


BMJ Open Prevalence and incidence of symptomatic pulmonary tuberculosis based on repeated population screening in a district in Ethiopia: a prospective cohort study

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ABSTRACT

Objective In Ethiopia, one-third of the estimated tuberculosis cases are not detected or reported. Incidence estimates are inaccurate and rarely measured directly. Assessing the ‘real’ incidence under programme conditions is useful to understand the situation. This study aimed to measure the prevalence and incidence of symptomatic pulmonary tuberculosis (PTB) during 1 year in the adult population of Dale in Ethiopia.

Design A prospective population-based cohort study.

Setting Every household in Dale was visited three times at 4-month intervals.

Participants Individuals aged ≥ 15 years.

Outcome measures Microscopy smear positive PTB (PTB s+), bacteriologically confirmed PTB (PTB b+) by microscopy, GeneXpert, or culture and clinically diagnosed PTB (PTB c+).

Results Among 136 181 individuals, 2052 had presumptive TB (persistent cough for 14 days or more with or without *haemoptysis, weight loss, fever, night sweats, chest pain or difficulty breathing*), in the first round of household visits including 93 with PTB s+, 98 with PTB b+ and 24 with PTB c+; adding those with PTB who were already on treatment, the total number of PTB was 201, and the prevalence was 147 (95% CI: 127 to 168)/100 000 population. Out of all patients with PTB, the proportion detected by symptom screening was in PTB s+ 65%, PTB b+ 67% and PTB c+ 44%. During 96 388 person-years follow-up, 1909 had presumptive TB, 320 had PTB and the total incidence of PTB was 332 (95% CI: 297 to 370)/100 000 person-years, while the incidence of PTB s+, PTB b+ and PTB c+ was 230 (95% CI: 201 to 262), 263 (95% CI: 232 to 297) and 68 (95% CI: 53 to 86)/100 000 person-years, respectively.

Conclusion The prevalence of symptomatic sputum smear-positive TB was still high, only one-third of prevalent PTB cases notified and the incidence rate highest in the age group 25–34 years, indicating ongoing transmission. Finding missing people with TB through repeated symptom screening can contribute to reducing transmission.

BACKGROUND

Tuberculosis (TB) is an infectious disease transmitted by mycobacterial droplets from

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This study included a large sample and worked closely with the national tuberculosis programme and the community structures that contributed to its sustainability.
- ⇒ We report not only the prevalence but also the incidence of symptomatic pulmonary tuberculosis during 1 year, which is often not reported elsewhere.
- ⇒ The study screened a very high proportion of households in the district, giving an accurate measure of the burden of tuberculosis, where the probability of missing people with tuberculosis is small.
- ⇒ Tuberculosis cases notified were chosen the year before the study because we could not separate the patients identified by the screening from those who attended the health services themselves.
- ⇒ Only symptomatic patients with tuberculosis were reported, and it is known that many patients are more or less asymptomatic.

coughing patients. The global End TB strategy aims to reduce the sources of infection by curing infected individuals with effective anti-TB drugs and has helped reduce the incidence of TB worldwide. The estimated global incidence of TB has recently decreased by 9% from 2015 to 2019, but still 11% less than the End TB targets set for 2020. The incidence of TB is unevenly distributed globally with the highest estimated TB incidence rate in Africa, at 226/100 000 population in 2019. However, the TB incidence rate in Africa declined by 16% from 2015 to 2019, which is greater than the average global decline but still not fast enough to reach the Sustainable Development Goal milestones.^{1–4} Ethiopia achieved the first milestone of End TB with a 31% decrease in the estimated incidence rate from 2015 to 2020 (192 to 132/100 000 population).

The national X-ray-based TB survey in Ethiopia in 2010 reported *prevalence* estimates of

108 per 100 000 population for smear-positive pulmonary tuberculosis (PTB s+) and 277/100 000 population for bacteriologically confirmed pulmonary tuberculosis (PTB b+).⁵ Only two studies have investigated the pulmonary TB (PTB) *incidence*, both *based on screening of respiratory symptoms*. A study in a central district of Ethiopia in 2013 reported that the incidence of PTB s+ was 214/100 000 person-years and that of PTB b+ was 232/100 000 person-years,⁶ while a study in the northern part of the country in 2011 reported that the incidence of PTB s+ was 311/100 000 person-years.⁷ However, notifications in the country indicate that one-third of TB cases are still undetected, and more than half of them are in those aged 15–34 years old. Hence, the true incidence of TB is unknown and under-researched because generating these estimates requires massive resources.^{8,9}

Therefore, locally available data using the existing health system may help to understand the epidemiology of the disease as well as to validate national estimates, since these are not accurate in areas with disparities in health outcomes and programme implementation. The ‘missed’ or ‘diagnosed late’ individuals are important sources of TB transmission.^{5,10} Repeated assessment of subnational population-level incidence and prevalence patterns may help the programme quantify the impact of the control efforts to support local decision-making.^{10–12}

Dale district was part of a community-based project with active TB case-finding implemented in 2010.¹³ The study initially showed high notification rates in the district, which gradually decreased over time (215/100 000 in 2011 to 66/100 000 in 2015). It is not clear to what extent the decline reflects a real decline in TB incidence or is the result of going back to the routine health service delivery strategy without a systematic screening of the community. The impact has therefore not been sufficiently described and documented. Hence, this study aimed to measure the prevalence and incidence of symptomatic PTB through repeated population-based screening in the adult population of the Dale district in southern Ethiopia.

METHODS

Study design and population

This was a population-based prospective cohort study including repeated symptom screening in three consecutive rounds of household visits, from October 2016 to September 2017, in Dale district of southern Ethiopia. The target population was everyone who resided in the 36 administrative units (*kebeles*) in the district. The population data were obtained from the district health offices and each *kebele*. A persistent cough for 14 days or more with or without *haemoptysis*, *weight loss*, *fever*, *night sweats*, *chest pain* or *difficulty breathing* was taken as a sign of presumptive TB. Individuals with presumptive TB were enrolled after informed consent, and the population ≥ 15 years are included in this report. The total population denominator for the population aged ≥ 15 years was 136 181, based on official data from the Central Statistics Agency

in Ethiopia.¹⁴ The coverage of households screened is based on the number of households visited over the number of households registered at each time point. The prevalence of PTB was calculated by dividing the number of patients diagnosed during the first round of visits by the population covered. The incidence rate was calculated by dividing the number of patients with PTB identified during the follow-up period (ie, in the second and third rounds of household visits) by person-years of observation-time. We used the strengthening of the Reporting of Observational Studies in Epidemiology cohort reporting guidelines (online supplemental file 1).¹⁵

Study setting

The Dale district is a densely populated rural community with 10 health centres, 2 clinics and 36 health posts; TB care follows the End TB strategy.¹⁶ Since 2010, the non-governmental organisation REACH Ethiopia has been developing an innovative model using close-to-community providers, including in the Dale district, contributing to community TB care implementation in Ethiopia.^{6,13} Microscopy, but not GeneXpert nor X-ray examination, can be performed at health centres. The primary test for PTB diagnosis is sputum smear microscopy, which is cost-efficient and accessible, but has low sensitivity.^{17–19} The only GeneXpert equipment in the area is located outside of Dale district in the town administration of Yirgalem.

Patient and public involvement

No patients were involved in setting the research question or the outcomes, the conduct, interpretation, writing or dissemination of the results. The study was conducted in close collaboration with the Dale district National TB and Leprosy Programme (NTLP). They were informed about the study in advance and were actively involved throughout the design and implementation and in dissemination of the results. The project team organised consultative meetings with participants from regional, zonal and woreda level organisations, non-governmental organisations and religious institutions throughout the full study period. Village-women were included as representatives for the population in Dale.

Data collection

As a first step of the screening, trained female health extension workers (HEWs) familiar with the village went door-to-door, asking if any household member had respiratory symptoms compatible with TB, including those not at home during the survey. HEWs are well-established and trusted by the communities. Those identified with symptoms were carefully followed and asked to come to the health post for a test. This also applied to household members not at home at the time of the visit. Health personnel offered to come to the home to collect sputum for persons having difficulties in reaching the health facilities.

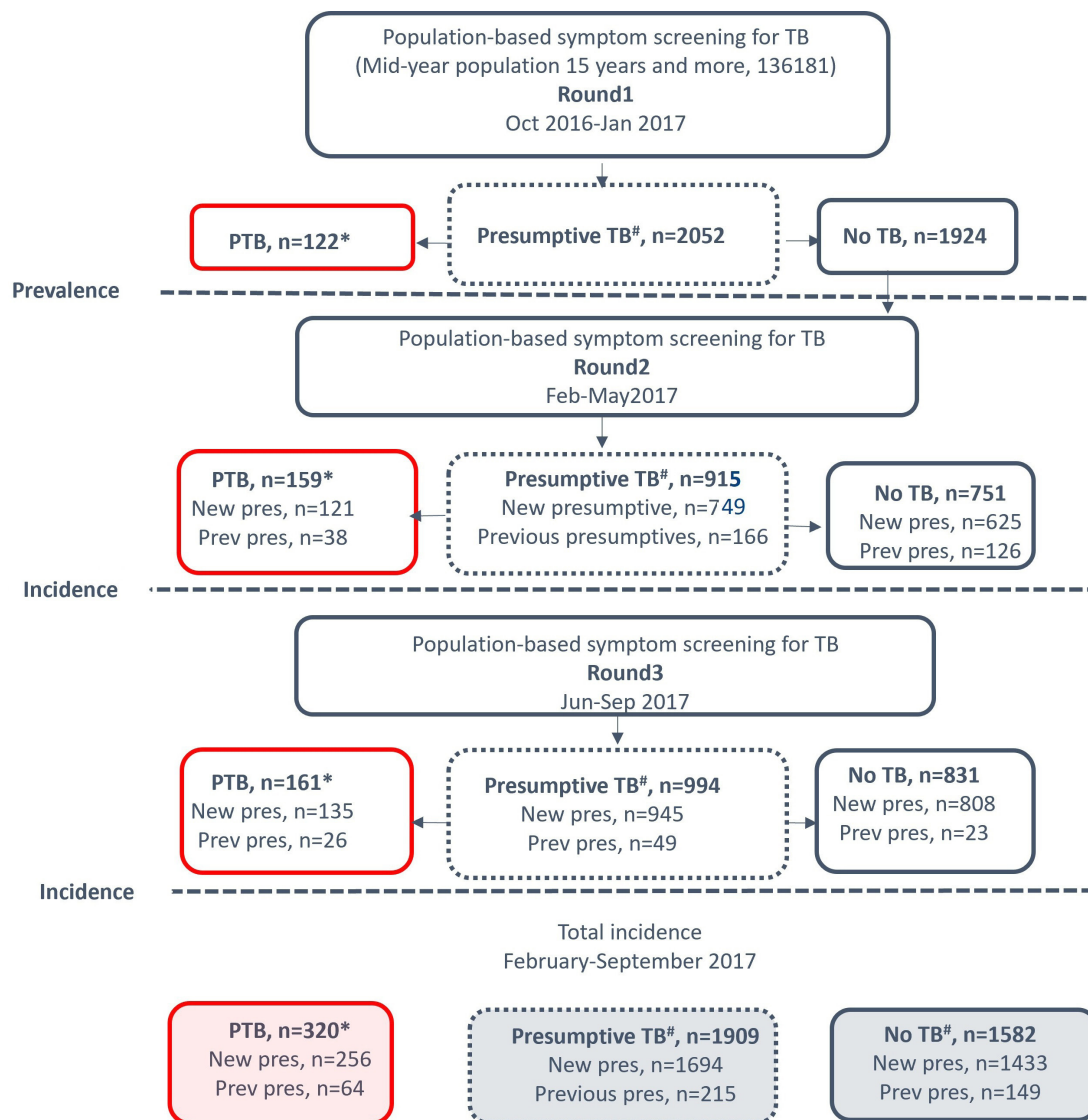


Figure 1 Study flow chart showing three rounds of household screening for TB in Dale district, 2016–2017. PTB, pulmonary TB; TB, tuberculosis. PTB: pulmonary tuberculosis. New pres: first episode of presumptive TB. Prev presumptive: the participant has been identified with presumptive TB in a previous round of household visits and enrolment dates were minimum 30 days apart. ‡Population denominator, estimates from Central Statistics Agency (CSA) in Ethiopia (estimated from a population census of 2007); Some patients had more than one episode.

Pretested semi-structured questionnaires were used to identify individuals with respiratory symptoms compatible with PTB and to collect clinical, demographic and socio-economic data (online supplemental file 2). Individuals identified with presumptive TB were asked to come to the health post to provide sputum. The sputum samples were collected and transported to the health centre for smear microscopy. Once identified by the study, participants received care, free of charge, as in the routine TB programme. If individuals were diagnosed with TB, they were treated according to the NTLP guidelines.²⁰ For patients diagnosed with drug-resistant TB, second-line drugs and follow-up were available at the nearby Yirgalem Hospital that initiates drug resistance TB treatment—free of charge. Individuals diagnosed with other diseases were referred for treatment. To ensure the quality of the laboratory, 50% of the slides were randomly selected

from participating catchment facilities and retested at the regional laboratory. Smear-positive samples were further validated by GeneXpert. Those already on TB treatment at the time of the survey were not included in the screening data of new incident cases. However, aggregate surveillance data from the NTLP on the number of patients already on TB treatment were added to those detected by screening in the prevalence calculation to facilitate comparison with other studies. Aggregated notification data were obtained from the NTLP from 2011 to 2018. Quarterly TB data were used to track those notified with PTB s+ or PTB c+ before, during, and after the study period to evaluate the impact of interventions on routine TB notification. The project ensured that all patients with TB identified through the project were registered in the TB register.²¹

**Table 1** Results of three rounds of testing individuals with presumptive tuberculosis in Dale, 2016–2017

| Household visits | Presumptive TB episodes*, n | PTB, n | PTB b+, n | PTB c+, n | % presumptive PTB with PTB | | | |
|------------------|--|--------|-----------|-----------|----------------------------|---------------------|---------------------|------|
| | | | | | PTB ¹ | PTB b+ ¹ | PTB c+ ¹ | |
| Round 1 | New presumptive; only tested once | 1729 | 76 | 71 | 5 | 4 | 4 | 0.3 |
| | New presumptive; TB with a repeat test | 323 | 46 | 27 | 19 | 14 | 8 | 5.9 |
| | New presumptive; all† | 2052 | 122 | 98 | 24 | 6 | 5 | 1.2 |
| Round 2 | New presumptive; only tested once | 630 | 72 | 71 | 1 | 11 | 11 | 0.2 |
| | New presumptive; TB with a repeat test | 119 | 49 | 19 | 30 | 41 | 16 | 25.2 |
| | New presumptive; all† | 753 | 121 | 90 | 31 | 16 | 12 | 4.1 |
| | Previous presumptive | 166 | 38 | 19 | 19 | 23 | 11 | 11.4 |
| | Total | 919 | 159 | 109 | 50 | 17 | 12 | 5.4 |
| Round 3 | New presumptive; only tested once | 900 | 121 | 119 | 2 | 13 | 13 | 0.2 |
| | New presumptive; TB with a repeat test | 45 | 14 | 11 | 3 | 31 | 24 | 6.7 |
| | New presumptive; all† | 945 | 135 | 130 | 5 | 14 | 14 | 0.5 |
| | Previous presumptive | 49 | 26 | 15 | 11 | 53 | 31 | 22.4 |
| | Total | 994 | 161 | 145 | 16 | 16 | 15 | 1.6 |
| Rounds 1+2+3 | New presumptive | 3746 | 378 | 318 | 60 | 10 | 8 | 2.0 |
| | Previous presumptive | 215 | 64 | 34 | 30 | 30 | 16 | 14.0 |

*The number of episodes is higher than the number of individuals as some were identified more than once.
†New presumptive all means only tested once plus repeat tests within the same round.
PTB¹, PTB means the proportion of presumptive TB cases with a positive bacteriological test result plus clinically diagnosed PTB; PTB, pulmonary TB; PTB b+, bacteriologically confirmed PTB; PTB c+, clinically diagnosed; TB, tuberculosis.

Operational definitions

As mentioned above, the term ‘presumptive TB’ was used to define individuals who had respiratory symptoms compatible with TB.²² ‘New presumptive’ was used the first time an individual was identified in the study as having symptoms of TB. Those with presumptive TB who tested negative for TB were included in the denominator for the consecutive rounds. If they were identified as having presumptive TB in a consecutive round of household visits (more than 30 days apart), they were classified as ‘previous presumptive with a new episode’. *PTB s+* was defined as at least one positive result by smear microscopy. *PTB b+* included having at least one positive result by smear microscopy, GeneXpert or culture. *PTB c+* was based on a clinical decision to start anti-TB treatment in those with persistent symptoms and negative bacteriological results; this diagnosis was usually (if not always) also supported by radiological findings. *PTB b+* and *PTB c+* both indicated a diagnosis of PTB. The ‘screening prevalence’ of PTB was calculated based on individuals identified with PTB in the first round (October 2016 to January 2017) of household visits divided by the total adult population (per 100 000 population). The ‘total prevalence’ also included patients who were already on TB treatment at the time of the

first screening round. The incidence was calculated based on the number of individuals newly identified with PTB in the second (February to May 2017) and third (June to September 2017) rounds of household visits divided by the person-years observation time (per 100 000 person-years). Person-years were calculated from the date of enrolment for screening or the end of follow-up on 31 September 2017, for all study participants. ‘Notification’ is based on TB register.

Diagnosis

For diagnosis, two spot sputum samples were collected according to standard procedures. Sputum smear-positive samples were sent for confirmation of diagnosis by GeneXpert at Yirgalem Hospital and by culture at the Armauer Hansen Research Institute in Addis Ababa. The use of GeneXpert for all samples was not feasible at the time of the study and was mainly limited to validation for smear-positive (drug-resistant TB diagnosis). In addition, smear-negative samples from HIV positive persons and persistent coughers still symptomatic after a course of broad-spectrum antibiotic were sent for analysis by GeneXpert and cultured in line with NTLP guidelines. Data on TB diagnosis, treatment and treatment outcome

were obtained from the TB register in the health centre. It was not possible to disentangle those identified through the household screening from those who approached the health centre on their own initiative. Individuals with chest X-ray abnormalities²³ were transferred to Yirgalem Hospital for clinical diagnosis of TB.

Data quality and analysis

Data were entered into Excel (Microsoft Office Proofing Tool 2016, Microsoft Corporation). The data quality was assessed by frequency distributions, cross-tabulations and double-entry of a 10% random sample of the data. The difference between the first and second data entries was 0.1%, and no systematic errors were detected. Stata V.14 and OpenEpi²⁴ were used for analyses.

RESULTS

Population-based symptom screening

The coverage of households screened was high, ranging from 96% to 98% in the three rounds of household visits, (online supplemental file 3). **Figure 1** shows a flow chart of the population in the three rounds of household screening. During the study-period, 3746 out of 136 181 persons in the screened target population were identified with presumptive TB. Of these, 442 persons were diagnosed with PTB. In total 352 cases had PTB b+; among them 263 were positive by smear microscopy, GeneXpert and culture, and 52 were positive by smear microscopy only, 34 were positive by GeneXpert only and 3 were positive by culture only. Of the 90 PTB c+ cases, 72 had the GeneXpert test (71 negatives and 1 error test), and none had culture tests. Chest X-ray was taken of 142 persistent coughers who needed further examination after broad spectrum antibiotic treatment; 86 had findings suggestive of PTB, 55 had normal and one unclear X-ray finding.

Table 1 shows results of three rounds of testing individuals with presumptive TB. The number of individuals presumed to have PTB was highest in the first round and halved in the two following rounds. The proportions of PTB cases among individuals with presumptive TB were 6%, 17% and 16% across the three rounds; the proportions of individuals with PTB b+ were 5%, 12% and 15%, respectively; and the proportions of PTB c+ were 5%, 10% and 13%, respectively. The proportion of PTB among individuals with presumptive TB who completed a course of broad-spectrum antibiotics and returned for another test was higher in the second and third rounds (14%, 41% and 31% for rounds 1, 2 and 3, respectively). Seventeen TB cases with symptoms of PTB were eventually diagnosed with extrapulmonary TB but not PTB, and excluded from the study (online supplemental table 1). Four individuals were identified with rifampicin resistance among 263 PTB b+ cases with rifampicin resistance test results. Women had a significantly higher prevalence and incidence of presumptive TB, a lower proportion with PTB b+ cases and a lower prevalence and incidence of PTB than men.

Prevalence of symptomatic PTB

Table 2 shows the total prevalence of PTB in the study area in first round of visits. Among the population of 136 181, 2052 had presumptive TB, 93 were diagnosed with PTB s+, 98 with PTB b+ and 24 with PTB c+. The total number of patients with PTB detected by symptom screening was 122; adding 49 PTB b+ (all of them PTB s+) and 30 PTB c+ patients who were already on TB treatment at the first round, the total number of PTB cases was 201, and the prevalence rate of PTB was 147 (95% CI: 127 to 168)/100 000 population. In those detected by screening, the prevalence rates of PTB b+ and PTB

Table 2 Total prevalence and percentage detected with pulmonary tuberculosis in the first round of visits in Dale, October 2016 to January 2017

| Covariate | Number of PTB during screening | | Number of PTB before screening | | Total prevalence of PTB | | % detected by screening | |
|--------------|--------------------------------|--------|--------------------------------|--------|-----------------------------|-----------------------------|-------------------------|--------|
| | PTB b+ | PTB c+ | PTB b+ | PTB c+ | PTB b+ per 100 000 (95% CI) | PTB c+ per 100 000 (95% CI) | PTB b+ | PTB c+ |
| Total | 98 | 24 | 49 | 30 | 108 (90 to 125) | 39 (29 to 50) | 67 | 44 |
| Age in years | | | | | | | | |
| 15–24 | 27 | 7 | 23 | 5 | 100 (76 to 132) | 24 (13 to 41) | 54 | 58 |
| 25–34 | 31 | 7 | 15 | 6 | 135 (100 to 179) | 38 (21 to 64) | 67 | 54 |
| 35–44 | 26 | 2 | 4 | 2 | 126 (86 to 177) | 17 (5 to 40) | 87 | 50 |
| 45–54 | 7 | 4 | 4 | 5 | 82 (43 to 143) | 67 (33 to 123) | 64 | 44 |
| 55+ | 7 | 4 | 3 | 12 | 65 (33 to 116) | 104 (61 to 166) | 70 | 25 |
| Sex | | | | | | | | |
| Male | 56 | 15 | 27 | 17 | 122 (98 to 151) | 47 (33 to 66) | 67 | 47 |
| Female | 42 | 9 | 22 | 13 | 93 (72 to 118) | 32 (21 to 48) | 66 | 41 |

n, number; PTB, pulmonary TB; PTB b+, bacteriologically confirmed PTB; PTB c+, clinically diagnosed PTB; TB, tuberculosis.

c+ were 72 (95% CI: 57 to 86) and 17 (95% CI: 10 to 24)/100 000 population, respectively. The prevalence rate of PTB s+ was 68 (95% CI: 54 to 82)/100 000 population from screening and 104 (95% CI: 87 to 121)/100 000 population including patients already on treatment. The percentages of patients detected by screening were as follows: PTB s+, 65%; PTB b+, 67%; and PTB c+, 44%. Among both PTB b+ and PTB c+ patients detected, only

one out of three had been identified by the health system (online supplemental tables 2–6).

Incidence of symptomatic PTB

The overall observation time was 96 388 person-years, with 1909 individuals identified with presumptive TB, 254 with PTB b+ (including 222 smear-positive) and 66 with PTB c+ (table 3). The total number of PTB cases

Table 3 Incidence of presumptive and pulmonary tuberculosis in the adult population in Dale, February to September 2017

| Visits | Covariate | Presumptive TB | PTB incidence | | | Proportion of presumptive TB with PTB (%) | | |
|-----------|--------------|---------------------|---------------------------------------|-----------------------------|-----------------------------|---|--------|--------|
| | | Episode per 100 000 | PTB ¹ per 100 000 (95% CI) | PTB b+ per 100 000 (95% CI) | PTB c+ per 100 000 (95% CI) | PTB ¹ | PTB b+ | PTB c+ |
| Round 2 | Total | 1920 (1798–2047) | 333 (284 to 388) | 228 (188 to 274) | 104 (78 to 137) | 17 | 12 | 5 |
| | Age in years | | | | | | | |
| | 15–24 | 1034 (891–1194) | 281 (210 to 369) | 212 (151 to 289) | 68 (37 to 117) | 27 | 21 | 7 |
| | 25–34 | 1750 (1524–2000) | 429 (322 to 559) | 336 (244 to 453) | 92 (48 to 160) | 25 | 19 | 5 |
| | 35–44 | 2065 (1773–2392) | 324 (218 to 465) | 228 (141 to 350) | 96 (44 to 182) | 16 | 11 | 5 |
| | 45–54 | 3096 (2652–3595) | 298 (176 to 474) | 130 (257 to 258) | 167 (82 to 308) | 10 | 4 | 5 |
| | 55+ | 4039 (3493–4647) | 342 (202 to 543) | 106 (39 to 236) | 235 (123 to 408) | 8 | 3 | 6 |
| | Sex | | | | | | | |
| | Male | 1697 (1537–1869) | 337 (269 to 418) | 223 (169 to 290) | 114 (76 to 163) | 20 | 13 | 7 |
| | Female | 2140 (1960–2331) | 329 (262 to 408) | 233 (178 to 303) | 96 (62 to 141) | 15 | 11 | 4 |
| Round 3 | Total | 2040 (1916–2170) | 330 (282 to 384) | 297 (252 to 349) | 32 (194 to 522) | 16 | 15 | 2 |
| | Age in years | | | | | | | |
| | 15–24 | 895 (763–1043) | 322 (246 to 415) | 305 (232 to 396) | 17 (4 to 46) | 36 | 34 | 2 |
| | 25–34 | 2126 (1878–2399) | 521 (403 to 662) | 455 (346 to 587) | 66 (30 to 125) | 25 | 21 | 3 |
| | 35–44 | 2222 (1923–2556) | 187 (110 to 297) | 152 (84 to 253) | 35 (9 to 95) | 8 | 7 | 2 |
| | 45–54 | 3617 (3142–4144) | 180 (91 to 320) | 162 (78 to 297) | 18 (1 to 89) | 5 | 4 | 0.50 |
| | 55+ | 3856 (3334–4438) | 307 (178 to 496) | 287 (163 to 470) | 20 (10 to 100) | 8 | 7 | 1 |
| | Sex | | | | | | | |
| | Male | 1757 (1595–1930) | 319 (253 to 396) | 294 (231 to 369) | 25 (10 to 52) | 18 | 17 | 1 |
| | Female | 2318 (2134–2516) | 341 (274 to 420) | 300 (238 to 375) | 40 (20 to 72) | 15 | 13 | 2 |
| Round 2+3 | Overall | 1981 (1893–2071) | 332 (297 to 370) | 263 (232 to 297) | 68 (53 to 86) | 18 | 14 | 4 |
| | Age in years | | | | | | | |
| | 15–24 | 964 (865–1071) | 302 (248 to 364) | 259 (210 to 317) | 43 (25 to 69) | 32 | 27 | 5 |
| | 25–34 | 1940 (1769–2122) | 475 (394 to 569) | 396 (322 to 482) | 79 (49 to 121) | 25 | 21 | 4 |
| | 35–44 | 2145 (1932–2374) | 254 (186 to 340) | 189 (132 to 264) | 65 (34 to 113) | 12 | 9 | 3 |
| | 45–54 | 3361 (3031–3719) | 238 (159 to 344) | 146 (86 to 234) | 91 (46 to 160) | 7 | 4 | 3 |
| | 55+ | 3946 (3562–4359) | 324 (224 to 454) | 198 (123 to 304) | 125 (68 to 213) | 8 | 5 | 3 |
| | Sex | | | | | | | |
| | Male | 1727 (1612–1848) | 328 (279 to 382) | 259 (216 to 308) | 69 (48 to 95) | 19 | 15 | 4 |
| | Female | 2230 (2100–2366) | 336 (287 to 391) | 268 (224 to 317) | 67 (47 to 94) | 15 | 12 | 3 |

PTB, pulmonary TB; PTB¹, PTB means the proportion of presumptive TB cases with a positive bacteriological test result plus clinically diagnosed PTB; PTB b+, bacteriologically confirmed PTB; PTB c+, clinically diagnosed.

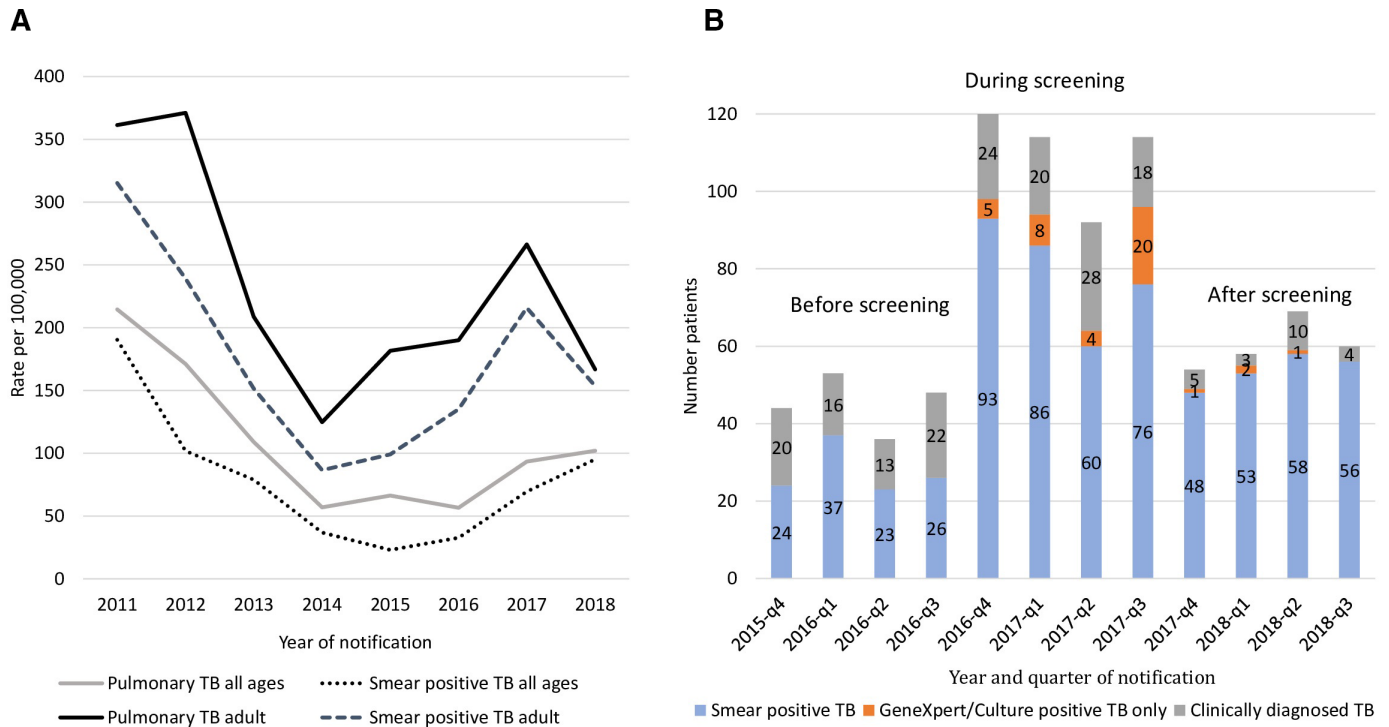


Figure 2 Case notification of patients with pulmonary TB in Dale district (A) rate per 100 000 population by category 2011–2018, and (B) absolute number of patients before, during and after screening from quarter 4 2015 to quarter 3 2018 (source National TB and Leprosy Programme). TB, tuberculosis.

was 320. The incidence of PTB was 332 (95% CI: 297 to 370)/100 000 person-years; the incidence rates of PTB s+, PTB b+ and PTB c+ were 230 (95% CI: 201 to 262), 263 (95% CI: 232 to 297) and 68 (95% CI: 53 to 86)/100 000 person-years, respectively (online supplemental table 7). The incidence rates of PTB s+ and PTB b+ were highest among 25–34 years old (online supplemental table 8).

PTB rate ratio comparison by sex

We estimated the ratios of the notification rate to the total prevalence rate (including cases already on TB treatment in the first round of the survey) as well as to the incidence rates for PTB b+, PTB c+ and PTB s+. The prevalence-to-notification rate ratios for PTB s+ were 1.28:1 for all adults, 1.2:1 for men and 1.4:1 for women. The ratios of the prevalence rate to the incidence rate were 0.45:1 for all adults, 0.52:1 for men and 0.40:1 for women. The ratios of the notification rate to the incidence rate of PTB b+ were 0.35:1 for all adults, 0.42:1 for men and 0.28:1 for women (online supplemental table 9).

PTB notification trend by year

Figure 2 shows (A) case notification rate 2011–2018 (B) and the number of patients before (four-quarters), during and after screening. The PTB s+ notification rates were 81 (95% CI: 66 to 96), 231 (95% CI: 206 to 257) and 150 (95% CI: 130 to 170)/100 000 population, respectively. The notification rates increased threefold during the project year and then decreased after the project but were higher than before the project. The notification rates had wide ranges between catchment areas,

particularly before the start of the current project (online supplemental tables 10–12).

DISCUSSION

This systematic symptom-based population-based TB screening in a district of Ethiopia found a point prevalence of smear-positive TB of 104/100 000 population, twice the level found in Ethiopia's 2010 national prevalence survey using smear-microscopy among symptomatic (58/100 000), where half of the cases were identified not by symptoms but by X-ray screening alone.⁵ Only one-third of individuals with TB were detected by the routine NTLN services. The incidence of PTB was 332/100 000 person-years, highest among those with persistent symptoms and in those aged 25–34 years old. Higher TB rates in young people in a community indicates high transmission, since with falling rates the median age of patients with TB increases as the infected population becomes older.^{2 25 26}

Our study showed a prevalence similar to that found in a 2013 local symptom-based survey from central Ethiopia, with a PTB s+ prevalence rate of 109 (67–150)/100 000 population,⁶ while other symptom-based studies reported a higher prevalence of PTB s+: 169/100 000 population in northern Ethiopia in 2011,²⁷ 139/100 000 population in southern Ethiopia in 2016²⁸ and 78–174/100 000 population in other studies from different rural areas in Ethiopia, demonstrating how the disease burden varies across the country.^{12 29–31} Compared with our data from



Ethiopia, a systematic review of national TB prevalence surveys (including X-ray and not based on symptoms) in Africa has revealed a higher prevalence of PTB s+ in Kenya (230/100 000) and Uganda (174/100 000), but a comparable prevalence in Ghana (111/100 000) and a lower prevalence in Gambia (90/100 000) and Rwanda (74/100 000). The difference in prevalence rates across studies could be due to differences in methods, year of study and location. Studies based on smear microscopy alone had lower prevalence rates than studies using the more sensitive tools GeneXpert and culture.^{27 28 32}

In the current study, two out of three individuals with PTB s+ remained undetected in the communities, which is in agreement with a systematic review in Ethiopia showing a point prevalence of undiagnosed PTB s+ of 79 (56–113)/100 000, with an active-to-passive case finding ratio of 2.3:1,³² which is also comparable to our prevalence of 72 (57–86)/100 000 population. Similarly, two individuals out of five with PTB c+ remained undetected. PTB c+ contributed 20–36% to the total prevalence and incidence of PTB in our study; 44% of PTB c+ cases were detected by screening. In general, all PTB c+ diagnoses were based on chest X-ray. Overall, active TB case finding increases TB detection through community engagement with HEWs, thereby improving community awareness and access to TB treatment.^{33 34} A lower prevalence of HIV and TB-HIV co-infections in the region³⁵ may have contributed to a lower prevalence of TB compared with the other studies. TB mainly affects women due to socio-economic disadvantages and domestic responsibilities. Women accounted for only 44% of the nationally notified cases in 2020 in Ethiopia, and such trends persisted for several years.¹¹ The prevalence of PTB was not statistically different by sex in this study.

The incidence of PTB s+ was 230 (201–262)/100 000 person-years, which is similar to the most recent report based on symptom screening, 214 (163–263)/100 000 person-years for PTB s+ from central Ethiopia in 2013, but lower than 311 (240–382)/100 000 person-years in northern Ethiopia in 2011.^{6 7} The age group 25–34 years had the highest incidence of PTB s+ cases, with no difference by sex; this may indicate heightened recent community transmission.

Individuals with presumptive TB for more than one round of screening (previous presumptive) were more likely to have PTB b+ (16%) than a new presumptive TB case (8%).³⁶ Similar trends were seen in a study in Guinea-Bissau, where smear-negative chronic coughers had a 5% higher smear-positivity rate after a month than new presumptive TB cases.³⁷ As expected, this study found more cases of PTB with a longer follow-up of chronic coughers after negative results than those initially identified with presumptive TB, thus emphasising the need to reach this population with feasible interventions and follow-up that can improve the identification of more TB cases.^{37 38}

Our study allowed us to directly calculate the prevalence-to-incidence ratio. In an ideal world where the duration of

the TB disease episode is not much more than 6 months (from disease onset to rapid start and completion of treatment) the ratio should be close to 0.5. In our study, of those with PTB s+, the ratio was 0.45:1 overall; 0.52:1 in men and 0.4:1 in women. These findings with a low ratio are likely due to the systematic and repeated screening with high coverage. Our prevalence-to-incidence ratio was lower than the study from another region of Ethiopia that reported rate ratio of 0.6:1.⁶

In prevalence surveys, the true incidence is normally unknown, and notification rates are used to estimate the incidence while taking into consideration underdiagnoses and under-reporting. The prevalence-to-notification rate ratio in PTB s+ cases in our study was 1.28:1, consistent with the finding that only one-third of patients with TB were detected and notified; therefore, showing that they had TB for a long time before diagnosis. In national surveys, the prevalence-to-notification rate ratios in PTB s+ patients have been reported to be 1.19:1 in Ethiopia, 0.62:1 in Gambia and 5.8:1 in Nigeria.³⁹

The notification rate increased threefold during the intervention year, indicating that the decline of TB notifications since the previous intervention did not only reflect decline in TB incidence but also less case-finding activities. The decreasing incidence is a function of early detection and effective treatment of infectious cases. In our study, it may be too early to see that the reduced transmission leads to lower TB incidence. Besides, we may have missed TB cases during our initial screening since we only included symptomatic persons and mainly confirmed the diagnosis using smear-positive microscopy. Although some smear-negative patients were started on treatment as clinical cases, others could be identified as smear-positive during subsequent rounds of screening. This delay may have resulted in continued transmission and persistently high incidence.

This study had two main strengths. First, the project worked in close collaboration with the NTLF, and very few people declined to participate. Due to the large study population, the data provide precise estimates of the prevalence and incidence of PTB. Second, the engagement of existing health systems and community structures increased the community involvement, thus contributing to its sustainability. Challenges include that only symptomatic patients with TB were reported, and it is known that many patients are more or less asymptomatic.^{40 41} However, since the same screening method is used in three rounds of visits, we are able to compare prevalence and incidence and assess changes over time. Individuals who did not participate in the first round of household visits, either because they were unavailable at the time of the visit or they did not come for sputum testing, may have been diagnosed with PTB in the second round (ie, prevalent but counted as incident cases). This may have overestimated the incidence. However, the number should be low because the coverage of households screened was high and screening-questions included household members who were not at home at the time of

the visit. We cannot rule out that there was some drop-off in the referral process of presumptive TB and sample collection, but none were reported as lost to follow-up and the proportion was probably very low. Finally, since the patients detected by screening could not be separated from those who attended health services by themselves, the year before the study was chosen as ‘notification’.

From a public health perspective, in this study, two-thirds of symptomatic individuals with smear-positive PTB were undetected and transmitting TB in the community. Why individuals with symptoms of the deadly disease in a setting with reasonably accessible health services do not seek treatment is a major question. Increasing access by lowering the cost of care (patients should not have travel and other-related expenses to seek care), better diagnostic tools and addressing the impact of stigma are important factors to consider. Based on the study results, community screening for respiratory symptoms at intervals (every 3–4 months) may improve case findings and reduce delay in TB diagnosis in the community.

CONCLUSIONS

The prevalence rate of symptomatic sputum microscopy-positive TB was still high and similar to the magnitude found in the district at the start of a previous project and only one-third of PTB cases were notified. The incidence rate was highest in the age group 25–34 years. These findings indicate low TB case finding in the community and ongoing transmission of PTB. Cost-effective interventions implemented under routine programme conditions that engage the existing health system structures are needed to find the missing people with TB, decrease transmission and contribute to a sustained decline in the incidence of TB in a society.

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