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Could repeated prevalence surveys lead to decreasing tuberculosis prevalence in a community?

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SUMMARY

SETTING: Tiruvallur District, South India, where one baseline tuberculosis (TB) disease prevalence survey followed by three repeat prevalence surveys were conducted every 2.5 years between 1999 and 2008, and where the DOTS strategy was implemented in 1999.

OBJECTIVE: To rule out the possibility that the observed decline in TB prevalence was influenced by conducting repeat prevalence surveys, we compared the findings from two surveys: the third repeat survey conducted in 2006–2008 and an independent single survey in a neighbouring area conducted in 2008–2009.

DESIGN: An independent survey was conducted to estimate the prevalence of TB in the same district in 2008–2009 using a different set of villages and employing repeat survey methodology. The independent survey findings were compared with those of the third repeat survey.

RESULTS: The estimated prevalence rate of culture- and smear-positive TB was respectively 401 per 100 000 and 186 per 100 000 population in the third repeat survey area. The corresponding rates were 340 and 184/100 000 in the independent survey area. The difference in prevalence was not significant (culture $P = 0.09$; smear $P = 0.93$).

CONCLUSION: The estimated prevalence rates in the two different sample survey areas were comparable, indicating that the repeated prevalence surveys in the study area did not influence the observed decline in TB disease prevalence.

KEY WORDS: TB; DOTS; prevalence; repeated surveys; epidemiology

AN ESTIMATED 9.0 million people developed tuberculosis (TB) and 1.5 million died from the disease in 2013, with India accounting for 24% of total cases.[1] The internationally recommended DOTS strategy was initiated by the Revised National TB Control Programme (RNTCP) in India in 1993,[2] and implemented in Tiruvallur District, South India, in 1999. Prevalence surveys were conducted in five blocks of Tiruvallur District, among a mainly agricultural population of 538 365 (2001 census), with 464 931 (86%) rural population and 269 105 (50%) males.

From May 1999 to April 2000, 32 663 adults were screened for TB and 216 cases were identified in the community baseline survey. Five cases had already been identified in health facilities and were receiving treatment, and 58 patients who were not on treatment became initial defaulters.[3] The RNTCP case-finding performance in this area showed a decline in smear-positive pulmonary TB (PTB) case notifications from 73 per 100 000 population in 2000 to 50/100 000 in 2009 ($P < 0.0001$), with the treatment success rate varying from 73% to 86% (average 78%). The yearly performance from 2000 to 2008 has been reported elsewhere.[4] Under the RNTCP, there is a supervisory TB unit for every 500 000 population; all TB cases diagnosed in any of the surveys were referred to the TB unit for treatment.

To investigate the epidemiological impact of the DOTS strategy in this area, three prevalence surveys were conducted at 2.5-year intervals by the National Institute for Research in TB (NIRT) in a representative population sample. The findings of the baseline survey conducted in 1999–2001 and of the first repeat survey conducted 2.5 years later (2001–2003) have been reported elsewhere.[5,6] The annual decline was estimated at 11.3% for culture-positive TB and 9.0% for smear-positive TB during the DOTS period.[6] A second repeat survey conducted 5 years from baseline (2003–2006) showed an overall decline of 12.6% (95% confidence interval [CI] 11.2–14.0) per annum for culture-positive TB and 12.3% (95%CI 8.6–15.8) for smear-positive TB.[7] A third

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repeat survey was undertaken at 7.5 years from baseline, in 2006–2008. An annual decline of 7.6% for smear-positive TB was estimated between the baseline survey in 1999–2001 and the third repeat survey in 2006–2008.[4]

It could be argued from these findings that conducting repeated prevalence surveys in the same area from 1999 onwards could have had an influence on the observed decline in TB prevalence. To investigate this concern, an independent survey was conducted in 2008–2009 in specific sites in the overall study area where no prevalence surveys had previously been conducted. The estimated prevalence of TB in the independent and the third repeat surveys were then compared. The results are reported here.

MATERIALS AND METHODS

The surveys were conducted in 53 randomly selected villages (50/208 villages and 3/10 urban units) in the five blocks (population 514 582) in the study area in which the earlier surveys had been conducted between 1999 and 2008. The survey methods used have been described elsewhere.[4–7] A single, independent sample survey was conducted in 2008–2009 in the same five blocks using a different random sample of 38 villages and one urban unit. The same survey methodology used in the repeat surveys was adopted in the independent survey. The sample size of 42 471 persons was chosen based on the repeat survey findings, a prevalence of 5/1000, a precision of 20% at 95%CI, coverage of 90% and a design effect of 2, and screened for PTB. The sample size chosen for the independent survey was sufficient to have adequate power (99%) based on the difference between the prevalence in the repeat survey area and that of the independent survey area. The independent survey identified 98.4% (41 773/42 471) of the sample population.

All persons aged $\geqslant$15 years in all the surveys were registered by door-to-door census. Especially trained field investigators interviewed all persons at home, identified new persons with chest symptoms (i.e., those with a cough of $\geqslant$2 weeks, chest pain or fever for 1 month, or haemoptysis at any time in the last 6 months) as well as those with a history of previous chemotherapy for TB. A quality check of symptom screening was performed by a supervisor among a random sample of 5% of all subjects examined for symptoms, and corrective measures were taken as needed.

The study participants were also screened by chest radiograph (mass miniature radiography [MMR]) for TB. The radiograph was read independently by two readers and, in case of disagreement, by a third reader. For persons with an abnormal chest radiograph and/or chest symptoms, and for previously treated TB cases, two sputum samples (one spot and one overnight) were collected and examined by fluorescence microscopy for acid-fast bacilli (AFB). The decontaminated sputum sample was cultured for *Mycobacterium tuberculosis* on solid Löwenstein-Jensen media, and all laboratory investigations were conducted per World Health Organization (WHO)/International Union Against Tuberculosis and Lung Disease guidelines.[8]

All patients diagnosed with TB disease were referred to a health facility for treatment under the RNTCP. The study participants were informed of the purpose of the survey, and all provided written informed consent to participate in the study. The studies were approved by the Ethics Committee of the NIRT.

Case definitions

All of the patients diagnosed (including cases reported as having present/past chemotherapy, as well as diagnosed/undiagnosed cases in passive case finding) were classified as follows: 1) patients with a positive culture for *M. tuberculosis*, regardless of smear result, were considered culture-positive cases, and 2) patients with a positive smear containing more than three AFB, regardless of culture, were considered smear-positive cases.

Data management and estimation of prevalence

All data were double-entered and verified, with permissible values only for each data item, using the data entry package MicroPro DataStar (MicroPro International Corp, San Rafael, CA, USA). All survey records were identified by a unique number allotted by the field investigators. Prevalence rates were estimated after adjustments for non-coverage by radiograph and sputum for sex and age distributions, and overall estimates of culture-positive and smear-positive TB were obtained as reported earlier.[5]

Data analysis and statistical methods

The data from the third repeat survey and from the independent survey were used to estimate culture- and smear-positive TB prevalence rates. For the purposes of comparison, the estimated prevalence rates were standardised against the age and sex distributions in the baseline survey (1999–2001) population in the five blocks. Next, the pooled variance of the prevalence was estimated with appropriate weighting and stratification to blocks. To investigate whether there was a difference, we considered the hypothesis that the prevalence (proportion) of TB in the two surveys was not different. The difference in prevalence between the two surveys was compared using the Z-test.[9] A P value <0.05 was considered statistically significant.

RESULTS

Radiographic/symptom and sputum coverage

The population eligible for investigation in the survey areas consisted of permanent residents in the com-

Table 1 Characteristics of the sample population in the third repeat survey and the independent prevalence survey

Sample population characteristics	Third repeat survey *n* (%)	Independent survey *n* (%)
Sex		
Male	44 996 (48.8)	20 420 (48.9)
Female	47 259 (51.2)	21 353 (51.1)
Age, years		
15–34	43 702 (47.4)	19 034 (45.6)
35–54	32 480 (35.2)	14 452 (34.6)
⩾55	16 073 (17.4)	8 287 (19.8)
Total	92 255 (100)	41 773 (100)

munity. The characteristics of the sample population of the third repeat survey (2006–2008) and the independent survey (2008–2009) are shown in Table 1. Although the proportion of males and females was similar in each survey, the proportion of persons in the different age groups was statistically significantly different. The proportion of eligible participants covered by the various investigations was consistently high in both surveys: ⩾89% for chest radiograph and/or symptom inquiry, and 96% for sputum examination amongst those eligible (Table 2). Among the participants eligible for sputum examination in the two surveys, respectively 8937 (97.2%) and 4308 (98.2%) provided two sputum samples. The estimated prevalence rates were standardised against the age and sex distribution of the baseline survey population for comparison (Table 3).

Radiographic and laboratory investigations

MMR coverage was respectively 89% and 90% in the third repeat and independent surveys. The computed κ value of respectively 0.57 and 0.53 in the two surveys indicated modest agreement between the two readers.

As regards the quality of the microbiological investigations, the proportion of smear-positive, culture-positive (35% vs. 41%, $P = 0.38$), smear-negative, culture-positive (57% vs. 50%, $P = 0.12$) and smear-positive, culture-negative samples (8% vs. 9%, $P = 0.24$) was stable between the two surveys.

Prevalence of tuberculosis

The proportion of TB cases (those reported to have received/be currently receiving anti-tuberculosis treatment) among all diagnosed cases was 28% in the third repeat survey and 15% in the independent survey.

Table 3 Comparison of the prevalence of culture- and smear-positive tuberculosis between the third repeat survey and the independent prevalence survey

	Prevalence rate		
	Third repeat survey* /100 000	Independent survey† /100 000	Difference between two prevalence rates *P* value‡
Culture-positive TB			
Total	401	340	0.09
Sex, *n*			
Male	689	607	0.23
Female	126	83	0.08
Age, years, *n*			
15–34	120	89	0.24
35–54	486	366	0.07
⩾55	991	899	0.48
Smear-positive TB			
Total	186	184	0.93
Sex, *n*			
Male	317	311	0.89
Female	62	62	0.99
Age, years, *n*			
15–34	68	34	0.05
35–54	236	183	0.23
⩾55	406	543	0.15

* Performed in the 53 clusters where three surveys were carried out earlier at 2.5-year intervals and standardised against the population of the baseline survey (1999–2001).
† Performed among 39 different clusters in the same study area and standardised against the population of the baseline survey (1999–2001).
‡ $P < 0.05$ (statistically significant).
TB = tuberculosis.

The overall standardised prevalence of culture-positive TB was respectively 401 and 340/100 000 in the third repeat and the independent surveys (Table 3); the difference was not statistically significant ($P = 0.09$). Similarly, the estimated overall standardised prevalence of smear-positive TB was respectively 186 and 184/100 000 in the two surveys (Table 3); again, the difference was not statistically significant ($P = 0.93$).

The overall nonstandardised prevalence of culture- and smear-positive TB was respectively 400 and 186/100 000 in the third repeat survey, and respectively 363 and 201/100 000 in the independent survey. Again, the prevalence rates were not statistically significantly different for culture-positive ($P = 0.31$) or smear-positive TB ($P = 0.57$). Also, the overall proportion of culture- and smear-positive TB among the number of persons with sputum examined in these two surveys was not statistically different (culture-positive 0.0361, 95%CI 0.0323–0.0399 vs. 0.0313, 95%CI 0.0261–0.0365, $P = 0.15$; smear-positive

Table 2 Screening coverage in the third repeat and independent prevalence surveys

Survey	Population *n*	Examined by radiography *n* (%)	Enquired about symptoms *n* (%)	Eligible for sputum testing *n* (%)	Sputum examined *n* (%)
Third repeat survey	92 255	82 470 (89)	84 010 (91)	9 561 (11)	9 186 (96)
Independent survey	41 773	37 692 (90)	38 621 (92)	4 573 (12)	4 369 (96)

0.0168, 95%CI 0.0142–0.0194 vs. 0.0173, 95%CI 0.0134–0.0212, $P = 0.83$) (data not shown).

The standardised prevalence rates of both surveys were not significantly different by age (15–34, 35–54 and $\geqslant 55$ years) or sex (males and females) for both culture- and smear-positive TB (Table 3). The estimated prevalence obtained from the independent survey would represent the prevalence during 2008–2009 in those villages that were not covered in the repeated prevalence surveys conducted during 1999–2008.

In addition, the overall prevalence without adjustments for non-coverage by MMR and sputum was calculated as the number of individuals diagnosed with TB divided by the number of individuals eligible to participate in the survey. Thus, the estimated prevalence of culture-positive TB in the third repeat survey and in the independent survey was respectively 360 and 328/100 000; again the difference was not statistically significant ($P = 0.42$). For smear-positive TB, the prevalence in the two surveys was also not significantly different (168 vs. 182, $P = 0.61$).

DISCUSSION

We previously reported an observed rapid annual decline in the prevalence of TB during the period 1999–2006, estimated at 12.6% for culture-positive TB and 12.3% for smear-positive TB.[7] In the third repeat survey (2006–2008), conducted at 7.5 years, the overall annual decline was re-estimated at 7.6% for smear-positive PTB and 5.8% for culture-positive PTB.[4] Concerns were raised as to whether the higher decline in TB prevalence was due to the effect of the repeated prevalence surveys. To address this concern, an independent survey was conducted during 2008–2009 in the same district using a different set of villages to estimate the prevalence of TB and compare the findings with those from the third repeat survey.

The estimated prevalence of culture-positive and smear-positive TB (401 and 186/100 000 in the third repeat survey and 340 and 184/100 000 in the independent survey) was not significantly different, nor were the estimates stratified by age group and sex. The lack of difference in prevalence might be attributable to the effectiveness of the RNTCP in the study area, with the effect that cases were diagnosed in a timely manner and became non-infectious rapidly, or that the actively detected cases were in the early stages of the disease—often such cases did not start treatment and the duration of infectiousness was not shortened. Another plausible explanation for not seeing an effect of the active case-finding activities under the repeat prevalence surveys might be that the frequency of the surveys was not high enough, or that the incidence of disease in the area was not high enough for case finding to make a difference.

On the other hand, the public in the survey area came to know about DOTS treatment over time, and the TB patients in the community may have approached health facilities on their own, despite earlier diagnosis in the active case-finding surveys. In addition, under the RNTCP, a public-private partnership scheme implemented for TB had succeeded in paving the way for wider cooperation with the private sector on other public health programmes in this area.[10] Even in high-prevalence settings, however, it has been observed that community surveys are of little help in reducing the spread of TB, as they identify cases who are less symptomatic and less infectious.[3] A systematic review reported that the individual and community-level benefits from active screening for TB remain uncertain and that the benefits of earlier diagnosis on patient outcomes and transmission had not been established.[11] The recent ZAMSTAR trial conducted in Zambia and in the Western Cape province of South Africa reported that community-level enhanced TB case finding had no effect on the reduction in TB.[12] Based on the study findings, the observed decline in TB prevalence does not therefore appear to have been influenced to any significant degree by the repeated surveys conducted in the community.

Limitations

The study has a number of limitations. Human immunodeficiency virus infection rates, levels of multidrug-resistant TB and socio-economic conditions were assumed to be the same in each of the surveyed areas in Tiruvallur District. Also, the independent survey and the third repeat survey were not conducted at the same period of time. Finally, the DOTS performance indicators (namely the case detection and treatment success rates) were not available village by village for comparison in the study area.

CONCLUSION

The difference between the estimated TB disease prevalence rates in the repeat and the independent survey areas was not statistically significant. Repeated TB disease prevalence surveys in the community do not therefore appear to have influenced the observed decline in TB disease prevalence. Future surveys should be conducted in a similar manner to the earlier surveys and follow the guidelines described in the 2011 WHO handbook.[13] Emphasis needs to be placed on ensuring that all cases detected under such surveys are registered for treatment under the RNTCP as a routine survey strategy, as it has been observed that such cases often do not start treatment. Future surveys should also be conducted using different sampling populations, especially where an effective TB control programme is implemented, to

avoid the survey effect in measuring the burden of TB disease. Repeat surveys should be conducted with a sample size calculation that includes an anticipated decline in the prevalence estimate to assess an impact of the TB control programme in the relevant survey area.

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FW is a staff member of the WHO. The author alone is responsible for the views expressed in this publication and they do not necessarily represent the decisions or policies of the WHO.

Conflicts of interest: none declared.

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RESUME

CONTEXTE : Le district de Tiruvallur, en Inde du Sud, où ont été réalisées une enquête de départ et trois enquêtes successives sur la prévalence de la tuberculose (TB) tous les 2,5 ans entre 1999 et 2008, et où la stratégie DOTS a été mise en œuvre en 1999.

OBJECTIF : Informer l'hypothèse selon laquelle le déclin observé de la prévalence de la TB était influencé par la réalisation d'enquêtes de prévalence répétées en comparant les résultats de deux enquêtes, c'est-à-dire la 3e enquête répétée réalisée en 2006–2008 et une enquête indépendante unique dans une zone proche en 2008–2009.

SCHEMA : Une enquête indépendante a été réalisée afin d'estimer la prévalence de la maladie tuberculeuse dans le même district en 2008–2009, en utilisant un autre ensemble de villages et en employant la méthode de l'enquête répétée ; les résultats de cette enquête ont ensuite été comparés à ceux de la 3e enquête répétée.

RESULTATS : Le taux estimé de prévalence de la TB à frottis et culture positifs a été respectivement de 401 et 186 par 100 000 habitants dans la zone de la 3e enquête répétée. Les taux correspondants ont été de 340 et 184 dans la zone d'enquête indépendante. La différence entre les taux de prévalence n'a pas été significative (culture $P = 0,09$; frottis $P = 0,93$).

CONCLUSION : Les taux de prévalence estimés dans les deux enquêtes portant sur des zones d'échantillonnage indépendantes ont été comparables, indiquant que les enquêtes de prévalence répétées n'ont pas influencé le déclin observé de la prévalence de la maladie tuberculeuse.

RESUMEN

MARCO DE REFERENCIA: En el distrito de Tiruvallur en el sur de la India, se llevó a cabo una encuesta inicial de prevalencia de tuberculosis (TB), seguida de tres encuestas de control con intervalos de 2 años y medio, de 1999 al 2008. En el año 1999 se introdujo en el país la estrategia DOTS.

OBJETIVO: Descartar la posibilidad de que la ejecución repetida de encuestas de prevalencia tuviese una influencia en la disminución observada de la prevalencia de TB, al comparar los resultados de dos encuestas: la tercera encuesta realizada entre el 2006 y el 2008 y una encuesta independiente única realizada en una zona adyacente en el 2008 y el 2009.

MÉTODOS: Se llevó a cabo una encuesta única con el fin de establecer la prevalencia de enfermedad tuberculosa en el mismo distrito en el 2008 y el 2009 con un muestreo diferente de pueblos y se aplicó mismo método adoptado en las encuestas longitudinales; los resultados de la encuesta independiente se compararon con los resultados de la tercera repetición de la encuesta.

RESULTADOS: La tasa de prevalencia de TB con cultivo positivo fue 401 por 100 000 habitantes y la tasa de tuberculosis con baciloscopia positiva fue 186/100 000 en la zona de la tercera repetición de la encuesta. Las tasas correspondientes en la zona donde solo se realizó una encuesta fueron 340 y 184/100 000. La diferencia de la prevalencia no fue estadísticamente significativa ($P = 0,09$ para el cultivo y $P = 0,93$ para la baciloscopia).

CONCLUSIÓN: Las tasas de prevalencia calculadas en las dos zonas de muestreo fueron comparables, lo cual indica que las encuestas repetidas no influyeron en la disminución observada de la prevalencia de TB en la zona estudiada.