# National survey of tuberculosis prevalence in Viet Nam

Nguyen Binh Hoa,<sup>a</sup> Dinh Ngoc Sy,<sup>a</sup> Nguyen Viet Nhung,<sup>a</sup> Edine W Tiemersma,<sup>b</sup> Martien W Borgdorff<sup>c</sup> & Frank GJ Cobelens<sup>c</sup>

**Objective** To estimate the prevalence of tuberculosis in Viet Nam with data from a population-based survey, compare it with the prevalence estimated by the World Health Organization, and identify major demographic determinants of tuberculosis prevalence. **Methods** A cross-sectional survey with multistage cluster sampling, stratified by urban, rural and remote areas, was done in 2006–2007 in 70 communes. All inhabitants aged  $\geq 15$  years were invited for cough and chest X-ray examination. Participants with findings suggestive of tuberculosis provided sputum specimens for smear examination and culture. Point prevalence estimates, 95% confidence intervals and design effects were calculated. Confidence intervals and *P*-values were adjusted for the cluster design.

**Findings** Of 114 389 adult inhabitants, 94 179 (82.3%) were screened. Of 87 314 (92.7%) screened by both questionnaire and chest X-ray, 3522 (4.0%) had productive cough, 518 (0.6%) had a recent history of tuberculosis and 2972 (3.4%) had chest X-ray abnormalities suggestive of tuberculosis. Sputum tests were done for 7648 participants. Sputum test, bacterial culture or both confirmed 269 tuberculosis cases, 174 of which were smear-positive. The prevalence rate of smear-positive tuberculosis was 145 per 100 000 (95% confidence interval: 110–180) assuming no tuberculosis in persons aged < 15 years. Prevalence was 5.1 times as high in men as in women, increased with age, was higher in rural than in urban or remote areas and showed a north-to-south gradient.

**Conclusion** In Viet Nam, the tuberculosis prevalence rate based on positive sputum smear tests was 1.6 times as high as previously estimated. Age and sex patterns were consistent with notification data. Tuberculosis control should remain a high priority in Viet Nam.

Une traduction en français de ce résumé figure à la fin de l'article. Al final del artículo se facilita una traducción al español. الترجمة العربية لهذه الخلاصة في نهاية النص الكامل لهذه المقالة.

# Introduction

Tuberculosis is still a major cause of morbidity and mortality worldwide. In 2006, an estimated 9.2 million new tuberculosis cases occurred, resulting in 1.7 million deaths. The Viet Nam National Tuberculosis Control Programme (NTP) is based on the principles of DOTS, the core control strategy recommended by the World Health Organization (WHO).<sup>2</sup> According to WHO estimates, since 1997 Viet Nam has reached and exceeded the global targets for tuberculosis control, 2,3 i.e. to detect > 70% of new smear-positive pulmonary tuberculosis cases and cure > 85% of these detected cases. If these targets were met, tuberculosis incidence in Viet Nam would predictably decrease over the period 1997–2004 by 44%.<sup>3,4</sup> Although there was indeed a small decrease in tuberculosis notification rates among women and persons older than 35 years, this was offset by an increase among young men, which led to stabilization in notification rates during this period.<sup>3</sup> In 2006, WHO estimated that Viet Nam ranked 12th among the tuberculosis high-burden countries<sup>1</sup>, with a prevalence of smear-positive tuberculosis of 89 per 100 000 population. (WHO, unpublished data, 2008).

A major question for the Viet Nam NTP is whether these estimates are correct. However, the tuberculosis burden and case detection rate are unknown, because they can only be measured directly if the incidence is known. Tuberculosis incidence is difficult to measure, but tuberculosis prevalence can be assessed by cross-sectional surveys and can be used to estimate the rate at which tuberculosis patients are detected and put on treatment as part of a tuberculosis control programme (i.e. the patient diagnostic rate, PDR). <sup>5,6</sup> The PDR provides information about the burden of tuberculosis and, if determined at different times,

can show the impact of tuberculosis control measures. We aimed to measure the burden of tuberculosis disease, as revealed by a nationwide representative cross-sectional survey, by estimating the tuberculosis prevalence in Viet Nam and comparing this to the tuberculosis prevalence estimated by WHO¹. We also identified the major demographic determinants of tuberculosis prevalence.

### Methods

# Study setting and population

We did a population-based cross-sectional survey based on multistage cluster sampling, stratified by urban, rural and remote areas. A sample size of approximately 105 000 adults (15 years or older) was calculated based on 95% confidence interval (CI) boundaries of 71 and 129 per 100 000 for an observed prevalence of 100 per 100 000 population and a design effect factor due to cluster sampling of 1.5.7

Clusters had an approximate population size of 2240 inhabitants (1500 adults), and 70 clusters were selected. Districts were selected with sampling probability proportional to the population in the 1999 census (General Statistics Office of Vietnam, unpublished data, 2002). In the selected districts, communes and sub-communes were selected by simple random sampling. Briefly, all communes or sub-communes were assigned a random number and in each district one was selected and used as the starting point. Other sub-communes were added until the required number of inhabitants (2240 people) was obtained by first going north from the selected sub-commune and then adding sub-communes along a clockwise route.

Smear-positive tuberculosis is usually rare in people younger than 15 years, and it is difficult to collect sputum samples

Correspondence to Edine W Tiemersma (e-mail: tiemersmae@kncvtbc.nl).

(Submitted: 28 May 2009 - Revised version received: 18 September 2009 - Accepted: 20 September 2009 - Published online: 22 February 2010)

<sup>&</sup>lt;sup>a</sup> National Tuberculosis Programme Viet Nam, Hanoi, Viet Nam.

<sup>&</sup>lt;sup>b</sup> KNCV Tuberculosis Foundation, PO Box 146, 2501 CC The Hague, Netherlands.

<sup>&</sup>lt;sup>c</sup> Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands

from children. Therefore the population eligible for the survey included all residents aged  $\geq 15$  years in the selected clusters who were present during the survey census. A resident was defined as a person who had lived in the household concerned for at least 3 months. To avoid participation bias, short-term guests in households were excluded from the survey.

#### Measurements

The survey was conducted from September 2006 to July 2007. In each cluster, data were collected during 14-day periods. First, the survey team conducted a house-to-house census based on population lists provided by the local authorities, to see who was present, to inform survey subjects about procedures and to collect household data. Subsequently persons suspected of having tuberculosis were identified by screening all eligible inhabitants during an interview and by chest X-ray with mobile X-ray units. Individuals with findings suggestive of tuberculosis were interviewed in depth and were asked to submit three sputum specimens. The first and third specimens were examined by smear test by the survey team in the district laboratory. The second (morning) specimen was transported to national and regional reference laboratories for smear examination, culture and species identification. At the reference laboratories, all slides were stored for selection of all (100%) positive smears and a 10% random sample of all negative smears from each sampling unit was used for re-reading. All X-ray images were transported to central X-ray reading units for re-reading of 100% of those scored as abnormal, a 20% random sample of those scored as normal in the field in the first 20 clusters and a 10% random sample of those scored normal in the subsequent  $50\,$ clusters. For this purpose, all X-ray images were given a serial number in chronological order, and a serial number of < 10 was randomly chosen. Then every tenth subsequent serial number was chosen for re-reading. For example, if serial number 7 was chosen, the 17th, 27th, etc. images were re-read.

#### **Definitions**

A person suspected of having tuberculosis was defined as any survey participant with chest X-ray abnormalities consistent with tuberculosis, productive cough for more than 2 weeks, current tuberculosis

treatment or a history of tuberculosis in the preceding 2 years. A smear-positive pulmonary tuberculosis case was defined by the presence of either two or more positive smears, one positive smear plus an abnormal chest X-ray result consistent with tuberculosis, or one positive smear plus a positive culture. A culture-positive case was defined as a participant with a positive culture. A bacteriologicallyconfirmed case was defined as a case with smear-positive or culture-positive pulmonary tuberculosis (or both). A new case was defined as a participant who had never had treatment for tuberculosis or who had taken anti-tuberculosis drugs for < 1 month.<sup>8,9</sup> Final classification of each tuberculosis case was done by a consensus panel that included an international expert not involved in the design or implementation of the study.

### **Data analysis**

All data were double-entered in an Epi-Data Software database (EpiData Association, Odense, Denmark); discrepancies were checked against the raw data. Data were analysed with Stata version 9SE software (Stata Corporation, College Station, TX, United States of America). Our primary analysis calculated overall prevalence rates; additional subgroup analyses were done to estimate stratumspecific prevalence rates by age group, sex and geographic area. In all analyses, population weightings were used to adjust for the stratified sampling design, for differences between clusters in population growth since 1999 and for differences in cluster size. Differences in departure from the cluster sample size of 1500 were found by calculating the overall exact sampling probability as:

 $A \times B \times C$ 

where A is the individual sampling probability, calculated as 1 divided by the sampling interval of a given stratum. For example, the sampling interval for urban areas was 746 890; i.e. after ranking districts in decreasing number of inhabitants (largest district first), the district inhabited by every 746 891st person was selected. B is the correction factor for the differential growth in population size between the years 1999 and 2006, calculated by dividing the population of each sampled district in 2006 by the census population of that district in 1999. The correction factor C for differential

cluster size was calculated by the number of participants in each cluster divided by the mean cluster size.

Point prevalence estimates, 95% CIs and design effects were calculated with the Stata "svy" commands. CIs were adjusted for the cluster design by first-order Taylor linearization. <sup>10</sup> *P*-values were adjusted by the second-order correction of Rao & Scott for the Pearson  $\chi^2$  test. <sup>11</sup> To test for trends, we used the non-parametric Cuzick test.

The PDR was calculated as the number of newly-reported cases of smear-positive tuberculosis per 100 000 population per year (notification rate) divided by the prevalence of new cases of smear-positive tuberculosis per 100 000.5

### **Ethical approval**

The Research Board of the National Hospital for Tuberculosis and Respiratory Diseases in Hanoi gave scientific and ethical approval for the study.

### Results

The census recorded 114 389 adult residents in the selected population clusters. Of these, 103 924 (91.0%) were present on the day of the census and thus considered eligible to participate in the survey, and 94 179 (82.3%) participated (Fig. 1). With respect to age and sex, the eligible population closely reflected the demographic characteristics of the Vietnamese population; in contrast, non-participants were younger and more often male (Fig. 2).

Of the participants, 6444 (6.8%) had been interviewed to screen for cough, 328 (0.3%) had the results of a chest X-ray examination and 87 314 (92.7%) had both. Of the remaining 93 participants, 81 (0.10%) were screened with a chest Xray but the results were not recorded and 12 (0.01%) were identified as suspected of having tuberculosis based on history only. Of the 87 314 participants who had both the screening interview and chest X-ray examination, 2972 (3.4%) participants suspected of having tuberculosis were identified based on chest X-ray abnormalities only, 3522 (4.0%) were identified based on productive cough only and 518 (0.6%) were identified based on both chest X-ray abnormalities and productive cough (Table 1).

The proportion of persons suspected of having tuberculosis who had both productive cough and chest X-ray abnormali-

ties was higher among men (0.9%) than among women (0.3%). This proportion also increased with age, from 0.1% in the group aged 15-24 years to 2.2% in the group aged  $\geq 65$  years. Chest X-ray abnormalities, with or without productive cough, were more frequent in the southern (4.6%) than in the northern (3.7%) or the central (3.6%) region of the country, but the differences were not statistically significant.

Smear examination, culture or both tests done for 7648 participants identified 269 tuberculosis cases, and 174 of these were smear-positive (Fig. 1). Six participants (3.4%) were on tuberculosis treatment, 16 (9.2%) had a history of tuberculosis treatment in the preceding 2 years and three (1.7%) had both current and past tuberculosis treatment. Fourteen participants (8.0%) had received tuberculosis treatment more than 2 years before the survey.

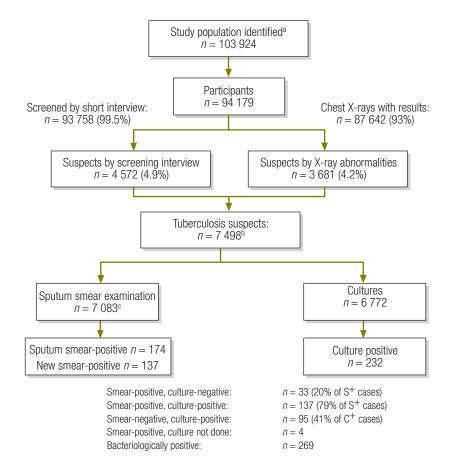
In-depth interview data were available for 264 participants with tuberculosis (98.1%). Productive cough for more than 2 weeks was reported by 131 (49.6%), any cough for more than 2 weeks by 145 (54.9%), any cough of any duration by 178 (67.4%) and any symptom suggestive of tuberculosis by 196 (74.2%). There were no significant differences in the frequency of cough or other symptoms between smear-positive and smearnegative cases (data not shown).

Based on 174 identified cases among 94 179 participants, the weighted prevalence of smear-positive tuberculosis was 196.8 per 100 000. The prevalence rate of smear-positive tuberculosis was higher in men than in women (351.1 versus 69.3 per 100 000; P < 0.001) and increased significantly with age, from 42.2 per 100 000 in the group aged 15–24 years to 429.3 per 100 000 in the group aged  $\geq$  65 (Table 2).

The prevalence of smear-positive tuberculosis was significantly lower in remote areas (134.3 per 100 000) as compared with urban (203.2 per 100 000) and rural areas (219.4 per 100 000). It was also higher in southern than in central and northern Viet Nam; this difference approached statistical significance (Table 2).

The weighted prevalence of bacteriologically-positive tuberculosis was 307.2 per 100 000 adult population (95% CI: 248.8–365.6) (Table 2). The prevalence rate of bacteriologically-positive tuberculosis was also significantly higher in men than in women (536.4 versus 117.8)

Fig. 1. Schematic diagram of the study design and data collection in a tuberculosis prevalence survey, Viet Nam, 2006–2007



C+, culture-positive; S+, sputum-positive.

- <sup>a</sup> Eligible and present during the census in the first days of field work.<sup>a</sup>
- b There were 755 participants with both chest X-ray abnormalities and either persistent productive cough or recent history of tuberculosis treatment.<sup>b</sup>
- <sup>c</sup> This figure excludes 565 people who were tested but who were not suspected of having tuberculosis. <sup>c</sup>

per 100 000; P < 0.001). As with smear-positive tuberculosis, the prevalence rate

of bacteriologically confirmed disease was lower in remote (232.3 per 100 000) than

Fig. 2. Age and sex distribution of the participating population in prevalence survey versus the general population of Viet Nam, 2006–2007

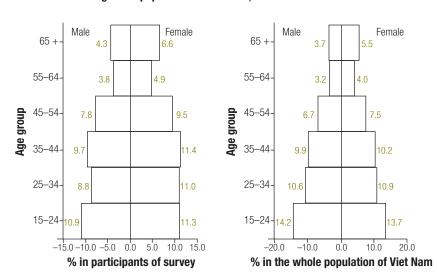


Table 1. Data for productive cough and chest X-ray results, by subgroups, among 87 314 participants in a tuberculosis prevalence survey in Viet Nam, 2006–2007

	No. with inter- view and CXR results	CXR abnormal and productive cough		CXR abnormal and no productive cough		CXR normal and productive cough		CXR normal and no productive cough					
		No.	%	P-value	No.	%	<i>P</i> -value	No.	%	P-value	No.	%	<i>P</i> -value
Total	87 314	518	0.6		2972	3.4		3522	4.0		80 302	92.0	
Sex				< 0.001			< 0.001			< 0.001			< 0.001
Male	39 776	369	0.9		1758	4.4		2126	5.3		35 523	89.3	
Female	47 530	149	0.3		1214	2.6		1396	2.9		44 771	94.2	
Unknown	8	-			-			-			8		
Age (years)				$< 0.001^{a}$			$< 0.001^{a}$			$< 0.001^{a}$			$< 0.001^{a}$
15–24	19 274	14	0.1	$< 0.001^{b}$	198	1.0	$< 0.001^{b}$	362	1.9	$< 0.001^{b}$	18 700	97.0	< 0.001 <sup>b</sup>
25–34	17 065	38	0.2	$< 0.001^{b}$	237	1.4	$< 0.001^{b}$	602	3.5	$< 0.001^{b}$	16 188	94.9	< 0.001 <sup>b</sup>
35–44	18 584	63	0.3	< 0.001 <sup>b</sup>	481	2.6	$< 0.001^{b}$	790	4.3	$0.338^{b}$	17 250	92.8	< 0.001 <sup>b</sup>
45–54	15 338	103	0.7	0.211 <sup>b</sup>	656	4.3	< 0.001 <sup>b</sup>	718	4.7	< 0.001 <sup>b</sup>	13 861	90.4	< 0.001 <sup>b</sup>
55–64	7 685	96	1.2	< 0.001 <sup>b</sup>	436	5.7	< 0.001 <sup>b</sup>	450	5.9	< 0.001 <sup>b</sup>	6 703	87.2	< 0.001 <sup>b</sup>
≥ 65	9 351	204	2.2	$< 0.001^{b}$	963	10.3	$< 0.001^{b}$	600	6.4	$< 0.001^{b}$	7 584	81.1	< 0.001 <sup>b</sup>
Unknown	17	_			1			-			16	94.1	
Area													
Urban	23 903	142	0.6	$0.646^{\circ}$	937	3.9	0.151°	810	3.4	$0.262^{\circ}$	22 014	92.1	0.862°
Remote	26 694	188	0.7	0.159°	686	2.6	$0.014^{\circ}$	1440	5.4	$0.006^{\circ}$	24 380	91.3	$0.306^{\circ}$
Rural	36 717	188	0.5	0.111°	1349	3.7	$0.322^{\circ}$	1272	3.5	$0.072^{\circ}$	33 908	92.3	$0.280^{\circ}$
Region													
North	41 436	273	0.7	$0.083^{d}$	1240	3.0	0.083 <sup>d</sup>	2190	5.3	< 0.001 <sup>d</sup>	37 733	91.1	$0.009^{d}$
Central	14 146	84	0.6	$0.565^{d}$	421	3.0	$0.736^{d}$	498	3.5	$0.365^{d}$	13 143	92.9	$0.265^{d}$
South	31 732	161	0.5	0.063 <sup>d</sup>	1311	4.1	0.062 <sup>d</sup>	834	2.6	< 0.001 <sup>d</sup>	29 426	92.7	0.027 <sup>d</sup>

CXR, chest X-ray.

in urban (282.0 per 100 000) and rural areas (344.2 per 100 000), but this difference was not significant. In addition, it was lower in central (209.4 per 100 000) than in southern (367.4 per 100 000) or northern Viet Nam (286.1 per 100 000).

A detailed analysis of the age-specific and sex-specific prevalence rates showed male-to-female ratios of 1.9 or higher, irrespective of how a tuberculosis case was defined. A similar pattern was observed for chest X-ray abnormalities consistent with tuberculosis. Overall, the prevalence rate of smear-positive tuberculosis in men was 5.1 times as high as in women, and the prevalence rate of all bacteriologically confirmed tuberculosis was 4.6 times as high in men as in women (Table 3).

The PDR of new smear-positive tuberculosis in the year 2006 was 0.60 (95% CI: 0.49–0.78). This PDR was higher among women (0.86) than among men (0.50), highest in the group aged 25–34 years (0.94) and lowest in the group aged 35–44 years (0.56). The PDR was slightly higher in the southern (0.66) than in the

northern and central regions of Viet Nam (0.54), as shown in Table 4.

# **Discussion**

The survey showed a weighted prevalence rate of smear-positive tuberculosis among the population aged ≥ 15 years of 196.8 per 100 000. Assuming that there were no smear-positive tuberculosis cases among the population younger than 15 years, the national prevalence rate of smear-positive tuberculosis in the total population (all age groups) would be 145 per 100 000 (95% CI: 110-180). This number is 1.6 times as high as the previous WHO estimate for Viet Nam in 2006 (89 per 100 000). Thus, the burden of tuberculosis in Viet Nam is probably considerably greater than assumed. Although we did not measure morbidity or mortality in this survey, this prevalence represents substantial morbidity and mortality directly related to tuberculosis and, potentially, to other diseases. 12 WHO estimates, based on tuberculin survey data from the 1990s,<sup>13</sup> are clearly too low, and the difference between the earlier estimate and our figures illustrates that tuberculosis prevalence, and probably incidence, cannot be reliably inferred from such data with Styblo's rule. 14,15

Of the 174 smear-positive cases detected, 39 (22%) were currently on tuberculosis treatment or had been treated for tuberculosis for  $\geq 1$  month. Thus, most smear-positive cases were not known to the NTP.

Tuberculosis control in Viet Nam is based on passive case-finding among patients who present with persistent productive cough.<sup>2</sup> In this survey, only 53% of those identified with smear-positive tuberculosis indicated they had persistent productive cough. Thus, a considerable proportion of the tuberculosis cases we detected would not have been diagnosed in NTP facilities although some of the cases (specifically those with mild complaints) would probably have been diagnosed by the NTP at a later time.

Smear-positive cases accounted for 64% of all bacteriologically-positive cases.

a P-value for trend.

<sup>&</sup>lt;sup>b</sup> P-value for the difference between this age group compared with all other age groups combined.

<sup>°</sup> P-value for the difference between this area compared with the other two areas together.

<sup>&</sup>lt;sup>d</sup> P-value for the difference between this region compared with the other two regions together.

Table 2. Estimated prevalence of tuberculosis in Viet Nam, according to sputum smear-positive and bacteriologically confirmed cases in survey participants ≥ 15 years old, 2006–2007

Characteristic	No. of survey		Sputum smea	r-positive cases	3	Bacteriologically confirmed cases				
	participants	No. of cases	Weighted prevalence (per 100 000) <sup>a</sup>	95% CI	<i>P</i> -value	No. of cases	Weighted prevalence (per 100 000) <sup>a</sup>	95% CI	<i>P</i> -value	
Total	94 179	174	196.8	149.6-243.9		269	307.2	248.8-365.6		
Sex <sup>b</sup>					< 0.001				< 0.001	
Male	42 603	142	351.1	262.3-439.9		212	536.4	431.3-641.5		
Female	51 567	32	69.3	39.2-99.3		57	117.8	75.0-160.7		
Age (years)c					< 0.001 <sup>d</sup>				< 0.001 <sup>d</sup>	
15–24	20 935	7	42.2	11.8-72.6	< 0.001e	10	54.8	21.9-87.6	< 0.001e	
25-34	18 682	16	83.5	23.7-143.2	$0.002^{e}$	27	136.4	62.8-210.0	< 0.001e	
35-44	19 794	47	246.7	156.8-336.6	0.063e	63	321.0	221.9-420.0	0.695e	
45–54	16 285	41	233.5	144.7-322.2	0.315 <sup>e</sup>	59	343.9	227.6-460.2	0.463 <sup>e</sup>	
55–64	8 137	24	328.7	187-470.4	$0.030^{e}$	38	599.0	288.2-909.9	0.012e	
≥ 65	10 328	39	429.3	238.8–619.7	$< 0.001^{d}$	72	764.4	492.0-1036.9	< 0.001 <sup>e</sup>	
Area									0.267	
Urban	26 357	52	203.2	132.2-274.2	0.862f	72	282.0	188.3-375.7	0.151 <sup>f</sup>	
Remote	27 545	37	134.3	92.1-176.5	$0.027^{f}$	63	232.3	131.5-333.0	0.119 <sup>f</sup>	
Rural	40 277	85	219.4	144.6-294.2	0.170 <sup>f</sup>	134	344.2	258.8-429.7	0.106 <sup>f</sup>	
Region									0.087	
North	45 679	71	162.5	117.0-208.0	$0.129^{g}$	124	286.1	217.7-354.6	0.4749	
Central	14 656	21	152.2	95.7-208.7	$0.212^{g}$	29	209.4	131.6-287.2	$0.048^{g}$	
South	33 844	82	256.4	151.6–361.1	$0.053^{g}$	116	367.4	249.2-485.7	0.121 <sup>g</sup>	

CI, confidence interval.

This proportion was relatively high compared to other recent prevalence surveys within the region<sup>16–19</sup> and may reflect the dynamics of the tuberculosis epidemic in Viet Nam. Our higher figure may also be explained by the fact that only the second sputum specimen was cultured, a

procedure that may be less sensitive than culturing two specimens, as was done in the other surveys. We may therefore have underestimated the prevalence of culture-positive tuberculosis.

Most smear-positive tuberculosis cases (89%) had chest X-ray abnormali-

ties consistent with tuberculosis. This association suggests that, together with direct smear examination, chest X-ray may be an important tool for tuberculosis case-finding. There was a strong and statistically significant correlation with age, both for the prevalence of chest

Table 3. Male-to-female ratios of the tuberculosis prevalence rate³ per 100 000 persons ≥ 15 years, by age group, in Viet Nam, 2006–2007

Age group _		ear-positive rculosis	Smear-positive tuberculosis			e-positive erculosis	Bacteriologically confirmed tuberculosis		
(years)	M:F	<i>P</i> -value <sup>a</sup>	M:F	<i>P</i> -value <sup>a</sup>	M:F	<i>P</i> -value <sup>a</sup>	M:F	<i>P</i> -value <sup>a</sup>	
15–24	2.0	0.421	2.0	0.421	2.9	0.194	2.9	0.193	
25-34	10.6	0.005	6.0	0.003	4.8	0.004	5.7	0.002	
35–44	7.7	< 0.001	6.3	< 0.001	5.0	< 0.001	5.7	< 0.001	
45-54	34.0	0.001	20.4	< 0.001	12.0	< 0.001	13.6	< 0.001	
55-64	35.8	< 0.001	52.2	< 0.001	16.1	< 0.001	20.9	< 0.001	
≥ 65	1.9	0.091	2.2	0.036	2.6	0.01	2.2	0.007	
All ages	4.8	< 0.001	5.1	< 0.001	4.5	< 0.001	4.6	< 0.001	

M:F, male to female ratio.

<sup>&</sup>lt;sup>a</sup> Weighted for stratification by area, differential population growth between 1999 and 2006 and different cluster size.

<sup>&</sup>lt;sup>b</sup> Data on sex were missing for 9 cases.

<sup>&</sup>lt;sup>c</sup> Data on age were missing for 18 cases.

d P-value for trend.

<sup>&</sup>lt;sup>e</sup> P-value for the difference between this age group compared with all other age groups combined.

 $<sup>{}^{\</sup>mathrm{f}}\textit{P}\text{-}\mathrm{value}$  for the difference between this area compared with the other two areas together.

 $<sup>{}^{\</sup>rm g}{\it P}{
m -value}$  for the difference between this region compared with the other two regions together.

<sup>&</sup>lt;sup>a</sup> Weighted for stratification by area, differential population growth between 1999 and 2006, and different cluster size.

X-ray abnormalities and persistent productive cough, and for the prevalence of bacteriologically-confirmed tuberculosis. Tuberculosis notification rates in Viet Nam also tend to increase with age.

Interestingly, the increase in prevalence rate occurred at a much earlier age in men than in women, which was reflected in very high male-to-female ratios in the group aged 45-64 years. The overall male-to-female ratios for the prevalence rate of tuberculosis were 4.5 to 5.1, depending on the type of tuberculosis (Table 3). This is 1.7 times as high as the notification rate of new smear-positive tuberculosis (2.8) in the NTP in 2006. Our higher ratio strongly suggests that the sex difference in tuberculosis notification in Viet Nam reflects a true difference in disease occurrence rather than a difference in access to diagnosis and treatment, as some studies have suggested. 16,20-22 A nationwide study carried out in 2002 in the same 70 clusters we used showed longer delays in diagnosis among women than among men (although the difference was small),20 but an analysis of tuberculosis laboratory data in the north of Viet Nam suggested that women were more likely than men to have or request a sputum smear examination.<sup>23</sup>

In Viet Nam, the considerably higher PDR in women (0.86) compared with men (0.50) suggests that the case detection rate is higher in the former. Although the PDR<sup>5</sup> is not the same as the case detection rate, comparing the PDR between populations or subpopulations can provide information about the relative completeness of case detection. The PDR was lowest in the groups aged 35-44 (0.56) and  $\geq$  65 years (0.66) and lower among men than among women. This result suggests that the NTP should increase efforts to find male tuberculosis patients and focus on these two age groups. Because the PDR relates to cases found and treated by the NTP only, this raises the question of whether men, especially in the group aged 35-44 years, are diagnosed more often by private physicians than by the publicly-operated NTP.

Our survey confirmed that other characteristics of the tuberculosis notification pattern reflect features of the underlying tuberculosis epidemic in Viet Nam. Specifically, our data reflect the north–south gradient<sup>2</sup> and the relatively low prevalence rates in remote, mountainous areas compared to the urban and low-lying rural areas.<sup>6</sup>

Table 4. Estimated patient diagnosis rates for the Viet Nam National Tuberculosis Programme, by sex, age group and geographic region, 2006–2007

Category	Annual notification rate (per 100 000)	Annual prevalence rate (per 100 000)	PDR <sup>a</sup>	95% CI
Total	93	155	0.60	0.49-0.78
Sex				
Male	137	273	0.50	0.40-0.66
Female	49	57	0.86	0.59-1.59
Age (years)				
15-24	32	42	0.76	0.44-2.70
25-34	69	73	0.94	0.55-3.15
35-44	93	166	0.56	0.37-1.10
45–54	135	182	0.74	0.53-1.26
55–64	176	228	0.77	0.50 - 1.72
≥ 65	254	384	0.66	0.45-1.27
Region				
North	66	123	0.54	0.40-0.80
Central	77	143	0.54	0.39-0.88
South	131	200	0.66	0.48-1.02

CI, confidence interval; PDR, patient diagnostic rate.

Although prevalence surveys such as ours are useful to evaluate the performance of tuberculosis programmes, they are logistically difficult to perform, time-consuming and expensive. Practical preparations for our survey began in mid-2005; recruitment started in September 2006 and lasted 9 months. Data entry, cleaning, analysis and reporting lasted another one-and-a-half years. Total survey costs, including the purchase of mobile X-ray units, were estimated to be 1 000 000 United States dollars.

Our survey had limitations. First, the eligible population did not include adults who were present in the sampled clusters for less than 3 months, who were incarcerated or who lived in military barracks (i.e. the mobile population) during the survey period. This is a potential drawback because it is not known how well the survey sample population represented the mobile population and thereby the total Vietnamese population. Because the mobile population probably contains a higher proportion of young men than the survey population, our survey may have either underestimated or overestimated the prevalence of tuberculosis. Young men, who were under-represented in the survey sample, tended to have a higher prevalence rate of tuberculosis than women of the same age, but a lower prevalence rate than older men. Second,

rather than any cough we used persistent productive cough as a screening criterion. This might have decreased the sensitivity of our case-finding method. In fact, among the smear-positive tuberculosis cases we identified, persistent cough was more commonly mentioned in the indepth interview (by 145 persons) than persistent productive cough (by 131 persons). Finally, this survey did not collect data on human immunodeficiency virus (HIV) infection. Further studies are needed to identify the prevalence of HIV and tuberculosis co-infection in the population and its significance for the total burden of tuberculosis in Viet Nam, because the increasing prevalence of HIV infection in parts of Viet Nam may have increased the burden of HIV and tuberculosis co-infection.2

The results of this first national prevalence survey showed a prevalence of tuberculosis in Viet Nam that was 1.6 times as high as previously estimated. A significant number of tuberculosis smearpositive and smear-negative cases remain undiagnosed and present a potential source of transmission in the community. The NTP should develop, implement and evaluate additional approaches to tuberculosis control, including special efforts to find boys and men with tuberculosis. Approaches that should be considered include: (i) the introduction of active case-

<sup>&</sup>lt;sup>a</sup> Calculated from the notification rates for new smear-positive tuberculosis cases and the weighted prevalence rates of new smear-positive tuberculosis cases as estimated from the prevalence survey, weighted for stratification by area, differential population growth from 1999 to 2006 and differential cluster size. Source: WHO 2008.<sup>1</sup>

finding based on chest X-ray screening in high-risk groups, and (ii) widening the eligibility criteria for smear examination to other tuberculosis-related symptoms in addition to cough. The control of tuberculosis should remain a high priority for the Vietnamese Ministry of Health.

### **Acknowledgements**

The authors thank the Viet Nam National Tuberculosis Control Programme

board of directors and tuberculosis staff involved in the survey, and all the individuals living in the study sites for taking part. They also thank Mr Nico Kalisvaart, Dr Marleen Vree and Dr Ikushi Onozaki for technical support with data management, data analysis and review of the cases of tuberculosis detected.

**Funding:** This study was supported financially by the Viet Nam Ministry of

Health, the Government of the Netherlands, KNCV Tuberculosis Foundation, the Global Fund To Fight AIDS, Tuberculosis and Malaria, and the World Health Organization.

**Competing interests:** None declared.

## ملخص

# المسح الوطنى لانتشار السل في فييت نام

الغرض قياس انتشار السل في فييت نام من بيانات المسح السكاني، ومقارنتها مع انتشار السل التقديري لمنظمة الصحة العالمية، والتعرف على المحددات الدموغرافية لانتشاره.

الطريقة أجري المسح المقطع العرضي مع اعتيان عنقودي متعدد المراحل، مقسم إلى طبقات حضرية وريفية ونائية، في عامي 2006-2007 في 70 منطقة. ودعا الباحثون جميع السكان في عمر أقل من أو يساوي 15 سنة لإجراء فحص السعال وفحص الأشعة السينية عليهم. ومن اكتشف لديه من المشاركين نتائج تشير إلى احتمال الإصابة بالسل كان عليه أن يعطي عينات من القشع (البلغم) للقيام بفحص اللطاخة واستزراعها. وحسب الباحثون نقط الانتشار التقديرية، وفاصلات الثقة %95، وتأثير التصميم. وأجرى الباحثون تصحيحاً لفاصلات الثقة وقيمة قوة الاحتمالات P على تصميم المجموعة العنقودية.

الموجودات من 114389 شخصاً بالغاً من السكان، أجري التحري على 94179 فرداً (بنسبة 82.3%). منهم 87314 (92.7%) أجري التحري عليهم عن طريق كل من الاستبيان والتصوير الشعاعي، وكان لدى 3522 شخصاً (4.0%) سعال

منتج للبلغم، وكان لدى 518 شخصاً ((0.60)) سوابق حديثة للإصابة بالسل، وكان لدى 2972 شخصاً ((0.60)) صوراً شعاعية غير طبيعية توحي بالإصابة بالسل. أجريت اختبارات البلغم على 7648 مشاركاً. وأكد اختبار البلغم أو المؤرعة البكتيرية أو كلاهما على الإصابة بالسل لدى 269 حالة، وكانت 174 حالة منهما إيجابية اللطاخة. وكان معدل انتشار اللطاخات الإيجابية للسل 145 لكل 100 ألف (فاصلة الثقة (0.00)9: 110 بافتراض عدم الإصابة بالسل بين الأفراد أقل من عمر 15 سنة. وكان الانتشار أكثر بـ5.1 ضعفاً بين الرجال عن النساء، وازداد الانتشار مع ازدياد العمر، وكان أعلى في المناطق الريفية عن المناطق الحضرية أو المناطق النائية، وأظهر الانتشار تدرجاً من الشمال إلى الجنوب.

الاستنتاج كان انتشار السل في فييت نام، بناء على نتائج اختبارات لطاخات البلغم الإيجابية، أكثر بـ 1.6 مرة من التقديرات السابقة. وكانت أنهاط العمر والجنس متسقة مع بيانات التبليغ. ولا بد أن تظل مكافحة السل أولوية قصوى في فييت نام.

### Résumé

## Enquête nationale sur la prévalence de la tuberculose au Viet Nam

Objectif Estimer la prévalence de la tuberculose au Viet Nam à partir des données d'une enquête en population, comparer cette estimation à la prévalence estimée par l'Organisation mondiale de la Santé et identifier les principaux déterminants géographiques de la prévalence de la tuberculose. Méthodes Une étude transversale avec sondage en grappes à plusieurs degrés, stratifiée selon la nature des zones (urbaines, rurales ou éloignées), a été réalisée sur la période 2006-2007 dans 70 communes. Tous les habitants de 15 ans et plus ont été invités à répondre à un questionnaire concernant la toux et à subir une radiographie thoracique. Les participants présentant des résultats évocateurs de tuberculose ont fourni des échantillons d'expectorations en vue d'un examen de frottis et d'une mise en culture. Des estimations ponctuelles de la prévalence, les intervalles de confiance à 95 % correspondants et les effets du type d'étude ont été déterminés. Les intervalles de confiance et les valeurs de p ont été ajustés pour tenir compte de l'utilisation du sondage en grappe.

**Résultats** Sur 114 389 habitants adultes, 94 179 (82,3 %) ont fait l'objet d'un dépistage. Sur les 87 314 individus (92,7 %) dépistés à la fois par questionnaire et par radiographie thoracique, 3522 (4,0 %) présentaient

une toux productive, 518 (0,6 %) des antécédents récents de tuberculose et 2972 (3,4 %) des anomalies radiologiques évocatrices de tuberculose. Des examens d'expectorations ont été effectués pour 7648 participants. Les examens d'expectorations, les cultures bactériennes ou l'un et l'autre de ces examens ont permis de confirmer 269 cas de tuberculose, dont 174 cas frottis positifs. Le taux de prévalence de la tuberculose à frottis positifs était de 145 pour 100 000 (intervalle de confiance à 95 % : 110-180), en supposant que la tuberculose était absente chez les moins de 15 ans. La prévalence de la maladie était 5,1 fois plus élevée chez les hommes que chez les femmes, augmentait avec l'âge, était plus importante en milieu rural qu'en milieu urbain ou dans des zones reculées et obéissait à un gradient Nord-Sud.

**Conclusion** Au Viet Nam, le taux de prévalence de la tuberculose déterminé d'après les examens de frottis positifs était 1,6 fois plus élevé que le taux précédemment estimé. Les schémas de répartition selon l'âge et le sexe relevés étaient cohérents avec les données de notification. La lutte contre la tuberculose doit rester fortement prioritaire dans ce pays.

### Resumen

### Encuesta nacional sobre la prevalencia de tuberculosis en Viet Nam

**Objetivo** Estimar la prevalencia de tuberculosis en Viet Nam a partir de los datos de una encuesta poblacional, compararla con la prevalencia estimada por la Organización Mundial de la Salud, e identificar los principales determinantes demográficos de la prevalencia de tuberculosis. **Métodos** En 2006-2007 se llevó a cabo en 70 comunas un estudio transversal mediante muestreo polietápico por conglomerados, estratificado por zonas urbanas, rurales y remotas. Se invitó a todos los habitantes ≥ 15 años a someterse a un cribado de tos y una radiografía torácica. Los participantes con resultados indicativos de tuberculosis proporcionaron muestras de esputo para baciloscopia y cultivo. Se hicieron estimaciones de la prevalencia momentánea y se calcularon los intervalos de confianza del 95% y los efectos de diseño. Los intervalos de confianza y los valores de *P* se ajustaron en función del diseño de los conglomerados. Resultados De un total de 114 389 habitantes adultos, se cribó a 94 179 (82,3%). De los 87 314 (92,7%) que se sometieron tanto al cuestionario como a la radiografía de tórax, 3522 (4,0%) presentaban tos con expectoración, 518 (0,6%) tenían antecedentes recientes de tuberculosis, y 2972 (3,4%) presentaban signos radiológicos indicativos de la enfermedad. Se analizó el esputo de 7648 participantes. El análisis de esputo, el cultivo bacteriano o ambas cosas confirmaron 269 casos de tuberculosis, 174 de los cuales eran bacilíferos. La prevalencia de tuberculosis bacilífera fue de 145 por 100 000 (intervalo de confianza del 95%: 110-180), suponiendo que no hubiera casos de tuberculosis entre los menores de 15 años. La prevalencia fue 5,1 veces mayor en los hombres que en las mujeres, aumentaba con la edad, era mayor en las zonas rurales que en las zonas urbanas o remotas, y mostraba un gradiente norte-sur.

**Conclusión** En Viet Nam, la prevalencia de tuberculosis deducida de los casos con esputo positivo fue 1,6 veces mayor que la estimada anteriormente. La distribución por edad y sexo fue congruente con los datos de notificación. El control de la tuberculosis debería seguir siendo de la máxima prioridad en Viet Nam.

### References

- Global tuberculosis control: surveillance, planning, financing: WHO report 2008. Geneva: World Health Organization; 2008 (WHO/HTM/TB/2008.393).
- Huong NT, Duong BD, Co NV, Quy HT, Tung LB, Bosman M et al. Establishment and development of the National Tuberculosis Control Programme in Vietnam. Int J Tuberc Lung Dis 2005;9:151–6. PMID:15732733
- Vree M, Duong BD, Sy DN, Co NV, Borgdorff MW, Cobelens FG. Tuberculosis trends, Vietnam. Emerg Infect Dis 2007;13:796–7. PMID:18044050
- Dye C, Gamett GP, Sleeman K, Williams BG. Prospects for worldwide tuberculosis control under the WHO DOTS strategy. *Lancet* 1998;352:1886– 91. doi:10.1016/S0140-6736(98)03199-7 PMID:9863786
- Borgdorff MW. New measurable indicator for tuberculosis case detection. *Emerg Infect Dis* 2004;10:1523–8. PMID:15498151
- Vree M, Hoa NB, Sy DN, Co NV, Cobelens FG, Borgdorff MW. Low tuberculosis in mountainous Vietnam is not due to low case detection: a cross-sectional survey. BMC Infect Dis 2007;7:109. doi:10.1186/1471-2334-7-109 PMID:17880701
- Williams B, Gopi PG, Borgdorff MW, Yamada N, Dye C. The design effect and cluster samples: optimising tuberculosis prevalence surveys. *Int J Tuberc Lung Dis* 2008;12:1110–5. PMID:18812038
- World Health Organization, International Union Against Tuberculosis and Lung Disease, Royal Netherlands Tuberculosis Association.. Revised international definitions in tuberculosis control. *Int J Tuberc Lung Dis* 2001;5:213–5. PMID:11326818
- 9. Enarson D, Rieder H, Arnadottir T, Trebucq A. *Management of tuberculosis:* a guide for low income countries, 5th ed. Paris: International Union Against Tuberculosis and Lung Disease; 2000.
- Royall RM. Model robust confidence intervals using maximum likelihood estimators. Int Stat Rev 1986;54:221–6. doi:10.2307/1403146
- Rao JN, Scott AJ. A simple method for the analysis of clustered binary data. Biometrics 1992;48:577–85. doi:10.2307/2532311 PMID:1637980
- Liang HY, Li XL, Yu XS, Guan P, Yin ZH, He QC et al. Facts and fiction of the relationship between pre-existing tuberculosis and lung cancer risk: a systematic review Int J Cancer 2009. Epub 11 June 2009
- Styblo K. The relationship between the risk of tuberculosis infection and the risk of developing infectious tuberculosis. *Bull Int Union Tuberc Lung Dis* 1985;60:117–9.

- van Leth F, van der Werf MJ, Borgdorff MW. Prevalence of tuberculosis infection and incidence of tuberculosis: a re-assessment of the Styblo rule. *Bull World Health Organ* 2008;86:20–6. doi:10.2471/BLT.06.037804 PMID:18235886
- Dye C. Breaking a law: tuberculosis disobeys Styblo's rule. Bull World Health Organ 2008;86:4. doi:10.2471/BLT.07.049510 PMID:18235879
- Cambodia, National Tuberculosis Control Program. National tuberculosis prevalence survey. Cambodia 2002. Phnom Penh: NTCP; 2005.
- 17. Report on nationwide random survey for the epidemiology of tuberculosis in 2000. Beijing: Ministry of Health; 2002.
- Tupasi TE, Radhakrishna S, Rivera AB, Pascual ML, Quelapio Ml. The 1997 nationwide tuberculosis prevalence survey in the Philippines. *Int J Tuberc Lung Dis* 1999;3:471–7. PMID:10383058
- Hong YP, Kim SJ, Lew WJ, Lee EK, Han YC. The seventh nationwide tuberculosis prevalence survey in Korea, 1995. *Int J Tuberc Lung Dis* 1998;2:27–36. PMID:9562108
- Huong NT, Vree M, Duong BD, Khanh VT, Loan VT, Co NV et al. Delays in the diagnosis and treatment of tuberculosis patients in Vietnam: a cross-sectional study. BMC Public Health 2007;7:110. doi:10.1186/1471-2458-7-110 PMID:17567521
- Borgdorff MW, Nagelkerke NJD, Dye C, Nunn P. Gender and tuberculosis: a comparison of prevalence surveys with notification data to explore sex differences in case detection. *Int J Tuberc Lung Dis* 2000;4:123–32. PMID:10694090
- Holmes CB, Hausler H, Nunn P. A review of sex differences in the epidemiology of tuberculosis. *Int J Tuberc Lung Dis* 1998;2:96–104. PMID:9562118
- Huong NT, Duong BD, Linh NN, Van LN, Co NV, Broekmans JF et al. Evaluation of sputum smear microscopy in the national tuberculosis control programme in the north of Vietnam. *Int J Tuberc Lung Dis* 2006;10:277–82. PMID:16562707
- Buu TN, Houben RMGJ, Quy HT, Lan NTN, Borgdorff MW, Cobelens FGJ. HIV and tuberculosis in Ho Chi Minh City, Vietnam, 1997–2002. *Int Emerg Infect Dis* 2007;13:1463–9.