Final report

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Prevalence of latent TB infection among South African gold miners

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Executive summary

Background

Tuberculosis (TB) has largely contributed to illness and death among gold miners in South Africa for decades. TB control is failing in spite of a well-implemented TB control programme that not only meets international targets but also already has an active case-finding programme.

This failure of TB control is largely attributable to the escalating HIV epidemic, as is being seen elsewhere in sub-Saharan Africa. A proof of concept, cluster randomised study among South African gold miners (henceforth referred to as the parent study) has commenced. The parent study, as part of SIMRAC Health 701 (Effect of community-wide isoniazid preventive therapy on tuberculosis among South African gold miners), aims to demonstrate that community-wide isoniazid preventive therapy (IPT) in addition to the standard TB control programme is an effective way of rapidly reducing the burden of TB infection and disease, and can improve TB control in high HIV prevalence areas. Modelling suggests that, if effective, this strategy would need to be combined with other sustained measures in order to maintain long term control of TB. Such measures could include reducing silica dust exposure and continuous targeted IPT for those at high risk of developing TB.

The effectiveness of community-wide IPT as a strategy to reduce TB incidence is likely to be influenced by the prevalence of latent TB infection (LTBI) among the mining workforce. Determining the prevalence of LTBI, as part of the preparation for the parent study, will help us to understand the results of the parent study, and assists with modelling the predicted effect of community-wide TB preventive therapy on TB incidence in the long term.

Objectives

The objectives of this study were to determine, in a representative sample of gold miners:

- The prevalence of LTBI as measured by tuberculin skin tests (TST).
- Factors associated with a positive test for LTBI (defined as TST response ≥ 10mm).
- Prevalence of radiological TB disease and silicosis (defined as ILO score ≥ 1/0).

Methods

The results of tuberculin skin tests (TST) among individuals in two age groups (less than 30 years; 30 years or more) as a proxy for intensity of exposure to TB infection were compared. Factors associated with a positive test for LTBI (defined as TST response ≥ 10mm) were investigated, and measured the prevalence of radiological TB disease and silicosis (defined as ILO score ≥ 1/0) in this sample. This study was supported as part of Health 701.

Results

520 participants were recruited to the study, and read 429 TSTs (105/130 <30y; 324/390 ≥30y). Using the mirror method our estimated prevalence of LTBI is high at 89%, and similar to a 1968 survey of new recruits to a gold mine in Orange Free State. A high percentage (45.5%) of HIV-positive participants had a zero TST response compared to 13% and 13.5% with zero TST response in the HIV-negative and status-unknown participants respectively. In participants with TST >0, there was no significant difference between size of response by either HIV status or age stratum. The strongest risk factors associated with a positive TST were HIV status and current underground work. Participants who worked underground had four times the risk of a positive TST compared to those who never worked underground. The prevalence of silicosis was high. The prevalences were 3.8%, 3.9%, 8.1% and 10.3% in shafts 1, 2, 3 and 4 respectively.

Conclusion

This is the first study to describe the prevalence of and risk factors for LTBI among a representative sample of in-service gold miners. The prevalence of LTBI among gold miners is very high and supports the need to evaluate community-wide IPT to control TB among miners, who not only have a very high prevalence of latent TB infection, but also have prevalent risk factors for TB, namely HIV infection and silicosis. These results are consistent with the high prevalence of LTBI found among new recruits (Laing 1968) and silicotic gold miners (Cowie 1994) and Chinese slate workers (MRC 1992). The strong association between positive test for LTBI and current underground work in this study suggests that dust and silica exposure, which are known risk factors for pulmonary TB, may also be risk factors for LTBI. This has not previously been described. The high prevalence of silicosis confirms the findings of previous studies and supports the need for the Mine Health and Safety Council's silicosis programme. The lack of small TST responses (1-5 mm) indicative of exposure to environmental mycobacteria in a setting with a high incidence of non-tuberculous mycobacterial disease has not been described before.

There was no association between a positive test for LTBI and age, and this may be explained by high levels of exposure to TB in this population before entering employment, and residual confounding by HIV status. A Tanzanian study investigating TST responses in TB patients found that although HIV co infected patients were more likely to demonstrate anergy to TST, the distribution of positive response sizes did not differ by HIV status.[6] Our findings, in a sample of healthy gold miners, are similar. Due to sensitivity around HIV testing within the mining industry the study was redesigned to exclude HIV testing and collecting blood specimens for new tests of LTBI. As a result the study was limited in its ability to accurately estimate the prevalence of and determine risk factors for LTBI.

Recommendation

Isoniazid TB preventive therapy targeted to known HIV-infected individuals and silicotics should be introduced as standard of care in accordance with the Department of Health and Mine Health and Safety Council guidelines.

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1 Introduction

1.1 Background

Tuberculosis (TB) has been a major cause of illness and death among gold miners in South Africa for decades. TB incidence has risen, despite a well-run TB control programme, and now exceeds 4000 per 100,000 employees per year. TB control is failing in South African gold mines, despite a well-implemented TB control programme that not only meets international targets but also already has an active case-finding programme. This failure of TB control is largely attributable to the escalating HIV epidemic, as is being seen elsewhere in sub-Saharan Africa. There is no good evidence to guide the choice of further intervention in this situation.

Mathematical modelling (SIMRAC Health 701) suggests that community-wide TB preventive therapy with isoniazid (IPT) could have a rapid impact on TB incidence. Community-wide preventive therapy has been used in the past in situations of epidemic tuberculosis, but previous work has not clearly established whether the observed reduction in TB incidence was attributable to this intervention. There is unlikely to be support for such a radical strategy without good evidence of its effectiveness, especially now that the HIV epidemic has transformed the epidemiology of TB. Among workforces in South African gold mines antiretroviral therapy (ART) implementation commenced in 2002, and if community-wide preventive therapy is not formally evaluated, it may be hard to separate out the effect of these two interventions.

A proof of concept, cluster randomised study among South African gold miners, SIMRAC Health 701 Phase 2 (Effect of community-wide isoniazid preventive therapy on tuberculosis among South African gold miners, henceforth referred to as the parent study) has commenced which aims to demonstrate that community-wide TB preventive therapy in addition to the standard TB control programme is an effective way of rapidly reducing the burden of TB infection and disease, and can improve TB control in high HIV prevalence areas. If the intervention is effective in reducing TB incidence at the population level, this strategy could be applied to other communities with high TB transmission, such as settings with high-density living and /or working conditions, especially where a large proportion of the population have increased susceptibility to TB, particularly due to HIV infection. Three gold mining companies, AngloGold, Gold Fields and Harmony, are participating in this study, in three geographical regions (Gauteng, North West and Free State provinces) in South Africa.

The modelling also suggests that:

- TB transmission among miners is more intense than occurs in equivalent general populations, or non-silica exposed miners
- Because of the high transmission rates, an unusually high proportion of miners are latently infected with TB

- HIV infection greatly increases the risk of progression to TB disease following TB infection. In the context of high TB transmission rates and a high percentage of miners latently infected with TB infection, the impact of the HIV epidemic has been profound.

In the pre-HIV era, the prevalence of latent TB infection, as measured by tuberculin skin test (TST), among new recruits[1] and miners with silicosis[2] was very high. The prevalence of latent TB infection in the current era of HIV is unknown. Determining the prevalence of latent TB infection is of importance to the mining industry because it adds to the understanding of TB epidemiology among miners, provides a measure of the effectiveness of the current TB control programme and provides further insights into which strategies, in addition to the directly-observed treatment short course (DOTS) strategy, may be effective in reducing TB rates.

The effectiveness of community-wide TB preventive therapy as a strategy to reduce TB incidence is likely to be influenced by the prevalence of latent TB infection among the mining workforce. Multi drug resistant (MDR) and the recent emergence of extensively drug-resistant (XDR) TB also have potential implications for the effectiveness of this strategy. Determining the prevalence of latent TB infection helps us to understand the results of the parent study, and assists with modeling the predicted effect of community-wide TB preventive therapy on TB incidence in the long term.

As part of the preparation for the parent study it is important to determine the prevalence of latent TB infection. The results of TSTs among individuals in two age groups (less than 30 years; 30 years or more) as a proxy for intensity of exposure to TB infection was compared.

1.2 Project outputs

1.2.1 Primary output

To determine the prevalence of latent TB infection (LTBI) as measured by tuberculin skin test (TST) among gold miners.

1.2.2 Secondary outputs

i) To determine whether the prevalence of latent TB infection differs significantly by age group (<30 versus ≥30 years) as a proxy for duration of exposure to high risk of TB transmission.

ii) To investigate factors associated with a positive test for latent infection.

1.3 Enabling outputs and timetable

1.3.1 Preparation phase

This comprised of:

- Obtaining ethical approval.

- Appointment and training of staff.
- Selecting participating shafts.
- Obtaining stakeholder approval and participation.
- Determining the sampling frame.

1.3.2 Enrolment and study procedures

This comprised of:

- Obtaining individual informed consent.
- Administration of questionnaire.
- Obtaining and reading the most recent standard or mini chest radiograph for silicosis and old or active TB.
- Administering and reading tuberculin skin test.
- Data capture from medical records.

1.3.3 Data analysis and write up

This comprised of:

- Integrating data sets.
- Conducting data analysis,
- Writing up the final report and communicating results to stakeholders.

1.3.4 Study and data management

This comprised of:

- Conducting monthly project meetings.
- Providing quarterly reports.
- Developing case report forms.
- Developing databases, double entry and verification of data.

Table 1-1 Summary of Enabling Outputs and date of completion

Enabling output	Date completion
Preparation phase	25/11/2005
Enrolment and study procedures	08/06/2006
Data analysis and write up	22/09/2006
Study and data management	09/06/2006

1.4 Sample size calculation for prevalence of latent TB infection

The sample size required was estimated as 400 individuals. Below is an outline of the assumptions used and justifications for the sample size.

There were no existing data on the prevalence of TB infection among a representative sample of mineworkers, but among mineworkers with silicosis (who are likely to be older and to have had greater than average exposure to TB infection) prior to the HIV epidemic, 99% had a positive TST.

With 400 individuals, the prevalence of latent TB infection can be estimated with the following degree of precision:

Prevalence of latent TB infection	*Precision*
95%	± 2.2%
90%	± 3.0%
80%	± 3.9%
70%	± 4.5%
60%	± 4.8%

To look at the prevalence of latent TB among individuals with high and low intensity of exposure to TB (as measured by duration of employment, and using age as a proxy), individuals in the age group <30 years were over-sampled, so that 30% of individuals included in the study were aged less than 30 years. Overall this would give 120 individuals aged less than 30 years and 280 individuals aged 30 years or more.

1.5 Accomplishment of project outputs

All primary and secondary outputs were fully accomplished.

1.6 Structure of the report

Chapter 2 details the methodology of the study, chapter 3 describes the results. General discussion and recommendations follow in chapters 4 and 5 respectively.

2 Research methodology

2.1 Study site and design

This study was a cross-sectional survey and was conducted in four gold mineshafts in Gauteng province. These shafts belong to the mining companies participating in the parent study. Two of the shafts are from AngloGold Ashanti, one from GoldFields and one from Harmony. Each mining house has health service facilities that provide comprehensive health care for employees, including a primary health clinic (PHC) attached to each shaft, and an Occupational Health Centre (OHC). The OHC provides surveillance for occupational diseases by conducting annual fitness examinations for employees which includes a screening chest radiograph.

Study participants were invited to attend shaft offices located near the crush area for the questionnaire survey, and the PHC for the tuberculin skin test. Where space in the crush area was limited a mobile facility was used.

2.2 Study population

Individuals were randomly selected from the Human Resource (HR) databases of the participating mineshafts and invited to participate in the study using the parading system.

2.2.1 Inclusion criteria

All employees working at the participating mine shafts and/or living in the participating mine hostel were eligible to participate.

2.2.2 Exclusion criteria

- Individuals who were currently receiving treatment for TB were excluded from the study of the prevalence of latent TB infection, but were invited to enrol in the remainder of the study.
- Individuals who were for any other reason unable to take part in the study of prevalence of latent infection (unwilling to undergo TST, unwilling or unable to return after 72 hours to have the TST read) were not enrolled in the part of the study investigating the prevalence of latent TB infection, but were invited to enrol in the remainder of the study.
- Individuals who declined permission to access their previous screening chest radiograph or medical records, or declined to take part in the questionnaire were excluded from the entire study.

2.3 Study procedures

Individuals who agreed to take part underwent the following procedures:

2.3.1 Questionnaire survey and examination for BCG scar

Examination by a trained research nurse for presence of a BCG scar and administration of a standardized questionnaire which covered the following information (Appendix 1):

- Demographic information such as, age, sex, place of residence, site of employment, duration of employment, employer (mining company or contracting company) current occupation, place of residence, and contact details to enable arrangement of a follow-up visit for reading of TST.
- History of prior or current TB treatment, or treatment for non-tuberculous mycobacterial (NTM) disease.
- Participant's HIV status based on self-report.
- History of prior or current isoniazid preventive therapy (IPT).
- History of prior or current ART.
- Presence or absence of symptoms suggesting active TB (new or worsening cough, cough for longer than two weeks, night sweats, weight loss).
- History of BCG vaccination.

Any individual with symptoms suggesting active TB disease (new or worsening cough, cough for longer than two weeks, night sweats or weight loss) was offered referral to the routine mine health services for further evaluation.

2.3.2 Tuberculin skin test

All participants who consented to and were eligible underwent tuberculin skin test using the Mantoux method with 2 tuberculin units of RT-23 in Tween-80 (Statens Serum Institute, Denmark). Skin reactions were read 3 days later as the maximum transverse diameter of the induration expressed in millimeters, using a digital caliper. Tests were administered and read by specially trained staff, who underwent quality control procedures during the course of the study.

Standard criteria for defining a positive TST were used:

- A TST result of > 10mm in an HIV-uninfected individual.
- In an individual who was known to be HIV-infected a TST result of > 5mm was considered positive irrespective of BCG scar presence.

2.3.3 Reading of most recent occupational screening chest radiograph

For all participants, the most recent (within the past 18 months) mini or standard sized routine occupational health screening chest radiograph was obtained and read by a trained member of the study team to determine:

- The radiological prevalence of previous TB.
- The radiological prevalence of active TB.

- The prevalence of silicosis, and grade according to a modified International Labour Organization (ILO) scoring system. The reader recorded the frequency of small opacities using the ILO 12-point scale, i.e. from 0/- to 3/+. Shape and size of small opacities were not recorded.

2.3.4 Review of medical records

Trained research staff reviewed the participant's medical records to check for agreement between information provided by the participant and information in the record concerning previous TB, current medication, HIV status, prior or current ART or IPT. All mine employees are issued with unique identification numbers (industry and company numbers) that facilitate access to individual health services records.

2.4 Criteria used for defining HIV status

Due to sensitivity around HIV testing within the mining industry the study was redesigned to exclude HIV testing and collecting blood specimens for new tests of LTBI, which is required to interpret TST results. HIV status was therefore based on self-report and information from the medical records..

- HIV-positive status was defined as participant self-reporting positive status, or a record of positive status in the medical records.
- HIV-negative status was defined as participant self-reporting negative status, which was confirmed by record of negative status in the medical records.
- HIV-unknown status was assigned to those who did not fit into either of the aforementioned categories.

2.5 Information systems

A study number was assigned to each participant and recorded on case report forms (CRFs). Locator information was recorded separately to assist with recalling individuals to have their TST read. Staff were trained in administering questionnaires and the completion of CRFs before the start of the study. CRFs were checked for completeness, accuracy and legibility immediately after completion, and any queries resolved prior to the participant departing.

Data recorded on CRFs were double entered by dedicated data encoders into a Microsoft Access study database. Range and consistency checks were implemented, and any data queries were submitted to the study coordinator for resolution against source documentation.

2.6 Ethical considerations

2.6.1 Ethical approval

The study was approved by the research ethics committees of the University of Kwa Zulu Natal, Durban, South Africa and the London School of Hygiene and Tropical Medicine, London, England. All study participants gave written informed consent to the study procedures and were provided with an information sheet about the study (Appendices 2 and 3).

2.6.2 Confidentiality

Confidentiality of data was strictly maintained. All Aurum research staff sign a confidentiality agreement on employment. Completed CRFs are stored in locked cabinets in a secure access-restricted room accessible only to authorized study staff and investigators. Forms containing locator information and identifiers are stored securely and separately from CRFs. CRFs and the main study databases used study numbers only, so that no loss of confidentiality would be possible should unauthorized access occur. Study databases are password protected. Master data files are password protected and access granted only to authorized investigators, staff, and monitors.

2.7 Statistical methods

Data were analysed using STATA software version 8.

The proportion of individuals with a positive TST and the 95% confidence intervals are reported overall and by age group (<30 years and ¤ 30 years) as a surrogate for intensity of exposure to TB infection.

The mirror method[5] was used to provide an additional estimate of the prevalence of latent TB infection. This is a method to estimate the prevalence of latent TB infection in populations where there may be small diameter TST responses due to environmental mycobacteria. The sensitivity of TST (ability to correctly identify individuals with TB infection) has been studied in TST surveys of TB patients and of healthy individuals living in areas with little exposure to environmental bacteria. In these surveys TST reaction sizes were found to follow an almost normal distribution. The mirror method assumes that:

- The specificity of TST (i.e. ability to correctly identify individuals without TB infection) at the mode (most frequent TST reaction size) is 100%.
- The number of participants with a TST response size greater than the mode is equal to the number of participants with a TST response less than the mode, i.e. TST reaction sizes follow a normal distribution. Doubling the number of participants with a reaction size greater

than the mode and adding this to the number of people with a reaction size at the mode should therefore estimate the number of participants with LTBI.

Differences in categorical variables were determined using a chi-squared or Fisher's exact test as appropriate. Differences in quantitative variables between two groups were assessed using the Wilcoxon rank sum test.

A logistic regression model was used to assess the association between risk factors (HIV status, silicosis status, age category, history of prior TB and NTM disease, history of BCG vaccination, presence of BCG scar, history of IPT and ART) and a positive TST result (defined as a TST response of ¤ 10mm). Results are reported as unadjusted and adjusted odds ratios with 95% confidence intervals.

The multivariable model was based on variables chosen from the univariable analysis which were associated with positive TST with p values of less than 0.2. A priori, age was included in the model because the the sampling scheme was stratified by age. Results were adjusted for age, current frequency of underground work, history of IPT and HIV status. The significance of each risk factor was assessed using the likelihood ratio test having adjusted for other variables in the model.

3 Results

3.1 Participation

1065 (83.5%) of the 1276 individuals who were randomly selected were invited to participate in the study. 600 (56.3%) of those who were invited were seen by a research nurse prior to the consenting process, and 520 (86.7%) of those seen consented to participate.

Recruitment from a shaft was terminated when the estimated target sample size for each age stratum had been reached; hence not all individuals who had been randomly selected were invited to participate.

Table 3.1 summarizes recruitment data for each shaft and demonstrates that there are slight differences between the shafts in terms of recruitment. These were due to differences between the shafts in HR procedures for inviting individuals, which were beyond our control. Overall, once an individual saw a research nurse who takes consent, uptake was consistently high.

Table 3-1 Summary of recruitment for each shaft

Shaft		**Invited (% of those selected)** **N (%)**	**Seen[1] (% of those invited)** **N (%)**	**Consented (% of those invited)** **N (%)**	**Consented (% of those seen)** **N (%)**
Shaft 1	Selected (N=250)	210 (84)	151 (71.9)	131 (62.3)	131 (86.8)
Shaft 2	Selected (N=280)	276 (98.6)	141 (51.17)	130 (47.1)	130 (92.2)
Shaft 3	Selected (N=375)	289 (77.1)	166 (57.4)	148 (51.2)	148 (89.2)
Shaft 4	Selected (N=371)	290 (78.2)	142 (49)	111 (38.3)	111 (78.2)
TOTAL	**Selected N=1276**	**1065 (83.5)**	**600 (56.3)**	**520 (48.8)**	**520 (86.7)**

[1]Defined as having seen the research nurse prior to consenting process

80 people who saw the research nurse declined to participate, and the main reasons given for declining consent were (percentages are given as a percentage of the 80 people who declined):

- 22 (27.5%): Will return another time.
- 18 (22.5%): Suspicious.
- 13 (16.3%): In a hurry.
- 9 (11.3%): Need time to think or consult.
- 6 (7.5%): Not interested.
- 12 (15%): Other reason

3.1.1 Comparison of participants with individuals who did not take part from the random selection

Shift, age, area of work (surface or underground), and gender data were not available for contract workers at shaft 4. Shift data was not available for some individuals at shaft 3. Hence it was difficult to interpret an overall comparison of participants with individuals who did not take part (non-participants).

Some differences were seen within each shaft between participants and non-participants, and are summarized in Table 3.2.

- In shaft 1, surface and contract workers were more likely to not participate (p=0.01)
- In shaft 2, surface workers, contract workers and individuals aged <30 years were more likely to not participate (p<0.05)
- In shaft 3 contract and night shift workers were more likely to not participate (p<0.05)

Table 3-2 Differences between participants and non-participants by shaft

Shaft		Participants N (%)	Non- participants N (%)	P-value
Shaft 1	**Area of work:**			
	Underground	127 (97)	105 (88.2)	0.012
	Surface	4 (3.1)	14 (11.8)	
	Employment status:			
	Employee	110 (84)	83 (69.7)	0.007
	Contractor	21 (16)	36 (30.3)	
Shaft 2	**Age stratum:**			
	<30	40 (30.8)	66 (44)	0.023
	¤30y	90 (69.2)	84 (56)	
	Area of work:			
	Underground	117 (90)	111 (74)	0.001
	Surface	13 (10)	39 (26)	
	Employment status:			
	Employee	112 (86.2)	104 (69.3)	0.001
	Contractor	18 (13.9)	46 (30.7)	
Shaft 3	**Shift:**			
	Day	104 (70.3)	125 (57.6)	0.019
	Night	11 (7.4)	35 (15.4)	
	Other	5 (3.4)	11 (4.8)	
	Not known	28 (18.9)	56 (24.7)	
	Employment status:			
	Employee	134 (90.5)	189 (83.3)	0.046
	Contractor	14 (9.5)	38 (16.7)	

3.2 Demographics of participants

520 participants were recruited, 130 (25%) aged less than 30 years and 390 (75%) aged 30 years and above. Median age was 26 years in the <30 years age stratum, and 43 years in the ¤30y age stratum.

Table 3-3 Demographics of participants by shaft

	Shaft 1 N (%)	Shaft 2 N (%)	Shaft 3 N (%)	Shaft 4 N (%)	Overall N (%)
Overall no. consented	131 (25)	130 (25)	148 (28.5)	111 (21.3)	**520**
Gender:					
Male	129 (98.5)	124 (95.4)	148 (100)	107 (96.4)	**508 (97.7)**
Female	2 (1.5)	6 (4.6)	0	4 (3.6)	**12 (2.3)**
Age strata:					
<30	33 (25.2)	37 (28.5)	46 (31.1)	14 (12.6)	**130 (25)**
30y+	98 (74.8)	93 (71.5)	102 (68.9)	97 (87.4)	**390 (75)**
Median age (years):					
<30	26	27	25.5	27	**26**
≥30	43	41	41	53	**43**
Age category (years):					
19-29	33 (25.2)	37 (28.5)	46 (31.1	14 (12.6)	**130 (25.0)**
30-39	29 (22.1)	37 (28.5)	38 (25.7)	14 (12.6)	**118 (22.7)**
40-49	56(42.8)	48 (36.9)	45 (30.4)	14 (12.6)	**163 (31.4)**
≥50	13 (9.9)	8 (6.2)	19 (12.8)	69 (62.2)	**109 (21.0)**
Country of origin:					
South Africa	69 (52.7)	62 (47.7)	73 (49.3)	53 (47.8)	**257 (49.4)**
Lesotho	35 (26.7)	32 (24.6)	22 (14.9)	7 (6.3)	**96 (18.5)**
Mozambique	16 (12.2)	26 (20)	33 (22.3)	47 (42.3)	**122 (23.5)**
Other	11 (8.4)	10 (7.7)	20 (13.5)	4 (3.6)	**45 (8.7)**
Ethnic group:					
Black	128 (97.7)	126 (96.9)	146 (98.7)	108 (97.3)	**508(97.7)**
White	3 (2.3)	4 (3.1)	2 (1.4)	3 (2.7)	**12 (2.3)**
Duration of employment (years):					
Median	16	13	12	30	**16**
Range	<1-34	1-36	<1-36	<1-42	**<1-42**
Ever worked underground:					
Yes	129 (98.5)	123 (94.6)	147 (99.3)	111 (100)	**510 (98.1)**
No	2 (1.5)	7 (5.4)	1 (0.7)	0	**10 (1.9)**
Current frequency of underground work:					
≥Twice a week	128 (97.7)	117 (90.0)	146 (98.7)	107 (96.4)	**498 (95.8)**
Never	3 (2.3)	13 (10.0)	2 (1.4)	4 (3.6)	**22**
Employment status:					
Employee	105 (80.2)	109 (83.9)	134 (90.5)	88 (79.3)	**436 (83.9)**
Contractor	26 (19.9)	21 (16.2)	14 (9.5)	23 (20.7)	**84 (16.2)**
Occupational level [1]:					
Job group 3-8	122 (93.1)	122 (93.9)	142 (96)	103 (92.8)	**489 (94)**
Union rep / Artisan	4 (3.1)	3 (2.3)	1 (0.7)	4 (3.6)	**12 (2.3)**
Official	5 (3.8)	5 (3.9)	5 (3.4)	4 (3.6)	**10 (3.7)**
Residence:					
Hostel	91 (69.5)	84 (64.6)	109 (73.7)	47 (42.3)	**331 (63.7)**
House	34 (26.0)	43 (33.1)	35 (23.7)	47 (42.3)	**159 (30.6)**
Other	6 (4.6)	3 (2.3)	4 (2.7)	17 (15.3)	**30 (5.8)**

[1] Occupational level by self report

In keeping with the demographics of the mining industry, most participants were black males of South African origin, lived in hostels and were in job group 3-8. Most participants were employees (rather than contractors) and worked underground at least twice weekly.

The demographics of participants according to shaft are shown in Table 3.3. Significant differences in demographics were found between the shafts. Participants from shaft 4 were older, only 12.6% participants were in the <30y age stratum (p=0.005), and the median age in ⌑30y age stratum was 53 years. Participants from shaft 4 were less likely to live in a hostel (p<0.001), and a higher proportion (43%) were from Mozambique (p<0.001). In keeping with participants being older, the median duration of employment was also greater in this shaft (p<0.001).

The demographics of participants according to age stratum are summarised in Table 3.2.b. Compared to those in the 30y+ age stratum, participants in the <30y age stratum are significantly more likely to be female, contract workers, South African in origin, and to live in a house rather than a hostel.

Table 3-4 Demographics of participants by age stratum

Characteristic	**<30 years N=130**		**⌑30y N=390**		**P-value**
	Number	**(%)**	**Number**	**(%)**	
Gender:					
Male	120	(92.3)	388	(99.5)	<0.001
Female	10	(7.7)	2	(0.5)	
Country of origin:					
South Africa	93	(71.5)	164	(42.1)	
Lesotho	9	(6.9)	87	(22.3)	<0.001
Mozambique	26	(20.0)	96	(24.6)	
Other	2	(1.5)	43	(11.0)	
Ethnic group:					
Black	126	(96.9)	382	(98.0)	0.506
White	4	(3.1)	8	(2.1)	
Duration of employment (years):					
Median duration	2		19		<0.001
Range	<1-13		1-42		
Ever worked underground:					
Yes	126	(96.9)	384	(98.5)	0.277
No	4	(3.1)	6	(1.5)	
Current frequency of underground work:					
≥Twice a week	125	(96.2)	373	(95.6)	1.0
Never	5	(3.9)	17	(4.4)	
Employment status:					
Employee	97	(74.6)	339	(86.9)	0.001
Contractor	33	(25.4)	51	(13.1)	
Occupational level:					
Job group 3-8	124	(95.4)	365	(93.6)	0.844
Union rep / Artisan	2	(1.5)	10	(2.6)	
Official	4	(3.1)	15	(3.9)	
Residence:					
Hostel	64	(49.2)	267	(68.5)	<0.001
House	63	(48.5)	96	(24.6)	
Other	3	(2.3)	27	(6.9)	

3.3 Prevalence of latent TB infection as measured by tuberculin skin test

3.3.1 Distribution of TST responses

429 TST responses were read in total. The number of TSTs read by shaft, age stratum and HIV status were:

- 112 from shaft 1, 108 from shaft 2, 113 from shaft 3 and 96 from shaft 4.
- 105 in the <30y age stratum, and 324 in the ≥30y age stratum.
- 115 in HIV-negative participants, 33 in HIV-positive participants, and 281 in participants whose HIV status was not known.

Figure 3.1 is a histogram demonstrating the overall distribution of TST response. 16% of participants had zero TST response. In participants with a TST response greater than zero the responses follow a normal distribution. There were very few readings below 5 mm in size, which one might expect due to exposure to environmental mycobacteria.

Figure 3-1 Overall distribution of TST responses

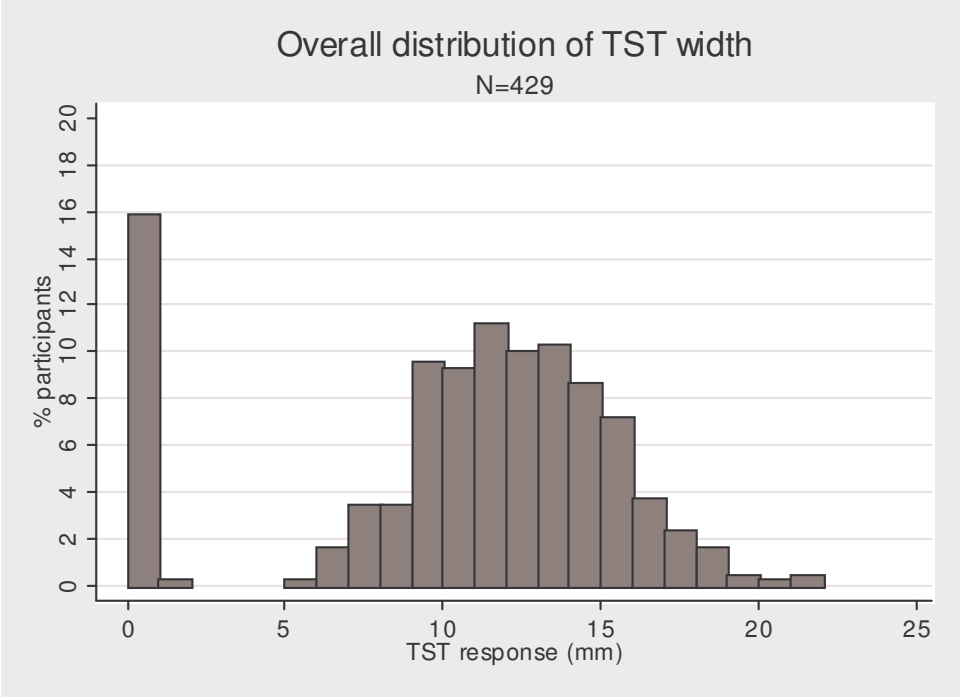

Figure 3.2 shows the distribution of TST response for each HIV status category. A high percentage (45.5%) of HIV-positive participants had a zero TST response compared to 13% and 13.5% with zero TST response in the HIV negative and HIV unknown categories respectively. The distributions of TST responses for HIV-negative and HIV-unknown participants were similar.

Figure 3-2 Distribution of TST response by HIV status

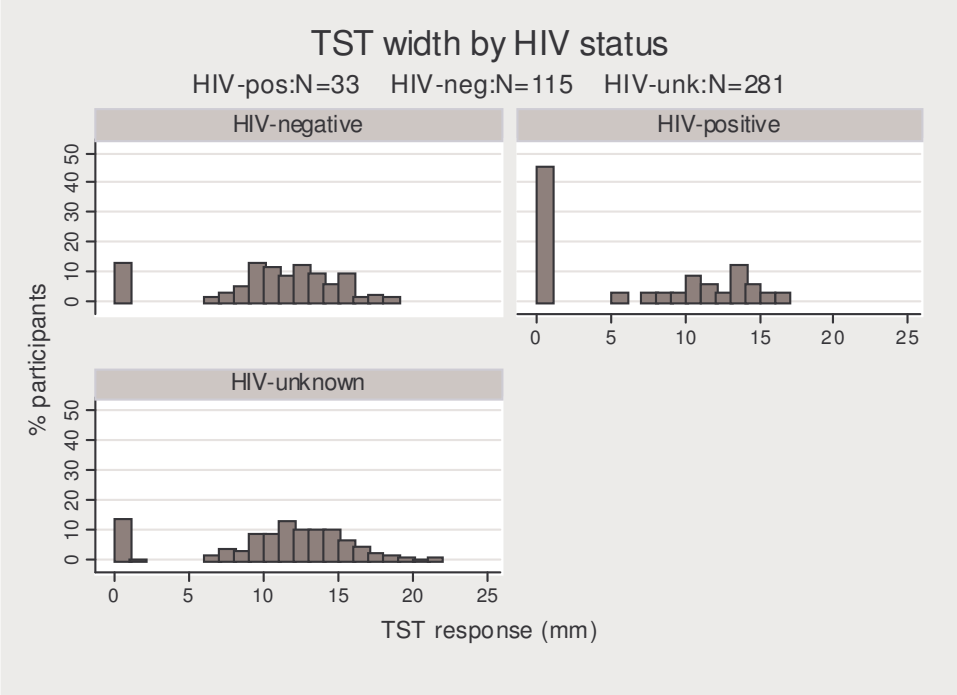

Figure 3.3 shows the distribution of TST responses for each age stratum. The distributions of TST response were similar for both age strata.

Figure 3-3 Distribution of TST response by age stratum

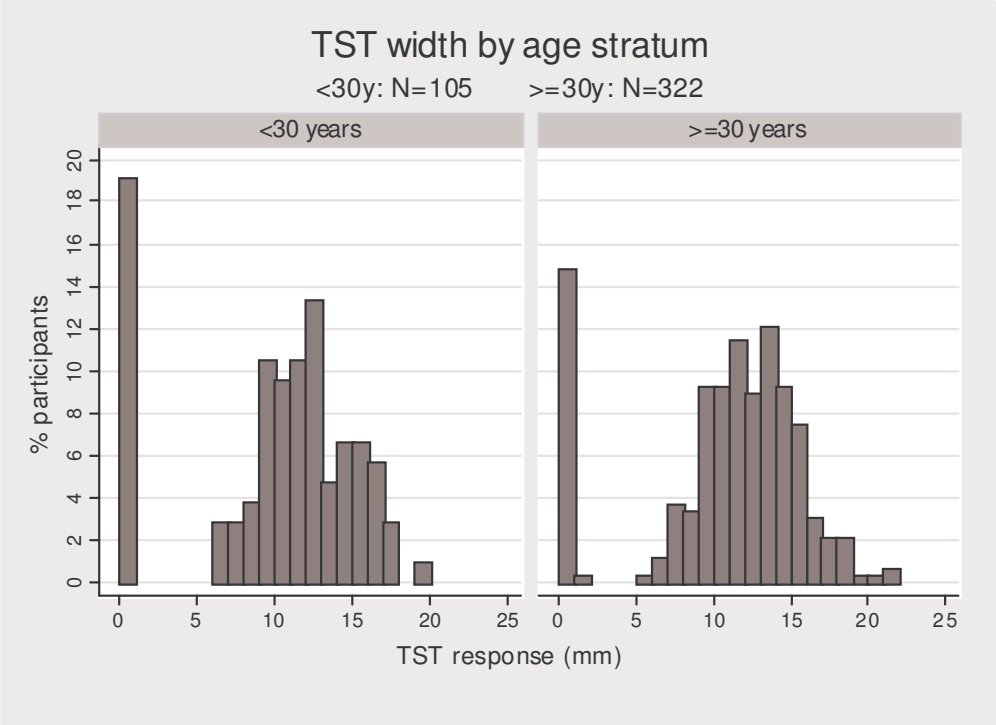

Table 3.5 summarises the TST response data. 68 (15.9%) of all participants had zero TST response. In all participants with a TST response greater than zero, mean (SD), mode and range for TST response were 12.35 mm (2.95), 12 mm and 1.4-21.83 respectively. In participants with TST >0, there was no significant difference between size of response by either HIV status or age stratum.

Table 3-5 Summary of TST responses

Characteristic		Zero TST response N=68		TST response >0mm N=361		MEAN (SD)	RANGE	P-value (ANOVA)
		Number	(%)	Number	(%)			
HIV status	Positive	15	(45.5)	18	(54.6)	11.84 (2.75)	5.82-16.17	0.284
	Negative	15	(13.0)	100	(87.0)	12.03 (2.75)	6.86-18.36	
	Unknown	38	(13.5)	243	(86.5)	12.52 (3.04)	1.4-21.83	
Age strata	<30y	20	(19.1)	85	(81.0)	12.12 (2.90)	6.3-19.09	0.406
	≥30y	48	(14.8)	276	(85.2)	12.42 (2.97)	1.4-21.83	

Mean, SD, range and p-value are based on those with TST response >0mm.

3.3.2 Prevalence of positive TST response and LTBI

Table 3.6 demonstrates the prevalence of positive TST using different criteria overall.

The prevalence of LTBI can be estimated using cut-points recommended by the CDC[3] of ¤ 5mm for positive TST in HIV-positive individuals, and ≥ 10 mm in HIV-negative individuals. Applying differential criteria for positive TST by HIV status for all participants, the prevalence of LTBI was between 66.4% if we assumed that all HIV-unknown participants were HIV-negative and 77.6% if we assumed that all HIV-unknown participants were HIV positive.

Table 3-6 Prevalence of positive TST response using different criteria

Criterion	Number with positive TST	Prevalence of positive TST %	95% CI %
TST ≥ 5 mm	360	83.9	80.4-87.4
TST ≥ 10 mm	281	65.5	61.0-70.0
TST ≥ 15 mm	69	16.1	12.6-19.6
TST ≥ 5 mm for HIV-positive TST ≥ 10 mm for HIV-negative and HIV-unknown	285	66.4	61.9-70.1
TST ≥ 5 mm for HIV-positive and HIV-unknown TST ≥ 10 mm for HIV-negative	333	77.6	73.7-81.6
Mirror method for mode of 12mm	382	89.0	

Alternatively, using the mirror method[5] for a mode of 12 mm, which assumes that specificity of TST is 100% at the mode, the overall prevalence of LTBI was estimated to be 89%.

Table 3.7 demonstrates the prevalence of positive TST in each age stratum using different criteria. There was little difference in the prevalence between the age strata. Applying differential criteria for positive TST according to HIV status, as detailed above, the range for prevalence of LTBI in the <30y stratum was 61.0-73.3%, and in the ¤ 30y stratum was 68.2-79.0%. Using age strata of age <26y and age ¤ 26y and applying differential criteria for HIV status, there was again little difference in prevalence between the age strata. The ranges for prevalence of LTBI were 68.3-85.4% and 66.2-76.8% for <26y and ¤ 26y respectively.

Table 3-7 Prevalence of positive TST response using different criteria by age stratum

Criterion	Age stratum			
	< 30 years		¤ 30 years	
	Prevalence of positive TST %	95% CI %	Prevalence of positive TST %	95% CI %
TST ≥ 5 mm	81.0	73.3-88.6	84.9	81.0-88.8
TST ≥ 10 mm	61.0	51.5-70.4	67.0	61.8-72.1
TST ≥ 15 mm	16.2	9.0-23.4	16.1	12.0-20.1
TST ≥ 5 mm for HIV-positive TST ≥ 10 mm for HIV-negative and HIV-unknown	61.0	51.5-70.4	68.2	63.1-73.3
TST ≥ 5 mm for HIV-positive and HIV-unknown TST ≥ 10 mm for HIV-negative	73.3	64.7-81.9	79.0	74.6-83.5

3.4 Investigation of factors associated with a positive test for latent infection

Table 3.8 shows a univariable analysis of risk factors for a positive test (defined as TST response ¤ 10 mm) for LTBI. In the univariable analysis a positive TST was significantly associated with male gender, black ethnic origin, current frequency of underground work ¤ twice a week, history of INH PT, and negative or unknown HIV status.

Table 3-8 Risk factors for positive TST, defined as TST response ¤ 10mm: Univariable analysis of TST response

Risk factor		TST-POSITIVE N=281		OR	95% CI	P-value
	Category	**Prevalence**	**(%)**			
Shaft	Shaft 1	70/112	(62.5)	1.0		0.083
	Shaft 2	62/108	(57.4)	0.81	0.47-1.39	
	Shaft 3	81/113	(71.7)	1.52	0.87-2.66	
	Shaft 4	68/96	(70.8)	1.46	0.81-2.61	
Gender	Male	279/422	(66.1)	1.0		
	Female	2/7	(28.6)	0.21	0.04-1.07	0.045
Age category (years)	19-29	64/105	(61.0)	1.0		0.172
	30-39	67/98	(68.4)	1.38	0.78-2.47	
	40-49	81/132	(61.4)	1.02	0.60-1.72	
	≥ 50	69/94	(73.4)	1.77	0.97-3.23	
Age stratum (years)	< 30	64/105	(61.0)	1.0		0.262
	≥ 30	217/324	(67.0)	1.30	0.82-2.05	
Country of origin	South Africa	129/209	(61.7)	1.0		0.451
	Lesotho	57/82	(69.5)	1.41	0.82-2.44	
	Mozambique	69/101	(68.3)	1.34	0.81-2.21	
	Other	26/37	(70.3)	1.47	0.69-3.13	
Ethnic origin	Black	281/421	(66.8)			<0.001
	White	0/8				
Residence	Hostel	181/272	(66.5)	1.0		0.821
	House	83/131	(63.4)	0.87	0.56-1.34	
	Other	17/26	(65.4)	0.95	0.41-2.21	
Occupational level	Job group 3-8	269/407	(66.1)	1.0		0.225
	Union rep/Artisan	7/10	(70)	1.2	0.30-4.70	
	Official	5/12	(41.7)	0.37	0.11-1.18	
Ever worked underground	Yes	278/421	(66)	1.0		0.104
	No	3/8	(37.5)	0.31	0.07-1.31	
Current freq of underground work	≥ Twice a week	275/411	(66.9)	1.0		0.005
	<Twice a week	0/0	(0)			
	Never	6/18	(33.3)	0.25	0.09-0.67	
Duration of employment (years)	<10	90/139	(64.8)	1.0		0.068
	10-19	81/128	(63.3)	0.94	0.57-1.55	
	20-29	59/92	(64.1)	0.97	0.56-1.69	
	≥ 30	50/65	(76.9)	1.81	0.93-3.56	
	Not known	1/5	(20)	0.14	0.01-1.25	
Reported TB contact in last 1 year	Yes	38/59	(64.4)	1.0		0.913
	No	195/299	(65.2)	1.04	0.58-1.85	
	Don't know	48/71	(67.6)	1.15	0.56-2.39	
BCG scar	Present	175/266	(65.8)	1.0		0.875
	Absent	80/121	(66.1)	1.01	0.64-1.6	
	Indeterminate	26/42	(61.9)	0.85	0.43-1.66	
History of TB[1]	Yes	22/38	(57.9)	0.70	0.36-1.38	0.308
	No	259/391	(66.2)	1.0		
History of NTM[1]	Yes	0				
	No	0				
History of ART[1,2] **in HIV positive patients**	Yes	4/11	(36.4)	0.69	0.15-3.04	0.62
	No	10/22	(45.5)	1.0		
History of IPT[1,3]	Yes	7/15	(46.7)	0.45	0.16-1.26	0.13
	No	274/414	(66.2)	1.0		
Silicosis	Definite (≥ 1/1)	13/17	(76.5)	1.75	0.56- 5.47	0.595
	Possible (0/1;1/0)	5/8	(62.5)	0.90	0.21- 3.81	
	No silicosis (0/0)	260/400	(65)	1.0		
Previous TB on CXR	Yes	10/16	(62.5)	0.87	0.31- 2.45	0.799
	No	269/410	(65.6)	1.0		
Active TB on CXR	Yes	1/2	(50)	0.53	0.03- 8.46	0.652
	No	278/424	(65.6)	1.0		
HIV status	Positive	14/33	(42.4)	0.42	0.19-0.93	0.010
	Negative	73/115	(63.5)	1.0		
	Unknown	194/281	(69)	1.28	0.81-2.02	

[1]Self report or from medical records; [2]All participants with history of ART were confirmed HIV positive from self-report or medical records; [3]17/18 of the participants with history of IPT were also confirmed HIV positive.

Unadjusted and adjusted odds ratios for associations between current frequency of underground work, HIV status, and age category and positive TST are shown in the multivariable analysis in Table 3.9. After multivariable analysis only HIV status and current frequency of underground work remained significantly associated with a positive test for LTBI. HIV-negative participants were 2.5 times more likely than HIV-positive participants to have a positive TST. Participants whose current frequency of underground work was > twice a week were 4 times more likely than those who never worked underground to have a positive TST.

Table 3-9 Risk factors for positive TST, defined as TST response ¤ 10mm: Multivariable analysis of TST response (N=429)

Risk factor	Category	N	Unadjusted OR	Adjusted OR (95% CI)	P-value (likelihood ratio test)
Age category (years)	19-29 30-39 40-49 50+	105 98 132 94	1.0 1.38 1.01 1.77	1.0 1.45 (0.80-2.62) 1.17 (0.68-2.02) 1.83 (0.99-3.39)	0.22
Current frequency of underground work	>Twice a week Never	411 18	1.0 0.25	1.0 0.25 (0.09-0.71)	0.007
HIV status	Positive Negative Unknown	33 115 281	0.42 1.0 1.28	0.40 (0.18-0.91) 1.0 1.19 (0.74-1.9)	0.02

3.5 Prevalence of radiological TB disease and silicosis by cluster

Table 3-10 Prevalence of radiological TB disease and silicosis by cluster

	Shaft				P Value
	Shaft 1	Shaft 2	Shaft 3	Shaft 4	
	Prevalence (%)	Prevalence (%)	Prevalence (%)	Prevalence (%)	
Silicosis[1]	5/131 (3.8)	5/130 (3.9)	12/148 (8.1)	11/107 (10.3)	0.105
Previous TB	6/131 (4.6)	4/130 (3.1)	7/148 (4.7)	6/108 (5.6)	0.824
Active TB	3/131 (2.3)	0	1/148 (0.7)	0	0.173

[1]Silicosis score is missing for one participant from shaft 4

Chest radiographs were available for 517 participants. Table 3.10 demonstrates the prevalence of silicosis (defined as silicosis score ¤1/0), previous and active TB by shaft. Shafts 3 and 4 had a higher prevalence of silicosis of a clinically important magnitude although the differences were not statistically significant, most likely due to small numbers in each shaft. The prevalence of radiological TB disease did not differ by shaft, and the numbers involved were very small. The study was not designed to examine differences by shaft.

4 Discussion

4.1 Prevalence of LTBI

Our estimated prevalence of LTBI of 89% using the mirror method certainly justifies offering treatment of LTBI infection on the basis of likely individual benefit, in addition to the potential additional benefit of community wide TB preventive therapy. This high prevalence supports the need to evaluate community-wide IPT to control TB among miners, who not only have a very high prevalence of latent TB infection, but also have prevalent risk factors for TB, namely HIV infection and silicosis.

The criteria that are widely used for defining a positive TST are those recommended by the American Thoracic Society (ATS) and the CDC. These criteria are designed to identify individuals at greatest risk of developing TB disease, in order that they can benefit from preventive treatment for LTBI. Based on the sensitivity and specificity of TST and the prevalence of TB in different groups, three cut-points are recommended to define a positive TST, and therefore LTBI. A ¤ 5mm cut-point is recommended for individuals at highest risk for developing TB disease, i.e. those who have been recently infected and those with increased risk of developing active TB following infection, in particular HIV positive individuals. A ≥ 10mm cut-point is recommended for those with an increased probability of recent infection or with conditions other than HIV that increase the risk of developing active TB following infection. Finally, ≥ 15mm cut-point is recommended for individuals considered to be at low risk.[3, 4] Given that the purpose of these cut-points is to identify those at greatest risk of developing TB disease in order to ensure that they benefit from preventive treatment, it is debatable whether the same criteria should be used in epidemiological surveys to measure the prevalence of LTBI in different populations. The positive and negative predictive values of TST are determined not only by its sensitivity and specificity (specificity varies according to geographical differences in NTM exposure), but also by the prevalence of LTBI in the population tested. A recent study in the Netherlands used routinely available TST data in TB patients and in healthy non-BCG vaccinated individuals to estimate the predictive values of TST and to thereby establish cut-point values in this population.[14] Where feasible, this may be the best way to establish cut-points for prevalence surveys of LTBI.

A major limitation of the study is that it was not possible to perform HIV testing. However, as detailed in chapter 3, using the CDC recommended differential cut-points according to HIV status, it was possible to determine a range for prevalence of LTBI of between 66.4% and 77.6%. A 1968 South African TST survey of new employees in a gold mine in what was formerly known as Orange Free State found that 11.1% of new employees were tuberculin negative (Heaf reaction grade zero).[1] Negative or equivocal grade 1 Heaf reactions were highest in the age group less than or equal to 25 years. Multiple puncture tests are no longer recommended for epidemiological surveys, as they are less accurate. Although a Heaf reaction grade zero is not directly equivalent to TST

response ⌑ 10mm, our estimated prevalence of LTBI of 89% using the mirror method is very similar to the 1968 survey. There have, to our knowledge, been no published TST surveys in representative samples of African gold miners other than the aforementioned 1968 survey.

4.2 Risk factors for a positive TST (≥10mm)

In this study the strongest risk factors associated with a positive TST were HIV status and current underground work. HIV negative and HIV unknown participants were more than twice as likely to have a positive TST compared to HIV positive participants, and participants who worked underground had four times the risk of positive TST compared to those who never worked underground. These associations persist after adjusting for confounding factors. Studies in South African gold miners have shown that HIV infection, silicosis, older age, underground work, and dusty occupations such as drilling are strong risk factors for pulmonary TB disease (PTB).[10,12,13] A recent survey in gold miners aged over 37 years calculated cumulative respirable dust and quartz exposures for each participant and showed that PTB is significantly associated with dust and silica exposure independently of the presence of silicosis. This study recommended urgent dust control measures in addition to TB control measures to halt the epidemic of PTB in gold miners.[11]

Dust and silica exposure are risk factors for PTB, and the strong association in our study between positive TST and current underground work suggests that they may also be risk factors for LTBI. A recent cross sectional TST survey in urban communities in Cape Town found that a significantly higher proportion of current or ex-smokers had a positive TST (defined as response ⌑ 10 mm) when compared to people who had never smoked, however they did not test HIV status. Smoking history was not assessed in the study, and it would have been interesting to compare. The Cape Town study hypothesized that smoking increased risk of LTBI by its effects on pulmonary host defences. Perhaps silica and dust exposure have a similar effect in gold miners.

In contrast to what was expected, and Laing's[1] study, age was not shown to be a risk factor for positive TST in our study. This could be explained by high exposure to TB at a young age in our study population that predates employment in the mines; hence duration of employment does not contribute to the risk of LTBI. It could also be due to residual confounding by HIV-positive status, which is more common in a younger age group.

4.3 TST response

A positive TST suggests infection with *Mycobacterium tuberculosis* (M. TB). False positive results occur most commonly due to antigens in tuberculin which are shared by M. TB and NTM, but in general the larger the size of the response the more likely it is to be due to M. TB. BCG vaccination can also cause false positive results, but this effect does not last longer than 10 years,[15,16] and hence is unlikely to affect TST responses in this study. The ability to mount a response to the tuberculin skin test is dependent on a functioning immune system. Immunosuppression, for

example in HIV positive individuals can result in cutaneous anergy, which compromises their ability to a response to TST. This results in false negative reactions particularly as CD4 lymphocyte counts decline.[3, 4]

The most interesting features of the histogram demonstrating the overall distribution of TST (figure 3.1) are the high percentage of zero TST responses, and the lack of low-grade TST responses which might be expected to arise as a result of exposure to NTM. The incidence of NTM disease and exposure to NTM in gold miners is high, hence it is difficult to explain the absence of these small responses.[1, 7] Monitoring during the course of the study of the staff who read the TSTs indicated that TST placing and reading procedures were satisfactory.

Given the high incidence and intense transmission of TB within the South African gold mining industry it is highly unlikely that the high percentage of zero TST responses reflects an absence of LTBI in these individuals. 45% of participants who were HIV positive had a zero TST response. Amongst HIV negative and unknown participants, similar percentages (13%) had zero TST response. However in participants who did mount a response there was no significant difference in size of response by HIV status. These findings are similar to those of a study looking at TST responses in patients with tuberculosis in Tanzania. It found that 24.6% of the 451 HIV positive and 3.3% of the 540 HIV negative TB patients demonstrated anergy (defined as TST reaction of less than or equal to 2mm) and that, among individuals with a positive reaction, HIV status made little difference to the distribution of reactions sizes. This study showed the limited value of a lower cut-point of 5mm to diagnose LTBI in patients with both TB and HIV where loss of TST sensitivity was due to anergy.[6]

Studies have been done which in addition to TST also test for anergy using skin test antigens such as tetanus toxoid and mumps to which most healthy individuals in a population will have been sensitized. Anergy tests are not standardized nor recommended by the CDC as part of screening for LTBI.[3] A community based study in the USA followed up a cohort of HIV infected and uninfected at risk women prior to the introduction of highly active antiretroviral therapy. Anergy testing and TST were administered. It was found that 41% of the 1343 HIV positive women were anergic (defined as zero TST response to any antigen) compared to 12% of the 390 HIV negative women. In the HIV positive women tuberculin reactivity was strongly and directly associated with CD4 lymphocyte counts, a CD4 count of ¤ 200 cells/mm^3 was associated with higher prevalence of reactivity. 19% of the HIV positive women who had a positive TST response (¤ 5mm) did not respond to the other antigens, which indicates the limited value of anergy testing.[8]

4.4 Prevalence of radiological TB disease and silicosis

The prevalence of silicosis is high in the participating mineshafts, and although the numbers are small and the results do not reach statistical significance, there are differences of a clinically important magnitude in the prevalence of silicosis between the mineshafts that participated in the

study. The prevalences of silicosis in shafts 3 and 4 were at least double those in shafts 1 and 2. Given the PTB epidemic in gold miners, the high prevalence of silicosis confirms the findings of previous studies and supports the need for the Mine Health and Safety Councils silicosis programme.

4.5 Demographics

It is interesting to note that even within the same province there were variations in the characteristics of participants by shaft. This is most clearly demonstrated by shaft 4 participants who were older, more likely to come from Mozambique and less likely to live in a hostel. It is difficult to establish whether this reflects the general composition of the workforce in this shaft due to missing data fields in the HR database.

The demographics of participants also vary by age stratum, but it is difficult to know how to interpret this in terms of the TST responses. Participants in the <30y age stratum were more likely than those in ¤ 30y stratum to be female, contract workers, South African in origin and to live in a house.

4.6 Limitations

Individuals were randomly selected from the workforce to participate in the study to ensure a representative sample. Only 56% of those individuals we paraded to take part in the study actually saw one of the research nurses who took consent. Contract workers and surface workers were less likely to participate in the study. These are potential sources of bias that limit our ability to accurately estimate the prevalence of LTBI overall and in these groups. Lack of certain data fields in the HR databases limited our comparisons of participants and non-participants.

Due to sensitivity around HIV testing within the mining industry the study was redesigned to exclude HIV testing and collecting blood specimens for new tests of LTBI. HIV status was based on self-report and information in the medical records as a surrogate. For 66% of participants it was not possible to confirm HIV status, and HIV status was assigned as unknown for the purposes of analysis. As a result the study was limited in its ability to accurately estimate the prevalence of and determine risk factors for LTBI.

5 Conclusion

The prevalence of LTBI among gold miners is very high (89%) and supports the need to evaluate community-wide IPT to control TB among miners, who not only have a very high prevalence of latent TB infection, but also have prevalent risk factors for TB, namely HIV infection and silicosis. HIV infection and underground work were found to be risk factors for LTBI. The strong association

between a positive test for LTBI and current underground work in this study suggests that dust and silica exposure, which are known risk factors for pulmonary TB, may also be risk factors for LTBI.

6 Recommendation

Isoniazid TB preventive therapy targeted to known HIV-infected individuals and silicotics should be introduced as standard of care in accordance with the Department of Health and Mine Health and Safety Council guidelines.

7 References

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