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Alexander M. Jordan	Date

Prevalence and Risk Factors of Tuberculosis Disease in South African Correctional Facilities in 2015

By

Alexander M. Jordan
MPH

Global Epidemiology

_____

Kenneth Castro, MD, FIDSA
Committee Chair

_____

Laura Podewils, PhD
Committee Member

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By

Alexander Jordan

B.S.E.H.

University of Georgia

2012

Thesis Committee Chair: Dr. Kenneth G. Castro, MD, FIDSA

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Prevalence and Risk Factors of Tuberculosis Disease in South African Correctional Facilities in 2015

Author: Alexander M. Jordan[1]

[1]Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, Georgia, USA

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ABSTRACT

Background: There is a lack of quality evidence pertaining to TB disease and its risk factors in sub-Saharan African prisons, the existing data indicate an epidemic of TB in prisons that far exceeds and likely serves to intensify the epidemic of TB in the general African population.

Methods: This is a secondary analysis of data collected during programmatic mass screening for TB conducted by the Aurum Institute and South African Department of Correctional Services in South African Correctional Facilities from January 2-December 18, 2015. A total of 31,668 inmates were screened for TB using self-reported symptoms and digital radiography (CAD). Inmates presenting with self-reported symptoms of fever, cough, unexplained weight loss, or heavy night sweats and/or chest X-ray abnormalities were asked to provide sputum for TB testing with GeneXpert MTB/RIF (GXP). Digital CXR abnormalities were assessed by human radiologists and those with a reading of 'Definite Pulmonary TB' were classified as positive for TB disease. HIV testing was conducted for all consenting inmates. Bivariate and multivariate logistic regression models were used to assess demographic and clinical factors associated with newly diagnosed TB disease.

Results: The overall prevalence rate of TB disease was estimated to be 2,653/100,000. TB prevalence rates differed between facilities and ranged from 933/100,000 to 6,240/100,000. Regression analysis indicated that the importance of symptoms as a predictor of TB disease may be dependent on HIV status, with symptoms being more predictive of TB disease in HIV negative inmates. Previous TB was associated with increased odds of newly diagnosed TB in inmates infected with HIV. In those known to be HIV negative, previous TB, self-reported symptoms, and increased age were associated with increased odds of newly diagnosed TB disease.

Discussion: This analysis reveals a high burden of TB disease in South African prisons. Our prevalence estimates are the first known to be reported for many of the facilities in our analysis. Our regression results provide evidence for future interventions to prevent and reduce TB disease in correctional facilities. This study provides evidence that routine TB and HIV screening should be adopted in South African correctional facilities.

Keywords: TB, tuberculosis, risk factors, prisons, South Africa

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Background

Tuberculosis (TB) disease in humans is caused by infection with *Mycobacterium tuberculosis* (*Mtb*). Mtb can infect the lungs (pulmonary) and other sites of the body (extra pulmonary). TB has been treatable and curable for decades but continues to cause extraordinary morbidity and mortality throughout the world[1]. TB was declared a global public health emergency in 1993[2]. In 2015, an estimated 10.4 million people became ill with TB disease and 1.4 million people died from TB disease[1]. Around 11% of TB cases in 2015 were HIV positive, with 0.4 million of the TB deaths occurring in those infected with HIV. An estimated 480,000 TB disease cases were infected with TB strains resistant to the first line drugs isoniazid and rifampin (multidrug-resistant TB; MDR-TB). The vast majority of the global incidence of TB disease lies in a limited number of countries that have been designated as 'high burden'.

Globally, progress has been made in reducing TB disease. TB mortality has been almost halved since 1990; from around 30/100,000 to 15/100,000 in 2015.[3]. It is estimated that TB disease prevalence was reduced from around 300/100,000 in 1990 to 174/100,000 in 2015. According to the World Health Organization (WHO) Global TB Report 2015 The Millennium Development Goal (MDG 6-Target 8) to halt and reverse TB incidence (compared to 1990) was achieved globally in all 6 WHO regions[1]. The expansion of a standardized approach to TB diagnosis and treatment cured an estimated 36 million people between 1995 and 2008 and saved an estimated 6 million individuals from death[4]. Central to the effort to drive down the global TB burden is the internationally recommended Directly Observed Treatment-Short Course (DOTS) strategy.[5] This strategy consists of 5 components; political and financial commitment, diagnosis by quality ensured sputum-smear microscopy, standardized short-course TB treatment under direct observation, regular supply of quality TB drugs, and standardized recording and reporting. New diagnostic platforms such as Cepheid's GeneXpert-MTB/RIF® (GeneXpert) assay have increased access to rapid, point of care diagnostics in many countries[6]. GeneXpert testing uses

nucleic acid amplification of sputum samples and allows for detection of TB disease as well as detection of resistance to the first line TB drug rifampicin. Globally, 3,763 GeneXpert machines had been obtained for public sector use at the end of 2014. The number of GeneXpert test cartridges used has also increased dramatically in recent years, from 550,000 in 2011 to 4.8 million in 2014[3]. Optimistically, the World Health Organization's new End TB strategy calls for a 95% reduction in TB deaths and a 90% reduction in incidence by 2035 (using 2015 numbers as baseline)[7]. The strategy to meet these goals is based on meeting the 90-90-90 targets, which are to reach at least 90% of all people with TB, at least 90% of key populations, and to achieve at least 90% treatment success[8]. The End TB Strategy is a continuation and intensification of the WHO's Stop TB Strategy, which aimed to halt and reverse the global TB pandemic as well as to halve TB prevalence and mortality by 2015 (linked with Millennium Development Goal 6). The new and more ambitious targets for global TB are also consistent with the 2015 United Nations' Sustainable Development Goals (SDGs)**.**

Despite the relative success in the last 2 decades, evidence suggests that the global decline in TB incidence has plateaued in recent years[9]. Between 2000 and 2014, the global incidence of TB decreased by an average of 1.5% per year, an insufficient rate of decline to meet the Stop TB Strategy's predetermined targets[8]. While the goal of halting the global TB pandemic was met globally, the goal to halve prevalence and mortality was not met by 2015 in the African or European Regions. Notably, 7 of 9 African high-burden countries reporting national data to the WHO in 2015 did not meet the 50% prevalence and mortality targets[3]. Around 1.5 million people still die annually from TB disease and TB has now surpassed HIV/AIDS as the top infectious killer of humans[8]. The End TB strategy aims to increase the rate of decline in TB incidence worldwide by recommending specific intervention packages to countries that focus on country-specific drivers of TB incidence[7].

Prevalence and Risk Factors of TB Disease in South African Correctional Facilities

The slow progress in driving down TB rates in sub-Saharan Africa is due in large part to the high prevalence of HIV/AIDS in most sub-Saharan nations[4]. Globally, a small percentage (5-15%) of those infected with TB will progress to symptomatic TB disease. However, those infected with HIV are 26 times more likely to progress to disease once infected with *Mtb*[3]. TB infection of those with HIV/AIDS can also accelerate the progression of AIDS and reduce the efficacy of antiretroviral therapy (ART)[10]. Going into 2016, the WHO recommended intensification of TB prevention, diagnosis, and treatment interventions (including ART) in order to prevent TB transmission and mortality in those with HIV[3]. The reduction of TB prevalence in Europe has been hindered by high rates of MDR-TB, especially in Eastern European nations[1].

The End TB strategy is composed of 3 pillars which focus on improving TB prevention and care, enhancing social and political policies to allow for broad engagement of communities and implementing partners, and intensified research and innovation[8]. Within the TB prevention component of this strategy, high risk populations are outlined as a critical area on which to focus prevention efforts. Expert consensus derived from numerous studies and systematic reviews has recommended that the TB prevention community consider certain demographic and clinical factors to be associated with TB. These include HIV infection, undernutrition, smoking, diabetes, silicosis, indoor air pollution, and alcohol abuse. The importance of each of these risk factors is region specific and may be determined by the presence of unknown factors. Early detection and treatment of populations who have a higher prevalence of these risk factors such as healthcare workers, prisoners, drug addicts, homeless individuals, migrants, refugees, and other populations which may have poor access to healthcare has been recommended as a way to reduce global TB incidence and mortality[4].

In order to meet the global targets of the End TB Strategy, critical knowledge gaps must be addressed: among these is the extent of the TB burden in correctional facilities.

Prevalence and Risk Factors of TB Disease in South African Correctional Facilities

TB in Prisons

There are approximately 10 million people currently detained worldwide, including pre-trial detainees.[11]. Prisons can function as reservoirs and amplifiers of the TB pandemic, as they serve to congregate individuals from disadvantaged sub-populations of society and subsequently facilitate prolonged contact between these individuals as well as prison staff and visitors.[12].

In the USA in 2014, 4.3% of TB cases in those aged 15 years or older were individuals who were incarcerated[13]. While the number of cases among inmates in the USA has declined more or less steadily since 1993, the percentage of all TB cases aged 15 years or older who were incarcerated has remained the same.

Studies have shown varying estimates for the risk for TB disease in prisons relative to the risk of TB in the general population. A USAID review of data from the Eastern European Union and Central Asia, Indonesia, Kazakhstan, Zambia, Malawi, and Tanzania estimated that TB incidence in prisons is 5-70 times higher than TB incidence in the community, using national prevalence as the 'community' estimate[11]. In 2006, a survey of TB control in Europe showed that prisons in Western and Eastern Europe have an average notification rate within prisons 17 times higher than that of the general population with rates generally increasing from West to East[14]. The high prevalence of TB observed in prisons is thought to be due to the association of incarceration with many other known risk factors for TB disease including HIV infection, intravenous drug use, homelessness, and mental illness. Furthermore, prison settings often facilitate the transmission of TB via inadequate ventilation systems, overcrowding, poor nutrition, poor healthcare, and inadequate TB control and case detection[15]. The WHO further specifies inadequate TB treatment regimens, drug shortages, inadequate laboratory services, and ineffective linkage between

national TB programs and prison health services, and inadequate case detection and research as contributing to the high levels of TB and MDR-TB in European Prisons[16].

The WHO Regional Office for Europe (WHO-Europe) has urged that effective TB prevention and DOTS must be implemented in prisons in order to prevent spread both within prisons and to the surrounding communities[16]. This recommendation is based upon evidence of the following:

- TB transmission is not contained by boundaries or walls.
- High levels of TB in prisons can have a significant impact on TB incidence in nearby communities due to mixing of civilians, prisoners, and prison staff.
- Poor living and health conditions that are common in many prisons facilitate the spread of TB.
- The risk of MDR-TB and/or TB/HIV coinfection is high in prisons.
- Governments have a duty to protect prisoners by providing access to health care at least equivalent to that available to the general community.

The WHO-Europe recommends that further research must be conducted that examines factors that may be associated with transmission of TB disease in prisons.

In 2009, the United States Agency for International Development (USAID), the Tuberculosis Coalition for Technical Assistance (TCTA), and International Committee of the Red Cross (ICRC) published updated guidelines for TB control in prisons[17]. These guidelines elaborated on 5 factors that characterize the spread of TB in prison settings:

- **Prisons receive TB** through intake of prisoners who come from areas with high rates of TB and poor health care and TB prevention.
- **Prisons concentrate TB** through overcrowding and poorly designed ventilation systems.

- **Prisons disseminate TB** through prisoner release and prisoner transfers combined with poor detection and treatment of TB cases.
- **Prisons worsen TB** by increasing the likelihood of an individual developing risk factors for TB disease such as malnutrition, drug addiction, HIV infection, and interrupted treatment for TB or HIV.
- **Prisons Export TB** to the outside community via contact between contagious prisoners and prison staff or visitors as well as upon release if TB disease went undiagnosed or if TB treatment is interrupted upon release [17].

TB in Prisons Globally

A number of studies have shown that TB infection and disease within prisons can serve as a source of infection for the surrounding community. A systematic review conducted by Baussano et al. in 2010 assessed the estimated incidence of TB in prisons from 19 studies from Spain, Israel, Hong Kong, USA, France, Brazil, Russia, and Ivory Coast[18]. The median estimated incidence of TB disease in these studies was 237.6/100,000 and 1,942.8/100,000 in high income and middle/low income countries respectively. The median rate of TB disease in these studies was 23 times higher than that of the median rate found in the respective general populations. The authors also estimated that 8.5% and 6.5% of TB cases in the general population were due to TB transmission in prisons in high and middle/low income countries respectively. This review underscores the paucity and poor quality of data being reported, especially from African and Central Asian correctional facilities.

One longitudinal analysis of TB trends in 26 Eastern European and Central Asian countries showed that the incarceration rate and total number of prisoners of a given country are significant predictors of overall TB trends in that population.[19] Logistic modelling of cross-sectional MDR-TB data from these same countries indicated that incarceration rates may also increase the rate of

primary MDR-TB infection[19]. A case control study conducted in Brazil using data from the national notification system as well as genetic fingerprinting for cluster identification showed that annual incidence of TB within the prison population was almost 40 times higher that of non-prisoners[20]. This study also showed that former prisoners made up 23% more of the cases in the community than those who had not been in prison and that a majority of the cases in the community belonged to clusters which also included strains found in the prison population. The data from this study also implies that many prisoners could have been infected due to transmission within the prisons, as TST rates upon entry to prison were around 7% and therefore prior infection would not account for many of the cases.

A cross-sectional study using both passive and active case finding in another Brazilian prison estimated a TB prevalence (based on bacteriologic confirmation by sputum and/or culture) of 4,712/100,000[21]. This was 69 times higher than the TB prevalence in the general population. This study found significant bivariate associations between Tb disease and low educational level, time incarcerated, productive cough, previous TB, smoking, and HIV infection. However, multivariate modeling results indicated that only previous TB disease and duration of cough were significantly associated with TB disease when controlling for other factors.

A study carried out in 1,317 inmates from 2 prisons in Tajikistan used CXR screening in conjunction with behavioral and demographic surveys to estimate the prevalence and risk factors for TB disease[22]. This study included inmates already on treatment and some former inmates. The prevalence of active TB in this study population as identified by WHO symptom scoring, CXR, and bacteriologic confirmation was 4.5%. Multivariate models identified self-reported HIV infection, previous active TB, and undernutrition as factor associated with active TB disease.

MDR-TB has become a major concern in Eastern European and Central Asian prisons[15]. One cross sectional study used 309 civilian and 291 prisoners with confirmed TB over the period 2001-2002 in Samara Oblast, Russia to estimate prevalence and risk factors for MDR-TB. The prevalence of MDR-TB in all cases, new civilian cases, and new prison cases were estimated to be 22.7%, 19.8% and 37.3% respectively. Factors associated with MDR TB disease were previous TB treatment for greater than 4 weeks, smoking, cavitation on CXR, and a history of imprisonment. Prevalence of resistance to isoniazid, rifampicin, streptomycin, ethambutol, and pyrazinamide were 38%, 25.2%, 34.6%, 14.7% and 7.2% respectively[23].

TB in African Prisons

There is currently a lack of reliable data concerning TB trends in prisons in Sub-Saharan Africa. One recent systematic review of TB in prisons was able to include only one study from Africa[18]. The studies which have been published generally indicate a large burden of TB within prisons which is partially driven by high HIV/AIDS prevalence.

A mass screening study done in 13 Zambian prisons in 2007 showed a minimum prevalence of 4,005/100,000 with prevalence of resistance to at least one TB drug in those with TB disease estimated to be 23.8%[24] Another mass screening effort conducted in 2010 in 6 Zambian prisons and surrounding worker camps by the Zambia Prisons Service and the Centre for Infectious Disease Research in Zambia (CIDRZ) found an estimated prevalence of 6,428/100,000[25]. The HIV prevalence among those with TB was estimated to be 37%.

A Malawian study using screening data from Zomba prison in 1996 estimated a TB prevalence of 5,142/100,000. This number was potentially biased upwards due to screening of only prisoners who were not on day-time community service. However, this may have been balanced by the rather strict inclusion criteria of CXR only for those with cough of 3 weeks or more[26]. Analysis Prevalence and Risk Factors of TB Disease in South African Correctional Facilities

from a mass screening done in 18 Malawian prisons in 2005 gave an estimated average prevalence of 705/100,000 (for smear positive TB). This study indicated higher TB prevalence in larger prisons[27].

A 1-year prospective study carried out in Cameroon including inmates from 10 major prisons (~45% of the national prison population) assessed incident pulmonary TB in any prisoners presenting with TB after a prison stay of 90 days or more. The incidence rate was estimated to be 1,700/100,000 person years. This was 9.4 times higher than the rate in the general Cameroonian population. This finding is striking due to the fact that these prisons were recipients of TB and HIV control interventions that followed international recommendations. This indicates that this rate estimate most likely underestimates the true TB burden in Cameroonian prisons and also implies that international recommendations are either inadequate to address the TB situation in Cameroon and/or that Cameroonian prison health workers and staff are not effectively implementing these recommendations[28].

While certain risk factors such as HIV infection, nutritional status, cell occupancy level, and smoking status are often considered in studies of TB in correctional settings, the importance of these factors may be contingent on the specific country, region, or facility in question.

Active case finding for 3 months in North Gondar Prison in Ethiopia including all inmates with cough for 1 week or more found that 10.4% of prisoners had active TB disease as diagnosed by sputum smear[29]. Almost 8% of enrollees were HIV (+). Of these, 47.4% had active TB. 34.6% of those with active TB were HIV (+) and 46.2% were classified as being underweight. This study indicates that high HIV prevalence and lack of nutritional resources for the incarcerated may be driving TB transmission.

A cross sectional study in 13 Ethiopian prisons in 2013 included all adult inmates who were HIV (+), previously diagnosed with TB in past 5 years, and/or scored a 5 on WHO recommended symptom screen[30]. The estimated prevalence from this population was 458.1/100,000, with

alcohol consumption, contact with a known TB case, and not having a prison-cell window associated with an active TB diagnosis. The results from this study showed that TB prevalence can vary widely between prison facilities in the same country, as the TB prevalence in this study ranged from 0 new TB cases detected to 1,528/100,000. The overall prevalence in these prisons is twice that of the estimated TB prevalence in the general Ethiopian population.

HIV/AIDS is a primary driver of the TB epidemic in sub-Saharan Africa[3]. A 2013 cross sectional study aimed to identify the risk factors that are associated with TB/HIV coinfection in people living with HIV/AIDS in Burkina Faso. Using multivariate logistic modelling, the authors determined that urban residence, a history of TB, higher number of individuals in the household, poor geographic access to care, CD4 counts below 200 /microliter, a history of STIs, and a history of pulmonary asthma were associated with TB infection in those with HIV/AIDs[31]. The results of this study also indicated that the significance of certain risk factors such as occupation and cardiovascular disease history may differ between regions within the same country.

TB in South African Prisons

Despite a dearth of quality evidence pertaining to TB disease and its risk factors in sub-Saharan African prisons, the existing data indicate an epidemic of TB in prisons that far exceeds and likely serves to intensify the epidemic of TB in the general African population. This public health crisis could be particularly dangerous in South Africa, a middle-income nation that has extremely high rates of TB and HIV/AIDs combined with the highest incarceration rate in Africa[32].

South Africa is considered high burden for TB, TB/HIV coinfection (TB/HIV), and MDR-TB based on the criteria compiled by The Stop TB Partnership[3]. South Africa has the highest TB incidence and prevalence rates in the world, the largest number of TB/HIV cases, and the second

highest number of detected drug resistant cases[33]. South Africa is one of 6 nations that make up 60% of the global total TB cases. In 2015, the incidence rate of TB in South Africa was 834/100,000. The incidence of TB/HIV was 473/100,000. Almost 57% of TB cases were infected with HIV. An estimated 3-5.9% of new TB cases were estimated to be infected with MDR-TB, while 7.1% of previously treated TB cases were estimated to have MDR-TB[1]. The total mortality rate (including TB/HIV) was 179/100,000 with 97,000 people dying from TB disease. The majority of these deaths (73,000) were in individuals who were co-infected with HIV/AIDS. While national TB prevalence surveys are currently underway in South Africa, the prevalence rate of TB as of 2014 was estimated to be 696/100,000, with 380,000 people sick with active TB[3]. Distressingly, South Africa has an estimated 20,000 people who have incident TB disease (new and relapse cases) who were not given notification of their TB status[1].

In 2013, tuberculosis was the leading 'underlying natural cause' of mortality for males and females in South Africa[34]. In order to address the devastating effect of TB, the South African government has taken major steps to reduce TB incidence and mortality. Notably, South Africa has made positive strides in recent years including improving treatment success rate and improved diagnosis through the large scale rollout of GeneXpert for TB diagnosis and detection of rifampin resistance[33]. As of 2015, South Africa accounted for 20% of the global total of procured GeneXpert modules[1]. HIV and TB care has largely been integrated across the public sector, with most HIV infected individuals receiving TB testing and treatment (where indicated)[8.] The South African Department of Health (DoH) also implemented a broad 4-year plan known as the National Strategic Plan on HIV, STIs, and TB 2012-2016 (NSP) [35]. This plan was formulated while taking into account successes of the South African response to the syndemic of TB and HIV in the years leading up to 2012. These successes include a large reduction in mother-to-child transmission of HIV, expanded population access to comprehensive HIV/AIDs and TB health services, an increase in the number of ART facilities nation-wide, and large numbers of

men receiving male circumcision. TB cure rates improved from 54% in 2000 to 71.1% and treatment success in new infectious TB was up to 77.1% in 2009. However, these numbers are still below the End TB Strategy target goal of a 90% cure rate[8].

During the 2012-2016 period, the strategic plan aimed to continue improvements in the fight against HIV/AIDS and TB by doing the following:

- Address social and structural barriers that increase the likelihood of HIV and TB infection.
- Prevent new HIV and Tb infections.
- Sustain health and wellness in the South African population.
- Increase protection of human rights and improve access to justice.

Prisoners and prison staff are considered key populations for interventions by the National Strategic Plan, especially in respect to prevention of new HIV and TB infections. The NSP also emphasizes greater focus on respiratory disease control and TB and HIV screening in prisons.

The NSP goals align with those of the WHO End TB Strategy[8]. The End TB strategy breaks countries down into subgroups based on the regionalized drivers of the TB epidemic. South Africa fits into 'Setting 2: Southern and Central African settings where HIV and mining are key drivers of the epidemic'. The intervention package outlined for this setting includes focusing on improved screening, treatment, and access to care for high risk populations including prisoners. The National Strategic Plan also elaborates on high risk population groups who are expected to be at higher risk of progressing from TB infection to TB disease. Three of these population groups are directly associated with prisons; these are HIV (+) individuals, mobile/migrant populations, and people living in poorly ventilated environments[35].

Prevalence and Risk Factors of TB Disease in South African Correctional Facilities

The South African Department of Correctional Services (DCS) has acknowledged the importance of the prison population in terms of TB and HIV/AIDS disease prevention. In 2013, the DCS collaborated with the South African DoH, the Joint United Nations Program on HIV/AIDS (UNAIDS), the United Nations Office of Drugs and Crime (UNODC), WHO, the Aurum Institute and other partners to produce guidelines for the management of TB, HIV, and STIs in correctional facilities[36]. These guidelines acknowledge that the correctional environment may enhance transmission of TB through overcrowding, high population turnover, and unhygienic conditions. The guidelines also state that the risk of TB and HIV/AIDS transmission is further increased due to prisoners coming from areas with high rates of TB and HIV/AIDS who may be undiagnosed or who may have their treatment interrupted due to arrest. DCS treatment guidelines align with the South African National Tuberculosis Management guidelines and emphasize early detection and screening as the most effective way to reduce TB and HIV/AIDS in correctional facilities. HIV testing and voluntary. All those newly diagnosed with HIV then undergo TB screening. Symptom based screening for TB is required for all incarcerated at entry/exit, self-presentation, or as campaign screening. Every incarcerated individual is supposed to be screened at least once a year.

In order to facilitate implementation of DCS guidelines in correctional facilities, a National Task Team consisting of the DoH, the DCS, the National Health Laboratory Service (NHLS), and clinical NGO teams including the Aurum institute was formed. The responsibility of this team is the oversight of ongoing implementation of comprehensive TB and HIV prevention, diagnosis, treatment, and care within correctional facilities[37].

Despite the increased focus on removing barriers to access to TB and HIV/AIDS care, especially in regards to high risk populations like prisoners, correctional facilities will most likely continue

lag behind other high risk communities due to budget constraints and stigma. Previous screening studies in done in South Africa showed that barriers such as security concerns, frequent transfers of inmates between facilities, competing health priorities, and insufficient staff contributed to less than adequate implementation of South African TB prevention guidelines, particularly as concerns DCS screening guidelines[38]. The DCS itself states that the burden of TB may be growing worse in part due to a shortage of trained health care staff, inadequate case detection, and improper treatment[36].

The prevalence of TB and factors associated with TB disease within the South African prison system remains largely unquantified. Global evidence suggests that ongoing transmission of TB both in and from prisons could serve as a substantial roadblock to meeting the End TB goals by the 2035 deadline. Despite the presence of relatively good infrastructure compared to most of its Southern African neighbors, the South African prison system has a number of characteristics which make it vulnerable to widespread TB transmission and disease. South Africa ranks 9th in the world and 1st in Africa in total prison population with 161,984 incarcerated individuals with an incarceration rate of 291/100,000 population as of March 2016.[32] Among the incarcerated, 27.9% are pre-trial detainees, 2.6% are female and 6.3% are foreign. Most distressingly, the average occupancy level of South African prisons is estimated to be at 133% official capacity. The South African Department of Health's 2013 Guidelines for the management of TB, HIV, and STIs in Correctional Facilities estimates that around 360,000 inmates move through the South African correctional facility system annually[36]. The DCS has estimated that the national TB prevalence rate is at 4.3%, with an estimated 30% of prisoners infected with HIV[37].

Data for South African prisons is sparse, with the existing literature indicating that TB incidence within prisons is higher than that for the general population. Only a handful of studies have reported representative TB prevalence estimates.

Prevalence and Risk Factors of TB Disease in South African Correctional Facilities

A systematic review of the epidemiology of TB in South African correctional facilities was conducted in 2014 as part of the Evidence to Inform South African Tuberculosis Policies Project (EVISAT) carried out by researchers from Stellenbosch University and funded by USAID and UNAIDS. This review was only able to find 3 studies which met its standards, 2 of which were cross-sectional with the other being a retrospective cohort study[39]. Overcrowding is an environmental factor that is thought to be linked to TB transmission within South African correctional facilities.

A modeling study done by Johnstone et al using data from Pollsmoor prison in Capetown estimated that the risk of TB transmission at current levels of overcrowding was 90% per year and that implementing international recommendations on cell occupancy would reduce TB transmission by >50%. It also estimated that decreased lock up time along with increased case finding would reduce TB transmission by 20%[40].

Analysis of a screening study carried out by the Aurum Institute in conjunction with local Department of Correctional Services (DCS) staff in Johannesburg Prison in 2010 estimated the prevalence of previously diagnosed and undiagnosed TB to be 1.0% and 3.5% respectively, with smoking and positive HIV status associated as risk factors with previously undiagnosed TB[41]. Another mass screening campaign carried out in 4 South African correctional facilities by the same organization identified a prevalence of 2.1% in 7,426 screened inmates[38]. The estimates from these studies are far above the estimated 2015 global prevalence rate of 174/100,000 and indicate a potentially huge burden of TB in the prisons of Southern Africa[1].

Conclusion

Despite being a treatable and curable disease, TB continues to wreak havoc on much of the world's population. While the TB epidemics in industrialized countries have mostly reached manageably low numbers, certain nations such as South Africa still experience debilitating

morbidity and mortality from TB disease. The TB epidemic in South Africa is driven by high HIV/AIDS prevalence and high numbers of individuals in high-risk populations such as miners and prisoners. Increasingly, international health organizations as well as South African health and correctional organizations are turning their attention to the problem of TB in South African correctional facilities. However, much work remains to be done if new guidelines and goals are to be met in time to affect change in the TB epidemic. Further research must be conducted that quantifies the extent of the TB burden in more representative samples of South African correctional facilities and elucidates region specific clinical, demographic, and environmental factors that may predict TB disease in prisons across South Africa. Said research will inform South African health authorities, South African Correctional Services, and international health organizations and allow a more informed approach for interventions targeted towards incarcerated individuals. This, in turn, will allow for more rapid reduction of TB transmission and prevalence in line with the goals laid out by the WHO End TB Strategy.

Objectives

1. To describe prevalence rates per 100,000 of TB disease for 16 South African prisons by facility.
2. To describe the yield of TB cases confirmed by GeneXpert-MTB/RIF in those with self-reported symptoms of cough, fever, weight loss, or night sweats and/or positive radiographs.
3. To elucidate the demographic, structural, and clinical factors associated with TB disease in 16 South African prisons.

Intended Audience

The results of this study are intended primarily for the South African DCS and implementing partners such as the Aurum Institute. The results will also be made available to any relevant government agency, research organization, or implementing partner involved in TB prevention, epidemiology, or control in correctional settings.

Methods

This evaluation was a secondary analysis of data collected by the Aurum Institute of Johannesburg, South Africa under the project title 'TB Screening, Detection, and Management in Identified Health Facilities of the Department of Correctional Services (DCS)-Data Analysis' (Appendix).This project was implemented through a collaboration between the Aurum Institute and the South African DCS to provide mass TB and HIV screening, including CAD digital chest X-ray (CXR) to all incarcerated persons in the country, in accordance with the South African Ministry of Health Guidelines for the Management of Tuberculosis, Human Immunodeficiency Virus, and Sexually-Transmitted Infections in Correctional Facilities. Inmates presenting with symptoms or chest X-ray abnormalities were asked to provide a sputum for TB testing with GeneXpert MTB/RIF. The Aurum Institute implemented mass TB / HIV screening programs in 16 Department of Correctional Services management areas in Gauteng, Limpopo, Mpumalanga and North West provinces from March 2013 to March 2016. The DCS management areas where the project was implemented are listed; Barberton, Baviaanspoort, Boksburg, Johannesburg, Kgosi Mampuru II, Klerksdorp, Krugersdorp, Kutama Sinthumule, Leeuwkop, Modderbee, Polokwane, Rooigrond, Rustenburg, Thohoyandou, Witbank, and Zonderwater. The goal of the project was to implement mass case finding for TB by using GeneXpert MTB/RIF sputum testing for any incarcerated persons self-reporting at least one symptom (cough, fever, night sweats, or weight loss) and/or a positive CXR. All persons willing to undergo HIV testing had a finger

prick blood sample collected and screened for HIV using a point of care HIV rapid test kit (UniGold). HIV positive screening tests were confirmed using point of care rapid confirmatory test kits (Abon). If the screening test was reactive and the confirmatory test was non-reactive, venous blood was collected for enzyme-linked immunosorbent assay (ELISA) & the ELISA result was interpreted as the final outcome of the HIV test.

Data Source

The data for the present evaluation will include a subset of the data collected from 16 management areas and includes screening results for 46,045 inmates screened from January to December 2015. Data from the standardized questionnaire will be merged with data from CXR screening in order to identify clinical diagnoses. An online directory linked to the South African National Health Lab System (NHLS), TrakCare, was used by data capturers at Aurum to establish GeneXpert results (linked via barcode on questionnaire) for all those who submitted sputum during screening.

Pre-analysis cleaning

- Prior to analysis, all inmates had names removed. The remaining prison ID was a unique identifier which neither I nor Emory Thesis committee members have the ability to link to individual inmates.
- All prison names were erased and assigned letter identifiers, for reasons of sensitivity to the South African DCS.
- Any prisoners without a prisoner ID or screening date were dropped from the dataset.
- Any duplicate observations (same screening date and prisoner ID) were dropped from the dataset.

- All data was stored on Rollin's School of Public Health H drive accessible to the thesis committee. All analysis and results will be shared with relevant researchers at the Aurum Institute in Johannesburg.

Statistical Analysis/Methods

Prior to analysis all data was de-duplicated. For our analysis we considered anyone with the same unique ID and screening date to be 'true' duplicates. Since many individuals were screened more than once over the course of 2015, we collapsed the dataset such that:

- Every individual has 1 row of data
- All individuals who never reported TB symptoms and who never tested positive for TB or HIV had data from the earliest date screened
- All individuals who never tested positive for TB or HIV but who were on antiretroviral treatment (ART) had data from the earliest date at which they were noted as being on ART.
- All individuals who reported any TB symptom in 2015 but never tested positive for TB or HIV and weren't on ART had data from the earliest date at which sputum was submitted
- All individuals who tested positive for TB but not HIV had data from the earliest date at which TB was diagnosed
- All individuals who tested positive for HIV but not TB had data from the earliest date at which HIV was diagnosed
- Individuals who tested positive for TB and HIV on different dates had data from the date at which they were diagnosed with TB, since this was our primary outcome of interest. In this situation the variable which denotes HIV status was updated to reflect the earlier HIV diagnosis.

Though we recognize that some prisoners who tested positive for TB and HIV on separate screening instances will lose the data from the date at which they screened positive for HIV, we believe this will be a very small number of individuals.

All data analyses were performed using SAS 9.4 (Cary, NC). The proportion of inmates with TB was calculated by taking the number of previously diagnosed TB cases and the number of previously undiagnosed cases identified through the screening program by GeneXpert or radiologist reading and dividing by the total number of inmates screened. We also calculated a prevalence rate by multiplying the same numerator and denominator by 100,000 (for a rate expressed as per 100,000 persons).

Calculation of GeneXpert Yield in those submitting sputum

Yield = (All those who submitted sputum and were TB positive by GeneXpert-MTB/RIF) / (All those screened who had at least one self-reported symptom and/or a computer automated radiograph suggestive of possible TB and submitted sputum)

The yield will be assessed for all those screened and for each prison. Separate total-screened and prison-specific yields will be calculated in those who received HIV testing, stratified by HIV test result.

Calculation of Total and Prison TB disease prevalence

TB Prevalence = (All individuals who tested positive via GeneXpert + individuals diagnosed with 'Definite TB' by radiologist + individuals on TB treatment at time of screening) / (All individuals who were screened and had data entered for prisoner ID and screening date)

TB/HIV Coinfection Prevalence = (individuals on antiretroviral treatment at time of screening + those testing positive for HIV with any of the TB numerator criteria listed above) / (all individuals who were screened, had ID and screening date, and consented to HIV testing)

Logistic regression analysis of factors potentially associated with TB or TB/HIV coinfection:

Logistic regression was used for our analysis of potential associated factors. The logistic model was chosen because our outcome variables are dichotomous. The logistic model is a linear model on the log odds scale. The estimated coefficients output in SAS for each predictor variable represent log-odds of the outcome given that predictor variable (log odds of the outcome in the exposed minus the log odds of the outcome in the unexposed). By exponentiation of the log-odds we arrive at the odds ratios which signify the odds of the outcome in those with the variable exposure of interest, compared to the level of the variable designated as the referent level. To assess which factors are associated with newly diagnosed TB disease or TB/HIV coinfection, we calculated the odds ratio of the outcome for each predictor variable and for any interaction terms of interest versus the referent group. All continuous variables were categorized as specified below and logistic bivariate analysis will be conducted for each potential risk factor and newly diagnosed TB disease. Bivariate associations were assessed between each predictor variable and the outcome using Wald Chi-square tests. Any plausible association less than 0.2 was considered for inclusion in the multivariate regression model. If any variable in our bivariate analyses included a numerator count of less than 5 then potential associations were assessed using Fisher's

exact test. Collinearity was assessed using the Emory University Department of Epidemiology's collinearity MACRO for SAS.

If any variables were significantly associated with one another ($p<=0.05$) only the one more highly associated with the outcome was included in the final model. We also assessed for effect modification of associations; when identified, models were presented stratified by the effect modifier or an interaction term was included in the final overall model. Variables which are biologically/environmentally plausible and significant ($p<=0.05$) were included in the final multivariate model. These thresholds were identified based on previous studies of similar size and objective[17,19].

Variable screening

The data analyzed in order to elucidate potential clinical, demographic, and structural factors associated with newly diagnosed TB disease and TB/HIV coinfection was taken from the responses of prisoners to the questions included in the Aurum questionnaire given to inmates at screening. Relevant factors included the following:

Questionnaire Variables

- Gender
- Age (will be categorized)
- Years of detention to date (will be categorized)
- Race
- Basis for screening
- Self-Reported symptoms:
    - Cough
    - Fever
    - Unexplained weight loss

  - Night sweats

- Prior TB Status:
  - If an inmate reported prior TB diagnosisthen this individual should also have responses for:
    - Current treatment status
    - Date of last TB diagnosis (presented categorically as <1 year ago, 1-2 years ago, or >2 years ago)

- Radiologist chest X-Ray Reading
- Self-Reported ART status
- HIV test results

Created variables

Using the questionnaire variables, the following variables were created for use in our analyses:

- Number of Symptoms:
  - 0: No reported symptoms
  - 1: Individual reported only 1 symptom
  - 2: Individual reported 2 or more symptoms
- Known HIV+:
  - 1: individual was either on antiretroviral treatment at time of screening or tested positive for HIV during screening
  - 0: individual either tested negative for HIV during screening or did not consent to HIV testing

Collinearity

Collinearity is an issue which arises when one or more predictor variables are associated (can be predicted) from one or more other predictor variables in the model. Strong relationships between predictor variables can yield unreliable regression coefficients for some predictors.

To assess collinearity in our multivariate logistic regression models, we used the collinearity MACRO developed by the Rollins School of Public Health Department of Epidemiology.

Running this macro (including all predictor variables of interest) provided us output tables with condition indices (CIs) and variance decomposition proportion (VDP) values for each variable in the model. Any variable with a CI greater than or equal to 30 and a VDP greater than 0.5 was considered to have a collinearity problem. If collinearity was indicated, the variable with the highest CI was dropped from the model and the MACRO was run again with the remaining variables. We proceeded sequentially in this manner until no collinearity issues are indicated.

Analysis

All regression analyses were performed using the proc logistic function of SAS 9.4 (Cary, NC).

This analysis elicited crude results, as well as factors stratified by HIV status. This analysis was first conducted among all persons in the sample, and then separately using only inmates with HIV/AIDS results.

Using logistic regression, we assessed associated factors for newly diagnosed (defined as all inmates screening positive by GeneXpert and/or chest radiography during screening) TB disease. To assess potential effect modification by HIV status we conducted logistic regression modeling for all inmates screened for TB disease and then compared bivariate effect estimates with those

obtained in bivariate logistic regression of the same variables stratified by HIV status. We repeated this process using only inmates with known HIV status.

Model 1 contained all individuals screened for TB disease. Models 2 and 3 were stratified models which assessed the effect of the same potential predictors in those with Known HIV infection (Model 2) and in those who were either known to be HIV negative or who had unknown HIV status (Model 3). Because the effect estimates differed substantially between Models 1, 2, and 3, multivariate analysis was conducted separately for Models 2 and 3. Results of multivariate analysis in Model 1 was not conducted due to observed effect modification by HIV status. To further elucidate the effect of HIV on potential predictors of newly diagnosed TB disease, we ran Model 4 using only inmates with known HIV status. Due to our previous findings, we also conducted logistic regression in this subpopulation stratified by HIV status (Models 2 and 5). The observed effect estimates differed substantially when stratifying by HIV status. Therefore we conducted multivariate analysis only for Model 5 (multivariate regression results for HIV infected were already reported for Model 2).

The final models will include all variables which are found to not have collinearity issues, are interpretable, and plausibly associated with our newly diagnosed TB outcome with a p-value of 0.2 or less in bivariate analysis. Interaction will be considered for any pairing of variables which have been selected for inclusion in the model and which have been previously identified as effect modifiers based on literature review. If any interaction terms are included, we will then conduct likelihood ratio tests for significance of the term. Any term with $p \leq 0.05$ will be included in the final model. Odds ratios and 95% confidence intervals will be presented for all demographic, clinical, and structural factors. Any factor which has an odds ratio with a p-value of <0.05 will be considered to be significantly associated with the outcome.

Results

All tables and figures mentioned in the following results section are listed in the appendix at the end of this document.

Total screened population and exclusions

Estimated prison populations for 2015 were obtained from the Aurum Institute (Table 1). Every facility except Facility B was at 100% capacity or higher, as estimated by dividing the 2015 estimated population by the prison capacity estimates as provided by the Aurum Institute. Overall prison capacity was 132.92%. Facilities I and D exceeded capacity by the greatest amount (185.15 and 169.55% respectively). The proportion of total prison population present at TB screening was 55.23% overall, but differed widely across facilities. Of the 31,843 individuals present at screening, 175 reported being on TB treatment at the time of screening. These 175 individuals were removed from all analyses except the TB prevalence calculations shown in Table 5. A total of 31,668 individuals were screened for TB disease. Facilities which had less than 30% of their estimated 2015 population screened were excluded from all yield and TB prevalence estimates. Four facilities (M, N, O, and P) were thus excluded and are not represented in Tables 2-5 or Figure 2. Only 7,584 inmates (23.95%) were of known HIV status (designated as those who consented to HIV testing or were on ART at the time of screening) (Table 1). Any facility for which <5% of screened inmates were of known HIV status was excluded from TB/HIV coinfection prevalence estimates, HIV prevalence estimates, and HIV-stratified GeneXpert yield calculations. Facilities A, D, and I were excluded for this reason and are not represented in Table 4 or the coinfection column for Table 5. All individuals who did not report being on TB treatment at the time of screening were included in our logistic regression analysis of potential risk factors. Figure 1 illustrates inclusions, exclusions, and total numbers of inmates screened by symptom questionnaire and CAD as well as the number of inmates testing positive for TB disease by GeneXpert or radiologist. Table 6 shows the relative distributions of

demographic and clinical factors in those who were included in TB prevalence estimates versus all screened and those who were excluded due to <30% facility TB screening coverage. The distribution of demographic and clinical factors in those included in TB prevalence estimates was similar to the distribution in all individuals screened for TB. The 296 inmates who were excluded from prevalence and yield estimates were similar to those included in terms of age, race, radiologist results, ART status, and proportion of those infected with HIV. Those who were excluded were more likely to be male, to have had previous TB (9.8 vs 4.59%), to exhibit current TB symptoms, and to have a known HIV status. Those who were excluded were less likely to be newly incarcerated and less likely to have a CAD reading of 50 or higher. Despite these differences, the total number of inmates excluded due to low facility screening coverage represented less than 1% of those screened for TB and therefore their exclusion is unlikely to affect the validity of our prevalence or yield estimates.

GeneXpert yield

The proportions of inmates screened as TB positive by symptom questionnaire or CAD in the 12 facilities which met our TB screening criteria are shown in Table 2. Figure 1 illustrates the flow of the screening algorithm employed in this study as well as the GeneXpert and Radiologist results. A total of 31,374 inmates from 12 facilities were included in our GeneXpert yield analyses. A total of 18,734 screened inmates from these facilities submitted sputum for GeneXpert testing. During the screening process, all inmates who had at least one self-reported symptom of cough, fever, night sweats, or unexplained weight loss and/or a CAD result indicative of possible TB should have submitted sputum for analysis with GeneXpert. However, the proportion of inmates indicated for sputum submission who actually submitted sputum varied widely across facilities (Table 2). While overall sputum submission in those with symptoms was high (89.5%), Facilities A and D had very low sputum submission (22.45 and 5.62% respectively). Overall sputum submission in asymptomatic inmates (indicated by CAD only) was

very low at 38.49%. Sputum submission in asymptomatic ranged from 4.26% (Facility I) to 100% (Facility H). The overall and facility specific yield of GeneXpert is shown in Table 3. A total of 166 (0.89%) inmates tested positive by GeneXpert, of which 158 (95.2%) were symptomatic.

Separate yield calculations were made for 9 facilities which had at least 5% of their respective screened populations with known HIV status (Table 4). The proportion of HIV infected in those with known HIV status from these facilities was 28.19%. The facility specific proportion of HIV infection ranged from 12.44% (Facility K) to 78,38 (Facility F). A total of 81 inmates with known HIV status were diagnosed by GeneXpert, giving a total yield of 1.43%. The GeneXpert yield was higher in HIV+ versus HIV- inmates (2.4% vs 1.04%). Yield in those reporting symptoms was also higher in HIV+ versus HIV- (2.46 vs 1.08). All but 2 of the inmates testing positive by GeneXpert were symptomatic, making a representative comparison of the HIV stratified yield in symptomatic versus asymptomatic inmates impossible.

TB Prevalence

Table 5 shows estimated TB prevalence for 12 Facilities. Estimated prevalence rates are given in Table 5 and Figure 2. For Facilities B, C, E, J, and L, more inmates were screened for TB than were estimated to be in the respective facilities. This is due to a very high turnover in South African prisons, which resulted in differing facility populations at the time of screening versus the time when the population estimate was made. The percent prevalence of coinfection is shown for 9 facilities which met screening and HIV status requirements. Including those who reported being on TB treatment at the time of screening, a total of 31,547 inmates (72.84%) were screened. With the exception of Facilities B and F, all facilities were at > 100% capacity. A total of 837 inmates had TB disease in these 12 facilities, giving an overall prevalence of 2,653/100,000. The prevalence of TB disease ranged from 933/100,000 (Facility L) to 6,240/100,000 (Facility A). In all with TB disease, 173 inmates were TB positive at the time of screening (548/100,000) while

166 (529/100,000) were newly diagnosed by GeneXpert and 498 (1587/100,000) were newly diagnosed by radiologist reading alone. The percent prevalence of TB disease in those with known HIV status was 1.42%. Out of the 7,489 inmates with known HIV status, 63 were coinfected with HIV/TB (0.84%). This coinfection proportion estimate should be viewed with caution, as HIV testing consent was low. A total of only 7 inmates were diagnosed with rifampicin resistant TB disease (prevalence: 22/100,000). Notably, 5 of these inmates were from Facility G.

Factors associated with newly diagnosed TB disease

Demographic and clinical characteristics of all 31,668 screened individuals who did not report being on TB treatment at the time of screening are listed in Table 6. The majority (75%) of inmates were aged 25-44 years. The vast majority of screened inmates were male (96.9%) and identified as black/African race (93.3%). The amount of time spent in incarceration ranged widely in the population. Most inmates had been incarcerated for relatively short amounts of time, with 37.13% having been incarcerated less than 1 year and 20.8% incarcerated from 1-2 years. The proportions of inmates reporting incarceration for 3-4 years, 5-9 years, and 10 years or more were 15.8%, 17.1%, and 6.9% respectively. A substantial number of inmates (4.5%) reported having had TB before. Of these individuals, 67.1% reported their last date of being TB positive as ‘more than 2 years ago’. Most inmates had at least one self-reported symptom (61.6%), with cough being the most frequently reported (45%), followed by night sweats (23%). Of those reporting symptoms, 10,126 (32%) reported only 1 symptom, while 9,380 (29.6%) reported 2 or more symptoms. Digital radiography results from computer automated detection (CAD) were indicative of possible TB disease in 5,573 (17.6%) inmates. Of these, 511 inmates were classified as having ‘Definite TB’ by human radiologists. Overall, 2,115 (6.68%) inmates were either on anti-retroviral treatment at the time of screening or tested positive for HIV during screening.

Prior to running each multivariate logistic regression model, a collinearity MACRO was used to assess bivariate and multivariate collinearity. No collinearity problems were identified.

Model 1: All inmates which were screened for TB disease

Risk factor analysis was done using variables that apply at the individual level. All 31,668 inmates who did not report being on TB treatment at the time of screening were included in Model 1. Although not every inmate included in this model consented to HIV testing, we created a 'Known HIV+' variable which compares all inmates known to have HIV to all those either known to be HIV- or with unknown HIV status. This variable categorization treats those with unknown HIV status as if they were HIV negative, giving a conservative estimate of the effect of HIV infection. A total of 684 inmates were newly diagnosed with TB disease in this population. Model 1 (results shown in Table 7) assessed potential bivariate associations between newly diagnosed TB disease (by GeneXpert or Radiologist) and demographic and clinical variables across the entire screened population. Age, male gender, years incarcerated, previous TB, black/African race, cough, number of symptoms, and known HIV+ status were all independently associated with newly diagnosed TB in bivariate logistic regression analysis ($P \leq 0.05$). Interestingly, symptom variables cough and 'number of symptoms' were significantly protective in this population in bivariate analysis. Because the majority (93.3%) of the screened population was black/African, and therefore logically accounted for most newly diagnosed TB cases (652), race was not considered for subsequent multivariate modelling. Although we included each of the 4 screening symptoms in bivariate analysis, we did not consider individual symptoms for inclusion in the multivariate. We instead considered the 'number of symptoms' variable, which considered an inmate's symptom status based on report of no symptoms, only 1 symptom, or ≥ 2 symptoms. Because known HIV positive status was significantly harmful (OR=1.43 (1.1, 1.86; p=0.008)), even when considering those with unknown HIV status in the denominator (giving a

conservative estimate) we conducted stratified bivariate logistic regression in those known to be HIV positive and in those known to be HIV negative/HIV unknown. All the same variables were considered in the stratified analysis as in Model 1, except for HIV status (stratification variable). A variable which compared those self-reporting current ART was included in bivariate analysis for known HIV infected inmates (Model 2). Because the estimated ORs in the HIV+ group differed substantially from the ORs estimated in Model 1, adjusted ORs will be reported separately for those known to be HIV+ (Model 2) and those known to be HIV- or HIV unknown (Model 3).

Model 2: Known HIV+ only

Results for Model 2 are shown in Table 8. This model contained only the 2,115 individuals who were known to be infected with HIV, either through self-report of ART or newly diagnosed HIV. A total of 63 inmates were newly diagnosed with TB disease in this population. In those known to be HIV+, only previous TB was significantly associated with newly diagnosed TB disease in bivariate analysis (aOR=4.29 (2.54, 7.25; p=<0.0001). Because years incarcerated was close to significant in those incarcerated for 5-9 years (using those incarcerated for less than a year as the reference group), we included years incarcerated in the model. Age was also included, as we thought it necessary to adjust for age when estimating the effect of years incarcerated. When adjusting for age, years incarcerated, and previous TB, only previous TB was significantly associated with newly diagnosed TB disease (aOR: 4.2 (2.43, 7.25; p=<0.0001)).

Model 3: Known HIV- and HIV unknown

Results for Model 3 are shown in Table 9. This model contained the 29,553 inmates who either tested negative for HIV or who did not consent to HIV testing. A total of 621 inmates were newly diagnosed with TB disease by GeneXpert or radiologist in this population. Age, male gender, years incarcerated, previous TB, current cough, and number of symptoms were

significantly associated with newly diagnosed TB disease in bivariate analysis. Like in Model 1, current cough and number of symptoms were significantly protective of newly diagnosed TB. Because current cough and number of symptoms were likely collinear, only number of symptoms was included in the multivariate model. Age, male gender, years incarcerated, and previous TB were also included. When adjusting for these variables, age was significantly associated with increased odds of newly diagnosed TB disease. Using those aged 15-24 as the reference group, inmates aged 25-44 years were 2.26 times more likely to be newly diagnosed with TB disease (CI: 1.73, 4.09; p=<0.0001). Inmates aged 45 and older were 5.21 times more likely to be newly diagnosed with TB disease than those aged 15-24 (CI: 3.30, 8.22; p=<0.0001). Male gender was also significantly harmful (aOR: 2.32 (CI: 1.13, 4.77; p=0.02). Inmates reporting having had TB previously were over 14 times as likely to have newly diagnosed TB in this population (CI: 12.00, 17.35, p=<0.0001). Using those with no reported symptoms as the reference group, inmates reporting 1 symptom were 0.57 times as likely to have newly diagnosed TB, indicating a significant protective effect (0.5, 0.7; p=<0.0001). Those reporting 2 or more symptoms were also less likely to have newly diagnosed TB (aOR=0.77 (0.63, 0.94; p=0.009)).

Model 4: Those with known HIV status

Infection with HIV is a widely accepted risk factor for TB disease[1]. Due to low consent to HIV testing in our population screened for TB, Model 1 was not able to adequately control for HIV status. Model 3, which included only those known to be HIV negative or HIV unknown may not have completely controlled for HIV negative status since many inmates were likely HIV positive but did not consent to HIV testing and were therefore included in the HIV negative-HIV unknown group. Therefore, to estimate the effect of newly diagnosed HIV on the odds of newly diagnosed TB we ran Model 4 (Table 10) using only the 7,584 inmates with known HIV status. Bivariate analyses were also conducted for age, race, time incarcerated, previous TB, symptoms, and number of symptoms. Results for Model 4 are shown in Table 10. The outcome of interest

in this model was newly diagnosed TB by GeneXpert or by radiologist reading. A total of 109 (1.44%) inmates with known HIV status were newly diagnosed with TB disease. Bivariate results for Model 4 are found in Table 10. Those aged 25-44 and those aged 45 and older had significantly increased odds of newly diagnosed TB, using those aged 15-24 as the reference group. Previous TB, current cough, night sweats, unexplained weight loss, having 2 or more symptoms, and newly diagnosed HIV infection were all harmfully associated with the odds of newly diagnosed TB disease.

Because effect modification by HIV status was found in Models 1-3, we also stratified Model 4 by HIV status. The estimated ORs for bivariate analysis of Model 4 were compared with bivariate ORs from Model 2 (HIV+ only) and Model 5 (HIV- only). We identified substantial differences in the estimated effects of age, previous TB, and symptoms between Model 4 and the stratified Models 2 and 5. This indicates that effect modification by HIV status may be occurring. We therefore ran multivariate models separately for Model 2 (reported above) and Model 5.

Model 5: Known HIV-

Results of Model 5 are shown in Table 11. This model included the 5,469 individuals who consented to HIV testing and were found to be HIV negative. In this group, a total of 46 inmates (0.84%) were newly diagnosed with TB disease. Results of bivariate logistic regression (Table 11) showed significant harmful effects of age, previous TB, symptoms, and number of symptoms on the odds of newly diagnosed TB disease. The variables age, years incarcerated, previous TB status, and 'number of symptoms', were included in the multivariate model for this group. When adjusting for these variables, inmates aged 25-44 years were over 4 times as likely to be newly diagnosed with TB disease when compared to those ages 15-24 (CI: 1.28, 13.64; p=0.02). Inmates who reported having had TB previously were 5.41 times as likely to have newly diagnosed TB when adjusting for relevant factors (CI: 1.85, 15.79; p=0.002). Inmates who reported 1 symptom were more than 8 times as likely to have newly diagnosed TB compared to

those reporting no symptoms (CI: 1.06, 62.38; p=0.04). Inmates who reported 2 or more symptoms were around 20 times as likely to have newly diagnosed TB compared to those with no symptoms (CI: 2.72, 146.66; p=0.003). The confidence intervals for the 'number of symptoms' variable are notably wide, due to only having 1 inmate who was newly diagnosed with TB with no reported symptoms in those known to be HIV negative.

Importantly, the magnitude of the estimated effect of these variables on newly diagnosed TB disease in those known to be HIV negative (Model 5) differs from the estimated effects in those who were combined HIV negative and HIV unknown (Model 3). Increased age was associated with similar effect estimates in both models, but in Model 5 only age of 25-44 was significantly associated with increased odds of newly diagnosed TB disease. Inmates reporting previous TB disease were more likely to be newly diagnosed with TB disease in both Model 3 and Model 5. However, the magnitude of the effect estimate differed drastically when excluding those with unknown HIV status (Model 5 aOR: 5.41 vs Model 3 aOR: 14.43). Most notably, the estimated effect of symptoms (1-2 or more) switched over from protective in Model 3 to highly harmful in Model 5 (Model 3 aORs: 0.57 (1 symptom) and 0.77 (2 or more symptoms) vs Model 5 aORs: 8.15 (1 symptom) and 19.99 (2 or more symptoms)). We cannot compare the effect estimates for male gender because there was no newly diagnosed TB in females with known HIV negative status.

Discussion

The TB screening conducted by Aurum Institute and the South African DCS in 2015 which provided data for this study reached 31,843 inmates, or 55.23% of the estimated combined facility population. Screening coverage varied by facility. In the 12 facilities with screening coverage $\geq$30%, far more new TB cases were diagnosed by radiologist reading than by GeneXpert testing (498 vs. 166). Combining inmates who reported being on TB treatment with

those newly diagnosed by GeneXpert or radiologist gave an overall prevalence rate of 2,653/100,000. Estimated facility prevalence rates ranged from 933/100,000 (Facility L) to 6,240/100,000 (Facility A). This indicates that facility specific factors may play a role in determining the extent of the TB burden in South African correctional facilities. Our overall prevalence estimate is much higher than the 2015 global prevalence rate (174/100,000)[3] as well as the 2014 national prevalence rate in South Africa (696/100,000). Our estimated total prevalence rate of TB (2,653/100,000) and our estimated prevalence rate of previously undiagnosed TB (2,116/100,000) are similar to the rates estimated in previous studies conducted in South African correctional facilities. These estimated the overall prevalence of TB disease to be around 2,100/100,000, with the prevalence of previously undiagnosed TB disease to be around 3500/100,000 [38,41]. Our percent prevalence estimate for newly diagnosed HIV/TB coinfection in those with known HIV status is 0.84%. Our results indicate a large burden of coinfection in the 12 facilities included in these estimates.

The overall yield of GeneXpert yield was low in our screening, at 0.89% of all those submitting sputum. It was slightly higher in symptomatic inmates (0.92%). Our results indicate that the absolute yield of TB cases by GeneXpert testing is higher in symptomatic HIV+ individuals when compared to symptomatic HIV- individuals. Previous studies have shown that GeneXpert may be less sensitive in individuals infected with HIV[42]. This may mean that HIV-infected inmates with TB disease were missed by GeneXpert testing. Previous research has shown that chest radiography may have greater sensitivity in detecting pulmonary TB disease in HIV infected individuals compared to bacteriological methods[44]. This may explain the much higher yield of new TB diagnoses via CAD/radiologist alone in our screened population, especially if a high proportion of screened inmates with unknown HIV status were infected with HIV. Our results imply that CAD may be an efficient method of pre-screening for TB. Far fewer inmates were indicated for sputum submission by CAD than by symptom questionnaire (5,549 vs 19,249),

while more inmates were newly diagnosed with TB by radiologists than by GeneXpert (498 vs. 166). Screening results also indicate an extraordinary overall percent prevalence of HIV infection in those with known status (28.19%). HIV infection prevalence differs widely across facilities as does the proportion of screened inmates with known HIV status.

We made use of 5 logistic regression models in our assessment of demographic and clinical factors associated with newly diagnosed TB disease. Because the significance and magnitude of bivariate OR estimates changed for many potential predictors when stratifying the overall population model (Model 1) by HIV status, we conclude that HIV was modifying the effect of other potential predictor variables. We conducted separate multivariate modelling for Known HIV infected and for combined known HIV uninfected/HIV unknown. Only previous TB was significantly associated with newly diagnosed TB disease in those known to be infected with HIV. Increasing age, male gender, and previous TB were significantly associated with increased odds of newly diagnosed TB in those who were either known to be HIV negative or who had unknown HIV status (Model 3). Having had 1 symptom or 2 or more symptoms were significantly protective in this group. Because symptom variables were either harmful or very close to null in the known HIV infected population (Model 2), we believe that the surprising observed protective effect of symptoms in this combined HIV negative/unknown group may be due to modification of symptom effect by HIV status. We hypothesize that this observed modifying effect could be due to the decreased likelihood of immunocompromised individuals displaying symptoms, even when they have TB disease.[45] Model 2 showed that symptoms are not associated with increased odds of new TB diagnosis by GeneXpert or radiologist in this HIV infected population. Because the combined HIV known negative and persons with unknown HIV status group likely included many individuals who were infected with HIV, the effect of symptoms in Model 3 should be viewed with caution. To further understand the effects of demographic and clinical variables on the odds of newly diagnosed TB disease when sufficiently

controlling for HIV infection, Model 4 was run using only the 7,584 inmates for whom HIV status was known. HIV infection was significantly harmful in bivariate analysis of this group (OR: 3.74 (2.22, 6.31; p-value: <0.0001)). Because of the observed modifying effect of HIV observed in previous models, Model 4 was stratified by HIV status in the same way as Model 1. Bivariate ORs were compared between overall HIV known (Model 4), HIV infected (Model 2), and known HIV negative (Model 5). Our results indicated that HIV status was modifying the effects of age, previous TB, and symptoms. Therefore, multivariate analysis was run separately for persons known to be HIV infected (Model 2) and known to be HIV uninfected (Model 5). As reported previously, only previous TB was significantly associated with newly diagnosed TB disease in those known to be infected with HIV when controlling for other relevant variables (aOR: 4.2 (2.43, 7.25)). Multivariate analysis of the same variables in those known to be HIV negative showed age, previous TB, and having TB symptoms to have a significant harmful association with the odds of newly diagnosed TB. The observed aORs for 1 reported symptom (8.15) and 2 or more symptoms (19.99) support previous evidence that the effect of symptoms is modified by HIV status and that symptoms are less reliable predictors of TB disease in those who are infected with HIV. Our results support previous studies which found that HIV infection, higher symptom scores, and previous TB were associated with increased odds of TB disease[29, 30].

We sought to analyze facility overcrowding as a potential risk factor, as is implied by the Pollsmoor modeling study by Johnstone-Robertson et al[40]. However, the fact that all but 2 facilities with adequate screening coverage were at 100-150% official capacity made comparison difficult, as there is essentially no reference population in the data. Our overall overcrowding estimates (total: 132.9% (range: 96.8-185.15%)) are nonetheless useful in providing further evidence that South African facilities are drastically overcrowded.

In summary, the estimated prevalence rates for 12 South African correctional facilities included in this study ranged from from 933/100,000 to 6,240/100,000. The percent prevalence of TB/HIV

coinfection in these facilities was 0.84%. The estimated percent prevalence of HIV infection in 9 facilities meeting our HIV testing criteria was 28.19% overall. Previous TB was identified as a predictor of newly diagnosed TB disease in inmates with known HIV infection. Age of 24-44 years, previous TB diagnosis, and having 1 or more symptoms were identified as predictors of newly diagnosed TB disease in inmates known to be HIV negative.

Limitations/Strengths

This study has several limitations. Our population estimates are based on collated monthly population estimates made by the Aurum Institute in 2015 and do not completely account for population mobility. Therefore, we have some facilities which had greater than 100% of estimated population screened. However, population mobility is an inherent characteristic of the South African correctional system. Because of Aurum Institute's close collaboration with the South African DCS in implementing TB and HIV prevention and care, it is likely that the Aurum institute has the most accurate numbers available. A notable limitation to our study is that only 55% of the estimated combined population of our 16 facilities was screened. This means that our estimated facility level prevalences could be biased upwards or downwards. Because the Aurum Institute conducts blanket screenings in these prisons, we believe that these facilities received better screening coverage than what is illustrated in our findings. Instead of low screened population, the low screening percentages from certain facilities likely reflects gaps in data collection from these facilities. We therefore do not have any reason to believe that inmates who were not screened were any more or less likely to have TB disease. Also, by excluding facilities with particularly poor TB screening coverage (<30%) we hope to avoid biasing prevalence estimates through any associated facility level factors such as low health care staff or facility staff which could be associated with both screening coverage and TB disease prevalence. Although sputum submission was good in those reporting symptoms (89.50%) it was very low in

asymptomatic individuals (38.49%). This means that TB cases were likely missed, especially in those who did not report symptoms. We were also unable to locate radiologist readings for 1,044 inmates (18.81%) who were indicated via CAD score of 50 or higher. Any of these inmates who were asymptomatic and had TB disease would not have appeared in our results, thereby giving us an underestimate of TB prevalence. Furthermore, this study would have benefited from verification of a subset of samples by gold standard culture. This would have allowed us to assess the sensitivity and specificity of GeneXpert and radiologist readings. Given the predominance of new TB diagnoses based on radiologist reading alone, it would also have been desirable to have a subset of radiographs verified by expert readers.

Another limitation to the study is low HIV test consent in those screened for TB (~24%). This made it difficult to accurately estimate HIV prevalence or TB/HIV coinfection. Because HIV consent could conceivably be associated with factors related to likelihood for HIV infection, the HIV percent prevalence reported in table 4 could be under or over estimated. These estimates should therefore be interpreted with caution. While our TB prevalence estimates are likely underestimated, the estimated percent prevalence of HIV infection could be an overestimate due to the inclusion of individuals on ART at the time of screening in the HIV prevalence numerator. Bias could be introduced into the prevalence estimates due to individuals reporting ART being included in the HIV-infected numerator, while individuals who were not on ART were not included in the denominator unless they consented to HIV testing.

The lack of a gold-standard diagnostic test means that we can only present absolute numbers for our assessment of GeneXpert yield. We cannot assess how many cases were missed by GeneXpert. A study carried out in prisoners in Malaysia found that GeneXpert missed around 50% of HIV+ TB cases as confirmed by culture[42]. Poor sputum submission (38.49%) in those who were asymptomatic makes a meaningful comparison of GeneXpert yield in symptomatic and asymptomatic individuals difficult. Low HIV testing coverage combined with low sputum

submission in asymptomatic inmates makes assessment of GeneXpert yield stratified by symptom status and HIV status impossible.

The fact that all questionnaire items were self-reported means that not all responses were accurate. While this likely biased our results to some extent, our estimated prevalence rates and risk factors are in line with previous findings from South Africa. Therefore, we do not believe that a substantial number of inmates falsified their responses. Low HIV consent also made the estimation of risk factors for newly diagnosed TB disease difficult. However, we believe that by stratifying our multivariate logistic regression models by HIV status we avoided estimate bias due to effect modification by HIV infection. The fact that all questionnaire items were self-reported means that not all individual responses were accurate. While this may have biased our results to some extent, our estimated prevalence rates and risk factors are in line with previous findings from South Africa. Therefore, we do not believe that a substantial number of inmates falsified their responses. Another limitation of our risk factor analysis is our inability to control from previously identified risk factors such as drug use, alcohol use, or nutritional status. However, we do not believe that the variables observed to be significantly associated with newly diagnosed TB models in our models are confounded or highly associated with any of the known risk factors not included on the questionnaire. Recent risk factor analysis in Johannesburg prison by Telisinghe et al. did not identify self-reported smoking or drinking to be associated with newly diagnosed TB disease when controlling for relevant factors.[41] Nutritional status has been found to be a risk factor in correctional facilities in some sub-Saharan nations.[43] However, nutrition may not be as lacking in South African facilities compared to less developed sub-Saharan nations.

Analysis of this screening data was complicated initially by a large amount of duplication. This was addressed by conducting careful, tedious data cleaning over the course of several weeks.

When considering this analysis and its limitations, it is important to understand that this data was collected programmatically in an extremely difficult work environment over the course of an

entire year. While observing TB screening in 2016, the author observed that many data capturers in some of these facilities relied solely on their own rapport with 'trustee' inmates to keep themselves safe. In one facility, an inmate was stabbed in a hall while data capturers were passing unguarded through to a medical ward. This incident did not seem to be unusual for the data capturers in question, and leads this author to believe that this type of occurrence is not uncommon. A shortage of guards in observed facilities made the screening process stressful for data capturers, and could understandably lead to some errors in data collection and recording.

Despite sub optimal screening, sputum submission, and radiologist data reporting, the 31,843 inmates who were present at screening, enumerated, and recorded appropriately constitute one of the largest populations ever screened for TB in the course of 1 year. Likewise, the 18,734 constitute one of the largest ever systematically assessed by GeneXpert and reported. We believe that the large number of inmates screened will allow us to estimate TB disease prevalence rates that are as representative of the true prevalence rate as is feasible with such a large programmatic TB screening, with the caveat that the prevalence estimates are likely under estimates. The strength of this study lies in the large size of the population screened for TB disease. To our knowledge, this is the largest study ever which examines newly diagnosed TB disease in correctional facilities in South Africa. The results of this study are strengthened through use of multiple diagnostic methods. Our results also represent correctional facilities from across South Africa, increasing the generalizability of our findings to other facilities in South Africa and other middle income, high burden TB nations.

Conclusion

Despite the shortcomings of our data, we have observed and reported a high prevalence of newly diagnosed TB disease in 12 South African correctional facilities. This data supports the

hypothesis that correctional facilities can serve as reservoirs for TB disease[15, 16, 17]. For some facilities included in this screening, this is likely the first time any representative prevalence estimates have been made. These prevalence estimates should be used by South African DCS and implementing partners to prioritize available resources in addressing the high-risk prison population as a way of addressing the overall burden of TB disease in South Africa. Previous TB in inmates infected with HIV, newly diagnosed HIV in those undergoing HIV testing, and increased age, previous TB, and any 1 or more symptoms in those known to be HIV negative were identified as risk factors for newly diagnosed TB disease in the 16 facilities. These results support past research and provide a firmer evidence base for future interventions seeking to reduce the burden of TB disease in correctional facilities. Furthermore, the heterogeneity of effect estimates when stratifying by HIV status illustrate the importance of HIV in the epidemiology and ecology of TB disease. In this study, the modifying effect of HIV on the effect of symptoms was especially noteworthy. Based on our results, CAD appears to be an effective pre-screen tool that could potentially make radiography screening more available and efficient by optimizing the time and effort of human radiologists. Smaller studies should be carried out in this setting which use the same screening algorithm with a gold-standard diagnostic tool to verify a sample of potential TB cases as indicated by CAD and/or GeneXpert. This will allow assessment of sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of these tools in the South African correctional setting, thereby informing us as to how many cases may be missed in screening strategies such as this. Efforts must be made to increase the uptake of HIV testing as well as the follow-through on established screening protocol and sputum submission in South African prisons. Future screenings must ensure that more female inmates are captured and recorded in the screening process. While the author acknowledges the difficulty of data collection in this environment, future screening efforts should endeavor to include extra questionnaire items in order to capture inmates' status as to other important risk factors for TB

disease, such as nutritional status, history of alcohol/drug use, and number of facility health staff and guards.

This study has provided substantial evidence that TB disease is dire problem in South African correctional facilities, and is exacerbated by the huge burden of HIV/AIDS in South Africa, both nationally and within the correctional system. Understanding the burden of TB disease in correctional facilities is the necessary first step to addressing and fighting the TB epidemic in this setting. The results of this study should be considered and followed-up on by the South African DCS as well as the broader TB research community.

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APPENDIX

Screening Protocol: TB Screening, Detection and Management in Identified Health Facilities of the Department of Correctional Services (DCS) _ Data Analysis. Project Name: GeneXpert in Correctional Centers Programme Evaluation. Project Reference: AUR6-10-117b. 29/09/2015.

Table 1: Population and Total Screened for TB and HIV for 16 South African Correctional Facilities in 2015

Facility	Estimated Prison Capacity	2015 Prison Population (% capacity)	Total No. present at Screening (%)	No. on TB treatment at time of screening (%)[a]	Total No. Screened for TB (%)	Total No. Screened for HIV[b, c]
A	3,039	3863 (127.11)	1314 (34.02)	3 (0.23)	1311 (99.77)	49 (3.74)
B	1,748	1692 (96.80)	2160 (127.66)	11 (0.51)	2149 (99.26)	581 (27.04)
C	2,859	3832 (134.03)	4178 (109.03)	37 (0.89)	4141 (99.11)	1385 (33.45)
D	4,864	8247 (169.55)	2900 (35.16)	28 (0.97)	2872 (99.03)	1 (0.03)
E	1,831	2642 (144.29)	3816 (144.44)	7 (0.18)	3809 (99.82)	1210 (31.77)
F	3,024	3024 (100)	2393 (79.13)	10 (0.42)	2383 (99.58)	481 (20.18)
G	3,249	4005 (123.27)	3744 (93.48)	27 (0.72)	3717 (99.28)	584 (15.71)
H	4,005	4602 (114.91)	2841 (61.73)	6 (0.21)	2835 (99.79)	1267 (44.69)
I	970	1796 (185.15)	816 (45.43)	7 (0.86)	809 (99.14)	37 (4.57)
J	1,598	1603 (100.31)	1604 (100.01)	13 (0.81)	1591 (99.19)	114 (7.17)
K	4,301	5277 (122.69)	2138 (40.51)	19 (0.89)	2119 (99.11)	1133 (53.47)
L	1,672	2728 (163.16)	3643 (133.54)	5 (0.14)	3638 (99.86)	648 (17.81)
M	5,400	7,673 (142.09)	6 (0.78)	0 (-)	6 (100)	1 (16.67)
N	2,177	3,266 (150.02)	215 (6.58)	1 (0.47)	214 (99.53)	76 (35.51)
O	808	1030 (127.48)	34 (3.30)	0 (-)	34 (100)	9 (26.47)
P	1,836	2,380 (129.63)	41 (1.72)	1 (2.44)	40 (97.56)	8 (20.00)
Total	**43,381**	**57,660 (132.92)**	**31,843 (55.23)**	**175 (0.55)**	**31,668 (99.45)**	**7,584 (23.95)**

a: percentage of those present at screening
b: includes those who reported being on ART at time of screening
c: percentage screened is out of the those screened for TB

Figure 1: Population present at screening, population screened, and results of symptom and CAD screening in 12 South African Correctional Facilities in 2015

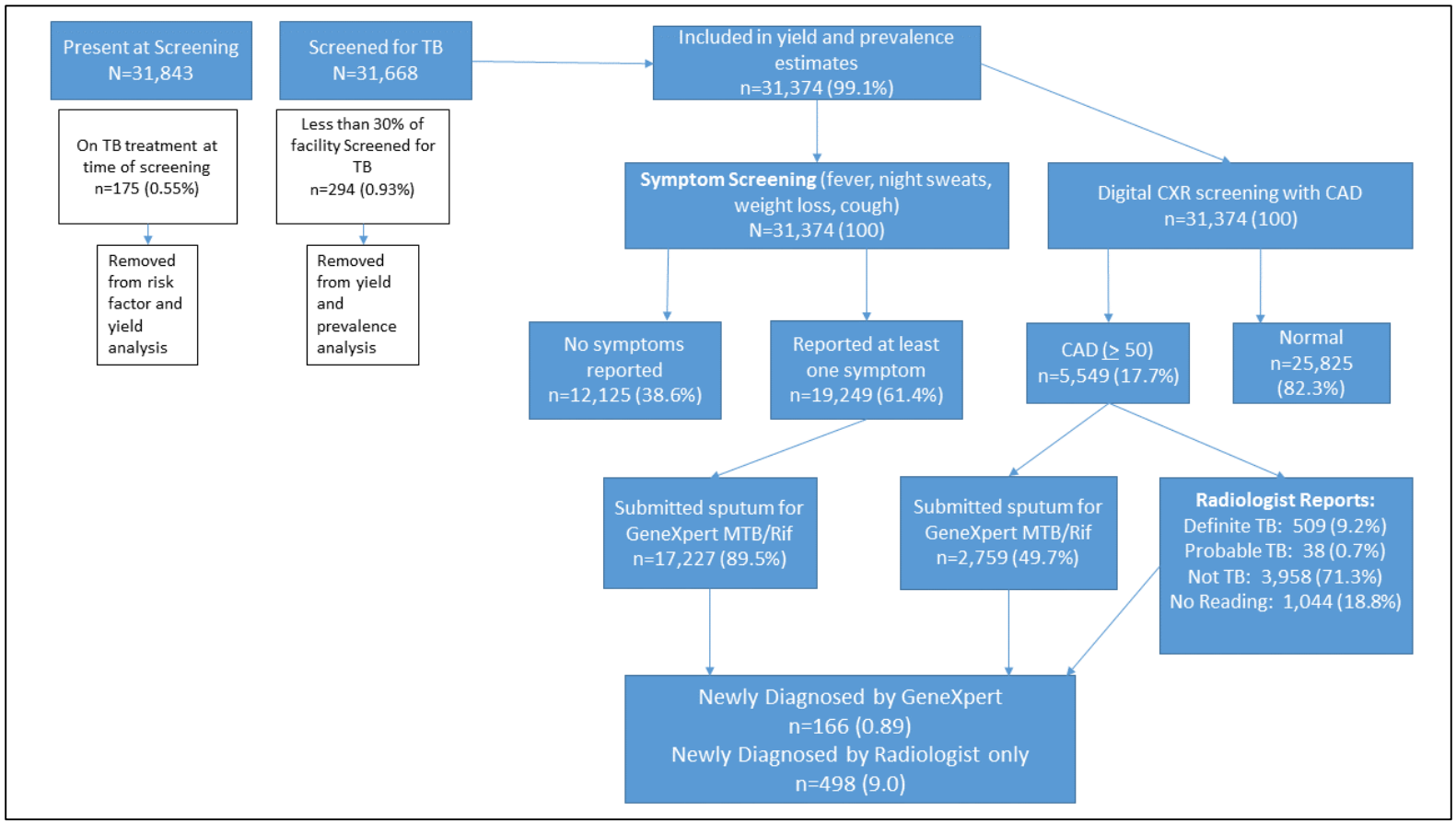

Table 2: TB Screening Results by Symptom and Computer Automated Detection (CAD) for 12 South African Correctional Facilities in 2015 (n=31,374)

Facility	No. Reporting any TB Symptom[a]	CAD+ (>=50)[b]	CAD+ only (asymptomatic)	Symptomatic and submitted sputum (%)	Asymptomatic and submitted sputum (%)
A	49 (3.74)	620 (47.29)	588 (44.85)	11 (22.45)	46 (7.82)
B	1394 (65.87)	525 (24.43)	438 (20.38)	1386 (99.43)	323 (73.74)
C	2608 (62.98)	745 (17.99)	637 (15.4)	2324 (89.11)	547 (85.87)
D	445 (15.49)	935 (32.56)	728 (25.34)	25 (5.62)	31 (4.26)
E	3726 (97.82)	590 (15.49)	27 (0.71)	3662 (98.28)	2 (7.41)
F	1669 (70.04)	152 (6.38)	105 (4.41)	1564 (93.71)	24 (22.86)
G	1887 (50.77)	524 (14.10)	403 (10.84)	1045 (55.38)	194 (48.14)
H	2157 (76.08)	248 (8.75)	196 (6.91)	2157 (100)	196 (100)
I	53 (6.55)	225 (27.81)	215 (26.57)	15 (28.30)	9 (4.19)
J	415 (26.08)	594 (37.34)	479 (30.11)	206 (49.64)	56 (11.69)
K	1471 (69.42)	93 (4.39)	40 (1.89)	1458 (99.12)	23 (57.50)
L	3375 (92.77)	298 (8.19)	59 (1.62)	3374 (99.97)	56 (94.92)
Total	**19,249 (61.35)**	**5549 (17.69)**	**3915 (12.48)**	**17,227 (89.50)**	**1507 (38.49)**

a: Symptoms: current cough, fever, drenching night sweats, or unexplained weight loss as reported by inmate

b: a CAD cutoff of 50 was used in this screening. This means that any inmate with a score of 50 or higher (out of 100) was indicated to submit sputum for GeneXpert testing and digital radiograph was sent to human radiologist for assessment

Table 3: GeneXpert Yield of newly diagnosed TB disease in self-reported symptomatic and asymptomatic inmates in 12 South African Prisons in 2015 (n=31,374)

Facility	Total GeneXpert Positive (% yield)	GeneXpert Positive in symptomatic (% yield)	GeneXpert Positive in asymptomatic, CAD+ (% yield)
A	3 (5.26)	1 (9.09)	2 (4.35)
B	7 (0.41)	7 (0.51)	0 (-)
C	34 (1.18)	31 (1.33)	3 (0.55)
D	3 (5.36)	3 (12)	0 (-)
E	38 (1.04)	38 (1.04)	0 (-)
F	16 (1.01)	16 (1.02)	0 (-)
G	17 (1.37)	15 (1.44)	2 (1.03)
H	22 (0.93)	21 (0.97)	1 (0.51)
I	0 (-)	0 (-)	0 (-)
J	4 (1.53)	4 (1.94)	0(-)
K	7 (0.47)	7 (0.48)	0 (-)
L	15 (0.44)	15 (0.44)	0 (-)
Total	**166 (0.89)**	**158 (0.92)**	**8 (0.53)**

Table 4: Results of TB Symptom and CAD screening and Yield of GeneXpert for newly diagnosed TB disease in those with known HIV status in 9 South African prisons in 2015 (n=7,403)

Facility	Total No. with Known HIV Status[a]	HIV prevalence (%)	No. Reporting any symptom and submitted sputum	No. asymp-tomatic (CAD+ only) and submitted sputum	No. GeneXpert Positive	Overall Yield of GXP	Genexpert+ and symptomatic (% yield	GeneXpert+ in asymptomatic (% yield)
B								
HIV+	234	40.28	159	26	0	0	0	0
HIV-	347		266	38	3	0.99	3 (1.13)	0
C								
HIV+	313	22.6	237	34	5	1.85	5 (2.11)	0
HIV-	1072		726	158	10	1.13	9 (1.24)	1 (0.63)
E								
HIV+	260	21.49	258	0	10	3.88	10 (3.88)	0
HIV-	950		937	0	12	1.28	12 (1.28)	0
F								
HIV+	377	78.38	228	6	5	2.14	5 (2.19)	0
HIV-	104		82	0	1	1.22	1 (1.22)	0
G								
HIV+	99	16.95	43	4	4	8.51	3 (6.98)	1 (25)
HIV-	485		114	12	2	1.59	2 (1.75)	0
H								
HIV+	387	30.54	311	2	9	2.88	9 (2.89)	0
HIV-	880		671	5	8	1.18	8 (1.19)	0
J								
HIV+	76	66.67	26	6	0	0	0	0
HIV-	38		34	0	1	2.94	1 (2.94)	0

K								
HIV+	141	12.44	93	3	1	1.04	1 (1.08)	0
HIV-	992		616	10	2	0.32	2 (0.32)	0
L								
HIV+	200	30.86	188	1	5	2.65	5 (2.66)	0
HIV-	448		357	3	3	0.83	3 (0.84	0
Total HIV+	**2087**		**1543**	**82**	**39**	**2.4**	**38 (2.46)**	**1 (1.22)**
Total HIV-	**5316**		**3803**	**226**	**42**	**1.04**	**41 (1.08)**	**1 (0.44)**
Total	**7403**	**28.19**	**5346**	**308**	**81**	**1.43**	**79 (1.48)**	**2 (0.65)**

a: individuals who reported TB treatment at the time of screening are excluded from this analysis
Note: Facilities A, D, and I are excluded due to less than 5% screened with known HIV status

Table 5: Prevalence of TB Disease and TB/HIV Coinfection in 12 South African Prison Facilities in 2015 (n=31,547)

Facility	Total No. with known TB or screened for TB[a] (%)	TB Treat--ment at time of screen (%)	Newly diagnosed with TB by GXP (%)	Newly Diagnosed with TB by Radiologist only (%)	Total with TB Disease (%)	TB Prevalence Rate (per 100,000)	No. with Known HIV status (%)[c, d]	No. TB+ (%)	No. with TB/HIV Coinfection (%)
A[b]	1314 (34.02)	3 (0.23)	3 (0.23)	76 (5.81)	82 (6.24)	6,240	49 (3.73)	-	-
B	2160 (127.66)	11 (0.51)	7 (0.33)	36 (1.68)	54 (2.50)	2,500	581 (26.96)	10 (1.72)	7 (1.20)
C	4178 (109.03)	37 (0.89)	34 (0.82)	28 (0.68)	99 (2.37)	2,370	1385 (33.16)	16 (1.16)	6 (0.43)
D[b]	2900 (35.16)	28 (0.97)	3 (0.10)	82 (2.86)	113 (3.90)	3,897	1 (0.03)	-	-
E	3816 (144.44)	7 (0.18)	38 (1.00)	32 (0.85)	77 (2.02)	2,018	1210 (33.17)	23 (1.90)	11 (0.91)
F	2393 (79.13)	10 (0.42)	16 (0.67)	53 (2.24)	79 (3.30)	3,301	481 (20.13)	14 (2.91)	13 (2.7)
G	3744 (93.48)	27 (0.72)	17 (0.46)	37 (1.00)	81 (2.16)	2,163	584 (15.60)	8 (1.37)	5 (0.86)
H	2841 (61.73)	6 (0.21)	22 (0.78)	45 (1.60)	73 (2.57)	2,570	1267 (44.63)	18 (1.42)	10 (0.79)
I[b]	816 (45.43)	7 (0.86)	0 (-)	18 (2.22)	25 (3.06)	3,064	37 (4.55)	-	-
J	1604 (100.01)	13 (0.81)	4 (0.25)	59 (3.72)	76 (4.74)	4,738	114 (7.13)	4 (3.51)	3 (2.63)
K	2138 (40.51)	19 (0.89)	7 (0.33)	18 (0.85)	44 (2.06)	2,058	1133 (53.02)	4 (0.35)	2 (0.18)
L	3643 (133.54)	5 (0.14)	15 (0.41)	14 (0.39)	34 (0.93)	933	648 (17.81)	9 (1.39)	6 (0.93)
Total	**31,547 (72.84)**	**173 (0.55)**	**166 (0.53)**	**498 (1.60)**	**837 (2.65)**	**2,653**	**7490 (23.74)**	**106 (1.42)**	**63 (0.84)**

a: this includes those who reported being on TB treatment at the time of screening
b: Not considered for HIV or coinfection prevalence due to too few inmates with known HIV status
c: this excludes those who reported being on TB treatment at time of screening
d: percent of those with known HIV status

Figure 2: Prevalence Rate of TB Disease in 12 South African Correctional Facilities in 2015 (n=31,547)

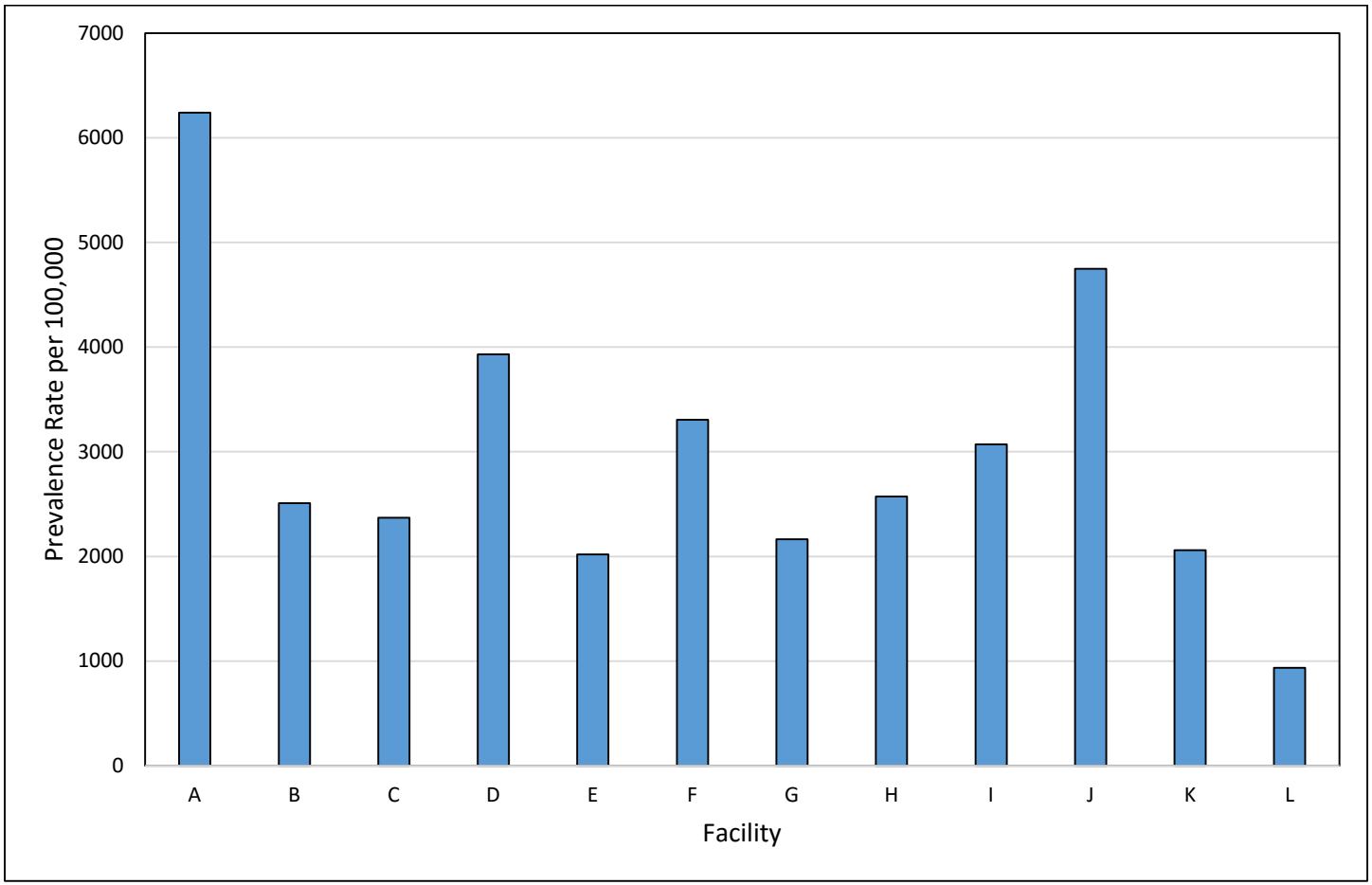

Table 6: Demographic and clinical characteristics of all inmates screened for TB, all inmates included in TB prevalence estimates, and all inmates excluded from prevalence estimates in 16 South African Prisons in 2015 (n=31,668)

Characteristic	All Screened (%) (n=31,668)	Included in TB prevalence analysis (n=31,547)[a]	Excluded from prevalence analysis (n=296)[b]	P-value[d]
Age				
15-24 years	4,091 (12.92)	4,075 (12.92)	39 (13.18)	0.75
25-44 years	23,745 (74.98)	23,654 (74.98)	218 (73.65)	
45 and older	3,725 (11.76)	3,709 (11.76)	39 (13.18)	
Missing	107 (0.34)	109 (0.35)	0	
Gender				
Male	30,691 (96.91)	30,566 (96.89)	293 (98.99)	0.006
Female	872 (2.75)	876 (2.78)	1 (0.34)	
Missing	105 (0.33)	105 (0.33)	2 (0.68)	
Race				
Black/African	29,554 (93.32)	29,434 (93.30)	286 (96.62)	0.20
Mixed Race	1,217 (3.84)	1,220 (3.87)	4 (1.35)	
Indian/Asian	177 (0.5)	176 (0.56)	1 (0.34)	
White/European	594 (1.88)	591 (1.87)	5 (1.69)	
Other	55 (0.17)	55 (0.17)	0	
Missing	71 (0.22)	71 (0.23)	0	
Years Incarcerated				
Less than 1 year (newly incarcerated)	11,757 (37.13)	11,780 (37.34)	46 (15.54)	<0.0001

1-2 years	6,575 (20.76)	6,491 (20.58)	115 (38.85)	
3-4 years	5,010 (15.82)	4,974 (15.77)	58 (19.59)	
5-9 years	5,398 (17.05)	5,375 (17.04)	50 (16.89)	
10 years or more	2,182 (6.89)	2,176 (6.90)	26 (8.78)	
Missing	746 (2.36)	751 (2.38)	1 (0.34)	
Basis for screening				
New Admission	3,411 (10.79)	3,407 (10.80)	30 (10.14)	<0.0001
Campaign	13,726 (43.42)	13,718 (43.48)	82 (27.70)	
Bi-annual screening	13,665 (43.23)	13,575 (43.03)	160 (54.05)	
Referred	684 (2.16)	666 (2.11)	23 (7.77)	
Contact	126 (0.4)	125 (0.40)	1 (0.34)	
Missing	56 (0.18)	56 (0.18)	0	
Previous TB				
Yes	1,412 (4.46)	1,449 (4.59)	29 (9.80)	<0.0001
No	30,199 (95.36)	30,037 (95.21)	266 (89.86)	
Missing	57 (0.18)	61 (0.19)	1 (0.34)	
Time since previous diagnosis				
Less than a year	255 (18.46)	283 (19.53)	12 (4.05)	
1-2 years	199 (14.41)	203 (14.01)	4 (1.35)	0.01
More than 2 years ago	927 (67.13)	927 (63.98)	12 (4.05)	
Missing	31 (2.20)	36 (2.48)	1 (3.45)	
Symptoms				
Cough	14,257 (45.02)	14,133 (44.80)	222 (75.00)	<0.0001
Fever	6,314 (19.94)	6,173 (19.57)	176 (59.46)	<0.0001
Night Sweats	7,290 (23.02)	7,157 (22.69)	176 (59.46)	<0.0001

Weight Loss	5,461 (17.24)	5,429 (17.21)	74 (25.00)	0.0003
Missing[c]	4 (0.01)	5 (0.02)	0	
Symptoms				
Any symptom	19,506 (61.60)	19,367 (61.39)	259 (87.50)	<0.0001
No symptoms	12,162 (38.40)	12,180 (38.61)	37 (12.50)	
Number of Symptoms				
1 symptom	10,126 (31.98)	10,142 (32.15)	49 (16.55)	<0.0001
2 or more symptoms	9,380 (29.60)	9,225 (29.24)	210 (70.95)	
CAD Reading				
CAD≥50	5573 (17.60)	5,603 (17.76)	24 (8.11)	<0.0001
CAD < 50	26,095 (82.40)	25,944 (82.24)	272 (91.89)	
Radiologist Reading				
'Definite TB'	511 (1.61)	533 (1.69)	2 (8.33)	0.82
'Probable Tuberculosis'	38 (0.12)	41 (0.13)	0	
Not TB	3,966 (71.16)	3,981 (71.05)	8 (33.33)	
Missing	1,058 (18.98)	1,048 (18.70)	14 (58.34)	
Known HIV Status				
No. with known HIV status	7,584 (23.95)	7,541 (23.90)	94 (31.76)	0.002
No. with unknown HIV status	24,084 (76.05)	24,006 (76.10)	202 (68.24)	
ART Status				
ART+	1432 (4.52)	1,444 (4.58)	13 (4.39)	0.88
ART-	30,236 (95.48)	30,103 (95.42)	283 (95.61)	
Known HIV+				

Known HIV+	2,115 (27.89)	2,127 (28.21)	19 (20.21)	0.83
Known HIV-	5,469 (72.11)	5,414 (71.79)	75 (79.79)	
Missing	24,084 (76.05%)	24,006 (76.09)	0	
Total	**31,668**	**31,547**	**296**	

a: included those reporting TB treatment at time of screening
b: excluded due to low screening coverage in facility
c: those missing all symptoms were considered as not having reported symptoms in analyses
d: p-values comparing included vs excluded inmates; calculated using chi-square test, if any cells in a 2-way comparison contain less than 5 individuals then p-value was calculated using Fisher's exact test

Table 7: Model 1, Bivariate Associations between Demographic and Clinical Variables and Newly Diagnosed TB Disease by GeneXpert or Radiologist in All inmates screened for TB disease in 16 South African Prisons in 2015 (n=31,668)

Factor	N=31,668 (%)	Newly Diagnosed with TB (N = 684)	TB Negative (N = 30,984)	Bivariate Analysis			
				OR	95% Confidence Interval		P-value
					Lower	Upper	
Age							
15-24 years	4091 (12.92)	26 (3.80)	4,065 (13.12)	ref	-	-	-
25-44 years	23745 (74.98)	493 (72.08)	23,252 (75.05)	3.32	2.23	4.92	<0.0001
45 and older	3725 (11.76)	163 (23.83)	3,562 (11.50)	7.15	4.72	10.85	<0.0001
Gender							
Female	872 (2.75)	9 (1.32)	863 (2.79)	ref	-	-	-
Male	30,691 (96.91)	674 (98.54)	30,017 (96.88)	2.15	1.11	4.17	0.023
Race							
Black/African	29,554 (93.32)	652 (95.32)	28,902 (93.28)	ref	-	-	-
Non-African	2,043 (6.45)	30 (4.39)	2,013 (6.50)	0.66	0.46	0.96	0.028
Years Incarcerated							
Less than 1 year (newly incarcerated)	11,757 (37.13)	182 (26.61)	11,575 (37.36)	ref	-	-	-
1-2 years	6,575 (20.76)	159 (23.25)	6,416 (20.71)	1.58	1.27	1.95	<0.0001
3-4 years	5010 (15.82)	110 (16.08)	4,900 (15.81)	1.43	1.12	1.81	0.0035
5-9 years	5,398 (17.05)	162 (23.68)	5,236 (16.90)	1.97	1.59	2.44	<0.0001

10 years or more	2,182 (6.89)	60 (8.77)	2,122 (6.85)	1.80	1.34	2.42	<0.0001
Previous TB							
No	30,199 (95.36)	439 (64.18)	29,760 (96.05)	ref	-	-	-
Yes	1412 (4.46)	245 (35.82)	1,167 (3.77)	14.23	12.04	16.82	<0.0001
Cough							
No	17,388 (54.91)	405 (59.21)	16,983 (54.81)	ref	-	-	-
Yes	14,257 (45.02)	278 (40.64)	13,979 (45.12)	0.83	0.72	0.97	0.0211
Fever							
No	25,336 (80.01)	565 (82.60)	24,771 (79.95)	ref	-	-	-
Yes	6,314 (19.94)	117 (17.11)	6,197 (20)	0.83	0.68	1.01	0.0654
Night Sweats							
No	24,359 (76.92)	524 (76.61)	23,835 (76.93)	ref	-	-	-
Yes	7,290 (23.02)	157 (22.95)	7,133 (23.02)	1.00	0.84	1.20	0.9898
Weight Loss							
No	26,180 (82.67)	562 (82.16)	25,618 (82.68)	ref	-	-	-
Yes	5,461 (17.24)	120 (17.54)	5,341 (17.24)	1.02	0.84	1.25	0.813
No. of Symptoms							
No symptoms	12,162 (38.40)	344 (50.29)	11,818 (38.14)	ref	-	-	-
1 symptom	10,126 (31.98)	150 (21.93)	9,976 (32.20)	0.52	0.43	0.63	<0.0001

2 or more symptoms	9,380 (29.6)	190 (27.78)	9,190 (29.66)	0.71	0.59	0.85	0.0002
HIV Status							
Known HIV- and HIV Unknown	29,553 (93.32)	621 (90.32)	28,932 (93.38)	ref	-	-	-
Known HIV+	2,115 (6.68)	63 (9.21)	2,052 (6.62)	1.43	1.1	1.86	0.0076

Table 8: Model 2, Bivariate Associations between Demographic and Clinical Variables and Newly Diagnosed TB Disease by GeneXpert or Radiologist in those Known to be HIV+ in 16 South African Prisons 2015 (n=2,115)

Factor	**Known HIV Positive** **N=2,115 (%)**	Newly Diagnosed with TB (N =63) (%)	TB Negative (N = 2,052) (%)	Bivariate Analysis				Multivariate Analysis			
				OR	95% Confidence Interval		P-value	aOR	95% Confidence Interval		P-value
					Lower	Upper			Lower	Upper	
Age											
15-24 years	131 (6.19)	3 (4.76)	128 (6.24)	Ref	-	-	-	ref	-	-	-
25-44 years	1,719 (81.28)	49 (77.78)	1,670 (81.38)	1.25	0.39	4.07	0.70	0.9	0.27	3	0.86
45 and older	263 (12.43)	11 (17.46)	252 (12.28)	1.86	0.51	6.79	0.35	1.02	0.26	3.9	0.98
Gender											
Female	21 (0.99)	0	21 (0.99)	Ref	-	-	-	-	-	-	-
Male	2,086 (98.63)	63 (100)	2,023 (98.59)	-	-	-	-	-	-	-	-
Race											
Black/African	2,049 (96.88)	62 (98.41)	1,987 (96.83)	Ref	-	-	-	-	-	-	-
Non-African	63 (2.98)	0	63 (3.07)	-	-	-	-	-	-	-	-
Years Incarcerated											
Less than 1 year	803 (37.97)	16 (25.40)	787 (38.35)	ref	-	-	-	ref	-	-	-
1-2 years	407 (19.24)	15 (23.81)	392 (19.10)	1.88	0.92	3.85	0.08	1.71	0.83	3.53	0.14

3-4 years	356 (16.83)	12 (19.05)	344 (16.76)	1.72	0.80	3.67	0.16	1.39	0.64	3.02	0.41
5-9 years	409 (19.34)	16 (25.40)	393 (19.15)	2	0.99	4.05	0.05	1.52	0.74	3.15	0.26
10 years or more	112 (5.30)	3 (4.76)	109 (5.31)	1.35	0.39	4.72	0.64	1.2	0.34	4.27	0.78
Previous TB											
No	1,831 (86.70)	39 (61.90)	1,792 (87.46)	ref	-	-	ref	-	-	-	-
Yes	281 (13.30)	24 (23.10)	257 (12.54)	4.29	2.54	7.25	<0.0001	4.2	2.43	7.25	<0.0001
Cough											
No	917 (43.42)	25 (39.68)	892 (43.53)	ref	-	-	-	-	-	-	-
Yes	1,195 (56.58)	38 (60.32)	1,157 (56.47)	1.17	0.70	1.96	0.54	-	-	-	-
Fever											
No	1,544 (73.04)	48 (76.19)	1,496 (72.94)	ref	-	-	-	-	-	-	-
Yes	570 (26.96)	15 (23.81)	555 (27.06)	0.84	0.47	1.52	0.57	-	-	-	-
Night Sweats											
No	1,373 (64.95)	39 (61.90)	1,334 (65.04)	ref	-	-	-	-	-	-	-
Yes	741 (35.05)	24 (38.10)	717 (34.96)	1.15	0.68	1.92	0.61	-	-	-	-
Weight Loss											
No	1,539 (72.94)	44 (69.84)	1,495 (73.03)	ref	-	-	-	-	-	-	-
Yes	571 (27.06)	19 (30.16)	552 (26.97)	1.17	0.68	2.02	0.58	-	-	-	-
No. of Symptoms											

No symptoms	514 (24.30)	15 (23.81)	499 (24.32)	ref	-	-	-	-	-	-	-
1 symptom	694 (32.81)	22 (34.92)	672 (32.75)	1.09	0.56	2.12	0.80	-	-	-	-
2 or more	907 (42.88)	26 (41.27)	881 (42.93)	0.98	0.52	1.87	0.96	-	-	-	-
ART Status at screening											
ART+	1,432 (67.71)	42 (66.67)	1,390 (67.74)	ref	-	-	-	-	-	-	-
ART-	683 (32.29)	21 (33.33)	662 (32.26)	1.05	0.62	1.79	0.86	-	-	-	-

Table 9: Model 3, Bivariate Associations between Demographic and Clinical Variables and Newly Diagnosed TB Disease by GeneXpert or Radiologist in those Known to be HIV- or HIV unknown in 16 South African Prisons 2015 (n=29,553)

Factor	**Known HIV Negative and HIV Unknown (N=29,553) (%)**	Newly Diagnosed with TB (N =621) (%)	TB Negative (N = 28,932) (%)	Bivariate Analysis				Multivariate Analysis			
				OR	95% Confidence Interval		P-value	aOR	95% Confidence Interval		P-value
					Lower	Upper			Lower	Upper	
Age											
15-24 years	3,960 (13.40)	23 (3.70)	3,937 (13.61)	ref	-	-	-	ref	-	-	-
25-44 years	22,026 (74.53)	444 (71.50)	21,582 (74.60)	3.52	2.31	5.36	<0.0001	2.66	1.73	4.09	<0.0001
45 and older	3,462 (11.71)	152 (24.48)	3,310 (11.44)	7.86	5.06	12.22	<0.0001	5.21	1.73	4.09	<0.0001
Gender											
Female	851 (2.88)	9 (1.45)	842 (2.91)	ref	-	-	-	ref	-	-	-
Male	28,605 (96.79)	611 (98.39)	27,994 (96.76)	2.04	1.05	3,96	0.035	2.32	1.13	4.77	0.02
Race											
Black/African	27,505 (93.07)	590 (95.01)	26,915 (93.03)	ref	-	-	-	-	-	-	-
Non-African	1,980 (6.70)	30 (4.83)	1,950 (6.74)	0.7	0.49	1.02	0.061	-	-	-	-
Years Incarcerated											
Less than 1 year	10,954 (37.07)	166 (26.73)	10,788 (37.29)	ref	-	-	-	ref	-	-	-

1-2 years	6,168 (20.87)	144 (23.19)	6,024 (20.82)	1.55	1.24	1.95	0.0001	1.14	0.9	1.22	0.28
3-4 years	4,654 (15.75)	98 (15.78)	4,556 (15.75)	1.4	1.09	1.8	0.0092	0.94	0.72	1.22	0.64
5-9 years	4,989 (16.88)	146 (23.51)	4,843 (16.74)	1.96	1.57	2.45	<0.0001	1.18	0.93	1.5	0.17
10 years or more	2070 (7)	57 (9.18)	2,013 (6.96)	1.84	1.36	2.5	<0.0001	0.82	0.59	1.14	0.244
Previous TB											
No	28,368 (96.17)	400 (64.41)	27,968 (96.85)	ref	-	-	-	ref	-	-	-
Yes	1,131 (3.83)	221 (35.59)	910 (3.15)	16.98	14.23	20.27	<0.0001	14.43	12	17.35	<0.0001
Cough											
No	16,471 (55.77)	380 (61.29)	16,091 (55.65)	ref	-	-	-	-	-	-	-
Yes	13,062 (44.23)	240 (38.71)	12,822 (44.35)	0.793	0.67	0.93	0.005	-	-	-	-
Fever											
No	23,792 (80.55)	517 (83.52)	23,275 (80.49)	ref	-	-	-	-	-	-	-
Yes	5,744 (19.45)	102 (16.48)	5,642 (19.51)	0.81	0.66	1.01	0.06	-	-	-	-
Night Sweats											
No	22,986 (77.83)	485 (78.48)	22,501 (77.81)	ref	-	-	-	-	-	-	-
Yes	6,549 (22.17)	133 (21.52)	6,416 (22.19)	0.96	0.79	1.17	0.7	-	-	-	-
Weight Loss											
No	24,641 (83.44)	518 (83.68)	24, 123 (83.44)	ref	-	-	-	-	-	-	-

Yes	4,890 (16.56)	101 (16.32)	4,789 (16.56)	0.98	0.79	1.22	0.87	-	-	-	-
No. of Symptoms											
No symptoms	11,648 (39.41)	329 (52.98)	11,319 (39.12)	ref	-	-	-	ref	-	-	-
1 symptom	9,432 (31.92)	128 (20.61)	9,304 (32.16)	0.47	0.39	0.58	<0.0001	0.57	0.5	0.7	<0.0001
2 or more	8,473 (28.67)	164 (26.41)	8,309 (28.72)	0.68	0.56	0.82	<0.0001	0.77	0.63	0.94	0.009

Table 10: Model 4, Bivariate Associations between Demographic and Clinical Variables and Newly Diagnosed TB by GeneXpert or Radiologist in those with Known HIV Status in 16 South African Prisons in 2015 (n=7,584)

Factor	N=7,584 (%)	Newly Diagnosed with TB by GXP or CXR (N =109)	TB Negative (N = 7,475)	Bivariate Analysis			
				OR	95% Confidence Interval		P-value
					Lower	Upper	
Age							
15-24 years	1261 (16.63)	6 (5.50)	1,255 (16.79)	ref	-	-	-
25-44 years	5591 (73.72)	88 (80.73)	5,503 (73.62)	3.35	1.46	7.67	0.0043
45 and older	715 (9.43)	15 (13.76)	700 (9.36)	4.48	1.73	11.60	0.002
Gender							
Female	68 (0.90)	0 (0)	68 (0.91)	-	-	-	-
Male	7484 (98.68)	109 (100)	7,375 (98.66)	-	-	-	-
Race							
Black/African	7022 (92.59)	104 (95.41)	6,918 (92.55)	ref	-	-	-
Non-African	540 (7.12)	4 (3.67)	536 (7.17)	2.01	0.74	5.49	0.17
Years Incarcerated							
Less than 1 year (newly incarcerated)	3662 (48.29)	44 (40.37)	3,618 (48.40)	ref	-	-	-
1-2 years	1415 (18.66)	23 (21.10)	1,392 (18.62)	1.36	0.82	2.26	0.2371
3-4 years	984 (12.87)	18 (16.51)	966 (12.92)	1.53	0.88	2.66	0.1304
5-9 years	1052 (13.87)	19 (17.43)	1,033 (13.82)	1.51	0.88	2.60	0.135
10 years or more	365 (4.81)	4 (3.67)	361 (4.83)	0.91	0.33	2.55	0.8593

Previous TB							
No	7191 (94.82)	81 (74.31)	7,110 (95.12)	ref	-	-	-
Yes	379 (5.00)	28 (25.69)	351 (4.70)	7.00	4.50	10.90	<0.0001
Cough							
No	3318 (43.75)	30 (27.52)	3,288 (43.99)	ref	-	-	-
Yes	4257 (56.13)	78 (71.56)	4,179 (55.91)	2.05	1.34	3.12	0.0009
Fever							
No	5600 (73.84)	74 (67.89)	5,526 (73.93)	ref	-	-	-
Yes	1980 (26.11)	35 (32.11)	1,945 (26.02)	1.34	0.90	2.02	0.1527
Night Sweats							
No	5362 (70.70)	62 (56.88)	5,300 (70.90)	ref	-	-	-
Yes	2219 (29.26)	47 (43.12)	2,172 (29.06)	1.85	1.26	2.71	0.0016
Weight Loss							
No	5727 (75.61)	68 (62.39)	5,659 (75.71)	ref	-	-	-
Yes	1847 (24.39)	41 (37.61)	1,806 (24.16)	1.89	1.28	2.79	0.0014
No. of symptoms							
No symptoms	1899 (25.04)	16 (14.68)	1,883 (25.19)	ref	-	-	-
1 symptom	2,739 (36.12)	35 (32.11)	2,704 (36.17)	1.52	0.84	2.76	0.1652
2 or more symptoms	2,946 (38.84)	58 (53.21)	2,888 (38.64)	2.36	1.36	4.12	0.0025
Newly diagnosed HIV							
no	5,469 (88.90)	46 (68.66)	5,423 (89.12)	ref	-	-	-
yes	683 (11.10)	21 (31.34)	662 (10.88)	3.74	2.22	6.31	<0.0001

Table 11: Model 5, Bivariate and Multivariate Associations between Demographic and Clinical Variables and Newly Diagnosed TB by GeneXpert or Radiologist in individuals known to be HIV- in 16 South African Prisons in 2015 (n=5,469)

Factor	N=5,469 (%)	Newly Diagnosed with TB by GXP or CXR (N =46)	TB Negative (N = 5,423)	Bivariate Analysis				Multivariate Analysis			
				OR	95% Confidence Interval		P-value	aOR	95% Confidence Interval		P-value
					Lower	Upper			Lower	Upper	
Age											
15-24 years	1,130 (20.66)	3 (6.52)	1,127 (20.78)	ref	-	-	-	ref	-	-	-
25-44 years	3,872 (70.80)	39 (84.78)	3,833 (70.68)	3.82	1.18	12.39	0.026	4.17	1.28	13.64	0.02
45 and older	452 (8.26)	4 (8.70)	448 (8.26)	3.35	0.75	15.05	0.11	4.06	0.89	18.57	0.071
Gender											
Female	47 (0.86)	0	47 (0.87)	-	-	-	-	-	-	-	-
Male	5,398 (98.70)	46 (100)	5,352 (98.69)	-	-	-	-	-	-	-	-
Race											
Black/African	4,973 (90.93)	42 (91.30)	4,931 (90.93)	ref	-	-	-	-	-	-	-
Non-African	477 (8.72)	4 (8.70)	473 (8.72)	1.00	0.36	2.82	0.99	-	-	-	-
Years Incarcerated											
Less than 1 year	2,859 (52.28)	28 (60.87)	2,831 (52.20)	ref	-	-	-	ref	-	-	-
1-2 years	1,008 (18.43)	8 (17.39)	1,000 (18.44)	0.81	0.37	1.78	0.60	0.74	0.33	1.65	0.46
3-4 years	628 (11.48)	6 (13.04)	622 (11.47)	0.98	0.40	2.37	0.96	0.93	0.38	2.27	0.88
5-9 years	643 (11.76)	3 (6.52)	640 (11.80)	0.47	0.14	1.56	0.22	0.39	0.12	1.30	0.12
10 years or more	253 (4.63)	1 (2.17)	252 (4.65)	0.40	0.05	2.96	0.37	0.30	0.04	2.30	0.25
Previous TB											

No	5,360 (98.01)	42 (91.30)	5,318 (98.06)	ref	-	-	-	ref	-	-	-
Yes	98 (1.79)	4 (8.70)	94 (1.73)	5.39	1.89	15.33	0.002	5.41	1.85	15.79	0.002
Cough											
No	2,401 (43.90)	5 (10.87)	2,396 (44.18)	ref	-	-	-	-	-	-	-
Yes	3,062 (55.99)	40 (86.96)	3,022 (55.73)	6.34	2.5	16.09	0.0001	-	-	-	-
Fever											
No	4,056 (74.16)	26 (56.52)	4,030 (74.31)	ref	-	-	-	-	-	-	-
Yes	1,410 (25.78)	20 (43.48)	1,390 (25.63)	2.23	1.24	4.01	0.007	-	-	-	-
Night Sweats											
No	3,989 (72.94)	23 (50)	3,966 (73.13)	ref	-	-	-	-	-	-	-
Yes	1,478 (27.03)	23 (50)	1,455 (26.83)	2.72	1.52	4.88	0.0007	-	-	-	-
Weight Loss											
No	4,188 (76.58)	24 (75.78)	4,164 (76.78)	ref	-	-	-	-	-	-	-
Yes	1,276 (23.33)	22 (47.83)	1,254 (23.12)	3.04	1.70	5.45	0.0002	-	-	-	-
No. of Symptoms											
No symptoms	1,385 (25.32)	1 (2.17)	1,384 (25.52)	ref	-	-	-	ref	-	-	-
1 symptom	2,045 (37.39)	13 (28.26)	2,032 (37.47)	8.85	1.16	67.72	0.036	8.15	1.06	62.38	0.044
2 or more symptoms	2,039 (37.28)	32 (69.57)	2,007 (37.01)	22.06	3.01	161.59	0.002	19.99	2.72	146.66	0.003