The first national tuberculosis prevalence survey of Lao PDR (2010–2011)

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Summary

Objective The objective of the study was to measure the prevalence of bacteriologically confirmed pulmonary tuberculosis (TB) in Lao PDR in 2010–2011.

Method A nationwide, multistage cluster-sampled cross-sectional survey was undertaken in 2010–2011. All consenting participants ≥15 years were screened for pulmonary TB with chest X-ray and symptom questionnaire. Two sputum specimens for bacteriological examination by microscopy and culture were collected from those who screened positive. Prevalence was estimated using multiple imputation and inverse probability weighting methods.

Results Of 39 212 eligible participants from 50 clusters, 6290 participants provided at least one sputum sample for smear and culture. There were 237 bacteriologically confirmed pulmonary TB cases, 107 of which were smear-positive. Chest X-ray screening alone identified 230 (97.0%) cases compared with 118 (49.8%) by symptom screening alone. The estimated prevalence of smear-positive and bacteriologically confirmed TB in those ≥15 years was 278 per 100 000 (95%C.I. 199–356) and 595 per 100 000 (95%C.I. 457–733), respectively. Prevalence significantly increased with age and was higher in men than women.

Conclusions The prevalence of TB in Lao PDR is almost twice as high than previous estimates, with the greatest burden in the older population. Case detection efforts remain the primary goal of the national TB programme with case notifications being very low in comparison with the estimated number of prevalent cases. The survey observed major limitations with the diagnostic strategy of passive (symptom based) case finding that uses only direct smear microscopy for confirmation.

Keywords tuberculosis, prevalence survey, Laos, Asia, epidemiology

Introduction

Tuberculosis (TB) remains a major global health problem and is ranked as the second-most common cause of infectious disease-related deaths worldwide. In 2011, it was estimated that there were nine million new TB cases, 12 million prevalent cases (60% of which were in Asia alone) and 1.4 million TB deaths in 2011 [1]. Lao PDR is a landlocked country, and although not among the highest TB burden countries globally, it is geographically surrounded by them, that is Cambodia, China, Myanmar, Thailand and Vietnam. Lao PDR, with a population of 6.3 million (2011), is also one of the poorest countries in South East Asia, but has moved from being a lower- to a lower-middle-income economy with a gross national income of USD 1090 (2011) per capita [2]. Life expectancy at birth is 67 years, and the under-5 mortality rate is 42 per 1000 live births (2011).

The National TB Control Programme (NTP) was established in 1995, and as of 2011, the DOTS strategy had reached full country coverage in all 17 provinces, all 140 districts hospitals, and had reached 95% coverage of its 904 health centres. Whilst expanding coverage, the case notification rate (new and relapse) had rapidly increased from 42 per 100 000 in 2000 to 64 per 100 000 in 2005, but this has stagnated since 2006. Case detection rate remained at 32% (2011), and treatment success of new smear-positive TB cases has remained above 90% since 2005.

Based on these case notification data, WHO had estimated a decline in TB prevalence (all forms, all ages)
from 472 per 100 000 in 1990 to 289 per 100 000 in 2007 (reported in 2009). Thus, the country had met Millennium Development Goal 6 (MDG) and was still on track to meet the Stop TB Partnership target to halve prevalence of TB disease in 2015 compared to the 1990 level. However, given the challenges of TB surveillance in the country, it was assumed that the number of notifications was further underestimated especially given that TB diagnosis is currently based on passive case detection, that is the self-presentation of patients with respiratory symptoms to health facilities followed by confirmatory smear microscopy.

A tuberculin survey (1996–1997) was previously used to estimate the incidence of TB in Lao PDR, but it is now recognised that results from such surveys are difficult to interpret [3, 4]. Thus, given the challenges of estimating the true incidence of TB, prevalence could be assessed with a nationally representative cross-sectional survey as per recommended guidance [5]. The NTP conducted its first national TB prevalence survey in 2010–2011 to estimate the prevalence of bacteriologically confirmed TB and thus provide a more accurate baseline upon which future national and international investments in TB control can be measured against.

Methods
Survey design
A nationwide, population-based, cross-sectional survey based on multistage cluster sampling was undertaken between July 2010 and December 2011. A sample size of 40 000 people, ≥15 years, from 50 clusters was calculated based upon an estimated smear-positive pulmonary TB prevalence (≥15 years) of 251 per 100 000 (as reported by WHO in 2009) with a relative precision of 0.25, an expected participation rate of 80% and a design effect of 1.3. Approximately 800 people from each cluster were systematically chosen by sampling probability proportional to the size of the population ≥15 years (extrapolated from the 2005 census: Lao Statistics Bureau (LSB)) with selection sorted by provinces, districts and villages. If a selected village did not have the requisite 800 people, then the nearest neighbouring village was additionally selected to participate in the survey. Clusters were not selected based on geographical strata.

Survey procedures
Field operations, undertaken by three survey teams, took between 7–10 days per cluster. Each team conducted a household census of the cluster village(s) and invited all eligible people to the survey site. Only those ≥15 years who had lived in the household for at least 14 days immediately prior to the field operation were eligible to participate. Participants who provided informed written consent (and assent if <18 years) were interviewed with a structured questionnaire. Acknowledgement of either a cough for two weeks or more within the past month (chronic cough) and/or haemoptysis within the past month classified them as a participant who screened positive (PSP). All participants were invited to have a full-size conventional chest X-ray (CXR) in the field that was immediately read by a radiologist. If the CXR showed any abnormal lung field shadows, then the participant was also classified as a PSP irrespective of the questionnaire results. All PSPs were asked to provide a spot sputum specimen, and an early morning sputum specimen the following day. For quality assurance and case management purposes, all CXRs were re-read by independent senior radiologists from Mahosot Hospital, Vientiane.

Laboratory examinations
In addition to the national reference TB laboratory in Vientiane, two culture laboratories were established specifically for the survey in Luangnamtha and Savannakhet. The Centre d’Infectiologie Christophe Mérieux du Laos (CICML) in Vientiane supported the national TB laboratories by formally identifying Mycobacterium tuberculosis (MTB). Sputum specimens collected in the field were transported on ice in cool boxes to one of the three culture laboratories. Specimens were examined for smear and prepared for culture within three days of collection. Two direct smears with two sputum specimens per PSP were prepared, stained with carbol fuchsin by Ziehl–Neelsen method then followed by high-powered fields (1000x) microscopic examination. All slides positive for acid-fast bacilli (AFB) were cross-checked by a second microscopist for confirmation. Each specimen was decontaminated with 4% sodium hydroxide and inoculated onto two slopes of solid Kudoh-modified Ogawa medium without centrifugation [6]. Inoculated media were observed for up to eight weeks of incubation prior to being discarded as negative. Except for overt contamination, all visible colonies grown on culture media were confirmed for AFB by microscopy, and susceptibility testing to para-nitrobenzoic acid (PNB) (500 μg/ml) in Löwenstein–Jensen medium to identify Mycobacterium tuberculosis complex. All subcultures of mycobacteria were sent to the CICML for further identification of MTB and resistance to rifampicin and/or isoniazid using the GenoType® MTBDRplus (Hain Lifescience Gmbh, Germany) test.
Survey case definitions

A smear-positive pulmonary TB case was defined by the presence of either at least one positive smear plus a positive culture (definite case) or at least one positive smear plus a CXR consistent with TB (probable case). A smear-negative pulmonary TB case was defined by the presence of either two positive cultures (definite), only one positive culture with greater than four colonies plus a CXR consistent with TB (definite), only one positive culture with greater than four colonies (probable) or only one positive culture less than five colonies plus a CXR consistent with TB (probable). A bacteriologically confirmed TB case was defined as an individual with either smear-positive or smear-negative, culture-positive pulmonary TB. A new case was defined as a participant who had never had treatment for TB. Final classification of every participant with any positive laboratory results was done by a panel of experts from WHO, Korean Institute of Tuberculosis and Soutien Pneumologue International.

Data entry and analysis

Single entry of all data occurred in Filemaker Pro (v11, Filemaker Inc., Santa Clara, USA). All identifier fields, that is name, age and survey identification number, and all positive results (i.e. any positive symptom, abnormal CXR and positive laboratory results) in the database were visually re-checked with the corresponding forms and registries. Data were analysed using two best practice methods to estimate both smear-positive TB and bacteriologically confirmed TB prevalence [7]. A complete-case analysis without weighting using robust standard errors to account for cluster sample survey design was initially undertaken, and the final prevalence estimates were derived from individual-level analyses that utilised robust standard errors with multiple imputation for missing values and inverse probability weighting. Analyses were undertaken using Stata (v12.1, Stata Corporation, USA). Analyses were as per protocol; that is, people who were screened but not eligible to participate, or those who submitted specimens but were not eligible were excluded from the final analyses. Smear-positive TB prevalence divided by smear-positive TB notification rates (2011) was used to estimate the ratio of prevalence to notification (P:N); the propagation of uncertainty for the ratio used the variance of the prevalence estimate and assumed notification rate as constant. Between-group comparisons utilised the test of proportions. Trend analysis for proportions utilised Royston’s method when comparing proportions across age groups.

Ethical approval

In addition to the National Ethics Committee of Health Research in Lao PDR, the protocol was also reviewed and approved by the WHO Global Task Force on TB Impact Measurement and the Korean Institute of Tuberculosis.

Results

Survey population

A total of 78,819 individuals were enumerated in the survey census (Figure 1), of whom 46,079 were eligible and invited to participate. The median number of eligible individuals across all 50 clusters was 865 (range: 784–1743). Of those eligible, 39,212 (85.1%) participated in the survey. The median number of participants across all 50 clusters was 799 (range: 693–822). The median age of participants was 36 years (IQR: 24,50). Participation was significantly higher among females than among males (87.8% vs. 82.1%, p < 0.05), and higher in rural compared with urban clusters (90.0% vs. 79.7%, p < 0.05). Participation was lowest in the younger age groups, especially males; however, overall participation was higher than expected (85.1%). The survey eligible population was similar to the national population structure by age group and sex, except for those in the 15–24 year age group whereby 4–5% less men and women were eligible to participate than anticipated.

Screening outcomes and sputum submission

All 39,212 participants were interviewed for symptom screening, but results were only available for 39,100 (99.7%). A total of 39,163 (99.9%) participants were screened by CXR, and 39,051 of them had both interview and CXR results available. The proportion of PSP increased with age, was higher in men than women and rural than urban participants (Table 1). Of the 6346 (16.2%) PSPs, 1927 (30.4%) were eligible by symptoms only, 3107 (49.0%) were eligible by CXR only, and 1312 (20.7%) were eligible by both. Of these, 6290 (99.1%) submitted at least one sputum sample, and 6253 (98.5%) submitted two specimens. Smear and culture results were available for all those who submitted a sample.

Study cases

Of 237 (3.8%) bacteriologically confirmed TB cases, 107 were smear-positive and 130 were smear-negative. The median age of all cases was 55 years (IQR: 40–68), with
Individuals enumerated in census: 78,819

Eligible study population: 46,079 (58.5%)

Participants: 39,212 (85.1%)

Ineligible individuals:
- 21,517 (27.3%) Children
- 11,223 (14.2%) Non-resident adults

Non-attendees: 6,867 (14.9%)
- Males 3,875 (17.9% of all eligible males)
- Females 2,992 (12.2% of all eligible females)

Eligible study population:
- 46,079 (58.5%)
- Participants 39,212 (85.1%)

Participants who had symptom screening: 39,212 (100%)
Participants who had CXR screening: 39,100 (99.7%)
Screened using both symptom and CXR: 39,051 (99.6%)

Eligible for sputum examination: 6,346 (16.2%)
- Eligible by both symptom and CXR screening: 13,12 (20.7%)
- Eligible by symptom screening only: 19,27 (30.4%)
- Eligible by CXR screening only: 3,107 (49.0%)

Submitted spot and morning specimens: 6,253 (98.5%)
Submitted a spot but not a morning specimen: 37 (0.6%)

2 smear and 2 culture results available: 6,253 (100%)
1 smear (spot) and 1 culture (spot) results available: 37 (100%)

Any smear-positive: 186
- Smear-positive culture result:
  - MTB: 94
  - Negative: 62
  - NTM: 30
  - Contaminated: 0

Any smear-negative: 6,104
- Smear-negative culture result:
  - MTB: 132
  - Negative: 4,519
  - NTM: 1,414
  - Contaminated: 39

Smear-positive TB cases: 107
- Definite TB cases: 94
- Probable TB cases: 13

Smear-negative TB cases: 130
- Definite TB cases: 101
- Probable TB cases: 29

Central Panel
Total TB survey cases: 237

Figure 1 Data flow of the national TB survey.
men accounting for 157 (66%) of them. CXR alone identified 230 (97.0%) bacteriologically confirmed TB cases with a corresponding sensitivity, specificity and positive predictive value (PPV) of 97.1%, 88.7% and 5.0%, respectively (Table 2). By comparison, symptom screening alone identified 118 (49.8%) of cases with a corresponding sensitivity, specificity and PPV of 49.8%, 92.0% and 3.6%, respectively. However, symptom screening alone would still identify 71 (66.4%) of all smear-positive cases.

Of the bacteriologically confirmed TB cases, 9 (3.8%) had a past history of anti-TB treatment only, 1 (0.4%) person was currently on treatment only, and 5 (2.1%) had both past and current anti-TB treatment histories. 74 (63%) of 118 symptomatic TB cases initially sought health care before being diagnosed with TB (public health facility: 44 (37.3%); private health facility: 3 (2.5%); pharmacy 13 (11.0%); village health volunteer 4 (3.4%); unknown facility: 10 (8.5%)).

**Prevalence**

The estimated prevalence using complete-case analysis without weighting was very similar to the method using multiple imputation and inverse probability weighting (Table 3). Given that all who submitted sputum samples

| Table 1 Screening outcomes for participants by sex, age and strata† |
|---------------------------------|----------------|----------------|----------------|----------------|
| Category                       | No. with symptom screening and/or CXR results | Symptom eligible only | % | CXR eligible only | % | Symptom and CXR eligible | % |
| National                       | 39 212 | 1927 | 4.9 | 3107 | 7.9 | 1312 | 3.4 |
| Sex                            |       |     |     |      |      |      |     |
| Male                           | 17 738 | 1010 | 5.7 | 1748 | 9.9 | 760 | 4.3 |
| Female                         | 21 474 | 917  | 4.3 | 1359 | 6.3 | 552 | 2.6 |
| Age (years)                    |       |     |     |      |      |      |     |
| 15–24                          | 9879  | 315  | 3.2 | 265  | 2.7 | 48  | 0.5 |
| 25–34                          | 8491  | 291  | 3.4 | 343  | 4.1 | 96  | 1.1 |
| 35–44                          | 7566  | 390  | 5.2 | 497  | 6.6 | 135 | 1.8 |
| 45–54                          | 6171  | 371  | 6.0 | 631  | 10.2 | 236 | 3.8 |
| 55–64                          | 3869  | 307  | 8.0 | 647  | 16.7 | 319 | 8.3 |
| 65+                            | 3236  | 253  | 7.9 | 724  | 22.4 | 478 | 14.8 |
| Strata                         |       |     |     |      |      |      |     |
| Urban                          | 10 209 | 391  | 3.8 | 863  | 8.5 | 249 | 2.5 |
| Rural                          | 29 003 | 1536 | 5.3 | 2244 | 7.7 | 1063 | 3.7 |

†Forty-nine participants had a questionnaire but no available chest X-ray (CXR) results, and 112 participants had a CXR but no available questionnaire results. Therefore the denominators used in this table are as follows: symptom eligible only, N = 39 100; CXR eligible only, N = 39 163; symptom and CXR eligible, N = 39 051.

| Table 2 Survey cases by screening outcome |
|------------------------------------------|----------------|----------------|----------------|----------------|
| Symptom result                           | CXR result     | No. of participants who submitted at least one sputum sample | No. of participants with smear-positive sputum | % | No. of participants who are S+C+ (MTB) | % | No. of participants who are S-C+ (MTB) | % | No. of participants who are B+ MTB | % |
| Eligible Not eligible                     | 1885 | 27 | 1.4 | 3 | 0.2 | 4 | 0.2 | 7 | 0.4 |
| Eligible Eligible                        | 1312 | 82 | 6.3 | 68 | 5.2 | 43 | 3.3 | 111 | 8.5 |
| Not eligible Eligible                    | 3085 | 77 | 2.5 | 36 | 1.2 | 83 | 2.7 | 119 | 3.9 |
| Others† Others†                          | 8 | 0 | – | 0 | – | 0 | – | – | – |
| Total                                     | 6290 | 186 | 3 | 107 | 1.7 | 130 | 2.1 | 237 | 3.8 |

S+, smear-positive; C+, culture-positive; B, bacteriologically confirmed; CXR, chest X-ray.

†Others include those who had either symptom or chest X-ray data only.
had available laboratory results, the larger differences in bacteriologically confirmed prevalence between the two methods are a reflection of the proportion of non-attendees who were predominantly males, those in the 25–34 year age group and living within urban strata. The prevalence of smear-positive pulmonary TB in those ≥15 years was estimated at 278 per 100 000 (95% C.I. 199–417), whereby bacteriologically confirmed pulmonary TB prevalence for the same age group was estimated at 595 per 100 000 (95% C.I. 457–733).

Prevalence was higher in men than in women, increased with age and was higher in rural than urban clusters. Of note, the estimated bacteriologically confirmed TB prevalence was more than 1% in those aged ≥55 years. The bacteriologically confirmed TB prevalence by cluster was variable; whilst five clusters had a prevalence of zero, nine clusters, all in rural areas, had a prevalence of more than 1% (Figure 2). The ratio of prevalence (smear-positive TB survey cases) to notification (new smear-positive cases ≥15 years) in 2011 was 3.6 (95% C.I. 2.6–4.5) (Table 4). This ratio was higher in men than in women, and highest in those <35 years followed by those ≥65 years, and lowest in 55–64 year age group.

### Table 3 Prevalence of smear-positive and bacteriologically-confirmed pulmonary TB among population aged >15 years

| Category | Number of participants | Number of TB cases | Method 1: Prevalence (95% C.I.) | Method 2: Prevalence (95% C.I.) | Number of TB cases | Number of smear-positive cases | Method 1: Prevalence (95% C.I.) | Method 2: Prevalence (95% C.I.) |
|----------|------------------------|--------------------|---------------------------------|---------------------------------|--------------------|------------------------------|---------------------------------|---------------------------------|
| National Sex |                        |                    |                                 |                                 |                    |                              |                                 |                                 |
| Male     | 17 738                 | 75                 | 424 (303–546)                  | 420 (299–576)                   | 157                | 889 (671–1107)               | 855 (646–1064)                  |                                 |
| Female   | 21 474                 | 32                 | 150 (88–211)                   | 152 (88–302)                    | 80                 | 142 (134–185)                | 145 (120–164)                   |                                 |
| Age (years) |                        |                    |                                 |                                 |                    |                              |                                 |                                 |
| 15–24    | 9879                   | 8                  | 81 (15–148)                    | 80 (11–134)                     | 14                 | 142 (46–238)                 | 145 (41–249)                    |                                 |
| 25–34    | 8491                   | 12                 | 142 (33–250)                   | 184 (16–174)                    | 22                 | 260 (134–385)                | 292 (120–464)                   |                                 |
| 35–44    | 7566                   | 15                 | 199 (100–298)                  | 201 (98–409)                    | 37                 | 491 (317–664)                | 484 (307–661)                   |                                 |
| 45–54    | 6171                   | 25                 | 406 (235–577)                  | 412 (234–470)                   | 44                 | 714 (467–961)                | 714 (461–968)                   |                                 |
| 55–64    | 3869                   | 19                 | 493 (284–701)                  | 513 (279–973)                   | 43                 | 1116 (696–1536)              | 1131 (704–1557)                 |                                 |
| 65+      | 3236                   | 28                 | 871 (525–1217)                 | 866 (503–2110)                  | 77                 | 2409 (1672–3147)             | 2410 (1665–3156)                |                                 |
| Strata   |                        |                    |                                 |                                 |                    |                              |                                 |                                 |
| Urban    | 10 209                 | 23                 | 226 (117–336)                  | 264 (130–510)                   | 42                 | 412 (295–530)                | 436 (307–565)                   |                                 |
| Rural    | 29 003                 | 84                 | 291 (195–386)                  | 283 (186–259)                   | 195                | 674 (494–855)                | 663 (477–848)                   |                                 |

†Complete-case analysis without weighting using robust standard errors to account for cluster sample survey design. Prevalence is per 100 000 population.
‡Robust standard errors with multiple imputation and inverse probability weighting. Imputation utilised the ice Stata commands with the following potential predictive variables: age group 15–24, age group 25–34, age group 35–44, age group 45–54, age group 55–64, female sex, rural stratum, field chest X-ray result, presence of cough for two weeks or more, and current anti-TB treatment. For imputation analyses for S+C+ estimates, presence of cough for two weeks or more was replaced with current cough as a variable. For imputation analyses for S-C+ estimates, current anti-TB treatment was not used as a variable. The design effect was 2.18 and 3.15 for smear-positive and bacteriologically confirmed prevalence estimates respectively. The between-cluster variation (k) was 0.74 and 0.68 for smear-positive and bacteriologically confirmed prevalence estimates respectively. Prevalence is per 100 000 population.

![Figure 2](image_url) Prevalence of bacteriologically confirmed pulmonary TB.

### Discussion

The first national TB prevalence survey in Lao PDR identified a high prevalence of smear and bacteriologically confirmed pulmonary TB in those ≥15 years during 2010–2011. Based on these results, WHO re-estimated...
the prevalence of TB (all ages, all forms) in 2011 to be 540 (95% CI 353–767) per 100 000 [8]. This estimate was almost twice as high as the previous WHO estimate in 2007 (289 per 100 000) that was used in the initial sampling design for the survey. The re-estimated prevalence was 64% that of the revised 1990 estimate, thus implying that the country had already met the MDG related to TB and Stop TB Partnership targets. The revised increase in prevalence is similar to those that occurred following recent prevalence surveys in the neighbouring countries of Cambodia, Myanmar and Vietnam [9–11]. It is not known as to what factors, and their attributable contribution, led to the overall decline in TB prevalence in Lao PDR from 1990 to 2011, but country-wide DOTS expansion and free anti-TB medication are likely to play a part. Unlike surveys before DOTS expansion in the Philippines (1997) and China (2000) where a large proportion of detected prevalent cases were under treatment, it is therefore of note that this survey identified only six (2.5%) TB cases who were currently under treatment, and 14 (5.9%) who had been previously treated [12, 13]. High-quality treatment and management may account for this. Furthermore, consistent growth of gross domestic product by more than 6% over the past decade with gradual improvement in socio-economic conditions are likely contributors to an overall decline in prevalence as well [2].

The survey noted that TB prevalence significantly increased with age. It is estimated that the prevalence in those ≥65 years was as much as ten-fold higher than those less than 25 years of age. This is a similar pattern observed in other South East Asia countries where there is also a shifting of the TB burden into the older age groups as TB control improves and transmission of infection decreases [14–16]. Furthermore, given the social constructs in Asia, the added risk of transmission will be to children who live with and are being cared for by older family members. The prevalence of chronic cough and haemoptysis also rises with age—in men more so than women. The chronicity of such symptoms in older people may suggest a lower recognition of TB disease and thus reluctance to seek care, which are intimately linked to health services that may not meet the needs of this population.

In an efficient and well-functioning TB surveillance system, it is expected that TB notifications from the NTP would be similar to TB prevalence. However, this gap (as defined by the P:N ratio) is discernibly large, and likely due to an underdiagnosis of TB cases, which is consistent with a case detection rate of 32% (2011). The higher P:N ratios in men and in those <35 and ≥65 years of age suggests a combination of lower case detection and/or disease recognition in these subgroups. Specifically, in the older population, this gap could also be explained by the chronic nature of disease and thus a longer duration of illness. Endogenous TB re-activation in the older population, as oppose to new infections in the younger population, will most likely make a greater contribution to TB burden as the population ages and as overall transmission decreases. Targeted age- and sex-specific case detection efforts could be strategies that the NTP utilises to detect these ‘missed’ TB cases. Given that the private health sector in Lao PDR plays a minimal role in TB diagnosis and management, it is unlikely that these subgroups are being diagnosed but not reported to the NTP in this sector. Nonetheless, inventory studies will assist in quantifying the true level of under-reporting.

The ability to diagnose new TB cases using the current national TB strategy of passive case detection and use of only smear microscopy has its limitations. The survey suggested that through active case finding, nearly half of culture-confirmed MTB cases did not acknowledge TB symptoms to begin with and were thus only discovered through CXR examination. Furthermore, of those culture-confirmed cases with TB symptoms, only 30% were sputum smear positive; that is, the ones that would have most likely been detected by routine practice. Without culture, smear microscopy would have been hampered by its inability to discriminate MTB from non-tuberculous mycobacteria (NTM). As shown in the survey, nearly half of the smear-positive results were either culture negative (62/186, 33%) or culture positive for NTM (30/186, 16%).

The diagnostic challenge is further exemplified by the contribution of smear-negative disease to the overall TB burden especially with increasing age. The gap between the rate of smear-positive cases and bacteriologically confirmed cases highlights this case. Smear-negative TB is
known to be more common in settings with HIV epidemics. However, given the low-HIV rate in Lao PDR, there is also a tendency to see more smear-negative disease in the older population, especially as the overall population in Lao PDR is ageing, thus lowering the possibility of diagnosing TB based purely on microscopy especially in these age groups. The clinical recognition of TB disease should also be reviewed, especially given that almost two-thirds of TB cases identified through the survey had initially sought care. This further illustrates that the current diagnostic processes, that is smear microscopy, clinical and radiological examinations, subsequent review and referral mechanisms, need to be closely examined with a view to increasing the sensitivity of case detection. Much like other prevalence surveys, CXR was a more sensitive screening tool than symptom screening in identifying bacteriologically confirmed TB cases [17]. This adds to the body of evidence that suggests that CXR can be important for the early identification of cases via active screening methods. However in Lao PDR, there is still a great opportunity to detect more symptomatic smear-positive cases in the community by improving the efficiency of the current diagnostic strategy. From the survey, the prevalence of smear-positive TB with chronic cough was estimated to be 185 per 100 000, whereas the annual notification rate (2011: all ages, all forms) was 68 per 100 000. Although this difference is as much a function of health seeking behaviour as it is to access, clinical management and diagnostic service delivery, it highlights the potential opportunity to identify more symptomatic smear-positive cases. Much like in Cambodia and China, the efficient implementation of the current passive case finding strategy along with DOTS decentralisation, community DOTS and strengthened case finding of smear-negative TB could effectively reduce the number of these symptomatic cases over time [13, 15].

Due to the following limitations, the population-based prevalence estimates are likely to be conservative. Firstly, the survey was not designed to identify TB in those less than 15 years of age or those with extrapulmonary TB. Secondly, as the survey was cross-sectional in design, the screening tools would only identify those with signs and/or symptoms at one point in time; therefore, other participants may have developed disease throughout the year that were not initially detected during the survey. Furthermore, many of those who denied symptoms at the time of screening may have been screened positive by CXR during the early stage of disease and therefore may only develop symptoms and become smear-positive as their disease progressed. Thirdly, the central level radiologists identified 460 false-negative CXRs. The delay in reading them and the required logistical challenges prevented the possibility of collecting specimens from these misclassified participants. However, upon review of all these CXRs, none had TB shadows with cavities; therefore, it was unlikely that any smear-positive cases were missed. Fourthly, most of the non-participants were young men, but despite the greatest TB burden being in older men, and assuming that younger men were fitter and healthier, then their overall contribution to the burden is likely to be low. Finally, the possibility of over-decontamination and the degradation of specimens during transportation may have underestimated the true number of bacteriologically confirmed cases.

In conclusion, the first national TB prevalence survey of Lao PDR was successfully undertaken and provided evidence for a higher than previously estimated prevalence of disease. The demographic distribution follows a similar pattern found in other countries in the region and reflects the TB epidemiology that is progressing through a transitional phase of overall country development. CXR screening alone identified more bacteriologically confirmed TB cases than by symptom screening alone in a high TB burden low-HIV setting. These data could inform the appropriate screening algorithm for any future case finding strategy; however, the cost-effectiveness of such needs to be further examined. The survey acknowledges the limitations of current case detection efforts, along with the screening and diagnostic methods by which it does so. In the light of limited infrastructure, skilled human and financial resources, focussed case detection efforts should be the immediate priority for the national TB programme of Lao PDR.

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