

## An evaluation of symptom and chest radiographic screening in tuberculosis prevalence surveys

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### SUMMARY

**SETTING:** A tuberculosis (TB) prevalence survey was performed in 2002 in two urban communities in Cape Town, South Africa. The population was 36 334 in 2001, and the TB notification rate was 341 per 100 000 population for new smear-positive TB in 2002.

**OBJECTIVE:** To evaluate the relative contributions of symptom and chest radiographic (CXR) screening in the detection of subjects with smear- and/or culture-positive TB in prevalence surveys.

**DESIGN:** Information on symptoms, CXR abnormalities, sputum smear and culture was gathered from a random cluster sample of 1170 adults (aged  $\geq 15$  years). Smear and/or culture-positive TB was used as the gold standard.

**RESULTS:** Of 1170 adults, 29 had bacteriologically pos-

itive TB (smear- and/or culture-positive). The presence of any abnormalities on CXR had the highest sensitivity for detecting subjects with bacteriologically positive TB (0.97, 95%CI 0.90–1.00). Specificity for any abnormalities on CXR was 0.67 (95%CI 0.64–0.70). The specificity of any of five TB-related symptoms was 0.68 (95%CI 0.65–0.71). Individual symptoms had low sensitivities, ranging from 0.10 for fever to 0.54 for cough of  $\geq 2$  weeks.

**CONCLUSION:** In this TB prevalence survey, CXR screening, but not symptom screening, was a sensitive alternative to sputum examination of all participants.

**KEY WORDS:** sensitivity; specificity; active case finding; community survey

THE PURPOSE of a tuberculosis (TB) prevalence survey is not only to obtain a reliable estimate of the prevalence of TB disease in a community or country as the basis for planning by National TB Programmes (NTPs),<sup>1</sup> but also to compare TB amongst different communities within a country,<sup>2,3</sup> or to evaluate the outcomes of the NTP over time.<sup>4–6</sup>

Bacteriological confirmation is the gold standard for diagnosing TB. However, it is not always feasible to gather sputum specimens from all participants in a prevalence survey. Alternative methods have therefore been developed that include screening for symptoms<sup>2,6,7</sup> or chest radiography (CXR).<sup>1,3,4,8–10</sup> In most surveys either one or both<sup>5,11–13</sup> of these methods are used to select subjects for sputum examination. However, with each approach, some TB cases will be missed, resulting in the prevalence of TB being underestimated.

This will vary according to the choice of screening method(s) and sequence of their use.

The aim of the present study was to determine the sensitivity and specificity of symptom and CXR screening for detecting subjects with smear-positive and/or culture-positive TB in prevalence surveys. We used data from a TB prevalence survey in which information on symptoms, CXR and sputum smear and culture were available for all participants. Smear-positive TB alone as well as bacteriologically positive TB (smear- and/or culture-positive) was used as the gold standard.

### METHODS

The study area—two urban communities in Cape Town, South Africa—had a population of 36 334 in 2001 and most (98%) were of mixed ethnicity (categorised as ‘coloured’).<sup>14</sup> The TB notification rate was 341 per 100 000 population for new smear-positive TB and 612/100 000 for bacteriologically confirmed TB in 2002.

<sup>†</sup> deceased.

This TB prevalence survey formed part of a larger study investigating the burden of lung diseases in this community, the Lung Health Survey 2002 (article submitted). The protocol for the Lung Health Survey was approved by the ethics committees of Stellenbosch University and the University of Cape Town. Permission to perform the study was obtained from the City of Cape Town and the Western Cape Provincial Department of Health. The health committees of the community were involved in the study and informed consent was obtained from all participants.

A cluster sampling design was used to select the survey population. Eight hundred and thirty nine (15%) residential addresses were randomly selected and all individuals living at these addresses were eligible for the study. A census of the survey population was carried out by enumerating all people living in the selected households. Written informed consent was obtained from the head of each household and from all individual participants. If the head of the household did not give consent for the household to be enrolled in the survey, it was replaced with a household on an adjacent address, first to the right and then to the left. All adults (aged  $\geq 15$  years) completed a pre-coded questionnaire under the supervision of a trained field worker. The questionnaire contained questions on the presence and duration of symptoms of cough, haemoptysis, weight loss, night sweats and fever.

Postero-anterior CXRs were performed using 200 mA X-ray machines (Tingle x-ray products inc., Vance, AL, USA) and consisted of  $35 \times 43$  cm radiographs. Large CXRs were used because this technology was available and we could transport participants to the CXR facility. An experienced pulmonologist used a standardised reporting form to assess all CXRs for abnormalities consistent with TB (including parenchymal, pleural and central structure abnormalities) and for any other abnormalities. A stratified sample of 31% of the CXRs was re-read by a second reader.<sup>15</sup>

Sputum samples were decontaminated with NaOH within 3 days using standard procedures.<sup>16</sup> The concentrated decontaminated sputum sediment was re-suspended in 2 ml of phosphate buffer (68 mM, pH 6.8) and inoculated onto Löwenstein-Jensen (LJ) slants. LJ slants were incubated at 37°C for 6 weeks. Ziehl-Neelsen (ZN) smears were prepared from each sample and scored according to the guidelines of the International Union Against Tuberculosis and Lung Disease (The Union).<sup>17</sup> Bacteriologically positive TB was defined as at least one positive smear and/or one positive culture. A second sputum specimen was requested when the first sample was positive on smear and/or culture.

The demographic, symptom and CXR profile of those who could and those who could not produce a sputum specimen were compared using logistic regression. Odds ratios (OR) were calculated. Sensitivity and specificity with 95% confidence intervals (CIs), adjusted for the clustering at address level, were

calculated for the following variables: cough for  $\geq 2$  weeks, haemoptysis, night sweats, weight loss, fever, presence of at least one of the preceding five symptoms (any symptom), any abnormalities on CXR and TB-related abnormalities on CXR. Data were analysed using STATA 8.0 for Windows (Stata Corporation, College Station, TX, USA).

## RESULTS

Of 3483 adults who filled in a questionnaire, 2608 (75%) had a CXR and attempted to produce a sputum specimen. Of these, 45% (1170 subjects) were able to produce a sputum specimen. Those who could

**Table 1** Demographics, symptoms and CXR abnormalities for those who could and those who attempted but could not produce a sputum sample

	Total <i>n</i>	Produced sputum <i>n</i>	With sputum %	OR (95%CI)*
Sex				
Female	1553	598	39	1
Male	1055	572	54	1.89 (1.62–2.20)
Age, years				
15–24	704	255	36	1
25–34	521	252	48	1.65 (1.29–2.10)
35–44	560	256	46	1.48 (1.19–1.85)
45–54	356	176	49	1.72 (1.35–2.19)
55+	467	231	49	1.72 (1.33–2.23)
Cough $\geq 2$ weeks				
No	2183	892	41	1
Yes	328	209	64	2.54 (1.99–3.25)
Unknown	97	69	71	
Haemoptysis				
No	2550	1124	44	1
Yes	48	40	83	6.34 (2.92–13.76)
Unknown	10	6	60	
Night sweats				
No	2343	988	42	1
Yes	258	179	69	3.11 (2.32–4.15)
Unknown	7	3	43	
Fever				
No	2509	1112	44	1
Yes	83	53	64	2.22 (1.38–3.56)
Unknown	16	5	31	
Weight loss				
No	2253	960	43	1
Yes	338	204	60	2.05 (1.61–2.62)
Unknown	17	6	35	
Any symptoms				
No	1950	780	40	1
Yes	657	389	59	2.18 (1.82–2.61)
Unknown	1	1	100	
Abnormal CXR				
No	1906	763	40	1
Yes	702	407	58	2.07 (1.73–2.46)
TB-related abnormalities on CXR				
No	2271	949	42	1
Yes	337	221	66	2.65 (2.09–3.37)
Total	2608	1170	45	

\* Adjusted for clustering on address level.  
CXR = chest radiograph; OR = odds ratio; CI = confidence interval.

**Table 2** Sensitivity and specificity for symptom and CXR screening for bacteriologically positive TB

	Bacteriologically positive <i>n</i>	Total <i>n</i>	Bacteriologically positive %	Sensitivity (95%CI)	Specificity (95%CI)
Cough					
No cough or cough <2 weeks	12	892	1.3	0.54 (0.31–0.76)	0.82 (0.79–0.84)
Cough ≥2 weeks	14	209	6.7		
Unknown	3	69	4.3		
Haemoptysis					
No	22	1124	2.0	0.24 (0.08–0.40)	0.92 (0.88–0.96)
Yes	7	40	17.5		
Unknown	0	6	0.0		
Night sweats					
No	15	988	1.5	0.48 (0.27–0.70)	0.86 (0.83–0.88)
Yes	14	179	7.8		
Unknown	0	3	0.0		
Fever					
No	26	1112	2.3	0.10 (0.00–0.21)	0.96 (0.94–0.97)
Yes	3	53	5.7		
Unknown	0	5	0.0		
Weight loss					
No	15	960	1.6	0.48 (0.29–0.67)	0.83 (0.81–0.86)
Yes	14	204	6.9		
Unknown	0	6	0.0		
Symptoms					
No symptoms	9	780	1.2	0.69 (0.50–0.88)	0.68 (0.65–0.71)
Any symptoms	20	389	5.1		
Unknown	0	1	0.0		
CXR					
Normal CXR	1	763	0.1	0.97 (0.90–1.00)	0.67 (0.64–0.70)
Abnormal CXR	28	407	6.9		
TB-related abnormalities on CXR					
No	3	949	0.3	0.90 (0.79–1.00)	0.83 (0.81–0.85)
Yes	26	221	11.8		
Total	29	1170			

CXR = chest radiograph; TB = tuberculosis; CI = confidence interval.

produce a sputum specimen were older ( $\chi^2$  for trend 19.79,  $P < 0.001$ ), more likely to be male (OR 1.89, 95%CI 1.62–2.20), to have symptoms (OR for presence of at least one of five symptoms 2.18, 95%CI 1.82–2.61) and to have TB-related abnormalities on CXR (OR 2.65, 95%CI 2.09–3.37) than those who attempted but could not produce a sputum specimen (Table 1). Bacteriologically positive TB was diagnosed in 29 subjects and sputum smear-positive TB alone was diagnosed in 20 subjects.

For bacteriologically positive TB, the sensitivity for any abnormalities on CXR was high (0.97, 95%CI 0.90–1.00), but the specificity for any abnormalities on CXR was lower than for symptoms (Table 2). Presence of any of the five symptoms had lower sensitivity (0.69, 95%CI 0.50–0.88) than CXR. Among the different symptoms, the sensitivity was highest for cough of ≥2 weeks (0.54, 95%CI 0.31–0.76) and specificity was highest for fever (0.96, 95%CI 0.94–0.97). Three cases had no TB-related CXR abnormalities: two had a single scanty positive sputum with negative culture and one had a single culture-positive sputum. Screening for symptoms did not reveal any extra TB cases in addition to CXR screening for TB-related abnormalities (Table 3).

**Table 3** Agreement between CXR and symptom screening for the 29 bacteriologically positive TB cases

	TB-related abnormalities on CXR		Total
	No <i>n</i>	Yes <i>n</i>	
Cough ≥2 weeks			
No	3	9	12
Yes	0	14	14
Unknown	0	3	3
Haemoptysis			
No	3	19	22
Yes	0	7	7
Night sweats			
No	3	12	15
Yes	0	14	14
Fever			
No	3	23	26
Yes	0	3	3
Weight loss			
No	3	12	15
Yes	0	14	14
Any symptoms*			
No	3	6	9
Yes	0	20	20
Total	3	26	29

\* Presence of at least one of the five symptoms.  
CXR = chest radiograph; TB = tuberculosis.

**Table 4** Sensitivity and specificity for symptom and CXR screening for smear-positive TB

	Smear-positive <i>n</i>	Total	Smear-positive %	Sensitivity (95%CI)	Specificity (95%CI)
Cough					
No cough or cough <2 weeks	6	892	0.7	0.67 (0.43–0.90)	0.82 (0.79–0.84)
Cough ≥2 weeks	12	209	5.7		
Unknown	2	69	2.9		
Haemoptysis					
No	14	1124	1.2	0.30 (0.10–0.50)	0.92 (0.88–0.96)
Yes	6	40	15.0		
Unknown	0	6	0.0		
Night sweats					
No	8	988	0.8	0.60 (0.36–0.84)	0.85 (0.83–0.88)
Yes	12	179	6.7		
Unknown	0	3	0.0		
Fever					
No	18	1112	1.6	0.10 (0.00–0.23)	0.96 (0.94–0.97)
Yes	2	53	3.8		
Unknown	0	5	0.0		
Weight loss					
No	10	960	1.0	0.50 (0.29–0.71)	0.83 (0.81–0.86)
Yes	10	204	4.9		
Unknown	0	6	0.0		
Symptoms					
No symptoms	5	780	0.6	0.75 (0.55–0.95)	0.67 (0.64–0.70)
Any symptoms	15	389	3.9		
Unknown	0	1	0.0		
CXR					
Normal CXR	1	763	0.1	0.95 (0.85–1.00)	0.66 (0.63–0.69)
Abnormal CXR	19	407	4.7		
TB-related abnormalities on CXR					
No	2	949	0.2	0.90 (0.77–1.00)	0.82 (0.80–0.85)
Yes	18	221	8.1		
Total	20	1170			

CXR = chest radiograph; TB = tuberculosis; CI = confidence interval.

The results for smear-positive TB were comparable with those for bacteriologically positive TB (Table 4). Any abnormalities on CXR had the highest sensitivity (0.95, 95%CI 0.85–1.00) and the presence of any of five TB-related symptoms had a lower sensitivity (0.75, 95%CI 0.55–0.95). When screening for any abnormalities on CXR, one of the 20 smear-positive TB cases would have been missed. This missed case had a single scanty positive smear and was culture-negative.

## DISCUSSION

This study shows that in TB prevalence surveys CXR screening is a good alternative to sputum examination of whole populations. Our results suggest that the number of people who would have to undergo sputum examination can be greatly reduced if the study population is first screened by CXR. With this approach, almost all bacteriologically positive TB cases will be detected. About 3–5% of smear- and/or culture-positive cases may be missed. However, the current study suggests that these cases are not likely to be highly infectious, and may even represent false-positive sputum results. Screening for any abnormalities is more sensitive than screening for TB-related abnor-

malities on CXR and it is therefore preferred as a screening tool, even though specificity is lower and thus more survey participants (33% vs. 17% of the total survey population) will have to undergo sputum examination. The sensitivity of symptoms as a screening method for smear- and/or culture-positive TB cases was low, even when we looked at the presence of at least one of five symptoms. Only 20 of 29 bacteriologically positive TB cases were detected by this method.

A well known limitation of CXR is that readings are highly subjective and inter- and intra-reader variability can be considerable.<sup>18–20</sup> Although in the current study<sup>15</sup> and another recently reported study,<sup>21</sup> inter- and intra-reader agreement were better than in previous studies, it is recommended that for the purpose of TB prevalence surveys radiographs be read by more than one reader.

We included only subjects who produced a sputum specimen in the analyses. As those who produced a sputum specimen were more often males and older than those who could not produce a sputum specimen, this group is not representative of the population. However, the fact that those who attempted but could not produce a sputum specimen were less often symptomatic and had fewer TB-related and other abnormalities on CXR suggests that these people were less

likely to have TB than those who managed to produce a sputum specimen. It is acknowledged that this does not entirely exclude the possibility that this group contained TB cases that we failed to diagnose.

The current study confirms the results of a study done by Gothi et al.,<sup>22</sup> which concluded that CXRs were a satisfactory screening tool in TB prevalence surveys but that adding symptom screening did not lead to detection of more TB cases. Several TB prevalence surveys have been performed in collaboration with the World Health Organization in which symptom, CXR and sputum smear and culture information was available for a proportion of subjects or for the whole survey population.<sup>23–27</sup> However, the sensitivity and specificity of symptoms and CXR were not reported. A number of studies have described the use of symptoms and CXR as a diagnostic tool in a clinical situation.<sup>28–30</sup> In these clinic-based studies, predictive models or diagnostic scores to distinguish subjects with and without TB were developed. However, these are not applicable to survey settings, as in clinical settings the prevalence of TB as well as the prevalence of symptoms and abnormalities on CXR is higher.

The results obtained in this study may be useful for other researchers who are planning TB prevalence surveys and are considering the use of CXR screening. Several points should be considered. In the current study we used conventional CXRs. Mass miniature radiographs (MMR) are often used in TB surveys<sup>4,8,12</sup> because the equipment is easier to transport. However, MMR may be more difficult to read because the CXRs are smaller and the sensitivity of MMR to detect any abnormalities may be lower than for conventional CXRs, resulting in more TB cases being missed during screening.

We did not present information on the costs of the different procedures, as these vary from country to country and are highly dependent on circumstances such as transport, manpower and accessibility in the study area.

Another point to consider is the influence of human immunodeficiency virus (HIV) infection on smear results and CXR abnormalities. It is known that TB patients with HIV are more likely to be smear-negative and to have atypical radiographic abnormalities.<sup>31–33</sup> A limitation of the present study was that HIV testing was not performed, but the estimated prevalence of HIV infection in the study area is lower than the 12.4% (95%CI 8.8–15.9) obtained from women attending antenatal clinics in the Western Cape Province in 2002.<sup>34</sup> Special care should be taken in areas of higher HIV prevalence and more attention should be paid to CXRs with atypical abnormalities. Additional studies need to investigate the reliability of CXR screening in high HIV incidence areas.

Although symptom screening was not effective in this population, results obtained in surveys in other communities may be different, as linguistic, ethnic and

cultural beliefs may influence responses to questions concerning symptoms. The sensitivity of symptom screening may be lower if people who do not consider their symptoms to be caused by TB respond negatively to a question concerning cough—for example, those who consider a chronic cough to be normal or smoking-related. In areas with a high incidence of diseases causing cough, such as asthma and chronic obstructive pulmonary disease (COPD), the specificity of the symptom cough may be lower.

## CONCLUSION

In the study site in Cape Town, South Africa, CXR screening was a valuable tool for detecting bacteriologically and smear-positive patients in a TB prevalence survey, while symptom screening was not. Factors such as the expected prevalence of TB, the presence of HIV, costs and accessibility of the study area have to be considered when deciding whether CXR screening is preferable to taking sputum from the total population in the area being studied.

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## R É S U M É

**CONTEXTE :** En 2002, on a pratiqué une enquête de prévalence de la tuberculose (TB) dans deux collectivités urbaines à Cape Town, Afrique du Sud. La population étudiée a été de 36 334 personnes en 2001 et le taux de déclaration de TB de 341 nouveaux cas de TB à bacilloscopie positive pour 100 000 en 2002.

**OBJECTIF :** Évaluer les contributions relatives du tri par symptômes ou par clichés thoraciques dans la détection de sujets atteints d'une TB à bacilloscopie ou à culture positives dans des enquêtes de prévalence.

**SCHÉMA :** On a rassemblé les informations sur les symptômes, les anomalies des clichés thoraciques (CXR), les résultats des frottis et des cultures dans un échantillon en grappes randomisé de 1.170 adultes ( $\geq 15$  ans). On a utilisé comme gold standard la positivité d'un frottis et/ou d'une culture.

**RÉSULTATS :** Sur 1170 adultes, 29 étaient atteints d'une TB positive à l'examen bactériologique (positivité du frottis et/ou de la culture). La présence d'une anomalie radiologique quelconque a eu la sensibilité la plus élevée pour la détection de sujets atteints de TB confirmée par l'examen bactériologique (0,97, IC95% 0,90–1,00). La spécificité pour n'importe quelle anomalie du CXR a été de 0,67 (IC95% 0,64–0,70). La spécificité pour n'importe lequel de cinq symptômes liés à la TB était de 0,68 (IC95% 0,65–0,71). Les sensibilités sont faibles pour les symptômes individuels et d'étendent entre 0,10 pour la fièvre et 0,54 pour une toux durant plus de 2 semaines.

**CONCLUSION :** Dans cette enquête de prévalence de la TB, le tri par CXR mais non le tri par symptômes s'est avéré une alternative sensible à l'examen des expectorations de l'ensemble des participants.

**MARCO DE REFERENCIA:** En 2002, se llevó a cabo un estudio de prevalencia de la tuberculosis (TB) en dos comunidades urbanas de Ciudad del Cabo en Sudáfrica. La población fue de 36 334 personas en 2001 y la tasa de declaración de TB fue de 341 por 100 000 para los casos nuevos con baciloscopia positiva en 2002.

**OBJETIVO:** Evaluar la contribución relativa del cribado por los síntomas y la radiografía de tórax (CXR) en la detección de individuos con TB y baciloscopia o cultivo positivos en los estudios de prevalencia.

**DISEÑO:** Se recogió información sobre los síntomas, las anomalías de la CXR, la baciloscopia y el cultivo de las muestras de esputo con un muestreo aleatorio por conglomerados de 1170 adultos ( $\geq 15$  años). Se utilizó como criterio referencia la TB con baciloscopia o cultivo positivos.

**RESULTADOS:** De los 1170 adultos, 29 presentaron TB

bacteriológicamente confirmada (frotis, cultivo o ambos positivos). La presencia de toda anomalía en la CXR exhibió la más alta sensibilidad para la detección de individuos con TB bacteriológicamente positiva (0,97 ; IC95% 0,90–1,00). La presencia de cualquier anomalía radiográfica tuvo una especificidad de 0,67 (IC95% 0,64–0,70). La especificidad para la presencia de cualquiera de los cinco síntomas asociados con TB fue de 0,68 (IC95% 0,65–0,71). Los síntomas individuales tuvieron una sensibilidad baja, entre 0,10 para la fiebre y 0,54 para la tos de  $>2$  semanas de duración.

**CONCLUSIÓN:** En este estudio de prevalencia, el cribado por la CXR constituyó una alternativa sensible al examen microscópico del esputo en todos los participantes, pero no así el cribado por la presencia de síntomas.

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