

**INCREASED YIELD OF SMEAR POSITIVE PULMONARY TB CASES BY SCREENING PATIENTS WITH  $\geq 2$  WEEKS COUGH, COMPARED TO  $\geq 3$  WEEKS AND ADEQUACY OF 2 SPUTUM SMEAR EXAMINATIONS FOR DIAGNOSIS.**

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**Summary**

**Background**

RNTCP recommends examining three sputum smears for AFB from Chest Symptomatics (CSs) with cough of  $\geq 3$  weeks for diagnosis of Pulmonary TB (PTB). A previous multi-centric study from Tuberculosis Research centre (TRC) has shown that the yield of sputum positive cases can be increased if duration of cough for screening was reduced to  $\geq 2$  weeks. Other studies have shown that two smear examinations are adequate for diagnosis of smear positive PTB. To validate the above findings, a cross sectional multi-centric study was repeated in different settings in five geographical areas in India.

**Methods**

Three primary and secondary level health facilities with high out-patient attendance were selected from two Tuberculosis Units (TU) in each of the 15 selected districts to screen about 10,000 new adult outpatients from each state. For patients who did not volunteer history of cough, symptoms were elicited using a structured simple questionnaire. All the CSs were referred for sputum examination.

**Results**

A total of 96,787 out-patients were registered. Among them 69,209 (72%) were new adult out-patients. Using  $\geq 2$  weeks of cough instead of  $\geq 3$  weeks as the criterion for screening, there was an overall increase of 58% in CS and 23% increase in the detection of smear-positive cases. Among 211 patients, 210 were positive at least by one smear from the initial two specimens. Increase in the work-load if 2 smears were done for patients with cough of  $\geq 2$  weeks cough were 2 specimens (i.e.13 to 15) per day for an adult OPD of 150.

**Conclusion**

The yield of sputum positive PTB cases can be improved by screening patients with  $\geq 2$  weeks cough and two specimens are adequate for diagnosis. [Indian J Tuberc 2008; 55: 77-83]

**Key words:** Chest symptomatic, RNTCP, Sputum smear examination-AFB

**INTRODUCTION**

Following a phased rapid expansion from 1997, the Government of India's DOTS-based Revised National Tuberculosis Control Programme (RNTCP) achieved nation-wide coverage in early 2006.<sup>1</sup> RNTCP recommends that the diagnosis of Pulmonary TB (PTB) is made by the examination of three sputum smears for AFB from chest symptomatics (CSs) with a history of cough of three weeks or more.<sup>2</sup>

A previous multi-centric study undertaken by Tuberculosis Research Centre (TRC), Chennai,

compared the yield of sputum smear positive PTB cases among CSs with a cough of  $\geq 2$  weeks versus  $\geq 3$  weeks, and found an increase in the yield if the duration of cough for screening was reduced to  $\geq 2$  weeks.<sup>3</sup> Various studies have shown that PTB cases can be diagnosed by doing two smears examination rather than the present recommended three, saving time as well as cost.<sup>4-6</sup> A recent systematic review suggested that reducing the recommended number of specimens from 3 to 2 could also potentially increase case detection by improving the quality of examination of the first two specimens<sup>7</sup>. To validate these findings, we undertook the current study in different settings in five geographical areas in India.

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## OBJECTIVES

1. To assess the yield of smear positive cases among chest symptomatics with cough of two weeks or more compared to three weeks or more.
2. To compare the efficacy of two smear examinations instead of three to diagnose smear positive PTB cases among chest symptomatics.

## METHODS

### Study design

In this cross sectional multi-centric study, adopting a multi-stage stratified sampling procedure, five States; Andhra Pradesh, Maharashtra, Orissa, Rajasthan and West Bengal where RNTCP coverage was >50%, were conveniently selected. From each of these States, three districts were selected; one each with a low, medium and high case detection rate as per the RNTCP performance report of the fourth quarter 2004. A convenient sample of two TB Units (TUs) [refer footnote <sup>1</sup>] in each district was selected, and three primary and three secondary level health facilities with high Out Patient Department (OPD) attendance were selected in those TUs, to screen about 10,000 new adult outpatients from each State. From the primary health facilities, one non-microscopy and two microscopy centres with a daily average of 50 new adults out-patients were selected. Similarly from the secondary level health facilities, two taluk level hospitals and one Government hospital with daily about 100 new adults patients were included. The duration of the data collection for the primary level centres was a minimum of 10 days or until the target of 500 was achieved. For secondary level centres, a minimum of one week or until the target of 700 was reached. Duration of intake was from December 2005 to March 2006.

### Definitions

**New adult out-patient** – A patient making their first visit to a health facility for the current illness, aged  $\geq 15$  years, during the study period.

**Chest Symptomatic (CS):** A new adult out-patient with a history of a cough of two weeks or more, with or without expectoration, or with a history of haemoptysis. The chest symptomatics were analysed in two groups. First, those who had cough of  $\geq 2$  weeks and the second group, those who had cough of  $\geq 3$  weeks.

**Smear positive PTB:** At least one sputum, positive for AFB by smear microscopy.

Medical officers and health workers in the study centres were trained about the study procedures and were asked to ensure that sputum examination was done on all patients with chest symptoms who fulfilled the criteria of a chest symptomatic. All out-patients were asked about their main complaints. If a patient did not spontaneously give a history of cough, then it sought after using a structured simple questionnaire.

All CSs were given a referral slip for sputum examination. In case of non-microscopy centres, arrangements were made for collection and transport of sputum specimens to the nearest microscopy centre. Patients with chest symptoms were asked to return on the following day to provide an early morning sample and a second spot specimen. Daily out-patient load at each facility according to age and sex, were collected using the OPD attendance register maintained at the facility.

To ensure accuracy of data collection, the respective State and District TB Officers, and TRC staff made frequent supervisory visits to the health facilities involved in the study.

### Statistical analysis

The data were scrutinised and computerized, verified keying in twice, edited and corrected for discrepancy and missing information. Data was analysed using SPSS/PC version 13.0. The Chi-square test was used to test difference in proportions. The level of statistical significance was defined as  $p \leq 0.05$ .

<sup>1</sup>A TB Unit under RNTCP is a sub-district supervisory and monitoring unit covering approximately 500,000 population.

**RESULTS**

During the study period, a total of 96,787 out-patients were registered in the selected centres of the five states. Among them, 69,209 (72%) fitted the criteria for new adult out-patients; 13,394 from Andhra Pradesh, 16,002 from Maharashtra, 11,017 from Orissa, 12,916 from Rajasthan and 15,880 from West Bengal. (Table 1). Using  $\geq 2$  weeks instead of  $\geq 3$  weeks as the criterion for screening of chest symptomatics for sputum microscopy, there was an overall increase of 58% in chest symptomatics i.e. an increase from 1,625 to 2,560 (range 50-69%). The increase in the detection of smear-positive PTB cases was

23% (range 18 to 40%). Among the 17% (441/2,560) who did not complain of a cough spontaneously, the rate of smear positivity was 5.7% (25/435) compared to 9.1% (190/2088) among those who complained spontaneously, a non-significant difference.

The increase in the number of CSs using cough of  $\geq 2$  weeks for screening was maximum among 15-25 year age group (Table 2) and minimum among the 56-65 age group. There was 38% increase in positivity rate among the younger age group. There was, however, no difference in the increase in the CSs and positivity rate between males and females (62% vs 55%, and 29% vs 21%).

**Table 1:** Proportion of chest symptomatics and sputum positivity rate state-wise

State	New adult out patients	Cough $\geq 2$ weeks*				Cough $\geq 3$ weeks				Increased %	
		CS	S+ve	Per 100000 new adult OPD		CS	S+ve	Per 100000 new adult OPD		CS	S+ve
(a)	(b)	n(%)	n(%)	CS	S+ve	n(%)	n(%)	CS	S+ve	(k)	(l)
		(c)	(d)	(e)	(f)	(g)	(h)	(i)	(j)	(e-i)/e	(f-j)/f
Andhra Pradesh	13394	465 (3.5)	64 (13.8)	3472	478	309 (2.3)	54 (17.5)	2307	403	50	19
Orissa	11017	423	43 (3.8)	3840 (10.2)	390	250 (2.3)	34 (13.6)	2269	309	69	26
Maharashtra	16002	640 (4.0)	40 (6.2)	4000	250	398 (2.5)	34 (8.5)	2487	212	61	18
Rajasthan	12916	355 (2.7)	33 (9.3)	2749	255	233 (1.8)	28 (12.0)	1804	217	52	18
West Bengal	15880	677 (4.3)	35 (5.2)	4263	220	435 (2.7)	25 (5.7)	2739	157	56	40
Total	69209	2560 (3.7)	215 (8.4)	3699 <sup>a</sup>	311 <sup>a</sup>	1625 (2.3)	175 (10.8)	2348 <sup>a</sup>	253 <sup>a</sup>	58 <sup>b</sup>	23 <sup>b</sup>

\*including all cases  $> 3$  weeks

CS = chest symptomatic; S+ve = smear positive.

<sup>a</sup> Estimated for one lakh New adult OPD based on the total

<sup>b</sup> Calculated based on the formula given

New adult out-patients screened in the primary and secondary health facilities were 25,650 and 43,559 respectively. The increase in the CSs was 57% and 58% and positivity rate were 19% and 25% in primary and secondary facilities respectively.

Among 935 CSs with  $\geq 2$  weeks of cough, 23 (2.5%) patients did not give sputum. Amongst the 1,625 CSs with  $\geq 3$  weeks of cough, 14 (0.9%) did not give sputum which was statistically significant ( $p < 0.01$ ).

Three samples were given by 2383 patients. As per the existing RNTCP definition of a smear positive PTB case, two or three specimens were positive for 199 (8.4%). If only the first 2 specimens were considered, both specimens were positive in 161 (6.8%). This was statistically significant ( $p < 0.001$ ) by McNemar's test. However, if one positive sputum was taken as the criterion for diagnosis of a smear positive PTB case, the positivity was similar whether two or three specimens were considered i.e. 211 (8.9%) cases detected if three specimens were considered and 210 (8.8%) if only the first two specimens were considered.

**Table 2:** Distribution of chest symptomatics in different age groups

Age	New adult out patients	Cough $\geq 2$ weeks*				Cough $\geq 3$ weeks				Increased %	
		CS	S+ve	Per 100000 new adult OPD	CS	S+ve	CS	S+ve	Per 100000 new adult OPD	CS	S+ve
(a)	(b)	n(%)	n(%)	(e)	(f)	n(%)	n(%)	(i)	(j)	(k)	(l)
		(c)	(d)			(g)	(h)			(e-i)/e	(f-j)/f
15 - 25	21689	551 (2.5)	47 (8.5)	2540	217	317 (1.5)	34 (10.7)	1462	157	74	38
26 - 35	16375	526 (3.2)	51 (9.7)	3212	311	339 (2.1)	41 (12.1)	2070	250	55	24
36 - 45	11627	453 (3.9)	50 (11.0)	3896	430	287 (2.5)	44 (15.3)	2468	378	58	14
46 - 55	7933	396 (5.0)	38 (9.6)	4992	479	248 (3.1)	31 (12.5)	3126	391	60	23
56 - 65	7789	422 (5.4)	20 (4.7)	5418	257	301 (3.9)	17 (5.6)	3864	218	40	18
> - 66	3796	212 (5.6)	9 (4.2)	5585	237	133 (3.5)	8 (6.0)	3504	211	59	13
Total	69209	2560 (3.7)	215 (8.4)	3699 <sup>a</sup>	311 <sup>a</sup>	1625 (2.3)	175 (10.8)	2348 <sup>a</sup>	253 <sup>a</sup>	58 <sup>b</sup>	23 <sup>b</sup>

\* including all cases  $\geq 3$  weeks

CS = chest symptomatic; S+ve = smear positive.

<sup>a</sup> Estimated for one lakh New adult OPD based on the total

<sup>b</sup> Calculated based on the formula given

We estimated the increase in the work-load for the laboratory in the respective health facility by reducing the duration of cough to  $\geq 2$  weeks for screening. Considering an average daily OPD attendance of 150, the number of specimens to be examined for diagnosis will be around 13 per day for screening chest symptomatics if a criterion of  $\geq 3$  weeks cough is utilised. If  $\geq 2$  weeks' cough and two sputum examinations were utilised, the average work-load per day would be 15 specimens per day. Thus with a change to  $\geq 2$  weeks' cough and 2 smear examinations, the increase in work-load will be only two specimens per day (Table 3).

## DISCUSSION

According to the current RNTCP recommendations, any patient with cough of  $\geq 3$

weeks should be screened for TB by doing three sputum examinations. This study confirms that the detection of smear positive PTB cases can be improved if the screening criterion is changed to a history of cough for  $\geq 2$  weeks. The findings of this study validate those shown by the earlier study done in 2002 in a different setting which showed 47% increase in sputum positive cases among CSs with  $\geq 2$  weeks cough.<sup>3</sup> Baily et al in 1967 reported an increased yield of 16% smear positive cases when the screening criterion used was cough of  $\geq 2$  weeks (44 of 622 with  $\geq 2$  weeks vs 37 of 275 with  $\geq 3$  weeks).<sup>8</sup> Our study also has similar findings.

In this study, the highest incremental yield of CSs and smear positive cases were found in the age group of 15-25 years. Vigilance should thus be high for history of cough when screening the

**Table 3:** Estimated work-load per microscopy centre per day in primary and secondary health facilities

	Primary health facility		Secondary health facility		Total		Cough 2 weeks or more with 2 specimens
	Cough $\geq 2$ weeks	Cough $\geq 3$ weeks	Cough $\geq 2$ weeks	Cough $\geq 3$ weeks	Cough $\geq 2$ weeks	Cough $\geq 3$ weeks	
New adult out patients per day (n)	46	46	104	104	150	150	150
Out patient with cough %	4.0	2.4	3.7	2.3	-	-	-
Patients with cough per year (n)	508	329	1157	719	1664	1048	-
<b>Smear examined per year (n)</b>							
For diagnosis ( three smears per patients )	1523	988	3470	2157	4993	3145	3328
For follow-up	381	247	868	539	1248	786	1248
Total	1904	1235	4338	2696	6241	3931	4576
Average smears per day	6	4	14	9	21	13	15

younger age groups attending out-patient facilities in India.

Another important finding of our study was the similar smear positivity rate among OPD subjects who voluntarily complained of cough and those from whom the symptom was elicited. Similar finding was reported in an earlier study also.<sup>3</sup> This emphasises the need to actively detect symptomatics among the passively attending OPD attendees.

This study also investigated the diagnostic value of the third sputum specimen for the diagnosing of smear positive PTB cases. Three specimens were given by 2,383 patients, of whom 211 were positive on at least one specimen out of the three. Only one patient, however, was positive on the third specimen alone (0.5%). Another study from this centre also showed just 0.8% (8/962) of suspects positive by the third specimen alone.<sup>4</sup> A recent study in Moldova and Uganda also concluded that the third serial sputum smear examination was inefficient in diagnosing sputum smear positive PTB.<sup>9</sup>

As per the RNTCP definition for a new smear positive PTB case, two or three specimens were positive among 199 patients. If only the first two samples were considered, 161 patients were positive on both smears, with thus a loss of 38 (19%) patients. As, however, many studies have reported that the incremental yield from the third specimen is negligible. If the first two specimens are considered with a case definition of at least one positive smear, then 210 out of 211 smear positive PTB cases would be detected i.e. two smears are an efficient method to diagnose smear positive PTB.<sup>4-7,9,10</sup> Even though the positive smear was not confirmed by culture in the study since it was done under programme conditions, it has been reported that among patients with only one of the two smears positive, 90% were positive by culture<sup>11</sup>.

A concern raised was that if the screening criterion for a chest symptomatic is reduced from  $\geq 3$  weeks to  $\geq 2$  weeks, there would be an increase in the laboratory work-load. However, we estimated from the study findings that the increase would only be in the order of two to three specimens per day if

the number of specimens is also reduced from the present recommended three to two. This small increase is manageable by virtually all microscopy centres under RNTCP.

## CONCLUSION

**The yield of sputum smear positive PTB cases can be improved if patients with  $\geq 2$  weeks history of cough are screened to diagnose such cases. In addition, two sputum smear examinations are as efficient as three for diagnosis. There is no significant increase in the work-load by screening CSs with  $\geq 2$  weeks cough if a methodology of only two sputum smear examinations is utilised.**

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On behalf of the Tuberculosis Association of India