

The 1997 Nationwide Tuberculosis Prevalence Survey in the Philippines*

T.E. Tupasi,¹ S. Radhakrishna,² A.B. Rivera,¹ M.L.G. Pascual,¹ M.I.D. Quelapio,¹ V.M. Co,¹ M.L.A. Villa,¹ G. Beltran,³ J.D. Legaspi,³ N.V. Mangubat,¹ J.N. Sarol Jr.,⁴ A.C. Reyes,¹ A. Sarmiento,⁵ M. Solon,⁶ F.S. Solon⁶ and M.J. Mantala⁷

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ABSTRACT

Setting: The Philippines is a developing country where tuberculosis (TB) remains a significant public health problem. **Objective:** To determine the prevalence of TB as a basis for setting the targets of the National Tuberculosis Control Program. **Study Population and Methods:** A multi-stage cluster survey of a random sample of 21,960 subjects from 36 clusters nationwide was undertaken from 2 April to 31 July 1997. BCG scar verification and tuberculin testing was performed for subjects aged 2 months and over, and chest radiography screening was done on subjects 10 years and older. Sputum samples were collected from individuals who were initially assessed to have abnormal chest radiographs to determine the prevalence of bacillary tuberculosis. Acid-fast smear by modified Kinyoun's technique and culture on Lowenstein Jensen were done to demonstrate *Mycobacterium tuberculosis*. **Results:** The prevalence of active pulmonary TB was 42/1,000 population. The prevalence of culture-positive and smear-positive cases was 8.1 and 3.1/1,000, respectively. The prevalence was similar in urban and rural areas. **Conclusion:** Morbidity from TB remains high. Allowing for methodological differences from the survey in 1981-1983, the prevalence of active pulmonary TB was unchanged. There was only a minimal decrease, of 37% for smear-positive cases and 25% for culture-positive cases, in the 14-year interval. (*Phil J Microbiol Infect Dis* 2000; 29(2):104-111)

Key words: Philippines, *M. tuberculosis*, prevalence survey

INTRODUCTION

The first national tuberculosis prevalence survey in the Philippines was undertaken in 1981-1983.¹ The findings from that survey showed that the prevalence of bacteriologically confirmed tuberculosis was 8.6/1,000 population for culture positive and 6.6/1,000 for smear positive tuberculosis. The prevalence of radiographic findings suggestive of active pulmonary tuberculosis (PTB) was 4.2%. The annual risk of infection was 2.5%.

The Department of Health (DOH) deemed it necessary to undertake the 1997 Nationwide Tuberculosis Prevalence Survey (NTPS) in order to determine the present magnitude of the tuberculosis problem. The results of this survey will serve as the basis for the course of action that the DOH will take to control tuberculosis in the Philippines.

MATERIALS AND METHODS

Study design and study population

This multi-stage cluster study was undertaken to determine the prevalence of active pulmonary tuberculosis and bacillary disease. The estimated sample size for the national prevalence survey was 21,600 subjects. This was based on the assumptions that the estimate of the overall prevalence among those aged 10 years and over were within 25% of the true value with 95% confidence; the presumptive prevalence of bacillary tuberculosis was 6/1,000; the expected coverage by radiographic examination was 85%; the expected coverage by sputum examination among those persons with radiographic abnormalities was 100%; about 73% of the population was aged 10 years and above; and that the design effect was 1.25 for the use of cluster sampling instead of simple random sampling.

A stratified multi-stage design was utilized in selecting the sample population. The population was selected from three strata: Metro Manila, other urban areas and rural areas. The allocation of clusters across strata was in proportion to the population sizes (PPS), based on the 1995 census from the Philippine National Statistics Office.

The first stage was the selection of provinces or cities within each stratum. Accordingly, five cities within Metro Manila, 10 Provinces representing other urban areas, and 21 provinces representing the rural areas were selected. In each province selected, a municipality was drawn first, and then a barangay (village) chosen based on PPS. Each cluster comprising 600 subjects was randomly selected from the barangay following a predetermined procedure.

Survey procedures

The field survey was undertaken by six teams from 1 April to 31 July 1997. Registration of the subjects in the cluster was done through house-to-house visits, at which time bacille Calmette Guerin (BCG) coverage was ascertained and tuberculin testing was performed in subjects aged 2 months and over. The tuberculin test induration was measured 2- 3 days later during a cluster assembly of the subjects. Results of the tuberculin tests will be reported separately. Chest radiography screening was done on individuals aged 10 years or older using mobile units equipped with 200-300 MA x-ray machines and a standard 10 x14 inch chest film. The chest films were interpreted initially by field readers and later read independently by two senior radiologists. In case of any discrepancy in the readings, a referee reader was consulted. The chest radiography was read following the diagnostic standards and classification of tuberculosis as recommended by the American Thoracic Society.²

All those deemed to have an abnormal chest radiograph by the field readers were requested to submit three sputum specimens collected on three separate occasions following recommended procedures.³ In some subjects who were unable to expectorate spontaneously, sputum was induced by nebulized super- saturated saline aerosol. The sputum specimens were then shipped to the research laboratory in ice within 24-72 hours of collection.

Laboratory procedures

A direct smear was prepared from each sputum specimen in the central research laboratory prior to processing. Screening microscopy of the smear was done with a fluorescence microscope using the auramine-rhodamine stain.⁴ Smears that were positive by screening microscopy were stained by the acid-fast modified Kinyoun's technique.⁵ The stained sputum smears were read independently by two readers, with a referee consulted in case, of discrepancy.

The sputum specimen was liquefied and decontaminated with 4% NAOH in N-acetyl L-cysteine. The processed specimen was then centrifuged at 3000 x G in a refrigerated centrifuge for 20 minutes. A portion of the sediment of the specimen was inoculated onto two slants of Lowenstein Jensen (LJ) medium and the remainder was stored at -70°C. The culture tubes were incubated in CO₂ at 37°C and inspected weekly to determine the presence of bacterial growth. The identification of *M. tuberculosis* was confirmed using standard biochemical methods. In case of contamination of the culture tube, the stored processed sediment from the specimen was again decontaminated and another set of LJ tubes was inoculated with the reprocessed specimen. Susceptibility to isoniazid, rifampicin, streptomycin and pyrazinamide was determined; these results will be reported separately.

Data processing and analysis

Data obtained from the field survey and the procedures performed were coded on the survey instrument and edited by the field interviewers. Field and laboratory data were computerized at the headquarters using Epi Info version 6.1⁷ Data were validated by double entry and files were later merged. Analysis of the data was done using SPSS version 7.5.⁸

Statistical analysis consisted primarily of the estimation of prevalence rates (proportions). Estimates of the prevalence were initially obtained for each cluster and weighted variance error per stratum was computed to derive the overall variance of the prevalence estimate. The standard error of the prevalence estimate was derived from the square root of the variance. The formula accounted only for the variation in the cluster level and variation for the other stages was not considered.⁹ Consequently, the computed sampling errors are likely to be underestimates. Confidence intervals were computed assuming that the prevalence estimates follow normal distribution upon repeated sampling.

To correct for non-coverage in 19% of the population eligible for chest radiography, the observed estimates were adjusted based on the relative risk in those not examined. There was strong evidence that those with chest symptoms (cough of 2 weeks or more, hemoptysis, chest and/or back pain of one month or more, fever of one month or more) presented for x-ray more often than those without; the proportions were 92% and 84%, respectively ($p < 0.001$). This association was evident in either sex: 93% and 86% in males, respectively ($p < 0.001$) and 90% and 83% females, respectively ($p < 0.001$), and was also present in the various age groups. The magnitude of this association was utilized to obtain the relative risk (RR) of a person without a radiograph having chest symptoms compared to a person with one. The RR of a person without a radiograph having chest symptoms has been considered to approximate the RR of that person having radiographic tuberculosis. If the RR was assumed to be lower in those who were not examined, this was taken to be 0.46 for males aged 10-19, 20-29, 30-39, 40-49, and 0.8 for males aged 50 years or more; for females, it was taken to be 0.69 for all ages.

To adjust for the non-coverage by sputum examination in approximately 14% of the eligible population, the culture-positive and smear-positive yields observed in subjects according to their radiographic abnormality were applied to those subjects without sputum specimens. The prevalence of bacillary disease among those not examined was estimated after the above adjustment of estimates of radiographic tuberculosis was applied among those who had no chest radiography.

RESULTS

Population surveyed

A total of 21,960 persons were surveyed from 21 rural and 15 urban clusters. Of these, 3,048 (13.9%) were from Metro Manila, 6,111 (27.8%) from other urban areas, and 12,801 (58.3%) from the rural areas. These were proportionate samples of the national population, which comprised 13.78% in Metro Manila, 28.95% in other urban areas, and 57.27% in rural areas. Males constituted 50.2% of the total population surveyed.

Approximately half of the total population was under 20 years of age, including 27.6% who were aged under 10 years. However, only 47.6% of the population surveyed in Metro Manila were aged under 20 years, compared to about 51% in other urban areas as well as in the rural areas. There were proportionately more individuals in the age-group 20-39 years in Metro Manila (35.1%) than in the other urban (27.9%) and rural (27%) areas. Conversely, proportionately less individuals aged 40 years and over were noted in Metro Manila (17.3%) than in the other urban (21%) or rural areas (22.3%).

Coverage of examinations done in the survey

Of the 15,905 (72.4%) subjects aged 10 years or older who were eligible for chest x-ray examination, 12,850 (81%) were x-rayed. Of these, 1,619 were considered to have abnormal chest radiography, and 1,390 (86%) had sputum specimens submitted for bacteriological examination during the cluster activities. To improve on the coverage of sputum collection, another attempt to collect sputum was made about 3-5 months after the fieldwork, and additional 151 patients submitted specimens. Thus, a total of 1,541 (95%) sputum specimens were eventually collected from the 1,619 individuals with abnormal chest x-rays. Only those collected from the first 1390 (86%) of the 1619 eligible individuals were analyzed, as the results of the last 151 individuals may not accurately reflect the situation during the

actual survey. However, data from the latter were used to validate the predicted numbers of smear-positive and culture-positive cases from among those not sampled in the general collection of specimens.

Observed prevalence of tuberculosis

Of the 1,619 subjects initially considered to have abnormal chest x-ray by the field readers, a total of 537 ($42/1,000 \pm 3.3$; 95% confidence interval [CI] 35-48) of the 12,850 individuals examined had radiographic findings suggestive of tuberculosis. This included minimal lesions in 442 ($34.4/1,000$) and moderate or advanced lesions in 91 ($7.1/1,000$), including 34 ($2.6/1,000$) with cavitation.

There was a positive correlation between the prevalence of radiographic abnormalities suggestive of pulmonary tuberculosis (PTB) and age. Those in the 10-19 year age group had the lowest prevalence ($6/1,000$) and those in the group aged 60-69 years had the highest prevalence ($122/1,000$). The preponderance of males ($53/1,000$) compared to females ($31/1,000$) was noted in all ages. When the two sexes were combined, the prevalence in the rural ($41/1,000$) and the urban ($42/1,000$) areas, however, was similar.

Bacillary disease was confirmed in 127 of 1,390 individuals studied among the 1,619 subjects who were eligible for sputum examination. These included 47 who had positive direct smears and 124 who had positive cultures; of these, three were smear-positive and culture-negative, 44 were both smear- and culture-positive, and 80 were smear-negative and culture-positive. The observed prevalence was $11.2/1,000 \pm 1.22$ (95% CI, 8.78-13.55) for culture-positive and $4.3/1,000 \pm 1.36$ (95% CI, 1.71-7.04) for smear-positive cases. When extrapolated to the entire population surveyed, assuming no sputum-positive cases occurred in children under 10 years of age, the culture-positive rate was $8.11/1,000 \pm 0.88$ (95% CI, 6.35-9.81) and the smear-positive rate was $3.1/1,000 \pm 0.99$ (95% CI, 1.24-5.10) population.

There was a higher prevalence of culture-positive tuberculosis in males compared to females (16.41 vs $6.37/1,000$, respectively). This was also observed for smear positive cases (6.49 vs $2.07/1,000$, respectively). When both sexes were combined, the prevalence of culture-positive and smear-positive cases was similar for the total urban (11.1 and $5.0/1,000$, respectively) compared to the rural area (11.4 and $3.8/1,000$, respectively). In the urban area, the rates in Metro Manila were lower ($7.4/1,000$ for culture-positive and $3.3/1,000$ for smear-positive cases) than in other urban areas (12.6 and $5.8/1,000$, respectively). There was no consistent association between age and the prevalence of bacteriologically confirmed tuberculosis. The highest prevalence in the total population was observed in the age group 40-49 years for both culture-positive and smear-positive cases ($20.65/1,000$ and $8.92/1,000$, respectively). The corresponding prevalence of pulmonary tuberculosis observed in the 1981-1983 nationwide survey is shown for comparison (Table 1).

Adjustment of prevalence rates for non-coverage

The adjusted prevalence of radiographic tuberculosis in the total population, after correcting for non-coverage in 19% of the population eligible for chest radiography, was $38/1,000 \pm 3.1$ (95% CI, 32-45) overall; it was $49/1,000$ for males compared to $29/1,000$ for females, assuming that the relative risk for tuberculosis was lower in those not examined by chest x-ray (Table 2). Assuming that the prevalence was the same among those examined and those who were not, the adjusted prevalence for radiographic changes suggestive of PTB was $42 \pm 3.3/1,000$ (95% CI, 35-48) overall - $53/1,000$ in males and $30/1,000$ in females.

The adjusted prevalence of radiographic tuberculosis in Metro Manila was $36/1,000$, in other urban areas it was $40/1,000$, and in combined urban areas it was $39/1,000$, compared to $38/1,000$ for the combined rural areas. Assuming equal risk in those not examined, it was similar in the total urban areas ($42/1,000$) and in the rural areas ($41/1,000$).

The predicted numbers of culture-positive and smear-positive cases in the 229 subjects who did not provide sputum specimens for examination were 12.5 and 3.1, respectively. These predicted numbers were subsequently validated by results obtained from sputum smear testing of specimens from 151 of the

229 subjects collected 3-5 months after the actual survey, from which six culture-positive and two smear-positive cases were observed; in the remaining 88 non-examined subjects, the expected numbers of culture-positive and smear-positive cases were 5.0 and 1.4, respectively. The sum of observed plus, expected smear-positive and culture-positive cases among those not examined would then be 11.0 and 3.4, respectively, compared to the 12.5 and 3.1 predicted. Accordingly, of the 1,619 subjects with a radiographic abnormality, the estimated total number of culture-positives was 136.5 (124 ± 12.5), and the estimated number of smear-positives was 50.1 (47 ± 3.1).

To correct for the non-coverage of approximately 19% of the population eligible for chest radiography, the adjusted prevalence rates were 9.8/1,000 culture-positive and 3.6/1,000 smear-positive cases. The adjusted prevalence of culture-positive cases was 6.4/1,000 and that of smear-positive cases 2.8/1,000 in Metro Manila, 10.6 and 4.8/1,000, respectively, in other urban areas, 9.0 and 4.1/1,000, respectively in the total urban area, and 10.1 and 3.4/1,000, respectively, in rural areas. The prevalence of culture-positive and smear-positive cases was 13.9 and 5.4/1,000, respectively, in males, and 5.8 and 1.9/1,000, respectively, in females. For the age group 10-29 years, it was 4.0 and 1.5/1,000, respectively, for those aged 30-49, it was 15.7 and 5.3/1,000, respectively; and for those 50 years and older, it was 16.5 and 7.1/1,000, respectively.

Table 1. Observed prevalence (per 1000) of pulmonary tuberculosis in the 1981-1983 and 1997 nationwide tuberculosis prevalence surveys, in subjects aged 10 years and over

	1981-1983				1997			
	No. eligible	Active PTB	Culture-positive TB	Smear-positive TB	No. eligible	Active PTB	Culture-positive TB	Smear-positive TB
Total Area	16,349	42	12.5	9.5	15,905	42	11.2	4.3
Urban	5,455	41	13.1	5.0	6,648	42	11.1	5.0
Rural	10,894	45	12.3	10.9	9,257	41	11.4	3.8
Sex								
Male	7,929	50	16.2	12.6	7,817	53	16.4	6.5
Female	8,420	35	9.3	6.9	8,080	31	6.4	2.1
Age (years)								
10-19	5,863	5	1.3	0.4	4,989	6	3.7	1.2
20-29	3,618	20	9.1	7.1	3,308	24	7.5	3.0
30-39	2,387	51	18.4	14.4	2,936	48	17.5	4.4
40-49	1,882	69	20.6	17.4	1,977	60	20.6	8.9
50-59	1,248	105	32.4	27.3	1,179	89	13.8	7.0
≥ 60	1,351	137	28.7	18.8	1,273	121	20.3	8.9

Table 2. Adjusted prevalence (per 1,000) of pulmonary tuberculosis in subjects aged 10 years and over, 1997

	Active PTB	Culture-positive TB	Smear-positive TB
Total	38-42	9.8	3.6
Area			
Metro Manila	36-40	6.4	2.8
Other urban	40-43	10.6	4.8
Total urban	39-42	9.0	4.1
Rural	38-41	10.1	3.4
Sex			
Male	49-53	13.9	5.4
Female	29-30	5.8	1.9
Age (years)			
10-29	12-13	4.0	1.5
30-49	48-53	15.7	5.3
≥ 50	100-103	16.5	7.1

Comparison between the 1997 and the 1981-1983 National Tuberculosis Prevalence Surveys

In comparing the 1997 and 1981-1983 surveys, methodological differences in the field work and laboratory techniques between the two surveys were taken into account. Chest radiography was performed using 10 x 14 inch films in the 1997 survey and a 70 mm photofluorogram in the 1981-1983 survey. While the rates of total radiographic abnormalities suggestive of pulmonary tuberculosis were identical in the two surveys (4.2/1,000), there was a 58% reduction in moderate or far advanced disease (7.1 vs 1.7/1,000) and a 48% reduction in cavitary disease (2.6 vs 4.7/1,000). Conversely, there was an increase of 39.6% in cases with minimal lesions.

There was not much difference in the prevalence of culture-positive cases: 8.1/1,000 in the 1997 NTPS vs 8.6/1,000 in the 1981-1983 NTPS. To allow for a meaningful comparison, the observed culture-positive and smear-positive rates in the 1997 NTPS were standardized using the frequency of observed radiographic abnormalities in the 1981-1983 population (Table 3). The expected number of positive cultures in 1981-1983 using the methods employed in the current survey should have been 185.5, which would exceed the actual observed yield of 156 in 1981-1983 by 1.2 (185.5/156) times. The difference in the expected and observed yields was statistically significant ($X^2 = 4.82$, $p < 0.05$).

Table 3. Comparison of prevalence rates (per 1,000) in the 1981-1983 and 1997 surveys in subjects aged 10 years and over

	1981-1983	1997
Radiologically active pulmonary tuberculosis	42	42
Bacillary disease		
Culture-positive		
Observed	12.5	11.2
Standardized	-	9.4
Extrapolated	8.6	8.1
Smear-positive		
Observed	9.5	4.3
Standardized	-	6.0
Extrapolated	6.6	3.1

Although the culture technique used was essentially the same, homogenization and centrifugation were probably more efficient in the 1997 NTPS. This being so, when comparing the two surveys, the observed culture-positive yield of 11.2/1,000 in 1997 should be adjusted by 0.84 times (156/185.5, i.e., 9.4/1,000), which should then be compared to the observed prevalence of 12.5/1,000 in the 1981-1983 survey. This would indicate a 25% reduction in the culture-positive case prevalence.

The smear-positive yield using the methods employed in the 1997 NTPS, on the other hand, was appreciably lower by a factor of 29% (84.0/119). The difference between expected and observed rates was also statistically significant ($X^2 = 16.84$, $p < 0.001$). This finding suggests an underestimation by acid-fast bacilli (AFB) smear on direct smears in the present survey. The prevalence of smear-positive patients in the 1997 NTPS was appreciably lower than in the 1981-1983 NTPS (3.1/1,000 vs 6.6/1,000). With standardization to correct for underestimation by adjusting the observed rate of 4.3/1,000 in persons 10 years or older by 1.4 times (119/84), the adjusted prevalence rate would be 6.0/1,000 in those 10 years or older. Compared to the 9.5/1,000 reported in 1981-1983, this would reflect a 37% reduction in smear-positive cases.

DISCUSSION

Since the first survey in 1981-1983, this has been the only systematic study undertaken nationwide to measure the magnitude of the problem of tuberculosis in the Philippines using standard epidemiological tools. The coverage attained with the various examinations in this survey was comparable to that of the 1981-1983 survey, and was deemed satisfactory. However the initial target of 85% coverage for chest radiography was not met, and the initial coverage in sputum collection was far

from ideal. To arrive at reasonable estimates of the prevalence of both bacillary disease and radiographic tuberculosis, a logical method of correcting the effect of this non-coverage was employed based on a judicious assessment of the characteristics of those not examined compared to those examined. Based on the finding that the prevalence of subjects with TB symptoms among those who were examined radiographically was significantly higher than in those who were not examined, the observed rates reported herein might actually be overestimates of the true prevalence if the total eligible population were examined.

All the parameters of disease were higher in males compared to females, but were essentially similar for urban and rural populations. The observed prevalence of bacillary tuberculosis of 8.1/1,000 population for culture-positive cases and 3.1/1,000 population for smear-positive cases implies that in a population of approximately 70 million Filipinos, there are approximately 200,000 to 500,000 people who are effectively infecting 10-20 persons each per annum. This translates to 2-10 million new cases of TB infection per year. As a result, the Philippines is reported as one of the top 22 countries that are cumulatively contributing 80% of estimated cases globally.¹⁰

After adjusting for technological differences between the present survey and that performed 15 years previously, the observed rates showed a minimal decline in bacillary disease. These findings are consistent with our observation that although the prevalence of radiographic findings suggestive of PTB was identical in the two surveys, there were more minimal lesions and fewer patients with moderate or far advanced and cavitary disease in the present survey. Consequently, there were more patients with low bacillary load in the present survey that could not be identified by a direct smear but from whom bacteria could still be isolated with the culture techniques applied.

Nevertheless, the reported parameters of tuberculous disease in this survey indicate that the morbidity due to tuberculosis has remained substantially high. From 1980-1996, there was a reported increase in the number of tuberculosis cases notified in the Philippines.¹⁰

As of 1996, the coverage of directly observed treatment, short course (DOTS) was only 2% of the population.¹⁰ Prior to that, in 1993, an evaluation of the National TB Control Program undertaken in four regions in the Philippines showed that there was no actual monitoring and supervision of patient treatment and response. Treatment of newly diagnosed cases was often delayed, and coverage was inadequate, primarily due to the inconstant supply of drugs.¹¹

More recently, improved cure rates, of from 60% to more than 80% of smear-positive cases, were reported from the World Health Organization-assisted pilot projects on DOTS in three provinces. As of February 1998, 8% of the Philippine population had access to DOTS, and 25% of the population by the end of 1998. It is planned that this will increase to 50% by 1999 and 100% by 2001.¹² It is anticipated that the prevalence of tuberculosis will decline with the implementation of DOTS similar to the progressive drop in the prevalence of tuberculosis and the number of tuberculosis cases notified in Korea in the period 1965-1995 as the coverage of DOTS among new cases increased, particularly in the past 15 years.^{10,13}

CONCLUSION

Morbidity from tuberculosis remains high in the Philippines. Compared to the first survey in 1981-1983, the decline in the prevalence of bacillary disease is minimal. Replicating the success of DOTS through its planned incremental implementation nationwide should greatly enhance the National TB Control Program of the Philippines.

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