-status or not. The study included patients with all forms of TB (smear-positive and negative pulmonary TB, and extra-pulmonary TB) and with any treatment categories (new, relapse, other re-treatment and others). The patients whose serum was not obtained and who were not confirmed as TB were all excluded from the analysis.

3. Study Regimens

The unlinked anonymous HIV testing was applied. Minimum unidentifiable data on patient's basic demographic information and TB were taken in the data collection form. The form and the serum sample of each patient were labeled by a unique study number.

4. Laboratory Procedures

Particle agglutination assay (Serodia HIV1/2, FUJIREBIO, Tokyo, Japan) and immunochromatography (Determine HIV1/2, ABOTT, Germany) were simultaneously used. The serum, which reacted to both tests, was considered as positive. Those which reacted to only one test were further examined by confirmatory HIV testing.

5. Data Management and Analysis

All data collection forms were carefully checked for errors prior to the analysis. The CENAT staff responsible for data management and the analysis did link demographic data with HIV test result. All data was entered into a computerized database and analyzed using STATA8.

6. Ethical Consideration

The unlinked anonymous HIV testing was applied based on the ethical approach. Informed consent to the study was taken from all participants who agreed for blood drawing. The protocol of the surveillance was reviewed and accepted by the Institutional Review Board, Ministry of Health, Cambodia.

III. RESULTS

2,668 patients were contacted in total. 4 were excluded due to missing the data collection forms and 19 were also excluded due to not being obtained serum from. The reasons that serum was not obtained were; the patient refused HIV test because he/she had already known HIV-positive status (10); the patient refused because of other reasons (2); the patient died before blood drawing (1); blood drawing was technically difficult (1). Of 2,645, 13 were not confirmed as TB because; the diagnoses of smear-negative pulmonary TB was made without chest X-ray (6); the diagnosis of smear-negative pulmonary TB was made without smear test (3); the site of extra pulmonary TB was not mentioned (4). Finally, 2,632 patients were analyzed in the surveillance.

Overall HIV sero-prevalence among all TB patients was 9.9%.

Characteristics of the all participants and the HIV sero-prevalence rates by these characteristics were shown in Table 1. The HIV sero-prevalence among male and female were almost same as 10.0% and 9.8%, respectively. Higher HIV sero-prevalence was seen more among the sexually active age groups (age 25 to 34, and 35 to 44), non-Cambodian, other re-treatment cases, smear-negative pulmonary TB, extra-pulmonary TB, and smear-negative pulmonary and extra-pulmonary TB (p-value <0.05).

Table 2 showed sex distribution and the HIV sero-prevalence in each age group. In the sexually active age groups, the prevalence among male was higher than female except the age group 15 to 24. The difference of the HIV sero-prevalence between male (2.6%) and female (9.8%) was statistically significant in the age group 15 to 24 (p-value 0.03).

The HIV sero-prevalence rates of all TB patients by province were shown with those in 2003 in Table 3. The prevalence in Phnom Penh was the highest at 26% which declined from 34.3% between 2003 and 2005. In some provinces which had high prevalence in 2003 showed high prevalence again in 2005 besides two provinces (Siem Reap and Prey Veng).

The analysis was conducted by disease forms and geographical areas among only new TB cases (Table 4). Disease forms were categorized smear-positive pulmonary TB with/without extra-pulmonary TB, or smear-negative pulmonary TB and/or extra-pulmonary TB. All provinces were categorized by five areas according to geographical and socio-economical similarities (Phnom Penh, Thai border area, Coastal area, North east area, and Others).

Among smear-positive pulmonary TB with/without extra-pulmonary TB cases, overall HIV sero-prevalence declined from 11.4% to 5.2% between 2003 and 2005. In HIV hot areas such as Phnom Penh and Coastal area, decline were observed. Among smear-negative pulmonary TB and/or extra-pulmonary TB cases, an overall number of the cases taken for the survey in 2005 was 46% bigger than that of 2003 (590 and 859), but the HIV sero-prevalence remained same as 18.5% between 2003 and 2005. However, increase of the HIV sero-prevalence was seen in Thai border area, Coastal area, and Others.

The risk factors on HIV sero-prevalence were analyzed by logistic regression model (Table 5). The factors which were significantly associated to the HIV sero-prevalence were; Thai border area, Coastal area, Phnom Penh, all age groups except more than 65, non-Cambodian, not-new treatment category, and smear-negative pulmonary TB and/or extra-pulmonary TB.

IV. DISCUSSION

HIV sero-prevalence of all TB patients in the whole country in 2005 was 9.9% which was lower than 11.8% in 2003. In the comparison of new smear-positive pulmonary TB, which was more reliable for TB diagnosis in the resource limited setting, HIV sero-prevalence dropped from 11.4% to 5.2% between 2003 and 2005.

There are several possible reasons for this drop. One of the reasons is that the HIV epidemic in Cambodia is declining. Generally, smear-positive pulmonary TB is seen in both HIV positive and negative people, while smear-negative pulmonary TB and extra-pulmonary TB are more frequently seen in HIV positive people when they become immunocompromised (Aaron L, Saadoun D, Calatroni I, et al., 2004). Therefore, the HIV-seroprevalence among smear-positive pulmonary TB might reflect the early stage of HIV

infection, although the HIV sero-prevalence among smear-negative pulmonary TB and extra-pulmonary TB cases might reflect HIV infections happened in several years ago which was the peak of HIV epidemic in Cambodia (NCHADS, 2004). Cambodia NCHADS reported the national antenatal clinic (ANC) HIV prevalence had a peak of 2.82% in about 1999 and then, it was declining very slowly down to 2.73% in 2002 (NCHADS, 2004). It is inferred that the decline of the HIV sero-prevalence among smear-positive TB cases in 2005 reflected the recent HIV epidemic trend in Cambodia.

Another reason is that the ambulatory Directly Observed Treatment, in Short-course (DOTS) expansion of NTP to the peripheral health centers between 2003 and 2005 improved case detection of new HIV-negative, smear-positive pulmonary TB. NTP started the approach of ambulatory DOTS expansion in 1999 and started the DOTS service newly at 264 health centers at the beginning of 2003 and at all health centers at the beginning of 2005. Improvement of case detection possibly diluted the HIV sero-prevalence among new smear-positive pulmonary TB in 2005.

To the contrary to the decline of HIV sero-prevalence among new smear-positive pulmonary TB, HIV epidemic did not show any change among smear-negative pulmonary TB and/or extra-pulmonary TB cases between 2003 and 2005. Actually, the number of these patients has enormously increased with 45.5% growth in two years, though growth of new smear-positive pulmonary TB cases was 7.4%. This result suggests that HIV epidemic impact worsen morbidity and mortality of TB patients, even though HIV epidemic is slowly declining. It is inferred that HIV infection among smear-negative pulmonary and extra-pulmonary cases were occurred in the late 1990's when the HIV epidemic in Cambodia was at peak. It can be said that TB epidemic in Cambodia has been hit by the hardest HIV epidemic of several years ago right now.

Yamada N. and Yanai H et al. (2003) revealed that HIV epidemic had been increasing numbers of both HIV-positive and HIV-negative TB for a decade after the HIV epidemic peak in Chiang Rai, Thailand. Cambodia is a next country to Thailand and there are many similarities in geographic and cultural characteristics and HIV epidemic trend between two countries. Based on such a precedent case of Chiang Rai, Thailand, it is estimated that

HIV epidemic continues to effect on TB epidemic and increase TB patients for next several years in Cambodia.

Against such a serious circumstance of TB/HIV dual epidemic, there are urgent needs of interventions such as; the wide introduction of HIV counseling and testing for TB patients; the improvement of capacities of both TB services and integrated general health services for diagnosis and management of complicated TB/HIV cases; collaboration of TB and HIV services; the wide usage of anti-retroviral (ARV) treatment; strengthening referral system between health centers and referral hospitals; more usage of preventive measures such as Cotrimoxazole to TB/HIV patients and Isoniazide to people living with HIV/AIDS.

The TB/HIV surveillance revealed the some HIV hot spots in the country; Phnom Penh, Thai border area and Coastal area. It is inferred that these areas are where both internal and external migrations of people are quite active. It has been focused that migration is one of the risk factors of HIV transmission (UN Regional Taskforce on Mobile Populations and HIV Vulnerability, 2004). Actually, it has been identified in Thailand that many Cambodian fishermen work at some ports in Thailand which are HIV epidemic areas (Press B, 2004, and Program for Appropriate Technology in Health [PATH]/Mekong, May 2002). However, there were a few HIV related studies/programs conducted for Cambodian migrants in Cambodia because of the sensitive nature of this issue (Press B, 2004). The high HIV prevalence in areas where active migration of people is suspected suggests the importance of the intervention against migration as well as series of interventions against TB/HIV epidemics.

Especially, the HIV epidemic in Thai border area has been the most growing among three HIV hot spots. Although, in the analysis by sex (Table 2), the HIV sero-prevalence of female was significantly higher than male at age group 15-24, out of 11 HIV-positive cases among these female, 5 were from Thai border area. Marital state or occupations of them were not able to be investigated by this surveillance, however, it is a concern that transmission between migrant workers to their young wives are happening. Reviewing current HIV control strategies and re-planning interventions for current situation are urgently necessary for this area, because other hot spots such as Phnom Penh and Coastal provinces did not show worsening of the HIV epidemic among TB patients.

Siem Reap and Prey Veng used to be provinces with high HIV sero-prevalence in 2003, however, the HIV sero-prevalence among TB declined in 2005. Although quality control of the TB services should be reviewed first of all, it might be useful to examine the effects of interventions against HIV infection conducted in these provinces for last several years. Siem Reap started ARV treatment in the Chronic Disease Clinic with collaboration with some non-governmental organization (NGO) (Medecins Sans Frontieres [MSF], 2004). Prey Veng, which has been know as one of sources of migrant fishermen working in Thailand because of low socio-economic situation, have an unique intervention against HIV infection of mobile population conducted by other NGO; a movie of the tragic story caused by HIV infection in a family which husband got HIV infection in Thailand was shown in many villages and left big impact (PATH/Mekong, May, 2002). Lessons learned by previous excellent programs should be applied for interventions in other provinces.

V. CONCLUSION

The TB/HIV surveillance was effective for monitoring the serious impact of TB/HIV dual epidemics, estimating the trend and future course, and identifying the risk factors for HIV infection among TB patients.

This TB/HIV surveillance is unique as one of the TB/HIV epidemic report from Asia. There are many reports on the relationship between TB and HIV infection from Africa (Siriaryapon P, Yanai H, Glynn JR, et al., 2002). Because the HIV epidemic trend and cultures are totally different between Africa and Asia, our surveillance is useful for other Asian countries as well as Cambodia itself.

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Table 1. Characteristics of the Cambodia TB/HIV surveillance 2005 participants and HIV prevalence

	Total		HIV- positive	%HIV	OR#	p-value
All TB cases	2632		261	9.9%		
Sex						
Male	1302	(49.5%)	130	10.0%	reference	
Female	1330	(50.5%)	131	9.8%	0.99	0.91
Age Group						
0-14	52	(2.0%)	4	7.7%	15.79	<0.01
15-24	226	(8.6%)	14	6.2%	12.51	<0.01
25-34	420	(16.0%)	104	24.8%	62.37	<0.01
35-44	587	(22.3%)	103	17.5%	40.33	<0.01
45-54	498	(18.9%)	26	5.2%	10.44	<0.01
55-64	468	(17.8%)	8	1.7%	3.30	0.13
>=65	381	(14.5%)	2	0.5%	reference	
Nationality						
Cambodian	2611	(99.2%)	253	9.7%	reference	
non Cambodian	21	(0.8%)	8	38.1%	5.74	<0.01
Treatment Category						
New	2533	(96.2%)	246	9.7%	reference	
Relapse	68	(2.6%)	9	13.2%	1.42	0.34
Other re-treatment	3	(0.1%)	0	0.0%	-	-
Others	24	(0.9%)	6	25.0%	3.10	0.02
Not Recorded	4	(0.2%)	0	0.0%	-	-
TB Site						
Sm(+)/PTB* only	1747	(66.4%)	95	5.4%	reference	
Sm(+)/PTB +EPTB†	2	(0.1%)	0	0.0%	-	
Sm(-)/PTB‡ only	421	(16.0%)	62	14.7%	3.00	<0.01
EPTB only	441	(16.8%)	98	22.2%	4.97	<0.01
Sm(-)/PTB +EPTB	21	(0.8%)	6	28.6%	6.96	<0.01

OR: Odds ratio

* Sm(+)/PTB: Smear-positive Pulmonary TB

† EPTB: Extra Pulmonary TB

‡ Sm(-)/PTB: Smear-negative Pulmonary TB

Table 2. Comparison of HIV sero-prevalence by sex in each age group of the Cambodia TB/HIV surveillance 2005 participants

Age Group	Total	Male	Female	Male %HIV	Female %HIV	OR*	p-value
0-14	52	27	29	11.1%	3.4%	3.26	0.30
15-24	226	114	112	2.6%	9.8%	0.25	0.03 [†]
25-34	420	205	217	27.3%	25.8%	0.89	0.61
35-44	587	302	286	19.2%	15.7%	1.28	0.26
45-54	498	215	283	6.5%	4.2%	1.57	0.26
55-64	468	243	229	1.2%	2.2%	0.56	0.42
>=65	381	203	180	0.5%	0.6%	0.89	0.93

* OR: Odds ratio of HIV-positive in male compared to female

[†] p-value=0.03 is statistically significant at the 5% level.

Table 4. Comparison of HIV prevalence of New Smear-Positive Pulmonary TB cases between the Cambodia TB/HIV surveillance 2003 and 2005

	2003		2005	
	Total	%HIV	Total	%HIV
All New TB	2149	10.1%	2533	9.7%
Area				
Phnom Penh	280	31.4%	226	26.5%
Thai Border Provinces	427	9.8%	545	14.7%
Coastal Provinces	127	12.6%	152	13.2%
North East Provinces	102	6.9%	112	4.5%
Others	1213	5.4%	1498	5.4%
All Sm(+)⁺PTB +/- EPTB	1559	11.4%	1674	5.2%
Area				
Phnom Penh	141	22.7%	97	19.6%
Thai Border Provinces	323	8.7%	347	8.1%
Coastal Provinces	98	11.2%	105	9.5%
North East Provinces	63	7.9%	80	3.8%
Others	933	5.5%	1045	2.6%
All Sm(-)⁻PTB and/or EPTB	590	18.5%	859	18.5%
Area				
Phnom Penh	139	41.7%	129	31.8%
Thai Border Provinces	104	19.2%	198	26.3%
Coastal Provinces	29	17.2%	47	21.3%
North East Provinces	39	10.3%	32	6.3%
Others	279	7.9%	453	11.9%

Note: 1. New smear-positive pulmonary TB cases include those who having only smear-positive pulmonary TB and those who have both smea-positive pulmonary TB and extra-pulmonary TB: 2. Thai Border Provinces include Oudor Meanchey, B. Meanchey, Siem Reap, Battam Bang, and Pailin provinces: 3. Coastal Provinces include Kampot, Krong Kep, Kg Som, and Koh Kong provinces: 4. North East Provinces include Pheah Vihear, Stung Treng, Kratie, Mondul Kiri, and Rattanakiri provinces:5. Others include Kandal, Svay Rieng, Pursat, Kg Thom, Takeo, Kg Speu, Prey Veng, Kg Chnnang, and Kg Cham.

Table 5. Logistic Regression Analysis of risk factors on HIV prevalence in Cambodia, 2005 January

factor	AOR*	95%C.I	p-value
Area†			
Others	reference		
North East provinces	1.07	(0.44-2.62)	0.88
Thai border provinces	2.36	(1.69-3.33)	<0.01
Coastal provinces	2.79	(1.59-4.89)	<0.01
Phnom Penh	4.07	(2.70-6.15)	<0.01
Age group			
0-14	8.16	(1.41-47.12)	<0.01
15-24	10.43	(2.32-47.03)	<0.01
25-34	57.82	(14.03-238.39)	<0.01
35-44	43.11	(10.48-177.45)	<0.01
45-54	11.06	(2.58-47.36)	<0.01
55-64	3.90	(0.82-18.64)	0.09
more than 65	reference		
Sex			
Male	reference		
Female	0.97	(0.72-1.29)	0.82
Nationality			
Cambodian	reference		
Non-Cambodian	3.40	(1.22-9.28)	0.02

* AOR: Adjusted Odds Ratio

† Area Category: Others; Kandal, Svay Rieng, Pursat, Kg Thom, Takeo, Kg Speu, Prey Veng, Kg Chnnang, Kg Cham: North East Provinces: Preah Vihear, Stung Treng, Kratie, Mondul Kiri, Rattanakiri: Thai Border: Oudor Meanchey, B. Meanchey, Siem Reap, Battam Bang, Pailin: Costal Provinces: Kampot, Krong Kep, Kg Som, Koh Kong

Category			
New	reference		
Not-new	2.49	(1.30-4.78)	<0.01
TB-site			
Smear-positive PTB [‡] +/- EPTB [#]	reference		
Smear-negative PTB and/or EPTB	3.83	(2.85-5.15)	<0.01

‡ PTB: pulmonary TB

EPTB: extra-pulmonary TB

‡ PTB: pulmonary TB

EPTB: extra-pulmonary TB

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