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National tuberculosis prevalence surveys in Asia, 1990–2012: an overview of results and lessons learned

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Abstract

OBJECTIVE AND METHODS In many countries, national tuberculosis (TB) prevalence surveys are the only way to reliably measure the burden of TB disease and monitor trends. They can also provide evidence about the current performance of TB care and control and how this could be improved. We developed an inventory of Asian surveys from 1953 to 2012 and then compiled and analysed a standard set of data for all national surveys implemented between 1990 (the baseline year for 2015 global TB targets) and 2012.

RESULTS There were 21 surveys in 12 countries between 1990 and 2012; published results were available for 18. The participation rate was at least 80% and often much higher except for two surveys in Thailand. The prevalence of bacteriologically-positive TB disease among adults aged ≥15 years varied widely among countries (1.2 per 1000 population in China in 2010 to 15 per 1000 population in Cambodia in 2002), but age and sex distribution patterns were consistent with a progressive increase in rates of disease by age, and men accounting for 66–75% of prevalent cases. A high proportion of cases (40–79% across all surveys) did not report TB symptoms that met screening criteria (generally cough of 2–3 weeks or more, and blood in the sputum) and were only detected due to chest X-ray screening of all survey participants; this proportion increased over time in countries with repeat survey data. The ratio of prevalent cases to cases notified to national TB programmes was typically around two, but was as high as three in Lao PDR and Pakistan even after the internationally recommended TB control strategy had been implemented nationwide for several years. Four countries (China, Cambodia, the Republic of Korea and the Philippines demonstrated declines in smear or culture-positive pulmonary TB prevalence of approximately 50% over 10 years.

CONCLUSIONS National TB prevalence surveys in Asia show that large reductions in the prevalence of TB disease can be achieved within a decade, that men bear much more of the burden than women and that the epidemic is ageing. Comparisons among countries show that more can be achieved in TB control in some countries with existing strategies and technologies. However, with many prevalent cases not reporting classic TB symptoms, all countries face the challenge of defining and implementing strategies that will result in earlier detection and treatment of cases.

keywords tuberculosis, prevalence survey, Asia, epidemiology, public health

Introduction

Measuring the burden of tuberculosis (TB) and monitoring time trends are critical for planning TB control interventions, assessing their impact on population health and for evaluation of whether global targets for reductions in disease burden are achieved. Current global targets are set for 2015: the target in the Millennium Development Goals (MDGs) is that TB incidence should be falling by 2015; the Stop TB Partnership targets set within the context of the MDGs are to halve TB prevalence and death rates by 2015 compared with 1990.

Ideally, nationwide disease surveillance systems should provide direct measurements of the number of TB cases and deaths from TB. However, most countries with a high TB burden do not yet have notification systems that capture all cases. In particular, cases diagnosed in the private sector may not be reported, and health systems in many countries lack the reach and quality required to ensure that all (or virtually all) cases are diagnosed. This includes most, if not all, of the 22 high TB burden countries that account for about 80% of the world's estimated cases. Vital registration systems with sufficient coverage and quality to allow direct measurement of TB mortality exist in 124 of WHO's 194 member states, but most of these are in Europe and Latin America (China, which ranks second globally in terms of numbers of TB cases, is a notable exception).

Given these gaps in routine surveillance, the only way to obtain an unbiased estimate of the burden of TB disease in many TB-endemic countries, and to monitor trends, is to conduct population-based national surveys of the prevalence of TB disease. Such surveys can also be used to better understand TB epidemiology (e.g. the distribution of disease by age, sex and geographical variation), to produce more precise estimates of TB incidence, to understand why people with TB disease have not been diagnosed by health providers and notified to national TB control programmes (NTPs) and to make associated changes to policies and strategies for TB care and control. When repeat surveys are implemented with intervals of approximately 10 years, trends can be assessed. Nonetheless, nationwide TB prevalence surveys are large studies that are expensive and logistically challenging to implement. In 2007, the WHO Global Task Force on TB Impact Measurement (hereafter the Task Force) developed a set of criteria to identify countries where surveys would be justified. These criteria are described in detail elsewhere [63]. A total of 53 countries met the criteria and from these a set of 22 global focus countries that would receive priority attention and support from the Task Force and partners were selected. A total of 20 national surveys will be implemented between 2009 and 2015, including in 15/22 global focus countries.

In the 1990s and 2000s, most surveys were implemented in Asia. This study provides a historical listing of national TB prevalence surveys completed between 1953 and 2012 and synthesises the major results and lessons learned from surveys completed between 1990 and 2012.

Methods

Identification of surveys conducted in Asia (1953–2012)

All national TB disease prevalence surveys conducted in Asia since the 1950s were identified using information previously compiled by WHO (for surveys conducted up to 2008, PubMed was searched using the terms: 'tuberculosis', 'prevalence' and 'surveys'), documents with regular updates on TB prevalence surveys produced by the Task Force since 2008 [64] and discussions with NTPs during WHO regional meetings in Asia. A total of 49 national TB prevalence surveys conducted in 16 Asian countries between 1953 and 2012 were identified (Table 1). For the purposes of maintaining relevance to current efforts in TB care and control, and given that 1990 is the baseline year for 2015 global TB targets, we focused our attention on surveys conducted between 1990 and 2012.

Standard variables used to summarise survey results

Key characteristics of survey design, implementation, analysis and reporting (for example, the eligible population, the target sample size and number of clusters, screening strategy, laboratory tests performed and statistical methods used to analyse data) and a standard set of results (variables defined in Box 1) were summarised for 18 of the 21 surveys conducted in 1990–2012. The three surveys that were excluded were Malaysia (2003), as uptake of facility-based chest X-ray screening was low and results have not been published; Thailand (2006), due to low coverage of specimen collection among those considered eligible for sputum examination by chest X-ray screening; and Indonesia (2010), because the survey was implemented as part of a general health survey that did not include either TB screening or systematic use of culture examinations. Trend data were summarised for four countries that had repeat survey data since 1990 and comparable survey methods: Cambodia, China, Republic of Korea and the Philippines.

Box 1 Standard variables used to summarise survey results

The variables used to summarise results from the 18 surveys for which results have been published in reports or papers were as follows:

- the size of the eligible population;
- the number of people who participated in survey operations and associated participation rate;
- the absolute number of smear-positive and bacteriologically-positive cases that were identified (overall and disaggregated by sex and age group);
- the prevalence rate for smear-positive and bacteriologically-positive TB, per 1000 population (overall and disaggregated by sex and age group);
- the sex ratio (male to female) of prevalence;
- the proportion of smear-positive and bacteriologically-positive cases that did not report TB symptoms that met NTP screening criteria;
- the prevalence to notification (P:N) ratio for smear-positive TB;
- drug susceptibility test results;
- healthcare-seeking behaviour among TB cases that reported symptoms;
- place of treatment for individuals on TB treatment at the time of the survey.

Table 1 National TB Prevalence surveys in Asia – historical listings and upcoming surveys planned to commence in 2015 or 2016

National surveys	Number of surveys	Year	References
Bangladesh	4	1964	Ministry of Health – Bangladesh [17]
		1987	Ministry of Health – Bangladesh [18]
		2007–09	Zaman K *et al*. [68]
		2015*	–
Cambodia	2	2002	Ministry of Health – Cambodia [19]
		2011	Mao *et al*. [16]
China	5	1979	Ministry of Public Health – China [37]
		1984	Ministry of Public Health – China [38]
		1990	Ministry of Public Health – China [39]
		2000	Ministry of Public Health – China [40]
		2010	Wang *et al*. [59]
Taiwan, China	4	1958–59	Quo 1959 [46], Lin *et al*. [15]
		1962–63	Lin *et al*. [15]
		1967–68	Lin *et al*. [15]
		1972–73	Lin *et al*. [15]
DPR Korea	1	2016*	–
Indonesia	4	1979–82	Aditama [1]
		2004	Ministry of Health – Indonesia [21], Soemantri *et al*. [48]
		2010	Ministry of Health – Indonesia [22]
		2013–14	To be published
Japan	5	1953	Yamaguchi [67], Omura *et al*. [45]
		1958	Ministry of Health and Welfare – Japan [36], Omura *et al*. [45]
		1963	Wakamatsu [58]
		1968	Muranaka [41]
		1973	Shimao [47]
Lao PDR	1	2010–11	Ministry of Health – Lao PDR [23]
Malaysia	2	1970	Chia and Huang [3]
		2003	Dye [8]
Mongolia	1	2014–15*	–
Myanmar	3	1972	Thein Nyunt *et al*. [51]
		1994	Ministry of Health – Myanmar [24]
		2009–10	Ministry of Health – Myanmar [25]
Nepal	1	2015*	–
Pakistan	3	1959	Dolin [6]
		1987	Dolin [6]
		2011	National TB control programme – Pakistan [43]
Philippines	3	1981	National Institute of Tuberculosis – Philippines [42], Department of Health – Philippines [5]
		1997	Tropical Disease Foundation Inc and Department of Health [53], Tupasi *et al*. [56], Tupasi *et al*. [57]
		2007	Tropical Disease Foundation Inc and Department of Health [54], Tupasi *et al*. [55]
		2015*	–
Republic of Korea	7	1965	Ministry of Health & Social Affairs and the Korean National Tuberculosis Association [29]
		1970	Ministry of Health & Social Affairs and the Korean National Tuberculosis Association [30]
		1975	Ministry of Health & Social Affairs and the Korean National Tuberculosis Association [31]
		1980	Ministry of Health & Social Affairs and the Korean National Tuberculosis Association [32]
		1985	Ministry of Health & Social Affairs and the Korean National Tuberculosis Association [33]

Table 1 (*Continued*)

National surveys	Number of surveys	Year	References
		1990	Ministry of Health & Social Affairs and the Korean National Tuberculosis Association, Hong *et al.* [13, 34]
		1995	Ministry of Health & Social Affairs and the Korean National Tuberculosis Association [35], Hong *et al.* [14]
Singapore	1	1975	Ministry of Health – Singapore [26]
Thailand	5	1960–64	Sunakorn [50]
		1977	Daramas *et al.* [4]
		1991–1992	Sriyabhaya *et al.* [49], Ministry of Health – Thailand [27]
		2006	Not published
		2012	Ministry of Health – Thailand [28]
Sri Lanka	1	1970	WHO [61]
Viet Nam	1	2006–7	Hoa *et al.* [10], Hoa *et al.* [11]
		2016*	–

*Survey planned to commence in 2015 or 2016.

Data sources and statistical analysis

The main sources of data were survey reports and articles published in peer-reviewed journals. In a few instances where these did not include the required information, data were obtained directly from lead survey investigators. When the coefficient of variation (k) of the cluster-specific TB prevalences was not reported, it was derived from the design effect (DEFF) or the confidence interval of the overall TB prevalence in surveys where the DEFF was not known [52, 63]. 95% confidence intervals for the proportion of isolates detected as MDR-TB were derived using the exact binomial approach, using the number of cases found with MDR-TB strains out of the total number of prevalent cases tested for drug susceptibility and assuming that missing data (prevalent cases not tested for drug susceptibility) were missing completely at random. The prevalence: notification (P:N) ratio was calculated as the smear-positive TB prevalence measured in the survey divided by the notification rate for smear-positive TB among those aged ≥15 years in the main year of the survey. Notification rates were calculated using notification data reported to WHO and United Nations population estimates (2012 revision) for the main year of the survey. The P:N ratio for bacteriologically-positive TB could not be calculated because notification data for smear- and culture-positive TB combined were not routinely compiled by most NTPs prior to 2014.

We did not conduct any meta-analyses to provide summary results across all surveys, as our objective in this study was rather to provide a comprehensive summary of the results from individual surveys and a synthesis of the lessons learned based on common findings in multiple surveys. However, meta-analyses using the data presented in this study (e.g. on male:female ratios or the age distribution of cases) could be the subject of future publications.

Ethical approval

All 18 prevalence surveys used in the final analysis were approved by in-country ethics committees. For surveys implemented since 2009, protocols were also reviewed by the WHO Global Task Force on TB Impact Measurement, including to ensure that ethical issues were appropriately addressed.

Results

Main survey characteristics

The main characteristics of the 18 surveys for which detailed results were available are shown in Table 2 (see Table S1 for a fuller summary).

The number of participants enrolled varied widely from 12 850 (the Philippines, 1997) to 1 461 190 (China, 1990) people, but was usually in the range 20 000–65 000 from 40 to 95 clusters. Surveys with a planned sample size of over 100 000 people were restricted to China, Pakistan and Viet Nam, and the number of clusters only exceeded 100 in China, Indonesia, the Republic of Korea and Thailand (1991 only). Most surveys used stratified sampling; urban (and/or the capital) and rural (and/or remote) were the most common strata used. Nine of the surveys were restricted to those aged ≥15 years (all surveys since 2009), five were restricted to those aged ≥10 years, two surveys in the

Table 2 Surveys in Asia 1990–2012 and their main characteristics

Country	Main year	Age of eligibility (Years unless specified)	Planned sample size/participants	Geographical area excluded*	Number of clusters	Stratified sampling	Screening strategy†		Bacteriology	
							Symptoms interview	CXR	Smear	Culture
China	1990	≥3 months	Not reported /1 461 190	Non-mainland ‡	928	Province	Not done	Fluoroscopy if abnormal then CXR §	2	2
Republic of Korea	1990	≥5	Not reported /48 976	None	190	Urban/ Rural	Not done	Abnormal	2 smear from 1 sputum	2
Thailand	1991	≥10	35 800	None	133	Urban/ Rural/ Bangkok	TB-suspected symptoms	Abnormal	3	1
Myanmar	1994	≥10	36 100/37 424	Unknown	41	Yangon/ Urban/ Rural	Cough ≥2 weeks	Not done	3	N/A only inner Yangon
Republic of Korea	1995	≥5	Not reported /64 713	None	203	Urban/ Rural	Not done	Abnormal	2 smear from 1 sputum	2
Philippines	1997	≥10	15 905/12 850	Unclear due to replacement after selection (two provinces, one municipality and a few clusters)	36	Manila/ Urban/ Rural	Not done	TB suggestive	3	3
China	2000	≥3 months	418 456/365 097	Non-mainland ‡	257	Province	Cough/ expectoration ≥3 weeks or haemoptysis	Fluoroscopy if abnormal then CXR §	3	2
Cambodia	2002	≥10	21 098/22 160	4/24 provinces, <3% of population	42	Urban/ Rural	Cough 3 weeks and/or haemoptysis	Abnormal	2	2
Indonesia	2004	≥15	62 000/50 154	None	1250 census blocks	Urban/ Rural	Any duration of productive cough/ sputum ± blood within a month	Not done	3	N/A (1 only in limited clusters)
Philippines	2007	≥10	30 000/20 625	18 barangays	50	Manila/ Urban/ Rural	Not done	Abnormal	3	3
Viet Nam	2007	≥15	105 000/94 179	None	70	Urban/ Rural/ Remote	Cough ≥2 weeks	TB suggestive	3	1

Table 2 (*Continued*)

Country	Main year	Age of eligibility (Years unless specified)	Planned sample size/participants	Geographical area excluded*	Number of clusters	Stratified sampling	Screening strategy†		Bacteriology	
							Symptoms interview	CXR	Smear	Culture
Bangladesh	2008	≥15	50 000/52 098	3/64 districts	40	Urban/ Semi-urban/ Rural	No screening	No screening	2–3	N/A (only undertaken in those who were S+)
Myanmar	2009	≥15	49 690/51 367	32/325 townships	70	States/ Divisions	Cough ≥3 weeks	Abnormal	2	2
China	2010	≥15	264 000/252 940	Non-mainland ‡	176	Province	Cough/ expectoration, haemoptysis ≥2 weeks	Abnormal	3	2
Cambodia	2011	≥15	39 680/37 417	None	62	Urban/ Rural	Cough ≥2 weeks and/or haemoptysis	Abnormal	2	2
Lao PDR	2011	≥15	40 000/39 212	None	50	Not stratified	Cough ≥2 weeks and/or blood sputum	Abnormal	2	2
Pakistan	2011	≥15	133 000/105 913	Unsecured zones, 6.5% of the national population	95	Not stratified	Cough ≥2 weeks or current TB treatment	Abnormal	2	1
Thailand	2012	≥15	78 840/62 536	Bangkok	83, number of PSU: 24 provinces	Urban/ Rural	Clinical scoring¶	Abnormal	2	2

CXR, Chest X-ray. S+, smear-positive. PSU, primary sampling unit.
*Although some surveys excluded certain geographical areas from their sampling frames, national surveys were included when most populations were covered.
†Criteria for eligibility of sputum examination.
‡Excluded Hong Kong Special Administrative Region, Macao Special Administrative Region, and Taiwan, China.
§In China 1990 & 2000, tuberculin skin tests performed in 0–14 years, and if positive, then fluoroscopy was undertaken.
¶A participant was screened positive when the clinical scoring was 3 or more points. The symptoms included cough of at least 2 weeks (Yes: 3 points); coughing up blood over the past month (3 points); cough of less than 2 weeks (2 points); unintentional body weight loss in the past month (1 point); fever 1 + weeks within the last 2 weeks (1 point); drenching night sweats in the past month (1 point).

Republic of Korea included those aged ≥5 years, and two surveys in China included all those aged ≥3 months.

The most common screening strategy during the 1990s was a chest X-ray, either a mass miniature X-ray or fluoroscopy, for the entire eligible population; those screening X-ray positive (any lung shadows or signs pathognomonic of TB) were then considered eligible for sputum examination. Between 2000 and 2008, surveys used a variety of screening and diagnostic methods, prompting WHO to produce standardised guidance on these and other survey methods [62]. In addition to chest X-ray screening, an interview with each participant that included questions about TB symptoms was introduced during the 2000s (using the NTP's definition of 'TB suspect', typically an individual with a chronic cough for more than 2–3 weeks and/or blood in the sputum). Since 2009, all surveys participants were screened using both direct chest X-ray (using either conventional or digital technologies) and an interview about symptoms, with participants who screened positive on either or both considered eligible for sputum examination.

In 15 surveys, participants eligible for sputum examination were tested using both smear microscopy and culture. In Indonesia (2004) and Myanmar (1994), testing included smear microscopy, but culture examination was not systematically performed. In Bangladesh, culture examinations were restricted to participants with sputum smear-positive results. Except for Viet Nam, all surveys used a simple inoculation method without centrifuging for primary culture.

Size of eligible population, survey participation rates and prevalence rates

The size of the eligible population, the participation rate, the number of prevalent cases identified and prevalence rates are shown in Table 3. The percentage of the eligible survey population that agreed to participate was ≥80% in 15 surveys and ≥90% in 9 of these. The participation rate could not be assessed for one survey (Myanmar, 1994) because a complete census of the population to enumerate those eligible to participate in the survey (i.e. the denominator) and those not eligible was not carried out. In general, participation rates were higher for females, middle and older age groups and rural residents, compared with males, younger age groups and urban residents.

The smear-positive TB prevalence per 1000 population aged ≥15 years varied from 0.66 (95% C.I. 0.53–0.79) in China (2010) to 4.4 (95% C.I. 3.5–5.6) in Cambodia (2002). The prevalence of bacteriologically-positive TB per 1000 population aged ≥15 years varied from 1.2 (95% C.I. 1.0–1.4) in China (2010) to 15 (95% C.I. 12–18) in Cambodia (2002). The proportion of bacteriologically-positive cases that were smear-positive varied widely, from 30% in Cambodia (2002) to 68% in Pakistan.

Age and sex distribution of cases

For 17 surveys, data on the prevalence of smear-positive TB cases disaggregated by sex were available (Figure 1). The male:female ratio of prevalence rates ranged from 1.7 in Pakistan to 5.1 in Viet Nam. In surveys for which culture results were also available, the male:female ratio of the prevalence of bacteriologically-positive TB varied from 1.5 in Pakistan to 4.5 in Viet Nam.

In 14 surveys that used chest X-ray screening, data on the prevalence of smear-positive TB disaggregated by age were available (Figure 2). In most surveys, TB prevalence rates increased progressively with age. In all countries, the most recent survey showed that TB prevalence rates peaked in the oldest age group of ≥65 years old. The pattern was similar for the absolute number of cases in most recent surveys (data not shown), with the notable exceptions of Myanmar (2011) and Viet Nam in which the absolute number of cases was highest in those aged 35–44 years.

Percentage of survey cases that screened negative for TB symptoms or had no symptoms

For 12 surveys, it was possible to assess the proportions of cases that met survey symptom screening criteria or whether they had any symptoms (Figure 3). The proportion of smear-positive cases that did not screen positive based on reported TB symptoms (typically a cough of more than 2–3 weeks duration and/or blood in the sputum) ranged from 34% in Lao PDR to 68% in Viet Nam. Among bacteriologically-positive TB cases, the proportion of cases that did not screen positive based on reported TB symptoms was higher still, ranging from 40% in Pakistan to 79% in Myanmar (2009).

In three repeat surveys that asked all participants about TB symptoms, the percentage of smear-positive TB cases that did not meet the symptom screening criteria or did not report any TB-related symptoms increased substantially compared with earlier surveys. In Cambodia, the percentage that screened negative for symptoms rose from 38% in 2002 to 56% in 2011; in the Republic of Korea, the percentage who did not report any symptoms rose from 39% to 60% between 1990 and 1995; and in China, the percentage of asymptomatic cases rose from 6% to 26% between 2000 and 2010 [20, 35, 40].

Table 3 Summary of the eligible population, participation rates and the number of prevalent cases identified

Country	Year	Age of eligibility (years unless specified)	Eligible population	Number (%) of participants identified in survey operations	Number of smear-positive cases	Number of bacteriologically-positive cases	Proportion of smear-positive in bacteriologically-positive cases	Prevalence per 1000 (95% C.I.: smear-positive cases			Prevalence per 1000 (95% C.I.): bacteriologically-positive cases		
								Rate	95% C.I.	k*	Rate	95% C.I.	k*
Bangladesh	2008	≥15	63 716	52 098 (82)	33	33†	N/A	0.79	0.47–1.3	1.58*	N/A	N/A	N/A
Cambodia	2002	≥10	23 084	22 160 (96)	81	271	30	3.6‡,§	2.8–4.6	0.28	12‡,§	10–15	0.47
Cambodia	2011	≥15	40 423	37 417 (93)	103	314	33	2.7‡	2.1–3.5	0.59	8.3‡	7.1–9.8	0.54
China	1990	≥3 months	1 493 334	1461 190 (98)	1827	2389	76	1.3¶	1.2–1.4	0.93*	1.8¶	1.7–1.9	0.79*
China	2000	≥3 months	375 599	365 097 (97)	447	584	77	1.2**	1.1–1.4	0.57*	1.6**	1.4–1.8	0.68*
China	2010	≥15	263 281	252 940 (96)	188	347	54	0.66	0.53–0.79	0.88	1.2	1.0–1.4	0.48
Indonesia	2004	≥15	53 155	50 154 (94)	80	Not done	N/A	1.5	0.94–2.0	N/A	N/A	N/A	N/A
Lao PDR	2011	≥15	46 079	39 212 (85)	107	237	45	2.8††	2.0–3.6	0.74	6.0††	4.6–7.3	0.68
Myanmar	1994	≥10	Not known ‡‡	37 424 (Not known)	39	Not done	N/A	1.0	0.7–1.4	0.92*	N/A	N/A	N/A
Myanmar	2009	≥15	57 607	51 367 (89)	123	311	40	2.4‡	1.9–3.2	0.82	6.1‡	5.0–7.5	0.69
Pakistan	2011	≥15	131 329	105 913 (81)	233	341	68	2.7††	2.2–3.2	0.68	4.0††	3.3–4.6	0.55
Philippines	1997	≥10	15 905	12 850 (81)	47	127	37	3.6	2.8–4.5	Undefined	9.6	7.5–12	0.44*
Philippines	2007	≥10	22 867	20 625 (90)	60	151	40	2.6§§	1.7–3.6	0.79	6.6§§	5.1–8.1	0.55
Republic of Korea	1990	≥5	50 960	48 976 (96)	70	118	59	1.4	Not known	Not known	2.4	1.8–3.0	1.18*
Republic of Korea	1995	≥5	73 194	64 713 (88)	60	142	42	0.93	Not known	Not known	2.2	1.8–2.6	0.57*
Thailand	1991	≥10	47 046	35 844 (76)	73	101	72	1.7	Not known	Not known	2.4	Not known	Not known
Thailand	2012	≥15	78 839	62 536 (79)	58	142	41	1.0††,***	0.56–1.8	1.27*	2.4††,***	1.8–3.2	0.52*
Viet Nam	2007	≥15	103 924	94 179 (91)	174	269	65	2.0	1.5–2.4	0.79	3.1	2.5–3.7	0.62

*k is the coefficient of variation of the cluster-specific TB prevalences. For these marked countries, k of the cluster-specific TB prevalences was not reported and derived from the confidence interval of the overall TB prevalence in surveys where the design effect (DEFF) was not known [52, 63].

†The survey in Bangladesh only undertook culture examination from those individuals whose specimens were positive for acid-fast bacilli, that is no cultures were examined from individuals that were smear-negative.

‡Imputation analyses were undertaken but as participation rates were high and imputed estimates were close to that derived from cluster-level models, the latter method was officially reported.

§The estimated smear-positive and bacteriologically-positive prevalence for TB, adjusted for participants who were ≥15 years of age is 4.4 per 1000 (95% C.I. 3.5–5.6) and 15 per 1000 (95% C.I. 12–18), respectively.

¶The estimated smear-positive and bacteriologically-positive prevalence for TB, adjusted for participants who were ≥15 years of age is 1.70 per 1000 (95% C.I. 1.66–1.74) and 2.21 per 1000 (95% C.I. 2.16–2.26), respectively.

**The estimated smear-positive and bacteriologically-positive prevalence for TB, adjusted for participants who were ≥15 years of age is 1.37 per 1000 (95% C.I. 1.23–1.53) and 1.78 per 1000 (95% C.I. 1.63–1.95), respectively.

††Estimates based upon the use of robust standard errors with missing value imputation and inverse probability weighting.

‡‡The denominator was not reported.

§§The estimated smear-positive and bacteriologically-positive prevalence for TB, adjusted for participants who were ≥15 years of age is 3.2 per 1000 (95% C.I. 3.5–5.6) and 7.8 per 1000 (95% C.I. 6.0–9.5), respectively.

***Not analysed at the cluster level but at the area (urban/rural) level.

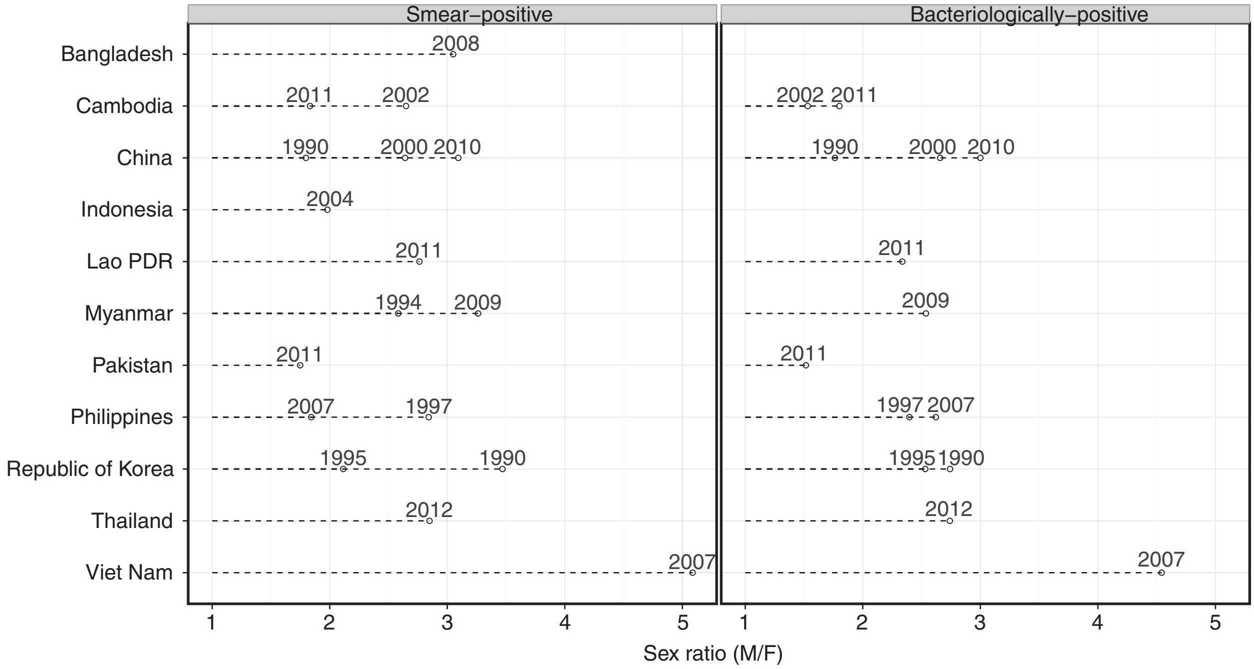

Figure 1 Sex ratio (male to female) of identified prevalent TB cases. There were no available sex-disaggregated data from Thailand (1991). The prevalence of bacteriologically-positive TB was not available from Bangladesh (2008), Indonesia (2004) and Myanmar (1994) because culture was not systematically used for all positively screened participants.

Prevalence to notification ratios

For 11 surveys in which chest X-ray screening was carried out, the ratio of smear-positive prevalence to smear-positive notifications (P:N) could be calculated (Figure 4). This ranged from 1.7 in Cambodia (2011) and China (2010) to 7.6 in China (2000). However, surveys conducted since 2007 typically had P:N ratios of around 2 (range: 1.4–3.2), with higher values for surveys in Lao PDR and Pakistan. In most countries, the ratio tended to be narrower in younger age groups and wider in older ones (data not shown). Except for the Philippines in 2007, the P:N ratio was higher in males compared with females. The P:N ratio for male and female smear-positive cases was as low as 1.1 for female cases in Cambodia (2002). Since 2007, the most noticeable discrepancy between men and women was in Viet Nam, where the P:N ratio for men was almost twice as that for women (2.8 *vs*. 1.6).

False-positive smear results

Although the isolation of non-tuberculous mycobacteria from smear-positive samples was very limited in seven surveys with available data, between 3% (Pakistan) and 43% (Lao PDR) of participants with a smear-positive result were not counted as TB cases because they did not fulfil the survey case definition of smear-positive TB, that is they did not show any culture isolates of MTB and/or their chest X-ray showed no signs of TB disease.

Drug susceptibility test results and the prevalence of MDR-TB

For 14 surveys in which drug susceptibility testing was performed for rifampicin and isoniazid, most countries tested more than 50% of MTB isolates and MDR-TB was detected in 0–11% of them (Table 4). Four countries had repeat survey data, allowing trends in the burden of MDR-TB and the numbers of people in the population in need of second-line TB treatment to be assessed. Striking findings included a large fall in the absolute number of prevalent cases of MDR–TB in China (and an approximate halving of numbers in need of expensive second-line treatments) and very low levels of drug resistance among TB cases in Cambodia.

Trends in prevalence rates in countries that have implemented repeat surveys

Four countries had repeat survey data since 1990 that allowed trends in the prevalence of smear-positive and

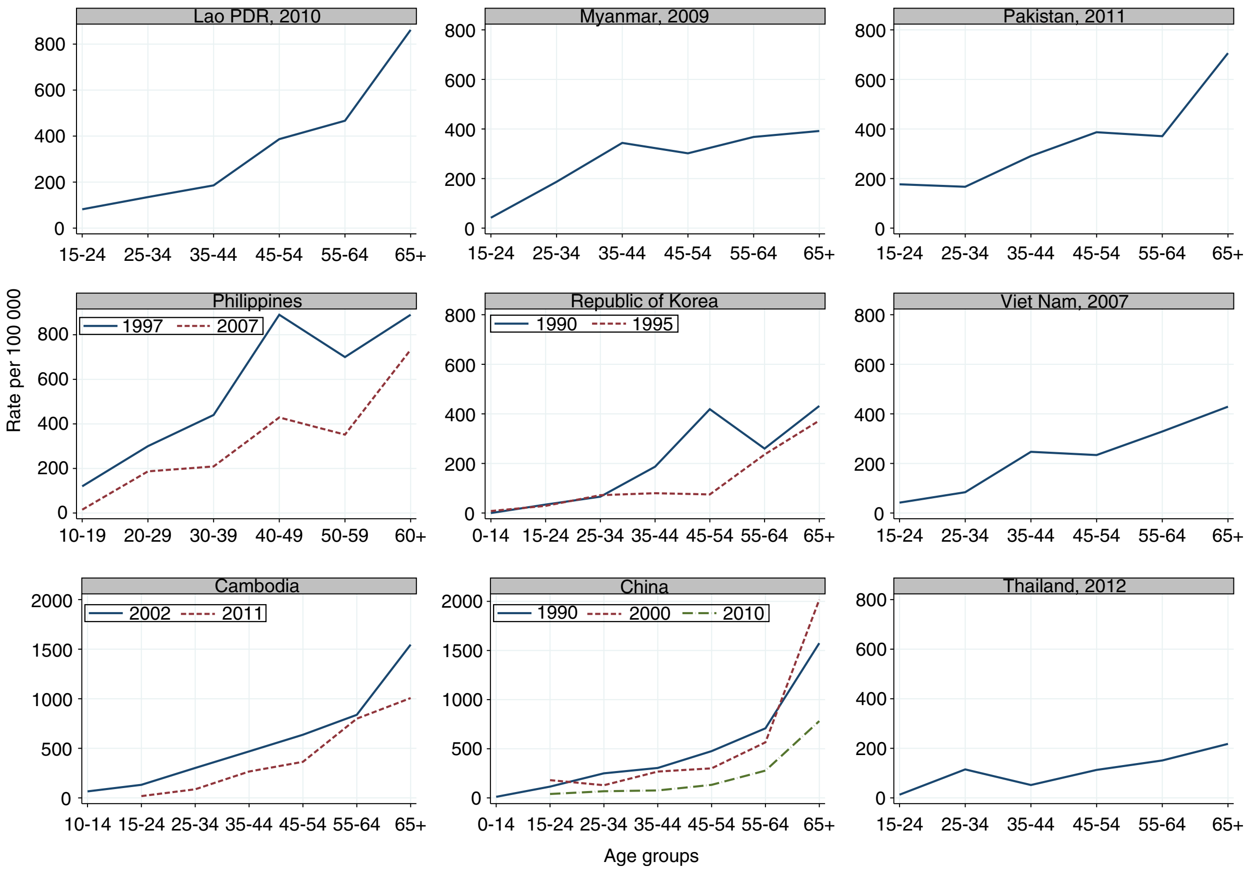

Figure 2 Age-specific, smear-positive TB prevalence. Smear-positive age-disaggregated data not available from Thailand (1991), Indonesia (2004) and Myanmar (1994). Data from Bangladesh (2008) were not shown because there were only 33 smear-positive TB cases.

bacteriologically-positive TB to be assessed: Cambodia, China, the Philippines and the Republic of Korea. Large reductions in TB prevalence were demonstrated in all repeat surveys (Figure 5).

Repeat surveys were also implemented between 1990 and 2012 in Myanmar (1994, 2009) and Thailand (1991, 2006, 2012). However, changes to screening and/or diagnostic methods in the most recent survey preclude an unbiased comparison of results. In Thailand, the 2012 survey used direct chest X-ray screening on-site as opposed to miniature mass radiography (MMR) in the 1991 and 2006 surveys; MMR is less sensitive than full-size chest X-ray and likely led to underestimation of the number of culture-positive TB cases in 1991. In Myanmar, the 1994 survey did not include chest X-ray screening or culture examination. Nonetheless, a reduction in the prevalence of smear-positive TB was documented in Thailand (1.7 per 1000 in 1991 to 1.0 per 1000 in 2012) despite an increase in TB due to HIV in the 1990s, and a 35% reduction in the prevalence of those who screened symptom-positive and had smear-positive TB occurred in Myanmar between 1994 and 2009 [25].

Health care-seeking behaviour and notification of diagnosed cases to the NTP

All surveys except Thailand (1991) and Myanmar (1994) reported health care-seeking behaviour data. Although behaviour among participants reporting a chronic cough was studied in most recent surveys, the most complete (8 surveys) and standardised data were about the current place of treatment for survey participants who were on TB treatment (Table 5). In six countries, around 80% or more of those on TB treatment were being treated in the public sector; the exceptions were Republic of Korea (1995) and Lao PDR, for which figures were around 50% (however, in Lao PDR the place of treatment was unknown for half of those on treatment). The proportion of TB patients being treated in the private sector halved between 2002 and 2011 in Cambodia, and in the most

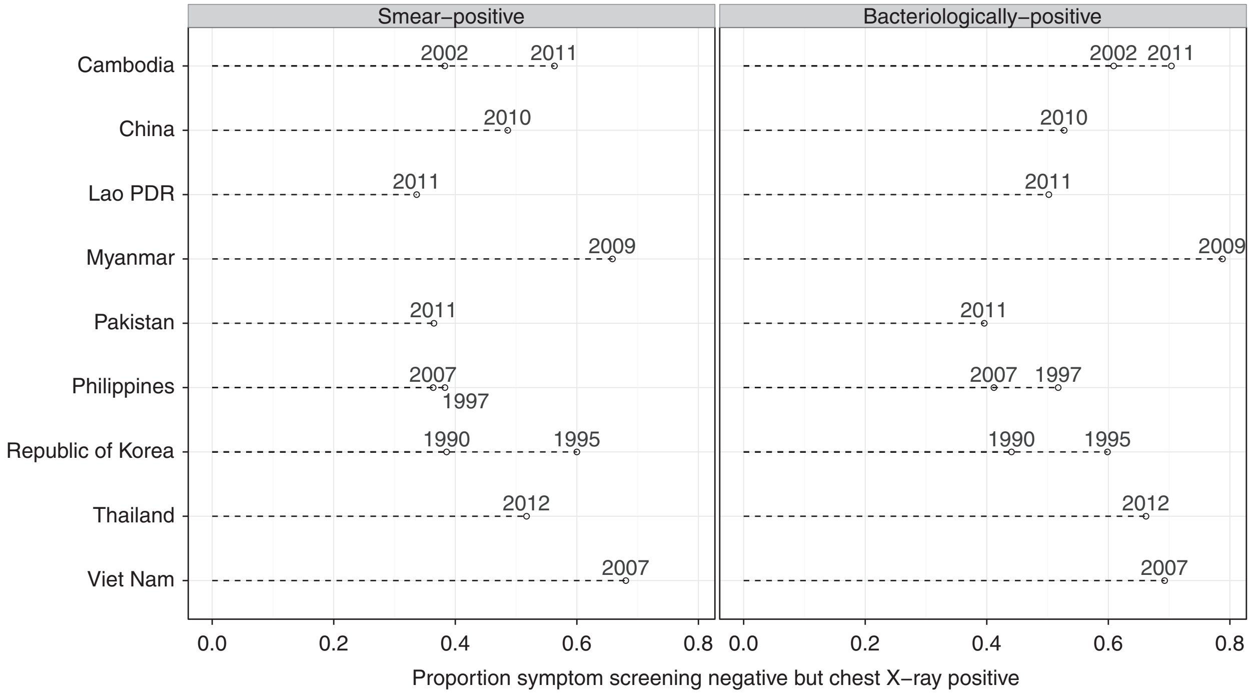

Figure 3 Proportion symptom screen negative among prevalent TB cases. There were no available data from Bangladesh (2008), China (1990, 2000), Indonesia (2004), Myanmar (1994) or Thailand (1991). Surveys conducted by the Republic of Korea (1990 and 1995) and the Philippines (1997 and 2007) did not use symptom screening; however, symptom-related data were collected from all detected TB cases.

Figure 4 TB prevalence (smear-positive) to TB case notification (new smear-positive) ratio. Notification data were calculated using smear-positive TB country notifications to WHO and the UN population estimates (2012 revision) for the main year of the survey. Notification data not available from China (1990), the Republic of Korea (1990), Myanmar (1994), the Philippines (1997) or Thailand (1991). Data were not shown for Bangladesh (2008) because estimated prevalence was likely to be underestimated.

Table 4 Drug sensitivity testing of *Mycobacterium tuberculosis* isolates from detected cases

Country	Main year	Number of bacteriologically-positive TB cases detected by the survey	Number (%) of MTB isolates tested	Number (%, 95% C.I.) of isolates with MDR-TB detected*
Bangladesh	2008	33†	29 (88)	1 (3.4, 0.1–17.8)
Cambodia	2002	271	245 (90)	0 (0, 0–1.5)
Cambodia	2011	314	193 (61)	0 (0, 0–1.9)
China	1990	2389	1595 (67)	36 (2.3, 1.6–3.1)
China	2000	584	392 (67)	42 (11, 7.8–14.2)
China	2010	347	280 (81)	19 (6.8, 4.1–10.4)
Lao PDR	2011	237	226 (95)	2 (0.9, 0.1–3.2)
Pakistan	2011	341	182 (53)	5 (2.7, 0.9–6.3)
Philippines	1997	127	55 (43)	2 (3.6, 0.4–12.5)
Philippines	2007	151	130 (86)	5 (3.8, 1.3–8.7)
Republic of Korea	1990	118	113 (96)	8 (7.1, 3.1–13.5)
Republic of Korea	1995	142	131 (92)	7 (5.3, 2.2–10.7)
Thailand	2012	142	130 (92)	0 (0, 0–2.8)
Viet Nam	2007	269	212 (79)	10 (4.7, 2.3–8.5)

*95% confidence intervals were derived using the exact binomial approach based on the number of cases found with MDR-TB strains out of the total number of prevalent cases tested for drug susceptibility, assuming that missing data (prevalent cases not tested for drug susceptibility) were missing completely at random.
†The survey in Bangladesh only undertook culture examination from those individuals whose specimens were positive for acid-fast bacilli, that is no cultures were examined from individuals that were smear-negative.

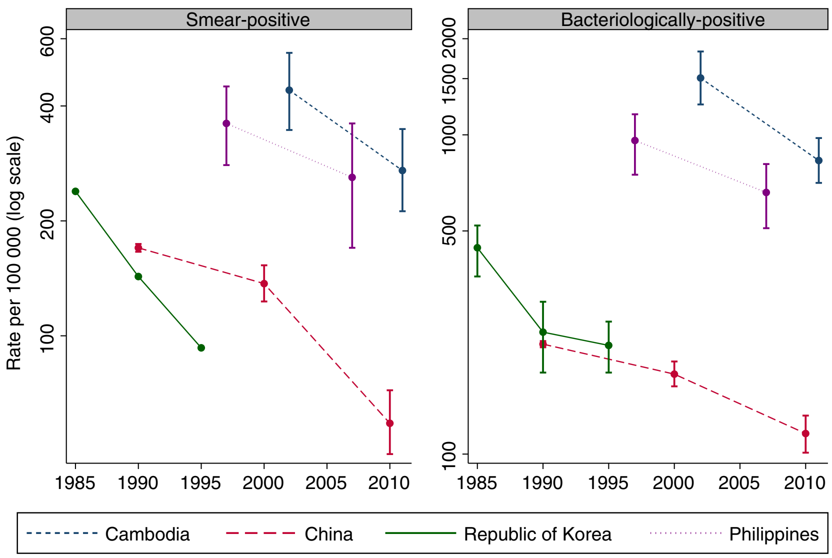

Figure 5 Trends in TB prevalence – four countries with repeat survey data. Prevalence rates refer to survey cases who were ≥15 years from China and Cambodia. For survey cases from the Republic of Korea and the Philippines, prevalence rates refer to survey cases who were ≥5 or ≥10 years, respectively. Standard errors and confidence intervals were not reported for smear-positive data in the three surveys from the Republic of Korea.

recent survey in China (2010), the number of patients reporting treatment in the private sector was almost negligible. The proportion of those on TB treatment who were bacteriologically-positive at the time of the survey was almost always very low (3–4%).

Information about whether TB patients had been notified to the NTP (or national TB surveillance system) was scarce. Verification using a case-based electronic national surveillance system was only possible in China, where 72% of people on TB treatment at the time of the survey had been notified through the national infectious diseases reporting system. Similar analyses using local registration data found under-reporting of approximately 20% in Viet Nam, Myanmar (2009) and Thailand (2012), assuming that all TB cases in local registries were notified to the NTP.

Table 5 Health care-seeking behaviour among participants on TB treatment at the time of the survey, and detected TB cases

Country	Year	Number of bacteriologically-positive TB cases detected by the survey	Number (%) of bacteriologically-positive TB cases detected by the survey who were currently on treatment	Number of survey participants currently on TB treatment	Number (%) of survey participants currently on TB treatment treated in the public sector	Number (%) of survey participants currently on TB treatment treated in the private sector	Number (%) of survey participants currently on TB treatment: unknown sector	Detected TB cases on treatment (%) reported to NTP at the time of the survey
Cambodia	2002	271	11 (4)	42	34 (81)	8 (19)	0 (0)	34 (81)
Cambodia	2011	314	6 (2)	80	72 (90)	6 (8)	2 (3)	72 (90)
China	2010	347	Not known	123	122 (99)	1 (1)	0 (0)	99 (72)
Republic of Korea	1995	142	6 (4)	71	34 (48)	33 (47)*	4 (6)	Not known
Myanmar	2009	311	11 (4)	79	63 (80)	15 (19)	1 (1)	63 (80)
Lao PDR	2011	237	6 (3)	42	21 (50)	0 (0)	21 (50)	21 (50)
Thailand	2012	142	6 (4)	60	48 (80)	3 (5)	9 (15)	48 (80)
Viet Nam	2007	269	39 (22)†	407‡	324 (80)	29 (7)	54 (13)	–(80–93)§

*In the Republic of Korea, 12 of the 33 cases were treated in the hospital sector which at the time may or may not have reported to the NTP.
†These data refer to the 174 smear-positive cases detected in the survey. These 39 cases refer to those currently on treatment or had been treated for ≥1 month.
‡Those reported to have been recently treated for TB within two years including those currently on treatment.
§Total detected TB cases reported to the NTP were not in the reference. Only a percentage was reported in the reference that was derived from imputation methods (Hoa *et al.* [12]).

For prevalent TB cases not on TB treatment, available data on health care-seeking behaviour varied markedly (see supplementary material, Table S2 for a summary). Key findings included that a variable proportion (range, 27–66%) of those who screened symptom-positive during surveys reported having previously sought some form of care in a medical facility, that visits to private health facilities, pharmacies and self-medication were common and that a large proportion of TB cases (with or without reported symptoms) had not sought care at all (range 10–56%).

Discussion

Our summary of results from national TB prevalence surveys in Asia shows that the burden of TB disease remains high in many countries, while also varying considerably from a relatively low bacteriologically-positive prevalence of 1.2 per 1000 in China (2010) to over 5 per 1000 adult population in Cambodia (2011), Lao PDR, Myanmar (2009), Pakistan and the Philippines (2007). Surveys in Cambodia, Lao PDR, Myanmar and Viet Nam have also demonstrated that the burden of TB disease was much higher than previously estimated using findings from tuberculin surveys, while in China, the results from contemporaneous prevalence and tuberculin surveys were contradictory in terms of trends. Together with other evidence, these findings have contributed to the increased priority given to TB prevalence surveys as a method to measure the burden of TB disease at global and national levels, as well as a WHO recommendation that tuberculin surveys should not be used to estimate the burden of TB disease.

It is encouraging that repeat surveys in four countries (Cambodia, China, the Philippines and Republic of Korea) demonstrate that reductions in TB prevalence of approximately 50% can be achieved within 10 years. In each case, the concomitant lowering of the prevalence of smear-positive TB and the ratio of prevalent smear-positive to notified smear-positive TB cases (P:N ratio), and a shift of the peak prevalence of TB to older age groups, suggest that efforts to improve TB control were a contributory factor alongside others such as economic growth and general improvements in living standards. A reduction in the prevalence of smear-positive TB is consistent with the focus of TB control in the years between the repeat and previous survey, that is prioritisation of the detection and cure of the most infectious cases (those who are smear-positive) within the framework of the DOTS strategy recommended by WHO between the mid-1990s and 2006. Reductions in TB prevalence in China and the Philippines occurred during a period of nation-wide expansion of DOTS, and in Cambodia, they occurred during a period when DOTS services were decentralised beyond hospitals to include health centres [16, 55, 59]. The low proportion of bacteriologically-positive cases on treatment among survey cases in almost all recent surveys conducted several years after DOTS implementation also suggests an increase in the quality of TB treatment over time. In turn, earlier conversion to bacteriologically negative status could have helped to cut transmission.

As transmission declines, most incident cases will arise from past rather than recent infection. The average latency period between acquisition of infection and onset of disease increases as the age distribution of cases shifts towards older age groups; a tendency amplified by an ageing population. The TB epidemic in Asia is a progressively ageing epidemic; in most countries, the highest rates and absolute numbers of cases are now found in the oldest age groups.

All surveys reinforce other evidence (for example, from routinely reported case notification data and research studies [2, 44]) that the burden of TB disease in men is two to three times higher than in women, with sex ratios (male:female) ranging from 1.7 in Lao PDR and Pakistan to 5.1 in Viet Nam. This means that, overall, men account for about two-thirds to three-quarters of the burden of TB disease in Asia. Survey results about the proportion of cases with MDR-TB are also consistent with national surveys of drug resistance [65].

One of the most striking and consistent findings is that a high percentage of people with bacteriologically-positive TB did not report symptoms that met screening criteria. Among surveys conducted since 2007, the percentage of prevalent TB cases that screened symptom negative was typically in the range 40–60%. In all repeat surveys, this proportion increased over time. These observations have important implications. First, many people with bacteriologically-positive TB, including a large proportion of smear-positive cases, are unlikely to seek health care unless they suffer from another condition and will be a source of ongoing transmission in the community until symptoms worsen. Second, even if they do seek care, it is unlikely (with existing screening criteria) that they would be referred for further laboratory testing and a resulting TB diagnosis on the basis of reported symptoms. Third, as basic TB care services improve, most TB cases with ‘classic’ TB symptoms should be detected, but as the proportion of cases without such symptoms increases a prompt diagnosis becomes, on average, harder to make. Furthermore, a large share of TB cases was only identified in these surveys because the entire eligible survey population was screened using chest X-ray. Updated control strategies that enable earlier diagnosis and treatment, such as widening the current screening criteria and more systematic use of chest X–ray screening, along with raised awareness of healthcare providers about the magnitude and characteristics of TB cases in the community, are required.

More encouragingly, cross-country comparisons of the P:N ratio show that in several countries, it should be possible to achieve much more with strategies and technologies for TB care and control that are already available. The overall P:N ratio in Cambodia (2011), China (2010), the Philippines (2007) and Thailand (2012) was less than two, suggesting that countries with higher ratios (especially Lao PDR and Pakistan) have scope to improve. Comparisons by sex reinforce this conclusion: systematically lower P:N ratios for women show considerable potential to lower this ratio among men. While the burden of TB disease is much higher in men, P:N ratios indicate that women are probably accessing available diagnostic and treatment services in primary care more effectively. They also indicate that cases among older age groups tend to be detected less effectively; explanations may include lower access to health care for financial or other reasons and that TB symptoms are tolerated for longer as older individuals are more prone to have chronic health conditions, leading to delayed investigations.

Standardised survey data from multiple countries on patterns of healthcare-seeking behaviour could help to identify actions that NTPs and/or health services in general could take to shorten the time to TB diagnosis and to ensure prompt provision of high-quality care. Unfortunately, data collected in Asian surveys up to 2012 are relatively limited and not well standardised. However, they do show that, in at least some settings, a large share of people with bacteriologically-positive TB and who reported symptoms had sought care at private healthcare facilities or at pharmacies/drug sellers. This reinforces the need for continuous engagement with the full range of healthcare providers in the public and private sectors, especially in Asian countries in which a large share of total health expenditures and usage of first-line TB drugs occur in the private sector [60, 66]. In the future, efforts are needed to standardise the data that are collected on healthcare-seeking behaviour as part of surveys and to ensure that under-reporting of detected cases to NTPs is measured so that routine TB surveillance can be strengthened if necessary.

Challenges and failures during surveys implemented in the 2000s prompted WHO and technical partners to publish guidance that included standardised survey methods and examples of best practices [63]. Lessons learned about the process of preparing, implementing and reporting on surveys from the Asian surveys described in this

Box 2 Important lessons for other countries and future TB prevalence surveys regarding how to design, prepare, implement and report results

- The time needed to procure the necessary equipment, especially X-ray equipment, is often underestimated. Countries have different rules and regulations for the procurement of equipment and consumables, which must be fully understood when survey preparations are initiated.
- Laboratories must be prepared for the required increase in capacity. Surveys typically require 5 000–10 000 primary cultures to be examined in 6–12 months, in addition to those from routinely collected sputum specimens. Therefore, the annual increase in the number of specimens to be processed for culture is approximately 50–100% for small or mid-sized countries. Efficient scheduling, human resource and procurement capacity should be carefully assessed for the duration of the survey so that a laboratory can process routine and survey specimens without compromising the quality of laboratory work. It may be necessary to involve more than one laboratory if services can be standardised and quality assured.
- Eligibility criteria must be clearly enforced. Individuals should be enrolled only if they are resident in the survey site for a clearly defined and context-appropriate period of time (typically 2–4 weeks), to avoid enrolment bias due to people moving to the survey site for free chest X-ray screening.
- Exclusions of specific geographical areas must be done at the time of protocol development. Exceptions can be considered but these should be for truly exceptional situations that cannot be anticipated in advance, such as a natural disaster or new developments that affect the personal security of the survey team.
- Community engagement is essential but should not be done too early. Smooth enrolment of participants and high participation rates are strongly enabled by early involvement of community leaders. Raising awareness about the survey should not be carried out prematurely, however, because this can encourage people from neighbouring areas to move to survey clusters, in particular to benefit from free chest X-ray screening.
- The optimal cluster size is 500–800 people. This corresponds to the number of people who can be screened by chest X-ray in one week, which is the maximum time that a survey site can be kept operational. The typical number of clusters will range from 50 to 70.
- Data management must be given high priority. In many surveys, one of the weakest aspects of implementation has been data management (especially in the laboratory), which in turn has delayed analysis and dissemination of results. The necessary people with appropriate expertise and experience as well as other resources must be identified before protocol development to ensure that data management is carried out according to best practices.
- Data analysis must be given high priority. The analysis of survey data, especially adjustments for intercluster variability and multiple imputation of missing values should be carried out by experts familiar with and able to implement best practices [9]. This requires support from qualified statisticians. Holding a workshop to discuss results and their interpretation shortly after survey completion is very helpful for facilitating prompt consensus about and wide dissemination of results.
- Chest X-ray screening in communities with immediate feedback of screening results facilitates participation and high sputum collection rates. The failure of surveys in Malaysia, 2003 (in which participants were invited to a separate facility to undergo X-ray examination rather than screening being performed in the field) and Thailand, 2006 (delayed feedback of X-ray examination results) provided evidence that strongly supported the use of on-site radiological screening. This has been adopted in every survey in Asia since 2009.
- A smear-positive result does not always mean TB. In more recent surveys, for case management purposes and survey case definitions, detected smear-positive specimens are being tested with Xpert® MTB/RIF or LPA to ensure accurate diagnosis of cases for whom smear results and clinical findings are inconsistent.
- Achieving high participation rates becomes more challenging as countries become more urbanised, and as overall income levels rise. Participation rates in almost all Asian surveys have been high. However, achieving high participation rates has been harder in urban areas and also in wealthier areas as well as in young people (especially men). Once access to health services is very good, there is little incentive to access free services (especially chest X-ray screening) provided during surveys.

study, to complement those arising from actual survey results, are summarised in Box 2. These include the importance of clearly enforcing eligibility criteria, when to define any geographical areas to exclude from the survey, the optimal cluster size, the role and magnitude of community engagement and the need to give high priority to and mobilise the right expertise for data management and data analysis.

There are several limitations to the survey data presented in this study. Most data are for adults only, due to well-recognised problems with the inclusion of children in surveys with currently available screening and diagnostic technologies [7]. HIV testing was not performed in any survey, primarily for logistical reasons and concerns about the impact on survey participation rates. In three surveys (Myanmar, 1994; Bangladesh, 2008; Indonesia, 2004), the only laboratory test used to diagnose TB in most participants was smear microscopy and chest X-ray screening was not provided, leading to a probable underestimation of TB prevalence. Analysis of the 1994 Myanmar survey did not account for clustering, and we were unable to establish whether the analyses performed for four other surveys (China 1990, 2000; Republic of Korea 1990, 1995) did so.

There is also one major geographical gap in the coverage of national TB prevalence surveys in Asia: no national survey has been conducted in India, even though the country accounts for about 24% of the global TB burden. Surveillance data in India are not yet reliable enough to provide a direct measure of disease burden (there are no vital registration data with accurate coding of cause of death to measure mortality; and under-reporting of cases from the private sector as well as underdiagnosis mean that notification data are not a good proxy for TB incidence). A national TB prevalence survey would be very valuable for providing reliable population-based data about the burden of TB disease in the country.

Conclusions

National TB prevalence surveys in Asia show that TB prevalence is still high in most countries, that large reductions in TB burden can be achieved with well-implemented TB control strategies, that more men than women have TB disease in this region and that TB epidemics are ageing. Comparisons between countries show that more can be achieved in TB control in most countries. However, with many prevalent cases not reporting classic TB symptoms, all countries face the challenge of defining and implementing strategies that will result in effective detection and treatment of cases with milder forms of the disease.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1 Surveys in Asia 1990–2012 and their main characteristics.

Table S2 Healthcare-seeking behaviour among symptomatic participants and detected TB cases.

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