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TB prevalence in Zimbabwe: a national cross-sectional survey, 2014

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Abstract

BACKGROUND: We conducted the first national TB prevalence survey to provide accurate estimates of bacteriologically confirmed pulmonary TB disease among adults aged ≥15 years in 2014.

METHODS: A TB symptoms screen and chest X-ray (CXR) were used to identify presumptive TB cases who submitted two sputum samples for smear microscopy, liquid and solid culture. Bacteriological confirmation included acid-fast bacilli smear positivity confirmed using Xpert® MTB/RIF and/or culture. Prevalence estimates were calculated using random effects logistic regression with multiple imputations and inverse probability weighting.

RESULTS: Of 43,478 eligible participants, 33,736 (78%) were screened; of these 5,820 (17%) presumptive cases were identified. There were 107 (1.9%) bacteriologically confirmed TB cases, of which 23 (21%) were smear-positive. The adjusted prevalences of smear-positive and bacteriologically confirmed TB disease were respectively 82/100,000 population (95% CI 47–118/100,000) and 344/100,000 (95% CI 268–420/ 100,000), with an overall all-ages, all-forms TB prevalence of 275/100,000 population (95% CI 217–334/100,000). TB prevalence was higher

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in males, and age groups 35–44 and ≥65 years. CXR identified 93/ 107 (87%) cases vs. 39/107 (36%) using the symptom screen.

CONCLUSION: Zimbabwe TB disease prevalence has decreased relative to prior estimates, possibly due to increased antiretroviral therapy coverage and successful national TB control strategies. Continued investments in TB diagnostics for improved case detection are required.

RÉSUMÉ

Nous avons réalisé la première enquête nationale de prévalence de la TB au Zimbabwe pour fournir des estimations précises sur la TB pulmonaire confirmée bactériologiquement chez l'adulte âgé ≥15 ans en 2014.

Un dépistage symptomatique de la TB et une radiographie thoracique (CXR) ont été réalisés pour identifier les cas suspects de TB ayant soumis deux échantillons d'expectorations pour microscopie des frottis et cultures en milieux liquide et solide. La confirmation bactériologique reposait sur un test de dépistage des bacilles acido-alcoolo-résistants positif par microscopie des frottis, confirmé par test Xpert® MTB/ RIF et/ou culture. Les estimations de la prévalence ont été calculées en utilisant une régression logistique à effets aléatoires avec imputations multiples et pondération des probabilités inverses.

Sur 43 478 participants éligibles, 33 736 (78%) ont été dépistés. Parmi eux, 5 820 (17%) cas suspects ont été identifiés. Un total de 107 (1,9%) cas de TB confirmée bactériologiquement a été identifié, dont 23 (21%) à microscopie positive. Les prévalences ajustées des cas de TB à microscopie positive et confirmàe bactériologiquement étaient respectivement de 82/100 000 habitants (IC 95% 47–118/100 000) et 344/100 000 (IC 95% 268–420/100 000), avec une prévalence globale de la TB (tout âge et toute forme confondu(e)) de 275/100 000 habitants (IC 95% 217–334/100 000). La prévalence de la TB était plus élevée chez les hommes, ainsi que dans les tranches d'êge 35–44 et ≥65 ans. La CXR a identifié 93/107 (87%) cas contre 39/107 (36%) pour le dépistage symptomatique.

La prévalence de la TB au Zimbabwe a diminué par rapport aux estimations antérieures, possiblement du fait d'une plus grande couverture en traitements antirétroviraux et de la réussite des stratégies nationales de contrôle de la TB. Des investissements continus sont nécessaires pour le diagnostic de la TB afin d'améliorer la détection des cas.

Keywords

pulmonary tuberculosis; bacteriologically confirmed tuberculosis; smear-positive tuberculosis

In 2005, Zimbabwe was ranked by the WHO to be among the countries with the highest TB prevalences in the world (409/100,000 population),[1] compounded by hyper-endemic HIV/ AIDS. Since the inception of the antiretroviral therapy (ART) programme, ART coverage has increased dramatically from 2% in 2005 to 89% in 2018.[2,3]

Despite concerted efforts to improve TB control approaches nationally,[3,4] high WHO prevalence and incidence estimates, together with declining national notification rates of smear-positive TB disease from 142/100,000 population (2002) to 85/100,000 population (2013)[3] suggests that there may be a large proportion of underdiagnosed and/or

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underreported cases in Zimbabwe. True TB disease prevalence remained unknown; however, reliable data are critical to monitoring efforts towards the achievement of national and global TB control targets.

We undertook a nationally representative, population-based survey in order to estimate the prevalence of bacteriologically confirmed pulmonary TB disease among adults aged ≥15 years in Zimbabwe in 2014. We also determined the frequency of symptoms and chest X-ray (CXR) abnormalities suggestive of TB among survey cases and investigated factors associated with bacteriologically confirmed TB disease among presumptive TB cases.

MATERIALS AND METHODS

Study design, sampling and sample size

We conducted a population-based, cross-sectional survey with multistage cluster sampling, stratified by urban and rural areas, in all 10 provinces of Zimbabwe between January and December 2014. Zimbabwean provinces are divided into districts and the districts into wards, which are, in turn, subdivided into enumeration areas (EAs). The sampling frame included 1,963 wards, from which 75 wards (22 urban and 53 rural) were selected with probability proportionate to their 2012 population size.[5] Within each selected ward, simple random sampling was used to select one EA (cluster) constituting between 540–600 eligible adults (individuals aged ≥15 years, either permanent residents in the selected households or visitors who had lived in the selected household more than 14 days before the survey). EAs with less than 540 eligible adults were merged with two or three sequential EAs in a clockwise manner to form clusters of 540–600 eligible adults. In clusters with >600 adults, a consecutive number of adults was recruited up to a maximum of 660 adults to cater for clusters with <600 adults. To avoid bias, the survey excluded high TB risk populations and those in congregate settings who were not representative of the general population, that is, in prisons, hospitals, orphanages and refugee camps. We determined the sample size to be 44,951, assuming a prevalence of smear-positive pulmonary TB disease of 190/100,000 population (≥15 years),[4] a relative precision to be tolerated at 95% confidence level (95% CI) of 25%, a 0.4 co-efficient of variation, a cluster size of 600 adults, a design effect of 1.18 and an expected 85% participation rate.

TB screening procedures

Eligible individuals provided a written informed consent, followed by a symptom screening interview and CXR to identify presumptive TB cases; those with TB suggestive symptoms or an abnormal CXR suggestive of TB, or both. TB suggestive symptoms included cough of any duration, drenching night sweats or history of haemoptysis in the previous 12 months. Field CXR images were read by the field medical officer and TB suggestive signs included lung opacities, cavitation, fibrosis, pleural effusion and calcification. CXR images were retrospectively assessed centrally by an experienced radiologist for quality and validity. Post-survey blinded CXR analysis of radiological-bacteriological mismatches was done by the radiologist to determine the final CXR result. Information on TB risk factors was then collected from presumptive cases.

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Laboratory processes

All presumptive TB cases were requested to submit one spot and one morning sputum sample for bacteriological confirmation. Participants unable to have CXRs taken due to refusal, pregnancy, ill health or physical challenges were also requested to provide sputum samples. Sputum samples were sent to the National Microbiology Reference Laboratory (NMRL; Harare, Zimbabwe) for decontamination with 4% sodium hydroxide, sputum fluorescence microscopy and two sputum cultures, one in Mycobacteria Growth Indicator Tube (MGIT) and one on Löwenstein-Jensen (LJ) slope.

All acid-fast bacilli (AFB) smear-positive samples were re-tested using the Xpert® MTB/RIF assay (Cepheid, Sunnyvale, CA, USA) to ascertain the presence of *Mycobacterium tuberculosis* (MTB). MGIT (in BACTECTM MGIT™ 960 machines; BD, Franklin Lakes, NJ, USA) and LJ cultures were incubated at 37°C for up to 42 days. Cultures were positive if there was growth on LJ slope, in MGIT or both. Positive MTB growth was confirmed using the MPT64 antigen test (Standard Diagnostics Inc, Gyeonggi-do, Republic of Korea) and Ziehl-Neelsen stain. All culture-positive samples were tested using Xpert to determine rifampicin resistance. The NMRL participated in external quality assurance programmes provided by TB reference laboratories in Belgium, Uganda and South Africa.

Bacteriologically confirmed TB disease was defined as 1) sputum smear-positive with confirmed MTB using Xpert, and/or 2) culture-positive, regardless of sputum smear status. Participants who were either sputum smear-negative/culture-negative or smear-positive/Xpert-negative (possibly non-tuberculous mycobacteria [NTM]) were classified as not having TB disease.

Data management and analysis

Data were entered using CSPro v6.1 (US Census Bureau, Suitland-Silver Hill, MD, USA; and ICF International, Fairfax, VA, USA) and analysed using Stata v13.1 (StataCorp, College Station, TX, USA) and SPSS v20 (IBM Corp, Armonk, NY, USA) according to internationally recommended guidance.[6,7] Briefly, for adjusted prevalence, we applied logistic regression with robust standard errors to account for the clustered design, multiple imputations for participants with missing laboratory results and inverse probability weighting for differentials in participation in the survey by age, sex and cluster.[6] Risk factors for presumptive TB disease were evaluated using univariate and multivariable random effects logistic regression models.

Ethical considerations

The survey obtained approval from the Medical Research Council of Zimbabwe, Harare, Zimbabwe. All participants provided written informed consent prior to enrolment.

RESULTS

Of the 85,636 enumerated individuals, 43,478 (51%) were eligible and 33,736 (78%) participated in the survey (Figure 1). Participation rate varied by cluster from 47% to

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100%. Rural participants accounted for 73% and females 58%; the median age was 33 years (interquartile range [IQR] 23–47).

Symptom and chest X-ray screening results for participants

Among the 33,736 participants, 33,694 (99%) received symptom screening. Of these, 1,833 (5%) reported at least one TB symptom. The most common TB symptom was cough of any duration (n = 1,415, 77%), followed by drenching night sweats (n = 560, 31%) and haemoptysis any time in the past 12 months (n = 310, 17%). Among those with cough of any duration, 1,068 (76%) had cough of >2 weeks, 344 (24%) had cough of <2 weeks and 3 (0.3%) had a cough of undefined duration. Among the 33,736 eligible participants, 32,500 (96%) had a CXR taken, and of these, 3,431 (11%) were identified as presumptive TB cases.

A total of 5,820 participants were eligible to submit sputum samples (Figure 1), 1,833 (31%) by symptom screen, 3,431 (59%) by CXR screen, 628 (11%) by both screening methods and 1,184 (20%) based on CXR exemption and symptom screen-negative. Of these, 5,705 (98%) submitted at least one sputum sample. These included 5,705 (100%) spot and 5,441 (95%) morning sputum samples.

Bacteriological results

Among the 5,705 participants with at least one sputum sample, a total of 206 (4%) were smear-positive (Figure 1). Of these, 23 (11%) cases were MTB confirmed on Xpert. Of the 5,705 participants, respectively 1,074 (19%), 4,608 (81%) and 23 (0.4%) had positive, negative and contaminated cultures. Of the positive cultures, 110 (10%) were MTB and 964 (90%) were NTM. Of the 110 MTB culture-positive cases, 21 (19%) were smear-positive. In all 21 smear-positive/MTB culture-positive participants and in an additional two, one smear-positive/ NTM culture-positive and one smear-positive/culture-negative, MTB was confirmed using Xpert. A total of 112 bacteriological cases were identified with five (4%) smear-negative/MTB culture-positive cases being excluded from analysis due to suspected laboratory cross contamination. Among the 107 bacteriological survey cases, 23 (21%) were smear-positive and 13 (12%) had Xpert rifampicin resistance.

TB prevalence estimates

Overall, the adjusted prevalence of smear-positive TB and bacteriologically confirmed TB disease among individuals aged ≥15 years was respectively 82/ 100,000 population (95% CI 47–118) and 344/ 100,000 population (95% CI 268–420) (Table 1). Prevalence in men (413/100,000 population, 95% CI 303–523) was higher than in women (288/100,000 population, 95% CI 189–386). Adjusted TB prevalence by age group peaked at 35–44 years and ≥65 years, and prevalence did not vary between geographic strata. When the adjusted prevalence was accounted for pulmonary TB in children and extrapulmonary TB, the all-ages, all-forms nationwide TB prevalence was 275/100,000 population (95% CI 217–334).

Screening results among survey cases

Respectively 39 (36%) and 93 (87%) of the 107 TB survey cases were identified using the symptom and CXR screening tools. Among the 84 smear-negative/ culture-positive cases,

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respectively 24 (29%) and 70 (83%) were identified using the symptom screen and CXR. Of the 107 survey cases, 68 (64%) reported no TB symptoms, including 58 (69%) of smear-negative/ culture-positive cases (Figure 2). Cough of >2 weeks was the most (n = 28, 26%) frequently reported TB symptom among the survey cases.

Risk factors for TB

Of the 5,820 presumptive TB cases, 5,717 (98%) responded to the TB risk factors assessment. The results of univariate and multivariate logistic regression are shown in Table 2. In the multivariate analysis, the odds of having TB were greatest among former tobacco smokers (adjusted odds ratio [aOR] 2.96, 95% CI 1.54–5.70) and those with TB contact within 2 years (aOR 2.29, 95% CI 1.25–4.18) when compared to never smokers and non-TB contacts, respectively.

DISCUSSION

In the first-ever, nationally representative, population-based TB prevalence survey in Zimbabwe, we found that TB prevalence remained high (275/ 100,000 population) in the ART era. We observed a high prevalence of bacteriologically confirmed TB disease (344/100,000 population) with a lower smear-positive TB disease prevalence (82/100,000). CXR screening performed better than symptom screening in identifying both presumptive and confirmed TB cases. Independent TB risk factors were tobacco smoking, history of TB contact, and the 25– 34 and 35–44 years age groups.

Participation in the survey (78%) was lower than the expected 85% and compared to Zambia (2013 2014) and Malawi (2013–2014) which reported >80%;[8,9] however, participation was comparable with that in Tanzania (2011–2012) (77%).10 The low participation was attributed to population hypermobility and the relatively long duration (minimum 2 weeks) between census enumeration and invitation to survey participation.

Relative to prior WHO estimates (409/100,000 population in 2013) based on TB notification data,[1] TB prevalence has decreased in Zimbabwe. This apparent decline may be real due to scale-up of national ART coverage, or may be due to biases in prior estimates based on a paper surveillance system which was prone to under- or over-reporting. TB prevalence estimates for Southern Africa have been reported for Malawi (2013–2014) and Zambia (2013–2014) which were respectively 452 and 638/ 100,000 population for bacteriologically confirmed TB disease and respectively, 220 and 319/100,000 population for smear-positive TB disease.[8,9] We observed a low smear-positive TB disease prevalence relative to bacteriologically confirmed TB disease, most probably due to the poor sensitivity of smear microscopy compared to culture. With 68% of TB-HIV co-infected patients in 2014 in Zimbabwe,[11] the paucibacillary nature of HIV-associated TB may have contributed to the low smear-positive TB disease prevalence. Alternatively, the observed low smear-positive TB disease prevalence against a higher smear-positive notification rate of 155/100,000 population in 2014 may indicate successful TB control strategies. However, the national TB control programme (NTP) was anchored on smear microscopy, which might have over-estimated TB notification rates given that in this survey, a large proportion of smear-positive cases were NTM.

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More males than females had TB, consistent with findings from other TB prevalence studies.[8–10,12–16] Biological and behavioural differences (increased risk to infection exposure in males through smoking and mining exposures) have been suggested to explain the disparity.[17] Consistent under-recognition of these disparities[18–20] raises a critical need to prioritise men in TB control activities. Peak prevalence rates were observed in those aged 35–44 and ≥65 years. In Tanzania (2011–2012), Pakistan (2010–2011) and Vietnam (2006–2007),[10,14,16] prevalence peaked among those aged ≥65 years, and was attributed to reactivation of TB due to waning immunity. On the contrary, younger age groups were the most affected in Kenya (2015–2016), Zambia (2013–2014) and Malawi (2013–2014).[8,9,13] The peak prevalence in the 35–44 years age group in our survey could be explained by the HIV epidemic in Zimbabwe, which has the highest prevalence within that age group among both males and females,[21] although this is disproportionately higher among females (17%) than males (11%).[22]

TB prevalence was comparable for rural and urban areas. However, programmatic data show lower TB case notifications in rural than in urban areas, probably due to reduced and delayed access to TB diagnostics, such as primarily seeking care from traditional healers.[23] Improved access to diagnostics and synergistic partnership between the NTP and traditional healers may be key in controlling TB in rural areas, as has proven effective in South Africa and Gambia.[24,25]

Most TB cases were smear-negative, lacking typical signs and symptoms of TB, and could have been missed cases under programmatic settings. Consistent with findings from TB prevalence surveys,[9] this survey showed that cough may not be sensitive enough to screen for TB disease, particularly for smear-negative TB.[26] Smoking and history of TB contact are well-known TB risk factors,[27,28] and were associated with TB in this survey. The small proportion of presumptive TB cases with history of TB contact in our survey suggests that programmatic identification of undiagnosed TB cases in this population is likely to be more cost effective using active case-finding approaches.[29]

Since 2014, the survey results enabled the NTP to identify critical gaps in TB control and led to the successful implementation of several interventions: 1) the replacement of smear microscopy by Xpert as the initial diagnostic test, 2) increased roll-out of Xpert instruments, 3) the incorporation of CXR into the TB screening algorithm, 4) the installation of digital CXRs in district hospitals, and 5) active case-finding using mobile units fitted with digital CXRs and Xpert instruments in 2017 in low-notifying/high-burden districts among high risk population groups, mainly people living with HIV, refugees, contacts of TB patients, miners and prisoners.[30,31] The successes of these interventions, including the success of ART roll-out and TB preventive therapy, may have contributed in part to the removal of Zimbabwe from the list of 30 high TB burden countries. Interventions in the pipeline include real-time monitoring of Xpert instruments use and reporting of results, enhanced public-private partnerships and integrated approaches to HIV-TB care.

The major strength of the survey was the use of Xpert to confirm smear-positive TB disease. Our study had some limitations. First, the study was confined to an adult population with pulmonary TB and excluded paediatric and extrapulmonary TB. Thus, an all-ages, all-forms

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TB disease prevalence estimate was achieved through imputation methods. Second, we were unable to estimate the prevalence of HIV-TB co-infections due to lack of data on HIV status.

In conclusion, although lower than WHO estimates, the prevalence of TB disease in Zimbabwe remains high. To achieve a more accurate evaluation of TB prevalence in Zimbabwe, better TB case detection strategies and tools are needed. Incorporating Xpert testing or an equivalently performing molecular diagnostic tool in the second national TB disease prevalence survey should improve case detection.

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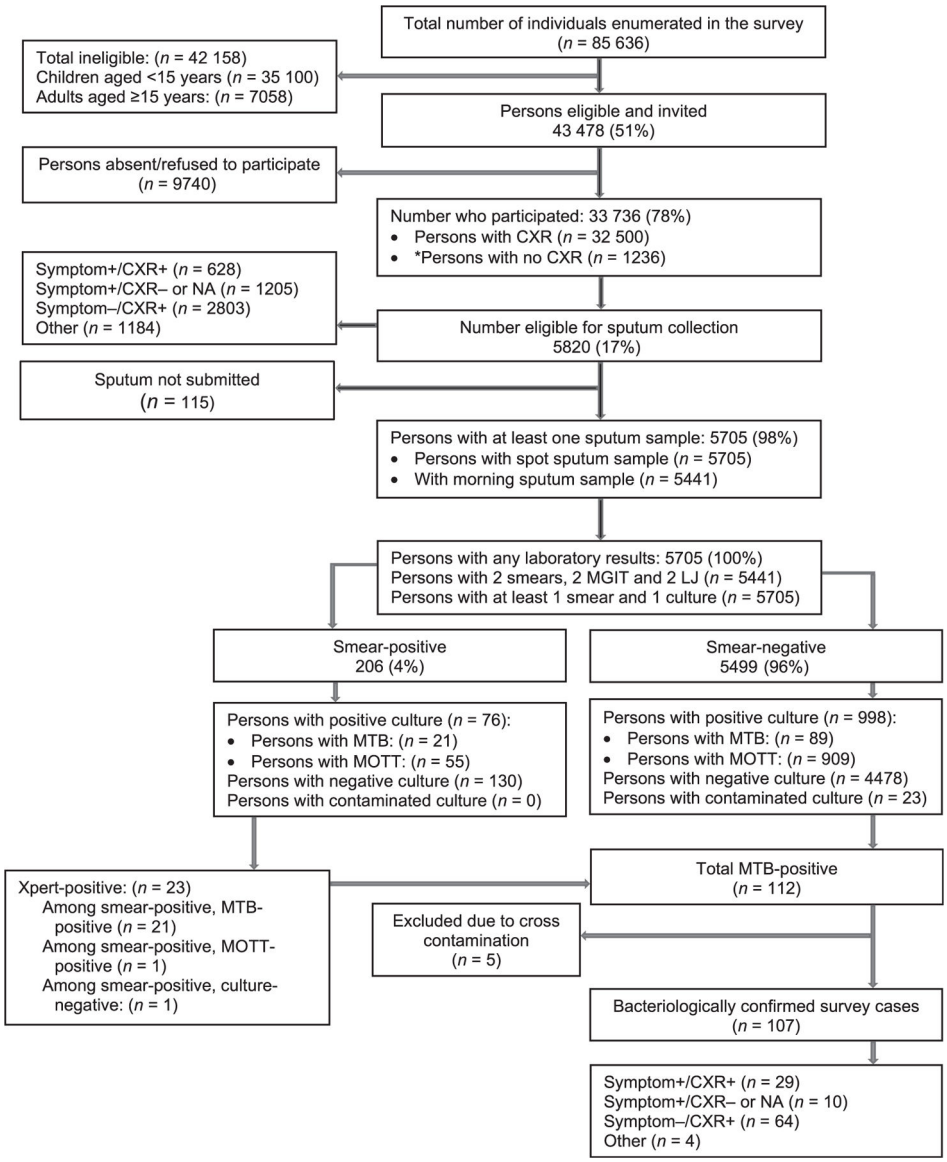

Figure 1.

Flow chart of participants screened for TB in the national TB prevalence survey of Zimbabwe, 2014. * Cases exempted from or missing CXR. CXR = chest X-ray; + = positive; – = negative; NA = not applicable; MGIT = Mycobacteria Growth Indicator Tube; LJ = Lowenstein-Jensen; MTB = *Mycobacterium tuberculosis*; MOTT = mycobacteria other than tuberculosis.

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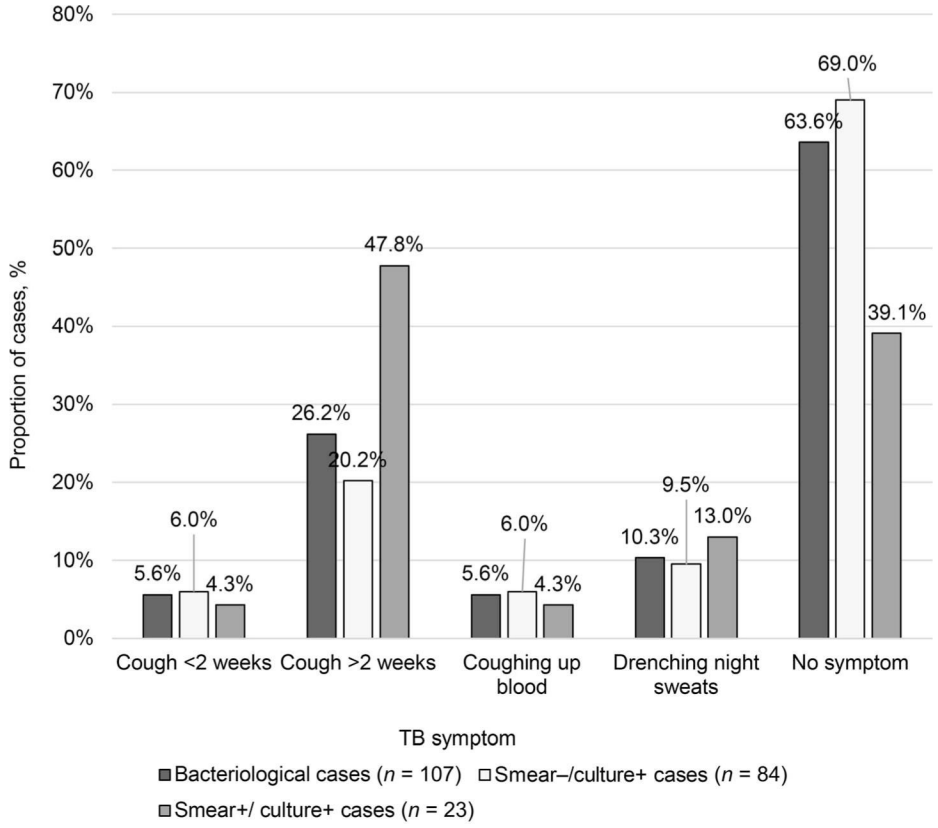

Figure 2.

Proportion of TB suggestive symptoms among the bacteriologically confirmed TB survey cases. + = positive; – = negative.

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Table 1

Adjusted prevalence (per 100,000 population) for smear and bacteriologically confirmed PTB disease among adults ≥15 years in Zimbabwe

		Smear-positive PTB		Bacteriologically confirmed PTB	
Characteristic	**Total *N***	***n***	**Adjusted prevalence (95% CI)**	***n***	**Adjusted prevalence (95% CI)**
Total	33,736	23	82 (47–118)	107	344 (268–420)
Sex					
Male	14,195	13	103 (43–163)	58	413 (303–523)
Female	19,541	10	65 (27–104)	49	288 (189–386)
Age group, years					
15–24	4,297	5	52 (21–131)	11	129 (68–245)
25–34	3,342	8	138 (70–274)	28	373 (255–546)
35–44	2,720	5	85 (34–215)	30	546 (371–804)
45–54	1,419	3	75 (23–248)	10	310 (168–570)
55–64	1,149	1	35 (5–277)	13	490 (276–869)
≥65	1,268	1	47 (7–341)	15	547 (310–962)
Strata					
Rural	24,639	14	64 (36–114)	76	337 (243–431)
Urban	9,097	9	116 (38–193)	31	355 (228–482)

PTB = pulmonary TB; CI = confidence interval.

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Table 2

Logistic regression analysis for factors associated with PTB

Variable	Total (*n* = 5,717) *N*	PTB (*n* = 106) *n*	No PTB (*n* = 5,611) *n*	cOR (95% CI)	aOR (95% CI)
Age group, years					
15–24	992	11	981	1	1
25–34	1,166	28	1,138	2.19 (1.09–4.43)	1.84 (0.90–3.77)
35–44	1,118	29	1,089	2.37 (1.18–4.78)	1.85 (0.90–3.80)
45–54	732	10	722	1.24 (0.52–2.92)	0.95 (0.39–2.30)
55–64	684	13	671	1.73 (0.77–3.88)	1.30 (0.56–2.98)
≥65	1,025	15	1,010	1.32 (0.61–2.90)	1.13 (0.50–2.53)
Sex					
Female	3,376	49	3,327	1	1
Male	2,341	57	2,284	1.69 (1.15–2.49)	1.17 (0.69–1.97)
Strata					
Rural	4,401	76	4,325	1	1
Urban	1,316	30	1,286	1.33 (0.89–2.04)	1.32 (0.83–2.10)
Current TB contact					
No	5,457	96	5,361	1	1
Yes	257	10	247	2.26 (1.16–4.39)	1.81 (0.91–3.61)
TB contact in the past 2 years					
No	5,407	92	5,315	1	1
Yes	307	14	293	2.76 (1.55–4.90)	2.29 (1.25–4.18)
Past TB treatment history					
No	4,945	87	4,858	1	1
Yes	771	19	752	1.41 (0.85–2.33)	1.18 (0.71–1.99)
Smoking status					
Never	4,517	65	4,452	1	1
Current	819	25	794	2.16 (1.35–3.44)	2.30 (1.18–4.50)
Former	380	16	364	3.01 (1.72–5.26)	2.96 (1.54–5.70)
Alcohol consumption					

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Variable	Total (n = 5,717)	PTB (n = 106)	No PTB (n = 5,611)		
	N	*n*	*n*	cOR (95% CI)	aOR (95% CI)
No	4,509	77	4,432	1	1
Yes	1,204	29	1,175	1.42 (0.92–2.19)	0.83 (0.47–1.50)
Work in dusty environments					
No	1,948	33	1,915	1	1
Yes	3,752	73	3,679	1.15 (0.76–1.74)	1.08 (0.69–1.70)
Previous HIV test					
No	1,960	30	1,930	1	1
Yes	3,754	76	3,678	1.33 (0.87–2.04)	1.19 (0.75–1.89)

PTB = pulmonary TB; cOR = crude odds ratio; CI = confidence interval; aOR = adjusted OR.