

## Screening tuberculosis suspects using two sputum smears

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### SUMMARY

**SETTING:** Ntcheu district hospital, Malawi.

**OBJECTIVE:** To assess a screening strategy for tuberculosis (TB) suspects using two sputum smears.

**DESIGN:** A strategy of screening all TB suspects with two sputum smears for 6 months (1 July–31 December 1998) was compared with the period 1 January to 30 June 1998 during which the strategy of screening TB suspects with three sputum smears was in use. All chest radiographs of patients with negative sputum smears were assessed, and in those with pulmonary cavities and extensive disease a third sputum smear was examined. Data were collected from the laboratory sputum register and the TB register. The two 6-month periods were compared.

**RESULTS:** In the laboratory register, using a two-sputum strategy, 186 (16%) of 1152 TB suspects were smear-positive, a result that was no different than when the three-sputum strategy was used, where 173 (16%) of

1106 TB suspects were smear-positive. The clinical pattern of TB using the different screening strategies was similar, with 58% of registered patients smear-positive with the two-sputum strategy and 54% smear-positive with the three-sputum strategy. In the first 6 months 3177 sputum smears were examined compared to 2266 smears in the second 6 months, a 29% reduction in the number of smears examined. The cost of consumables using the strategy of three sputum smears was USD \$731 compared with USD \$521 using the strategy of two sputum smears.

**CONCLUSIONS:** Screening TB suspects using two sputum smears is as effective as screening using three sputum smears, and is associated with less laboratory work and savings in costs.

**KEY WORDS:** sputum smear examination; pulmonary tuberculosis

IT IS CURRENTLY recommended by both the World Health Organization (WHO)<sup>1</sup> and the International Union Against Tuberculosis and Lung Disease (IUATLD)<sup>2</sup> that pulmonary tuberculosis (PTB) suspects submit three sputum specimens for smear examination for presence of acid-fast bacilli (AFB). The epidemic of associated human immunodeficiency virus (HIV) and tuberculosis (TB) in sub-Saharan Africa has led to a huge increase in the number of suspects submitting sputum for smear examination. In an operational research study conducted in 40 hospitals (three central, 22 district and 15 mission hospitals) in Malawi in the first quarter of 1998, 17 479 patients submitted sputum samples for smear examination, of whom 12 292 were new patients (unpublished observations). Examining three sputum smears for each new suspect constitutes a huge workload for the small number of hospital laboratory staff.

A large study conducted with the IUATLD in Tanzania showed that among suspects with a complete set of three sputum smears examined, the incremental yield of smear-positive cases was 83.4% with the first specimen,

12.2% with the second and 4.4% with the third.<sup>3</sup> Several other studies have shown similar results.<sup>4,5</sup> A study conducted in Blantyre,<sup>5</sup> Malawi, found that the yield of smear-positive cases was 83% with the first specimen, 13% with the second and 4% with the third. Such results suggest that under routine conditions the incremental yield from a third smear after two examinations is relatively small, and that screening with two sputum specimens could be the basis for case-finding in low-income, high prevalence countries.

We decided to screen pulmonary tuberculosis (PTB) suspects with two sputum smears during a 6-month period in one district in Malawi, and compare results with those obtained in the previous 6 months when screening was carried out using three sputum smears.

### METHODS

*Screening and management of patients:  
January–June 1998*

The study was carried out in Ntcheu district hospital, situated in the Central region of Malawi. In the first 6

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months, 1 January to 30 June 1998, the district followed established national guidelines of screening TB suspects using three sputum smears.<sup>6</sup> With this screening process, a patient is classified as having smear-positive PTB if 1) at least two sputum specimens are positive for AFB by microscopy, or 2) one sputum specimen is positive for AFB by microscopy and there are radiographic abnormalities consistent with PTB. A patient is classified as having smear-negative PTB if the sputum smears are negative, there is no clinical response to broad spectrum antibiotics and the chest radiograph shows abnormalities consistent with PTB.

#### *Screening and management of patients: July–December 1998*

From 1 July to 31 December 1998, the screening process was changed so that all TB suspects submitted two sputum specimens as 1) an on the spot specimen and 2) an early morning specimen the next day. All sputum specimens were examined in the Ntcheu hospital laboratory for AFB using the Ziehl-Neelsen stain. Specimens were not marked by health workers or laboratory staff as early morning or 'on the spot', and differentiating the smear-positive yield between the two different sputum specimens in this study was not possible. Previous research in Malawi suggests that the yield from early morning and 'on the spot' sputum is similar.<sup>5</sup>

Smear-positive PTB patients were diagnosed according to national guidelines,<sup>6</sup> and received standardised anti-tuberculosis treatment according to the Ntcheu district policy. Suspects who were sputum smear-negative proceeded to have a chest radiograph in the district hospital (the only radiographic facility in Ntcheu district is situated in the hospital). Suspects who were judged by the district health officer or a senior clinical officer to have radiographic pulmonary infiltrates, intrathoracic lymphadenopathy and fibrosis were registered and treated for smear-negative PTB, and those with evidence of disease in other sites (e.g., pleural effusion, pericardial effusion) were registered and treated for extra-pulmonary TB. Suspects judged to have pulmonary cavities, extensive radiographic changes or large pleural effusions submitted one extra sputum on the spot. Those found to be sputum smear-positive on this third sputum specimen were treated for smear-positive PTB and those who were sputum negative were treated for smear-negative PTB/extra-pulmonary TB.

#### *Training of health staff*

All district health staff were briefed during May and June about the change of screening strategy from three sputum specimens to two sputum specimens, and a briefing letter was distributed to officers in charge of health centres. Clinical staff in the hospital also received a one-day training course on reading chest radiographs, with particular emphasis on identifying pulmonary cavities.

#### *Data collection and analysis*

The district registers were inspected for each of the 6-month periods in 1998. Data were collected from the Laboratory Register on the number of new TB suspects submitting sputum specimens, the number of sputum smears examined per suspect and the number of patients with sputum smears positive for AFB. The total number of sputum smears examined during each 6-month period was calculated. Data were collected from the Tuberculosis Register on the pattern of TB, and the proportion of PTB patients with smear-positive and smear-negative disease. Chest radiographs performed on all patients with smear-negative PTB, pleural effusion, pericardial effusion and miliary TB during the second 6 months were kept, and read at a later date by an independent observer (ADH), with a view to determining whether pulmonary cavities were present and whether a third sputum specimen should or should not have been performed.

#### *Cost analysis*

In 1997 the total cost of a single sputum smear examination in Ntcheu district hospital was calculated at US\$1.9.<sup>7</sup> This figure included costs of staff, equipment, consumables, transport, general overheads, supervision and buildings. A change from a three-sputum to a two-sputum smear examination strategy results in a change in consumable costs only, other cost factors remaining stable. The cost of consumables (e.g., slides, reagents) for one sputum smear examination was calculated in 1997 at US\$0.23. Using this figure, the laboratory cost of consumables for the screening strategy with three smears was compared with the cost of the screening strategy with two smears.

#### *Statistics*

$\chi^2$  test with Yates correction was used to assess differences in proportions between results in the two 6-month periods, with differences at the 5% level being regarded as significant. Odds ratios (OR), their 95% confidence intervals (CI) and *P* values were also calculated where appropriate.

## **RESULTS**

#### *Laboratory register*

In the first 6 months of 1998, 1106 new TB suspects submitted sputum specimens, and 1152 new TB suspects submitted sputum specimens in the second 6 months. The number of sputum smears examined for each patient and the number of patients with positive AFB smears is shown in Table 1. In both 6-month periods, just over 90% of patients submitted sputum specimens in accordance with the guidelines (i.e., three or two sputum samples). Of 998 patients submitting three sputum samples between January to June 1998, 160 (16%) were smear-positive, which

**Table 1** Laboratory Register: results of using different sputum smear screening strategies

	January–June 1998 Screening with three sputum smears	July–December 1998 Screening with two sputum smears
No. of TB suspects submitting sputum	1106	1152
No. (%) of TB suspects who submitted		
3 sputum specimens	998 (90.2)	36 (3.1)*
2 sputum specimens	80 (7.2)	1042 (90.4)
1 sputum specimen	28 (2.6)	74 (6.5)
No. (%) of TB suspects smear-positive	173 (15.6)	186 (16.1)

\* In the 6 months from July–December 1998, this includes 23 patients who submitted a third sputum because of chest radiographic findings such as cavities or extensive disease. The other 13 patients submitted a third sputum at the time of the change-over in July because of misunderstandings by health care workers.

was no different from that for July to December 1998, where 165 (16%) of 1042 patients submitting two sputum specimens were smear-positive. Significantly more patients (6.5%) in the second 6-month period submitted only one sputum specimen compared with the first 6 months (2.6%, OR 3.23, 95%CI 1.97–5.35,  $P < 0.05$ ). There were 3177 sputum smears examined in the first 6 months and 2266 smears examined in the second 6 months, representing a 29% reduction in the number of smears examined.

#### *Tuberculosis Register*

There were 305 registered TB patients in the first 6 months of 1998 and 303 in the second 6 months. The type of TB is shown in Table 2. There were no differences in the proportion of patients with smear-positive PTB, smear-negative PTB and extra-pulmonary TB.

#### *Chest radiograph review and submission of a third sputum*

A total of 127 patients had smear-negative PTB or extra-pulmonary TB; 123 chest radiographs had been performed and were available for review. Fifteen patients had pulmonary cavities. Nine patients with pulmonary cavities submitted a third sputum and in two patients this was smear-positive. In six patients with pulmonary cavities, no third sputum was submitted. Eight patients judged to have extensive radiographic disease ( $n = 4$ ) or a large pleural effusion ( $n = 4$ ) also submitted a third sputum specimen; one patient with a large pleural effusion was smear-positive. Of 23 patients submitting a third sputum, three (13%) were found to be smear-positive.

#### *Cost calculations*

The cost of consumables using the three sputum strategy was US\$731, while the cost of that using two sputum smears was \$521, a saving of \$210.

## DISCUSSION

This study shows that under routine conditions a strategy of screening TB suspects with two sputum smears was as effective as screening suspects with three sputum smears. During the two 6-month periods, the total numbers of patients submitting sputum samples and the proportions found to be smear-positive were similar. The clinical pattern of TB was also similar, with no difference in the proportion of patients registered with smear-positive PTB.

In both 6-month periods, the number of patients registered with smear-positive PTB was less than the number found smear-positive in the laboratory register—this failure to register all smear-positive patients has already been documented as a country-wide problem, and reflects death or transfer of patients to another district before registration is carried out.<sup>8</sup> Whatever screening strategy is put in place, complete adherence to guidelines is usually impossible to achieve under routine conditions.

Previous operational research has shown that of 12 292 new suspects submitting sputum in 40 hospitals in the first quarter of 1998, 89% submitted three sputum samples, 8% submitted two sputum samples and 3% submitted one sample (unpublished observations). The results of this study are in line with these findings: in both 6-month periods, there was adher-

**Table 2** Tuberculosis Register: results of using different sputum smear screening strategies

	January–June 1998 Screening with three sputum smears	July–December 1998 Screening with two sputum smears
No. of TB patients registered	305	303
No. (%) of TB patients registered with		
Smear-positive PTB	165 (54.1)	176 (58.1)
Smear-negative PTB	91 (29.8)	75 (24.7)
Extra-pulmonary TB	49 (16.1)	52 (17.2)

ence to guidelines in just over 90% of patients. However, it is of concern that nearly 7% of patients using a two sputum screening strategy submitted only one sputum. If the two-sputum strategy is used more extensively, it will be important for supervisors to ensure that the proportion of patients giving just one sputum remains as low as possible. The extra supervision required to ensure that two sputum specimens are collected may, of course, offset the cost savings resulting from the reduction in laboratory workload.

There are many causes of a false negative sputum smear, with potential problems occurring at the level of sputum collection, sputum processing, smear examination and laboratory administration.<sup>9</sup> Although our strategy of a third sputum in smear-negative patients with radiographic cavities or extensive disease resulted in only an additional three patients being found smear-positive, we believe that this practice should be continued. Patients with cavitating lung disease are often sputum smear-positive.<sup>10</sup> If clinical staff find that an increasing proportion of their 'smear-negative' TB cases have pulmonary cavities, questions might be asked about the quality of smear examination in the laboratory.

The results of this study are encouraging. The almost 30% reduction in workload using a two sputum screening strategy might encourage overstretched laboratory staff to spend more time examining sputum smears. Unfortunately, in this study we have no data on time spent examining sputum smears, and we are therefore unable to calculate staff time variables. In a resource-poor country such as Malawi, the savings in cost with no loss of effectiveness is another welcome finding. However, we would caution against extrapolating these results to other resource-poor countries with a high burden of tuberculosis. The extent of laboratory services, the number of laboratory staff and laboratory performance may vary considerably from country to country,<sup>11</sup> and each tuberculosis control programme should carefully assess whether the sputum screening processes need to be changed before embarking on their own operational research to test different strategies.

The Malawi National Tuberculosis Control Programme intends to continue this initiative in Ntcheu district. It also intends to expand the strategy to sev-

eral other districts, and evaluate the results over a 6- to 12-month period. If similar encouraging results are found, a two-sputum screening strategy may become national policy.

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#### RÉSUMÉ

**CADRE :** L'hôpital de district de Ntcheu au Malawi.

**OBJECTIF :** Apprécier une stratégie de dépistage des sujets suspects de tuberculose (TB) au moyen de deux frottis d'expectoration.

**SCHEMA :** L'on a comparé une stratégie de dépistage de tous les suspects de TB au moyen de deux frottis d'expectoration entre le 1er juillet et le 31 décembre 1998 par comparaison avec la période du 1er janvier au 30 juin 1998, pendant laquelle la stratégie comportait

trois frottis d'expectoration. Les clichés thoraciques des patients dont les expectorations étaient négatives ont été examinés, et chez ceux montrant des cavités pulmonaires ou une maladie étendue, l'on a pratiqué un troisième frottis d'expectoration. Les données ont été relevées au niveau du registre des expectorations du laboratoire et du registre de la TB. Les deux périodes de 6 mois ont été comparées.

**RÉSULTATS :** Dans le registre du laboratoire, 186 (16%)

des 1152 suspects de TB ont eu une expectoration positive dans la stratégie à deux frottis, ce qui n'est pas différent des 173 (16%) de 1106 suspects de TB à bacilloscopie positive avec la stratégie à trois frottis. Le type clinique de TB s'est avéré similaire dans les deux stratégies de dépistage, avec 58% des patients enregistrés comme positifs avec la stratégie à deux expectorations et 54% avec la stratégie à trois expectorations. Au cours des 6 premiers mois, 3177 frottis ont été examinés contre 2266 au cours du deuxième semestre, ce qui correspond

à une réduction de 29% dans le nombre de frottis examinés. Le coût des produits fut de US\$731 avec la stratégie à trois frottis contre US\$521 pour la stratégie à deux frottis.

**CONCLUSIONS :** Le dépistage des suspects de TB par une stratégie comportant deux frottis d'expectoration est aussi efficace que celle qui recourt à trois frottis, et implique moins de travail pour le laboratoire ainsi que des coûts réduits.

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#### RESUMEN

**MARCO DE REFERENCIA :** Hospital Distrital Ntcheu, Malawi.

**OBJETIVO :** Evaluar una estrategia de catastro para sospechosos de tuberculosis (TB) utilizando dos exámenes de esputos.

**MÉTODO :** Se comparó una estrategia de catastro de los sospechosos de TB con dos exámenes de esputo, entre el 1 de julio y el 31 de diciembre de 1998, con otro grupo en el que se efectuaron tres exámenes de esputos, entre el 1 de enero y el 30 de junio de 1998. Se evaluaron todas las radiografías de tórax de los pacientes con esputo negativo, y en aquellos con cavidades pulmonares y enfermedad extendida se realizó un tercer examen de esputo. Los datos se obtuvieron del registro de TB. Se compararon los dos períodos de 6 meses.

**RESULTADOS :** En el registro de laboratorio, 186 (16%) de 1152 sospechosos de TB eran positivos utilizando la

estrategia de dos exámenes de esputo, lo que es similar a 173 (16%) de 1106 sospechosos de TB que eran positivos utilizando la estrategia de tres exámenes. El esquema clínico de TB utilizando las diferentes estrategias fue similar, con 58% de los pacientes registrados con esputo positivo usando la estrategia de dos exámenes y 54% de casos con esputo positivo con la estrategia de tres exámenes. Se examinaron 3177 esputos en los primeros 6 meses y 2266 en los 6 meses siguientes, o sea con una reducción de las láminas examinadas del 29%. El costo de insumos usando la estrategia de tres exámenes fue de 731 dólares, comparado con un costo de 521 dólares cuando se utilizaban dos exámenes.

**CONCLUSIONES :** El catastro de los sospechosos de TB usando dos exámenes de esputo es tan efectivo como el que usa tres exámenes, y está asociado con menos trabajo de laboratorio y menor costo.

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