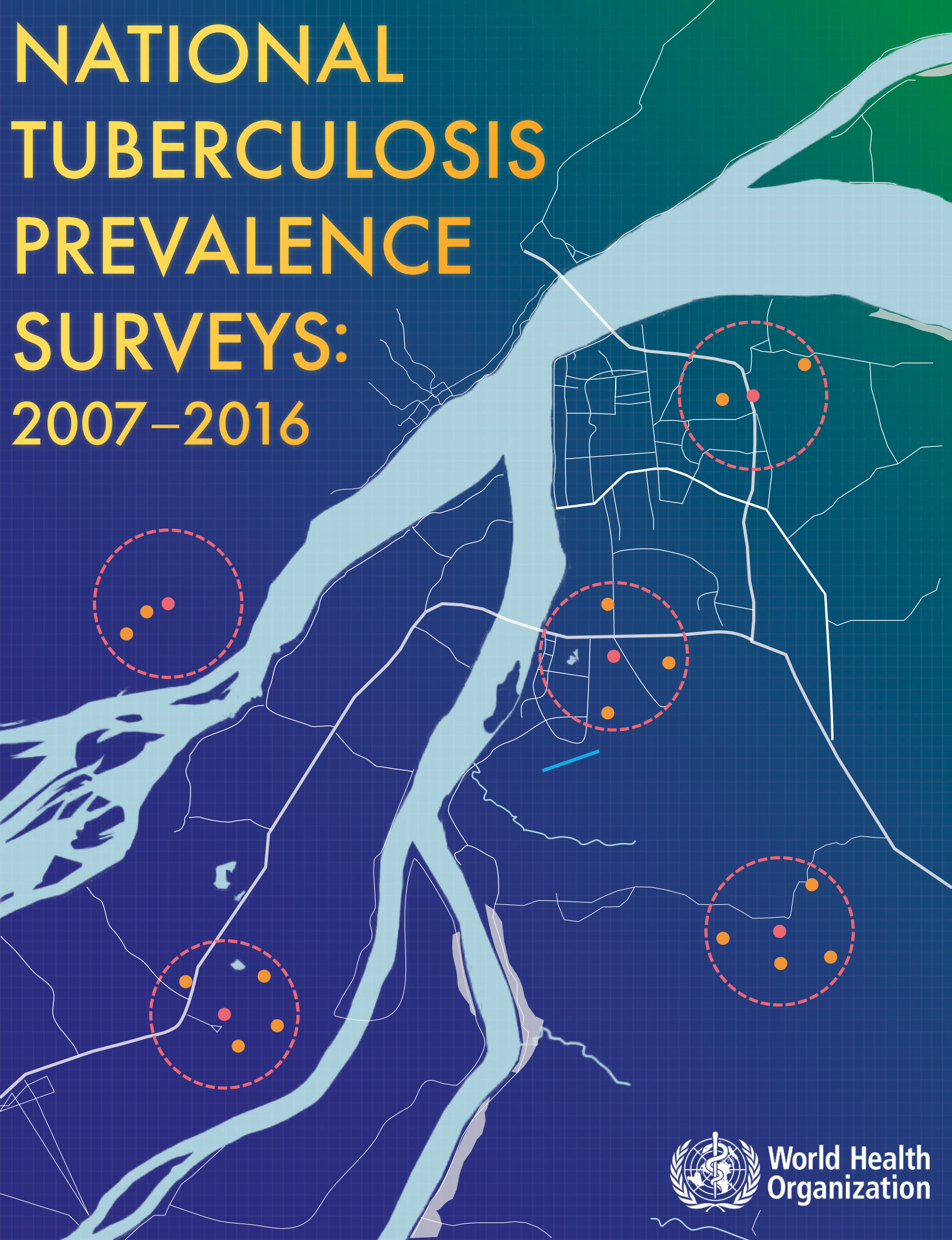
NATIONAL TUBERCULOSIS PREVALENCE SURVEYS: 2007–2016



World Health Organization

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Preface

At the time of publication of this book in early 2021, tuberculosis (TB) remains a major cause of ill health and one of the top causes of death worldwide.

During the period 2000–2015, global and national efforts to reduce the burden of TB disease had the aim of achieving global TB targets that were set as part of the United Nations (UN) Millennium Development Goals (MDGs), the World Health Organization's (WHO) Stop TB Strategy (2006–2015) and the Stop TB Partnership's Global Plan to Stop TB (2006–2015). Three targets were set: to halt and reverse TB incidence by 2015; to halve the TB mortality rate by 2015 compared with 1990; and to halve the prevalence of TB disease by 2015 compared with 1990.

In 2006, WHO established a Global Task Force on TB Impact Measurement, convened by the TB monitoring, evaluation and strategic information (TME) unit of WHO's Global Tuberculosis Programme. The Task Force's aim was to ensure a robust, rigorous and consensus-based assessment of whether the 2015 TB targets were achieved at global, regional and national levels. At its second meeting, held in 2007, the Task Force agreed on three strategic areas of work for the period 2007–2015: strengthening of routine national surveillance systems (notification and vital registration) in all countries; national TB prevalence surveys in 22 global focus countries; and periodic review of the methods used by WHO to translate surveillance and survey data into estimates of TB disease burden. The 22 global focus countries were a prioritised subset of 53 countries considered eligible to implement a national TB prevalence survey: 13 in Africa and 9 in Asia.

Global recognition of the importance of national TB prevalence surveys was reinforced and supported by considerable national interest in and commitment to implementing such surveys, which had started to grow and intensify in many countries during the early-mid 2000s.

In 2007, however, the goal of completing a large number of national TB prevalence surveys in a relatively short period of time was a daunting task. The number of recent national surveys was small, and global and national experience and expertise in their design, implementation and analysis was scarce. Between 1990 and 2006, only a handful of countries in Asia successfully completed a national TB prevalence survey. No national survey had been attempted in the WHO African Region since the 1950s, with the sole exception of a survey in Eritrea in 2005 that was limited by the diagnostic methods used to detect people with TB.

What followed was an unprecedented national, regional and global effort to implement national TB prevalence surveys. Between 2007 and the end of 2016, 24 countries implemented a total of 25 national surveys using methods recommended by WHO. The 24 countries comprised 18 of the 22 global focus countries and six other countries. The 25 surveys consisted of 13 in Asia and 12 in Africa.

The outcome is a wealth of new data. These data were crucial to WHO's assessment of whether the 2015 TB targets were met at global, regional and country levels, by providing a much better understanding of the burden of TB disease, including its distribution by age and sex, and reliable evidence about trends in countries where a repeat survey was done. The data have also provided new evidence about the symptoms experienced by people with undiagnosed TB in the community, the extent of gaps between the number of people with TB in the community and the number of people officially detected with TB, and health care-seeking behaviour in the public and private sectors, in turn shining new light on reasons for delays in diagnosing people with TB and for the underreporting of people diagnosed with TB to national authorities. Collectively, survey findings have informed the policies, plans and programmatic actions needed to address gaps in TB diagnosis and treatment and to reduce the burden of TB disease. Finally, the 24 countries have a robust baseline for assessing progress towards new global targets set in the UN Sustainable Development Goals (2016–2030) and WHO's End TB Strategy (2016–2035).

At the global level, efforts to support the design, implementation, analysis and reporting of national TB prevalence surveys between 2007 and 2016 were led and coordinated by a subgroup of the WHO Global Task Force on TB Impact Measurement. This subgroup was led by staff in WHO's TME unit.

In 2016, it was our collective view that the methods, results, successes achieved, challenges faced and lessons learned from the 25 national surveys implemented 2007–2016 should be comprehensively documented in a book. We viewed such a product as a global public good, that should be available to all those with an interest in and commitment to using survey findings, now and in the future.

As with implementation of the 25 surveys themselves, the book is the result of a major global, regional and national collaborative and collective effort, with more than 450 contributors from all around the world. We are proud of the final product, wholeheartedly thank all those who made it possible, and hope that it will be a valuable resource for many people for many years to come.

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The core team prepared the five cross-cutting chapters that form Part I of the book. Chapter 1 was prepared by Katherine Floyd, Philippe Glaziou, Irwin Law and Ikushi Onozaki. Chapter 2 and Chapter 3 were prepared by Irwin Law, with contributions from Katherine Floyd, Philippe Glaziou, Sayori Kobayashi, Ikushi Onozaki and Marina Tadolini (WHO consultant). Chapter 4 was prepared by Katherine Floyd. Chapter 5 was prepared by Katherine Floyd, Irwin Law and Charalambos Sismanidis, with contributions from Philippe Glaziou.

The country-specific chapters for the 25 national TB prevalence surveys that were completed 2007–2016, which form Part II of the book, were prepared by the WHO core team together with key members of the national survey teams and people who provided technical assistance to these teams. Sayori Kobayashi and Irwin Law produced and checked the final datasets and reports that were used for each chapter in close collaboration with national survey teams, analysed the data and produced the standard sets of figures and tables that are featured in each chapter. The text of each chapter was drafted by national survey teams in collaboration with the WHO core team; all chapters were reviewed and finalized by Katherine Floyd and Irwin Law.

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Abbreviations

AFB	acid-fast bacilli
BCG	Bacille Calmette-Guérin
C&NCD	Communicable and Noncommunicable Disease Administration
CAD	computer aided detection
CDC	Centers for Disease Control and Prevention
CI	confidence interval
CXR	chest X-ray
DDR	direct digital radiography
DOTS	directly observed treatment, short course
FATA	Federally Administered Tribal Areas
FIND	Foundation for Innovative New Diagnostics
FM	fluorescence microscopy
GCP	good clinical practice
GDMP	good data management practices
GFC	global focus countries
Global Fund	Global Fund to Fight AIDS, Tuberculosis and Malaria
HBC	high TB burden country
HEPA	high efficiency particulate air
HIV	human immunodeficiency virus
IGRA	interferon gamma release assay
JATA	Japan Anti-Tuberculosis Association
JICA	Japanese International Cooperation Agency
k	coefficient of between cluster variation
LED	light-emitting diode
LJ	Löwenstein–Jensen media
LPA	line-probe assay
MDG	Millennium Development Goal
MDR-TB	multidrug-resistant tuberculosis
MGIT	mycobacteria growth indicator tube
MMR	mass miniature radiography
MoH	ministry of health
MRCG	Medical Research Council Unit, The Gambia
MTB	*Mycobacterium tuberculosis*
NTM	nontuberculous mycobacteria
NTLP	National Tuberculosis and Leprosy Program
NTP	national tuberculosis programme
NTRL	national TB reference laboratory
ODPC	Office of Disease Prevention and Control

P:N	prevalence:notification
PIN	personal identification number
PNB	para-nitrobenzoic acid
PPS	probability proportional to size
RIF	rifampin
RIT	Research Institute of Tuberculosis
SDG	Sustainable Development Goal
SOP	standard operating procedure
SRL	supranational reference laboratory
TB	tuberculosis
TBMU	TB management unit
UI	uncertainty interval
UN	United Nations
UNAIDS	Joint United Nations Programme on HIV/AIDS
US	United States
WHO	World Health Organization
ZIMSTAT	Zimbabwe National Statistics Agency
ZN	Ziehl-Neelsen

PART I

An overview of the 25 surveys implemented 2007–2016

Examining chest X-rays in the field during the 2010–2011 national TB prevalance survey of Ethiopia
Photo credit: Yasunori Ichimura

Chapter 1
Introduction

This book is about national surveys of the prevalence of tuberculosis (TB) disease that were completed between 2007 and 2016. During this 10-year period there was an unprecedented national, regional and global effort to implement such surveys. Particular attention was given to a group of 22 global focus countries (GFCs) in Asia and Africa that, in 2007, were selected by the World Health Organization (WHO) Global Task Force on TB Impact Measurement *(1)*.

Between 2007 and the end of 2016, 24 countries implemented a total of 25 national TB prevalence surveys[1] using methods recommended by WHO *(2)*; the 24 countries comprised 18 of the 22 GFCs, and six other countries. The book documents the survey methods used, results and their implications, successes achieved, challenges faced, and lessons learned for future surveys. It ends with a discussion of prevalence surveys post-2016.

This opening chapter explains the rationale for conducting national TB prevalence surveys; provides a historical overview of where, when and how they were implemented in the years up to 2007; and describes why prevalence surveys in 22 GFCs became one of three strategic areas of work pursued by the WHO Global Task Force on TB Impact Measurement between 2007 and 2015. It ends with a summary of the 25 national TB prevalence surveys that were completed between 2007 and 2016, which are the subject of the rest of the book.

1.1 Why are national TB prevalence surveys needed?

Dr Robert Koch announced that he had discovered *Mycobacterium tuberculosis (M. tuberculosis)* as the cause of TB on 24 March 1882, an event now marked annually as World TB Day *(3)*. At that time, TB was one of the leading causes of death in European countries, with cause-of-death data from national vital registration (VR) systems showing mortality rates of over 100 per 100 000 population per year. National laws that made reporting of TB cases compulsory were introduced in these and various other industrializing (and now high-income) countries. In combination, these national notification and VR systems have allowed the burden of TB disease (in terms of numbers of cases and deaths each year) to be reliably monitored using routine health information systems for several decades, with a few time series covering a span of more than 100 years (**Fig. 1.1**).

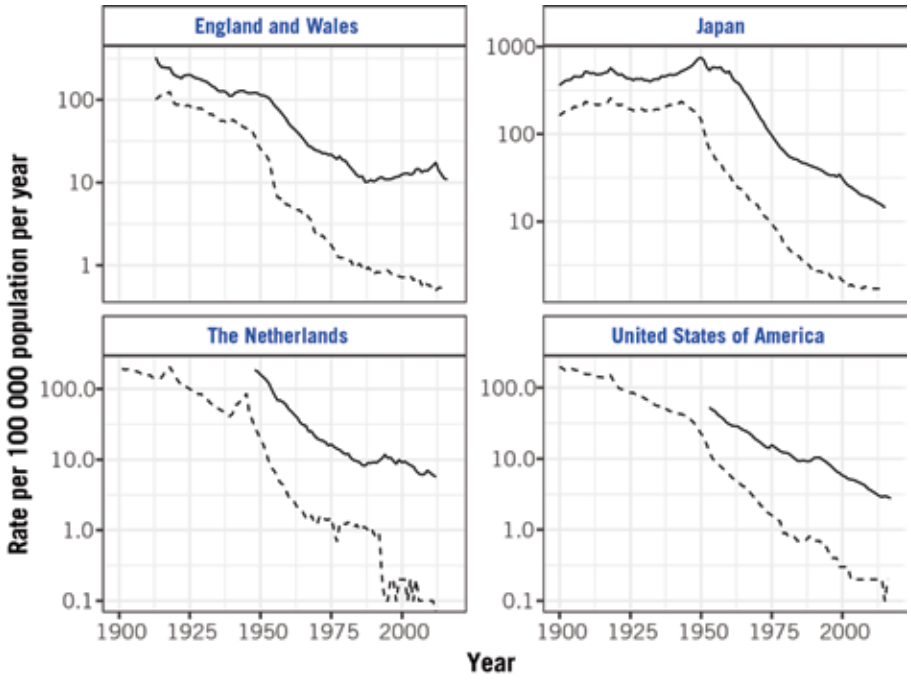
The ultimate goal is that all countries can reliably track their TB epidemics using national notification and VR systems. However, although all countries have national notification systems for TB, and report notification data to WHO on an annual basis *(4)*, the number of notified cases each year is generally not a good proxy for the actual number of new cases. This is due to (1) underreporting, especially in countries with large private sectors or in which people with TB seek care in public facilities that are not linked to the national TB programme (NTP) and associated reporting systems; and (2) underdiagnosis, especially in countries where there are geographic or financial barriers to seeking health care. In the early 2000s, national VR systems of high quality and coverage had not been established in many parts of the world (including most countries with a high burden of TB), and there was limited progress between 2000 and 2012 *(5)*.

In the absence of national notification and VR systems of high quality and coverage, national population-based surveys of the prevalence of TB disease provide an alternative way of measuring the burden of TB disease. Such surveys allow direct measurement of the number of TB cases in the population at a given point in time, and the distribution of cases by age and sex. Repeat surveys allow assessment of trends, and of the impact of interventions to reduce the burden of disease in the period since the last survey. Other benefits of surveys include documentation of health care seeking behaviour in the public and private sectors; identification of reasons why people with TB were not diagnosed before the survey or officially reported

[1] The country that implemented two surveys was the Philippines.

Fig. 1.1

Trends in TB incidence (solid line) and TB mortality (dashed line) based on data from national notification and national VR systems, selected countries



VR: vital registration.
Sources: Public Health England (2017) (*6*), The Research Institute of Tuberculosis/JATA (2018) (*7*), National Institute for Public Health and the Environment, Ministry of Health, Welfare and Sport (2016) (*8*) and Centers for Disease Control and Prevention (*9*).

to national authorities (or both); and development or improvement of strategies and interventions for TB case finding, diagnosis and treatment.

1.2 The first wave of national TB prevalence surveys: 1953–1960

The first national TB prevalence surveys were implemented in the 1950s, in East Asia and Africa (Fig. 1.2).[1]

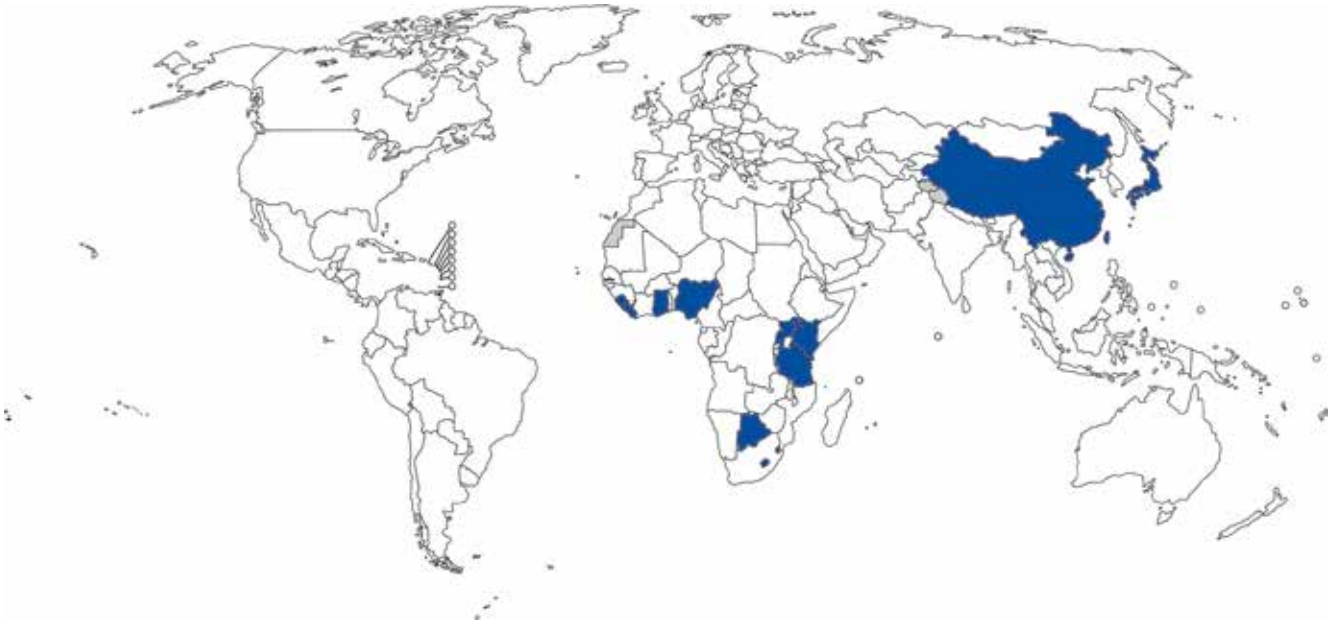
The first survey was implemented in Japan in 1953, followed by a repeat survey in 1958 *(12-14)*. These surveys used mass miniature radiography (MMR) as an initial screening tool for pulmonary TB; diagnosis was based on smear microscopy and culture. MMR was developed in 1936, and free-of-charge MMR was one of 12 interventions for TB control recommended by the first World Health Assembly in July 1948 *(15)*. Results from the first survey in Japan alarmed national authorities by revealing a high prevalence of radiologically active and bacteriologically confirmed cases (3.4% and 0.75% of the population, respectively). They also showed that most cases (79%) had not been diagnosed before the survey and were in those aged 30 years or over. As a result, a systematic programme of MMR screening, previously restricted to those under the age of 30 years, was expanded to cover the whole population. Registration and case-holding systems were also introduced.

WHO implemented a series of surveys in 12 African countries between 1955 and 1960 *(16)*. Of these, 11 were national surveys: Basutoland (Lesotho), Bechuanaland (Botswana), Gambia, Ghana, Liberia, Nigeria, Sierra Leone, Swaziland (Eswatini), Tanganyika (United Republic of Tanzania), Uganda and Zanzibar. A survey was also implemented in Kenya, excluding Nairobi and the country's northern province. Survey investigations were based on a technical guide published by WHO *(17)*, and included tuberculin skin tests, chest X-rays and sputum examination by direct microscopy. In five countries, X-ray examination was not possible because the necessary equipment was not available. Culture examinations were generally done for all smear-positive specimens and a random sample of smear-negative specimens. The estimated prevalence of bacteriologically

[1] A full historical listing of all surveys implemented up to 2012 in Asia is provided in Onozaki et al. (2015) *(10)*. For surveys in Africa, a listing is provided in WHO (2007) *(11)*.

Fig. 1.2

Countries that implemented a national TB prevalence survey, 1953–1960



Grey, not applicable.

confirmed TB was 1.5%, with men (2%) having a higher prevalence than women (0.7%); however, there were proportionally more smear-positive cases in women (0.4%) than in men (0.5%).

Pakistan conducted a survey in 1959, but from the available information it is not clear whether this was a national or subnational survey *(18)*. In 1955–1959, India carried out subnational TB prevalence surveys *(19)*.

1.3 National TB prevalence surveys in Asia in the 1960s and 1970s

In the 1960s and 1970s, 14 countries implemented a total of 19 national TB prevalence surveys (Fig. 1.3). Multiple surveys were implemented in Japan (three), the Republic of Korea (three) and Thailand (two).[1]

After surveys in 1953 and 1958, repeat surveys were implemented in Japan in 1963, 1968 and 1973. These showed a rapid reduction in the number of cases, with an annual decline estimated at about 10% per year up to the late 1970s – one of the fastest national declines in TB disease burden ever recorded (Fig. 1.1).

[1] A full historical listing of all surveys implemented up to 2012 in Asia is provided in Onozaki et al. (2015) *(10)*. For surveys in Africa, a listing is provided in WHO (2007) *(11)*.

Elsewhere in the WHO Western Pacific Region, national surveys were implemented in China (1979), Malaysia (1970), the Republic of Korea (1965, 1970 and 1975), Samoa (1975) and Singapore (1975).

Outside the WHO Western Pacific Region, surveys were conducted in Bangladesh (1964), Indonesia (1979–1982), Iraq (1970), Libya (1976), Myanmar (1972), Netherlands (1970), Sri Lanka (1970) and Thailand (1960–1964 and 1977). Most of these surveys used MMR for screening, and sputum and culture examination for diagnosis.

Several subnational surveys in south India were also implemented under the leadership of the National Tuberculosis Institute in Bangalore from 1961 to 1968 *(20)*.

1.4 The 1980s and 1990s: A period of few national TB prevalence surveys

Few national TB prevalence surveys were implemented in the 1980s and 1990s; six countries implemented a total of 11 surveys (Fig. 1.4).[1]

In Asia, the series of surveys at 5-year intervals that started in the Republic of Korea in 1965 was continued,

Fig. 1.3

Countries that implemented a national TB prevalence survey in the 1960s and 1970s

Grey, not applicable.

with a further four surveys completed in 1980, 1985, 1990 and 1995. The survey in 1995 was the last to be carried out in the country. The other five countries in Asia that implemented surveys were Bangladesh (1987), China (1984 and 1990), Pakistan (1987), Philippines (1981 and 1997) and Thailand (1991–1992).

Reasons for the relatively small number of surveys included:

- In 1974, WHO recommended that MMR should not be used for TB case finding *(21)*. This recommendation affected investments in mobile radiographic equipment, and NTPs prioritized bacille Calmette-Guérin (BCG) vaccination and the diagnosis and treatment of people seeking medical care over systematic screening programmes in the general population.
- There were declines in disease burden in countries that had previously implemented surveys. In countries such as Japan, the Republic of Korea, Singapore and Sri Lanka, these declines meant that increasingly large sample sizes would be required, which were prohibitive for logistical and cost reasons.
- In some countries, increased urbanization and improved living conditions led to reduced willingness among the general population to participate in surveys. For example, in the Republic of Korea, where seven national surveys were conducted every 5 years from 1965 to 1995, urban participants progressively increased from 34% (1965) to 74% (1995) of the total, and survey participation rates declined from 96% (1965) to 87% (1995) *(22, 23)*. Similarly, in the five national surveys in Japan from 1953 to 1973, participation declined from 99% to 89% *(24)*.
- In a growing number of countries, the quality and coverage of routine TB surveillance data improved. These data provided most if not all of the information needed to monitor the TB epidemic and inform TB policy, strategy and planning.

1.5 The early to mid 2000s: Few national TB prevalence surveys, but growing interest in them

From 2000 to 2006, six surveys that used a variety of methods were implemented (Table 1.1).

Fig. 1.4

Countries that implemented a national TB prevalence survey in the 1980s and 1990s

Grey, not applicable.

Only two of these surveys (China, 2000 and Cambodia, 2002) used both smear microscopy and culture for diagnostic testing, and achieved a sufficiently high participation rate for results to be nationally representative. The surveys in Eritrea (2004) and Indonesia (2004) used smear microscopy only *(25);* the survey in Malaysia (2003)had a very low participation rate in urban areas; and the survey in Thailand collected sputum samples only from those who reported symptoms, owing to delays in reading MMRs.

Recognizing the value of updated guidance and greater standardization in survey methods, the WHO Regional Office for the Western Pacific took the initiative to develop a handbook on national TB prevalence surveys *(11)*; this later became known as the *red book*. Recommendations drew heavily on the 2002 survey in Cambodia.

Although the number of national TB prevalence surveys implemented during this period was small, there was growing interest in them. This occurred in the context of a series of developments that started in the early to mid 1990s:

- The World Health Assembly agreed the first-ever targets for global TB control in 1991 *(26)*. The targets were to detect 70% of new smear-positive pulmonary TB cases and to successfully treat 85% of these cases by 2000, a target date that was later reset to 2005 *(27)*. The first indicator became commonly known as the case detection rate. The numerator was the annual number of new cases of smear-positive TB notified to national authorities in a year, and the denominator was an estimate of the incidence of smear-positive TB (i.e. the number of new cases of smear-positive TB) in the same year.
- WHO declared TB a global health emergency in 1993 *(28)*.
- In 1994, WHO published a framework for effective TB control *(29)*. This was subsequently branded as the DOTS strategy, which was WHO's recommended approach to TB control until the end of 2005.[1] The DOTS strategy had five components,[2]

[1] The DOTS strategy was succeeded by the Stop TB Strategy (*30*) in 2006 (which included an updated version of DOTS as its first component) and by the End TB Strategy in 2016.

[2] The five components of the DOTS strategy were; political commitment; diagnosis by quality-assured sputum smear microscopy; standardized short-course chemotherapy with direct observation of treatment (DOT); a regular and uninterrupted supply of high-quality anti-TB drugs; and a standardized system for recording and reporting of cases and their treatment outcomes.

Table 1.1

National TB prevalence surveys implemented in 2000–2006

Country	Year	Specific survey characteristics
China	2000	The last national survey to include all age groups (>3 months of age); fluoroscopy used for screening; smear microscopy and culture used for diagnostic testing.
Cambodia	2002	Screening done using an interview about symptoms and direct CXR with onsite full-size film development using portable equipment; smear microscopy and culture used for diagnostic testing.
Malaysia	2003	Symptom screening done at home and CXR screening at a health facility; smear microscopy and culture used for diagnostic testing; survey results were not usable owing to a low participation rate in urban areas.
Eritrea	2004	Sputum smear specimens taken from all participants but no CXR screening; smear microscopy used for diagnostic testing (no culture).
Indonesia	2004	Implemented as part of a national health demographic survey. Sputum specimens taken from any participant reporting a productive cough of any duration; no CXR screening; smear microscopy used for diagnostic testing (no culture).
Thailand	2006	An interview about symptoms and MMR were used for screening. Survey results were not usable because sputum samples were not collected from participants who had an abnormal MMR but did not report symptoms, due to delays in reading MMRs and providing feedback about results.

CXR: chest X-ray; MMR: mass miniature radiography.

and its main aim was to achieve the global targets of a 70% case detection rate and an 85% treatment success rate for smear-positive pulmonary TB cases. By 2000, almost all WHO Member States had adopted the DOTS strategy *(31)*.

- In 1999, TB was declared a crisis in the WHO Western Pacific Region. In response, WHO established the Stop TB Special Project, which aimed to halve 2000 levels of TB prevalence and mortality by 2010. This was the first time that a regional target for TB prevalence had been set *(32)*.
- The United Nations (UN) Millennium Development Goals (MDGs) were adopted by all UN Member States in 2000 *(33)*. Targets were defined for each of the eight MDGs. One of the targets under MDG 6 was that the TB incidence rate (new cases per 100 000 population per year) should be declining by 2015. The MDG framework also included four other TB indicators: prevalence per 100 000 population, the mortality rate, the case detection rate and the treatment success rate.
- In the context of the MDGs, regional targets set in the WHO Western Pacific Region and a resolution passed at a summit of the Group of Eight (G8) countries in Okinawa, Japan, the Stop TB Partnership set global targets to halve TB prevalence and mortality (per 100 000 population) by 2015 compared with levels in 1990 *(34)*. This was the first time that a global target for TB prevalence was set.

From 2000 until 2015, national, regional and global efforts in TB control focused on achievement of the targets set by the World Health Assembly, the UN and the Stop TB Partnership.

Up to 2005, the greatest attention was given to the World Health Assembly targets of a 70% case detection and 85% treatment success rate. There was considerable interest in estimates of TB incidence, because it was the denominator of the first target.

After a series of consultations, the first estimates of TB incidence produced by WHO for the national, regional and global levels were for 1997 *(35)*. Subsequently, WHO published updated estimates annually in its global TB report. Given that notification data in many countries were not a good proxy for TB incidence (owing to underreporting and underdiagnosis), and in the frequent absence of other direct measurements of TB disease (e.g. prevalence surveys or cause-of-death data from national VR systems), these estimates relied heavily on two things: expert opinion about the gap between notifications and the true level of TB incidence, and tuberculin survey data.

National authorities, including ministries of health and their NTPs whose performance in making progress towards the World Health Assembly targets was being regularly assessed and reported, became increasingly interested in improving the evidence available to inform estimates of TB incidence, in particular through the implementation of a national TB prevalence survey. This interest was reinforced by growing evidence and

consensus that methods used to estimate TB incidence from tuberculin survey data were problematic *(36, 37)*; the inclusion of TB prevalence as an MDG indicator; the setting of regional and global targets for reductions in TB prevalence; and the launch of the Stop TB Strategy.

1.6 The decade 2007–2016: a period of unprecedented national, regional and global efforts to implement national TB prevalence surveys

In 2006, the DOTS strategy was succeeded by the Stop TB Strategy *(30)* which, in line with the MDGs, had an end date of 2015. The new strategy had three targets for 2015, all of which were related to reductions in TB disease burden. The targets were that TB incidence should be falling (in line with the TB target under MDG 6), and that 1990 levels of TB prevalence and mortality (per 100 000 population) should be halved by 2015 (thus incorporating the targets that had been set by the Stop TB Partnership for the MDG indicators of prevalence and mortality). From 2006 to 2015, efforts in TB control at national, regional and global levels were focused on achieving the three "impact" targets of the Stop TB Strategy.

In June 2006, WHO established a Global Task Force on TB Impact Measurement *(1)*. The main aim of the Task Force was to ensure that assessment of whether the 2015 targets were achieved at global, regional and national levels was robust, rigorous and consensus-based *(38)*. After its first meeting in 2006, which focused on a review of available methods to estimate TB disease burden *(39)*, the second meeting in December 2007 was used to discuss and reach agreement on strategic areas of work to be pursued by the Task Force between 2008 and 2015. Three strategic areas of work were defined: strengthening of routine surveillance systems (notification and VR) in all countries; implementing national TB prevalence surveys in 22 GFCs; and periodic review of the methods used to translate surveillance and survey data into estimates of TB disease burden *(40)*.

The 22 GFCs for national TB prevalence surveys (13 in Africa and 9 in Asia) were selected based on four major

Table 1.2

The four groups of criteria used to identify countries in which national surveys of the prevalence of TB disease could be justified in the period up to 2015

Group of criteria	Explanation
Group 1 →	
1. Estimated prevalence of smear-positive TB ≥100 per 100 000 population *and* 2. Accounts for ≥1% of the estimated total number of smear-positive TB cases globally *and* 3. CDR for smear-positive TB ≤50% or >100%	• Major contribution to the global burden of TB disease. Sample size small enough to make surveys feasible in terms of cost and logistics. • Excludes countries whose contribution to the global burden of TB disease is insignificant for the purposes of global and regional assessments of burden and impact. • CDR ≤50% or >100% indicates weak reporting systems and problematic TB estimates, respectively.
Group 2 →	
1. Estimated prevalence of smear-positive TB ≥70 per 100 000 population *and* 2. Accounts for ≥1% of the estimated total number of smear-positive TB cases globally *and* 3. Estimated HIV prevalence rate in the adult population (15–49 years) ≥1%	• Less stringent criteria for the TB prevalence rate, but incorporates countries with high HIV prevalence and therefore where there is potential for a rapid increase in TB incidence and prevalence rates.
Group 3 →	
1. Estimated prevalence of smear-positive TB ≥200 per 100 000 population *and* 2. Accounts for ≥0.5% of the estimated total number of smear-positive TB cases globally	• Less stringent criteria for a country's contribution to the global burden of TB disease, but incorporates countries with particularly high TB prevalence per 100 000 population.
Group 4 →	
1. Nationwide survey implemented between 2000 and 2007 *or* 2. Nationwide survey planned before 2010	• Prior survey data allow monitoring of trends. • High motivation of NTP to conduct a survey.

CDR: case detection rate; HIV: human immunodeficiency virus; NTP: national TB programme.
When the criteria were applied in December 2007, the sources of data used were WHO (2007) (*41*), the WHO global TB database and UNAIDS/WHO (2006) (*42*).

Table 1.3

The 22 GFCs for TB prevalence surveys selected by the WHO Global Task Force on TB Impact Measurement

Region and country	Criteria met (group number as defined in Table 1.2)	High-burden country?[a]	Data from baseline survey conducted between around 1990 and 2008?
WHO African Region			
Ethiopia	1,3	Yes	No
Ghana	1,2	No	No
Kenya	2,4	Yes	No
Malawi	1,2,3,4	No	No
Mali	1,2,3,4	No	No
Mozambique	1,2,3	Yes	No
Nigeria	1,2,3,4	Yes	No
Rwanda	1,2,3	No	No
Sierra Leone	1,2,3	No	No
South Africa	2,3	Yes	No
Uganda	1,2,3,4	Yes	No
United Republic of Tanzania	1,2,3,4	Yes	No
Zambia	2,3	No	No
WHO Eastern Mediterranean Region			
Pakistan	1,4	Yes	Yes (1987)
WHO South-East Asia Region			
Bangladesh	4	Yes	Yes (2008–2009)
Indonesia	4	Yes	Yes (2004)
Myanmar	4	Yes	Yes (1994)
Thailand	2,4	Yes	Yes (1991, 2006)
WHO Western Pacific Region			
Cambodia	2,3	Yes	Yes (2002)
China	4	Yes	Yes (1990, 2000)
Philippines	4	Yes	Yes (1981, 1997, 2007)
Viet Nam	4	Yes	Yes (2007)

GFC: global focus country; WHO: World Health Organization.

[a] "High burden" refers to the 22 high TB burden countries (HBCs) that were defined by WHO for the period 1998–2015. The 22 HBCs were the countries that ranked first to 22nd in terms of their estimated number of incident cases of TB per year. In 2015, WHO reviewed and updated the definition and a list of 30 HBCs was defined for the period 2016–2020.

groups of criteria (Table 1.2) and are shown in Table 1.3 *(2)*.

A total of 53 countries met one of the four groups of criteria shown in Table 1.2. There were two major reasons for selecting a subset of 22 GFCs. The first was that providing the necessary technical support to all of the 53 countries would be challenging if not impossible, given the relatively limited expertise at that time in the design and implementation of prevalence surveys at both global and country levels. The second was that, in combination, the GFCs accounted for a substantial share of the estimated number of TB cases in each of the four WHO regions where routine surveillance systems were weakest (i.e. the African, Eastern Mediterranean, South-East Asia and Western Pacific regions).[1]

From the beginning of 2008, substantial efforts were made to design and implement national TB prevalence surveys, and to analyse and report results. At the global level, these efforts were led and coordinated under the

[1] The other two WHO regions – the European Region and the Region of the Americas – already had relatively strong notification and VR systems.

umbrella of the WHO Global Task Force on TB Impact Measurement, and more specifically by a Task Force subgroup on national TB prevalence surveys that was led by WHO staff in the Global Tuberculosis Programme's TB monitoring and evaluation unit.

Examples of key actions, activities and products of the Task Force subgroup on national TB prevalence surveys included:

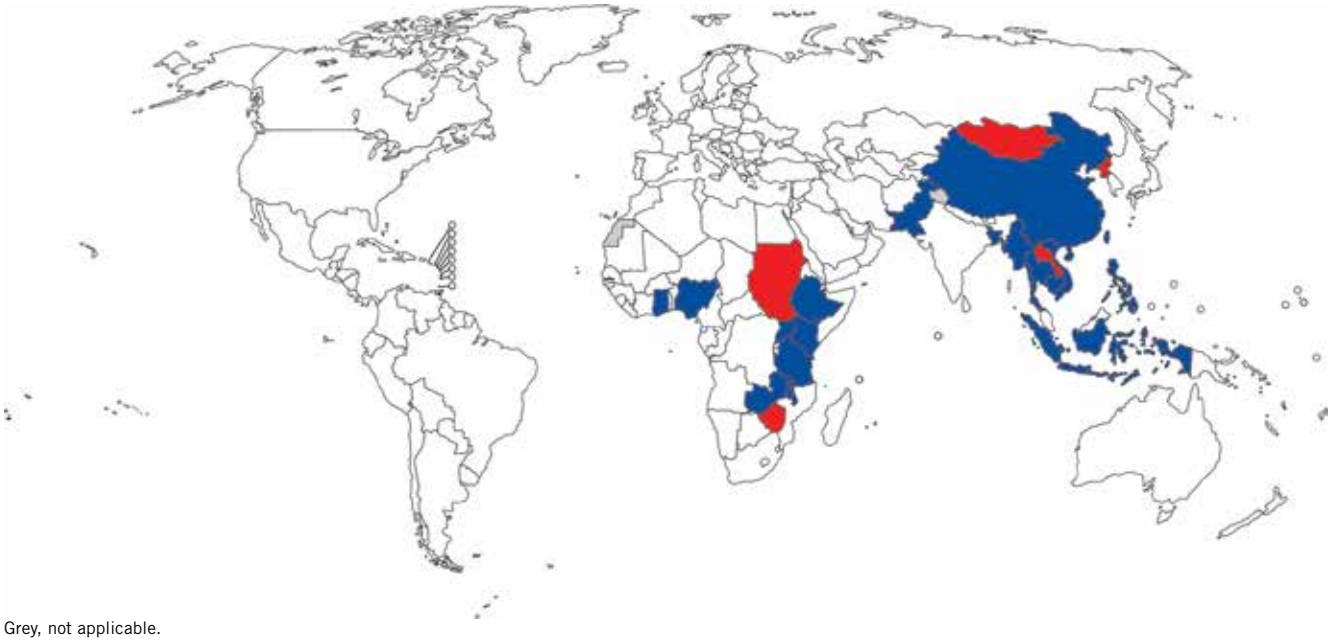
- sending high-level letters from WHO to the ministers of health of each GFC, to explain why the country had been selected as a priority for a national TB prevalence survey and to offer guidance and support from the Task Force;
- organization of multicountry workshops for protocol development;
- development of updated guidance on standardized methods for undertaking national TB prevalence surveys in the form of a handbook, which became known as the *lime book (2)*. This was used as the foundation of all national TB prevalence surveys implemented from 2010 to 2016 and was produced as a major collaborative effort among technical agencies, financial partners and lead investigators involved in surveys implemented in the 1990s and 2000s, with a total of 50 co-authors;
- expert reviews of protocols, using a checklist based on guidance provided in the *lime book (2)*;
- organization of multicountry workshops hosted by countries that had recently launched survey field operations (Ethiopia in October 2010, Cambodia in July 2011 and Ghana in May 2013), to enable a mixture of support for all countries combined with an opportunity to observe a survey at first hand;
- organization of study tours to countries where surveys were being implemented for countries that were in the preparation phase; and
- coordination and provision of technical assistance to all countries, with an emphasis on Asia–Asia, Asia–Africa and Africa–Africa (AA) collaboration.

This global effort reinforced and supported the considerable interest in and commitment to implementing a national TB prevalence survey that had been growing and intensifying in many countries during the early 2000s (including in those outside the list of 22 GFCs).

Fig. 1.5

The 24 countries that implemented a national TB prevalence survey in 2007–2016 and that are the subject of this book

Of the 13 GFCs in Africa, nine completed a survey (blue); all nine GFCs in Asia completed at least one survey (blue). Six other countries completed a survey but were not GFCs (red).



Grey, not applicable.
GFC: global focus country; WHO: World Health Organization.

Table 1.4

The 25 national TB prevalence surveys implemented in 2007–2016, which are the subject of this book

Country	Year of survey	GFC?
Bangladesh	2015–2016	Yes
Cambodia	2010–2011	Yes
China	2010	Yes
Democratic People's Republic of Korea	2016	No
Ethiopia	2010–2011	Yes
Gambia	2012	No
Ghana	2013	Yes
Indonesia	2013–2014	Yes
Kenya	2015–2016	Yes
Lao People's Democratic Republic	2010–2011	No
Malawi	2013–2014	Yes
Mongolia	2014–2015	No
Myanmar	2009–2010	Yes
Nigeria	2012	Yes
Pakistan	2011	Yes
Philippines	2007	Yes
Philippines	2016	Yes
Rwanda	2012	Yes
Sudan	2013–2014	No
Thailand	2012–2013	Yes
Uganda	2014–2015	Yes
United Republic of Tanzania	2012	Yes
Viet Nam	2007	Yes
Zambia	2013–2014	Yes
Zimbabwe	2014	No

GFC: global focus country.

The creation of a new source of financing in 2002, in the form of the Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund), helped to turn this interest and commitment into reality. The Global Fund helped to finance 22 surveys implemented between 2007 and 2016.[1] Domestic resources contributed to funding for 12 surveys,[2] the United States (US) government contributed to funding for nine surveys, and other donors contributed to funding for 13 surveys.

All of this interest and commitment culminated in a decade of unprecedented global, regional and national efforts to implement national TB prevalence surveys, with particular attention to 22 GFCs. The 25 surveys that were implemented in 24 countries in 2007–2016 according to methods set out in the *lime book* are shown in Table 1.4 and Fig. 1.5;[3] they included 18 of the 22 GFCs.[4] For context, Fig. 1.6 shows a timeline of all surveys conducted between the 1950s and 2016.

This book provides comprehensive documentation of the 25 national TB prevalence surveys implemented in 2007–2016 that are listed in Table 1.4. Part I includes cross-cutting chapters: methods (Chapter 2); results and their implications (Chapter 3); successes, challenges and lessons learned (Chapter 4); and a discussion of prevalence surveys post-2016 (Chapter 5). Part II contains 25 country-specific profiles, which provide details about each survey in a standardized format.

The book represents the collective effort and contribution of more than 450 people, with leadership and coordination provided by WHO.

References

1. WHO Global Task Force on TB Impact Measurement [website]. Geneva: World Health Organization; 2019 (https://www.who.int/tb/areas-of-work/monitoring-evaluation/impact_measurement_taskforce/en/, accessed 12 June 2019).
2. Tuberculosis prevalence surveys: a handbook. Geneva: World Health Organization; 2011 (https://apps.who.int/iris/bitstream/handle/10665/44481/9789241548168_eng.pdf, accessed 22 November 2019).
3. Sakula A. Robert Koch: centenary of the discovery of the tubercle bacillus, 1882. Thorax. 1982;37(4):246–51 (https://www.ncbi.nlm.nih.gov/pubmed/6180494, accessed 22 November 2019).
4. Global tuberculosis report. Geneva: World Health Organization; 2018 (https://apps.who.int/iris/bitstream/handle/10665/274453/9789241565646-eng.pdf?ua=1, accessed 22 November 2019).
5. Mikkelsen L, Phillips DE, AbouZahr C, Setel PW, de Savigny D, Lozano R et al. A global assessment of civil registration and vital statistics systems: monitoring data quality and progress. Lancet. 2015;386(10001):1395–406 (https://www.ncbi.nlm.nih.gov/pubmed/25971218, accessed 22 November 2019).

[1] Further details about survey budgets and sources of funding are provided in Chapter 2 (see in particular Table 2.5).

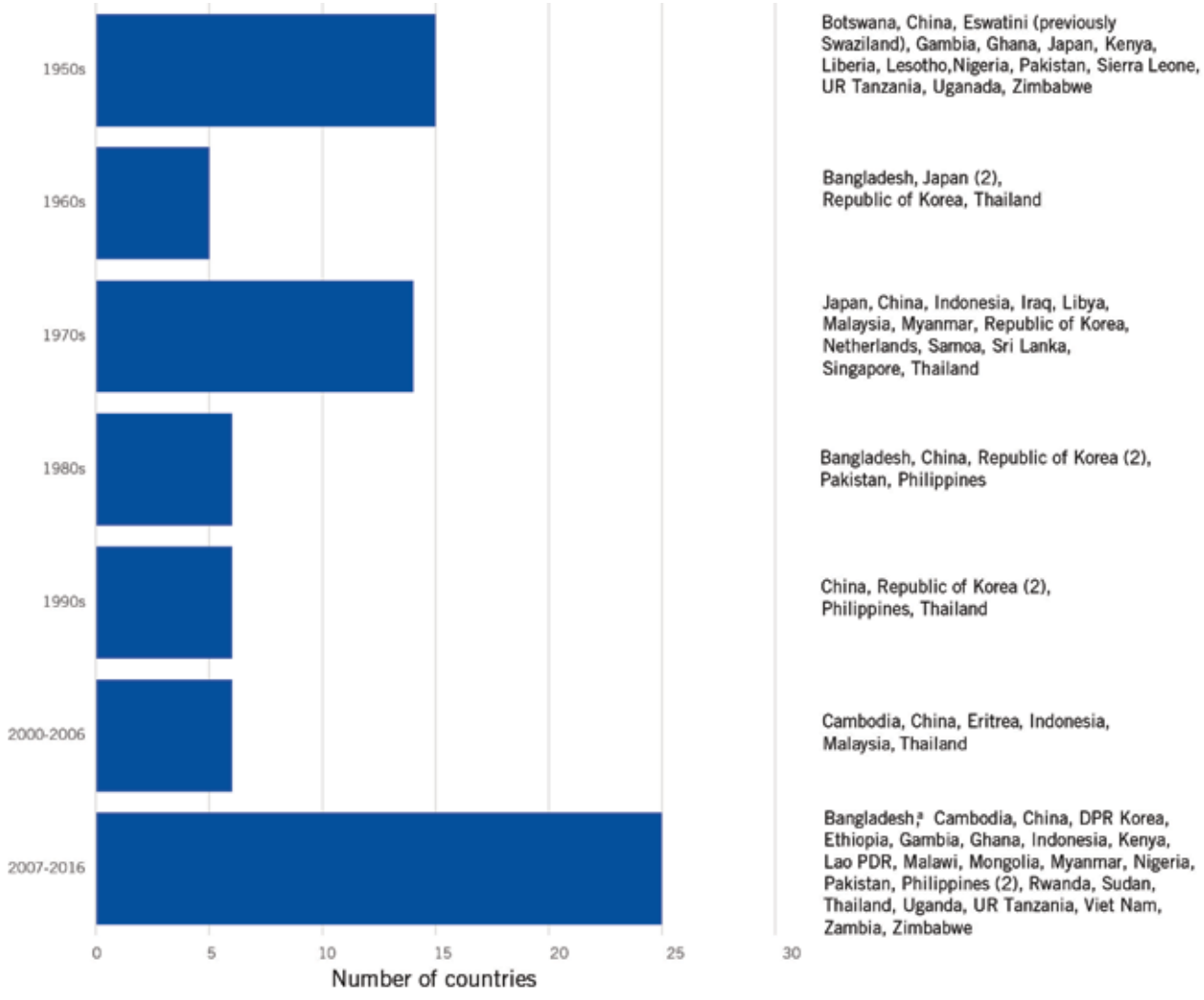
[2] The only survey that relied on domestic funding alone was the one in China.

[3] There was one survey implemented during this period that did not use the screening algorithm recommended in the *lime book*. This was a 2008 survey in Bangladesh, which took sputum samples from the entire eligible population (without screening based on symptoms and chest X-ray). Results appeared to considerably understate the true burden of TB disease, likely probably due to challenges in processing large numbers of samples; this was confirmed by results from the 2015 survey.

[4] The four GFCs that had not implemented a survey by the end of 2016 were Mali, Mozambique, Sierra Leone and South Africa. Mozambique implemented a survey in 2018–2019 and South Africa implemented a survey in 2017–2019.

Fig. 1.6

National surveys of the prevalence of TB disease, 1950–2016



DPR Korea: Democratic People's Republic of Korea; Lao PDR: Lao People's Democratic Republic; UR Tanzania: United Republic of Tanzania

[a] The survey listed is the one in Bangladesh in 2015, which is featured in this book. There was also a survey in 2008, but this did not use the screening and diagnostic algorithm recommended in the *lime book* and for this reason is not counted in the total of 25 surveys.

6. Public Health England. Historical TB notification data tables to end December 2017 (Table no. 1). 2018 (https://www.gov.uk/government/publications/tuberculosis-tb-annual-notifications-1913-onwards, accessed 19 June 2019).
7. Statistics of TB [website]. The Tuberculosis Surveillance Center; 2018 (https://www.jata.or.jp/rit/ekigaku/en/statistics-of-tb/, accessed 19 July 2019).
8. National Institute for Public Health and the Environment; Ministry of Health WaS. Curvekaart tuberculose in Nederland 1901–2015. Netherlands: 2016 (https://www.rivm.nl/documenten/curvekaart-tuberculose-in-nederland1901-2015, accessed 24 July 2019).
9. Centers for Disease Control and Prevention (CDC). Reported tuberculosis in the United States, 2017. Atlanta, GA: US Department of Health and Human Services, CDC; 2018 (https://www.cdc.gov/nchs/nvss/mortality_historical_data.htm, accessed 19 June 2019).
10. Onozaki I, Law I, Sismanidis C, Zignol M, Glaziou P, Floyd K. National tuberculosis prevalence surveys in Asia, 1990–2012: an overview of results and lessons learned. Trop Med Int Health. 2015;20(9):1128–45 (https://www.ncbi.nlm.nih.gov/pubmed/25943163, accessed 22 November 2019).
11. World Health Organization. Assessing tuberculosis prevalence through population-based surveys. Geneva, Switzerland 2007 (https://apps.who.int/iris/handle/10665/206962, accessed 20 November 2019).
12. Yamaguchi M. Survey of tuberculosis prevalence in Japan, 1953. Bull World Health Organ. 1955;13(6):1041–73 (https://www.ncbi.nlm.nih.gov/pubmed/13284568, accessed 22 November 2019).

13. Yamaguchi M, Oka H, Kumabe H, Yosano H. Survey of tuberculosis prevalence in Japan, 1954: trends in tuberculosis from 1953 to 1954. Bull World Health Organ. 1959;21:145–59 (https://www.ncbi.nlm.nih.gov/pubmed/13846395, accessed 22 November 2019).
14. Shimao T. [Surveys of tuberculosis prevalence]. Bull Int Union Tuberc. 1982;57(2):127–33 (https://www.ncbi.nlm.nih.gov/pubmed/6983377, accessed 22 November 2019).
15. First world health assembly. Draft resolution on tuberculosis proposed by the delegation of Czechoslovakia. Geneva: World Health Organization; 1948 (https://apps.who.int/iris/bitstream/10665/98189/1/WHA1_Prog-29_eng.pdf, accessed 6 May 2019).
16. Roelsgaard E, Iversen E, Blocher C. Tuberculosis in tropical Africa. An epidemiological study. Bull World Health Organ. 1964;30:459–518 (https://www.ncbi.nlm.nih.gov/pubmed/14178027, accessed 22 November 2019).
17. Technical guide for tuberculosis survey team. WHO/TUB/Technical Guide/1, Geneva: World Health Organization; 1958 (https://apps.who.int/iris/bitstream/10665/75224/1/WHO_TUB_Techn.Guide_1_1958_eng.pdf, accessed 22 November 2019).
18. Dolin P. WHO report of a visit to Pakistan. December 5–19. Geneva: World Health Organization; 1997.
19. Indian Council of Medical Research. Tuberculosis Sub-Committee. Tuberculosis in India: a sample survey, 1955–58. New Delhi:1959.
20. National Tuberculosis Institute Bangalore. Tuberculosis in a rural population of South India: a five-year epidemiological study. Bull World Health Organ. 1974;51(5):473–88 (https://www.ncbi.nlm.nih.gov/pubmed/4549498, accessed 22 November 2019).
21. WHO expert committee on tuberculosis: ninth report. WHO Technical Report Series, No. 552, Geneva: World Health Organization; 1974 (https://apps.who.int/iris/bitstream/10665/41095/1/WHO_TRS_552_eng.pdf, accessed 19 May 2019).
22. Hong YP, Kim SJ, Lew WJ, Lee EK, Han YC. The seventh nationwide tuberculosis prevalence survey in Korea, 1995. Int J Tuberc Lung Dis. 1998;2(1):27–36 (https://www.ncbi.nlm.nih.gov/pubmed/9562108, accessed 22 November 2019).
23. Ministry of Health and Social Affairs, Korean National Tuberculosis Association. Report on the tuberculosis prevalence survey in Korea. 1965.
24. Shimao T. [Tuberculosis prevalence survey in Japan]. Kekkaku. 2009;84(11):713–20 (https://www.ncbi.nlm.nih.gov/pubmed/19999593, accessed 22 November 2019).
25. Sebhatu M, Kiflom B, Seyoum M, Kassim N, Negash T, Tesfazion A et al. Determining the burden of tuberculosis in Eritrea: a new approach. Bull World Health Organ. 2007;85(8):593–9 (https://www.ncbi.nlm.nih.gov/pubmed/17768517, accessed 22 November 2019).
26. Resolution WHA44.8: tuberculosis control programme, 3rd ed, Handbook of resolutions and decisions of the World Health Assembly and the Executive Board, Geneva, World Health Organization. 1993 (https://www.who.int/tb/publications/tbresolution_wha44_8_1991.pdf?ua=1, accessed 22 November 2019).
27. Stop tuberculosis initiative. Report by the director-general. Fifty-third world health assembly, Geneva: World Health Organization; 2000 (https://apps.who.int/iris/handle/10665/260193, accessed 22 November 2019).
28. TB: a global emergency, WHO report on the TB epidemic (WHO/TB/94.177) [website]. Geneva 1994 (https://apps.who.int/iris/handle/10665/58749, accessed 21 June 2019).
29. Framework for effective TB control. WHO/TB/1994.179, Geneva: World Health Organization; 1994 (https://apps.who.int/iris/handle/10665/58717, accessed 22 November 2019).
30. Raviglione MC, Uplekar MW. WHO's new Stop TB Strategy. Lancet. 2006;367(9514):952–5 (https://www.ncbi.nlm.nih.gov/pubmed/16546550, accessed 22 November 2019).
31. Global tuberculosis report. Geneva: World Health Organization; 2014 (https://apps.who.int/iris/bitstream/10665/137094/1/9789241564809_eng.pdf?ua=1, accessed 22 November 2019).
32. van Maaren P, Tomas B, Glaziou P, Kasai T, Ahn D. Reaching the global tuberculosis control targets in the Western Pacific Region. Bull World Health Organ. 2007;85(5):360–3 (https://www.ncbi.nlm.nih.gov/pubmed/17639220, accessed 22 November 2019).
33. Millennium development goals [website]. (https://www.un.org/millenniumgoals/, accessed 3 May 2019).
34. Global tuberculosis report. Geneva: World Health Organization; 2006 (https://apps.who.int/iris/bitstream/handle/10665/144567/9241563141_eng.pdf, accessed 12 June 2019).
35. Dye C, Scheele S, Dolin P, Pathania V, Raviglione MC. Consensus statement. Global burden of tuberculosis: estimated incidence, prevalence, and mortality by country. WHO Global Surveillance and Monitoring Project. JAMA. 1999;282(7):677–86 (https://www.ncbi.nlm.nih.gov/pubmed/10517722, accessed 22 November 2019).
36. van Leth F, van der Werf MJ, Borgdorff MW. Prevalence of tuberculous infection and incidence of tuberculosis: a re-assessment of the Styblo rule. Bull World Health Organ. 2008;86(1):20–6 (https://www.ncbi.nlm.nih.gov/pubmed/18235886, accessed 22 November 2019).
37. Styblo K. The relationship between the risk of tuberculous infection and the risk of developing infectious tuberculosis. Bull Int Union Tuberc Lung Dis. 1985;60:117–9.
38. Global tuberculosis report. Geneva: World Health Organization; 2015 (https://apps.who.int/iris/bitstream/handle/10665/191102/9789241565059_eng.pdf, accessed 12 June 2019).
39. Dye C, Bassili A, Bierrenbach AL, Broekmans JF, Chadha VK, Glaziou P et al. Measuring tuberculosis burden, trends, and the impact of control programmes. Lancet Infect Dis. 2008;8(4):233–43 (https://www.ncbi.nlm.nih.gov/pubmed/18201929, accessed 22 November 2019).
40. TB impact measurement policy and recommendations for how to assess the epidemiological burden of TB and the impact of TB control. Stop TB policy paper no. 2, Geneva: World Health Organization; 2009 (https://apps.who.int/iris/bitstream/handle/10665/44231/9789241598828_eng.pdf, accessed 22 November 2019).
41. Global tuberculosis control: surveillance, planning, financing : WHO report 2007. Geneva: World Health Organization; 2007 (https://apps.who.int/iris/handle/10665/43629, accessed 22 November 2019).
42. UNAIDS, World Health Organization. 2006 report on the global AIDS epidemic. Geneva: UNAIDS and World Health Organization; 2006 (https://data.unaids.org/pub/report/2006/2006_gr_en.pdf, accessed 22 November 2019).

Chapter 2
Methods

Background

Guidance on national surveys of the prevalence of TB disease was published by WHO in 2007 *(1)* and 2011 *(2)*, with the 2011 edition becoming known as the *lime book*. The 2011 handbook was a major collaborative effort of technical agencies, financial partners and lead investigators involved in surveys implemented in the 1990s and 2000s, and had a total of 50 co-authors. Examples of important changes in the 2011 edition were a definitive recommendation on which screening strategy to use (as opposed to the first edition, which provided four options); improved guidance on sampling design, data management and analysis, and reporting of survey results; a new chapter on repeat surveys; and more country case studies from recent surveys to illustrate what the guidance meant in practice.

The national surveys featured in this book are the 25 surveys implemented between 2007 and 2016 that followed the methods set out in the *lime book*.[1] This chapter provides an overview of the key methods used, structured according to 13 major topics: survey objectives, eligibility criteria, definition of a prevalent survey TB case, screening and diagnostic testing strategies, sampling design, field operations, additional testing for HIV infection and drug susceptibility, central-level activities, data management and analysis, additional studies, reporting and dissemination of results, ethics approval, and budgeting and financing.

2.1 Survey objectives

The primary objective of all national TB prevalence surveys implemented in the period 2007–2016 was to estimate the burden of disease caused by TB; specifically, the national prevalence of smear-positive and bacteriologically positive pulmonary TB among the general population aged 15 years and above.[2] Over time, increasing emphasis was given to the prevalence of bacteriologically confirmed TB, especially following a 2013 update to WHO-recommended case definitions, and associated recording and reporting of cases *(3)*.

Other objectives included measuring trends in the burden of disease caused by TB (e.g. the surveys in Cambodia, China, Myanmar and the Philippines, which were repeat surveys); and to use survey results, alongside an in-depth analysis of surveillance and programmatic data, as the basis for a comprehensive update of estimates of disease burden (incidence and mortality as well as prevalence).

Most surveys implemented in the period 2007–2016 also collected data on the health care seeking behaviour of symptomatic participants and TB cases, to assess whether care had been sought and, if so, where (e.g. in the public or private health care sectors, and in which types of facilities or services). Some surveys further investigated reasons why cases were not diagnosed before the survey, and the extent to which people with TB were being treated by health care providers that were not linked to the NTP. All surveys collected data on those who were on (or had a past history of) anti-TB treatment at the time of the survey, and on the type of health facility in which treatment was provided. These data were used to evaluate case finding and care policies, as well as the performance of routine TB surveillance.

[1] Only one national survey implemented over the period 2007–2016 was not included. This was the 2008 survey in Bangladesh, which did not use the screening strategy recommended in the *lime book*. Instead, sputum samples were taken from all individuals considered eligible based on age and residency.

[2] The Philippines used a 10-year-old eligibility threshold for its 2007 survey.

Table 2.1

Eligibility criteria to participate in a national TB prevalence survey, 2007–2016

Country	Year	Age of eligibility (years)	Residency criteria
Bangladesh	2015–2016	≥15	Lived in the cluster for ≥2 weeks before the census
Cambodia	2010–2011	≥15	Lived in the household for ≥2 weeks before the census
China	2010	≥15	Lived in the household for ≥6 months before the census
DPR Korea	2015–2016	≥15	Registered in the living administrative unit for ≥2 weeks before the census
Ethiopia	2010–2011	≥15	Permanent residents who stayed in the household for ≥1 night in the 14 days before the census, and temporary visitors who stayed in the household for ≥14 days before the census
Gambia	2011–2013	≥15	Residents who spent ≥1 night in the household in the 4 weeks before the census day; visitors who arrived in the household ≥4 weeks before the census
Ghana	2013	≥15	Permanent residents who lived in the household for ≥1 day in the past 14 days, or visitors who lived in the household for ≥7 days in the past 14 days
Indonesia	2013–2014	≥15	Lived in the household for ≥1 month before the census
Kenya	2015–2016	≥15	Lived in the selected cluster for ≥30 days before the census
Lao PDR	2010–2012	≥15	Slept in the household for 14 days before the census
Malawi	2013–2014	≥15	Slept in the household for ≥14 days before the census
Mongolia	2014–2015	≥15	Slept in the household for 14 days before the census
Myanmar	2009–2010	≥15	Lived in the household for ≥2 weeks before the census
Nigeria	2012	≥15	Slept in the household for ≥14 days before the census
Pakistan	2010–2011	≥15	Slept in the household the night before the census
Philippines	2007	≥10	No residency criteria
Philippines	2016	≥15	Lived in the household for ≥2 weeks before the census
Rwanda	2012	≥15	Lived in the household for ≥1 month before the interview
Sudan	2013–2014	≥15	Household members resident in the selected household for the past 6 months, and visitors who spent ≥3 weeks in the household before the census
Thailand	2012–2013	≥15	Permanent residents based on household registration, or temporary residents or nonresidents who had slept in the household for ≥2 weeks before the census
Uganda	2014–2015	≥15	Permanent residents who stayed ≥1 night in the household in the past 2 weeks; temporary visitors who arrived ≥2 weeks before census
UR Tanzania	2011–2012	≥15	Slept in the household for 2 weeks before the census
Viet Nam	2006–2007	≥15	Lived in the household for ≥3 months before the census
Zambia	2013–2014	≥15	Slept in the household 24 hours before the census
Zimbabwe	2014	≥15	Permanent residents who had slept ≥1 night in the 14 days before the census; non-residents who had slept in the household for ≥14 days before the census

DPR Korea, Democratic People's Republic of Korea; Lao PDR, Lao People's Democratic Republic; UR Tanzania, United Republic of Tanzania.

2.2 Eligibility criteria

Eligibility to participate in a national TB prevalence survey was based on two criteria: age and residency (Table 2.1). Of the 25 surveys implemented in the period 2007–2016, 24 used the age criterion recommended in the *lime book* (i.e. individuals aged ≥15 years).[1] The exception was the 2007 survey in the Philippines (implemented before the publication of WHO guidance on national TB prevalence surveys), in which all those aged 10 years and above were considered eligible. In most surveys, a resident was defined as someone who had lived in the household for

[1] Diagnosis of TB among children is difficult with the diagnostic tools used in prevalence surveys. For example, it is hard for children to produce sputum samples (especially given the paucibacillary nature of TB in children) and chest X-rays are not suitable for use in healthy children with a low risk of TB disease. A further problem is the larger sample size needed to estimate the number of cases among children.

at least 2–4 weeks at the time of the survey census.[1] The exceptions were the surveys in Pakistan and Zambia (which classified a resident as someone who had slept in the household the night before the census), and those in China (6 months residency), Sudan (6 months residency) and Viet Nam (3 months residency).

2.3 Definition of a prevalent survey TB case

In 2007, a prevalent case of TB was defined as follows:

- a definite case of smear-positive pulmonary TB: at least one specimen acid-fast bacilli (AFB) positive by smear microscopy and culture-positive for *M. tuberculosis*;
- a probable case of smear-positive pulmonary TB: at least one specimen AFB positive by smear microscopy and chest X-ray consistent with TB disease according to the reading by the central radiology team, and culture-negative or not available; and
- a case of smear-negative culture-positive pulmonary TB: two smear-negative slides and culture-positive for *M. tuberculosis*.

Prevalent survey cases of smear-positive TB and smear-negative culture-positive TB were both classified as bacteriologically confirmed TB *(1)*.

In December 2010, WHO endorsed the rapid molecular test Xpert®MTB/RIF for the simultaneous diagnosis of TB and rifampicin-resistant TB *(4)*, and in 2013, WHO reviewed its recommended routine case definitions for TB and issued an update *(3)*. In the context of prevalence surveys documented in this book, bacteriologically confirmed TB was defined as a positive culture and/or positive Xpert MTB/RIF result for *M. tuberculosis*. Smear was not used to define a *definite* case of TB; rather, it was used to disaggregate cases according to their smear status. Smear-positive TB was defined as a bacteriologically confirmed case (by culture and/or Xpert MTB/RIF) with at least one AFB-positive smear result.

Careful review of laboratory and chest X-ray results by a diagnostic panel, before finalizing the list of survey TB cases, was a standard part of national TB prevalence surveys. This was done not only to ensure the quality of survey results, but also for clinical management of those with positive laboratory results (not all of whom were eventually considered to have TB disease or were included in the list of prevalent TB cases). Participants with missing culture or Xpert results (or both) would require use of other evidence (e.g. smear and chest X-ray results) for them to be defined as a TB case. Instances of misdiagnosis or overdiagnosis could arise through data management errors, cross-contamination in the laboratory or false-positive laboratory results. In particular, participants with a single positive bacteriological result but no other supportive evidence of TB disease required special attention. For example, survey participants with a single scanty culture-positive result (i.e. <5 or 10 *M. tuberculosis* colonies on solid media) or a positive Xpert MTB/RIF result from a centrifuged sediment were not categorized as prevalent TB cases unless there was chest X-ray evidence of TB disease.

Once the final list of survey cases was available, two categories were defined for the purposes of analysis and presentation of results: smear-positive pulmonary TB and bacteriologically confirmed pulmonary TB. Given the diagnostic technologies currently available and the logistics of population-based surveys, prevalence surveys focus on the measurement of active pulmonary TB disease in adults. Surveys cannot be used to directly measure the prevalence of extrapulmonary disease in adults or the prevalence of TB disease in children.

2.4 Screening and diagnostic testing strategies

The screening and diagnostic testing strategies used in surveys implemented in the period 2007–2016 are summarized in **Table 2.2**.

2.4.1 Screening

Most surveys used two screening tools: an interview about TB symptoms and chest X-ray. Generally, individuals with symptoms that met screening criteria and/or a chest X-ray showing any lung shadow or findings suggestive of TB were considered eligible for sputum examination. Participants that screened negative on both interview and chest X-ray were categorized as not eligible for sputum examination, and were therefore assumed not to have TB.

The main symptom screening criterion was a chronic cough (i.e. ≥2 weeks in most surveys), since this has been the primary screening criterion for TB in routine health services. Nine countries used cough ≥2 weeks as the only symptom screening criterion. The symptom screening criteria in seven other countries was cough ≥2 weeks or haemoptysis, or both. A few surveys considered individuals to be screen positive if they reported a history

[1] The aim of residency criteria is to exclude individuals who intentionally move into the household in anticipation of receiving health care from the survey team, thus potentially biasing results.

Table 2.2

Screening methods used in national TB prevalence surveys, 2007–2016

Country	Symptom screening	Radiography screening	Other screening criteria
Bangladesh	Scoring system: eligible if the total score was ≥3 [a]	Direct digital	Chest X-ray exempted [a]
Cambodia	Cough for ≥2 weeks or haemoptysis (or both)	Conventional	Chest X-ray exempted
China	Cough for ≥2 weeks or haemoptysis of any duration (or both)	Conventional	Participants with known active pulmonary TB with normal chest X-ray, and those who were chest X-ray exempted
DPR Korea	Cough for ≥15 days or haemoptysis (or both)	Conventional	None
Ethiopia	Cough for ≥2 weeks	Conventional	Participants who were exempt from or declined chest X-ray but met one of the following criteria: weight loss ≥3 kg in the past month, night sweats ≥2 weeks, fever ≥2 weeks or contact with a TB patient in the past year
Gambia	Cough for ≥2 weeks, or cough <2 weeks with ≥2 other symptoms, or no cough with ≥3 other symptoms: chest pain, night sweats, shortness of breath, loss of appetite, weight loss, fever or haemoptysis	Direct digital	Chest X-ray exempted
Ghana	Cough for ≥2 weeks	Direct digital	Chest X-ray exempted
Indonesia	Cough for ≥2 weeks or haemoptysis (or both)	Direct digital	Chest X-ray exempted but had at least one of the following symptoms: cough, haemoptysis, fever, chest pain, night sweats, loss of appetite or shortness of breath
Kenya	Cough for ≥2 weeks	Direct digital	Chest X-ray exempted
Lao PDR	Cough for ≥2 weeks within the past month or haemoptysis within the past month (or both)	Conventional	None
Malawi	Any of the following symptoms for at least 1 week: cough, sputum production, haemoptysis, chest pain, weight loss, night sweats, fatigue, fever or shortness of breath	Conventional	None
Mongolia	Cough for ≥2 weeks	Direct digital	Chest X-ray exempted
Myanmar	Cough for ≥3 weeks or haemoptysis (or both)	Conventional	Chest X-ray exempted
Nigeria	Cough for ≥2 weeks	Computed radiography	None
Pakistan	Cough for ≥2 weeks, or cough of any duration if there was no available chest X-ray result	Direct digital	Participants on TB treatment at the time of the survey
Philippines (2007)	N/A [b]	Conventional	None
Philippines (2016)	Cough for ≥2 weeks or haemoptysis (or both)	Direct digital	Chest X-ray exempted
Rwanda	Cough of any duration	Direct digital	Chest X-ray exempted
Sudan	Cough for ≥2 weeks	Direct digital	Chest X-ray exempted or a participant was currently on TB treatment
Thailand	Scoring system: eligible if the total score was ≥3 [c]	Direct digital	Chest X-ray exempted [c]
Uganda	Cough for ≥2 weeks	Conventional	Chest X-ray exempted
UR Tanzania	Any of the following symptoms: cough for ≥2 weeks, haemoptysis, fever for ≥2 weeks, weight loss or excessive night sweats	Computed radiography	None

Table 2.2

Continued

Country	Symptom screening	Radiography screening	Other screening criteria
Viet Nam	Productive cough for ≥2 weeks	Digital scan onsite and mass miniature radiography (70x70 mm)	Chest X-ray exempted or currently on anti-TB treatment or history of TB in preceding 2 years
Zambia	Any one of the following symptoms for ≥2 weeks: cough, fever or chest pain	Direct digital	None
Zimbabwe	Any one of the following symptoms: cough of any duration, haemoptysis in the past 12 months or drenching night sweats	Direct digital	Chest X-ray exempted

DPR Korea, Democratic People's Republic of Korea; Lao PDR, Lao People's Democratic Republic; UR Tanzania, United Republic of Tanzania.

[a] In Bangladesh, a participant was eligible if their total score was 3 points or more: cough ≥2 weeks (3 points), cough <2 weeks (1 point), haemoptysis in the past month (3 points), weight loss in the past month (1 point), fever ≥1 week in the past month (1 point) and night sweats in the past month (1 point). If the chest X-ray was exempted, then a clinical score of 1 or 2 classified a participant as symptom-screen positive.

[b] In the Philippines, symptom screening was not used as a selection criterion for sputum submission, but an interview about TB symptoms and TB history was done for participants aged 20 years or more.

[c] In Thailand, a participant was eligible if their total score was 3 or more (or ≥1 with chest X-ray exempted): cough for ≥2 weeks (3 points), haemoptysis over the past month (3 points), cough <2 weeks (2 points), weight loss in the past month (1 point), fever ≥1 week within the past 2 weeks (1 point) and night sweats in the past month (1 point).

of TB, even in the absence of symptoms and chest X-ray abnormalities.

In nine surveys, the sensitivity of symptom screening was increased by broadening criteria, including combinations of cough of any duration, loss of body weight, chest pain, night sweats and fever. In the 2007 survey in the Philippines, eligibility for sputum submission was based only on chest X-ray screening. In Bangladesh and Thailand, a points-scoring system based on reported symptoms was used.[1]

Since professional reading by a radiologist was not possible in most field sites, reporting of any chest X-ray abnormalities (especially lung abnormalities that were consistent with TB) was encouraged in all surveys, to increase the sensitivity of screening. In 17 surveys, participants who declined chest X-ray investigation or were exempt from having a chest X-ray were automatically eligible for sputum submission; in three countries (Ethiopia, Indonesia and Pakistan) this only applied if the participant reported symptoms.

A single posterior–anterior (PA) image by radiography was used for chest X-ray screening in all surveys.[2] From 2007, there was a transition from conventional to digital chest X-ray imaging systems. In nine surveys, film images were developed using an automatic film processor (a standard practice in surveys before 2007), but other surveys deployed digital X-ray systems. Advantages of digital systems included no requirement for removal of chemicals; immediate availability of the images for chest X-ray reading in the field; more efficient transmission of images to a central unit; and simpler image archiving and retrieval. Computer radiography with an imaging plate and image reader was used in the surveys in Nigeria and the United Republic of Tanzania, whereas direct digital radiography (DDR) with a flat panel detector subsequently became the standard technology for other countries.

Depending on the accessibility of cluster sites and available funding, countries selected a variety of chest X-ray delivery options, including X-ray vans, X-ray containers loaded on a truck or portable X-ray units, or combinations of these options.

Computer-aided detection for reading chest X-ray images was tested in the context of national TB prevalence surveys. However, as of the end of 2016, their performance was not considered satisfactory, especially for diagnosis *(5)*.

[1] In Bangladesh and Thailand, a participant with a symptom score of 3 points or more was eligible for sputum submission: a cough of ≥2 weeks or more (3 points), a cough of less than 2 weeks (1 point), haemoptysis in the past month (3 points), weight loss in the past month (1 point) fever of ≥1 week in the past month (1 point) and night sweats in the past month (1 point). In Thailand, if participants did not have a chest X-ray, then a score of 1 or more made them eligible for sputum submission.

[2] Given the required dose of radiation and the lower quality of images that are produced, WHO does not recommend either MMR or fluoroscopy.

2.4.2 Diagnostic testing

Sputum specimens were collected from all participants who screened positive according to the screening strategy described in **Section 2.4.1**. In general, two smear examinations and two culture examinations (or at least one culture examination when laboratory capacity was limited) were undertaken for each participant. From 2013, in all but one country (Sudan), Xpert MTB/RIF was systematically used in addition to culture, rather than as a substitute for culture (**Table 2.3**).

Direct Ziehl-Neelsen (ZN) light microscopy was the standard technology used for smear examinations in most surveys, consistent with its use in routine clinical practice. However, following WHO's 2011 recommendation to use light-emitting diode (LED) microscopy, this method was used in some of the later surveys *(6)*. In both cases, the direct smear method was used in most surveys (20/25), in preference to smear from concentrated sediment (interpretation of results from smears using the concentrated method was a challenge in Ghana and Malawi owing to possible cross-contamination while making the smears and inoculating culture). In most surveys, at least two sputum specimens were examined (the exception was the Philippines in 2016), and this was usually done in one or more designated laboratories. In Pakistan, Rwanda and the United Republic of Tanzania, testing was carried out onsite or at the nearest hospital laboratory.

In two repeat surveys in Asia (those in Cambodia and the Philippines), a simple primary culture method (i.e. Ogawa-Kudoh method), without centrifugation of specimens, was used to enable direct comparisons with previous survey results. Most other countries used the more sensitive concentration method with Löwenstein-Jensen (LJ media), in line with the latest WHO recommendations. Only Gambia, Ghana,[1] Zambia and Zimbabwe had sufficient resources to use liquid culture – that is, mycobacteria growth indicator tube (MGIT) – for primary culture. The use of a second culture increased the number of positive results by almost 20%, suggesting that the testing of only one culture was a limitation of the surveys in Ethiopia, Kenya, Indonesia,[2] Pakistan, the United Republic of Tanzania and Viet Nam.

For identification of *M. tuberculosis* complex, rapid immunochromatographic assays (strip tests for speciation) to identify cultured isolates are recommended. These assays provide a definitive identification of all types of *M. tuberculosis*. Capilia or SD MPT64TB Ag kits were used in several surveys. However, biochemical testing such as niacin production, nitrate reduction and growth on p-nitrobenzoic acid were used in settings where national TB reference laboratories had not yet introduced rapid identification tests.

Where Xpert MTB/RIF (or line probe assays [LPA]) were used to systematically confirm cases – that is, in Bangladesh, Ghana, Indonesia, Kenya, Malawi, Mongolia, Pakistan, the Philippines (2016), Sudan (LPA), Uganda, Zambia and Zimbabwe[3] – a large proportion of Xpert-negative or LPA-negative individuals was observed among those with positive AFB microscopy results (and negative culture results or no culture results) (**Table 3.7**). Hence, confirmatory testing of smear-positive specimens using Xpert MTB/RIF (or LPA) was encouraged. Xpert MTB/RIF was used in all screen-positive individuals (in addition to culture) in the surveys in Bangladesh, Kenya and the Philippines (2016). Given the risk of DNA cross-contamination, Xpert MTB/RIF testing of a direct sputum specimen was recommended (testing of a concentrated sputum sediment was only recommended as a confirmatory test for smear positivity, in place of culture).

2.4.3 Screening methods in repeat prevalence surveys

Repeat surveys are typically undertaken every 7–10 years. During that time interval, screening and diagnostic practices can change with the adoption of improved techniques and technologies. Therefore, differences in screening and diagnostic methods between consecutive surveys can potentially generate biases that need to be accounted for when interpreting results.

In Thailand, the 2012 survey used digital chest X-ray as opposed to the less sensitive MMR used in the 1991 and 2006 surveys. In China, the 1990 survey used chest fluoroscopy for symptomatic individuals, and sputum samples were only taken if this test was abnormal. In contrast, in the 2000 and 2010 surveys in China, participants with symptoms but normal fluoroscopic examination (2000) or normal chest radiography (2010) were also asked to submit sputum samples. The 1994 survey in Myanmar and the 2004 survey in Indonesia did not systematically perform

[1] Ghana used both LJ and MGIT, but only MGIT was used to define a survey TB case.

[2] Owing to laboratory capacity constraints, two sputum samples were obtained from participants in 52 clusters (33%), and one sample from the remaining 104 clusters.

[3] Pakistan was the first country to use Xpert MTB/RIF in a national TB prevalence survey, but it was only used for specimens that were smear positive with undetermined culture results.

Table 2.3

Diagnostic methods used in national TB prevalence surveys, 2007–2016

Country	Smear		Primary culture		Xpert MTB/RIF	MTB identification test for positive cultures	HIV testing	Drug susceptibility testing
	Number of samples	Type	Number of samples	Type				
Bangladesh	2	Direct FM	2	Concentrated LJ	Yes, for all participants who screened positive	Capilia	No	Yes
Cambodia	2	Direct FM	2	Direct Ogawa	No	Capilia	No	Yes
China	3	Direct ZN	2	Direct LJ	No	PNB	No	Yes
DPR Korea	2	Concentrated FM	2	Concentrated LJ	No	MPT64	No	No
Ethiopia	2	Direct FM	1	Concentrated LJ	No	Capilia	No	Only as a post-survey activity
Gambia	2	Direct FM	2	Concentrated MGIT	No [a]	MGIT™ TBc Identification Test	No	Only as a post-survey activity [a]
Ghana	2	Concentrated ZN	2	Concentrated MGIT [b]	Yes, for smear-positive specimens, and if cultures were contaminated	PNB, capilia	No	Yes [c]
Indonesia	2	Direct ZN	2 samples for 52 clusters, 1 sample for 104 clusters	Concentrated LJ	Yes, for smear-positive specimens or non-conclusive cultures	MPT64, niacin	No	No
Kenya	2	Direct FM	2	Concentrated LJ	Yes, for all participants who screened positive	MPT64	No [d]	Yes
Lao PDR	2	Direct ZN	2	Direct Ogawa	No	PNB, LPA	No	Yes
Malawi	2	Concentrated FM	2	Concentrated LJ	Yes, for smear-positive specimens, and if cultures were contaminated	Capilia	No [e]	Yes [c]
Mongolia	2	Direct FM	2	Direct Ogawa	Yes, for smear-positive specimens	PNB, niacin	No	Yes
Myanmar	2	Direct FM	2	Direct Ogawa	No	Niacin, PNB, capilia	No	No
Nigeria	2	Direct ZN	2	Concentrated LJ	No	MPT64	No	No

Table 2.3

Continued

Country	Smear		Primary culture		Xpert MTB/RIF	MTB identification test for positive cultures	HIV testing	Drug susceptibility testing
	Number of samples	Type	Number of samples	Type				
Pakistan	2 (1 onsite, 1 at central)	Direct ZN	1	Direct Ogawa	Yes, for smear-positive specimens without culture confirmation	PNB, MPB64: all culture-positive specimens, and LPA or Xpert MTB/RIF used with smear-positive specimens without culture confirmation.	No	Yes
Philippines (2007)	3	Direct FM	3	Concentrated LJ and direct Ogawa	No	Niacin, catalase, nitrate testing	No	Yes
Philippines (2016)	1 [f]	Direct FM	1 [f]	Direct Ogawa	Yes, for all participants who screened positive	MPT64	No	Yes
Rwanda	2	Direct FM	2	Concentrated LJ	No	MPT64	Yes	Yes
Sudan	2	Direct FM	2	Direct Ogawa	No	Capilia, LPA [g]	No	No
Thailand	2	Direct ZN	2	Direct Ogawa	No [h]	Simple immunochromato-graphic assay	No	No
Uganda	2	Direct ZN	2	Concentrated LJ	Yes, for smear-positive specimens, and if cultures were contaminated	MPT64	Yes	Only as a post-survey activity
UR Tanzania	3 (2 on site, 1 at central)	Direct FM	1	Concentrated LJ	Yes [i]	PNB	Yes	Only as a post-survey activity
Viet Nam	3	Direct ZN	1	Concentrated LJ	No	Niacin	No	All positive isolates were tested but results were not officially reported
Zambia	2	Concentrated FM	2	Concentrated MGIT	Yes, for all participants who screened positive [j]	Capilia	Yes	No
Zimbabwe	2	Concentrated FM	2	Concentrated LJ and MGIT	Yes, for all smear-positive specimens [k]	MPT64	No [d]	Yes [c]

DPR Korea, Democratic People's Republic of Korea; FM, fluorescence microscopy; HIV, human immunodeficiency virus; Lao PDR, Lao People's Democratic Republic; LJ, Löwenstein-Jensen media; LPA, line probe assays; MGIT, mycobacterial growth indicator tube; MTB, *Mycobacterium tuberculosis*; PNB, para-nitrobenzoic acid; TB, tuberculosis; UR Tanzania, United Republic of Tanzania; ZN, Ziehl-Neelsen stain.

[a] In Gambia, Xpert MTB/RIF was used to determine if survey cases were rifampicin-resistant but not as part of the survey.

[b] In Ghana, concentrated LJ and MGIT were both used in the survey, but only MGIT was used to define a TB survey case.

[c] In Ghana, Malawi and Zimbabwe, rifampicin resistance was detected using Xpert MTB/RIF only.

[d] In Kenya and Zimbabwe, TB cases detected by the survey were offered HIV counselling and testing as part of routine treatment management but were not directly tested as part of the survey.

[e] In Malawi, instead of HIV testing, all participants were asked if they had ever been tested for HIV and, if willing, to disclose their status.

[f] In the Philippines (2016), if the first sample was not of sufficient volume, a second sample was also used.

Table 2.3

Continued

[g] In Sudan, LPA was used to test all culture-positive and all smear-positive samples.
[h] In Thailand, Xpert MTB/RIF was used after the study for quality assurance purposes for smear-positive, culture-negative samples.
[i] In UR Tanzania, Xpert MTB/RIF was only used on smear-positive slides to confirm the presence of MTB at the Antwerp SRL, but was not part of the original protocol.
[j] In Zambia, Xpert MTB/RIF was also performed on some smear-negative culture contaminated samples or smear-negative culture indeterminate samples if the chest X-ray was suggestive of TB.
[k] In Zimbabwe, in addition to smear-positive samples all culture-positive samples were also tested for rifampicin resistance using Xpert MTB/RIF.

culture examination, but culture was used in the repeat surveys in 2009 and in 2014, respectively. In Myanmar, the 1994 survey did not include chest X-ray screening but it was used in the 2009–2010 survey. In Cambodia, the 2002 and 2011 surveys used similar screening and diagnostic methods. In the Philippines, the 1997 and 2007 surveys used only chest X-ray for screening. Although the 2016 Philippines survey used Xpert MTB/RIF for diagnostic confirmation, comparisons with the 2007 survey results could still be made because the same culture method (Ogawa) was used in both surveys.

2.5 Sampling design

A comprehensive description of the recommended sampling design is outlined in **Chapter 5** of the *lime book (2)*.

2.5.1 Sample size

Until the advent of rapid molecular tests (in particular, Xpert MTB/RIF in 2010), smear examination was the main test used for TB diagnosis in most countries. From the mid-1990s until the mid-2000s, routine reporting of notified cases of smear-positive pulmonary TB and their treatment outcomes was a core component of WHO's recommended global TB strategy, global TB monitoring undertaken by WHO and national TB surveillance systems. Hence, up to 2015, sample size calculations were based on the expected national prevalence of smear-positive pulmonary TB among adults. The expected prevalence was generally based on the assumption of a prevalence to notification ratio of 2:1. For repeat surveys, the sample size calculation was based on the expected decline in the prevalence of smear-positive pulmonary TB since the previous survey *(7)*. After 2015, following WHO's 2013 update to TB case definitions, sample size was calculated based on the expected prevalence of bacteriologically confirmed pulmonary TB in adults.

The calculated samples sizes for surveys implemented in the period 2007–2016 are shown in **Table 2.4**. They ranged from 30 000 in the Philippines (2007) to 264 000 in China (2010). Of note, Indonesia and Mongolia aimed to obtain subnational estimates, and Thailand's survey was designed as two independent surveys: one for the Bangkok area and another for areas outside Bangkok.

2.5.2 Cluster number and size

Both logistical and statistical issues are relevant when determining the number and size of clusters to be sampled. At least 50 clusters are strongly recommended, as a compromise between minimizing sampling design effects (which requires more and smaller clusters) and reducing logistical constraints (by having fewer clusters). All surveys implemented in the period 2007–2016 had 50 or more clusters (**Table 2.4**). Cluster sizes of 400–800 were generally recommended, because this size makes it possible to complete chest X-ray screening within 7–10 days. Most surveys had a cluster size of 500–900 people, apart from those in China (1500 people), Pakistan (1400) and Viet Nam (1500). The introduction of high-capacity direct digital chest X-ray units made it feasible to screen 250–300 people per day, thus enabling completion of field operations in each cluster in fewer than 5 working days.

2.5.3 Stratification

Most surveys used stratified designs to increase sampling efficiency, such as urban versus rural strata, or geographically defined strata (**Table 2.4**). Probability proportional to size (PPS) sampling was applied to the selection of primary sampling units (regions, states, zones or provinces), followed by smaller secondary sampling units (districts, townships, subdistricts and municipalities), and so on until reaching the level of geographical area that comprised the population size of a cluster. The last stage of cluster selection sometimes used simple random sampling.

2.5.4 Sampling frame

The sampling frame defines the areas of the country from which clusters are selected. Ideally, all clusters should be included in the sampling frame to ensure optimal national representativeness. However, certain areas were excluded in several surveys because of security concerns or geographic inaccessibility. Excluded areas generally covered less than 5% of the total population (**Table 2.4**). In several surveys, some clusters that were initially

Table 2.4

Sampling and survey design, 2007–2016

Country	Planned sample size	Planned number of clusters	Cluster size	Stratified sampling	Geographical areas excluded initially from sampling frame	Geographical areas excluded during field operations
Bangladesh	100 000	125	800	Urban, rural	None	One cluster was replaced for security reasons
Cambodia	39 680	62	640	Urban, rural, others	None	None
China	264 000	176	1500	Urban, rural	None	None
DPR Korea	69 442	100	700	Urban, rural	None	Five clusters in Anpyon, Kyongsong and Pukchang county were replaced by five others in the same counties due to inaccessibility
Ethiopia	46 514	85	550	Urban, rural, pastoralist	37 out of 810 woredas (3% of the national population) were excluded from the sampling frame for security reasons and due to logistical challenges; two clusters (kebele) were replaced before field operations started due to logistical challenges	None
Gambia	55 281	80	700	Not stratified	None	Three clusters were replaced due to a large uninhabited area in the urban area around the capital (one cluster), military installations and areas around the president's residence (two clusters)
Ghana	63 905	98	650	Urban, rural	None	None
Indonesia	78 000	156	500	Sumatra, Java-Bali and others, with each stratified into urban/rural	None	None
Kenya	72 000	100	720	Urban, rural	None	One cluster in Mandera was excluded for security reasons
Lao PDR	40 000	50	800	Not stratified	None	None
Malawi	37 200	74	500	Urban, semi-urban, rural	None	None
Mongolia	49 000	98	600 (city) / 500 (other)	City, provincial centre, rural	None	None
Myanmar	49 690	70	710	Region, state	32 townships were excluded for security reasons	Five townships (Bokepyin, Kunlon, Kyarinnseikkyi, Mindat and Nattalin) were replaced by others within the same township during the pre-visit, owing to security and transportation problems, and an insufficient population aged 15 years and above

Table 2.4

Continued

Country	Planned sample size	Planned number of clusters	Cluster size	Stratified sampling	Geographical areas excluded initially from sampling frame	Geographical areas excluded during field operations
Nigeria	49 000	70	700	Six zones	None	Three clusters in the states of Borno and Yobe were excluded for security reasons; these were replaced in the states of Adamawa, Bauchi and Gombe
Pakistan	133 000	95	1400	Not stratified	The Federally Administered Tribal Areas, district Dera Bugti in Balochistan and 17 tehsils of Khyber Pakhtunkhwa were excluded for security reasons; this accounted for 6.4% of the national population	Three clusters from Balochistan (Awaran, Lehri and Quetta) were replaced by other clusters (Hub in Balochistan, Khan Pur in Punjab, and Sharda in Azad-Jammu and Kashmir) for security reasons
Philippines (2007)	30 000	50	600	Metro Manila, other urban, rural	Four barangays in other urban strata and 14 barangays in rural strata were excluded for security reasons and due to inaccessibility	None
Philippines (2016)	54 000	108	500	National Capital Region, region 3 and 4A; Rest of Luzon; Visayas; Mindanao	Before field operations started, one cluster in Basilan province was excluded for security reasons (this accounted for <1% of the national population)	Three clusters (Maco, Madaya and Sipangkot barangays) were replaced for security reasons, and one cluster (Holy Spirit barangay) was dropped because the local authorities refused house-to-house mobilization and interviews
Rwanda	44 500	73	610	Not stratified	None	None
Sudan	91 131	114	800	Urban, rural	None	Four clusters (two in Darfur State, one in Gazira and one in South Kordofan) were cancelled for security reasons, and one was removed due to a protocol violation
Thailand [a]	74 700	83	900	Urban, rural	None	None
Uganda	40 180	70	580	Urban, rural	None	None
UR Tanzania	46 792	62	750	Urban, semi-urban, rural, Zanzibar	None	None
Viet Nam	105 000	70	1500	Urban, rural, remote	None	None
Zambia	54 400	66	825	Urban, rural	None	None
Zimbabwe	44 951	75	600	Urban, rural	None	Two clusters (Chiredzi and Macheke) were replaced due to logistical issues (e.g. weather, equipment failure)

DPR Korea, Democratic People's Republic of Korea; Lao PDR, Lao People's Democratic Republic; UR Tanzania, United Republic of Tanzania.

[a] The Bangkok metropolitan area was excluded.

selected were excluded after the sampling stage had been completed, owing to security concerns or natural disasters.

2.6 Field operations

The main activities conducted during field operations include a census in each cluster, screening of participants, and the collection and transportation of sputum specimens. The survey census and collection of sputum specimens are summarized below (screening methods are described in Section 2.4.1).

2.6.1 Survey census

In each survey cluster, a population listing was typically obtained by local volunteers 1–2 weeks in advance of the arrival of the survey investigators. In some surveys, the survey investigators (or staff from the bureau of statistics) undertook the census. At the beginning of field operations, the survey investigators would confirm the population listing, and assess each enumerated person's eligibility to participate, based on their age and residential status (Table 2.1).

During the census, data on household assets were collected in several surveys to measure socioeconomic status (in Kenya, Malawi, Mongolia, Myanmar, the Philippines, Rwanda, the United Republic of Tanzania, Viet Nam and Zambia). In some of the surveys, it was possible to evaluate the relationship between household poverty and TB disease *(8)*.[1]

2.6.2 Sputum collection and transportation

Typically, two sputum samples (spot and the following morning) were collected. It was often a challenge to obtain quality sputum samples, compared with routine sputum collection for coughing patients who are seeking medical care. Despite a WHO recommendation to take two spot specimens 1 hour apart on the same day (i.e. front loading) *(9)*, in the setting of prevalence surveys, a spot sample followed by a morning sample the next day was generally advised. An additional second spot sample (i.e. a third specimen) was collected in some surveys, especially when the quality of the first specimen was poor.

Sputum specimens were transported via cold chain to a designated laboratory, ideally within 3 days of specimen collection to allow for rapid culturing and to avoid contamination. A maximum processing time of 7 days after collection in the field was recommended, provided that the cold chain was maintained.

2.7 Additional testing for HIV infection and drug susceptibility

2.7.1 HIV testing

Information about the HIV status of TB patients is essential both for individual patient care and for understanding the epidemiology of TB. However, HIV testing was not usually done as part of survey field operations owing to logistical constraints (Table 2.3). Only seven of the 25 surveys collected data about HIV status, and all seven of these were in Africa. In Zambia, HIV testing was offered in the field to every survey participant as part of the survey; in Rwanda, Uganda and the United Republic of Tanzania, HIV testing was offered as part of the survey to all participants that screened positive based on symptom screening or chest X-ray criteria (or both), with an opt-out modality. When incorporated in the survey, HIV testing was implemented according to national guidelines, and included pre- and post-test counselling. In Malawi, given the high population coverage of HIV testing, all survey participants were asked to report their HIV status to survey investigators. In Kenya and Zimbabwe, the HIV status of survey cases was obtained from linkage with available records in routine disease information systems.

2.7.2 Testing for drug susceptibility

National TB prevalence surveys are not designed to precisely estimate the prevalence of drug-resistant TB, owing to the small number of survey cases. However, drug susceptibility testing was usually done for all survey cases to inform case management (Table 2.3). In some surveys that used Xpert MTB/RIF, rifampicin-susceptibility status was recorded.

2.8 Central-level activities

Apart from the organisational and logistical aspects of surveys, the main activities conducted at the central level (as opposed to in the field) were the confirmatory reading of chest X-rays and the review of participants with positive laboratory results.

[1] This study combined individual-level data from some of these countries, and found no relationship between household socioeconomic level and TB disease. However, because of the small numbers of TB cases usually detected, prevalence surveys are not an efficient study design for investigating TB risk factors.

2.8.1 Central chest X-ray reading

A second reading of chest X-rays taken in the field was done centrally by trained radiologists, to provide quality assurance of field chest X-ray readings, and a formal interpretation that could be used in determining the final list of survey cases. In surveys undertaken before the use of Xpert MTB/RIF, probable TB survey cases were defined using positive smear results and chest X-ray readings, especially when culture was negative or not available. In the later surveys done in Bangladesh, Kenya and the Philippines, central chest X-ray readings were also used to define a case when culture positivity was weak[1] and there was no other positive evidence on Xpert MTB/RIF or smear.

In most surveys, all chest X-rays were reread; however, in countries with limited capacity, all abnormal chest X-rays and 10–20% of normal chest X-rays were reread. Some surveys attempted to have the central reading undertaken at the same time as field operations, but since this required major logistical organization and strong internet connectivity, it rarely happened.

2.8.2 Central review of participants with positive laboratory results

Each survey conducted a review of all cases by a panel that typically comprised the survey coordinator, a radiologist, a medical officer, head of laboratory and the data manager. The panel was responsible for the final interpretation of radiographic and laboratory results for all participants with any positive laboratory results (e.g. smear, culture or Xpert MTB/RIF). The panel had two objectives: to define and confirm the status of TB survey cases; and to refer patients for further investigations and treatment, as needed. Typically, the panel reviewed only one to three cases each week. All panel decisions were documented.

2.9 Data management and analysis

Given the sample size of a typical TB prevalence survey and the need to enter data from different sources (census, household surveys, symptom screening, field and central chest X-ray readings, and laboratory and final diagnostic panel decisions), data management is a crucial, and often underestimated component of a survey (as discussed in **Chapter 4**). In surveys implemented in the period 2007–2014, data were mostly collected on paper and then entered into a database at the central level. Subsequently, the digitalization of survey data management increased with the use of computers, personal digital assistants, tablets, digital chest X-rays, barcoding and internet-connectivity in the field.

The survey in Ghana (in 2013) was the first to rely predominantly on electronic data entry, and the survey in Zambia was the first to be virtually "paper-free". The growing use of digital technologies increased the speed and efficiency with which data could be cleaned and analysed, and helped to improve data quality. It also required additional investment in equipment and, in particular, staff with specialist information technology skills. In areas with poor internet connectivity and unreliable power supply, complete reliance on digital systems was not possible. Furthermore, although such technologies have many advantages, overreliance on digital systems occasionally led to insufficient attention to data quality checks. Thus, systems using paper remain relevant, especially for data quality assurance and back-up purposes.

Following data cleaning, analysis of survey results usually required specialist technical assistance to ensure the correct application of best-practice methods *(10)*. Prevalence estimates were produced using three statistical approaches (cluster-based analysis, and two models based on individual-level analysis and multiple imputation for missing data). Multiple imputation of missing data and inverse probability weighting was the recommended method to report final results, unless there was a clear and documented justification to use one of the other two methods. With one exception, all national surveys implemented in the period 2007–2016 were analysed using the recommended methods.[2]

2.10 Additional studies

In surveys conducted before 2007 it was common to implement, in parallel, a tuberculin survey; the Viet Nam survey (2007) was the last survey to do this *(11)*. The practice was discontinued following updated WHO policy guidance in 2009 about the limited usefulness of tuberculin surveys *(12)*.

Data about diseases or health conditions other than TB – for example, smoking, chronic obstructive pulmonary

[1] Weak positive culture is defined as one to nine colonies of *M. tuberculosis*.

[2] The 2007 survey in Viet Nam was analysed before the development and publication of these methods. The 2007 survey in the Philippines was initially not analysed using the recommended methods, but was reanalysed using these methods in 2009.

Table 2.5

Total budget and sources of funding for national TB prevalence surveys, 2007–2016

Country	Total budget (US$ millions)	Global Fund	US government	Domestic funding	Other
Bangladesh	3.6	●	●	–	–
Cambodia	1.0	●	●	–	●
China	5.6	–	–	●	–
DPR Korea	1.4	●	–	●	–
Ethiopia	2.8	●	–	●	●
Gambia	1.9	●	–	–	●
Ghana	2.2	●	–	–	●
Indonesia	4.6	●	●	–	–
Kenya	5.2	●	●	–	●
Lao PDR	1.3	●	●	–	–
Malawi	2.2	●	–	●	–
Mongolia	1.1	●	–	●	●
Myanmar	0.9	–	●	–	●
Nigeria	3.1	●	–	●	●
Pakistan	4.4	–	●	–	●
Philippines (2007)	Not known	●	–	–	●
Philippines (2016)	2.4	●	–	●	–
Rwanda	2.4	●	–	–	●
Sudan	1.9	●	–	●	–
Thailand	1.9	●	–	●	–
Uganda	2.8	●	–	–	–
UR Tanzania	3.4	●	●	●	●
Viet Nam	1.1	●	–	●	●
Zambia	5.4	●	●	–	●
Zimbabwe	3.5	●	–	–	–

DPR Korea, Democratic People's Republic of Korea; Global Fund, Global Fund to Fight AIDS, Tuberculosis and Malaria; Lao PDR, Lao People's Democratic Republic; UR Tanzania, United Republic of Tanzania; US, United States of America.
● yes; – no

disease, obesity (body mass index was measured) and diabetes – were collected in a few surveys to assess TB risk factors. These data were not systematically collected or analysed across all surveys. However, data on the health care seeking behaviour of survey participants with symptoms suggestive of TB (e.g. cough ≥2 weeks) in the United Republic of Tanzania, Viet Nam and Zambia were published *(13-15)*. These data highlighted the location where care was initially sought, and therefore the missed opportunities to diagnose TB, but they also highlighted that many symptomatic participants did not seek care.

2.11 Reporting and dissemination of results

A report was produced for all 25 surveys, and results from 11 surveys were published in a peer-reviewed journal *(7, 16-52)*.[1] The process took about 1.3 years (and sometimes up to 3 years) from the time of completing field operations to official dissemination of results or publication of findings.

Some survey investigators published results that extended beyond the primary objective of estimating national TB prevalence. Examples include the health care

[1] Ghana and Rwanda submitted a paper at the time of writing. Thailand produced one report in Thai only.

seeking behaviour of survey participants in the United Republic of Tanzania, Viet Nam and Zambia *(13-15)*; the characteristics of participants with non-tuberculosis mycobacteria and the use of computer-aided reading of chest X-rays in Zambia *(53, 54)*; the diagnosis and treatment of TB in the private sector, and the association between TB and household expenditure in Viet Nam *(55, 56)*. Pooled survey data have been used to help understand differences in TB burden by sex, and the effect of household poverty on TB *(8, 57)*.

2.12 Ethics approval

All surveys were approved by their respective national ethical review boards, and all protocols were reviewed and approved by partner agencies (e.g. those providing technical assistance) and the WHO Global Task Force on TB impact measurement.

2.13 Budgeting and financing

As reported by the survey teams, the Global Fund was a crucial source of financing for all but three surveys (**Table 2.5**; further details in individual country profiles). Other international funders, especially the US government, also made major contributions to survey funding. Some countries were able to fully or partially fund their surveys from domestic resources. Most of the international technical assistance for the 25 surveys was funded by the US government and the Japan International Cooperation Agency.

References

1. World Health Organization. Assessing tuberculosis prevalence through population-based surveys. Geneva, Switzerland 2007 (https://apps.who.int/iris/handle/10665/206962, accessed 20 November 2019).
2. World Health Organization. Tuberculosis prevalence surveys: a handbook. Geneva, Switzerland 2011 (https://apps.who.int/iris/bitstream/handle/10665/44481/9789241548168_eng.pdf, accessed 27 November 2019).
3. World Health Organization. Automated real-time nucleic acid amplification technology for rapid and simultaneous detection of tuberculosis and rifampicin resistance: Xpert MTB/RIF system. Policy statement. Geneva, Switzerland 2011 (https://apps.who.int/iris/bitstream/handle/10665/44586/9789241501545_eng.pdf, accessed 28 November 2019).
4. World Health Organization. Definitions and reporting framework for tuberculosis (updated 2014). Geneva, Switzerland 2013 (www.who.int/iris/bitstream/10665/79199/1/9789241505345_eng.pdf, accessed 28 November 2019).
5. World Health Organization. Chest radiography in tuberculosis detection: summary of current WHO recommendations and guidance on programmatic approaches. Geneva, Switzerland 2016 (https://apps.who.int/iris/bitstream/10665/252424/1/9789241511506-eng.pdf, accessed 28 November 2019).
6. World Health Organization. Fluorescent light-emitting diode (LED) microscopy for diagnosis of tuberculosis policy. Policy statement. Geneva, Switzerland 2011 (https://apps.who.int/iris/bitstream/handle/10665/44602/9789241501613_eng.pdf, accessed 28 November 2019).
7. Mao TE, Okada K, Yamada N, Peou S, Ota M, Saint S et al. Cross-sectional studies of tuberculosis prevalence in Cambodia between 2002 and 2011. Bull World Health Organ. 2014;92(8):573–81 (https://www.ncbi.nlm.nih.gov/pubmed/25177072, accessed 28 November 2019).
8. Siroka A, Law I, Macinko J, Floyd K, Banda RP, Hoa NB et al. The effect of household poverty on tuberculosis. Int J Tuberc Lung Dis. 2016;20(12):1603–8 (https://www.ncbi.nlm.nih.gov/pubmed/27931334, accessed 28 November 2019).
9. TB diagnostics and laboratory strengthening - WHO policy [website]. 2007 (https://www.who.int/tb/areas-of-work/laboratory/policy_diagnosis_pulmonary_tb/en/, accessed 26 April 2019).
10. Floyd S, Sismanidis C, Yamada N, Daniel R, Lagahid J, Mecatti F et al. Analysis of tuberculosis prevalence surveys: new guidance on best-practice methods. Emerg Themes Epidemiol. 2013;10(1):10 (https://www.ncbi.nlm.nih.gov/pubmed/24074436, accessed 28 November 2019).
11. Hoa NB, Cobelens FG, Sy DN, Nhung NV, Borgdorff MW, Tiemersma EW. First national tuberculin survey in Viet Nam: characteristics and association with tuberculosis prevalence. Int J Tuberc Lung Dis. 2013;17(6):738–44 (https://www.ncbi.nlm.nih.gov/pubmed/23676155, accessed 28 November 2019).
12. TB impact measurement policy and recommendations for how to assess the epidemiological burden of TB and the impact of TB control. Stop TB policy paper no. 2, Geneva: World Health Organization; 2009 (https://apps.who.int/iris/bitstream/handle/10665/44231/9789241598828_eng.pdf, accessed 22 November 2019).
13. Chanda-Kapata P, Kapata N, Masiye F, Maboshe M, Klinkenberg E, Cobelens F et al. Health seeking behaviour among individuals with presumptive tuberculosis in Zambia. PLoS One. 2016;11(10):e0163975 (https://www.ncbi.nlm.nih.gov/pubmed/27711170, accessed 28 November 2019).
14. Hoa NB, Tiemersma EW, Sy DN, Nhung NV, Vree M, Borgdorff MW et al. Health-seeking behaviour among adults with prolonged cough in Vietnam. Trop Med Int Health. 2011;16(10):1260–7 (https://www.ncbi.nlm.nih.gov/pubmed/21692960, accessed 28 November 2019).
15. Senkoro M, Hinderaker SG, Mfinanga SG, Range N, Kamara DV, Egwaga S et al. Health care-seeking behaviour among people with cough in Tanzania: findings from a tuberculosis prevalence survey. Int J Tuberc Lung Dis. 2015;19(6):640–6 (https://www.ncbi.nlm.nih.gov/pubmed/25946352, accessed 28 November 2019).
16. Adetifa IM, Kendall L, Bashorun A, Linda C, Omoleke S, Jeffries D et al. A tuberculosis nationwide prevalence survey in Gambia, 2012. Bull World Health Organ. 2016;94(6):433–41 (https://www.ncbi.nlm.nih.gov/pubmed/27274595, accessed 28 November 2019).
17. Bonsu F, Addo KK, Alebachew Z, Gyapong J, Badu-Peprah A, Gockah R et al. National population-based tuberculosis prevalence survey in Ghana, 2013. Int J Tuberc Lung Dis. 2020 Mar 1;24(3):321-328. (https://pubmed.ncbi.nlm.nih.gov/32228763/, accessed 20 March 2020).

18. Department of Public Health Federal Republic of Nigeria. Report of the first national TB prevalence survey 2012, Nigeria. 2014 (https://www.who.int/tb/publications/NigeriaReport_WEB_NEW.pdf, accessed 9 October 2017).
19. Disease Control Bureau of the Ministry of Health – Chinese Center for Disease Control and Prevention. Report on the 5th national tuberculosis epidemiological survey in China – 2010. Beijing, China: 2011.
20. Enos M, Sitienei J, Ong'ang'o J, Mungai B, Kamene M, Wambugu J et al. Kenya tuberculosis prevalence survey 2016: challenges and opportunities of ending TB in Kenya. PLoS One. 2018;13(12):e0209098 (https://www.ncbi.nlm.nih.gov/pubmed/30586448, accessed 28 November 2019).
21. Hoa NB, Sy DN, Nhung NV, Tiemersma EW, Borgdorff MW, Cobelens FG. National survey of tuberculosis prevalence in Viet Nam. Bull World Health Organ. 2010;88(4):273–80 (https://www.ncbi.nlm.nih.gov/pubmed/20431791, accessed 28 November 2019).
22. Institute of Epidemiology Disease Control & Research, Ministry of Health & Family Welfare Government of the People's Republic of Bangladesh. National tuberculosis prevalence survey, Bangladesh 2015–2016. Dhaka, Bangladesh: 2017.
23. Kapata N, Chanda-Kapata P, Ngosa W, Metitiri M, Klinkenberg E, Kalisvaart N et al. The prevalence of tuberculosis in Zambia: results from the first national TB prevalence survey, 2013–2014. PLoS One. 2016;11(1):e0146392 (https://www.ncbi.nlm.nih.gov/pubmed/26771588, accessed 28 November 2019).
24. Kebede AH, Alebachew Z, Tsegaye F, Lemma E, Abebe A, Agonafir M et al. The first population-based national tuberculosis prevalence survey in Ethiopia, 2010–2011. Int J Tuberc Lung Dis. 2014;18(6):635–9 (https://www.ncbi.nlm.nih.gov/pubmed/24903931, accessed 28 November 2019).
25. Law I, Sylavanh P, Bounmala S, Nzabintwali F, Paboriboune P, Iem V et al. The first national tuberculosis prevalence survey of Lao PDR (2010–2011). Trop Med Int Health. 2015;20(9):1146–54 (https://www.ncbi.nlm.nih.gov/pubmed/25939366, accessed 28 November 2019).
26. Migambi P, Gasana M, Uwizeye CB, Kamanzi E, Ndahindwa V, Kalisvaart N et al. Prevalence of tuberculosis in Rwanda: Results of the first nationwide survey in 2012 yielded important lessons for TB control. PLoS One. 2020 Apr 23;15(4):e0231372. https://pubmed.ncbi.nlm.nih.gov/32324750/, accessed 20 April 2020).
27. Ministry of Health. Technical report of the Zambia national tuberculosis prevalence survey (2013–2014). 2015 (https://www.moh.gov.zm/docs/reports/zntbs13-14_final.pdf, accessed 12 October 2017).
28. Ministry of Health – Cambodia. Report of the second national tuberculosis prevalence survey, 2011. 2012 (http://open_jicareport.jica.go.jp/pdf/12120325.pdf, accessed 28 November 2019).
29. Ministry of Health – Federal Democratic Republic of Ethiopia. First Ethiopian national population based tuberculosis prevalence survey. Ethiopian Health and Nutrition Research Institute; 2011.
30. Ministry of Health – Mongolia. Report of the first national tuberculosis prevalence survey in Mongolia (2014–2015). Ulaanbaatar, Mongolia: 2016.
31. Ministry of Health – Myanmar. Report on national TB prevalence survey 2009–2010. Yangon, Myanmar: 2010.
32. Ministry of Health – Republic of Indonesia, National Institute of Health Research and Development. Indonesia tuberculosis prevalence survey 2013–2014. Jakarta, Indonesia: 2015.
33. Ministry of Health – Thailand. Fourth tuberculosis prevalence survey in Thailand, 2012. Bangkok, Thailand: 2015.
34. Ministry of Health – Viet Nam. National tuberculosis prevalence survey in Vietnam, 2006–2007. Hanoi, Viet Nam: 2008.
35. Ministry of Health (national tuberculosis leprosy and lung disease program). National tuberculosis prevalence survey of Kenya 2015–2016. 2016.
36. Ministry of Health (national tuberculosis program). National tuberculosis prevalence survey of Sudan 2013–2014 (report). 2018.
37. Ministry of Health and Child Care. The Zimbabwe national population based tuberculosis prevalence survey. 2014.
38. Ministry of Health and Social Welfare. The first national tuberculosis prevalence survey in the United Republic of Tanzania. 2013.
39. Ministry of Health and Social Welfare. The Gambian survey of tuberculosis prevalence report. Medical Research Council Unit, The Gambia; 2014.
40. Ministry of Health National TB Control Programme. Technical report: Malawi tuberculosis prevalence survey (2013–2014). 2016.
41. Ministry of Health Uganda and Makerere University School of Public Health. Population-based survey of prevalence of tuberculosis disease in Uganda 2014–15 (report). Makerere University School of Public Health; 2016.
42. Ministry of Public Health – DPRK. Report of DPRK national TB prevalence survey 2015–2016. Pyongyang, Democratic People's Republic of Korea: 2017.
43. National TB control program – Pakistan. Prevalence of pulmonary tuberculosis among the adult population of Pakistan, 2010–2011. Islamabad, Pakistan: 2013.
44. National TB Control Programme (Ghana Health Service). Ghanaian national population based tuberculosis prevalence survey in 2013 (report). 2016.
45. National Tuberculosis Centre – Ministry of Health – Lao PDR. Report of the first report of the first national tuberculosis prevalence survey of Lao PDR (2010–2011). Vientiane, Lao PDR: 2013.
46. Philippines: Department of Health Republic of the Philippines, Foundation for the Advancement of Clinical Epidemiology Inc, Philippine Council for Health Research and Development. National tuberculosis prevalence survey 2016. Manila, Philippines: 2018.
47. Qadeer E, Fatima R, Yaqoob A, Tahseen S, Ul Haq M, Ghafoor A et al. Population based national tuberculosis prevalence survey among adults (>15 years) in Pakistan, 2010–2011. PLoS One. 2016;11(2):e0148293 (https://www.ncbi.nlm.nih.gov/pubmed/26863617, accessed 28 November 2019).
48. Rwanda Ministry of Health. The first national tuberculosis prevalence survey in Rwanda (2012). 2015.
49. Senkoro M, Mfinanga S, Egwaga S, Mtandu R, Kamara DV, Basra D et al. Prevalence of pulmonary tuberculosis in adult population of Tanzania: a national survey, 2012. Int J Tuberc Lung Dis. 2016;20(8):1014–21 (https://www.ncbi.nlm.nih.gov/pubmed/27393533, accessed 28 November 2019).
50. Tropical Disease Foundation Inc and Department of Health. Final report of the nationwide tuberculosis prevalence survey 2007. Navotas City, Philippines: 2008.
51. Tupasi TE, Radhakrishna S, Chua JA, Mangubat NV, Guilatco R, Galipot M et al. Significant decline in the tuberculosis burden in the Philippines ten years after initiating DOTS. Int J Tuberc Lung Dis. 2009;13(10):1224–30 (https://www.ncbi.nlm.nih.gov/pubmed/19793426, accessed 28 November 2019).

52. Wang L, Zhang H, Ruan Y, Chin DP, Xia Y, Cheng S et al. Tuberculosis prevalence in China, 1990–2010; a longitudinal analysis of national survey data. Lancet. 2014;383(9934):2057–64 (https://www.ncbi.nlm.nih.gov/pubmed/24650955, accessed 28 November 2019).

53. Chanda-Kapata P, Kapata N, Klinkenberg E, Mulenga L, Tembo M, Katemangwe P et al. Non-tuberculous mycobacteria (NTM) in Zambia: prevalence, clinical, radiological and microbiological characteristics. BMC Infect Dis. 2015;15:500 (https://www.ncbi.nlm.nih.gov/pubmed/26545357, accessed 28 November 2019).

54. Melendez J, Philipsen R, Chanda-Kapata P, Sunkutu V, Kapata N, van Ginneken B. Automatic versus human reading of chest X-rays in the Zambia national tuberculosis prevalence survey. Int J Tuberc Lung Dis. 2017;21(8):880–6 (https://www.ncbi.nlm.nih.gov/pubmed/28786796, accessed 28 November 2019).

55. Hoa NB, Cobelens FG, Sy DN, Nhung NV, Borgdorff MW, EW T. Diagnosis and treatment of tuberculosis in the private sector, Vietnam. Emerg Infect Dis. 2011;17(3):562–4 (https://www.ncbi.nlm.nih.gov/pubmed/21392464, accessed 28 November 2019).

56. Hoa NB, Tiemersma EW, Sy DN, Nhung NV, Gebhard A, Borgdorff MW et al. Household expenditure and tuberculosis prevalence in VietNam: prediction by a set of household indicators. Int J Tuberc Lung Dis. 2011;15(1):32–7 (https://www.ncbi.nlm.nih.gov/pubmed/21276293, accessed 28 November 2019).

57. Horton KC, MacPherson P, Houben RM, White RG, Corbett EL. Sex differences in tuberculosis burden and notifications in low- and middle-income countries: a systematic review and meta-analysis. PLoS Med. 2016;13(9):e1002119 (https://www.ncbi.nlm.nih.gov/pubmed/27598345, accessed 28 November 2019).

Use of a digital chest X-ray during the 2015-2016 national TB prevalence survey of Kenya
Photo credit: Jane Rahedi Ong'ang'o / KEMRI

Chapter 3
Results and their implications

3.1 Survey population, enrolment and participation

Table 3.1 shows the size of the planned sample population in national tuberculosis (TB) prevalence surveys implemented in 2007–2016. The table also shows the actual size of the eligible population, the number of people who participated, the participation rate and the number of participants who screened positive for sputum examination.

3.1.1 Participation

The participation rate was high in most surveys, at ≥80% of the eligible population in 19 of 25 surveys (Fig. 3.1 and Table 3.1). The six countries with lower participation rates were Gambia, Nigeria, the Philippines (in 2016), Thailand, the United Republic of Tanzania and Zimbabwe.

In general, participation rates were higher among females, and middle and older age groups, compared with males and younger age groups (see Part II for details). Reasons for non-participation were not routinely documented, but included previous work-related health assessments or ease of access to health facilities (both of which reduced the incentive to participate for the purposes of having a chest X-ray examination), as well as lack of time.

Achieving high levels of participation in highly urban settings, especially capital cities, was challenging in almost all countries. The most extreme example was the Bangkok metropolitan area of Thailand, in which only 26% of the eligible population participated. Results from Bangkok were subsequently excluded from the final analysis.

In the Republic of Korea, the repetition of prevalence surveys every 5 years was discontinued after 1995 because of declining participation (in the context of an increasingly urbanized and modern environment) and a reduction in disease burden, which would have necessitated much larger sample sizes *(1)*. In countries that were not able to achieve a high participation rate in surveys implemented in 2007–2016, careful consideration of whether a future survey should be attempted will be needed, especially if there are further increases in the proportion of the population living in urban or more economically developed areas. This is discussed further in Chapter 5.

3.1.2 Eligibility for sputum examination

The proportion of participants who were eligible for sputum examination averaged 16%, ranging from a low of 4% of screened participants in China to a high of 40% in the 2016 survey in the Philippines (Table 3.1). The proportion was more than 20% in Bangladesh, Indonesia, Mongolia, Myanmar, the Philippines (2007 and 2016) and Sudan, due to high yields from chest X-ray screening.

In 15 of 25 surveys, chest X-ray screening identified more participants eligible for sputum examination than symptom screening (Table 3.1). However, the opposite applied in Malawi, the United Republic of Tanzania and Zambia; these African countries used a broader range of symptoms with the aim of increasing the sensitivity of the screening algorithm in a high HIV prevalence setting.[1] Of the other seven surveys, screening yields were similar, and one survey (Philippines 2007) did not systematically use symptoms for screening purposes.

3.2 TB prevalence and updated estimates of TB disease burden

3.2.1 Prevalence of pulmonary TB disease

Surveys showed that the estimated prevalence of pulmonary TB per 100 000 population was high in many countries, but there was also considerable variation

[1] The symptom screening criteria used in Malawi were any symptom for at least 1 week, including cough, sputum production, haemoptysis, chest pain, weight loss, night sweats, fatigue, fever or shortness of breath; in the United Republic of Tanzania, cough of ≥2 weeks, or haemoptysis or fever of ≥2 weeks, or weight loss or excessive night sweats; and in Zambia, cough of ≥2 weeks, or fever of ≥2 weeks, or chest pain of ≥2 weeks.

Table 3.1

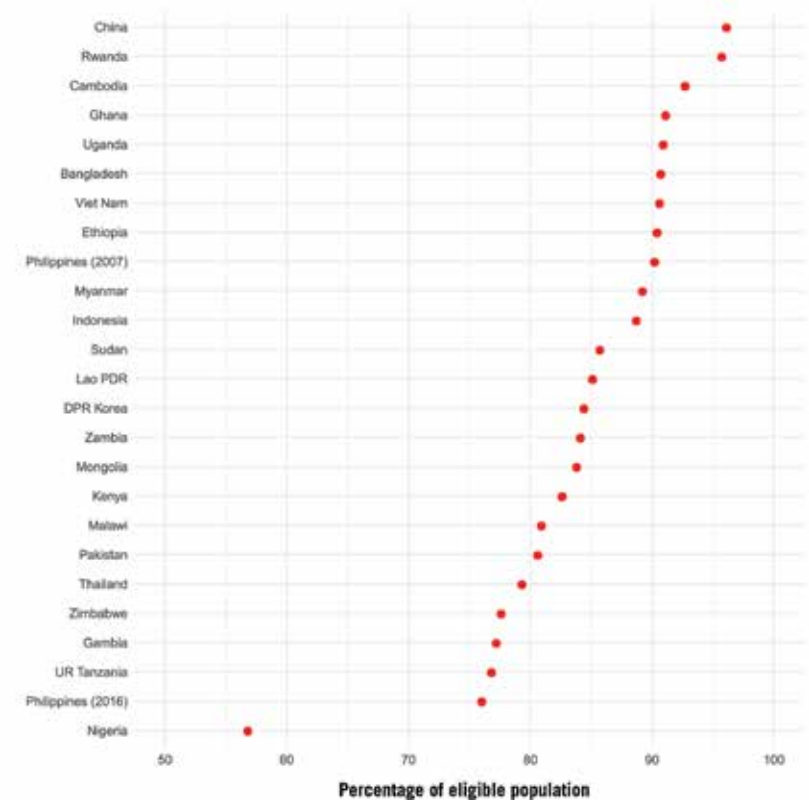
Summary of sampling population, survey participants and screening outcomes

Country	Timeframe of field operations	Planned sample population	Number of people eligible to participate	Survey participants		Number of participants eligible for sputum examination													
				Number	Rate (%)	Sym+, CXR+	%	Sym+, CXR-/ N/A	%	Sym-, CXR+	%	Others	%	Any Sym+	%	Any CXR+	%	Total eligible	%
Africa																			
Ethiopia	2010–2011	46 514	51 667	46 697	90%	806	1.7%	2220	4.8%	3013	6.5%	41	0.09%	3026	6.5%	3819	8.2%	6080	13%
Gambia	2011–2013	55 281	55 832	43 100	77%	1026	2.4%	2436	5.7%	2384	5.5%	102	0.24%	3462	8.0%	3410	7.9%	5948	14%
Ghana	2013	63 905	67 757	61 726	91%	771	1.2%	1198	1.9%	4387	7.1%	1942	3.1%	1969	3.2%	5158	8.4%	8298	13%
Kenya	2015–2016	72 000	76 291	63 050	83%	1241	2.0%	2896	4.6%	5184	8.2%	394	0.62%	4137	6.6%	6425	10%	9715	15%
Malawi	2013–2014	37 200	39 026	31 579	81%	381	1.2%	2334	7.4%	717	2.3%	N/A	N/A	2715	8.6%	1098	3.5%	3432	11%
Nigeria	2012	49 000	77 797	44 186	57%	746	1.7%	1720	3.9%	2222	5.0%	N/A	N/A	2466	5.6%	2968	6.7%	4688	11%
Rwanda	2012	44 500	45 058	43 128	96%	545	1.3%	2092	4.9%	2107	4.9%	3	0.01%	2637	6.1%	2652	6.1%	4747	11%
Sudan	2013–2014	91 131	96 979	83 202	86%	1823	2.2%	840	1.0%	9838	12%	5040	6.1%	2663	3.2%	11 661	14%	17 541	21%
Uganda	2014–2015	40 180	45 293	41 154	91%	552	1.3%	2162	5.3%	2298	5.6%	130	0.32%	2714	6.6%	2850	6.9%	5142	12%
Tanzania	2011–2012	46 792	65 664	50 447	77%	804	1.6%	3459	6.9%	2039	4.0%	N/A	N/A	4263	8.5%	2843	5.6%	6302	12%
Zambia	2013–2014	54 400	54 830	46 099	84%	1505	3.3%	2948	6.4%	2255	4.9%	N/A	N/A	4453	10%	3760	8.2%	6708	15%
Zimbabwe	2014	44 951	43 478	33 736	78%	628	1.9%	1205	3.6%	2803	8.3%	1184	3.5%	1833	5.4%	3431	10%	5820	17%
Total					**83%**		**1.8%**		**4.7%**		**6.2%**		**1.7%**		**6.5%**		**8.0%**		**14%**
Asia																			
Bangladesh	2015–2016	100 000	108 834	98 710	91%	3077	3.1%	4217	4.3%	13 300	13%	N/A	N/A	7294	7.4%	16 377	17%	20 594	21%
Cambodia	2010–2011	39 680	40 423	37 417	93%	710	1.9%	1206	3.2%	2699	7.2%	165	0.44%	1916	5.1%	3409	9.1%	4780	13%
China	2010	264 000	263 281	252 940	96%	797	0.32%	4665	1.8%	2189	0.87%	2174	0.86%	5462	2.2%	2986	1.2%	9825	3,9%
DPR Korea	2015–2016	70 000	71 877	60 683	84%	1028	1.7%	1916	3.2%	1858	3.1%	N/A	N/A	2944	4.9%	2886	4.8%	4802	7,9%
Indonesia	2013–2014	78 000	76 576	67 944	89%	4459	6.6%	4093	6.0%	6743	10%	151	0.22%	8552	13%	11 202	16%	15 446	23%
Lao PDR	2010–2012	40 000	46 079	39 212	85%	1312	3.3%	1927	4.9%	3107	7.9%	N/A	N/A	3239	8.3%	4419	11%	6346	16%
Mongolia	2014–2015	49 000	60 031	50 309	84%	817	1.6%	1729	3.4%	7064	14%	749	1.5%	2546	5.1%	7881	16%	10 359	21%
Myanmar	2009–2010	49 690	57 607	51 367	89%	1258	2.4%	433	0.84%	9364	18%	1180	2.3%	1691	3.3%	10 622	21%	12 235	24%
Pakistan	2010–2011	133 000	131 329	105 913	81%	2819	2.7%	2598	2.5%	5042	4.8%	12	0.01%	5417	5.1%	7861	7.4%	10 471	10%
Philippines	2007	30 000	22 867	20 643	90%	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	5378	26%
Philippines	2016	54 000	61 466	46 689	76%	1444	3.1%	1371	2.9%	10 702	23%	5080	11%	2815	6.0%	12 146	26%	18 597	40%
Thailand	2012–2013	90 000	78 839	62 536	79%	526	0.84%	1757	2.8%	3767	6.0%	N/A	N/A	2283	3.7%	4293	6.9%	6050	10%
Viet Nam	2006–2007	105 000	103 924	94 179	91%	518	0.55%	3522	3.7%	2972	3.2%	993	1.1%	4040	4.3%	3490	3.7%	8005	8,5%
Total					**87%**		**2.3%**		**3.3%**		**9.3%**		**2.2%**		**5.7%**		**12%**		**17%**

CXR, chest X-ray; DPR Korea, Democratic People's Republic of Korea; Lao PDR, Lao People's Democratic Republic; N/A, not applicable; Sym, symptom; Tanzania, United Republic of Tanzania; +, positive; -, negative.

Fig. 3.1

Participation rate in 25 surveys (24 countries) implemented in 2007–2016



DPR Korea, Democratic People's Republic of Korea; Lao PDR, Lao People's Democratic Republic; UR Tanzania, United Republic of Tanzania.

among countries and between Africa and Asia (Fig. 3.2 and Table 3.2).

In African countries, the prevalence of smear-positive pulmonary TB per 100 000 population aged 15 years or above ranged from 74 (95% confidence interval [CI]: 48–99) in Rwanda to 319 (95% CI 232–406) in Zambia. Similarly, the prevalence of bacteriologically confirmed pulmonary TB per 100 000 population aged 15 years or above ranged from 119 (95% CI: 79–160) in Rwanda to 638 (95% CI: 502–774) in Zambia. There was great variation in the proportion of bacteriologically confirmed pulmonary TB cases that were smear-positive in Africa, from a low of 24% in Zimbabwe to a high of 62% in Rwanda (Table 3.2).

In Asian countries, the prevalence of smear-positive pulmonary TB per 100 000 population aged 15 years or above ranged from 66 (95% CI: 53–79) in China to 434 (95% CI: 350–518) in the Philippines (in 2016). Similarly, the prevalence of bacteriologically confirmed TB per 100 000 population aged 15 years or above ranged from 119 (95% CI: 103–135) in China to 1159 (95% CI: 1016–1301) in the Philippines (in 2016). As in surveys in African countries, the proportion of bacteriologically confirmed pulmonary TB cases that were smear-negative varied widely, from 33% in Cambodia to 68% in Pakistan (Table 3.2).

The systematic use of culture (as well as Xpert® MTB/RIF in three of the later surveys)[1] identified more smear-negative than smear-positive pulmonary TB cases in all but the following eight surveys: China, the Democratic People's Republic of Korea, Nigeria, Pakistan, Rwanda, Sudan, Viet Nam and Zambia (Table 3.2).

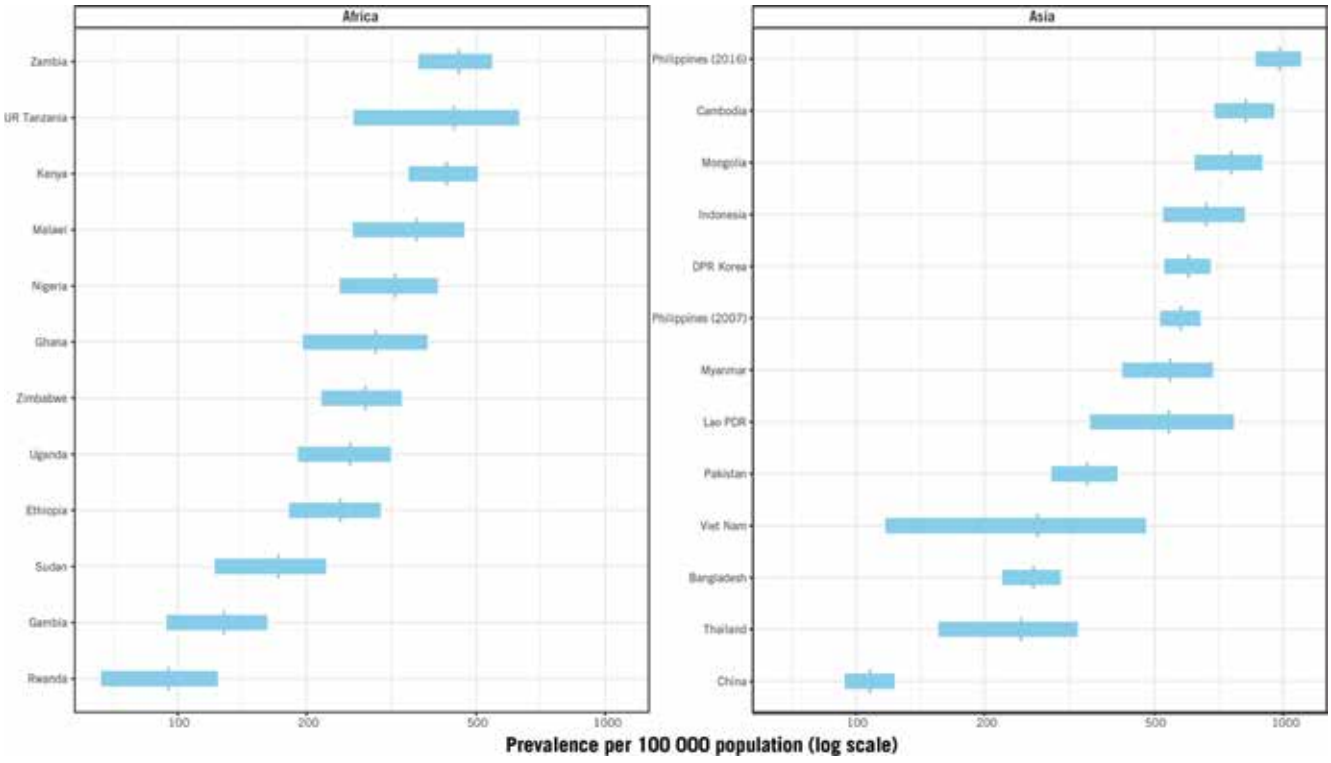
3.2.2 Prevalence of pulmonary TB disease disaggregated by age and sex

The distribution of prevalent cases by age is shown in Fig. 3.3a for surveys in African countries and Fig. 3.3b for surveys in Asian countries. In the latter, there was

[1] Bangladesh (2015), Kenya (2015) and the Philippines (2016).

Fig. 3.2

Estimates of the prevalence of bacteriologically confirmed pulmonary TB in those aged ≥15 years in 25 surveys (24 countries) implemented in 2007–2016



DPR Korea, Democratic People's Republic of Korea; Lao PDR, Lao People's Democratic Republic; UR Tanzania, United Republic of Tanzania.

a clear pattern in which prevalence increased with age (an exception was the Democratic People's Republic of Korea). In African countries, this pattern was only observed in Ghana and Rwanda, although in Malawi and the United Republic of Tanzania there was an increase between the age groups of 45–54 years and of 65 years or more, after an earlier peak in the age group 35–44 years. In most African countries, there was a peak in prevalence per 100 000 population in the age groups 35–44 or 45–54 years,[1] which could be explained at least in part by the impact of the HIV epidemic.

As transmission declines, more incident cases arise from past rather than recent infection. Therefore, a pattern in which prevalence increases with age suggests that transmission is falling. It is encouraging that prevalence surveys indicated that transmission is potentially declining in many Asian countries as well as in Ghana, Malawi, Rwanda and the United Republic of Tanzania. In other countries, surveys suggested considerable community transmission.

A striking finding across all surveys was the much higher burden of TB disease in men compared with women (Fig. 3.4). The male to female ratio of the prevalence of bacteriologically confirmed TB was 2.3 (95% CI: 2.0–2.6) overall, but ranged from 1.2 in Ethiopia to more than 4 in Uganda and Viet Nam. It was higher in Asia (2.6) than in Africa (2.0). These results mean that men account for about 66–70% of the burden of TB disease among adults in Asia and Africa.

3.2.3 Estimates of the prevalence of TB, all ages and all forms

Following surveys, estimates of the prevalence of TB for all ages (i.e. including those aged <15 years) and all forms (i.e. including extrapulmonary as well as pulmonary TB) were updated by WHO in consultation with national authorities. Fig 3.5 compares the updated estimates with the most recent estimates published before survey results became available.

[1] The estimated absolute number of TB cases in each age group is shown in Fig. 3 of the country profiles in Part II.

Table 3.2

Estimated prevalence of smear-positive and bacteriologically confirmed pulmonary TB

Country	Smear-positive pulmonary TB				Bacteriologically confirmed pulmonary TB				Proportion of bacteriologically confirmed cases that were smear-positive
	Number of cases	Prevalence per 100 000 population aged ≥15 years [a]	95% confidence interval	*k* [b]	Number of cases	Prevalence per 100 000 population aged ≥15 years [a]	95% confidence interval	*k* [b]	
Africa									
Ethiopia	47	108	73–143	0.7	110	277	208–347	0.4	39
Gambia	34	90	53–127	1.3	77	212	152–272	0.7	42
Ghana	64	111	76–145	0.9	202	356	288–425	0.7	31
Kenya	123	230	174–286	0.7	305	558	455–662	0.7	41
Malawi	62	220	142–297	1.1	132	452	312–593	1.1	49
Nigeria	107	318	225–412	0.9	144	524	378–670	0.7	61
Rwanda	27	74	48–99	N/A[c]	40	119	79–160	0.7	62
Sudan	57	87	52–121	1.3	112	183	128–238	1.3	48
Uganda	66	174	111–238	0.9	160	401	292–509	0.8	43
UR Tanzania [c]	134	275	232–326	0.6	N/A	N/A	N/A	N/A	N/A
Zambia	135	319	232–406	0.8	265	638	502–774	0.7	50
Zimbabwe	23	82	47–118	N/A [d]	107	344	268–420	0.3	24
Asia									
Bangladesh	108	113	87–139	0.7	278	287	244–330	0.5	39
Cambodia	103	271	212–348	0.6	314	831	707–977	0.5	33
China	188	66	53–79	0.9	347	119	103–135	0.5	55
DPR Korea	187	330	283–377	2.0	340	587	520–655	0.6	56
Indonesia	165	257	210–303	0.7	426	759	590–961	0.5	34
Lao PDR	107	278	199–356	0.7	237	595	457–733	0.7	47
Mongolia	88	204	143–265	1.5	248	560	455–665	0.9	36
Myanmar	123	242	186–315	0.8	311	613	502–748	0.7	39
Pakistan	233	270	217–323	0.6	341	398	333–463	0.6	68
Philippines (2007)	55	280	190–370	1.0	136	660	530–800	0.6	42
Philippines (2016)	173	434	350–518	0.6	446	1159	1016–1301	0.6	37
Thailand	58	104	55–195	1.0	142	242	176–332	0.5	43
Viet Nam	174	197	150–244	0.8	269	307	249–366	0.6	64

DPR Korea, Democratic People's Republic of Korea; Lao PDR, Lao People's Democratic Republic; N/A, not applicable; TB, tuberculosis; UR Tanzania, United Republic of Tanzania.

[a] Estimates are based on the use of robust standard errors with missing value imputation and inverse probability weighting for all countries except the United Republic of Tanzania, for which a cluster-level model of analysis was used.

[b] *k* is the coefficient of variation of the cluster-specific TB prevalences.

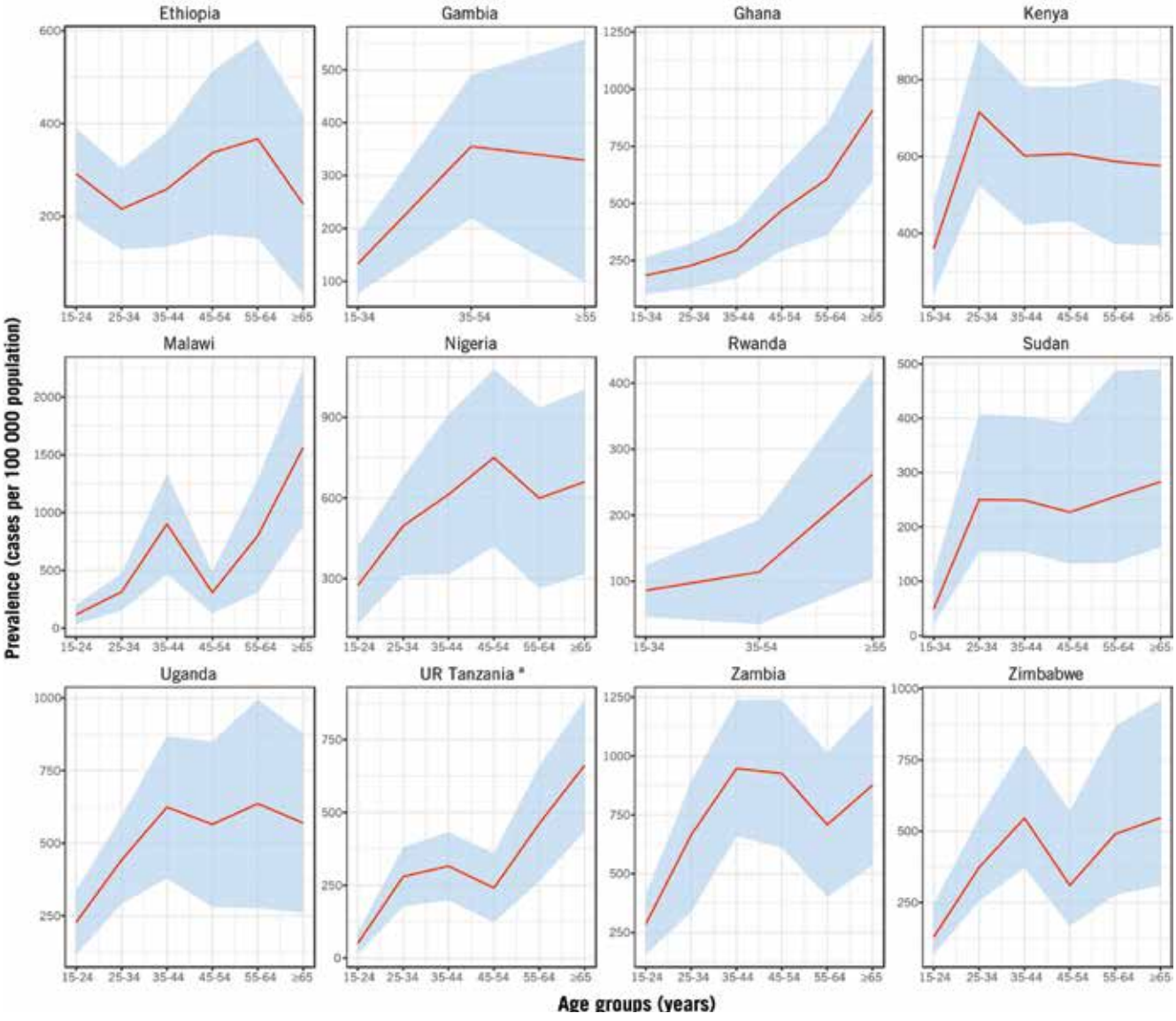
[c] The number of bacteriologically confirmed pulmonary TB cases could not be verified for the United Republic of Tanzania.

[d] For Rwanda and Zimbabwe, *k* could not be calculated because the design effect was less than one.

Fig. 3.3a

Estimated age-specific prevalence of bacteriologically confirmed pulmonary TB for surveys implemented in Africa in 2010–2016

The red line denotes the best estimate and the blue shaded areas are the 95% confidence intervals.



UR Tanzania, United Republic of Tanzania.

[a] Bacteriologically confirmed TB cases could not be verified for United Republic of Tanzania, so smear-positive TB prevalence rates are shown instead.

In all countries, estimates of TB prevalence based on national surveys were much more precise than presurvey estimates (i.e. uncertainty intervals were much narrower). In most countries, best estimates based on surveys were also within the uncertainty interval of presurvey estimates. Best estimates of TB prevalence based on survey results were higher than presurvey estimates in 15 countries (most noticeably in Ghana, Indonesia, Lao People's Democratic Republic, Malawi, Mongolia, the Philippines (2016) and the United Republic of Tanzania) and lower in 10 countries (most noticeably in Ethiopia, Gambia and Zimbabwe).

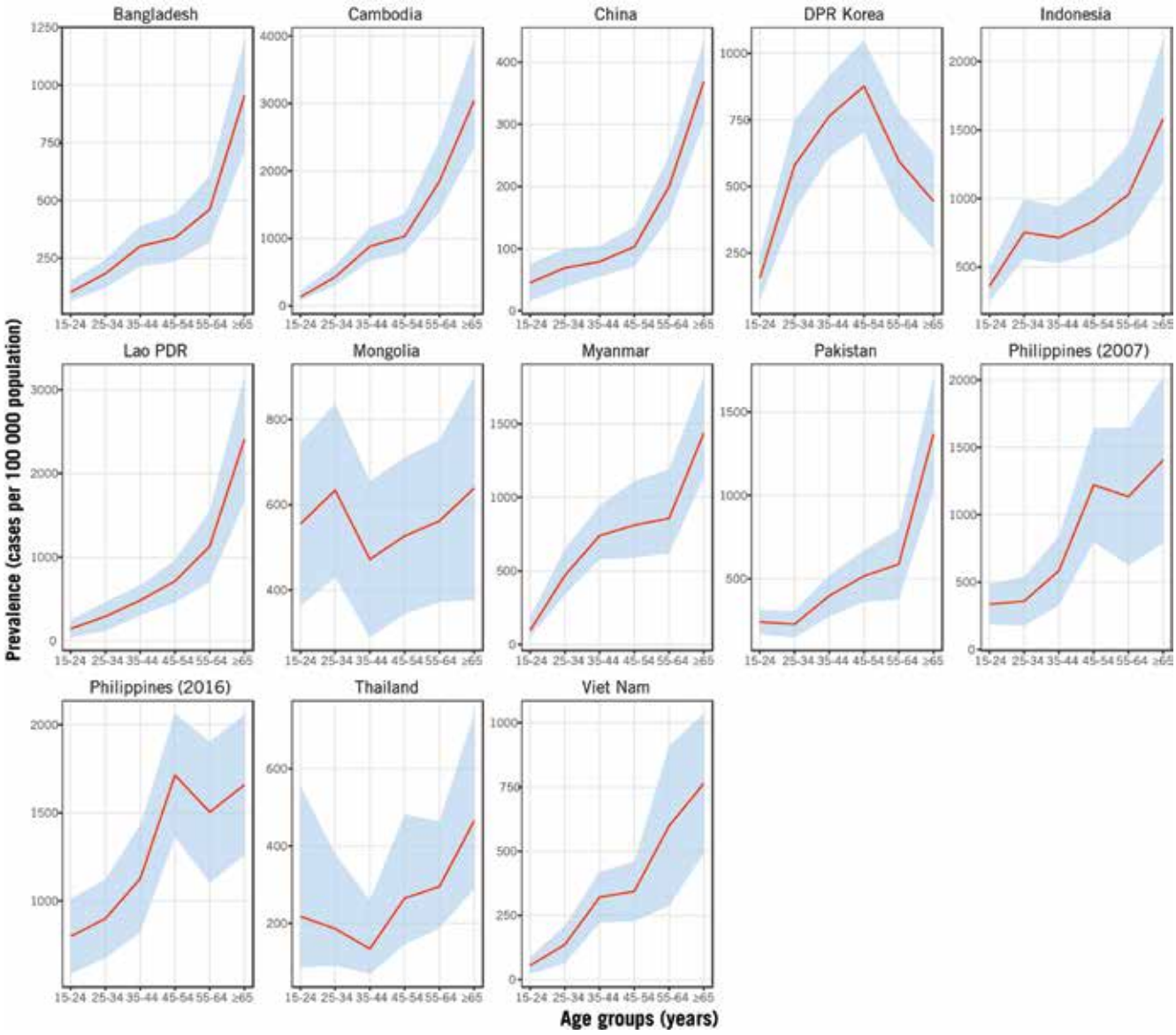
3.3 Trends in TB prevalence measured in repeat surveys

Among countries that conducted prevalence surveys between 2007 and 2016, three countries had undertaken at least one survey in the preceding 20 years: Cambodia (2002), China (1990, 2000 and 2010) and the Philippines

Fig. 3.3b

Estimated age-specific prevalence of bacteriologically confirmed pulmonary TB for surveys implemented in Asia in 2007–2016

The red line denotes the best estimate and the blue shaded areas are the 95% confidence intervals.



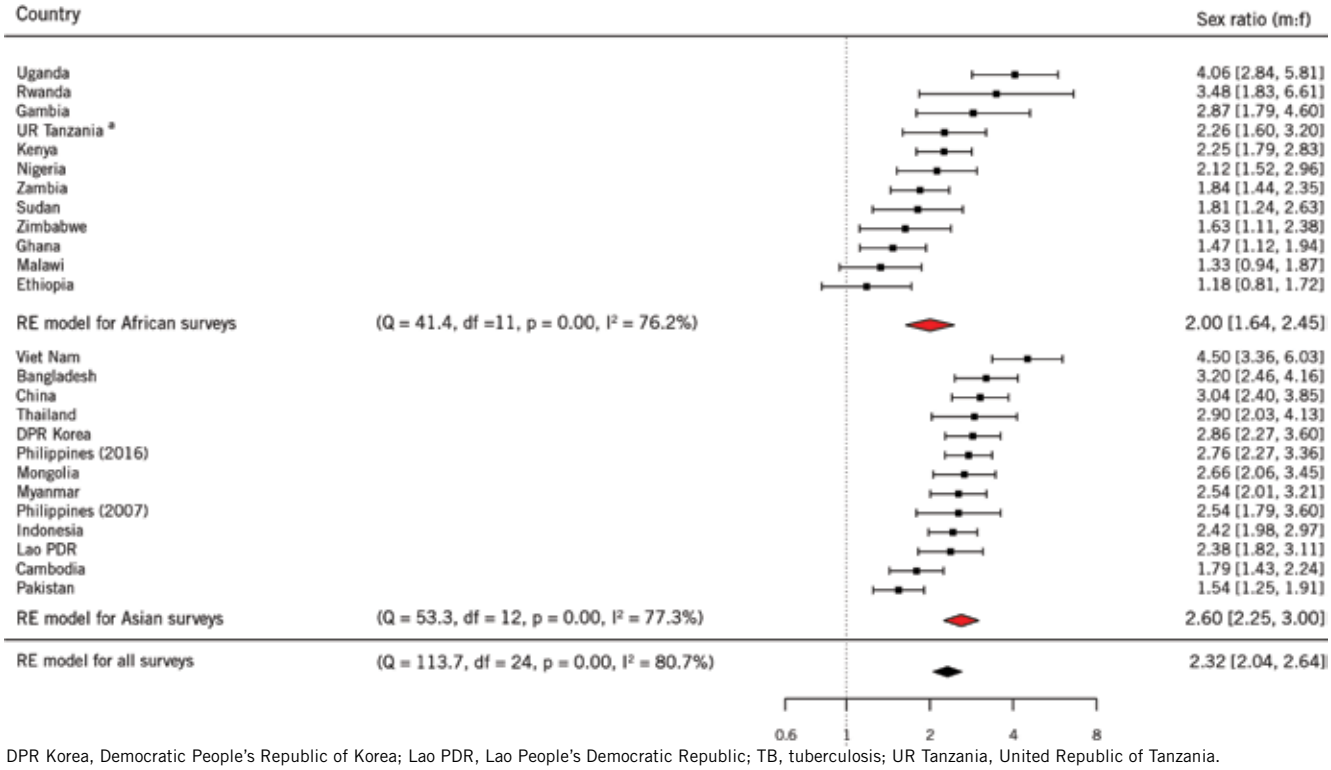
DPR Korea, Democratic People's Republic of Korea; Lao PDR, Lao People's Democratic Republic; TB, tuberculosis.

(1997 and 2007). Trends in TB prevalence based on surveys conducted since 2007 are shown in Fig. 3.6.

The repeat surveys in Cambodia and China demonstrated that substantial reductions in TB prevalence can be achieved within 10 years. Observed reductions in the prevalence of smear-positive pulmonary TB in particular were consistent with the prioritization given to detection and cure of the most infectious cases within the framework of the DOTS strategy, which was recommended by WHO between the mid-1990s and 2006 (see also Chapter 1). The reduction in TB prevalence in China between 2000 and 2010 occurred during a period of nationwide expansion of DOTS (from half to all of the country). The reduction in Cambodia occurred during a period when DOTS services were expanded to health centres as well as hospitals, making TB diagnostic and treatment services much more accessible *(2-4)*. However, the Philippines fourth national survey, in 2016, showed concerning results. Following a reduction in TB prevalence between 1997 and 2007, no decline occurred

Fig. 3.4

The sex ratio (male to female) of bacteriologically confirmed pulmonary TB cases detected in prevalence surveys implemented in 2007–2016

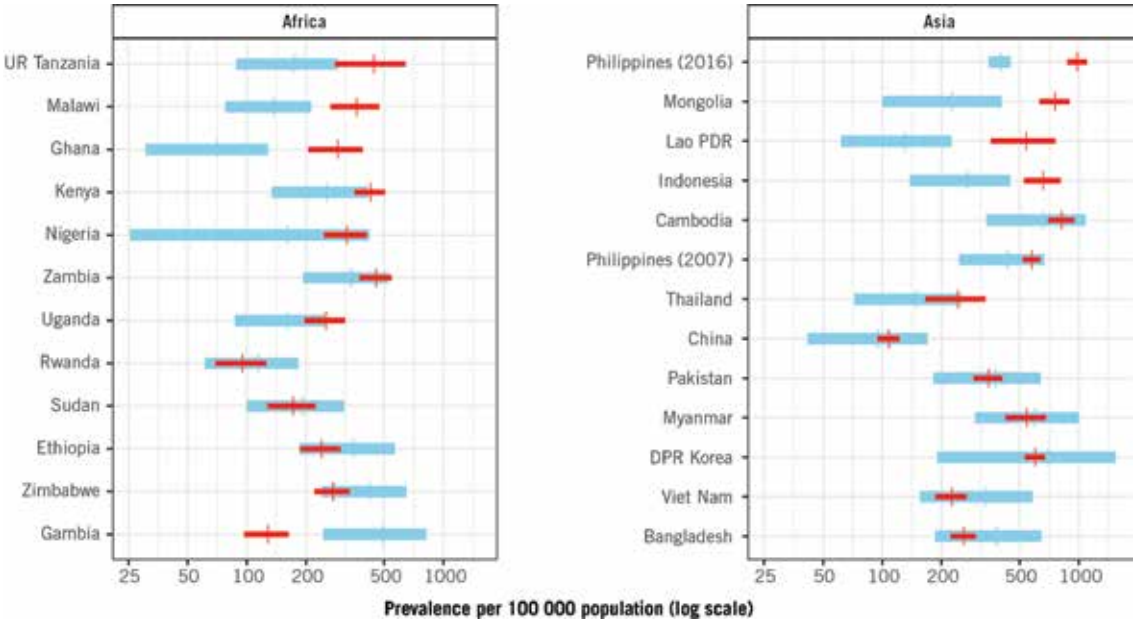


DPR Korea, Democratic People's Republic of Korea; Lao PDR, Lao People's Democratic Republic; TB, tuberculosis; UR Tanzania, United Republic of Tanzania.
[a] The sex ratio of smear–positive TB cases is shown for the United Republic of Tanzania.

Fig. 3.5

Estimates of TB prevalence (all ages, all forms of TB) for 25 surveys (24 countries), before (in blue) and after (in red) results became available from national TB prevalence surveys implemented in 2007–2016

Countries are listed in decreasing order according to the before–after difference.

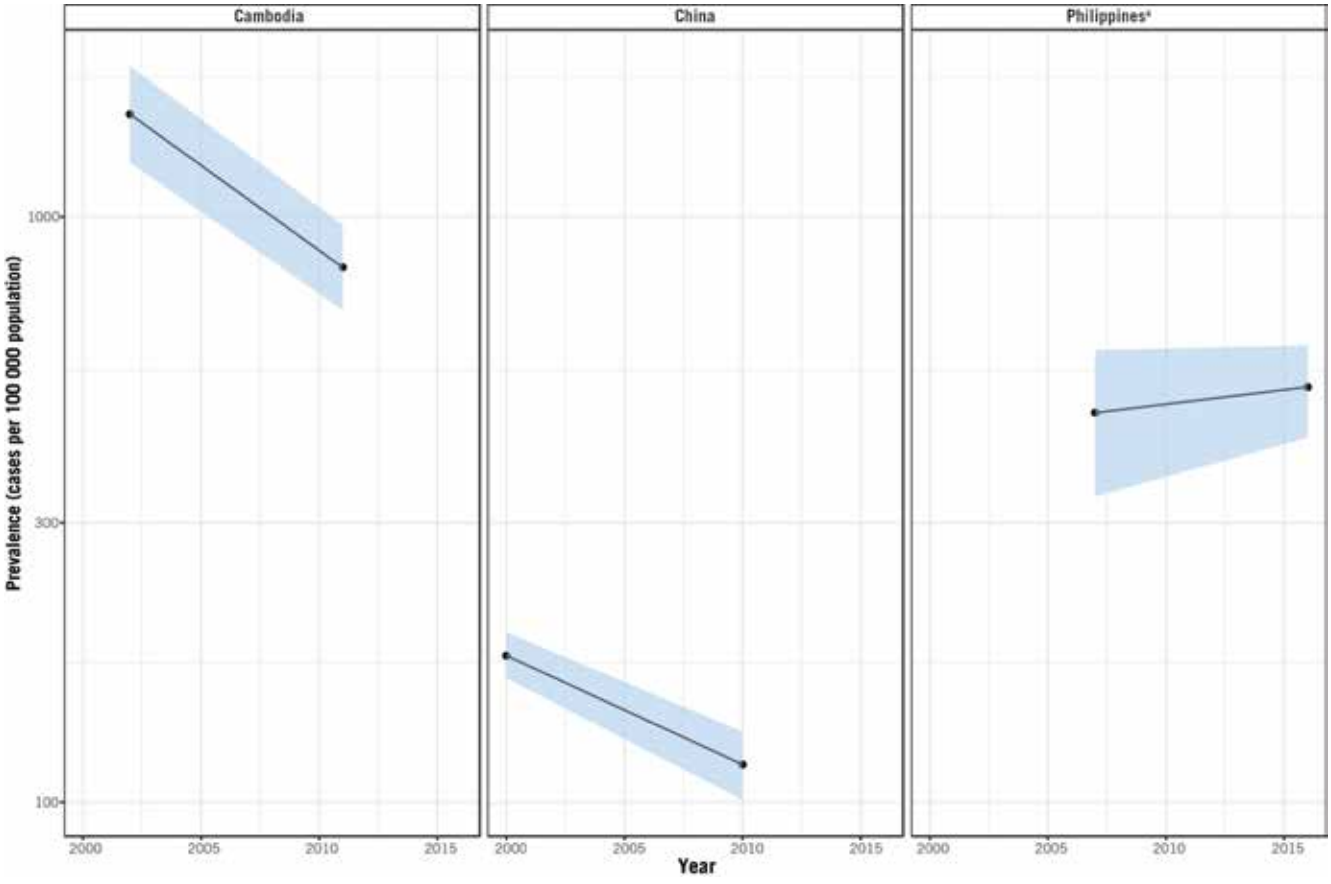


DPR Korea, Democratic People's Republic of Korea; Lao PDR, Lao People's Democratic Republic; UR Tanzania, United Republic of Tanzania.

Fig. 3.6

Trends in bacteriologically confirmed pulmonary TB measured in repeat surveys in Cambodia, China and the Philippines

Shaded areas represent uncertainty intervals.



[a] The trend is for culture-confirmed cases.

between 2007 and 2016. This may be linked to broader determinants of the TB epidemic, notably levels of poverty and undernutrition *(5)*.

Although not featured in this book, repeat surveys in Myanmar in 2018 and Viet Nam in 2017 showed large reductions in disease burden from 2009 to 2018 and from 2007 to 2017, respectively *(6)*.

3.4 Proportion of survey cases reporting symptoms that met screening criteria

A consistent finding in all surveys was that a high proportion of people with bacteriologically confirmed pulmonary TB did not report symptoms that met screening criteria. Although symptom screening criteria varied between countries (Table 3.2), only about half of the bacteriologically confirmed pulmonary TB cases (median 48%, range 21–70%) would have been identified if relying on symptom screening alone (Table 3.3). Other cases were identified due to chest X-ray screening.

Among countries that used chronic cough alone as a symptom screening criterion, the proportion of people with bacteriologically confirmed pulmonary TB that did not report this symptom ranged from 36% in Nigeria to 79% in Mongolia. When chronic cough or haemoptysis (or both) were used, the proportion ranged from 43% in the Democratic People's Republic of Korea and Indonesia to 79% in Myanmar. When cough and other TB-related symptoms were used, the proportion ranged from 30% in Malawi to 66% in Thailand (Fig. 3.7, Table 3.3).

These findings can be explained by the fact that a prevalence survey identifies many people in the earlier stages of TB disease, before symptoms become more serious. These people will remain a source of transmission

Table 3.3

Screening outcomes of bacteriologically confirmed pulmonary TB cases

Country	Number of bacteriologically confirmed TB cases	Symptom screening definition [a]	Symptom positive, chest X-ray positive	Symptom positive, chest X-ray negative/ N/A	Symptom negative, chest X-ray positive	Other screening category [a]	Proportion identified by symptom screening (%)	Proportion identified by chest X-ray screening (%)
Ethiopia	110	Cough ≥2 weeks	45	12	53	0	52%	89%
Ghana	202	Cough ≥2 weeks	67	15	85	35	41%	75%
Kenya	305	Cough ≥2 weeks	115	32	154	4	48%	88%
Mongolia	248	Cough ≥2 weeks	44	7	194	3	21%	96%
Nigeria	144	Cough ≥2 weeks	76	16	52	N/A	64%	89%
Sudan	112	Cough ≥2 weeks	43	8	45	16	46%	79%
Uganda	160	Cough ≥2 weeks	63	16	81	0	49%	90%
Viet Nam	269	Cough ≥2 weeks	48	23	181	17	26%	85%
Cambodia	314	Cough ≥2 weeks or haemoptysis	88	5	218	3	30%	97%
China	347	Cough ≥2 weeks or haemoptysis	143	17	182	5	46%	94%
DPR Korea	340	Cough ≥2 weeks or haemoptysis	187	7	146	N/A	57%	98%
Indonesia	426	Cough ≥2 weeks or haemoptysis	217	25	184	0	57%	94%
Lao PDR	237	Cough ≥2 weeks or haemoptysis	111	7	119	N/A	50%	97%
Myanmar	311	Cough ≥3 weeks or haemoptysis	65	1	231	14	21%	95%
Philippines (2016)	446	Cough ≥2 weeks or haemoptysis	132	18	298	18	34%	96%
Bangladesh	278	Other	79	27	172	N/A	38%	90%
Gambia	77	Other	32	12	33	0	57%	84%
Malawi	132	Other	25	67	40	N/A	70%	49%
Pakistan	341	Other	157	41	142	1	58%	88%
Philippines (2007) [b]	136	Other	N/A	N/A	N/A	N/A	N/A	N/A
Rwanda	40	Other	15	4	21	0	N/A	90%
Thailand	142	Other	42	6	94	N/A	N/A	96%
UR Tanzania [c]	134	Other	55	18	48	13	N/A	77%
Zambia	265	Other	115	46	104	N/A	N/A	83%
Zimbabwe	107	Other	29	10	64	4	N/A	87%

DPR Korea, Democratic People's Republic of Korea; Lao PDR, Lao People's Democratic Republic; N/A, not applicable; UR Tanzania, United Republic of Tanzania.

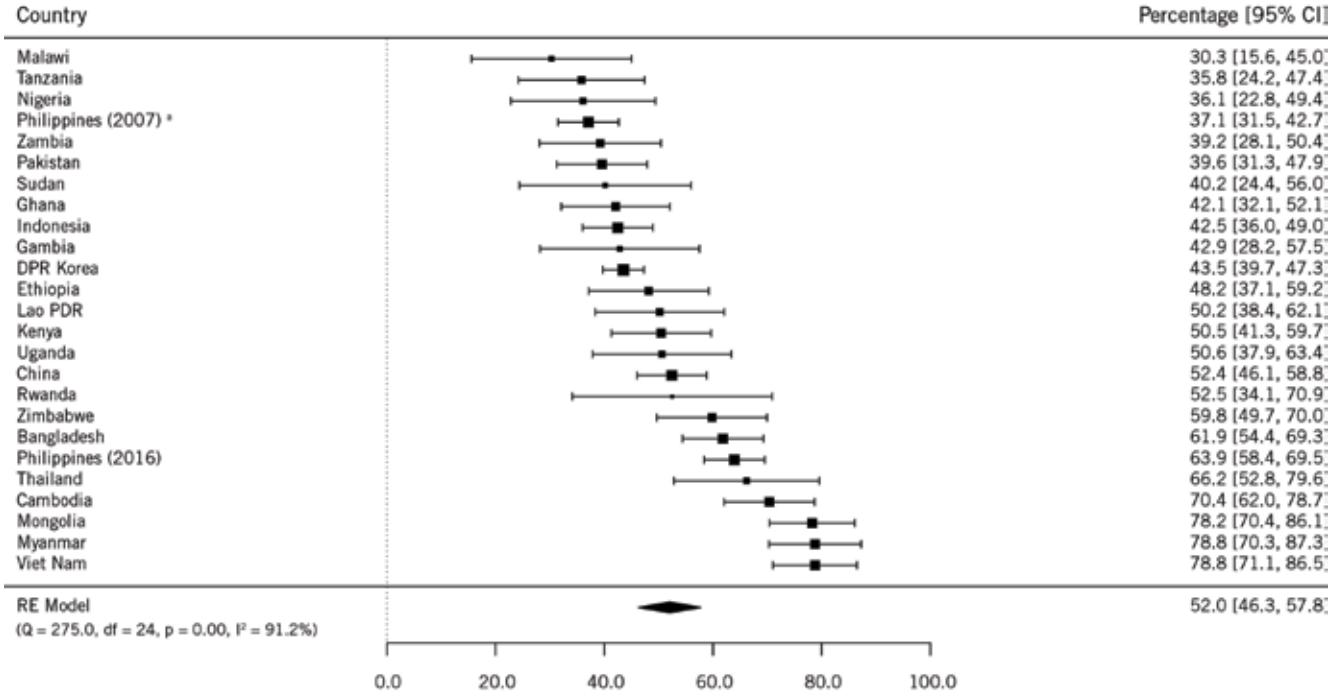
[a] Other screening criteria generally included more symptoms or symptoms of longer duration. See country specific chapters in **Part II** for details.

[b] In the Philippines (2007), a symptom interview was not used to screen participants.

[c] In the United Republic of Tanzania, only smear-positive TB survey cases were reported.

Fig. 3.7

Proportion of prevalent TB cases that were symptom–screen negative in surveys implemented in 2007–2016



DPR Korea, Democratic People's Republic of Korea; Lao PDR, Lao People's Democratic Republic; UR Tanzania, United Republic of Tanzania.
[a] The Philippines (2007) survey did not use symptom screening; however, symptom–related data were collected from all detected TB cases.

until they experience symptoms that prompt them to seek health care. Even if they had sought care at an earlier stage, it is unlikely (with existing screening criteria) that they would have been referred for further laboratory testing on the basis of reported symptoms.

As access to TB diagnostic and treatment services improve, the proportion of prevalent cases in the community that do report the 'classic' symptoms of pulmonary TB should fall. A prevalence survey in which a high proportion of cases do not report symptoms may indicate relatively good access to TB diagnosis and care, whereas a low proportion tends to suggest that access needs to be improved. An example of this was Nigeria, where many cases found in the survey already had symptoms that should have prompted care seeking and prompt diagnostic testing at health facilities. An increased proportion of cases not reporting symptoms in a repeat survey is consistent with improved health care services. This was a pattern found in the 2010–2011 survey in Cambodia, in which the prevalence of people with smear-positive pulmonary TB that reported symptoms fell by 56% compared with 2002.

Among those who do seek care, widening the use of chest X-ray screening in primary health care facilities and raising awareness among health care staff about the magnitude and characteristics of TB cases in the community could contribute to earlier diagnosis.

3.5 Detection and reporting gaps

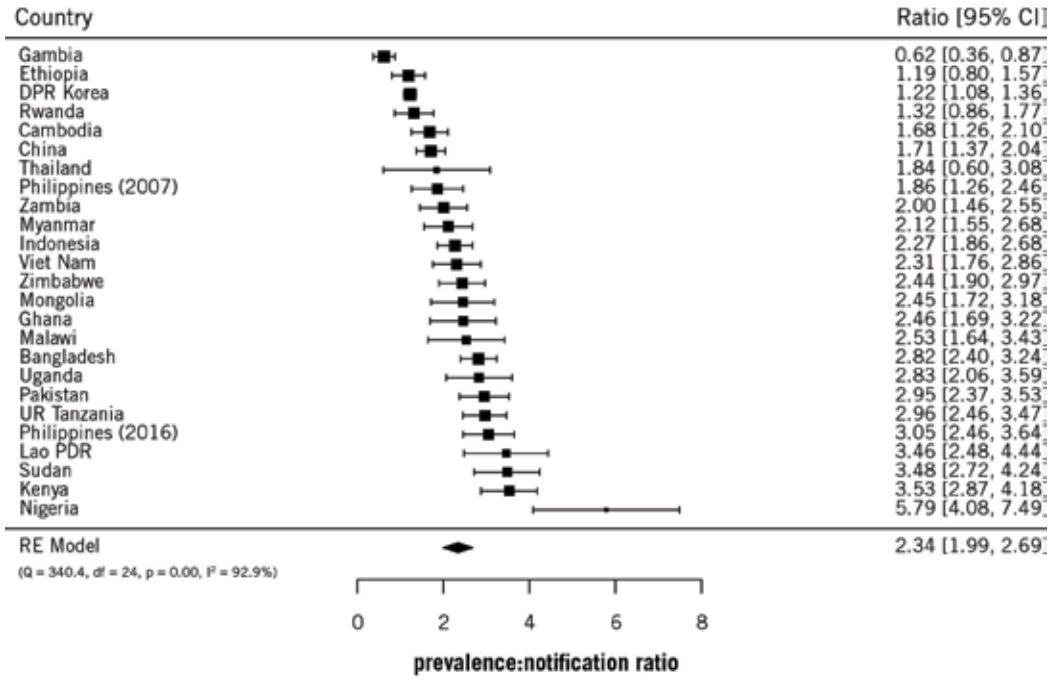
When measurements of prevalence are compared with official case notification data, prevalence surveys can identify gaps in detection and reporting. Overall ratios of prevalent (P) to notified (N) cases are shown in Fig. 3.8a, and ratios disaggregated by sex are shown in Fig. 3.8b–d.[1] Ratios ranged from 0.62 in Gambia to 5.8 in Nigeria. For all countries except the Philippines in 2007 and Zimbabwe, the ratio was higher in men than women.

Cross-country and male/female differences in the P:N ratio show that in several countries it should be possible

[1] The P:N ratio is an approximate indicator (expressed in years) of case detection by the NTP *(7)*. The higher the ratio, the longer the time taken for a prevalent case to be notified to the NTP. Some cases may exit the pool of prevalent cases without being notified, for example because they self-cure or die, or because they are detected and treated by providers not linked to official reporting systems.

Fig. 3.8a

TB prevalence to TB notification (P:N) ratio in surveys implemented in 2007–2016 [a]

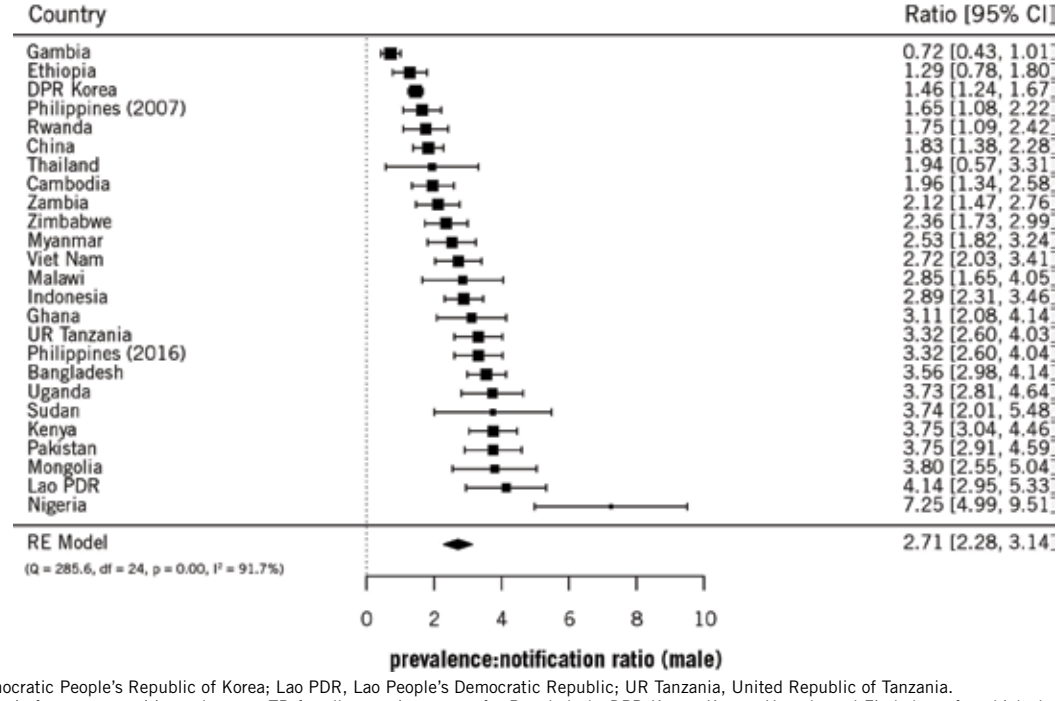


DPR Korea, Democratic People's Republic of Korea; Lao PDR, Lao People's Democratic Republic; UR Tanzania, United Republic of Tanzania.

[a] The comparison is for smear–positive pulmonary TB for all countries except for Bangladesh, DPR Korea, Kenya, Uganda and Zimbabwe, for which the comparison is for bacteriologically confirmed pulmonary TB.

Fig. 3.8b

TB prevalence to TB notification (P:N) ratio (male) in surveys implemented in 2007–2016 [a]

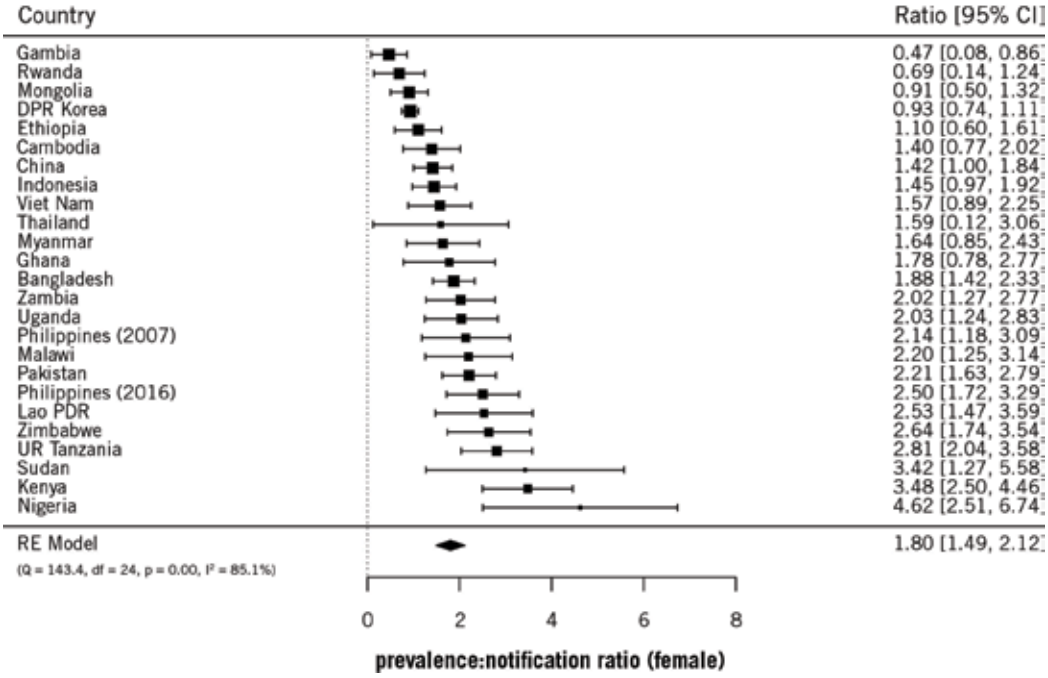


DPR Korea, Democratic People's Republic of Korea; Lao PDR, Lao People's Democratic Republic; UR Tanzania, United Republic of Tanzania.

[a] The comparison is for smear–positive pulmonary TB for all countries except for Bangladesh, DPR Korea, Kenya, Uganda and Zimbabwe, for which the comparison is for bacteriologically confirmed pulmonary TB.

Fig. 3.8c

TB prevalence to TB notification (P:N) ratio (female) in surveys implemented in 2007–2016 [a]

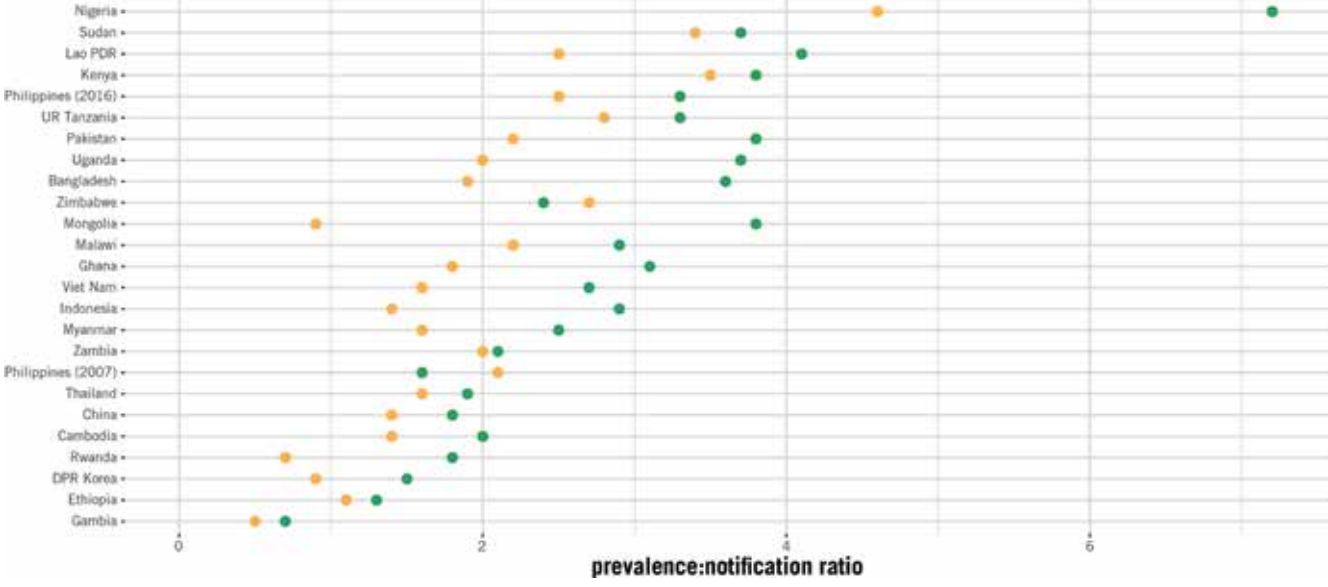


DPR Korea, Democratic People's Republic of Korea; Lao PDR, Lao People's Democratic Republic; UR Tanzania, United Republic of Tanzania.

[a] The comparison is for smear–positive pulmonary TB for all countries except for Bangladesh, DPR Korea, Kenya, Uganda and Zimbabwe, for which the comparison is for bacteriologically confirmed pulmonary TB.

Fig. 3.8d

Comparison of the TB prevalence to TB notification (P:N) ratio between men (green) and women (orange) in surveys implemented in 2007–2016 [a]



DPR Korea, Democratic People's Republic of Korea; Lao PDR, Lao People's Democratic Republic; UR Tanzania, United Republic of Tanzania.

[a] The comparison is for smear-positive pulmonary TB for all countries except for Bangladesh, DPR Korea, Kenya, Uganda and Zimbabwe, for which the comparison is for bacteriologically confirmed pulmonary TB.

to achieve better (i.e. lower) ratios with strategies and technologies for TB diagnosis and treatment that are already available, and to close reporting and detection gaps for men. Although the burden of TB disease was consistently higher in men, P:N ratios were systematically lower among women, suggesting that women were accessing available diagnostic and treatment services more effectively *(8)*. Development of strategies to improve care seeking and diagnosis among men are warranted in many countries.

In some countries, P:N ratios also indicated that older people with TB were detected less effectively (**Fig. 3.9**). This may reflect financial and geographical accessibility barriers. Older people may also have greater tolerance of symptoms or associate symptoms with other chronic health conditions, leading to delayed care seeking and associated investigations.

In Indonesia *(9)* and Viet Nam *(10)*, the records of survey participants on treatment at the time of the survey were linked to the records of newly detected cases from routine TB surveillance, enabling the magnitude of underreporting of detected cases to be measured. In Indonesia, of the participants who reported that they were on TB treatment, only 19% (24/125) were identified in the national TB register, which helps to explain the high P:N ratio. In Viet Nam, 10% (37/353) of the participants that screened positive and were recently treated for TB had not been reported to the NTP.

Whenever possible, future surveys should include comparison of the records of cases on treatment at the time of the survey with a national case-based electronic TB database, to assess the level of underreporting. Alternatively, or in addition,[1] national inventory studies *(11)* can be used to measure levels of underreporting. A good example was the national inventory study in Indonesia, which was prompted by findings from the national TB prevalence survey.[2]

3.6 HIV testing and the prevalence of HIV

Although HIV testing is a routine part of TB case management, collection of data about HIV status was not standardized in prevalence surveys implemented in 2007–2016. Reasons included variation in national HIV testing policies, the logistics of taking blood samples in the field, and the concern that survey participation might be negatively affected by refusing an HIV test. None of the surveys in Asia included HIV testing. HIV testing results or the HIV status of participants (or both) were obtained as part of the surveys in seven African countries: Kenya, Malawi, Rwanda, Uganda, the United Republic of Tanzania, Zambia and Zimbabwe (**Table 3.4**).

HIV testing during field operations was done in only four countries: Rwanda, Uganda, the United Republic of Tanzania and Zambia. In Rwanda, Uganda and the United Republic of Tanzania, only those eligible for sputum examination were offered an HIV test. In Zambia, HIV testing was offered to all survey participants. In Zambia, 2063 (6.7%) of those tested were HIV-positive. In Rwanda, Uganda and the United Republic of Tanzania, the proportions of those tested who were HIV-positive were 4.9%, 9.6% and 5.0%, respectively.

In Malawi, all participants were asked if they had ever been tested for HIV, and were invited to disclose their status; verbal acknowledgement of HIV status was provided for 19 703 (62%) participants, of which 1840 (9.3%) reported that they were HIV-positive. In Kenya and Zimbabwe, records of survey cases were linked to records from routine HIV treatment and care programmes. The proportion of survey cases who were HIV-positive was 13% in Kenya and 51% in Zimbabwe.

HIV prevalence among prevalent TB cases was systematically lower than HIV prevalence among newly notified cases (**Fig. 3.10**), probably reflecting the faster progression of TB disease in people living with HIV, which prompts earlier care seeking. It is also plausible that the expansion of HIV care programmes since the early 2000s contributed to earlier detection and treatment of TB among people living with HIV.

3.7 Health care seeking behaviour

Patterns of health care seeking behaviour can help to identify actions that could be taken to shorten the time to TB diagnosis and treatment. They may also indicate care providers that need to be better engaged with the NTP, including to ensure reporting of detected cases.

Although there was limited standardization in the data on health care seeking behaviour that were collected during surveys implemented in 2007–2016, it was clear that a large proportion of symptomatic participants had not sought care before the survey (**Table 3.5**). The median proportion of those reporting symptoms that

[1] Cases detected before survey investigations are typically not as well documented as survey cases detected during investigations, particularly in countries where culture or Xpert MTB/RIF are not routinely used.

[2] Results and lessons learned from this study were documented in the 2018 WHO global TB report (*12*).

Fig. 3.9

TB prevalence to TB notification (P:N) ratio by age group in surveys implemented in 2007–2016 [a]

DPR Korea, Democratic People's Republic of Korea; Lao PDR, Lao People's Democratic Republic; UR Tanzania, United Republic of Tanzania.

[a] The comparison is for smear-positive pulmonary TB for all countries except for Bangladesh, DPR Korea, Kenya, Uganda and Zimbabwe, for which the comparison is for bacteriologically confirmed pulmonary TB.

Table 3.4

HIV status of participants and bacteriologically confirmed pulmonary TB cases

	Participants						Participants who screened positive								Bacteriologically confirmed pulmonary TB cases					
Country	Number of participants who were tested for HIV, or had documented HIV status	% [a]	HIV-positive	%	HIV-negative	%	Total screened positive	Number of participants who were tested for HIV, or with documented HIV status	%	HIV-positive	%	HIV-negative	%	Total TB cases	Number who were tested for HIV or with reported HIV status	%	HIV-positive	%	HIV-negative	%
Kenya [b]	N/A	N/A	N/A	N/A	N/A	N/A	9715	N/A	N/A	N/A	N/A	N/A	N/A	305	245	80%	41	17%	204	67%
Malawi [c]	19 703	62%	1840	9.3%	17 863	91%	3432	2066	60%	339	16%	1708	83%	132	78 [a]	59%	22	28%	52	67%
Rwanda [d]	N/A	N/A	N/A	N/A	N/A	N/A	4747	4445	94%	218	4.9%	4227	95%	40	36	90%	1	2.8%	35	97%
Uganda [d]	N/A	N/A	N/A	N/A	N/A	N/A	5142	4386	85%	422	9.6%	3964	90%	160	145	91%	39	27%	106	73%
UR Tanzania [d,e]	N/A	N/A	N/A	N/A	N/A	N/A	6302	6302	100	318	5.0%	5984	95%	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Zambia [f]	30 584	66%	2062	6.7%	28 522	93%	6708	N/A	N/A	N/A	N/A	N/A	N/A	265	134	51%	36	27%	98	73%
Zimbabwe [g]	N/A	N/A	N/A	N/A	N/A	N/A	5820	N/A	N/A	N/A	N/A	N/A	N/A	107	83	78%	42	51%	41	49%

HIV, human immunodeficiency virus; N/A, not applicable; UR Tanzania, United Republic of Tanzania.

[a] For Malawi and Zambia, the denominator is the total number of survey participants as shown in Table 3.1.

[b] In Kenya, HIV testing was not done as part of the survey. HIV data were obtained from the national HIV reporting system of linked TB cases.

[c] In Malawi, there was verbal reporting of HIV status only. Of 2066 participants who screened positive, 19 had unknown status. For 48 out of 78 bacteriologically confirmed TB cases, their HIV status was unknown.

[d] In Rwanda, Uganda and the United Republic of Tanzania, only those who screened positive were tested for HIV during field operations.

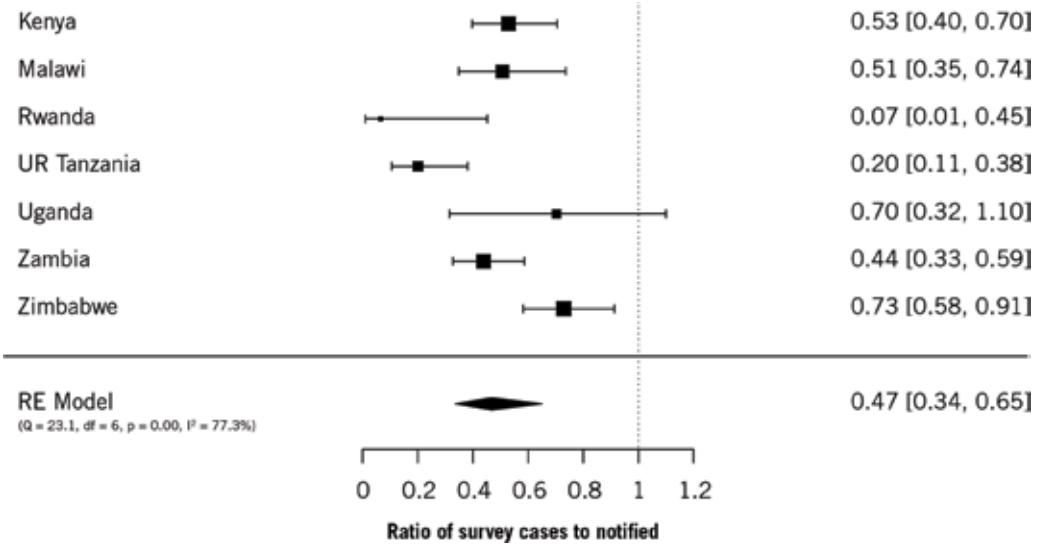
[e] In the United Republic of Tanzania, bacteriologically confirmed TB cases could not be verified.

[f] In Zambia, all survey participants were invited to be tested for HIV during field operations.

[g] In Zimbabwe, all bacteriologically confirmed TB cases detected by the survey were offered HIV counselling and testing as part of routine treatment management and were not directly tested as part of the survey.

Fig. 3.10

HIV prevalence in TB survey cases compared with HIV prevalence in notified TB cases expressed as a ratio, in surveys implemented in 2007–2016



UR Tanzania, United Republic of Tanzania.

met screening criteria who had not yet sought care was 42% (range, 10–67%), suggesting that there are barriers to accessing health services.

Among those that had sought health care, most did so within the public sector (Table 3.6). In a few countries (mostly in Asia), 30% or more of the symptomatic participants sought care in the private sector; examples included Bangladesh, Indonesia, Malawi, Myanmar and the Philippines (in 2016). Pharmacies were also an important point of care in a few countries, especially in Asia. The observed proportion of cases treated in the private health sector is a useful measure of the need for engagement of NTPs with the private sector.

3.8 Diagnostic performance of smear microscopy

High proportions of false-positive results from direct microscopic examination of smears were observed in several surveys (Table 3.7). In these surveys, TB was ruled out based on results from culture and Xpert MTB/RIF (or LPA), with false-positive results probably due to nontuberculous mycobacteria.

These findings provide evidence that sputum smear microscopy is also likely to be an unreliable diagnostic test for TB in the context of active case finding, unless high positive predictive values can be demonstrated in the population group targeted by active case finding.

Commonly used diagnostics – particularly direct microscopic examination of sputum smear samples – need to be upgraded with better technology, including WHO-approved rapid diagnostics that are more sensitive and more specific than sputum microscopy.

3.9 Conclusions

The 25 national TB prevalence surveys implemented in Africa and Asia between 2007 and 2016 provided a better understanding of the national, regional and global burden of TB disease, and of gaps in TB detection and treatment. The surveys showed a much higher burden in men than women, an ageing epidemic in most of Asia and a peak in prevalence in the younger age groups in most African countries. They also showed that actions are needed to improve access to health care and to ensure prompt diagnosis when care is sought, especially among men. Repeat surveys in Asian countries have demonstrated that substantial reductions in the burden of TB disease can be achieved within 10 years, and all 25 surveys provide a valuable baseline for future assessment of trends.

Table 3.5

Health care seeking behaviour among participants who were symptom-screen positive

Country	Participants who were symptom-screen positive	No action taken	%	Location of care sought																			
				Consulted medical facility	%	Type of facility						Pharmacy	%	Traditional	%	Other	%	Unspecified	%	Self-treated	%	Unknown	%
						Public facility	%	Private facility	%	Other facility	%													
Africa																							
Ethiopia	3026	1932	64%	848	28%	628	74%	199	23%	21	2.5%	40	1.3%	3	0.10%	N/A	N/A	55	1.8%	N/A	N/A	148	4.8%
Gambia	3462	1424	41%	1706	49%	1398	82%	220	13%	88	5.2%	17	0.49%	14	0.40%	24	0.69%	N/A	N/A	N/A	N/A	277	8.0%
Ghana	1969	264	13%	793	40%	695	88%	61	7.7%	37	4.7%	324	17%	20	1.0%	N/A	N/A	N/A	N/A	567	29%	1	0.10%
Kenya[a]	4137	2763	67%	1257	30%	1047	N/A	198	N/A	3	N/A	56	N/A	9	N/A	N/A	N/A	N/A	N/A	N/A	N/A	117	2.8%
Malawi	2715	1096	40%	1280	47%	901	70%	379	30%	N/A	N/A	32	1.2%	41	1.5%	4	0.15%	N/A	N/A	236	8.7%	26	0.96%
Nigeria	2466	604	24%	800	32%	628	79%	172	21%	N/A	N/A	319	13%	11	0.45%	9	0.36%	3	0.12%	680	28%	40	1.6%
Rwanda[a]	2855	1934	68%	921	32%	941	N/A	48	N/A	38	N/A	101	N/A	54	N/A	N/A	N/A	N/A	N/A	0	0	N/A	N/A
Sudan	2663	575	22%	1308	49%	1077	82%	90	6.9%	141	11%	52	2.0%	49	1.8%	N/A	N/A	69	2.6%	N/A	N/A	610	23%
Uganda	2714	1059	39%	1201	44%	1038	86%	146	12%	17	1.4%	421	16%	11	0.41%	N/A	N/A	N/A	N/A	22	0.81%	0	0%
UR Tanzania	3388	1688	50%	481	14%	445	93%	36	7.5%	N/A	N/A	147	4.3%	11	0.32%	257	7.6%	155	4.6%	N/A	N/A	649	19%
Zambia	4453	2534	57%	1829	41%	1680	92%	75	4.1%	74	4.0%	16	0.36%	1	0.02%	N/A	N/A	N/A	N/A	N/A	N/A	73	1.6%
Zimbabwe[a]	1833	1130	62%	486	26%	438	N/A	45	N/A	N/A	N/A	17	N/A	13	N/A	N/A	N/A	N/A	N/A	N/A	N/A	217	12%
Asia																							
Bangladesh[b]	26 882	12 947	48%	6545	24%	1816	28%	2182	33%	2547	39%	6533	24%	23	0.10%	191	0.71%	N/A	N/A	643	2.4%	N/A	N/A
Cambodia	1916	197	10%	1261	66%	947	75%	305	24%	9	0.71%	401	21%	21	1.10%	6	0.31%	N/A	N/A	28	1.5%	2	0.10%
China	5462	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
DPR Korea	2944	1192	41%	1743	N/A	1743	100%	N/A	N/A	N/A	N/A	N/A	N/A	3	0.10%	N/A	N/A	N/A	N/A	0	0%	6	0.20%
Indonesia	8552	3685	43%	2231	26%	1178	53%	672	30%	381	17%	2636	31%	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Lao PDR	3239	1210	37%	1148	35%	990	86%	106	9.2%	52	4.5%	690	21%	26	0.80%	N/A	N/A	N/A	N/A	N/A	N/A	165	5.1%
Mongolia	2546	1179	46%	950	37%	920	97%	30	3.1%	N/A	N/A	222	8.7%	2	0.08%	59	2.3%	N/A	N/A	N/A	N/A	30	1.2%
Myanmar	1691	440	26%	363	22%	197	54%	166	46%	N/A	N/A	271	16%	243	14%	39	2.3%	N/A	N/A	307	18%	28	1.7%
Pakistan	5417	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Philippines (2007)[c]	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Philippines (2016)[a]	2815	1142	41%	530	N/A	359	67%	162	31%	9	1.7%	4	N/A	10	N/A	N/A	N/A	N/A	N/A	1130	N/A	18	0.64%
Thailand[d]	2283	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Viet Nam	4172	2248	54%	1228	29%	1029	84%	199	16%	N/A	N/A	671	16%	25	0.60%	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

DPR Korea, Democratic People's Republic of Korea; Lao PDR, Lao People's Democratic Republic; N/A, not applicable; UR Tanzania, United Republic of Tanzania.

[a] a In Kenya, the Philippines (2016), Rwanda and Zimbabwe participants could select more than one category.

[b] In Bangladesh, data on health care seeking behaviour were available for participants who reported at least one TB symptom (i.e. cough, haemoptysis, weight loss, fever, night sweats).

[c] In Philippines (2007), there was no symptom screening and therefore no health seeking behaviour data obtained.

[d] In Thailand, limited data were available and were not reported.

Table 3.6

Location of treatment for participants who were on treatment at the time of the survey

Country	Number of participants who were on treatment at the time of the survey	Public sector	%	Private sector	%	Other sector	%	Unknown sector	Location of treatment for participants who were on treatment at the time of the survey
Africa									
Ethiopia	75	54	72%	7	9.3%	3	4.0%	11	15%
Gambia	38	38	100%	0	0%	0	0%	0	0%
Ghana	48	42	88%	1	2.1%	5	10%	0	0%
Kenya[a]	62	23	37%	0	0%	1	1.6%	38	61%
Malawi[a]	12	10	83%	2	17%	0	0%	0	0%
Nigeria	82	56	68%	14	17%	5	6.1%	7	8.5%
Rwanda	21	–	–	–	–	–	–	–	–
Sudan	104	69	66%	1	1.0%	4	3.8%	30	29%
Uganda	61	57	93%	4	6.6%	0	0%	0	0%
UR Tanzania	88	–	–	–	–	–	–	–	–
Zambia	114	61	54%	1	0.9%	0	0%	52	46%
Zimbabwe	84	–	–	–	–	–	–	–	–
Asia									
Bangladesh	57	16	28%	10	18%	18	32%	13	23%
Cambodia	80	72	90%	6	7.5%	0	0%	2	2.5%
China	73	72	99%	0	0%	1	1.4%	0	0%
DPR Korea	106	101	95%	0	0%	0	0%	5	4.7%
Indonesia	125	68	54%	52	42%	5	4.0%	0	0%
Lao PDR	42	21	50%	0	0%	0	0%	21	50%
Mongolia	129	126	98%	0	0%	3	2.3%	0	0%
Myanmar	79	63	80%	14	18%	0	0%	2	2.5%
Pakistan	146	–	–	–	–	–	–	–	–
Philippines (2007)	–	–	–	–	–	–	–	–	–
Philippines (2016)[b]	170	134	79%	15	8.8%	24	14%	1	0.59%
Thailand	66	53	80%	3	4.5%	3	4.5%	7	11%
Viet Nam	64	46	72%	2	3.1%	0	0%	16	25%

DPR Korea, Democratic People's Republic of Korea; Lao PDR, Lao People's Democratic Republic; UR Tanzania, United Republic of Tanzania.
– no data were available.

[a] In Kenya and Malawi, data were available only for participants who were eligible for sputum submission.
[b] In the Philippines (2016), some participants identified more than one location.

Table 3.7

Percentage of smear-positive results that were not confirmed TB.

Results shown for surveys in which specimens were tested using smear microscopy, rapid molecular tests and culture [a]

Country	Number of participants with at least one smear-positive specimen	Participants with smear-positive specimens excluded as a TB case	
		Number	%
Bangladesh	125	17	14%
Ghana	198	138	70%
Indonesia	291	126	43%
Kenya	141	18	13%
Malawi	163	101	62%
Mongolia	92	5	5.4%
Pakistan	236	29	12%
Philippines (2016)	183	10	5.5%
Sudan	61	4	6.6%
Uganda	91	25	27%
Zambia	356	221	62%
Zimbabwe	206	183	89%

[a] Results are shown for surveys in which specimens were tested using smear microscopy and the systematic use of rapid molecular tests. All surveys used Xpert MTB/RIF except Sudan which used line probe assay (LPA). Bangladesh and Kenya used both culture and Xpert MTB/RIF whereas other surveys used Xpert (or LPA) to confirm smear-positive specimens only.

References

1. Hong YP, Kim SJ, Lew WJ, Lee EK, Han YC. The seventh nationwide tuberculosis prevalence survey in Korea, 1995. Int J Tuberc Lung Dis. 1998;2(1):27–36 (https://www.ncbi.nlm.nih.gov/pubmed/9562108, accessed 22 November 2019).
2. Mao TE, Okada K, Yamada N, Peou S, Ota M, Saint S et al. Cross-sectional studies of tuberculosis prevalence in Cambodia between 2002 and 2011. Bull World Health Organ. 2014;92(8):573–81 (https://www.ncbi.nlm.nih.gov/pubmed/25177072, accessed 28 November 2019).
3. Tupasi TE, Radhakrishna S, Chua JA, Mangubat NV, Guilatco R, Galipot M et al. Significant decline in the tuberculosis burden in the Philippines ten years after initiating DOTS. Int J Tuberc Lung Dis. 2009;13(10):1224–30 (https://www.ncbi.nlm.nih.gov/pubmed/19793426, accessed 28 November 2019).
4. Wang L, Zhang H, Ruan Y, Chin DP, Xia Y, Cheng S et al. Tuberculosis prevalence in China, 1990–2010; a longitudinal analysis of national survey data. Lancet. 2014;383(9934):2057–64 (https://www.ncbi.nlm.nih.gov/pubmed/24650955, accessed 28 November 2019).
5. Global tuberculosis report 2017. Geneva: World Health Organization; 2017 (http://apps.who.int/iris/bitstream/10665/259366/1/9789241565516-eng.pdf?ua=1, accessed 1 February 2020).
6. Global tuberculosis report 2019. Geneva: World Health Organization; 2019 (https://apps.who.int/iris/bitstream/handle/10665/329368/9789241565714-eng.pdf, accessed 1 February 2020).
7. Borgdorff MW. New measurable indicator for tuberculosis case detection. Emerg Infect Dis 2004: 10: 1523–1528.
8. Horton KC, MacPherson P, Houben RM, White RG, Corbett EL. Sex Differences in tuberculosis burden and notifications in low- and middle-income countries: a systematic review and meta-analysis. PLoS Med 2016: 13: e1002119.
9. Ministry of Health – Republic of Indonesia, National Institute of Health Research and Development. Indonesia tuberculosis prevalence survey 2013–2014. Jakarta, Indonesia: 2015.
10. Hoa NB, Cobelens FG, Sy DN, Nhung NV, Borgdorff MW, EW T. Diagnosis and treatment of tuberculosis in the private sector, Vietnam. Emerging infectious diseases. 2011;17(3):562–4 (https://www.ncbi.nlm.nih.gov/pubmed/21392464, accessed 28 November 2019).
11. World Health Organization. Assessing tuberculosis under-reporting through inventory studies. Geneva, Switzerland 2012 (https://www.who.int/tb/publications/inventory_studies/en/, accessed 20 November 2019).
12. Global tuberculosis report 2018. Geneva: World Health Organization; 2018 (https://apps.who.int/iris/bitstream/handle/10665/274453/9789241565646-eng.pdf?ua=1, accessed 1 February 2020).

Chapter 4
Successes, challenges and lessons learned

Chapter 3 provided an overview of the main results from the 25 national TB prevalence surveys completed between 2007 and the end of 2016, including what they showed about the distribution of TB disease by age and sex. The overview also showed trends over time (for any countries that completed repeat surveys) and their implications for policy, planning and programmatic action.

In addition to the major success of producing valuable new data, this chapter highlights other aspects of survey success. It also identifies the main challenges that were faced during the process from deciding to implement a survey through to finalizing and disseminating the results. Lessons learned from both survey successes and challenges, which should be useful for informing future surveys, are then summarized.

For all three topics, this chapter synthesizes the more detailed assessments of successes, challenges and lessons learned that are reported by those who led or contributed to each survey in the country-specific chapters (Part II) of this book.

4.1 Successes

Survey successes are summarized in Table 4.1.

All surveys provided an up-to-date direct measurement of the burden of TB disease, and other valuable information about the status of the TB epidemic and access to care. This information was used to inform national policy, national strategic plans, advocacy and resource mobilization. Of the 25 surveys, 21 were in countries that completed either their first-ever national TB prevalence survey (n=18) or the first survey to include culture testing (n=3) according to the screening and diagnostic algorithm recommended in the *lime book (1)*. In 2011, Ethiopia became the first African country in decades to implement a national survey using this algorithm; also impressive was the short time (about 1 year) between the decision by Ethiopia's Ministry of Health to conduct a survey and the start of field operations. Three countries completed repeat surveys that enabled assessment of trends in TB disease burden: Cambodia, China and the Philippines.

Most countries (19 of 25) also succeeded in achieving a high participation rate (more than 80%). Nine countries (Bangladesh, Cambodia, China, Ethiopia, Ghana, the Philippines in 2007, Rwanda, Uganda and Viet Nam) managed to achieve participation rates of 90% or more, with an exceptionally high participation rate (96%) in China and Rwanda.

Other survey successes identified by multiple countries included good data management (n=6), a strong laboratory (n=5), and timely finalization and dissemination of results (n=8). Surveys that described laboratory work as a "survey success" included those in which the laboratory used was either part of a long-established research unit (e.g. Gambia) or a national reference laboratory. In the survey in Uganda, the national reference laboratory was also a supranational reference laboratory.

Survey successes mentioned by a single country were:

- the ability to generate subnational (provincial) as well as national estimates of prevalence (China, reflecting the survey's very large sample size);
- full domestic funding for the survey (China);
- capacity development for health care workers during the survey (Cambodia);
- smooth field operations (Cambodia);
- the enhancement of laboratory and operational research capacity (Ghana); and
- the opportunity to see challenges in case management and surveillance in the most remote areas of the country, often for the first time (Lao People's Democratic Republic).

4.2 Challenges

The major challenges faced in surveys are summarized in Table 4.2, with the top five challenges shown in Fig. 4.1.

Table 4.1

Survey successes as reported by countries (see Part II for details)

Country	First national survey completed (ever or for many years)[a]	Repeat national survey completed	Up-to-date direct measurement of TB disease burden and other valuable information about the status of the TB epidemic and access to care provided	Direct measurement of trends in TB disease burden	High participation rate (>80%)	Good data management [b]	Strong laboratory [c]	Timely finalization and dissemination of results [d]
Bangladesh	•		•		•	•		
Cambodia		•	•	•	•			•
China		•	•	•	•			•
DPR Korea	•		•		•			
Ethiopia	•		•		•			
Gambia	•		•				•	
Ghana	•		•		•	•		
Indonesia	•		•		•			
Kenya	•		•		•			
Lao PDR	•		•		•			
Malawi	•		•		•	•		•
Mongolia	•		•		•		•	
Myanmar	•		•		•		•	•
Nigeria	•		•					
Pakistan	•		•		•			
Philippines (2007)		•	•	•	•			
Philippines (2016)		•	•	•		•		
Rwanda	•		•		•			
Sudan	•		•		•			
Thailand	•		•					
Uganda	•		•		•	•	•	•
UR Tanzania	•		•					
Viet Nam	•		•		•			•
Zambia	•		•		•	•		•
Zimbabwe	•		•				•	•

[a] The survey in Bangladesh was the first national survey that used the methods recommended in the *lime book* (*1*); the survey in Ethiopia was the first in the country as well as the first in decades in Africa that used culture; the survey in Indonesia was the first for decades using both X-ray and culture; and the survey in Myanmar was the first in the country to use culture.
[b] Countries that had a data management plan, had no major data issues in the field, and took <1 year to clean data after field operations were completed.
[c] Countries that did not have have laboratory protocol violations and had high culture confirmation of smear-positive cases (≥85%).
[d] Countries that did not have long delays before results were accepted by public health authorities, and provided an official report and/or paper within a few years of completing field operations.

Table 4.2

Major challenges faced in surveys as reported by countries (see Part II for details)

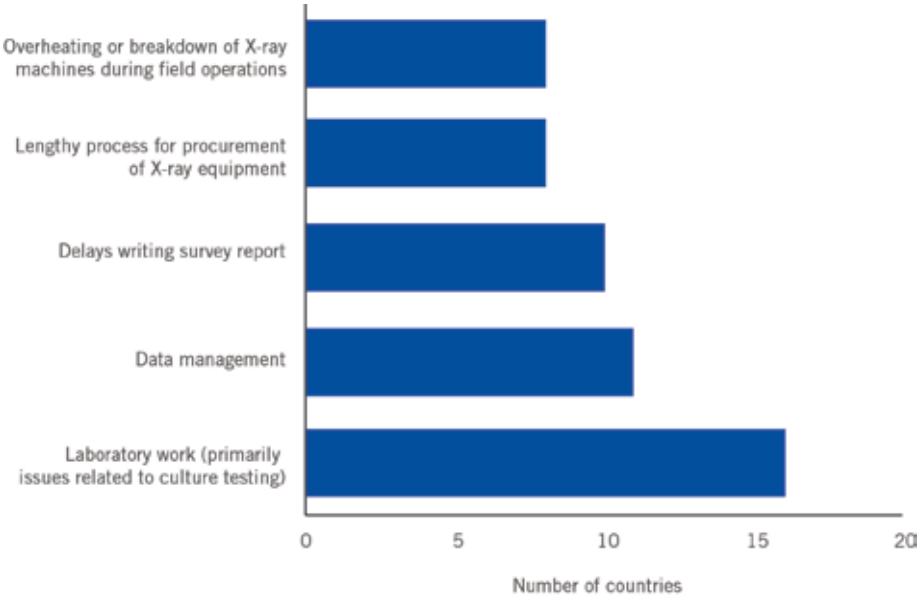
Country	Time to secure funding or funding interruptions during survey	Lengthy process to procure X-ray equipment	Security issues	Gaps between population in national and survey census	Internal migration affecting residential eligibility criteria	Participation (≤80%)[a]	Overheating or breakdown of X-ray machines during field operations	Data management	Laboratory work (primarily issues related to culture testing)	Delays in central reading of X-rays or difficulties in retaining radiologists	Delays in writing the survey report
Bangladesh		●					●		●		
Cambodia				●				●	●		
China				●	●				●		
DPR Korea	●							●			●
Ethiopia		●						●	●	●	
Gambia		●				●					●
Ghana		●					●		●	●	●
Indonesia		●							●		●
Kenya		●						●		●	
Lao PDR	●								●		●
Malawi	●						●		●	●	●
Mongolia							●				
Myanmar		●			●		●		●		●
Nigeria			●			●		●	●		●
Pakistan			●					●	●		
Philippines (2007)			●						●		
Philippines (2016)						●		●	●		
Rwanda		●						●	●		
Sudan			●				●	●	●		
Thailand				●		●					●
Uganda	●						●				
UR Tanzania	●							●	●		●
Viet Nam					●						
Zambia											
Zimbabwe							●	●		●	

[a] In addition, many countries reported challenges with participation in at least one of the following subcategories: the first survey clusters, younger age groups, men and urban (especially wealthier) areas.

● yes

Fig. 4.1

Top five challenges in 25 surveys as reported by countries



The top challenge, identified by 16 countries, was laboratory-related work (primarily issues related to culture testing). Examples of such challenges included:

- potential cross-contamination of samples during transportation from the field to the laboratory (e.g. Bangladesh and Malawi);
- a need to rely on only two laboratories owing to difficulties in standardizing laboratory work (Cambodia);
- the difficulty of standardizing techniques when multiple laboratories were used (e.g. China and the Philippines);
- a lower yield than expected from culture specimens (e.g. China, Pakistan, Rwanda and the United Republic of Tanzania);
- backlogs and delays in culture inoculation, linked to the high volume of specimens (e.g. Sudan and the United Republic of Tanzania);
- testing of only one specimen (instead of the recommended number of two) using culture in some (e.g. Indonesia) or all (e.g. Ethiopia) clusters owing to limited laboratory capacity;
- the time required to establish the laboratory capacity needed for culture testing (e.g. this took 2 years in Lao People's Democratic Republic);
- use of sputum cups that were suboptimal for culture testing (Myanmar);
- security issues in the part of the country where the national reference laboratory was located, which limited monitoring and technical assistance (Nigeria); and
- difficulties maintaining a cold chain, especially in hot or heatwave conditions (e.g. Pakistan and the Philippines).

Despite these issues, in 15 of 16 countries, the number of culture-confirmed survey cases was considerably higher than the number of survey cases that were smear positive, as expected. The exception was the United Republic of Tanzania, for which it was concluded that culture results could not be used (and hence the results in this book are restricted to smear-positive cases).

The second most frequent challenge, identified by 11 countries, was data management. Examples of such challenges included:

- slow data entry (e.g. Cambodia, the Democratic People's Republic of Korea and Nigeria);
- use of software designed for a national census that was not suited to a prevalence survey (e.g. Ethiopia);
- overreliance on internet connectivity in the field for electronic data entry (Kenya and Sudan), which was later resolved through use of a local area

network (Kenya) or paper-based recording of data as a backup (Sudan);

- linking data from the field with laboratory results when different data management systems were used (e.g. Kenya);
- transcription errors and serious difficulties in matching records for the same individual when multiple paper-based forms were used to collect data (e.g. Pakistan, Rwanda and the United Republic of Tanzania) – this caused long delays in the production of a final, clean dataset in Pakistan (>1 year) and the United Republic of Tanzania, while intensive efforts were needed by the survey team in Rwanda to successfully ameliorate the problem;
- difficulties with the data management system that were hard to resolve until the survey implementing agency (rather than an externally contracted separate agency) assumed direct responsibility for it (e.g. the Philippines); and
- delayed sharing of datasets and different data management processes between the survey team and the national statistics agency (e.g. Zimbabwe).

Challenges related to X-ray equipment – either the initial process to procure it (eight countries) or breakdowns or overheating in the field (eight countries) – were also common. One or both of these two challenges affected 10 countries in total.

Producing a final survey report was a considerable challenge in 10 countries. The main reasons were the lack of a budget specifically for this activity, that the contracts of members of the survey team who could have worked on the report expired before they were able to spend time on writing the report, and no funding was available for the option of employing someone to help the survey team to produce it.

The other challenges identified by at least three countries were:

- the time taken to secure funding, or interruptions to funding during the survey;
- security issues;
- discrepancies between the national census data and the survey census;
- internal migration, which affected the proportion of the population eligible to participate according to residential criteria;
- participation; and
- delays in central reading of X-rays.

Even in countries that achieved high participation rates, many countries experienced challenges with participation in at least one of the following subcategories: the first survey clusters, younger age groups, men, and urban (especially wealthier) areas.

Other challenges mentioned by a single country were:

- interruption to field operations during the long winter season (Mongolia);
- expiry of X-ray software licences due to delays in starting the survey, with the software then having to be repurchased (Nigeria);
- lack of access to national census data by the survey team responsible for the prevalence survey, and the changing of bureau of statistics staff for each cluster (Nigeria);
- extreme rainfall that forced field operations to be suspended for 1 month (Nigeria);
- a natural disaster (a flood) that delayed field operations (Pakistan);
- high staff turnover (Sudan);
- some recommendations from external monitoring missions not being implemented in a timely manner (United Republic of Tanzania);
- some myths and misconceptions about TB in the community, which had an effect on the participation rate (Zambia);
- the need for field staff to work long hours when participants arrived at the main survey camp site relatively late in the day, especially in rural areas (Zambia);
- hot weather conditions that affected participation (Zimbabwe);
- religious groups that were opposed to modern medical interventions (Zimbabwe); and
- issues with retrieval of X-ray images because the archiving and communications system was controlled by an X-ray supplier in the Netherlands (Zimbabwe).

Table 4.3

Lessons learned for future surveys as reported by countries (see Part II for details)

Topic	Lessons learned
First-ever surveys	• These are strongly facilitated by the use of experts from other countries that have recently completed a survey successfully and of international experts that have already supported multiple surveys; it is important to have continuity of support from these experts throughout the survey. • Many surveys benefited from "AA collaboration" (Asia–Asia, Asia–Africa and Africa–Africa) and technical assistance from international agencies.
Repeat surveys	• These are facilitated if at least some of the same national staff and international experts involved in the previous survey are involved in the repeat survey.
Stakeholder commitment and involvement, and regular communication among stakeholders	• Involvement of and ownership by the national TB programme and, more broadly, the Ministry of Health are especially important, even if another agency is contracted to implement the survey. • The roles and responsibilities of each stakeholder should be clearly defined. • Good collaboration with the national bureau of statistics is essential for proper sampling design.
Survey team leadership, management capacity and monitoring	• A high level of leadership and management capacity in the team responsible for implementing the survey is a major contributor to a successful survey. • All survey procedures should be carefully monitored to prevent protocol violations, or to ensure prompt remedy if violations occur.
Community engagement and survey participation	• Involvement of stakeholders and community leaders at local level is essential; use of the media to inform people about the survey can also be helpful. Participation can be increased by extended hours of field operations (including in the evenings and on weekends), provision of transport to those living far from the survey field site, and high levels of motivation of the field and survey teams.
X-ray equipment procurement and breakdowns	• Procurement needs to be planned well in advance, and national regulations checked to ensure that what is ordered complies with the regulations. • If equipment is procured from an international supplier, it is important to ensure that there is a contract to provide local support in the event of breakdowns. The availability of in-country servicing of equipment is essential to ensure timely repairs and troubleshooting. • Back-up machines should be available in case of breakdowns.
Data management	• A competent and responsive data management team that is involved from survey design to completion is essential. • Use of multiple paper-based forms for the same individual should be avoided. • Electronic data management facilitates timely entry, validation and analysis of survey data. • Internet connectivity may be a challenge in some parts of a country; solutions identified included use of a local area network in the field with later uploading of data to a central server and use of paper forms as a back-up. • Use of bar codes (as opposed to writing individual identifiers by hand) reduces errors in data entry and matching of records.
Laboratory issues	• It is essential to ensure that good laboratory practices are maintained and standardized in all involved laboratories, and are properly monitored throughout the survey, including during periods of high volume and throughput of specimens to be tested. • Strong leadership from the principal investigator and survey team can help to identify and resolve problems in a timely way, as can following the advice of an expert technical advisory group for the survey. • Xpert MTB/RIF is useful for checking smear-positive results that are negative on culture, or for which the culture result is missing. • Surveys that described the quality of laboratory work as a "survey success" included countries where the laboratory that was used was either part of a long-established research unit (Gambia) or a national reference laboratory (including one, in Uganda, that was a supranational reference laboratory).
Security issues	• Survey protocols should clearly define how clusters will be replaced in the event of security or other issues that require cluster replacement. • How clusters were replaced should also be documented in the final survey report.
Production of final survey report	• A budget should be allocated specifically for the writing of the survey report. In several countries, the report was delayed because no funding had been allocated to prepare and write the survey report.
Delays in reading X-rays	• It may be necessary to allocate a budget specifically for reading X-rays. In some surveys, additional funds had to be mobilized at the end of the survey (including from WHO) to enable review by qualified radiographers. A local supplier for software and for archiving or communication of images should be used if possible.

WHO: World Health Organization.

4.3 Lessons learned

Lessons were learned from both successes and challenges. These lessons, which are important for guiding and informing future surveys, are summarized in Table 4.3. They included the following:

- There is much value in cross-country collaboration and international technical assistance from experts with experience of supporting multiple surveys, especially for countries implementing their first-ever (or first for many years) survey. Asia–Asia, Asia–Africa and Africa–Africa collaborations (collectively referred to as "AA collaboration") were all strongly promoted and facilitated by the WHO Global Task Force on TB Impact Measurement's subgroup on national TB prevalence surveys.
- There is high value in having at least some continuity in the national staff and international experts involved in repeat surveys.
- It is important to have stakeholder commitment and involvement, and regular communication among stakeholders, throughout a survey.
- Strong leadership and management of the survey team are major contributors to survey success.
- Procurement needs to be planned well in advance, and national regulations checked, to ensure that the ordered equipment complies with national regulations.
- The availability of in-country servicing for X-ray equipment, and the availability of back-up machines, help to ensure that issues during field operations (e.g. overheating or breakdown) can be resolved quickly.
- Laboratory work must be carefully planned, maintained and closely monitored throughout a survey; advice from laboratory experts or an expert technical advisory group must be promptly acted upon.
- Xpert MTB/RIF can be helpful to check smear-positive results when culture results are missing or negative.[1]
- A competent and responsive data management team is essential; this team should be involved from the initial stages of survey preparations through to completion of data analysis and report writing.
- Electronic data capture systems can significantly facilitate and increase the efficiency of data collection, validation and analysis.
- Use of multiple paper-based forms for the same individual should be avoided.
- A budget should be allocated specifically for the writing of the final survey report.
- Involvement of stakeholders and community leaders at local level is essential; also, use of the media can facilitate community engagement and participation.

These lessons learned echo and reinforce the 11 factors that were identified in the *lime book* as prerequisites for the successful implementation of a national TB prevalence survey *(1)*. The 11 prerequisites were: strong commitment and leadership from the NTP, the ministry of health and a core group of professionals; identification of a suitable institute, organization or agency to lead and manage the survey; adequate laboratory capacity, especially for culture; compliance with the regulations of the national radiation authority; reliable and timely procurement and logistics; funding; assurance of security in the field for survey teams and participants; professional data managers and associated data management practices; community participation; expert review and clearance of protocols, including ethical clearance; external support and technical assistance.

[1] Further discussion of the role of molecular tests in addressing challenges with culture testing in prevalence surveys is included in Chapter 5.

Reference

1. Tuberculosis prevalence surveys: a handbook. Geneva: World Health Organization; 2011 (https://apps.who.int/iris/bitstream/handle/10665/44481/9789241548168_eng.pdf, accessed 22 November 2019).

Transporting chest X-ray equipment during the 2016 national TB prevalence survey of the Philippines
Photo credit: Raldy Benavente / FACE Inc (Philippines)

Chapter 5
Future direction

The introductory chapter of this book highlighted that national notification and vital registration systems can be used to reliably monitor the burden of TB disease (in terms of numbers of cases and deaths each year) in many high-income countries, with a few countries having time series of data that cover a span of more than 100 years. It also highlighted that while the ultimate goal is that all countries can reliably track their TB epidemics using such systems, in the early 2000s this goal had not been achieved in many countries with a high burden of TB. Although all countries (including high TB burden countries) had national notification systems for TB and were reporting notification data to WHO on an annual basis, in most countries the number of notified cases was not a good proxy for the actual number of new cases. This was due to a mixture of underreporting of detected cases, duplicated case reporting, some level of overdiagnosis of bacteriologically unconfirmed cases and underdiagnosis. National VR systems of high quality and coverage had yet to be established in many parts of the world.

This situation was the reason for the establishment of the WHO Global Task Force on TB Impact Measurement in 2006. The task force had the aim of ensuring a robust, rigorous and consensus-based assessment of whether TB targets set for 2015 in the UN MDGs and the WHO Stop TB Strategy were achieved. It included national surveys of the prevalence of TB disease in 22 global focus countries (GFCs) as one of its three strategic areas of work during the period 2007–2015 *(1)*. Such surveys were recognized as providing an alternative way of directly and reliably measuring the burden of TB disease, with repeat surveys allowing assessment of trends. Other recognized benefits of surveys were that they could be used to document the distribution of disease by age and sex; to better understand health care seeking behaviour in the public and private sectors; to identify reasons why people with TB were not diagnosed before the survey or officially reported to national authorities (or both); and to inform the development or improvement of strategies and interventions for TB case finding, diagnosis and treatment.

As illustrated in **Chapter 3** and in the country-specific chapters that form **Part II** of this book, a substantial new body of knowledge was generated by the 25 surveys completed in 24 countries[1] (including 18 of the 22 GFCs) between 2007 and 2016. Data were used to update estimates of TB disease burden, including time trends in the three countries that conducted repeat surveys, and to inform national policy, national strategic plans, advocacy and resource mobilization. **Chapter 4** then synthesized survey successes (including and beyond the generation and use of survey data), challenges and lessons learned during the time between the initial decision to implement a survey and dissemination of results, based on the more detailed descriptions provided in **Part II**.

Looking forward, and building on **Chapter 3** and **Chapter 4**, this final chapter of **Part I** addresses three important questions:

- Are national TB prevalence surveys still relevant?
- Where do national TB prevalence surveys remain relevant?
- Should national TB prevalence surveys be done differently in future?

5.1 Are national TB prevalence surveys still relevant?

In 2013, WHO published a TB surveillance checklist of standards and benchmarks that can be used to assess the quality and coverage of national notification and VR systems *(2)*. Although much progress in strengthening national TB notification systems was made between 2007 and 2016, at the end of this period, most countries with a high burden of TB still lacked systems that met the levels of quality and coverage necessary for notification data to provide a direct measure of TB incidence *(3)*. In WHO's *Global tuberculosis report 2019*, the data used to estimate TB incidence in high TB burden countries were sourced mainly from national TB prevalence surveys *(4)*. In the

[1] Two surveys were implemented in the Philippines (2007 and 2016).

Table 5.1

Suggested epidemiological criteria for assessing whether a country should consider implementing a prevalence survey post-2016 for two major groups of countries, as discussed by the WHO Global Task Force on TB Impact Measurement in April 2016

Criteria	Explanation
Group 1 → Countries that conducted a national prevalence survey in 2007–2016[a] (Fig. 5.1)	
1. Estimated prevalence of bacteriologically confirmed TB ≥250 per 100 000 population aged ≥15 years during the previous survey. *and* 2. More than 7 years since the last survey.[a]	• Sample size small enough (<70 000 individuals) to make surveys feasible in terms of cost and logistics. • Time between surveys sufficient to allow a statistically meaningful comparison of prevalence.
Group 2 → Countries that did not implement a national prevalence survey in 2007–2016 (Fig. 5.2)	
1. Estimated TB incidence[b] ≥150 per 100 000 population per year (all forms, all ages). *and* 2. No nationwide VR system with standard coding of causes of deaths. *and* 3. Infant mortality rate >10/1000 live births.	• Sample size[b] small enough (<70 000 individuals) to make surveys feasible in terms of cost and logistics, taking into account added uncertainty due to the use of rapid molecular tests with performance that may be inferior to culture. • No reliable direct measurement of TB disease burden. • Indirect indicator of low access to quality health services, as defined in the WHO checklist of standards and benchmarks for TB surveillance and VR.

VR: vital registration; WHO: World Health Organization.

[a] Surveys conducted before 2000 may lack comparability with surveys implemented according to the screening and diagnostic algorithm recommended in the *lime book (8)*. An interval of about 7–10 years between two surveys is recommended.

[b] Country-specific prevalence estimates have not been published by WHO post-2016 because prevalence is not a high-level indicator of the End TB Strategy. For sample size calculations, prevalence in the age group 15 years or more may be predicted from incidence.

same report, estimates of TB mortality were based on national VR data for 123 countries (including nine of the 30 included in WHO's list of high TB burden countries). Given this situation, the rationale for using national TB prevalence surveys as an alternative way to directly measure the burden of TB disease and trends remained as valid at the end of 2016 as it was in 2007.

5.2 Where do national TB prevalence surveys remain relevant?

In April 2016, the WHO Global Task Force on TB Impact Measurement held a meeting to discuss progress achieved during the period 2007–2015, and its work in the post-2015 era of the UN Sustainable Development Goals (SDGs, which succeeded the MDGs) and WHO's End TB Strategy (which succeeded the Stop TB Strategy) *(5)*. The SDGs, set for 2030, were adopted by all UN Member States in September 2015 *(6)*. The End TB Strategy was adopted by all WHO Member States at the World Health Assembly in 2014; it covers the period 2016–2035, with milestones for 2020 and 2025 and targets for 2030 and 2035 *(7)*.

During its April 2016 meeting, the task force agreed on an updated mission and five strategic areas of work, initially for the period 2016–2020 (likely to apply and be extended to 2021–2025). National TB prevalence surveys were retained under the new third strategic area of work, which was defined as "Priority studies to periodically measure TB disease burden". The task force meeting was also used to discuss the countries in which national TB prevalence surveys remained relevant. The suggested epidemiological criteria for assessing whether a country should consider implementing a survey are shown in Table 5.1, and the countries in each of the two groups defined in Table 5.1 (based on data available at the end of 2019) are shown in Fig. 5.1 and Fig. 5.2.

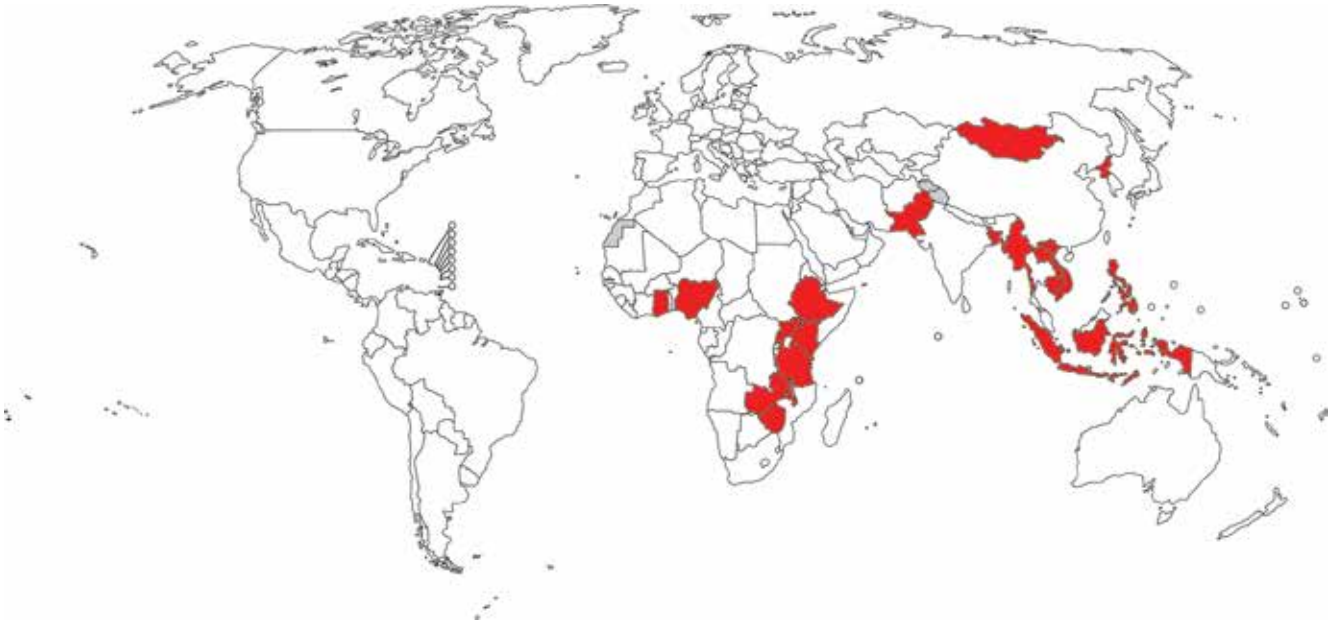
Among the 24 countries in Group 1 (i.e. those that implemented a survey in 2007–2016 and that met the criteria shown in Table 5.1), it is worth highlighting that five did not meet the criteria for a further survey because of their relatively low measured level of TB disease burden; these countries were China, Gambia, Rwanda, Sudan and Thailand. In these countries, the focus should be on maintaining or strengthening national notification and VR systems.

Of the 29 countries in Group 2, four stood out in terms of their share of estimated TB disease burden from a global perspective: Democratic Republic of the Congo, India, Mozambique and South Africa. Of these, South Africa completed a survey in 2019, Mozambique completed one in 2020 and India started a survey in 2019. In addition, surveys were completed in Namibia (2018), Nepal (2019) and Lesotho (2019), and planning for a survey in Botswana was initiated in 2018.

For any country meeting the epidemiological criteria shown in Table 5.1, it was stressed that survey feasibility

Fig. 5.1

Countries that conducted a national TB prevalence survey in 2007–2016 and that met the Group 1 criteria based on data available at the end of 2019 (N=19, red) [a]



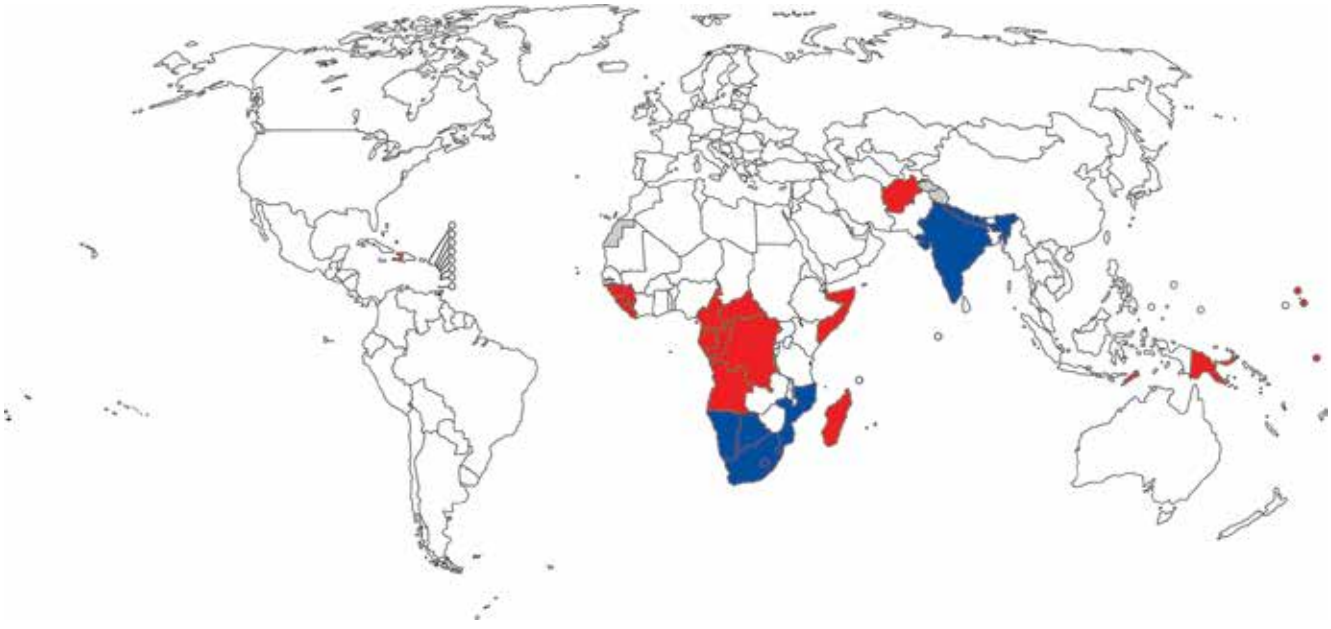
Grey, not applicable.

[a] These 19 countries are Bangladesh, Cambodia, Democratic People's Republic of Korea, Ethiopia, Ghana, Indonesia, Kenya, Lao People's Democratic Republic, Malawi, Mongolia, Myanmar, Nigeria, Pakistan, Philippines, Uganda, United Republic of Tanzania, Viet Nam, Zambia and Zimbabwe.

Fig. 5.2

Countries that met the Group 2 criteria for implementing a national TB prevalence survey based on data available at the end of 2019 [a]

Countries that had already completed or started implementation of a survey by the end of 2019 are shown in blue and remaining countries are shown in red.



Grey, not applicable.

[a] The 8 countries in blue are Botswana, Eswatini, India, Lesotho, Mozambique, Namibia, Nepal and South Africa. The 21 other countries in red are Afghanistan, Angola, Cameroon, Central African Republic, Congo, Democratic Republic of the Congo, Djibouti, Equatorial Guinea, Gabon, Guinea, Guinea-Bissau, Haiti, Kiribati, Liberia, Madagascar, Marshall Islands, Papua New Guinea, Sierra Leone, Somalia, Timor-Leste and Tuvalu.

must also be carefully assessed. As set out in the *lime book (8)*, there are 11 prerequisites for a survey to be feasible:

- there is strong commitment and leadership from the NTP, ministry of health and a core group of professionals;
- a suitable institute, organization or agency to lead and manage the survey can be identified;
- there is adequate laboratory capacity;
- X-ray equipment can comply with the regulations of the national regulatory authority;
- reliable and timely procurement and logistics is possible;
- funding is available;
- security in the field for survey teams and participants can be assured;
- data management can be done according to recommended standards;
- community participation is likely to be sufficiently high, including in urban areas;
- expert review and clearance of protocols, including ethical clearance, can be undertaken; and
- external support and technical assistance are available if needed.[1]

These prerequisites remain valid post-2016. Among the countries in Group 2, several are likely to face challenges in meeting the feasibility criteria; examples include Afghanistan, Democratic Republic of the Congo and Papua New Guinea.

5.3 Should national TB prevalence surveys be done differently in future?

The successes, challenges and lessons learned during surveys completed in 2007–2016 (Chapter 4) are useful for informing surveys implemented after 2016. They clearly show what challenges are likely to be encountered and how these can be prevented or mitigated.

For the top three challenges that affected by far the largest number of countries (i.e. between 10 and 16), it is worth considering what could be done differently to avoid or mitigate them in future surveys. The top three challenges were:

- laboratory work, notably issues related to culture testing;
- data management; and
- delays in producing the final survey report.

5.3.1 Are there alternatives to relying on culture testing of samples from all survey participants who meet survey screening criteria?

The reference standard test for diagnosis of active pulmonary TB disease is culture of *M. tuberculosis* from sputum samples. In many countries with a high burden of TB, sputum smear microscopy remained the most commonly used diagnostic test for TB in the period 2007–2016.[2] For these two reasons, testing of sputum samples using both smear microscopy and culture to diagnose TB was the method recommended for national TB prevalence surveys in the *lime book (8)* (see also Chapter 2). As stated in the *lime book*:

> Surveys of the prevalence of TB disease aim to measure the burden of *bacteriologically confirmed* pulmonary TB in the community… as such, laboratory tests of sputum samples (using sputum smear microscopy and culture) are a fundamental component of a prevalence survey.

Nonetheless, the challenges of culture testing in the context of a national TB prevalence survey were always well recognized. Challenges included the following:

- Samples taken among the general population in a field-site setting can be of poorer quality and lower volume than those taken in clinical settings. They are also likely to be more paucibacillary in nature, since on average those with TB disease will be at an earlier stage of disease progression compared with those diagnosed when seeking care at a health facility.
- There can be long transportation times between a survey cluster and the laboratory or laboratories being used for testing, and a cold chain needs to be maintained during these times. The recommended time between obtaining a sample and its arrival at the laboratory is 3 days or less, and no more than 5 days. If these times are exceeded, contaminated tubes or false-negative test results become likely.
- There is a risk of cross-contamination from positive to negative specimens.

[1] This is likely to be especially important for countries implementing a survey for the first time.

[2] Use of rapid molecular tests – notably the Xpert® MTB/RIF and Xpert Ultra cartridges – started following WHO's endorsement of Xpert MTB/RIF in 2010.

- The workload of culture testing generated by a prevalence survey may be challenging for laboratories to manage. Without careful planning it is possible for laboratories to become overloaded, affecting testing timeliness and quality.

For these reasons, in all surveys, culture results have been missing for some survey participants, and some results may have been false-negative or (if there was cross-contamination) false-positive.[1] Surveys have made use of expert panel reviews using all sources of evidence (symptom screen, X-ray, smear microscopy, sometimes a molecular test result) to make a final determination of whether someone with a missing culture result, or with a culture-negative but smear-positive or Xpert-positive result, should be classified as a survey case.

The challenges of culture testing not surprisingly led to growing interest in the role of Xpert (both the MTB/RIF® and more recent Xpert Ultra® assays) in a national TB prevalence survey, following WHO's endorsement of the Xpert MTB/RIF assay in December 2010, and publication of a policy update *(10)* and an implementation manual *(11)*. Compared with culture, the advantages of this molecular test include that it is rapid (results available within hours), is automated, does not require fresh samples to perform optimally and does not require stringent laboratory containment. Direct testing of sputa without centrifugation has the added advantage of minimizing cross-contamination.

Nonetheless, both Xpert assays also have disadvantages compared with culture. In particular, they have lower sensitivity and specificity. Results from evaluations by the Foundation for Innovative New Diagnostics (FIND) in which Xpert was compared with the reference standard of culture using sputum samples collected in clinical settings in a variety of countries are shown in Table 5.2.

The best estimate of sensitivity (the percentage of culture-positives identified by Xpert) was 83% for Xpert MTB/RIF, 88% for Xpert Ultra if trace results were used, and 85% for Xpert Ultra if trace results were not used.[2] These findings mean that if Xpert alone is used to test samples from survey participants that meet survey screening criteria (i.e. reported symptoms suggestive of TB or an abnormal chest X-ray), true cases of TB (that could be identified by culture) would be missed. Sensitivity may be improved by repeating Xpert testing on another sample (interpreting the test combination as positive if at least one of the two tests is found to be positive).

Table 5.2

Sensitivity and specificity of the Xpert® MTB/RIF and Ultra assays as measured in an evaluation by FIND

Assay	Sensitivity (%) compared with the reference standard of culture	Specificity (%) compared with the reference standard of culture
Xpert MTB/RIF	83 (78–87)	98 (96–99)
Xpert Ultra, if trace results are used	88 (84–91)	95 (93–97)
Xpert Ultra, if trace results are excluded[a]	85	97

FIND: Foundation for Innovative New Diagnostics.
Sources: Dorman et al. (2018) *(12)* and WHO (2017) *(13)*.
[a] Uncertainty bounds could not be calculated.

The best estimates of specificity (the percentage of culture-negatives found to be negative by Xpert) were 98% for Xpert MTB/RIF, 95% for Xpert Ultra if trace results were considered positive and 97% for Xpert Ultra if trace results were considered negative.[3]

In the setting of a population-based national TB prevalence survey, the proportion of screen-positive individuals (in terms of reported symptoms or an abnormal X-ray) with culture-positive TB disease will be low. In surveys implemented in 2007–2016, the proportion was typically in the range 1–5% (Fig. 5.3). This means that of those tested, typically 95–99% will be culture negative; if tested using an Xpert assay, given the specificity of Xpert MTB/RIF and Ultra (excluding trace results), 2–3% of this 95–99% would have a false-positive Xpert result. In other words, if 100 individuals who screen positive in a prevalence survey are tested with Xpert, about 1–5 people with TB will be correctly identified (in reality a bit less given that Xpert is less sensitive than culture) and about 2–3 people will have a false-positive result.

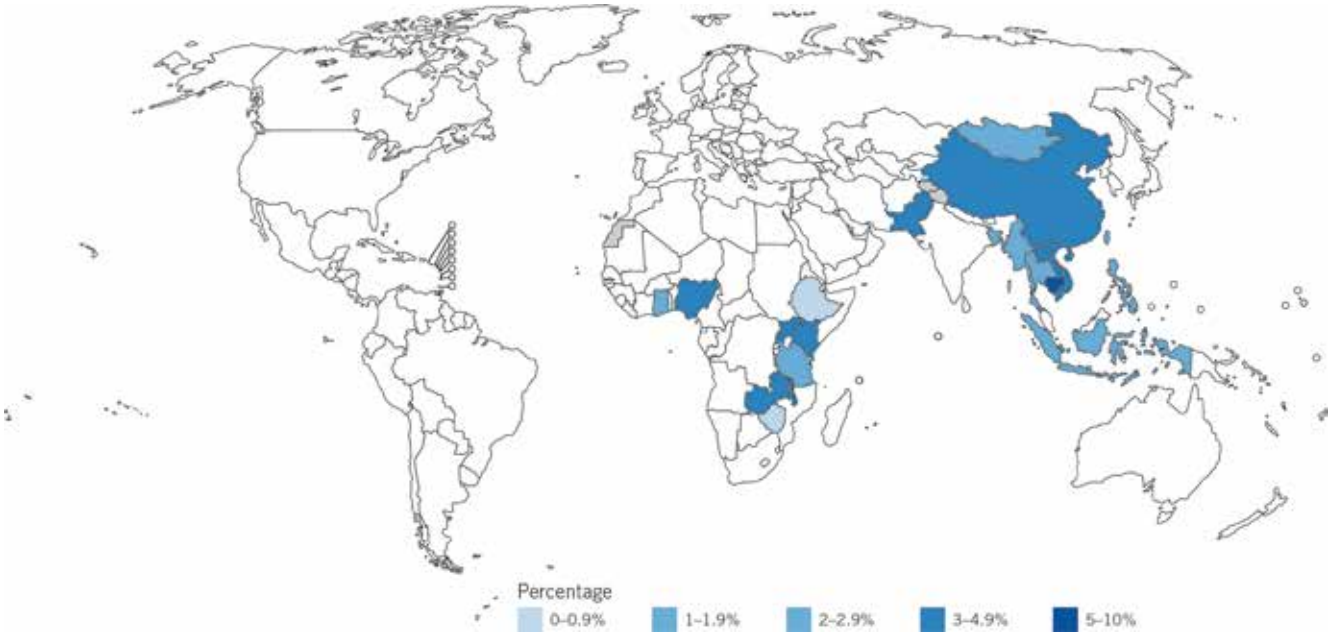
[1] A recent systematic review found that 2% (95% confidence interval [CI]: 1–2%) of all positive cultures were false-positive results due to laboratory cross-contamination. See Barac et al. (2019) *(9)*.

[2] For the detection of *M. tuberculosis*, Ultra incorporates two new multicopy amplification targets (IS6110 and IS1081) and a larger DNA amplification reaction chamber than Xpert MTB/RIF. The semiquantitative scale for Xpert Ultra results is as follows: trace, very low, low, medium or high. Trace corresponds to the lowest bacillary burden for detection of *M. tuberculosis* and indicates that only the multicopy targets were detected, as opposed to the TB-specific regions in the *rpoB* gene.

[3] The main explanation for false-positive Xpert results is that Xpert detects dead TB bacilli, whereas a culture-positive result requires live TB bacilli to be present. This means that Xpert may detect people who had TB in the past as well as those who have been infected by *M. tuberculosis* but contained the infection.

Fig. 5.3

Percentage of people who were eligible for sputum testing (i.e. they reported symptoms suggestive of TB or had an abnormal chest X-ray) that had culture confirmed pulmonary TB, for surveys implemented in 2007–2016



Grey, not applicable.

Table 5.3

Estimated percentage of Xpert-positive results that would be false-positive in a national TB prevalence survey, based on the specificity of Xpert estimated in the FIND evaluation

Percentage of people screened positive in a national TB prevalence survey who have bacteriologically confirmed TB (culture positive)	Estimated percentage of Xpert MTB/RIF positive results that will be false-positive	Estimated percentage of Xpert Ultra positive results that will be false-positive (assuming trace results are excluded)[a]
2	54 (49–59)	63
3	44 (39–49)	53
4	37 (32–42)	46
5	31 (20–29)	40

FIND: Foundation for Innovative New Diagnostics.
[a] There were insufficient data to estimate uncertainty intervals.

This means that between around one third and two thirds of Xpert-positive results would be expected to be false-positive results in the context of a national TB prevalence survey (Table 5.3). This is an unacceptable level of error when the main objectives of a survey are to reliably measure the level of pulmonary TB disease in the community and (in a repeat survey) trends in that level of TB disease.

These expectations were borne out in six national and two subnational TB prevalence surveys completed between 2015 and 2019, in which Xpert MTB/RIF or Xpert Ultra were used alongside culture for testing of all survey participants that screened positive.[1] These surveys showed a high proportion of discordant results. The discordance was higher for those reporting a previous history of TB disease compared with those reporting no history; this finding is as expected, given that in those with a treatment history, Xpert is more likely to detect dead TB bacilli. The estimated pooled sensitivity of Xpert MTB/RIF compared with culture was 73% (62–82%) and for Xpert Ultra (excluding trace results) it was 68% (55–79%);[2] the estimated pooled specificity of Xpert MTB/RIF was 98% (98–99%) and for Xpert Ultra it was 98% (97–99%).

[1] The national surveys were those in Bangladesh (2015), Kenya (2015), Myanmar (2017–2018), the Philippines (2016), South Africa (2018–2019) and Viet Nam (2017). The subnational surveys were implemented in 2019 as part of community randomized trials in South Africa and Zambia (the TREATS study).

[2] The pooled estimates of sensitivity for Xpert MTB/RIF and Xpert Ultra were based on a small number of prevalence surveys, with wide credibility intervals. There was no demonstrated statistical difference in the sensitivity of the two tests.

Recognizing the limitations of both culture and Xpert testing in the context of a national TB prevalence survey, WHO organized meetings between 2018 and 2020 to discuss the best way forward, based on accumulating evidence from surveys in which Xpert and culture were used alongside each other. As of early 2020, one option under consideration for countries without the capacity to conduct high-quality culture testing in the context of a national prevalence survey was as follows: the use of two Xpert Ultra tests on two separate sputum samples for all participants who screen positive (to maximize sensitivity), followed by culture testing for any participant with an Xpert Ultra positive test result (thus addressing the suboptimal specificity of Xpert Ultra by using the reference standard as a confirmatory test to eliminate false-positive Xpert Ultra results). Prevalence estimates would then need to be adjusted to account for the lower sensitivity of the Xpert Ultra test (i.e. adjustment for false-negative Xpert Ultra results).

A final set of recommendations related to the diagnostic algorithm to be used in future surveys, designed to make optimal use of both culture and Xpert, is planned for publication in a new edition of the WHO handbook on prevalence surveys that will succeed the *lime book*.[1]

5.3.2 Adapting and using the principles of good clinical practice that have been established for clinical trials in the context of national TB prevalence surveys

Good clinical practice (GCP) is a set of internationally recognized ethical and scientific quality requirements that must be followed when designing, conducting, recording and reporting clinical trials that involve people *(14)*. They have been used in the context of drug development in particular.

Adapting GCP principles to the context of a national TB prevalence survey could help to prevent or mitigate challenges related to data management. They could also contribute to enhancing survey quality more broadly, by strengthening oversight, monitoring processes and ensuring that any recommendations are implemented in a timely way. An independent evaluation of national TB prevalence surveys conducted in 2015 included a recommendation to explore the relevance of GCP to future national TB prevalence surveys *(5)*.

GCP requirements are designed to ensure two things: the protection of the rights, safety and well-being of all participants; and that data are comprehensive and accurate. To facilitate their use, roles and responsibilities are defined as follows:

- The sponsor or sponsors provide the financing for a survey. Examples include external agencies (e.g. the Global Fund to Fight AIDS, Tuberculosis and Malaria, development agencies or the national government) and may include a mixture of agencies. Sponsors can request regular reports from survey implementing agencies, and reports may be linked to periodic release of funds.
- The principal investigator represents all survey investigators. That person is responsible for leading the development of the protocol and standard operating procedures (SOPs) and for ensuring review. The principal investigator is also responsible for the recruitment of competent staff, and leads the writing of the final report and scientific papers.
- Investigators contribute to survey design (including the development of a protocol and SOPs, and ethics review and approval), implementation of field operations including quality control, analysis of results and preparation of a survey report. During field operations, this includes ensuring the accuracy, completeness, legibility and timeliness of the data reported in data collection tools. Data that are derived from source documents should be consistent with the source documents; if this is not the case, discrepancies should be explained. To achieve maximum data quality, a standard set of quality assurance procedures[2] should be in place. These include checking that batches of newly entered records are consistent with defined standards.
- Survey monitors assess the implementation of survey operations, including checking protocol modifications and checking for protocol violations. They may conduct batch checks of data. They advise investigators about their findings and provide recommendations for corrective actions if needed. They also report to an independent data monitoring committee (or board) and may assist the principal investigator to prepare the final

[1] At the time of writing, this was planned for publication in 2021.

[2] Quality assurance is a process of systematic activities designed to ensure, assess and confirm the quality of the data collected during a survey. Quality-assured data are those that are suitable for their intended purpose in terms of their accuracy, timeliness, accessibility and comparability between database and source documents.

report. In the context of GCP, study monitors represent the sponsor.

- An independent data monitoring committee (or board) may be established by the sponsor to assess the progress of the survey at regular intervals (based on reports from survey monitors) and to provide recommendations to the sponsor about whether to continue, modify or stop the survey.

The first three of these elements were present in all national TB prevalence surveys implemented in 2007–2016. Survey monitoring by external experts (the fourth element) was also commonly in place, provided by staff of international agencies or by people who had held senior roles in previous surveys in other countries (via the Asia–Asia, Asia–Africa and Africa–Africa collaboration highlighted in **Chapter 4**). However, a formal and independent data monitoring committee was not established for any of the surveys (although many had oversight from a survey committee, expert advisory group or equivalent). It was also the case that there was not necessarily any obligation for investigators to implement all of the recommendations made by external experts.

WHO initiated the development of guidance on the adaptation and use of GCP and good data management practices (GDMP) within the context of national population-based surveys of TB disease (including national TB prevalence surveys) and health facility based surveys in 2019, in collaboration with WHO/TDR – the WHO Special Programme for Research and Training in Tropical Diseases, which has conducted extensive training in the application of GCP in clinical trials. The final document will provide guidance on how to implement the key GCP/GDMP principles to maximize data credibility (i.e. comprehensive and accurate data collected in an ethical manner) within the scope of population-based surveys and health facility based surveys.

Other challenges related to data management can be addressed using the lessons learned from previous surveys (documented in **Chapter 4**). Examples of lessons learned are that:

- a competent and responsive data management team is essential, and this team should be involved from the initial stages of survey preparations through to completion of data analysis and report writing;
- electronic data capture systems in the field and laboratories can significantly facilitate and increase the efficiency of data collection, validation and analysis; and
- use of multiple paper-based forms for the same individual should be avoided.

5.3.3 Invest more resources in the work required once results are finalized, especially to ensure the timely production of survey reports and effective communication of findings and their implications

In 10 of the 25 surveys implemented in 2007–2016, producing the final survey report took a considerable amount of time (more than 1 year in 8 countries). The presence of a permanent full-time survey monitor (in line with GCP) could help to address this challenge, since one of that person's responsibilities would be to provide regular reports with material that could subsequently be used in the final survey report. More generally, more resources for report writing (people with the right skills and time, and funding for production costs including editing and printing) need to be committed when a survey budget is first developed and approved.

Experience in several countries also highlighted the importance of good communication of results to key decision-makers (e.g. planners, policy-makers and those with responsibility for communicable diseases in the ministry of health). During discussions, emphasis should be given to survey validity; quality assurance procedures; monitoring (including external monitoring); and how survey findings provide valuable information for decision-making on policies, prioritization and future budgeting for TB control. When to engage with national and local media also needs careful thought.

The last chapter of the *lime book (8)*, on "Analysis and reporting", focused on best-practice methods for the analysis of survey data and how to present results.[1] The book did not include a subsequent chapter on the production of a survey report and communication of results. Such additional guidance will be part of the next WHO edition of this handbook.

References

1. Global tuberculosis report 2015. Geneva: World Health Organization; 2015 (https://apps.who.int/iris/bitstream/handle/10665/191102/9789241565059_eng.pdf, accessed 8 January 2020).
2. WHO. Standards and Benchmarks for tuberculosis surveillance and vital registration systems. WHO, 2014 http://apps.who.int/iris/bitstream/10665/112673/1/9789241506724_eng.pdf?ua=1.

[1] This guidance was subsequently updated and published in a journal article by Floyd et al. (2013) *(15)*.

3. Anderson L, Floyd K, Sismanidis B. Strengthening national notification systems for direct measurement of TB cases: an overview of progress. Geneva: World Health Organization; 2018 (https://www.who.int/tb/advisory_bodies/impact_measurement_taskforce/meetings/tf7_background_1_strengthen_notification.pdf, accessed 22 January 2020).
4. Global tuberculosis report 2019. Geneva: World Health Organization; 2019 (https://apps.who.int/iris/bitstream/handle/10665/329368/9789241565714-eng.pdf, accessed 1 February 2020).
5. WHO Global Task Force on TB Impact Measurement. Report of the sixth meeting of the full Task Force (19–21 April 2016, Glion-sur-Montreux, Switzerland). Geneva: World Health Organization; 2016 (https://www.who.int/tb/advisory_bodies/impact_measurement_taskforce/meetings/tf6_report.pdf?ua=1, accessed 8 January 2020).
6. Sustainable development goals [website]. New York: United Nations; 2016 (https://sustainabledevelopment.un.org/topics/sustainabledevelopmentgoals, accessed 22 January 2020.
7. Uplekar M, Weil D, Lonnroth K, Jaramillo E, Lienhardt C, Dias HM et al. WHO's new End TB Strategy. Lancet. 2015;385(9979):1799–801 (https://www.ncbi.nlm.nih.gov/pubmed/25814376, accessed 22 January 2020).
8. Tuberculosis prevalence surveys: a handbook. Geneva: World Health Organization; 2011 (https://apps.who.int/iris/bitstream/handle/10665/44481/9789241548168_eng.pdf, accessed 22 November 2019).
9. Barac A, Karimzadeh-Esfahani H, Pourostadi M, Rahimi MT, Ahmadpour E, Rashedi J et al. Laboratory cross-contamination of Mycobacterium tuberculosis: a systematic review and meta-analysis. Lung. 2019;197(5):651–61.
10. Policy update: Xpert MTB/RIF assay for the diagnosis of pulmonary and extrapulmonary TB in adults and children. Geneva: World Health Organization; 2013 (https://apps.who.int/iris/bitstream/handle/10665/112472/9789241506335_eng.pdf, accessed 14 February 2020).
11. Xpert MTB/RIF implementation manual: technical and operational 'how-to'; practical considerations. Geneva: World Health Organization; 2014 (https://apps.who.int/iris/bitstream/handle/10665/112469/9789241506700_eng.pdf, accessed 14 February 2020).
12. Dorman SE, Schumacher SG, Alland D, Nabeta P, Armstrong DT, King B et al. Xpert MTB/RIF Ultra for detection of Mycobacterium tuberculosis and rifampicin resistance: a prospective multicentre diagnostic accuracy study. Lancet Infect Dis. 2018;18(1):76–84.
13. WHO meeting report of a technical expert consultation: non-inferiority analysis of Xpert MTB/RIF Ultra compared to Xpert MTB/RIF. Geneva: World Health Organization; 2017 (https://apps.who.int/iris/bitstream/handle/10665/254792/WHO-HTM-TB-2017.04-eng.pdf?sequence=1, accessed 22 January 2020).
14. International Conference on Harmonisation Working Group. ICH harmonised tripartite guideline: guideline for good clinical practice E6 (R1). International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. Washington, DC. 1996.
15. Floyd S, Sismanidis C, Yamada N, Daniel R, Lagahid J, Mecatti F et al. Analysis of tuberculosis prevalence surveys: new guidance on best-practice methods. Emerg Themes Epidemiol. 2013;10(1):10 (https://ete-online.biomedcentral.com/articles/10.1186/1742-7622-10-10, accessed 14 February 2020).

PART II

Country-by-country survey profiles

BANGLADESH

2015–2016

Summary statistics

Participation rate	91%
Bacteriologically confirmed TB (≥15 years)	
• Prevalence per 100 000 population	287
• Male:female ratio	3.2
Prevalence:notification ratio (Bacteriologically confirmed TB, ≥15 years)	2.8

Surveyed clusters (N=125)[a]

Key people

Name	Role	Organization
Mahmudur Rahman	Principal investigator (PI)	Institute of Epidemiology, Disease Control and Research (IEDCR)
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Mohammad Mushtuq Husain	Co-investigator and chief coordinator	IEDCR
S.M. Mostofa Kamal	Co-investigator and laboratory manager	National TB Reference Laboratory (NTRL), National Institute of Diseases of the Chest and Hospital (NIDCH)
Asif Mujtoba Mahmud	Co-investigator	IEDCR
Iqbal Ansary Khan	Co-investigator	IEDCR
Akter Hossain	Co-investigator and central radiologist	IEDCR
Ahmad Raihan Sharif	Co-investigator and data manager	IEDCR
Mahbubur Rahman	Co-investigator and assistant data manager	IEDCR
Vikarunnessa Begum	Co-investigator	WHO Bangladesh
Mohammed Sayeedur Rahman	Co-investigator and survey coordinator	WHO Bangladesh
Ashaque Husain	Chairperson, Executive Committee	TB-Leprosy, Directorate General of Health Services (DGHS)
Ahmed Hussain Khan	Chairperson, Executive Committee	TB-Leprosy, DGHS
Md Mozammel Haque	Chairperson, Executive Committee	TB-Leprosy, DGHS
Md Quamrul Islam	Chairperson, Executive Committee	TB-Leprosy, DGHS
Shahid Md Sadiqul Islam	Chairperson, Executive Committee	TB-Leprosy, DGHS
Rouseli Haq	Chairperson, Executive Committee	TB-Leprosy, DGHS
Md Ehteshamul Huq Choudhury	Chairperson, Executive Committee	TB-Leprosy, DGHS
Md Jahangir Alam Sarker	Member secretary, Executive Committee	National TB Control Programme
Md Ashraf Uddin	Member secretary, Executive Committee	National TB Control Programme
Ikushi Onozaki	Technical assistance (survey advisor)	WHO headquarters
Irwin Law	Technical assistance (design and analysis)	WHO headquarters
Sayori Kobayashi	Technical assistance (data management)	WHO headquarters
J. Sean Cavanaugh	Technical assistance (design and analysis)	US Centers for Disease Control and Prevention (CDC)
Shua Chai	Technical assistance (survey advisor)	US Centers for Disease Control and Prevention (CDC)
Mourad Gumusboga	Technical assistance (laboratory)	Supranational Reference Laboratory (SRL), Antwerp, Belgium
Susumu Hirao	Technical assistance (X-ray interpretation)	Research Institute of Tuberculosis/Japan Anti-Tuberculosis Association (RIT/JATA)

Survey organization and financing

Implementing agency:
Institute of Epidemiology, Disease Control and Research (IEDCR)

Finance	Amount (US$)
USAID	1 689 004
The Global Fund	1 849 334
TB CARE II	56 440
Total budget	3 594 778

Data sources

- National Tuberculosis Prevalence Survey, Bangladesh 2015–2016. Institute of Epidemiology, Disease Control & Research (IEDCR), Directorate General of Health Services, Ministry of Health & Family Welfare, Government of the People's Republic of Bangladesh; 2017.
- Survey dataset.

[a] The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Survey design and methodology

Sampling design	
Sampling frame	Whole country
Sampling design	Multistage cluster sampling using PPS
Strata	Urban/rural
Sampling unit	Urban: ward/mohalla or para Rural: union/mouza or village
Sample size assumptions	
• Smear-positive prevalence	100 per 100 000 (≥15 years)
• Precision	0.25
• Design effect	1.3
• *k*	0.6
• Response rate	80%
• Sample size (estimated)	100 000
Number of clusters	125[a]
Cluster size	800
Eligibility criteria	
• Age	≥15 years
• Residency	Lived in the cluster for at least 2 weeks before the census

[a] One cluster was replaced by another in the same district, due to a security issue (the planned survey site was set on fire by people from a neighbouring village).

Screening criteria	
Interview[a]	Cough ≥2 weeks (3 points) Cough <2 weeks (1 point) Haemoptysis in the past month (3 points) Weight loss in the past month (1 point) Fever ≥1 week in the past month (1 point) Night sweats in the past month (1 point) Symptom-screen positive: Total clinical score ≥3 points Clinical score 1 or 2 with chest X-ray exempted
Chest X-ray[b]	Any lung abnormality
Other	N/A

[a] An in-depth interview on health-care seeking behaviour was done only for participants who reported any TB symptoms (cough, haemoptysis, weight loss, fever, night sweats).
[b] Portable digital direct radiography.

Laboratory methodology	
Smear	Two samples (spot, morning): direct preparation FM (LED, auramine stain)
Culture	Two samples (spot, morning): concentrated preparation, LJ media
Identification of MTB	Capilia
TB drug susceptibility test	Done
Xpert® MTB/RIF	One sample (morning). A spot sample was used if the following conditions were met: morning sample was not available; smear-positive but Xpert-negative in a morning sample; smear-negative and Xpert-negative in a morning sample, but a spot sample was smear-positive.
HIV test	Not done

Analysis and reporting

Field data collection	Paper (interview)/ electronic (census)
Database	SQL
Method of analysis	MI+IPW
Results first published in a report/paper	August 2017
Official dissemination event	August 2018

Key survey results

Prevalence[a]	Smear-positive TB		Bacteriologically confirmed TB	
	Number per 100 000 population	95% CI	Number per 100 000 population	95% CI
Total	113	87–139	287	244–330
Male	187	141–234	452	379–526
Female	48	30–67	143	109–178
15–24 years	45	21–69	103	65–152
25–34 years	77	39–116	183	122–244
35–44 years	138	74–202	302	215–389
45–54 years	137	72–202	338	235–441
55–64 years	147	64–229	462	317–607
≥65 years	333	185–480	954	715–1 194
Urban	131	78–185	316	239–392
Rural	103	77–129	270	220–321

[a] Age ≥15 years unless otherwise specified.

	Design effect	*k*
Smear-positive TB	1.5	0.8
Bacteriologically confirmed TB	1.6	0.5

Other sputum results	Number	%
Total smear-positive participants	125	–
Smear-positive participants without MTB confirmation[a]	17	14
Isolates with MDR-TB detected[b]	1	0.6

[a] This includes culture with no evidence of MTB (i.e. culture-negative, NTM, contaminated, N/A) and Xpert-negative.
[b] DST was done for 157 subjects.

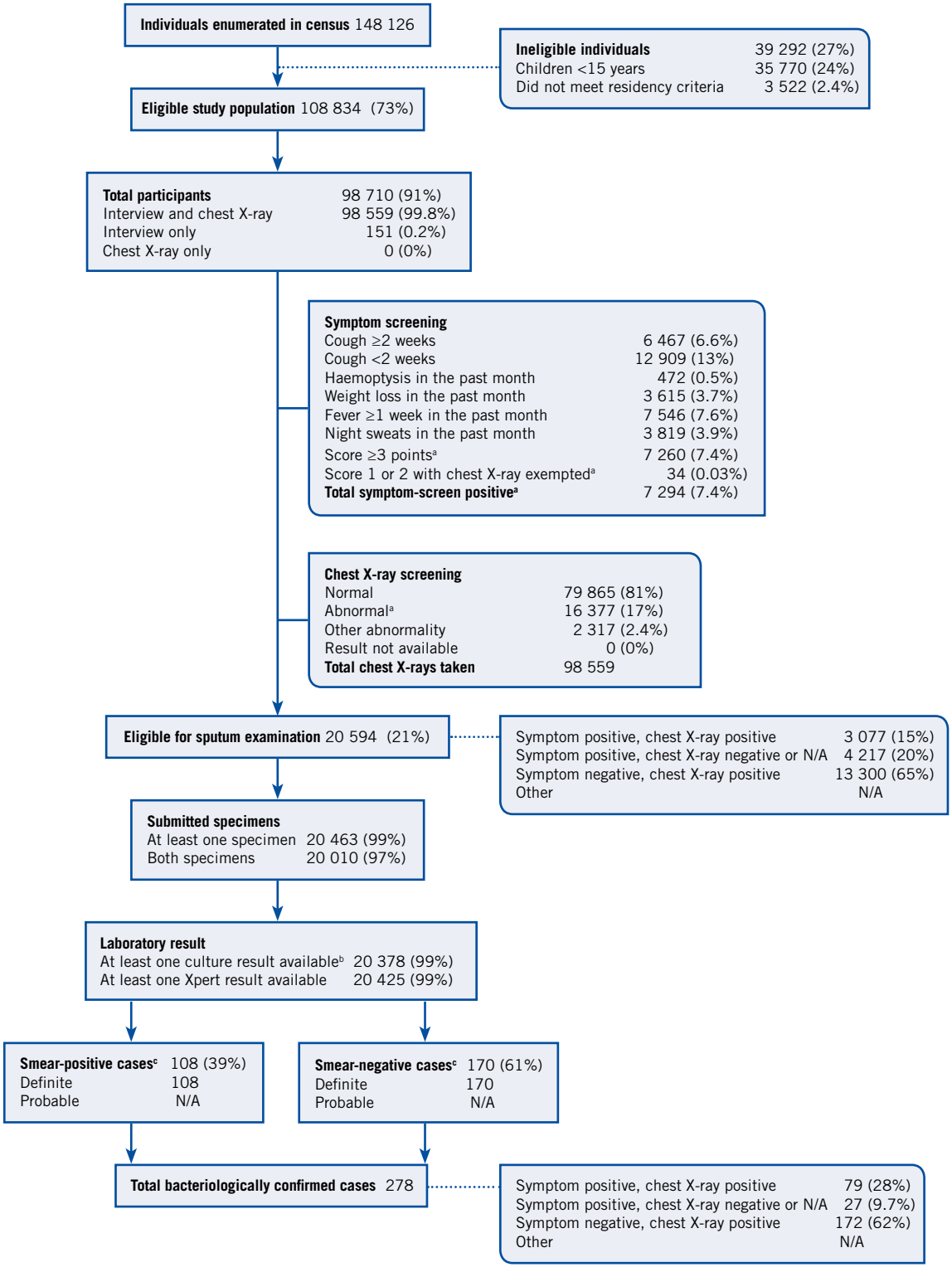
Health-care seeking behaviour among participants who reported symptoms	Number	%
Participants who reported symptoms[a]	26 882	–
Location of care sought		
• Consulted medical facility	6 545	24
Public facility	*1 816*	*28*
Private facility	*2 182*	*33*
Other (NGO, village doctor)	*2 547*	*39*
• Pharmacy	6 533	24
• Traditional healer	23	0.1
• Other[b]	191	0.7
Self-treated	643	2.4
No action taken	12 947	48

[a] Data on health-care seeking behaviour were available for participants who reported at least one of TB symptoms (cough, haemoptysis, weight loss, fever, night sweats).
[b] Ayurvedic/homeo/unani (177), not specified (14).

Survey participants currently on TB treatment	Number	%
Total participants currently on TB treatment	57	–
• Treated in the public sector	16	28
• Treated in the private sector	10	17
• Treated in other sector	18	32
• Treated in unknown sector	13	23
Bacteriologically confirmed TB cases detected by the survey who were currently on TB treatment	9	3.2

Survey flow: census to final outcomes

Field operations: March 2015 to April 2016



[a] Eligible for sputum collection.
[b] Cultures that were either contaminated and/or missing without a definitive result (i.e. MTB, NTM, negative) were excluded.
[c] Definite: MTB confirmed by culture and/or Xpert. Probable: no definition.

Fig. 1: Participation rate by age and sex

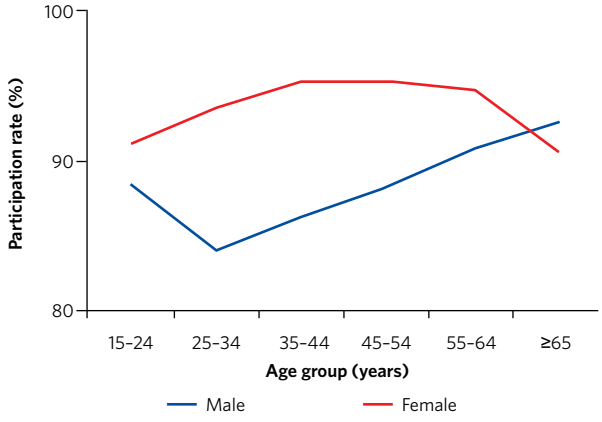


Fig. 2: TB prevalence per 100 000 population by age

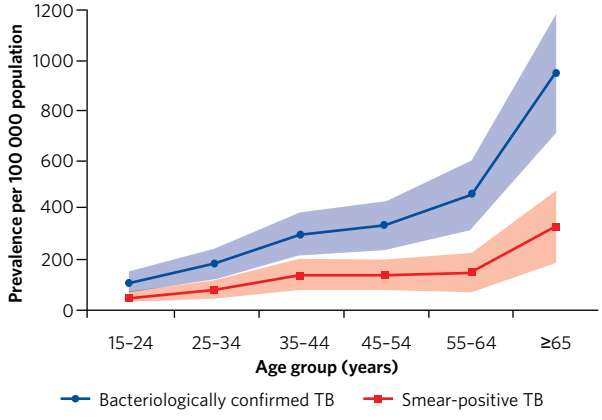


Fig. 3: Estimated number of bacteriologically confirmed TB cases and prevalence per 100 000 population, by age[a]

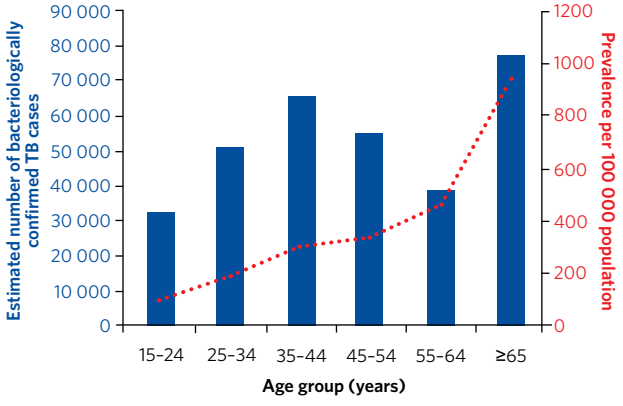


Fig. 4: Cluster variation of the number of bacteriologically confirmed TB cases[b]

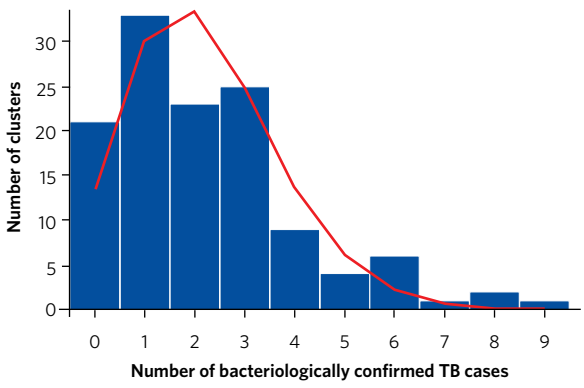


Fig. 5: Ratio of bacteriologically confirmed TB prevalence to notifications by age and by sex[c]

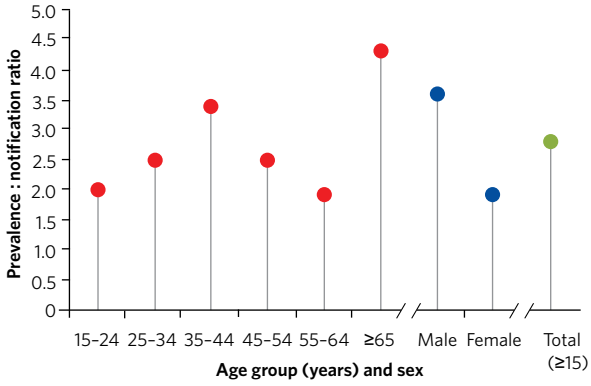
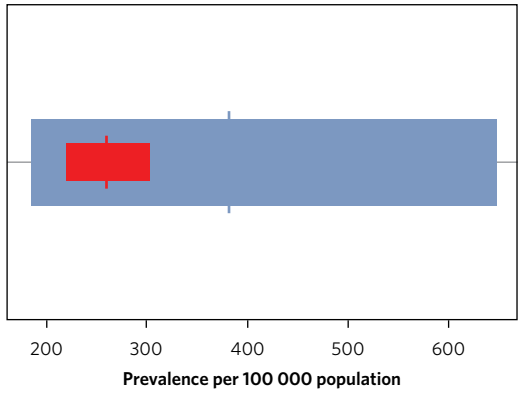


Fig. 6: Estimates of TB prevalence (all ages, all forms of TB) before (in blue) and after (in red) the national TB prevalence survey[d]



[a] The estimated number of bacteriologically confirmed TB cases is the product of age-specific prevalence per 100 000 population and population estimates from the UN Population Division (2015 revision).

[b] The data suggest that the distribution of cases by cluster (blue bars) is significantly different from the theoretical distribution (red line) (mean 2.22, variance 3.63, $p<0.05$). The theoretical distribution assumes cases are distributed at random i.e. no clustering effect.

[c] Notification rates were estimated using notifications of bacteriologically confirmed pulmonary TB (2015) obtained from the NTP, and population estimates from the UN Population Division (2015 revision).

[d] The blue bar denotes the best estimate of prevalence and its range that was indirectly derived from the estimate of incidence previously published by WHO, adjusted to the year of the prevalence survey based on previously published trends in incidence.

Background

Bangladesh's population was 161 million in 2015. It was one of the 22 high tuberculosis (TB) burden countries (HBCs) defined by WHO as a top priority for global efforts in TB control in 1998 and throughout the Millennium Development Goal (MDG) era (2000–2015), and one of the top 30 HBCs defined by WHO for the period 2016–2020. In 2015, Bangladesh was a lower-middle-income country with an average gross national income (GNI) per person of US$ 1190 per year *(1)*. The prevalence of HIV in the general population aged 15–49 years was <0.1% (95% confidence interval [CI]: <0.1–<0.1%) *(2)*, and it was estimated that 0.1% (95% CI: 0.08–0.2%) of TB patients were coinfected with HIV *(3)*.

In Bangladesh in the 1960s and 1970s, TB services were based in TB clinics or hospitals, and then expanded to 124 upazila health complexes (UHCs) between 1980 and 1986 (the period of the second health and population plan). During the third health and population plan (1986–1991), TB services were integrated with leprosy under the Mycobacterial Disease Control unit of the Directorate General of Health Services (DGHS). The National TB Control Programme (NTP) adopted the WHO-recommended DOTS strategy during the fourth health and population plan (1992–1998); it was implemented in four upazilas in November 1993 and expanded to cover all upazilas by mid-1998 *(4-6)*.

The notification rate increased from 45 per 100 000 population in 1990 to 102 per 100 000 population in 2010 *(7)*. WHO estimated incidence to be 227 (95% CI: 200–256) per 100 000 population and prevalence to be 404 (95% CI: 211–659) per 100 000 population in 2014. The case detection rate was 53% (95% CI: 47–60) in 2014 *(8)*.

Bangladesh carried out national TB prevalence surveys in 1964–1966, in 1987–1988 and in 2007–2009 *(9–11)*. In contrast to the methodology recommended by the WHO Global Task Force on TB Impact Measurement, the 2007–2009 survey was based on "smear from everybody"; that is, without screening, sputum samples were collected from every eligible participant for smear examinations (and a subsequent chest X-ray was taken if a smear was positive). Adjusted smear-positive TB prevalence in those aged 15 years or more in the 2007–2009 survey was 79 (95% CI: 47–134) per 100 000 population.

In December 2007, Bangladesh was one of the 22 global focus countries for a national TB prevalence survey selected by the WHO Global Task Force on TB Impact Measurement. Recognizing that a new prevalence survey – carried out in accordance with recommended methods – was needed to understand the current TB burden *(12)* and to measure the impact of the NTP, the Ministry of Health decided in 2012 to implement a fourth national TB prevalence survey. Field operations were conducted from March 2015 to April 2016.

Photo credit: Irwin Law

Key methods and results

There were 125 survey clusters in two strata (urban and rural), with a target cluster size of 800 individuals. A total of 148 126 individuals from 9594 households were enumerated in the survey census, of whom 108 834 (73%) were eligible and invited to participate. Of these, 98 710 (91%) did so. All participants were screened according to the 2011 algorithm recommended by WHO; that is, using a chest X-ray and an interview about symptoms *(12)*. A total of 20 594 participants (21%) were eligible for sputum examination; of these, 20 463 (99%) submitted at least one sputum specimen and 20 010 (97%) submitted two sputum specimens.

Sputum from 20 425 participants was tested with Xpert® MTB/RIF. Of these participants, 269 (1.3%) were positive for *Mycobacterium tuberculosis* (MTB); of these, 12 (4.4%) were also rifampicin (RIF) resistant, 231 (86%) were RIF sensitive and 26 (9.6%) were indeterminate. Due to potential cross-contamination, 13 Xpert-positive results were annulled.

A total of 278 bacteriologically-confirmed pulmonary TB cases were identified, including 108 (39%) cases of smear-positive TB. Of these 278 cases, 132 (47%) were confirmed by both culture and Xpert MTB/RIF, 22 (7.9%) only by culture, and 124 (45%) only by Xpert MTB/RIF (the accompanying culture result was either culture MTB negative, nontuberculous mycobacteria or contaminated). Among 124 cases that were diagnosed only by Xpert MTB/RIF, 103 were smear-negative.

The prevalence of smear-positive TB was 113 (95% CI: 87–139) per 100 000 population (among those aged ≥15 years), and for bacteriologically confirmed TB it was 287 (95% CI: 244–330) per 100 000 population. The prevalence of smear-positive and bacteriologically confirmed TB per 100 000 population did not vary by strata.

Other key results were:

- the male to female ratio was 3.9 for smear-positive TB and 3.2 for bacteriologically confirmed TB;
- prevalence per 100 000 population increased with age and was especially high in those aged 55 years or more; the absolute number of TB cases was consistently high in all age groups, with two peaks in those aged 35–44 years and 65 years or more;
- among bacteriologically confirmed TB cases, 38% were symptom-screen positive, and among the smear-positive cases, 48% were symptom-screen positive;
- for smear-positive pulmonary TB, the ratio of prevalence to notifications (P:N ratio) was 2.8 overall, but varied from 1.9 in those aged 55–64 years to 4.3 in those aged 65 years or more, and was higher for men than women (3.6 versus 1.9);
- among the bacteriologically confirmed TB cases, 90% had no previous history of anti-TB treatment and only 3.2% were on anti-TB treatment at the time of the survey; and
- of the 101 bacteriologically confirmed and 48 smear-positive TB survey cases that screened positive for symptoms and were not on anti-TB treatment at the time of the survey, 32 (32%) and 15 (31%), respectively, had previously sought care in a public or private health facility for their symptoms.

Photo credit: Irwin Law

Implications of results

Based on the results from the national TB prevalence survey, the overall prevalence (for all forms and all ages) was estimated at 260 (95% CI: 220–301) per 100 000 population. This was lower than the pre-survey estimate of 404 (95% CI: 211–659) per 100 000 population *(6, 8)*. However, it was higher than had been anticipated by national authorities based on the country's notification data and the results from the 2007–2009 survey. Possible explanations for the lower-than-expected burden include improved access and use of TB diagnostic services, better case detection and treatment of TB cases in the community (especially in urban areas), and reductions in the level of poverty and undernourishment in the decade prior to the survey *(1, 13)*. The estimated incidence was 221 (95% CI: 160–290) per 100 000 population, which was similar to the pre-survey estimate of 227 (95% CI: 200–256) per 100 000 population *(6, 8)*.

Other implications included:

- a need for case detection to be improved by including chest X-ray examination in the diagnostic algorithm, given that only one third of survey TB cases met the symptom screening criteria according to the scoring system used, and the remaining cases were identified as eligible for diagnostic testing only by chest X-ray;
- a need for strategies to improve access to diagnosis and treatment for men and those aged 55 years or more, given the higher prevalence and higher ratio of prevalence to notifications in these groups;
- a need for improved diagnostic capacity to detect the large pool of smear-negative disease;
- a need for strengthened community awareness about TB and efforts to reduce stigma associated with the disease, given that about half of participants who reported at least one TB symptom had not sought care for their symptoms at the time of the survey; and
- a need for informal private providers to be integrated into public-private networks given that among participants who reported at least one TB symptom, 24% sought care in pharmacies as the first point of care.

Major successes, challenges and lessons learned

The 2015–2016 national TB prevalence survey in Bangladesh was carried out successfully. As with the survey in Kenya, this was one of the first national TB prevalence surveys that used both culture and Xpert MTB/RIF for all participants who screened positive.

A key factor in the success of the survey was the strong leadership, strong technical capacity and collaborative culture of the implementing agency. Together with extensive experience with health research, the team had good channels of communication with the Ministry of Health, the NTP, the National TB Reference Laboratory, nongovernmental organizations and external partners such as WHO and the United States Centers for Disease Control and Prevention. Ensuring that only one agency was responsible for the survey helped to streamline funding mechanisms, procurement and human resource management.

Another reason for success was the ingenuity and responsiveness of the information technology (IT) team. This included medical and epidemiological officers, a data manager and software engineers. Practical understanding of the survey in combination with technical capacity ensured a system that was fit for purpose, and which could provide a high-quality dataset shortly after field operations were completed. The use of barcodes and real-time data entry using tablets helped to minimise transcription errors and the overall workload of the survey team. The use of paper as a backup for key variables assisted with validation of data and for tracking of individuals during field operations.

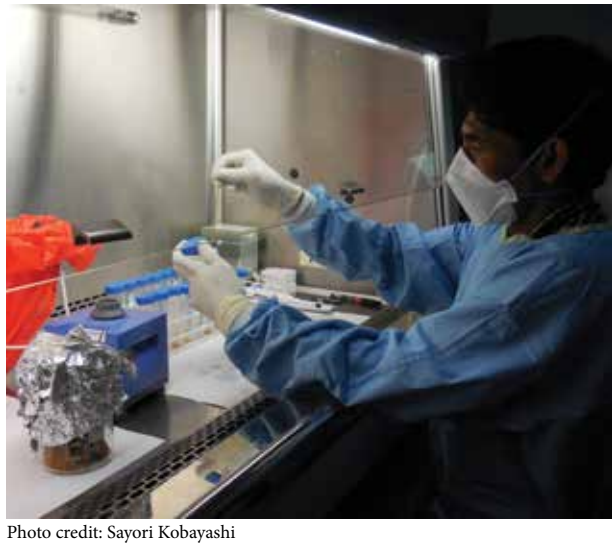


Photo credit: Sayori Kobayashi

Challenges faced during the survey, and associated lessons learned, are listed below.

- A lengthy procurement process that took more than 12 months. Some laboratory equipment was only received after the pilot survey had been completed.
- Field operations had to be rescheduled several times due to the failure (due to overheating) of some digital chest X-ray machines. None of the five machines were simultaneously functional, which slowed survey implementation and increased overall costs (e.g. for human resources). There was no local vendor of the equipment to provide service support. Procurement of major capital from international suppliers should always include local support.
- Potential cross-contamination of specimens from the field to the laboratory. In defining a survey TB case, laboratory source documents were examined to identify any potential clustering of positive Xpert MTB/RIF results. All available data from those with any results that were consecutively positive (because they were processed in the same numerical order) were reviewed, and 13 results from three clusters were excluded. It is essential to ensure that good laboratory practices are maintained in situations of high volume and throughput.
- One cluster had to be replaced by another due to local conflict – the planned survey site was set on fire by people from a neighbouring village. While such situations are likely to be infrequent, survey protocols should clearly define how clusters will be replaced in such circumstances, and cluster replacement should be documented including in the final survey report.

References

1. The World Bank. (https://data.worldbank.org/country, accessed April 2017).
2. UNAIDS. (http://aidsinfo.unaids.org/, accessed May 2017).
3. World Health Organization. Global tuberculosis database. Geneva: WHO; 2017 (http://www.who.int/tb/data/en/, accessed April 2017).
4. National tuberculosis prevalence survey, Bangladesh 2015–2016. Bangladesh: Institute of Epidemiology, Disease Control & Research (IEDCR), Directorate General of Health Services, Ministry of Health & Family Welfare, Government of the People's Republic of Bangladesh; 2017.
5. WHO Tuberculosis Programme. (1994). WHO Tuberculosis Programme: framework for effective tuberculosis control. World Health Organization. (http://www.who.int/iris/handle/10665/58717, accessed January 2018).
6. World Health Organization. Global tuberculosis programme. Global tuberculosis control report 1997. Geneva: WHO; (https://apps.who.int/iris/bitstream/handle/10665/63354/WHO_TB_97.225_(part1).pdf?sequence=1, accessed January 2018).
7. World Health Organization. Global tuberculosis report 2013. Geneva: WHO; 2013 (http://reliefweb.int/sites/reliefweb.int/files/resources/9789241564656_eng.pdf, accessed May 2017).
8. World Health Organization. Global tuberculosis report 2015. Geneva: WHO; 2015 (http://apps.who.int/iris/bitstream/10665/191102/1/9789241565059_eng.pdf, accessed July 2017).
9. Government of Bangladesh. The report of the tuberculosis survey of Bangladesh. National TB prevalence survey in Bangladesh. 1973. National Tuberculosis Control and Research Project. Ministry of Health and Family Planning, Government of Bangladesh; 1973.
10. Zaman K, Hossain S, Banu S, Quaiyum MA, Barua PC, Salim MA et al. Prevalence of smear-positive tuberculosis in persons aged ≥ 15 years in Bangladesh: results from a national survey, 2007–2009. Epidemiol Infect. 2012;140(6):1018–1027 (https://www.ncbi.nlm.nih.gov/pubmed/21880168, accessed March 2018).
11. Directorate General of Health Services. Report on the national prevalence survey on tuberculosis in Bangladesh, 1987–88. Dhaka: Ministry of Health and Family Welfare, Government of Bangladesh; 1989.
12. World Health Organization. Tuberculosis prevalence surveys: a handbook. Geneva: WHO; 2011 (https://apps.who.int/iris/bitstream/handle/10665/44481/9789241548168_eng.pdf, accessed August 2017).
13. Food and Agriculture Organization of the United Nations (FAO). FAOSTAT, Bangladesh. (http://www.fao.org/faostat/en/#country/16, accessed March 2018).

CAMBODIA

2010–2011

Summary statistics

Participation rate	93%
Bacteriologically confirmed TB (≥15 years)	
• Prevalence per 100 000 population	831
• Male:female ratio	1.8
Prevalence:notification ratio (smear-positive TB, ≥15 years)	1.7

Surveyed clusters (N=62)[a]

Key people

Name	Role	Organization
Mao Tan Eang	Chairman	National Centre for TB and Leprosy Control (CENAT)
Peou Satha	Survey coordinator/chief of radiology	CENAT
Pheng Sok Heng	Chief of laboratory	CENAT
Koy Bonamy	Chief of census	CENAT
Tieng Sivanna	Chief of statistics	CENAT
Kouet Pichenda	Field team leader	CENAT
Keo Sokonth	Field team leader	CENAT
Saint Saly	Field team leader	CENAT
Chea Manith	Field team leader	CENAT
Kosuke Okada	Supervisor (project leader)	Research Institute of Tuberculosis/Japan Anti-Tuberculosis Association (RIT/JATA)
Norio Yamada	Supervisor (epidemiology/statistics)	RIT/JATA
Masaki Ota	Supervisor (epidemiology/data management)	RIT/JATA
Takashi Yoshiyama	Supervisor (chest X-ray examination (diagnosis))	RIT/JATA
Kunihiko Ito	Supervisor (chest X-ray examination (diagnosis))	RIT/JATA
Hiroyuki Nishiyama	Supervisor (chest X-ray examination (diagnosis))	RIT/JATA
Yutaka Hoshino	Supervisor (chest X-ray examination (film shooting))	RIT/JATA
Hiroko Matsumoto	Supervisor (bacteriological examination (quality assurance))	RIT/JATA
Tetsuhito Sugamoto	Supervisor (bacteriological examination (culture, identification and DST))	RIT/JATA
Kiyomi Yamamoto	Coordinator/data management	RIT/JATA
Ikushi Onozaki	Technical assistance (survey advisor)	WHO headquarters
Rajendra Yadav	Technical assistance (survey advisor)	WHO Cambodia
Emily Bloss	Technical assistance (survey advisor)	US Centers for Disease Control and Prevention (CDC)
Sara Whitehead	Technical assistance (survey advisor)	US Centers for Disease Control and Prevention (CDC)
Philippe Glaziou	Technical assistance (statistics)	WHO headquarters
Charalampos Sismanidis	Technical assistance (analysis)	WHO headquarters
Sian Floyd	Technical assistance (analysis)	London School of Hygiene & Tropical Medicine

Survey organization and financing

Implementing agency:
The National Centre for TB and Leprosy Control (CENAT)

Finance	Amount (US$)
The Global Fund	203 650
JICA	760 300
USAID	53 600
Total budget	1 017 550

Data sources

- Report of the second national TB prevalence survey, 2011. Phnom Penh: Cambodia Ministry of Health; 2012.
- Survey dataset.

[a] The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Survey design and methodology

Sampling design	
Sampling frame	Whole country
Sampling design	Multistage cluster sampling using PPS
Strata	Urban/rural/others[a]
Sampling unit	District/commune/village
Sample size assumptions	
• Smear-positive prevalence	256 per 100 000 (≥15 years)
• Precision	0.25
• Design effect	1.4
• *k*	0.5
• Response rate	90%
• Sample size (estimated)	39 680
Number of clusters	62
Cluster size	640
Eligibility criteria	
• Age	≥15 years
• Residency	Resided ≥2 weeks in the household prior to the census

[a] Mondulkiri, Rattanakiri, Preah Vihear and Steung Treng.

Screening criteria	
Interview	Cough ≥2 weeks and/or haemoptysis
Chest X-ray[a]	Any lung abnormality[b]
Other	Chest X-ray exempted

[a] Conventional radiography.
[b] Other than a single small calcification nodule less than 10mm or pleural adhesion at costophrenic angles.

Laboratory methodology	
Smear	Two samples (spot, morning); direct preparation FM (LED, auramine stain), cross-examination by ZN for specific slides[a]
Culture	Two specimens (spot, morning); direct preparation, Ogawa media
Identification of MTB	Capilia
TB drug susceptibility test	Done[b]
Xpert® MTB/RIF	Not done
HIV test	Not done

[a] ZN was used on smears that were FM positive; those with positive cultures; those with negative smears and negative cultures but chest X-ray suggestive of active TB; and 5% of those smears that were FM negative as negative controls.
[b] 278 MTB strains were sent to RIT/JATA.

Analysis and reporting

Field data collection	Paper
Database	Microsoft® Access
Method of analysis	Survey analysis based on participants without imputation
Results first published in a report/paper	December 2012
Official dissemination event	February 2012

Key survey results

Prevalence[a]	Smear-positive TB		Bacteriologically confirmed TB	
	Number per 100 000 population	95% CI	Number per 100 000 population	95% CI
Total	271	212–348	831	707–977
Male	361	265–493	1 097	895–1 344
Female	197	127–303	609	486–763
15–24 years	18	4.3–71	130	74–227
25–34 years	87	41–185	427	304–598
35–44 years	266	169–420	881	667–1 163
45–54 years	364	218–607	1 029	780–1 358
55–64 years	799	534–1 194	1 844	1 388–2 446
≥65 years	1 007	653–1 550	3 046	2 353–3 936
Urban	134	61–292	593	357–983
Rural	310	236–408	882	738–1 055
Other	249	4.4–12 273	1 175	24–36 964

[a] Age ≥15 years unless otherwise specified.

	Design effect	*k*
Smear-positive TB	1.6	0.6
Bacteriologically confirmed TB	2.5	0.6

Other sputum results	Number	%
Total smear-positive participants	114	–
Smear-positive participants without MTB confirmation[a]	24	21
Isolates with MDR-TB detected	0	0

[a] This includes culture with no evidence of MTB (i.e. culture-negative, NTM, contaminated, N/A).

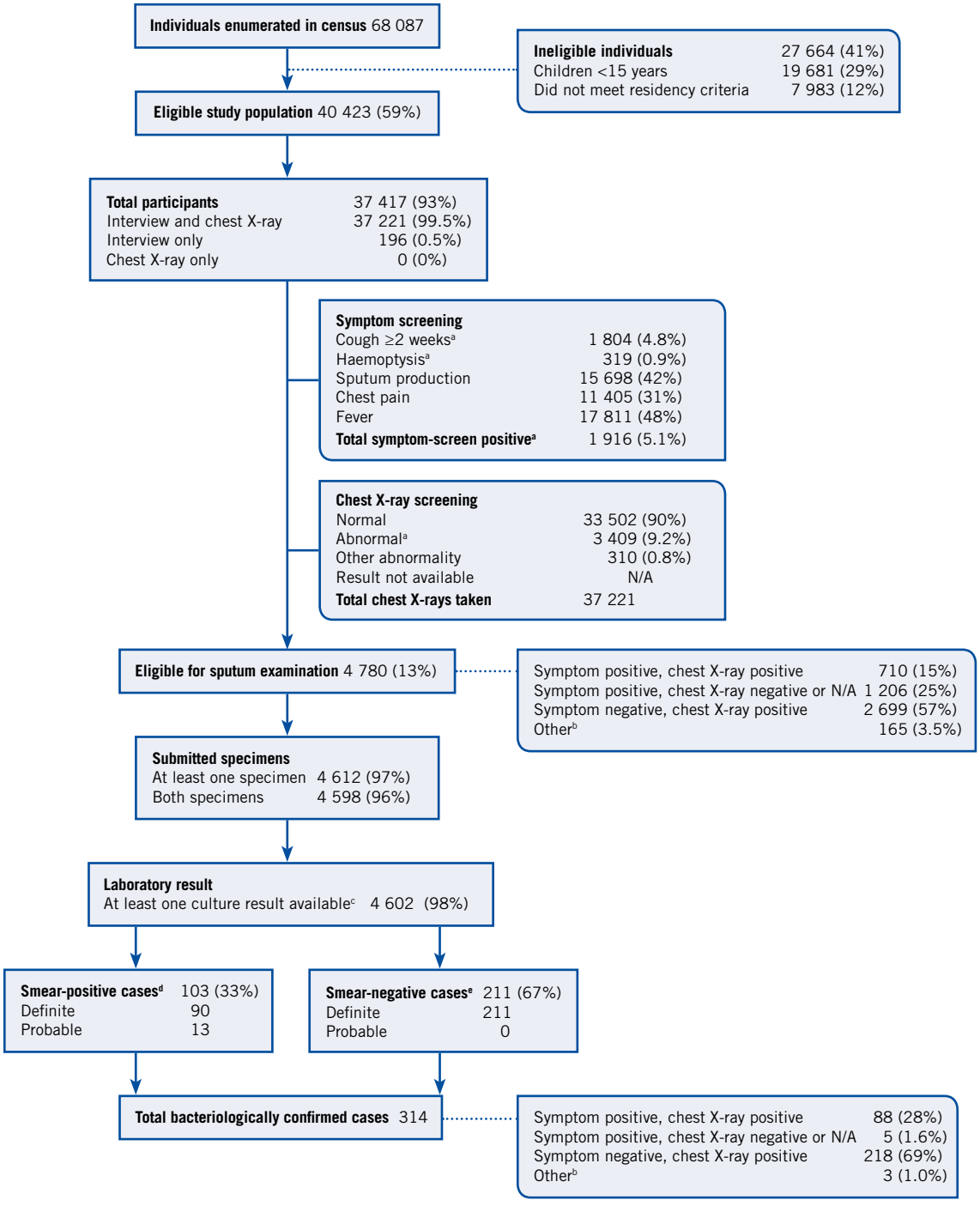
Health-care seeking behaviour among participants who were symptom-screen positive	Number	%
Participants who were symptom-screen positive[a]	1 916	–
Location of care sought		
• Consulted medical facility	1 261	66
Public facility	*947*	*75*
Private facility	*305*	*24*
Unspecified	*9*	*0.7*
• Pharmacy	401	21
• Traditional healer	21	1.1
Self-treated	28	1.5
Other[b]	6	0.3
No action taken	197	10
Unknown	2	0.1

[a] Cough ≥2 weeks and/or haemoptysis.
[b] Family member.

Survey participants currently on TB treatment	Number	%
Total participants currently on TB treatment	80	–
• Treated in the public sector	72	90
• Treated in the private sector	6	8.0
• Treated in unknown sector	2	2.0
Bacteriologically confirmed TB cases detected by the survey who were currently on TB treatment	6	1.9

Survey flow: census to final outcomes

Field operations: December 2010 to September 2011



[a] Eligible for sputum collection.
[b] Chest X-ray exempted and symptom-screen negative, and other.
[c] Cultures that were either contaminated and/or missing without a definitive result (i.e. MTB, NTM, negative) were excluded.
[d] Definite: MTB confirmed by culture. Probable: MTB not confirmed by culture but two smear-positive slides, or one smear-positive slide with chest X-ray suggestive of TB.
[e] Definite: MTB confirmed by culture. Probable: culture-positive (but MTB not confirmed) and chest X-ray suggestive of TB.

Fig. 1: Participation rate by age and sex

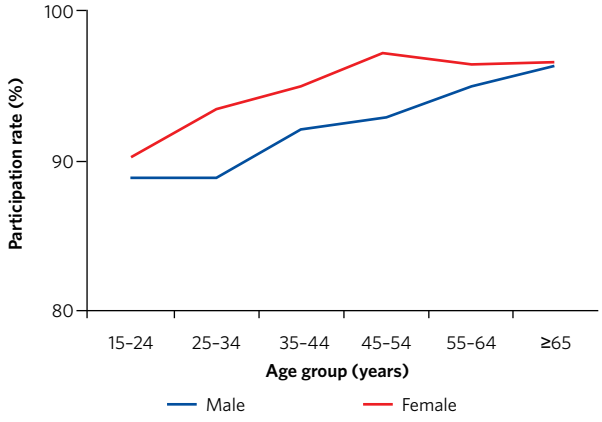


Fig. 2: TB prevalence per 100 000 population by age

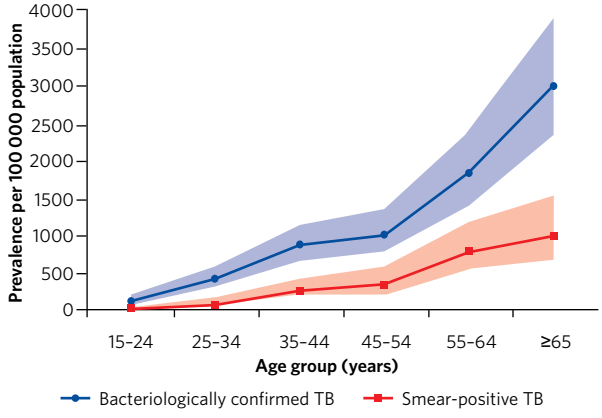


Fig. 3: Estimated number of bacteriologically confirmed TB cases and prevalence per 100 000 population, by age[a]

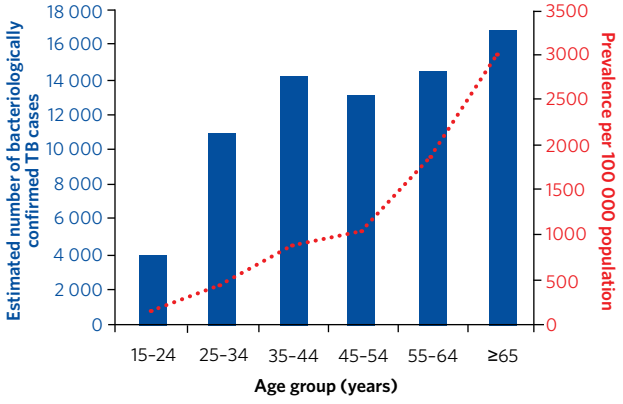


Fig. 4: Cluster variation of the number of bacteriologically confirmed TB cases[b]

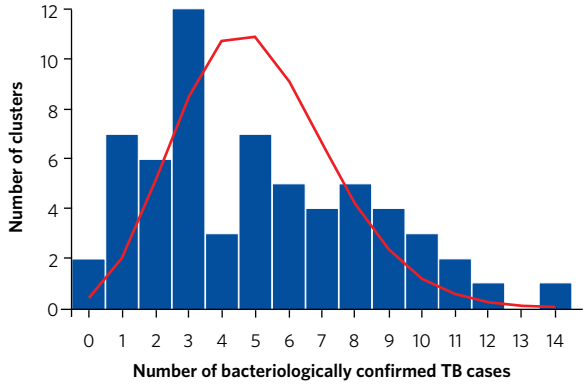


Fig. 5: Ratio of smear-positive TB prevalence to notifications by age and by sex[c]

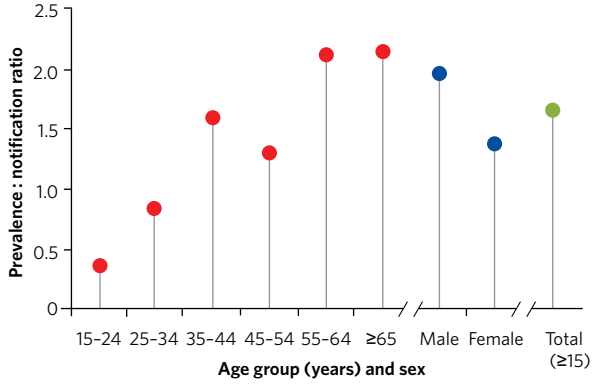
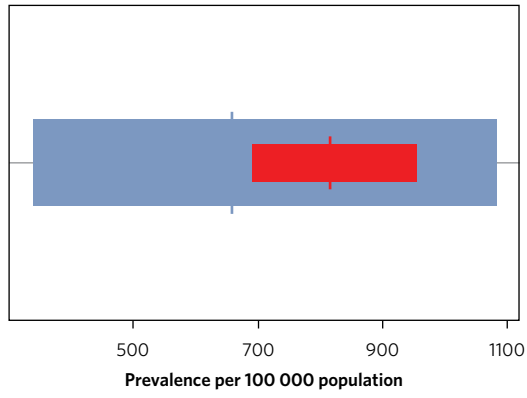


Fig. 6: Estimates of TB prevalence (all ages, all forms of TB) before (in blue) and after (in red) the national TB prevalence survey[d]



[a] The estimated number of bacteriologically confirmed TB cases is the product of age-specific prevalence and population estimates from the UN Population Division (2015 revision).

[b] The data suggest that the distribution of cases by cluster (blue bars) was significantly different from the theoretical distribution (red line) (mean 5.06, variance 11.0, $p<0.05$). The theoretical distribution assumes cases are distributed at random i.e. no clustering effect.

[c] Notification rates were estimate of using notifications obtained from the WHO global TB database, and population estimates from the UN Population Division (2015 revision).

[d] The blue bar denotes the best estimated prevalence and its range that was indirectly derived from the estimate of incidence previously published by WHO, adjusted to the year of the prevalence survey based on previously published trends in incidence.

Background

Cambodia's population was 15 million in 2011, and the average gross national income (GNI) per person was US$ 810 per year, making it a low-income country *(1)*. It was one of the 22 high tuberculosis (TB) burden countries (HBCs) defined by WHO as a top priority for global efforts in TB control in 1998 and throughout the Millennium Development Goal (MDG) era (2000–2015), and one of the top 30 HBCs defined by WHO for the period 2016–2020. In 2011, the prevalence of HIV in the general population aged 15–49 years was 0.8% (95% confidence interval [CI]: 0.7–0.9%) *(2)*, and it was estimated that 5.1% (95% CI: 4.6–5.6%) of TB patients were coinfected with HIV *(3)*.

Cambodia experienced a long period of political, economic and social turmoil following the regime of the Khmer Rouge (1975–1979), during which about three million people died *(4)* and many people left the country.[1] In the 1980s, there were few health personnel per capita. In 1992, the country began to be rebuilt with United Nations support.

In 1994, the National TB Programme (NTP) introduced the WHO-recommended DOTS strategy in hospitals *(5,6)*. Further decentralization to primary care health centres was implemented between 1999 and 2004, with technical support from WHO and the Japanese International Cooperation Agency (JICA). By 2001, DOTS had been introduced in 268 (31%) health centres, and by 2005 all 853 health centres had been covered. Subsequently, the NTP strengthened the community DOTS programme with support from USAID, the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund) and other partners. Treatment success rates were consistently maintained at above 90%.

The NTP implemented the country's first national TB prevalence survey in 2002, during the early stages of DOTS decentralization *(7)*. The results showed a prevalence of smear-positive pulmonary TB of 362 (95% CI: 284–461) per 100 000 population aged 10 years or older; the prevalence of bacteriologically confirmed TB was 1208 (95% CI: 997–1463) per 100 000 population. The notification rate of new smear-positive TB cases peaked in 2005, and subsequently stagnated for 3 years.

In December 2007, Cambodia was selected by the WHO Global Task Force on TB Impact Measurement as one of 22 global focus countries to undertake a national TB prevalence survey. The aim was to better understand the burden of TB disease at national and global levels, and to assess trends in countries with a baseline survey. A second national TB prevalence survey was needed to obtain an up-to-date measurement of the burden of TB disease and to assess trends since the 2002 survey. Planning for this second survey started in September 2009, and the survey was implemented in 2010–2011 *(8)*.

Key methods and results

There were 62 survey clusters in three strata (urban, rural and other[2]), with a target cluster size of 640 individuals. A total of 68 087 individuals from 12 651 households were enumerated in the survey census, of whom 40 423 (59%) were eligible and invited to participate. Of these, 37 417 (93%) did so. All participants were screened according to the 2011 algorithm recommended by WHO; that is, using chest X-ray and an interview about symptoms *(9)*. A total of 4780 participants (13%) were eligible for sputum examination, of whom 4612 (97%) submitted at least one sputum specimen and 4598 (96%) submitted two sputum specimens.

A total of 314 bacteriologically confirmed pulmonary TB cases were identified, including 103 cases of smear-positive TB. The prevalence of smear-positive TB was 271 (95% CI: 212–348) per 100 000 population (among those aged ≥15 years) and for bacteriologically confirmed TB it was 831 (95% CI: 707–977) per 100 000 population. When extrapolated to all forms of TB and to all ages, prevalence was 817 (95% CI: 690–954) per 100 000 population. There was variation between the three geographical strata, with a significantly lower prevalence per 100 000 population in urban areas than in rural and other regions.

[1] The original report is in the Khmer language; excerpts have been translated by the Documentation Center of Cambodia for the Cambodian Genocide Program.

[2] In the 2002 survey, four provinces (Mondulkiri, Rattanakiri, Preah Vihear and Steung Treng) were excluded because of serious difficulties in accessing these provinces and their relatively small population (<3% at that time). In the 2010 survey, for the purposes of comparisons between the two surveys, these four provinces were grouped into a stratum separate from the areas covered in the 2002 survey.

Other key results were:

- the male to female ratio was 1.8 for smear-positive TB and 1.8 for bacteriologically confirmed TB;
- prevalence per 100 000 population increased with age and was especially high in those aged 55 years and above; however, given the population distribution, the absolute number of bacteriologically confirmed TB cases was consistently high in most age groups (from those aged 25 years and above);
- among bacteriologically confirmed TB cases, 30% were symptom-screen positive, and among the smear-positive cases, 44% were symptom-screen positive;
- for smear-positive pulmonary TB, the ratio of prevalence to notifications (P:N ratio) was 1.7 overall, but varied from 0.4 in those aged 15–24 years to 2.2 in those aged 65 years or more, and was slightly higher for men than for women (2.0 versus 1.4);
- among bacteriologically confirmed TB cases, 90% had no previous history of anti-TB treatment and only 1.9% were on anti-TB treatment at the time of the survey; and
- of the 88 bacteriologically confirmed and 41 smear-positive TB survey cases that screened positive for symptoms and were not on anti-TB treatment at the time of the survey, 62 (70%) and 27 (66%), respectively, had previously sought care in a public or private health facility for their symptoms.

Comparing the results between the 2002 and 2011 surveys (for the population aged ≥15 years and for the same or equivalent provinces):

- there was a statistically significant decline of 38% and 46% in smear-positive and bacteriologically confirmed TB prevalence per 100 000 population, respectively; prevalence per 100 000 population was reduced in all age groups, although not all of the reductions were statistically significant;
- the prevalence of those with smear-positive TB who reported symptoms decreased by 56%, while the prevalence of smear-positive TB among those who did not report symptoms decreased by only 8%; and
- the P:N ratio declined from 2.0 to 1.7 between the two surveys, with an especially large change in those aged 15–24 years; and the P:N ratio in elderly men remained high.

Implications of results

The 2011 survey showed that the prevalence of TB fell significantly in the nine years between 2002 and 2011. A key factor in this reduction was the expansion of DOTS from hospitals to health centres, which was achieved with technical support from a JICA project. As part of DOTS expansion, enormous efforts were made by the NTP and its development partners to detect and treat the most infectious cases, and to increase their treatment success rate to more than 90%. The NTP in Cambodia maintained facility-level DOTS services at hospital and health-centre level as the core of TB control, while also expanding efforts to encompass community-level DOTS and public–private mix DOTS. Other factors that could have contributed to a reduction in TB prevalence included a reduction in the prevalence of HIV coinfection and a more than a doubling of GNI per capita between 2002 and 2011 (US$ 320 to US$ 810) *(10)*.

There were clear differences in the extent to which the prevalence of TB fell in those screening symptom-positive (56% decline, 2002–2011) compared with those screening symptom-negative (8% decline, 2002–2011). These differences are consistent with the emphasis on passive detection of self-referring symptomatic TB cases under the DOTS strategy. In 2002, symptomatic smear-positive TB cases with a cough of 2 weeks or longer or haemoptysis (62%) were more common than

Photo credit: Kosuke Okada

asymptomatic TB cases (38%). By 2011, symptomatic smear-positive TB cases accounted for 44% of all cases. Only 23% of people with smear-negative, culture-positive TB met the 2011 NTP definition of an individual with presumptive TB.

This evolution in the TB epidemic had two major programmatic implications. The first was a need to strengthen diagnostic capacity for outpatients with respiratory symptoms, by reviewing and updating the diagnostic algorithm which had previously relied heavily on smear microscopy. Suggested updates included more extensive use of chest X-ray for people with any respiratory symptom, including a referral system for people with smear-negative presumptive TB to a health facility equipped to carry out chest X-rays, and the replacement of smear microscopy with more sensitive diagnostic tools, such as Xpert® MTB/RIF. The second implication was that active case detection activities should be expanded to specific groups with a high prevalence of TB, such as the elderly, household contacts of people with smear-positive TB and people coinfected with HIV.

Other implications included:

- a need to improve the capacity of health-care workers to clinically recognize TB disease, given that 55% of those with smear-positive TB and cough of any duration had already sought care (and 45% of these cases had consulted a public health facility); more than half (55%) of those with smear-negative, culture-positive TB and a cough of any duration had also previously sought care; and
- a need to consider the wider use of TB preventive therapy, especially among older people with a chest X-ray suggestive of inactive TB and negative bacteriological test results.

Major successes, challenges and lessons learned

Major successes included smooth survey operations conducted in a highly transparent manner, a high participation rate, capacity development of health workers at the central and local level, and rapid dissemination of key results at a large dissemination event (in February 2012, within 5 months of the completion of field operations). Funding was mobilized from several sources (JICA, the Global Fund and USAID) and was efficiently managed. After the survey, staff and equipment (e.g. chest X-ray machines) deployed for the survey were used to undertake active case finding in specific geographical hotspots identified by the survey and in specific subpopulations (e.g. the elderly).

Challenges were limited, but included a need to rely on two laboratories, given issues with standardizing laboratory work in other parts of country; slow data entry; some gaps between the population identified in the survey census and the national census data due to seasonal migration; and rescheduling of one cluster operation due to border security issues.

Important lessons learned for future surveys were that:

- institutional memory from a previous survey substantially facilitates a subsequent survey; the core staff of the 2002 survey led the 2011 survey, and the same international experts (from WHO and JICA) provided technical assistance; and
- the availability of trained staff and survey equipment previously mobilized for active case detection in high-risk populations (in the case of Cambodia, since 2006) can help to ensure smooth survey operations.

Photo credit: Kosuke Okada

Photo credit: Kosuke Okada

The expertise and experience of those involved in leading and managing the 2002 and 2011 surveys in Cambodia proved to be an invaluable source of assistance to surveys in other countries. Survey staff from Cambodia provided direct technical assistance to the surveys in Ethiopia, Kenya, Lao People's Democratic Republic, Malawi, Rwanda and Uganda. In addition, two training courses were held in Cambodia during the 2011 survey, which provided survey coordinators and their technical partners with an opportunity to witness and learn from a model survey operation at first-hand. Staff from the Cambodia survey played a crucial role in Asia–Asia and Asia–Africa collaborations that were strongly promoted by WHO to support surveys implemented from 2009–2015.

References

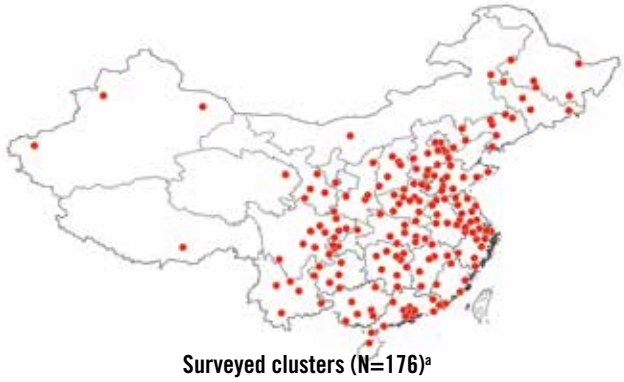
1. The World Bank (https://data.worldbank.org/country, accessed April 2017).
2. UNAIDS (http://aidsinfo.unaids.org/, accessed April 2017).
3. World Health Organization. Global Tuberculosis Database. 2017. (http://www.who.int/tb/country/en/, accessed April 2017).
4. Report of the Research Committee on Pol Pot's Genocidal Regime Phnom Penh, Cambodia: 1983 (http://www.dccam.org/, accessed May 2017). The original report is in the Khmer language; excerpts have been translated by the Documentation Center of Cambodia for the Cambodian Genocide Program.
5. WHO Tuberculosis Programme. (1994). WHO Tuberculosis Programme: framework for effective tuberculosis control. World Health Organization. (http://www.who.int/iris/handle/10665/58717, accessed January 2018).
6. World Health Organization. Global tuberculosis programme. Global tuberculosis control report 1997. Geneva: WHO; (https://apps.who.int/iris/bitstream/handle/10665/63354/WHO_TB_97.225_(part1).pdf?sequence=1, accessed January 2018).
7. Report of the national TB prevalence survey, 2002. Phnom Penh: Cambodia Ministry of Health; 2005.
8. Report of the second national TB prevalence survey, 2011. Phnom Penh: Cambodian Ministry of Health; 2012 (http://open_jicareport.jica.go.jp/pdf/12120325.pdf, accessed January 2018).
9. World Health Organization. Tuberculosis prevalence surveys: a handbook (WHO/HTM/TB/2010.17). Geneva: WHO; 2011 (https://apps.who.int/iris/bitstream/handle/10665/44481/9789241548168_eng.pdf, accessed August 2017).
10. Mao TE, Okada K, Yamada N, Peou S, Ota M, Saint S et al. Cross-sectional studies of tuberculosis prevalence in Cambodia between 2002 and 2011. Bull World Health Organ. 2014;92(8):573–581 (https://www.ncbi.nlm.nih.gov/pubmed/25177072, accessed May 2017).

CHINA

2010

Summary statistics

Participation rate	96%
Bacteriologically confirmed TB (≥15 years)	
• Prevalence per 100 000 population	119
• Male:female ratio	3.0
Prevalence:notification ratio (smear-positive TB, ≥15 years)	1.7



Surveyed clusters (N=176)[a]

Key people

Name	Role	Organization
Wang Lixia	Principal investigator	National Center for Tuberculosis Control and Prevention, Chinese Center for Disease Control and Prevention (NCTB, China CDC)
Zhang Hui	Survey coordinator	NCTB, China CDC
Cheng Shiming, Chen Mingting, He Guangxue	Survey design	NCTB, China CDC
Jiang Shiwen	Survey design, data collection	NCTB, China CDC
Zhao Yanlin	Survey design, laboratory manager	NCTB, China CDC
Ruan Yunzhou	Survey design, data collection and analysis	NCTB, China CDC
Du Xin, Chen Wei	Sampling	NCTB, China CDC
Zhou Lin	Diagnosis	NCTB, China CDC
Zhou Xinhua	Radiology coordinator	Beijing Tuberculosis and Thoracic Tumor Research Institute
Li Renzhong	Data collection and analysis	NCTB, China CDC
Xia Yinyin	Data manager, data analysis	NCTB, China CDC
Xu Caihong, Li Jun	Data manager	NCTB, China CDC
Wang Shengfen	Data analysis, laboratory manager	NCTB, China CDC
Chen Yude	Technical assistance (survey design, quality control, data analysis)	Peking University Health Science Center
Wang Xiexiu	Technical assistance (survey design, quality control, data analysis)	Tianjin Center for Disease Control and Prevention
Jin Shuigao	Technical assistance (survey design, quality control, data analysis)	China CDC
Tang Danlin	Technical assistance (survey design)	China-Japan friendship hospital
Qian Yuanfu, Wang Zhongren, Duanmu Hongjin, Zhao Fengzeng	Technical assistance (survey design)	Beijing Tuberculosis and Thoracic Tumor Research Institute
Wu Zhenglai	Technical assistance (survey design)	Peking Union Medical College
Zhu Guilin	Technical assistance (survey design)	Chinese Anti-tuberculosis Association
Tu Dehua	Technical assistance (radiology)	Beijing Research Institute for Tuberculosis Control
Pan Yuxuan, Zou Jiqian, Zhu Lizhen	Technical assistance (radiology)	Beijing Tuberculosis and Thoracic Tumor Research Institute
Shi Hongsheng	Technical assistance (data analysis)	Beijing Tuberculosis and Thoracic Tumor Research Institute
Cao Jiping	Technical assistance (data analysis)	Hebei Center for Disease Control and Prevention
Xu Weiguo	Technical assistance (data analysis)	Jiangsu Center for Disease Control and Prevention
Zheng Suhua, Zhang Zongde	Technical assistance (data analysis)	Beijing Tuberculosis and Thoracic Tumor Research Institute

Survey organization and financing

Implementing agency:

National TB Control Programme NCTB*

Finance	Amount (US$)
Ministry of Health, China	5 620 520
Total budget	5 620 520

* A leading group, technical advisory group and survey office were set up at all administrative levels (national, provincial, prefectural, county/district) to support survey implementation. There were 160 field survey teams in 31 provinces (autonomous regions and municipalities).

Data sources

- Disease Control Bureau of the Ministry of Health – Chinese Center for Disease Control and Prevention. Report on the 5th national tuberculosis epidemiological survey in China – 2010. Beijing, China: Military Medical Science Press; 2011.
- Wang L, Zhang H, Ruan Y, Chin DP, Xia Y, Cheng S et al. Tuberculosis prevalence in China, 1990–2010; a longitudinal analysis of national survey data. Lancet. 2014;383(9934):2057–2064.

[a] The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Survey design and methodology

Sampling design	
Sampling frame	Whole country
Sampling design	Multistage cluster sampling using PPS
Strata	Urban/rural
Sampling unit	Province/prefecture/county/township/village
Sample size assumptions	
• Smear-positive prevalence	116 per 100 000 (≥15 years)
• Precision	0.15
• Design effect	1.8
• *k*	0.7
• Response rate	95%
• Sample size (estimated)	264 000
Number of clusters	176
Cluster size	1 500
Eligibility criteria	
• Age	≥15 years
• Residency	Individuals who lived for ≥6 months in the household

Screening criteria	
Interview[a]	Cough ≥2 weeks and/or haemoptysis for any duration
Chest X-ray[b]	Any lung abnormality
Other	Participants with known active pulmonary TB with normal chest X-ray, and chest X-ray exempted

[a] The questionnaire on the socioeconomic conditions was done only for active pulmonary TB patients.
[b] Conventional radiography.

Laboratory methodology	
Smear	Three samples (spot, night and morning): direct preparation, ZN
Culture	Two samples out of three (spot, night and morning) selected[a]: direct preparation, LJ media
Identification of MTB	PNB
TB drug susceptibility test	Done
Xpert® MTB/RIF	Not done
HIV test	Not done

[a] Two samples were selected based on their smear result (-, +, ++, +++, ++++) and appearance (bloody, mucopurulent or salivary). Samples with higher smear grades and better appearance were selected for culture.

Analysis and reporting

Field data collection	Paper
Database	SPV
Method of analysis	Complex sampling method-based weighted adjustment
Results first published in a report/paper	December 2011
Official dissemination event	March 2011

Key survey results

Prevalence[a]	Smear-positive TB		Bacteriologically confirmed TB	
	Number per 100 000 population	95% CI	Number per 100 000 population	95% CI
Total	66	53–79	119	103–135
Male	99	74–123	177	149–204
Female	32	23–42	59	46–72
15–24 years	20	0.8–39	45	16–75
25–34 years	35	15–55	69	38–100
35–44 years	38	21–55	79	55–104
45–54 years	67	38–95	103	71–135
55–64 years	136	90–181	200	151–249
≥65 years	188	138–238	369	303–435
Urban	49	25–74	73	46–99
Rural	78	64–93	153	133–172

[a] Age ≥15 years unless otherwise specified.

	Design effect	*k*
Smear-positive TB	1.7	0.9
Bacteriologically confirmed TB	1.4	0.5

Other sputum results	Number	%
Total smear-positive participants	207	–
Smear-positive participants without MTB confirmation[a]	61	30
Isolates with MDR-TB detected[b]	19	6.8

[a] This includes culture with no evidence of MTB (i.e. culture-negative, NTM, contaminated, N/A).
[b] A total of 280 MTB strains were examined.

Health-care seeking behaviour among participants who were symptom-screen positive	Number	%
Participants who were symptom-screen positive[a]	5 462	–
Location of care sought		
• Consulted medical facility	N/A	N/A
Public facility	N/A	N/A
Private facility	N/A	N/A
Other	N/A	N/A
• Pharmacy	N/A	N/A
• Traditional healer	N/A	N/A
No action taken	N/A	N/A
Unknown	N/A	N/A

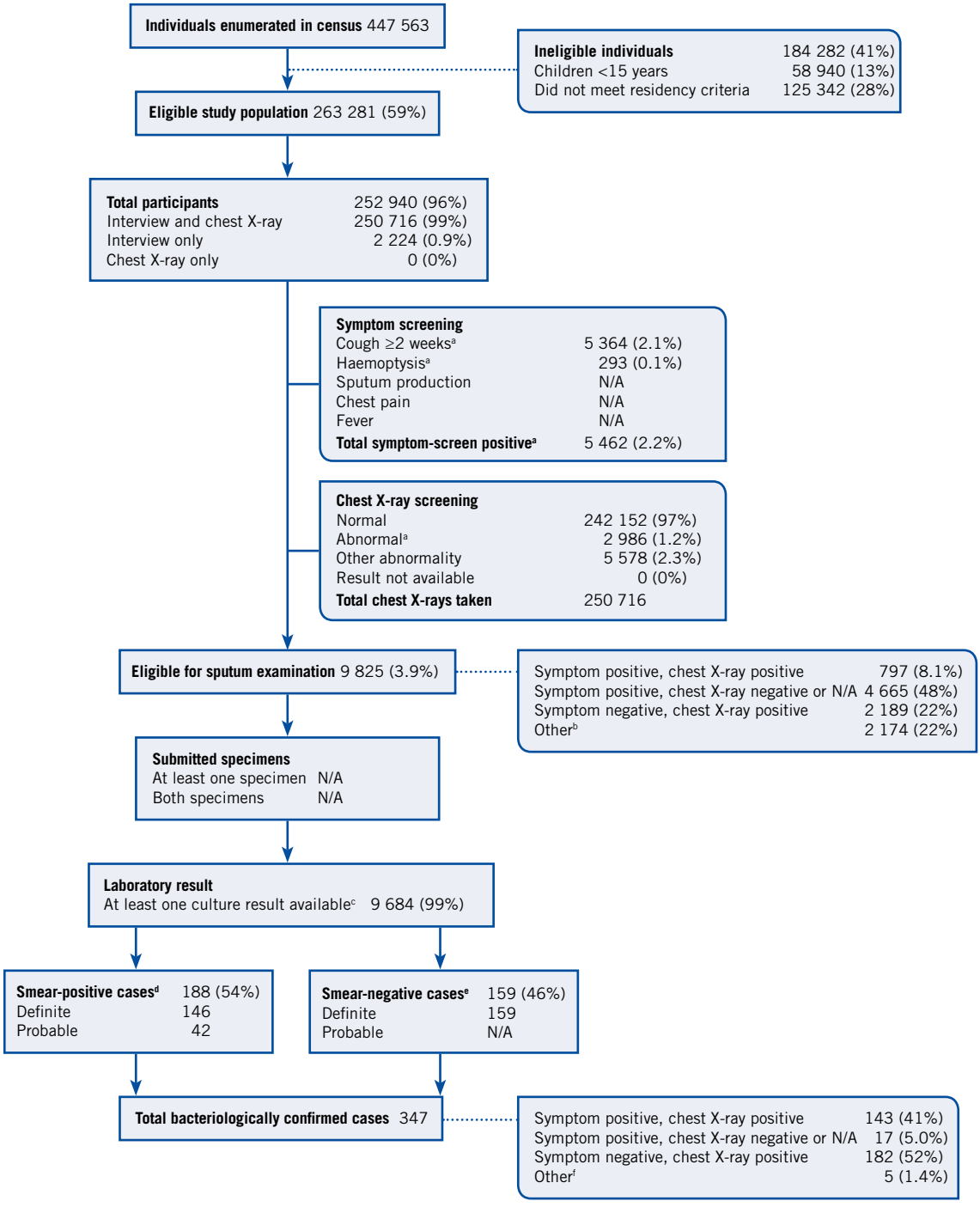
[a] Cough ≥2 weeks or haemoptysis for any duration.

Survey participants currently on TB treatment	Number	%
Total participants currently on TB treatment[a]	73	–
• Treated in the public sector	72	99
• Treated in the village/community clinic	1	1.4
• Treated in unknown sector	0	0
Bacteriologically confirmed TB cases detected by the survey who were currently on TB treatment	9	2.6

[a] Among 1 310 participants (active pulmonary TB patients), 1 301 were interviewed about their health-care seeking behaviour.

Survey flow: census to final outcomes

Field operations: April 2010 to July 2010



[a] Eligible for sputum collection.
[b] Chest X-ray exempted and symptom-screen negative (2 167), other (not specified) (7).
[c] Cultures that were either contaminated and/or missing without a definitive result (i.e. MTB, NTM, negative) were excluded.
[d] Definite: MTB confirmed by culture. Probable: MTB not confirmed by culture, and non NTM (all 42 participants had culture-negative results).
[e] Definite: MTB confirmed by culture. Probable: no definition.
[f] Chest X-ray exempted and symptom-screen negative (4), other (not specified) (1).

Fig. 1: Participation rate by age and sex

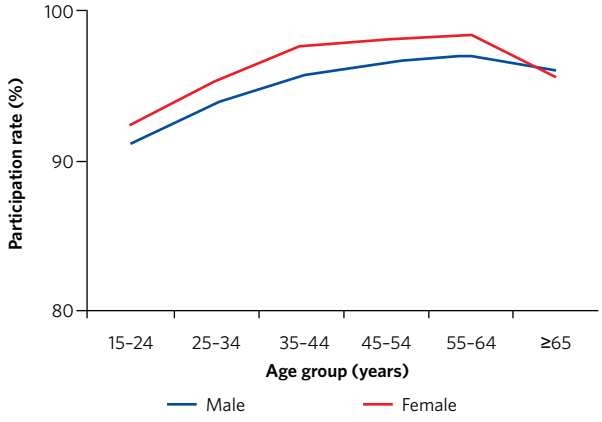


Fig. 2: TB prevalence per 100 000 population by age

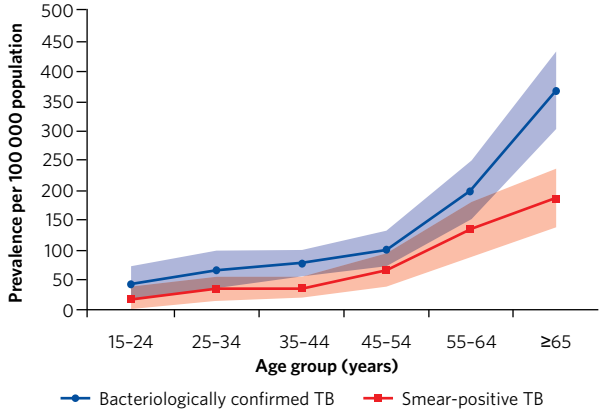


Fig. 3: Estimated number of bacteriologically confirmed TB cases and prevalence per 100 000 population, by age[a]

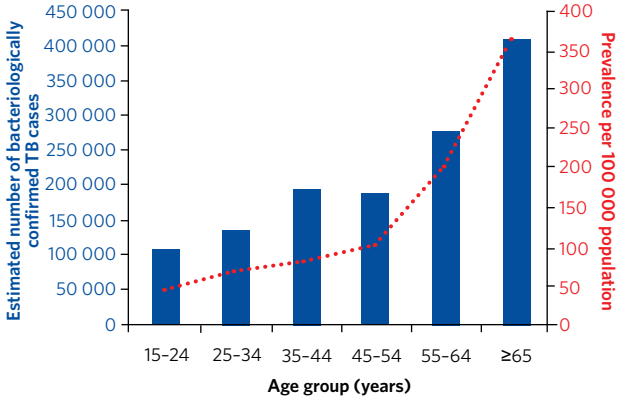


Fig. 4: Cluster variation of the number of bacteriologically confirmed TB cases[b]

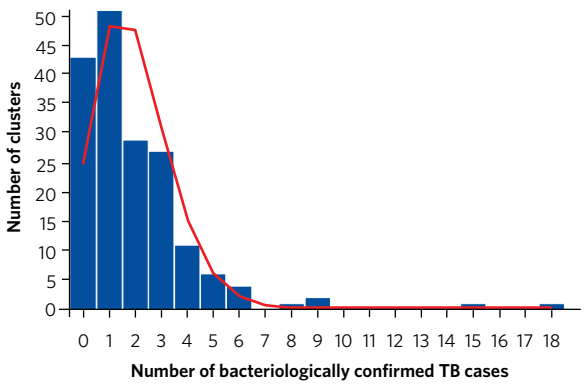


Fig. 5: Ratio of smear-positive TB prevalence to notifications by age and by sex[c]

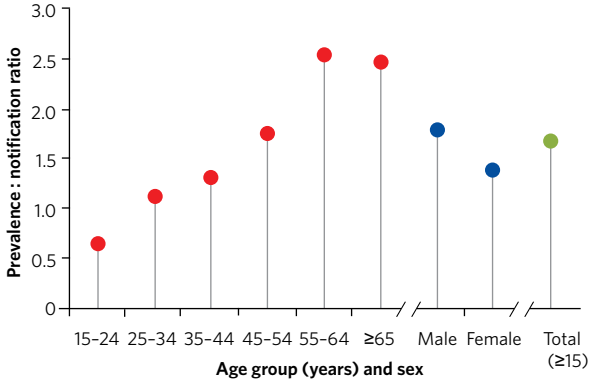
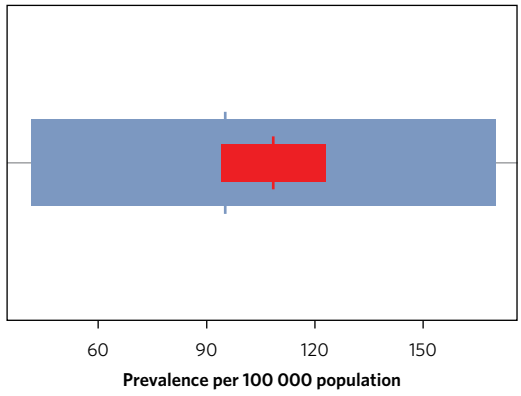


Fig. 6: Estimates of TB prevalence (all ages, all forms of TB) before (in blue) and after (in red) the national TB prevalence survey[d]



[a] The estimated number of bacteriologically confirmed TB cases is the product of age-specific prevalence and population estimates from the UN Population Division (2015 revision).

[b] The data suggest that the distribution of cases by cluster (blue bars) was significantly different from the theoretical distribution (red line) (mean 1.97, variance 5.55, $p<0.05$). The theoretical distribution assumes cases are distributed at random i.e. no clustering effect.

[c] Notification rates were estimated using notifications obtained from the WHO global TB database, and population estimates from the UN Population Division (2015 revision).

[d] The blue bar denotes the best estimate of prevalence and its range that was indirectly derived from the estimate of incidence previously published by WHO, adjusted to the year of the prevalence survey based on previously published trends in incidence.

Background

China's population was 1.3 billion in 2010, making it the most populous country in the world. China experienced rapid economic growth throughout the 1990s and 2000s, and by 2010 it was an upper-middle-income country with an average gross national income (GNI) per person of US$ 4340 *(1)*.

For most of the Millennium Development Goal (MDG) era (2000–2015), China ranked second (after India) in terms of the estimated number of new tuberculosis (TB) cases occurring each year. It was one of the 22 high tuberculosis (TB) burden countries (HBCs) defined by WHO as a top priority for global efforts in TB control in 1998 and throughout the Millennium Development Goal (MDG) era (2000–2015), and one of the top 30 HBCs defined by WHO for the period 2016–2020. In 2010, it was estimated that 1.5% (95% confidence interval [CI]: 1.2–1.8%) of TB patients in China were coinfected with HIV *(2)*.

The TB epidemic began to be addressed as a high priority and on a large scale in the 1990s. At that time, a TB control project funded by the World Bank and China's domestic resources was used to implement the WHO-recommended DOTS strategy in 13 provinces, which accounted for half the country's population *(3,4)*. National TB prevalence surveys implemented in 1990 and 2000 showed a 30% reduction in TB prevalence in areas where the project was implemented. In contrast, overall TB prevalence fell by less than 20% during this period *(5)*.

To accelerate progress in TB control, in 2001 the State Council of China launched a new 10-year TB control plan, which resulted in national coverage of DOTS by 2005. In the same year, China achieved the global TB control targets of detecting at least 70% of all estimated new smear-positive TB cases and successfully treating more than 85% of detected cases.

Photo credit: Yin Yin Xia

To assess progress made by 2010 in reducing the burden of TB, a national TB prevalence survey was implemented. This was the fifth such survey in China, following previous surveys in 1979, 1984–1985, 1990 and 2000. The 2010 survey was by far the largest national TB prevalence survey undertaken worldwide in the period 2000–2015, having a sample size of 260 000 people. The survey started in April 2010 and was completed in July 2010 *(6)*.

Key methods and results

There were 176 survey clusters in two strata (urban and rural); the target cluster size was 1500 individuals. A total of 447 563 individuals from 130 655 households were enumerated in the survey census, 263 281 (59%) of whom were eligible to participate. Of these, 252 940 (96%) did so. All participants were screened in line with the 2011 algorithm recommended by WHO; that is, using chest X-ray and a symptom-based questionnaire *(7)*. A total of 9825 participants (3.9%) were eligible for sputum examination.

Field operations were conducted by provincial teams, in contrast to the use of centrally managed cluster operations in other countries. Local reference laboratories were used for smear and culture. The central survey unit provided an operation manual, training of provincial staff, monitoring and supervision, and external quality assurance on diagnostic tools. Identification of isolated colonies and TB drug susceptibility testing were performed by the National TB Reference Laboratory in Beijing.

A total of 347 bacteriologically confirmed pulmonary TB cases was identified, including 188 cases of smear-positive TB. The prevalence of smear-positive TB was 66 (95% CI: 53–79) per 100 000 population (among those aged ≥15 years), and for bacteriologically confirmed TB it was 119 (95% CI: 103–135) per 100 000 population. When extrapolated to all forms of TB and to all ages, prevalence was 108 (95% CI: 94–123) per 100 000 population. The prevalence of bacteriologically confirmed TB was higher in rural than in urban areas, and higher in the western region (198 per 100 000 population; 95% CI: 167–229) than the central region (118 per 100 000 population; 95% CI: 81–154) and eastern region (65 per 100 000 population; 95% CI: 50–81). These three regions were

defined based on geography and economic status, with wealth generally declining from east to west.

Other key results were:

- the male to female ratio was 3.1 for smear-positive TB and 3.0 for bacteriologically confirmed TB;
- prevalence per 100 000 population increased with age, as did the absolute number of bacteriologically confirmed TB cases; over 60% (219/347) of prevalent TB cases were aged 55 or more;
- among the bacteriologically confirmed TB cases, 46% were symptom-screen positive, and of the smear-positive cases, 49% were symptom-screen positive;
- for smear-positive pulmonary TB, the ratio of prevalence to notifications (P:N ratio) was 1.7 overall, but varied from 0.7 in those aged 15–24 years to 2.5 in the age groups 55–64 years and 65 years or more; also, it was higher for men than for women (1.8 versus 1.4);
- among the bacteriologically confirmed TB cases, 85% had no previous history of anti-TB treatment and 2.6% were on anti-TB treatment at the time of the survey; and
- of the 153 bacteriologically confirmed survey cases that screened positive for symptoms and were not on anti-TB treatment at the time of the survey, 48% (73 of the 151 for whom there were results about health-care seeking behaviour) had previously sought care in a public or private health facility for their symptoms; and of the 87 smear-positive TB cases who reported symptoms but were not on anti-TB treatment at the time of the survey, 57% (49 of the 86 for whom there were results about health-care seeking behaviour) had previously sought care in a public or private health facility.

The survey showed that TB prevalence declined substantially between 1990 and 2010. Based on analysis of results according to the diagnostic protocol used in 1990 to allow for a fair comparison, the prevalence of smear-positive TB fell from 170 (95% CI: 166–174) per 100 000 population in 1990 to 59 (95% CI: 49–72) per 100 000 population in 2010. In the 1990s, the prevalence of smear-positive TB fell only in the provinces where DOTS was implemented. After 2000, declines were observed in all provinces. Of the total reduction in the prevalence of smear-positive TB from 1990–2010, 70% occurred after 2000.

Implications of results

The halving of TB prevalence in 20 years was assisted by a nationwide DOTS programme being implemented throughout the country's network of local centres for disease control, improved reporting and referral hospital systems, and a policy of free treatment for all patients with active pulmonary TB, alongside rapid socioeconomic development. Specifically, there were tremendous increases in GNI per capita (from US$ 330 in 1990 to US$ 4340 in 2010) and in living conditions overall (the human development index improved from 0.501 in 1990 to 0.699 in 2010) *(1,8)*. The overall fall in the prevalence of TB, in combination with the reduction in the proportion of prevalent cases with a previous history of TB, also had

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a major impact on reducing the burden of multidrug-resistant TB (MDR-TB).

Clear differences in TB prevalence between men and women, and across age groups and geographic regions also showed the need for considerable further efforts, such as policy or programmatic measures targeted to particular population groups and regions. TB control and policy should prioritize western and central China, rural areas, the elderly, ethnic minorities and those who are poor. It was also recognized that central and provincial governments should strengthen funding support and input for infrastructure, facilities and human resources for these areas and population groups.

The survey also showed that there was a need to improve TB notification and treatment of patients with TB within the hospital sector.

Major successes, challenges and lessons learned

The 2010 survey followed methods recommended in the first (2007) edition of WHO's handbook on prevalence surveys *(9)*. This included three modifications compared with the fourth (2000) survey:

- inclusion of adults (aged ≥15 years) only;[1]
- no tuberculin skin testing; and
- use of direct chest X-ray (posteroanterior) film images instead of fluoroscopy screening.

Major successes included implementation of the survey within two years of initiating planning; full mobilization of funding required for field operations at provincial level, which enabled field operations to be completed within four months; a high participation rate; a sample large enough to produce precise provincial as well as national estimates of TB prevalence; and prompt finalization of results and production of a survey report.

There were two major challenges. The first was the level of internal migration in China. The technical expert group established to provide advice on the survey suggested that the residential criteria for determining whether people were eligible to participate in the survey should be defined as "resident for one month at the time of the survey census". In practice, the definition of "six months residency in the household" was used since this was the official government definition. Using this more restrictive criterion, 10% of otherwise-eligible invitees were defined as non-permanent residents, and just over 20% of people identified by the survey census were not included in the survey because they had moved in the past six months. In addition, the survey team could not find 30% of the registered population in the survey clusters; this probably also reflected internal migration, especially of young men to urban areas.

The second challenge involved culture testing. Although the central team and the National TB Reference Laboratory made extensive efforts to standardize survey operations in all provinces, the yield from cultured sputum specimens was low or non-existent in some provinces. In other TB prevalence surveys in Asia, the number of smear-negative culture-positive TB cases was 1.2–2.0 times higher than the number of smear-positive TB cases.[2] Among 31 provinces in the prevalence survey in China, only six (19%) had a ratio of smear-negative culture-positive to smear-positive TB cases of 1.5 and above. Five other provinces had no yield from cultured sputum specimens.

References

1. The World Bank (https://data.worldbank.org/country, accessed April 2017).
2. World Health Organization. Global Tuberculosis Database. 2017. (http://www.who.int/tb/country/en/, accessed April 2017).
3. WHO Tuberculosis Programme. (1994). WHO Tuberculosis Programme: framework for effective tuberculosis control. World Health Organization. (http://www.who.int/iris/handle/10665/58717, accessed January 2018).
4. World Health Organization. Global tuberculosis programme. Global tuberculosis control report 1997. Geneva: WHO; (https://apps.who.int/iris/bitstream/handle/10665/63354/WHO_TB_97.225_(part1).pdf?sequence=1, accessed January 2018).
5. Wang L, Zhang H, Ruan Y, Chin DP, Xia Y, Cheng S et al. Tuberculosis prevalence in China, 1990–2010; a longitudinal analysis of national survey data. Lancet. 2014;383(9934):2057–2064 (https://www.ncbi.nlm.nih.gov/pubmed/24650955, accessed May 2017).
6. Disease Control Bureau of the Ministry of Health – Chinese Center for Disease Control and Prevention. Report on the 5th national tuberculosis epidemiological survey in China – 2010. Beijing, China: Military Medical Science Press; 2011.

[1] The 2000 survey included children as well as adults; for every case found among children, 8000 children were screened.

[2] Cambodia: 2.0 (smear-positive TB cases: smear-negative culture-positive TB cases = 103:211), Indonesia: 1.6 (165:261), Lao PDR: 1.2 (107:130), Mongolia: 1.8 (88:160), Myanmar: 1.5 (123:188) and Thailand: 1.5 (58:84).

7. World Health Organization. Tuberculosis prevalence surveys: a handbook (WHO/HTM/TB/2010.17). Geneva: WHO; 2011 (https://apps.who.int/iris/bitstream/handle/10665/44481/9789241548168_eng.pdf, accessed August 2017).

8. UNDP. Human development report – China, human development indicators. United Nations Development Programme (UNDP);(http://hdr.undp.org/en/countries/profiles/CHN, accessed May 2017).

9. World Health Organization. Assessing tuberculosis prevalence through population-based surveys. Geneva: WHO; 2007 (https://apps.who.int/iris/handle/10665/206962, accessed January 2018).

DEMOCRATIC PEOPLE'S REPUBLIC OF KOREA

2015–2016

Summary statistics

Participation rate	84%
Bacteriologically confirmed TB (≥15 years)	
• Prevalence per 100 000 population	587
• Male:female ratio	2.9
Prevalence:notification ratio (Bacteriologically confirmed TB, ≥15 years)	1.2

Surveyed clusters (N=100). Cluster location not provided.[a]

Key people

Name	Role	Organization
Kim Hyong Hun	Chair of steering committee	Ministry of Public Health (MoPH)
Ri Chan Hyok	Member of steering committee, principal investigator	MoPH
Choe Tong Chol	Member of steering committee	MoPH
Jo Won Ryong	Leader of central survey data management team	MoPH
Rim Gye Tong	Leader of central survey management team	MoPH
Choe Tal Bom	Leader of central survey interview team	Pyongyang Medical college under Kim Il Sung university
Ri Jong Chan	Leader of central survey chest X-ray team	Central TB Preventive Institute (CTPI)
Yun Jong Chol	Leader of central survey laboratory team	CTPI
Ko Jin Hyok	Survey coordinator	TB Programme Management Unit (PMU), MoPH
Partha Pratim Mandal	TB medical officer	WHO South-East Asia Regional Office (SEARO)
Mubeen Aslam	Global Fund programme coordinator	UNICEF, Democratic People's Republic of Korea
M. Bintari Dwihardiani	Technical assistance (survey advisor)	WHO Indonesia
Philippe Glaziou	Technical assistance (analysis)	WHO headquarters
Charalambos Sismanidis	Technical assistance (analysis)	WHO headquarters

Survey organization and financing

Implementing agency:
National TB Control Programme

Finance	Amount (US$)
Ministry of Public Health	481 963
Global Fund	896 026
Total budget	1 377 989

Data sources

- Report of DPRK National TB Prevalence Survey (2015–2016), Department of TB and Hepatitis, Ministry of Public Health DPR Korea; 2017.

[a] The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Survey design and methodology

Sampling design	
Sampling frame	Whole country
Sampling design	Multistage cluster sampling using PPS
Strata	Urban/rural/construction area Region (east, west, in-land)
Sampling unit	Province/city, county or district/Ri or Dong
Sample size assumptions	
• Smear-positive prevalence	220 per 100 000 (≥15 years)
• Precision	0.2
• Design effect	1.4
• *k*	0.5
• Response rate	85%
• Sample size (estimated)	70 000
Number of clusters	100
Cluster size	700
Eligibility criteria	
• Age	≥15 years
• Residency	Resident in the household for the last 2 weeks

Screening criteria	
Interview[a]	Cough more than 2 weeks and/or haemoptysis
Chest X-ray[b]	Any lung abnormality
Other	N/A

[a] An in-depth interview on health-care seeking behaviour was done for those who screened positive (symptom) and/or who had TB history.
[b] Conventional radiography.

Laboratory methodology	
Smear	Two samples (spot, morning): concentrated preparation, FM (LED, auramine stain)
Culture	Two samples (spot, morning): concentrated preparation, LJ media
Identification of MTB	SD Bioline TB Ag MPT64 rapid test
TB drug susceptibility test	Not done as per protocol
Xpert® MTB/RIF	Not done as per protocol
HIV test	Not done as per protocol

Analysis and reporting

Field data collection	Paper
Database	Microsoft Access®
Method of analysis	MI+IPW
Results first published in a report/paper	April 2018
Official dissemination event	October 2017

Key survey results

Prevalence[a]	Smear-positive TB		Bacteriologically confirmed TB	
	Number per 100 000 population	95% CI	Number per 100 000 population	95% CI
Total	330	283–377	587	520–655
Male	535	443–627	917	783–1 052
Female	164	118–210	319	256–382
15–24 years	42	0–84	155	70–240
25–34 years	333	218–448	579	410–748
35–44 years	417	302–531	764	611–916
45–54 years	525	400–651	877	705–1 049
55–64 years	341	207–474	595	410–781
≥65 years	265	137–393	444	264–624
Urban	330	267–394	577	489–665
Rural	361	288–434	659	555–764
Construction unit	66	0–138	102	0–219

[a] Age ≥15 years unless otherwise specified.

	Design effect	*k*
Smear-positive TB	1.5	0.5
Bacteriologically confirmed TB	2.0	0.5

Other sputum results	Number	%
Total smear-positive participants	203	–
Smear-positive participants without MTB confirmation[a]	10	4.9
Isolates with MDR-TB detected	NA	NA

[a] All were NTM.

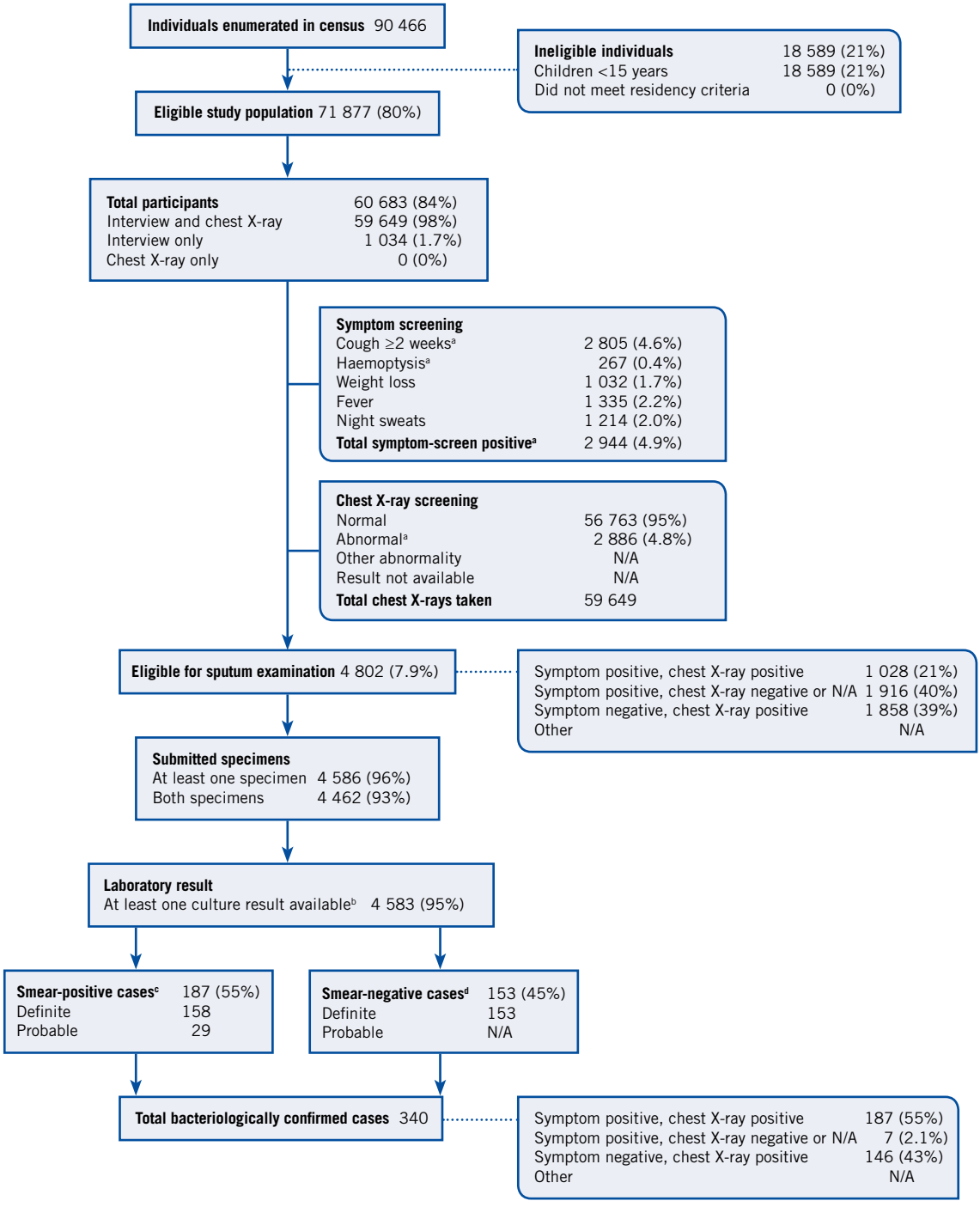
Health-care seeking behaviour among participants who were symptom-screen positive	Number	%
Participants who were symptom-screen positive[a]	2 944	–
Location of care sought		
• Consulted medical facility	1 743	N/A
Public facility	*1 743*	*100*
Private facility	*0*	*0*
Other (NGO, village doctor)	*0*	*0*
• Pharmacy	0	0
• Traditional healer	3	0.1
Self-treated	0	0
No action taken	1 192	41
Unknown	6	0.2

[a] Cough more than 2 weeks and/or haemoptysis.

Survey participants currently on TB treatment	Number	%
Total participants currently on TB treatment	106	–
• Treated in the public sector	101	96
• Treated in the private sector	0	0
• Treated in unknown sector	5	4.7
Bacteriologically confirmed TB cases detected by the survey who were currently on TB treatment	87	26

Survey flow: census to final outcomes

Field operations: October 2015 to May 2016



[a] Eligible for sputum collection.
[b] Cultures that were either contaminated and/or missing without a definitive result (i.e. MTB, NTM, negative) were excluded.
[c] Definite: MTB confirmed by culture. Probable: MTB not confirmed by culture but chest X-ray abnormal findings at central reading.
[d] Definite: MTB confirmed by culture, with having either chest X-ray abnormal findings at central reading or follow-up evidence. Probable: no definition.

Fig. 1: Participation rate by age and sex

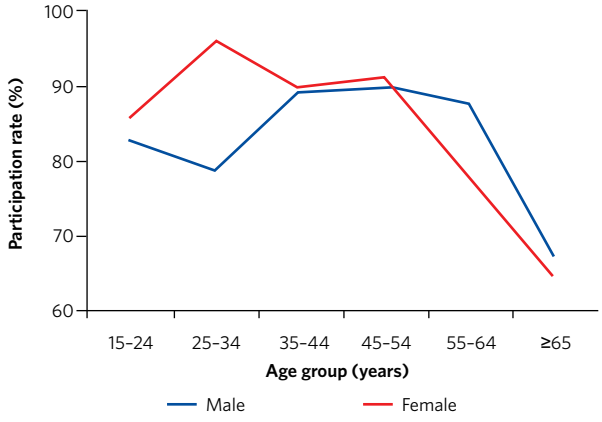


Fig. 2: TB prevalence per 100 000 population by age

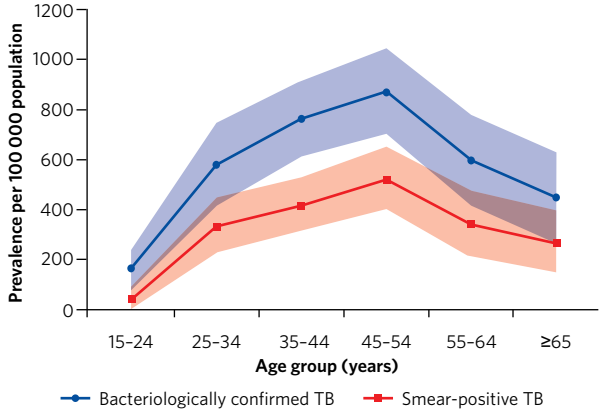


Fig. 3: Estimated number of bacteriologically confirmed TB cases and prevalence per 100 000 population, by age[a]

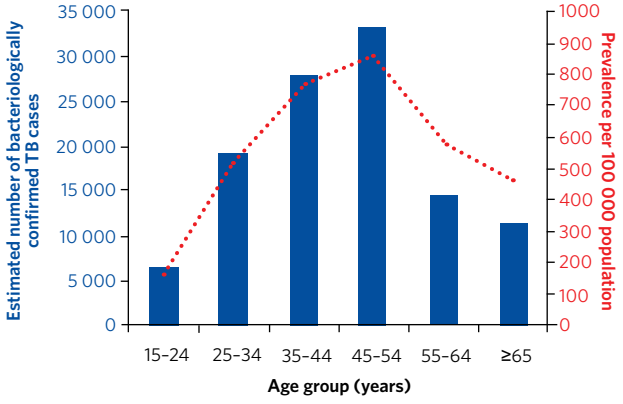


Fig. 4: Cluster variation of the number of bacteriologically confirmed TB cases[b]

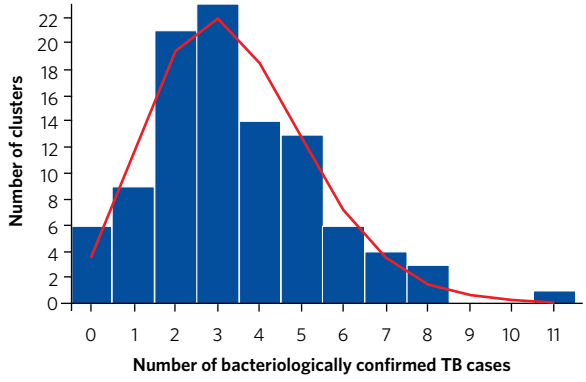


Fig. 5: Ratio of bacteriologically confirmed TB prevalence to notifications by age and by sex[c]

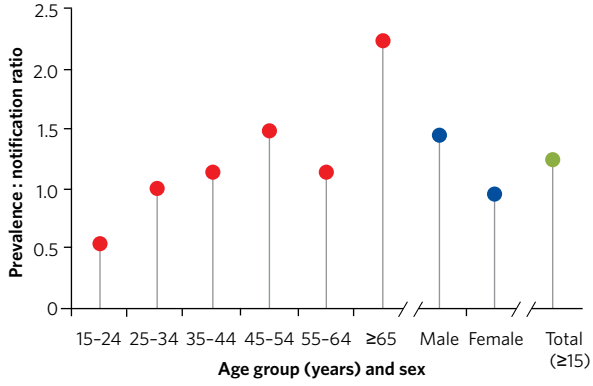
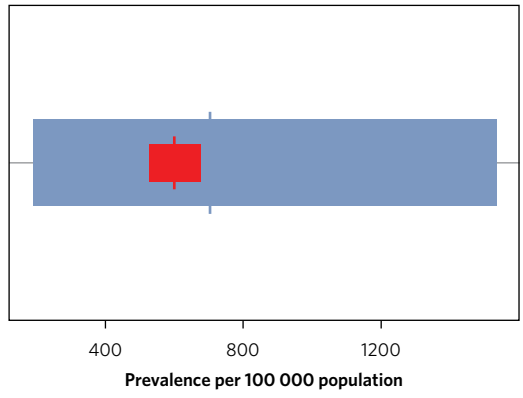


Fig. 6: Estimates of TB prevalence (all ages, all forms of TB) before (in blue) and after (in red) the national TB prevalence survey[d]



[a] The estimated number of bacteriologically confirmed TB cases is the product of age-specific prevalence and population estimates from the UN Population Division (2019 revision).

[b] The data did not suggest that the distribution of cases by cluster (blue bars) was significantly different from the theoretical distribution (red line) (mean 3.4, variance 4.22, p=0.12). The theoretical distribution assumes cases are distributed at random i.e. no clustering effect.

[c] Notification rates were estimated using notifications obtained from the WHO global TB database, and population estimates from the UN Population Division (2019 revision).

[d] The blue bar denotes the best estimate of prevalence and its range that was indirectly derived from the estimate of incidence previously published by WHO, adjusted to the year of the prevalence survey based on previously published trends in incidence.

Background

The Democratic People's Republic of Korea had a population of 25 million in 2015 and was classified as a low-income country *(1)*. The country was one of the top 30 high tuberculosis (TB) burden countries (HBCs) defined by the World Health Organization (WHO) for the period 2016–2020. Although no data about HIV prevalence were available *(2)*, it was estimated that 0.32% (95% confidence interval [CI]: 0.26–0.38) of TB patients were coinfected with HIV in 2015 *(3)*.

The country's National TB Control Programme (NTP) was established in 1968. By 2003, the NTP had adopted and expanded the WHO DOTS strategy nationally, including the establishment of a unified surveillance system for TB case registration. To estimate the burden of disease, the Democratic People's Republic of Korea conducted a national survey of the annual risk of TB infection (ARTI) in 2007 *(4)*. The estimated ARTI was 3.1% (95% CI: 2.8–3.3%); based on this result, the burden of new smear-positive pulmonary TB disease was estimated as 155±34 cases per 100 000 population per year. Thereafter, the notification rate for smear-positive pulmonary TB increased. Since 2010, reported treatment success rates were consistently 90% or higher. In mid-2013, the NTP decided to conduct a national TB prevalence survey to improve estimates of TB disease burden. Following 2 years of preparations, the NTP undertook a national TB prevalence survey between October 2015 and May 2016.

Key methods and results

There were 100 clusters across three population strata (defined as urban, rural and construction areas) and three geographical strata (defined as east, west and inland regions), with a target cluster size of 700 individuals. A total of 90 466 people were enumerated in the survey census, of whom 71 877 (80%) were eligible and invited to participate. Of these, 60 683 (84%) did so. All participants were screened according to the 2011 algorithm recommended by WHO; that is, using chest X-ray and an interview about symptoms *(5)*. A total of 4802 (7.9%) participants were eligible for sputum examination, of whom 4586 (96%) submitted at least one sputum sample and 4462 (93%) submitted two sputum samples.

A total of 340 bacteriologically confirmed pulmonary TB cases were identified, including 187 cases of smear-positive TB. The prevalence of smear-positive TB was 330 (95% CI: 283–377) per 100 000 population (among those aged ≥15 years), and for bacteriologically confirmed TB it was 587 (95% CI: 520–655) per 100 000 population. The prevalence of bacteriologically confirmed TB varied by strata: 577 (95% CI: 489–665) per 100 000 population in urban areas, 659 (95% CI: 555–764) per 100 000 population in rural areas and 102 (95% CI: 0–219) per 100 000 population in construction areas.

Photo credit: National TB Programme of DPRK

Other key results were as follows:

- the male to female ratio was 3.3 for smear-positive TB and 2.9 for bacteriologically confirmed TB;
- the prevalence per 100 000 population increased with age, with a peak in those aged 45–54 years, before declining with age; the absolute number of TB cases was high in those aged 25–54 years;
- among the bacteriologically confirmed TB cases, 57% were symptom-screen positive, and among the smear-positive TB cases, 66% were symptom-screen positive;
- for smear-positive pulmonary TB, the ratio of prevalence to notifications (P:N ratio) was 1.2 overall, but varied from 0.5 in those aged 15–24 years to 2.2 in those aged 65 years or more, and was higher for men than for women (1.5 versus 0.9);
- among the bacteriologically confirmed TB cases, 91% (310/340) had no previous history of TB treatment and 26% (87/340) were on treatment at the time of the survey; and
- of the 107 bacteriologically confirmed cases that screened positive for symptoms and were not on anti-TB treatment at the time of the survey, 96 (90%) had previously sought care in a public health facility for their symptoms; and of 123 smear-positive TB cases with TB symptoms, only 69 (56%) had sought care.

Photo credit: National TB Programme of DPRK

Photo credit: National TB Programme of DPRK

Implications of results

Based on the results from the national TB prevalence survey, the overall prevalence (for all forms and all ages) was estimated at 600 (95% CI: 527–676) per 100 000 population. This was higher than the pre-survey estimate of 490 per 100 000 population used in the initial design in 2012 *(4)*. Based on the survey, TB incidence was re-estimated at 513 per 100 000 population per year (95% CI: 446–584), equivalent to 131 000 new cases per year in 2017 *(6)*. This was also 1.2 times higher than the previous estimate of 442 (95% CI: 412–473) per 100 000 population in 2014 *(7)*. The survey findings were adopted by relevant stakeholders for the development of a new national TB control strategy (2019–2022) and a proposal to the Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund) (2018–2021).

Clear differences in TB prevalence between men and women and across age groups showed the need for considerable further efforts, such as policy or programmatic measures targeted to specific population groups. TB control and policy should give particular attention to men, given the high burden in men (especially in those of working age) and the large gap between prevalence and notifications (especially in those aged 45–54 and ≥65 years). It was also clear that central and provincial governments needed to strengthen funding support and other inputs for infrastructure, facilities and human resources in specific areas and population groups.

Other implications included the need to:

- strengthen community screening for TB to ensure earlier detection, treatment and notification of cases;
- review the surveillance system, given that a large proportion of TB cases (26%) on treatment were not notified to the NTP;
- review the use of and access to chest X-ray screening in the early detection of cases, given that 43% (146/340) of bacteriologically confirmed survey cases were only identified by chest X-ray;
- expand the range of laboratory tests to diagnose TB beyond smear and culture, recognizing that high-level negotiations would be required to ensure the sustainable use and expansion of Xpert MTB/RIF;
- strengthen health services, especially at the peripheral level (Ri/Dong clinic and city/county hospital) – for example, by raising health worker awareness of TB symptoms and making diagnostics more widely available; many bacteriologically confirmed cases had sought care before diagnosis, including nearly half of all symptomatic smear-positive TB cases, but not been diagnosed; and
- strengthen community awareness of TB, since more than 40% (1193/2944) of participants with chronic cough or haemoptysis (or both) at the time of the survey had not sought care for their symptoms – men accounted for the vast majority of symptomatic participants.

Major successes, challenges and lessons learned

Despite financial and technological constraints, the first national TB prevalence survey of the Democratic People's Republic of Korea managed to achieve its primary objective and field operations were successfully completed within a year.

Almost all national TB prevalence surveys since 2015 used Xpert MTB/RIF or Xpert Ultra, in addition to culture, as part of the diagnostic algorithm for all participants who screened positive. However, given important limitations, the Democratic People's Republic of Korea's survey was only able to use smear and culture, as was originally recommended in the *lime book (5)*. Other constraints included reliance on paper instead of electronic data collection systems, and conventional instead of digital mobile chest X-ray machines. The survey was among those that cost the least to implement, at US$ 1.4 million. The Global Fund contributed about US$ 900 000, with the remainder being supplied by the Ministry of Public Health.

The survey's high level of participation (84%) was probably due to strong leadership and extensive community engagement by the large survey teams (six teams of 25 people) and central survey team (>100 people).

Photo credit: National TB Programme of DPRK

There were few regular international missions to provide technical assistance, due to administrative challenges and access restrictions. A technical consultant from the national TB prevalence survey team of Indonesia provided some in-country advice (June 2016), and two laboratory experts from the supranational reference laboratory in Hong Kong Special Administrative Region reviewed laboratory progress and results (July 2016). There was good engagement with the WHO country office and WHO headquarters to support data review, final analysis and report writing. Collaboration with multiple international stakeholders, from procurement to dissemination, also helped to ensure that the survey was a success.

Major challenges included interruptions of funding in 2014 that led to a 1-year delay before field operations could be started. In addition, there were long delays in the procurement of mobile conventional chest X-ray machines. This meant that the survey could only start with two instead of four field teams during phase one of the survey (October to November 2015). Extended delays from the end of field operations to the final dissemination of results were due to insufficient human resources for data entry, analysis and report writing. Other challenges included the replacement of five clusters due to poor road conditions.

An important lesson learned for future surveys was the importance of good planning and collaboration for smooth implementation. Specifically, the procurement of laboratory and chest X-ray equipment should be completed before starting field operations, and sufficient lead times allowed for this purpose.

References

1. The World Bank (https://data.worldbank.org, accessed July 2017).
2. UNAIDS (https://aidsinfo.unaids.org/, accessed July 2017).
3. World Health Organization. Global Tuberculosis Database. 2017 (https://www.who.int/tb/data/en/, accessed July 2017).
4. Report of DPRK National TB Prevalence Survey (2015–2016), Department of TB and Hepatitis, Ministry of Public Health, Democratic People's Republic of Korea; 2017.
5. World Health Organization. Tuberculosis prevalence surveys: a handbook. Geneva: WHO; 2011 (https://apps.who.int/iris/bitstream/handle/10665/44481/9789241548168_eng.pdf, accessed August 2017).
6. World Health Organization. Global tuberculosis report 2017. Geneva: WHO; 2017 (https://www.who.int/tb/data/en/, accessed July 2017).
7. World Health Organization. Global tuberculosis report 2015. Geneva: WHO; 2015 (https://www.who.int/tb/data/en/, accessed July 2017).

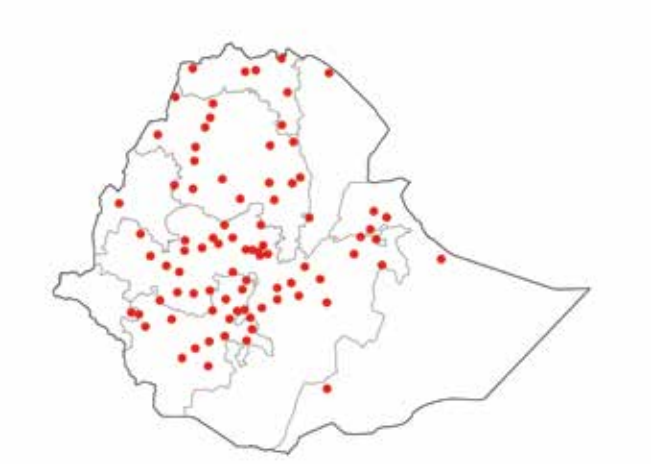
Photo credit: National TB Programme of DPRK

ETHIOPIA

2010–2011

Summary statistics

Participation rate	90%
Bacteriologically confirmed TB (≥15 years)	
• Prevalence per 100 000 population	277
• Male:female ratio	1.2
Prevalence:notification ratio (smear-positive TB, ≥15 years)	1.2



Surveyed clusters (N=85)[a]

Key people

Name	Role	Organization
Amha Kebede	Director general, principal investigator	Ethiopian Public Health Institute
Zeleke Alebachew	Survey coordinator	Ethiopian Public Health Institute
Fasil Tsegaye	Deputy survey coordinator	Ethiopian Public Health Institute
Almaz Abebe	Directorate director, Infectious and Non Infectious Disease Research	Ethiopian Public Health Institute
Eshetu Lema	Senior laboratory advisor	Ethiopian Public Health Institute
Mulualem Agonafer	Laboratory manager	Ethiopian Public Health Institute
Gashawtena Fantu	Central X-ray radiologist	Saint Paul's Hospital
Molla Endale	Central X-ray radiologist	Saint Paul's Hospital
Shewalem Negash	Central X-ray radiologist	Saint Paul's Hospital
Feleke Dana	Data manager	Ethiopian Public Health Institute
Menelik Balcha	Field team leader	Ethiopian Public Health Institute
Sale Workneh	Field team leader	Ethiopian Public Health Institute
Tedla Fiseha	Field team leader	Ethiopian Public Health Institute
Tibebu Biniam	Field team leader	Ethiopian Public Health Institute
Wilfred Nkhoma	Technical assistance (survey advisor)	WHO Regional Office for Africa (AFRO)
Ikushi Onozaki	Technical assistance (survey advisor)	WHO headquarters
Marina Tadolini	Technical assistance (survey advisor)	Consultant, Italy
Peou Satha	Technical assistance (survey advisor)	Consultant, Cambodia
Hazim Timimi	Technical assistance (data management)	WHO headquarters
Charalampos Sismanidis	Technical assistance (design and analysis)	WHO headquarters

Survey organization and financing

Implementing agency:
Ethiopian Public Health Institute, Ethiopian Health and Nutrition Research Institute

Finance	Amount (US$)
The Global Fund/Ministry of Health, Ethiopia	2 625 520
WHO	106 900
TB CAP Ethiopia	100 000
Total budget	2 832 420

Data sources

- First Ethiopian national population-based tuberculosis prevalence survey. Addis Ababa: Ministry of Health, Federal Democratic Republic of Ethiopia; Ethiopian Health and Nutrition Research Institute; 2011.
- Kebede AH, Alebachew Z, Tsegaye F, Lemma E, Abebe A, Agonafir M et al. The first population-based national tuberculosis prevalence survey in Ethiopia, 2010–2011. Int J Tuberc Lung Dis. 2014;18(6):635–639.
- Survey dataset.

[a] The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Survey design and methodology

Sampling design	
Sampling frame	773 of 810 woredas (districts)[a]
Sampling design	Multistage cluster sampling using PPS
Strata	Rural/urban/pastoralist
Sampling unit	Strata (urban, rural, pastoralist)/woreda/kebele
Sample size assumptions	
• Smear-positive prevalence	364 per 100 000 (≥15 years)
• Precision	0.2
• Design effect	1.5
• *k*	0.5
• Response rate	85%
• Sample size (estimated)	46 514
Number of clusters	85
Cluster size	550
Eligibility criteria	
• Age	≥15 years
• Residency	Permanent residents who stayed in the household at least one night in the 14 days prior to the census, and temporary visitors who stayed in the household at least 14 days prior to the census

[a] 37 woredas (3% of the total population) were excluded due to security and logistical challenges. Two clusters (kebele) were replaced before field operations started due to logistical challenges.

Screening criteria	
Interview[a]	Cough ≥2 weeks
Chest X-ray[b]	Any lung abnormality
Other	Those exempt from chest X-ray but with one of the following criteria were also requested to submit sputum specimens: weight loss ≥3 kg in the past month, night sweats ≥2 weeks, fever ≥2 weeks or contact with a TB patient in the past year.

[a] An in-depth interview about health-care seeking behaviour was done for participants who had a cough ≥2 weeks and for those with a history of TB treatment.
[b] Conventional radiography.

Laboratory methodology	
Smear	Two samples (spot, morning): direct preparation, FM (LED, auramine stain)
Culture	One sample (morning; if unavailable then spot): concentrated preparation, LJ media
Identification of MTB	Capilia
TB drug susceptibility test	Conducted as post-survey activity
Xpert® MTB/RIF	Not done
HIV test	Not done

Analysis and reporting

Field data collection	Paper
Database	CSPro
Method of analysis	MI+IPW
Results first published in a paper	December 2012
Official dissemination event	December 2011

Key survey results

Prevalence[a]	Smear-positive TB		Bacteriologically confirmed TB	
	Number per 100 000 population	95% CI	Number per 100 000 population	95% CI
Total	108	73–143	277	208–347
Male	133	80–185	304	219–388
Female	87	47–127	246	176–315
15–24 years	113	53–173	292	194–390
25–34 years	86	30–143	216	129–303
35–44 years	117	43–191	259	135–382
45–54 years	138	23–253	337	161–513
55–64 years	159	19–300	367	153–582
≥65 years	41	1–123	227	33–421
Urban	70	6–135	273	130–416
Rural	109	67–151	273	189–356
Pastoralist	170	60–280	316	163–468

[a] Age ≥15 years unless otherwise specified.

	Design effect	*k*
Smear-positive TB	1.3	0.7
Bacteriologically confirmed TB	1.3	0.4

Other sputum results	Number	%
Total smear-positive participants	61	–
Smear-positive participants without MTB confirmation[a]	28	46
Isolates with MDR-TB detected[b]	4	4.4

[a] This includes culture with no evidence of MTB (i.e. culture-negative, NTM, contaminated, N/A).
[b] 90 culture MTB-positive specimens were tested for drug susceptibility and 4 were identified as MDR-TB.

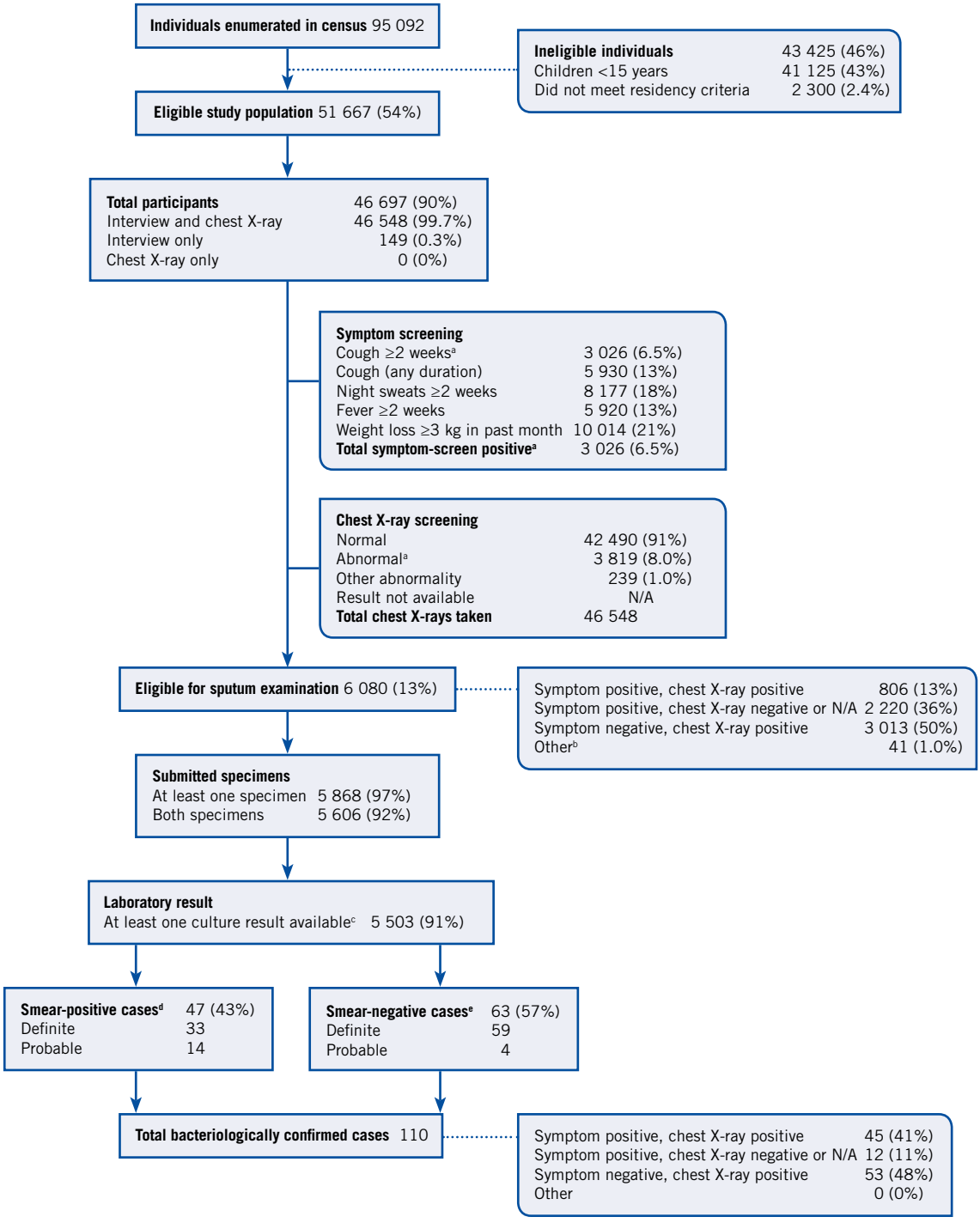
Health-care seeking behaviour among participants who were symptom-screen positive	Number	%
Participants who were symptom-screen positive[a]	3 026	–
Location of care sought		
• Consulted medical facility	848	28
Public facility	*628*	*74*
Private facility	*199*	*23*
Other	*21*	*2.5*
• Pharmacy	40	1.3
• Traditional healer	3	0.1
• Unspecified	55	1.8
No action taken	1 932	64
Unknown	148	4.8

[a] Cough ≥2 weeks.

Survey participants currently on TB treatment	Number	%
Total participants currently on TB treatment	75	–
• Treated in the public sector	54	72
• Treated in the private sector	7	9.3
• Treated in other sector	3	4.0
• Treated in unknown sector	11	15
Bacteriologically confirmed TB cases detected by the survey who were currently on TB treatment	3	2.7

Survey flow: census to final outcomes

Field operations: October 2010 to June 2011



[a] Eligible for sputum collection.
[b] One of the following: weight loss ≥3 kg in the past month, night sweats ≥2 weeks, fever ≥2 weeks or contact with a TB patient in the past year while chest X-ray exempted.
[c] Cultures that were either contaminated and/or missing without a definitive result (i.e. MTB, NTM, negative) were excluded.
[d] Definite: MTB confirmed by culture. Probable: MTB not confirmed by culture but chest X-ray consistent with TB.
[e] Definite: MTB confirmed by culture with chest X-ray consistent with TB. Probable: MTB confirmed by culture but without chest X-ray consistent with TB.

Fig. 1: Participation rate by age and sex

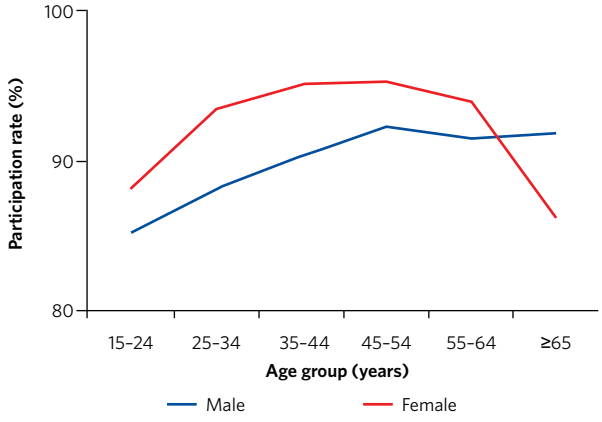


Fig. 2: TB prevalence per 100 000 population by age

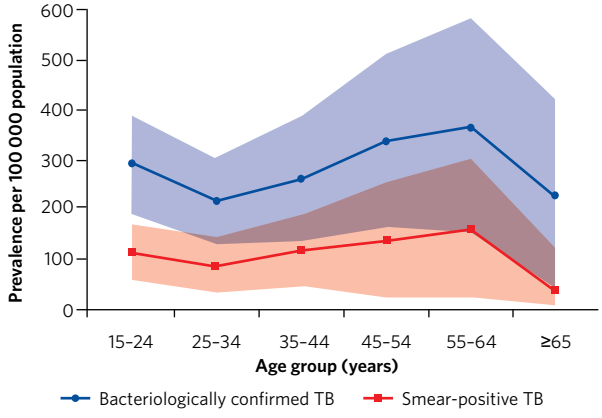


Fig. 3: Estimated number of bacteriologically confirmed TB cases and prevalence per 100 000 population, by age[a]

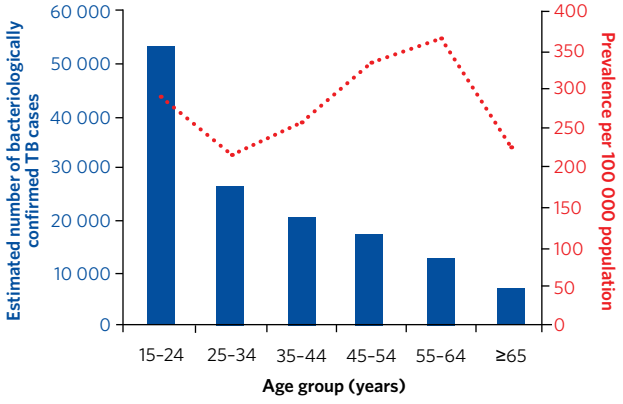


Fig. 4: Cluster variation of the number of bacteriologically confirmed TB cases[b]

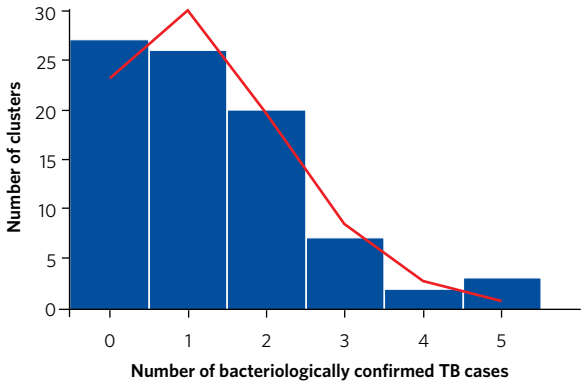


Fig. 5: Ratio of smear-positive TB prevalence to notifications by age and by sex[c]

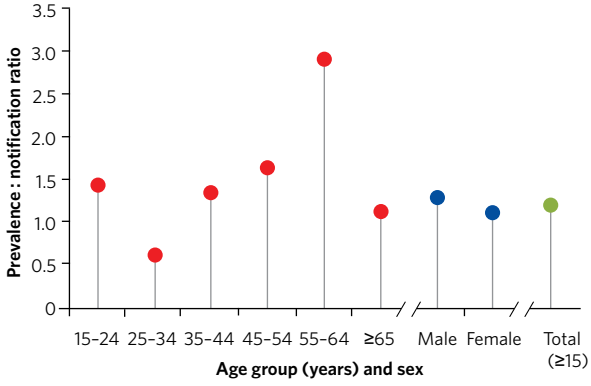
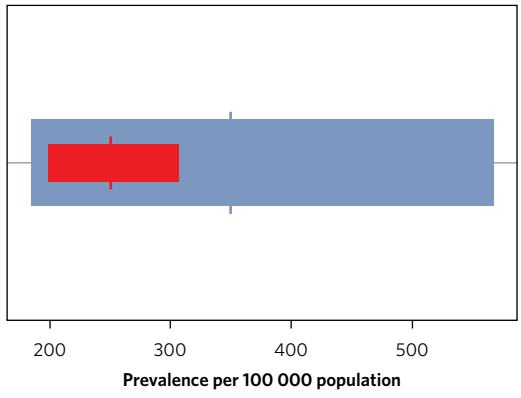


Fig. 6: Estimates of TB prevalence (all ages, all forms of TB) before (in blue) and after (in red) the national TB prevalence survey[d]



[a] The estimated number of bacteriologically confirmed TB cases is the product of age-specific prevalence and population estimates from the UN Population Division (2015 revision).

[b] The data did not suggest that the distribution of cases by cluster (blue bars) was significantly different from the theoretical distribution (red line) (mean 1.29, variance 1.59, p=0.12). The theoretical distribution assumes cases are distributed at random i.e. no clustering effect.

[c] Notification rates were estimated using notifications obtained from the WHO global TB database, and population estimates from the UN Population Division (2015 revision).

[d] The blue bar denotes the best estimate of prevalence and its range that was indirectly derived from the estimate of incidence previously published by WHO, adjusted to the year of the prevalence survey based on previously published trends in incidence.

Background

Ethiopia's population was 90 million in 2011, making it the second most populous country in Africa (after Nigeria) *(1)*. It was one of the 22 high tuberculosis (TB) burden countries (HBCs) defined by WHO as a top priority for global efforts in TB control in 1998 and throughout the Millennium Development Goal (MDG) era (2000–2015), and one of the top 30 HBCs defined by WHO for the period 2016–2020. In 2011, Ethiopia was a low-income country with an average gross national income (GNI) per person of US$ 390 per year *(1)*. In 2011, the prevalence of HIV in the general population aged 15–49 years was 1.3% (95% confidence interval [CI]: 1.1–1.5%) *(2)*, and it was estimated that 14% (95% CI: 13–16%) of TB patients were coinfected with HIV *(3)*.

Although WHO launched the DOTS strategy in the mid-1990s, the Government of Ethiopia began to implement the key components of the strategy earlier, in 1992. Nationwide coverage was reached in 2009. The Ministry of Health (MoH) reported that, in 2010, TB was the eighth leading cause of hospital admissions and the third leading cause of hospital deaths in Ethiopia *(4)*. Based on WHO estimates for the same year, Ethiopia had the seventh highest burden of TB globally in terms of estimated incident cases, and ranked third in Africa. Nonetheless, there was considerable uncertainty about the true level of the burden of TB disease. No national TB prevalence survey had been done, no direct measurements of TB mortality were available from vital registration, and the gap between notifications and incidence (due to underreporting or underdiagnosis of cases) was unquantified and hard to estimate. The national authorities in Ethiopia considered that the WHO estimate of TB incidence was too high.

To better understand the burden of TB disease, in December 2008 the MoH decided to implement a national TB prevalence survey. From this point onwards, the WHO Global Task Force on TB Impact Measurement considered Ethiopia as one of 22 global focus countries for a national TB prevalence survey. The survey was implemented in 2010–2011 *(4, 5)*.

Key methods and results

There were 85 survey clusters in three strata (urban, rural and pastoralist), with a target cluster size of 550 individuals. A total of 95 092 individuals from 19 267 households were enumerated in the survey census, of whom 51 667 (54%) were eligible and invited to participate. Of these, 46 697 (90%) did so. All participants were screened in line with the 2011 algorithm as recommended by WHO; that is, using chest X-ray and an interview about symptoms *(6)*. A total of 6080 participants (13%) were eligible for sputum examination, of whom 5868 (97%) submitted at least one sputum specimen and 5606 (92%) submitted two sputum specimens.

A total of 110 bacteriologically confirmed pulmonary TB cases was identified, including 47 cases of smear-positive TB. The prevalence of bacteriologically confirmed TB was 277 (95% CI: 208–347) per 100 000 population (among those aged ≥15 years), and for smear-positive TB it was 108 (95% CI: 73–143) per 100 000 population. When extrapolated to all forms of TB and to all ages, prevalence was 240 (95% CI: 182–298) per 100 000 population. There was no significant difference between the three geographical strata (urban, rural and pastoralist).

Other key results were:

- the male to female ratio for TB prevalence was 1.5 for smear-positive TB and 1.2 for bacteriologically confirmed TB;
- prevalence per 100 000 population increased with age and was highest in the age groups 45–54 and 55–64 years; there were also relatively large proportions of bacteriologically confirmed cases in younger age groups;
- among bacteriologically confirmed TB cases, 48% were symptom-screen negative, and among the smear-positive TB cases, 43% were symptom-screen negative;
- for smear-positive pulmonary TB, the ratio of prevalence to notifications (P:N ratio) was 1.2 overall, but varied from 0.6 in those aged 25–34 years to 2.9 in the 55–64 year age group. The ratio was slightly higher for men than for women (1.3 versus 1.1);
- among bacteriologically confirmed TB cases, 88% had no previous history of anti-TB treatment, and only 2.7% were on anti-TB treatment at the time of the survey; and
- of the 54 bacteriologically confirmed and 25 smear-positive TB survey cases that screened positive for symptoms and were not on anti-TB treatment at the time of the survey, 23 (43%) and 13 (52%), respectively, had previously sought care in a public or private health facility for their symptoms.

Photo credit: Marina Tadolini

Implications of results

The burden of smear-positive pulmonary TB was found to be lower than previously estimated. The observed smear-positive TB prevalence of 108 (95% CI: 73–143) per 100 000 population was about half of the level hypothesized to calculate the sample size of the survey, and about two thirds of the level estimated by WHO in 2009 (168 per 100 000 population). There were several reasons for the previous overestimation, including:

- a lack of accurate population-based baseline data prior to the survey;
- HIV prevalence in Ethiopia was previously assumed to be similar to the regional HIV prevalence for countries in sub-Saharan Africa, at 6%; results from sentinel HIV surveillance among women attending antenatal care suggested a level of 2.3% in 2009; and
- expansion of the DOTS strategy and the presence of a high-quality nationwide treatment programme may have contributed to the low observed prevalence of smear-positive TB.

On the basis of survey results, estimates of TB disease burden published by WHO were revised downwards, and the case detection rate, based on an updated estimate of TB incidence, was revised upwards.

Although the survey revealed a lower TB prevalence than previously estimated, almost all TB cases had not been previously notified to the National TB Programme (NTP). In addition, 54% (58/107) of the previously undetected cases in the community were among the younger age groups (15–34 years), suggesting high levels of transmission (including to the children of young parents with TB).

Other implications included:

- a need to strengthen community screening of TB, to ensure earlier detection and treatment of cases;
- a need to review the important role of chest X-ray screening in early detection of cases, given that half of bacteriologically confirmed cases did not report chronic cough and were only identified through such screening;
- a need to expand the range of laboratory tests being used to diagnose TB, to include culture or Xpert® MTB/RIF, or both; at the time of the survey, the only laboratory test in widespread use for TB diagnosis was sputum smear microscopy, but more than 50% of survey cases were sputum smear-negative;
- a need to understand that a smear-positive test result does not always indicate TB disease, especially in a community (as opposed to clinical) setting; of the 61 smear-positive participants, 27 were culture-negative and one had nontuberculous mycobacteria (NTM). In active TB case-finding activities, TB cannot be diagnosed based on smear examination alone; and
- a need for more funding to implement better screening, wider use of chest X-ray and improvements to diagnostics.

Major successes, challenges and lessons learned

This was the first-ever national TB prevalence survey in Ethiopia, and the first national survey in Africa in more than 50 years to be successfully implemented according to screening and diagnostic methods recommended in the 2011 edition of WHO's handbook on national TB prevalence surveys *(6)*. It only took just over 1 year between the decision to undertake a survey and the start of field operations. The population coverage (97%), participation rate (90%) and sputum collection rate (97%) were all very high.

Major challenges in the early stages of the survey included mismanagement of sputum specimens, backlogs in culture inoculation and a high culture contamination rate (up to 15% for cultures in the first week of the survey). With strong leadership from the principal investigator and the survey's technical working group, major efforts were made to address these challenges. Problems with management of sputum specimens were resolved, and the overall contamination rate for the survey was 6% (360/5868). Other challenges included delays in the procurement of chest X-ray equipment; difficulties in retaining radiologists during field operations; and the use of data management software that was not suited to the flow of data collection in a prevalence survey, which caused delays in data capture. Due to security and logistical challenges, 3% of the total population was excluded from the sampling frame (e.g. parts of Somaliland and areas bordering Eritrea).

Only one specimen per participant was taken for culture; therefore, the prevalence of culture-positive TB may have been underestimated. Nonetheless, the relatively high culture contamination rate may have contributed to higher culture yields than those found in other African surveys that used culture with Löwenstein-Jensen media.

An important lesson for future surveys was that the high level of commitment from different stakeholders was key to prompt survey preparation and implementation (the shortest preparation period of any survey in Africa in the period 2009–2015). This commitment had many benefits. For example, it ensured the early appointment of a full-time survey coordinator, close collaboration with the WHO Country Office and WHO headquarters, and excellent collaboration with the NTP. Other important benefits included Asia-Africa collaboration, combined with technical assistance from WHO and an independent consultant. Members of the survey team from Cambodia provided technical assistance to the Ethiopian survey team; the staff person leading WHO's global work on national TB prevalence surveys made more than 10 visits during the course of the survey; and an independent consultant (funded by the Italian Cooperation) provided regular assistance throughout the survey, from protocol development to reporting of results.

Photo credit: Zeleke Alebachew

Photo credit: Marina Tadolini

References

1. The World Bank (https://data.worldbank.org/country, accessed April 2017).
2. UNAIDS (http://aidsinfo.unaids.org/, accessed April 2017).
3. World Health Organization. Global Tuberculosis Database. 2017. (http://www.who.int/tb/country/en/, accessed April 2017).
4. Kebede AH, Alebachew Z, Tsegaye F, Lemma E, Abebe A, Agonafir M et al. The first population-based national tuberculosis prevalence survey in Ethiopia, 2010–2011. Int J Tuberc Lung Dis. 2014;18(6):635–639 (https://www.ncbi.nlm.nih.gov/pubmed/24903931, accessed April 2017).
5. First Ethiopian national population based tuberculosis prevalence survey. Addis Ababa: Ministry of Health, Federal Democratic Republic of Ethiopia; Ethiopian Health and Nutrition Research Institute; 2011 (http://www.ephi.gov.et/images/downloads/Tuberculosis%20Prevalence%20Survey.pdf, accessed May 2017).
6. World Health Organization. Tuberculosis prevalence surveys: a handbook (WHO/HTM/TB/2010.17). Geneva: WHO; 2011 (https://apps.who.int/iris/bitstream/handle/10665/44481/9789241548168_eng.pdf, accessed August 2017).

GAMBIA

2011–2013

Summary statistics

Participation rate	77%
Bacteriologically confirmed TB (≥15 years)	
• Prevalence per 100 000 population	212
• Male:female ratio	3.1
Prevalence:notification ratio (smear-positive TB, ≥15 years)	0.6

Surveyed clusters (N=80)[a]

Key people

Name	Role	Organization
Ifedayo Adetifa	Principal investigator	Medical Research Council (MRC) Unit-The Gambia
Ma Ansu Kinteh	Survey coordinator	MRC Unit-The Gambia
Martin Antonio	Unit microbiologist and head of MRC TB Reference Laboratory	MRC Unit-The Gambia
Ramatoulie Manne	Radiology coordinator	MRC Unit-The Gambia
Beatrice dei Alorse	Radiology coordinator	MRC Unit-The Gambia
Simon Donkor	Data manager	MRC Unit-The Gambia
Adedapo Bashorun	Field team leader	MRC Unit-The Gambia
Christopher Linda	Field team leader	MRC Unit-The Gambia
Semeeh Omoleke	Field team leader	MRC Unit-The Gambia
Lindsay Kendall	Biostatistician	MRC Unit-The Gambia
David Jeffries	Biostatistician	MRC Unit-The Gambia
Edward Demba	Scientific officer-mycobacteriology	MRC Unit-The Gambia
Catherine Bi Okoi	Scientific officer-mycobacteriology	MRC Unit-The Gambia
Kodjovi Mlaga	Scientific officer-mycobacteriology	MRC Unit-The Gambia
William dei Alorse	Scientific officer-mycobacteriology	MRC Unit-The Gambia
Umberto D'Alessandro	Epidemiologist/head of Disease Control and Elimination Theme	MRC Unit-The Gambia
Elina Cole	Senior project administrator	MRC Unit-The Gambia
Ikushi Onozaki	Technical assistance (survey advisor)	WHO headquarters
Marina Tadolini	Technical assistance (survey advisor)	Consultant, Italy
Charalampos Sismanidis	Technical assistance (design and analysis)	WHO headquarters
Sian Floyd	Technical assistance (analysis)	London School of Hygiene & Tropical Medicine, UK
Etienne Leroy Terquiem	Technical assistance (radiology advisor)	Consultant, France
Jan van den Hombergh	Technical assistance (radiology advisor)	PharmAccess, Tanzania
John Mayanda	Technical assistance (radiology advisor)	PharmAccess, Tanzania
Bimbo Fasan	Technical assistance (radiology advisor)	Lagos state university teaching hospital, Nigeria

Survey organization and financing

Implementing agency:
The Medical Research Council Unit-The Gambia

Finance	Amount (US$)
The Global Fund	1 844 198
Medical Research Council United Kingdom	16 979
Total budget	1 861 177

Data sources

- The Gambian Survey of Tuberculosis Prevalence, Ministry of Health and Social Welfare. The Gambia, Medical Research Council Unit, April 2014.
- Adetifa IM, Kendall L, Bashorun A, Linda C, Omoleke S, Jeffries D et al., A tuberculosis nationwide prevalence survey in Gambia, 2012, Bull World Health Organ 2016;94:433–441.
- Survey dataset.

[a] The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Survey design and methodology

Sampling design	
Sampling frame	Whole country
Sampling design	Multistage cluster sampling using PPS
Strata	No stratification was used, but final analysis accounted for urban/rural
Sampling unit	Region/enumeration area
Sample size assumptions	
• Smear-positive prevalence	292 per 100 000 (≥15 years)
• Precision	0.2
• Design effect	1.5
• *k*	0.5
• Response rate	85%
• Sample size (estimated)	55 281
Number of clusters	80[a]
Cluster size	700
Eligibility criteria	
• Age	≥15 years
• Residency	Residents who spent at least one night in the household in the 4 weeks before the census day; visitors who arrived in the household 4 weeks or more before the census day

[a] Three clusters were replaced with back-up clusters due to a large uninhabited area in the urban part around the capital (one cluster) and to the military installations and area around the president's residence (two clusters).

Screening criteria	
Interview[a]	Cough ≥2 weeks Cough <2 weeks with ≥2 other TB symptoms[b] No cough with ≥3 other TB symptoms[b]
Chest X-ray[c]	Any lung or mediastinum abnormality
Other	Chest X-ray exempted

[a] An in-depth interview about health-care seeking behaviour was done for TB symptomatic participants and for those with previous (within 5 years) or current history of TB.
[b] Chest pain, night sweats, shortness of breath, loss of appetite, weight loss, fever, haemoptysis.
[c] Mobile direct digital radiography.

Laboratory methodology	
Smear	Two samples (spot/spot or spot/morning): direct preparation, FM (LED, auramine stain)
Culture	Two samples (spot/spot or spot/morning): concentrated preparation, MGIT media, sub-cultured onto a LJ slope for speciation purposes
Identification of MTB	MGIT™ TBc Identification Test
TB drug susceptibility test	Xpert MTB/RIF for all survey TB cases, not as part of the survey
Xpert® MTB/RIF	Done for all survey TB cases, not as part of the survey
HIV test	Not done

Analysis and reporting

Field data collection	Paper
Database	SQL
Method of analysis	MI+IPW
Results first published in a report/paper	April 2014
Official dissemination event	May 2014

Key survey results

Prevalence[a]	Smear-positive TB		Bacteriologically confirmed TB	
	Number per 100 000 population	95% CI	Number per 100 000 population	95% CI
Total	90	53–127	212	152–272
Male	148	88–208	333	233–433
Female	41	0–83	109	54–164
15–34 years	56	24–88	133	76–190
35–54 years	144	65–223	355	219–490
≥55 years	159	0–367	329	99–558
Urban	96	43–148	266	164–368
Rural	86	32–140	109	54–164

[a] Age ≥15 years unless otherwise specified.

	Design effect	*k*
Smear-positive TB	1.8	1.3
Bacteriologically confirmed TB	1.6	0.7

Other sputum results	Number	%
Total smear-positive participants	36	–
Smear-positive participants without MTB confirmation[a]	8	22
Isolates with DR-TB (rifampicin resistance) detected	3	3.9

[a] This includes culture with no evidence of MTB (i.e. culture-negative, NTM, contaminated, N/A).

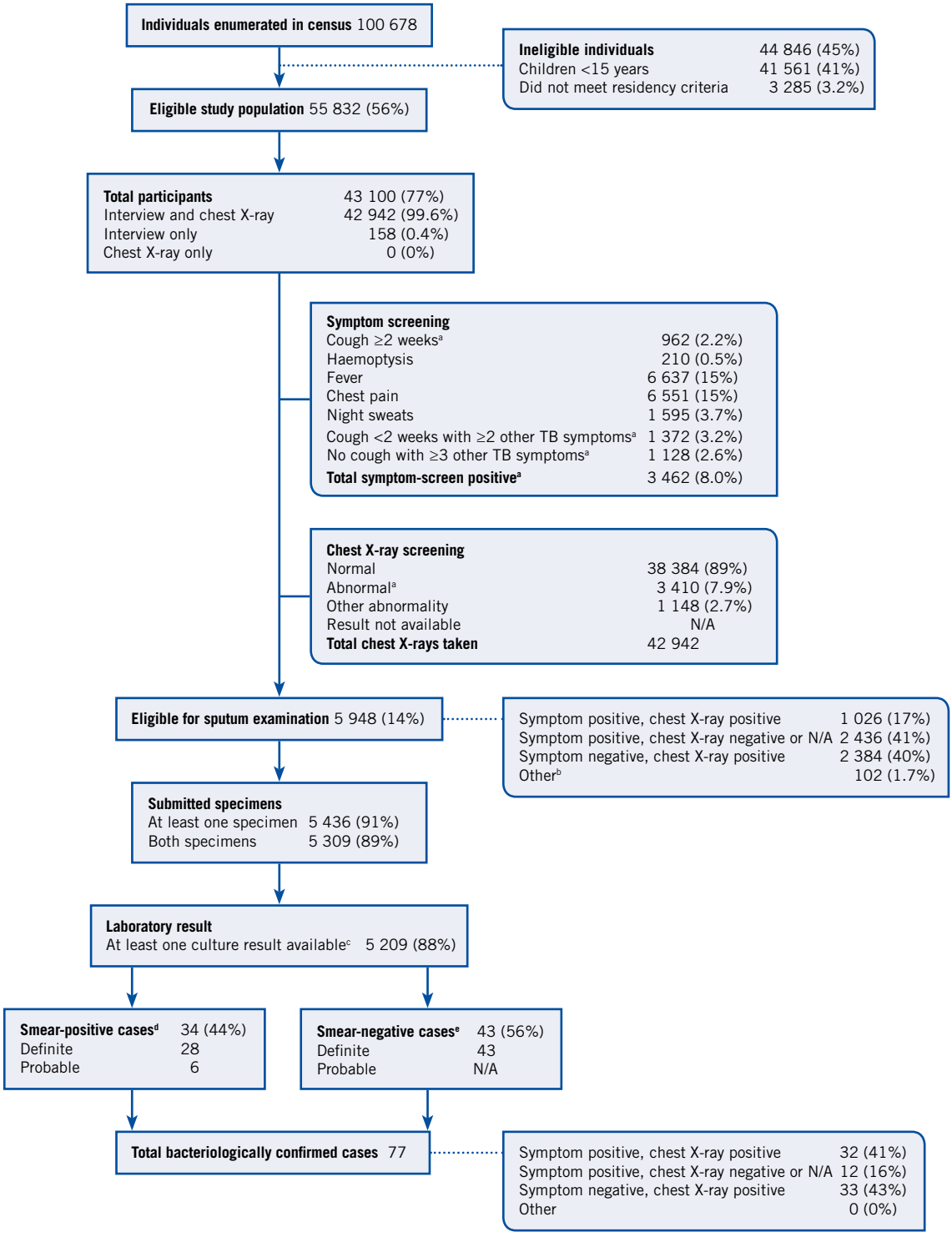
Health-care seeking behaviour among participants who were symptom-screen positive	Number	%
Participants who were symptom-screen positive[a]	3 462	–
Location of care sought		
• Consulted medical facility	1 706	49
Public facility	*1 398*	*82*
Private facility	*220*	*13*
Other (NGOs, MRC facility)	*88*	*5.2*
• Pharmacy	17	0.5
• Traditional centre	14	0.4
• Other	24	0.7
Self-treated	N/A	N/A
No action taken	1 424	41
Unknown	277	8.0

[a] Cough ≥2 weeks, or cough <2 weeks with ≥2 other TB symptoms, or no cough with ≥3 other TB symptoms.

Survey participants currently on TB treatment	Number	%
Total participants currently on TB treatment[a]	38	–
• Treated in the public sector	38	100
• Treated in the private sector	N/A	N/A
• Treated in other sector	N/A	N/A
Bacteriologically confirmed TB cases detected by the survey who were currently on TB treatment	4	5.0

Survey flow: census to final outcomes

Field operations: December 2011 to January 2013



[a] Eligible for sputum collection.
[b] Chest X-ray exempted and symptom-screen negative.
[c] Cultures that were either contaminated and/or missing without a definitive result (i.e. MTB, NTM, negative) were excluded.
[d] Definite: MTB confirmed by culture. Probable: MTB not confirmed by culture but two AFB positive or one AFB positive with chest X-ray suggestive of TB.
[e] Definite: MTB confirmed by culture. Probable: no definition.

Fig. 1: Participation rate by age and sex

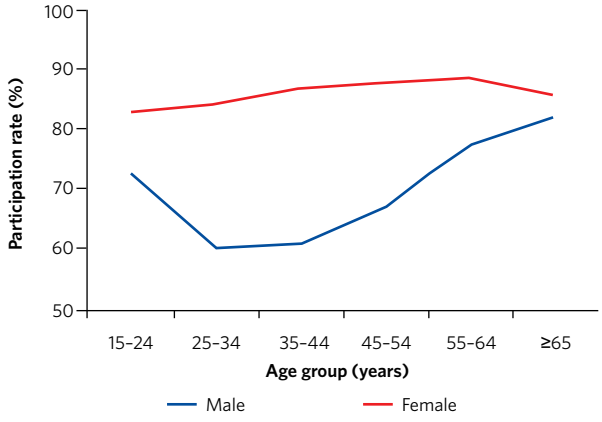


Fig. 2: TB prevalence per 100 000 population by age

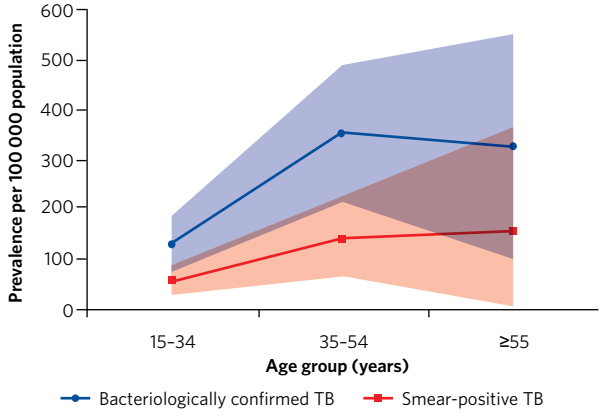


Fig. 3: Estimated number of bacteriologically confirmed TB cases and prevalence per 100 000 population, by age[a]

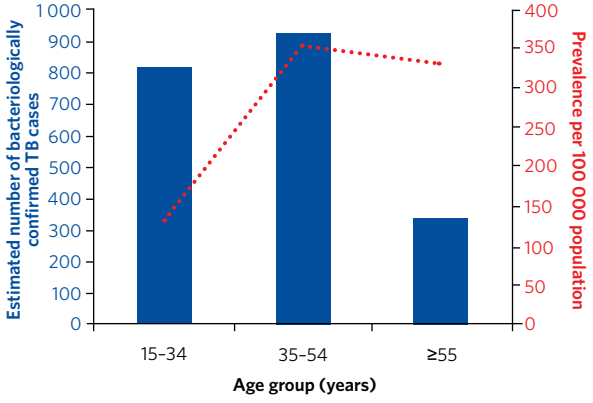


Fig. 4: Cluster variation of the number of bacteriologically confirmed TB cases[b]

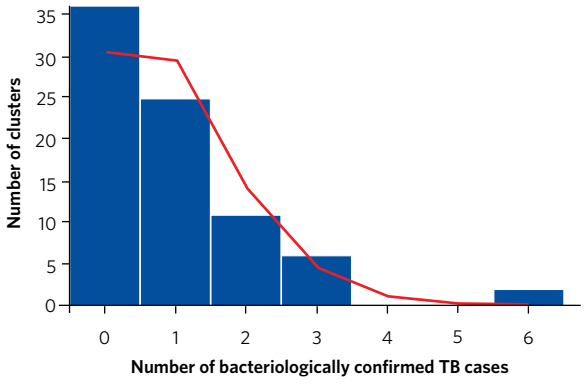


Fig. 5: Ratio of smear-positive TB prevalence to notifications by age and by sex[c]

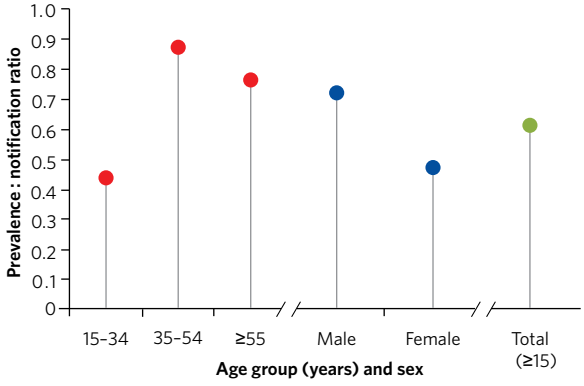
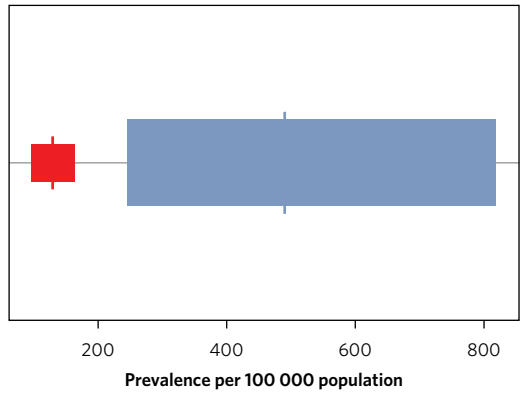


Fig. 6: Estimates of TB prevalence (all ages, all forms of TB) before (in blue) and after (in red) the national TB prevalence survey[d]



[a] The estimated number of bacteriologically confirmed TB cases is the product of age-specific prevalence and population estimates from the UN Population Division (2015 revision).

[b] The data did not suggest that the distribution of cases by cluster (blue bars) was significantly different from the theoretical distribution (red line) (mean 0.96, variance 1.53, p=0.06). The theoretical distribution assumes cases are distributed at random i.e. no clustering effect.

[c] Notification rates were estimated using notifications obtained from the WHO global TB database, and population estimates from the UN Population Division (2015 revision).

[d] The blue bar denotes the best estimate of prevalence and its range that was indirectly derived from the estimate of incidence previously published by WHO, adjusted to the year of the prevalence survey based on previously published trends in incidence.

Background

Gambia, a small country in West Africa, had a population of 1.8 million in 2012, and an average gross national income (GNI) per person of US$ 520 per year, making it a low-income country *(1)*. The prevalence of HIV in 2012 in the general population aged 15–49 years was 2.0% (95% confidence interval [CI]:1.6–2.4%) *(2)*, and it was estimated that 16% (95% CI: 15–18%) of tuberculosis (TB) patients were coinfected with HIV *(3)*.

Gambia established a National Leprosy and TB Programme (NLTP) in 1984. The WHO-recommended DOTS strategy was adopted in the mid-1990s, and was eventually expanded to reach national coverage *(4,5)*. The case notification rate for new TB cases peaked at 124 per 100 000 population in 2008 and then started to fall. The WHO estimate of TB prevalence in 2011 was 455 (95% CI: 225–764) per 100 000 population, with the case detection rate (notifications of new cases divided by incidence) estimated at 45% (95% CI: 38–55%). However, there was considerable uncertainty about the burden of TB disease, given that no national TB prevalence survey had previously been done, no direct measurements of TB mortality were available from vital registration, and the gap between notifications and incidence (due to underreporting or underdiagnosis of cases) had not been quantified and was difficult to estimate. National authorities in the Gambia considered that WHO estimates of TB incidence were too high.

To better understand the burden of TB disease in the country, a decision to implement a national TB prevalence survey was taken in 2008–2009. The survey started in December 2011 and was completed in January 2013 *(6,7)*. Gambia was not one of the 22 global focus countries for national TB prevalence surveys selected by the WHO Global Task Force on TB Impact Measurement in December 2007. Nevertheless, the country was on the Task Force's longer list of 53 countries considered to meet survey eligibility criteria.

Key methods and results

There were 80 survey clusters, with a target cluster size of 700 individuals. No stratification was used at the time of survey design, but urban and rural strata were examined during the analysis. A total of 100 678 individuals from 13 847 households were enumerated in the survey census, of whom 55 832 (56%) were eligible and invited to participate. Of these, 43 100 (77%) did so. All participants were screened according to the 2011 algorithm recommended by WHO; that is, using chest X-ray and an interview about symptoms *(8)*. A total of 5948 participants (14%) were eligible for sputum examination, of whom 5436 (91%) submitted at least one sputum specimen and 5309 (89%) submitted two sputum specimens.

A total of 77 bacteriologically confirmed pulmonary TB cases was identified, including 34 cases of smear-positive TB. The prevalence of smear-positive TB was 90 (95% CI: 53–127) per 100 000 population (among those aged ≥15 years), and for bacteriologically confirmed TB it was 212 (95% CI: 152–272) per 100 000 population. When extrapolated to all forms of TB and to all ages, prevalence was 128 (95% CI: 94–162) per 100 000 population. The prevalence of smear-positive and bacteriologically confirmed TB was higher in urban areas than in rural areas.

Photo credit: Ifedayo Adetifa

Other key results were:

- the male to female ratio for TB prevalence was 3.6 for smear-positive TB and 3.1 for bacteriologically confirmed TB;
- prevalence per 100 000 population was highest in the older age groups; however, the absolute number of bacteriologically confirmed TB cases was relatively high in the younger age groups (15–34 years and 35–54 years);
- among bacteriologically confirmed TB cases, 57% were symptom-screen positive, and of the smear-positive cases, 56% were symptom-screen positive;
- for smear-positive pulmonary TB, the ratio of prevalence to notifications (P:N ratio) was 0.6 overall, but varied from 0.4 in those aged 15–34 years to 0.9 in the 35–54 year age group; it was slightly higher for men than for women (0.7 versus 0.5);
- among bacteriologically confirmed TB cases, 16% had a previous history of anti-TB treatment and only 5.0% were on anti-TB treatment at the time of the survey;
- of the 40 bacteriologically confirmed and 15 smear-positive TB survey cases that screened positive for symptoms and were not on anti-TB treatment at the time of the survey, 24 (60%) and 12 (80%), respectively, had previously sought care in a public or private health facility for their symptoms; and
- three cases had rifampicin resistance based on Xpert® MTB/RIF testing; none of these rifampicin-resistant cases had a history of current or previous anti-TB treatment.

Photo credit: Ifedayo Adetifa

Photo credit: Ifedayo Adetifa

Implications of results

The estimated TB prevalence for all ages based on survey results was 128 per 100 000 population (95% CI: 94–162). This was only one quarter of the pre-survey estimate published by WHO. Estimated incidence was revised downwards to a best estimate of 175 per 100 000 population (95% CI: 135–215), and the case detection rate was revised upwards, to 71% (95% CI: 70–73%). At the same time, stable TB case notification rates indicated that efforts in TB control were still not sufficient.

This survey was the only one where the P:N ratio was less than one for all categories (all age groups, male and female). Possible explanations for this included an NTP that was able to efficiently detect and treat cases in the community as in high-resource settings, or over-diagnosis of smear-positive TB cases in routine health care services.

Other implications included:

- a need for interventions targeted or more tailored to men, especially those aged 35–54 years;
- a need for expanded use of chest X-ray combined with better capacity to interpret results, and greater use of culture and Xpert MTB/RIF (or both), to improve detection of people with smear-negative culture-positive disease;

- a need to consider targeted interventions among older people, including paying particular attention to this group during contact investigations and active case finding (given the cultural acceptance of chronic cough among the elderly); and
- a need for increased funding for implementation of targeted interventions, wider use and better interpretation of X-rays, and improvements to diagnostics.

Major successes, challenges and lessons learned

This was the first survey in Africa to have been outsourced by the NTP and conducted by a reputable research institute. In addition, it was the first survey for which results led to a statistically significant downward estimate of TB burden, thus confirming the value of undertaking a survey and validating the notion that WHO estimates were previously too high.

One major challenge was ensuring participation, particularly in urban areas. Overall, the target of an 85% participation rate was not achieved. The survey was also prolonged to 13 months, and the start of the survey was delayed due to logistical problems. A particular difficulty was the procurement of mobile X-rays, due to a combination of the high unit cost and the need to adhere to European Union procurement rules and procedures given that the implementing agency for the survey (Medical Research Council Unit, The Gambia (MRCG)) was an affiliate of the Medical Research Council UK. However, following the survey, the radiology equipment was handed over to the government to help improve TB diagnosis.

The MRCG laboratory had excellent capacity, made considerable efforts to ensure high-quality sputum samples and used best practices in the decontamination process. They pioneered the use of MGIT for primary diagnosis and identification of MTB. Nevertheless, culture contamination rates were relatively high (11%), in part because of the use of liquid culture. The relatively high contamination rate might have contributed to higher yields by culture (i.e. there were more smear-negative, culture-positive specimens than smear-positive, culture-positive ones). The contamination rate within the laboratory for routine samples was within the prescribed ranges for both solid and liquid media cultures.

The survey was fully implemented by MRCG staff. Although the NLTP was represented by a designated liaison person (deputy programme manager) for implementation and on the survey steering committee (NLTP manager), their involvement was relatively limited. More active engagement would have helped to build greater ownership of survey results and strengthened use of the results in national strategic planning.

Photo credit: Ifedayo Adetifa

Financial policies of the funder – the Global Fund to Fight AIDS, Tuberculosis and Malaria – meant that key survey staff reached the end of their contracts before the survey report was ready. This contributed to delays in publication of the official survey report.

References

1. The World Bank (https://data.worldbank.org/country, accessed April 2017).
2. UNAIDS (http://aidsinfo.unaids.org/, accessed April 2017).
3. World Health Organization. Global Tuberculosis Database. 2017. (http://www.who.int/tb/country/en/, accessed April 2017).
4. WHO Tuberculosis Programme. (1994). WHO Tuberculosis Programme: framework for effective tuberculosis control. World Health Organization. (http://www.who.int/iris/handle/10665/58717, accessed January 2018).
5. World Health Organization. Global tuberculosis programme. Global tuberculosis control report 1997. Geneva: WHO; (https://apps.who.int/iris/bitstream/handle/10665/63354/WHO_TB_97.225_(part1).pdf?sequence=1, accessed January 2018).
6. The Gambian survey of tuberculosis prevalence (GAMSTEP). Banjul, The Gambia: Medical Research Council Unit, The Gambia; 2014.
7. Adetifa IM, Kendall L, Bashorun A, Linda C, Omoleke S, Jeffries D et al. A tuberculosis nationwide prevalence survey in Gambia, 2012. Bull World Health Organ. 2016;94(6):433–441 (https://www.ncbi.nlm.nih.gov/pubmed/27274595, accessed August 2017).
8. World Health Organization. Tuberculosis prevalence surveys: a handbook (WHO/HTM/TB/2010.17). Geneva: WHO; 2011 (https://apps.who.int/iris/bitstream/handle/10665/44481/9789241548168_eng.pdf, accessed August 2017).

GHANA

2013

Summary statistics

Participation rate	91%
Bacteriologically confirmed TB (≥15 years)	
• Prevalence per 100 000 population	356
• Male:female ratio	1.4
Prevalence:notification ratio (smear-positive TB, ≥15 years)	2.5

Surveyed clusters (N= 98)[a]

Key people

Name	Role	Organization
Frank Bonsu	Principal investigator	Ghana Health Service, National TB Control Programme (NTP)
Kennedy Kwasi Addo	Co-principal investigator	Noguchi Memorial Institute, University of Ghana
John Gyapong	Co-investigator	University of Ghana
Ellis Owusu Dabo	Co-investigator	Kwame Nkrumah University of Science and Technology
Kwadwo Koram	Co-investigator	Noguchi Memorial Institute, University of Ghana
Augustina Badu Peprah	Co-investigator	Komfo anokye teaching hospital, Kumasi
Raymond Yaw Gockah	Survey coordinator	Ghana Health Service, NTP
Francisca Dzata	NTP laboratory focal point	Ghana Health Service, NTP
Michael Omari	Head of chest clinic laboratory	Korle bu teaching hospital, Laboratory
Robertson Adiei	Cartographer	Ghana Statistical Service, NTP
Nii Nortey Hanson Nortey	Deputy NTP manager	Ghana Health Service, NTP
Jane Amponsah	Data manager	Ghana Health Service, NTP
Sauda Ahmed	Assistant data manager	Ghana Health Service, NTP
Herve Awako	ICT manager	TABS Consult (data/IT management)
Prince Boni	Data planning	TABS Consult (data/IT management)
Zeleke Alebachew	Technical assistance (report writing)	Consultant, Ethiopia
Irwin Law	Technical assistance (survey advisor)	WHO headquarters
Wilfred Nkhoma	Technical assistance (survey advisor)	WHO Regional Office for Africa (AFRO)
Ikushi Onozaki	Technical assistance (survey advisor)	WHO headquarters
Marina Tadolini	Technical assistance (survey advisor)	Consultant, Italy
Charalampos Sismanidis	Technical assistance (analysis)	WHO headquarters

Survey organization and financing

Implementing agency:
National TB Control Programme

Finance	Amount (US$)
The Global Fund	2 100 000
WHO	100 000
Total budget	2 200 000

Data sources

- Bonsu F, Addo KK, Alebachew Z, Gyapong J, Badu-Peprah A, Gockah R et al. National population-based tuberculosis prevalence survey in Ghana, 2013. Int J Tuberc Lung Dis. 2020 Mar 1;24(3):321-328.
- Survey dataset.

[a] The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Survey design and methodology

Sampling design	
Sampling frame	Whole country
Sampling design	Multistage cluster sampling using PPS
Strata	Urban/rural
Sampling unit	Region/district/enumeration area
Sample size assumptions	
• Smear-positive prevalence	270 per 100 000 (≥15 years)
• Precision	0.2
• Design effect	1.4
• *k*	0.5
• Response rate	80%
• Sample size (estimated)	63 905
Number of clusters	98
Cluster size	650
Eligibility criteria	
• Age	≥15 years
• Residency	Permanent residents who lived in the household at least 1 day in the past 14 days, or visitors who lived in the household at least 7 days in the past 14 days

Screening criteria	
Interview[a]	Cough ≥2 weeks
Chest X-ray[b]	Any lung abnormality
Other	Chest X-ray exempted

[a] An in-depth interview about health-care seeking behaviour and exposure to risk factors was done only for those with cough of two weeks or more, sputum production, current TB treatment or a history of TB.
[b] Mobile digital radiography.

Laboratory methodology	
Smear	Two samples (spot, morning): concentrated preparation, ZN
Culture	Two samples (spot, morning): concentrated preparation, LJ media and MGIT media (but only MGIT was used for study case definition)
Identification of MTB	PNB, capilia
TB drug susceptibility test	Xpert MTB/RIF
Xpert® MTB/RIF	Done for smear-positive specimens, and if cultures were contaminated (where specimens were available).
HIV test	Not done

Analysis and reporting

Field data collection	Paper/electronic
Database	Microsoft® Access
Method of analysis	MI+IPW
Results first published in a paper	March 2020
Official dissemination event	March 2015

Key survey results

Prevalence[a]	Smear-positive TB		Bacteriologically confirmed TB	
	Number per 100 000 population	95% CI	Number per 100 000 population	95% CI
Total	111	76–145	356	288–425
Male	198	133–264	431	327–536
Female	49	21–76	303	223–382
15–24 years	49	14–84	185	104–265
25–34 years	35	1.6–69	228	130–326
35–44 years	101	38–164	295	174–416
45–54 years	223	129–317	470	294–645
55–64 years	245	63–426	607	362–854
≥65 years	212	77–347	908	597–1 219
Urban	142	89–195	293	216–372
Rural	75	39–111	429	315–542

[a] Age ≥15 years unless otherwise specified.

	Design effect	*k*
Smear-positive TB	1.5	0.9
Bacteriologically confirmed TB	2.0	0.7

Other sputum results	Number	%
Total smear-positive participants	198	–
Smear-positive participants without MTB confirmation[a]	138	70
Isolates with DR-TB (rifampicin) detected[b]	11	1.0

[a] This includes culture with no evidence of MTB (i.e. culture-negative, NTM, contaminated, N/A) and Xpert-negative.
[b] 1134 participants were tested with Xpert MTB/RIF and 11 were resistant to rifampicin.

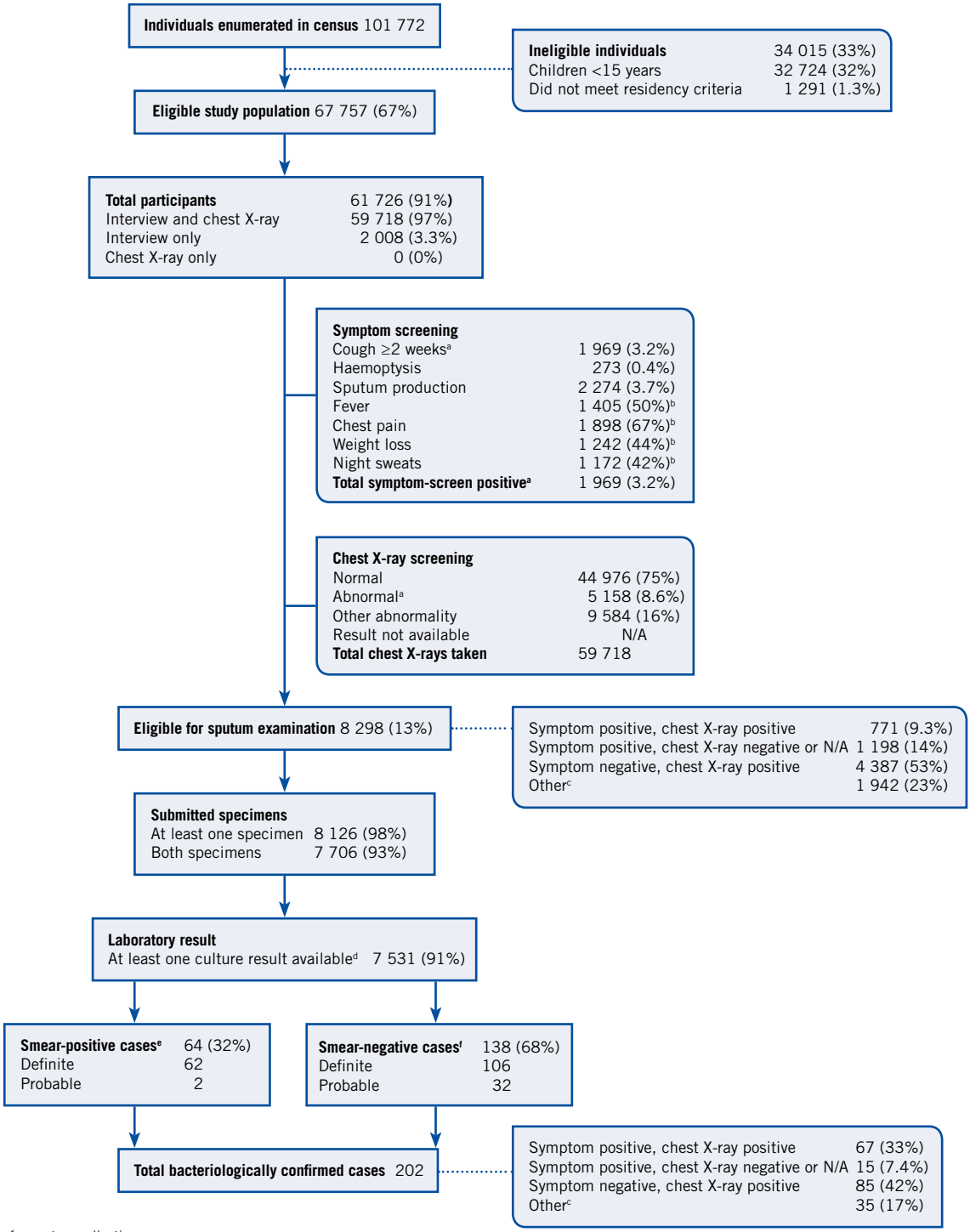
Health-care seeking behaviour among participants who were symptom-screen positive	Number	%
Participants who were symptom-screen positive[a]	1 969	–
Location of care sought		
• Consulted medical facility	793	40
Public facility	*695*	*88*
Private facility	*61*	*7.7*
Other[b]	*37*	*4.7*
• Pharmacy	324	17
• Traditional center	20	1.0
Self-treated	567	29
No action taken	264	13
Unknown	1	0.1

[a] Cough ≥2 weeks.
[b] Faith based health facility.

Survey participants currently on TB treatment	Number	%
Total participants currently on TB treatment	48	–
• Treated in the public sector	42	88
• Treated in the private sector	1	2.1
• Treated in other sector (faith based health facility)	5	10
Bacteriologically confirmed TB cases detected by the survey who were currently on TB treatment	9	4.5

Survey flow: census to final outcomes

Field operations: March to December 2013



[a] Eligible for sputum collection.
[b] The denominator included only participants who had the in-depth interview (N=2 821).
[c] Chest X-ray exempted and symptom-screen negative.
[d] Cultures that were either contaminated and/or missing without a definitive result (i.e. MTB, NTM, negative) were excluded.
[e] Definite: MTB confirmed by culture in at least one sample, or Xpert-positive in at least one sample with chest X-ray suggestive of TB. Probable: Xpert-positive in at least one sample without chest X-ray suggestive of TB.
[f] Definite: MTB confirmed by culture and/or Xpert in two samples, or culture and/or Xpert in one sample with chest X-ray suggestive of TB. Probable: MTB confirmed by culture and/or Xpert in one sample without chest X-ray suggestive of TB.

Fig. 1: Participation rate by age and sex

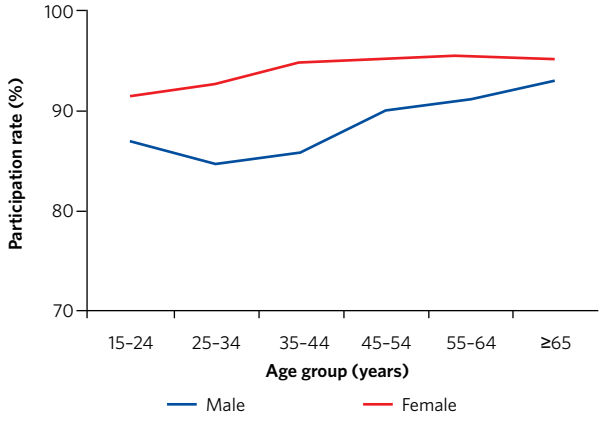


Fig. 2: TB prevalence per 100 000 population by age

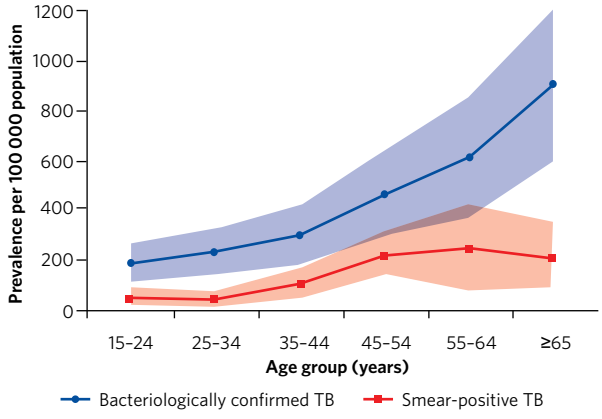


Fig. 3: Estimated number of bacteriologically confirmed TB cases and prevalence per 100 000 population, by age[a]

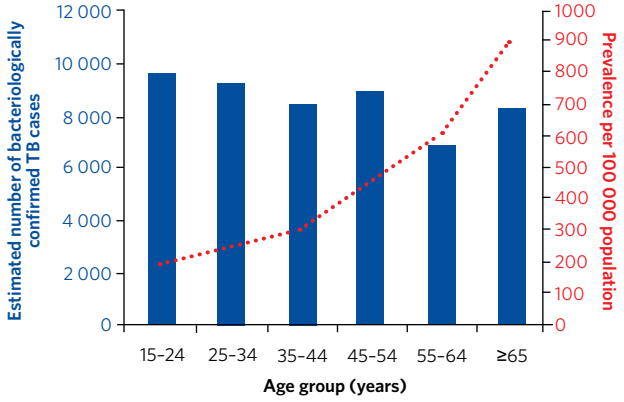


Fig. 4: Cluster variation of the number of bacteriologically confirmed TB cases[b]

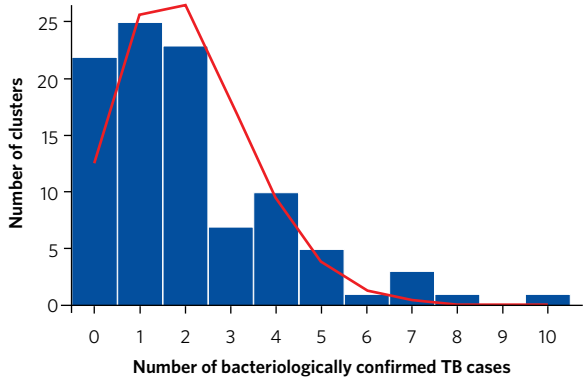


Fig. 5: Ratio of smear-positive TB prevalence to notifications by age and by sex[c]

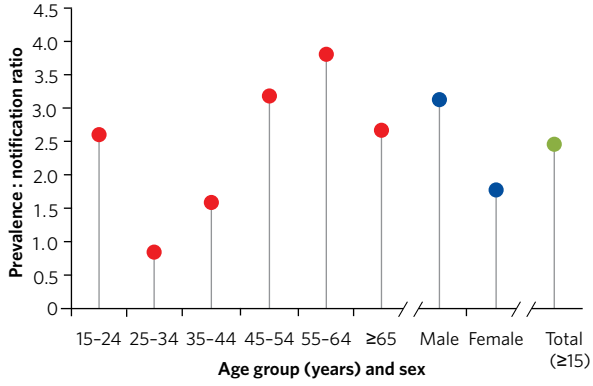
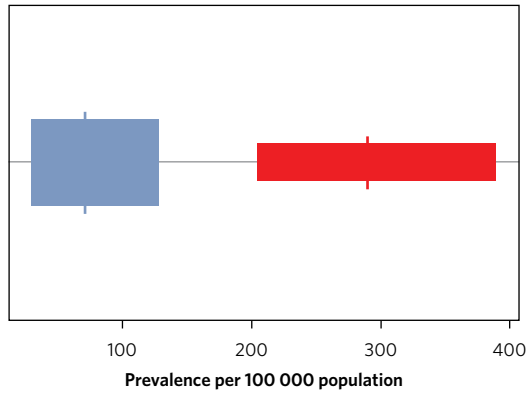


Fig. 6: Estimates of TB prevalence (all ages, all forms of TB) before (in blue) and after (in red) the national TB prevalence survey[d]



[a] The estimated number of bacteriologically confirmed TB cases is the product of age-specific prevalence and population estimates from the UN Population Division (2015 revision).

[b] The data suggested that the distribution of cases by cluster (blue bars) was significantly different from the theoretical distribution (red line) (mean 2.06, variance 4.08, $p<0.05$). The theoretical distribution assumes cases are distributed at random i.e. no clustering effect.

[c] Notification rates were estimate of using smear-positive pulmonary TB notifications (2013) obtained from the NTP, and population estimates from the UN Population Division (2015 revision).

[d] The blue bar denotes the best estimate of prevalence and its range that was indirectly derived from the estimate of incidence previously published by WHO, adjusted to the year of the prevalence survey based on previously published trends in incidence.

Background

Ghana, in West Africa, had a population of 26 million in 2013, and a gross national income (GNI) per person of US$ 1740, making it a lower-middle-income country *(1)*. In 2013, the prevalence of HIV in the general population aged 15–49 years was 1.5% (95% confidence interval [CI]: 1.2–2.0%) *(2)*, and it was estimated that 24% (95% CI: 20–27%) of tuberculosis (TB) patients were coinfected with HIV *(3)*.

The Ghana Tuberculosis Service was formally established with the appointment of its first director in 1959. It was restructured and renamed the National TB Control Programme (NTP) in 1994, the year in which implementation of the WHO-recommended DOTS strategy began *(4,5)*. Three national strategic plans for TB control were implemented during the period 1994–2013.

In its 2012 global TB report, WHO estimated that there were 20 000 (95% CI: 17 000–22 000) new cases of TB per year. Nonetheless, there was considerable uncertainty about estimates of the burden of TB disease, given that no national TB prevalence survey had been done since 1957; there were no direct measurements of TB mortality available from vital registration; and the gap between notifications and incidence (due to underreporting or underdiagnosis of cases) was not quantified and was difficult to estimate. A 2013 evaluation of TB surveillance using the WHO checklist of TB surveillance standards and benchmarks found that only four of the 13 standards expected from a high-performance surveillance system capable of providing direct and reliable measurements of the number of TB cases and deaths were fully met.

Photo credit: Irwin Law

In December 2007, Ghana was one of 22 global focus countries for a national TB prevalence survey selected by the WHO Global Task Force on TB Impact Measurement. In response, the Ministry of Health decided to implement a national TB prevalence survey in 2008, and secured funding from the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund). Field operations started in March 2013 and were completed in December 2013.

Key methods and results

There were 98 survey clusters in two strata (urban and rural), with a target cluster size of 650 individuals. A total of 101 772 individuals from 23 991 households were enumerated in the survey census, of whom 67 757 (67%) were eligible and invited to participate. Of these, 61 726 (91%) did so. All participants were screened according to the 2011 algorithm recommended by WHO; that is, using chest X-ray and an interview about symptoms *(6)*. A total of 8298 participants (13%) were eligible for sputum examination, of whom 8126 (98%) submitted at least one sputum specimen and 7706 (93%) submitted two sputum specimens.

A total of 202 bacteriologically confirmed pulmonary TB cases was identified, including 64 cases of smear-positive TB. The prevalence of smear-positive TB was 111 (95% CI: 76–145) per 100 000 population (among those aged ≥15 years) and for bacteriologically confirmed TB it was 356 (95% CI: 288–425) per 100 000 population. Bacteriologically confirmed TB prevalence was generally higher in rural than urban areas.

Other key results were:

- the male to female ratio was 4.0 for smear-positive TB and 1.4 for bacteriologically confirmed TB;
- prevalence per 100 000 population increased with age; however, the absolute number of TB cases was consistently high in all age groups;
- among bacteriologically confirmed TB cases, 41% were symptom-screen positive, and of the smear-positive cases, 64% were symptom-screen positive;

- for smear-positive pulmonary TB, the ratio of prevalence to notifications (P:N ratio) was 2.5 overall, but varied from 0.9 in those aged 25–34 years to 3.8 in those aged 55–64 years, and it was higher for men than for women (3.1 versus 1.8);
- among bacteriologically confirmed TB cases, 95% had no previous history of anti-TB treatment and only 4.5% were on anti-treatment at the time of the survey; and
- of the 73 bacteriologically confirmed and 37 smear-positive TB survey cases that screened positive for symptoms and were not on anti-TB treatment at the time of the survey, 33 (45%) and 17 (46%), respectively, had previously sought care in a public or private health facility for their symptoms.

Implications of results

The estimated TB prevalence (all forms, all ages) based on the survey (290 per 100 000 population; 95% CI: 196–384) was approximately three times higher than the pre-survey estimate (92 per 100 000 population; 95% CI: 44–158). Furthermore, the survey clearly revealed undiagnosed TB cases in the community, with many missed opportunities for diagnosis, including a high proportion of patients with chronic cough who visited both public and private health facilities but were not offered sputum examination. This was further compounded by the large proportion of people who self-treated, with a high usage of pharmacies as a first point of health care.

Based on survey findings, the national TB control implementation strategy (TB strategic plan 2015–2020) was updated to include:

- a revised screening and diagnostic algorithm that included chest X-ray and culture and/or Xpert® MTB/RIF in addition to smear microscopy and symptoms;
- introduction of a policy to use chest X-ray as part of active TB case finding in vulnerable populations and in health-care settings;
- wider use of Xpert MTB/RIF throughout the programme to detect bacteriologically confirmed cases and to exclude nontuberculous mycobacteria (NTM); and
- targeting of TB screening activities to specific subpopulations, such as men and the elderly.

In addition, the evidence of TB-related stigma and poor knowledge about TB in the general population prompted the development of a national communications strategy with stakeholders. The survey also highlighted gaps in the surveillance system that needed to be addressed; in particular, underreporting of smear-negative culture-positive TB cases to the NTP.

Photo credit: Irwin Law

Culture and Xpert MTB/RIF testing showed that a smear-positive test result did not always indicate TB disease, especially in a community setting as opposed to a clinical setting. In active TB case finding, TB cannot be diagnosed based on smear examination alone.

Major successes, challenges and lessons learned

The major overarching success was that the first national TB prevalence survey in Ghana in more than 50 years was successfully implemented, with a high participation rate. A key part of the success story was that the survey was led and coordinated by the NTP, with stakeholders from research institutes, the national statistical service, universities and the Ministry of Health. The survey team also benefited from substantial technical assistance, coordinated by the WHO Global Task Force on TB Impact Measurement.

Other successes included:

- the survey enhanced national capacity to conduct culture examinations, drug susceptibility testing and action-oriented operational research;
- collaboration with the private sector in data planning, management and storage made the survey one of the most technologically advanced (among those conducted in 2009–2016) in terms of data management; beyond the survey, this subsequently improved data management capacity within the NTP; and
- the active community screening, specimen collection and transportation required in the survey improved working relationships between the NTP and research institutes.

The survey faced several challenges. It took four years from the start of survey preparations in 2008 to reach the point at which field operations could be launched. The major reason for this delay was the substantial time taken to acquire digital X-ray units. When the survey was designed, the timely delivery of such units was expected from a large Netherlands-Ghana project to equip the district hospital network with digital equipment, based on a concessional loan and national counterpart funding. In practice, the project was not approved by the Dutch national parliament for several years and the NTP had to mobilize other funds to procure the X-ray units needed for the survey.

During field operations there were logistical challenges. Transportation across harsh terrain caused some breakdowns in container X-ray units, which needed to be replaced with portable units that had shockproof boxes. In one of the two laboratories used in the survey, there was a

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breakdown of the biosafety cabinet (due to a blocked high efficiency particulate air [HEPA] filter), which may have caused specimen cross-contamination. The breakdown necessitated temporary suspension of laboratory work for maintenance, and thus delayed inoculation of the collected specimens. Furthermore, culture confirmation occurred in less than 85% of smear-positive survey cases, and the exclusion of solid culture and FM smear results (done in parallel with MGIT culture and Ziehl-Neelsen [ZN] smear) highlighted the challenges encountered by at least one of the two laboratories.

Other challenges faced during the survey included a backlog of 20 000 chest X-rays that had to be read after field operations were completed; and delays in report writing and dissemination of results because survey staff had competing demands on their time. Future surveys would benefit from a dedicated budget and associated staff for report writing.

References

1. The World Bank (https://data.worldbank.org/country, accessed April 2017).
2. UNAIDS (http://aidsinfo.unaids.org/, accessed April 2017).
3. World Health Organization. Global Tuberculosis Database. 2017. (http://www.who.int/tb/country/en/, accessed April 2017).
4. WHO Tuberculosis Programme. (1994). WHO Tuberculosis Programme: framework for effective tuberculosis control. World Health Organization. (http://www.who.int/iris/handle/10665/58717, accessed January 2018).
5. World Health Organization. Global tuberculosis programme. Global tuberculosis control report 1997. Geneva: WHO; (https://apps.who.int/iris/bitstream/handle/10665/63354/WHO_TB_97.225_(part1).pdf?sequence=1, accessed January 2018).
6. World Health Organization. Tuberculosis prevalence surveys: a handbook (WHO/HTM/TB/2010.17). Geneva: WHO; 2011 (https://apps.who.int/iris/bitstream/handle/10665/44481/9789241548168_eng.pdf, accessed August 2017).

INDONESIA

2013–2014

Summary statistics

Participation rate	89%
Bacteriologically confirmed TB (≥15 years)	
• Prevalence per 100 000 population	759
• Male:female ratio	2.3
Prevalence:notification ratio (smear-positive TB, ≥15 years)	2.3

Surveyed clusters (N=156)[a]

Key people

Name	Role	Organization
Dina Bisara Lolong	Principal investigator	National Institute of Health Research and Development (NIHRD)
Francisca Srioetami	Regional coordinator	NIHRD
Lamria Pangaribuan	Regional coordinator	NIHRD
Ainur Rofiq	Regional coordinator	NIHRD
Retno Kusuma Dewi	Laboratory coordinator	National TB Programme (NTP)
Irfan Ediyanto	Vice laboratory coordinator	NTP
Aziza G. Icksan	Radiology coordinator	Persahabatan hospital
Narendro Arifia	Data manager	NIHRD
Safrizal	Field team leader	The National TB Prevalence Survey team (NPS team) of NIHRD
Darmawati	Field team leader	NPS team of NIHRD
Risnawati	Field team leader	NPS team of NIHRD
Ade Yoska Tilla Serihati	Field team leader	NPS team of NIHRD
Elisabeth Bernadeth	Field team leader	NPS team of NIHRD
Laura Valeria	Field team leader	NPS team of NIHRD
M.N. Farid	Technical assistance (statistics, data management)	TB Operational Research Group (TORG)
Pandu Riono	Technical assistance (statistics)	TORG
Jubaedi	Technical assistance (data management)	WHO Indonesia
M. Bintari Dwihardiani	Technical assistance (survey advisor)	WHO Indonesia
Ikushi Onozaki	Technical assistance (survey advisor)	WHO headquarters
Irwin Law	Technical assistance (survey advisor)	WHO headquarters
Marina Tadolini	Technical assistance (survey advisor)	Consultant, Italy
Charalampos Sismanidis	Technical assistance (analysis)	WHO headquarters
Philippe Glaziou	Technical assistance (analysis)	WHO headquarters

Survey organization and financing

Implementing agency:
National Institute of Health Research and Development

Finance	Amount (US$)
The Global Fund	4 241 005
TB Care 1	379 576
Total budget	4 620 581

Data sources

- Indonesia Tuberculosis Prevalence Survey 2013–2014. Ministry of Health, Republic of Indonesia; National Institute of Health Research and Development; in collaboration with Directorate General of Disease Control and Environment Health; 2015.

[a] The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Survey design and methodology

Sampling design	
Sampling frame	Whole country
Sampling design	Multistage cluster sampling using PPS
Strata	Urban/rural Three geographical regions (Sumatra, Java-Bali and others)
Sampling unit	Geographical region/village/census block
Sample size assumptions	
• Smear-positive prevalence	156 per 100 000 (≥15 years)
• Precision	0.2
• Design effect	1.5
• *k*	0.8
• Response rate	85%
• Sample size (estimated)	78 000
Number of clusters	156
Cluster size	500
Eligibility criteria	
• Age	≥15 years
• Residency	Individuals who lived in the household for at least one month prior to the census

Screening criteria	
Interview	Cough ≥2 weeks and/or haemoptysis
Chest X-ray[a]	Any lung or pleura abnormality
Other	Chest X-ray exempted with any TB symptoms[b]

[a] Direct digital radiography (portable).
[b] Cough, haemoptysis, fever, chest pain, night sweats, loss of appetite, shortness of breath.

Laboratory methodology	
Smear	Two samples (spot, morning): direct preparation, ZN
Culture	Two samples (spot, morning) for 52 clusters, one sample (morning) for 104 clusters: concentrated preparation, LJ media
Identification of MTB	MPT64 rapid test, niacin test
TB drug susceptibility test	Not done
Xpert® MTB/RIF	Done for smear-positive and non-conclusive culture samples
HIV test	Not done

Analysis and reporting

Field data collection	Paper/electronic
Database	Microsoft® Access
Method of analysis	MI+IPW
Results first published in a report/paper	September 2015
Official dissemination event	October 2014

Key survey results

Prevalence[a]	Smear-positive TB		Bacteriologically confirmed TB	
	Number per 100 000 population	95% CI	Number per 100 000 population	95% CI
Total	257	210–303	759	590–961
Male	393	315–471	1 083	873–1 337
Female	131	88–174	461	354–591
15–24 years	138	77–198	361	254–495
25–34 years	240	156–324	753	562–995
35–44 years	265	171–359	714	527–941
45–54 years	272	166–377	836	609–1 108
55–64 years	319	174–463	1 030	734–1 399
≥65 years	528	292–763	1 582	1 123–2 154
Urban	282	220–345	846	678–1 048
Rural	231	163–300	674	512–874

[a] Age ≥15 years unless otherwise specified.

	Design effect	*k*
Smear-positive TB	1.6	0.7
Bacteriologically confirmed TB	1.8	0.5

Other sputum results	Number	%
Total smear-positive participants	291	–
Smear-positive participants without MTB confirmation[a]	126	43
Isolates with MDR-TB detected	N/A	N/A

[a] This includes culture with no evidence of MTB (i.e. culture-negative, NTM, contaminated, N/A) and Xpert-negative.

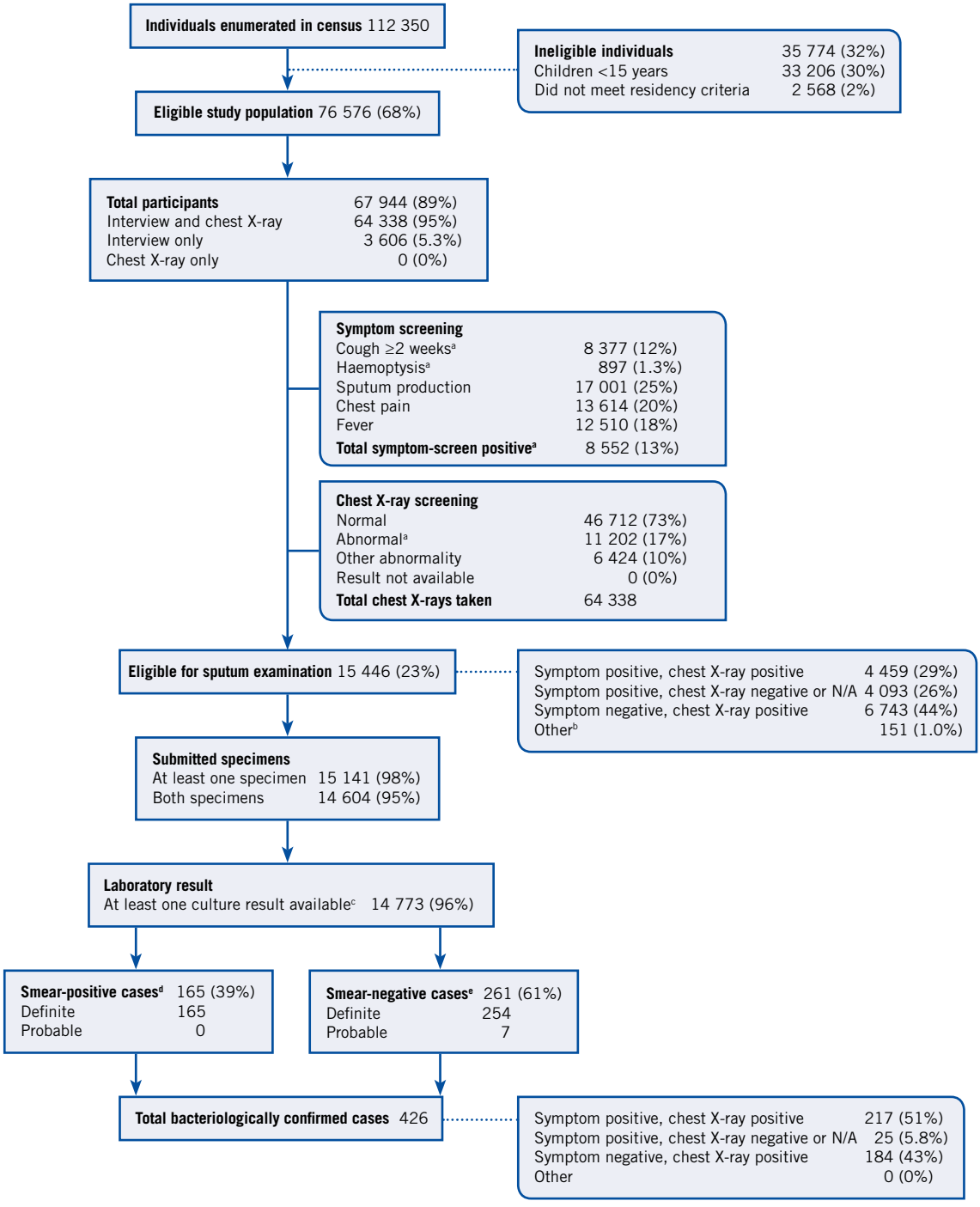
Health-care seeking behaviour among participants who were symptom-screen positive	Number	%
Participants who were symptom-screen positive[a]	8 552	–
Location of care sought		
• Consulted medical facility	2 231	26
Public facility	*1 178*	*53*
Private facility	*672*	*30*
Other[b]	*381*	*17*
• Pharmacy, shop	2 636	31
• Traditional centre	N/A	N/A
Self-treated	N/A	N/A
No action taken	3 685	43
Unknown	N/A	N/A

[a] Cough ≥2 weeks and/or haemoptysis.
[b] Nurse or midwife consultation.

Survey participants currently on TB treatment	Number	%
Total participants currently on TB treatment	125	–
• Treated in the public sector	68	54
• Treated in the private sector	52	42
• Treated in other sector	5	4.0
Bacteriologically confirmed TB cases detected by the survey who were currently on TB treatment	18	4.2

Survey flow: census to final outcomes

Field operations: April 2013 to June 2014



[a] Eligible for sputum collection.
[b] 151 pregnant women reported at least one of following TB symptoms: cough, haemoptysis, fever, chest pain, night sweats, loss of appetite, shortness of breath.
[c] Cultures that were either contaminated and/or missing without a definitive result (i.e. MTB, NTM, negative) were excluded.
[d] Definite: MTB confirmed by culture and/or Xpert. Probable: MTB not confirmed by culture and/or Xpert but chest X-ray suggestive of TB.
[e] Definite: MTB confirmed by culture and/or Xpert. Probable: For six out of seven, cultures were identified by niacin but not MPT64, with chest X-ray suggestive of TB. One case was a pregnant participant who was Xpert-positive, but whose culture specimen was contaminated.

Fig. 1: Participation rate by age and sex

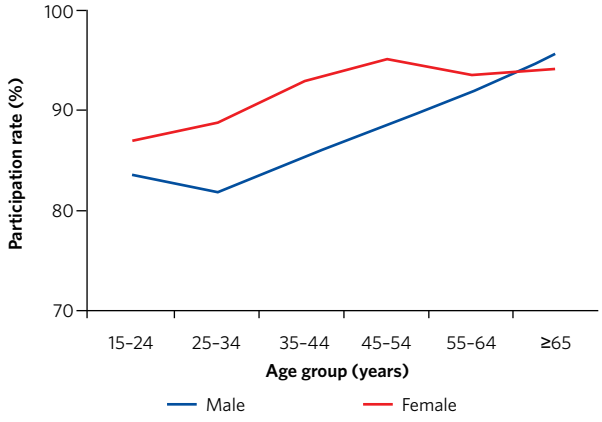


Fig. 2: TB prevalence per 100 000 population by age

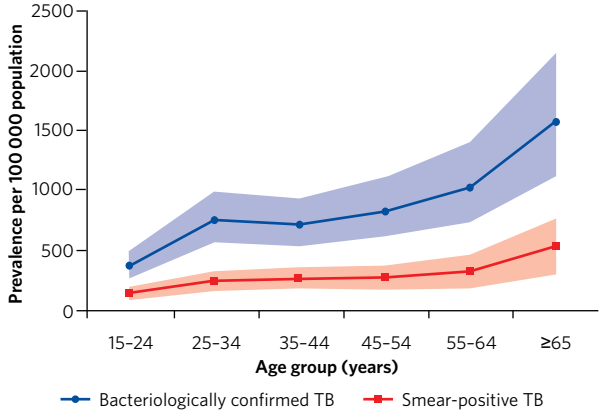


Fig. 3: Estimated number of bacteriologically confirmed TB cases and prevalence per 100 000 population, by age[a]

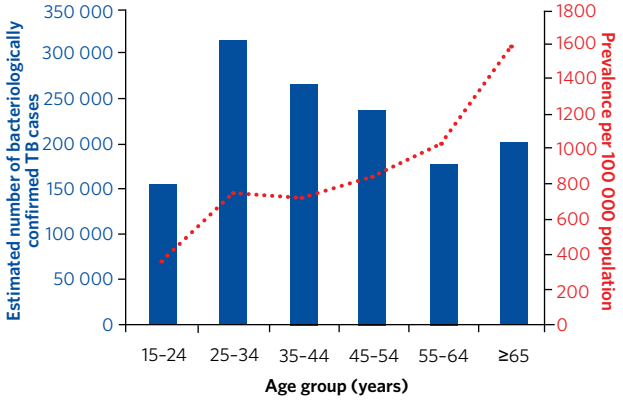


Fig. 4: Cluster variation of the number of bacteriologically confirmed TB cases[b]

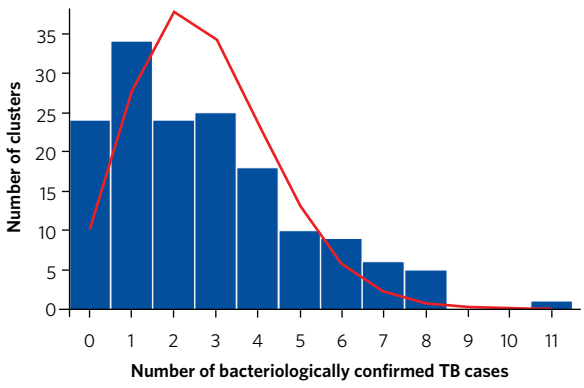


Fig. 5: Ratio of smear-positive TB prevalence to notifications by age and by sex[c]

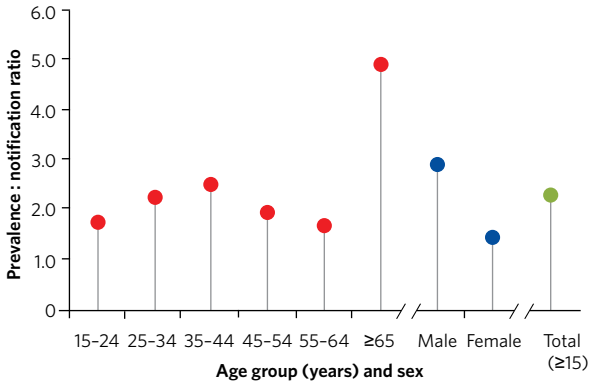
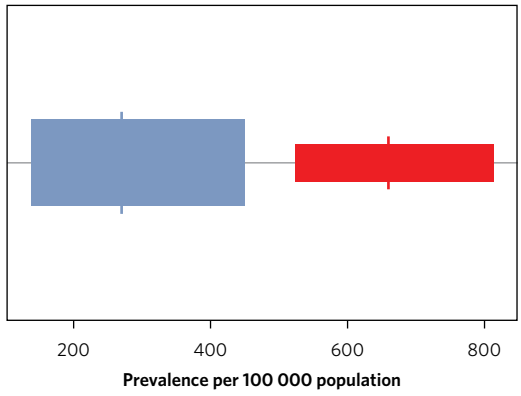


Fig. 6: Estimates of TB prevalence (all ages, all forms of TB) before (in blue) and after (in red) the national TB prevalence survey[d]



[a] The estimated number of bacteriologically confirmed TB cases is the product of age-specific prevalence and population estimates from the UN Population Division (2015 revision).

[b] The data suggested that the distribution of cases by cluster (blue bars) was significantly different from the theoretical distribution (red line) (mean 2.73, variance 5.09, $p<0.05$). The theoretical distribution assumes cases are distributed at random i.e. no clustering effect.

[c] Notification rates were estimated using smear-positive pulmonary TB notifications (2013) obtained from the NTP, and population estimates from the UN Population Division (2015 revision).

[d] The blue bar denotes the best estimate of prevalence and its range that was indirectly derived from the estimate of incidence previously published by WHO, adjusted to the year of the prevalence survey based on previously published trends in incidence.

Background

Indonesia's population was 251 million in 2013, making it the third most populous country in the world after China and India. In 2013, the average gross national income (GNI) per person was US$ 3740, making Indonesia an upper-middle-income country *(1)*. During the Millennium Development Goal (MDG) era (2000–2015), it consistently ranked among the top five countries in the world in terms of the estimated number of tuberculosis (TB) cases per year. It was one of the 22 high tuberculosis (TB) burden countries (HBCs) defined by WHO as a top priority for global efforts in TB control in 1998 and throughout the Millennium Development Goal (MDG) era (2000–2015), and one of the top 30 HBCs defined by WHO for the period 2016–2020. In 2013, the prevalence of HIV in the general population aged 15–49 years was 0.4% (95% confidence interval [CI]: 0.4–0.5%) *(2)*, and it was estimated that 4.7% (95% CI: 2.7–7.2%) of TB patients were coinfected with HIV *(3)*.

National TB control efforts started around 1970, with TB diagnosis and treatment in primary health-care facilities providing the backbone of the national TB programme (NTP). Indonesia adopted the WHO-recommended DOTS strategy in 1995 *(4,5)*. The estimated burden of TB disease published by WHO in 2013 included a TB incidence rate of 183 (95% CI: 164–207) per 100 000 population (equivalent to about 0.5 million cases per year), a TB prevalence of 272 (95% CI: 138–450) per 100 000 population (equivalent to a best estimate of 680 000 cases) and a TB mortality rate of 25 (95% CI: 14–37) per 100 000 population. These estimates drew on notification data and a national TB prevalence survey conducted in 2004. However, the 2004 prevalence survey used a screening algorithm based only on symptoms (with no chest X-ray) and confirmation of TB using smear alone (without culture). In addition, the gap between notifications and incidence (which reflects underdiagnosis and underreporting of detected cases) was hard to quantify. It was recognized that many health facilities were detecting TB cases but not notifying them to national authorities *(6,7)*.

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Given these limitations, and the size of the estimated TB burden as a proportion of the global total, Indonesia was one of the 22 global focus countries for a national TB prevalence survey selected by the WHO Global Task Force on TB Impact Measurement in December 2007. In Indonesia, it was also recognized that a national TB prevalence survey – adopting the 2011 WHO recommendations for screening and diagnostic methods *(8)* – would improve estimates of the burden of TB disease in the country. Survey planning started in January 2011, and the survey was implemented from April 2013 to June 2014.

Key methods and results

There were 156 clusters in three geographical strata (Sumatra, Java-Bali and others) and two population strata (urban and rural), with a target cluster size of 500 individuals. A total of 112 350 individuals from 34 947 households were enumerated in the survey census, of whom 76 576 (68%) were eligible and invited to participate. Of these, 67 944 (89%) did so. All participants were screened according to the 2011 algorithm recommended by WHO; that is, using chest X-ray and an interview about symptoms *(8)*. A total of 15 446 participants (23%) were eligible for sputum examination, of whom 15 141 (98%) submitted at least one sputum specimen and 14 604 (95%) submitted two sputum specimens.

A total of 426 bacteriologically confirmed pulmonary TB cases was identified, including 165 (39%) cases of smear-positive TB. The prevalence of smear-positive TB was 257 (95% CI: 210–303) per 100 000 population (among those aged ≥15 years), and for bacteriologically confirmed TB it was 759 (95% CI: 590–961) per 100 000 population. The prevalence of bacteriologically confirmed TB was higher in urban areas (846 per 100 000 population; 95% CI: 678–1048) than in rural areas (674 per 100 000 population; 95% CI: 512–874), and higher in Sumatra (913 per 100 000 population; 95% CI: 697–1177) and other regions (842 per 100 000 population; 95% CI: 635–1092) than in Java-Bali (593 per 100 000 population; 95% CI: 447–771).

Other key results were:

- the male to female ratio was 3.0 for smear-positive TB and 2.3 for bacteriologically confirmed TB;
- prevalence per 100 000 population increased with age; however, the absolute number of bacteriologically confirmed TB cases was relatively high in the young and middle-age groups (25–54 years);
- among bacteriologically confirmed TB cases, 57% were symptom-screen positive, and among smear-positive cases, 70% were symptom-screen positive;
- for smear-positive pulmonary TB, the ratio of prevalence to notifications (P:N ratio) was 2.3 overall, but varied from 1.7 in those 55–64 years to 4.9 in those aged 65 years or more, and was higher for men than for women (2.9 versus 1.4);
- among bacteriologically confirmed TB cases, 86% had no previous history of anti-TB treatment, and only 4.2% were on anti-TB treatment at the time of the survey;
- of the 225 bacteriologically confirmed and 101 smear-positive TB survey cases that screened positive for symptoms and were not on anti-TB treatment at the time of the survey, 147 (65%) and 38 (38%), respectively, had previously sought care in a public or private health facility for their symptoms; and
- only 20% of participants reported to be on anti-TB treatment were in the national TB electronic register (SITT); and this was also confirmed by the high level of under-reporting (41%) documented in the 2017 national inventory study (*9*).

Implications of results

The estimated TB prevalence of 660 (95% CI: 523–813) per 100 000 population (all forms of TB and all ages) based on the survey was much higher than the previous WHO estimate of 272 (95% CI: 138–450) per 100 000 population. TB incidence was re-estimated at 399 (95% CI: 274–546) per 100 000 population, equivalent to one million new cases per year and double the pre-survey estimate. The TB mortality rate was estimated at 41 (95% CI: 26–59) per 100 000 population, equivalent to 100 000 deaths per year *(10)*. The new estimates were used as the basis for the National TB Strategic Plan 2015–2019 and for a proposal to the Global Fund to Fight AIDS, Tuberculosis and Malaria.

Other implications included:

- a need for TB case notification to be legally mandated with enforcement to address the underreporting of detected TB cases. Regulations, tools, implementation guidelines,

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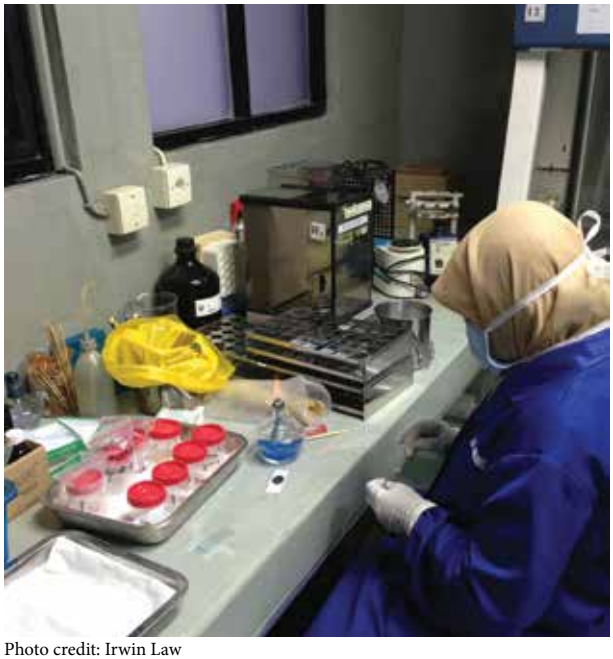
supervision mechanisms, and monitoring and evaluation tools should be prepared for this purpose;

- a need for intensified case finding for TB, which has since become one of the major strategies of the NTP;
- a need for improved access to health facilities, including via provision of universal health insurance, so that symptomatic individuals would be more likely to seek immediate treatment;
- a need for the general population to be made more aware that anti-TB treatment in standard health facilities is free of charge, to encourage people to seek care promptly;
- a need to use chest X-rays more widely, to improve case detection; for example, as part of community outreach or among key populations, such as prisoners, people living with HIV, people with comorbidities and the elderly;
- a need to increase the number of qualified laboratories to improve access to, and the speed of, diagnosis, especially in rural areas where geographical barriers hinder the rapid delivery of specimens to referral laboratories;
- a need for the NTP to implement innovative strategies to supervise TB service quality in all health facilities, including those in the private sector;
- a need to understand that a positive smear result should not be the basis for providing anti-TB treatment (especially in the context of active case finding in the community rather than in a clinic) given the low positive predictive value of smear microscopy without confirmatory testing, compared with culture; and
- a need for increased funding to implement all of the policy and programmatic measures listed above, especially given the major finding of the survey that the burden of TB disease was double the level previously estimated.



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Major successes, challenges and lessons learned

The overarching major success was that the survey was successfully implemented with high quality and a high participation rate, and that it was the first in the country for decades to include chest X-ray screening combined with diagnosis using culture as well as smear microscopy.

Several major challenges included those listed below.

- The procurement process for chest X-ray equipment was slow. It took 18 months and delayed the start of the survey. Subsequently, setting up and using the chest X-ray equipment in the field generated some problems with data collection. These were partly alleviated by the availability of in-country servicing of the equipment, which facilitated timely repairs and troubleshooting.
- Collecting and processing sputum specimens was demanding, and some contamination of specimens occurred. Morning specimens had higher rates of contamination (431 [3%] of 14 569 specimens) than spot specimens (47 [1%] of 4433).
- Culture failed to grow in some settings, perhaps because of geographical challenges (e.g. poor road conditions and the difficulty of maintaining a cold chain in the context of high temperatures and humidity), poor sample handling and the limited number of laboratories.
- The quality of laboratories may have varied, even though laboratory experts evaluated and validated the performance quality of the laboratories used in the survey.
- Limited culture capacity meant that it was only possible to culture two specimens for every participant who submitted sputum samples in one third of survey clusters; in the remaining survey clusters, only one specimen was cultured. To mitigate this problem, Xpert MTB/RIF was used when culture failed (e.g. from contamination in all tubes).

- It took time for the updated estimates of TB disease burden to be officially accepted at the higher levels of the Ministry of Health (MoH). Thus, although events to disseminate results were held in October 2014 (shortly after field operations were completed), acceptance of results and publication of the survey report were delayed. After further discussions and briefings, the updated disease burden estimates were agreed in July 2015, and the survey report was published in September 2015.

There were also some more minor challenges:

- field operations in a few clusters were delayed by forest fires and volcanic activity; and
- the participation rate was low in urban clusters, especially in economically wealthy areas in large cities. Most of the residents in these areas already had good access to health services, including annual health screening with chest X-ray, so the X-ray screening offered as part of the survey provided no incentive to participate.

Important lessons learned for future surveys included:

- even if the NTP or MoH is not directly involved in survey implementation, it is still important to ensure their involvement and ownership throughout the process, from design to dissemination of results. This facilitates survey implementation and rapid uptake and use of results;
- although prior prevalence surveys can be used to help assess trends in TB disease burden, this is challenging when previous surveys have used different (and less sensitive) screening and diagnostic methods; and
- to maintain high-quality laboratory services throughout the survey, laboratories need to be standardized and monitored frequently.

References

1. The World Bank (https://data.worldbank.org/country, accessed April 2017).
2. UNAIDS (http://aidsinfo.unaids.org/, accessed April 2017).
3. World Health Organization. Global Tuberculosis Database. 2017. (http://www.who.int/tb/country/en/, accessed April 2017).
4. WHO Tuberculosis Programme. (1994). WHO Tuberculosis Programme: framework for effective tuberculosis control. World Health Organization. (http://www.who.int/iris/handle/10665/58717, accessed January 2018).
5. World Health Organization. Global tuberculosis programme. Global tuberculosis control report 1997. Geneva: WHO; (https://apps.who.int/iris/bitstream/handle/10665/63354/WHO_TB_97.225_(part1).pdf?sequence=1, accessed January 2018).
6. Indonesia Tuberculosis Prevalence Survey 2013–2014. Ministry of Health, Republic of Indonesia; National Institute of Health Research and Development; in collaboration with Directorate General of Disease Control and Environment Health; 2015.
7. Tuberculosis Prevalence Survey in Indonesia 2004. National Institute of Health Research and Development, Ministry of Health- Republic of Indonesia; Jakarta, Indonesia; 2005.
8. World Health Organization. Tuberculosis prevalence surveys: a handbook (WHO/HTM/TB/2010.17). Geneva: WHO; 2011 (https://apps.who.int/iris/bitstream/handle/10665/44481/9789241548168_eng.pdf, accessed August 2017).
9. World Health Organization. Global tuberculosis report 2018. Geneva: WHO; 2018; (http://apps.who.int/iris/bitstream/handle/10665/274453/9789241565646-eng.pdf, accessed December 2018).
10. World Health Organization. Global tuberculosis report 2015. Geneva: WHO; 2015; (http://apps.who.int/iris/bitstream/10665/191102/1/9789241565059_eng.pdf, accessed January 2018).

KENYA

2015–2016

Summary statistics

Participation rate	83%
Bacteriologically confirmed TB (≥15 years)	
• Prevalence per 100 000 population	558
• Male:female ratio	2.3
Prevalence:notification ratio (Bacteriologically confirmed TB, ≥15 years)	3.5

Surveyed clusters (N=99)[a]

Key people

Name	Role	Organization
Joseph Sitienei	Principal investigator (PI)	National Tuberculosis, Leprosy and Lung Disease Program (NTLD-P)
Hillary Kipruto	Co-PI	WHO Kenya
Jane Ong'ang'o	Co-PI & study coordinator	Kenya Medical Research Institute
Bernard Langat	Co-investigator	NTLD-P
Enos Masini	Co-investigator	NTLD-P
Margaret Ndisha	Co-investigator	NTLD-P
Faith Ngari	Co-investigator	NTLD-P
Obadiah Njuguna	Co-investigator	NTLD-P
Janet Agaya	Co-investigator	Kenya Medical Research Institute
Jeremiah Chakaya	Co-investigator	Kenya Medical Research Institute
Joel Kangangi	Co-investigator	WHO Kenya
Maurice Maina	Co-investigator	United States Agency for International Development (USAID)
Brenda Mungai	Co-investigator	Centre for Health Solutions, Kenya
Rose Mwirigi	Co-investigator	National Tuberculosis Reference Laboratory
Anja Vant'Hoog	Co-investigator	Academic Medical Centre of the University of Amsterdam
Josephine Wahogo	Co-investigator & laboratory manager	National Tuberculosis Reference Laboratory
Veronica Manduku	Co-investigator & lead radiologist	Kenya Medical Research Institute
Geoffrey Okallo	Data management team leader	NTLD-P
Richard Kiplimo	Data manager	NTLD-P
Amos Ndombi	Data manager	NTLD-P
Dickson Kirathe	IT manager	NTLD-P
Martin Githiomi	IT officer	NTLD-P
Drusilla Nyaboke	Logistician	NTLD-P
Maureen Kamene Kimenye	Member of report writing committee	NTLD-P
Janice Njoroge	Communication specialist	Centre for Health Solutions, Kenya
James Ng'ang'a	Statistician	Kenya National Bureau of Statistics
Emily Bloss	Technical assistance (survey advisor)	US Centers for Disease Control and Prevention (CDC)
Martien W. Borgdorff	Technical assistance (survey advisor)	US Centers for Disease Control and Prevention (CDC) Kenya
Kevin Cain	Technical assistance (survey advisor)	US Centers for Disease Control and Prevention (CDC) Kenya
Julia Ershova	Technical assistance (survey advisor)	US Centers for Disease Control and Prevention (CDC)
Irwin Law	Technical assistance (survey advisor)	WHO headquarters
Wilfred Nkhoma	Technical assistance (survey advisor)	WHO Regional Office for Africa (AFRO)
Marina Tadolini	Technical assistance (survey advisor)	Consultant, Italy
Sayori Kobayashi	Technical assistance (data management)	WHO headquarters
Hazim Timimi	Technical assistance (data management)	WHO headquarters

Survey organization and financing

Implementing agency:

National Tuberculosis, Leprosy and Lung Disease Program

Finance	Amount (US$)
The Global Fund/USAID TB ARC	30 627
The Global Fund	4 530 712
USAID	491 892
WHO/USAID	121 612
Total budget	5 174 843

Data sources

- Kenya Tuberculosis Prevalence Survey 2016, Survey Report. National Tuberculosis, Leprosy and Lung Disease Program, Ministry of Health, Republic of Kenya; 2018 (https://www.nltp.co.ke/survey-reports-2/).
- Survey dataset.

[a] The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Survey design and methodology

Sampling design	
Sampling frame	Whole country
Sampling design	Multistage cluster sampling using PPS
Strata	Urban/rural
Sampling unit	Urban, rural/enumeration area
Sample size assumptions	
• Smear-positive prevalence	269 per 100 000 (≥15 years)
• Precision	0.2
• Design effect	1.7
• *k*	0.6
• Response rate	85%
• Sample size (estimated)	72 000
Number of clusters	100[a]
Cluster size	720
Eligibility criteria	
• Age	≥15 years
• Residency	Residents who lived in the selected cluster for at least 30 consecutive days prior to the census

[a] One cluster in Mandera was cancelled due to a security issue.

Screening criteria	
Interview[a]	Cough ≥2 weeks
Chest X-ray[b]	Any lung abnormality
Other	Chest X-ray exempted

[a] An in-depth interview about health-care seeking behaviour was done for all participants who reported any TB symptoms (cough, sputum production, haemoptysis, chest pain, fever, fatigue, night sweats, weight loss, shortness of breath).
[b] Direct digital radiography.

Laboratory methodology	
Smear	Two samples (spot, morning): direct preparation, FM (LED, auramine stain)
Culture	Two samples (spot, morning): concentrated preparation, LJ media
Identification of MTB	MPT64 rapid test
TB drug susceptibility test	Done
Xpert® MTB/RIF	Done for all morning samples and spot samples lacking a matching morning sample.
HIV test	HIV status was verbally obtained from participants. For prevalent TB cases, it was also obtained from the TB electronic and reporting system.

Analysis and reporting

Field data collection	Paper[a]/electronic
Database	SQL
Method of analysis	MI+IPW
Results first published in a report/paper	March 2018
Official dissemination event	March 2017

[a] The team used paper for field data collection throughout field operations in one cluster, due to the breakdown of the electronic system.

Key survey results

Prevalence[a]	Smear-positive TB		Bacteriologically confirmed TB	
	Number per 100 000 population	95% CI	Number per 100 000 population	95% CI
Total	230	174–286	558	455–662
Male	346	260–431	809	656–962
Female	138	79–196	359	258–460
15–24 years	218	133–303	360	242–478
25–34 years	259	164–353	716	526–906
35–44 years	297	164–430	602	422–782
45–54 years	234	101–367	607	432–781
55–64 years	118	24–211	587	372–803
≥65 years	125	24–226	576	368–783
Urban	335	213–456	760	539–981
Rural	175	126–224	453	357–549

[a] Age ≥15 years unless otherwise specified.

	Design effect	*k*
Smear-positive TB	1.8	0.7
Bacteriologically confirmed TB	2.5	0.7

Other sputum results	Number	%
Total smear-positive participants	141	–
Smear-positive participants without MTB confirmation[a]	18	13
Isolates with MDR-TB detected[b]	6	2.7

[a] This includes culture with no evidence of MTB (i.e. culture-negative, NTM, contaminated, N/A) and Xpert-negative.
[b] DST was conducted for 225 participants.

Health-care seeking behaviour among participants who were symptom-screen positive	Number	%
Participants who were symptom-screen positive[a]	4 137	–
Location of care sought[b]	1 257	30
• Consulted medical facility		
Public facility	*1047*	–
Private facility	*198*	–
Other	*3*	–
• Pharmacy	56	–
• Traditional healer	9	–
No action taken	2 763	67
Unknown	117	2.8

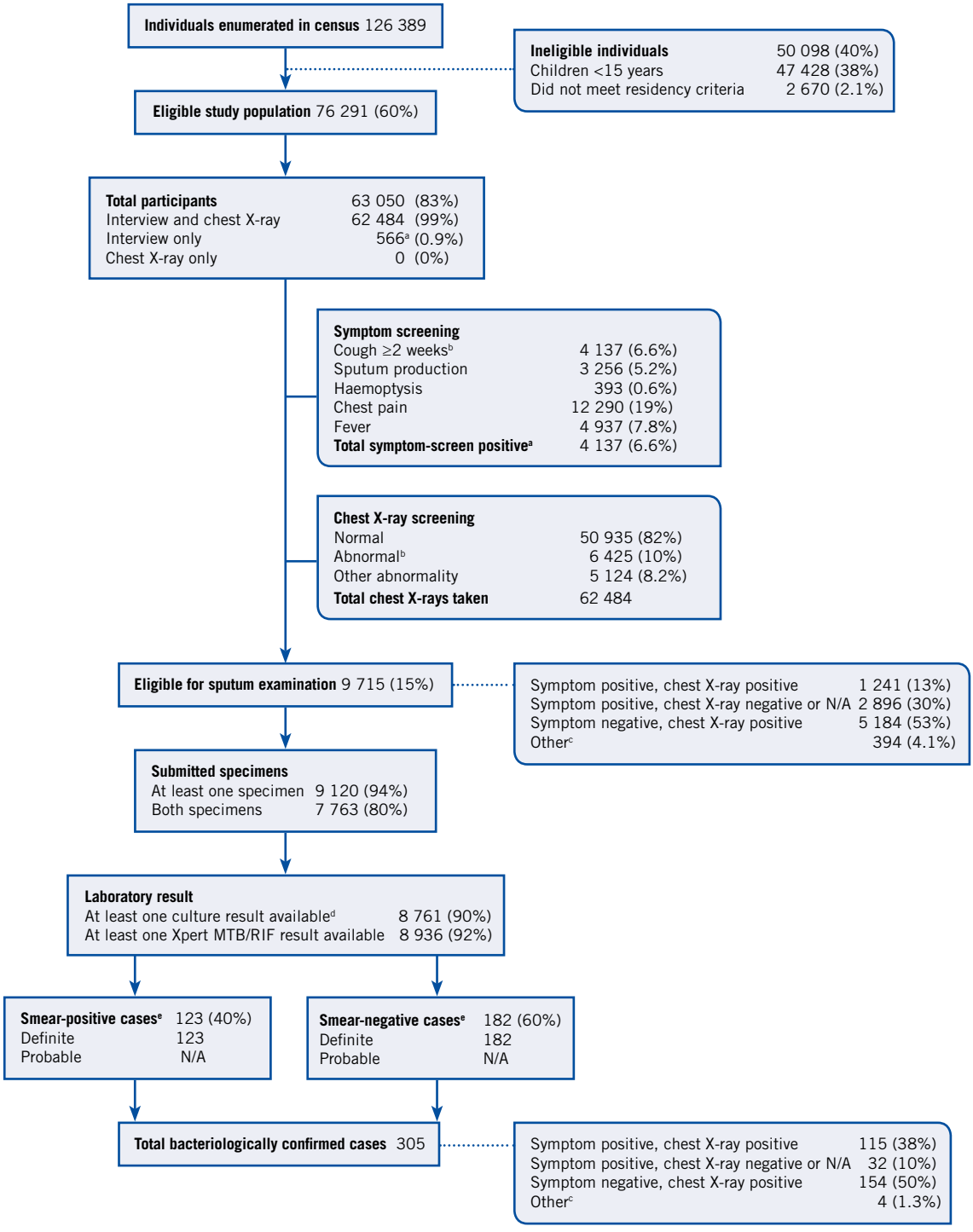
[a] Cough ≥2 weeks.
[b] The subtotals do not add up to 1257 because participants could select more than one category.

Survey participants currently on TB treatment	Number	%
Total participants currently on TB treatment[a]	62	–
• Treated in the public sector	23	37
• Treated in the private sector	0	0
• Treated in other sector	1	1.6
• Treated in unknown sector	38	61
Bacteriologically confirmed TB cases detected by the survey who were currently on TB treatment	15	4.9

[a] Data were available only for participants who were eligible for sputum submission.

Survey flow: census to final outcomes

Field operations: August 2015 to July 2016



[a] 429 participants declined a chest X-ray, and 137 participants did not have a chest X-ray due to malfunctioning X-ray machines.
[b] Eligible for sputum collection.
[c] Chest X-ray exempted and symptom-screen negative.
[d] Cultures that were either contaminated and/or missing without a definitive result (i.e. MTB, NTM, negative) were excluded.
[e] Definite: MTB confirmed by culture and/or Xpert. Probable: no definition.

Fig. 1: Participation rate by age and sex

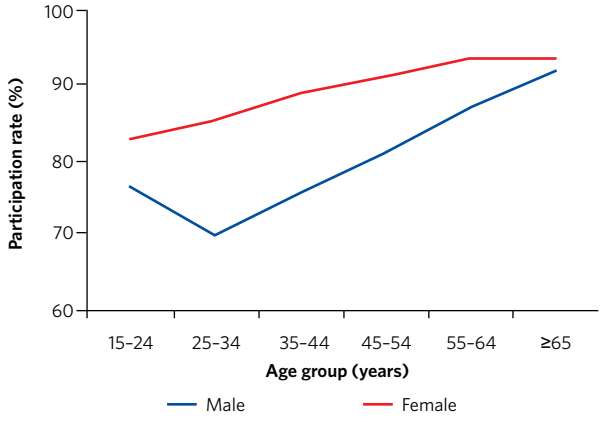


Fig. 2: TB prevalence per 100 000 population by age

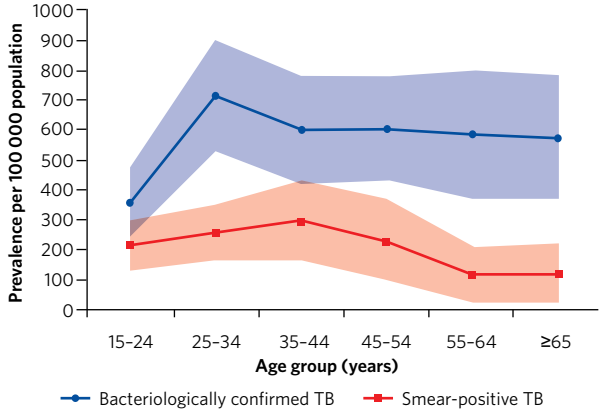


Fig. 3: Estimated number of bacteriologically confirmed TB cases and prevalence per 100 000 population, by age[a]

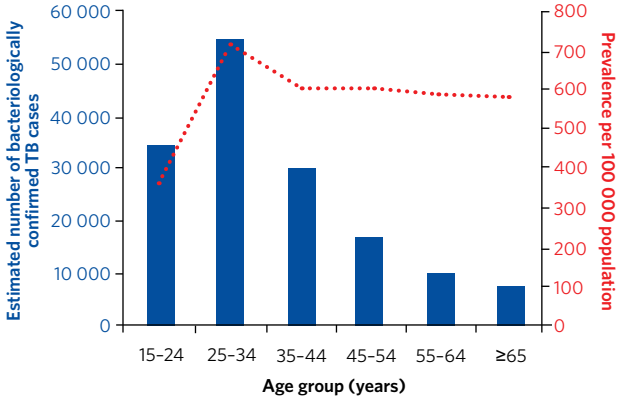


Fig. 4: Cluster variation of the number of bacteriologically confirmed TB cases[b]

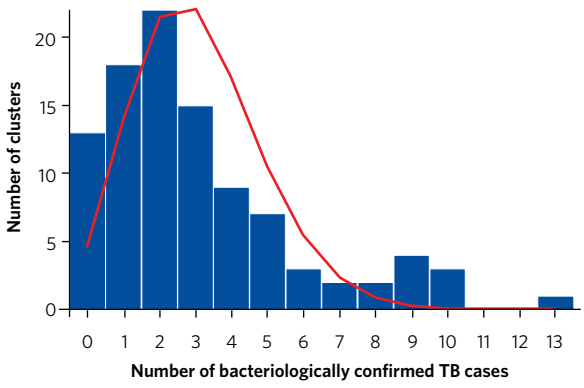


Fig. 5: Ratio of bacteriologically confirmed TB prevalence to notifications by age and by sex[c]

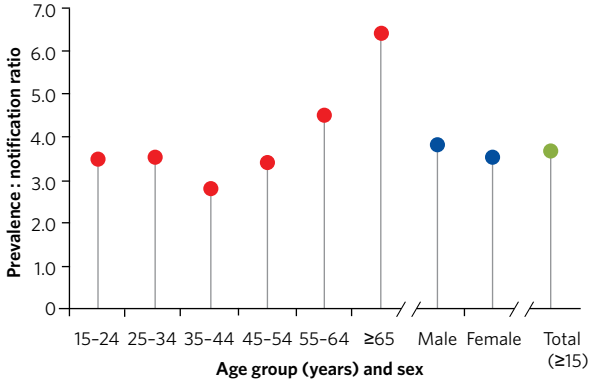
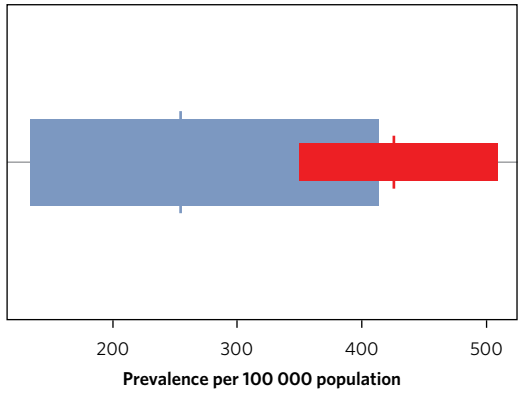


Fig. 6: Estimates of TB prevalence (all ages, all forms of TB) before (in blue) and after (in red) the national TB prevalence survey[d]



[a] The estimated number of bacteriologically confirmed TB cases is the product of age-specific prevalence and population estimates from the UN Population Division (2015 revision).

[b] The data suggested that the distribution of cases by cluster (blue bars) was significantly different from the theoretical distribution (red line) (mean 3.08, variance 7.63, $p<0.05$). The theoretical distribution assumes cases are distributed at random i.e. no clustering effect.

[c] Notification rates were estimated using bacteriologically confirmed pulmonary TB notifications (2015) obtained from the NTP, and population estimates from the UN Population Division (2015 revision).

[d] The blue bar denotes the best estimate of prevalence and its range that was indirectly derived from the estimate of incidence previously published by WHO, adjusted to the year of the prevalence survey based on previously published trends in incidence.

Background

Kenya had a population of 47 million in 2015. The average gross national income (GNI) per person was US$ 1310 per year, making it a low-income country *(1)*. It was one of the 22 high tuberculosis (TB) burden countries (HBCs) defined by WHO as a top priority for global efforts in TB control in 1998 and throughout the Millennium Development Goal (MDG) era (2000–2015), and one of the top 30 HBCs defined by WHO for the period 2016–2020.

Kenya's TB notification rate (new and relapse cases) increased from 50 per 100 000 population in 1990 to 287 per 100 000 population in 2005, then slowly decreased to 194 per 100 000 population in 2014. WHO estimates of TB incidence and prevalence in 2014 were 246 (95% confidence interval [CI]: 240–252) per 100 000 population and 266 (95% CI: 142–427) per 100 000 population, respectively *(2)*.

Like many other sub-Saharan African countries, from the mid-1980s Kenya was severely affected by the HIV/AIDS epidemic. From the mid-2000s, large investments in TB/HIV collaborative activities resulted in a high proportion (>90%) of TB patients knowing their HIV status, and high uptake of antiretroviral therapy among coinfected patients. An integrated TB/HIV data collection system was implemented in Kenya in 2005, enabling the collection of HIV-related information as a standard part of TB diagnosis and treatment. The prevalence of HIV among TB patients with an HIV test result was 57% in 2005, declining to 39% in 2012 *(2)*. In 2015, the prevalence of HIV in the general population aged 15–49 years was 5.6% (95% CI: 4.9–6.3%) *(3)*, and it was estimated that 33% (95% CI: 32–35%) of TB patients were coinfected with HIV *(4)*.

Photo credit: Irwin Law

A national TB prevalence survey (excluding the northern province and Nairobi) was implemented in Kenya in 1958–1959. As part of this survey, a tuberculin skin test was done for the whole population except infants aged under 1 month, and chest X-ray and bacteriological examinations (smear and culture) were done for all participants aged 10 years or more. The survey found a prevalence of approximately 3100 per 100 000 population, equivalent to 110 000 cases in the population of 3.5 million aged 10 years or more *(5, 6)*.

In December 2007, Kenya was one of the 22 global focus countries for a national TB prevalence survey that was selected by the WHO Global Task Force on TB Impact Measurement. In 2009, the Ministry of Health and the National Tuberculosis, Leprosy and Lung Disease Program (NTLD-P) decided to implement a second national TB prevalence survey. The survey started in July 2015 and was completed in July 2016 *(6)*.

Key methods and results

There were 99 survey clusters in two strata (urban and rural), with a target cluster size of 720 individuals. A total of 126 389 individuals from 31 955 households were enumerated in the survey census, of whom 76 291 (60%) were eligible and invited to participate. Of these, 63 050 (83%) did so. All participants were screened according to the 2011 algorithm recommended by WHO; that is, using a chest X-ray and an interview about symptoms *(7)*. A total of 9715 participants (15%) were eligible for sputum examination; of these, 9120 (94%) submitted at least one sputum specimen and 7763 (80%) submitted two sputum specimens. This was one of the first surveys to test all screen-positive participants with both culture and Xpert® MTB/RIF.

Valid Xpert MTB/RIF results were available for 8936 participants. Of these, 237 (2.7%) were Xpert positive for *Mycobacterium tuberculosis*, and six (2.5% of 237) were also rifampicin (RIF) resistant. Of 305 bacteriologically confirmed TB cases, 147 (48%) were confirmed by both culture and Xpert MTB/RIF, 68 (22%) were positive only by culture, and 90 (30%) were positive only by Xpert MTB/RIF.

A total of 305 bacteriologically confirmed pulmonary TB cases were identified, including 123 (40%) cases of smear-positive TB. The prevalence of smear-positive TB was 230 (95% CI: 174–286) per 100 000 population (among those aged ≥15 years), and for bacteriologically confirmed TB it was 558 (95% CI: 455–662) per 100 000 population. Prevalence rates for smear-positive and bacteriologically confirmed TB were higher in urban areas than in rural areas.

Other key results were:

- the male to female ratio was 2.5 for smear-positive TB and 2.3 for bacteriologically confirmed TB;
- the prevalence per 100 000 population was high for people aged 25 years or more, with a peak in those aged 25–34 years; the absolute number of bacteriologically confirmed TB cases in those aged under 45 years was relatively high;
- among bacteriologically confirmed TB cases, 48% were symptom-screen positive, and among smear-positive TB cases, 69% were symptom-screen positive;
- for bacteriologically confirmed TB, the ratio of prevalence to notifications (P:N ratio) was 3.5 overall, but varied from 2.8 in those aged 35–44 years to 6.4 in those aged 65 years or more, and was slightly higher for men than women (3.8 versus 3.5); these findings were consistent with the 2013 TB inventory study, which found a high level of under-reporting (21%) of smear-positive TB cases especially in those over 55 years of age (*8*);
- among bacteriologically confirmed TB cases, 72% had no previous history of anti-TB treatment and only 4.9% were on anti-TB treatment at the time of the survey; and
- of the 139 bacteriologically confirmed and 52 smear-positive TB survey cases that screened positive for symptoms and were not on anti-TB treatment at the time of the survey, 52 (37%) and 34 (43%), respectively, had previously sought care in a public or private health facility for their symptoms; this was similar to findings from a patient-pathway analysis (PPA) in 2013, in which of those who sought care, 58% and 41% respectively initially sought care in a public or private health facility (*9*); and
- although HIV testing was not done during field operations, the HIV status of bacteriologically confirmed TB cases was obtained from the national HIV electronic and reporting system; and of 305 bacteriologically confirmed TB cases, 41 (13%) were HIV-positive, 204 (67%) were HIV-negative and for 60 (20%) the status was unknown.

Implications of results

The survey showed that TB prevalence for all forms of TB and all ages, at 426 per 100 000 population (95% CI: 347–504), was significantly higher than the pre-survey estimate of 266 (95% CI: 142–427) per 100 000 population *(3)*. The burden of TB was much higher than that reported through routine surveillance, especially among men and older age groups.

The survey had several major programmatic, policy and funding implications:

- the high prevalence in younger age groups, especially among men, suggested considerable active transmission of TB in the general community;
- among confirmed TB cases, most (65%) of those with symptoms who did not seek treatment were men, consistent with greater reluctance among men to seek care for HIV (*10)*; together with the finding that men had a higher burden of TB disease, this showed a need for innovative approaches to reduce barriers to accessing care and associated delays in diagnosis and treatment for TB among men;
- among bacteriologically confirmed TB cases, more than half would have been missed if screening using the single criterion of cough of more than two weeks was relied upon; this

Photo credit: Irwin Law

suggested that the screening criteria used in routine clinical settings should be reviewed and that expanded use of chest X-ray as a screening tool should be considered;

- since more than half of the bacteriologically confirmed cases were smear-negative and were diagnosed by culture or Xpert MTB/RIF (or both), use of diagnostic tools besides smear microscopy should be expanded;
- about 70% of participants who reported a chronic cough did not seek care, even though the Kenya Demographic Health Survey of 2014 found that about 80% of those aged 15–49 years knew that TB is spread through the air by coughing (*11*); nonetheless, the general population may be unaware of the actual symptoms of TB, and consequently delay seeking care; this suggested that improving community awareness about TB symptoms as well as the availability of free TB services at public health facilities could help to improve health care seeking behaviour;
- the relatively high proportion of symptomatic cases who had sought some care before the survey but were not diagnosed with TB suggested a need to improve access to diagnostics and treatment, as well as a need to review the screening algorithm and develop strategies to improve patient awareness and health-care provider knowledge of TB symptoms; and
- the prevalence of HIV infection among bacteriologically confirmed TB cases with known HIV status (17%; 41/245[1]) was lower than that reported among notified TB cases (33%) (*12*); this suggested that while there has been a strong focus on the TB/HIV programme, a large TB burden exists among those who are HIV-negative, for which more programmatic action is required.

[1] 41 were HIV-positive and 204 were HIV-negative.

Major successes, challenges and lessons learned

The national TB prevalence survey in Kenya 2015–2016 was successfully implemented. This was the first African survey to use Xpert MTB/RIF and culture for all participants who screened positive, and despite the resulting increase in workload for the national reference laboratory, the survey demonstrated that using both tests was feasible. Good communication throughout the survey contributed to these achievements. This included high levels of community engagement (especially during visits prior to survey field operations) that fostered survey participation, and regular meetings and close collaboration between the NTLD-P, various implementing partners and technical agencies that facilitated effective project management and ownership of the final survey results.

Challenges faced during the survey, and associated lessons learned, included those listed below.

- The procurement process for digital chest X-ray machines by the WHO Regional Office for Africa was lengthy, which delayed the start of the survey by more than a year.

Photo credit: Marina Tadolini

- There was overreliance on the internet-based data management system in the field. Although electronic data collection in the field was innovative and efficient, enumeration data from the field had to be uploaded to the central server in Nairobi before other questionnaire data could be entered. For clusters that had good internet connection, this worked well, but for clusters with poor coverage, survey teams had to switch to a paper-based data collection system and were then faced with the issue of merging data from different systems. From about mid-way through field operations, development of a local area network in the field circumvented the need to upload data to the central server and improved the efficiency of electronic data management.
- There were problems in linking laboratory and field data because the laboratory health information system was different from the one used by the survey itself, and mismatching of barcodes (this typically happened when they were handwritten). It took five months from the end of field operations to complete data cleaning.
- One cluster (close to the border with Somalia) was cancelled due to security issues.
- Budgetary limitations constrained the number of central chest X-rays that could be read centrally. Initially, it was planned that all chest X-rays would be read by the central radiologists, but in practice this was limited to only specific categories of images (i.e. all those with abnormal results; 10% of normal images, as determined by the field teams; and all images with discordant findings between two field readers).

References

1. The World Bank. (https://data.worldbank.org/country, accessed January 2018).
2. World Health Organization. Global tuberculosis report 2015. Geneva: WHO; 2015 (http://apps.who.int/iris/bitstream/10665/191102/1/9789241565059_eng.pdf, accessed January 2018).
3. UNAIDS. (http://aidsinfo.unaids.org/, accessed January 2018).
4. World Health Organization. Global tuberculosis database. Geneva: WHO; 2017 (http://www.who.int/tb/data/en/, accessed January 2018).
5. Roelsgaard E, Nyboe J. A tuberculosis survey in Kenya. Bulletin of the World Health Organization. 1961;25(6):851–870 (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2555628/, accessed February 2018).
6. Kenya Tuberculosis Prevalence Survey 2016. Survey Report. National Tuberculosis, Leprosy and Lung Disease Program, Ministry of Health, Republic of Kenya; 2018 (https://www.nltp.co.ke/survey-reports-2/).
7. World Health Organization. Tuberculosis prevalence surveys: a handbook. Geneva: WHO; 2011 (https://apps.who.int/iris/bitstream/handle/10665/44481/9789241548168_eng.pdf, accessed August 2016).
8. Tollefson D, Ngari F, Mwakala M, Gethi D, Kipruto H, Cain K, Bloss E. Under-reporting of sputum smear-positive tuberculosis cases in Kenya. INt J Tuberc Lung Dis. 2016 Oct; 20(10):1334-1341.
9. Masini E, Hanson C, Ogoro J, Brown J, Ngari F, Mingkwan P, Makayova J, Osberg M. Using patient-patheway analysis to inform a differentiated program response to tuberculosis: the case of Kenya. JID 2017;216(S7):S714-23.
10. UNAIDS. Get on the Fast-Track, The life-cycle approach to HIV, 2016. (http://www.unaids.org/sites/default/files/media_asset/Get-on-the-Fast-Track_en.pdf, accessed March 2018).
11. Republic of Kenya. Demographic and Health Survey. 2014 (https://dhsprogram.com/pubs/pdf/fr308/fr308.pdf, accessed February 2018).
12. World Health Organization. Global tuberculosis report 2016. Geneva: WHO; 2016 (https://apps.who.int/iris/bitstream/handle/10665/250441/9789241565394-eng.pdf, accessed January 2018).

LAO PEOPLE'S DEMOCRATIC REPUBLIC

2010–2012

Surveyed clusters (N=50)[a]

Summary statistics

Participation rate	85%
Bacteriologically confirmed TB (≥15 years)	
• Prevalence per 100 000 population	595
• Male:female ratio	2.3
Prevalence:notification ratio (smear-positive TB, ≥15 years)	3.5

Key people

Name	Role	Organization
Phannasinh Sylavanh	Director and principal investigator	National TB Control Programme
Saveang Saisongkham	Deputy director	National TB Control Programme
Phouvang Vangvichit	Deputy director	National TB Control Programme
Soth Bounmala	Survey coordinator/field team leader	National TB Control Programme
Phonenaly Chittamany	Chief of statistics/field team leader	National TB Control Programme
Manikhone Ouanephongchaleune	Monitoring and evaluation/field team leader	National TB Control Programme
Bounkong Fongosa	Monitoring and evaluation/field team leader	National TB Control Programme
Thavone Phengsavatdy	Technical officer	National TB Control Programme
Liene Phonekeo	Finance officer	National TB Control Programme
Donekham Inthavong	Laboratory manager	National TB Control Programme
Phasouk Senephansiri	Laboratory co-manager	National TB Control Programme
Oroth Rajphol	Radiologist	Mahosot hospital, Lao People's Democratic Republic (Lao PDR)
Vongvilay Paphatsalang	Radiologist	Mahosot hospital, Lao People's Democratic Republic (Lao PDR)
Vatthana Nanthana	Country director advisor/translator	Damien Foundation, Lao People's Democratic Republic (Lao PDR)
Jacques Sebert	Medical officer	WHO Lao People's Democratic Republic (Lao PDR)
Irwin Law	Data manager/epidemiologist	National TB Control Programme
Fulgence Nzabintwali	Technical assistance/laboratory co-manager	National TB Control Programme
Phimpha Paboriboune	Scientific director	Centre d'Infectiologie Christophe Merieux du Laos
Vibol Iem	Scientist	Fondation Merieux, Lao People's Democratic Republic (Lao PDR)
Pierre L'Her	Technical assistance (pulmonologist, radiologist)	Soutien Pneumologique International, France
Etienne Leroy-Terquem	Technical assistance (pulmonologist)	Soutien Pneumologique International, France
Charalampos Sismanidis	Technical assistance (statistician)	WHO headquarters
Ikushi Onozaki	Technical assistance (survey advisor)	WHO headquarters
Sang Jae Kim	Technical assistance (laboratory advisor)	Korean Institute of Tuberculosis, Republic of Korea
Peou Satha	Technical assistance (radiology and survey advisor)	National Centre for TB and Leprosy Control, Cambodia

Survey organization and financing

Implementing agency:
National TB Control Programme

Finance	Amount (US$)
The Global Fund	1 275 070
USAID	16 000
Total budget	1 291 070

[a] The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Data sources

- Report of the first national tuberculosis prevalence survey in Lao PDR (2010–2011). Vientiane, Lao PDR: National Tuberculosis Centre, Department of Communicable Diseases, Ministry of Health - Lao PDR; 2014.
- Law I, Sylavanh P, Bounmala S, Nzabintwali F, Paboriboune P, Iem V et al. The first national tuberculosis prevalence survey of Lao PDR (2010–2011). Trop Med Int Health. 2015;20(9):1146–1154.
- Survey dataset.

Survey design and methodology

Sampling design	
Sampling frame	Whole country
Sampling design	Multistage cluster sampling using PPS
Strata	No stratification was used, but final analysis accounted for urban and rural.
Sampling unit	Province/district/village/enumeration area
Sample size assumptions	
• Smear-positive prevalence	251 per 100 000 (≥15 years)
• Precision	0.25
• Design effect	1.3
• *k*	0.4
• Response rate	80%
• Sample size (estimated)	40 000
Number of clusters	50
Cluster size	800
Eligibility criteria	
• Age	≥15 years
• Residency	Slept in the household for 14 days prior to the census

Screening criteria	
Interview[a]	Cough ≥2 weeks within the past month and/or haemoptysis within the past month
Chest X-ray[b]	Any lung abnormality
Other	N/A

[a] An in-depth interview about health-care seeking behaviour was done only for participants who had symptoms suggestive of TB.
[b] Conventional radiography.

Laboratory methodology	
Smear	Two samples (spot, morning): direct preparation, ZN
Culture	Two samples (spot, morning): direct preparation, Ogawa media
Identification of MTB	PNB, GenoType MTBDRplus (LPA)
TB drug susceptibility test	Done
Xpert® MTB/RIF	Not done
HIV test	Not done

Analysis and reporting

Field data collection	Paper
Database	Filemaker Pro 10
Method of analysis	MI+IPW
Results first published in a report/paper	January 2014
Official dissemination event	January 2013

Key survey results

Prevalence[a]	Smear-positive TB		Bacteriologically confirmed TB	
	Number per 100 000 population	95% CI	Number per 100 000 population	95% CI
Total	278	199–356	595	457–733
Male	420	299–541	855	646–1 064
Female	152	88–215	366	254–477
15–24 years	80	11–149	145	41–249
25–34 years	184	16–352	292	120–464
35–44 years	201	98–304	484	307–661
45–54 years	412	234–590	714	461–968
55–64 years	513	279–747	1 131	704–1 557
≥65 years	857	503–1 229	2 410	1 665–3 156
Urban	264	130–398	436	307–565
Rural	283	186–380	663	477–848

[a] Age ≥15 years unless otherwise specified.

	Design effect	*k*
Smear-positive TB	2.2	0.7
Bacteriologically confirmed TB	3.2	0.7

Other sputum results	Number	%
Total smear-positive participants	186	–
Smear-positive participants without MTB confirmation[a]	92	50
Isolates with MDR-TB detected[b]	2	0.9

[a] This includes culture with no evidence of MTB (i.e. culture-negative, NTM, contaminated, N/A).
[b] DST was done for 226 culture MTB-positive cases.

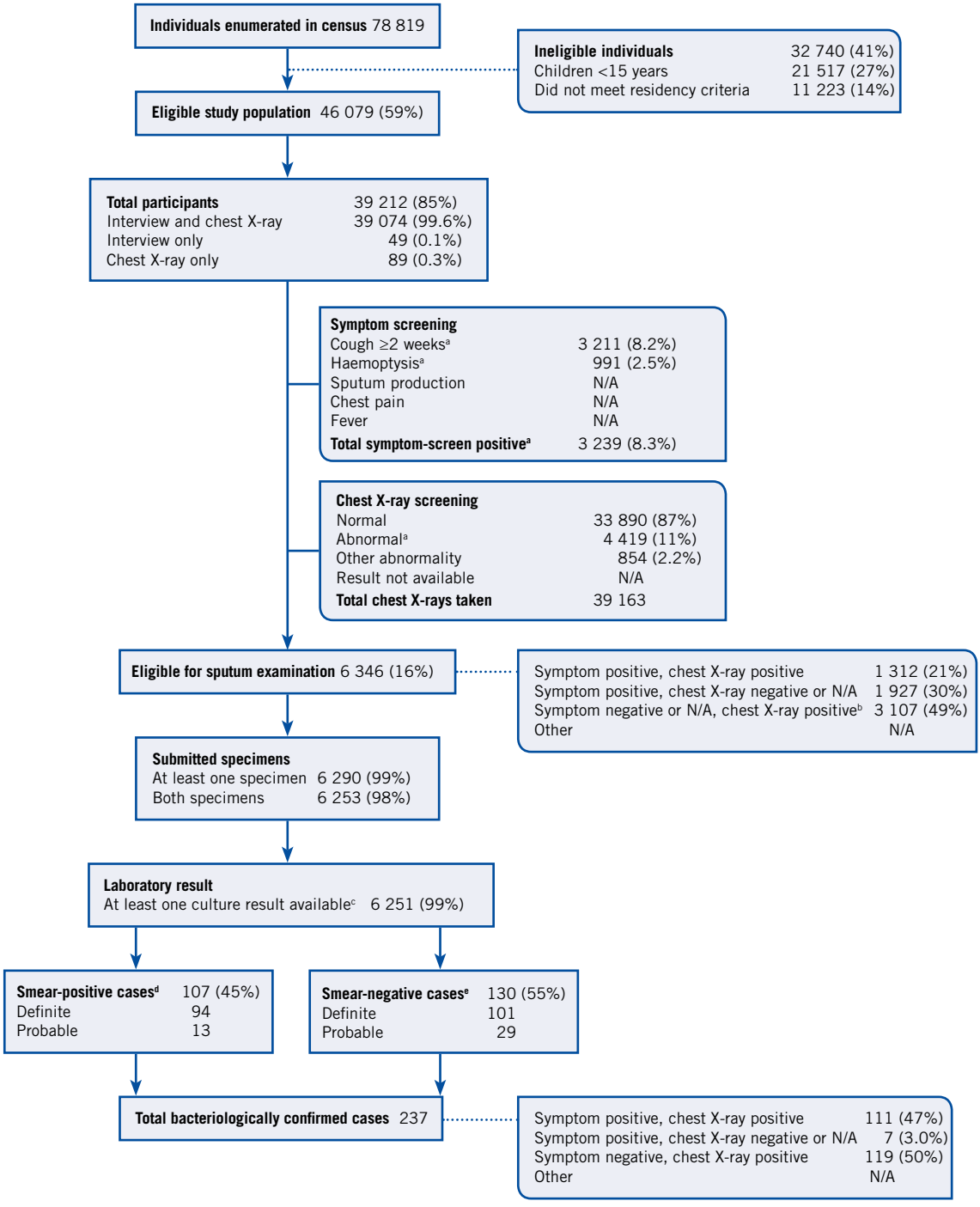
Health-care seeking behaviour among participants who were symptom-screen positive	Number	%
Participants who were symptom-screen positive[a]	3 239	–
Location of care sought		
• Consulted medical facility	1 148	35
Public facility	*990*	*86*
Private facility	*106*	*9.2*
Other[b]	*52*	*4.5*
• Pharmacy	690	21
• Traditional healer	26	0.8
Self-treated	N/A	N/A
No action taken	1 210	37
Unknown	165	5.1

[a] Cough ≥2 weeks and/or haemoptysis.
[b] Village health volunteer (32), another country (17) and other (3).

Survey participants currently on TB treatment	Number	%
Total participants currently on TB treatment	42	–
• Treated in the public sector	21	50
• Treated in the private sector	0	0
• Treated in unknown sector	21	50
Bacteriologically confirmed TB cases detected by the survey who were currently on TB treatment	6	2.5

Survey flow: census to final outcomes

Field operations: July 2010 to January 2012



[a] Eligible for sputum collection.
[b] Symptom-screening results were not available for eight people.
[c] Cultures that were either contaminated and/or missing without a definitive result (i.e. MTB, NTM, negative) were excluded.
[d] Definite: MTB confirmed by culture. Probable: MTB not confirmed by culture but chest X-ray suggestive of TB.
[e] Definite: MTB confirmed by two culture specimens, or by one culture with chest X-ray suggestive of TB. Probable: MTB confirmed by one culture with five or more colonies without chest X-ray suggestive of TB, or by one culture with less than five colonies and chest X-ray suggestive of TB.

Fig. 1: Participation rate by age and sex

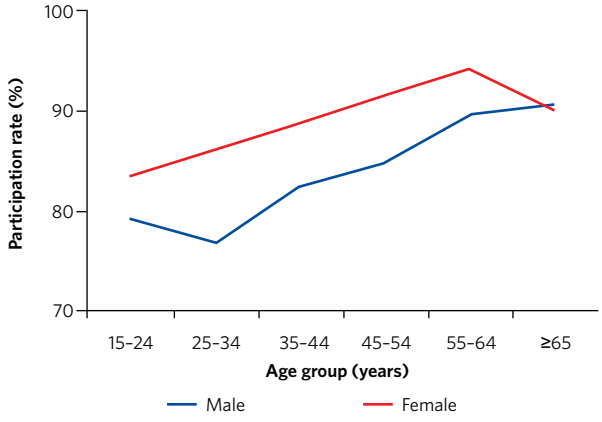


Fig. 2: TB prevalence per 100 000 population by age

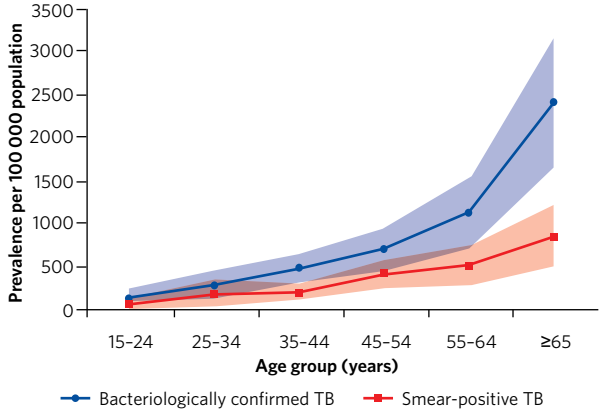


Fig. 3: Estimated number of bacteriologically confirmed TB cases and prevalence per 100 000 population, by age[a]

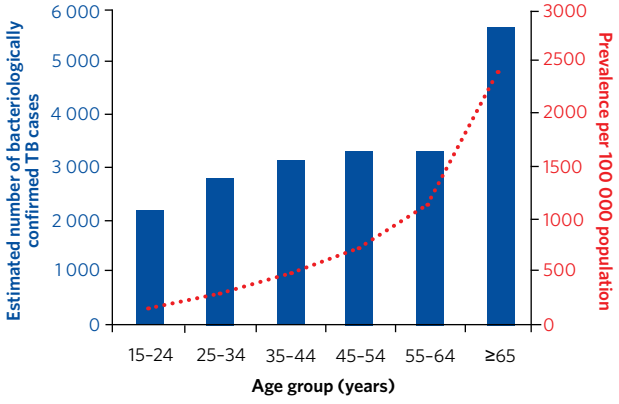


Fig. 4: Cluster variation of the number of bacteriologically confirmed TB cases[b]

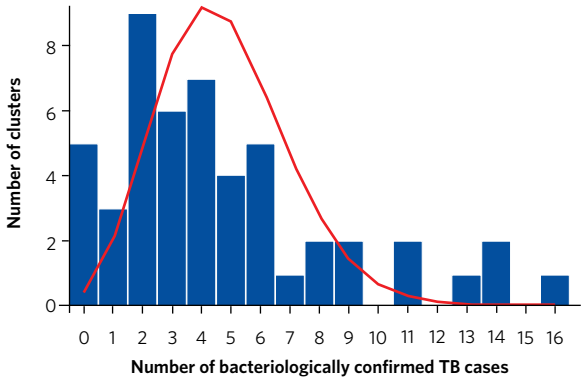


Fig. 5: Ratio of smear-positive TB prevalence to notifications by age and by sex[c]

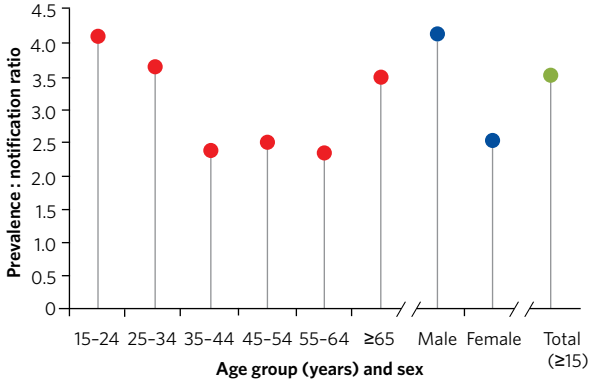
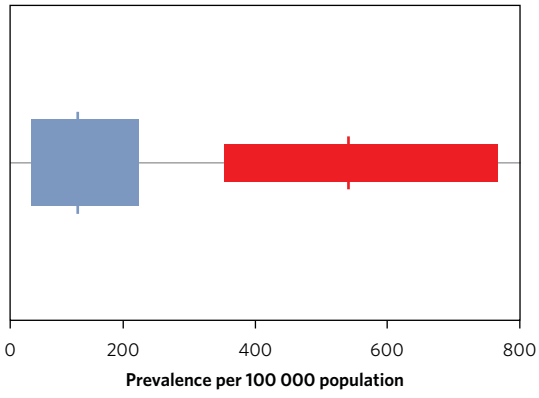


Fig. 6: Estimates of TB prevalence (all ages, all forms of TB) before (in blue) and after (in red) the national TB prevalence survey[d]



[a] The estimated number of bacteriologically confirmed TB cases is the product of age-specific prevalence and population estimates from the UN Population Division (2015 revision).

[b] The data suggested that the distribution of cases by cluster (blue bars) was significantly different from the theoretical distribution (red line) (mean 4.74, variance 15.5, $p<0.05$). The theoretical distribution assumes cases are distributed at random i.e. no clustering effect.

[c] Notification rates were estimated using notifications obtained from the WHO global TB database, and population estimates from the UN Population Division (2015 revision).

[d] The blue bar denotes the best estimate of prevalence and its range that was indirectly derived from the estimate of incidence previously published by WHO, adjusted to the year of the prevalence survey based on previously published trends in incidence.

Background

Lao People's Democratic Republic (PDR) is a landlocked country. In 2010, it had a population of 6.3 million and was one of the poorest countries in South-East Asia, with an average gross national income (GNI) per person of US$ 1000 per year, making it a lower-middle income country *(1)*. The prevalence of HIV in the general population aged 15–49 years was 0.2% (95% confidence interval [CI]: 0.2–0.3%) *(2)*, and it was estimated that 4.5% (95% CI: 3.7–5.4%) of tuberculosis (TB) patients were coinfected with HIV *(3)*.

The National TB Control Programme (NTP) was established in 1995. By 2005, the WHO-recommended DOTS strategy *(4,5)* had reached full country coverage across all 17 provinces and in all of the 140 district hospitals. As DOTS coverage expanded, the case notification rate (new and relapse cases) increased rapidly, from 41 per 100 000 population in 2000 to 65 per 100 000 population in 2005. Subsequently, the case notification rate stagnated, and the best estimate of the case detection rate (notifications of new cases divided by incidence) was 31% in 2011. Nonetheless, there was considerable uncertainty about the burden of TB disease, and the gap between notifications and incidence (due to underreporting or underdiagnosis of cases) was unclear *(6–8)*.

To better understand the burden of TB disease in the country, a decision to implement a national TB prevalence survey was taken in mid-2007. After three years of preparations, the survey was implemented from July 2010 to January 2012. Lao PDR was not one of the 22 global focus countries for national TB prevalence surveys identified by the WHO Global Task Force on TB Impact Measurement in December 2007. Nevertheless, Lao PDR was a regional priority for the WHO Western Pacific Region and was on the Task Force's longer list of 53 countries considered to meet survey eligibility criteria.

Key methods and results

There were 50 survey clusters (no stratification was used at the time of survey design, but both urban and rural strata were examined during the analysis), with a target cluster size of 800 individuals. A total of 78 819 individuals from 14 800 households were enumerated in the survey census, of whom 46 079 (59%) were eligible and invited to participate. Of these, 39 212 (85%) did so. All participants were screened in line with the 2011 algorithm recommended by WHO; that is, using chest X-ray and an interview about symptoms *(9)*. A total of 6346 people (16% of participants) were eligible for sputum examination, of whom 6290 (99%) submitted at least one sputum specimen and 6253 (99%) submitted two sputum specimens.

Photo credit: Jacques Sebert

A total of 237 bacteriologically confirmed pulmonary TB cases was identified, including 107 cases of smear-positive TB. The prevalence of smear-positive TB was 278 (95% CI: 199–356) per 100 000 population (among those aged ≥15 years) and for bacteriologically confirmed TB it was 595 (95% CI: 457–733) per 100 000 population. Prevalence in rural clusters was higher than in urban clusters.

Other key results were:

- the male to female ratio for TB prevalence was 2.8 for smear-positive TB and 2.3 for bacteriologically confirmed TB;
- prevalence per 100 000 population increased with age; the absolute number of bacteriologically confirmed TB cases was highest in the group aged 65 years or more, and consistently high in other age groups;
- among bacteriologically confirmed TB cases, 50% were symptom-screen positive, and among the smear-positive cases, 66% were symptom-screen positive;
- for smear-positive pulmonary TB, the ratio of prevalence to notifications (P:N ratio) was 3.5 overall, but varied from 2.4 in those aged 35–44 and 55–64 years to 4.2 in the age group 15–24 years; the ratio was higher for men than for women (4.3 versus 2.6);
- among bacteriologically confirmed TB cases, 6% had no previous history of anti-TB treatment, and only 3% were on anti-TB treatment at the time of the survey; and
- of the 113 bacteriologically confirmed and 67 smear-positive TB survey cases that screened positive for symptoms and were not on anti-TB treatment at the time of the survey, 42 (37%) and 27 (43%), respectively, had previously sought care in a public or private health facility for their symptoms.

Implications of results

Based on survey results, WHO estimated that the prevalence of TB (all ages, all forms of TB) in 2011 was 540 (95% CI: 353–767) per 100 000 population; estimates for previous years were also revised. The 2011 estimate was almost double the pre-survey WHO estimate that was used in the initial sampling design for the survey (289 per 100 000 population in 2007). The updated estimate of prevalence in 2011 was 64% lower than the revised 1990 estimate of 1490 (95% CI: 746–2490) per 100 000 population, indicating that the country had met the Millennium Development Goal target related to TB (that incidence should be falling by 2015) and the Stop TB Partnership target of halving TB prevalence between 1990 and 2015. Although it was not possible to quantify the relative contribution of the various factors that led to this decline, those considered to have played an important role included the countrywide expansion of DOTS and the associated availability of free anti-TB medication, increases in GNI per capita (from US$ 190 in 1990 to US$ 1120 in 2011) and improvements in overall

Photo credit: Jacques Sebert

living conditions (the Human Development Index was 0.397 in 1990 and 0.554 in 2011) *(6,7)*.

In common with other countries in Asia, the survey showed a markedly ageing TB epidemic, with prevalence in those aged 65 years or more as much as 10 times the level in those under 25 years of age. This suggested that transmission of infection was in decline and that endogenous re-activation of TB in older age groups, as opposed to new infections in the younger population, was likely to make a growing contribution to the overall TB burden.

The survey had several major programmatic, policy and funding implications, which included those listed below.

- It was clear that further efforts were needed to close gaps in case detection. The gap between prevalence and official notifications of new cases (the P:N ratio) was among the largest found in any survey conducted between 2009 and 2016. The particularly high P:N ratio for men compared with women, and for people aged under 35 years and 65 years or more, also indicated a need for interventions targeted to specific subpopulations.
- In addition to programmatic efforts, the high P:N ratio indicated a broader need to strengthen the health system, and the overall availability and acceptability of diagnostic and treatment services. The chronicity of symptoms in older people suggested a reluctance to seek care, possibly linked to health services that were not meeting the needs or expectations of this population.
- Diagnostic services should be improved, progressing from a reliance on sputum smear microscopy to greater use of chest X-ray and either culture or rapid tests (e.g. Xpert® MTB/RIF).
- A smear-positive test result does not always indicate TB disease, especially in a community (as opposed to a clinic) setting. In active TB case finding, TB cannot be reliably diagnosed based on smear examination alone.
- The ability of health-care workers to clinically recognize TB disease should be improved, given that one-third of symptomatic survey cases had already sought care in a public or private health facility, before being detected by the survey.

Photo credit: Irwin Law

Survey findings were used to prepare a funding application to the Global Fund to fight AIDS, TB and malaria, and to develop a new national strategic plan for TB.

Major successes, challenges and lessons learned

Major successes included completion of the survey with a small budget (US$ 1.3 million), a high participation rate and the fact that many NTP staff were able to see, first-hand and often for the first time, the challenges of TB surveillance and case management in the more remote areas of the country. The survey was successfully implemented with the use of entirely conventional or traditional survey methods (i.e. paper-based data collection instruments, conventional chest X-ray systems and the Kudoh culture method with Ogawa media).

Major challenges included the time taken to create the laboratory capacity needed for the survey (it took two years to refit the central-level laboratory), interruptions to funding, a need to mobilize additional funding towards the latter stages of the survey, and difficulties in ensuring that results were clearly understood and accepted by key stakeholders. It also took time to prepare the survey report due to the lack of staff needed for this task.

Important lessons learned for future surveys included:

- good financial planning is essential to ensure the smooth progress of a survey;
- good technical assistance throughout survey preparations and implementation can help to ensure survey quality, especially when a survey

has not previously been conducted in the country; in Lao PDR, three full-time international staff based in the country provided support throughout, including the training and pilot phases, during which revisions were made to the protocol and data-collection tools; additional support was provided by staff involved in the Cambodian surveys (2002 and 2010–2011), and country missions were undertaken by staff from WHO headquarters and other technical partners including the Korean Institute of Tuberculosis, Centre d'Infectiologie Christophe Mérieux du Laos and Soutien Pneumologique International (France); and

- a transparent and open communication strategy among all stakeholders helps to facilitate the adoption of new prevalence estimates (and programmatic implications).

References

1. The World Bank (https://data.worldbank.org/country, accessed April 2017).
2. UNAIDS (http://aidsinfo.unaids.org/, accessed April 2017).
3. World Health Organization. Global Tuberculosis Database. 2017. (http://www.who.int/tb/country/en/, accessed April 2017).
4. WHO Tuberculosis Programme. (1994). WHO Tuberculosis Programme: framework for effective tuberculosis control. World Health Organization. (http://www.who.int/iris/handle/10665/58717, accessed January 2018).
5. World Health Organization. Global tuberculosis programme. Global tuberculosis control report 1997. Geneva: WHO; (https://apps.who.int/iris/bitstream/handle/10665/63354/WHO_TB_97.225_(part1).pdf?sequence=1, accessed January 2018).
6. Law I, Sylavanh P, Bounmala S, Nzabintwali F, Paboriboune P, Iem V et al. The first national tuberculosis prevalence survey of Lao PDR (2010–2011). Trop Med Int Health. 2015;20(9):1146–1154 (https://www.ncbi.nlm.nih.gov/pubmed/25939366, accessed July 2017).
7. Report of the first national tuberculosis prevalence survey in Lao PDR (2010–2011). Vientiane, Lao PDR: National Tuberculosis Centre, Department of Communicable Diseases, Ministry of Health - Lao PDR; 2014.
8. World Health Organization. Global tuberculosis report 2013. Geneva: WHO; 2013 (http://apps.who.int/iris/bitstream/10665/91355/1/9789241564656_eng.pdf, accessed January 2018).
9. World Health Organization. Tuberculosis prevalence surveys: a handbook (WHO/HTM/TB/2010.17). Geneva: WHO; 2011 (https://apps.who.int/iris/bitstream/handle/10665/44481/9789241548168_eng.pdf, accessed August 2017).

MALAWI

2013–2014

Summary statistics

Participation rate	81%
Bacteriologically confirmed TB (≥15 years)	
• Prevalence per 100 000 population	452
• Male:female ratio	1.5
Prevalence:notification ratio (smear-positive TB, ≥15 years)	2.5

Surveyed clusters (N=74)[a]

Key people

Name	Role	Organization
James Mpunga	Principal investigator	National TB Control Programme (NTP)
Rhoda Banda	Survey coordinator	NTP
Alister Munthali	Co-principal investigator	Centre for Social Research, University of Malawi
Damson Kathyola	Co-investigator	Ministry of Health (MOH)
Isaiah Dambe	Co-investigator	NTP
Ishmael Nyasulu	Co-investigator	WHO Malawi
Suzgo Mzumara	Co-investigator (radiologist)	MOH
George B. Samuti	Chief of laboratory	Central Reference Laboratory, MOH
Daniel Nyangulu	Radiology coordinator	MOH
Charles Mandambwe	Data manager	NTP
Masy Chiocha	Data manager	Centre for Social Research, University of Malawi
Andrew Dimba	Field team leader	NTP
Henry Kanyerere	Field team leader	NTP
Lameck Mlauzi	Field team leader	NTP
Sidon Konyani	Technical assistance (epidemiologist)	Centre for Social Research, University of Malawi
Julia Ershova	Technical assistance (survey advisor)	US Centers for Disease Control and Prevention (CDC)
Irwin Law	Technical assistance (survey advisor)	WHO headquarters
Patrick Moonan	Technical assistance (survey advisor)	US Centers for Disease Control and Prevention (CDC)
Wilfred Nkhoma	Technical assistance (survey advisor)	WHO Regional Office for Africa (AFRO)
Ikushi Onozaki	Technical assistance (survey advisor)	WHO headquarters
Sian Floyd	Technical assistance (analysis)	London School of Hygiene & Tropical Medicine

Survey organization and financing

Implementing agency:
National TB Control Programme/Centre for Social Research, University of Malawi

Finance	Amount (US$)
Ministry of Health, Malawi	1 023 244
The Global Fund	1 211 836
Total budget	2 235 080

Data sources

- Malawi Tuberculosis Prevalence survey, technical report: Ministry of Health, National TB Control Programme; 2013–2014.
- Survey dataset.

[a] The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Survey design and methodology

Sampling design	
Sampling frame	Whole country
Sampling design	Multistage cluster sampling using PPS
Strata	Urban/semi-urban/rural
Sampling unit	Three major strata (urban, semi-urban, rural)/ward or area (urban), boma or town (semi-urban), traditional area (rural)/ enumeration area
Sample size assumptions	
• Smear-positive prevalence	278 per 100 000 (≥15 years)
• Precision	0.25
• Design effect	1.4
• *k*	0.5
• Response rate	80%
• Sample size (estimated)	37 200
Number of clusters	74
Cluster size	500
Eligibility criteria	
• Age	≥15 years
• Residency	Slept in the household for at least 14 days before the census

Screening criteria	
Interview[a]	Any symptoms[b] ≥1 week
Chest X-ray[c]	Any lung abnormality
Other	N/A

[a] An in-depth interview about health-care seeking behaviour was done only for those who screened positive.
[b] Cough, sputum production, haemoptysis, chest pain, weight loss, night sweats, fatigue, fever, shortness of breath.
[c] Conventional radiography.

Laboratory methodology	
Smear	Two samples (spot, morning): concentrated preparation[a], FM (LED, auramine stain), FM positives were re-confirmed by Xpert MTB/RIF.
Culture	Two samples (spot, morning): concentrated preparation, LJ media
Identification of MTB	Capilia
TB drug susceptibility test	Xpert MTB/RIF
Xpert® MTB/RIF	Any smear-positive specimens, and any specimens that were culture contaminated
HIV test	Not done[b]

[a] Protocol violation, originally direct preparation.
[b] Participants were interviewed about their HIV status.

Analysis and reporting

Field data collection	Paper/electronic
Database	Microsoft® Access
Method of analysis	MI+IPW
Results first published in a report/paper	May 2016
Official dissemination event	Pending

Key survey results

Prevalence[a]	Smear-positive TB		Bacteriologically confirmed TB	
	Number per 100 000 population	95% CI	Number per 100 000 population	95% CI
Total	220	142–297	452	312–593
Male	303	176–431	546	335–757
Female	149	85–213	374	246–501
15–24 years	46	5.6–86	120	36–205
25–34 years	219	81–356	315	156–474
35–44 years	423	199–647	902	468–1 336
45–54 years	146	21–271	309	131–487
55–64 years	369	45–693	800	310–1 290
≥65 years	645	261–1 028	1 564	888–2 241
Urban	555	281–830	1 014	486–1 542
Rural	169	96–242	373	239–506
Semi-urban	278	0–694	393	0–910

[a] Age ≥15 years unless otherwise specified.

	Design effect	*k*
Smear-positive TB	2.1	1.1
Bacteriologically confirmed TB	3.2	1.1

Other sputum results	Number	%
Total smear-positive participants	163	–
Smear-positive participants without MTB confirmation[a]	101	62
Isolates with DR-TB (rifampicin) detected[b]	9	4.7

[a] This includes culture with no evidence of MTB (i.e. culture-negative, NTM, contaminated, N/A) and Xpert-negative.
[b] 358 participants were tested with Xpert MTB/RIF, and 9 were resistant to rifampicin.

Health-care seeking behaviour among participants who were symptom-screen positive	Number	%
Participants who were symptom-screen positive[a]	2 715	–
Location of care sought		
• Consulted medical facility	1 280	47
Public facility	*901*	*70*
Private facility (including CHAM[b])	*379*	*30*
• Pharmacy	32	1.2
• Traditional centre	41	1.5
• Other	4	0.1
Self-treated	236	8.7
No action taken	1 096	40
Unknown	26	1.0

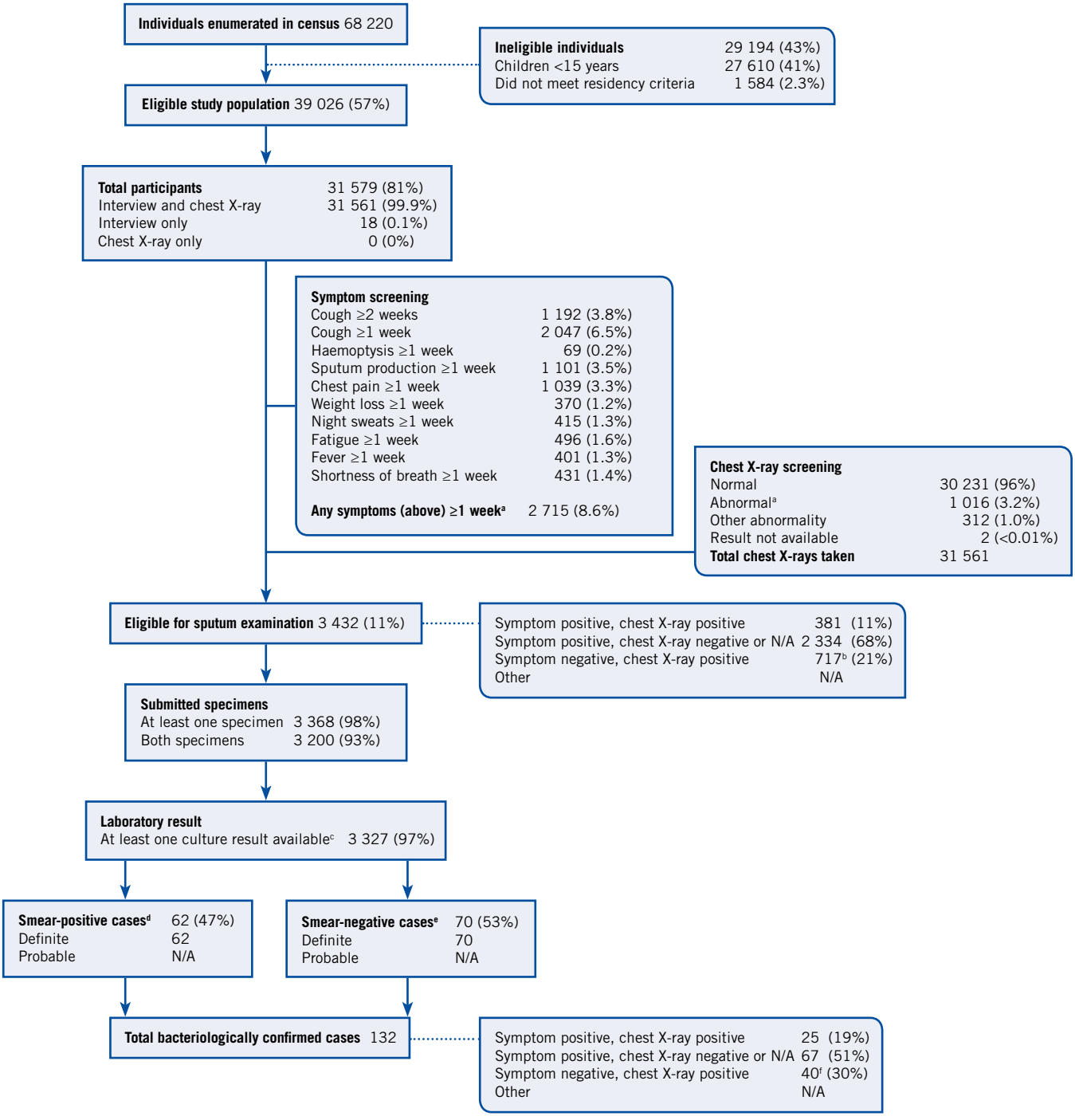
[a] Any symptoms (cough, sputum production, haemoptysis, chest pain, weight loss, night sweats, fatigue, fever, shortness of breath) ≥1 week.
[b] Christian Health Association of Malawi.

Survey participants currently on TB treatment	Number	%
Total participants currently on TB treatment[a]	12	–
• Treated in the public sector	10	83
• Treated in the private sector (CHAM)	2	17
• Treated in unknown sector	0	0
Bacteriologically confirmed TB cases detected by the survey who were currently on TB treatment	4	3.0

[a] Data were available only for participants who were eligible for sputum submission.

Survey flow: census to final outcomes

Field operations: June 2013 to May 2014



[a] Eligible for sputum collection.
[b] Out of 717, 82 participants were defined as "chest X-ray abnormal but not suggestive of TB", but were nonetheless requested to submit sputum samples. Teams were not consistent in their approach to sputum submission for participants with an abnormal chest X-ray (suggestive of TB or other abnormality).
[c] Cultures that were either contaminated and/or missing without a definitive result (i.e. MTB, NTM, negative) were excluded.
[d] Smear-positive was defined as a specimen with ≥4 AFBs. Definite: MTB confirmed by culture and/or Xpert. Probable: no definition.
[e] Definite: MTB confirmed by culture and/or Xpert. Probable: no definition.
[f] Four out of 40 were "abnormal but not suggestive of TB" on chest X-ray.

Fig. 1: Participation rate by age and sex

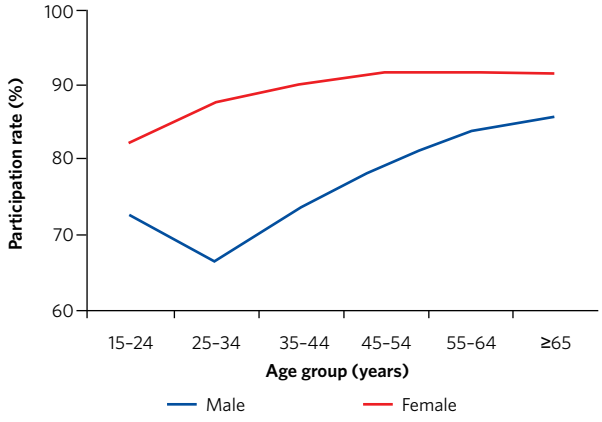


Fig. 2: TB prevalence per 100 000 population by age

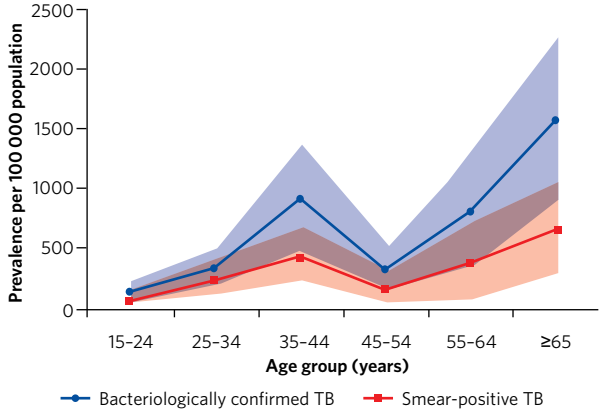


Fig. 3: Estimated number of bacteriologically confirmed TB cases and prevalence per 100 000 population, by age[a]

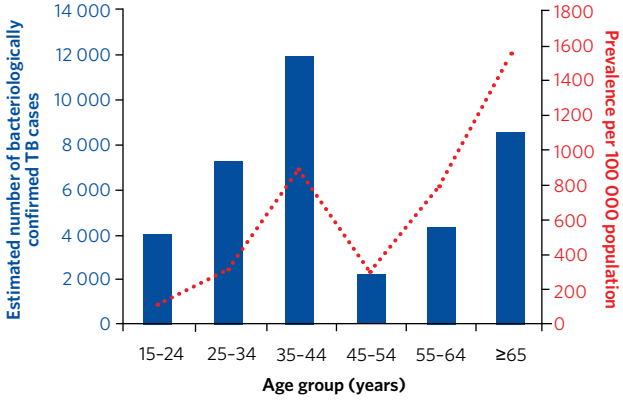


Fig. 4: Cluster variation of the number of bacteriologically confirmed TB cases[b]

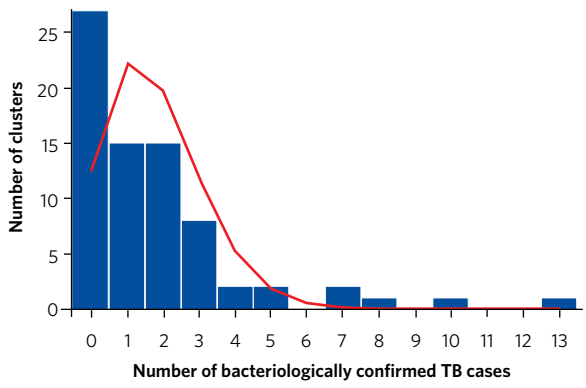


Fig. 5: Ratio of smear-positive TB prevalence to notifications by age and by sex[c]

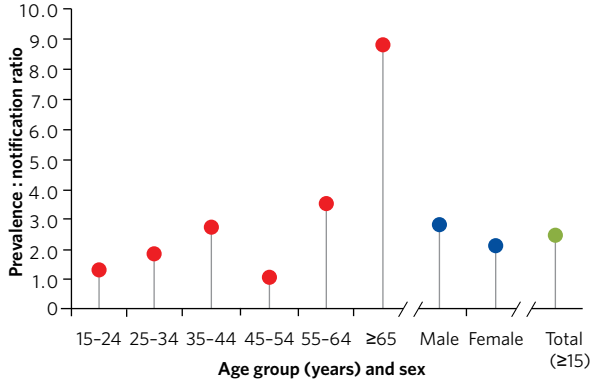
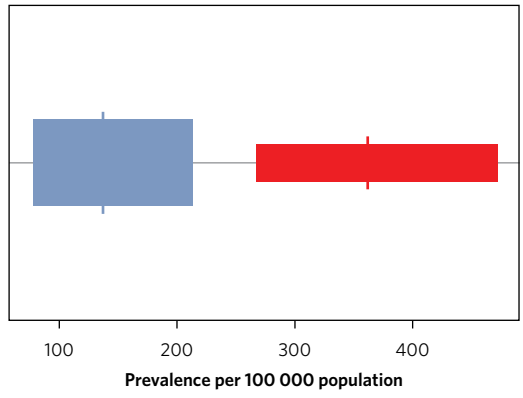


Fig. 6: Estimates of TB prevalence (all ages, all forms of TB) before (in blue) and after (in red) the national TB prevalence survey[d]



[a] The estimated number of bacteriologically confirmed TB cases is the product of age-specific prevalence and population estimates from the UN Population Division (2015 revision).

[b] The data suggested that the distribution of cases by cluster (blue bars) was significantly different from the theoretical distribution (red line) (mean 1.78, variance 5.82, $p<0.05$). The theoretical distribution assumes cases are distributed at random i.e. no clustering effect.

[c] Notification rates were estimated using smear-positive pulmonary TB notifications (2013) obtained from the NTP, and population estimates from the UN Population Division (2015 revision).

[d] The blue bar denotes the best estimate of prevalence and its range that was indirectly derived from the estimate of incidence previously published by WHO, adjusted to the year of the prevalence survey based on previously published trends in incidence.

Background

Malawi, in southern Africa, had a population of 16 million in 2013. The average gross national income (GNI) per person was US$ 390 per year, making it a low-income country *(1)*. In 2013, the prevalence of HIV in the general population aged 15–49 years was 9.9% (95% confidence interval [CI]: 9.1–11%) *(2)*, and it was estimated that 55% (95% CI: 49–62%) of tuberculosis (TB) patients were coinfected with HIV *(3)*.

The National Tuberculosis Control Programme (NTP) in Malawi began implementing what later became known as the DOTS strategy in 1984; it was one of the first model TB programmes in Africa. By 1999, DOTS had been expanded to all public health facilities, and facilities in the quasi-private sectors. TB remained one of the major public health concerns in Malawi throughout this period and worsened considerably following the emergence of the HIV epidemic in the late 1980s and 1990s. TB control was part of the Essential Health Package of the Malawi Government's Health Sector Strategic Plan for 2011–2016 *(4)*.

WHO estimated that, in 2010, there were 219 (95% CI: 203–236) new cases of TB per 100 000 population per year, equivalent to a best estimate of 33 000 (95% CI: 31 000–35 000) new cases per year. Nonetheless, estimates of the burden of TB disease were uncertain because no national TB prevalence survey had ever been done, there were no direct measurements of TB mortality available from vital registration, and the gap between notifications and incidence (due to underreporting or underdiagnosis of cases) had not been quantified and was hard to estimate. Malawi was one of the 22 global focus countries for a national TB prevalence survey selected by the WHO Global Task Force on TB Impact Measurement in December 2007.

To better understand the burden of TB, and with the new opportunity of funding from the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund) and the national budget, the Ministry of Health decided in 2010 to implement a national TB prevalence survey. The survey started in June 2013 and was completed in May 2014.

Key methods and results

There were 74 survey clusters in three strata (urban, semi-urban and rural), with a target cluster size of 500 individuals. A total of 68 220 individuals from 16 380 households were enumerated in the survey census, of whom 39 026 (57%) were eligible and invited to participate. Of these, 31 579 (81%) did so. All participants were screened according to the 2011 algorithm recommended by WHO; that is, using chest X-ray and an interview about symptoms *(5)*. A total of 3432 participants (11%) were eligible for sputum examination; of these, 3368 (98%) submitted at least one sputum specimen and 3200 (93%) submitted two sputum specimens.

A total of 132 bacteriologically confirmed pulmonary TB cases were identified, including 62 (47%) cases of smear-positive TB. The prevalence of smear-positive TB was 220 (95% CI: 142–297) per 100 000 population (among those aged ≥15 years), and for bacteriologically confirmed TB it was 452 (95% CI: 312–593) per 100 000 population. When extrapolated to all forms of TB and for all ages, prevalence was estimated as 362 (95% CI: 257–468) per 100 000 population. The prevalence per 100 000 population of both smear-positive and bacteriologically confirmed TB was higher in urban than in rural and semi-urban areas.

Photo credit: Julia Ershova

Other key results were:

- the male to female ratio was 2.0 for smear-positive TB and 1.5 for bacteriologically confirmed TB;
- prevalence per 100 000 population had two peaks, in those aged 35–44 years and the 65 years or over group; the absolute number of bacteriologically-confirmed cases was relatively high in the younger age groups (25–34 years and 35–44 years) and the elderly group (≥65 years);
- among bacteriologically confirmed TB cases, 70% were symptom-screen positive, and among smear-positive cases, 66% were symptom-screen positive;
- for smear-positive pulmonary TB, the ratio of prevalence to notifications (P:N ratio) was 2.5 overall, but varied from 1.1 in those aged 45–54 years to 9.0 in those aged 65 years or more, and was higher for men than women (2.9 versus 2.2);
- among the bacteriologically confirmed TB cases, 90% had no previous history of anti-TB treatment and only 3.0% were on anti-TB treatment at the time of the survey;
- of the 89 bacteriologically confirmed and 39 smear-positive TB survey cases that screened positive for symptoms and were not on anti-TB treatment at the time of the survey, 46 (52%) and 21 (54%), respectively, had previously sought care in a public or private health facility for their symptoms; and
- All participants were asked whether they had ever been tested for HIV and, if willing, were asked to disclose their status; of the 31 579 participants, 19 703 (62%) disclosed their HIV status, and of those, 1840 (9.3%) reported being HIV-positive; and among 132 bacteriologically confirmed TB cases, 22 (17%) were HIV-positive, 52 (39%) were HIV-negative, and the status of the remaining 44% was unknown (all data were based on the verbal interview).

Implications of results

The prevalence of TB in Malawi was significantly higher than the pre-survey estimate of 140 (95% CI: 72–229) per 100 000 population *(6)*. The fact that TB prevalence per 100 000 population increased with age suggested that the TB epidemic in Malawi had a downward trend. The elderly may also have more limited access to proper diagnosis and management.

The survey had several major programmatic, policy and funding implications:

- most TB cases in the community were HIV-negative, probably reflecting the effectiveness of TB and HIV interventions as well as a relatively poor detection rate of TB among HIV-negative people;
- most undiagnosed TB patients with symptoms had not visited a medical service, indicating that TB diagnostic capacity was inadequate and needed to be strengthened;
- the burden of TB was not evenly spread across the country: urban populations had a higher risk of acquiring and developing TB disease than did semi-urban and rural populations; active case finding strategies should be considered for these higher-risk populations;
- TB case finding strategies better customized to men should be developed and implemented; and
- microscopy contributed to only 47% of final TB diagnoses, suggesting that case detection and patient management would be improved by expanding the use of more sensitive and specific diagnostic tests.

Photo credit: Ikushi Onozaki

Major successes, challenges and lessons learned

The major overarching success was that the first national TB prevalence survey in Malawi was successfully implemented, with a good participation rate. This was done using conventional tools (e.g. film-based portable chest X-ray equipment and paper-based data collection tools) as dictated by the relatively small budget provided by the Global Fund and the national government.

Other successes included excellent collaboration between the NTP and the University of Malawi's Centre for Social Research, and between the survey team, NTP and technical partners, including the United States Centers for Disease Control and Prevention (US-CDC), the London School of Hygiene and Tropical Medicine, and WHO, which strongly facilitated survey implementation. Given the challenges faced in some other countries, data management was effective, with on-site data entry in the field, timely data cleaning and validation, and continuous support from the US-CDC. The final validated data set was available within a few months of the completion of field operations.

Challenges faced during the survey included those listed below.

- It took two years to secure government funding to support field activities and more than a year to procure conventional X-ray equipment. During the survey, interruptions to disbursement of funds caused some delays in field operations.
- A change of the lead technical adviser during the final stages of survey preparations meant that the survey team did not benefit from technical assistance during the pilot survey and the early stages of field operations. This contributed to some initial issues with data management, but these were subsequently rectified.
- The suboptimal environment in which chest X-rays were often taken. X-ray units, and the chemical liquids used to develop and fix films, tended to overheat in hot conditions. Field operations were sometimes delayed while the units were allowed to cool down. In addition, individual identifiers were written on the films by hand after the images had been developed. This caused problems with later archiving and retrieval of images for central reading, and potentially caused some images to be mislabelled (i.e. labelled with the wrong participant's name).
- Advice about sputum examination, which was not appropriate in the context of a prevalence survey, was provided to the central reference laboratory by an expert not directly involved in the survey. Although the intention was to conduct direct smear microscopy (to allow comparison with cases routinely detected by health services), in practice, centrifuged sediment was used for light-emitting diode (LED) fluorescent microscopy (FM). This was a protocol violation and resulted in many scanty smear-positive results. In 62% of the smear-positive specimens, *Mycobacterium tuberculosis* could not be detected by either culture or Xpert® MTB/RIF. In consultation with leading laboratory experts working with the Global Laboratory Initiative and the Supranational Reference Laboratory for Malawi, the survey re-categorized scanty 1–3 acid-fast bacilli (AFB) smears by concentrated LED FM as insignificant, and did not classify them as smear-positive.
- There were incidents of laboratory cross-contamination. Of the specimens from 192 participants who were positive by culture or Xpert MTB/RIF (or both), one third were found to be clustered in the laboratory logbook; that is, consecutive specimens were positive for *M. tuberculosis*. Following an extensive panel review of laboratory documents, chest X-rays and other information (e.g. data on family contacts), some laboratory cross-contamination was suspected. The panel concluded that a total of 60 participants with positive laboratory results should not be counted as TB cases. Of these 60, 29 had a very strong suspicion of cross-contamination and the remaining 31 had a single weak positive result (i.e. culture of fewer than five colonies) without other supportive evidence of TB disease other than symptoms. The final survey results may have underestimated TB prevalence.

Photo credit: Julia Ershova

- A substantial number of chest X-rays had to be read after field operations were completed.
- There was a considerable delay in the writing of the survey report because no one was available to undertake this task.

Important lessons for future surveys were:

- all survey procedures must be closely monitored to prevent protocol violations, or to ensure that any violations are promptly corrected;
- cross-contamination in the laboratory is a potential problem, and great care is needed to avoid cross-contamination compromising survey results; and
- it is important to ensure that someone is available to prepare the survey report, and to include adequate funding for this activity in the budget.

References

1. The World Bank (https://data.worldbank.org/country, accessed April 2017).
2. UNAIDS (http://aidsinfo.unaids.org/, accessed April 2017).
3. World Health Organization. Global Tuberculosis Database. 2017. (http://www.who.int/tb/country/en/, accessed April 2017).
4. Malawi health sector strategic plan 2011–2016: Moving towards equity and equality. Ministry of Health, Government of Malawi; 2011 (http://www.healthpromotion.gov.mw/index.php/2013-08-12-12-52-31/2013-08-12-12-52-32/policies-strategies?download=6:malawi-health-sector-strategic-plan-2011-2016, accessed July 2017).
5. World Health Organization. Tuberculosis prevalence surveys: a handbook (WHO/HTM/TB/2010.17). Geneva: WHO; 2011 (https://apps.who.int/iris/bitstream/handle/10665/44481/9789241548168_eng.pdf, accessed August 2017).
6. World Health Organization. Global tuberculosis report 2013. Geneva: WHO; 2013 (http://apps.who.int/iris/bitstream/10665/91355/1/9789241564656_eng.pdf, accessed January 2018).

MONGOLIA

2014–2015

Summary statistics

Participation rate	84%
Bacteriologically confirmed TB (≥15 years)	
• Prevalence per 100 000 population	560
• Male:female ratio	2.8
Prevalence:notification ratio (smear-positive TB, ≥15 years)	2.5

Surveyed clusters (N=98)[a]

Key people

Name	Role	Organization
Tugsdelger Sovd	Principal investigator	Ministry of Health
Puntsag Banzragch	Central panel team	National Center for Communicable Diseases
Naranbat Nyamadawa	Survey consultant	Mongolian Anti-Tuberculosis Coalition
Naranzul Dambaa	Survey coordinator	National Center for Communicable Diseases
Tsolmon Boldoo	Data manager	National Center for Communicable Diseases
Bayasgalan Purev	Central radiologist	National Center for Communicable Diseases
Buyankhishig Burneebaatar	Laboratory doctor	National Tuberculosis Reference Laboratory
Oyuntuya Tumenbayar	Laboratory doctor	National Tuberculosis Reference Laboratory
Ikushi Onozaki	Technical assistance (survey advisor)	WHO headquarters
Yasunori Ichimura	Technical assistance (survey advisor)	Chiba University, Japan
Norio Yamada	Technical assistance (survey advisor)	Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association (RIT/JATA)
M. Bintari Dwihardiani	Technical assistance (survey advisor)	WHO Indonesia
M.N. Farid	Technical assistance (survey advisor)	Central Bureau of Statistics, Jakarta
Satoshi Mitarai	Technical assistance (laboratory advisor)	RIT/JATA
Soe Nyunt-U	Technical/financial support	WHO Mongolia
Narantuya Jadambaa	Technical/financial support	WHO Mongolia

Survey organization and financing

Implementing agency:
National TB Programme, National Center for Communicable Diseases

Finance	Amount (US$)
Government of Mongolia	442 000
The Global Fund	617 000
WHO	34 700
Total budget	1 093 700

Data sources

- Report of the first national tuberculosis prevalence survey in Mongolia (2014–2015). Ulaanbaatar city, Mongolia: Ministry of Health; 2016.
- Survey dataset.

[a] The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Survey design and methodology

Sampling design	
Sampling frame	Whole country
Sampling design	Multistage cluster sampling using PPS
Strata	City (Ulaanbaatar, Darkhan and Erdenet cities)/provincial center (except Darkhan and Orkhon provinces)/rural (all soums except provincial center soums)
Sampling unit	City: khoroo (sub-district) in UB city, bagh in Darkhan and Erdenet cities Provincial center: bagh (sub-soum) Rural: soum (sub-province)
Sample size assumptions	
• Smear-positive prevalence	180 per 100 000 (≥15 years)
• Precision	0.25
• Design effect	1.2
• *k*	0.5
• Response rate	85%
• Sample size (estimated)	49 000
Number of clusters	98
Cluster size	600 (51 clusters in city strata); 500 (47 clusters in other strata)
Eligibility criteria	
• Age	≥15 years
• Residency	Slept in the household for 14 days prior to census

Screening criteria	
Interview	Cough ≥2 weeks
Chest X-ray[a]	Any lung abnormality
Other	Chest X-ray exempted

[a] Direct digital radiography by chest X-ray car and mobile apparatus.

Laboratory methodology	
Smear	Two samples (spot, morning): direct preparation, FM (LED, auramine stain). ZN for those smears that were FM positve
Culture	Two samples (spot, morning): direct preparation, Ogawa media
Identification of MTB	PNB, niacin test
TB drug susceptibility test	MTBDRplus test[a]
Xpert® MTB/RIF	Done for smear-positive specimens (from the early phase of field operations)[b]
HIV test	Not done

[a] Financial support was provided by Science and Technology Foundation Mongolia.
[b] Xpert MTB/RIF was done for 84 out of 92 smear-positive specimens.

Analysis and reporting

Field data collection	Paper
Database	Microsoft® Access
Method of analysis	MI+IPW
Results first published in a report/paper	December 2016
Official dissemination event	March 2017

Key survey results

Prevalence[a]	Smear-positive TB		Bacteriologically confirmed TB	
	Number per 100 000 population	95% CI	Number per 100 000 population	95% CI
Total	204	143–265	560	455–665
Male	349	235–464	840	646–1 033
Female	68	38–99	299	225–372
15–24 years	135	42–228	555	362–748
25–34 years	281	152–410	634	431–837
35–44 years	208	94–323	472	289–655
45–54 years	197	77–318	527	344–711
55–64 years	170	63–277	562	372–752
≥65 years	194	64–323	639	377–900
City	191	126–257	586	447–724
Provincial center	195	34–356	513	216–810
Rural	233	85–381	529	336–723

[a] Age ≥15 years unless otherwise specified.

	Design effect	*k*
Smear-positive TB	2.0	1.0
Bacteriologically confirmed TB	2.1	0.6

Other sputum results	Number	%
Total smear-positive participants	92	–
Smear-positive participants without MTB confirmation[a]	5	5.4
Isolates with MDR-TB detected[b]	22	9.4

[a] This includes culture with no evidence of MTB (i.e. culture-negative, NTM, contaminated, N/A) and Xpert-negative.
[b] 234 culture-positive samples were tested with Genotype MTBDRplus.

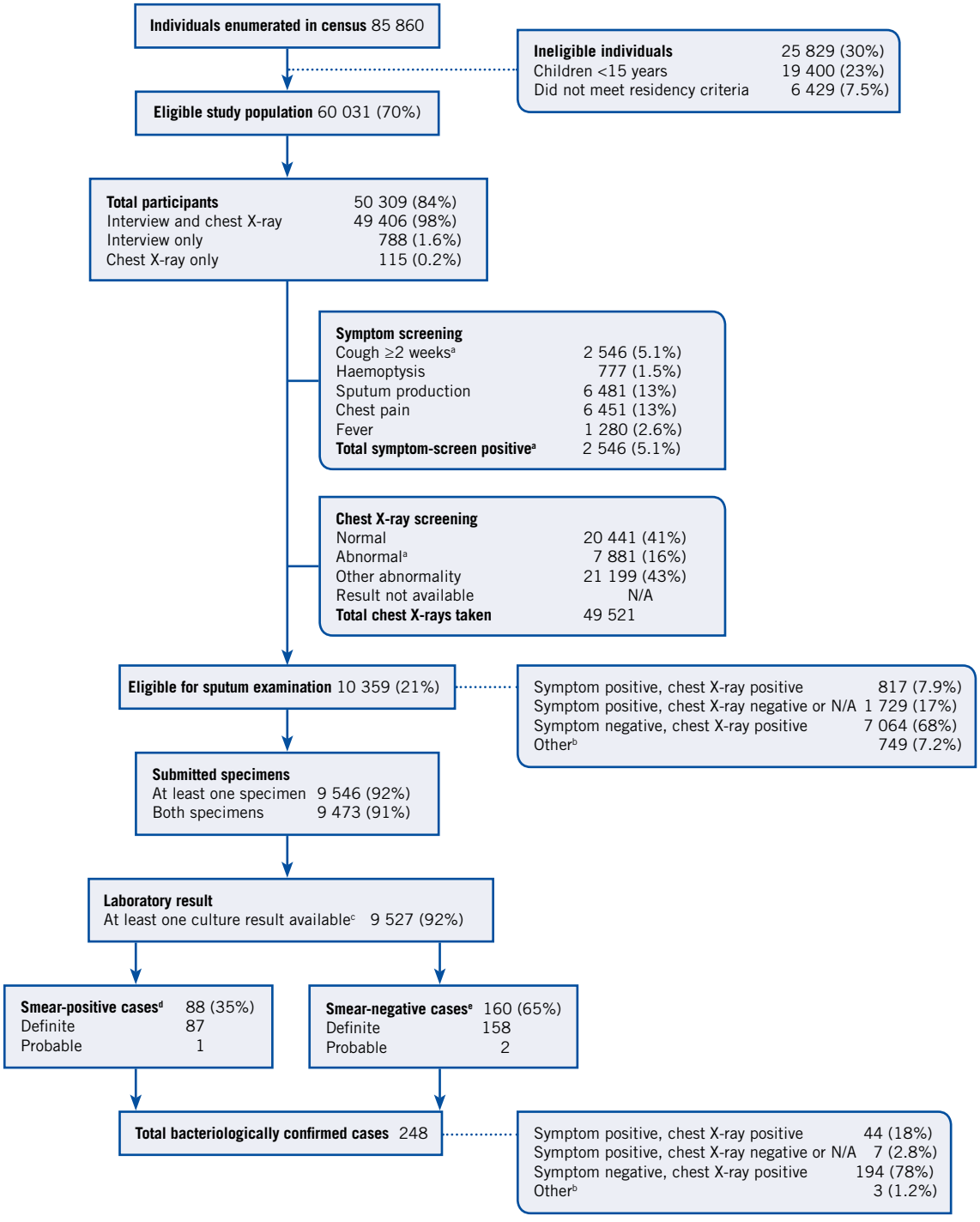
Health-care seeking behaviour among participants who were symptom-screen positive	Number	%
Participants who were symptom-screen positive[a]	2 546	–
Location of care sought		
• Consulted medical facility	950	37
Public facility	*920*	*97*
Private facility	*30*	*3.1*
• Pharmacy	222	8.7
• Traditional medicine hospital	2	0.1
• Others	59	2.3
• Unspecified	104	4.1
No action taken	1 179	46
Unknown	30	1.2

[a] Cough ≥2 weeks.

Survey participants currently on TB treatment	Number	%
Total participants currently on TB treatment	129	–
• Treated in the public sector	126	98
• Treated in the private sector	0	0
• Treated in other sector	3	2.3
Bacteriologically confirmed TB cases detected by the survey who were currently on TB treatment	11	4.4

Survey flow: census to final outcomes

Field operations: April 2014 to November 2015 (April to November 2014 for phase 1 (urban), April to November 2015 for phase 2 (rural))



[a] Eligible for sputum collection.
[b] Chest X-ray exempted and symptom-screen negative.
[c] Cultures that were either contaminated and/or missing without a definitive result (i.e. MTB, NTM, negative) were excluded.
[d] Definite: MTB confirmed by culture and/or Xpert. Probable: MTB not confirmed by culture and/or Xpert but chest X-ray suggestive of TB.
[e] Definite: MTB confirmed by culture. Probable: one scanty culture-positive without chest X-ray suggestive of TB but with chronic cough, and confirmed as TB cases by referral facilities.

Fig. 1: Participation rate by age and sex

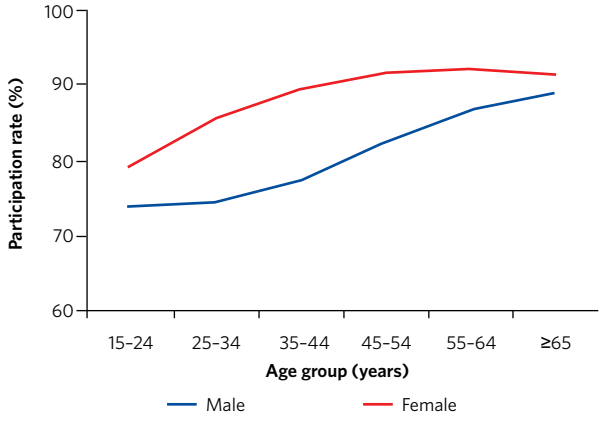


Fig. 2: TB prevalence per 100 000 population by age

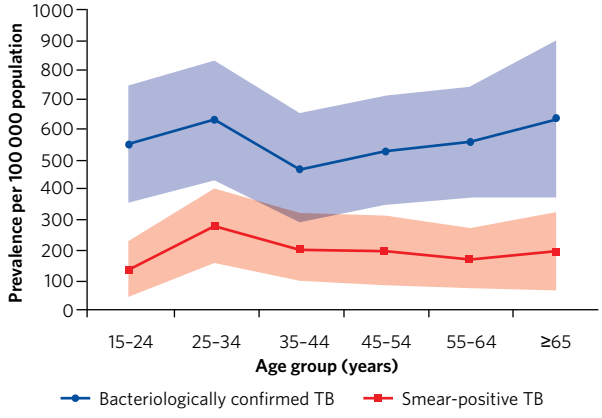


Fig. 3: Estimated number of bacteriologically confirmed TB cases and prevalence per 100 000 population, by age[a]

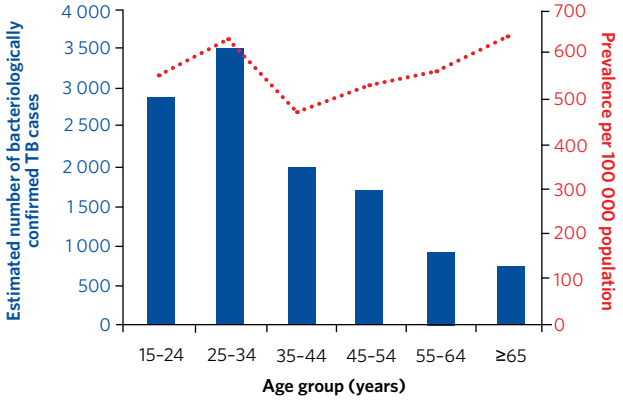


Fig. 4: Cluster variation of the number of bacteriologically confirmed TB cases[b]

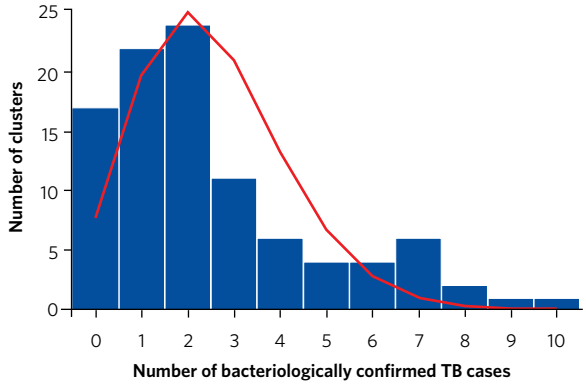


Fig. 5: Ratio of smear-positive TB prevalence to notifications by age and by sex[c]

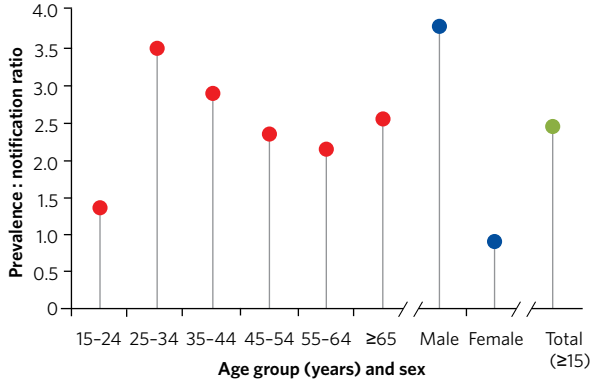
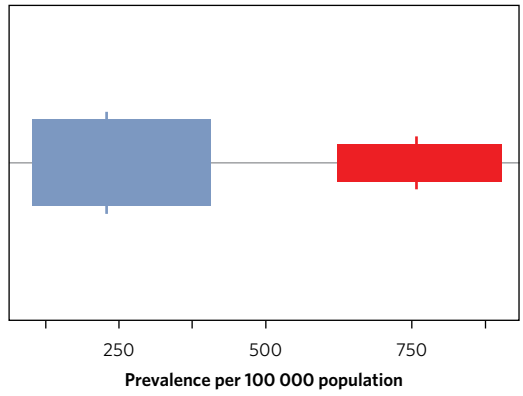


Fig. 6: Estimates of TB prevalence (all ages, all forms of TB) before (in blue) and after (in red) the national TB prevalence survey[d]



[a] The estimated number of bacteriologically confirmed TB cases is the product of age-specific prevalence and population estimates from the UN Population Division (2015 revision).

[b] The data suggested that the distribution of cases by cluster (blue bars) was significantly different from the theoretical distribution (red line) (mean 2.53, variance 5.49, $p<0.05$). The theoretical distribution assumes cases are distributed at random i.e. no clustering effect.

[c] Notification rates were estimate of using smear-positive pulmonary TB notifications (2014) obtained from the NTP, and population estimates from the UN Population Division (2015 revision).

[d] The blue bar denotes the best estimated prevalence and its range that was indirectly derived from the estimate of incidence previously published by WHO, adjusted to the year of the prevalence survey based on previously published trends in incidence.

Background

Mongolia is a landlocked country in East Asia that had a population of 2.9 million in 2014. The average gross national income (GNI) per person was US$ 4260 per year, making it an upper-middle-income country *(1)*. According to the Population and Housing Census of 2010, about 40% of the nation's population lived in the capital city of Ulaanbaatar *(2)*. In 2014, the prevalence of HIV in the general population aged 15–49 years was <0.1% (95% confidence interval [CI]: <0.1–<0.1%) *(3)*, and it was estimated that 0.18% (95% CI: 0.17–0.20%) of TB patients were coinfected with HIV *(4)*.

The National Tuberculosis (TB) Programme (NTP) introduced the WHO-recommended DOTS strategy in 1994, and the country subsequently improved TB detection and treatment outcomes *(5,6)*. The case notification rate (all types of TB) increased from 116 per 100 000 population in 1995 to 185 per 100 000 population in 2006, after which it decreased slowly. Treatment success was around 80–85% throughout the period 1999–2014. WHO estimated that the prevalence of TB was 254 (95% CI: 119–438) per 100 000 population in 2013. Although TB mortality declined from 3.2 per 100 000 population in 2000 to 1.9 per 100 000 population in 2013, TB remained the leading cause of death from communicable diseases in Mongolia *(7)*.

Between 1959 and 1961, and with the assistance of the Russian Federation, Mongolia undertook a large active TB screening programme that covered 88% of the total population. The survey estimated that 33% of the population had a positive tuberculin skin test result *(8)*. No study of a similar magnitude had previously been conducted in the country.

In 2011, in line with the Millennium Development Goals (MDGs) and the *Regional strategy to Stop TB in the Western Pacific (9)*, as endorsed by WHO's regional committee, the Government of Mongolia approved a 5-year national plan to stop and prevent TB. This plan included a national TB prevalence survey to measure the prevalence of bacteriologically confirmed pulmonary TB among those aged 15 years and more.

Key methods and results

Due to the scattered and sparse population in remote provinces and the cold winters, survey field operations were split into two phases: Phase 1 was mostly conducted in the capital city of Ulaanbaatar (2014); Phase 2 continued in the remote provinces (2015). Phase 1 was designed as an independent survey with a sample size large enough to provide TB prevalence estimates for the capital and urban areas, where most TB cases were notified *(7)*.

There were 98 survey clusters across three strata (city, provincial centre and rural), with a target cluster size of 600 individuals in cities and 500 individuals in other strata. A total of 85 860 individuals from 24 127 households were enumerated in the survey census, of whom 60 031 (70%) were eligible and invited to participate. Of these, 50 309 (84%) did so. All participants were screened according to the 2011 algorithm recommended by WHO; that is, chest X-ray and an interview about symptoms *(10)*. A total of 10 359 people (21% of participants) were eligible for sputum examination; of these, 9546 (92%) submitted at least one sputum specimen and 9473 (91%) submitted two sputum specimens.

A total of 248 bacteriologically confirmed pulmonary TB cases were identified, including 88 smear-positive TB cases. The prevalence of smear-positive TB was 204 (95% CI: 143–265) per 100 000 population among those aged ≥15 years, and for bacteriologically confirmed TB it was 560 (95% CI: 455–665) per 100 000 population. When extrapolated to all forms of TB and for all ages, prevalence was estimated as 757 (95% CI: 620–894) per 100 000 population. There was no significant variation in the prevalence of bacteriologically confirmed TB between the three strata, with the results being city, 586 (95% CI: 447–724) per 100 000 population; provincial centres, 513 (95% CI: 216–810) per 100 000 population; and rural sub-provinces, 529 (95% CI: 336–723) per 100 000 population.

Other key results were:

- the male to female ratio was 5.1 for smear-positive TB and 2.8 for bacteriologically confirmed TB;
- prevalence per 100 000 population was high in all age groups; however, the absolute number of bacteriologically confirmed TB cases was relatively high in the young age groups (15–24 years and 25–34 years);

Photo credit: M. Bintari Dwihardiani

- among bacteriologically confirmed TB cases, 21% were symptom-screen positive, and among the smear-positive cases, 34% were symptom-screen positive;
- for smear-positive pulmonary TB, the ratio of prevalence to notifications (P:N ratio) was 2.5 overall, but varied from 1.4 in those aged 15–24 years to 3.5 in the 25–34 year age group, and was much higher for men than for women (3.8 versus 0.9);
- among bacteriologically confirmed TB cases, 82% had no previous history of anti-TB treatment and only 4.4% were on anti-TB treatment at the time of the survey; and
- of the 48 bacteriologically confirmed and 27 smear-positive TB survey cases that screened positive for symptoms and were not on anti-TB treatment at the time of the survey, 17 (35%) and 14 (52%), respectively, had previously sought care in a public or private health facility for their symptoms.

Implications of results

Based on the first national TB prevalence survey, Mongolia was confirmed as a high TB burden country in the WHO Western Pacific Region, with considerable ongoing transmission in the community. The estimated national prevalence per 100 000 population was high, including among the younger age groups. These results suggested that TB should be reconsidered as a significant public health problem in Mongolia.

The prevalence of bacteriologically confirmed prevalence was uniformly high across all strata. High prevalence with high notification rates in congested urban areas suggested a higher overall burden of TB in these places, especially in the sprawling residential areas with little infrastructure (known as the ger districts). The seasonal pattern of TB also indicated higher rates of transmission in the winter months, a time of year with higher air pollution in the ger districts. Increasing urbanization in the five years prior to the survey led to the expansion of static ger areas around the centre of Ulaanbaatar and a more densely populated environment with increased air pollution; the former may have increased TB transmission, and the latter may have contributed to delays in diagnosis because of the increased frequency of common coughs and reduced likelihood of suspecting TB as the cause. The high prevalence in provincial centres and rural (sub-provinces) areas indicated challenges related to access to health facilities and diagnostic services.

The gap between prevalence and notification showed the limitations of existing approaches to case-finding, which relied upon symptom screening and smear microscopy. In the survey, smear-positive cases accounted for only 36% of bacteriologically confirmed cases; three-quarters of cases were symptom-screen negative, and were tested due to screening by chest X-ray (most smear-negative, culture-positive cases had small and atypical shadows in chest X-ray images). These findings suggested that access to high-quality chest X-rays should be improved, that

new diagnostic tools beyond smear such as Xpert® MTB/RIF should be introduced, and that diagnostic services should be decentralized across the country.

Because underreporting of detected cases to national authorities probably also contributed to the gap between prevalence and notifications, another identified priority was to strengthen the electronic reporting system with appropriate supervision.

While strengthening TB control efforts in general, the importance of giving particular attention to risk groups with a high TB prevalence and to remote areas with poorer access was also recognized, and reflected in Mongolia's 5-year national TB strategic plan for 2016–2020.

Major successes, challenges and lessons learned

Major successes included carrying out the first nationwide TB prevalence survey in Mongolia, and the first TB-related survey in the country for more than 50 years; achieving high population coverage (100%), with a participation rate of 84% and a sputum collection rate of more than 90%; reaching clusters located in remote areas with limited infrastructure; and examining all specimens to a high standard in one national reference laboratory. Specifically, specimens from remote clusters were transported using a nationwide sputum transportation system established in 2008; the overall culture (Ogawa) contamination rate was low (1.9%; 696/37 322 tubes); and all laboratory results were available, with an overall recovery rate of 87% (80 culture *Mycobacterium tuberculosis* [MTB]-positive among 92 smear-positive).

Survey successes were facilitated by excellent leadership from the NTP; good collaboration between the Ministry of Health, the survey team and local authorities and health centres during field operations; the appointment of a full-time survey coordinator and data management team early in the process; and close collaboration with external partners including the Global Fund to Fight AIDS, TB and Malaria, the WHO country office and WHO headquarters. Good technical assistance throughout survey preparations and implementation helped to ensure the high quality of the survey, especially given that Mongolia had no previous experience of undertaking a survey of this magnitude. Experts in prevalence surveys visited more than 10 times during the course of the survey, and provided regular assistance throughout, from protocol development to reporting of final results. Good financial planning (especially with financial contributions from the government) was also vital in ensuring the smooth progress of the survey, including the ongoing maintenance of chest X-ray machines during field operations.

Major challenges included interruptions to field operations during the long winter season; a lower participation rate among the young, men and urban clusters, especially in the wealthier parts of large cities; and postponement of field operations following a breakdown of both X-ray machines, since no backup machines were available.

Photo credit: M. Bintari Dwihardiani

Photo credit: M. Bintari Dwihardiani

References

1. The World Bank (https://data.worldbank.org/country, accessed April 2017).
2. 2010 population and housing census of Mongolia. Census monograph, Ulaanbaatar: National Statistical Office of Mongolia; 2011.
3. UNAIDS (http://aidsinfo.unaids.org/, accessed April 2017).
4. World Health Organization. Global Tuberculosis Database. 2017. (http://www.who.int/tb/country/en/, accessed April 2017).
5. WHO Tuberculosis Programme. (1994). WHO Tuberculosis Programme: framework for effective tuberculosis control. World Health Organization. (http://www.who.int/iris/handle/10665/58717, accessed January 2018).
6. World Health Organization. Global tuberculosis programme. Global tuberculosis control report 1997. Geneva: WHO; (https://apps.who.int/iris/bitstream/handle/10665/63354/WHO_TB_97.225_(part1).pdf?sequence=1, accessed January 2018).
7. Report of the first National Tuberculosis Prevalence Survey in Mongolia (2014–2015). Ulaanbaatar city, Mongolia: Ministry of Health; 2016.
8. Results of screening for TB in 1959–1961 in Mongolia. Mongolian Journal of Infectious Diseases. 2012;4(47).
9. WHO Regional Office for the Western Pacific. The regional strategic plan to stop TB in the Western Pacific. Manila, Philippines: WHO; 2000 (https://iris.wpro.who.int/bitstream/handle/10665.1/9849/Regional_Strategic_Plan_to_Stop_TB_WP_eng.pdf, accessed July 2017).
10. World Health Organization. Tuberculosis prevalence surveys: a handbook (WHO/HTM/TB/2010.17). Geneva: WHO; 2011 (https://apps.who.int/iris/bitstream/handle/10665/44481/9789241548168_eng.pdf, accessed August 2017).

MYANMAR

2009–2010

Surveyed clusters (N=70)[a]

Summary statistics

Participation rate	89%
Bacteriologically confirmed TB (≥15 years)	
• Prevalence per 100 000 population	613
• Male:female ratio	2.5
Prevalence:notification ratio (smear-positive TB, ≥15 years)	2.1

Key people

Name	Role	Organization
Win Maung	Vice-chair, lead SC, TC and CPD	Director of Disease Control
Thandar Lwin	Survey coordinator, lead WC	National Tuberculosis Programme (NTP)
Tin Mi Mi Khaing	SC and TC member	Regional TB officer, Yangon
Bo Myint	SC and TC member	Regional TB officer, Mandalay
Tin Tin Mar	TC and CPD member	National TB Reference Laboratory (NTRL)
Ti Ti	TC member and laboratory advisor	FIND
Wint Wint Nyunt	Lead laboratory unit	NTRL
San San Shein	TC member, lead radiology unit	Regional TB Centre, Mandalay
Moe Zaw	TC member, data manager	NTP
Hnin Wai Lwin Myo	TC member, data management, WC	NTP
Si Thu Aung	TC member, field team leader	NTP
Htay Lwin	Field team leader	State TB officer, Shan East
Htar Htar Oo	Field team leader	NTP
Thandar Thwin	TC member, field team leader	Regional TB Centre, Yangon
Myo Zaw	SC and TC member, monitoring & supervision	WHO Myanmar
Ikushi Onozaki	SC, TC, CPD and WC member	WHO headquarters
Norio Yamada	Technical assistance (epidemiology, analysis and WC)	Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association (RIT/JATA)
Kosuke Okada	SC and TC member, technical assistance (management)	Japan International Cooperation Agency (JICA)
Eva Nathanson	Coordination (supply and logistics), WC member	WHO Myanmar

CPD: central panel for diagnosis, SC: steering committee, TC: technical committee, WC: writing committee.

Survey organization and financing

Implementing agency:
National Tuberculosis Programme

Finance	Amount (US$)
WHO	15 000
Three diseases fund	270 000
JICA	114 000
Population Services International (PSI)	358 000
USAID	120 000
Total budget	877 000

Data sources

- Report on national TB prevalence survey, 2009–2010, Myanmar. Ministry of Health, Department of Health, Government of Myanmar.
- Survey dataset.

[a] The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Survey design and methodology

Sampling design	
Sampling frame	293 out of 325 townships[a]
Sampling design	Multistage cluster sampling using PPS
Strata	Region/state
Sampling unit	Region, state/township/ward/village
Sample size assumptions	
• Smear-positive prevalence	278 per 100 000 (≥15 years)
• Precision	0.2
• Design effect	1.3
• *k*	0.4
• Response rate	90%
• Sample size (estimated)	49 690
Number of clusters	70[b]
Cluster size	710
Eligibility criteria	
• Age	≥15 years
• Residency	Individuals who lived in the household for ≥2 weeks at the time of the census

[a] 32 townships were excluded from the sampling frame, mostly due to security issues.
[b] Five clusters (Bokepyin, Kyarinnseikkyi, Nattalin, Mindat, Kunlon) were replaced by others within the same township during the pre-visit, due to security/transportation problems and a population aged 15 years and above that was too small.

Screening criteria	
Interview	Cough ≥3 weeks and/or haemoptysis
Chest X-ray[a]	Any lung abnormality
Other	Chest X-ray exempted

[a] Conventional radiography (chest X-ray van or portable chest X-ray machine).

Laboratory methodology	
Smear	Two samples (spot, morning): direct preparation FM (auramine stain), ZN for those smears that were FM positive
Culture	Two samples (spot, morning): direct preparation, Ogawa media
Identification of MTB	PNB, niacin, capilia
TB drug susceptibility test	Not done
Xpert® MTB/RIF	Not done
HIV test	Not done

Analysis and reporting

Field data collection	Paper
Database	Epi Info
Method of analysis	Classic survey analysis, logit model
Results first published in a report/paper	November 2011
Official dissemination event	December 2010

Key survey results

Prevalence[a]	Smear-positive TB		Bacteriologically confirmed TB	
	Number per 100 000 population	95% CI	Number per 100 000 population	95% CI
Total	242	186–315	613	502–748
Male	398	301–525	931	743–1 166
Female	122	77–194	367	288–469
15–24 years	43	18–103	95	48–187
25–34 years	190	131–274	469	339–648
35–44 years	350	231–530	739	579–944
45–54 years	304	189–489	811	591–1 111
55–64 years	373	248–560	858	619–1 189
≥65 years	395	225–691	1 438	1 135–1 819
Region	192	137–267	523	421–649
State	369	236–578	838	560–1 252
Urban	331	216–506	903	662–1 232
Rural	216	154–304	527	410–677

[a] Age ≥15 years unless otherwise specified.

	Design effect	*k*
Smear-positive TB	2.2	0.8
Bacteriologically confirmed TB	3.2	0.7

Other sputum results	Number	%
Total smear-positive participants	132	–
Smear-positive participants without MTB confirmation[a]	16	12
Isolates with MDR-TB detected	N/A	N/A

[a] This includes culture with no evidence of MTB (i.e. culture-negative, NTM, contaminated, N/A).

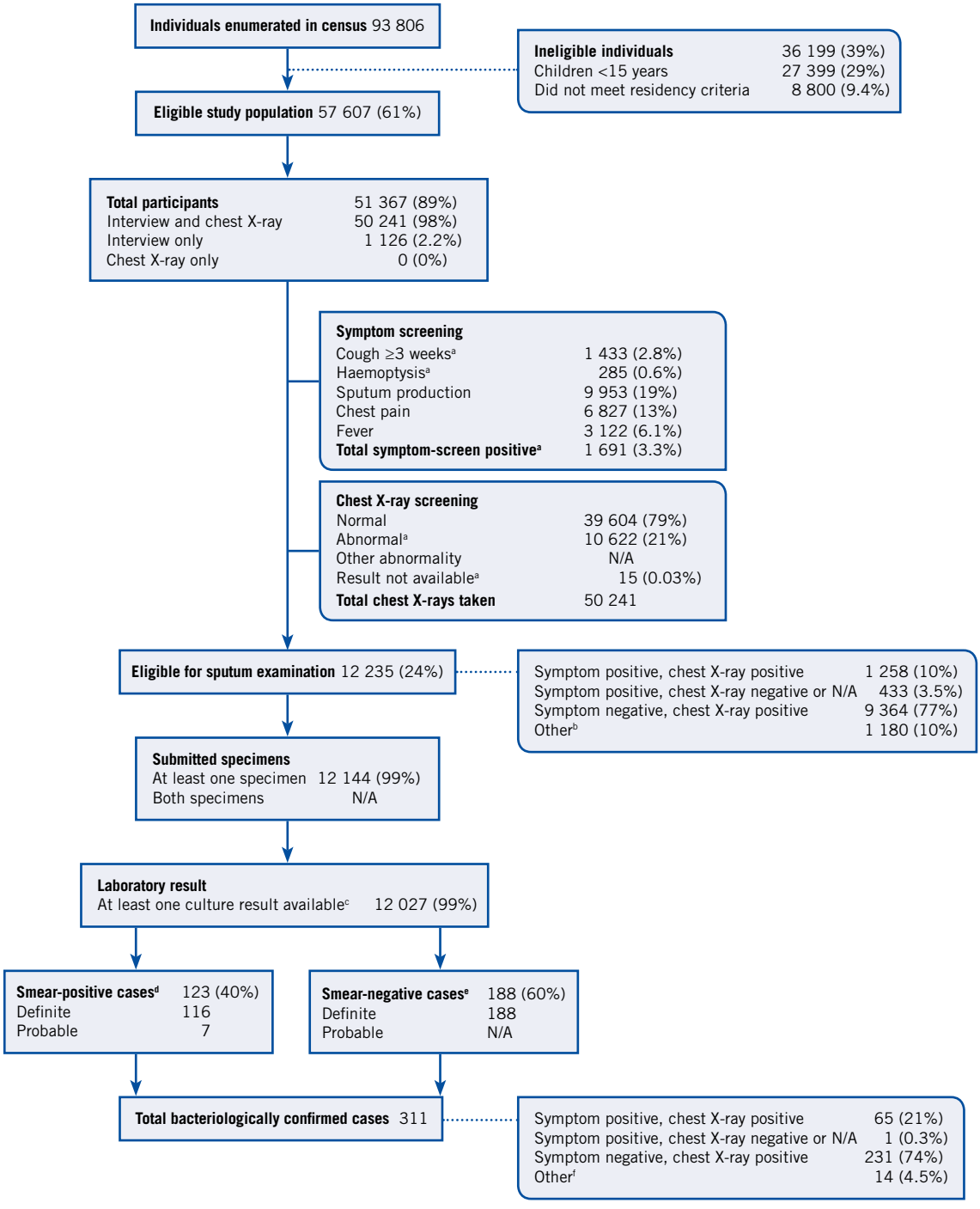
Health-care seeking behaviour among participants who were symptom-screen positive	Number	%
Participants who were symptom-screen positive[a]	1 691	–
Location of care sought		
• Consulted medical facility	363	22
Public facility	*197*	*54*
Private facility (general practitioner, specialist)	*166*	*46*
• Pharmacy	271	16
• Traditional healer	243	14
Self-treated	307	18
No action taken	440	26
Other	39	2.3
Unknown	28	1.7

[a] Cough ≥3 weeks and/or haemoptysis.

Survey participants currently on TB treatment	Number	%
Total participants currently on TB treatment	79	–
• Treated in the public sector	63	80
• Treated in the private sector (incl. general practitioner)	14	18
• Treated in unknown sector	2	2.5
Bacteriologically confirmed TB cases detected by the survey who were currently on TB treatment	13	4.2

Survey flow: census to final outcomes

Field operations: June 2009 to April 2010



[a] Eligible for sputum collection.

[b] Chest X-ray exempted and symptom-screen negative (1096), corrective action (rechecked results of the interview and chest X-ray) (70), chest X-ray uninterpretable and symptom-screen negative (14).

[c] Cultures that were either contaminated and/or missing without a definitive result (i.e. MTB, NTM, negative) were excluded.

[d] Definite: MTB confirmed by culture. Probable: MTB not confirmed by culture but two smear-positive, or one smear-positive with chest X-ray consistent with TB.

[e] Definite: MTB confirmed by culture with at least one of the following conditions met: culture-positive (≥1 colony) in both two specimens, culture-positive (1–4 colonies) in one specimen and chest X-ray consistent with TB, or culture-positive (≥5 colonies) in one specimen. Probable: no definition.

[f] Chest X-ray exempted and symptom-screen negative (12), symptom-screen negative and field chest X-ray negative (i.e. central chest X-ray healed TB) (1), symptom-screen negative and chest X-ray negative (field and central) (1) (the last two cases were from the corrective action).

Fig. 1: Participation rate by age and sex

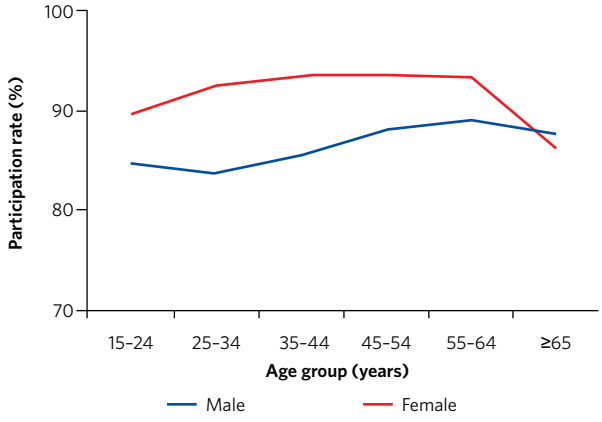


Fig. 2: TB prevalence per 100 000 population by age

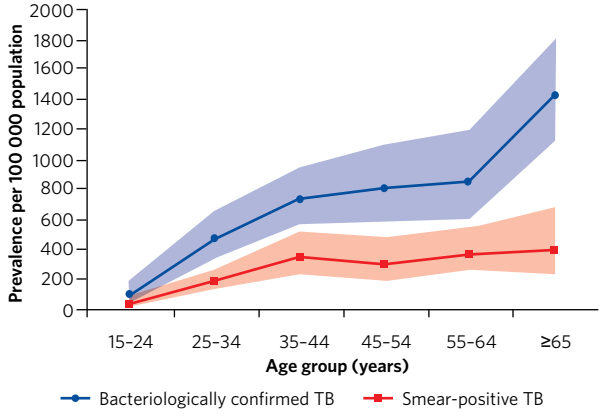


Fig. 3: Estimated number of bacteriologically confirmed TB cases and prevalence per 100 000 population, by age[a]

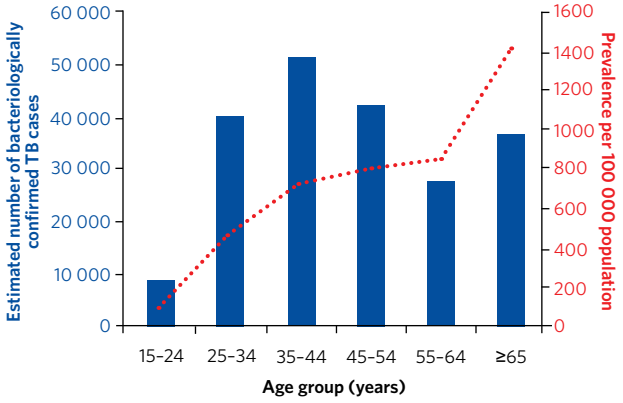


Fig. 4: Cluster variation of the number of bacteriologically confirmed TB cases[b]

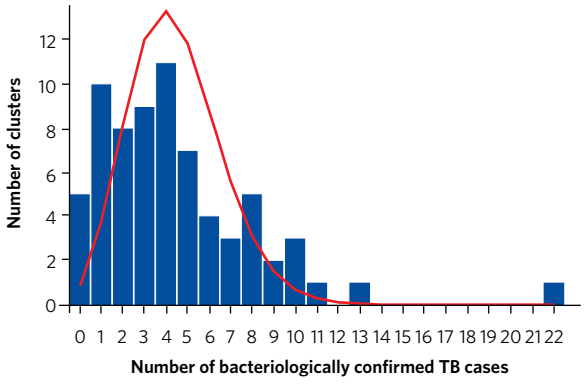


Fig. 5: Ratio of smear-positive TB prevalence to notifications by age and by sex[c]

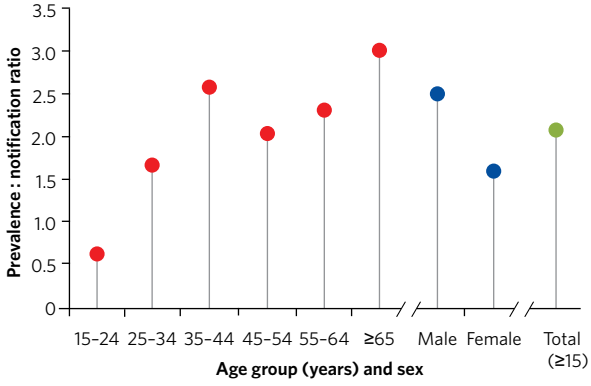
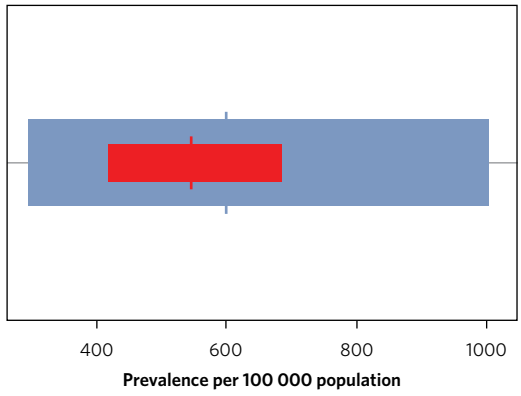


Fig. 6: Estimates of TB prevalence (all ages, all forms of TB) before (in blue) and after (in red) the national TB prevalence survey[d]



[a] The estimated number of bacteriologically confirmed TB cases is the product of age-specific prevalence and population estimates from the UN Population Division (2015 revision).

[b] The data suggested that the distribution of cases by cluster (blue bars) was significantly different from the theoretical distribution (red line) (mean 4.44, variance 13.61, $p<0.05$). The theoretical distribution assumes cases are distributed at random i.e. no clustering effect.

[c] Notification rates were estimated using notifications obtained from the WHO global TB database, and population estimates from the UN Population Division (2015 revision).

[d] The blue bar denotes the best estimate of prevalence and its range that was indirectly derived from the estimate of incidence previously published by WHO, adjusted to the year of the prevalence survey based on previously published trends in incidence.

Background

Myanmar is a country in South-East Asia that had a population of 51 million in 2009. It had an average gross national income (GNI) of US$ 630 per person per year, making it a low-income country *(1)*. It was one of the 22 high tuberculosis (TB) burden countries (HBCs) defined by WHO as a top priority for global efforts in TB control in 1998 and throughout the Millennium Development Goal (MDG) era (2000–2015), and one of the top 30 HBCs defined by WHO for the period 2016–2020. In 2009, the prevalence of HIV in the general population aged 15–49 years was 0.9% (95% confidence interval [CI]: 0.7–1.1%) *(2)*, and it was estimated that 11% (95% CI: 6.4–16%) of TB patients were coinfected with HIV *(3)*.

The National TB Programme (NTP) introduced the WHO-recommended DOTS strategy in 1997 *(4,5)*. As DOTS expanded, the case notification rate increased, from 67 (new and relapse cases) per 100 000 population in 2000 to 223 per 100 000 population in 2005. For smear-positive pulmonary TB specifically, the case notification rate increased from 38 per 100 000 population in 1999 to 76 per 100 000 population in 2005 *(6)*.

Myanmar carried out two national TB prevalence surveys before the introduction of DOTS: one in 1972 and one in 1994. The 1972 survey used chest X-ray (miniature photofluorography) and symptoms (cough, chest pain and haemoptysis) for screening and smear for diagnosis; culture testing was used in a limited number of clusters. The estimated prevalence of smear-positive pulmonary TB was 145 per 100 000 population among those aged 15 years or more. A tuberculin survey conducted at the same time suggested an annual risk of TB infection of 1.2%. Screening in the 1994 survey was based solely on symptoms, and diagnostic confirmation was limited to smear microscopy; chest X-ray and culture were conducted for a limited population but were not officially part of the protocol. The estimated prevalence of smear-positive pulmonary TB was 104 (95% CI: 72–137) per 100 000 population in participants aged 10 years or more.

In the context of continuing increases in case notifications throughout the late 1990s and 2000s, the NTP initiated plans in 2005 for a third national TB prevalence survey, this time with chest X-ray screening and diagnosis based on culture as well as smear, with technical assistance from the Research Institute of Tuberculosis/Japan Anti-Tuberculosis Association (RIT/JATA) and WHO. However, the sudden termination of a grant from the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund) in 2006 meant that survey operations were completed only in Yangon division (a pilot survey was also completed in Mandalay). A high prevalence of smear-positive and bacteriologically confirmed TB was confirmed in both the urban and rural parts of Yangon. The prevalence of smear-positive pulmonary TB was 279 (95% CI: 204–381) per 100 000 population among those aged 10 years or more, and the prevalence of bacteriologically confirmed TB was 534 (95% CI: 431–661) per 100 000 population in the same age group *(7)*.

Based on these results, the NTP advocated further for a national prevalence survey. Myanmar was also one of the 22 global focus countries for national TB prevalence surveys selected by the WHO Global Task Force on TB Impact Measurement in December 2007. Planning restarted in 2008, and the survey was launched in June 2009 in close collaboration with four major partners: Three Diseases Fund, Japanese International Cooperation Agency, United States Agency for International Development, Population Services International and WHO. The survey was completed in April 2010 *(8)*.

Key methods and results

There were 70 survey clusters in two strata (region and state, the latter having populations dominated by ethnic minorities), with a target cluster size of 710 individuals. A total of 93 806 individuals from 18 596 households were enumerated in the survey census, of whom 57 607 (61%) were eligible and invited to participate. Of these, 51 367 (89%) did so. All participants were screened according to the 2011 algorithm recommended by WHO; that is, chest X-ray and an interview about symptoms *(9)*. A total of 12 235 participants (24%) were eligible for sputum examination, of whom 12 144 (99%) submitted at least one sputum specimen.

A total of 311 bacteriologically confirmed pulmonary TB cases were identified, including 123 cases of smear-positive TB. The prevalence of smear-positive TB was 242 (95% CI: 186–315) per 100 000 population (among those aged ≥15 years), and for bacteriologically confirmed TB it was 613 (95% CI: 502–748) per 100 000 population. When extrapolated to all forms of TB and to all ages, prevalence was 544 (95% CI: 420–685) per 100 000 population. The prevalence of bacteriologically confirmed TB was much higher in the states (838 per 100 000 population; 95% CI: 560–1252) than in the regions (523 per 100 000

Photo credit: Kosuke Okada

population; 95% CI: 421–649). The prevalence of bacteriologically confirmed TB was higher in urban areas (903 per 100 000 population; 95% CI: 662–1232) than in rural areas (527 per 100 000 population; 95% CI: 410–677).

Other key results were:

- the male to female ratio was 3.3 for smear-positive TB and 2.5 for bacteriologically confirmed TB;
- prevalence per 100 000 population increased with age; however, the absolute number of bacteriologically confirmed TB cases was relatively high in the young to middle age groups (25–54 years);
- of the bacteriologically confirmed TB survey cases, 21% were symptom-screen positive, and among smear-positive cases, 34% were symptom-screen positive;
- for smear-positive pulmonary TB, the ratio of prevalence to notifications (P:N ratio) was 2.1 overall, but varied from 0.7 in those aged 15–24 years to 3.0 in those aged 65 years or more, and was higher for men than for women (2.5 versus 1.6);
- among bacteriologically confirmed TB survey cases, 86% had no previous history of anti-TB treatment and only 4.2% were on anti-TB treatment at the time of the survey; and
- of the 60 bacteriologically confirmed and 37 smear-positive TB survey cases that screened positive for symptoms and were not on anti-TB treatment at the time of the survey, 21 (35%) and 14 (38%), respectively, had previously sought care in a public or private health facility for their symptoms.

Implications of results

The 2009–2010 national TB prevalence survey revealed a high prevalence of TB in Myanmar despite efforts since the late 1990s to expand DOTS throughout the country. Although the estimated prevalence of smear-positive TB among all age groups (171 per 100 000 population; 95% CI: 131–223) was higher than the prevalence indicated in the 1994 survey, this did not mean that the burden of TB increased between 1994 and 2009 because the results were not directly comparable. The 1994 survey relied only on symptom screening and smear microscopy whereas the 2009–2010 survey used both chest X-ray and symptoms as screening tools. Prevalence results compared using the same screening criteria showed a 35% reduction in the prevalence of smear-positive pulmonary TB from 1994 to 2009–2010, suggesting that TB control efforts had a major impact.

In the 2009–2010 survey, the difference between the total number of smear-positive pulmonary cases and the number of those with classic TB symptoms (i.e. a chronic cough), and between the total number of bacteriologically confirmed cases and the number of smear-positive cases, suggested that the case detection strategies used at the time of the survey had serious limitations and that a comprehensive review of approaches to case finding was warranted. For example, TB could be considered as part of the differential diagnosis of anyone with undiagnosed chronic symptoms, regardless of the presence of cough or any respiratory illness. The expansion of diagnostic tests including chest X-ray and culture was included in the national strategic plan for TB control 2011–2015.

The finding that the prevalence of TB was higher in the states than in the regions suggested that specific efforts were needed to improve access to basic diagnostic services in the states, especially in the most remote areas.

Among the symptomatic TB cases, 24% (16/66) chose to initially seek care in pharmacies or from a traditional healer. This suggested that incorporating these providers into formal TB control and care networks could help to detect cases earlier.

The survey showed that chest X-ray was a more sensitive tool for TB detection than symptom screening. Therefore, anyone with an undiagnosed chest X-ray abnormality should be considered as a presumptive TB case and eligible for sputum examination. The diagnostic challenge was

further illustrated by the large share of smear-negative cases among all detected TB cases. Expanded use of Xpert® MTB/RIF was one of the strategies identified to address this challenge (major expansion of culture was not considered feasible, given the complexity of culture methods and the requirement for strict infection control measures).

Survey results showed that specific measures were needed in congested urban areas where prevalence rates were highest. Examples that were identified included intensified collaboration with the private sector, since this provided services at convenient hours for those living in urban areas.

Major successes, challenges and lessons learned

The survey was successfully implemented with a high participation rate and with a comparatively low survey-specific budget (US$ 1 million, excluding the costs of NTP staff who worked on the survey). Even after the withdrawal of the financing initially committed by the Global Fund, resources were mobilized from other sources following intensive efforts by the NTP and the WHO Country Office in particular. Provisional results were shared with key officials and partners within 4 months of completing field operations. Final results, including updated estimates of TB disease burden (incidence, prevalence and mortality), were fully disseminated to national and international partners in December 2010. These estimates informed the subsequent revision of the national strategic plan for TB, and contributed to the mobilization of additional funding for TB care and treatment in Myanmar.

Photo credit: Ikushi Onozaki

Challenges included the need to exclude 32 of 325 townships from the sampling frame due to security issues; the fact that residency criteria for survey eligibility meant that 9.4% of those otherwise eligible were not included in the survey (mostly the mobile population, including seasonal workers); and low participation rates in a few areas, notably a few urban clusters and remote areas. These challenges affected the coverage and representativeness of the survey. Delays in procuring chest X-ray equipment delayed the start of survey operations, and some equipment then failed during field operations. The sputum cups that were used were not optimal for the purposes of culture testing and may have caused some laboratory cross-contamination. Unfortunately, no staff were available to write a paper to summarize the key results and lessons learned from the survey in a peer-reviewed journal.

Survey results were analysed before guidance on analytical methods in the WHO handbook was finalized *(9)*. The results from analyses that were restricted to survey participants (not taking into account those eligible but not participating in the survey) were used as the official survey results. Although the survey was carried out rigorously and had a high participation rate with few missing data, later analysis (that included more extended imputation for missing data) estimated TB prevalence to be about 10% higher than results in the official survey report.

Important lessons learned included the value of the 2006 survey in Yangon for providing experience and expertise that were invaluable to the later national survey. Strong technical assistance from RIT/JATA and close collaboration with the WHO Country Office were also considered major contributions to the success of the survey.

References

1. The World Bank (https://data.worldbank.org/country, accessed April 2017).
2. UNAIDS (http://aidsinfo.unaids.org/, accessed April 2017).
3. World Health Organization. Global Tuberculosis Database. 2017. (http://www.who.int/tb/country/en/, accessed April 2017).
4. WHO Tuberculosis Programme. (1994). WHO Tuberculosis Programme: framework for effective tuberculosis control. World Health Organization. (http://www.who.int/iris/handle/10665/58717, accessed January 2018).
5. World Health Organization. Global tuberculosis programme. Global tuberculosis control report 1997. Geneva: WHO; (https://apps.who.int/iris/bitstream/handle/10665/63354/WHO_TB_97.225_(part1).pdf?sequence=1, accessed January 2018).
6. World Health Organization. Global tuberculosis report 2009. Geneva: WHO; 2009 (http://apps.who.int/iris/bitstream/10665/44035/1/9789241563802_eng.pdf?ua=1, accessed January 2018).
7. Annual report 2006. National Tuberculosis Programme, Myanmar; 2007.
8. Report on national TB prevalence survey, 2009–2010, Myanmar. Ministry of Health, Department of Health, Government of Myanmar;(https://www.who.int/tb/advisory_bodies/impact_measurement_taskforce/prevalencesurveymyanmar_2009-10report.pdf, accessed July 2017).
9. World Health Organization. Tuberculosis prevalence surveys: a handbook (WHO/HTM/TB/2010.17). Geneva: WHO; 2011 (https://apps.who.int/iris/bitstream/handle/10665/44481/9789241548168_eng.pdf, accessed August 2017).

NIGERIA

2012

Summary statistics

Participation rate	57%
Bacteriologically confirmed TB (≥15 years)	
• Prevalence per 100 000 population	524
• Male:female ratio	2.1
Prevalence:notification ratio (smear-positive TB, ≥15 years)	5.8

Surveyed clusters (N=70)[a]

Key people

Name	Role	Organization
Joshua Obasanya	Principal investigator	National TB and Leprosy Control Programme (NTBLCP)
Emmanuel Idigbe	Chairman technical committee	Nigeria Institute of Medical Research, Lagos
Chukwueme Nkemdilim	Deputy survey coordinator	National TB and Leprosy Control Programme
Osahon Ogbweiwe	Survey coordinator	Consultant, Nigeria
Philip Patrobas	In-country technical advisor	WHO Nigeria
Awe Ayodele	TB advisor to NTBLCP	WHO Nigeria
Abiola Tubi	Laboratory manager	Nigeria Centre for Disease Control (CDC-GAP)
Babalola Akin	Radiology coordinator	Gwagwalada specialist hospital
Gideon Zaphania	Central data manager	National TB and Leprosy Control Programme
Samuel Ogiri	Field team leader	WHO-National professional officer North-Central zone
Haruna Adamu	Field team leader	WHO-National professional officer North-East zone
Moses Onoh	Field team leader	Medical advisor, The Leprosy Mission Nigeria
Osakwe Puis Chijioke	Field team leader	WHO-National professional officer South-East zone
Daniel Olusoji James	Field team leader	WHO-National professional officer South-West zone
Jose Michael Madu	Field team leader	WHO-National professional officer South-South zone
Wilfred Nkhoma	Technical assistance (survey advisor)	WHO Regional Office for Africa (AFRO)
Ikushi Onozaki	Technical assistance (survey advisor)	WHO headquarters
Charalampos Sismanidis	Technical assistance (analysis)	WHO headquarters
Julia Ershova	Technical assistance (data management)	US Centers for Disease Control and Prevention (CDC)
Daniella Cirillo	Technical assistance (laboratory advisor)	Supranational Reference Laboratory Milan

Survey organization and financing

Implementing agency:
National TB and Leprosy Control Programme

Finance	Amount (US$)
Ministry of Health, Nigeria	1 226 871
The Global Fund	1 465 283
WHO	375 650
Total budget	3 067 804

Data sources

- Report first national TB prevalence survey 2012, Nigeria, Department of Public Health, Federal Republic of Nigeria.
- Survey dataset.

[a] The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Survey design and methodology

Sampling design	
Sampling frame	Whole country
Sampling design	Multistage cluster sampling using PPS
Strata	Six geographical zones (north central, north east, north west, south east, south south, south west). Final analysis accounted for urban and rural areas.
Sampling unit	Six geographical zones/local government area/enumeration area
Sample size assumptions	
• Smear-positive prevalence	346 per 100 000 (≥15 years)
• Precision	0.2
• Design effect	1.5
• *k*	0.5
• Response rate	85%
• Sample size (estimated)	49 000
Number of clusters	70[a]
Cluster size	700
Eligibility criteria	
• Age	≥15 years
• Residency	Slept in the household ≥14 days prior to the census

[a] Three clusters in the states of Borno and Yobe were excluded during field operations, due to security challenges. They were replaced with clusters in the states of Gombe, Bauchi and Adamawa.

Screening criteria	
Interview	Cough ≥2 weeks
Chest X-ray[a]	Any lung abnormality
Other	N/A

[a] Portable mobile X-ray unit (Min X-ray), computed radiography.

Laboratory methodology	
Smear	Two samples (spot, morning): direct preparation, ZN
Culture	Two samples (spot, morning): concentrated preparation, LJ media
Identification of MTB	MPT 64 rapid test
TB drug susceptibility test	Not done
Xpert® MTB/RIF	Not done
HIV test	Not done

Analysis and reporting

Field data collection	Paper/electronic
Database	Microsoft® Access
Method of analysis	MI+IPW
Results first published in a report/paper	November 2014
Official dissemination event	November 2014

Key survey results

Prevalence[a]	Smear-positive TB		Bacteriologically confirmed TB	
	Number per 100 000 population	95% CI	Number per 100 000 population	95% CI
Total	318	225–412	524	378–670
Male	484	333–635	751	538–965
Female	198	108–289	359	213–505
15–24 years	193	84–302	274	130–419
25–34 years	291	165–418	496	312–680
35–44 years	367	141–593	613	316–911
45–54 years	494	265–722	750	420–1 079
55–64 years	331	122–540	599	262–936
≥65 years	332	106–559	660	318–1 003
Urban	413	269–556	663	441–884
Rural	182	111–254	323	191–456

[a] Age ≥15 years unless otherwise specified.

	Design effect	*k*
Smear-positive TB	2.6	0.9
Bacteriologically confirmed TB	2.6	0.7

Other sputum results	Number	%
Total smear-positive participants	184	–
Smear-positive participants without MTB confirmation[a]	109	59
Isolates with MDR-TB detected	N/A	N/A

[a] This includes culture with no evidence of MTB (i.e. culture-negative, NTM, contaminated, N/A).

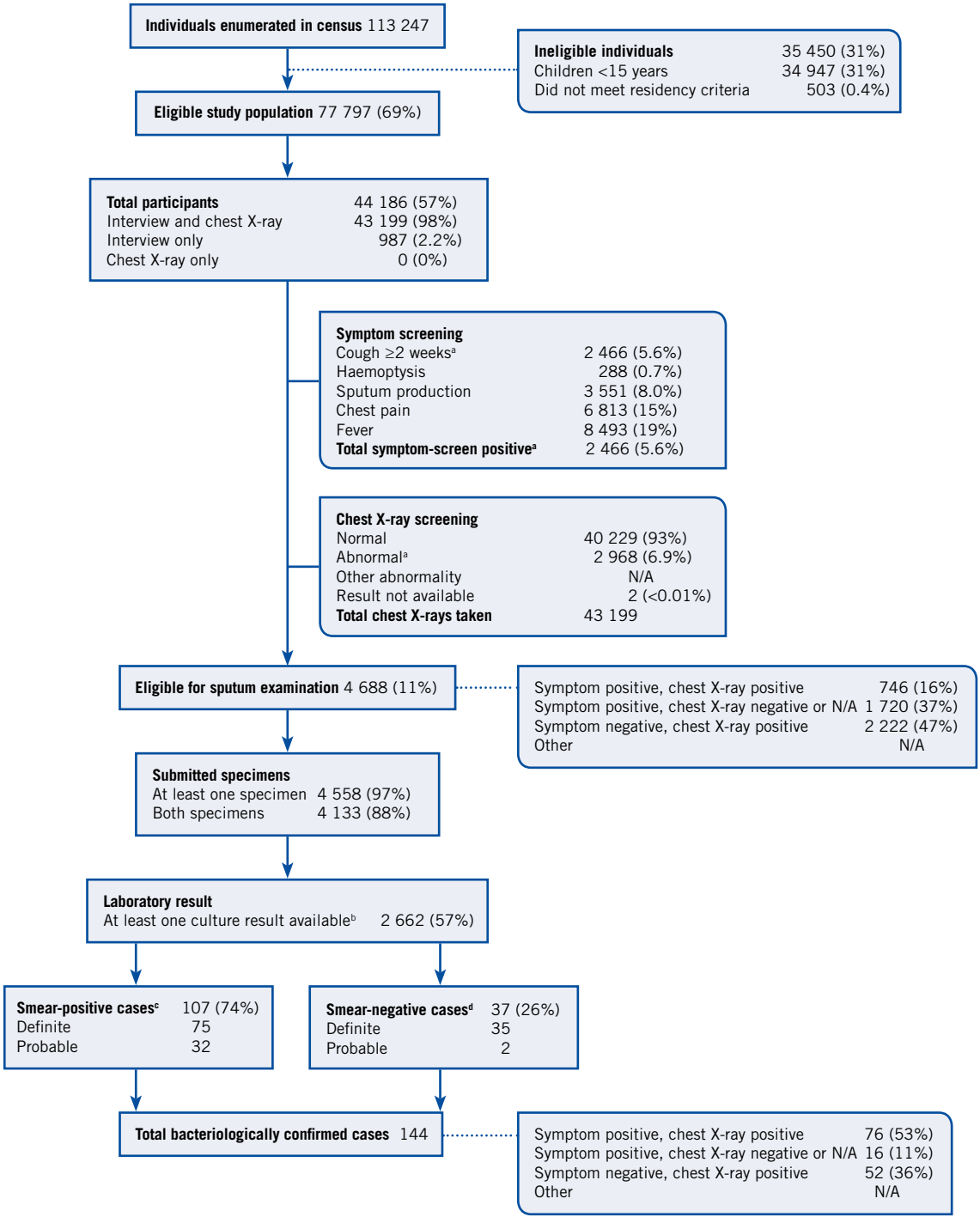
Health-care seeking behaviour among participants who were symptom-screen positive	Number	%
Participants who were symptom-screen positive[a]	2 466	–
Location of care sought		
• Consulted medical facility	800	32
Public facility	*628*	*79*
Private facility	*172*	*21*
• Pharmacy	319	13
• Traditional centre	11	0.4
• Other	9	0.4
• Unspecified	3	0.1
Self-treated	680	28
No action taken	604	24
Unknown	40	1.6

[a] Cough ≥2 weeks.

Survey participants currently on TB treatment	Number	%
Total participants currently on TB treatment	82	–
• Treated in the public sector	56	68
• Treated in the private sector	14	17
• Treated in other sector	5	6.0
• Treated in unknown sector	7	9.0
Bacteriologically confirmed TB cases detected by the survey who were currently on TB treatment	12	8.0

Survey flow: census to final outcomes

Field operations: February to November 2012



[a] Eligible for sputum collection.
[b] Cultures that were either contaminated and/or missing without a definitive result (i.e. MTB, NTM, negative) were excluded.
[c] Definite: MTB confirmed by culture. Probable: MTB not confirmed by culture, but chest X-ray suggestive of TB.
[d] Definite: MTB confirmed by culture. Probable: culture-positive without identification, and chest X-ray suggestive of TB.

Fig. 1: Participation rate by age and sex

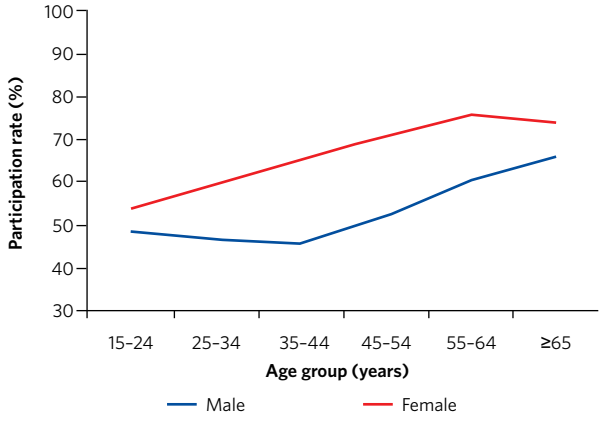


Fig. 2: TB prevalence per 100 000 population by age

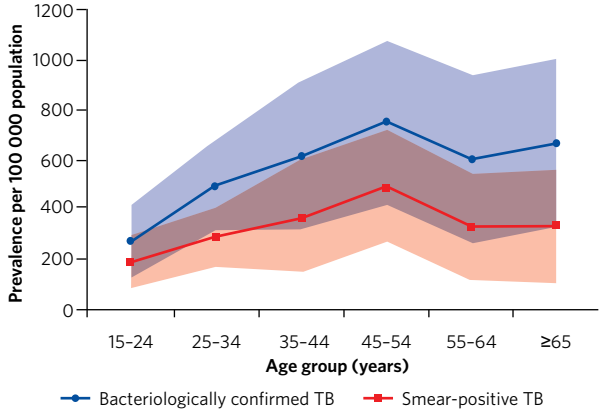


Fig. 3: Estimated number of bacteriologically confirmed TB cases and prevalence per 100 000 population, by age[a]

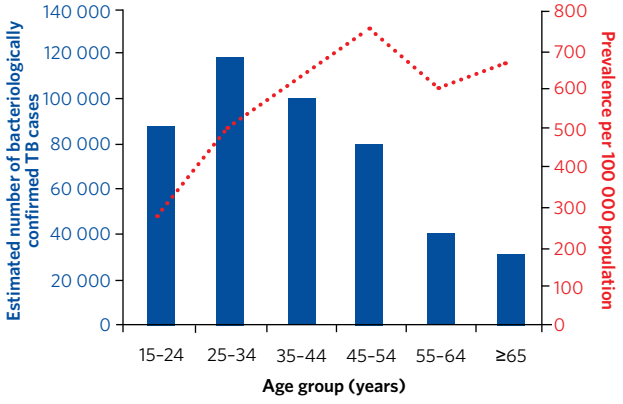


Fig. 4: Cluster variation of the number of bacteriologically confirmed TB cases[b]

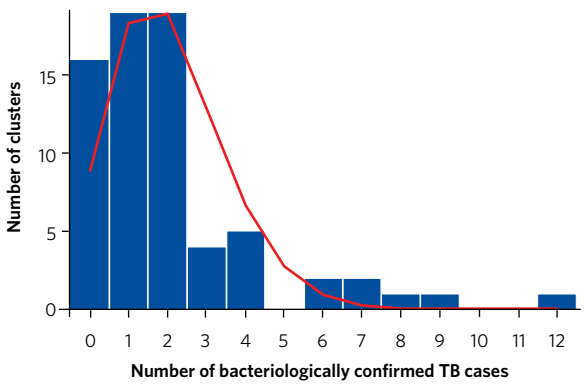


Fig. 5: Ratio of smear-positive TB prevalence to notifications by age and by sex[c]

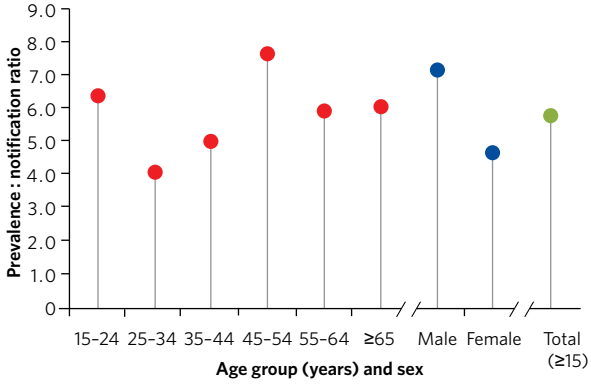
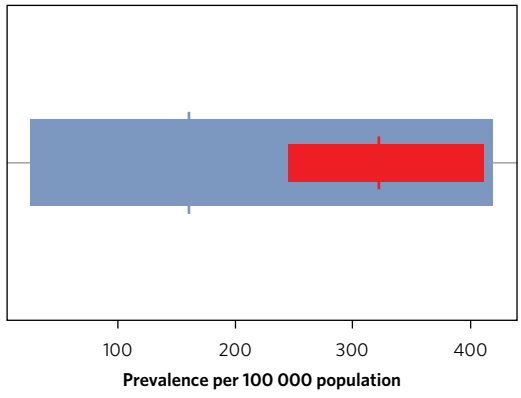


Fig. 6: Estimates of TB prevalence (all ages, all forms of TB) before (in blue) and after (in red) the national TB prevalence survey[d]



[a] The estimated number of bacteriologically confirmed TB cases is the product of age-specific prevalence and population estimates from the UN Population Division (2015 revision).

[b] The data suggested that the distribution of cases by cluster (blue bars) was significantly different from the theoretical distribution (red line) (mean 2.06, variance 5.42, $p<0.05$). The theoretical distribution assumes cases are distributed at random i.e. no clustering effect.

[c] Notification rates were estimated using notifications obtained from the WHO global TB database, and population estimates from the UN Population Division (2015 revision).

[d] The blue bar denotes the best estimate of prevalence and its range that was indirectly derived from the estimate of incidence previously published by WHO, adjusted to the year of the prevalence survey based on previously published trends in incidence.

Background

Nigeria's population was 168 million in 2012, making it the most populous country in Africa *(1)*. It was one of the 22 high tuberculosis (TB) burden countries (HBCs) defined by WHO as a top priority for global efforts in TB control in 1998 and throughout the Millennium Development Goal (MDG) era (2000–2015), and one of the top 30 HBCs defined by WHO for the period 2016–2020. In 2012, Nigeria was a lower-middle income country with an average gross national income (GNI) per person of US$ 2470 per year *(1)*. At that time the prevalence of HIV in the general population aged 15–49 years was 3.4% (95% confidence interval [CI]: 3.1–3.6%) *(2)*, and it was estimated that 24% (95% CI: 20–28%) of TB patients were coinfected with HIV *(3)*.

The National TB and Leprosy Control Programme (NTBLCP) was established in 1991 under Nigeria's Ministry of Health (MoH). By the end of 2009, the number of DOTS centres represented 56% of the targeted number of 6261, and 1025 facilities contained laboratories with microscopes, equivalent to one centre for every 149 000 people. By 2012, DOTS was being implemented in areas that accounted for 85% of the country's population. During DOTS expansion, case notifications consistently increased; however, they then plateaued between 2008 and 2012, despite an intensification of efforts to engage with public and private health-care providers outside the NTBLCP network (in 2012, these providers contributed 24% of case notifications).

Based on WHO estimates, in 2012 Nigeria ranked fourth in Africa and 11th globally in terms of estimated incident cases per year. Nonetheless, there was considerable uncertainty about estimates of the burden of TB disease, given that no national TB prevalence survey had previously been carried out, that there were no direct measurements of TB mortality available from vital registration, and that the gap between notifications and incidence (due to underreporting or underdiagnosis of cases) had not been quantified and was hard to estimate.

Photo credit: Philip Patrobas

In December 2007, Nigeria was selected by the WHO Global Task Force on TB Impact Measurement as one of 22 global focus countries for a national TB prevalence survey, with the aim of better understanding the burden of TB disease at national and global levels. In 2008, the MoH decided to implement a national TB prevalence survey. The survey started in February 2012 and was completed in November 2012 *(4)*.

Key methods and results

There were 70 survey clusters, with a target cluster size of 700 individuals (there were no strata, but urban and rural zones as well as six geographical zones were accounted for at the time of data analysis). A total of 113 247 individuals from 20 708 households were enumerated in the survey census, of whom 77 797 (69%) were eligible and invited to participate. Of these, 44 186 (57%) did so. All participants were screened according to the 2011 algorithm recommended by WHO; that is, using chest X-ray (computed radiography with the imaging plate) and an interview about symptoms *(5)*. A total of 4688 participants (11%) were eligible for sputum examination, of whom 4558 (97%) submitted at least one sputum specimen and 4133 (88%) submitted two sputum specimens.

A total of 144 bacteriologically confirmed pulmonary TB cases were identified, including 107 cases of smear-positive TB. The prevalence of smear-positive TB was 318 (95% CI: 225–412) per 100 000 population (among those aged ≥15 years) and for bacteriologically confirmed TB it was 524 (95% CI: 378–670) per 100 000 population. Prevalence was significantly higher in urban than in rural areas.

Other key results were:

- the male to female ratio was 2.4 for smear-positive TB and 2.1 for bacteriologically confirmed TB;

- prevalence per 100 000 population increased with age (with a peak among those aged 45–54 years); however, the absolute number of bacteriologically confirmed TB cases was relatively high in young age groups;
- among bacteriologically confirmed TB cases, 64% were symptom-screen positive, and among the smear-positive cases, 75% were symptom-screen positive;
- for smear-positive pulmonary TB, the ratio of prevalence to notifications (P:N ratio) was 5.8 overall, but varied from 4.1 in those aged 25–34 years to 7.7 among those aged 45–54 years, and was much higher for men then for women (7.2 versus 4.6);
- among bacteriologically confirmed TB cases, 85% had no previous history of anti-TB treatment and only 8% were on anti-TB treatment at the time of the survey; and
- of the 80 bacteriologically confirmed and 68 smear-positive TB survey cases that screened positive for symptoms and were not on anti-TB treatment at the time of the survey, 43 (54%) and 36 (53%), respectively, had previously sought care in a public or private health facility for their symptoms.

Photo credit: Philip Patrobas

Implications of results

The survey clearly demonstrated a high burden of TB disease in Nigeria, with an estimated prevalence of 323 (95% CI: 239–406) per 100 000 population (all forms of TB, all ages). The findings highlighted TB as a major public health problem that was much worse than previously thought, with a prevalence of 171 (95% CI: 44–382) per 100 000 population *(6)*. The age distribution of cases and the high proportion of symptomatic cases in the community also demonstrated considerable ongoing transmission. After adjustments to include children and extrapulmonary TB, estimates of TB disease burden published by WHO were revised substantially upwards: estimates of TB prevalence were doubled, those for TB incidence trebled and those for TB mortality were increased fivefold compared with the previously estimated levels. The best estimate of the case detection rate (notifications of new and relapse cases divided by estimated incidence) was revised downwards.

The survey had major programmatic, policy and funding implications. These included:

- a need to substantially improve access to basic DOTS services to diagnose and treat people with TB; this was particularly evident from the high ratio of prevalent to notified TB cases (among the highest found in any survey conducted since 1990), and the fact that 75% of smear-positive cases already had typical TB symptoms but had either not yet sought care, or had sought health care but not been diagnosed;
- a need for specific efforts in the hotspots where TB prevalence was highest – there was considerable variation in TB prevalence among survey clusters; and
- a need for increased domestic funding at the federal government level, and especially at the state and local government authority levels, complemented by more international funding.

Part of the reason for the large gap between the number of prevalent TB cases and the number of cases captured by the routine surveillance system could have been underreporting of detected cases. Possible solutions identified included strengthening linkages with all care providers and making TB notification mandatory by law.

Major successes, challenges and lessons learned

The major success of this survey was that it was the first of its kind in Nigeria and contributed to a much better understanding and robust measurement of the burden of TB disease in the country. It was also implemented and completed in the face of several challenges beyond the control of the NTBLCP and the survey team.

The biggest challenge outside the control of the NTBLCP and survey teams was the security situation in the country, which deteriorated during both preparations for and implementation of the survey. In August 2011, just as survey preparations (including all procurement) were almost complete and the survey was about to start, a terrorist attack occurred in the capital of Abuja. A bomb hidden in a car exploded underneath the United Nations (UN) building, killing 21 people and wounding 60 others (including WHO staff). Following this attack, the UN raised its rating of the security level and there was considerable debate about whether the survey should be cancelled.

Eventually, the MoH decided to launch the survey in February 2012. Only three of the original list of randomly selected clusters had to be replaced due to the security measures in place; nevertheless, the security situation had other serious repercussions:

- limited hours of operation for data collection during cluster operations (it was done from 7am to 5pm);
- negative attitudes, including advice (or instructions) from some community leaders not to participate in the survey;
- extremely limited access to the northern regions of the country (including the National TB Reference Laboratory used for the prevalence survey) for international staff;
- no international technical assistance to the National TB Reference Laboratory in Zaria, although local staff from the United States Centers for Disease Control and Prevention continued to provide support; and
- delays to the start of the survey that led to the expiry of the contract and associated licenses for X-ray software, which had to be re-procured.

Photo credit: Philip Patrobas

Linked to these repercussions, other major challenges included a low participation rate, especially in urban areas; a large number of positively-screened participants with missing culture results; and the possible under-performance of culture laboratories (related to lack of technical assistance). The implications of these challenges had to be investigated and adjusted for during analysis of survey data. Even with these data limitations, analyses that included imputation of missing data and sensitivity analysis showed that the limitations did not affect the main policy and programmatic implications drawn from the survey. For example, even if it was assumed that all those who refused to participate in the survey were healthy (i.e. without active TB disease), the number of detected TB cases still far exceeded the number of TB cases being detected and notified.

Other challenges faced during the survey included: oversampling during field operations, despite the low participation rate (although field teams correctly registered the population in enumeration areas, regardless of their willingness to participate); survey investigators did not have access to national census data; staff from the Bureau of Statistics, who joined cluster operations, changed for each cluster; a 1-month suspension of field operations due to extreme rainfall; slow data entry from the field and in the laboratory; and delays in finalizing the survey report due to the departure of the survey coordinator and the lack of a full-time officer in the NTBLCP to oversee the survey.

Important lessons learned for future surveys included the importance of ensuring that someone is available to prepare the survey report and of budgeting adequately for this activity; and working with the Bureau of Statistics, to inform them of the need to select clusters based on agreed survey methodology and not on their routine census activities.

References

1. The World Bank (https://data.worldbank.org/country, accessed April 2017).
2. UNAIDS (http://aidsinfo.unaids.org/, accessed April 2017).
3. World Health Organization. Global Tuberculosis Database. 2017. (http://www.who.int/tb/country/en/, accessed April 2017).
4. Report first national TB prevalence survey 2012 Nigeria: Department of Public Health, Federal Republic of Nigeria; 2014 (http://www.who.int/tb/publications/NigeriaReport_WEB_NEW.pdf, accessed May 2017).
5. World Health Organization. Tuberculosis prevalence surveys: a handbook (WHO/HTM/TB/2010.17). Geneva: WHO; 2011 (https://apps.who.int/iris/bitstream/handle/10665/44481/9789241548168_eng.pdf, accessed August 2017).
6. World Health Organization. Global tuberculosis report 2012. Geneva: WHO; 2012 (http://www.who.int/tb/publications/global_report/gtbr12_main.pdf, accessed June 2017).

PAKISTAN

2010–2011

Summary statistics

Participation rate	81%
Bacteriologically confirmed TB (≥15 years)	
• Prevalence per 100 000 population	398
• Male:female ratio	1.5
Prevalence:notification ratio (smear-positive TB, ≥15 years)	2.9

Surveyed clusters (N=95)[a]

Key people

Name	Role	Organization
Ejaz Qadeer	Principal investigator	National TB Control Programme (NTP)
Sabira Tahseen	Co-principal investigator	National TB Reference Laboratory (NTRL)
Razia Fatima	Co-principal investigator	NTP
Mohammad Asif	Survey coordinator	NTP
Alamdar Hussain Rizvi	Senior microbiologist	NTRL, NTP
Sabir Rehman	Radiology coordinator	NTP
Zia Samad	Data coordinator	NTP
Aisha Mariam	Field team leader	NTP
Abdul Mannan Soomro	Field team leader	NTP
Arshad Shamsi	Field team leader	NTP
Riaz Ahmed	Field team leader	NTP
Ghulam Nabi Shaikh	Field team leader	NTP
Zulfiqar Ul Hassan	Field team leader	NTP
Edine Tiemersma	Technical assistance (survey advisor)	KNCV Tuberculosis Foundation
Masja Straetemans	Technical assistance (survey advisor)	KNCV Tuberculosis Foundation
Nico Kalisvaart	Technical assistance (data management)	KNCV Tuberculosis Foundation
Amal Bassili	Technical assistance (survey advisor)	WHO Eastern Mediterranean Regional Office (EMRO)

Survey organization and financing

Implementing agency:
National TB Control Programme

Finance	Amount (US$)
TB CAP	3 131 770
TB CARE	1 240 787
Total budget	4 372 557

Data sources

- Prevalence of pulmonary tuberculosis among the adult population of Pakistan 2010–2011. Ministry of Health.
- Qadeer E, Fatima R, Yaqoob A, Tahseen S, Ul Haq M, Ghafoor A et al. Population based national tuberculosis prevalence survey among adults (≥15 years) in Pakistan, 2010–2011. PLoS One. 2016; 11(2).

[a] The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Survey design and methodology

Sampling design	
Sampling frame	Whole country excluding the Federally Administered Tribal Areas, district Dera Bugti in Balochistan and 17 tehsils of Khyber Pakhtunkhwa
Sampling design	Multistage cluster sampling using PPS
Strata	No stratification was used, but the final analysis accounted for four provinces and two regions (Punjab, Sindh, Balochistan, Khyber Pakhtunkhwa, Azad Jammu and Kashmir, Gilgit-Baltistan), and urban/rural
Sampling unit	Province/district/tehsil/union council
Sample size assumptions	
• Smear-positive prevalence	213 per 100 000 (≥15 years)
• Precision	0.2
• Design effect	2.5
• *k*	0.7
• Response rate	85%
• Sample size (estimated)	133 000
Number of clusters	95[a]
Cluster size	1 400
Eligibility criteria	
• Age	≥15 years
• Residency	Individuals who slept in the household the night before the census

[a] Three clusters in Balochistan (Lehri, Quetta, Awaran) were replaced by other clusters (Sharda in Azad-Jammu and Kashimir, Khan Pur in Punjab and Hub in Balochistan) due to security issues.

Screening criteria	
Interview[a]	Cough ≥2 weeks or cough of any duration with no chest X-ray result
Chest X-ray[b]	Any lung abnormality
Other	TB treatment at the time of the survey

[a] The first short screening consisted of questions about current TB treatment, current cough and its duration, and smoking behaviour. An in-depth interview (other TB symptoms and health-care seeking behaviour) was done only for those who screened positive.
[b] Digital radiography (portable).

Laboratory methodology	
Smear	Two samples (spot, morning): direct preparation, ZN (spot sample was examined in the field site, morning sample in the central laboratory)
Culture	One sample (morning): direct preparation, Modified Kudoh method
Identification of MTB	PNB, MPB64: all culture-positive samples LPA, Xpert MTB/RIF: smear-positive with culture-negative or contaminated or N/A
TB drug susceptibility test	Done
Xpert® MTB/RIF	Done only for smear-positive with culture-negative or contaminated or N/A
HIV test	Not done

Analysis and reporting

Field data collection	Paper/electronic
Database	EpiData version 3.1
Method of analysis	MI+IPW
Results first published in a report/paper	March 2014
Official dissemination event	March 2014

Key survey results

Prevalence[a]	Smear-positive TB		Bacteriologically confirmed TB	
	Number per 100 000 population	95% CI	Number per 100 000 population	95% CI
Total	270	217–323	398	333–463
Male	352	273–431	484	392–577
Female	197	145–249	320	253–388
15–24 years	180	120–239	242	168–315
25–34 years	163	100–226	228	149–307
35–44 years	293	196–391	398	275–521
45–54 years	392	254–530	517	362–671
55–64 years	386	231–540	587	377–797
≥65 years	691	439–942	1 369	1 028–1 710
Urban	209	147–270	310	234–386
Rural	321	241–401	471	377–564

[a] Age ≥15 years unless otherwise specified.

	Design effect	*k*
Smear-positive TB	2.0	0.6
Bacteriologically confirmed TB	2.4	0.6

Other sputum results	Number	%
Total smear-positive participants	236	–
Smear-positive participants without MTB confirmation[a]	29	12
Isolates with MDR-TB detected[b]	5	2.7

[a] This includes culture with no evidence of MTB (i.e. culture-negative, NTM, contaminated, N/A) and NAAT-negative.
[b] 182 strains were tested.

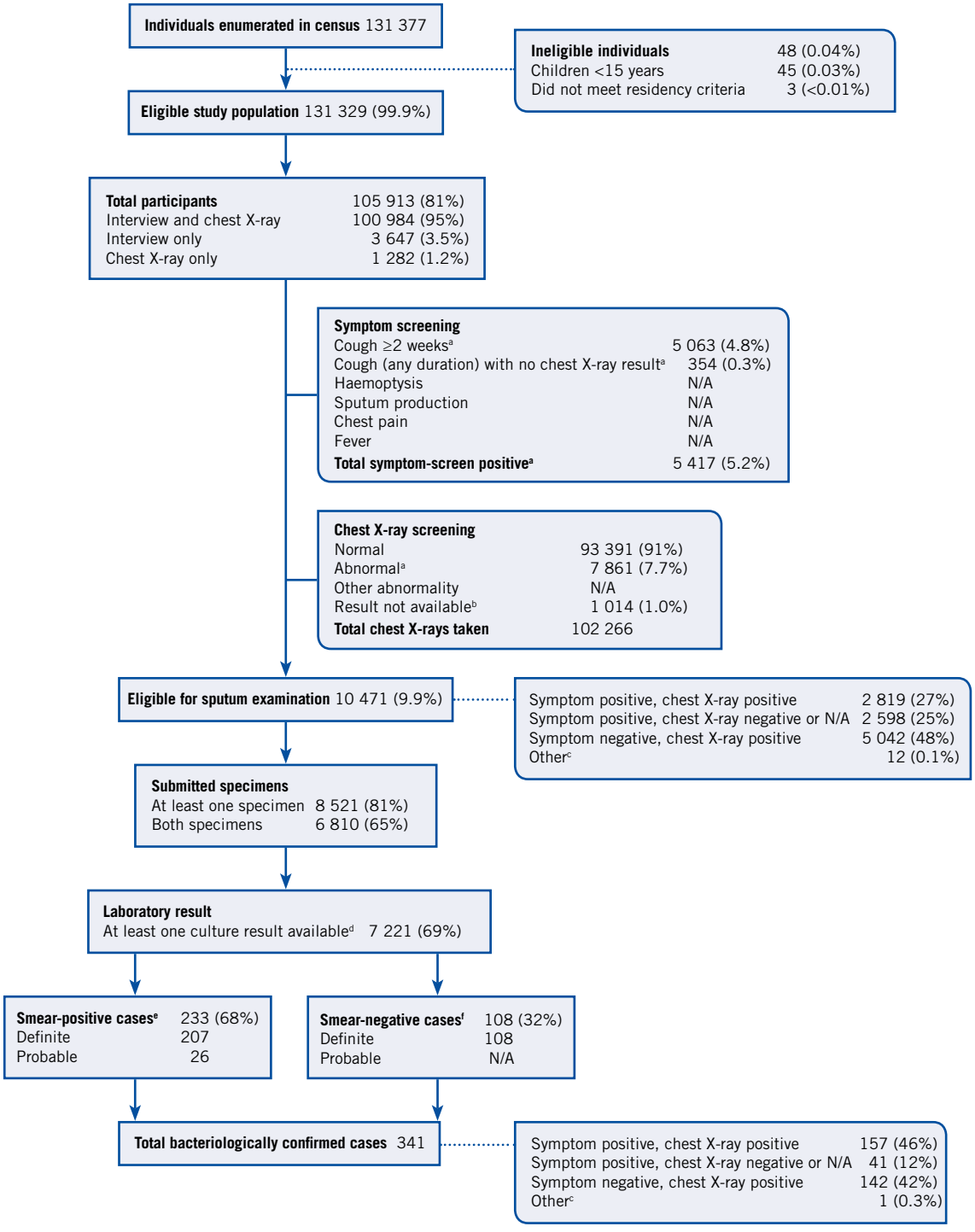
Health-care seeking behaviour among participants who were symptom-screen positive	Number	%
Participants who were symptom-screen positive[a]	5 417	–
Location of care sought		
• Consulted medical facility	N/A	N/A
Public facility	N/A	N/A
Private facility	N/A	N/A
Other	N/A	N/A
• Pharmacy	N/A	N/A
• Traditional healer	N/A	N/A
No action taken	N/A	N/A
Unknown	N/A	N/A

[a] Cough ≥2 weeks or cough of any duration with no chest X-ray result.

Survey participants currently on TB treatment	Number	%
Total participants currently on TB treatment	146	–
• Treated in the public sector	N/A	N/A
• Treated in the private sector	N/A	N/A
• Treated in unknown sector	N/A	N/A
Bacteriologically confirmed TB cases detected by the survey who were currently on TB treatment	26	7.6

Survey flow: census to final outcomes

Field operations: December 2010 to December 2011



[a] Eligible for sputum collection.
[b] The result was not entered on the form (933) or the form was not available (81).
[c] Current TB treatment with symptom-screen negative and chest X-ray normal.
[d] Cultures that were either contaminated and/or missing without a definitive result (i.e. MTB, NTM, negative) were excluded.
[e] Definite: MTB confirmed by culture and/or NAAT. Probable: MTB not confirmed by culture and/or NAAT, but two smear-positive or one smear-positive with chest X-ray suggestive of TB.
[f] Definite: MTB confirmed by culture (more than 5 colonies, or less than 5 colonies with chest X-ray suggestive of TB). Probable: no definition.

Fig. 1: Participation rate by age and sex

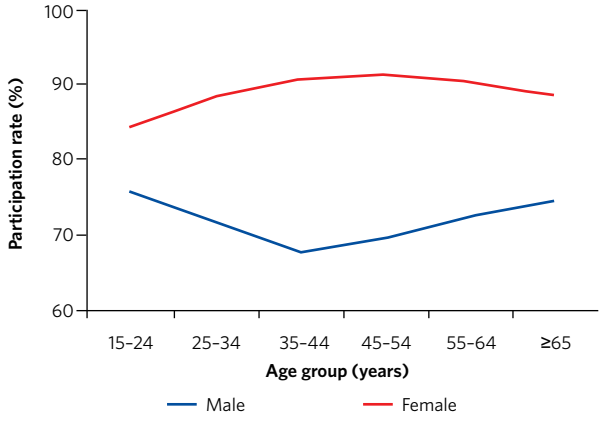


Fig. 2: TB prevalence per 100 000 population by age

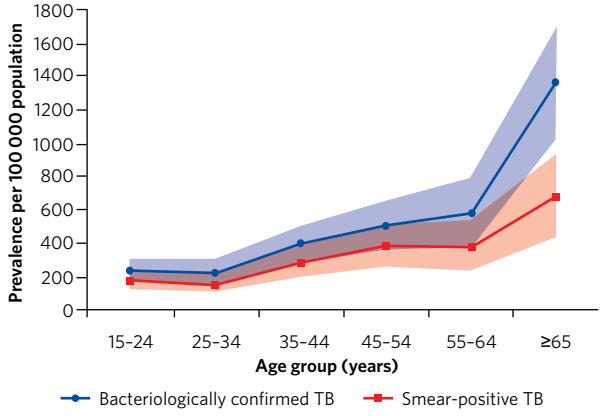


Fig. 3: Estimated number of bacteriologically confirmed TB cases and prevalence per 100 000 population, by age[a]

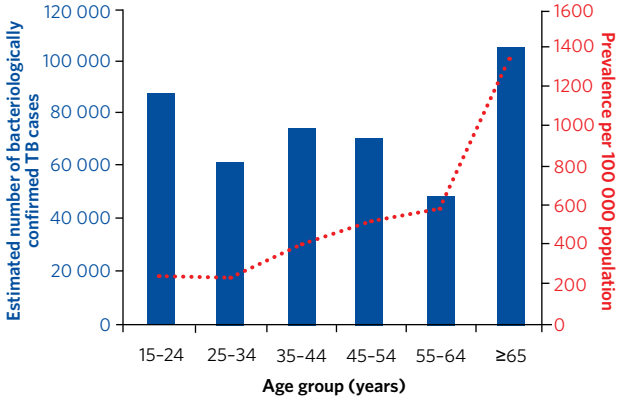


Fig. 4: Cluster variation of the number of bacteriologically confirmed TB cases[b]

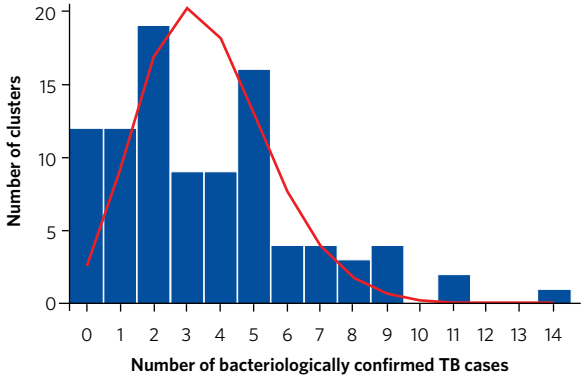


Fig. 5: Ratio of smear-positive TB prevalence to notifications by age and by sex[c]

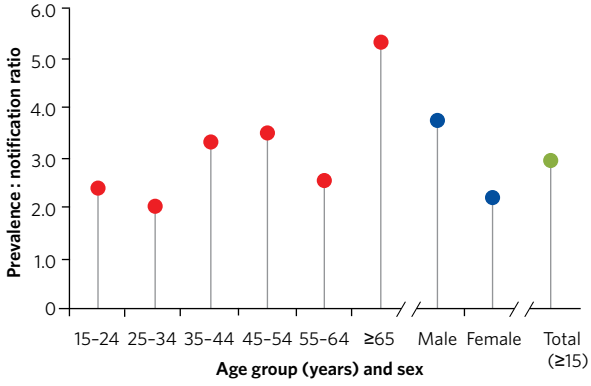
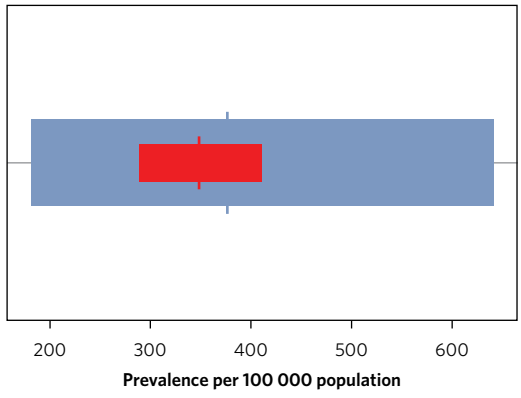


Fig. 6: Estimates of TB prevalence (all ages, all forms of TB) before (in blue) and after (in red) the national TB prevalence survey[d]



[a] The estimated number of bacteriologically confirmed TB cases is the product of age-specific prevalence and population estimates from the UN Population Division (2015 revision).

[b] The data suggested that the distribution of cases by cluster (blue bars) was significantly different from the theoretical distribution (red line) (mean 3.59, variance 8.33, $p<0.05$). The theoretical distribution assumes cases are distributed at random i.e. no clustering effect.

[c] Notification rates were estimated using notifications obtained from the WHO global TB database, and population estimates from the UN Population Division (2015 revision).

[d] The blue bar denotes the best estimate of prevalence and its range that was indirectly derived from the estimate of incidence previously published by WHO, adjusted to the year of the prevalence survey based on previously published trends in incidence.

Background

Pakistan's population was 173 million in 2011, and it had an average gross national income (GNI) per person of US$ 1150 per year, making it a lower-middle-income country *(1)*. It was one of the 22 high tuberculosis (TB) burden countries (HBCs) defined by WHO as a top priority for global efforts in TB control in 1998 and throughout the Millennium Development Goal (MDG) era (2000–2015), and one of the top 30 HBCs defined by WHO for the period 2016–2020. In 2011, the prevalence of HIV in the general population aged 15–49 years was <0.1% (95% confidence interval [CI]: <0.1–<0.1%) *(2)*, and it was estimated that 0.8% (95% CI: 0.6–0.9%) of TB patients were coinfected with HIV *(3)*.

The National TB Programme of Pakistan was revived in 2000 with a well-defined central unit, four TB control units at provincial level and one TB coordinator for each of the 139 districts. Implementation of the WHO-recommended DOTS strategy *(4,5)* began in 2000, and by 2005 full geographical coverage had been achieved in the public sector. The case notification rate (all forms of TB) increased from 7.7 per 100 000 population in 2000 to 153 per 100 000 population in 2010. In 2010, WHO estimated the incidence and prevalence of all forms of TB at 231 (95% CI: 190–276) per 100 000 population and 389 (95% CI: 191–657) per 100 000 population, respectively *(6–8)*.

Before 2010, three national TB prevalence surveys had been implemented: in 1960–1962, 1974–1978 and 1987–1989. The screening and diagnostic methods used in the last of these surveys were a chest X-ray and an interview about symptoms, followed by smear microscopy for those reporting TB symptoms or with an abnormal X-ray. The prevalence of smear-positive pulmonary TB was estimated to be 170 per 100 000 population *(7)*.

In December 2007, Pakistan was one of the 22 global focus countries selected as a priority for a national TB prevalence survey by the WHO Global Task Force on TB Impact Measurement. National authorities had also recognized the value of a fourth national TB prevalence survey. At the same time, the feasibility of a survey was extensively discussed due to security concerns. Eventually, it was decided to implement a survey that excluded the country's Federally Administered Tribal Areas and one district from Balochistan (Dera Bugti). Based on the most recent census data from these areas (from 1998), it was estimated that these excluded areas accounted for 6.5% of the country's population.

The fourth national TB prevalence survey started in December 2010 and was completed in December 2011.

Photo credit: NTP

Key methods and results

There were 95 clusters with a target size of 1400 individuals per cluster. No stratification was used at the time of survey design; however, results were later analysed separately for four provinces and two regions (Punjab, Sindh, Balochistan, Khyber Pakhtunkhwa, Azad Jammu and Kashmir, Gilgit-Baltistan), and for urban and rural areas. A total of 131 377 individuals from 33 324 households were enumerated in the survey census, of whom 131 329 (99.9%) were eligible and invited to participate. Of these, 105 913 (81%) did so. All participants were screened according to the 2011 algorithm recommended by WHO; that is, chest X-ray and an interview about symptoms *(9)*. A total of 10 471 people (10% of participants) were eligible for sputum examination; of these 8521 (81%) submitted at least one sputum specimen and 6810 (65%) submitted two sputum specimens.

A total of 341 cases of bacteriologically confirmed pulmonary TB were identified, including 233 cases of smear-positive TB. The prevalence of smear-positive pulmonary TB was 270 (95% CI: 217–323) per 100 000 population (among those aged ≥15 years), and for bacteriologically confirmed TB it was 398 (95% CI: 333–463) per 100 000 population. The prevalence of bacteriologically confirmed TB was higher in rural areas (471 per 100 000 population; 95% CI: 377–564) than in urban areas (310 per 100 000 population; 95% CI: 234–386).

Other key results were:

- the male to female ratio was 1.8 for smear-positive TB and 1.5 for bacteriologically confirmed TB;
- prevalence per 100 000 population increased with age; however, the absolute number of bacteriologically confirmed TB cases was consistently high in all age groups;
- among bacteriologically confirmed TB cases, 58% were symptom-screen positive, and among the smear-positive cases, 62% were symptom-screen positive;
- for smear-positive pulmonary TB, the ratio of prevalence to notifications (P:N ratio) was 2.9 overall, but varied from 2.1 in those aged 25–34 years to 5.3 in those aged 65 years or more, and was higher for men than for women (3.8 versus 2.2);
- among bacteriologically confirmed TB cases, only 7.6% were on anti-TB treatment at the time of the survey; no data about previous history of anti-TB treatment were available.

No data were available on whether participants with symptoms had sought health care.

Photo credit: NTP

Implications of results

Based on survey results, the overall prevalence of TB (all forms of TB, all ages) was estimated as 342 (95% CI: 284–406) per 100 000 population. This was similar to (but more precise than) the pre-survey estimate published by WHO (389 per 100 000 population; 95% CI: 191–657) *(8)*. This result showed that TB remained a major public health problem in Pakistan, requiring continued high-level political commitment and sustained funding.

The high number of previously undiagnosed cases detected in the community, and the fact that 68% of these were smear-positive, suggested that people may not recognize the symptoms of TB, and that when they do seek care they may not be diagnosed. These findings indicated a need to implement strategies to increase population awareness of TB symptoms, and to improve the availability and quality of services for TB diagnosis and treatment in the community. It was also recognized that further analysis of health-care seeking behaviour and of awareness of TB among health-care providers could help the programme to design specific interventions. The higher prevalence of TB in older age groups and in rural areas demonstrated a need for improved case finding in these groups and areas in particular. One proposed option was active engagement of trained community health workers to help identify and refer people with TB symptoms to health services.

Given the P:N ratio of 2.9, and results from a subsequent TB inventory study of the level of underreporting of detected TB cases in 2012, it was clear that both underreporting and underdiagnosis of TB needed to be addressed *(10)*. With a large private sector, and less than 1% of private providers reporting TB cases to national authorities at the time of the survey, factors identified as being of vital importance were much greater engagement of the private sector and mandatory notification of cases.

The survey was the first time the specimen transport system was successfully used for the transport of specimens via cold chain from field sites to the National TB Reference Laboratory (NTRL). This experience was used to improve specimen transportation undertaken as part of routine programmatic activities.

Major successes, challenges and lessons learned

Given the security and geographical challenges, the successful implementation of the survey was a major achievement.

Security concerns persisted throughout survey implementation. A complete security assessment was done and a handbook on security and safety was prepared in consultation with international experts in

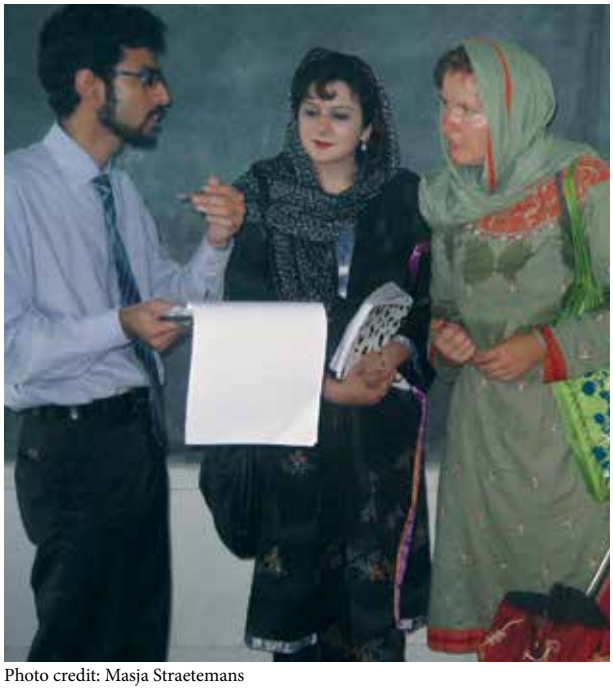


Photo credit: Masja Straetemans

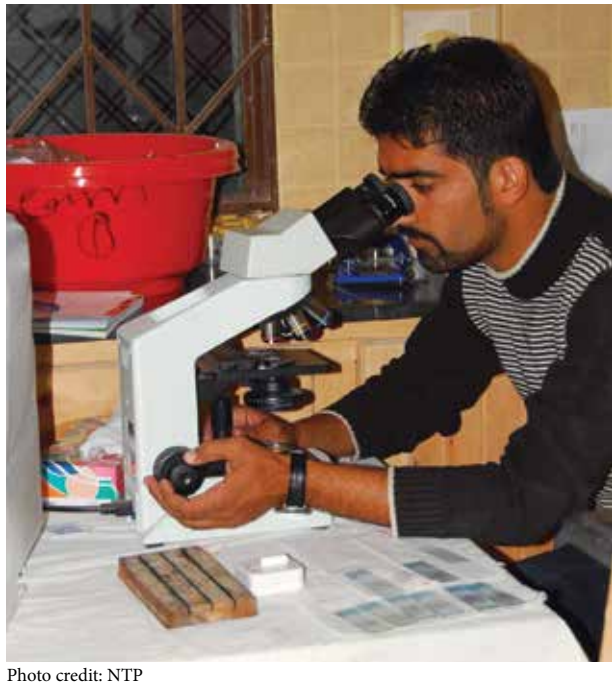


Photo credit: NTP

2010. Nonetheless, there were gaps in the monitoring and uptake of recommendations because those responsible for providing international technical assistance were not able to visit field sites. During the survey, three tehsils (administrative units) from Balochistan (Lehri, Quetta and Awaran) were replaced by three clusters (Sharda in Azad Jammu and Kashmir, Khan Pur in Punjab and Hub in Balochistan).

The survey was also affected by a natural disaster. A major flood, mainly in Sindh province, affected a large part of the country, including 12 survey clusters. The flood damaged local infrastructure and displaced people. The survey field team visited the affected areas last, by which time the situation had improved. There was also a heatwave during field operations, during which it was an enormous challenge to maintain a cold chain for sputum transportation from clusters in remote villages to the NTRL.

The NTRL achieved a lower than expected level of culture recovery, with only 69% (161/233) of the cases of smear-positive TB being confirmed by culture. Therefore, survey case definitions were amended to allow for the use of molecular tests (Genotype MTBDRplus or Xpert® MTB/RIF, or both), which were then used to confirm whether individuals with a smear-positive result had TB. Another 46 of the 233 smear-positive TB cases (20%) were bacteriologically confirmed in this way.

The survey faced major challenges with data management, and important lessons were learned that were subsequently used to help surveys in other countries. In particular, data collection in the field was based on multiple forms for each participant, rather than a single form. Besides needing to manage multiple forms, manual transcription errors when entering personal identification numbers (PINs) on the forms made it difficult to later match records (forms) for the same individual. Initially, about 8% of PINs were not available in the census register. It took more than a year of data cleaning and verification to produce the survey results. Data management challenges also delayed the follow-up of people with positive laboratory results.

References

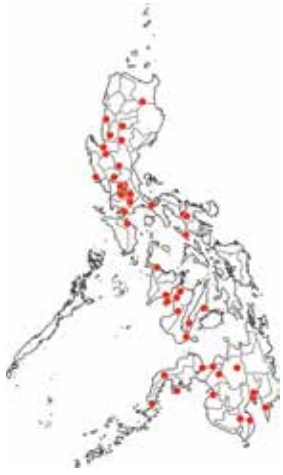
1. The World Bank (https://data.worldbank.org/country, accessed April 2017).
2. UNAIDS (http://aidsinfo.unaids.org/, accessed April 2017).
3. World Health Organization. Global Tuberculosis Database. 2017. (http://www.who.int/tb/country/en/, accessed April 2017).
4. WHO Tuberculosis Programme. (1994). WHO Tuberculosis Programme: framework for effective tuberculosis control. World Health Organization. (http://www.who.int/iris/handle/10665/58717, accessed January 2018).
5. World Health Organization. Global tuberculosis programme. Global tuberculosis control report 1997. Geneva: WHO; (https://apps.who.int/iris/bitstream/handle/10665/63354/WHO_TB_97.225_(part1).pdf?sequence=1, accessed January 2018).
6. Prevalence of pulmonary tuberculosis among the adult population of Pakistan 2010–2011. Ministry of Health; (http://www.ntp.gov.pk/uploads/Prevalence_Report.pdf, accessed July 2017).
7. Qadeer E, Fatima R, Yaqoob A, Tahseen S, Ul Haq M, Ghafoor A et al. Population based national tuberculosis prevalence survey among adults (>15 years) in Pakistan, 2010–2011. PLOS ONE. 2016;11(2); (http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0148293, accessed January 2018).
8. World Health Organization. Global tuberculosis report 2013. Geneva: WHO; 2013 (http://apps.who.int/iris/bitstream/10665/91355/1/9789241564656_eng.pdf, accessed January 2018).
9. World Health Organization. Tuberculosis prevalence surveys: a handbook (WHO/HTM/TB/2010.17). Geneva: WHO; 2011 (https://apps.who.int/iris/bitstream/handle/10665/44481/9789241548168_eng.pdf, accessed August 2017).
10. Fatima R. Investigation of presumptive tuberculosis cases by private health providers: lessons learnt from a survey in Pakistan. 2014;4(2):110–112; (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4539039/pdf/i2220-8372-4-2-110.pdf, accessed January 2018).

PHILIPPINES

2007

Summary statistics

Participation rate (chest X-ray)	90%
Bacteriologically confirmed TB (≥10 years)	
• Prevalence per 100 000 population	660
• Male:female ratio	2.6
Prevalence:notification ratio (smear-positive TB, ≥15 years)	1.9



Surveyed clusters (N=50)[a]

Key people

Name	Role	Organization
Thelma E. Tupasi	Principal investigator	Tropical Disease Foundation, Inc.
Ma. Imelda Quelapio	Co-investigator	Tropical Disease Foundation, Inc.
Jennifer Chua	Program manager	Tropical Disease Foundation, Inc.
Leilani Naval	Administrative coordinator	Tropical Disease Foundation, Inc.
Nellie Mangubat	Data processing coordinator	Tropical Disease Foundation, Inc.
Grace Egos	Laboratory coordinator	Tropical Disease Foundation, Inc.
Lena Ablis	Radiology coordinator	Makati Medical Center
Gerardo Beltran	Radiology consultant	Makati Medical Center
Joselito Legaspi	Radiology consultant	Makati Medical Center
Sistla Radhakrishna	Biostatic consultant	Consultant, Philippines
Jesus Sarol	Biostatistician	University of the Philippines-Manila
Ruffy Guilatco	Data management staff	Tropical Disease Foundation, Inc.
Maricar Galipot	Data management staff	Tropical Disease Foundation, Inc.
Genesis Ramos	Data management staff	Tropical Disease Foundation, Inc.
Vivian Lofranco	Field monitor	Department of Health
Onofre Edwin Merilles	Field monitor	Tropical Disease Foundation, Inc.
Ruth Orillaza-Chi	Field monitor	Tropical Disease Foundation, Inc.
Nona Rachel Mira	Field monitor	Tropical Disease Foundation, Inc.
Virgil Belen	Field monitor	Tropical Disease Foundation, Inc.
Albert Angelo Concepcion	Field monitor	Tropical Disease Foundation, Inc.

Survey organization and financing

Implementing agency:
National TB Control Programme, Department of Health/ Tropical Disease Foundation, Inc.

Finance	Amount (US$)
The Global Fund	N/A
World Health Organization	N/A
Total budget	N/A

Data sources

- Nationwide Tuberculosis Prevalence Survey 2007, final report, Republic of the Philippines. Tropical Disease Foundation Inc.; 2008.
- Tupasi TE, Radhakrishna S, Chua JA, Mangubat NV, Guilatco R, Galipot M et al. Significant decline in the tuberculosis burden in the Philippines ten years after initiating DOTS. Int J Tuberc Lung Dis. 2009;13(10):1224–1230.
- Floyd S, Sismanidis C. The 2007 Philippines nationwide TB survey confirmatory report of main results. London School of Hygiene & Tropical Medicine; 2008.
- Survey dataset.

[a] The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Survey design and methodology

Sampling design	
Sampling frame	Whole country[a]
Sampling design	Multistage cluster sampling using PPS
Strata	Metro Manila/other urban/rural
Sampling unit	Province/municipality/barangay
Sample size assumptions	
• Smear-positive prevalence	300 per 100 000 (≥10 years)
• Precision	N/A
• Design effect	1.25
• *k*	0.4
• Response rate	85% (for radiographic examination)
• Sample size (estimated)	30 000
Number of clusters	50
Cluster size	600
Eligibility criteria	
• Age	≥10 years (chest X-ray)
• Residency	N/A

[a] Four barangays in the "other urban" strata and 14 barangays in rural strata were excluded due to security issues and inaccessibility.

Screening criteria	
Interview[a]	The interview was conducted for each household about demographic and socio-economic factors, and also for participants ≥20 years about TB symptoms and the TB history. However, the interview result was not used as the selection criteria for sputum submission.
Chest X-ray[b]	Any lung abnormality (conducted for participants ≥10 years)
Other	N/A

[a] An in-depth interview about health-care seeking behaviour was done for participants ≥20 years who reported any TB symptoms (cough more than 2 weeks, haemoptysis, chest or back pain, fever, night sweats, weight loss).
[b] Conventional radiography.

Laboratory methodology	
Smear	Three samples (spot, morning and morning[a]): direct preparation, FM (auramine stain)
Culture[b]	Three samples (spot, morning and morning[a]): direct preparation for Ogawa media, and concentrated preparation for LJ media for pooled samples
Identification of MTB	Niacin, catalase test, nitrate production test
TB drug susceptibility test	Done
Xpert® MTB/RIF	Not done
HIV test	Not done

[a] Two morning samples were taken on the same day.
[b] As per protocol, initially concentrated LJ was done for the first 37 participants. Due to the heavy workload for the laboratory, the method was changed to direct Ogawa and pooled concentrated LJ for the remaining participants.

Analysis and reporting

Field data collection	Paper
Database	Microsoft® Access
Method of analysis	Multiple imputation
Results first published in a report/paper	July 2008
Official dissemination event	July 2008

Key survey results

Prevalence[a,b]	Smear-positive TB		Bacteriologically confirmed TB	
	Number per 100 000 population	95% CI	Number per 100 000 population	95% CI
Total	280	190–370	660	530–800
Male	350	240–480	970	780–1 180
Female	190	120–290	370	260–510
10–19 years	20	0–90	180	90–310
20–29 years	220	100–420	500	300–770
30–39 years	240	100–470	600	370–920
40–49 years	460	250–790	1 100	750–1 560
≥50 years	590	380–870	1 320	990–1 720
Metro Manila	430	0–870	640	160–1 120
Other urban	250	150–360	680	500–860
Rural	260	150–360	650	460–850

[a] Age ≥10 years.
[b] Results for total prevalence and the three geographic strata are from the multiple imputation model; other numbers are crude estimates.

	Design effect	*k*
Smear-positive TB	2.3	1.1
Bacteriologically confirmed TB	2.1	0.6

Other sputum results	Number	%
Total smear-positive participants	55	–
Smear-positive participants without MTB confirmation[a]	5	9.1
Isolates with MDR-TB detected[b]	5	3.8

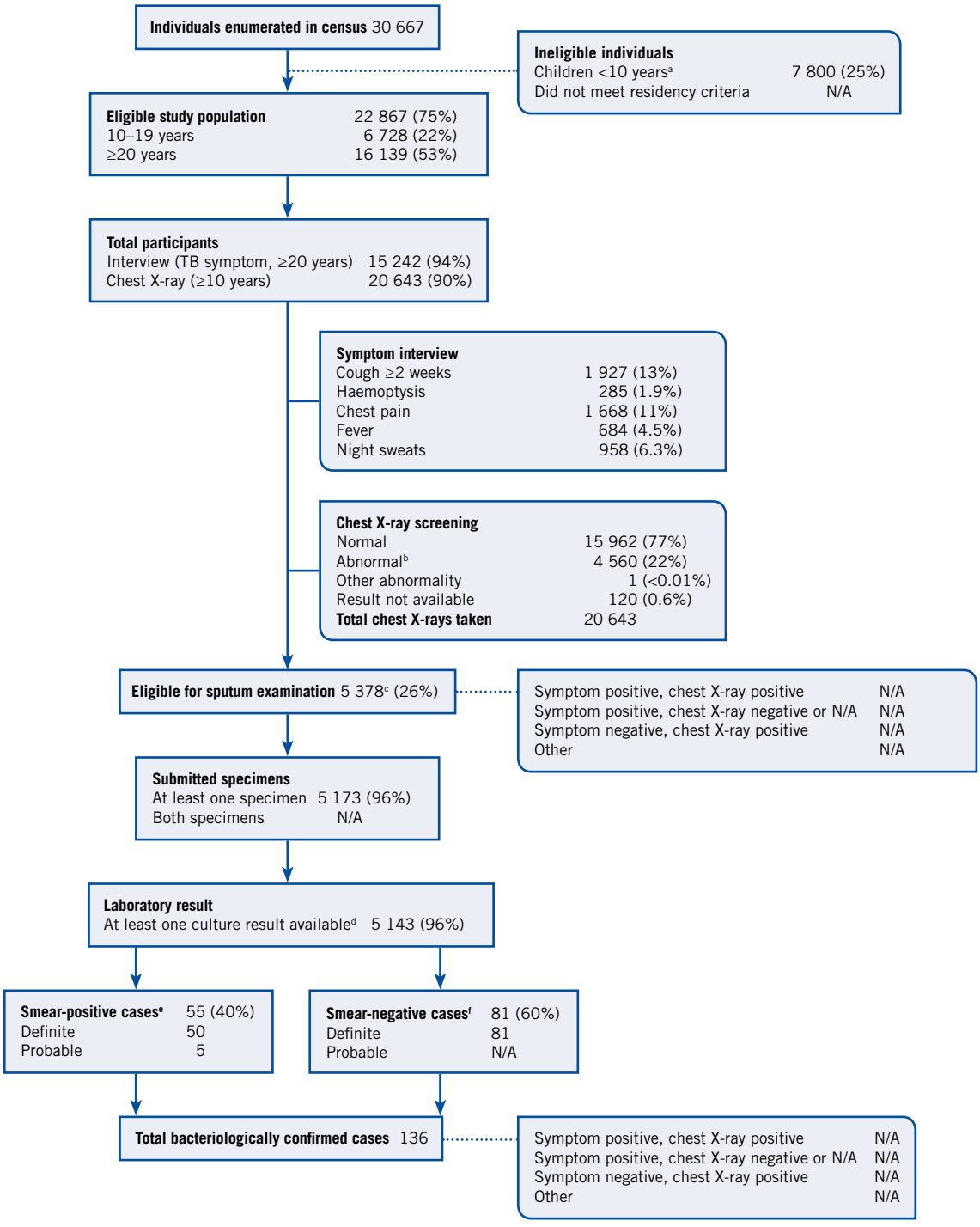
[a] This includes culture with no evidence of MTB (i.e. culture-negative, NTM, contaminated, N/A).
[b] DST was done for 131 participants.

Health-care seeking behaviour among participants who were symptom-screen positive	Number	%
Participants who were symptom-screen positive	N/A	N/A
Location of care sought		
• Consulted medical facility	N/A	N/A
Public facility	N/A	N/A
Private facility	N/A	N/A
• Pharmacy	N/A	N/A
• Traditional healer	N/A	N/A
No action taken	N/A	N/A
Unknown	N/A	N/A

Survey participants currently on TB treatment	Number	%
Total participants currently on TB treatment	N/A	N/A
• Treated in the public sector	N/A	N/A
• Treated in the private sector	N/A	N/A
• Treated in other sector	N/A	N/A
Bacteriologically confirmed TB cases detected by the survey who were currently on TB treatment	N/A	N/A

Survey flow: census to final outcomes

Field operations: July to December 2007



[a] BCG scar verification was undertaken for those aged 2 months–9 years, and a tuberculin skin test was done for two age groups (5–9 and 40–59 years) as well as those who had a chest X-ray suggestive of TB.

[b] Only chest X-ray, and not a symptom interview, was used as a screening tool to determine eligibility for sputum collection.

[c] The number eligible for sputum submission was more than the number with a field chest X-ray abnormality (i.e. 4560), because some consultant radiologists were involved in field screening and they found more chest X-ray abnormalities than field readers.

[d] Cultures that were either contaminated and/or missing without a definitive result (i.e. MTB, NTM, negative) were excluded.

[e] Definite: MTB confirmed by culture. Probable: MTB not confirmed by culture but chest X-ray suggestive of TB.

[f] Definite: MTB confirmed by culture. Probable: no definition.

Fig. 1: Participation rate by age and sex

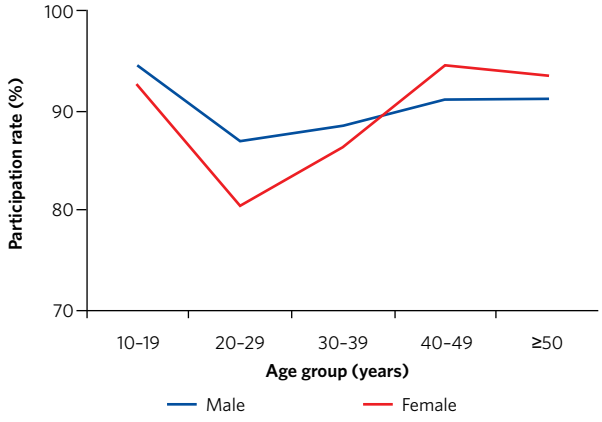


Fig. 2: TB prevalence per 100 000 population by age

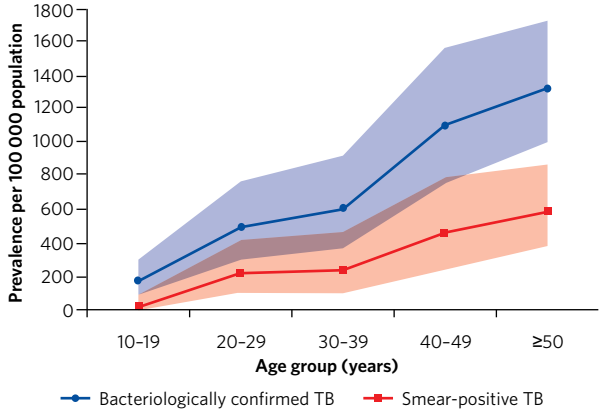


Fig. 3: Estimated number of bacteriologically confirmed TB cases and prevalence per 100 000 population, by age[a]

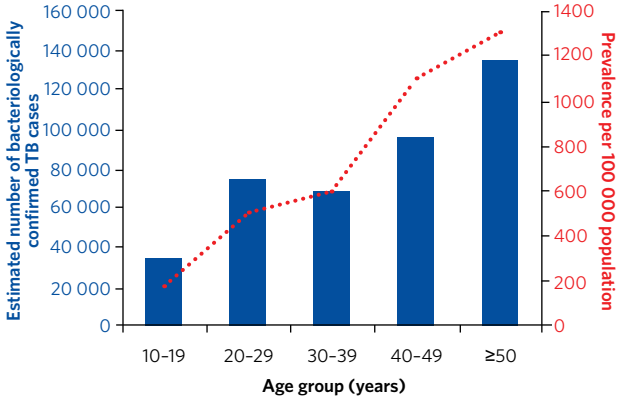


Fig. 4: Cluster variation of the number of bacteriologically confirmed TB cases[b]

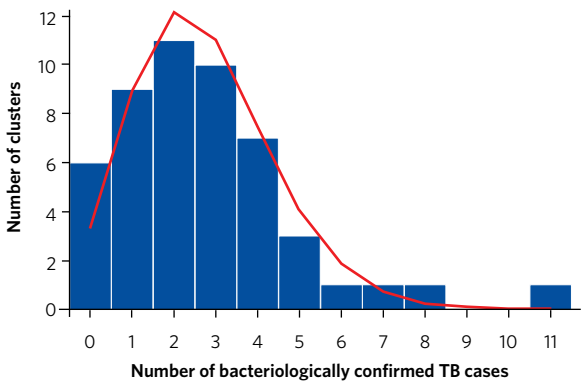


Fig. 5: Ratio of smear-positive TB prevalence to notifications by age and by sex[c]

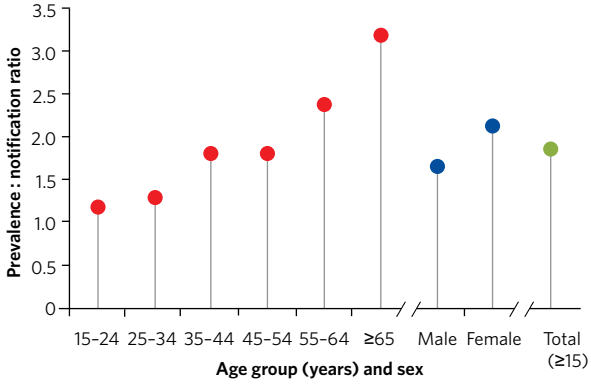
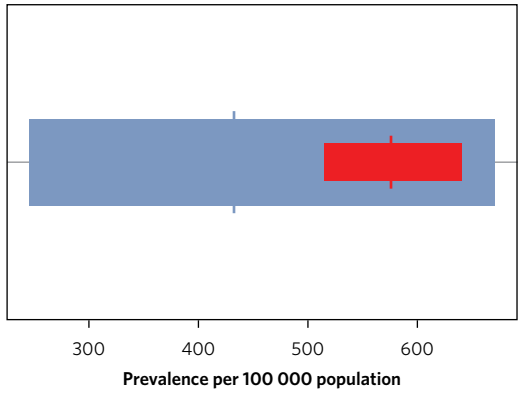


Fig. 6: Estimates of TB prevalence (all ages, all forms of TB) before (in blue) and after (in red) the national TB prevalence survey[d]



[a] The estimated number of bacteriologically confirmed TB cases is the product of age-specific prevalence and population estimates from the UN Population Division (2015 revision).

[b] The data did not suggest that the distribution of cases by cluster (blue bars) was significantly different from the theoretical distribution (red line) (mean 2.72, variance 4.70, p=0.08). The theoretical distribution assumes cases are distributed at random i.e. no clustering effect.

[c] Notification rates were estimated using notifications obtained from the WHO global TB database, and population estimates from the UN Population Division (2015 revision). As notification data in the WHO database was disaggregated by six age groups (as opposed to the five age groups used in the Philippines survey), crude prevalence rates for six age groups were recalculated for this figure.

[d] The blue bar denotes the best estimate of prevalence and its range that was indirectly derived from the estimate of incidence previously published by WHO, adjusted to the year of the prevalence survey based on previously published trends in incidence.

Background

The population of the Philippines was 88 million in 2007, and the average gross national income (GNI) per person was US$ 1900 per year, making it a lower-middle-income country *(1)*. It was one of the 22 high tuberculosis (TB) burden countries (HBCs) defined by WHO as a top priority for global efforts in TB control in 1998 and throughout the Millennium Development Goal (MDG) era (2000–2015), and one of the top 30 HBCs defined by WHO for the period 2016–2020. In 2007, the prevalence of HIV in the general population aged 15–49 years was <0.1% (95% confidence interval [CI]: <0.1–<0.1%) *(2)*, and it was estimated that 0.2 % (95% CI: 0.1–0.3%) of TB patients were coinfected with HIV *(3)*.

The National TB Control Programme (NTP) launched the WHO-recommended DOTS strategy in 1996 *(4,5)* and national coverage was achieved by 2005 *(5,6)*. In 2005, WHO estimated TB incidence and prevalence as 291 per 100 000 population and 450 per 100 000 population, respectively; the notification rate (new and relapse TB cases) was 165 per 100 000 population and had not changed significantly since 2000. The case detection rate (notifications of new and relapse cases divided by estimated incidence in the same time period) was 55% in 2005 *(8)*.

The Philippines had previously undertaken two national TB prevalence surveys, one in 1981–1983 and one in 1997. In the 1981–1983 survey, the prevalence of smear-positive TB was 660 per 100 000 population (among those ≥10 years) and the prevalence of culture-positive TB was 860 per 100 000 population. The prevalence of smear-positive TB in the 1997 survey (360 per 100 000 population; 95% CI: 280–450) was lower than in the 1981–1983 survey, but the prevalence of culture-positive TB in the 1997 survey (960 per 100 000 population; 95% CI: 750–1160) had not significantly changed. Drug susceptibility testing of 188 isolates from the 1997 survey showed that 4.3% of survey cases had multidrug-resistant TB (1.5% of people with no previous TB history and 15% of previously treated cases) *(6,9)*.

The Philippines NTP undertook a third national TB prevalence survey in 2007 to determine the burden of TB and the impact of the DOTS programme, which had been launched 10 years previously.

Key methods and results

There were 50 survey clusters across three strata (Metro Manila, other urban and rural), with a target cluster size of 600 individuals. A total of 30 667 individuals from 6259 households were enumerated in the survey census, of whom 22 867 (75%) were eligible for chest X-ray and were invited to participate. Of these, 20 643 (90%) were screened by chest X-ray. A total of 5378 people (26% of participants) were eligible for sputum examination based on their chest X-ray result; of these 5173 (96%) submitted at least one sputum specimen. An interview about symptoms was undertaken for 15 242 participants aged 20 years or more; however, this was not considered to be a screening tool for sputum submission *(6,9,10)*.

A total of 136 bacteriologically confirmed pulmonary TB cases were identified, including 55 cases of smear-positive TB. The prevalence of smear-positive TB was 280 (95% CI: 190–370) per 100 000 population (among those aged ≥10 years), and for bacteriologically confirmed TB it was 660 (95% CI: 530–800) per 100 000 population. When extrapolated to all forms of TB and to all ages, prevalence was 576 (95% CI: 515–640) per 100 000 population. There was no significant variation in prevalence among the three strata.

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Other key results were:

- the male to female ratio was 1.8 for smear-positive TB and 2.6 for bacteriologically confirmed TB;
- prevalence per 100 000 population increased with age, as did the absolute number of bacteriologically confirmed TB cases;
- among bacteriologically confirmed TB cases who were interviewed using a symptom questionnaire, 42% had a chronic cough, and among the smear-positive TB cases who were interviewed using a symptom questionnaire, 59% had a chronic cough;
- for smear-positive pulmonary TB, the ratio of prevalence to notifications (P:N ratio) was 1.9 overall, but varied from 1.2 in those aged 15–24 years to 3.2 in those aged 65 years or more, and was higher for women than men (2.1 versus 1.6); and
- among bacteriologically confirmed TB cases, 72% had no previous history of anti-TB treatment.

Data for those on anti-treatment at the time of the survey were not available. It was estimated that up to one third of participants with symptoms suggestive of TB had consulted a health facility and one quarter had taken no action.

Implications of results

Based on the prevalence surveys in 1997 and 2007, which followed a standard protocol and similar methodology, the prevalence of bacteriologically confirmed TB declined from 960 (95% CI: 750–1160) per 100 000 population to 660 (95% CI: 530–800) per 100 000 population. Smear-positive prevalence also declined, from 360 (95% CI: 280–450) per 100 000 population to 280 (95% CI: 190–370) per 100 000 population. Between 1996 and 2007, the Philippines NTP aggressively implemented its strategic plan for TB control in collaboration with private sector partners, increased its budgetary support, and continued to enhance the quality of DOTS services through training and retooling. The 2007 survey suggested that these efforts had contributed to a reduction in the burden of TB disease in the country.

Nonetheless, in the 2007 survey, the prevalence of bacteriologically confirmed TB was 2.6 times higher among males than among females, and it increased with age. This shifting of the burden into older age groups mirrored results from other surveys in Asia and indicated a maturing epidemic. Specific efforts were still required to reduce the burden in males and older age groups.

Among the participants who reported TB symptoms in the 2007 survey, only one third had previously consulted health facilities; nearly half of them had chosen to self-medicate and the rest had not taken any action. Although in comparison to the 1997 survey the proportion of symptomatic participants who consulted health facilities increased marginally and the proportion who took no action dropped, the proportion who had self-medicated almost doubled. Among those in the 2007 survey who took no action, 45% considered their symptoms to be harmless, 39% could not afford the cost of treatment and 4% found the distance to a health facility to be a barrier. These findings highlighted a need to improve access to health facilities, social support and advocacy to communities *(6)*.

Major successes, challenges and lessons learned

Major successes of the 2007 survey included completing the survey on time, despite challenges faced during field operations, and the high coverage of the survey's screening and diagnostic tests (e.g. 90% of the 22 867 participants aged 10 years or older were examined by chest X-ray).

Major challenges faced during the survey included the exclusion of some barangays (i.e. the smallest administrative unit) from the sampling frame because of security issues and inaccessibility, so the survey was not truly representative of the national population; it was difficult to define the study population in some congested areas because households were not clearly demarcated; logistical challenges were experienced in some barangays (e.g. households spread over several kilometres, or located in geographically challenging locations such as small islands or mountainous areas); and the quality of sputum samples was questionable in some clusters because of the absence of courier services, difficulties in maintaining the cold chain in tropical conditions and delays in processing specimens (this resulted in high specimen contamination rates; 6.9% of 13 926 specimens on Ogawa media and 8.3% of pooled specimens on LJ slopes *(6)*).

Photo credit: Leilani Naval


Photo credit: Leilani Naval

References

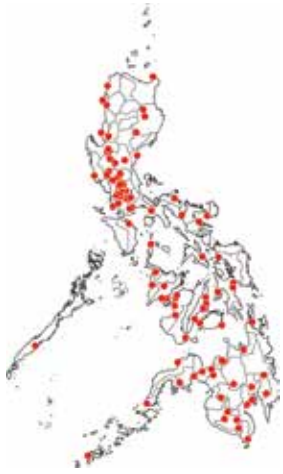
1. The World Bank (https://data.worldbank.org/country, accessed April 2017).
2. UNAIDS. (http://aidsinfo.unaids.org/, accessed May 2017).
3. World Health Organization. Global tuberculosis database. Geneva: WHO; 2017 (http://www.who.int/tb/data/en/, accessed April 2017).
4. WHO Tuberculosis Programme. (1994). WHO Tuberculosis Programme: framework for effective tuberculosis control. World Health Organization. (http://www.who.int/iris/handle/10665/58717, accessed January 2018).
5. World Health Organization. Global tuberculosis programme. Global tuberculosis control report 1997. Geneva: WHO; (https://apps.who.int/iris/bitstream/handle/10665/63354/WHO_TB_97.225_(part1).pdf?sequence=1, accessed January 2018).
6. Nationwide Tuberculosis Prevalence Survey 2007, final report, Republic of the Philippines. Tropical Disease Foundation Inc.; 2008.
7. World Health Organization. Global Plan to Stop TB – Phase 1: 2001 to 2005. Geneva: WHO; (http://www.stoptb.org/global/plan/plan0105.asp, accessed July 2017).
8. World Health Organization. Global Tuberculosis Control. Geneva: WHO; 2007
9. Tupasi TE, Radhakrishna S, Chua JA, Mangubat NV, Guilatco R, Galipot M et al. Significant decline in the tuberculosis burden in the Philippines ten years after initiating DOTS. Int J Tuberc Lung Dis. 2009;13(10):1224–1230.
10. Floyd S, Sismanidis C. The 2007 Philippines nationwide TB survey confirmatory report of main results. London School of Hygiene & Tropical Medicine; 2008.

PHILIPPINES

2016

Summary statistics

Participation rate	76%
Bacteriologically confirmed TB (≥15 years)	
• Prevalence per 100 000 population	1 159
• Male:female ratio	2.7
Prevalence:notification ratio (smear-positive TB, ≥15 years)	3.1



Surveyed clusters (N=106)[a]

Key people

Name	Role	Organization
Mary Ann Lansang	Principal investigator (PI)	Foundation for the Advancement of Clinical Epidemiology (FACE, Inc.)/University of the Philippines Manila (UP Manila)
Anna Marie Celina Garfin	Chair of the technical working group	Department of Health (DOH)
Marissa Alejandria	Co-PI	FACE, Inc./UP Manila
Myrna Mendoza	Co-PI	Foundation for the Control of Infectious Diseases, Inc. (FCID, Inc.)/UP Manila
Jacinto Blas Mantaring III	Co-PI	FACE, Inc./UP Manila
Noel Juban	Co-PI, field coordinator	FACE, Inc./UP Manila
Sonia Salamat	Co-field coordinator	FCID, Inc./UP Manila
Concepcion Ang	Laboratory manager	FCID, Inc./UP Manila
Joseph Adrian Buensalido	Laboratory manager	FCID, Inc./UP Manila
Johanna Patricia Cañal	Radiology coordinator	Philippine College of Radiology/UP Manila
Maria Lourdes Amarillo	Data manager	FACE, Inc./UP Manila
Olivia Sison	Data manager	FACE, Inc./UP Manila
Jose Rene Cruz	Field team leader	FACE, Inc.
Nori Jane Galagar	Field team leader	FACE, Inc.
Anjo Benedict Fabellon	Field team leader	FACE, Inc.
Rodelia Pascua	Field team leader	FACE, Inc.
Allison Noel	Field team leader	FACE, Inc.
Luis Anos	Field team leader	FACE, Inc.
Aser Sisona	Field team leader	FACE, Inc.
Irwin Law	Technical assistance (survey advisor)	WHO headquarters
Ikushi Onozaki	Technical assistance (survey advisor)	WHO headquarters
Yasunori Ichimura	Technical assistance (survey advisor)	Chiba University, Japan
Marina Tadolini	Technical assistance (survey advisor)	Consultant, Italy
M. Bintari Dwihardiani	Technical assistance (survey advisor)	Consultant, Indonesia
Julia Ershova	Technical assistance (data management)	US Centers for Disease Control and Prevention (CDC)
Hiroko Matsumoto	Technical assistance (laboratory)	Research Institute of Tuberculosis/Japan Anti-Tuberculosis Association (RIT/JATA)
Tetsuhiro Sugamoto	Technical assistance (laboratory)	RIT/JATA

Survey organization and financing

Implementing agency:
National TB Control Programme, Department of Health/ Philippine Council for Health Research and Development (PCHRD)/Foundation for the Advancement of Clinical Epidemiology (FACE, Inc.)

Finance	Amount (US$)
Department of Health, Philippines	1 987 462
The Global Fund	367 900
Total budget	2 355 362

Data sources

- National Tuberculosis Prevalence Survey 2016, Philippines: Department of Health, Republic of the Philippines; Foundation for the Advancement of Clinical Epidemiology, Inc.; Philippine Council for Health Research and Development; 2018.
- Survey dataset.

[a] The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Survey design and methodology

Sampling design	
Sampling frame	Whole country
Sampling design	Multistage cluster sampling using PPS
Strata	Four strata (National Capital Region, regions 3 and 4-A/rest of Luzon/Visayas/ Mindanao). In the final analysis, urban and rural were also considered.
Sampling unit	Four strata/province or HUC (Highly Urbanized Cities)/barangay
Sample size assumptions	
• Smear-positive prevalence	260 per 100 000 (≥15 years)
• Precision	0.25
• Design effect	1.8
• *k*	0.8
• Response rate	85%
• Sample size (estimated)	54 000[a]
Number of clusters	108[b]
Cluster size	500
Eligibility criteria	
• Age	≥15 years
• Residency	Individuals who lived for at least two weeks in the household prior to the census

[a] Six clusters (3000 individuals) were added to the original sample size (51 000), to ensure this sample size, in case of cancellation in the Autonomous Region in Muslim Mindanao due to security issues.

[b] One cluster in Basilan province was excluded before field operations started, due to security issues. During field operations, three clusters (Sipangkot, Madaya and Maco barangays) were replaced by others from the same provinces, due to problems of accessibility and security. Another cluster (Holy Spirit barangay) was dropped because the board of directors of the private subdivision in the selected area refused to allow the survey team to do house-to-house mobilization and interviews.

Screening criteria	
Interview[a]	Cough ≥2 weeks and/or haemoptysis
Chest X-ray[b]	Any lung or mediastinum abnormality
Other	Chest X-ray exempted

[a] An in-depth interview about health-care seeking behaviour was done for participants who reported cough ≥2 weeks and/or haemoptysis.

[b] Mobile digital X-ray machine.

Laboratory methodology	
Smear[a]	One or two samples (the morning sample was mainly used. If the morning sample's volume was inadequate, the second spot sample was also used): direct preparation, FM (LED, auramine stain)
Culture[a]	One or two samples (the morning sample was mainly used. If the morning sample's volume was inadequate, the second spot sample was also used): direct preparation, Ogawa media
Identification of MTB	MPT 64 rapid test
TB drug susceptibility test	Done
Xpert® MTB/RIF[a]	Done for all first spot specimens[b]
HIV test	Not done

[a] All participants who were eligible for sputum examination were asked to submit two sputum samples (spot and morning) for smear, culture and Xpert MTB/RIF. The additional spot sample was collected when the volume of previous sputum specimens (first spot and/or morning) was less than 3ml.

[b] If the first sample had an inadequate volume, a morning or second spot specimen was used. If all three specimens had less than 1ml each, the available specimens were pooled.

Analysis and reporting

Field data collection	Electronic
Database	Epi Info
Method of analysis	MI+IPW
Results first published in a report/paper	May 2018
Official dissemination event	August 2017

Key survey results

Prevalence[a]	Smear-positive TB		Bacteriologically confirmed TB	
	Number per 100 000 population	95% CI	Number per 100 000 population	95% CI
Total	434	350–518	1 159	1 016–1 301
Male	673	528–819	1 713	1 482–1 943
Female	205	141–270	627	516–739
15–24 years	330	197–463	799	586–1 011
25–34 years	326	195–458	900	677–1 123
35–44 years	470	298–641	1 126	821–1 430
45–54 years	665	438–891	1 714	1 364–2 064
55–64 years	488	285–691	1 504	1 104–1 903
≥65 years	503	310–696	1 659	1 261–2 058
NCR, 3, 4-A[b]	599	451–747	1 358	1 103–1 612
Rest of Luzon	258	138–378	1 038	787–1 288
Visayas	471	261–680	1 234	873–1 594
Mindanao	268	173–364	856	686–1 026

[a] Age ≥15 years unless otherwise specified.

[b] National Capital Region, regions 3 and 4-A.

	Design effect	*k*
Smear-positive TB	1.7	0.6
Bacteriologically confirmed TB	2.0	0.4

Other sputum results	Number	%
Total smear-positive participants	183	–
Smear-positive participants without MTB confirmation[a]	10	5.5
Isolates with MDR-TB detected[b]	9	3.9

[a] This includes culture with no evidence of MTB (i.e. culture-negative, NTM, contaminated, N/A) and Xpert-negative.

[b] DST was done for 232 culture MTB-positive specimens.

Health-care seeking behaviour among participants who were symptom-screen positive	Number	%
Participants who were symptom-screen positive[a]	2 815	–
Location of care sought[b]		
• Consulted medical facility	530	–
Public facility	*359*	*67*
Private facility	*162*	*31*
Other	*3*	*0.6*
Unspecified	*6*	*1.1*
• Pharmacy	4	–
• Traditional healer	10	–
Self-treated[b]	1 130	–
No action taken	1 142	41
Unknown	18	0.6

[a] Cough ≥2 weeks and/or haemoptysis.

[b] Participants could answer more than one category.

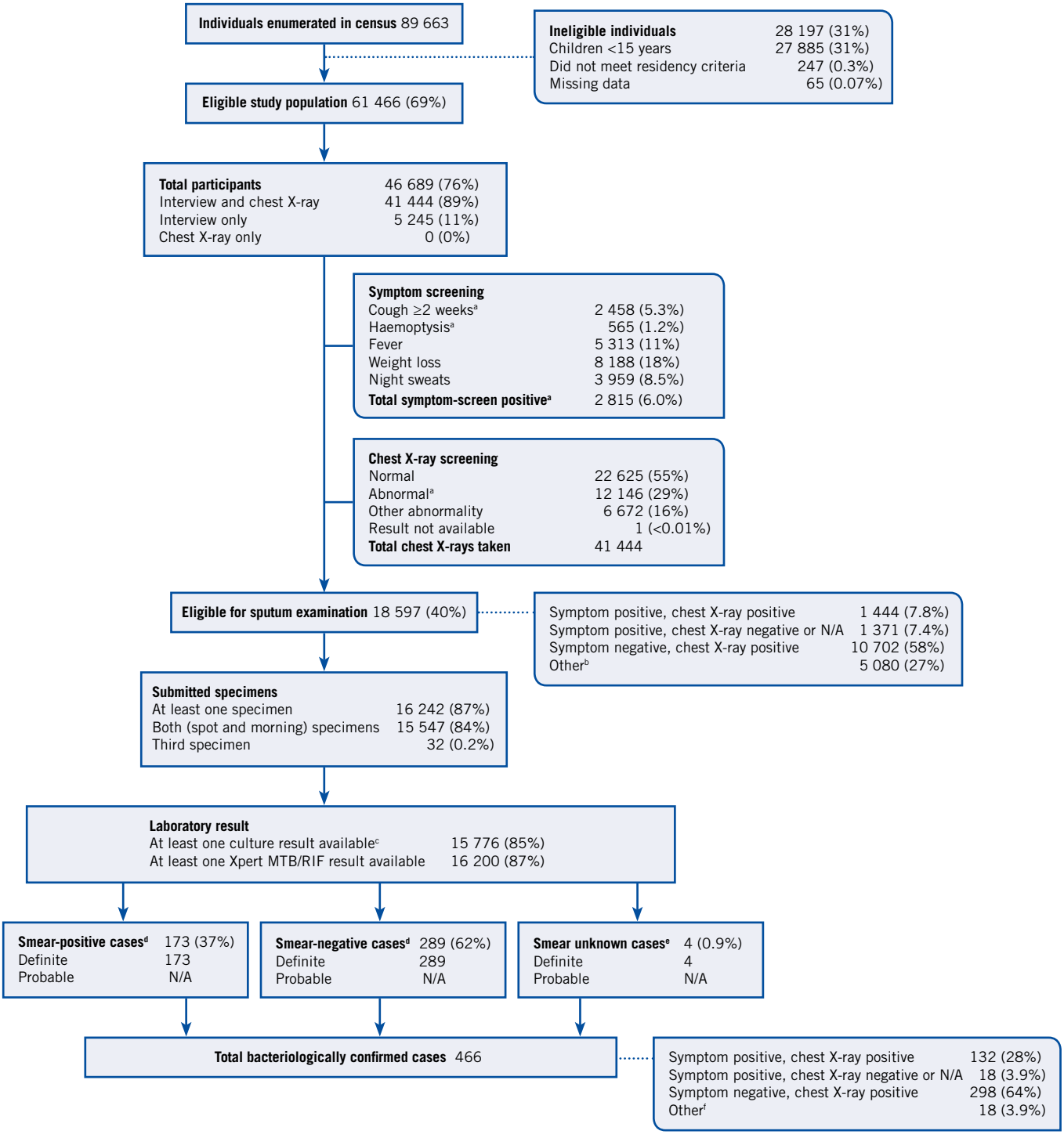
Survey participants currently on TB treatment	Number	%
Total participants currently on TB treatment[a]	170	–
• Treated in the public sector	134	–
• Treated in the private sector	15	–
• Treated in other sector[b]	24	–
• Treated in unknown sector	1	–
Bacteriologically confirmed TB cases detected by the survey who were currently on TB treatment	30	6.4

[a] Some participants answered more than one facility. The reason why they had multiple treatment places is unavailable.

[b] Private pharmacy (23), relatives (1).

Survey flow: census to final outcomes

Field operations: March to December 2016



[a] Eligible for sputum submission.
[b] Chest X-ray exempted and symptom-screen negative (5079), poor chest X-ray image and symptom-screen negative (1).
[c] Cultures that were either contaminated and/or missing without a definitive result (i.e. MTB, NTM, negative) were excluded.
[d] Definite: MTB confirmed by culture and/or Xpert. Probable: no definition.
[e] Definite: smear and culture not done, but MTB confirmed by Xpert. Probable: no definition.
[f] Chest X-ray exempted and symptom-screen negative.

Fig. 1: Participation rate by age and sex

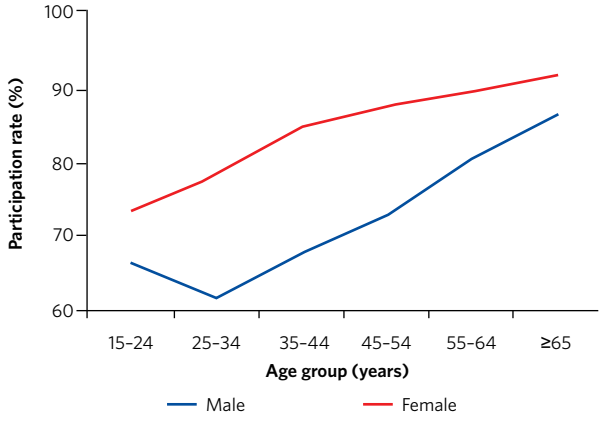


Fig. 2: TB prevalence per 100 000 population by age

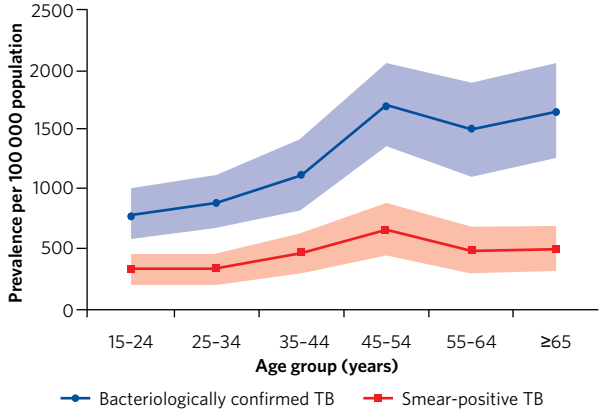


Fig. 3: Estimated number of bacteriologically confirmed TB cases and prevalence per 100 000 population, by age[a]

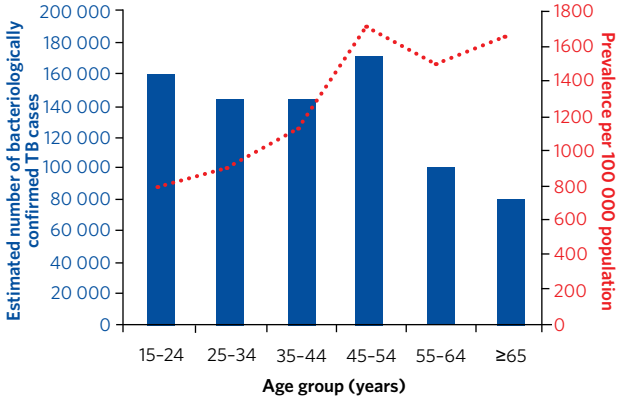


Fig. 4: Cluster variation of the number of bacteriologically confirmed TB cases[b]

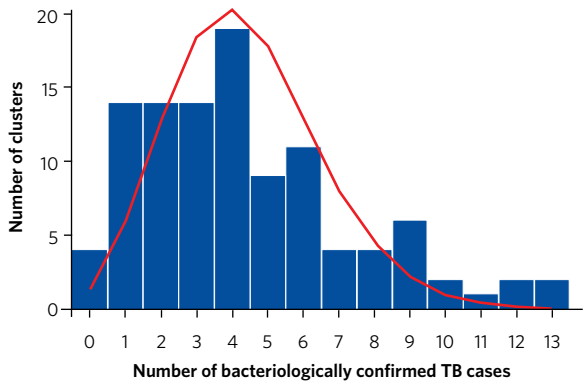


Fig. 5: Ratio of smear-positive TB prevalence to notifications by age and by sex[c]

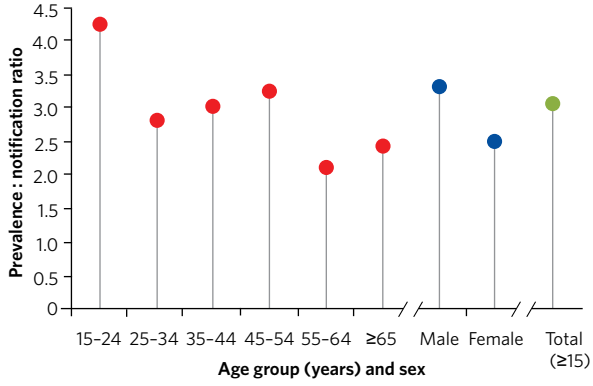
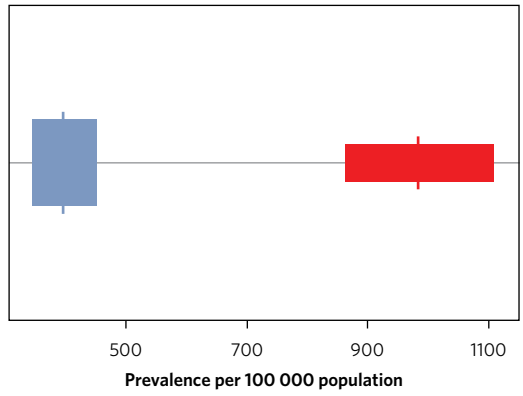


Fig. 6: Estimates of TB prevalence (all ages, all forms of TB) before (in blue) and after (in red) the national TB prevalence survey[d]



[a] The estimated number of bacteriologically confirmed TB cases is the product of age-specific prevalence and population estimates from the UN Population Division (2015 revision).

[b] The data suggested that the distribution of cases by cluster (blue bars) was significantly different from the theoretical distribution (red line) (mean 4.40, variance 9.12, $p<0.05$). The theoretical distribution assumes cases are distributed at random i.e. no clustering effect.

[c] Notification rates were estimated using smear-positive pulmonary TB notifications (2016) obtained from the NTP, and population estimates from the UN Population Division (2015 revision).

[d] The blue bar denotes the best estimate of prevalence and its range that was indirectly derived from the estimate of incidence previously published by WHO, adjusted to the year of the prevalence survey based on previously published trends in incidence.

Background

The Philippines had a population of 101 million in 2015 and was a lower-middle-income country with an average gross national income (GNI) per person of US$ 3520 per year *(1)*. It was one of the 22 high tuberculosis (TB) burden countries (HBCs) defined by WHO as a top priority for global efforts in TB control in 1998 and throughout the Millennium Development Goal (MDG) era (2000–2015), and one of the top 30 HBCs defined by WHO for the period 2016–2020. In 2015, the prevalence of HIV in the general population aged 15–49 years was <0.1% (95% confidence interval [CI]: <0.1–<0.1%) *(2)*, and it was estimated that 0.9% (95% CI: 0.5–1.4%) of TB patients were coinfected with HIV *(3)*.

Using findings from the 2007 national TB prevalence survey as well as other data, WHO estimated TB incidence at 285 (95% CI: 228–342) per 100 000 population in 2008; this remained static up to 2014 (288 per 100 000 population; 95% CI: 254–324). Prevalence was estimated to have decreased slightly, from 548 (95% CI: 499–597) per 100 000 population in 2008 to 417 (95% CI: 367–471) per 100 000 population in 2014 *(4,5)*. In December 2007, the Philippines was one of the 22 global focus countries selected by the WHO Global Task Force on TB Impact Measurement as a priority for a national TB prevalence survey during the period 2008–2015.

The fourth national TB prevalence survey in the Philippines was conducted from March to December 2016 *(6)*, following surveys in 1981–1983, 1997 and 2007. It was led by the National TB Control Programme, Department of Health and the Philippine Council for Health Research and Development, and was implemented by the Foundation for the Advancement of Clinical Epidemiology, Inc. The primary objective of the survey was to estimate the prevalence of pulmonary TB (bacteriologically confirmed; i.e. culture-positive TB or Xpert® MTB/RIF, or both) among the general population aged 15 years or more.

Photo credit: Julia Ershova

Key methods and results

There were 106 survey clusters in four strata – National Capital Region, regions 3 and 4-A; rest of Luzon; Visayas; and Mindanao. The target cluster size was 500 individuals. A total of 89 663 individuals from 19 707 households were enumerated in the survey census, of whom 61 466 (69%) were eligible and invited to participate. Of these, 46 689 (76%) did so. All participants were screened according to the 2011 algorithm recommended by WHO; that is, using a chest X-ray and an interview about symptoms *(7)*. A total of 18 597 participants (40%) were eligible for sputum examination; of these, 16 242 (87%) submitted at least one sputum specimen and 15 547 (84%) submitted two sputum specimens. Sputum specimens from 16 200 participants were tested with Xpert MTB/RIF. Of these, 397 (2.5%) were Xpert positive for *Mycobacterium tuberculosis*, and of these, 29 (7.3%) were also rifampicin (RIF) resistant, 358 (90%) were RIF susceptible and 10 (2.5%) were indeterminate. Of 466 bacteriologically confirmed TB cases, 159 (34%) were confirmed by both culture and Xpert MTB/RIF, 69 (15%) only by culture and 238 (51%) only by Xpert MTB/RIF.

Of the 466 bacteriologically confirmed TB cases, 173 (37%) were smear-positive. The prevalence of smear-positive TB was 434 (95% CI: 350–518) per 100 000 population (among those aged ≥15 years), and for bacteriologically confirmed TB it was 1159 (95% CI: 1016–1301) per 100 000 population. Although there was no statistically significant variation between the four geographical strata, the highly urbanized strata (National Capital Region, regions 3 and 4-A) had the highest prevalence of bacteriologically confirmed TB (1358 per 100 000 population; 95% CI: 1103–1612), followed by Visayas (1234 per 100 000 population; 95% CI: 873–1594), rest of Luzon (1038 per 100 000 population; 95% CI: 787–1288) and the more rural Mindanao (856 per 100 000 population; 95% CI: 686–1026).

Other key results were:

- the male to female ratio was 3.3 for smear-positive TB and 2.7 for bacteriologically confirmed TB;
- prevalence per 100 000 population was high in all age groups, especially in those aged 35 years or more, with the peak being in those aged 45–54 years; the absolute number of TB cases was high in the young and middle age groups (15–54 years);
- among bacteriologically confirmed TB cases, 32% were symptom-screen positive, and among the smear-positive cases, 51% were symptom-screen positive;
- for smear-positive pulmonary TB, the ratio of prevalence to notifications (P:N ratio) was 3.1 overall, but varied from 2.1 in those aged 55–64 years to 4.2 in the 15–24 years age group, and was higher for men than women (3.3 versus 2.5);
- among bacteriologically confirmed TB cases, 82% had no previous history of anti-TB treatment and only 6.4% were on anti-TB treatment at the time of the survey; and
- of the 138 bacteriologically confirmed and 82 smear-positive TB survey cases that screened positive for symptoms and were not on anti-TB treatment at the time of the survey, 35 (25%) and 22 (27%), respectively, had previously sought care in a public or private health facility for their symptoms.

Photo credit: Irwin Law

Implications of results

The prevalence of bacteriologically confirmed pulmonary TB was the highest of all national surveys implemented globally since 2007. Based on the survey, the estimated prevalence for all forms of TB and all ages was 982 (95% CI: 862–1100) per 100 000 population – this was almost 2.5 times higher than the pre-survey estimate (i.e. 417 per 100 000 population in 2014; 95% CI: 367–471) *(5)*.

Together with surveys in Bangladesh and Kenya, the 2016 survey in the Philippines was one of the first surveys to use both Xpert MTB/RIF and culture for all participants who screened positive. Although it was not surprising that the use of Xpert MTB/RIF increased the overall diagnostic yield, the prevalence of culture-confirmed TB alone was very high (587 per 100 000 population; 95% CI: 488–687) and showed that the Philippines was facing one of the highest burdens of TB in the world. When prevalence was extrapolated to all forms of TB and all ages, it was estimated that there were about 1 million people in the Philippines with TB in 2016, equivalent to 1 in 15 of all prevalent cases globally *(6)*.

Notwithstanding the limitation of a 76% participation rate, survey results were of high quality and provided a robust measurement of the burden of TB disease. Results from the 2016 prevalence survey were used to update estimates of TB incidence and mortality. The estimate of TB incidence after the survey was 554 (95% CI: 311–866) per 100 000 population in 2016, compared with the pre-survey WHO estimate (which had assumed a decline in incidence since 2007) of 288 (95% CI: 254–324) per 100 000 population in 2014; estimates for previous years were similarly revised upwards. The estimated mortality rate based on the survey was 21 (95% CI: 21–22) per 100 000 population in 2016, compared with a pre-survey estimate of 10 (95% CI: 9.1–11) in 2014; estimates for previous years were similarly revised upwards *(5, 8)*.

The sample size in 2016 was not designed to detect a specified effect size (e.g. 20% decline) in comparison with the 2007 survey, but rather to obtain an estimate of prevalence in 2016 with a specified precision. The 2016 survey was therefore not powered to detect small differences between it and the 2007 survey. Nonetheless, this limitation did not prevent an assessment of the trend in TB disease burden since 2007. Adjustments were made to ensure that the two datasets and methods were as comparable as possible, resulting in an upward adjustment of the 2007 survey results, to account for the more sensitive screening and diagnostic methods used in the 2016 survey. Based on these adjustments, the prevalence of culture-positive TB was 463 (95% CI: 333–592) per 100 000 population in 2007 and 512 (95% CI: 420–603) per 100 000 population in 2016 *(6)*. The probability that prevalence did not decline over the period 2007–2016 was estimated at 75%.

The lack of decline in TB prevalence since 2007 could be explained by a combination of case-detection gaps, significant delays in diagnosis, health system weaknesses, and broader social and economic influences on the TB epidemic. These broader influences included the level of poverty, with 22% of people living below the national poverty line in 2015; the level of undernourishment, with a prevalence of 14% in the general population in 2015 and no improvement since 2008; and low coverage of health insurance and social protection (e.g. coverage of only 4% in the poorest quintile in 2013), leading to financial barriers to accessing health services and high levels of TB-affected households facing catastrophic costs (35% in 2016–2017) *(1, 9)*. At a broader level, the poor and disadvantaged require adequate social protection strategies and increased PhilHealth TB benefit packages to reduce catastrophic costs associated with TB, especially multidrug-resistant TB (MDR-TB).[1]

Based on TB prevalence survey findings, the National TB Control Programme (NTP) initiated the development of new strategies with a national multisectoral approach. These included:

- introducing systematic screening among high-risk and vulnerable groups (including men, older age groups and those living in urban areas);
- improving the use of tools for screening and diagnosis, coupled with improved training of health-care providers and health-care delivery;
- initiatives to reduce geographic and financial barriers affecting access to health care;
- greater engagement of public-private mix partnerships, including effective implementation of existing legislation on mandatory notification of TB cases; and
- strengthening collaboration between the NTP and other health programmes, such as those for HIV, diabetes and lung health.

In discussions towards the end of 2016, it was anticipated that these strategic actions would be implemented with the full support of the Department of Health, and full mobilization of the health sector. Measures that were agreed to be needed included the deployment of sufficient human resources at national and subnational levels; increased domestic funding; a presidential executive order for drug regulation; establishment of a high-level steering group; and ensuring financial protection (and sustained poverty alleviation efforts) for more than 90% of the poor through increased coverage of PhilHealth and expanded social protection programmes.

Major successes, challenges and lessons learned

Major successes in the survey included:

- high-level commitment and excellent coordination by the implementing agency;
- reaching remote hamlets and villages that were included in the sampling frame, based on efficient logistical management of field teams and equipment and use of digital X-ray

Photo credit: Julia Ershova

[1] PhilHealth is the national health insurance programme.

machines, as well as effective use of social media and instant messaging;

- regular supervision of field teams and laboratories by central staff, which helped to ensure the quality of survey operations and standardization across the teams;
- double reading of each chest X-ray; that is, X-rays were read by one medical officer in the team and by another person (an off-site radiologist) who read the chest X-ray remotely, with a quick turnaround;
- use of Xpert MTB/RIF, which made up for challenges associated with MTB culture processes;
- almost 90% of specimens for culture being processed in 5 days or less; and
- the availability of a large team of highly skilled people to clean and analyse data.

Challenges faced during the survey included:

- a low participation rate (76% compared with a target of 85%) despite extended hours for field operations including evenings and weekends; lower participation was observed in men, younger age groups, those living in urban areas and higher income groups, as well as during the two months preceding national elections;
- the high sputum eligibility rate (40% of total participants screened) which led to a larger than expected laboratory workload;
- difficulties in standardizing techniques across six laboratories; the culture recovery rate[1] varied between 75% and 92% and contamination rates varied between 1.4% and 6.2% (*6*); and
- logistical issues arose in maintaining cold storage during transport from the field to the laboratory, which may have affected culture results.

During the preparation phase, one major lesson learned was the need for the implementing agency to have complete control of the design and implementation of the data management system. Initially, a private company was contracted to develop the system; however, because of the slow response times to adapt to changes in the survey protocols and data collection tools, plus ongoing costs, the company was replaced by an in-house team.

[1] Recovery rate of MTB: number of smear-positive MTB that are culture positive out of the number of smear-positive specimens.

References

1. The World Bank (https://data.worldbank.org/country, accessed April 2017).
2. UNAIDS. (http://aidsinfo.unaids.org/, accessed May 2017).
3. World Health Organization. Global tuberculosis database. Geneva: WHO; 2017 (http://www.who.int/tb/data/en/, accessed April 2017).
4. World Health Organization. Global tuberculosis control 2010. Geneva: World Health Organization; 2010 (http://apps.who.int/iris/bitstream/10665/44425/1/9789241564069_eng.pdf, accessed February 2018).
5. World Health Organization. Global tuberculosis report 2015. Geneva: WHO; 2015 (http://apps.who.int/iris/bitstream/10665/191102/1/9789241565059_eng.pdf, accessed July 2017).
6. National Tuberculosis Prevalence Survey 2016. Philippines: Department of Health, Republic of the Philippines; Foundation for the Advancement of Clinical Epidemiology, Inc.; Philippine Council for Health Research and Development; 2018.
7. World Health Organization. Tuberculosis prevalence surveys: a handbook (WHO/HTM/TB/2010.17). Geneva: WHO; 2011 (https://apps.who.int/iris/bitstream/handle/10665/44481/9789241548168_eng.pdf, accessed August 2017).
8. World Health Organization. Global tuberculosis report 2017. Geneva: WHO; 2017 (http://www.who.int/tb/data/en/, accessed February 2018).
9. Survey to estimate the proportion of households experiencing catastrophic costs due to TB (report of the NTP Zonal Dissemination Forum: 2016 National TB Prevalence Survey and 2016 Catastrophic Cost Study, on 14 September 2017). Department of Health, Republic of the Philippines; 2017.

RWANDA

2012

Summary statistics

Participation rate	96%
Bacteriologically confirmed TB (≥15 years)	
• Prevalence per 100 000 population	119
• Male:female ratio	3.9
Prevalence:notification ratio (smear-positive TB, ≥15 years)	1.3

Surveyed clusters (N=73)[a]

Key people

Name	Role	Organization
Michel Gasana	Principal investigator	Tuberculosis & Other Respiratory Communicable Diseases Division-Kigali, Rwanda
Claude Bernard Uwizeye	Principal investigator	US Centers for Disease Control and Prevention CDC-Kigali, Rwanda
Eveline Klinkenberg	Principal investigator	KNCV Tuberculosis Foundation
Pauline Basinga	Principal investigator	School of public health, National University of Rwanda
Patrick Migambi	Co-investigator and survey coordinator	Tuberculosis & Other Respiratory Communicable Diseases Division-Kigali, Rwanda
Julie Mugabekazi	Co-investigator	WHO Rwanda
Védaste Ndahindwa	Survey statistician	School of public health, National University of Rwanda
Elaine Kamanzi	Survey laboratory activities coordinator	National Reference Laboratory-Kigali, Rwanda
Jules Kamugunga Mulinzi	Survey data manager	Tuberculosis & Other Respiratory Communicable Diseases Division-Kigali, Rwanda
Alaine Umubyeyi Nyaruhirira	Laboratory advisor	Management Sciences for Health
Louise Kalisa	Survey radiology coordinator	Kigali University Teaching Hospital-Kigali, Rwanda
Calvin Mugabo	Field team leader	Tuberculosis & Other Respiratory Communicable Diseases Division-Kigali, Rwanda
Liliane Umutesi	Field team leader	Tuberculosis & Other Respiratory Communicable Diseases Division-Kigali, Rwanda
Ndeziki Mashengesho	Field team leader	Tuberculosis & Other Respiratory Communicable Diseases Division-Kigali, Rwanda
Nico Kalisvaart	Technical assistance (data management)	KNCV Tuberculosis Foundation
Ikushi Onozaki	Technical assistance (survey advisor)	WHO headquarters

Survey organization and financing

Implementing agency:
Tuberculosis and Other Respiratory Communicable Diseases Division, Rwanda Biomedical Center, the Ministry of Health

Finance	Amount (US$)
The Global Fund	1 840 893
US CDC	415 000
KNCV	36 741
WHO/OGAC (PEPFAR)	75 778
Total budget	2 368 412

Data sources

- The First National Tuberculosis Prevalence Survey 2012 in Rwanda, Institute of HIV/AIDS, Disease Prevention & Control, Tuberculosis & Other Respiratory Communicable Diseases Division, Republic of Rwanda, Ministry of Health, 2015.
- Migambi P, Gasana M, Uwizeye CB, Kamanzi E, Ndahindwa V, Kalisvaart N, Klinkenberg E. Prevalence of tuberculosis in Rwanda: Results of the first nationwide survey in 2012 yielded important lessons for TB control. PLoS One. 2020 Apr 23;15(4):e0231372.
- Survey dataset.

[a] The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Survey design and methodology

Sampling design	
Sampling frame	Whole country
Sampling design	Multistage cluster sampling using PPS
Strata	No stratification was used, but the final analysis accounted for province (Kigali city, North, East, South, West)
Sampling unit	Province/administrative sector/umudugudu (village)
Sample size assumptions	
• Smear-positive prevalence	304 per 100 000 (≥15 years)
• Precision	0.23
• Design effect	1.7
• *k*	0.6
• Response rate	95%
• Sample size (estimated)	44 500
Number of clusters	73[a]
Cluster size	610
Eligibility criteria	
• Age	≥15 years
• Residency	Individuals who lived in the household for at least 1 month prior to the interview

[a] Although the required number of clusters was 70, an additional 3 clusters were selected in Kigali to obtain more precise estimates.

Screening criteria	
Interview[a]	Cough (any duration)
Chest X-ray[b]	Any lung abnormality
Other	Chest X-ray exempted

[a] An in-depth interview about health-care seeking behaviour was done only for those who screened positive by interview and/or chest X-ray.
[b] Mobile chest X-ray truck, digital radiography.

Laboratory methodology	
Smear	Two samples (spot, morning): direct preparation in the facility close to the survey site (and the National Reference Laboratory also examined smear with the concentrated preparation), FM (LED, auramine stain)
Culture	Two samples (spot, morning): concentrated preparation, LJ media
Identification of MTB	MPT64 rapid test
TB drug susceptibility test	Done[a]
Xpert® MTB/RIF	Not done
HIV test	Offered to those who screened positive

[a] 38 TB cases were tested.

Analysis and reporting

Field data collection	Paper
Database	EpiData 3.1
Method of analysis	MI+IPW
Results first published in a report/paper	June 2015
Official dissemination event	January 2016

Key survey results

Prevalence[a]	Smear-positive TB		Bacteriologically confirmed TB	
	Number per 100 000 population	95% CI	Number per 100 000 population	95% CI
Total	74	48–99	119	79–160
Male	142	88–196	208	139–278
Female	24	4.7–43	53	20–86
15–34 years	57	27–86	86	46–125
35–54 years	66	21–110	114	35–193
≥55 years	159	54–263	262	104–421
Urban	N/A	N/A	N/A	N/A
Rural	N/A	N/A	N/A	N/A

[a] Age ≥15 years unless otherwise specified.

	Design effect	*k*
Smear-positive TB	0.91	N/A[a]
Bacteriologically confirmed TB	1.3	0.7

[a] *K* could not be computed for smear-positive TB because the design effect was less than one.

Other sputum results	Number	%
Total smear-positive participants	29	–
Smear-positive participants without MTB confirmation[a]	7	24
Isolates with MDR-TB detected[b]	2	5.2

[a] This includes culture with no evidence of MTB (i.e. culture-negative, NTM, contaminated, N/A).
[b] DST was done for 38 TB cases.

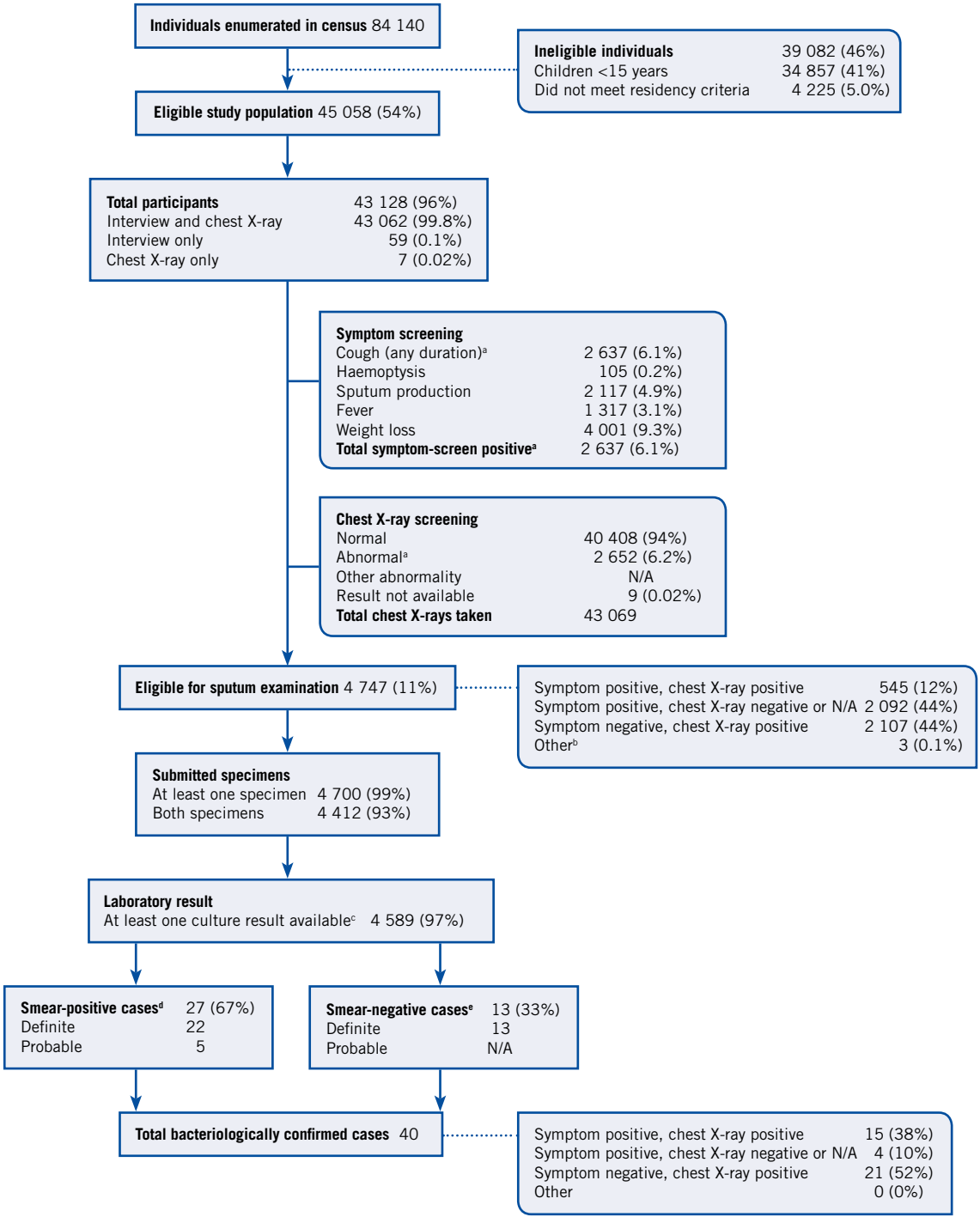
Health-care seeking behaviour among participants who were symptom positive	Number	%
Participants who were symptom positive[a]	2 855	–
Location of care sought[b]	921	32
• Consulted medical facility		
Public facility	*941*	–
Private facility	*48*	–
• Pharmacy	101	–
• Traditional center	54	–
• Other	38	–
Self-treated	0	0
No action taken	1 934	68
Unknown	N/A	N/A

[a] The in-depth interview identified 2855 participants who had a cough. This interview was in addition to the screening interview, and the extra participants who acknowledged a cough (304) were not included in the final screening outcomes.
[b] The subtotals do not add up to 921 because participants could select more than one health facility or groups within a facility (e.g. public facility includes health center, district hospital, referral hospital and community health worker).

Survey participants currently on TB treatment	Number	%
Total participants currently on TB treatment	21	–
• Treated in the public sector	N/A	N/A
• Treated in the private sector	N/A	N/A
• Treated in other sector	N/A	N/A
• Treated in unknown sector	N/A	N/A
Bacteriologically confirmed TB cases detected by the survey who were currently on TB treatment	2	5.0

Survey flow: census to final outcomes

Field operations: March to December 2012



[a] Eligible for sputum collection.
[b] Chest X-ray exempted and symptom-screen negative.
[c] Cultures that were either contaminated and/or missing without a definitive result (i.e. MTB, NTM, negative) were excluded.
[d] Definite: MTB confirmed by culture. Probable: MTB not confirmed by culture but two smear-positive specimens or one smear-positive with chest X-ray suggestive of TB.
[e] Definite: MTB confirmed by two cultures, or one culture with chest X-ray suggestive of TB. Probable: no definition.

Fig. 1: Participation rate by age and sex

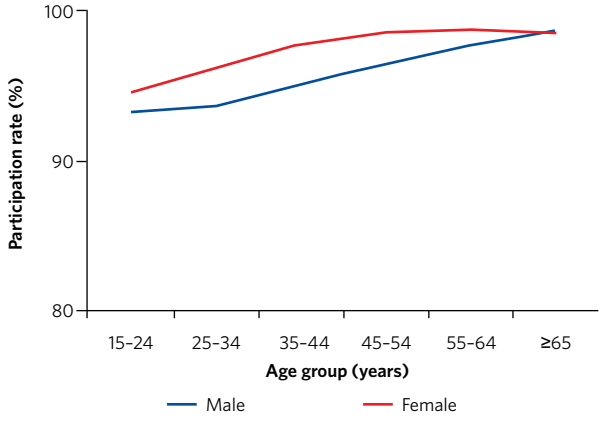


Fig. 2: TB prevalence per 100 000 population by age

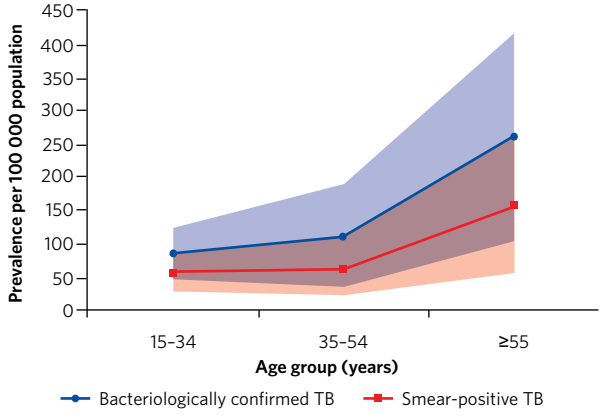


Fig. 3: Estimated number of bacteriologically confirmed TB cases and prevalence per 100 000 population, by age[a]

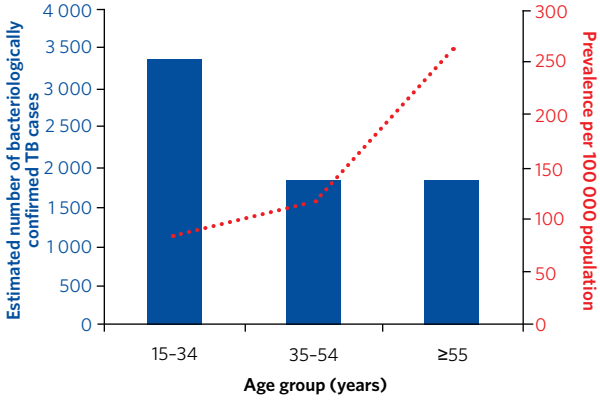


Fig. 4: Cluster variation of the number of bacteriologically confirmed TB cases[b]

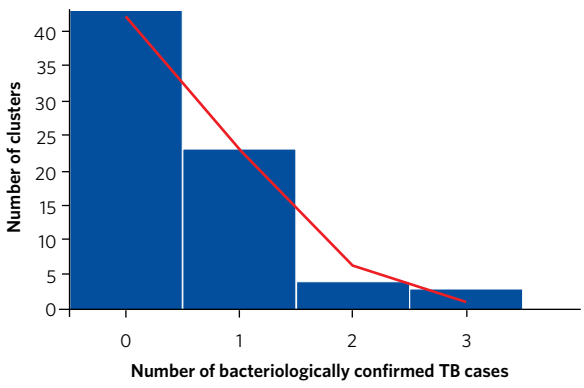


Fig. 5: Ratio of smear-positive TB prevalence to notifications by age and by sex[c]

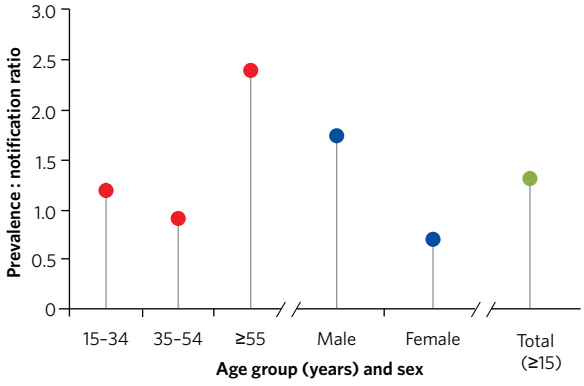
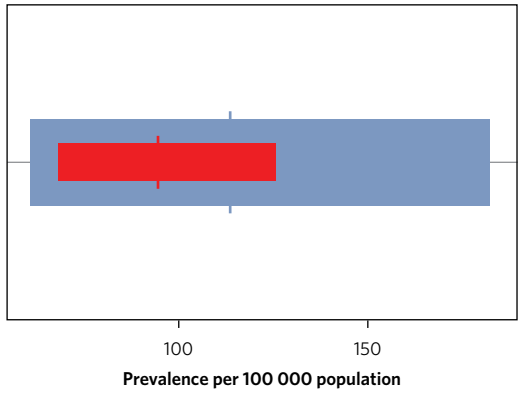


Fig. 6: Estimates of TB prevalence (all ages, all forms of TB) before (in blue) and after (in red) the national TB prevalence survey[d]



[a] The estimated number of bacteriologically confirmed TB cases is the product of age-specific prevalence and population estimates from the UN Population Division (2015 revision).

[b] The data did not suggest that the distribution of cases by cluster (blue bars) was significantly different from the theoretical distribution (red line) (mean 0.55, variance 0.61, p=0.27). The theoretical distribution assumes cases are distributed at random i.e. no clustering effect.

[c] Notification rates were estimate of using notifications obtained from the WHO global TB database, and population estimates from the UN Population Division (2015 revision).

[d] The blue bar denotes the best estimate of prevalence and its range that was indirectly derived from the estimate of incidence previously published by WHO, adjusted to the year of the prevalence survey based on previously published trends in incidence.

Background

Rwanda, in East Africa, had a population of 10 million in 2012, of which 85% lived in rural areas. The average gross national income (GNI) per person was US$ 640 per year, making it a low-income country *(1)*. The prevalence of HIV in the general population aged 15–49 years was estimated at 3.1% (95% confidence interval [CI]: 2.7–3.4%) in 2012 *(2)*, and it was estimated that 26% (95% CI: 25–27%) of TB patients were coinfected with HIV *(3)*.

In 1990, the Programme National de Lutte contre la Tuberculose – Rwanda's National Tuberculosis (TB) Control Programme (NTP) – was established within the Ministry of Health. At the same time, TB control activities were decentralized to the health-facility level (public and faith-based). The WHO-recommended DOTS strategy was implemented from the mid-1990s *(4,5)*. In 2005, a community DOTS strategy was launched to help make services more accessible; it included increasing the role of community health workers in the detection and management of TB patients. Nationwide coverage for community TB care was achieved in 2010. Collaborative TB/HIV activities were launched in 2005. By December 2012, 99% of notified TB cases (all forms) knew their HIV status, and of these cases, 26% were HIV-positive. Of the TB patients living with HIV in 2012, 99% were initiated on co-trimoxazole prophylaxis, and 75% were on antiretroviral treatment *(6)*.

The total number of reported TB cases (all forms of TB) increased after 1995 and peaked at 8283 in 2006. Subsequently, TB case notifications fell year on year, to 6207 in 2012. The TB notification rate followed a similar downward trend; after a peak in 2006, it fell to 59 per 100 000 population in 2012 (and 37 per 100 000 population for smear-positive pulmonary TB) *(7)*.

In the 2013 WHO global TB report, the estimated prevalence of TB in 1990 was 356 (95% CI: 173–603) per 100 000 population for all forms of TB and 114 (95% CI: 61–183) per 100 000 population in 2012 *(6)*. Over the same period, TB incidence was estimated to have fallen from 290 (95% CI: 259–323) per 100 000 population to 86 (95% CI: 77–96) per 100 000 population. The estimated TB case detection rate (for new and relapse cases) was 62% in 2012. However, there was no direct measurement of TB disease burden in Rwanda, and it was considered possible that the burden was lower than indicated in published estimates given the expansion in TB services and collaborative TB/HIV activities. In December 2007, Rwanda was one of the 22 global focus countries selected by the WHO Global Task Force on TB Impact Measurement as a priority for a national TB prevalence survey during the period 2008–2015. Following a decision by the NTP to carry out its first national TB prevalence survey, a survey was implemented between March and December 2012 *(7)*.

Photo credit: Kamugunga Jules

Key methods and results

There were 73 clusters in the survey, with a target cluster size of 610 individuals. Stratification was not used at the time of survey design; however, five provinces (Kigali city, North, East, South and West) were examined separately during the final analysis. A total of 84 140 individuals from 19 474 households were enumerated in the survey census, of whom 45 058 (54%) were eligible and invited to participate. Of these, 43 128 (96%) participated in the survey and were screened according to the 2011 algorithm recommended by WHO; that is, chest X-ray and a symptom screening interview *(8)*. A total of 4747 people (11% of participants) were eligible for sputum examination, of whom 4700 (99%) submitted at least one sputum specimen and 4412 (93%) submitted two sputum specimens.

A total of 40 bacteriologically confirmed pulmonary TB cases were identified, including 27 cases of smear-positive TB. The prevalence of smear-positive TB was 74 (95% CI: 48–99) per 100 000 population, and for bacteriologically confirmed pulmonary TB it was 119 (95% CI: 79–160) per 100 000 population (≥15 years). When extrapolated to all forms of TB and all ages, prevalence was estimated as 95 (95% CI: 66–124) per 100 000 population.

Other key results were:

- the male to female ratio was 5.9 for smear-positive TB and 3.9 for bacteriologically confirmed TB;
- prevalence per 100 000 population increased with age; however, the absolute number of TB cases was relatively high in the young age group (15–34 years);
- among bacteriologically confirmed TB cases, 48% were symptom-screen positive, and of the 27 smear-positive cases, 52% were symptom-screen positive;
- for smear-positive pulmonary TB, the ratio of prevalence to notifications (P:N ratio) was 1.3 overall, but varied from 0.9 in those aged 35–54 years to 2.4 in the 55 years or more age group, and was higher for men than for women (1.8 versus 0.7);
- among bacteriologically confirmed TB cases, 93% had no previous history of anti-TB treatment and only 5% were on anti-TB treatment at the time of the survey;
- of the 17 bacteriologically confirmed and 12 smear-positive TB survey cases that screened positive for symptoms and were not on anti-TB treatment at the time of the survey, 2 (12%) and 2 (17%), respectively, had previously sought care in a public or private health facility for their symptoms; and
- of those eligible for sputum examination, 94% (4445/4747) were offered HIV counselling and testing, of whom 5.2% (248/4747) refused; overall, 218 (4.9%) of those tested were HIV-positive, and 181 of the 218 (83%) already knew their HIV status; of 40 bacteriologically confirmed TB cases, 36 were tested for HIV and only 1 (2.8%) was HIV-positive.

Photo credit: Kamugunga Jules

Implications of results

The estimated prevalence of TB identified in the survey was lower than WHO estimates. This was a welcome finding, but also presented a challenge in terms of how to ensure continued funding to sustain efforts in TB control and further reduce this burden. It was recognized that finding and treating the remaining cases could require more costly interventions (on a per patient basis) than those used in the past.

The prevalence of HIV among TB cases detected in the survey was low. This probably reflected two factors: the short duration of illness for HIV-positive TB cases that are untreated in the community, and the effective TB screening programme among people living with HIV. People at higher risk for TB – including people living with HIV as well as prisoners, refugees and students in boarding schools – were already a priority for the NTP at the time of the survey. However, all diagnosed cases should be used as an entry point to find additional cases, including through strengthened contact tracing and continued active case finding.

The higher burden of TB among men and the elderly was consistent with routine surveillance data. However, men were five times more likely than women to have TB, whereas among notified TB cases there were only twice as many men as women. These findings suggested under-diagnosis among men and the elderly, and associated differences in health-care seeking behaviour.

Rwanda introduced a community health-insurance system in 1999 to improve access to health care. In 2012, 91% of the population was covered by this health insurance and 83% of the population could access a health-care facility within 2 hours of their home. Despite improving access to health care, survey data showed that people with TB or with symptoms meeting screening criteria did not always seek care, especially if they were poor, men or young adults. Overall, 70% of those with a cough who had not sought care at the time of the survey indicated that it was not important to do so; only 6% indicated that lack of money for transport was a barrier to accessing care *(7)*. It appeared that people in the general community were not identifying themselves as being at risk of developing TB disease, and that innovative approaches would be needed to raise awareness and enhance care-seeking among individuals with a cough.

The survey also suggested that the existing advocacy, communication and social mobilization strategy should be reviewed to incorporate innovative strategies to aid TB control. Possibilities that were identified included the use of role models or ambassadors, especially those with whom men could identify; raising awareness among health-care staff, given that only half of those who sought care for a chronic cough were asked to submit a sputum specimen for testing *(7)*; improving health-care staff awareness that men and the elderly are more likely to have TB than other groups and are underdiagnosed; and strategic case finding among the elderly, for example through routine outpatient screening for TB in this age group. After the survey, the NTP defined five high risk groups that required greater attention: children under 15 years, people over 55 years, prisoners, people living with HIV (PLHIV) and contacts of TB cases. In addition, the NTP developed plans to use chest X-ray as a screening tool among prisoners and PLHIV, and for the scale-up of Xpert®MTB/RIF as a diagnostic tool.

Contrary to expectations, one-third (16/54) of the participants with positive culture growth had nontuberculosis mycobacteria (NTM). This showed a need for further investigations to characterize the NTM problem in Rwanda, by conducting genotyping of the current cases, characterizing the affected population and determining the extent of the problem, as well as developing guidelines on treatment of NTM (such guidelines did not exist at the time of the survey).

Overall, the survey showed that current efforts in TB prevention, diagnosis and treatment needed to be maintained while also being supplemented by new strategies, to ensure early detection and treatment of all cases, with a specific focus on key populations.

Major successes, challenges and lessons learned

The Rwandan survey showed that the country's TB and TB/HIV services were well organized. However, since the number of detected cases was so small compared with the estimated burden when the survey was designed, it was hard to analyse in detail the characteristics of the detected TB cases.

Most survey equipment was procured by the Rwanda Biomedical Center. Delays occurred in procurement despite the process starting early. The original plan was to import portable digital X-ray units, but this was not possible because the national radiation authority did not approve the units. Digital units in a container system were procured instead. During field operations, one digital container was accidentally dropped and required a service.

Photo credit: Kamugunga Jules

A major success was that the overall participation rate was very high, at 96%. The area in which achieving high participation was a challenge was Kigali (the capital city); as in other surveys, this made it more difficult to estimate TB prevalence in highly urbanized areas. Rwanda was also one of the first countries to provide high-quality data on TB/HIV coinfection with a large proportion of survey participants requesting to be tested.

The survey was the first to successfully use a "paper-based horizontal data collection" approach. Without having the same individual survey form for each participant used throughout the screening process, individual data were collected independently and blindly from other information. However, more than in any other survey, this process required large and intensive amounts of human resource effort and a strong data management team.

An external review confirmed that the central laboratory carried out culture examination in accordance with their standard operating procedures; that is, concentrated Löwenstein–Jensen media recommended by WHO. Nonetheless, compared with surveys that used liquid media (i.e. mycobacteria growth indicator tube), or solid media without centrifuge (i.e. Ogawa method), the yields by culture were limited. Of the 54 culture positive participants, there were 38 participants with culture-confirmed TB, and 3 of the 38 were excluded from the final case list (in total there were 35 definite survey cases and 5 probable cases). They had only an indication of TB in one of the collected samples, which was not confirmed by an indication in another sample or the central chest X-ray reading. Therefore, it is likely that the prevalence of bacteriologically confirmed TB was underestimated.

References

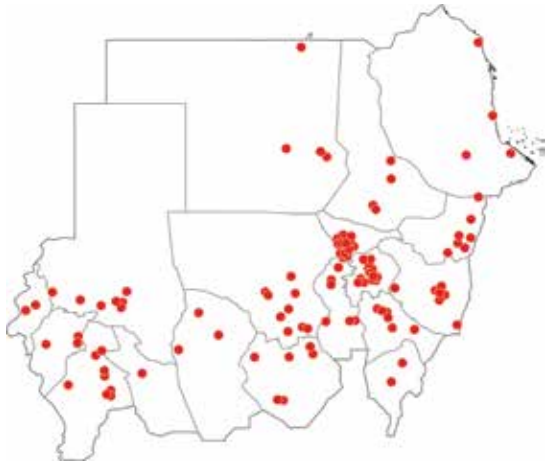
1. The World Bank (https://data.worldbank.org/country, accessed April 2017).
2. UNAIDS (http://aidsinfo.unaids.org/, accessed April 2017).
3. World Health Organization. Global Tuberculosis Database. 2017. (http://www.who.int/tb/country/en/, accessed April 2017).
4. WHO Tuberculosis Programme. (1994). WHO Tuberculosis Programme: framework for effective tuberculosis control. World Health Organization. (http://www.who.int/iris/handle/10665/58717, accessed January 2018).
5. World Health Organization. Global tuberculosis programme. Global tuberculosis control report 1997. Geneva: WHO; (https://apps.who.int/iris/bitstream/handle/10665/63354/WHO_TB_97.225_(part1).pdf?sequence=1, accessed January 2018).
6. World Health Organization. Global tuberculosis report 2013. Geneva: WHO; 2013 (http://apps.who.int/iris/bitstream/10665/91355/1/9789241564656_eng.pdf, accessed January 2018).
7. The First National Tuberculosis Prevalence Survey 2012 in Rwanda, Institute of HIV/AIDS, Disease Prevention & Control, Tuberculosis & Other Respiratory Communicable Diseases Division, Republic of Rwanda, Ministry of Health, 2015.
8. World Health Organization. Tuberculosis prevalence surveys: a handbook (WHO/HTM/TB/2010.17). Geneva: WHO; 2011 (https://apps.who.int/iris/bitstream/handle/10665/44481/9789241548168_eng.pdf, accessed August 2017).

SUDAN

2013–2014

Summary statistics

Participation rate	86%
Bacteriologically confirmed TB (≥15 years)	
• Prevalence per 100 000 population	183
• Male:female ratio	1.6
Prevalence:notification ratio (smear-positive TB, ≥15 years)	3.5



Surveyed clusters (N=109)[a]

Key people

Name	Role	Organization
Igbal Ahmed Elbasheer	Principal investigator	Public Health Institute (PHI)
Mona Hassen Mustafa	Survey coordinator	PHI
Sawsan Mustafa Abdalla	Survey coordinator	PHI
Heba Kamal Hamed Elneel	NTP manager (coordination between the survey team and TB states coordinators)	National TB Programme (NTP)
Asrar Mohammed Abdelsalam	Head of laboratory	National Tuberculosis Reference Laboratory
Majda Elsayed	Central radiologist	Consultant, Sudan
Nahid Abdelgader	Data manager	PHI
Abdelaeem	Field team leader	PHI
Ahmed Elhaj Ali	Field team leader	PHI
Alfakie	Field team leader	PHI
Fatih Alrahaman Ali Abdel-rahaman	Field team leader	PHI
Hasham Alamin Salem	Field team leader	PHI
Hashim Salah Hamza	Field team leader	PHI
Hozifa Omer Eljak	Field team leader	PHI
Mohammed Osman	Field team leader	PHI
Mustafa	Field team leader	PHI
Nazar Alnoor Ibrahim	Field team leader	PHI
Sami Abdel Hameed	Field team leader	PHI
Sumia Yousif Mohammed	Field team leader	PHI
Ayyed Muneam El-Dulaimi	Technical support	WHO Sudan
Mai Mohammed Eltigany	Technical support	WHO Sudan
Amal Bassili	Technical assistance (survey advisor)	WHO Eastern Mediterranean Regional Office (EMRO)
Sabira Tahseen	Technical assistance (survey advisor)	Consultant, Pakistan
Fasil Tsegaye	Technical assistance (survey advisor)	Consultant, Ethiopia
Ikushi Onozaki	Technical assistance (survey advisor)	WHO headquarters
Norio Yamada	Technical assistance (statistics)	Research Institute of Tuberculosis/Japan Anti-Tuberculosis Association (RIT/JATA)
Kiyohiko Izumi	Technical assistance (statistics)	RIT/JATA

Survey organization and financing

Implementing agency:
Public Health Institute (PHI)/National TB Programme

Finance	Amount (US$)
Government of Sudan	487 000
The Global Fund	1 400 709
Total budget	1 887 709

Data sources

- Survey dataset.

[a] The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Survey design and methodology

Sampling design	
Sampling frame	Whole country
Sampling design	Multistage cluster sampling using PPS
Strata	Urban/rural
Sampling unit	State/administrative unit/popular administrative unit (PAU)
Sample size assumptions	
• Smear-positive prevalence	239 per 100 000 (≥15 years)
• Precision	0.2
• Design effect	1.9
• *k*	0.7
• Response rate	85%
• Sample size (estimated)	91 131
Number of clusters	114[a]
Cluster size	800
Eligibility criteria	
• Age	≥15 years
• Residency	Household members resident in the selected household for the past 6 months, and visitors who spent ≥3 weeks in the household prior to the census

[a] 109 out of 114 PAUs were visited: four clusters (one in South Kordofan, two in Darfur State and one in Gazira) were cancelled due to security concerns and one due to non-compliance with eligibility criteria.

Screening criteria	
Interview[a]	Cough ≥2 weeks
Chest X-ray[b]	Any lung abnormality
Other	Any current TB treatment, chest X-ray exempted

[a] An in-depth interview about other TB symptoms and health-care seeking behaviour was done only for those who screened positive.
[b] Direct digital (portable).

Laboratory methodology	
Smear	Two samples (spot, morning): direct preparation, FM (LED, auramine stain)
Culture	Two samples (spot, morning): direct preparation, Ogawa media
Identification of MTB	Capilia LPA for all smear-positive and all culture-positive samples
TB drug susceptibility test	Not done
Xpert® MTB/RIF	Not done
HIV test	Not done

Analysis and reporting

Field data collection	Paper/electronic
Database	CSPro
Method of analysis	MI+IPW
Results first published in a report/paper	Pending
Official dissemination event	Pending

Key survey results

Prevalence[a]	Smear-positive TB		Bacteriologically confirmed TB	
	Number per 100 000 population	95% CI	Number per 100 000 population	95% CI
Total	87	52–121	183	128–238
Male	123	79–193	233	163–333
Female	58	32–105	143	98–208
15–24 years	27	9.2–82	49	21–111
25–34 years	122	68–220	250	154–407
35–44 years	157	88–279	249	154–403
45–54 years	67	27–168	227	132–390
55–64 years	87	31–246	255	134–486
≥65 years	114	51–253	282	163–489
Urban	150	93–243	275	178–425
Rural	55	29–108	137	89–210

[a] Age ≥15 years unless otherwise specified.

	Design effect	*k*
Smear-positive TB	1.8	1.1
Bacteriologically confirmed TB	2.7	1.1

Other sputum results	Number	%
Total smear-positive participants	61	–
Smear-positive participants without MTB confirmation[a]	4	6.6
Isolates with MDR-TB detected	N/A	N/A

[a] This includes culture with no evidence of MTB (i.e. culture-negative, NTM, contaminated, N/A) and LPA-negative.

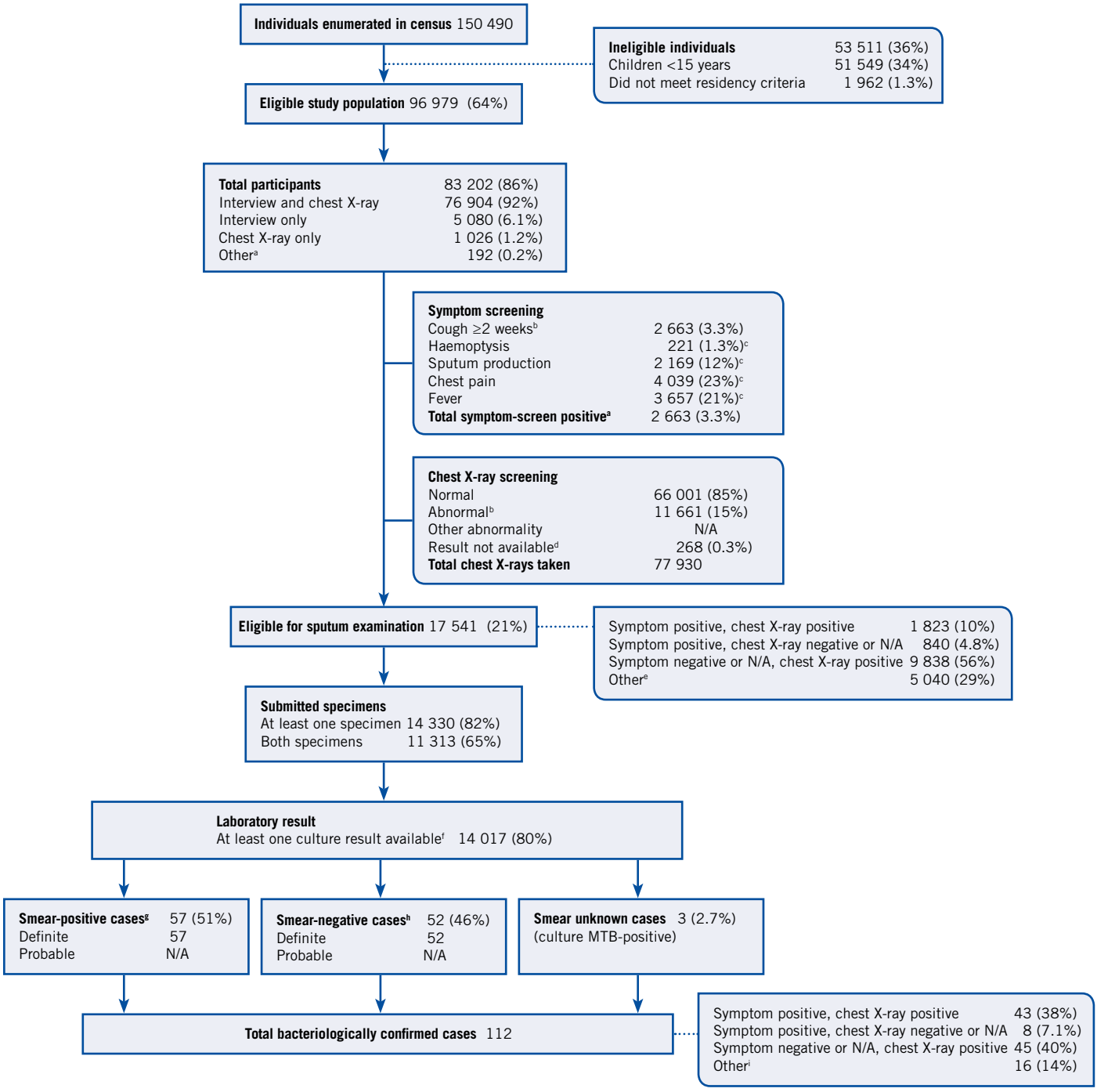
Health-care seeking behaviour among participants who were symptom-screen positive	Number	%
Participants who were symptom-screen positive[a]	2 663	–
Location of care sought		
• Consulted medical facility	1 308	49
Public facility	*1 077*	*82*
Private facility	*90*	*6.9*
Other (NGO)	*141*	*11*
• Pharmacy	52	2.0
• Traditional centre	49	1.8
No action taken	575	22
Other (unspecified)	69	2.6
Unknown	610	23

[a] Cough ≥2 weeks.

Survey participants currently on TB treatment	Number	%
Total participants currently on TB treatment	104	–
• Treated in the public sector	69	66
• Treated in the private sector	1	1.0
• Treated in other sector	4	4.0
• Treated in unknown sector	30	29
Bacteriologically confirmed TB cases detected by the survey who were currently on TB treatment	8	7.1

Survey flow: census to final outcomes

Field operations: February 2013 to March 2014



[a] Of 192 individuals, 80 were exempted from chest X-ray and were not screened by interview. In addition, 112 individuals did not attend the survey site and were not screened by interview or chest X-ray. Although a protocol violation, specimens were collected from these 112 individuals, and included in the final analysis (they were subsequently classified as off-site participants).

[b] Eligible for sputum collection.

[c] The denominator is 17 423 (on-site participants who screened positive).

[d] Poor quality of film (13) and result missing (255). 13 (poor quality of film) out of 268 were asked to submit sputum.

[e] Symptom-screen negative or missing and chest X-ray exempted (4899), symptom-screen negative and chest X-ray result N/A (13), symptom-screen negative or missing and chest X-ray negative but currently on TB treatment (10), off-site participants (112), symptom-screen negative or missing and chest X-ray negative, not currently on TB treatment but submitted sputum in error (6).

[f] Cultures that were either contaminated and/or missing without a definitive result (i.e. MTB, NTM, negative) were excluded.

[g] Definite: MTB confirmed by culture and/or LPA. Probable: no definition.

[h] Definite: MTB confirmed by culture. Probable: no definition.

[i] Symptom-screen negative and chest X-ray exempted (9), symptom-screen negative or missing and chest X-ray negative, not currently on TB treatment but submitted sputum in error (6), off-site participant (1).

Fig. 1: Participation rate by age and sex

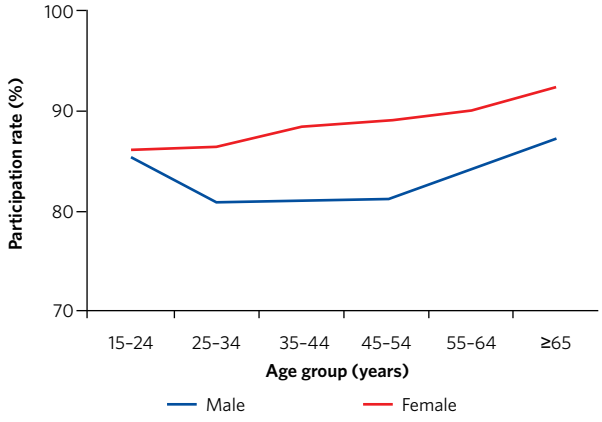


Fig. 2: TB prevalence per 100 000 population by age

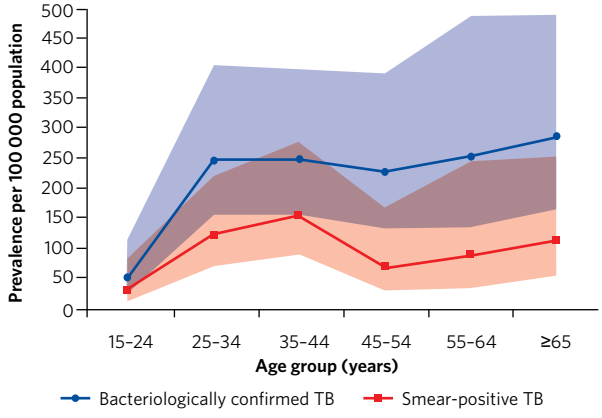


Fig. 3: Estimated number of bacteriologically confirmed TB cases and prevalence per 100 000 population, by age[a]

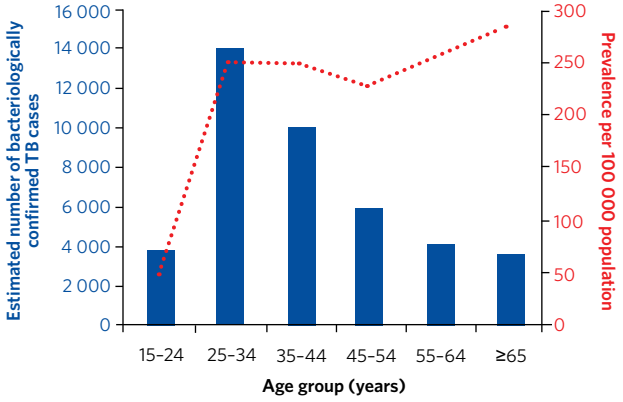


Fig. 4: Cluster variation of the number of bacteriologically confirmed TB cases[b]

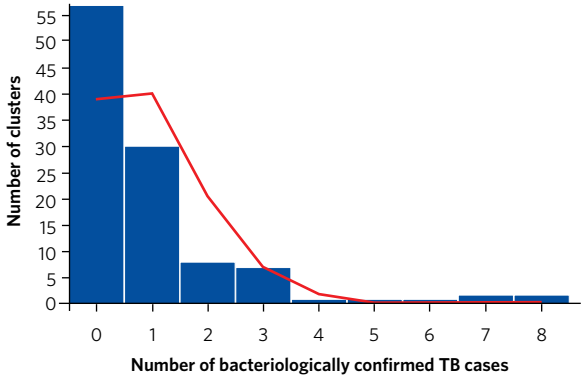


Fig. 5: Ratio of smear-positive TB prevalence to notifications by age and by sex[c]

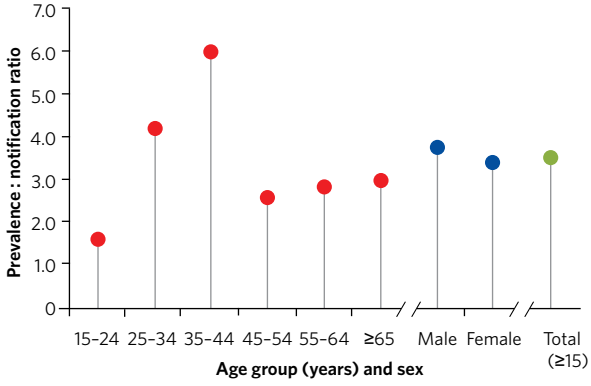
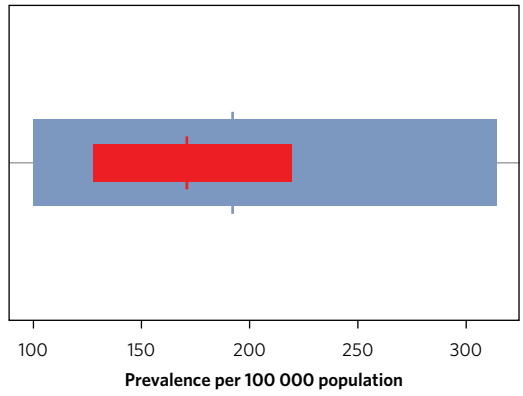


Fig. 6: Estimates of TB prevalence (all ages, all forms of TB) before (in blue) and after (in red) the national TB prevalence survey[d]



[a] The estimated number of bacteriologically confirmed TB cases is the product of age-specific prevalence and population estimates from the UN Population Division (2015 revision).

[b] The data suggested that the distribution of cases by cluster (blue bars) was significantly different from the theoretical distribution (red line) (mean 1.03, variance 2.90, $p<0.05$). The theoretical distribution assumes cases are distributed at random i.e. no clustering effect.

[c] Notification rates were estimated using smear-positive pulmonary TB notifications (2013) obtained from the NTP, and population estimates from the UN Population Division (2015 revision).

[d] The blue bar denotes the best estimate of prevalence and its range that was indirectly derived from the estimate of incidence previously published by WHO, adjusted to the year of the prevalence survey based on previously published trends in incidence.

Background

Sudan had a population of 39 million people in 2013, of which 88% were settled (i.e. in a permanent residence), including 33% in urban areas and 67% in rural areas (of whom 8% were nomads). The average gross national income (GNI) per person was US$ 1170, making it a lower-middle income country *(1)*. In 2013, the prevalence of HIV in the general population aged 15–49 years was 0.2% (95% confidence interval [CI]: 0.2–0.3%) *(2)*, and it was estimated that 4.4% (95% CI: 3.6–5.3%) of tuberculosis (TB) patients were coinfected with HIV *(3)*.

Nationwide coverage of DOTS was achieved in 2002. In March 2013, the Federal Ministry of Health of Sudan integrated management of disease-specific programmes, including TB, into a newly established Communicable and Noncommunicable Disease Administration (C&NCD) under the Directorate of Primary Health Care. State and locality TB programme officers were responsible for the implementation of TB control activities, including supervision of the TB management unit(s) in their area of responsibility. In 2013, there were 325 TB management units, usually from institutions that were part of the primary health-care network. The TB laboratory network was organized at three levels, with microscopy laboratories in each TB management unit, quality assurance performed by each of the 15 states, and one National TB Reference Laboratory.

The treatment success rate for new smear-positive pulmonary TB cases was 80–82% between 2002 and 2010. This dropped to 70% in 2011 *(4)* because some cases could not be evaluated due to the conflict in West Darfur, but returned to 80% in 2014 *(5)*. The case detection rate (notifications of new cases divided by estimated incidence) was estimated at 44% (95% CI: 37–54%) in 2012.

Sudan was not one of the 22 global focus countries for national TB prevalence surveys identified by the WHO Global Task Force on TB Impact Measurement in December 2007. However, it was on the Task Force's longer list of 53 countries considered to meet survey eligibility criteria. Given considerable uncertainty about estimates of the burden of TB disease, the lack of a previous national TB prevalence survey, the fact that no direct measurements of TB mortality were available from vital registration, and the difficulty in estimating the gap between notifications and incidence (due to underreporting or under-diagnosis of cases), it was decided to conduct the country's first national TB prevalence survey. The survey started in February 2013 and was completed in March 2014.

Key methods and results

There were 109 survey clusters in two strata (urban and rural), with a target cluster size of 800 individuals. A total of 150 490 individuals from 24 837 households were enumerated in the survey census, of whom 96 979 (64%) were eligible and invited to participate. Of these, 83 202 (86%) did so. Almost all participants were screened according to the 2011 algorithm recommended by WHO; that is, using chest X-ray and an interview about symptoms *(6)*. Out of 83 202 participants, 112 were not screened either by interview or chest X-ray; instead, they submitted sputum at home when survey teams visited. A total of 17 541 participants (21%) were eligible for sputum examination, of whom 14 330 (82%) submitted at least one sputum specimen and 11 313 (65%) submitted two sputum specimens.

A total of 112 bacteriologically confirmed pulmonary TB cases were identified, including 57 cases of smear-positive TB. The prevalence of smear-positive TB was

Photo credit: Fasil Tsegaye

87 (95% CI: 52–121) per 100 000 population (among those aged ≥15 years), and for bacteriologically confirmed TB it was 183 (95% CI: 128–238) per 100 000 population. When extrapolated to all forms of TB and to all ages, prevalence was 172 (95% CI: 122–222) per 100 000 population. The prevalence of smear-positive and bacteriologically confirmed TB was higher in urban than in rural areas.

Other key results were:

- the male to female ratio was 2.1 for smear-positive TB and 1.6 for bacteriologically confirmed TB;
- the prevalence per 100 000 population was consistently high for people aged 25 years and over, and people in the age groups 25–34 and 35–44 years accounted for a relatively large proportion of the absolute number of bacteriologically confirmed TB cases;
- among bacteriologically confirmed TB cases, 46% were symptom-screen positive, and among smear-positive cases, 56% were symptom-screen positive;
- for smear-positive pulmonary TB, the ratio of prevalence to notifications (P:N ratio) was 3.5 overall, but varied from 1.6 in those aged 15–24 years to 6.0 in the 35–44 years age group, and was slightly higher for men than for women (3.7 versus 3.4);
- among bacteriologically confirmed TB cases, 76% had no previous history of anti-TB treatment and 7.1% were on anti-TB treatment at the time of the survey; and
- of the 44 bacteriologically confirmed and 26 smear-positive TB survey cases that screened positive for symptoms and were not on anti-TB treatment at the time of the survey, 30 (68%) and 16 (62%), respectively, had previously sought care in a public or private health facility for their symptoms.

Photo credit: Fasil Tsegaye

Implications of results

The TB prevalence survey confirmed a burden of disease similar to pre-survey estimates of prevalence, i.e. 207 (95% CI: 104–345) per 100 000 population in 2012 *(4)*, while also producing more precise estimates. The survey showed that a high proportion of cases in the community had not yet reached TB diagnostic and treatment services, and high prevalence rates in the younger population (even in the context of low HIV prevalence among TB patients) confirmed ongoing transmission. Plausible explanations for a higher prevalence per 100 000 population in urban areas included large-scale displacement of people from rural areas due to insecurity and associated deterioration in economic conditions, in contrast with remote rural areas with nomadic populations and fewer opportunities to spread TB.

The survey had several major programmatic, policy and funding implications including those listed below.

- NTP services should be reoriented towards the hospital sector. Most survey cases that reported symptoms had sought treatment at general hospitals, rather than primary health centres (PHC), but in 2014 more than half of the country's hospitals lacked TB diagnostic services. There was a need to strengthen hospitals to include TB diagnostic services, supported by strengthening PHC centres, especially for treatment monitoring.
- Diagnosis with culture or other diagnostics beyond culture (e.g. Xpert® MTB/RIF) and use of chest X-ray as part of the screening algorithm for TB should be widely expanded.
- Case-finding activities should be intensified, and targeted particularly towards those aged 25–44 years and urban areas.
- There was a need to address inadequate knowledge of TB symptoms and the variable quality of services among health-care providers.
- Increased funding was required to implement the above-listed policy and programmatic measures.

Major successes, challenges and lessons learned

The major overarching success was that Sudan's first-ever national TB prevalence survey was successfully implemented, with a high participation rate. Advocacy through the media, and the involvement of stakeholders and community leaders at the state level, strongly facilitated survey participation.

The survey faced several major challenges that included those listed below.

- The harsh terrain and remoteness of much of the country made survey operations very demanding. This contributed to frequent breakdowns of equipment, problems with internet connectivity for electronic data collection (including the transfer of digital images from the field to the central level) and difficulties with the transportation of sputum samples.
- Several clusters that were initially selected in Darfur state and other bordering states were later excluded due to security concerns, which had knock-on effects for the survey schedule and logistics.
- There was a high turnover of staff.
- Relatively few morning sputum specimens were collected. While at least one sputum specimen was obtained for 82% of participants who were eligible for sputum examination, there were fewer morning specimens than spot specimens. Since morning samples typically yield more bacteriologically confirmed results, this may have led to underestimation of TB prevalence. The specimen-based imputation model used in the analysis of data helped to compensate for this problem.
- Backlogs delayed culture inoculation when field operations were accelerated without sufficient consideration of laboratory capacity (for 3460 out of 9664 morning specimens, inoculation occurred more than 7 days after collection). This may have resulted in some false-negative culture results, and contributed to the low culture confirmation of smear-positive survey cases.
- Data entry errors occurred on the tablet computers used in the field. Considerable efforts were needed to fix these errors in the absence of routine recording of data on paper as well as electronically (the paper form for symptom screening was introduced from the fourth cluster onward).

Important lessons learned for future surveys included:

- paper records are valuable to back up electronic records;
- different diagnostic techniques should be considered given the environmental challenges of maintaining the cold chain for specimens; and
- Africa-Africa and Asia-Africa collaborations are valuable, as is technical assistance from international agencies; the coordinator of the national TB prevalence survey in Ethiopia and a laboratory expert from Pakistan both provided assistance; the WHO Regional Office for the Eastern Mediterranean provided assistance during survey preparations, including protocol development, and the Research Institute of Tuberculosis (Japan) helped to clean and analyse the data.

Photo credit: Fasil Tsegaye

References

1. The World Bank (https://data.worldbank.org/country, accessed April 2017).
2. UNAIDS (http://aidsinfo.unaids.org/, accessed April 2017).
3. World Health Organization. Global Tuberculosis Database. 2017. (http://www.who.int/tb/country/en/, accessed April 2017).
4. World Health Organization. Global tuberculosis report 2013. Geneva: WHO; 2013 (http://apps.who.int/iris/bitstream/10665/91355/1/9789241564656_eng.pdf, accessed January 2018).
5. World Health Organization. Global tuberculosis report 2014. Geneva: WHO; 2014 (http://apps.who.int/iris/bitstream/10665/137094/1/9789241564809_eng.pdf, accessed January 2018).
6. World Health Organization. Tuberculosis prevalence surveys: a handbook (WHO/HTM/TB/2010.17). Geneva: WHO; 2011 (https://apps.who.int/iris/bitstream/handle/10665/44481/9789241548168_eng.pdf, accessed August 2017).

THAILAND

2012–2013

Summary statistics

Participation rate	79%
Bacteriologically confirmed TB (≥15 years)	
• Prevalence per 100 000 population	242
• Male:female ratio	3.3
Prevalence:notification ratio (smear-positive TB, ≥15 years)	1.8

Surveyed clusters (N=83 (non-Bangkok))[a]

Key people

Name	Role	Organization
Sriprapa Nateniyom	Principal investigator	Bureau of Tuberculosis
Sirinapha Jittimanee	Survey coordinator	Bureau of Tuberculosis
Saijai Smithtikarn	Laboratory coordinator	Bureau of Tuberculosis
Wilawan Dangsaart	Radiology coordinator	Bureau of Tuberculosis
Wiriya Madasin	Data manager	Bureau of Tuberculosis
Autagorn Chunmathong	Field team leader	Bureau of Tuberculosis
Runjuan Sukkavee	Field team leader	Bangkok Metropolitan Administration
Nuntaporn Meksawasdichai	Field team leader	Institute for Urban Disease Control and Prevention, Bangkok
Pattana Pokaew	Field team leader	ODPC 1, Chiangmai
Sakchai Chaiamahapurk	Field team leader	ODPC 2, Pitsanulok
Pavasuth Chutjuntaravong	Field team leader	ODPC 3, Nakhonsawan
Supaporn Wattanatoan	Field team leader	ODPC 4, Saraburi
Ratree Dokkabowt	Field team leader	ODPC 5, Ratchaburi
Ornnipa Iamsamang	Field team leader	ODPC 6, Chonburi
Narong Wongba	Field team leader	ODPC 7, Konkaen
Phalin Kamolwat	Field team leader	ODPC 9, Nakhonratchasima
Walaya Sitti	Field team leader	ODPC 10, Ubonratchathani
Kamonwan Imduang	Field team leader	ODPC 11, Nakhonsrithamarat
Auyporn Petborisuit	Field team leader	ODPC 12, Songkhla
Norio Yamada	Technical assistance (data analysis)	Research Institute of Tuberculosis/Japan Anti-Tuberculosis Association (RIT/JATA)
Hataichanok Pukcharern	Technical assistance (sampling methodology)	National Statistics Office, Thailand
Ikushi Onozaki	Technical assistance (survey methodology)	WHO headquarters

ODPC: The Office of Disease Prevention and Control

Survey organization and financing

Implementing agency:
National TB Programme, Bureau of Tuberculosis

Finance	Amount (US$)
Government of Thailand	100 080
The Global Fund	1 790 293
Total budget	1 890 373

Data sources

- Survey dataset.

[a] The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Survey design and methodology

Sampling design	
Sampling frame	Whole country (but results applied only to non-Bangkok clusters due to the low rate participation within the Bangkok region)
Sampling design	Multistage cluster sampling using PPS
Strata	Bangkok, non-Bangkok (urban) and non-Bangkok (rural)
Sampling unit	Bangkok: three zones[a]/enumeration areas Non-Bangkok: 12 regions (ODPC[b])/provinces/enumeration areas
Sample size assumptions	
• Smear-positive prevalence	118 per 100 000 (≥15 years)
• Precision	0.25
• Design effect	1.3
• *k*	0.5
• Response rate	85%
• Sample size (estimated)	90 000 (Bangkok: 15 300, non-Bangkok: 74 700)[c]
Number of clusters	100 (Bangkok: 17, non-Bangkok: 83)
Cluster size	900
Eligibility criteria	
• Age	≥15 years
• Residency	1) Permanent residents based on house registration or 2) temporary residents or non-residents who had slept in the household for at least 2 weeks before the census

[a] The three zones included: i) the inner-most geographic region, ii) the surrounding districts, iii) districts on the edge of the Bangkok metropolitan area.
[b] The Office of Disease Prevention and Control.
[c] An additional 17% of the required sample size for the survey within Bangkok was calculated due to concerns about a low participation rate.

Screening criteria	
Interview[a]	Cough ≥2 weeks (3 points) Haemoptysis over the past month (3 points) Cough <2 weeks (2 points) Weight loss in the past month (1 point) Fever ≥1 week in the past two weeks (1 point) Night sweats in the past month (1 point) Screened positive: total score ≥3 or score ≥1 with chest X-ray exempted
Chest X-ray[b]	Any lung abnormality
Other	N/A

[a] An in-depth interview about health-care seeking behaviour was done for those who screened positive and/or those who were currently on TB treatment.
[b] Direct digital radiography.

Laboratory methodology	
Smear	Two samples (spot, morning): direct preparation, ZN
Culture	Two samples (spot, morning): direct preparation, Ogawa modified Kudoh
Identification of MTB	Immunochromatographic assay
TB drug susceptibility test	Not done
Xpert® MTB/RIF	Done after the study for quality assurance only using smear-positive culture-negative samples
HIV test	Not done

Analysis and reporting

Field data collection	Paper
Database	iDataFax
Method of analysis	MI+IPW
Results first published in a report/paper	Pending
Official dissemination event	Pending

Key survey results (non-Bangkok survey)

Prevalence[a]	Smear-positive TB		Bacteriologically confirmed TB	
	Number per 100 000 population	95% CI	Number per 100 000 population	95% CI
Total	104	55–195	242	176–332
Male	159	82–306	376	264–535
Female	51	23–117	115	71–184
15–24 years	22	2.2–215	218	86–555
25–34 years	126	44–362	186	91–380
35–44 years	49	18–132	134	69–259
45–54 years	109	27–439	265	146–482
55–64 years	164	92–293	295	187–463
≥65 years	204	108–384	465	290–743
Urban	147	48–445	286	158–518
Rural	82	55–122	220	170–284

[a] Age ≥15 years unless otherwise specified.

	Design effect	*k*
Smear-positive TB	3.3	1.7
Bacteriologically confirmed TB	2.7	1.0

Other sputum results	Number	%
Total smear-positive participants	75	–
Smear-positive participants without MTB confirmation[a]	29	39
Isolates with MDR-TB detected	N/A	N/A

[a] This includes culture with no evidence of MTB (i.e. culture-negative, NTM, contaminated, N/A).

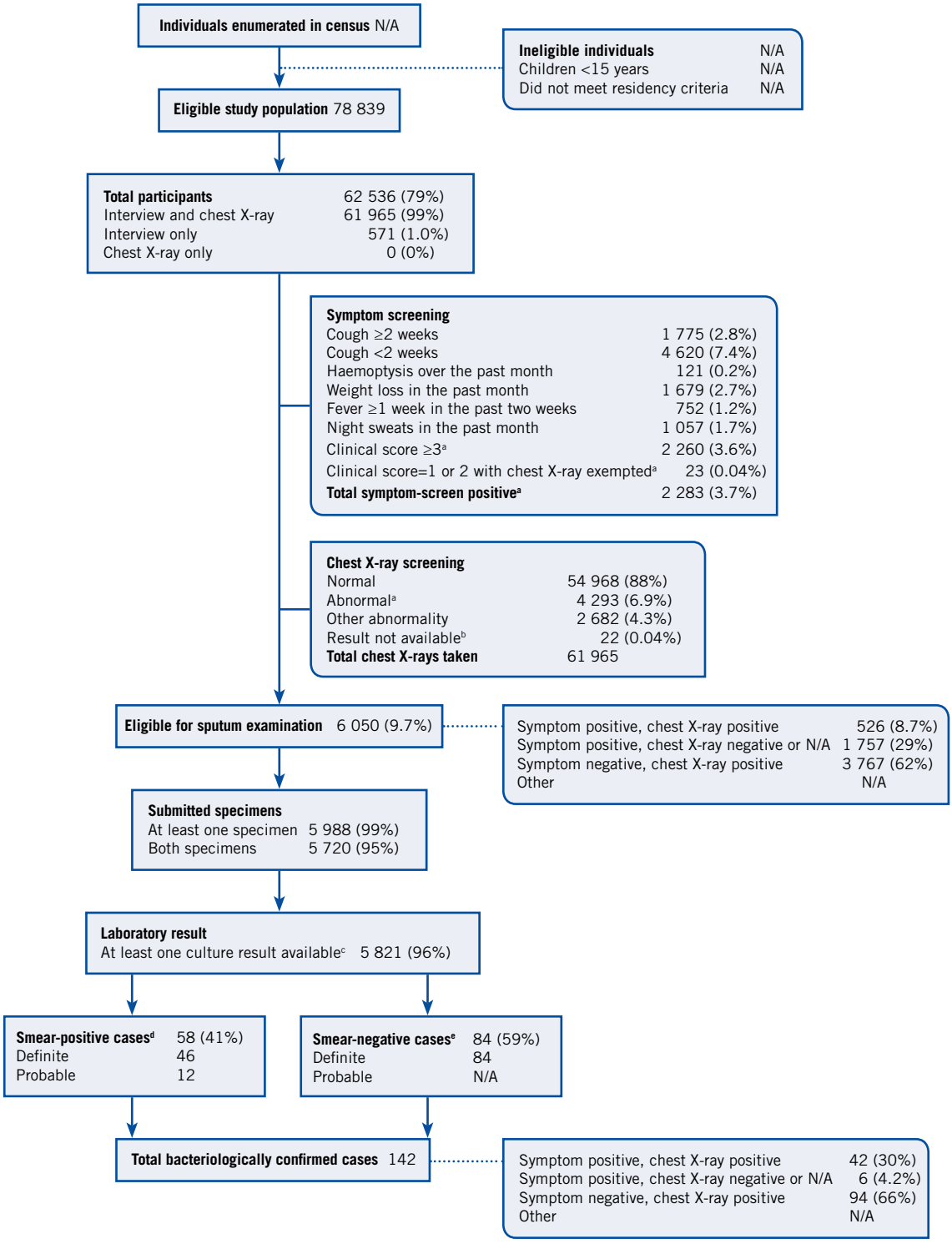
Health-care seeking behaviour among participants who were symptom-screen positive	Number	%
Participants who were symptom-screen positive[a]	2 283	–
Location of care sought		
• Consulted medical facility	N/A	N/A
Public facility	N/A	N/A
Private facility	N/A	N/A
Other	N/A	N/A
• Pharmacy	N/A	N/A
• Traditional centre	N/A	N/A
Self-treated	N/A	N/A
No action taken	N/A	N/A
Unknown	N/A	N/A

[a] Clinical score ≥3 or score ≥1 with chest X-ray exempted.

Survey participants currently on TB treatment	Number	%
Total participants currently on TB treatment	66	–
• Treated in the public sector	53	80
• Treated in the private sector	3	4.5
• Treated in other sector	3	4.5
• Treated in unknown sector	7	11
Bacteriologically confirmed TB cases detected by the survey who were currently on TB treatment	6	4.2

Survey flow: census to final outcomes (non-Bangkok survey)

Field operations: February to September 2012



[a] Eligible for sputum collection.
[b] The result was missing or could not be read due to the poor quality of the chest X-ray.
[c] Cultures that were either contaminated and/or missing without a definitive result (i.e. MTB, NTM, negative) were excluded.
[d] Definite: MTB confirmed by culture. Probable: MTB not confirmed by culture, but at least one smear-positive with chest X-ray suggestive of TB, or two smear-positive, or one smear-positive and confirmed as TB cases by referral health facilities.
[e] Definite: MTB confirmed by culture (one significant culture-positive, or two scanty culture-positive, or one scanty culture-positive with chest X-ray suggestive of TB), or confirmed as TB cases by referral health facilities. Probable: no definition.

Fig. 1: Participation rate by age and sex

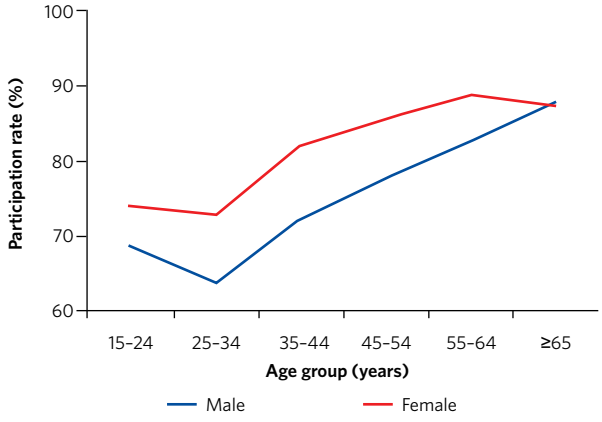


Fig. 2: TB prevalence per 100 000 population by age

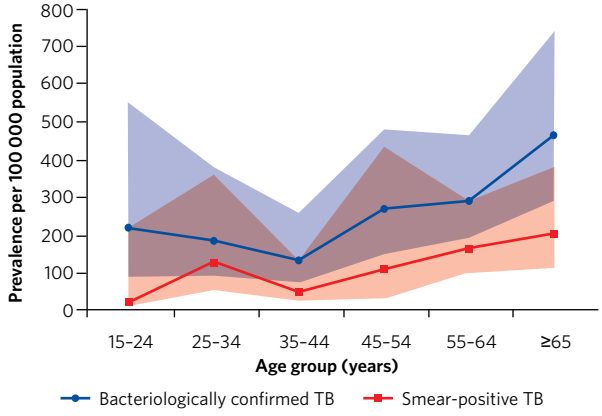


Fig. 3: Estimated number of bacteriologically confirmed TB cases and prevalence per 100 000 population, by age[a]

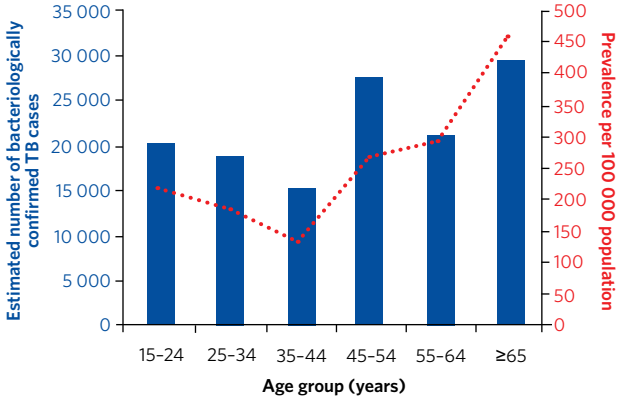


Fig. 4: Cluster variation of the number of bacteriologically confirmed TB cases[b]

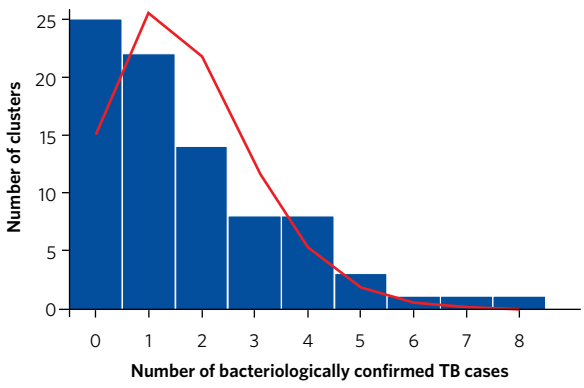


Fig. 5: Ratio of smear-positive TB prevalence to notifications by age and by sex[c]

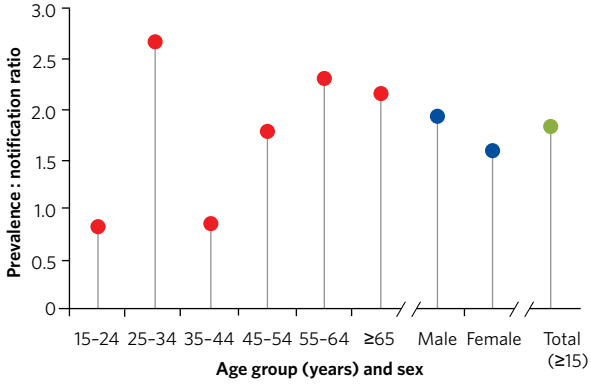
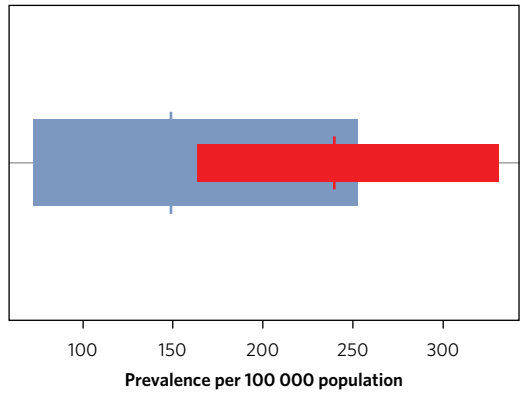


Fig. 6: Estimates of TB prevalence (all ages, all forms of TB) before (in blue) and after (in red) the national TB prevalence survey[d]



[a] The estimated number of bacteriologically confirmed TB cases is the product of age-specific prevalence and population estimates from the UN Population Division (2015 revision).

[b] The data suggested that the distribution of cases by cluster (blue bars) was significantly different from the theoretical distribution (red line) (mean 1.71, variance 3.16, $p<0.05$). The theoretical distribution assumes cases are distributed at random i.e. no clustering effect.

[c] Notification rates were estimated using notifications obtained from the WHO global TB database, and population estimates from the UN Population Division (2015 revision).

[d] The blue bar denotes the best estimate of prevalence and its range that was indirectly derived from the estimate of incidence previously published by WHO, adjusted to the year of the prevalence survey based on previously published trends in incidence.

Background

Thailand's population was 67 million in 2012, and the average gross national income (GNI) per person was US$ 5590 per year, making it an upper-middle-income country *(1)*. It was one of the 22 high tuberculosis (TB) burden countries (HBCs) defined by WHO as a top priority for global efforts in TB control in 1998 and throughout the Millennium Development Goal (MDG) era (2000–2015), and one of the top 30 HBCs defined by WHO for the period 2016–2020. In 2012, the prevalence of HIV in the general population aged 15–49 years was 1.2% (95% confidence interval [CI]: 1.0–1.4%) *(2)*, and it was estimated that 14% (95% CI: 13–16%) of TB patients were coinfected with HIV *(3)*.

In 1996, the Government of Thailand began to implement the WHO-recommended DOTS strategy *(4,5)*. By 2001, all districts had at least one public health-care facility implementing DOTS. The case notification rate for all forms of TB (new and relapse cases) decreased from 82 per 100 000 population in 1990 to 55 per 100 000 population in 2000, then increased to 101 per 100 000 population in 2010. The case detection rate (notifications of new cases divided by estimated incidence) reached 80% (95% CI: 67–97%) in 2011 *(6)*. Surveillance data from routine TB notification and vital registration systems were available to estimate the burden of TB disease in Thailand; however, underreporting from hospitals and the private sector limited their accuracy.

Before 2012, Thailand had already carried out four national TB prevalence surveys: in 1962, 1977, 1991–1992 and 2006. The observed prevalence of bacteriologically confirmed TB declined from 500 per 100 000 population (among those aged ≥15 years) in 1962 to 310 per 100 000 population (among those aged ≥15 years) in 1977 and 240 per 100 000 population (among those aged ≥10 years) in 1991 *(7)*. Although the 2006 survey used interviews and chest X-rays for screening, and culture for diagnostic confirmation, the survey could not be used to estimate prevalence due to a low participation rate (56%), untimely reading of chest X-rays (this was only done after each field cluster operation), and a low sputum submission rate from eligible participants (19%). The fifth national survey was implemented in 2012–2013.

Key methods and results (non-Bangkok survey)

All participants were screened according to the 2011 algorithm recommended by WHO; that is, using chest X-ray and an interview about symptoms *(8)*. The survey was undertaken in two phases: Phase 1 covered the non-Bangkok areas of the country from February to September 2012, and Phase 2 covered metropolitan Bangkok from April to July 2013.

Due to political instability at the time, and the low participation rate in urban settings in previous surveys, the survey design anticipated operational difficulties in metropolitan Bangkok. Therefore, Phase 1 (non-Bangkok areas) was designed as an entirely independent survey that would provide a large enough sample to estimate TB prevalence in non-Bangkok areas; the estimated sample size was 74 700 in 83 clusters. Phase 2 (metropolitan Bangkok) was allocated 17 clusters to complement Phase 1, with an estimated sample size of 15 300. Phase 1 was successfully completed with a participation rate of 79%. In Phase 2, most residents were not available, resulting in a participation rate of 26%. Therefore, the national TB programme (NTP) and the survey team decided to report only on the results of the Phase 1 survey. To estimate national prevalence, the prevalence per 100 000 population in the urban clusters of Phase 1 was assumed to be similar to the prevalence per 100 000 population in the Bangkok region.

Phase 1 included two strata (urban and rural), with a target cluster size of 900 individuals. No data were available on the numbers of individuals enumerated in the household census. 78 839 people were eligible and invited to participate. Of these, 62 536 (79%) did so. A total of 6050 participants (9.7%) were eligible for sputum examination based on chest X-ray and symptom screening. Of these, 5988 (99%) submitted at least one sputum specimen and 5720 (95%) submitted two sputum specimens.

A total of 142 bacteriologically confirmed pulmonary TB cases were identified, including 58 cases of smear-positive TB. The prevalence of bacteriologically confirmed TB was 242 (95% CI: 176–332) per 100 000 population (among those aged ≥15 years), and for smear-positive TB it was 104 (95% CI: 55–195) per 100 000 population. There was no significant difference between urban strata (286 per 100 000 population; 95% CI: 158–518) and rural strata (220 per 100 000 population; 95% CI: 170–284).

Photo credit: Sirin Jittimanee

Other key results were:

- the male to female ratio for TB prevalence was 3.1 for smear-positive TB and 3.3 for bacteriologically confirmed TB;
- the highest prevalence per 100 000 population was in those aged 45 years or more, and the absolute number of bacteriologically confirmed cases was also relatively high in the older age groups;
- among bacteriologically confirmed TB cases, 34% were symptom-screen positive, and among the smear-positive cases, 48% were symptom-screen positive;
- for smear-positive pulmonary TB, the ratio of prevalence to notifications (P:N ratio) was 1.8 overall, but varied from 0.8 in those aged 15–24 years to 2.7 in the 25–34 years age group, and was slightly higher for men than for women (1.9 versus 1.6); and
- among bacteriologically confirmed TB cases, 95% had no previous history of anti-TB treatment, and only 4.2% were on anti-TB treatment at the time of the survey.

Data on health-care seeking behaviour among TB cases were not available.

Implications of results

The survey showed that there was still a high burden of TB, and that the disease remained a public health threat. The updated national estimate (for all ages and all forms) of TB prevalence (236 per 100 000 population; 95% CI: 161–326) was higher than the pre-survey 2011 WHO estimate (182 per 100 000 population; 95% CI: 80–300) *(9, 10)*. However, this did not necessarily mean that the burden of TB had been increasing. Combining the results with data from previous surveys, as well as adjusting for the fact that the 2012 survey methods were more sensitive than those of previous surveys (owing to the use of direct chest X-ray with a digital system and the improved quality of culture testing in regional laboratories guided by the National TB Reference Laboratory), TB prevalence was still estimated to be declining, although to only a limited extent.

Assuming there were very few cases in those aged 10–15 years in 2012, the prevalence of bacteriologically confirmed TB in 2012 (242 per 100 000 population; 95% CI: 176–332, ≥15 years) was similar to the estimate from the 1991–1992 survey (240 per 100 000 population, ≥10 years) *(7)*. The 2012 survey even suggested that the prevalence of smear-negative culture-positive TB had increased. This may in part have been due to the impact of the HIV epidemic on the number of TB cases in the

late 1990s, but it may also reflect the higher sensitivity of methods used to detect smear-negative culture-positive TB in the 2012 survey. In addition, since programmatic efforts prioritized the detection and treatment of smear-positive TB cases, the impact of TB control efforts was more likely to be seen in the prevalence of smear-positive TB. The observed prevalence of smear-positive TB in 1991–1992 (170 per 100 000 population, ≥10 years) was higher than the level found in 2012 (104 per 100 000 population; 95% CI: 55–195, ≥15 years) *(7)*. Nonetheless, smear-positive TB accounted for only 41% of the total number of prevalent bacteriologically confirmed TB cases in the 2012 survey.

Age-specific estimates of TB prevalence in 2012 also suggested a long-term decline in the burden of TB. Those aged 45 years or more accounted for more than two thirds of TB cases, suggesting that reactivation of infection from the past was playing a greater role than recent infection. However, an ageing population also contributed to a relatively slow decline in the overall burden of TB.

The survey team traced the treatment provided to bacteriologically confirmed TB cases detected by the survey and found that only 45% (64/142) of patients had started treatment at a designated health centre or a nearby public hospital. Of the remainder, six died, four refused treatment and six were diagnosed as non-TB by hospitals; information was lacking on eight people who had moved outside of the survey site and on 54 (38%) for whom health facilities did not provide data, thereby limiting the analysis of treatment provision.

Photo credit: Sirin Jittimanee

The geographical variation in TB was also of concern. Among 142 bacteriologically confirmed patients detected by the survey, 81 (57%) were from the economically less-developed north-eastern region. Although confidence intervals were wide, results suggested that the level of TB prevalence in the north-eastern region could be more than twice that of other regions in Thailand.

The classical pathway to detect TB (i.e. chronic cough recognition to diagnosis by smear) would only have detected one-fifth of the bacteriologically confirmed TB survey cases (26/142). This showed the need for wider use of chest X-rays and more sensitive tools, such as molecular technologies, in the diagnostic pathway.

It was also evident that the case notification system needed improvement; for example, by introducing and monitoring mandatory notification of designated infectious diseases, including TB. Based on the survey, as many as 20% of the cases on anti-TB treatment may have been missed in the TB surveillance system.

Major successes, challenges and lessons learned

The national TB prevalence survey (non-Bangkok areas) was successfully carried out, and it provided the NTP and partners with a large and rich set of data. Estimates of TB prevalence based on the survey were more accurate and precise than those previously available, and trends were updated to show a slight decline overall.

The delay in starting Phase 2 made it hard to find staff to write and publish the official survey report, because many survey team members had moved to other positions. Nonetheless, the results were used in a timely manner to update the national TB strategy and plan.

It may not be possible to implement another national prevalence survey in Thailand in the future, given the difficulties in recruitment within the Bangkok region and in urban clusters, where the participation rate was only 65% overall. This was despite the extended hours of field activities in urban areas, including operating in the evenings and on weekends. Rapid urbanization means that the proportion of the population living in urban areas will continue to increase. In 2010, 44% of the population lived in urban areas, and this was projected to increase to 56% by 2020 *(11)*. Thus, to accurately monitor the burden of, and trends in, TB disease, either alternative survey methods would need to be developed or (preferably) the

surveillance system should be strengthened to meet the necessary quality and coverage standards, in particular to address the problem of underreporting of detected TB cases.

The complexity of a multistage cluster sampling design and probable underrepresentation of the urban population complicated the analysis (only 15 of the 83 clusters were in urban settings). In addition, there was also a large difference between the registered population and the actual number of people enumerated in the survey.

References

1. The World Bank (https://data.worldbank.org/country, accessed April 2017).
2. UNAIDS (http://aidsinfo.unaids.org/, accessed April 2017).
3. World Health Organization. Global Tuberculosis Database. 2017. (http://www.who.int/tb/country/en/, accessed April 2017).
4. WHO Tuberculosis Programme. (1994). WHO Tuberculosis Programme: framework for effective tuberculosis control. World Health Organization. (http://www.who.int/iris/handle/10665/58717, accessed January 2018).
5. World Health Organization. Global tuberculosis programme. Global tuberculosis control report 1997. Geneva: WHO; (https://apps.who.int/iris/bitstream/handle/10665/63354/WHO_TB_97.225_(part1).pdf?sequence=1, accessed January 2018).
6. World Health Organization. Global tuberculosis report 2013. Geneva: WHO; 2013; (http://apps.who.int/iris/bitstream/10665/91355/1/9789241564656_eng.pdf, accessed January 2018).
7. Sriyabhaya N, Payanandana V, Bamrungtrakul T, Konjanart S. Status of tuberculosis control in Thailand. Southeast Asian J Trop Med Public Health. 1993;24(3):410–419; (http://www.tm.mahidol.ac.th/seameo/1993-24-3/1993-24-3-410.pdf, accessed January 2018).
8. World Health Organization. Tuberculosis prevalence surveys: a handbook (WHO/HTM/TB/2010.17). Geneva: WHO; 2011. (https://apps.who.int/iris/bitstream/handle/10665/44481/9789241548168_eng.pdf, accessed August 2017).
9. World Health Organization. Global tuberculosis report 2015. Geneva: WHO; 2015; (http://apps.who.int/iris/bitstream/10665/191102/1/9789241565059_eng.pdf, accessed January 2018).
10. World Health Organization. Global tuberculosis control: WHO report 2011. Geneva: WHO; 2011; (http://apps.who.int/iris/bitstream/10665/44728/1/9789241564380_eng.pdf, accessed January 2018).
11. Department of Economic and Social Affairs. World urbanization prospect: the 2014 revision (CD Rom edition). United Nations; 2014; (https://esa.un.org/unpd/wup/CD-ROM/, accessed January 2018)

UGANDA

2014–2015

Summary statistics

Participation rate	91%
Bacteriologically confirmed TB (≥15 years)	
• Prevalence per 100 000 population	401
• Male:female ratio	4.1
Prevalence:notification ratio (Bacteriologically confirmed TB, ≥15 years)	2.8

Surveyed clusters (N=70)[a]

Key people

Name	Role	Organization
Frank Mugabe	Principal investigator - policy	Ministry of Health
Elizeus Rutebemberwa	Principal investigator - technical	School of Public Health, Makerere University
Bruce Kirenga	Co-principal investigator	School of Public Health, Makerere University
Samuel Kasozi	Study coordinator	School of Public Health, Makerere University
Harriet Kisembo	Study investigator, lead radiologist	Mulago hospital
Okot Martin Nwang	Study investigator	Senior consultant pulmonologist and head of medical panel, Mulago hospital & complex
William Worodria	Study investigator	Department of Medicine Mulago hospital & complex
Abel Nkolo	Study investigator	WHO Uganda
Emily Bloss	Study investigator	US Centers for Disease Control and Prevention (CDC)
Moses Joloba	Survey laboratory consultant and director	National TB Reference Laboratory
Kenneth Musisi	Laboratory manager	National TB Reference Laboratory
Rogers Sekibira	Data manager	School of Public Health, Makerere University
Ronald Anguzu	Field team leader	School of Public Health, Makerere University
Annet Nagudi	Field team leader	School of Public Health, Makerere University
Racheal Tumwebaze	Field team leader	School of Public Health, Makerere University
Wilfred Nkhoma	Technical assistance (survey advisor)	WHO Regional Office for Africa (AFRO)
Ikushi Onozaki	Technical assistance (survey advisor)	WHO headquarters
Marina Tadolini	Technical assistance (survey advisor)	Consultant, Italy
Peou Satha	Technical assistance (radiology)	Consultant, Cambodia
Julia Ershova	Technical assistance (data management)	US Centers for Disease Control and Prevention (CDC)
Charalampos Sismanidis	Technical assistance (analysis)	WHO headquarters

Survey organization and financing

Implementing agency:
Makerere University School of Public Health

Finance	Amount (US$)
The Global Fund	2 841 452
Total budget	2 841 452

Data sources

- Report on the population-based survey of prevalence of tuberculosis disease in Uganda 2014–15. Kampala, Uganda: Makerere University School of Public Health (pending official publication).
- Survey dataset.

[a] The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Survey design and methodology

Sampling design	
Sampling frame	Whole country
Sampling design	Multistage cluster sampling using PPS
Strata	Urban/rural
Sampling unit	Region/district/village
Sample size assumptions	
• Smear-positive prevalence	269 per 100 000 (≥15 years)
• Precision	0.25
• Design effect	1.5
• *k*	0.6
• Response rate	85%
• Sample size (estimated)	40 180
Number of clusters	70
Cluster size	580
Eligibility criteria	
• Age	≥15 years
• Residency	Permanent residents who stayed at least one night in the past two weeks; temporary visitors who arrived at least two weeks before census day

Screening criteria	
Interview	Cough ≥2 weeks
Chest X-ray[a]	Any lung abnormality
Other	Chest X-ray exempted

[a] Conventional radiography.

Laboratory methodology	
Smear	Two samples (spot, morning): direct preparation, ZN
Culture	Two samples (spot, morning): concentrated preparation, LJ media
Identification of MTB	MPT64 rapid test
TB drug susceptibility test	Not done as per protocol (post-survey study)
Xpert® MTB/RIF	Done on smear-positive specimens and/or if both samples were culture contaminated
HIV test	Offered to all participants who screened positive

Analysis and reporting

Field data collection	Paper
Database	Microsoft® Access
Method of analysis	MI+IPW
Results first published in a report/paper	August 2017
Official dissemination event	August 2017

Key survey results

Prevalence[a]	Smear-positive TB		Bacteriologically confirmed TB	
	Number per 100 000 population	95% CI	Number per 100 000 population	95% CI
Total	174	111–238	401	292–509
Male	314	216–413	734	554–914
Female	70	25–114	178	109–248
15–24 years	124	50–198	228	117–338
25–34 years	191	98–284	442	291–592
35–44 years	294	162–425	624	379–869
45–54 years	164	25–303	565	280–850
55–64 years	254	26–481	636	277–995
≥65 years	85	2–205	570	261–879
Urban	191	113–270	504	355–652
Rural	169	91–248	370	237–504

[a] Age ≥15 years unless otherwise specified.

	Design effect	*k*
Smear-positive TB	1.8	0.9
Bacteriologically confirmed TB	2.5	0.8

Other sputum results	Number	%
Total smear-positive participants	91	–
Smear-positive participants without MTB confirmation[a]	25	27
Isolates with MDR-TB detected	0	0

[a] This includes culture with no evidence of MTB (i.e. culture-negative, NTM, contaminated, N/A) and Xpert-negative.

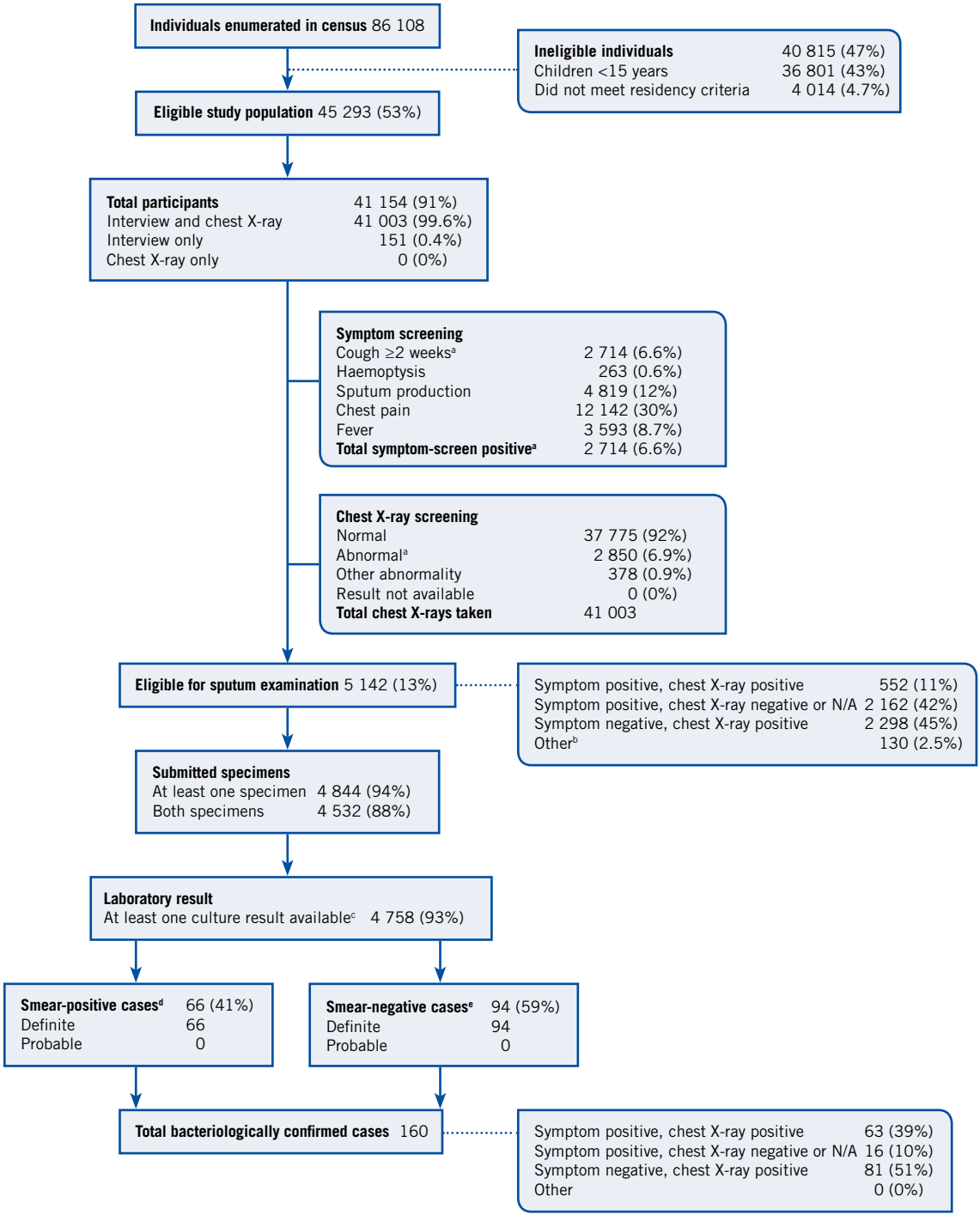
Health-care seeking behaviour among participants who were symptom-screen positive	Number	%
Participants who were symptom-screen positive[a]	2 714	–
Location of care sought		
• Consulted medical facility	1 201	44
Public facility	*1 038*	*86*
Private facility	*146*	*12*
Others (NGO)	*17*	*1.4*
• Pharmacy	421	16
• Traditional centre	11	0.4
Self-treated	22	0.8
No action taken	1 059	39
Unknown	0	0

[a] Cough ≥2 weeks.

Survey participants currently on TB treatment	Number	%
Total participants currently on TB treatment	61	–
• Treated in the public sector	57	93
• Treated in the private sector	4	7
• Treated in unknown sector	0	0
Bacteriologically confirmed TB cases detected by the survey who were currently on TB treatment	16	10

Survey flow: census to final outcomes

Field operations: October 2014 to July 2015



[a] Eligible for sputum collection.
[b] Chest X-ray exempted and symptom-screen negative.
[c] Cultures that were either contaminated and/or missing without a definitive result (i.e. MTB, NTM, negative) were excluded.
[d] Definite: MTB confirmed by culture and/or Xpert. Probable: MTB not confirmed by culture and/or Xpert, but chest X-ray consistent with TB.
[e] Definite: MTB confirmed by culture and/or Xpert with chest X-ray consistent with TB. Probable: culture weak positive (<20 colonies) in one sample and Xpert pending or N/A without negative evidence on chest X-ray (i.e. chest X-ray not taken).

Fig. 1: Participation rate by age and sex

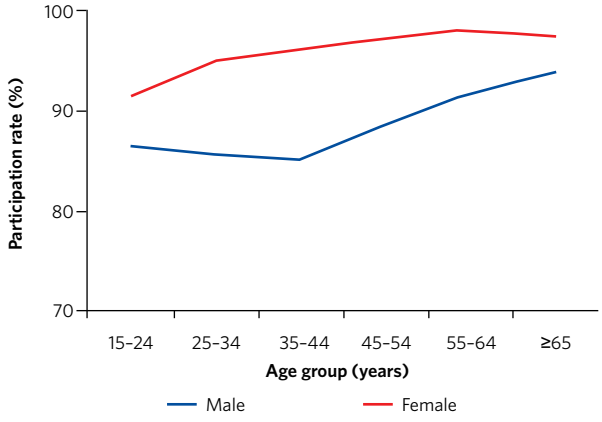


Fig. 2: TB prevalence per 100 000 population by age

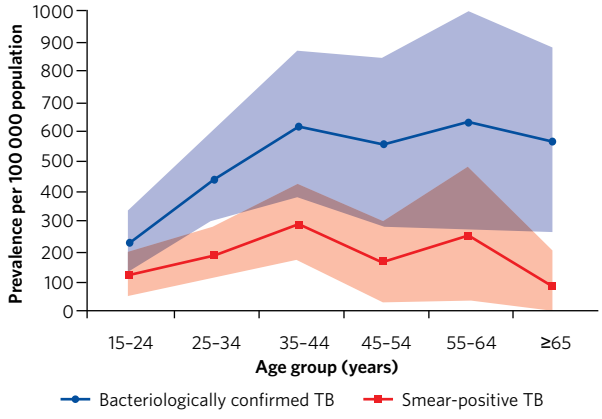


Fig. 3: Estimated number of bacteriologically confirmed TB cases and prevalence per 100 000 population, by age[a]

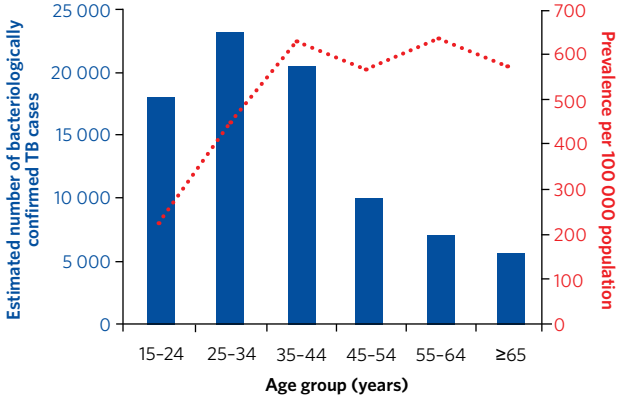


Fig. 4: Cluster variation of the number of bacteriologically confirmed TB cases[b]

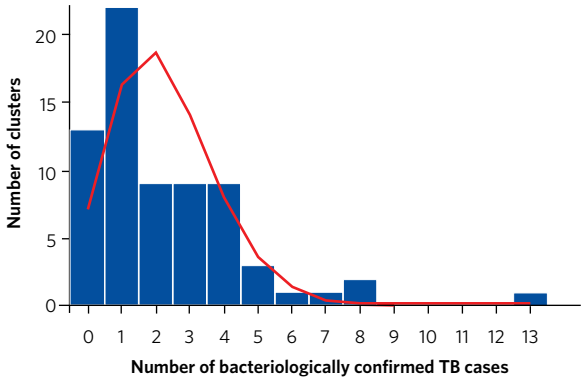


Fig. 5: Ratio of bacteriologically confirmed TB prevalence to notifications by age and by sex[c]

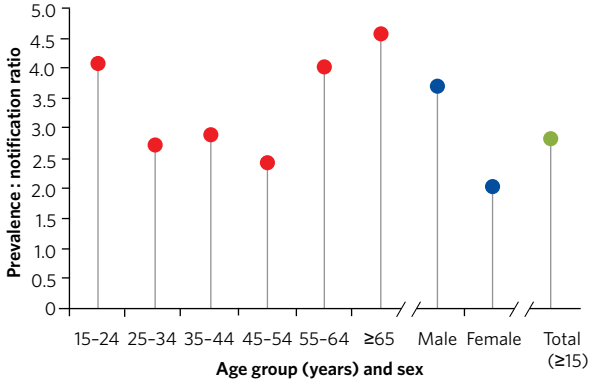
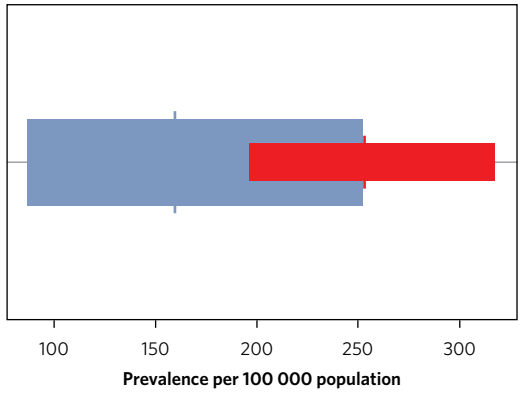


Fig. 6: Estimates of TB prevalence (all ages, all forms of TB) before (in blue) and after (in red) the national TB prevalence survey[d]



[a] The estimated number of bacteriologically confirmed TB cases is the product of age-specific prevalence and population estimates from the UN Population Division (2015 revision).

[b] The data suggested that the distribution of cases by cluster (blue bars) was significantly different from the theoretical distribution (red line) (mean 2.29, variance 5.42, $p<0.05$). The theoretical distribution assumes cases are distributed at random i.e. no clustering effect.

[c] Notification rates were estimated using bacteriologically confirmed pulmonary TB notifications (2015) obtained from the NTP, and population estimates from the UN Population Division (2015 revision).

[d] The blue bar denotes the best estimate of prevalence and its range that was indirectly derived from the estimate of incidence previously published by WHO, adjusted to the year of the prevalence survey based on previously published trends in incidence.

Background

The population of Uganda, in East Africa, was 37 million in 2014, with 48% aged under 15 years and 82% living in rural areas. The average gross national income (GNI) per person in 2014 was US$ 690, making it a low-income country *(1)*. Uganda was one of the 22 high tuberculosis (TB) burden countries (HBCs) defined by WHO as a top priority for global efforts in TB control in 1998 and throughout the Millennium Development Goal (MDG) era (2000–2015). The prevalence of HIV in the general population aged 15–49 years in 2014 was 7.1% (95% confidence interval [CI]: 6.7–7.7%) *(2)*, with declines evident since the early 1990s. In 2014, it was estimated that 45% (95% CI: 42–48%) of TB patients were coinfected with HIV *(3)*.

The National Tuberculosis and Leprosy Program (NTLP) was established in 1990, within the National Disease Control Department of the Ministry of Health (MoH). In 2015, the programme was staffed with a national programme manager and zonal TB and leprosy supervisors. The NTLP was responsible for policy formulation, planning, training, resource mobilization and setting standards for TB control. At the district level, TB control activities were the responsibility of district TB and leprosy supervisors, with oversight provided by the district health officer.

At the time of the survey design in 2008, WHO estimated that there were 311 (95% CI: 249–373) new TB cases per 100 000 population per year, equivalent to 98 356 new cases of TB per year (95% CI: 78 685–118 027). However, there was considerable uncertainty about estimates of the burden of TB disease, given that no national TB prevalence survey had ever been done, no direct measurements of TB mortality were available from vital registration, and the gap between notifications and incidence (due to underreporting or under-diagnosis of cases) had not been quantified and was difficult to estimate. For these reasons, as well as Uganda's share of the global and regional TB burden, the country was one of the 22 global focus countries for a national TB prevalence survey selected by the WHO Global Task Force on TB Impact Measurement in December 2007.

With the new opportunity of funding for a survey from the Global Fund to Fight AIDS, Tuberculosis and Malaria, in 2008 the MoH decided to implement a national TB prevalence survey. Following various challenges and delays, survey field operations started in October 2014 and were completed in July 2015 *(4)*.

Photo credit: Julia Ershova

Key methods and results

There were 70 survey clusters in two strata (urban and rural), with a target cluster size of 580 individuals. A total of 86 108 individuals from 17 535 households were enumerated in the survey census, of whom 45 293 (53%) were eligible and invited to participate. Of these, 41 154 (91%) did so. All participants were screened according to the 2011 algorithm recommended by WHO; that is, using chest X-ray and an interview about symptoms *(5)*. A total of 5142 participants (13%) were eligible for sputum examination, of whom 4844 (94%) submitted at least one sputum specimen and 4532 (88%) submitted two sputum specimens.

A total of 160 bacteriologically confirmed pulmonary TB cases were identified, including 66 cases of smear-positive TB. The prevalence of smear-positive TB was 174 (95% CI: 111–238) per 100 000 population and for bacteriologically confirmed TB it was 401 (95% CI: 292–509) per 100 000 population. The prevalence of bacteriologically confirmed TB was highest in those aged 35–44 years, at 624 (95% CI: 379–869) per 100 000 population. The prevalence of bacteriologically confirmed TB was higher in urban areas than in rural areas: 504 (95% CI: 355–652) per 100 000 population in urban areas and 370 (95% CI: 237–504) per 100 000 population in rural areas.

Other key results were:

- the male to female ratio was 4.5 for smear-positive TB and 4.1 for bacteriologically confirmed TB;
- prevalence increased with age, up to the age group 35–44 years, and it was consistently high in older age groups; however, the absolute number of bacteriologically confirmed TB cases was relatively high in younger age groups;
- of the TB survey cases, 49% were symptom-screen positive, and of the smear-positive cases, 55% were symptom-screen positive;
- for bacteriologically confirmed TB, the ratio of prevalence to notifications (P:N ratio) was 2.8 overall, but varied from 2.4 in those aged 45–54 years to 4.6 in the 65 years and over age group, and was higher for men than for women (3.7 versus 2.0);
- of the TB survey cases, 84% had no previous (or current) history of anti-TB treatment and 10% were on anti-TB treatment at the time of the survey; and
- of the 66 bacteriologically confirmed and 20 smear-positive TB survey cases that screened positive for symptoms and were not on anti-TB treatment at the time of the survey, 27 (41%) and 14 (70%), respectively, had previously sought care in a public or private health facility for their symptoms.

A total of 5142 individuals who screened positive were eligible for HIV testing, but 756 (15%) of these individuals were not tested during the survey. For those who were tested, 422 (9.6%) were found to be HIV-positive. Of the 160 bacteriologically confirmed cases, 15 (9%) did not have an HIV test and, of those tested, 39 (27%) were HIV-positive.

Implications of results

The estimated TB prevalence for all ages and all forms of TB based on the results from the survey (253 per 100 000 population; 95% CI: 191–315) was much higher than the pre-survey estimates (154 per 100 000 population; 95% CI: 85–243) *(6)*.

At the time of the survey, Uganda's NTLP screened for TB disease using chronic cough (i.e. cough >2 weeks). However, in the prevalence survey, half of the bacteriologically confirmed cases were initially identified for diagnostic testing based only on chest X-ray screening. This suggested that the NTLP should seriously consider ways of improving access to chest X-ray services. Since it was recognized that it might take time to expand such screening, a need for more research about how to improve symptom screening was also identified.

Photo credit: Marina Tadolini

Urban areas had a higher prevalence per 100 000 population than rural areas, and there were three times more cases of TB among men than women. Thus, the NTLP needed to give more attention to ensuring access to screening and enrolment on treatment among men and for people living in urban areas.

The TB/HIV data showed that integration of HIV services with anti-TB treatment should be continued.

Of participants with smear-positive specimens, 28% (25/91) did not have *Mycobacterium tuberculosis* (MTB). Thus, a smear-positive result alone was not adequate for the detection of TB cases, especially in the context of intensified case finding or active case detection strategies.

Before the survey, Uganda was in the list of 22 HBCs as defined by WHO. The survey identified a higher prevalence than expected, but the results were available only after a new list of 30 HBCs was defined by WHO for the period 2016–2020. The need for good communication between all levels of WHO, the NTLP and the MoH to determine the consequences of Uganda not being in the list of 30 TB HBCs (although it remained on the list of high TB/HIV burden countries) was recognized.

Photo credit: Irwin Law

Major successes, challenges and lessons learned

It was a major success to implement the country's first national TB prevalence survey. Survey preparations started in 2008, but there were long delays primarily due to the challenge of securing funding. Whereas prevalence surveys in other countries introduced technologies such as digital chest X-ray or electronic data collection in the field, the Ugandan survey used only conventional chest X-ray equipment and paper-based data collection because of limitations on funding and time. Data were entered into the database at central level upon completion of each cluster operation. Nonetheless, the quality of the survey was exceptionally high.

There were no major delays in survey implementation resulting from major accidents or equipment failure. However, the X-ray machine often had to be restarted due to excessive humidity and heat, which affected the auto-film processor. Therefore, X-ray examinations were often interrupted, and participants were kept waiting.

A high participation rate, both in rural and urban clusters, was achieved due to the dedication of the central and field teams, community involvement and careful preparation of survey operations (especially in big cities). A high sputum collection rate was also achieved. Uganda's survey was also one of the first to provide high-quality data on

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TB/HIV coinfection with a large proportion of survey participants requesting to be tested.

The biggest advantage of the survey in Uganda was that the country had its own National TB Reference Laboratory in Kampala – one of only a few laboratories in Africa qualified as a supranational reference laboratory. This laboratory produced highly reliable results for both Xpert® MTB/RIF and culture testing.

A large data management team at the central level cleaned and validated data in a timely and systematic way. This allowed the final validated dataset to be available within a few months of the end of the survey.

Given the elements described above, the survey in Uganda was one of the highest quality prevalence surveys in Africa.

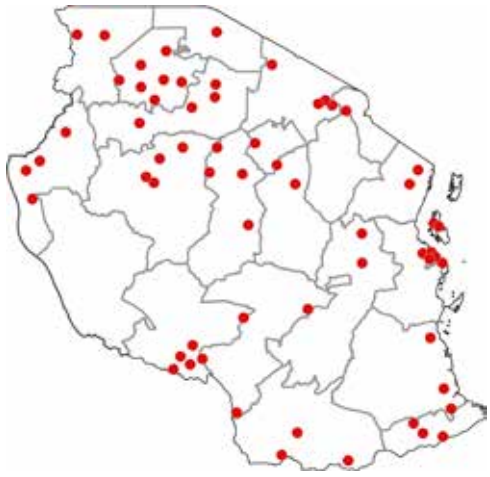
Clear demarcation between the terms of reference of the NTLP manager and the head of research team that actually undertook the survey facilitated smooth field operations and post-survey work. The survey team lacked experience in conducting a TB prevalence survey, because those trained through a WHO workshop had left the survey team by the start of the survey. This lack of experience resulted in some census sampling errors and lack of community participation during the pilot. Nonetheless, major challenges were ultimately solved by the survey team, with the support of intensive technical assistance during the early phases of the survey.

References

1. The World Bank (https://data.worldbank.org/country, accessed April 2017).
2. UNAIDS (http://aidsinfo.unaids.org/, accessed April 2017).
3. World Health Organization. Global Tuberculosis Database. 2017. (http://www.who.int/tb/country/en/, accessed April 2017).
4. Report on the population-based survey of prevalence of tuberculosis disease in Uganda 2014–15. Kampala, Uganda: Makerere University School of Public Health 2018.
5. World Health Organization. Tuberculosis prevalence surveys: a handbook (WHO/HTM/TB/2010.17). Geneva: WHO; 2011 (https://apps.who.int/iris/bitstream/handle/10665/44481/9789241548168_eng.pdf, accessed August 2017).
6. World Health Organization. Global tuberculosis report 2014. Geneva: WHO; 2014 (http://apps.who.int/iris/bitstream/10665/137094/1/9789241564809_eng.pdf?ua=1, accessed January 2018).

UNITED REPUBLIC OF TANZANIA

2011–2012



Surveyed clusters (N=62)[a]

Summary statistics

Participation rate	77%
Smear-positive TB (≥15 years)	
• Prevalence per 100 000 population	275
• Male:female ratio	2.3
Prevalence:notification ratio (smear-positive TB, ≥15 years)	3.0

Key people

Name	Role	Organization
Saidi M. Egwaga	Principal investigator (PI)	National Tuberculosis and Leprosy Programme (NTLP)
Godfrey S. Mfinanga	Co-PI	National Institute for Medical Research (NIMR), Muhimbili Medical Research Center
Deusdedit V. Kamara	Survey coordinator	NTLP
Senkoro Mbazi	Assistant survey coordinator	NIMR, Muhimbili Medical Research Center
Ahmed Khatib	Programme manager	Zanzibar Tuberculosis and Leprosy Programme
Basra Doulla	Laboratory manager	Central TB Reference Laboratory (CTRL), NTLP
Lulu Fundikira	Radiology coordinator	Muhimbili University of Health and Allied Sciences (MUHAS)
Raymond P. Shirima	Data manager	NTLP
Blasdus F. Njako	Field team leader	NTLP
Msaki John	Field team leader	NIMR
Rahim Ishumi	Field team leader	NIMR
Lugano Mtafya	Field team leader	NIMR
Moses Ringo	Field team leader	NIMR
Frank van Leth	Technical assistance (survey advisor)	KNCV Tuberculosis Foundation
Wilfred Nkhoma	Technical assistance (survey advisor)	WHO Regional Office for Africa (AFRO)
Ikushi Onozaki	Technical assistance (survey advisor)	WHO headquarters
Charalampos Sismanidis	Technical assistance (analysis)	WHO headquarters

Survey organization and financing

Implementing agency:

The National Tuberculosis and Leprosy Programme (NTLP)

Finance	Amount (US$)
PATH/USAIDS	29 673
The Global Fund	2 611 312
Other partners	521 184
MOH, Tanzania	200 000
Total budget	3 362 169

Data sources

- The First National Tuberculosis Prevalence Survey in the United Republic of Tanzania, final report: Ministry of Health and social welfare; 2013.
- M. Senkoro, S. Mfinanga, S. Egwaga, R. Mtandu, D.V. Kamara, D. Basra, et al. Prevalence of pulmonary tuberculosis in adult population of Tanzania: a national survey, 2012. Int J Tuberc Lung Dis 20(8):1014–1021.
- M. Senkoro, S.G. Hinderaker, S.G. Mfinanga, N. Range, D.V. Kamara, S. Egwaga, et al. Health care-seeking behaviour among people with cough in Tanzania: findings from a tuberculosis prevalence survey. Int J Tuberc Lung Dis 19(6):640–646.
- Survey dataset.

[a] The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Survey design and methodology

Sampling design	
Sampling frame	Whole country
Sampling design	Multistage cluster sampling using PPS
Strata	Urban/semi-urban/rural/Zanzibar
Sampling unit	Four strata/district/ward
Sample size assumptions	
• Smear-positive prevalence	261 per 100 000 (≥15 years)
• Precision	0.25
• Design effect	1.6
• *k*	0.6
• Response rate	80%
• Sample size (estimated)	46 792
Number of clusters	62
Cluster size	750
Eligibility criteria	
• Age	≥15 years
• Residency	Slept for the past 2 weeks in the household prior to the census

Screening criteria	
Interview[a]	Cough ≥2 weeks or haemoptysis or fever ≥2 weeks or weight loss or excessive night sweats
Chest X-ray[b]	Any lung (or mediastinum) abnormality
Other	N/A

[a] An in-depth interview was done only for those who screened positive, to obtain information on demographics, risk factors for TB, knowledge about TB and health-care seeking behaviour.
[b] Mobile X-ray unit, computed radiography.

Laboratory methodology	
Smear	Three samples (spot, morning and spot; both spot samples were examined in the field, and a morning sample was examined in the central laboratory): direct preparation, FM (LED, auramine stain)
Culture	One sample (morning): concentrated preparation, LJ media
Identification of MTB	PNB
TB drug susceptibility test	Done at the Antwerp SRL, not as part of the original protocol
Xpert® MTB/RIF	Done only for smear-positive slides to confirm the presence of MTB at the Antwerp SRL, not as part of the original protocol
HIV test	Done for participants who screened positive

Analysis and reporting

Field data collection	Paper
Database	EpiData
Method of analysis	Cluster-level[a]
Results first published in a report/paper	August 2013
Official dissemination event	July 2013

[a] Reported prevalence results are based on a re-analysis by WHO.

Key survey results

Prevalence[a]	Smear-positive TB		Bacteriologically confirmed TB	
	Number per 100 000 population	95% CI	Number per 100 000 population	95% CI
Total	275	232–326	N/A	N/A
Male	407	319–494	N/A	N/A
Female	179	130–228	N/A	N/A
15–24 years	51	13–88	N/A	N/A
25–34 years	280	178–381	N/A	N/A
35–44 years	316	199–433	N/A	N/A
45–54 years	241	123–359	N/A	N/A
55–64 years	462	264–660	N/A	N/A
≥65 years	662	436–888	N/A	N/A
Urban	328	184–471	N/A	N/A
Semi-urban	302	201–404	N/A	N/A
Rural	268	210–327	N/A	N/A

[a] Age ≥15 years unless otherwise specified. No TB cases were identified in Zanzibar.

	Design effect	*k*
Smear-positive TB	1.9	0.6
Bacteriologically confirmed TB	N/A	N/A

Other sputum results	Number	%
Total smear-positive participants	162	–
Smear-positive participants without MTB confirmation[a]	N/A	N/A
Isolates with MDR-TB detected	N/A	N/A

[a] This could not be calculated because not all 162 smear-positive participants were tested with culture and/or Xpert MTB/RIF.

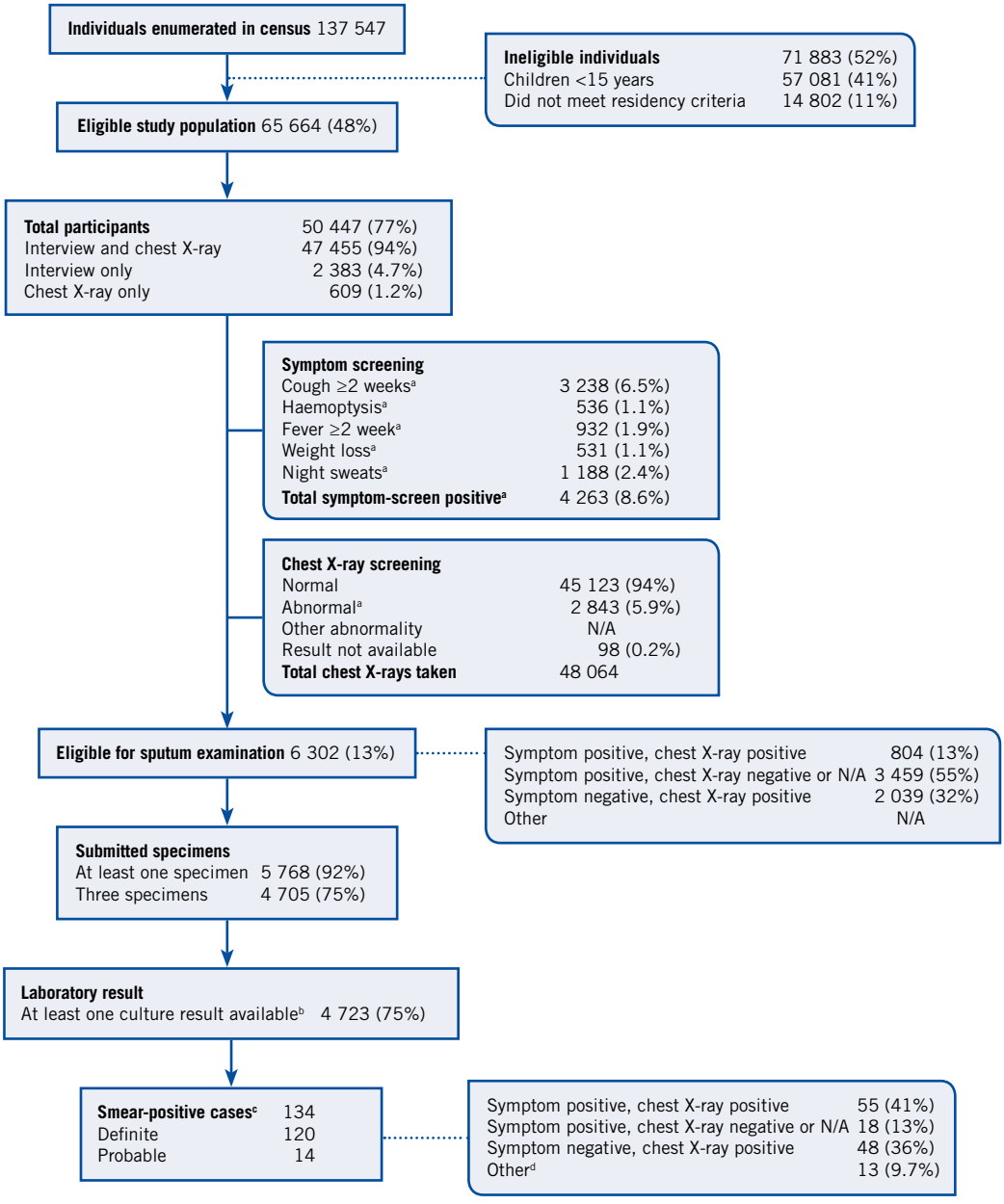
Health-care seeking behaviour among participants who were symptom-screen positive	Number	%
Participants who were symptom-screen positive[a]	3 388	–
Location of care sought		
• Consulted medical facility	481	14
Public facility (incl. mission hospital)	*445*	*93*
Private facility	*36*	*7.5*
• Pharmacy	147	4.3
• Traditional centre	11	0.3
• Other[b]	412	12
Self-treated	N/A	N/A
No action taken	1 688	50
Unknown	649	19

[a] Data on health-care seeking behaviour were only available for participants who reported cough ≥2 weeks and/or haemoptysis.
[b] This included 257 dispensaries and 155 unspecified locations.

Survey participants currently on TB treatment	Number	%
Total participants currently on TB treatment	88	–
• Treated in the public sector	N/A	N/A
• Treated in the private sector	N/A	N/A
• Treated in other sector	N/A	N/A
Smear-positive TB cases detected by the survey who were currently on TB treatment	5	3.7

Survey flow: census to final outcomes

Field operations: December 2011 to November 2012



[a] Eligible for sputum collection.
[b] Cultures that were either contaminated and/or missing without a definitive result (i.e. MTB, NTM, negative) were excluded.
[c] Definite: MTB confirmed by culture (NTRL) and/or Xpert (Antwerp SRL). Probable: MTB not confirmed by culture or Xpert, but chest X-ray final reading "consistent with TB". Please see the main text for further details.
[d] 13 were screened negative, and these people were not part of the total number of people eligible for sputum examination. The reason for their sputum submission was unknown.

Fig. 1: Participation rate by age and sex

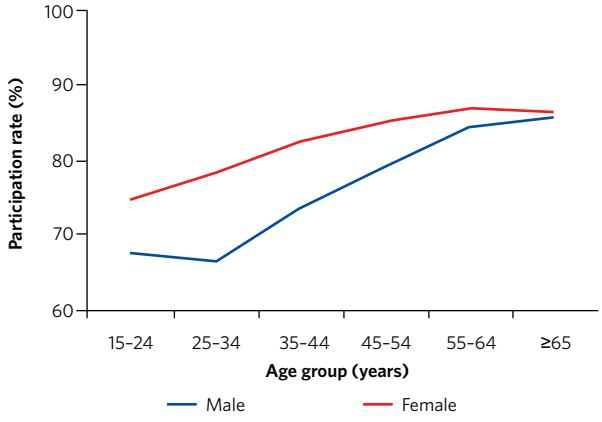


Fig. 2: TB prevalence per 100 000 population by age

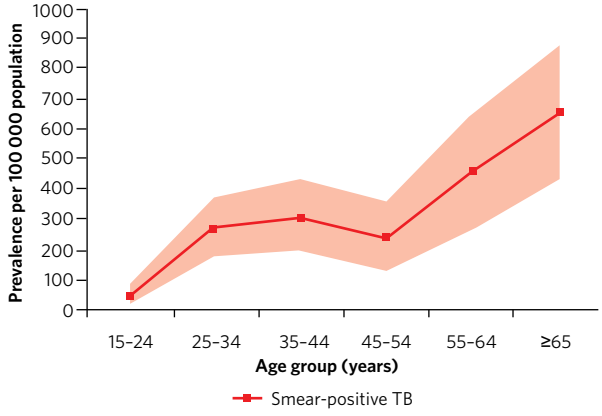


Fig. 3: Estimated number of smear-positive TB cases and prevalence per 100 000 population, by age[a]

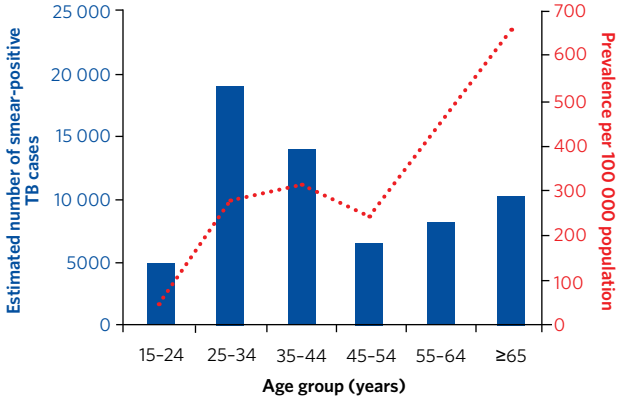


Fig. 4: Cluster variation of the number of smear-positive TB cases[b]

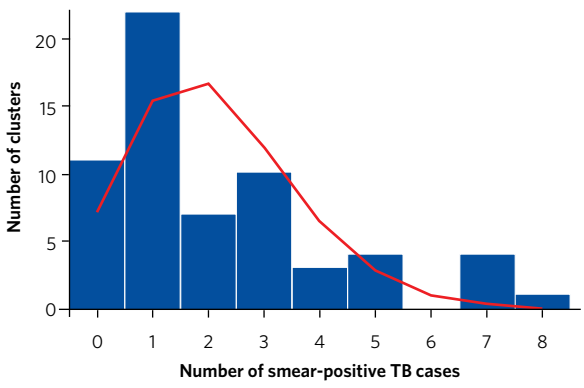


Fig. 5: Ratio of smear-positive TB prevalence to notifications by age and by sex[c]

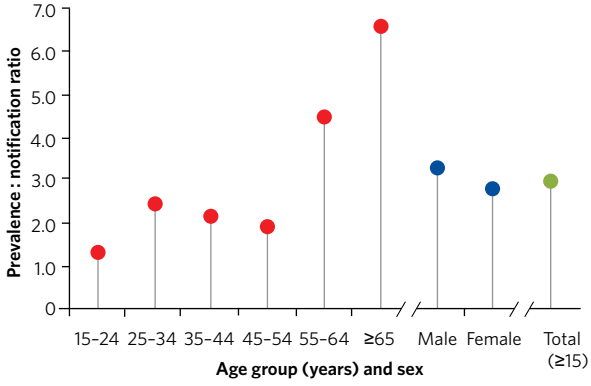
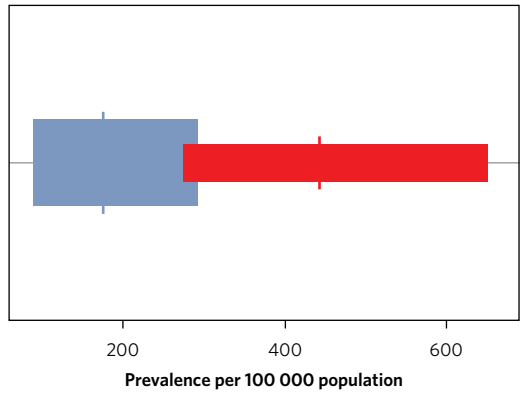


Fig. 6: Estimates of TB prevalence (all ages, all forms of TB) before (in blue) and after (in red) the national TB prevalence survey[d]



[a] The estimated number of smear-positive TB cases is the product of age-specific prevalence and population estimates from the UN Population Division (2015 revision).

[b] The data suggested that the distribution of cases by cluster (blue bars) was significantly different from the theoretical distribution (red line) (mean 2.16, variance 4.24, $p<0.05$). The theoretical distribution assumes cases are distributed at random i.e. no clustering effect.

[c] Notification rates were estimated using notifications obtained from the WHO global TB database, and population estimates from the UN Population Division (2015 revision).

[d] The blue bar denotes the best estimate of prevalence and its range that was indirectly derived from the estimate of incidence previously published by WHO, adjusted to the year of the prevalence survey based on previously published trends in incidence.

Background

In 2012, the United Republic of Tanzania, in East Africa, had a population of 48 million. It was a low-income country with an average gross national income (GNI) per person of US$ 780 per year *(1)*. The United Republic of Tanzania was one of the 22 high tuberculosis (TB) burden countries (HBCs) defined by WHO as a top priority for global efforts in TB control in 1998 and throughout the Millennium Development Goal (MDG) era (2000–2015), and one of the top 30 HBCs defined by WHO for the period 2016–2020. In 2012, the prevalence of HIV in the general population aged 15–49 years was 5.2% (95% confidence interval [CI]: 4.6–5.9%) *(2)*, and it was estimated that 38% (95% CI: 33–44%) of TB patients were coinfected with HIV *(3)*.

The United Republic of Tanzania's National Tuberculosis and Leprosy Programme (NTLP) was established in 1977. During the 1980s it became the first country in the world to use an approach to TB control that later became known as the DOTS strategy, and was considered a "model" DOTS programme *(4)*. Before the national TB prevalence survey of 2012, WHO estimated the incidence of all forms of TB at 169 (95% CI: 159–180) per 100 000 population and the prevalence at 177 (95% CI: 93–286) per 100 000 population *(5)*. These estimates were primarily based on data from case notifications, corrected for detection and reporting gaps of the surveillance system of TB cases, as best understood by experts. To move away from expert opinion and instead use a robust, nationally representative, direct measurement to estimate the burden of TB disease in the country, it was decided to conduct a national TB prevalence survey. A detailed survey protocol was first developed in 2006, but funds were only secured in 2010. In the intervening period, the United Republic of Tanzania became one of the 22 global focus countries for a national TB prevalence survey selected by the WHO Global Task Force on TB Impact Measurement. The survey started in December 2011 and was completed in November 2012 *(6)*.

Key methods and results

In 2012, the United Republic of Tanzania became only the second country in Africa to complete a national TB prevalence survey that used the screening and diagnostic methods recommended in the latest guidance issued by WHO *(7)*. There were 62 clusters sampled in four strata (urban, semi-urban, rural and Zanzibar) across the country, with a target cluster size of 750 individuals. A total of 137 547 individuals was enumerated in the survey census, of whom 65 664 (48%) were eligible (non-residents and children were ineligible) and invited to participate. Of these, 50 447 (77%) did so. They were screened according to the 2011 algorithm recommended by WHO; that is, using both a chest X-ray and an interview about symptoms *(7)*. A total of 6302 participants (13%) screened positive and were eligible for sputum examination; of these, 5768 (92%) submitted at least one sputum specimen, and 4705 (75%) submitted three sputum specimens.

A total of 134 smear-positive pulmonary TB cases were identified in the survey. This translated into an estimate of smear-positive TB prevalence in the country, among those aged 15 years or more, of 275 (95% CI: 232–326) per 100 000 population in 2012. There were no significant

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differences among three geographical strata (urban, semi-urban and rural) in the level of smear-positive TB prevalence among those aged 15 years or more. No TB cases were identified in Zanzibar.

Other key results were:

- the male to female ratio for TB prevalence was 2.3 for smear-positive pulmonary TB;
- prevalence increased with age, with a notably high level per 100 000 population (and estimated number of smear-positive cases) in those aged 25–44 years;
- among smear-positive pulmonary TB cases, 44% were symptom-screen positive;
- for smear-positive pulmonary TB, the ratio of prevalence to notifications (P:N ratio) was 3.0 overall, but varied from 1.3 in those aged 15–24 years to 6.6 in those aged 65 years or more; the ratio was slightly higher for men than for women (3.3 versus 2.8);
- among smear-positive pulmonary TB cases, 93% had no previous history of anti-TB treatment, and only 3.7% were receiving treatment at the time of the survey; and
- among participants who screened-positive, 5.0% (318 of 6302) tested HIV-positive.

No data on health-care seeking behaviour among smear-positive TB cases were collected.

Unfortunately, the number of bacteriologically confirmed TB cases could not be validated. In the survey, field teams prioritized the detection of smear-positive individuals in the field and the early treatment of these people. Microscopy laboratories – using light-emitting diode fluorescence microscopy (LED FM) – were set up in every cluster site by senior laboratory staff from the Central TB Reference Laboratory (CTRL). However, this had an unintended negative effect on the quality of samples collected, and on testing by culture. For example, many samples (possibly as many as half) took more than a week to reach the CTRL; and a preliminary survey report stated there were 100 TB cases with a smear-positive result[1] and 73 with a culture-positive result *(6)* - such a finding had never previously been observed in a national TB prevalence survey that followed the 2011 WHO guidelines *(7)*. This in turn led to concerns that the number of culture-positive TB cases from the survey was underestimated. Following discussion and review of laboratory results with external partners including the country's Supranational Reference Laboratory (SRL) in Antwerp, Belgium, as well as WHO, there was consensus that the culture results from the prevalence survey could not be used *(8–10)*.

In an attempt to confirm the validity of the smear-positive test results, and following discussions between the NTLP in the United Republic of Tanzania, the head of the Central TB Reference Laboratory (CTRL), the survey team, the KNCV Tuberculosis Foundation (the main technical partner) and WHO, it was agreed to send all specimen slides classified as smear-positive for testing using Xpert® MTB/RIF to the SRL Antwerp. A positive Xpert result would exclude false-positive microscopy as well as NTM (without the presence of MTB in the case of mixed infection). Results from the SRL (which became available in September 2014) concluded that "*...an estimate of prevalence based on microscopy-positives could be justified*" *(11)*. The final case count, combining SRL Antwerp and survey CTRL results, was a total of 134 smear-positive TB cases, compared with 100 from the initial analysis based only on survey CTRL findings *(8–10)*. This final count is the one used in this profile.

To estimate the prevalence of bacteriologically confirmed TB among those aged 15 years or more, data from the neighbouring countries of Ethiopia, Malawi, Rwanda, Uganda and Zambia were used. From surveys in these five countries, the combined estimate of the ratio of bacteriologically confirmed to smear-positive TB was 2.16:1 (standard deviation [SD]: 0.46).[2] This ratio was applied to the smear-positive prevalence estimate for the United Republic of Tanzania, resulting in an estimate of the prevalence of bacteriologically confirmed TB of 590 (95% CI: 330–860) per 100 000 population. A further step of extrapolation to all forms of TB and all ages resulted in an estimated TB prevalence of 443 (95% CI: 258–629) per 100 000 population.

[1] The NTLP's smear-positive case definition: two smear-positive specimens regardless of culture result, one smear-positive specimen with chest X-ray abnormality consistent with TB, or smear-positive specimen with a culture positive result.

[2] To extrapolate the prevalence of bacteriologically confirmed TB among those aged ≥15 years to the prevalence of TB for all ages and all forms of TB, it was assumed that 45% of the general population were children, that extrapulmonary TB accounted for 23% (SD 9%) of all TB cases (based on 2008-2012 notification data) and that the ratio of childhood to adult TB was 0.07 (SD 0.03).

Implications of results

The estimated prevalence of TB (443 per 100 000 population; 95% CI: 258–629, all forms, all ages) was higher than the pre-survey WHO estimate (2012) of 177 (95% CI: 93–286) per 100 000 population *(5)*. However, the re-estimated time series of prevalence showed a continual decline since 2005.

A striking finding of the survey was that 52% of the identified smear-positive TB cases were aged 45 years or more. This indicated that prevalent TB was largely driven by progression from a much earlier acquisition of a latent infection. In contrast, routine programmatic data from 2012 showed that only 28% of notified TB cases were aged 45 years or more, indicating important gaps in the detection of cases in the middle to older age groups. The large proportion of prevalent TB cases in older age groups points towards a historic positive effect of NTLP control strategies; however, differences with the estimated number of notified TB cases suggested a need for the NTLP to reassess its screening and diagnostic strategies (for example, to widen the range of symptoms considered when screening for TB in routine practice, and expand the use of chest X-ray), and to create better community awareness about the symptoms of TB. The strong emphasis of the NTLP on TB/HIV activities may have taken attention away from a large, unidentified population of older HIV-negative people with TB. The post-survey estimate of the case detection rate (notifications of new cases divided by estimated incidence) in 2015 was only 36% (95% CI: 21–77), compared with a pre-survey estimate of 79% (95% CI: 74–84%) *(12,13)*.

Major successes, challenges and lessons learned

Due to serious limitations with culture examinations, it was difficult to accurately estimate the burden of bacteriologically confirmed TB. Nonetheless, collaborative post-survey activities with all partners made the survey results (especially estimates of the prevalence of smear-positive pulmonary TB) useful for the NTLP. One key message was the age distribution of prevalent cases, which suggested an epidemiological shift towards older people and potentially reactivation of previous infection, which has been a sign of effective population-wide TB control activities in other countries in the past *(14)* and is consistent with a shift observed more recently in Asian countries that have implemented prevalence surveys. The identification of a higher burden of TB disease among those who were HIV-negative compared with those who were HIV-positive was also helpful. The survey team, to their credit, published their results in a peer-reviewed journal *(14–16)*.

In addition to the major challenge with culture testing, other challenges and associated lessons learned included:

- smear microscopy in the field is technically feasible, but in practice it can be fraught with potential contamination issues;
- multiple paper forms were used for data collection (including handwritten individual identifiers), and administrative errors made it difficult or impossible to match the personal identifiers on these forms with laboratory specimens and other clinical information; digital data entry and barcoding is vital to ensure the quality of data management in future surveys;
- there was erroneous oversampling of study participants in the initial clusters, to increase participation. Such protocol violations need to be avoided;
- some recommendations from external monitoring missions were not implemented in a timely manner, thus potentially impacting on survey quality;
- vehicles with computerized radiography equipment had to be checked and serviced during the survey and given the technology used, additional manual steps and human resources were required to develop images before reading

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compared with more recent digital radiography systems;

- the agreement to reach consensus between key stakeholders on the actual number of TB cases took more than a year; and
- there were delays in disbursement of funds to support survey operations.

References

1. The World Bank. (https://data.worldbank.org/country, accessed April 2017).
2. UNAIDS. (http://aidsinfo.unaids.org/, accessed May 2017).
3. World Health Organization. Global tuberculosis database. Geneva: WHO; 2017 (http://www.who.int/tb/data/en/, accessed April 2017).
4. Enarson D A. Principles of IUATLD collaborative tuberculosis progammes. Bull Int Union Tuberc Lung Dis 1991; 66 (4): 195–200.
5. World Health Organization. Global tuberculosis report 2012. Geneva: WHO; 2012 (http://www.who.int/tb/publications/global_report/gtbr12_main.pdf, accessed May 2017)
6. United Republic of Tanzania – Ministry of Health and Social Welfare. The first national tuberculosis prevalence survey in the United Republic of Tanzania – interim report. Tanzania: 2013.
7. World Health Organization. Tuberculosis prevalence surveys: a handbook. Geneva: WHO; 2011 (https://apps.who.int/iris/bitstream/handle/10665/44481/9789241548168_eng.pdf, accessed August 2016).
8. Supranational Reference Laboratory. Final report. Technical assistance and support. Antwerp, Belgium: SRL; 2013.
9. Supranational Reference Laboratory. Final report on Xpert MTB/RIF testing of survey sputum smears positive for acid-fast bacilli. Antwerp, Belgium: SRL; 2013.
10. World Health Organization. Addendum to the report of the first national TB prevalence survey of the United Republic of Tanzania. Geneva: WHO; 2015.
11. Van Deun, A. Final report on Xpert MTB/RIF testing of survey sputum smears positive for acid-fast bacilli by the Supra-National TB Reference Laboratory (SRL) in Antwerp, Belgium. 3 September 2014.
12. World Health Organization. Global tuberculosis report 2013. Geneva: WHO; 2013 (http://apps.who.int/iris/bitstream/handle/10665/91355/9789241564656_eng.pdf?sequence=1, accessed May 2017)
13. World Health Organization. Global tuberculosis report 2015. Geneva: WHO; 2015 (http://apps.who.int/iris/bitstream/handle/10665/191102/9789241565059_eng.pdf;jsessionid=DA5FF20A3580FAAD2F9FA0267F9D1724?sequence=1, accessed May 2017)
14. Senkoro M, Mfinanga S, Egwaga S, Mtandu R, Kamara DV, Basra D et al. Prevalence of pulmonary tuberculosis in adult population of Tanzania: a national survey, 2012. Int J Tuberc Lung Dis. 2016;20(8):1014–1021 (https://www.ncbi.nlm.nih.gov/pubmed/27393533, accessed January 2018).
15. Senkoro M, Hinderaker SG, Mfinanga SG, Range N, Kamara DV, Egwaga S et al. Health care-seeking behaviour among people with cough in Tanzania: findings from a tuberculosis prevalence survey. Int J Tuberc Lung Dis. 2015;19(6):640–646 (https://www.ncbi.nlm.nih.gov/pubmed/25946352, accessed January 2018).
16. Senkoro M, Kumar AM, Chinnakali P, Mfinanga SG, Egwaga S, Kamara V et al. Population impact of factors associated with prevalent pulmonary tuberculosis in Tanzania. Int J Tuberc Lung Dis. 2016;20(10):1326–1333 (https://www.ncbi.nlm.nih.gov/pubmed/27725043, accessed January 2018).

VIET NAM

2006–2007

Summary statistics

Participation rate	91%
Bacteriologically confirmed TB (≥15 years)	
• Prevalence per 100 000 population	307
• Male:female ratio	4.5
Prevalence:notification ratio (smear-positive TB, ≥15 years)	2.3

Surveyed clusters (N=70)[a]

Key people

Name	Role	Organization
Dinh Ngoc Sy	Principal investigator	National Tuberculosis Control Programme/National lung hospital
Nguyen Viet Nhung	Principal investigator, survey coordinator	National Tuberculosis Control Programme/National lung hospital
Nguyen Binh Hoa	Survey coordinator, data manager, field team leader	National Tuberculosis Control Programme/National lung hospital
Nguyen Van Hung	Laboratory manager	National Tuberculosis Control Programme/National lung hospital
Do Trong Nghia	Radiology manager	National Tuberculosis Control Programme/National lung hospital
Nguyen Van Cu	Field team leader	National Tuberculosis Control Programme/National lung hospital
Chu Manh Dung	Field team leader	National Tuberculosis Control Programme/National lung hospital
Nguyen Cong Chi	Field team leader	National Tuberculosis Control Programme/National lung hospital
Ha Thuc Van	Field team leader	National Tuberculosis Control Programme/Danang Hospital for TB and Lung Diseases
Bao Thuyet	Field team leader	National Tuberculosis Control Programme/Danang Hospital for TB and Lung Diseases
Vu Ngoc Tuan	Field team leader	National Tuberculosis Control Programme/Pham Ngoc Thach hospital
Pham Vuong Khac Thai	Field team leader	National Tuberculosis Control Programme/Pham Ngoc Thach hospital
Tran Ngoc Thach	Field team leader	National Tuberculosis Control Programme/Pham Ngoc Thach hospital
Thai Anh Sam	Field team leader	National Tuberculosis Control Programme/Pham Ngoc Thach hospital
Frank G.J. Cobelens	Technical assistance (survey advisor)	Academic Medical Center, University of Amsterdam
Martien W. Borgdorff	Technical assistance (survey advisor)	Academic Medical Center, University of Amsterdam
Edine W. Tiemersma	Technical assistance (data analysis)	KNCV Tuberculosis Foundation
Nico Kalisvaart	Technical assistance (data management)	KNCV Tuberculosis Foundation
Agnes Gebhard	Technical assistance (analysis on social economic status)	KNCV Tuberculosis Foundation
Marleen Vree	Technical assistance (analysis)	Landsteiner Institute, Medical Center Haaglanden, The Hague, The Netherlands

Survey organization and financing

Implementing agency:
National Tuberculosis Control Programme

Finance	Amount (US$)
Government of Viet Nam (Ministry of Health)	893 000
Government of the Netherlands	92 000
The Global Fund	10 000
WHO	57 000
Total budget	1 052 000

Data sources

- Viet Nam National Tuberculosis Programme, national TB prevalence survey in Vietnam, 2006–2007. Ministry of Health, Viet Nam; Hanoi November 2008.
- Hoa NB, Sy DN, Nhung NV, Tiemersma EW, Borgdorff MW, Cobelens FG. National survey of tuberculosis prevalence in Viet Nam. Bull World Health Organ. 2010;88(4):273–280.
- Hoa NB, Cobelens FG, Sy DN, Nhung NV, Borgdorff MW, Tiemersma EW. Yield of interview screening and chest X-ray abnormalities in a tuberculosis prevalence survey. Int J Tuberc Lung Dis. 2012;16(6):762–767.
- Hoa NB, Tiemersma EW, Sy DN, Nhung NV, Vree M, Borgdorff MW et al. Health-seeking behaviour among adults with prolonged cough in Vietnam. Trop Med Int Health. 2011;16(10):1260–1267.

[a] The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Survey design and methodology

Sampling design	
Sampling frame	Whole country
Sampling design	Multistage cluster sampling using PPS
Strata	Urban, rural and remote districts
Sampling unit	District/commune/sub-commune
Sample size assumptions	
• Smear-positive prevalence	100 per 100 000 (≥15 years)
• Precision	0.2
• Design effect	1.5
• *k*	0.6
• Response rate	80%
• Sample size (estimated)	105 000
Number of clusters	70
Cluster size	1 500
Eligibility criteria	
• Age	≥15 years
• Residency	Lived in the household for at least three months prior to the census

Screening criteria	
Interview[a]	Productive cough ≥2 weeks
Chest X-ray[b]	Any lung abnormality
Other	Current TB treatment or history of TB in preceding two years or chest X-ray exempted

[a] An in-depth interview about TB related symptoms and health-care seeking behaviour was conducted among people who screened positive on any one of the screening criteria.

[b] Mobile mass miniature radiography system based on photofluorography and mobile direct digital X-ray unit (slot scan system).

Laboratory methodology	
Smear	Three samples (one spot immediately, one early morning and one spot on or before the transport day): direct preparation, ZN
Culture	One sample (morning): concentrated preparation, LJ media
Identification of MTB[a]	Niacin
TB drug susceptibility test	Done[b]
Xpert® MTB/RIF	Not done
HIV test	Not done

[a] Species identification was done for positive cultures.

[b] All *M.tuberculosis* isolates were tested for resistance to isoniazid, rifampicin, ethambutol and streptomycin but results were not officially reported, since measurement of levels of drug resistance was not a primary objective of the survey.

Analysis and reporting

Field data collection	Paper
Database	EpiData version 3.1
Method of analysis	Adjustment of standard errors for cluster design
Results first published in a report/paper	November 2008
Official dissemination event	November 2008

Key survey results

Prevalence[a]	Smear-positive TB		Bacteriologically confirmed TB	
	Number per 100 000 population	95% CI	Number per 100 000 population	95% CI
Total	197	150–244	307	249–366
Male	351	262–440	536	431–642
Female	69	39–99	118	75–161
15–24 years	42	12–73	55	22–88
25–34 years	84	24–143	136	63–210
35–44 years	247	157–337	321	222–420
45–54 years	234	145–322	344	228–460
55–64 years	329	187–470	599	288–910
≥65 years	429	239–620	764	492–1 037
Urban	203	132–274	282	188–376
Rural	219	145–294	344	259–430
Remote	134	92–177	232	131–333

[a] Age ≥15 years unless otherwise specified.

	Design effect	*k*
Smear-positive TB	2.7	0.8
Bacteriologically confirmed TB	2.6	0.6

Other sputum results	Number	%
Total smear-positive participants	186	–
Smear-positive participants without MTB confirmation[a]	49	26
Isolates with MDR-TB detected	N/A	N/A

[a] This includes culture with no evidence of MTB (i.e. culture-negative, NTM, contaminated, N/A).

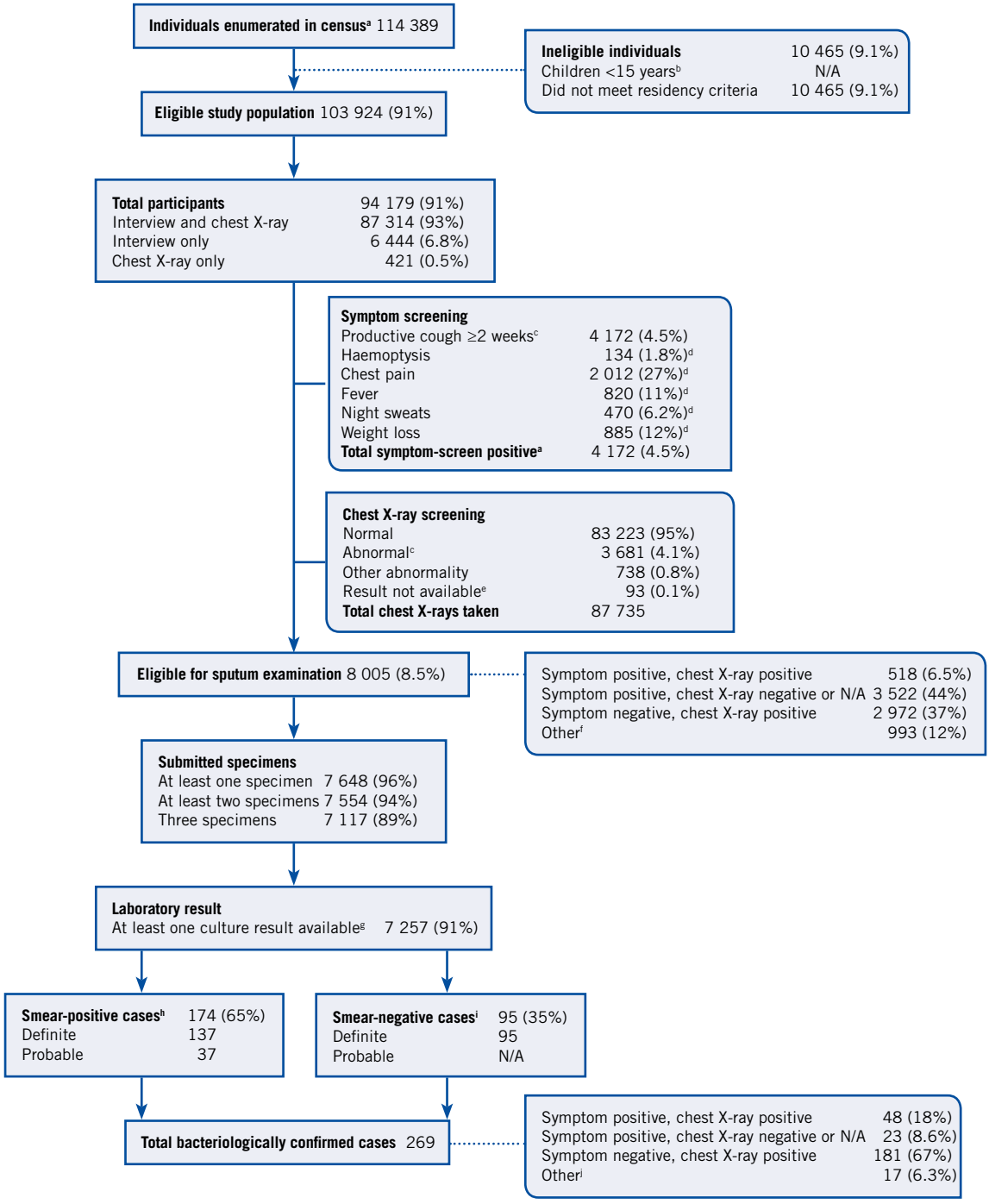
Health-care seeking behaviour among participants who were symptom-screen positive	Number	%
Participants who were symptom-screen positive[a]	4 172	–
Location of care sought		
• Consulted medical facility	1 228	29
Public facility	*1 029*	*84*
Private facility	*199*	*16*
• Pharmacy	671	16
• Traditional centre	25	0.6
Self-treated	N/A	N/A
No action taken	2 248	54
Unknown	N/A	N/A

[a] Productive cough ≥2 weeks.

Survey participants currently on TB treatment	Number	%
Total participants currently on TB treatment	64	–
• Treated in the public sector	46	72
• Treated in the private sector	2	3.1
• Treated in unknown sector	16	25
Bacteriologically confirmed TB cases detected by the survey who were currently on TB treatment	10	3.7

Survey flow: census to final outcomes

Field operations: September 2006 to July 2007



[a] There were 137 549 individuals in the census, and only adults (≥15 years) were counted for the prevalence survey.
[b] 23 160 children (6–14 years) from the same population as the prevalence survey participated in a concurrent tuberculin survey (see reference 11).
[c] Eligible for sputum collection.
[d] The denominator is the number of participants who had an in-depth interview (N=7580).
[e] The results were not recorded.
[f] Currently on TB treatment, including participants who screened positive (symptom and/or chest X-ray) (64), history of TB in the two years preceding the survey, including participants who screened positive (symptom and/or chest X-ray) (364), chest X-ray exempted and symptom-screen negative (58), and participants who were not eligible for sputum submission but submitted sputum based on the team leader's decision (507).
[g] Cultures that were either contaminated and/or missing without a definitive result (i.e. MTB, NTM, negative) were excluded.
[h] Definite: MTB confirmed by culture. Probable: MTB not confirmed by culture but either two or more positive smears, one positive smear with chest X-ray consistent with TB.
[i] Definite: MTB confirmed by culture. Probable: no definition.
[j] One was chest X-ray exempted and 16 were included due to the team leader's decision.

Fig. 1: Participation rate by age and sex

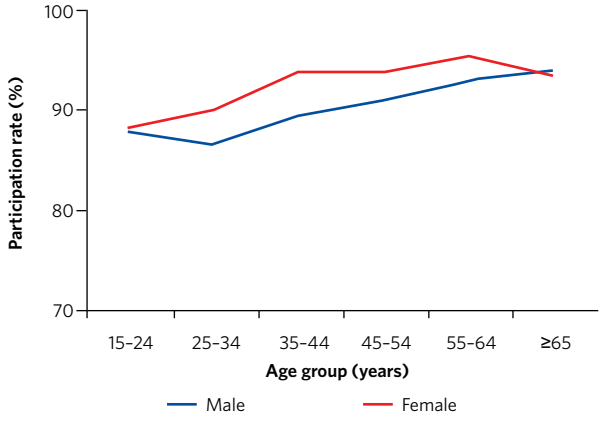


Fig. 2: TB prevalence per 100 000 population by age

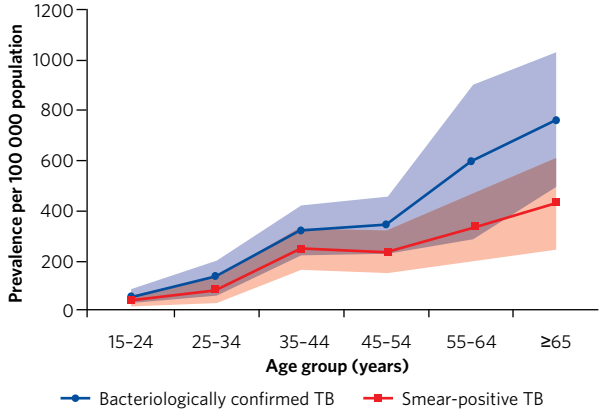


Fig. 3: Estimated number of bacteriologically confirmed TB cases and prevalence per 100 000 population, by age[a]

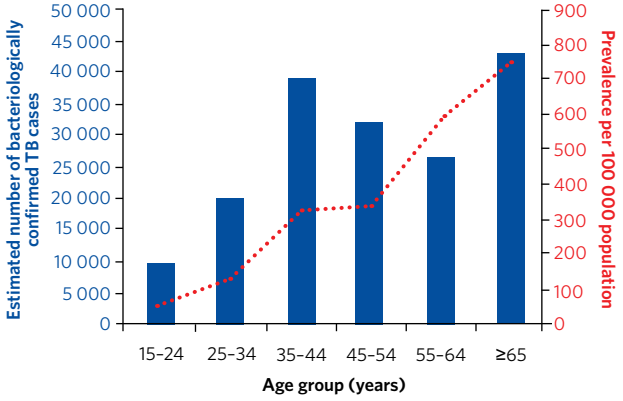


Fig. 4: Cluster variation of the number of bacteriologically confirmed TB cases[b]

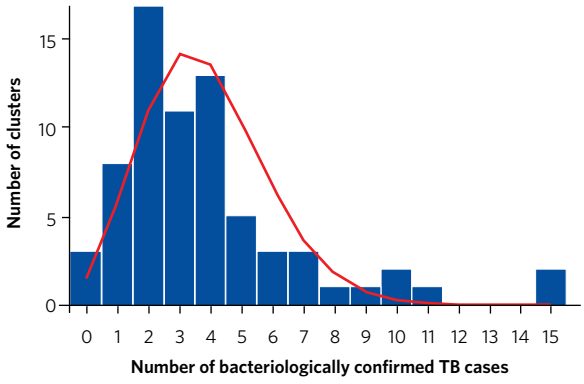


Fig. 5: Ratio of smear-positive TB prevalence to notifications by age and by sex[c]

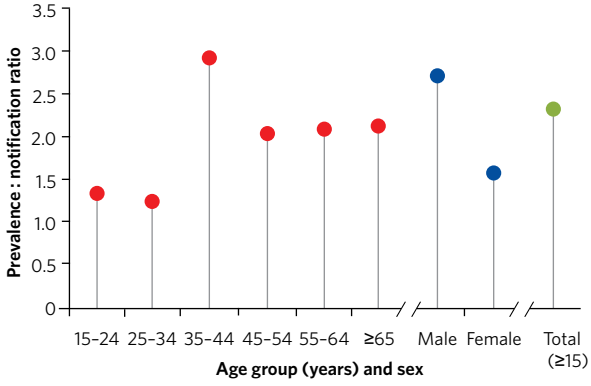
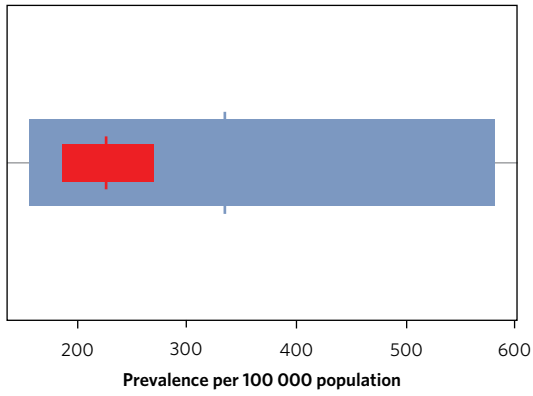


Fig. 6: Estimates of TB prevalence (all ages, all forms of TB) before (in blue) and after (in red) the national TB prevalence survey[d]



[a] The estimated number of bacteriologically confirmed TB cases is the product of age-specific prevalence and population estimates from the UN Population Division (2015 revision).

[b] The data suggested that the distribution of cases by cluster (blue bars) was significantly different from the theoretical distribution (red line) (mean 3.84, variance 9.35, $p<0.05$). The theoretical distribution assumes cases are distributed at random i.e. no clustering effect.

[c] Notification rates were estimated using notifications obtained from the WHO global TB database, and population estimates from the UN Population Division (2015 revision).

[d] The blue bar denotes the best estimate of prevalence and its range that was indirectly derived from the estimate of incidence previously published by WHO, adjusted to the year of the prevalence survey based on previously published trends in incidence.

Background

Viet Nam is the easternmost country on the Indochinese Peninsula in South-East Asia, and in 2006 its population was 83 million. The average gross national income (GNI) per person was US$ 760 per year, making it a low-income country *(1)*. It was one of the 22 high tuberculosis (TB) burden countries (HBCs) defined by WHO as a top priority for global efforts in TB control in 1998 and throughout the Millennium Development Goal (MDG) era (2000–2015), and one of the top 30 HBCs defined by WHO for the period 2016–2020. In 2005, the prevalence of HIV in the general population aged 15–49 years was 0.4% (95% confidence interval [CI]: 0.3–0.5%) *(2)*, and it was estimated that 7.0% (95% CI: 6.2–7.8%) of TB patients were coinfected with HIV *(3)*.

In 1995, the National TB Control Programme (NTP) in Viet Nam began implementing the WHO-recommended DOTS strategy *(4,5)* and achieved nationwide DOTS coverage in 1999 *(6)*. Based on mathematical models, it was predicted that TB prevalence and incidence would start to decline in Viet Nam when 70% of its new smear-positive TB cases were detected and 85% of cases were successfully treated *(7)*. According to WHO estimates, Viet Nam reached and exceeded these targets in 1997 *(8)*. However, its notification rate (new and relapse) increased from 73 per 100 000 population in 1990 to 111 per 100 000 population in 2000. A small decrease in TB notification rates among women and older adults was offset by an increase among young men, resulting in stabilization of notification rates during this period *(8)*. Given that the epidemiology of TB in Viet Nam did not follow the predicted pattern, and that estimates of TB incidence (used as the denominator for estimates of the case detection rate) were based on tuberculin surveys[1] conducted in the 1990s, the NTP decided to implement a national TB prevalence survey in 2006–2007. The objectives of the survey were to obtain a direct measure of the burden of TB disease, and to better understand the epidemiology of TB and the effectiveness of TB control efforts in Viet Nam.

[1] Tuberculin surveys were used to estimate the annual risk of infection but did not provide a direct measure of the burden of TB disease.

Key methods and results

There were 70 clusters in three strata (urban, rural and remote), with a target cluster size of 1500 individuals. A total of 114 389 individuals from 34 271 households were enumerated in the survey census, of whom 103 924 (91%) were eligible and invited to participate. Of these, 94 179 (91%) were screened by chest X-ray and symptom screening interview, in line with the WHO 2011 algorithm *(9)*. A total of 8005 people (8.5% of participants) were eligible for sputum examination. Of these, 7648 (96%) submitted at least one sputum specimen and 7117 (89%) submitted three sputum specimens *(10,11)*.

A total of 269 bacteriologically confirmed pulmonary TB cases were identified, including 174 cases of smear-positive TB. The prevalence of smear-positive TB was 197 (95% CI: 150–244) per 100 000 population (among those aged ≥15 years) and for bacteriologically confirmed TB it was 307 (95% CI: 249–366) per 100 000 population. When extrapolated to all forms of TB and to all ages, prevalence was estimated as 266 (95% CI: 117–477) per 100 000 population. There was no significant variation in prevalence between the three strata (urban, rural and remote). However, in the middle geographical zone of the country, where there are more remote and mountainous areas, prevalence was 209 (95% CI: 132–287) per 100 000 population, which was significantly lower than the level of 286 (95% CI: 218–355) per 100 000 population in the

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northern zone and of 367 (95% CI: 249–486) per 100 000 population in the southern zone *(10,11)*.

Other key results were:

- the male to female ratio was 5.1 for smear-positive TB and 4.5 for bacteriologically confirmed TB;
- prevalence per 100 000 population increased with age, and the absolute number of bacteriologically TB cases was also relatively large in older age groups (≥35 years);
- among bacteriologically confirmed TB cases, 26% were symptom-screen positive, and among the smear-positive cases, 53% were symptom-screen positive;
- for smear-positive pulmonary TB, the ratio of prevalence to notifications (P:N ratio) was 2.3, but varied from 1.3 in those aged 15–34 years to 2.9 in the 35–44 year age group, and was higher for men than for women (2.7 versus 1.6);
- among bacteriologically confirmed TB cases, 79% had no previous history of anti-TB treatment and only 4% were on anti-treatment at the time of the survey; and
- of the 196 bacteriologically confirmed and 134 smear-positive TB survey cases that screened positive for symptoms,[2] and were not on anti-TB treatment at the time of the survey, 62 (32%) and 46 (34%), respectively, had previously sought care in a public or private health facility for their symptoms.

Implications of results

The survey found that the prevalence of smear-positive TB among those aged 15 years or more was 197 (95% CI: 150–244) per 100 000 population. Assuming that there were no smear-positive TB cases in those aged under 15 years, the national prevalence of smear-positive TB (all age groups) was 145 (95% CI: 110–180) per 100 000 population. Therefore, the prevalence of smear-positive TB was 1.6 times higher than the level of 90 per 100 000 population in 2006 that had been estimated prior to the survey (based on data from tuberculin surveys).

The prevalence survey demonstrated that the previous estimates based on tuberculin survey data from the 1990s were too low. Nonetheless, the distribution of TB by age, sex and geography was similar to patterns observed in case notification data. Specifically, the burden of TB was much higher in men than in women, and the epidemic was a progressively ageing one, with the highest burden found in the oldest age groups. The survey also confirmed a relatively low burden in the remote, mountainous areas compared with urban and low-lying rural areas. To address the high TB burden in older people and men, active case finding efforts were expanded, with specific attention paid to those groups.

Only about one half of the smear-positive TB cases found in the survey reported a productive cough of ≥2 weeks duration. Given that detection of TB cases in health facilities used a screening algorithm based on the presence of a persistent productive cough, a large proportion of TB cases would not have met the standard screening criteria. Furthermore, over a third of the bacteriologically confirmed cases were smear-negative, so that without culture (which was not routinely done), many cases could not be confirmed. These findings highlighted important limitations in the TB screening and diagnostic algorithms used for routine care (i.e. a presumptive TB case was identified only by symptoms – mainly a cough for ≥2 weeks). They also highlighted the need to widen the eligibility criteria for smear examination to other TB-related symptoms in addition to cough, and to expand the use of culture for TB diagnosis. Broader symptom screening criteria and greater use of chest X-ray were implemented in Viet Nam following the prevalence survey.

The survey also showed that nearly 30% (1228/4172) of people with prolonged productive cough had visited a health-care provider, and of these, 84% (1029) had visited a public health-care facility. A common first point of contact was a pharmacy, which highlighted the important role this sector could play in TB case-finding activities, especially through the referral of a person with

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[2] Health-care seeking behaviour data were available for survey cases with any TB symptoms, not just for those with chronic cough.

presumptive TB to appropriate health-care providers. In addition, TB patients waited on average about one month before seeking care, which demonstrated the need to increase awareness in the general population about TB symptoms, and the need to improve the diagnostic practices of providers to ensure appropriate and timely diagnosis and management of TB.

Major successes, challenges and lessons learned

The survey provided the first ever direct measurement of TB disease burden at the national level in Viet Nam. It also provided a large amount of other information about the TB epidemic, much of which was published in a timely fashion *(11–15)*. For example, data collected during, or in association with, the survey provided information about:

- the relationship between TB and household expenditure (as a proxy for socio-economic status);
- health-care seeking behaviour among people with presumptive TB;
- the distribution and frequency of mycobacteria other than TB;
- the yield of interview screening and chest X-ray abnormalities;
- diagnosis and treatment of TB in the private sector;
- comparisons between TB prevalence and the annual risk of tuberculous infection; and
- the quality and coverage of the national TB surveillance system.

The results were also used to evaluate and improve approaches to TB control within Viet Nam, and the experience gained during the survey helped to build global and regional capacity to conduct prevalence surveys.

The inclusion criteria used in the survey posed some challenges. Specifically, adults who were not present in the sampled clusters for at least three months, or who were incarcerated or who lived in military barracks (i.e. the mobile population), were not included in the survey. As a result, it was not known how well the survey sample represented the mobile population, and therefore the total Vietnamese population. The proportion of young men in the mobile population was relatively high at the time of the survey; thus, this group was underrepresented in the survey sample. The prevalence of TB among men of this age group was higher than that among women of the same age, but lower than the prevalence among older men.

Photo credit: Frank Cobelens

References

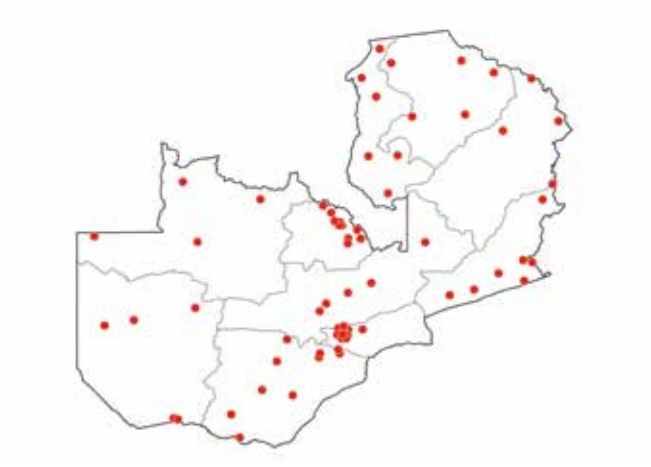
1. The World Bank (https://data.worldbank.org/country, accessed April 2017).
2. UNAIDS (http://aidsinfo.unaids.org/, accessed April 2017).
3. World Health Organization. Global Tuberculosis Database. 2017. (http://www.who.int/tb/country/en/, accessed April 2017).
4. WHO Tuberculosis Programme. (1994). WHO Tuberculosis Programme: framework for effective tuberculosis control. World Health Organization. (http://www.who.int/iris/handle/10665/58717, accessed January 2018).
5. World Health Organization. Global tuberculosis programme. Global tuberculosis control report 1997. Geneva: WHO; (https://apps.who.int/iris/bitstream/handle/10665/63354/WHO_TB_97.225_(part1).pdf?sequence=1, accessed January 2018).
6. Huong NT, Duong BD, Co NV, Quy HT, Tung LB, Bosman M et al. Establishment and development of the National Tuberculosis Control Programme in Vietnam. Int J Tuberc Lung Dis. 2005;9(2):151–156 (https://www.ncbi.nlm.nih.gov/pubmed/15732733, accessed January 2018).
7. Dye C, Maher D, Weil D, Espinal M, Raviglione M. Targets for global tuberculosis control. Int J Tuberc Lung Dis. 2006;10(4):460–462 (https://www.ncbi.nlm.nih.gov/pubmed/16602414, accessed January 2018).
8. Vree M, Bui DD, Dinh NS, Nguyen VC, Borgdorff MW, Cobelens FG. Tuberculosis trends, Vietnam. Emerg Infect Dis. 2007;13(5):796–797 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2738473/, accessed January 2018).
9. World Health Organization. Tuberculosis prevalence surveys: a handbook (WHO/HTM/TB/2010.17). Geneva: WHO; 2011 (https://apps.who.int/iris/bitstream/handle/10665/44481/9789241548168_eng.pdf, accessed August 2017).
10. Viet Nam National Tuberculosis Programme, national TB prevalence survey in Vietnam. Ministry of Health, Viet Nam.
11. Hoa NB, Sy DN, Nhung NV, Tiemersma EW, Borgdorff MW, Cobelens FG. National survey of tuberculosis prevalence in Viet Nam. Bull World Health Organ. 2010;88(4):273–280 (http://www.who.int/bulletin/volumes/88/4/09-067801/en/, accessed January 2018).
12. Hoa NB, Cobelens FG, Sy DN, Nhung NV, Borgdorff MW, Tiemersma EW. Yield of interview screening and chest X-ray abnormalities in a tuberculosis prevalence survey. Int J Tuberc Lung Dis. 2012;16(6):762–767 (https://www.ncbi.nlm.nih.gov/pubmed/22507287, accessed January 2018).
13. Hoa NB, Cobelens FG, Sy DN, Nhung NV, Borgdorff MW, Tiemersma EW. First national tuberculin survey in Viet Nam: characteristics and association with tuberculosis prevalence. Int J Tuberc Lung Dis. 2013;17(6):738–744 (https://www.ncbi.nlm.nih.gov/pubmed/23676155, accessed January 2018).
14. Hoa NB, Tiemersma EW, Sy DN, Nhung NV, Vree M, Borgdorff MW et al. Health-seeking behaviour among adults with prolonged cough in Vietnam. Trop Med Int Health. 2011;16(10):1260–1267 (https://www.ncbi.nlm.nih.gov/pubmed/21692960, accessed January 2018).
15. van Leth F, Guilatco RS, Hossain S, Van't Hoog AH, Hoa NB, van der Werf MJ et al. Measuring socio-economic data in tuberculosis prevalence surveys. Int J Tuberc Lung Dis. 2011;15 Suppl 2:S58–63 (https://www.ncbi.nlm.nih.gov/pubmed/21740660, accessed January 2018).

ZAMBIA

2013–2014

Summary statistics

Participation rate	84%
Bacteriologically confirmed TB (≥15 years)	
• Prevalence per 100 000 population	638
• Male:female ratio	1.7
Prevalence:notification ratio (smear-positive TB, ≥15 years)	2.0



Surveyed clusters (N=66)[a]

Key people

Name	Role	Organization
Nathan Kapata	Principal investigator	National TB and Leprosy Control Programme
Pascalina Chanda Kapata	Survey coordinator and co-principal investigator	Ministry of Health
William Ngosa	Assistant survey coordinator	Ministry of Health
Mine Metitiri	Assistant survey coordinator	Ministry of Health
Lutinala Nalomba Mulenga	Chest diseases laboratory team lead	Ministry of Health
Mathias Tembo	Tropical Diseases Research Centre laboratory team lead	Ministry of Health
Patrick Katemangwe	University teaching hospital laboratory team lead	Ministry of Health
Mazyanga Mazuba Liwewe	HIV laboratory team lead	Ministry of Health
Veronica Sunkuntu	Radiology team lead	Ministry of Health
Chris Silavwe	Data manager	Ministry of Health
Chitani Mbewe	Field team leader	Ministry of Health
Sam Msariri	Field team leader	Ministry of Health
Mashina Chomba	Field team leader	Ministry of Health
Jane Shawa	Field team leader	Ministry of Health
Eveline Klinkenberg	Technical assistance (survey advisor)	KNCV Tuberculosis Foundation
Nico Kalisvaart	Technical assistance (data management)	KNCV Tuberculosis Foundation
Julia Ershova	Technical assistance (data management)	US Centers for Disease Control and Prevention (CDC)

Survey organization and financing

Implementing agency:
National TB and Leprosy Control Programme

Finance	Amount (US$)
Government of Zambia	1 639 303
USAID	2 000 000
US CDC	1 737 264
Total budget	5 376 567

Data sources

- National tuberculosis prevalence survey 2013–2014 technical report. Zambia: Ministry of Health, Government of the Republic of Zambia; 2015.
- Kapata N, Chanda-Kapata P, Ngosa W, Metitiri M, Klinkenberg E, Kalisvaart N et al. The prevalence of tuberculosis in Zambia: Results from the first national TB prevalence survey, 2013–2014. PLoS One. 2016;11(1):e0146392.

[a] The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Survey design and methodology

Sampling design	
Sampling frame	Whole country
Sampling design	Multistage cluster sampling using PPS
Strata	Urban/rural
Sampling unit	Province/district/ward/census supervisory area
Sample size assumptions	
• Smear-positive prevalence	199 per 100 000 (≥15 years)
• Precision	0.25
• Design effect	1.5
• *k*	0.6
• Response rate	85%
• Sample size (estimated)	54 400
Number of clusters	66
Cluster size	825
Eligibility criteria	
• Age	≥15 years
• Residency	Slept in the household 24 hours prior to the census

Screening criteria	
Interview[a]	Cough ≥2 weeks or fever ≥2 weeks or chest pain ≥2 weeks
Chest X-ray[b]	Any lung abnormality
Other	N/A

[a] An in-depth interview about other TB symptoms and health-care seeking behaviour was undertaken only for those who screened positive.
[b] Direct digital radiography (portable).

Laboratory methodology	
Smear	Two samples (spot, morning): concentrated preparation, FM (auramine stain)
Culture	Two samples (spot, morning): concentrated preparation, MGIT media
Identification of MTB	Capilia
TB drug susceptibility test	Not done
Xpert® MTB/RIF	Done[a]
HIV test	Done for participants who consented

[a] Xpert MTB/RIF was conducted for all smear-positive, some smear-negative with culture contaminated, or smear-negative culture indeterminate but chest X-ray suggestive of TB.

Analysis and reporting

Field data collection	Electronic
Database	Microsoft® Access
Method of analysis	MI+IPW
Results first published in a report/paper	September 2015
Official dissemination event	January 2016

Key survey results

Prevalence[a]	Smear-positive TB		Bacteriologically confirmed TB	
	Number per 100 000 population	95% CI	Number per 100 000 population	95% CI
Total	319	232–406	638	502–774
Male	445	309–580	833	641–1 024
Female	221	139–303	487	353–621
15–24 years	154	71–236	285	157–412
25–34 years	422	245–599	664	337–891
35–44 years	496	315–676	947	660–1 237
45–54 years	323	139–507	926	611–1 240
55–64 years	333	149–517	708	401–1 013
≥65 years	288	91–485	876	535–1 218
Urban	583	391–775	993	714–1 273
Rural	187	130–243	460	344–577

[a] Age ≥15 years unless otherwise specified.

	Design effect	*k*
Smear-positive TB	2.3	0.8
Bacteriologically confirmed TB	3.3	0.7

Other sputum results	Number	%
Total smear-positive participants	356	–
Smear-positive participants without MTB confirmation[a]	221	62
Isolates with MDR-TB detected	N/A	N/A

[a] This includes culture with no evidence of MTB (i.e. culture-negative, NTM, contaminated, N/A) and Xpert-negative.

Health-care seeking behaviour among participants who were symptom-screen positive	Number	%
Participants who were symptom-screen positive[a]	4 453	–
Location of care sought		
• Consulted medical facility	1 829	41
Public facility	*1 680*	*92*
Private facility	*75*	*4.1*
Other facility	*74*	*4.0*
• Pharmacy	16	0.4
• Traditional centre, Faith based organization	1	0.02
Self-treated	N/A	N/A
No action taken	2 534	57
Unknown	73	1.6

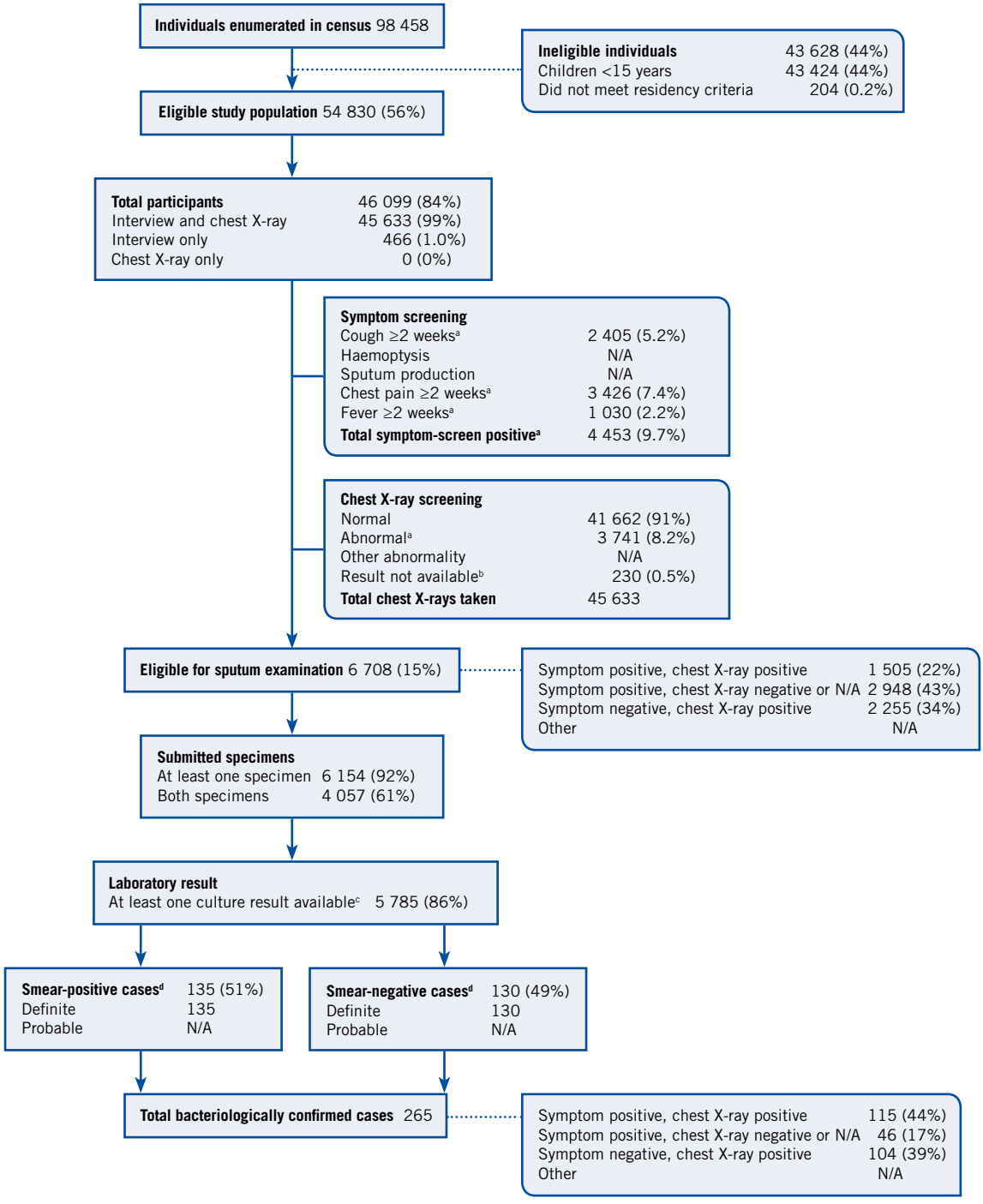
[a] Cough ≥2 weeks or fever ≥2 weeks or chest pain ≥2 weeks.

Survey participants currently on TB treatment	Number	%
Total participants currently on TB treatment[a]	114	–
• Treated in the public sector	61	54
• Treated in the private sector	1	0.9
• Treated in unknown sector	52	45
Bacteriologically confirmed TB cases detected by the survey who were currently on TB treatment	7	2.6

[a] Data were available only for participants who were eligible for sputum submission.

Survey flow: census to final outcomes

Field operations: August 2013 to July 2014



[a] Eligible for sputum collection.
[b] Results were not interpretable (19), missing (136), or not available for other non-specified reasons (75). Among 230 participants, 19 who had uninterpretable chest X-ray images were requested to submit sputum samples.
[c] Cultures that were either contaminated and/or missing without a definitive result (i.e. MTB, NTM, negative) were excluded.
[d] Definite: MTB confirmed by culture and/or Xpert. Probable: no definition.

Fig. 1: Participation rate by age and sex

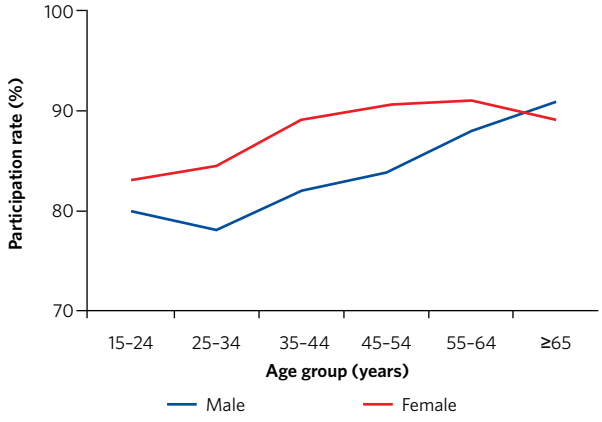


Fig. 2: TB prevalence per 100 000 population by age

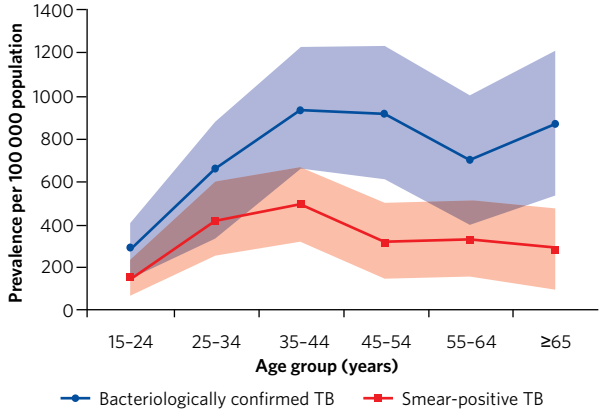


Fig. 3: Estimated number of bacteriologically confirmed TB cases and prevalence per 100 000 population, by age[a]

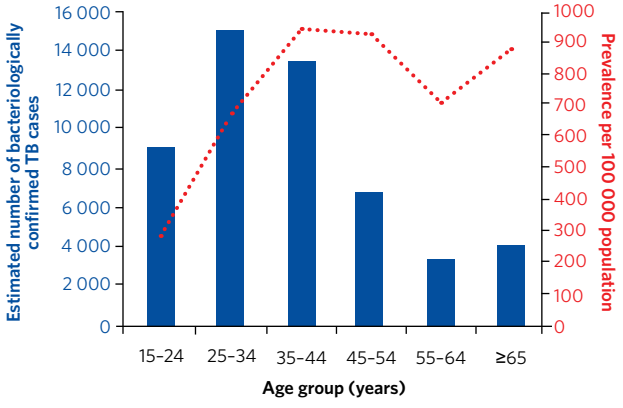


Fig. 4: Cluster variation of the number of bacteriologically confirmed TB cases[b]

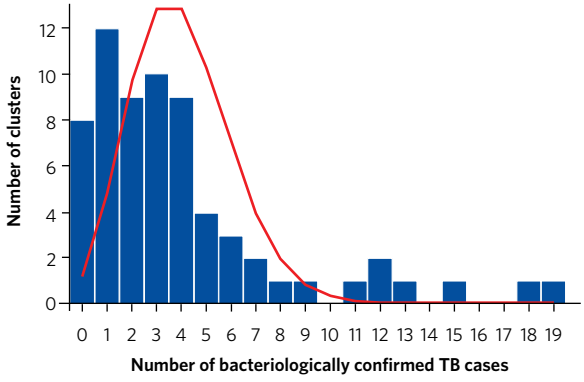
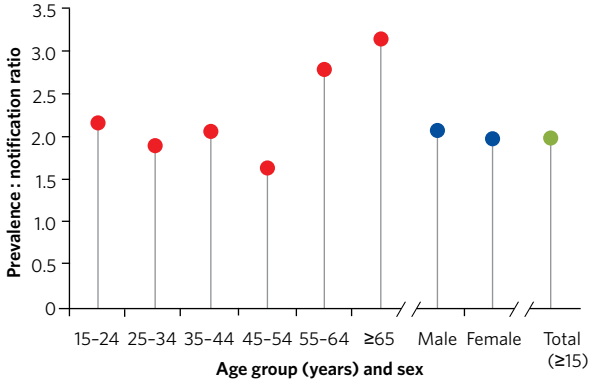
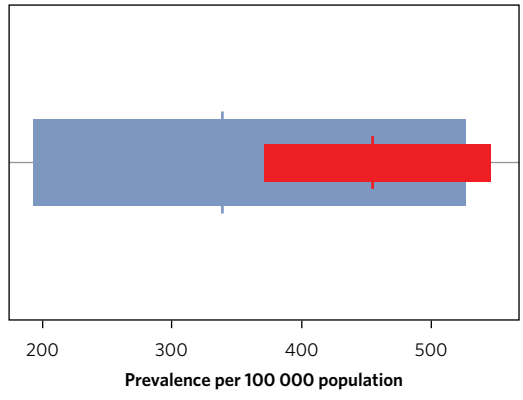


Fig. 5: Ratio of smear-positive TB prevalence to notifications by age and by sex[c]



Data source: smear-positive pulmonary TB notified cases from NTP data (2014) (including cases diagnosed by Xpert MTB/RIF)

Fig. 6: Estimates of TB prevalence (all ages, all forms of TB) before (in blue) and after (in red) the national TB prevalence survey[d]



[a] The estimated number of bacteriologically confirmed TB cases is the product of age-specific prevalence and population estimates from the UN Population Division (2015 revision).

[b] The data suggested that the distribution of cases by cluster (blue bars) was significantly different from the theoretical distribution (red line) (mean 4.02, variance 17.8, $p<0.05$). The theoretical distribution assumes cases are distributed at random i.e. no clustering effect.

[c] Notification rates were estimated using smear-positive pulmonary TB notifications (2014) obtained from the NTP (including TB cases diagnosed by Xpert MTB/RIF), and population estimates from the UN Population Division (2015 revision).

[d] The blue bar denotes the best estimate of prevalence and its range that was indirectly derived from the estimate of incidence previously published by WHO, adjusted to the year of the prevalence survey based on previously published trends in incidence.

Background

Zambia, a landlocked country in Southern Africa, had a population of 16 million in 2014. Its average gross national income (GNI) per person was US$ 1740, making it a lower-middle-income country *(1)*. It was one of the top 30 high TB burden countries (HBCs) defined by WHO for the period 2016–2020. The prevalence of HIV in the general population aged 15–49 years was 13% (95% confidence interval [CI]: 13–14%) in 2014 *(2)*, and it was estimated that 61% (95% CI: 55–66%) of TB patients were coinfected with HIV *(3)*.

Zambia's National TB Control Programme (NTP) was established in 1964. It operated as a vertical programme in the health sector until 1993, when it was combined with the AIDS and sexually transmitted infections (STI) programme. After initiating implementation of the DOTS strategy in 1995, the NTP moved from hospitals to community-based programmes. However, during a period of health sector decentralization in the late 1990s, the national programme almost collapsed. There was a loss of structure, staff training and guidance at all levels, and interruptions to drug supplies were frequent. The NTP was reorganized in 2000 and subsequently strengthened *(4)*.

The HIV epidemic led to a dramatic increase in the TB notification rate throughout the 1990s, from 216 cases per 100 000 population in 1990 to 524 cases per 100 000 population in 2004. Subsequently, notification rates started to fall, to a level of 365 cases per 100 000 population in 2010. The highest notification rate was in Lusaka (the capital city), followed by areas in the Copperbelt and southern provinces (especially along the railway lines). WHO estimated that, in 2012, TB incidence was 427 (95% CI: 385–470) per 100 000 population, prevalence was 388 (95% CI: 197–642) per 100 000 population and the case detection rate (notifications of new cases divided by estimated incidence) was 68% (95% CI: 62–75%) *(5)*.

In 2012, there was no direct measurement of TB disease burden in Zambia, and routine notification data were the main source of information to assess progress towards TB targets. However, the gap between notifications and incidence due to underreporting and underdiagnosis of cases was difficult to estimate. It was also recognized that the HIV epidemic had increased the level of TB disease burden, and that this might have been exacerbated by growing levels of poverty. For these reasons, it was decided to carry out Zambia's first national TB prevalence survey, to obtain a direct measure of TB disease burden in the community, inform policy-makers and provide baseline data for future evaluation of programmatic achievements.

Survey preparations began in 2008, but funding was delayed when the Global Fund to Fight AIDS, Tuberculosis and Malaria suspended all funding to Zambia, with the exception of essential activities. Survey preparations resumed in 2012, in close collaboration with the KNCV Tuberculosis Foundation, following agreement that the US Government would provide financial support for the survey through the TB CARE project. The survey started in August 2013 and was completed in July 2014 *(6–9)*.

Key methods and results

There were 66 survey clusters in two strata (urban and rural), with a target cluster size of 825 individuals. A total of 98 458 individuals in 17 485 households were enumerated in the survey census, of which 54 830 (56%) were eligible and invited to participate. All 46 099 participants (84% of the total eligible) were screened according to the 2011 algorithm recommended by WHO; that is, chest X-ray and a symptom screening interview *(10)*. A total of 6708 people (15% of participants) were eligible for sputum examination, of whom 6154 (92%) submitted at least one sputum specimen and 4057 (61%) submitted two sputum specimens.

A total of 265 bacteriologically confirmed pulmonary TB cases were identified, including 135 cases of smear-positive TB. The estimated prevalence of smear-positive TB was 319 (95% CI: 232–406) per 100 000 population among those aged 15 years or more, and for bacteriologically confirmed TB it was 638 (95% CI: 502–774) per 100 000 population. When extrapolated to all forms of TB and to all ages, prevalence was 455 (95% CI: 366–544) per

Photo credit: Zambia NTP


Photo credit: Julia Ershova

100 000 population. The prevalence of bacteriologically confirmed TB was higher in urban areas than in rural areas (993 versus 460 per 100 000 population).

Other key results were:

- the male to female ratio was 2.0 for smear-positive TB and 1.7 for bacteriologically confirmed TB;
- prevalence per 100 000 population increased with age, up to the 35–44 years age group, and was consistently high above 45 years; however, the absolute number of TB cases was relatively high in the younger age groups;
- of the bacteriologically confirmed TB cases, 61% were symptom-screen positive, and of the smear-positive cases, 67% were symptom-screen positive;
- for smear-positive pulmonary TB, the ratio of prevalence to notifications (P:N ratio) was 2.0 overall, but varied from 1.6 in those aged 45–54 years to 3.2 in the 65 years and over age group, and was slightly higher for men than for women (2.1 versus 2.0); and
- of the bacteriologically confirmed TB cases, 14% of cases had no previous history of anti-TB treatment and only 2.6% were on anti-TB treatment at the time of the survey.

Data on health-care seeking behaviour among survey TB cases were not available.

The risk of TB was also analysed in terms of socio-economic status using wealth tertiles. In rural areas, the risk of TB was higher among the highest wealth tertile than among the lowest and middle tertiles. The opposite was true in urban areas, where the lowest and middle wealth tertiles had a prevalence that was twice as high as that found in the highest wealth tertile.

HIV pre-test counselling was conducted for 44 761 (97%) of the 46 099 survey participants. Of those who underwent pre-test counselling, 30 605 (68%) consented to be tested, of whom 30 584 (99.9%) were tested. Of those tested, 2063 (6.7%) were HIV-positive, 28 431 were HIV-negative and 90 had an indeterminate result. Of 265 bacteriologically confirmed TB cases, 134 were tested for HIV and 36 (27%) were HIV-positive.

HIV prevalence was four times higher among individuals with bacteriologically confirmed TB (27% [95% CI: 17–36%]) than among those without (6.5% [95% CI: 5.4–7.5%]). The prevalence of both smear-positive and bacteriologically confirmed pulmonary TB among HIV-positive people was more than four times higher than among HIV-negative people. However, there were still more TB cases among HIV-negative people, highlighting the high burden of TB at community level irrespective of the HIV epidemic.

Table 1: Bacteriologically confirmed TB prevalence by wealth index

Wealth index[a]	Bacteriologically confirmed TB	
	Prevalence per 100 000 population	95% CI
Rural		
Highest	610	423–797
Middle	364	224–505
Lowest	483	294–672
Urban		
Highest	603	386–820
Middle	1251	911–1592
Lowest	1208	750–1666

[a] Please refer to the official report for an explanation of how the index was derived.

Table 2: Pulmonary TB prevalence by HIV status

HIV status	Prevalence per 100 000 population	95% CI
	Smear-positive TB	
HIV-positive	887	424–1350
HIV-negative	182	129–236
	Bacteriologically confirmed TB	
HIV-positive	1726	1029–2423
HIV-negative	387	294–480

Implications of results

The survey showed that the prevalence of bacteriologically confirmed TB was higher than that estimated before the survey. In particular, the burden of TB among HIV-negative people had been underestimated.

The survey also showed that many TB cases were likely to be missed (or detected late) when services rely on passive case finding alone. Of the symptomatic cases found during the survey, 97% (258/265) were not yet on treatment. The fact that half of the symptomatic cases not on treatment had already sought care for their symptoms also demonstrated a need to strengthen health services; for example, by raising health worker awareness of TB symptoms and by making diagnostics more widely available.

Just over half of survey cases (51%; 134/265) were in those aged 25–44 years, with prevalence peaking in those aged 35–44 years. The economic consequences of this disease burden warrant further investigation, especially in the context of the End TB Strategy milestone for 2020, that no TB-affected households face catastrophic costs as a result of TB disease *(11)*.

The finding that 49% (130/265) of survey cases were smear-negative and that 39% of survey cases did not meet symptom screening criteria (despite using a wider range of screening symptoms than most other surveys) indicated a need to improve capacity to diagnose cases of culture-positive but smear-negative TB and to carefully assess the use of chest X-ray during the diagnostic process (particularly in the context of active case finding).

Just over one third of the survey cases (34%; 89/258) that had not been detected before the survey were in the Copperbelt province, highlighting that coverage of diagnostic and treatment services needed to be improved in this particular "hotspot". The socio-demographic disparities evident in the survey results also showed a need for more targeted efforts for certain population groups: men, the urban poor and those living in densely populated farming areas.

The large number of symptomatic participants with nontuberculous mycobacteria (NTM) showed that NTM should be better characterized in Zambia, to enable the appropriate management of clinically relevant cases of NTM. Of the 6123 culture results available, 923 (15%) were NTM. Just over half (478/923) of individuals with a positive result had an abnormal chest X-ray, and 71% (655/923) were symptomatic (i.e. had either cough, chest pain or fever).

The fact that a large proportion (62%, 221/356) of participants with a smear-positive result were found not to have *Mycobacterium tuberculosis* (MTB) showed

Photo credit: Julia Ershova

that a smear-positive result alone may not be adequate for the detection of TB cases, especially in the context of intensified case finding or active case detection strategies.

Major successes, challenges and lessons learned

Field operations were implemented within the expected timeframe with minimal interruptions and with a high participation rate overall (84%). One of the reasons for this was that the hard-to-reach rural areas were covered in the early part of the survey, during the drier parts of the year. The participation rate was lower (~49%) in the early stages of the survey (a common finding in surveys); this lower rate was also linked to the long distances to be travelled in the more remote and sparsely populated parts of the country. The survey teams encountered some myths and misconceptions among community members about TB, which had some impact on the overall participation rate. Measures implemented to improve participation rates included use of in-cluster community sensitization, involvement of the local political and traditional leadership, and ongoing community education using mainstream television and community radio stations to disseminate the objectives and procedures of the survey.

The 7-day period used for cluster operations was manageable, but sometimes required field staff to work long hours, depending on the flow of participants. For example, in rural areas, participants tended to report to the cluster site later in the day, meaning that the teams had to work late into the night to clear the queue of participants, which in turn meant that transport had to be provided to those coming from locations far from the main survey camp site. This was a valuable lesson for future surveys, because without providing such support the participation rate might have been lower.

The survey in Zambia was one of the first surveys to use digitalized data management from the household census through to central X-ray reading and laboratory management. It became the first national TB prevalence survey that used hand-held size apparatus to collect data in field conditions. There were initial problems with data-capture devices (e.g. pairing up of barcode scanners, short battery life and fragile barcodes), but these were resolved during the early stages of the survey. The efficiency of the fully digitalized data management system, use of direct digital chest X-ray units and good overall organization meant that the time between completion of field operations and dissemination of results and final publication was relatively short (14 months).

References

1. The World Bank (https://data.worldbank.org/country, accessed April 2017).
2. UNAIDS (http://aidsinfo.unaids.org/, accessed April 2017).
3. World Health Organization. Global Tuberculosis Database. 2017. (http://www.who.int/tb/country/en/, accessed April 2017).
4. The National Tuberculosis and Leprosy Programme, TB manual (3rd ed). Zambia: Ministry of Health;(http://www.who.int/hiv/pub/guidelines/zambia_tb.pdf?ua=1, accessed July 2017).
5. World Health Organization. Global tuberculosis report 2013. Geneva: WHO; 2013 (http://apps.who.int/iris/bitstream/10665/91355/1/9789241564656_eng.pdf?ua=1, accessed January 2018).
6. Chanda-Kapata P, Kapata N, Klinkenberg E, Mulenga L, Tembo M, Katemangwe P et al. Non-tuberculous mycobacteria (NTM) in Zambia: prevalence, clinical, radiological and microbiological characteristics. BMC Infect Dis. 2015;15:500 (https://www.ncbi.nlm.nih.gov/pubmed/26545357, accessed May 2017).
7. Chanda-Kapata P, Kapata N, Klinkenberg E, William N, Mazyanga L, Musukwa K et al. The adult prevalence of HIV in Zambia: results from a population based mobile testing survey conducted in 2013–2014. AIDS Res Ther. 2016;13:4 (https://www.ncbi.nlm.nih.gov/pubmed/26793264, accessed May 2017).
8. Kapata N, Chanda-Kapata P, Ngosa W, Metitiri M, Klinkenberg E, Kalisvaart N et al. The prevalence of tuberculosis in Zambia: Results from the first national TB prevalence survey, 2013–2014. PLOS ONE. 2016;11(1):e0146392 (https://www.ncbi.nlm.nih.gov/pubmed/26771588, accessed May 2017).
9. National tuberculosis prevalence survey 2013–2014 technical report. Zambia: Ministry of Health, Government of the Republic of Zambia; 2015.
10. World Health Organization. Tuberculosis prevalence surveys: a handbook (WHO/HTM/TB/2010.17). Geneva: WHO; 2011 (https://apps.who.int/iris/bitstream/handle/10665/44481/9789241548168_eng.pdf, accessed August 2017).
11. World Health Organization. The End TB Strategy. Geneva, WHO; 2014 (http://www.who.int/tb/strategy/en/, accessed July 2017).

ZIMBABWE

2014

Summary statistics

Participation rate	78%
Bacteriologically confirmed TB (≥15 years)	
• Prevalence per 100 000 population	344
• Male:female ratio	1.4
Prevalence:notification ratio (Bacteriologically confirmed TB, ≥15 years)	2.5

Surveyed clusters (N=75)[a]

Key people

Name	Role	Organization
Charles Sandy	Principal investigator	National Tuberculosis Control Programme (NTP)
Junior Mutsvangwa	Co-principal investigator	Biomedical Research and Training Institute
Ronnie Matambo	Survey coordinator	Biomedical Research and Training Institute
Dumisani Ndlovu	Radiology coordinator	Biomedical Research and Training Institute
Ellen Munemo	Laboratory manager	National Microbiology Reference Laboratory
Eve Marima	Data manager	The Zimbabwe National Statistics Agency (ZIMSTAT)
Hebert Mutunzi	Technical working group member, laboratory	NTP
Mkhokeli Ngwenya	Technical working group member, survey design	NTP
Joconiah Chirenda	Technical working group member, survey design	University of Zimbabwe, College of Health Sciences
Nicholas Siziba	Technical working group member, M&E	NTP
Peter Shiri	Technical working group member, M&E	NTP
Martin Mapfurira	NTP officer	NTP
Patrick Hazangwe	Technical assistance	WHO Zimbabwe
Wilfred Nkhoma	Technical assistance (survey advisor)	WHO Regional Office for Africa (AFRO)
Ikushi Onozaki	Technical assistance (survey advisor)	WHO headquarters
Marina Tadolini	Technical assistance (survey advisor)	Consultant, Italy
Fasil Tsegaye	Technical assistance (survey advisor)	International Union Against Tuberculosis and Lung Disease
Kunihiko Ito	Technical assistance (radiology)	Research Institute of Tuberculosis/Japan Anti-Tuberculosis Association (RIT/JATA)
Mourad Gumusboga	Technical assistance (laboratory advisor)	Supranational Reference Laboratory, Antwerp Belgium
Hazim Timimi	Technical assistance (data management)	WHO headquarters
Norio Yamada	Technical assistance (analysis)	RIT/JATA
Kosuke Okada	Technical assistance (reporting)	RIT/JATA

Survey organization and financing

Implementing agency:
The National Tuberculosis Control Programme/Biomedical Research and Training Institute

Finance	Amount (US$)
The Global Fund	3 464 437
Total budget	3 464 437

Data sources

- Republic of Zimbabwe – Ministry of Health and Child Care. Report of the First National Population-based Tuberculosis Prevalence Survey. Republic of Zimbabwe, Ministry of Health and Child Care, August 2015.
- Survey dataset.

[a] The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Survey design and methodology

Sampling design	
Sampling frame	Whole country
Sampling design	Multistage cluster sampling using PPS
Strata	Urban/rural
Sampling unit	Ward/enumeration area
Sample size assumptions	
• Smear-positive prevalence	190 per 100 000 (≥15 years)
• Precision	0.25
• Design effect	1.2
• *k*	0.4
• Response rate	85%
• Sample size (estimated)	44 951
Number of clusters	75[a]
Cluster size	600
Eligibility criteria	
• Age	≥15 years
• Residency	Permanent residents who had slept at least one night out of the last 14 days on the day of census, or non-residents who had slept in the household for 14 days or more before the day of the census

[a] Two clusters (Macheke and Chiredzi) were replaced with other communities within the same district (same strata), due to difficulties in reaching the cluster site following severe rainfall as well as community apathy after long delays due to a breakdown of the mobile X-ray unit.

Screening criteria	
Interview[a]	Cough of any duration, current night sweats, haemoptysis at any time in the past 12 months prior to study
Chest X-ray[b]	Any lung abnormality
Other	Chest X-ray exempted

[a] An in-depth interview about health-care seeking behaviour was done only for those who screened positive.
[b] Chest X-ray truck, mobile digital radiography.

Laboratory methodology	
Smear	Two samples (spot, morning): concentrated preparation, FM (LED, auramine stain)
Culture	Two samples (spot, morning): concentrated preparation, LJ media and MGIT media (for all)
Identification of MTB	MPT64 rapid test
TB drug susceptibility test	Done using Xpert MTB/RIF (all smear-positive and culture-positive specimens)
Xpert® MTB/RIF	All smear-positive specimens (and all culture-positive specimens for rifampicin resistance testing)
HIV test	Done at referral centre for all bacteriologically confirmed TB cases

Analysis and reporting

Field data collection	Paper
Database	CSPro
Method of analysis	MI+IPW
Results first published in a report/paper	August 2015
Official dissemination event	March 2017

Key survey results

Prevalence[a]	Smear-positive TB		Bacteriologically confirmed TB	
	Number per 100 000 population	95% CI	Number per 100 000 population	95% CI
Total	82	47–118	344	268–420
Male	103	43–163	413	303–523
Female	65	27–104	288	189–386
15–24 years	52	21–131	129	68–245
25–34 years	138	70–274	373	255–546
35–44 years	85	34–215	546	371–804
45–54 years	75	23–248	310	168–570
55–64 years	35	4.5–277	490	276–869
≥65 years	47	6.6–341	547	310–962
Urban	116	38–193	355	228–482
Rural	64	36–114	337	243–431

[a] Age ≥15 years unless otherwise specified.

	Design effect	*k*
Smear-positive TB	0.97	N/A[a]
Bacteriologically confirmed TB	1.1	0.3

[a] *k* could not be calculated for smear-positive TB because the design effect was less than one.

Other sputum results	Number	%
Total smear-positive participants	206	–
Smear-positive participants without MTB confirmation[a]	183	89
Isolates with DR-TB (rifampicin) detected[b]	13	12

[a] This includes culture with no evidence of MTB (i.e. culture-negative, NTM, contaminated, N/A) and Xpert-negative.
[b] Xpert MTB/RIF was done only to test for rifampicin resistance among 107 bacteriologically confirmed cases.

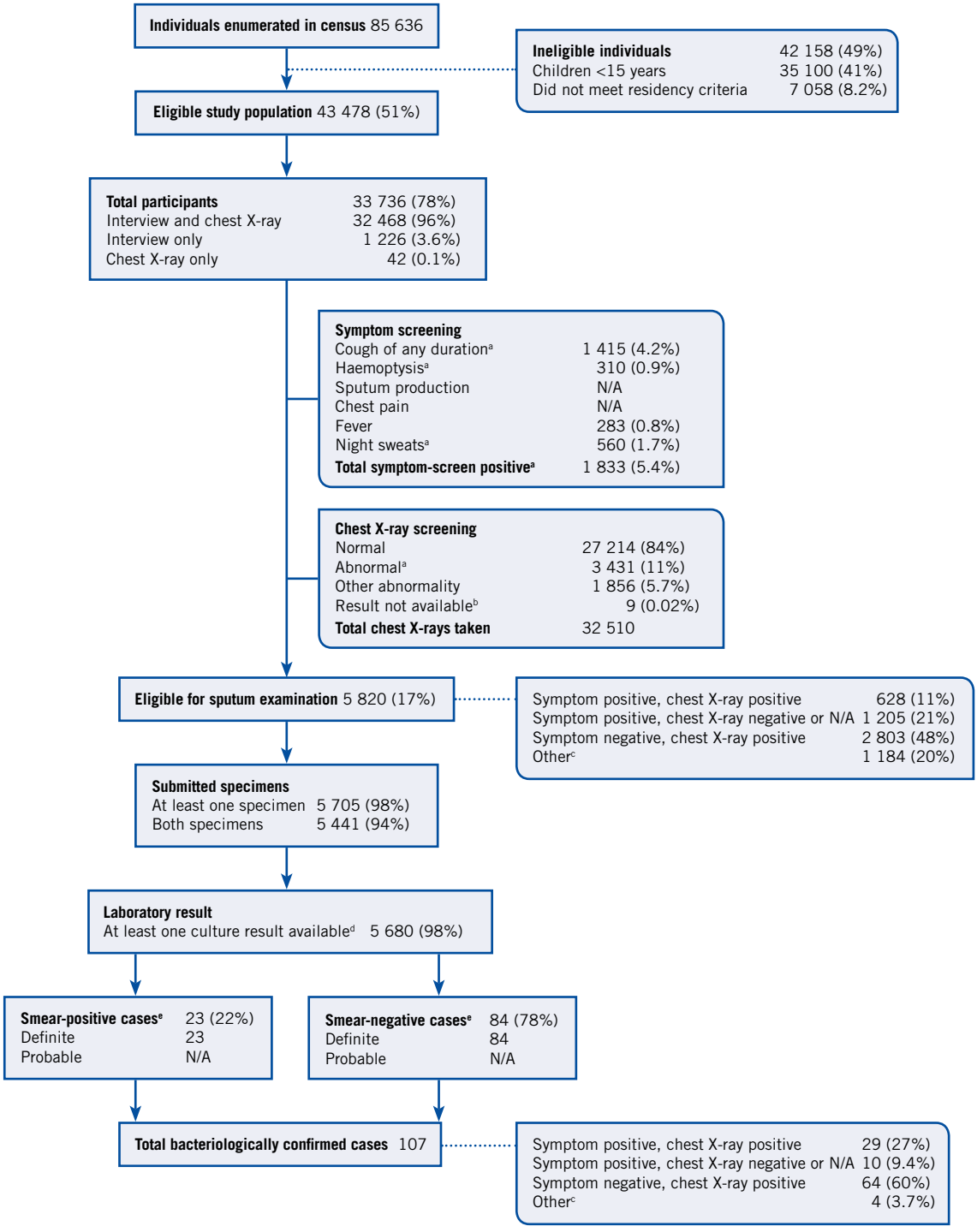
Health-care seeking behaviour among participants who were symptom-screen positive	Number	%
Participants who were symptom-screen positive[a]	1 833	–
Location of care sought[b]	486	26
• Consulted medical facility		
Public facility	*438*	–
Private facility	*45*	–
• Pharmacy	17	–
• Traditional centre, faith healer	13	–
Self-treated	N/A	N/A
No action taken	1 130	62
Unknown	217	12

[a] Cough (any duration), current night sweats, and/or haemoptysis at any time in the last 12 months prior to the survey.
[b] Participants could answer more than one category.

Survey participants currently on TB treatment	Number	%
Total participants currently on TB treatment	84	–
• Treated in the public sector	N/A	N/A
• Treated in the private sector	N/A	N/A
• Treated in other sector	N/A	N/A
Bacteriologically confirmed TB cases detected by the survey who were currently on TB treatment	2	1.9

Survey flow: census to final outcomes

Field operations: January 2014 to December 2014



[a] Eligible for sputum collection.
[b] Chest X-ray taken but results were missing.
[c] Chest X-ray exempted and symptom-screen negative.
[d] Cultures that were either contaminated and/or missing without a definitive result (i.e. MTB, NTM, negative) were excluded.
[e] Definite: MTB confirmed by culture and/or Xpert. Probable: no definition.

Fig. 1: Participation rate by age and sex

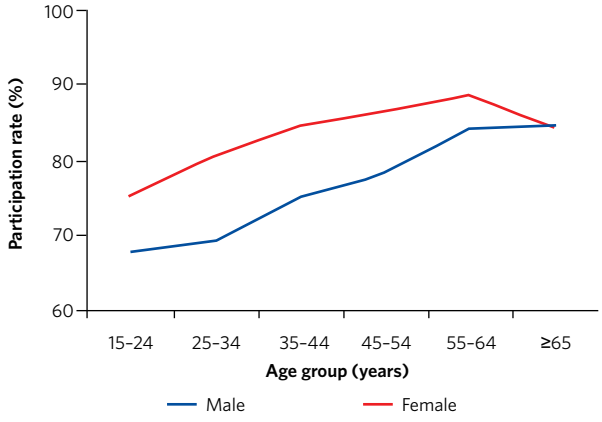


Fig. 2: TB prevalence per 100 000 population by age

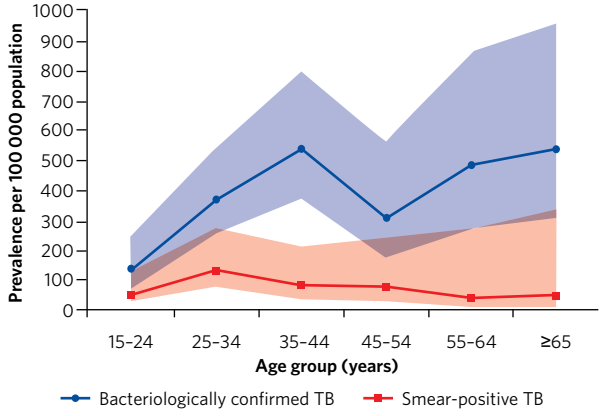


Fig. 3: Estimated number of bacteriologically confirmed TB cases and prevalence per 100 000 population, by age[a]

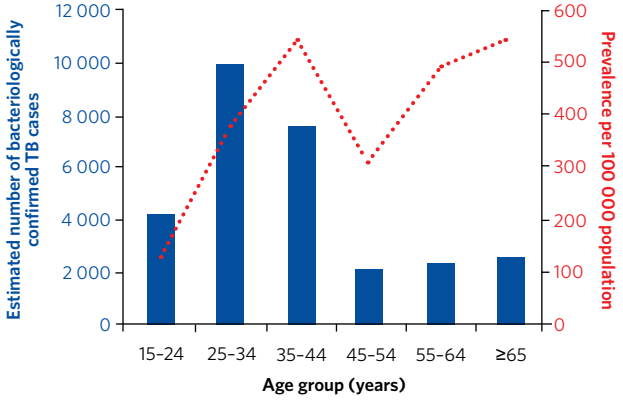


Fig. 4: Cluster variation of the number of bacteriologically confirmed TB cases[b]

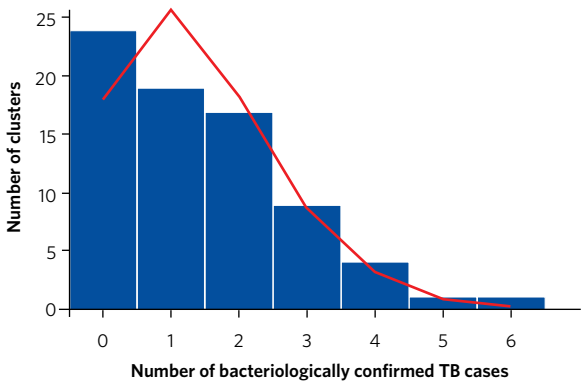


Fig. 5: Ratio of bacteriologically confirmed TB prevalence to notifications by age and by sex[c]

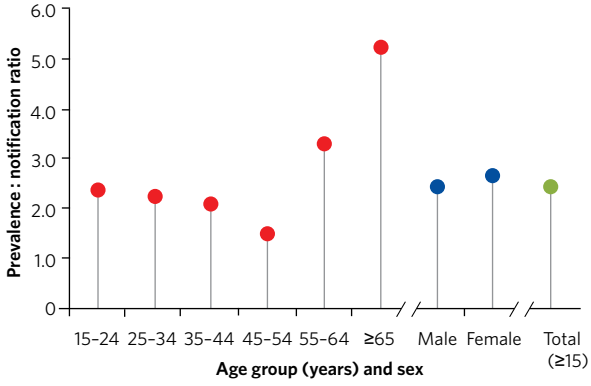
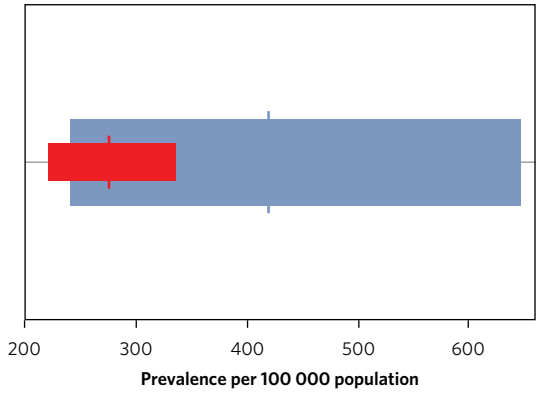


Fig. 6: Estimates of TB prevalence (all ages, all forms of TB) before (in blue) and after (in red) the national TB prevalence survey[d]



[a] The estimated number of bacteriologically confirmed TB cases is the product of age-specific prevalence and population estimates from the UN Population Division (2015 revision).

[b] The data did not suggest that the distribution of cases by cluster (blue bars) was significantly different from the theoretical distribution (red line) (mean 1.43, variance 1.90, p=0.06). The theoretical distribution assumes cases are distributed at random i.e. no clustering effect.

[c] Notification rates were estimated using bacteriologically confirmed pulmonary TB notifications (2014) obtained from the NTP, and population estimates from the UN Population Division (2015 revision).

[d] The blue bar denotes the best estimate of prevalence and its range that was indirectly derived from the estimate of incidence previously published by WHO, adjusted to the year of the prevalence survey based on previously published trends in incidence.

Background

Zimbabwe is a landlocked country in Southern Africa. In 2014, it had a population of 15 million, and a gross national income (GNI) per person of US$ 840, making it a low-income country *(1)*. It was one of the 22 high tuberculosis (TB) burden countries (HBCs) defined by WHO as a top priority for global efforts in TB control in 1998 and throughout the Millennium Development Goal (MDG) era (2000–2015), and one of the top 30 HBCs defined by WHO for the period 2016–2020. The prevalence of HIV in the general population aged 15–49 years was 15% (95% confidence interval [CI]: 14–16%) in 2014 *(2)*, and it was estimated that 69% (95% CI: 64–74%) of TB patients were coinfected with HIV *(3)*.

Zimbabwe's National TB Programme (NTP) was established in the late 1960s *(4)*. The WHO-recommended DOTS strategy *(5,6)* was adopted in 1996 and nationwide coverage was achieved in 1998 *(7,8)*. In 2014, there were 220 functional TB diagnostic centres within the public health system, and TB diagnosis and treatment was provided free of charge within the public health sector.

The case notification rate declined from 2004, reaching a low of 302 per 100 000 population in 2007, probably influenced by health-system challenges in the context of an economic recession. With improved TB financing starting from 2008, case notifications increased, likely reflecting a mixture of better access to services and improved disease surveillance. TB notifications started to decline again from 2011 (332 per 100 000 population). In 2013, before the national TB prevalence survey, the TB prevalence was estimated as 409 (95% CI: 235–630) per 100 000 population; TB incidence was estimated at 552 (95% CI: 474–643) per 100 000 population; and the case detection rate (notifications of new cases divided by estimated incidence) was estimated at 42% (95% CI: 36–49) *(7)*. However, these estimates were not informed by any direct measurement of disease burden.

The NTP initiated preparations for a national TB prevalence survey in 2012, with financing from the Global Fund to Fight AIDS, Tuberculosis and Malaria. The objective was to obtain a direct measurement of the burden of TB disease, and better quantification of the gap between this burden and case notifications. The survey started in January 2014 and was completed in December 2014 *(8)*.

Key methods and results

There were 75 survey clusters in two strata (urban and rural), with a target cluster size of 600 individuals. A total of 85 636 individuals from 19 629 households were enumerated in the survey census, of whom 43 478 (51%) were eligible and invited to participate. Of these, 33 736 (78%) participated and were screened according to the 2011 algorithm recommended by WHO; that is, using chest X-ray and a symptom screening interview *(9)*. A total of 5820 people (17% of participants) were eligible for sputum examination, of whom 5705 (98%) submitted at least one sputum specimen and 5441 (94%) submitted two sputum specimens. The Zimbabwean survey was one of only a few national surveys during the period 2009–2015 that used the mycobacteria growth indicator tube (MGIT) for culture, and in which smear-positive specimens were tested with Xpert® MTB/RIF.

A total of 107 bacteriologically confirmed pulmonary TB cases were identified, including 23 cases of smear-positive TB. Among the survey population of people aged 15 years or more, the prevalence of smear-positive TB was 82 (95% CI: 47–118) per 100 000 population, and for bacteriologically confirmed TB it was 344 (95% CI: 268–420) per 100 000 population. When extrapolated to all forms of TB and to all ages, prevalence was 275 (95% CI: 217–334) per 100 000 population. There was no significant difference between the two strata; in urban areas the prevalence of bacteriologically confirmed was 355 (95% CI: 228–482) per 100 000 population, and in rural areas it was 337 (95% CI: 243–431) per 100 000 population.

Photo credit: Charles Sandy

Other key results were:

- the male to female ratio was 1.6 for smear-positive TB and 1.4 for bacteriologically confirmed TB;
- prevalence per 100 000 population had two peaks, in those aged 35–44 years and ≥65 years; however, the absolute number of TB cases was relatively high in younger age groups;
- among bacteriologically confirmed TB cases, 36% were symptom-screen positive, and among the smear-positive cases, 61% were symptom-screen positive;
- for bacteriologically confirmed pulmonary TB, the ratio of prevalence to notifications (P:N ratio) was 2.5 overall, but varied from 1.5 in those aged 45–54 years to 5.3 in the 65 years or over age group, and was slightly lower for men than for women (2.4 versus 2.7);
- among bacteriologically confirmed TB cases, 81% had no previous history of anti-TB treatment and only 1.9% were on anti-TB treatment at the time of the survey; and
- of the 38 bacteriologically confirmed and 13 smear-positive TB survey cases that screened positive for symptoms and were not on anti-TB treatment at the time of the survey, 17 (45%) and 7 (54%), respectively, had previously sought care in a public or private health facility for their symptoms.

Although not directly part of the survey itself, the HIV status of the bacteriologically confirmed TB cases was obtained from referral centres. Of the 107 cases, 42 (39%) were HIV-positive, 41 (38%) were HIV-negative and the HIV status of the remaining 24 (22%) was unknown. The proportion of cases who were HIV-positive (39%) was higher than the proportion in the population aged 15–49 years (15%) *(2)*, but lower than in the clinical setting, where it was 60% (19 290 / 32 018), based on NTP notification of TB cases (all age groups) by HIV status in 2014.

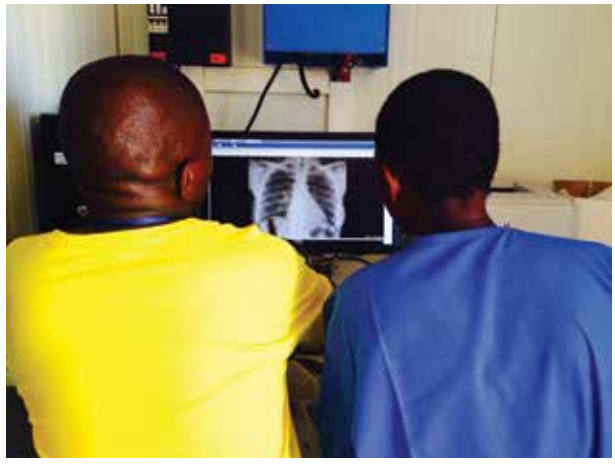


Photo credit: Marina Tadolini

Implications of results

The smear-positive prevalence of 82 per 100 000 population was much lower than the estimated prevalence used during the sample size calculation (i.e. 190 per 100 000 in the adult population).

The survey showed the challenges that the NTP faces in detecting cases. Two peaks in TB prevalence per 100 000 population were observed: one in those aged 35–44 years and the other in those aged 65 years or more. Apart from the impact of HIV, other factors contributing to the higher prevalence in the former group probably included higher rates of urbanization and mixing in congregated settings. It was recognized that the NTP should strengthen TB/HIV activities in collaboration with the national HIV/AIDS programme. The high prevalence among the elderly indicated that intensified efforts to detect cases in this subpopulation might be warranted.

Although there were as many TB cases in urban areas as in rural areas, case notification rates were lower in rural areas. Possible explanations included poorer accessibility to medical services, and challenges with diagnosis and clinical management in rural areas; for example, TB diagnosis in rural areas was more dependent on smear microscopy since not all district hospitals were equipped with X-ray machines (or more advanced diagnostic tools) at the time of the survey. Proposed solutions included referral mechanisms from health centres to district hospitals, or outreach services to the community by mobile teams.

The number of smear-negative culture-positive TB cases (84 cases) was almost four times the number of smear-positive culture-positive cases (23 cases). The former group cannot be definitively diagnosed under normal programmatic conditions if routine diagnostic services rely on smear microscopy alone. Among the smear-positive participants, "smear-positive" but "culture/Xpert-negative/non-TB" accounted for 89% (183/206). This finding highlighted major concerns about the positive predictive value of smear examination in the context of routine health services. The survey thus demonstrated that the diagnostic services available at the time of the survey (which depended mostly on smear microscopy) needed to be thoroughly reviewed. For example, there was a need to assess the role of chest X-ray for individuals with severe or chronic respiratory symptoms (or both), and to expand referral services, so that presumptive TB cases with negative smears could access care at facilities equipped with chest X-ray, culture or Xpert MTB/RIF.

Major successes, challenges and lessons learned

The survey was successfully implemented within one calendar year, and preliminary results were available within six months of completing field operations. Although the survey team in Zimbabwe did not participate in preparatory workshops organized by WHO for global focus countries, two visits to prevalence surveys in Malawi and Rwanda, and technical assistance from the Ethiopian deputy survey coordinator, greatly assisted the team's understanding of how to organize and undertake a survey. This external technical support was vital in ensuring a good-quality survey.

Despite a high contamination rate (1432 (13%) out of 11 138 samples – spot and morning – with MGIT), the performance of culture testing was high with the support of the Supranational Reference Laboratory in Antwerp, Belgium to ensure quality management of culture testing.

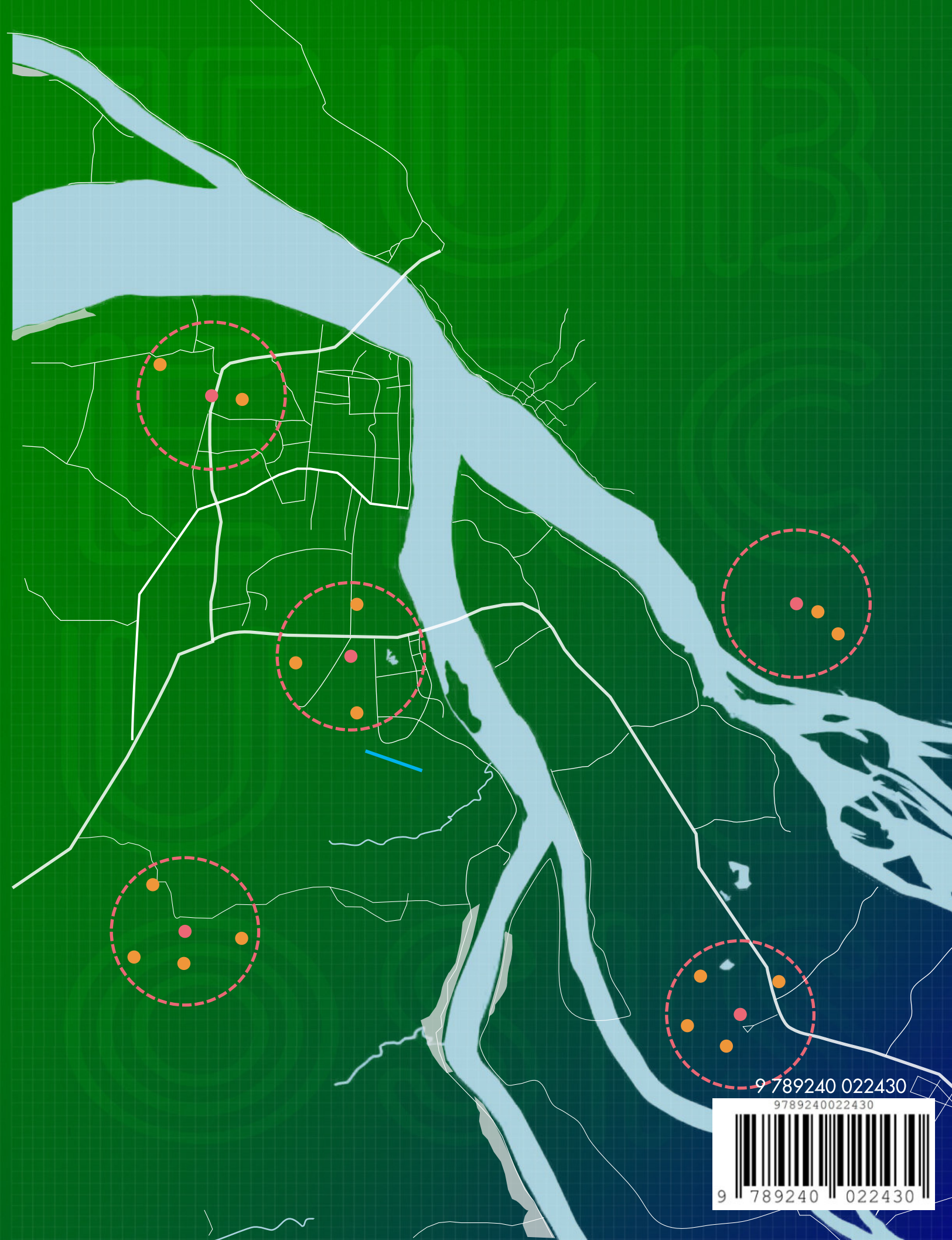
Challenges faced during the survey included:

- a participation rate that was lower-than-targeted (i.e. 78%), especially in men aged 15–54 years and women aged 15–24 years; factors that affected participation included damage to the digital chest X-ray system in a container due to poor road conditions; hot weather conditions which discouraged participation; and the presence of some religious groups who objected to any modern medical interventions;
- retrieval of X-ray images was sometimes problematic because the archiving and communication system was controlled by the X-ray unit supplier in the Netherlands; there was also a backlog in central reading of X-rays due to the limited access to the internet; these challenges were resolved through in-country technical assistance provided by the Research Institute of Tuberculosis/Japan Anti-Tuberculosis Association;
- delays in the communication of laboratory results and follow-up of confirmed TB cases resulted in delayed case management and loss to follow-up; as a result, not all confirmed TB cases were tested for HIV as planned; and
- the lack of clarity of defined roles, responsibilities and deliverables during survey preparations among the four key partners – the survey team, the laboratory, the NTP and the Zimbabwe National Statistics Agency (ZIMSTAT); survey implementation and data management were done by the Biomedical Research Institute and ZIMSTAT, respectively; however, the delayed sharing of datasets and different data management processes between the two agencies made survey management a challenge; other data management issues related to excessive delays caused by double data entry, and the lack of a barcoding system during field data collection.

Photo credit: Charles Sandy

References

1. The World Bank (https://data.worldbank.org/country, accessed April 2017).
2. UNAIDS (http://aidsinfo.unaids.org/, accessed April 2017).
3. World Health Organization. Global Tuberculosis Database. 2017. (http://www.who.int/tb/country/en/, accessed April 2017).
4. Republic of Zimbabwe – Ministry of Health and Child Welfare. National Tuberculosis Control Program, External Review Report. Republic of Zimbabwe, Ministry of Health and Child Welfare; 2011.
5. WHO Tuberculosis Programme. (1994). WHO Tuberculosis Programme: framework for effective tuberculosis control. World Health Organization. (http://www.who.int/iris/handle/10665/58717, accessed January 2018).
6. World Health Organization. Global tuberculosis programme. Global tuberculosis control report 1997. Geneva: WHO; (https://apps.who.int/iris/bitstream/handle/10665/63354/WHO_TB_97.225_(part1).pdf?sequence=1, accessed January 2018).
7. World Health Organization. Global tuberculosis report 2014. Geneva: WHO; 2014 (http://apps.who.int/iris/bitstream/10665/137094/1/9789241564809_eng.pdf?ua=1, accessed January 2018).
8. Republic of Zimbabwe – Ministry of Health and Child Care. Report of the First National Population-based Tuberculosis Prevalence Survey. Republic of Zimbabwe, Ministry of Health and Child Care, 2015.
9. World Health Organization. Tuberculosis prevalence surveys: a handbook (WHO/HTM/TB/2010.17). Geneva: WHO; 2011 (https://apps.who.int/iris/bitstream/handle/10665/44481/9789241548168_eng.pdf, accessed August 2017).



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