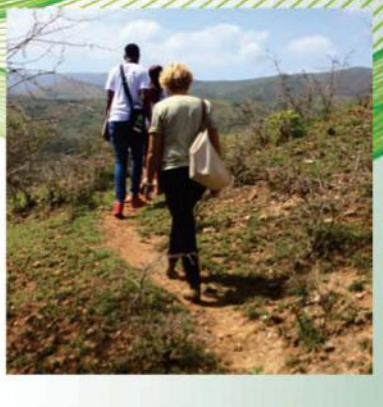
The First National TB Prevalence Survey

South Africa 2018

Short Report



FOREWORD

South Africa (SA) is one of the 30 high burden tuberculosis (TB) countries contributing 87% of the estimated incident TB cases worldwide, on its own SA accounts for 3% of cases globally. Among these 30 high burden TB countries, the country is among the 14 countries with the highest burden of TB, TB/HIV and multi-drug resistant TB (MDR-TB). The country's TB epidemic is driven by a number of factors including low socio-economic status and a high HIV co-infection burden. Additionally, delayed health-seeking behaviour among individuals with TB, as well as a high burden of undiagnosed disease in communities also drive the TB epidemic.

In August 2017 we commenced the first ever national TB prevalence survey, a survey that used Xpert MTB/RIF Ultra technology and liquid culture to test for TB among the adult population (≥ 15 years) in 110 clusters across South Africa. The Survey was conducted in line with international guidelines in accordance with the World Health Organization recommendations for conducting national TB prevalence surveys.

This report represents a milestone in the history of TB management and research. It provides a precise estimate of the TB burden as well as health seeking behaviour of TB patients and those reporting TB symptoms.

The Survey confirms the estimated high burden of TB in SA, identifies existing gaps and provides recommendations for improving TB management. We urge all stakeholders to work with the Government though the National TB Programme to ensure that the findings of this report are used to inform strategies that will have a meaningful impact towards ending TB in the country.

We take this opportunity to express our gratitude to the highly-competent team of Survey Investigators and local and international technical experts. We thank the Survey Participants, volunteers and communities that offered their time and support that enabled us to successfully conduct the Survey in the country. We thank the Global Fund to Fight AIDS, TB and Malaria, the Bill and Melinda Gates Foundation and the United States Agency for International Development for their financial support that helped make the Survey a reality.

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1. INTRODUCTION

South Africa is one of the 30 high burden tuberculosis (TB) countries that collectively contribute to 87% of the estimated incident cases worldwide, and the country accounts for 3% of cases globally. Adjusting for population size, South Africa is often ranked the highest in terms of incidence rate for TB. The high rates of TB have been fueled from the early 1990s by the HIV epidemic that negatively impacted TB control in the country. That pattern has now reversed since the aggressive scale up of antiretroviral treatment. Evidence of declines of TB incidence date back to 2008 and this has been consistent between laboratory confirmed pulmonary TB (PTB) incidence rates and notification data reported by the National Department of Health.

In the 2019 Global TB report, the HIV co-infection rate among notified TB cases in South Africa was 59%, which highlights the continued importance of HIV to the TB epidemic. What stands out however in that report is the large difference in the modelled estimates of the burden of TB disease reported by the World Health Organization (WHO) compared with the number of notified TB cases who were started on treatment. While model estimates do have limitations, the gap is still large and would impact on efforts aimed at ending TB by 2035.

Several efforts aimed at finding additional cases have been initiated. However, these have not provided much additional benefit and raised uncertainty around the accuracy of the modelled estimates which are based on reported TB notifications. Primary transmission of TB is a major driver of the epidemic and any missed cases are in fact missed opportunities with long term consequences. Thus, resolving the uncertainty of the true burden of TB disease through implementation of a national survey was needed. This would also assist in providing information about possible population groups that are being missed.

Before the current survey, South Africa had never conducted a national TB prevalence survey and one was overdue. Since 2007, 33 surveys following standardized WHO methodologies have been conducted in 31 countries. Importantly these surveys provide population level TB estimates at community level using an active case finding strategy as opposed to passive case finding that is used in routine practice. Furthermore, notification data only accounts for patients started on treatment, and previous studies have highlighted inaccuracies and under reporting within these data. The TB prevalence surveys conducted thus far in other countries have provided important insights to guide programmes to develop effective strategic plans aimed at Ending TB by 2035. The prevalence survey data from these countries have also been incorporated into the global WHO TB models to improve the accuracy of the estimates reported annually.

The aim of the First National TB Prevalence Survey was to enhance TB control in the country by informing the National TB programme (NTP) about the current epidemiological situation of TB disease and offering insight on ways in which TB control can be improved.

The objectives were:

i) To estimate the prevalence of bacteriologically confirmed pulmonary TB disease at a national level among the adult population (15 years and older) of the Republic of South Africa

ii) To identify the extent to which people with pre-existing TB or with symptoms suggestive of pulmonary TB seek care and if so from which type of facility.

2. METHODOLOGY

The survey followed the WHO handbook *(Tuberculosis prevalence surveys: a handbook)*, for national TB prevalence surveys. Population proportionate cluster sampling (PPS) was performed and individuals aged 15 years and older within the selected clusters were screened for symptoms suggestive of TB using a symptom screening questionnaire, and lung abnormalities suggestive of TB via digital chest X-ray (CXR). Those who screened positive by one or both modalities were eligible for sputum examination and were requested to submit two sputum samples, which were tested for TB using Xpert® MTB/RIF Ultra (Xpert Ultra) and liquid culture on the Bactec MGIT 960 (Becton Dickinson, USA) system. Prevalence estimates calculated accounted for sampling design and appropriate adjustments for participation and missing data.

The survey was conducted on behalf of the South African National Department of Health (NDOH) by the South African Medical Research Council (SAMRC), the Human Sciences Research Council (HSRC) and the National Institute for Communicable Diseases (NICD).

2.1 Sampling

The sample size was calculated based on historical data of smear-positive TB cases (350/100,000 adult population in 2013) and aimed for a relative precision of 20%. Sampling took into account the heterogeneous TB prevalence across the country with the nine provinces divided into three TB burden strata. Gauteng and Limpopo provinces comprised the low burden stratum; Free State, KwaZulu-Natal, and Mpumalanga provinces, the medium burden stratum; and Eastern Cape, Northern Cape, North West, and Western Cape provinces the high burden stratum. A selected fixed cluster size of 500 was used, with a resulting design effect of 1.44 (coefficient of variation k=0.5). Allowing for a participation rate of 85%, the required sample size was estimated at 54,873 individuals aged 15 years and above from 110 clusters. A stratified sampling design was applied to increase the precision and representativeness of the overall national prevalence estimate.

2.2 Inclusion and exclusion criteria

Individuals meeting the criteria below were included in the survey:

- persons aged 15 years and older
- persons who had slept in the house for at least 10 nights in the prior two weeks
- persons who could provide informed consent (assent and parental or guardian consent were required for those younger than 18 years).

Individuals meeting the criteria below were excluded:

- persons under the age of 15 years
- those living in congregate settings, including prisons, hospitals, hotels, diplomatic compounds, schools, universities, dormitories and student hostels
- persons who were visiting the area and had not slept in the house for at least 10 nights in the prior two weeks.

2.3 Survey operations

The survey activities are summarized in Figure 1. The survey implementation consisted of four main stages: (i) stakeholder engagement at various levels and starting at provincial level; (ii) a pre-survey visit to each cluster for survey preparation, social mobilization in the community, and pre-survey listing activities; (iii) the core data collection of household census (enumeration of individuals in each household), screening and specimen collection procedures and laboratory testing; and (iv) review of results to identify survey TB cases to inform the data analysis. The NTP was responsible for treatment of all cases identified.

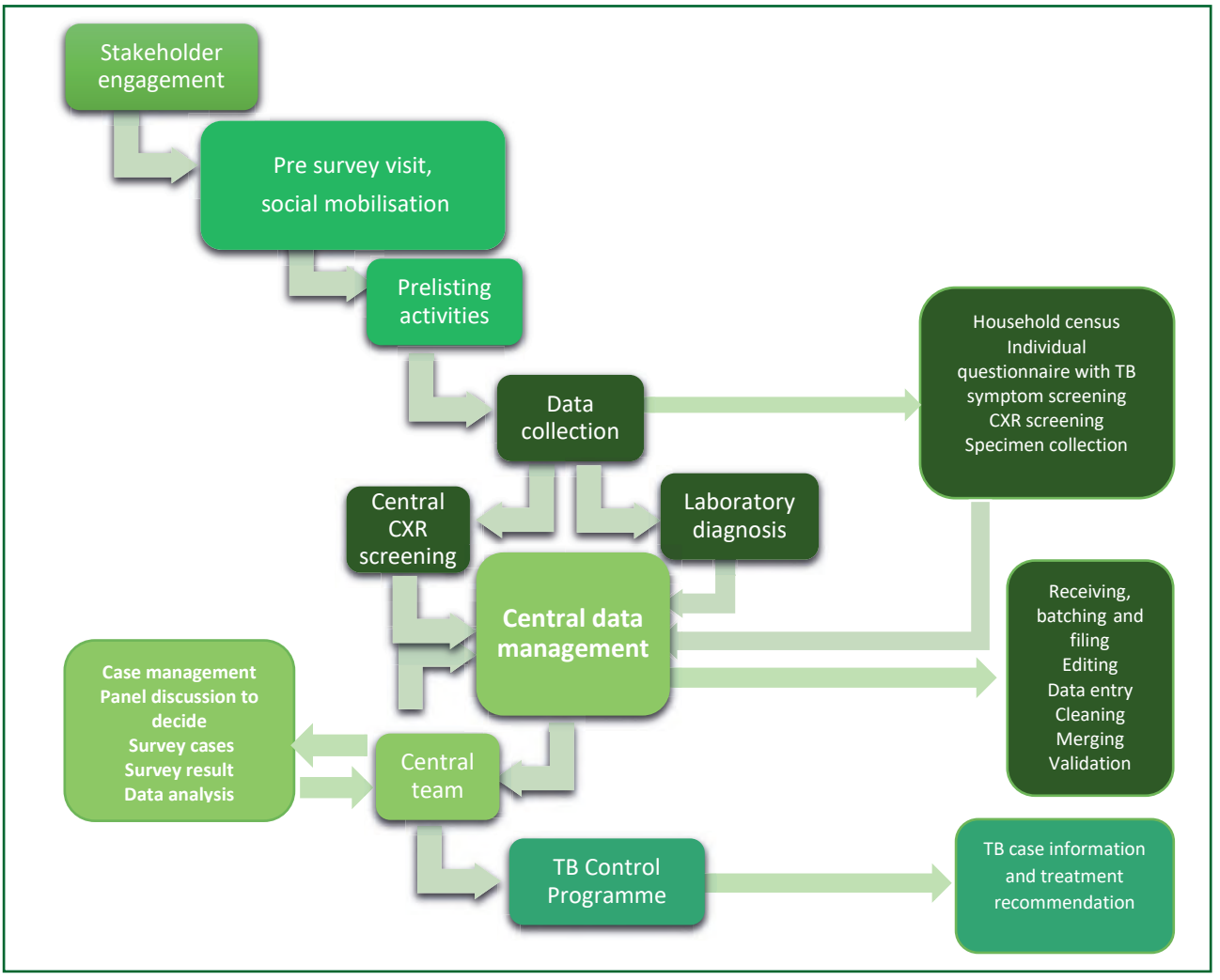


Figure 1: Survey flow diagram

In each cluster the provincial, district and local level stakeholders were consulted before work could begin. A census of the target population in the cluster was conducted prior to the formal survey operations. A household questionnaire was administered to the head of the household. The questionnaire listed all the household members and collected their demographic information. Individuals eligible to participate were provided an invitation slip to present themselves at the temporary survey site in the area. The site was capacitated to provide facilities for participant interviews, specimen collection and CXR using a mobile CXR truck (Figure 2). Participant interviews collected individual demographic information, information about current and past TB treatment, and HIV status. Participants could decline to disclose their HIV status. A symptom screen was also completed during the interview and those with any one or more of the following symptoms were eligible for sputum examination: (i) cough of any duration, (ii) unexplained weight loss, (iii) drenching night sweats, or (iv) unexplained fever. Those who reported these symptoms were asked about care seeking for the symptoms. Additionally, all participants had a CXR taken and if any abnormalities suggestive of TB were observed, they were also eligible for sputum examination. Participants who could not undergo a CXR for any reason (because they declined to consent for the CXR, or were pregnant, or had disabilities that made it impossible to take the CXR, or were bed ridden and not able to attend the screening site) were eligible for sputum examination regardless of the symptom findings. CXRs were read in the field by medical officers (MOs) who were trained to over-read so as to increase the sensitivity of screening and to avoid missing any potential TB cases.

Participants eligible for sputum examination were asked to produce two sputum samples, one on the spot and the second one an hour later. All samples were couriered under cold chain conditions and tested at the Centre for Tuberculosis (CTB) at the NICD. The first sample was tested with Xpert® MTB/RIF Ultra (Cepheid, USA) and the second underwent liquid culture on the Bactec MGIT 960 (Becton Dickinson, USA) with further speciation to confirm the presence of *Mycobacterium tuberculosis* complex in positive cultures.

Participants who were eligible for sputum exami-nation were also asked to have a dried blood spot (DBS) sample taken for HIV testing. HIV testing was performed by the Centre for HIV and STIs (CHIVSTI) at the NICD using two assays, (i) the Genscreen Ultra HIV Ag/Ab (BioRad, Hercules, California, USA), which was used as the primary screen, and (ii) the Murex HIV Ag/Ab Combination (Diasorin, Saluggia, Italy), which served as the confirmatory assay for those that tested positive on the Genscreen. All samples that were positive on the confirmatory assay were reported as positive. If the results of the two assays were discordant the screen assay was repeated. If the results were still discordant then the Genscreen HIV-1 Western Blot (BioRad) assay was performed to confirm the final test result.

2.4 Central CXR reading

All field CXRs that were reported to have abnormalities suggestive of TB by MOs in the field were also reviewed by a central radiologist. The radiologist also reread 20% of all CXRs that were reported as normal by the MOs. An external CXR reading panel also read the CXRs of participants who had Xpert Ultra positive and / or culture positive results.

2.5 Case definition

Due to concerns related to possible false-positive results from Xpert Ultra in low pre-test probability settings such as surveys, the final definition of a survey TB case aimed to be conservative but robust. The final case definition was derived following input from the WHO technical support team as well as several workshops they held on the topic. A TB case in this survey was defined as any *Mycobacterium tuberculosis* complex culture positive case irrespective of Xpert Ultra results assuming there was no cross-contamination. When the culture was not positive for *Mycobacterium tuberculosis* complex (this included negative cultures, contaminated cultures, and cases where culture was not done because there was no sample), additional survey TB cases were defined as follows: (i) Xpert Ultra results were positive (trace results were re-classified as negative), (ii) the participant did not have a history of a previous TB episode (i.e. no history of TB past or current), and (iii) the CXR findings were suggestive of active TB as confirmed by an external CXR reading panel.

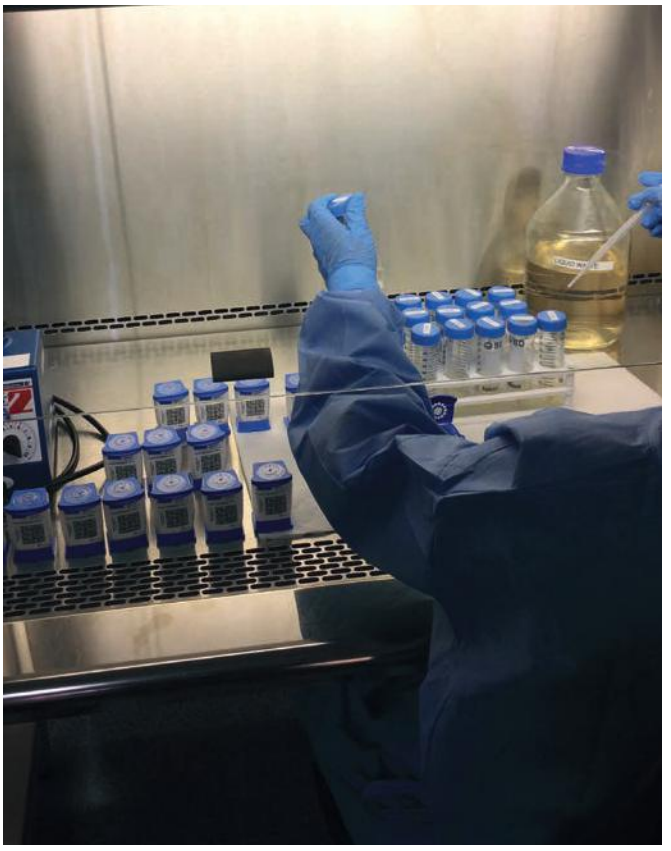
The final HIV status for this survey was determined using the DBS result where this was available, and by self-reported status where there was no DBS result. HIV status was classified as unknown where there was no self-reported status and no DBS result.

Figure 2: Survey Field team and participants: a survey site with tents and mobile X-ray equipment in a rural area.

2.6 Linking survey participants to care

All Xpert Ultra and culture positive results were sent to the TB programme through the district TB coordinator in which the cluster was located. The coordinators were responsible for ensuring that the participants with these positive results were traced and started on TB treatment.

Participants who gave a blood sample for HIV received a barcoded voucher that they presented at the clinic if they wanted their HIV results. The barcoded voucher was given to the participant at the time of DBS sample collection. When the participant presented at the clinic for HIV results, the clinic followed the national HIV testing and screening guidelines to test the participant. The clinics followed the national HIV testing and screening guidelines before release of these results to participants. Participants who were found to have acute and/or other medical concerns on screening or on CXR were referred to their local clinic for further evaluation and management.



2.7 Ethical considerations

The protocol was approved by the SAMRC research ethics committee (Reference EC001 2/2012). All participants gave informed consent for participation. Participants aged under 18 years signed an assent form and their legal guardian gave the informed consent for their participation. Participants were provided with reimbursements for their time spent on the survey. The reimbursements included food and household grocery items or mobile phone credit (i.e. airtime) to the value of R50 (approximately USD5 at the time) and were introduced from cluster 10 onwards.

2.8 Data management and analysis

All field records were captured on tablets and entered into a RedCap application specially designed for the survey. Staff were trained on how to use the application, which had built-in validity checks to ensure data accuracy and completeness. The application was also made available to the laboratory staff and the central radiologist to enter laboratory results and central CXR readings against the unique identifier allocated to each participant. The data manager worked closely with the field data staff in each team to review the data regularly for consistency and completeness, and also liaised closely with the laboratory staff, the radiologist and the case management team. To inform data analysis, the case management team reviewed the data of all participants with laboratory positive results, and decided on the survey cases with the input from the external CXR panel.

Data analysis was conducted using STATA Version 15.0 (College Station, Texas, USA). Frequency and percentage distributions were generated to describe the survey data. Prevalence was estimated based on the number of TB cases detected as defined above among participants. Three methods were considered to estimate the prevalence of bacteriologically confirmed tuberculosis: (1) cluster-level analysis, (2) individual-level analysis, and (3) estimation with inverse probability weighting (IPW), and with multiple value imputation (MI). The latter, which accounted for missing data and non-participation, was the most robust option to derive the estimates. This is the option that is recommended by WHO and generally used in other TB prevalence surveys. The imputation model included the following variables: age group, CXR panel reading, cough of more than two weeks, HIV status, sex, TB burden strata, and race.

3. RESULTS

3.1 Overview of sampling and participation

Survey activities were completed in 110 clusters across South Africa, as shown in Figure 3 based on PPS sampling. The first cluster was enrolled in August 2017 in Kwa-Zulu Natal Province and the last cluster was completed in July 2019 in the Western Cape Province.

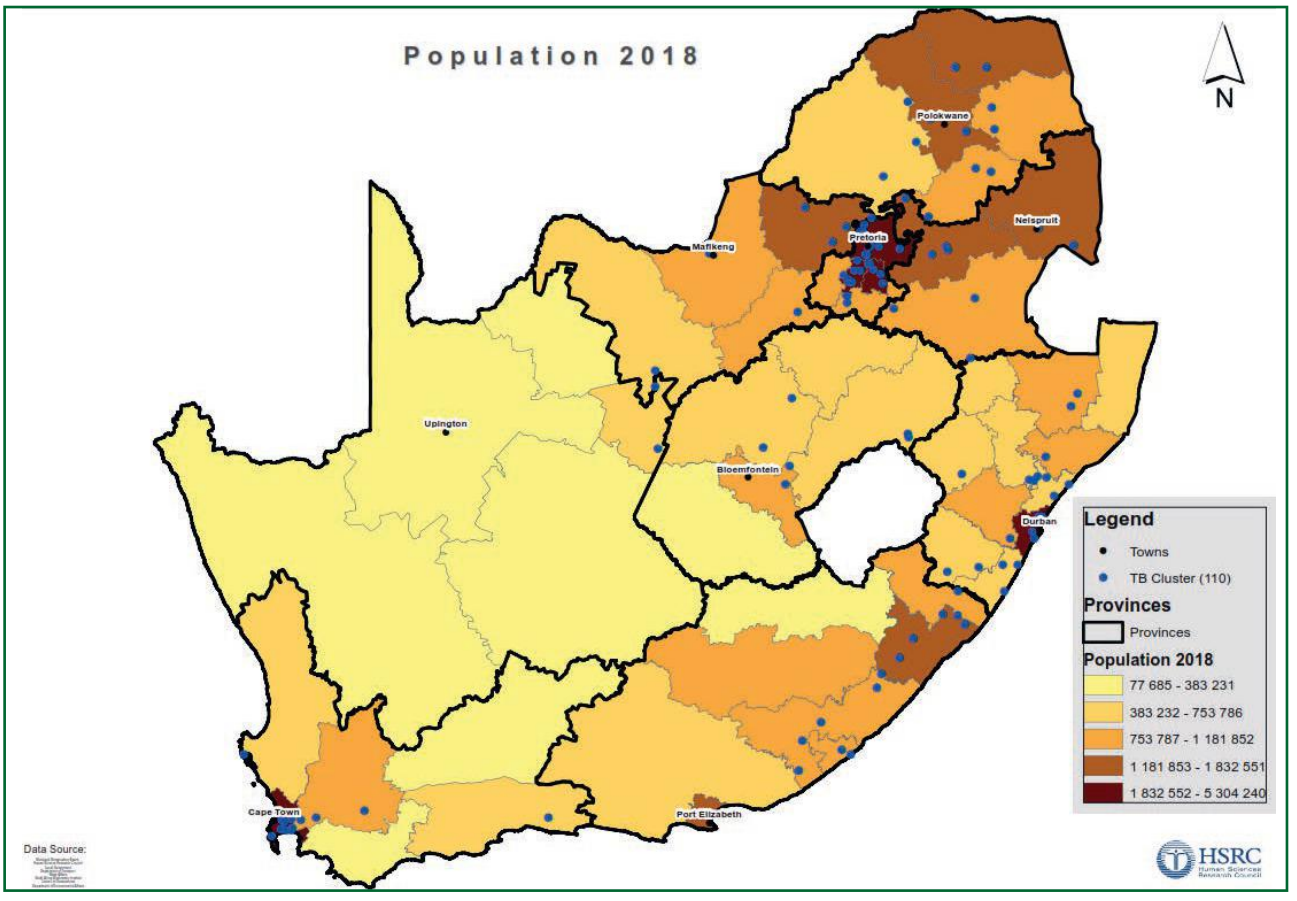


Figure 3: National TB prevalence survey: location and distribution of survey clusters

A total of 68,771 people were enumerated across the 110 clusters. Figure 4 shows a comparison of the national population (National census, 2011) and the population enumerated in the survey at household level. There were some differences between the populations including (i) a lower percentage of children aged 0-14 years (both males and females) enumerated compared to the national population (6.9% compared to 10.9% among those 0-4 years, 21.7% compared to 30.1% overall for 10-14 years), (ii) higher proportions of females in the survey population when compared to the national population (19.5% compared to 17.8% in those aged 15- 24 years, and 11.0% compared to 9.4% in those aged 45-54 years), and (iii) a higher proportion of older males enumerated compared to the national population, 6.3% compared to 4.1%.

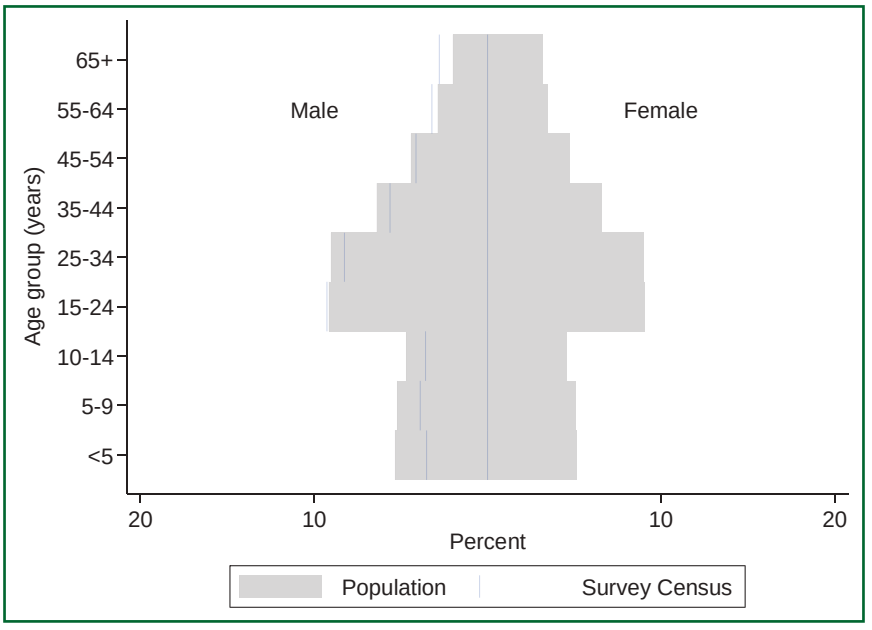


Figure 4: Comparison of the national population (National census, 2011) and the population enumerated at household level (TB survey census)

3.2 Survey participation

Survey participation varied across clusters and was generally lower in clusters that were in urban areas when compared to those in rural areas (Figure 5). Following very low participation rates in the earlier clusters, a decision was made to provide reimbursements to participants for their time spent on survey activities. This had a positive effect in most rural communities but this was not the case in urban settings. In addition, tailored messaging about the survey in the local media was increased. The net effect was an improvement in the average participation rate after the interventions. However, despite these efforts, the overall participation rate was 66.1%, which was lower than the target participation rate of 85%.

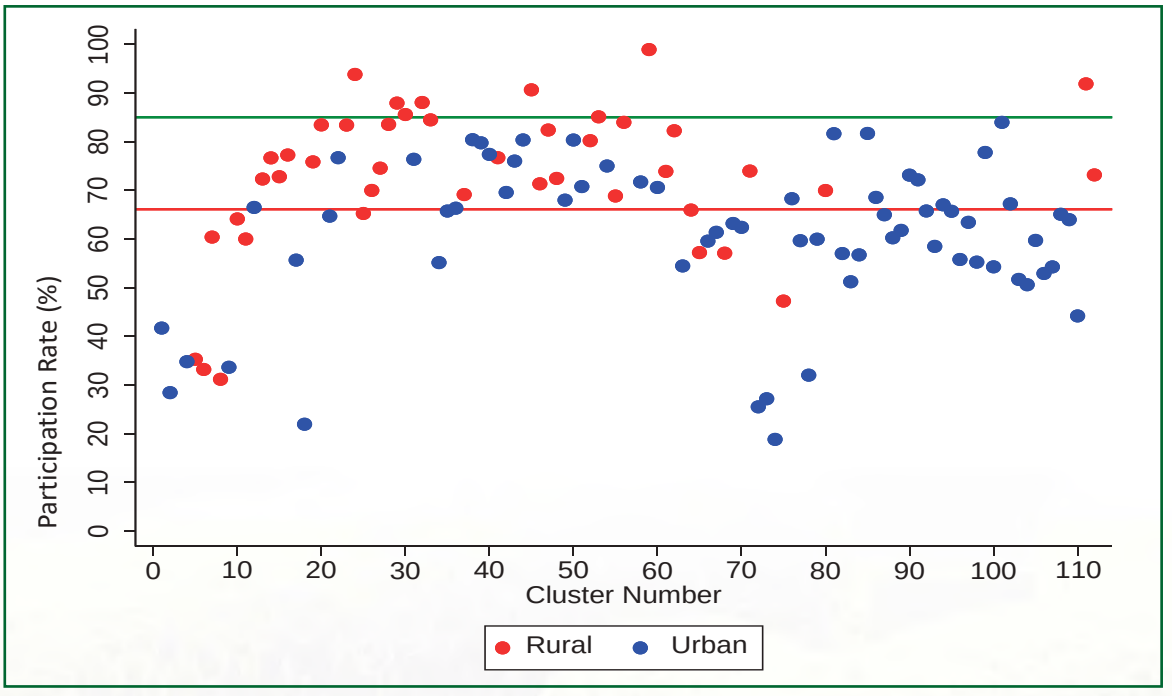


Figure 5: Participation rate per cluster (in chronological order) stratified by cluster geotype: Target participation rate (green line: 85%), average survey participation rate (red line 66.1%)

Participation was low for both sexes with that of men consistently lower than for women in all age categories (Figure 6). Participation was lowest among the youth but improved with increasing age. The lowest participation rate was observed in men aged 25-34 years while the highest was among females aged 55-64 years.

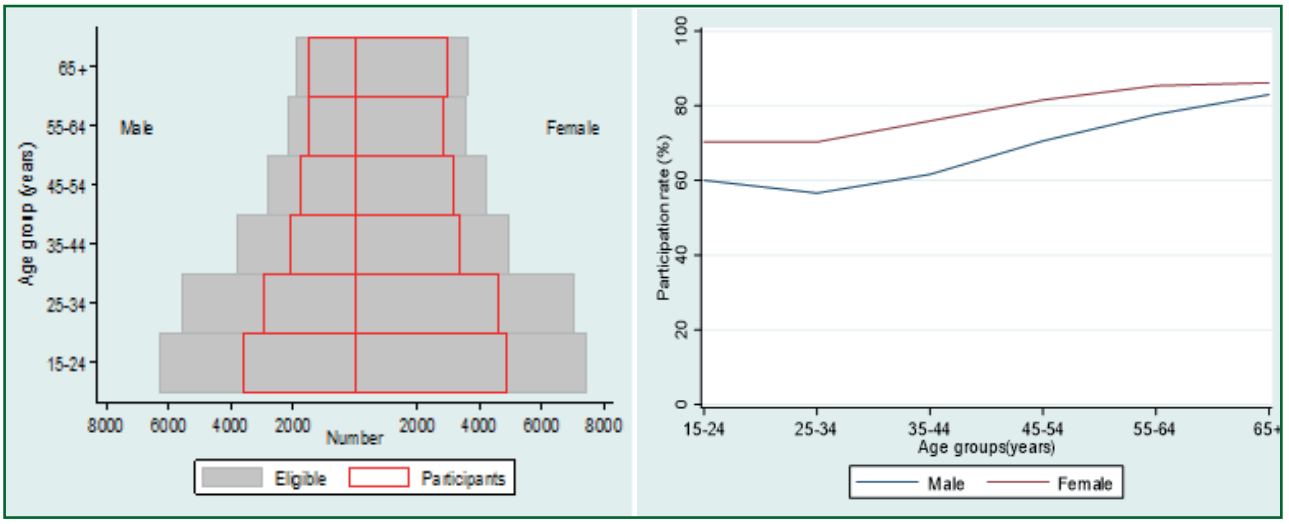


Figure 6: Participation by age and sex compared to the eligible population as enumerated at household level

3.3 Characteristics of survey participants

Among the 68,771 enumerated people, 53,250 (77.4%) met the survey inclusion criteria and 35,191 (66.1%) participated (Figure 7), median age 37 years (IQR 25-55), and 13,388 (38.0%) were males. Approximately a quarter of participants 25.8% (9,066) were positive on screening based on symptoms and/or CXRs; median age 49 years (IQR 33-63); and 3,849 (42.5%) were males. Among these 82.9% had a valid Xpert Ultra and 80.6% had a valid culture result available (Figure 7), and 7,292 (80.4%) had both a valid Xpert Ultra and culture result.

Screening for TB by symptoms and CXR findings

Among the 9,066 participants who were eligible for sputum examination, 19.1% (1,733) had both symptoms and abnormal CXR findings suggestive of TB as read by MOs in the field. The majority of participants screened positive by only one modality; 39.3% (3,566) screening positive by CXR findings only and 37.9% (3,435) by symptoms only, and in 3.7% (332) CXRs were not done (Figure 8).

Total population enumerated at the household level	• 68,771
Individuals eligible to participate at household level	• 53,250 (77.4% of enumerated)
Eligible individuals who participated	• 35,191 (66.1% all eligible = participation rate)
Participants screened positive (symptoms and/or abnormal CXR)	• 9,066 (25.8% of participants) eligible for sputum collection
Valid Xpert Ultra result	• 7,521 (82.9% of screened positive)
Valid culture result	• 7,305 (80.6% of screened positive)

Figure 7: Summary of the enumerated population and survey participants

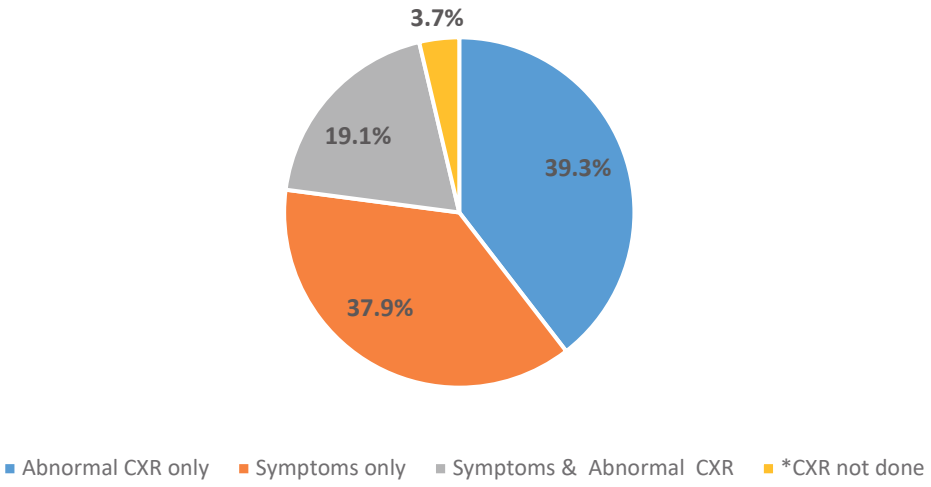


Figure 8: Eligibility for sputum examination by symptoms and CXR findings, N = 9,066
**CXR was not done because the participant declined to consent, or was pregnant, or had disabilities that made it impossible to take the CXR, or was bedridden and not able to attend the screening site.*

3.4 Culture and Xpert Ultra Results

Among the 9,066 participants eligible for sputum examination there were 220 with culture positive results and 223 with Xpert Ultra positive results (Table 1). Among the 223 participants with Xpert Ultra positive results, 144 also had positive culture results, while 66 had negative culture results, 9 had contaminated samples and 4 did not have a culture result.

Table 1: Culture and Xpert Ultra results among participants eligible for sputum examination, N = 9,066

Culture results	Xpert Ultra results				Total
	Xpert Ultra positive	Xpert Ultra negative*	Invalid	Not done/ Rejected	
Culture positive	144	74	0	2	220
Culture negative	66	6,460	11	49	6,586
Culture contaminated	9	383	0	4	396
Non-tuberculous mycobacteria	0	145	0	0	145
Not done/Rejected/ Sputum not collected	4	224	1	1,490	1,719
Total	**223**	**7,286**	**12**	**1,545**	**9,066**

** 71 trace Xpert Ultra cases were found, and were regarded as negative*

3.5 TB survey cases

A total of 234 cases met the survey TB case definition (Figure 9). These comprised of 220 culture positive cases, of which 144 were Xpert Ultra positive, 74 were Xpert Ultra negative and two were not tested by Xpert Ultra. An additional 14 cases that were classified as TB survey cases were Xpert Ultra positive, culture was not positive for *Mycobacterium tuberculosis* complex as per the survey definition, did not have a history of TB, and had CXR findings that were suggestive of active TB as confirmed by the external CXR reading panel.

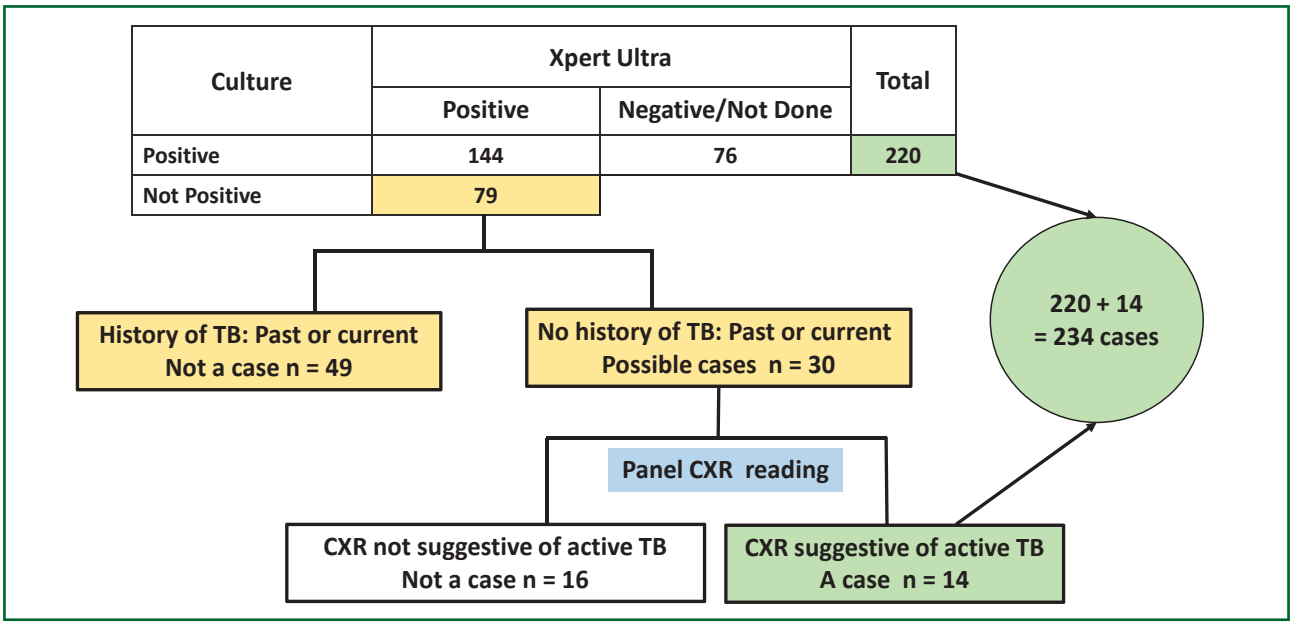


Figure 9: Survey TB cases by culture and Xpert Ultra, N = 234.
Trace Xpert Ultra results were regarded as negative.

Symptoms and CXR findings among survey TB cases

Among the 234 survey cases more than half (135; 57.7%) had CXR abnormalities only without reported symptoms; 82 (35.0%) were symptomatic with CXR abnormalities, 16 (6.8%) reported symptoms only and one (0.4%) case did not report symptoms and had not undergone CXR (Figure 10). CXR abnormalities among survey cases were confirmed by an external CXR reading panel.

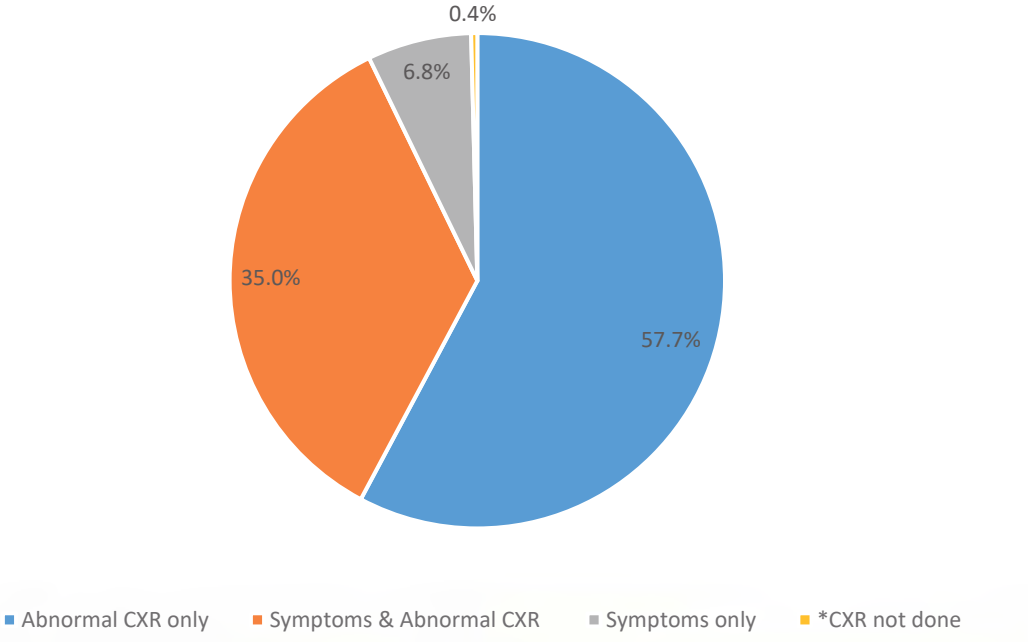


Figure 10 Symptoms and/or abnormal CXR among survey cases, N = 234
*CXR was not done because the participant declined to consent, or was pregnant, or had disabilities that made it impossible to take the CXR, or was bedridden and not able to attend the screening site.

3.6 HIV status among survey participants

Table 2: HIV status among survey participants, N = 35,191

	Participants with a known HIV status			HIV prevalence among participants with a known HIV status		
Category	**Total**	**Known HIV status**	**%**	**HIV Negative**	**HIV Positive**	**% HIV Positive**
All participants	35,191	26,877	76.4	22,289	4,588	**17.1**
All Screen positive participants	9,066	7,061	77.9	5,414	1,647	**23.3**
Screen positive participants by symptoms only	5,168	4,173	80.7	3,156	1,017	**24.4**
Screen positive participants by CXR only	3,566	2,641	74.1	2,060	581	**22.0**
Survey cases	234	191	81.6	136	55	**28.8**
***Programme cases**	178	162	91.0	68	94	**58.0**

*HIV status determined by a DBS result and in its absence the self-reported status. HIV status unknown: no DBS result and no self-reported status. *Programme cases: individuals already on treatment through the NTP prior to enrolment into the survey.*

HIV status was known for 76.4% (26,877) of participants (Table 2). HIV testing on DBS was done on 2,189 (24.1%) of the screen positive participants. Among those with a known HIV status, there was a sequential increase in the percentage of participants with HIV starting with all participants (17.1%), followed by screen positive participants (23.3%), then survey cases (28.8%) and finally programme cases (58.0%) enrolled into the survey. Programme cases were individuals who were already on treatment through the NTP prior to enrolment into the survey. The percentage of participants with HIV among programme cases was very similar to the notification data (59%).

The percentage of participants with HIV increased as the number of symptoms increased reaching 45.4% among those who reported 4 symptoms (Table 3). Of the 107 survey cases who did not report any symptoms, and had a known HIV status, 83 (77.6%) were HIV negative.

Table 3: HIV infection stratified by number of symptoms among participants identified as survey cases with a known HIV status, N = 191

TB survey cases with a known HIV status				
Number of TB Symptoms	**HIV Positive**	**HIV Negative**	**Total**	**% HIV co-infection**
0	24	83	107	**22.4**
1	10	24	34	**29.4**
2	10	14	24	**41.7**
3	6	9	15	**40.0**
4	5	6	11	**45.4**
Total	**55**	**136**	**191**	**28.8**

Symptoms included cough, fever, night sweats and unexplained weight loss

3.7 Estimated prevalence of bacteriologically confirmed pulmonary TB

Table 4: Estimated prevalence of bacteriologically confirmed pulmonary TB (≥15 years), by sex and by age group, South Africa, 2018 (Method: IPW+MI)

Prevalence per 100,000 population		95% CI
Sex		
Male	**1,094**	**835 – 1,352**
Female	**675**	**494 - 855**
Age group (years)		
15-24	**432**	**232 - 632**
25-34	**902**	**583 – 1,221**
35-44	**1,107**	**703 – 1,511**
45-54	**1,063**	**682 – 1,443**
55-64	**845**	**505 – 1,186**
≥65	**1,104**	**680 – 1,528**

The estimated prevalence of pulmonary TB in males 15 years and older was more than 1,000 per 100,000 population and was approximately 1.6 times that of women. Prevalence peaked in those aged 35-44 years and in those aged 65 years and older and was lowest among those aged 15-24 years (Table 4).

The survey estimated the prevalence of bacteriologically confirmed pulmonary TB in South Africa at 852 (95% CI 679-1,026) per 100,000 population among individuals 15 years and older. Using this survey estimate, the prevalence of TB for all forms of TB and ages in South Africa were calculated adjusting for individuals less than 15 years (29%), a rate ratio of child to adult TB (0.6) and the proportion of notified cases that are extra-pulmonary TB (9.7%). This was performed by the WHO using standard methods. **The estimated prevalence of TB (all ages, all forms) in South Africa in 2018 was 737 (95% CI 580-890) per 100,000 population.**

3.8 Estimated number of TB cases in the community

Figure 11 shows the estimated number of TB cases in the community for 2018 using the point estimate data from Table 4 and stratified by age. The highest estimated number of cases was among those aged 25-34 years. Although the estimated number of cases in those aged 65 years and older was lower than some of the other age groups, the prevalence was above 1%.

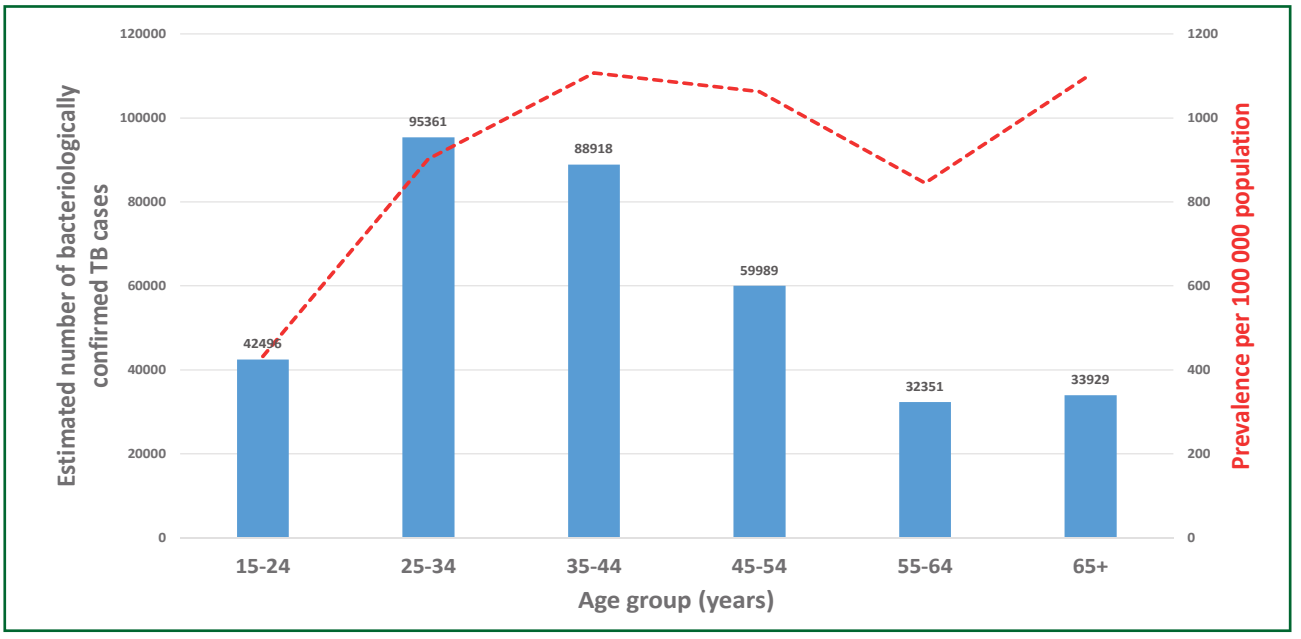


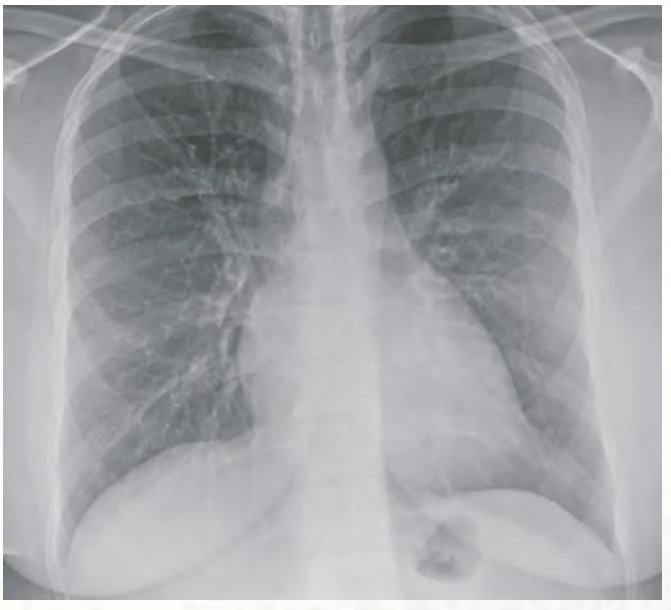
Figure 11: Comparison of the estimated number of bacteriologically confirmed TB cases (blue bar) with prevalence (red line) by age group (≥15years), South Africa, 2018

3.9 The Prevalence to Notification (P:N) ratio

The ratio of the bacteriologically confirmed pulmonary TB cases (Figure 9) to the case notification rate (2018) (prevalence to notification, P:N ratio) is shown in Table 5. Across all age groups and in both males and females more cases were estimated than were notified. The largest gap was in those aged 15-24 years and the elderly 65 years and older where the P: N ratios were 2.91 and 2.88 respectively. The ratios for males and females were 1.89 and 1.70 respectively.

Table 5: Ratio of prevalence to notification for pulmonary TB, ≥15 years, South Africa, 2018

Category	P:N ratio
Total	1.75
Male	1.89
Female	1.70
15-24 years	2.91
25-34 years	1.61
35-44 years	1.55
45-54 years	1.66
55-64 years	1.63
≥65 years	2.88



3.10 Health care seeking among participants with symptoms of TB

Among the 5,168 survey participants who reported at least one TB symptom, the majority 3,442 (66.6%) did not report seeking care for the symptoms at the time of their participation in the survey. Among these, more males (71.3%) than females (63.4%) did not seek care (Table 6).

The percentage of symptomatic participants who did not seek care was highest in younger participants and decreased with increasing age starting at 82.3% in those aged 15-24 years, then 62.9% in those 45-54 years old and 54.8% in those 65 years and older. Fifty-six percent (56.4%) of HIV positive participants had not sought care for their symptoms compared to 68.6% of those who were HIV negative.

Table 6: Number and percentage of symptomatic participants who had not sought care, N = 3,442

Category	Number of symptomatic participants	Number of participants that did not seek care	% of participants that did not seek care
Male	2,104	1,500	71.3
Female	3,064	1,942	63.4
15-24 years	678	558	82.3
25-34 years	869	688	79.2
35-44 years	850	573	67.4
45-54 years	859	540	62.9
55-64 years	897	526	58.6
≥65 years	1,016	557	54.8
HIV negative	3,156	2,164	68.6
HIV positive	1,017	574	56.4

Among the 3,442 participants with symptoms who had not sought care, the majority 2,071 (60.2%), indicated that they were planning to seek care. A further 917 (26.6%) felt their symptoms were not serious enough for them to seek care, 223 (6.5%) reported not having sufficient money to travel a health facility, and 189 (5.5%) reported that the health care facility was too far away for them to attend (Figure 12a).

Among the 1,726 participants with symptoms who had a sought care, more that 90% had attended a government facility, with the majority attending a community clinic (1,497; 86.7%) and 139 (8.1%) seeking care from the private sector (Figure 12b).

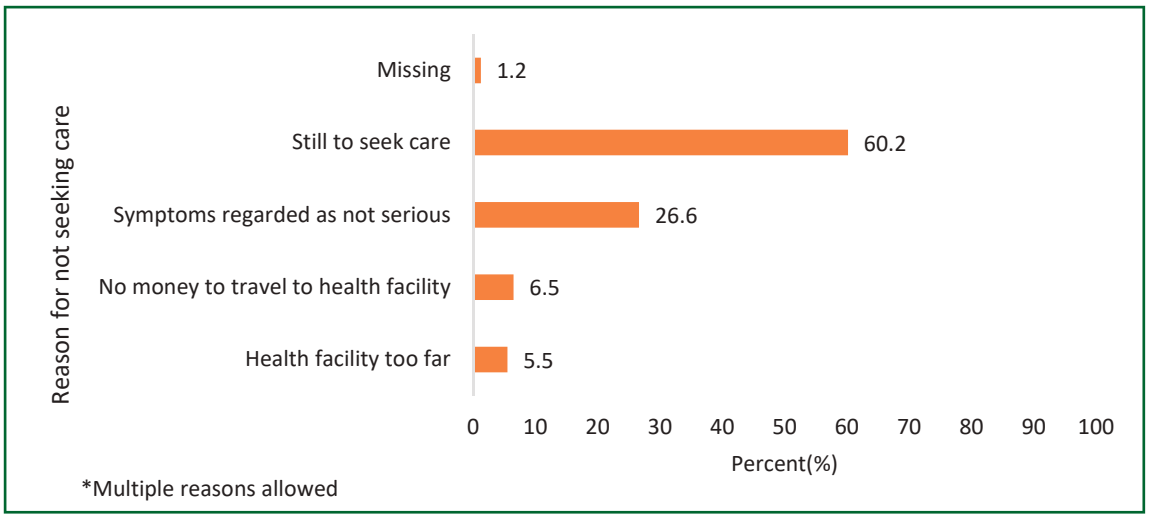


Figure 12a: Reasons for not seeking care by symptomatic participants, N = 3,442

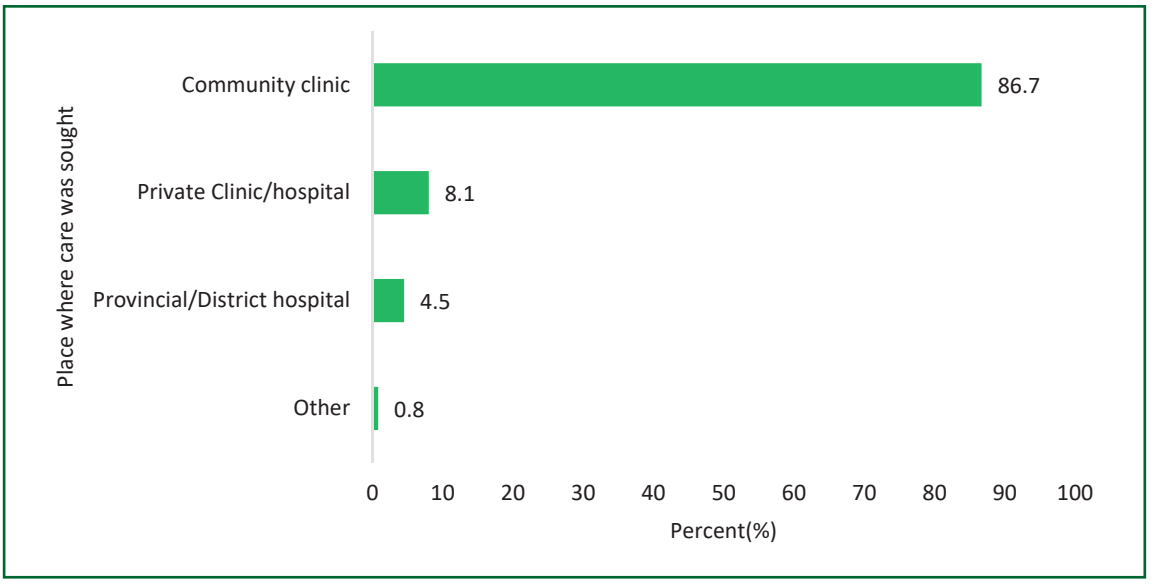


Figure 12b: Place where care was sought by symptomatic participants, N = 1,726

Of the 234 participants identified as TB cases in the survey 41 (17.5%) who were symptomatic had sought care for their symptoms before the survey: 31 attended a community clinic, 4 attended a government hospital and 6 attended a private sector facility. Among these 41 participants 8 (19.5%) were on treatment for TB at the time of enrolment into the survey.

4. DISCUSSION AND PROGRAMMATIC IMPLICATIONS

4.1 South Africa has a high TB burden including many people with undetected TB in the community

The prevalence of TB (all forms, all ages) in South Africa in 2018 was 737 (95% CI 580-890) per 100,000 population. Restricted to pulmonary TB and based on the survey findings, prevalence was lowest in the youth (15-24 years), and peaked in those aged 35-44 years and the elderly aged 65 years and older where it exceeded 1%; (1,107/100,000 (95% CI 703–1,511), and 1,104/100,000 (95% CI 680–1,528), respectively. TB prevalence was higher in males than in females. The estimated number of TB cases was more than the cases notified in the same year which is an important finding implying risk for ongoing transmission. The largest prevalence to notification gap was in the youth aged 15-24 years and in those 65 years and older. To effectively deal with the TB epidemic this gap needs to be closed. The three important findings identified from this survey related to these issues are that:

i) Men often have TB and are undetected or not reported to the NTP

The TB burden was higher among males, with a prevalence almost 1.6 times that of females. This finding is consistent with findings from other TB prevalence surveys in Africa and Asia. The disproportionately high TB prevalence of TB among men has previously been associated with delays in seeking care and access barriers. Similar concerns have been noted in the HIV programme and joining efforts to provide male friendly health services are needed.

ii) Sub-clinical TB is underestimated as a contribution to the TB burden

An important finding in this survey was a very high proportion (57.8%) of TB cases in participants who did not report any TB symptoms at the time of the survey and yet had bacteriological confirmation of TB. A review of surveys in Asia reported a range between 40% and 79% of TB cases without symptoms, hence this finding is not new, but it partly explains the gap in undetected TB. Sub-clinical TB is an emerging area that requires further research both in terms of tools to detect it and appropriate treatment and management regimens. Individuals with sub-clinical TB, though not "overtly suffering" from TB when they present, represent a phase in the continuum of TB disease and may in time develop symptoms and present to care. They do however have the propensity to infect others even at this early stage and efforts to address this issue will be important if the long term goals to "End TB" are to be realized.

iii) TB in HIV-negative individuals is also common

The percentage of survey cases with HIV (28.8%) was half that reported for those participants on treatment in the programme (58.0%). This finding is also consistent with information reported in the literature of a higher burden of HIV negative TB when active case finding efforts are undertaken. Interestingly, among TB cases who did not report symptoms, the majority were HIV negative (78%). Thus, the higher than expected prevalence of TB in this survey was in part driven by undetected TB among HIV negative individuals. It is however important to note that HIV positive TB cases were more likely to be symptomatic. These individuals therefore would have a greater likelihood of being detected through the programme as the current screening approach is based on symptoms. In addition more than two-thirds of HIV negative symptomatic participants had not sought care for their symptoms. Thus, a strategy to detect HIV negative cases earlier is needed and should include both patient as well as healthcare provider education.

4.2 Care seeking for individuals with TB symptoms is delayed

Care seeking among participants with symptoms suggestive of TB was delayed with almost two-thirds having not sought care at the time of their participation in the survey, and 60.2% of these reporting that they were still planning to seek care. A further 26.6% regarded the symptoms as not serious and thus did not seek care. In-depth qualitative research is needed to better understand the reasons for delayed care seeking so as to inform interventions to address this gap. In addition, interventions to increase knowledge of TB and awareness of TB symptoms and their importance are still needed. Approximately a fifth (19.5%) of symptomatic participants who were survey TB cases who had sought care for their symptoms had been diagnosed and started on treatment. There should thus also be heightened vigilance in assessing TB symptoms among those who attend health facilities in order to promote early diagnosis.

5. STRENGTHS AND LIMITATIONS

The survey was a nationally representative population-based survey that has for the first time provided a national estimate of the true burden of TB in South Africa. This was made possible by close collaboration of major public institutions in the country working with the Department of Health. The prevalence estimates derived followed WHO standardized methodology ensuring the robustness of estimates and allowing comparisons to be made with other countries and regions. Additionally, important issues were uncovered that will help future strategies to be formulated to effectively address the TB epidemic.

As with other national surveys of this scale there were a number of limitations that may have impacted the prevalence estimates. A major limitation was the performance of Xpert Ultra in active case finding activities. Given the specificity of Xpert Ultra [98% (95% CI 97-99%)], the rate of false-positive results for TB disease is high in low prevalent settings like the general community as was targeted by this survey (This is unlike in individuals who attend routine care). A history of TB can reduce specificity even further. Therefore, the survey case definition was amended to ensure that a positive culture result or a CXR suggestive of active TB was used to confirm Xpert Ultra positive results in those with no history of TB treatment. The analysis thus used a conservative approach. The participation rate of 66.1% was below the target level of 85% and missing data which occurred due to various reasons probably impacted the estimates calculated. The well established methodologies of multiple imputation with inverse probability weighting were used to account for these limitations allowing robust estimates to be derived. The HIV status for many participants was based on self-report (24.1% of those eligible for sputum examination were tested for HIV on DBS), and interpretation of the descriptive analysis should be viewed with this potential limitation in mind.

6. CONCLUSIONS

The First National Tuberculosis Prevalence Survey, South Africa, 2018, identified a high TB burden, higher in males than in females and high prevalence of TB among individuals aged 35-44 years and the elderly 65 years and older. The largest prevalence to notification gap was in the youth aged 15-24 years and in those 65 years and older. A higher proportion of TB was detected among HIV-negative individuals, with most reporting no symptoms. HIV positive participants identified as TB cases had more symptoms and hence they are more likely to be detected and treated in contrast to those who are HIV negative who are less likely to report symptoms and potentially contribute to ongoing transmission of TB. Sub-clinical TB has emerged as another area that requires further research and will be important for long term control efforts. Although TB symptoms at first may be perceived to be benign leading to delays in heath seeking, this perception needs to be corrected as TB remains the number one infectious disease cause of mortality in South Africa. In addition, a high index of suspicion, evaluation and follow-up of people presenting with TB-related symptoms by health care providers is needed to improve case detection.

Knowing starts with getting screened for TB

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