Tuberculosis infection among healthcare trainees in South India

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Abstract

Background: Pulmonary tuberculosis (TB) is a mycobacterial infection which can lead to poor respiratory health and even death. Carried by airborne droplets, TB is well-transmitted in crowded hospitals where infectious individuals are in close proximity with others. For this reason, healthcare workers and trainees in high burden countries such as India are at great risk of being exposed to and acquiring TB.

Objective: We investigated the prevalence of TB infection among healthcare trainees in a private university in Manipal and Mangalore, India. We also assessed knowledge, attitudes and practices (KAP) of TB infection control among trainees.

Methods: Eligible medical and nursing undergraduate students in Manipal university (n=443) were recruited and assessed for exposure to TB, and latent TB status using the tuberculin skin test. Trainees with at least two years of exposure to hospital settings were compared with trainees with no exposure to hospital settings. Eligible internship year and post-graduate residents in medicine (n=486) were administered a questionnaire assessing their knowledge, attitudes and practices (KAP) related to TB infection control.

Results: The prevalence of TB infection among undergraduate trainees in medicine and nursing was 5.1% (95% CI 3.1-7.2). Being posted in pulmonary medicine departments was associated with both an increase in TST induration size of 1.42mm (95% CI 0.66, 2.19) and 3.11 times adjusted odds of TST positivity (95% CI 1.31, 7.36). Among interns and post-graduate students, being a post-graduate was associated with a knowledge score increase of 3.6% (95% CI 1.4-6.0). Knowledge score for TB infection control at 50.5% (95% CI 48.7-52.2) was significantly lower than transmission and risk factors for TB 67.5% (95% CI 65.6-69.4). Overall, 76.75% reported that they do not always wear a mask when working with a TB patient.

Conclusion: The prevalence of TB infection among healthcare undergraduate students is lower than reported elsewhere in India. However, the results are unique to this context and cannot be generalized to all healthcare undergraduates in India. We identified gaps in knowledge, attitudes and perception of TB infection control among medical interns and post-graduates. This presents a source of vulnerability to TB infection that is amenable to institutional interventions.

Résumé

Contexte: La tuberculose pulmonaire (TB) est une infection mycobactérienne qui peut conduire à une mauvaise santé respiratoire et même la mort. Porté par des gouttelettes, la TB est bien transmise dans les hôpitaux où les individus infectieux sont proches d'autres. Ainsi, les travailleurs de la santé sont à grand risque d'être exposés à la TB et infectées par la TB.

Objectif: Cette recherche a étudié la prévalence de l'infection TB parmi les étudiants dans une école de médecine et un hôpital privé en Inde. Nous avons évalué aussi les connaissances, attitudes et pratiques (CAP) de contrôle de la tuberculose chez les étudiants.

Méthodes: La prévalence de l'infection tuberculeuse et les facteurs de risqué ont été estimés entre les étudiants de premier cycle en médecine et en soins infirmiers (n=443) à l'Université de Manipal à Manipal en Inde. Les étudiants qui ont au moins deux années d'exposition aux milieux hospitaliers ont été comparés avec les étudiants sans exposition aux milieux hospitaliers. Connaissances, attitudes et pratiques (CAP) liées à la contrôle de la TB ont été évalués parmi les internes et les étudiants postdoctorales en médecine (n = 486) à Manipal et Mangalore, Inde.

Résultats: La prévalence de l'infection de la TB chez les étudiants de premier cycle a été de 5,1% (IC 95% 03.01- 07.02). Le travail dans les départements pulmonaires a été associée à une augmentation de taille de l'induration de 1.42mm (IC à 95% 0,66, 2,19) et 3.11 fois l'odd ratio ajusté pour positivité du TST (IC à 95% 1,31, 7,36). Pour les marques de connaissances, les étudiants postdoctoraux en médecine ont marqué de 3,6% (IC à 95% de 1,4 à 6,0) plus élevé que les internes. Le marque de la connaissance de la contrôle de la TB à 50,5% (IC 95%, 48,7-52,2) était significativement plus faible que le score de la connaissance de transmission et les facteurs de risque pour la TB 67,5% (IC à 95% de 65,6 à 69,4). 76,75% ont déclaré qu'ils ne portent pas toujours un masque lorsque'ils travaillent avec un patient tuberculeux.

Conclusion: La prévalence de l'infection TB chez les étudiants de premier cycle de santé est inférieure à celle apporté ailleurs en Inde. Cependant, les résultats sont propres à ce contexte et ne peuvent être généralisés à tous les étudiants de premier cycle en soins de santé en Inde. Nous avons identifié les déficits de connaissances, attitudes chez les étudiants. Cela représente un lieu où les institutions peuvent intervenir pour réduire le risque de contracter la TB.

Preface

To investigate nosocomial TB infection and infection control in young healthcare trainees in India, in collaboration with our research partners I designed and undertook two main projects in Manipal and Mangalore, South India. This thesis reports results from these projects in order to develop a broader understanding of nosocomial TB infection.

- **Chapter 1** offers an introduction to tuberculosis in healthcare settings in India.
- **Chapter 2** provides a comprehensive review of published literature on nosocomial TB infection and TB infection control in healthcare settings.
- **Chapter 3** informs regarding broad social and economic context of our studies.
- **Chapter 4** outlines the overall objective of this work, and details the specific objectives of the two research projects.
- **Chapters 5 and 6** details the methodology used for each study and provide the results of studies two manuscripts prepared for publication.
- **Chapter 7** offers a discussion of the overall results and explores the implications of our findings, providing recommendations for future research.

The results from our studies have been prepared for submission as two manuscripts as detailed below. The first focuses on TB infection risk factors and the second on knowledge attitudes and practices regarding infection control. These manuscripts will be presented at conferences in the upcoming months. The results from the study will be distributed to the Manipal University in the form of a report to inform future decision-making and provide an impetus for potential interventions to improve infection control.

<u>Conferences</u>

Ghiasi, M., ... Pai, M. Tuberculosis infection among healthcare trainees in South India. (2016, June). Poster to be presented at the Canadian Society for Epidemiology and Biostatistics (CSEB) National Student Conference, Winnipeg, Canada.

Ghiasi, M., ... Pai, M. Tuberculosis infection among healthcare trainees in South India. (2016, April). Poster presented at the McGill Epidemiology, Biostatistics and Occupational Health Research Day, Montreal, Canada.

Ghiasi, M., ... Pai, M. Prevalence and risk factors of tuberculosis infection among healthcare trainees in South India. (2016, April). Poster presented at the Infectious Diseases and Immunity in Global Health (IDIGH) Research Day, Montreal, Canada.

Manuscripts

Ghiasi, M., Saravu, K., Nair, S., Mukhopadhyay, C., George, L.S., Pai, M. *Prevalence and risk factors of tuberculosis infection among healthcare trainees in South India.* To be submitted.

Ghiasi, M., Saravu, K., Baliga, S., Mukhopadhyay, C., Nair, S., Pai, M. *Tuberculosis infection control knowledge, attitudes and practices among medical interns and post-graduate residents in South India.* To be submitted.

Author contributions

The project investigating the prevalence of latent TB infection among junior healthcare trainees was conceptualized by MP, KS, SN and MG. MG wrote the study protocol with feedback from KS, SN, MP. Questionnaire for assessing risk-factors in latent TB infection study was made by MP, and adapted, modified, pre-tested by MG, KS, SN, LSG, CM. MG supervised the administration and reading of TST by hired technician and managed data collection and counseling by medical volunteers. MG conducted all data entry, cleaning, statistical analysis, results interpretation, and writing of the manuscript.

The project investigating knowledge, attitudes and practices of senior healthcare trainees was conceptualized by MG, KS, MP. MG wrote the study protocol and developed the questionnaire, revised with input from KS with valuable contributions from all study co-coordinators. Questionnaires were pre-tested by CM and MG. Data were anonymously collected in the field by KS, SB, MG. MG conducted all data entry, cleaning, statistical analysis, results interpretation, and writing of the manuscript.

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List of Abbreviations

aOR	Adjusted odds ratio
ARTI	Annual risk of TB infection
BCG	Bacillus Calmette-Guérin
CI	Confidence interval
DOTS	Directly Observed Treatment Short course
HCW	Healthcare worker
HIV	Human immunodeficiency virus
LTBI	Latent tuberculosis infection
MDR-TB	Multidrug-resistant TB
Mtb	Mycobacterium tuberculosis
OR	Odds ratio
PPD	Purified protein derivative
RNTCP	Revised National Tuberculosis Control Program
SD	Standard deviation
SES	Socioeconomic status
TB	Tuberculosis
TBIC	Tuberculosis infection control
TST	Tuberculin skin test
XDR-TB	Extensively drug-resistant TB
WHO	World Health Organization

1 Introduction

Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis* that infects millions each year. While in 90% of cases the infection remains latent, approximately 10% of those infected or 9.6 million people worldwide develop active TB each year and 1.5 million die from the disease. India is the country with the world's highest burden of TB, and in 2014 accounted for 25% of global cases of TB (World Health Organization, 2015b). The WHO's 'END TB' strategy has called for the worldwide reduction of deaths due to TB by 95% by 2035 (World Health Organization, 2015a). However, the emergence of multi-drug resistant (MDR-TB) and extensively drug resistant (XDR-TB) threatens this ambitious goal.

Hospital settings can facilitate the transmission of TB infection between patients and healthcare workers (HCWs) in close proximity. Nosocomial TB infection has put healthcare workers and students in high burden countries at serious risk. Although the prevalence, risk and risk factors for TB are heterogeneous and depend on the context, the average prevalence of LTBI among HCWs in low to middle income countries worldwide is estimated to be 54% (ranging from 33% to 79%) with annual risk of infection as high as 14.3% (R. Joshi, Reingold, Menzies, & Pai, 2006). The World Health Organization has developed comprehensive guidelines for TB infection control (TBIC) in healthcare facilities (World Health Organization, 2009). However, in healthcare facilities across high burden countries there are limited policies and partial implementation of TBIC measures in place. For example, the WHO recommends surveillance of HCWs for TB, in many high burden countries routine TB testing is not done for HCWs and trainees.

India’s high TB burden combined with a surge of drug-resistant strains of the disease presents a serious risk in healthcare settings, particularly to young healthcare trainees (Pai & Christopher, 2011). There have been very few studies in the country focusing on the prevalence of LTBI in trainees, and identifying the risk factors and how much trainees know about and engage in TB infection control. Better understanding of TB and TBIC practices in healthcare trainees will allow for the development of appropriate policies and evidence-based interventions that will reduce nosocomial TB infection and protect the next generation of HCWs against TB.

2 Review of Literature

2.1 Etiology and pathogenesis of TB

Tuberculosis (TB) is caused by *Mycobacterium tuberculosis* (Mtb) which can infect any part of the body. The most common form of the disease is pulmonary TB which affects the lungs, while extra-pulmonary forms of the disease can infect areas including the central nervous system, body fluids and lymph nodes. Pulmonary TB is airborne and transmitted by 1-5 micron large aerosolised droplets from infectious individuals (Centers for Disease Control and Prevention, 2013). In 90% of those infected by Mtb, the infection is contained by the immune system and remains latent. However, 5% of individuals develop active TB disease in 2 years following infection. Another 5% with latent TB infection develop the active disease over the course of their lifetime (Figure 2.1) (Behrman et al., 2013).

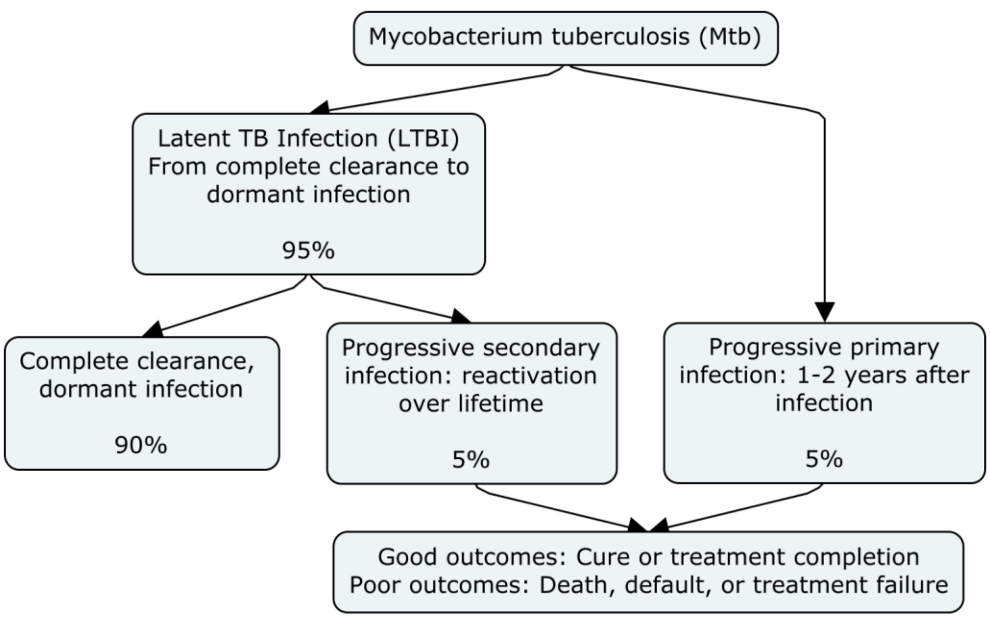
There are treatment options for both latent and active tuberculosis infection. Those with latent TB infection (LTB), who are at high risk of developing active TB disease, have the option of undergoing multiple treatment regiments, including prophylactic treatment for 6 to 9 months with isoniazid (INH). Those diagnosed with active TB, based on appropriate diagnostic algorithms including microbiological confirmation, typically undergo a four-drug regimen of isoniazid (INH), rifampicin (RIF), ethambutol (EMB), and pyrazinamide (PZA) for 6 to 9 months. These regimens are modified in the case where drug-susceptibility testing detects infection with drug-resistant strains of Mtb.

2.2 Epidemiology of TB

In 2014, the World Health Organization estimated 9.6 million new cases of TB and 1.5 million deaths from TB (Appendix 1) (World Health Organization, 2015b). TB is the leading cause of death due to an infectious disease worldwide, followed by HIV which had a mortality of 1.2 million in 2014. Among those whose cause of main death is classified as HIV, nearly a third of total deaths (approximately 390,000) were attributed to active TB infection. HIV and TB coinfections interact as a syndemic, tremendously worsening the outcomes for one another (Kwan & Ernst, 2011).

India has the world's highest burden of TB accounting nearly 25% of the absolute number of global cases of TB. with a prevalence of 2.5 million (95% CI 1.7-3.5), incidence of 2.2 million (95% CI 2.0-2.3) and an estimated 220,000 deaths (95% CI 150,000-350,000)) (World Health Organization, 2015b). However, only a fraction of actual cases are reported to the state-run national TB surveillance and control program, the Revised National Tuberculosis Control Program (RNTCP). The case detection rate (CDR), which is the number of new and relapse TB cases notified to national TB control program divided by the estimated number of incident cases, was 74% (95% CI 70-80) in 2014. The estimated 26% of cases unaccounted for are believed to be missed due to poor diagnostics and poor reporting (Glaziou, Sismanidis, Floyd, & Raviglione, 2015; World Health Organization, 2015b).

Figure 2.1 Progression of tuberculosis after infection with Mycobacterium tuberculosis (Mtb)



2.3 Revised National TB Control Programme (RNTCP)

The Revised National TB Control Programme (RNTCP) in India was launched in 1997 and has been making tremendous strides in combating TB. Between 1990 and 2013, the country saw a 51% reduction in incidence and 42% reduction in mortality (World Health Organization, 2014a). Between 1995 and 2010 the case detection rate (CDR) had remained around 59%, between 2010 and 2014, the case detection rate CDR jumped to 74% (World Health Organization, 2015b). Treatment success, assessed via smear or culture, has jumped from 25% to 88% in new cases and 70% in re-treatment between 1995 and 2013 (Central TB Division, 2014). In 2017, the program ends its third 5-year phase which focused on rapid, early detection of TB and providing better Directly Observed Treatment Short course (DOTS) services, and engaging all care providers (Sachdeva, Kumar, Dewan, Kumar, & Satyanarayana, 2012). Despite progress, the number of cases and fatality from TB is still high in the country, and the emergence of DR-TB seriously threatens these successes.

2.4 Drug Resistant TB (DR-TB)

One of the major TB threats around the world today is the rapid rise of drug-resistant TB (DR-TB) which do not respond to first-line drugs such as isoniazid (INH) and rifampicin (RIF). In 2014, an estimated 123,000 multi-drug resistant TB (MDR-TB) cases of TB were detected, representing only a fraction of some 480,000 estimated cases thought to have occurred in India, China and Russia (World Health Organization, 2015b). In India, an estimated 2.2% of new TB cases and 15% of retreatment cases were MDR-TB. Again, these cases are thought to be a fraction of the actual numbers as drug susceptibility testing (DST) is only done for 18% of cases in the country (World Health Organization, 2014a).

Regional reports highlight a dire situation. HIV anti-retroviral treatment (ART) centers in Mumbai, India have found that 25% of new TB cases and 44% of retreatment cases among HIV patients are showing drug resistance (Isaakidis et al., 2014). Other studies in Mumbai have found a six-fold increase in MDR-TB in Mumbai, India between 2005-2013 (Dalal et al., 2014). In Karnataka state of India, a prevalence resistance to at least one drug has been detected in 61% to 75% of hospital TB culture specimens (Abraham et al.; Gaude & Hattiholli, 2015). In Mumbai, totally drug-resistant TB strains have also been reported (Udwadia, Amale, Ajbani, & Rodrigues, 2012).

2.5 BCG vaccination

Bacille Calmette-Guérin (BCG) vaccine is currently the only approved vaccine to reduce risk of TB infection. In India the vaccine has routinely been administered after birth since mid-twentieth century, with an estimated national coverage of 91% in 2014 (World Health Organization, 2014b). The overall efficacy of BCG has been found to be highly variable in adults, ranging between 0% to 80% efficacy in randomized control trials (Behr & Small, 1997). The largest BCG trial, conducted in South India, showed no protective effect (The Tuberculosis Prevention Trial, 1979). However, vaccine has been found to be protective for TB in children, and against various forms of extrapulmonary TB such as meningeal in adults (Mangtani et al., 2014; Roy et al., 2014).

2.6 Latent TB Infection (LTBI)

Latent tuberculosis infection (LTBI) has been defined as “lasting tuberculosis immune response” as a result of immune sensitization to Mtb antigens without any symptoms and clinical manifestations (Mack et al., 2009). Some with latent TB infection will progress to active disease, suggesting the presence of immune-contained live Mtb bacilli in those individual. Here LTBI is reservoir of disease which can progress to active, infectious TB. The identification and treatment of LTBI is therefore essential in preventing future cases of TB (Esmail, Barry, Young, & Wilkinson, 2014). However, it is unclear whether this detectable sustained immune response always requires the presence of live viable bacilli. For this reason it has been suggested that LTBI should be viewed as a spectrum conditions ranging from potentially eliminated infection to subclinical disease, all of which can result in immune sensitization without any symptoms present (Barry et al., 2009).

Cell-mediated immune response as a result of Mtb antigen sensitization can be detected in-vivo using the tuberculin skin test (TST) or in-vitro using interferon-γ release assays (IGRAs). For screening purposes, either TST or IGRAS can be used. However, TSTs and IGRAs cannot distinguish stages on the LTBI spectrum, or between LTBI and active TB. Nor can these diagnostic tests distinguish between old and new infections (Pai et al., 2014). Given the limited evidence on the performance of IGRAs in high-burden settings, and the complexity and cost of these tests, the World Health Organization recommends the continued use of TST in high-burden low-resource settings (World Health Organization, 2011). Additionally, IGRAs have shown poor performance in repeat testing, and are not recommended for serial testing (Canadian Thoracic Society & Public Health Agency of Canada, 2013).

The tuberculin skin test, conducted using the Mantoux technique, can be done in one-step or two steps. A specified tuberculin unit (TU) of purified protein derivative (PPD) is injected interadermally in the forearm. It must be noted that in India, TST for prevalence surveys and diagnostic purposes has been conducted in the past using 1TU of PPD-RT 23, which is no longer recommended in WHO guidelines (Chadha, Jagannatha, Vaidyanathan, & Jagota, 2003). For the measurement of induration sizes, cut-offs exist to call a test negative or positive depending on national guidelines and the personal profile of a given individual. For example, in the Canadian guidelines, an induration of 5mm and greater among those with HIV and an induration of 10mm or more among healthcare personnel is considered at high risk of progression to active disease (Canadian Thoracic Society & Public Health Agency of Canada, 2013).

In the one-step procedure, the size of the induration formed is assessed between 48-72 hours later by a trained reader. In the two-step procedure the injection process is repeated several weeks later and a second reading done to assess reaction boosting. A booster reaction occurs because some individuals with past TB infection have reduced immune response to the first TST and the test may be falsely negative. However, on a subsequent TST conducted from 1 week to 1 year after, their immune response will be boosted and they may test positive. If not conducted in close proximity, it is difficult to distinguish whether a positive result is due to boosting or due to a new infection. The two-step TST procedure allows for the detection of boosting, while reducing the possibility of future misinterpretation of a positive reaction. Two-step TST is generally recommended where TST will be administered at regular intervals as part of routine testing (Canadian Thoracic Society & Public Health Agency of Canada, 2013).

Neither TST nor IGRAs are considered gold-standard diagnostics for LTBI. TST sensitivity has been estimated to be between 77% (95% CI 71-82) and specificity 97% (95% CI 95-99) in non-BCG vaccinated and 59% (95% CI 46-73) in BCG vaccinated populations (Pai, Zwerling, & Menzies, 2008). BCG vaccination can confound the results of TST by reducing specificity and increasing false-positives for latent TB infection. However, meta-analyses have shown that effect of BCG on TST is completely attenuated and virtually disappears between 10 years to 15 years after vaccination (Farhat, Greenaway, Pai, & Menzies, 2006; Wang, Turner, Elwood, Schulzer, & FitzGerald, 2002).

Due to the high prevalence of TB disease in India, many in the country are exposed to *M. tuberculosis* each year. The country has a high annual risk of TB infection (ARTI) of 1.5% based on nationwide TST surveys of children conducted between 2000 and 2003. However, great regional variation has been noted, whereby an ARTI of 1.9% was found in Northern regions, and an ARTI of 1.0% in Southern regions (Chadha, 2005). Various prevalence surveys similarly show heterogeneous distribution of LTBI across different regions in India, but estimate an overall infection prevalence of 38%-44% in the population country-wide (Chakraborty, 2004).

2.7 Hospital-associated nosocomial infection

Hospital settings provide a milieu in which respiratory infectious diseases such as TB can be transmitted from patients to other patients and healthcare workers. Hospital-associated TB infection puts patients at risk and contributes to surging epidemics of multi-drug resistance TB. There has been some work focusing on the transmission of resistant strains of TB in hospital settings, particularly among immunocompromised patients. For example, Bantubani et al. (2014) identified nosocomial transmission as a core factor in outbreaks of MDR-TB and XDR-TB in South African hospitals. S. Basu et al. (2007) developed a model suggesting that in 2007 nine out of every ten cases of XDR-TB in KwaZulu-Natal, South Africa occurred in hospitals. The increased prevalence of multi-drug resistant TB (MDR-TB) and extensively drug resistant TB (XDR-TB) has created a pressing need to identify risk factors and implement effective TB control strategies in healthcare settings.

2.8 Healthcare workers and nosocomial infection

Healthcare workers (HCWs) are at elevated risk of being exposed to and acquiring TB infection as an occupational hazard. HCW absenteeism and loss of workers due to TB disease and death can have negative effects for the healthcare system (Trajman & Menzies, 2010). A number of reviews have focused on identifying the extent of nosocomial infection among HCWs and risk factors in low-burden and high-burden settings. R. Joshi et al. (2006) conducted a systematic review of 51 studies, examining LTBI in HCWs in low to middle-income countries. They found an average prevalence of 54% (ranging from 33% to 79%) and an annual risk for LTBI of 0.5% to 14.3% among HCWs. A follow up study by D. Menzies, Joshi, and Pai (2007) found a LTBI prevalence of 24% (95% CI 4-46) in HCWs high income countries. Baussano et al. (2011) conducted a systematic review of ARTI in HCWs in countries with low, intermediate and high TB incidence to identify the annual risk for LTBI. They reported higher risk in HCWs than general populations, providing a pooled estimate of 8.4% for annual risk of infection among healthcare workers in high TB-incidence countries.

Many factors affect the risk of transmission and progression to active TB among HCWs. These include individual factors, such as individual health and susceptibility, level of occupational exposure, and broader factors such as TB infection control measures (TBIC) and adherence to these measures (von Delft et al., 2015). Seidler, Nienhaus, and Diel (2005) conducted a review of TB risk factors in low-incidence countries, although they did not provide an overall pooled estimate due to the heterogeneity of included studies, they identified a number of risk factors associated with infection including being in wards with TB patients. They also identified occupational roles, such as nurse or physicians in internal medicine, or respiratory therapists and others to be at higher risk of tuberculosis infection. The main risk factors identified by R. Joshi et al. (2006) in their systematic review were certain occupations within the hospital such as nurses, and certain locations such as TB facilities and laboratories.

Nosocomial TB transmission has only been studied in the Indian context in recent years. Gopinath et al. (2004) conducted a retrospective study looking at 10 years of records belonging to a cohort of HCWs in Tamil Nadu, reporting incidences of active pulmonary and extra-pulmonary TB. They found higher levels of incident disease among HCWs. Rao, Aggarwal, and Behera (2004) followed a group of medical residents in Chandigarh, India and found elevated risk of TB infection, particularly extra-pulmonary disease. Khayyam, Patra, Sarin, and Behera (2010) also found elevated risk of TB among HCWs in a speciality TB care hospital in New Delhi, although at rates lower than reported in other studies. In a large study of 726 HCWs in Sevagram, India, Pai et al. (2005) reported a LTBI prevalence of 41% (95% CI 38-45) using TST, and 40% (95% CI 37-43) using QuantiFERON TB Gold. BCG vaccination had little impact on TST and IFN-gamma assay results.

Risk factors for nosocomial infection of HCWs in Indian contexts are thought to include: patient-related factors that increased risk of exposure, poor or absent TBIC, and poor patient and practitioner knowledge regarding TB transmission though the relative importance of each is unknown (Devasahayam Jesudas Christopher & Thangakunam, 2013; Pai, Kalantri, Aggarwal, Menzies, & Blumberg, 2006). A case-control study in Vellore, India found that low BMI (<19kg/m2) was associated with increased risk of TB infection among healthcare workers, as well working in medical wards and microbiological laboratories (Mathew et al., 2013). A study in Sevagram, India found increasing age and years in the health profession were significant risk factors for both IFN-gamma assay and TST positivity (Pai et al., 2005).

2.9 Nosocomial infection among healthcare trainees

The risk of tuberculosis to medical and nursing trainees working in hospital settings has been historically described as a point of concern in previously high-burden countries. As early as 1924, Heimbeck (1928) in Norway was using the Pirquet method, the predecessor to the Mantoux method, to assess the prevalence of infection among healthcare trainees and the effectiveness of the then newly-developed BCG vaccine. In the decades that followed, a number of studies were conducted to examine the use of the then novel TB diagnostic tools Mantoux tuberculin skin test and chest X-rays. Some of these studies focused on trainees in medical and nursing programs. In an extensive narrative review, Soper and Amberson (1938) summarized results of studies investigating the prevalence and incidence of TB among medical and nursing students in the United States, noting that students had "disproportionate increase in positive reactions to tuberculin during their training."

In more contemporary times, a number of studies have been conducted in high burden countries to examine tuberculosis infection and skin test conversion among healthcare trainees, often as part of larger studies examining TB in healthcare workers. In their systematic review of prevalence and risk studies in low to middle income countries, R. Joshi et al. (2006) stratified medical and nursing trainees and found LTBI infection rates ranging from 2% (95% CI 0-6) in Iran (Golchin & Rostami, 2005), to 25% (95% CI 21-30) in India (Pai et al., 2005) and 40% (95% CI 26-54) in Uganda (Kayanja, Debanne, King, & Whalen, 2005). The overall LTBI prevalence among medical and nursing students was calculated to be 12% (95% CI 10-13).

However, studies focusing on prevalence and risk of TB infection and disease among healthcare trainees in India have been limited. Christopher et al. (2010) followed a cohort nursing students in Tamil Nadu, India and found significantly an LTBI prevalence of 47.8% in the group. In a follow-up study, a higher annual risk of TB infection (7.8%) was observed in this group than the general population (1.8%) (D. J. Christopher et al., 2011). Based on the results of these studies, Pai and Christopher (2011) published an article calling for action to protect healthcare trainees, highlighting that these students were particularly vulnerable to nosocomial TB infection in their early clinical exposures. A more recent study in Pune, India investigated active TB prevalence among 662 medical trainees including interns and residents. They reported a high TB disease prevalence of 3.9% with an incidence of 3,279 cases/100,000 person-years which was 15 times higher than incident cases in the regional community (Basavaraj et al., 2016).

2.10 Infection control in healthcare settings

The document *WHO Policy on TB Infection Control in Health-Care Facilities, Congregate Settings and Households* provides a comprehensive set of recommendations for TB infection control (TBIC) at national, subnational and facilities level managerial activities. At the level of facilities they identified three types of controls: administrative controls, including patient management and interventions; environmental controls: including isolation rooms, ventilation and ultraviolet germicidal irradiation (UVGI); and personal protective equipment: including face masks and N95 respirators (World Health Organization, 2009). India developed its own national airborne infection control (AIC) guidelines in 2010 (India Ministry of Health and Family Welfare, 2010).

Despite these guidelines, TBIC is not widely implemented in high burden countries. A study in Uganda examined TBIC implementation in 51 facilities using qualitative and quantitative surveys and found structural barriers, lack of human resources, stigma associated with TB, limited managerial support among critical factors that challenged effective implementation of TBIC measures (Buregyeya et al., 2013). A study in South Africa surveying 52 health facilities found that only 50% of TBIC measures recommended by the South African national health department were actually implemented (Malangu & Mngomezulu, 2015). A study examining the implementation of TBIC in a region of China found similar implementation gaps including some 28% of study HCWs reported collecting sputum samples in common waiting areas (Chen et al., 2016). This highly risky practice exposes other vulnerable patients and healthcare workers to potential TB infection.

WHO guidelines recommend active screening of healthcare workers for TB infection (World Health Organization, 2009). Routine screening for LTBI of all healthcare workers and trainees, particularly at point of entry to healthcare institutions, is common practice in many low-TB burden countries (Canadian Thoracic Society & Public Health Agency of Canada, 2013). However, a study in a hospital for drug-resistant TB in South Africa found that despite screening policies in place, implementation was partial with only 19% of HCWs being screened for TB (Tudor, Van der Walt, Hill, & Farley, 2013). A study in Portugal investigated factors that led to reduced screening in the country among some 39,000 physicians and 57,000 nurses and found the lack of offering screening to be the most important factor, in addition to concerns regarding potential LTBI treatment (Meireles, Gaio, & Duarte, 2015).

Systematic reviews have shown that the implementation of administrative infection control measures is most critical in reducing nosocomial TB transmission in high and low income settings (R. Joshi et al., 2006; D. Menzies et al., 2007). Administrative controls including effective triage and isolation policies are simple and inexpensive to implement, and can have great impact on protecting healthcare workers (Trajman & Menzies, 2010). Parmar et al. (2015)

examined the implementation of airborne infection control (AIC) guidelines in India in 35 healthcare institutions between 2009 and 2011. They reported improved administrative TBIC practices after the implementation of guidelines, combined with recommendations tailored to the institutions. A major limitation of the study was that it relied on self-reports from institutions and conducted no objective validation.

A longitudinal interventional study in Brazil found that basic administrative infection control measures including improved isolation policies for TB patients and patients of unknown status, reduction in sputum test result turnaround times, and protective mask education had a significant impact in reducing LTBI among physicians and nurses (Albuquerque da Costa et al., 2009). The implementation of interventions at all levels requires healthcare workers to actively engage in TBIC practices.

2.11 Engagement of trainees with TB infection control

Literature focused on healthcare trainees' knowledge and approaches to TB and TBIC was retrieved using a systematic search strategy as described in Appendix 2. Among literature identified, 12 studies assessing trainees took place in Indian contexts, while 20 took place outside India (Table 2.1). The vast majority focused on assessing knowledge of TB among trainees, particularly knowledge regarding the Directly Observed Treatment Short course (DOTS) strategy for diagnoses and treatment of TB. Three studies involved interventions to ameliorate knowledge and practices. Six studies identified focused specifically on TB infection control.

Knowledge regarding TB and TBIC

Almost all studies focused on assessing levels of knowledge and many found serious gaps in knowledge. Among the studies conducted in India, nine focused on knowledge of TB using RNTCP guidelines as the standard and one specifically on infection control, two were comparisons with performance of students in other countries. RNCTP guidelines are part of the national Indian medical curriculum so it was expected that students, interns and post graduates would perform well.

Kutare, Rosario, and Goudb (2012) reported that among interns very few could correctly identify modes of TB transmission (18.8%) and cough for three weeks as a symptom of TB (38.2%). M. Basu and Das (2014) found that around two-thirds (65.4%) of interns were able to identify droplets as a mode of TB transmission and a similar number recognized two weeks of cough as a symptom of TB. By contrast Balamurugan and Swaminathan (2013) found that among interns and post-graduates, 92.7% could correctly identify droplets as a mode of TB transmission, however there were gaps in knowledge in other areas such as treatment. Rupali and Gautam (2014) also had similar findings among interns, finding that 96.5% could identify TB routes of transmission correctly. Poor knowledge regarding other RNTCP guidelines was also found. Mehta, Bassi, Singh, and Mehta (2012) found that only 21% of interns and post-graduates knew that you could be sputum-negative and still carry infectious pulmonary TB. Bogam and Sagare (2011) conducted a workshop training post-graduates in RNTCP, and found improvements in knowledge scores.

Nalabothu and Menon (2014) examined knowledge of MDR/XDR TB, and found among medical post-graduates less than half (42.8%) could correctly define MDR-TB, and even fewer (25.7%) XDR-TB correctly. (Rupali & Gautam, 2014) similarly found that less than 40% had correct knowledge regarding MDR-TB etiology and diagnostics. Giri and Phalke (2013) conducted a workshop for final year med students and looked at definitions of MDR-TB. They found that before the workshop only 39% could correctly define MDR-TB while after this number had risen to 95.3%.

Kulkarni et al. (2013) conducted a semi-structured cross-sectional survey among medical students in Mangalore, India focusing on broad infection control practices, with a small portion focused on TB. They found the majority knew about cough hygiene for patients (86.6%), and sputum collection standards (81.3%). They also reported that the majority of students knew that healthcare workers should wear a mask to protect themselves (80%), however, it was unclear what was meant by a "mask" (i.e. surgical or N95 masks). Baveja and Dalal (2012) investigating mask use among medical students found that only 6% knew N95 masks are appropriate for protection against TB.

Similarly, studies conducted among medical and nursing students in Brazil (Mussi, Traldi, & Talarico, 2012; Teixeira et al., 2008), China (Zhao, Ehiri, Li, Luo, & Li, 2013), Iran (Behnaz, Mohammadzade, Mousavi-e-roknabadi, & Mohammadzadeh, 2014; Charkazi, Kouchaki, Nejad, & Gholizade, 2010; Vahedian, Faroughi, Khakshour, & Saeidi, 2014), Nigeria (Olakunle et al., 2014), Peru (Kiefer, Shao, Carasquillo, Nabeta, & Seas, 2009), Serbia (Nagorni-Obradovic, Vukovic, Markovic, Pesut, & Vukovic, 2012), Taiwan (Chang, Hung, Chou, & Ling, 2007), Turkey (Akin et al., 2011), Uganda (Kamulegeya, Kizito, & Balidawa, 2013) and USA (Jackson, Harrity, Hoffman, & Catanzaro, 2007; Karakousis et al., 2007) found moderate to poor knowledge regarding the basic of TB. Two studies in Italy reported moderate to good knowledge regarding TB etiology and epidemiology, but poor knowledge regarding clinical aspects such as diagnosis and treatment (Laurenti et al., 2013; Montagna et al., 2014). Comparing medical students to paramedics in Oman, Al-Jabri, Dorvlo, Al-Rahbi, Al-Abri, and Al-Adawi (2006) found better knowledge among medical students, and Maciel, Meireles, Silva, Fiorotti, and Dietze (2007) had similar findings when comparing medical and nursing students to economics students in Brazil.

Some studies found significant associations between various factors and level of knowledge. Emili, Scott, Upshur, Schmuck, and John (2002) examined knowledge among final year medical students in India, Canada and Uganda and found that knowledge was not poor in any group, but significantly different depending on curriculum. Teixeira et al. (2008) found that those had previous lectures on TB were more likely to answer knowledge questions correctly. In India, Kutare et al. (2012) found interns who had had TB clinic postings were more likely to have higher knowledge scores.

TB and TBIC attitudes and practices

Comparing across three countries, Emili et al. (2002) found that curriculum differences and exposure to patients did not have a strong effect on attitudes towards patients with TB and students across three countries, with one being a non-endemic area had similar attitudes. However, they found that level of knowledge, curriculum and experience did have a positive effect on appropriate practices for providing care to TB patients. Akin et al. (2011) also found that greater knowledge among nursing and midwifery students was associated with more positive attitudes towards TB. van der Westhuizen et al. (2015) conducted an education intervention among healthcare undergraduates in South Africa and found a 20% increase in scores regarding knowledge of N95 masks and other TB and TBIC measures, as well improved their perception of risk and likelihood to refuse to provide care to high risk patients without self-protection.

In examining mask use as a critical aspect of personal protection against pulmonary TB, the role of personal experiences, the presence of resources, and the role of peers, supervisors and institutions was highlighted. In India, Baveja and Dalal (2012) found that although a significant portion (90%) of students expressed fear regarding TB transmission from a coughing patient, in general TB risk perception and management was poor among medical students. In terms of mask use, Teixeira et al. (2008) found that those with more knowledge were less likely to wear masks, while those with more clinical experience were more likely to wear masks. Kamulegeya et al. (2013) found that those with personal TB history were not more likely to report using masks when dealing with TB patients.

The importance of social norms in a hospital was highlighted by results from several studies. Kamulegeya et al. (2013) found that 28.7% of interns and nurses didn't wear masks because it was not common practices. The important role of supervisors in infection control was highlighted in a number of studies. van der Westhuizen et al. (2015) found that 73% of trainees reported that their superiors gave them orders that "made [it] difficult to protect themselves". Kamulegeya et al. (2013) found that 27.8% of interns and nurses reported not using masks because they were not available. van der Westhuizen et al. (2015) reported that 49% of students indicated masks were not frequently or always available, and hospitals did not always isolate patients with MDR-TB.

Limitations of studies

The literature identified had a number of serious limitations associated with it. Many studies had relatively small sample sizes of healthcare workers and used convenience sampling, with studies in India ranging from 36 to 268 participants with a mean of 147 participants. Almost all studies conducted developed and used their own survey instruments, which makes it very difficult to draw comparisons between studies. While some studies described pretesting and assessed the reliability, validity of their instrument, the majority did not report conducting any kind of pretesting or pilot testing of their instrument.

For studies that reported the questions that they had asked, some questions appeared to be vague or ambiguous or poorly worded such as "TB is dreadful disease" (Nagorni-Obradovic et al., 2012). Some questions reported were inaccurate as per the recommendations of the World Health Organization, for example one study considered the use of surgical masks for protection against TB as a safe practice for healthcare workers (Behnaz et al., 2014), which is against recommended guidelines. Many papers did not list the questions that they had asked as part of their survey at all and offered a vague description of the measure, which made it very difficult to assess what had actually been measured.

Scoring systems for questionnaires were also very heterogeneous across literature, and for some papers it was unclear how questions had been scored and scores aggregated. As well, for papers that had converted continuous scoring variables to categorical, such as 'good knowledge', the basis for categorical cut-off lines was unclear. Some studies conducted comparison of groups without clear justification as to why these groups were chosen. For example comparing tuberculosis knowledge among medical and nursing students versus economics students, the former performed exceptionally well of course (Maciel et al., 2007).

For studies that conducted educational intervention, the baseline and follow-up surveys were conducted immediately before and after a short intervention within the same day (Bogam & Sagare, 2011; Giri & Phalke, 2013; van der Westhuizen et al., 2015). This meant that there was no exploration of whether information had been retained and knowledge levels had changed over the long-term, but merely if material could be recalled over the very short term.

Table 2.1 Studies regarding knowledge, attitudes and practices of TB and TB infection control among healthcare trainees (n=32)

First author	Year	Country	Target HCWs	Size	Outcome measure	
Van der Westhuizen*	2015	South Africa	Undergraduate: medical, physiotherapy	326	Knowledge, Attitudes, Practices	TB Infection Control
Rupali	2014	India (Maharashtra)	Internship: medical	85	Knowledge	TB only
Nalabothu	2014	India (Puducherry)	Post-graduate: medical	140	Knowledge	TB only
Basu	2014	India (West Bengal)	Internship: medical	156	Knowledge	TB only
Vahedian	2014	Iran	Undergraduate: medical, public health	90	Knowledge	TB only
Behnaz	2014	Iran	Undergraduate: medical	145	Knowledge, Attitudes, Practices	TB and TB Infection Control
Montagna	2014	Italy	Undergraduate: medical, nursing	2220	Knowledge, Attitudes, Practices	TB and TB Infection Control
Olakunie	2014	Nigeria	Undergraduate: medical	241	Knowledge	TB only
Zhao	2013	China	Undergraduate: medical	1486	Knowledge	TB only
Kulkarni	2013	India (Karnataka)	Undergraduate: medical	268	Knowledge	TB Infection Control
Balamurugan	2013	India (Tamil Nadu)	Internship, postgraduate: medical	150	Knowledge	TB only
Giri*	2013	India (Uttar Pradesh)	Final year med students	86	Knowledge	TB only
Laurenti	2013	Italy	Undergraduate: medical	183	Knowledge, Attitudes, Practices	TB only
Kamulegeya	2013	Uganda	Internship: medical, nursing	209	Knowledge, Attitudes, Practices	TB Infection Control
Mussi	2012	Brazil	Undergraduate and professional: nursing	76	Knowledge	TB only
Mehta	2012	India (Haryana)	Internship, postgraduate: medical	112	Knowledge	TB only
Kutare	2012	India (Karnataka)	Internship: medical	207	Knowledge	TB only
Baveja	2012	India (Maharashtra)	Undergraduate: medical	200	Knowledge, Attitudes	TB only
Nagorni-Obradovic	2012	Serbia	Undergraduate: medical, dental	350	Knowledge	TB only
Bogam*	2011	India (Maharashtra)	Post-graduate: medical	36	Knowledge	TB only
Akin	2011	Turkey	Undergraduate: nursing, midwifery	615	Knowledge, Attitudes	TB only
Charkazi	2010	Iran	Internship: medical	80	Knowledge	TB only
Kiefer	2009	Peru	Undergraduate: medical, nursing, technician	11	Knowledge, Attitudes	TB only
Teixeira	2008	Brazil	Undergraduate: medical	1094	Knowledge, Attitudes, Practices	TB and TB Infection Control
Marciel	2007	Brazil	Undergraduate: medical, nursing	605	Knowledge	TB only
Chang	2007	Taiwan	Undergraduate: nursing	865	Knowledge, Attitudes	TB only
Karakousis	2007	USA	Post-graduate: medical	131	Knowledge	TB only
Jackson	2007	USA	Undergraduate: medical and allied	1480	Knowledge, Attitudes	TB only

			health			
Al-Jabri	2006	Oman	Undergraduate: medical, paramedic	417	Knowledge	TB only
Marciel	2005	Brazil	Undergraduate: nursing	178	Knowledge, Attitudes, Practices	TB only
Emili	2002	Canada, India, Uganda	Undergraduate: medical	160	Attitudes	TB only
Emili	2001	Canada, India, Uganda	Undergraduate: medical	160	Knowledge, Practices	TB only

3 Research context

3.1 Study Context

The primary data for this study were collected in Manipal and Mangalore, two cities in the South Canara region on the coast of Karnataka state in south west India. Manipal is located within the Udupi City Municipality with a population consisting almost exclusively of 28,0000 Manipal University students, faculty and staff (Manipal University, 2016a). Udupi City Municipality has a total population of 144,960 and an average literacy of 93.6% (2011). The TB context of the region can be examined through case notification rate, which is the number of cases of TB disease reported to the national surveillance system. Udupi District has an annual total case notification rate of 77 per 100,000 population (2013) (Central TB Division, 2014). Mangalore city has a population of 488,968 and an average literacy of 93.7% (2011) (Census Organization of India, 2011). The Dakshina Kannada district in which Mangalore is located has an annual total case notification rate of 78 per 100,000 population (2013) (Central TB Division, 2014). By contrast, Karnataka overall reports literacy of 73.4% (2011) and an annual TB case notification rate of 98 per 100,000 (2013) (Census Organization of India, 2011; Central TB Division, 2014). India overall has a literacy rate of 74.0%, and a total TB case notification rate of 114 per 100,000 population (2014) (Central TB Division, 2015).

The two studies were conducted in two private tertiary teaching hospitals which are part of the private Manipal Health Systems consisting of 13 hospitals across India and affiliated educational institutions. The two teaching hospitals are associated respectively with Manipal University in Manipal and Mangalore. Kasturba Hospital, Manipal is a 1612 bed hospital with 300 consultants providing comprehensive tertiary care (Manipal Group Hospitals, 2016a). KMC Hospitals in Mangalore are respectively a 220-bed and 600-bed with over 200 consultants (Manipal Group Hospitals, 2016b, 2016c). To obtain an estimate of potentially infectious TB patient load, records for all TB suspect sputum samples sent for assessment using acid-fast bacilli (AFB) smear from Kasturba Hospital to the Department of Microbiology between Nov 28, 2013 and May 7, 2015 were examined. Among 14,178 samples that were sent for assessment during this 15-month period, 1,362 (9.6%) were reported as AFB-positive. This suggests that during this period at least a thousand sputum-smear positive and potentially infectious individuals passed through the hospital.

KMC hospitals are private and generally well-resourced hospitals with infection control committees. However, in our locations on interest, guidelines on TB infection control were limited. Based on personal interviews, the present infection control systems for TB control offer are partially and inconsistently implemented throughout hospitals. Healthcare workers in the hospitals undergo routine hematologic screening for sugar, cholesterol and blood-borne pathogens including hepatitis C. Students offered vaccines for pathogens such as hepatitis B. However, routine TB testing and monitoring and reporting for healthcare workers is not in place.

In out-patient areas, patients showing symptoms are TB are not screened or prioritized. Patients showing symptoms of TB are offered surgical masks, but often after seeing a healthcare worker and being admitted to wards. Accompanying family members are not offered masks. TB suspects are only moved to isolation wards after sputum smear confirmation, which can be up to 24 hours after the patient has spent time in general wards. In a sampling of waiting areas and wards, there were no posters or information regarding TB infection control and hygiene. Cross ventilation and mechanical ventilation in clinics, general and isolation wards is limited. In certain locations, designated cross-ventilation though present, is obstructed. N95 masks for healthcare workers are generally only available in isolation wards.

Undergraduate students in medicine and nursing learn about TB in course of their education as part of the national medical curriculum, in courses such as microbiology, community medicine and others. However, when starting rotations in the hospital they generally do not receive orientation with respect to TB infection control. Interns and post-graduates on the other hand do receive orientation depending on where they will be working. However, they can engage in procedures such as bronchoscopy that put them at risk. Undergraduate medical students are not permitted to go to isolation wards, while interns and post-graduates can be assigned to those locations. Medical students are generally not assigned proven TB suspects for history taking. However there is no policy in place with respect to TB suspects, and undergraduate medical students can be assigned to take their medical histories.

3.2 Study Populations

As per the standard national curriculum, undergraduate medical students in all MBBS programs in India are trained for 5.5 years in four sections. In pre-clinical MBBS I (semester 1 & 2) students do not have any exposure to clinical settings. MBBS II (semesters 3, 4, 5) is considered a para-clinical section as students begin to have limited postings of 3 hours per day starting at 3rd semester. MBBS III (semesters 6, 7, 8, 9) is considered a clinical section, and by semester 7 students begin to have postings of 6 hours and more per day, 3 hours in the morning and 3 hours in the afternoon. Students receive training in para-clinical and clinical subjects such as microbiology, medicine, community medicine after the third semester.

The final year of undergraduate medical studies consists of the internship year where students are rotate full-time in various specialties. Following the completion of the internship program, the MBBS degree and a license to practice as physicians is conferred to trainees. Trainees can elect to work in healthcare, or continue on with their post-graduate educational training in MD/DNB (for medical specialties) or MS/DNB (for surgical specialties) for 3 additional years. Undergraduate trainees in at the Manipal College of Nursing (MCON), Manipal, India are enrolled in 4-year BSc Nursing or 3-year Diploma in General Nursing and Midwifery programs, with an internship of 6 months. Both programs can be followed by Post Basic Diplomas for advanced training. Students in both programs begin receiving foundational supervised clinical practice during the first year onwards.

Manipal University is a private hospital, and although there are a limited number of reduced cost seats available per state policies, the majority of students pay full tuition fees. In addition, depending on the program, there is a large population of international students including foreign and Indian non-resident students. In 2015, for MBBS programs overall program fees for the program are approximately USD $62,000 for Indian students and USD $207,700 for foreign students and non-residents. For BSc nursing, overall program fees were USD $6118 for Indian students, and USD $18,500 for foreign students and non-residents (Manipal University, 2016b).

3.3 Study Rationale

The studies included in this project involve two distinct populations (I) medical and nursing undergraduate trainees (II) internship year and post-graduate medical trainees in the same hospital setting. Although both dimensions of this project could have been conducted on the same population, such an approach would not enable us to address the question of place-based exposures and risk of TB.

For our study on prevalence of LTBI, the aim was to understand the impact of place-based exposure on the prevalence of TB infection. We opted to assess this only in medical and nursing undergraduate trainees at the earliest stages of their training, and after exposure of around two years to similar clinical settings. While we used self-reporting of exposures as a measure, we also had extensive administrative information on student postings which we could use to corroborate with self-reports. Post-graduate trainees generally come to Manipal University from very diverse locations across India, and have been exposed to clinical settings in a variety of places for highly variable lengths of time. Therefore this population could not be reliably assessed in order to assess the association between TB infection and clinical settings.

For knowledge, attitudes and practices regarding infection control our aim was to identify the level of knowledge of trainees, and how they interact with place-based infection control measures. We opted to assess this only in internship and post-graduate students because they all have undergone the same standard national medical curriculum. Therefore their knowledge could be generalized to a broader population of early-career physicians and give us insight as to gaps in knowledge associated with the undergraduate medical curriculum. Unlike undergraduate medical and nursing students who have very limited clinical posting, internship and post-graduate students are fully embedded in hospital settings. Therefore, their attitudes and practices give us more insight regarding barriers in attitudes and perceptions that may perpetuate place-based exposure and risk.

4 Objectives

4.1 Overall objectives

The goal of this work is to establish baselines tuberculosis infection prevalence, its risk factors, as well as knowledge, attitudes and practices of tuberculosis infection control among healthcare trainees working in tertiary-care training hospitals in South India.

4.2 Specific objectives

This work is divided in two components, due to the different scope of each project, and the different trainee populations involved as described in study rationale. These projects are related under the broader goal of establishing a baseline for future infection control interventions.

Baseline prevalence of latent tuberculosis infection (LTBI)

1. Measure the prevalence of TB infection among medical and nursing trainees through tuberculin skin test (TST) screening
2. Measure the impact of exposure to various clinical setting as a risk factor amenable to institutional intervention
3. Identify other risk factors associated with TB infection among trainees

Baseline knowledge, attitudes and practices with respect to TB infection control

1. Measure knowledge, attitudes and practices of medical interns and post-graduates regarding TB transmission and infection control
2. Measure the associations between personal factors, knowledge, attitudes and self-reported practices

5 Results: Manuscript 1

Prevalence and risk factors of tuberculosis infection among healthcare trainees in south India

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Background: Pulmonary tuberculosis (TB) is an airborne bacterial infection that can lead to poor respiratory health. Healthcare workers and trainees working in crowded hospitals in high burden countries such as India are at great risk of being exposed to and acquiring the infection.

Objectives: We examined prevalence of latent TB infection and its demographic and occupational risk factors among medical and nursing undergraduates in Manipal, India.

Methods: Eligible participants (n=443) included trainees before exposure to clinical settings (pre-clinical) and trainees exposed to clinical settings for at least 2 years (clinical). Cross-sectional questionnaires and physical assessment were conducted to obtain demographic and health information, and to evaluate exposure to TB in clinical and community settings. Each participant underwent the tuberculin skin test (TST) procedure to assess their latent TB infection status. Differences in infection prevalence across groups were examined using descriptive data. Risk factors for TST reaction induration size and binary TST positivity status based on a cut-off of 10mm were assessed using adjusted multivariable models.

Results: The overall prevalence of TB infection among all trainees was 5.1% (95% CI 3.1-7.2). Among medical trainees, we found a prevalence of 4.8% (95% CI 1.3-8.3) and 9.3% (95% CI 4.4-14.1) before and after clinical exposure, respectively. Among nursing trainees, we found a prevalence of 1.6% (95% CI 0-4.7) and 1.8% (95% CI 0-5.3) before and after clinical exposure, respectively. Having been posted in pulmonary medicine wards and pulmonary out-patient departments was associated with both an increase in TST induration size (b=1.42mm, 95% CI 0.66, 2.19) and increased odds of TST positivity (aOR 3.11, 95% CI 1.31, 7.36).

Conclusions: Compared to studies elsewhere in India, we found a low prevalence of TB infection among healthcare trainees in Manipal University, India reflective in part of the unique context of the study. However, consistent with studies in healthcare workers we identified increased odds of infection associated with being posted in a high risk area of the hospital.

Keywords: tuberculosis, healthcare trainees, nosocomial infection

5.1.1 INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by Mycobacterium tuberculosis. 9.5 million people worldwide develop active TB each year and 1.5 million die from the disease (World Health Organization, 2015b). India is the country with the world's highest burden of TB, and in 2013 accounted for 25% of global cases of TB (2.0-2.3 million) (Central TB Division, 2014). Healthcare workers (HCWs) are at elevated risk of being exposed to and acquiring TB as an occupational hazard, particularly in high-TB burden, low and middle-income countries, with the prevalence of LTBI among HCWs has been estimated to be anywhere between 33% to 79% (R. Joshi et al., 2006).

Nosocomial TB transmission has only been studied in the Indian context in recent years, with the first papers being published in 2004 (Gopinath et al., 2004; Rao et al., 2004). Golpinath et al. (2004) investigated retrospectively 10-years records of a cohort of HCWs in Tamil Nadu, reporting incidence of active pulmonary and extra-pulmonary TB. They found higher levels of incident disease among HCWs (Gopinath et al., 2004). Rao et al. (2004) followed a group of medical residents in Chandigarh, India and found elevated risk of TB infection, particularly extra-pulmonary disease (Rao et al., 2004). Khayyam et al. (2010) also found elevated risk of TB among healthcare workers in a TB care hospital in New Delhi, although at rates lower than reported in other studies (Khayyam et al., 2010).

Christopher et al. (2010) followed a cohort nursing students in Tamil Nadu, India and found significantly an LTBI prevalence of 47.8% in the group (D. J. Christopher et al., 2010). In a follow-up study, higher annual risk of TB infection (7.8%) among this group than the general population (1.8%) (D. J. Christopher et al., 2011). Based on the results of these studies, Pai and Christopher (2011) published an article calling for action to protect healthcare trainees, highlighting that these students were particularly vulnerable to nosocomial TB infection in their early clinical exposures (Pai & Christopher, 2011). A second study in Pune, India investigated active TB prevalence among 662 medical trainees including interns and residents. They reported a high TB disease prevalence of 3.9% with an disease incidence 15 times higher than incident cases in the regional community (Basavaraj et al., 2016). Given the lack of studies focusing on prevalence of LTBI among healthcare trainees India, the present study was designed to add to current knowledge in a different setting in order to examine context-dependent differences in LTBI prevalence, but also identify common risk factors across studies to inform broader TB infection control efforts.

5.1.2 METHODS

Study setting

This cross-sectional study took place in Kasturba Medical College and Manipal College of Nursing, Manipal University, Manipal, India in June- October, 201. The university and associated hospital are private institutions with high entry fees and a sizeable international student body.

Population and recruitment

The objective of this study was to screen all eligible students for potential tuberculosis infection, for this reason no sample size limit was estimated. However, for analytical purposes we estimated the minimum sample size necessary to be 327 trainees, after adjusting for a 25% reduction from total due to ineligibility, refusal to participate or drop-out. Students in pre-clinical and clinical stages of their education in medical and nursing program were approached for participation in the study. Participants were enrolled in the study following signing of written informed consent. Those under 18, past positive TST, previous treatment for TB (pulmonary or extra-pulmonary), severe allergic reactions and other medical contraindications were excluded from the study. Non-participants were asked to fill an anonymous non-participant form.

Self-administered questionnaire

Personal demographics, exposures and other factors were self-reported. This information was supplemented with administrative data indicating the participation of groups of trainees in clinical activities. We adopted the questionnaire used by Rajnish Joshi et al. (2007), modified for use in this study context and to collect additional data based on study objectives, feedback from local experts and validation during pretesting (Appendix 3).

Personal demographics and medical history

Information was collected about personal factors including: age, sex, educational and occupational experience, nationality, birth country, and state of residence, family income, assets and occupation. Due to income means significantly higher than the general population in India, the revised Kuppuswamy socioeconomic status (SES) scale (Oberoi, 2015) could not be used to stratify the population. A modified 4-category SES index was constructed using household monthly income, and where no income reported family assets and parental education and occupation.

History of previous TST and TB disease assessment was collected. Medical history and conditions which may increase susceptibility to tuberculosis infection, including immunosuppressive conditions such as diabetes (Dooley & Chaisson, 2009), HIV (Pontillo et al., 2013). Weight and height were measured to generate BMI. Bacille Calmette Guérin (BCG) vaccination status was assessed using self-reported data and physical inspection of BCG scars. While since 1985 India has had a universal BCG vaccination program, in 1997 this coverage only extended to 72% of the population (World Health Organization, 2015c). As well, BCG vaccination cannot be assumed in students born in other countries where it has been phased out.

Community exposures

All individuals were asked nine questions assessing their potential TB exposure in community settings, they were asked further questions about dates of exposure and time to create opportunity for recall, and allow us to assess the quality of the recalled information by examining certainty of estimates. Community exposures were then collapsed into an index of community exposure for whether an individual reported having definitively been exposed to TB in at least one community setting.

Clinical exposures

For students in clinical stages of their education information was collected about length of postings in various departments including medicine, pulmonary medicine and DOTS treatment centers. For nursing students information regarding procedures conducted was collected. Participants were also asked if they had ever been in direct contact, within a conversational distance, with a sputum-positive pulmonary TB patient (Pai et al., 2005). The responses were collapsed into a categorical measure conditional whether a participant reported 'Yes' or 'Yes, but don't know if sputum positive' and 'No' and 'Don't know'.

Tuberculin skin test (TST)

A one-step TST procedure was conducted using 0.1 ml of 2 tuberculin unit (TU) Purified Protein Derivative RT23/Tween 80, as the current standard recommended dose by the WHO is 2 TU (Rieder, Chadha, Nagelkerke, van Leth, & vanderWerf, 2011). The PPD supplier was Arkray Healthcare Pvt. Ltd., an Indian company. There is no other PPD supplier in India, and PPD from Staten Serum Institut (SSI), the original supplier in Denmark, was not available because of short supply and long delays in production.

A trained research technician administered the test on the anterior portion of forearm, approximately 5-10 cm below the elbow joint. The test was read 48 hours after application, with a few read within 72 hours which is the acceptable range limit. The technician demarcated the transverse diameter of the induration using ballpoint pen, and measured in millimeters the induration using a clear ruler (Rieder et al., 2011). The size of the induration was also converted to a binary categorical variables based on study definitions, with a reported induration of ≥10mm being considered positive.

The results were reported in the study form, and individuals were sent to be processed in a private room by a consulting physician. The consulting physician took a blinded second reading for study quality assessment. The consulting physician provided individuals with a signed result of their TST test, and explained the meaning of results to individual participants. Those with TST indurations of 10mm or higher (the standard cut-off used in India) or 5mm depending for those with HIV and indicated immunosuppressive conditions or showing signs of active TB were given a referral and encouraged to visit the hospital for further chest X-ray and microbiological testing to rule out active TB. The study did not follow-up with assessment outcomes.

Ethical considerations

This project was reviewed and approved by the central ethics committees in Manipal University, India and McGill University, Canada. Permission was also obtained from stakeholders including Deans at Kasturba Medical College and the Manipal College of Nursing.

Statistical Analysis

Anonymized data was entered in Epi Info 7 software (CDC, Atlanta, GA), encrypted, and analyzed using Stata 12 (Stata Corporation, College Station, TX). Baseline characteristics were described for the overall population and stratified by clinical exposure status as a result of being enrolled in a given program. Further characteristics such as clinical history, community exposures, self-reported clinical exposure, postings and activities considered high-risk were also reported descriptively. The distribution of TST reaction size was described, and positive TST results were described stratified by program year in order to allow for comparison of prevalence across groups and overall. Two TST results were obtained for each individual, the first by a single trained study reader, and the second as a quality check by 13 secondary blinded readers who were providing consultations to participants. We used this as a quality check, and to determine the consistency of results conducted interrater reliability analysis (Cohen's κ).

Based on our literature review, 18 potential predictors were assessed for association with TST reaction size, a continuous outcome reported on the millimeter scale, and LTBI status, a dichotomous outcome reported as positive or negative. Continuous predictors were age and BMI. Dichotomous predictors were sex, pre-clinical or clinical status, BCG history, BCG scar, clinical exposure, community exposure, nationality, birth place, state of residence, posting in medicine, posting in pulmonary wards or OPD, posting in DOTS clinic, past TST, past TB assessment. Categorical predictors were SES, program. Variables were evaluated using univariate generalized linear models for continuous outcome, and univariate logistic regression model for dichotomous outcome.

Adjustment co-variates for generalized linear models and logistic models were identified using an iterative, purposeful selection of adjustment covariates as described by Hosmer and Lemeshow (Bursac, Gauss, Williams, & Hosmer, 2008; Hosmer Jr, Lemeshow, & Sturdivant, 2013). After univariate analysis, any covariate with a Wald statistic $p \leq 0.25$ was included in a full model. Co-variates with significantly missing data (under 75% of total participants) were excluded. In the full model, co-variates not meeting a Wald statistics $p \leq 0.05$ were dropped to create a reduced model. If none met this criterion covariates were assessed using backward-stepwise selection to create the reduced model. The full set of covariates were then iteratively added to the reduced model to create an extended model which included any variables that are significant in presence of other variables and lead to threshold change in outcome point-estimate ($\Delta\hat{\beta}$ >20%).

For the univariable and multivariable generalized linear models with continuous TST induration size as the outcome, the adjusted b-coefficients with 95% confidence intervals (CI) were presented. For multivariable logistic models with binary TST positivity as outcome, adjusted ORs with 95% confidence intervals were presented. Due to extremely low prevalence, clinical risk factors including HIV status, diabetes, and other immunosuppressive conditions were recorded, but only used for counseling purposes by physicians and not as a covariate in our analysis.

5.1.3 RESULTS

Participants

There were 763 total healthcare trainees eligible for participation in the study, and participation rates are summarized in Figure 5.1. 489 (64.1%) were successfully recruited into the study. The nearly one third who did not participate did not so for various reasons: refusal, not contactable, or were under 18 years of age. 19.3% of non-participants completed a non-participant form used to help us determine if there was any bias. After recruitment and following filling out the information form, 46 (9.4%) of individuals were excluded from the analysis: 27 were excluded from participation in TST due to reported past TB history, allergies, and health conditions, and another 19 did not return for reading of their TST results.

Demographic characteristics

The baseline characteristics for the overall population and pre-clinical exposure and post-clinical exposure groups can be found in Table 5.1. The overall characteristics between the two groups are overall slightly imbalanced due to low participation and exclusion of 1st year diploma nursing students. However when comparing within strata based on program enrollment, i.e. medicine only, characteristics such as BMI, income, etc. are balanced and comparable across groups.

Overall 85% of participants were between the ages of 18-21, with a mean age of 19.8 years and range of 18-33 years. 66% of participants were female with an overall BMI mean of 22.6 kg/m^2 (95% CI 22.2-23.0). Only 64% of participants reported their income. For individuals where income information was missing we used assets, parental education and occupation as proxies for socio-economic status. More than 80% of participants would be considered upper class based on Kuppuswamy's socioeconomic status scale relative to national standards (Oberoi, 2015). Therefore we stratified participants on a modified SES scale relative to this context. More than two-thirds of participants (71%) were not in-state Karnataka residents, 10% of participants were not born in India, and another 10% did not have Indian nationality.

Clinical history was examined through a series of questions about past BCG vaccination, TST testing and TB assessment. 82% of individuals reported having received BCG vaccination at birth or after birth. The latest reported vaccination after birth was 1998 or 17 years prior to the study. Among those who gave permission for inspection of BCG scar, a scar was observed among 79%. Individuals who reported having tested positive for TST or TB before were excluded from the study. 16 (4%) participants reported testing negative for TST in the past, and 16 (4%) participants reported having been assessed for TB disease before, and not having tested positive.

In order to assess participant self-selection bias we used administrative data and name analytics code we developed to assign gender to the full database of names of individuals enrolled in courses, with a margin of uncertainty associated with unisex names and names with unique spellings. We estimated that the population of all classes was approximately 65.7% female, and the population of non-participants was 65.5% female. Based on this information we do not expect any gender bias associated with non-participation. We also requested non-participants to fill out a physical non-participant form. 53 non-participants, representing a fifth (19%) of total non-participants, filled out this form. Proportionally, students in medicine were over-represented among those filling out non-participant forms, while students in nursing were under-represented. Non-participants who had agreed to fill out the non-participant form were 83% female, on average 20 years of age (95% CI 19.8-20.5). 96% reported not having been treated for TB before, and 83% reported not having had TST done before.

Exposures and clinical experience

Exposure history was examined with respect to whether individuals had worked in healthcare settings before as shown in Table 5.2. Only 13 of 443 (3%) reported having worked in healthcare settings outside their clinical postings. The length of time was generally short term, and the roles were classified as low-exposure including 'volunteer', 'research assistant' and 'observership'. 54 (12%) indicated having been exposed with certainty to TB positive individuals in at least one or more community setting including households or student residences. While the questionnaires asked for length, dates and whether exposure source had been sputum or culture positive during the time of exposure, these variables were excluded due to high recall uncertainty. 163 (37%) of participants reported with certainty having had direct contact, though the majority were uncertain about whether the exposure source was sputum smear/culture positive or not. This number did not include those who had reported being uncertain about having been exposed in clinical settings.

Data was collected about specific exposures to high risk clinical settings and clinical activities for those in the clinical group (Table 5.3). For clinical postings, all upper-year medical trainees reported being posted in medicine wards for a mean of 100 days (95% CI 97-105) and pulmonary medicine ward for a mean of 19 days (95% CI 16-21). Only 1 trainee reported being posted in the adult isolation ward. 132 (94.3%) reported having been posted to the pulmonary out-patient department (OPD) for a mean of 27.2 days (95% CI 23-32). 15 (10.7%) reported having been posted to a DOTS clinic for a mean of 2 days (95% CI 0.6-3.7) at the Government District Hospital in Ajjarkad, Udupi. Among upper-year nursing (BSc and diploma), 95 (99%) reported being posted in medicine wards for fa mean of 34 days (95% cI 24-43). 14 (14.6%) reported being posted in pulmonary medicine ward for a mean of 26 days (95% CI 23-29), although 11 of 14 were BSc nursing students. Only 3 reported having been posted to a DOTS clinic for a mean of 1.5 days (95% CI 0-7.8). Very few nursing trainees reported performing or helping with any procedures from a list of procedures for a patient with known or suspected pulmonary TB (Table 5.4).

Prevalence of TB infection

The accepted standard deviation for repeated readings, accounting for intra- inter- and within-subject variation is 3mm, we used this as a threshold to examine agreement between study and blind readers (Dick Menzies, 1999). 94.1% of results were within 3mm of each other, with near perfect agreement at this threshold with a Cohen's κ=0.93 (95% CI 0.90-0.96, $p<0.0001$). In 23 cases, a third reader was brought in to resolve a discordance of more than 3mm.

The distribution of reaction sizes is shown in Figure 5.2. The mean size for pre-clinical exposure was 3.89mm (95% CI 3.56-4.22) for post-clinical exposure 3.86mm (95% CI 3.47-4.25). Results for 443 participants were dichotomized to estimate prevalence of TB infection based on pre-set cut-offs. 23 tested positive (≥10mm) and 420 negative (<10mm), for an overall prevalence of 5.1% (95% CI 3.1-7.2). MBBS III students had a prevalence of 4.8% (95% CI 1.3-8.3), while MBBS VII students had a prevalence of 9.3% (95% CI 4.4-14.1) (Table 5.5).

Risk factors for LTBI

The association between TST induration size and personal characteristics and exposures was assessed using univariable and multivariable generalized linear regression models (Table 5.6). Covariates were adjusted for clinical status, self-reported in clinical exposure, posting in pulmonary medicine (clinic and out-patient department) and posting in general medicine wards. In the unadjusted model, female gender, self-reported BCG vaccination, and being born in India were associated with decrease induration size while posting in pulmonary medicine was associated with increased induration size. In the adjusted model, self-reported BCG vaccination was associated with decreased TST induration size (-0.75mm, 95% CI -1.43, -0.08). Posting in pulmonary medicine was associated with increased TST induration size (b=1.42mm, 95% CI 0.66, 2.19).

The association between TST positivity (cut-off ≥10mm) and personal characteristics and exposures was assessed using univariable and multivariable logistic regression models (Table 5.7). In the unadjusted model, self-reported direct exposure in clinical settings and posting in pulmonary medicine were associated with TST positivity. In the adjusted model, adjusted for posting in pulmonary medicine, only posting in pulmonary medicine was associated with increased odds of TST positivity (aOR 3.11, 95% CI 1.31, 7.36).

5.1.4 DISCUSSION

Summary

This study found an overall TB prevalence of 5.1%, which varied across nursing and MBBS programs though not significantly. The study also found that overall, the major risk factor identified for both increased induration size and TST positivity was having been posted in pulmonary medicine wards or out-patient departments for a mean of 27.2 days or more.

Our prevalence results are similar to baseline results found in healthcare workers and students in non-endemic countries such as Italy (Durando et al., 2013; Lamberti et al., 2015), but significantly lower than high endemic countries including Brazil (Maciel et al., 2005), India (D. J. Christopher et al., 2011), Zimbabwe (Corbett et al., 2007). The low prevalence observed in a high endemic country might be in part explained by the unique context of the study and limited student exposure and partial infection control measures in place.

Manipal is located within the Udupi City Municipality with a population consisting almost exclusively of 28,0000 Manipal University students, faculty and staff. Udupi City Municipality has a total population of 144,960 and an average literacy of 93.6%. The district annual total case notification rate of 77 per 100,000 population (2013) (Central TB Division, 2014), which although high is lower than the national average.

Manipal could be considered a low-endemic enclave in a high endemic region. The participants in this study had significantly higher socio-economic status than the general population, and nearly 71% from outside the state, and 10% were not Indian nationals. The fee barrier to enrolling in the school selects for a unique population. In 2015, for MBBS programs overall program fees are approximately USD $62,000 for Indian students and USD $207,700 for foreign nationals. For BSc nursing, overall program fees were USD $6118 for Indian students, and USD $18,500 for foreign nationals. Similarly the hospital system is better resourced than public hospitals in the region.

Students in the early MBBS and nursing programs in Manipal generally have limited exposure to patients in their initial years. For example, while 3 hours of each day after the third semester is spent in clinics, students spend a significant number of these hours receiving passive instruction and not engaging in practical activities that would expose them to serious risk. Furthermore, while the use of N95 masks is not hospital policy, partial infection control measures exist. For example, while masks are not used in general and there is limited cross-ventilation in general and isolation wards, undergraduate trainees are not permitted to go to respiratory isolation wards.

In this study we found that having being posted to pulmonary wards and pulmonary out-patient clinic was significantly associated with latent TB infection. Several past studies among HCWs have identified work in specific locations in hospitals to be associated with greater risk of TB infection (R. Joshi et al., 2006; Mathew et al., 2013; Seidler et al., 2005). Unlike HCWs students do not spend significant amounts of time in the pulmonary wards and out-patient departments. For example, medical students spent on average 19 days in pulmonary medicine wards, and 27 days in the pulmonary out-patient department. Nevertheless, an elevated risk in these areas is plausible given the dense presence of patients with infectious TB and limited infection control measures in place. The results would suggest a need to assess and implement improved respiratory infection control in these high risk locations.

Strengths and limitations

This study had a large number of participating students. Despite the large number of participants, we had an overall participation rate of 64.1%, excluding a program that did not choose to participate this rate would be 69.2%. The number tested was higher in some groups than others, at 98% in Diploma nursing year 3 versus 59% in year MBBS 7. In the pre-clinical groups, many individuals had to be excluded due to not being age eligible. Though, based on administrative data and non-participant feedback, we don't believe that the reasons for lack of participation were due to health issues or suspected infection, nevertheless there is potential for selection bias. The findings from participant population in the study may not be generalizable to other populations.

We also used a comprehensive questionnaire combined with administrative data to identify exposures and risk factors for TB. For assessing exposures, we relied on recall from students. While exposure in clinical settings for medical students could be confirmed in part using administrative records, we nevertheless anticipate some recall bias. Students may not have known if someone had TB, which would lead to reduced estimates of exposure, but they also had great challenge in knowing if people 'with TB' had already been treated for TB and not infectious -- which would overestimate their exposure.

We had a trained TST reader whose readings were validated with a blind reader. This study used a one-step TST. Since this was not part of routine testing we don't anticipate TST prevalence would have been significantly different with two-step testing, as studies have shown that one-step testing works well for population surveys (Murthy et al., 2013). However, we had no choice but to use an Indian PPD of unknown quality. The PPD by Arkray Healthcare Pvt. Ltd. has not been validated and shown to be bioequivalent to established standards such as the PPD RT23 by SSI, Denmark. Another study from India that used the same PPD found a lower prevalence of TB infection compared to QuantiFERON-TB Gold (Mathad et al., 2014).

5.1.5 CONCLUSIONS

We found a low prevalence of TB among students in medical and nursing programs in Manipal compared to other institutions in India. We found an association between being posted to pulmonary wards or clinics and both induration size and skin test positivity. In order to assess the actual risk of conversion as a result of exposure, it's necessary to conduct longitudinal studies for longer periods of exposure. The identification of infection control gaps in high risk settings such as pulmonary wards and clinics is recommended. Medical and nursing students in India are routinely vaccinated and asked to conduct hematological testing, and routine TB testing could be integrated in this program. Given that hospitals in India rely on local PPD supplies, we also encourage future studies to establish the sensitivity and specify of PPD products made in India. The establishment of clear guidelines for infection control, routine testing, and long term surveillance of TB infection prevalence and incidence among medical and nursing students will ensure that future healthcare workers are protected.

5.1.6 ACKNOWLEDGMENTS

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Disclosure: We do not declare any potential conflicts of interest.

5.1.7 TABLES AND FIGURES

Figure 5.1 Participation in study of tuberculosis infection among medical and nursing trainees in Manipal, India

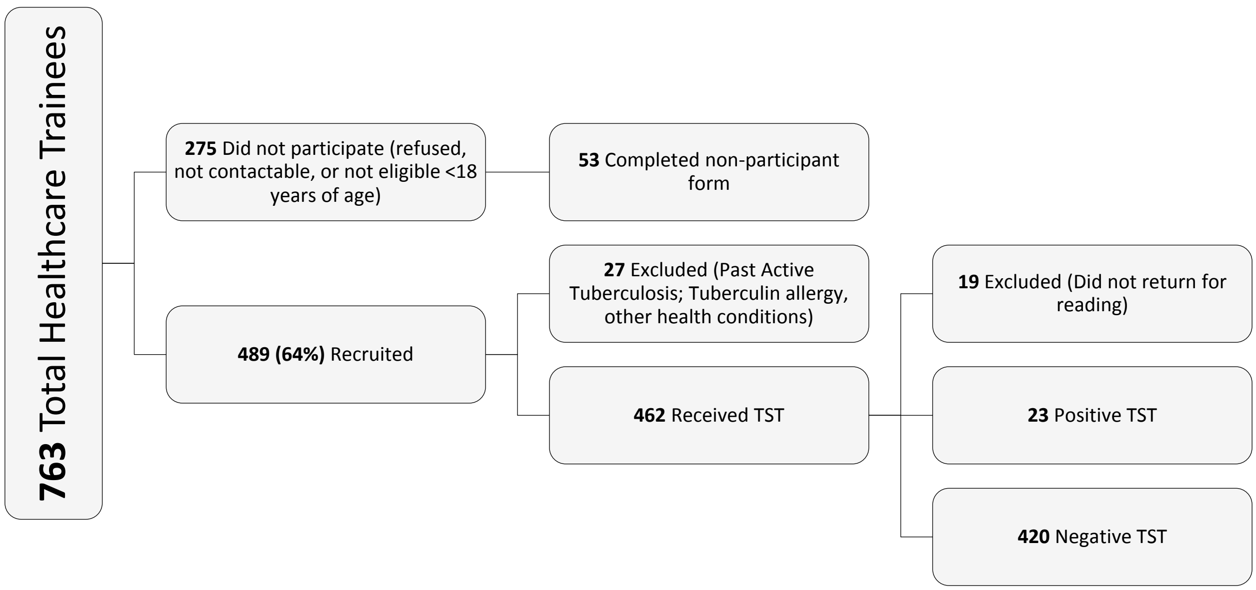

Figure 5.2 Histogram of one-step tuberculin skin test (TST) reaction size for medical and nursing trainees (n=443)

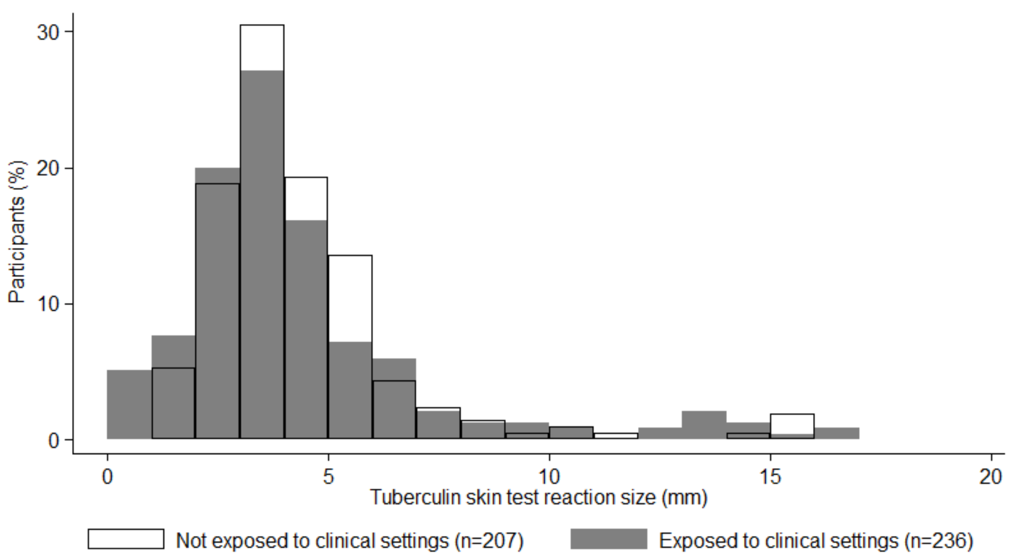

Table 5.1 Baseline characteristics of medical and nursing trainee participants

	Overall	(N=443)	**Preclinical**	(N=207)	**Clinical**	(N=236)
Gender						
Male	132	30%	71	34%	61	26%
Female	307	69%	134	65%	173	73%
Unknown	4	1%	2	1%	2	1%
Age (range)	19.8 years (18-33)		18.9 years (18-25)		20.6 years (19-33)	
BMI (range)	22.6 kg/m2 (13.7-45.2)		23.1 kg/m2 (15.8-45.2)		22.2 kg/m2 (13.7-44)	
Income						
<Rs. 30K	73	16%	19	9%	54	23%
Rs 30 -90K	69	16%	32	15%	37	16%
>Rs 90K	133	30%	75	36%	58	25%
Unknown	168	38%	81	39%	87	37%
Socio-Economic Status*						
Low	45	10%	12	6%	33	14%
Middle-low	86	19%	37	18%	49	21%
Middle-high	43	10%	16	8%	27	11%
High	247	56%	128	62%	119	50%
Unknown	22	5%	14	7%	8	3%
Nationality/residence						
Not born in India	46	10%	24	12%	22	9%
Foreign nationality	46	10%	22	11%	24	10%
In-state (Karnataka)	133	30%	46	22%	87	37%
Clinical history						
BCG reported	363	82%	153	74%	210	89%
BCG scar present**	281	79%	121	58%	160	68%
TST in past	16	4%	5	2%	11	5%
Assessed for TB	16	4%	1	0%	15	6%

*SES index composed of income, where not available: assets, parental education, and occupation.
**BCG Scar N=357 gave permission to examine scar.

Table 5.2 Trainee Exposure History

	Overall (N=443)		Preclinical (N=207)		Post-clinical (N=236)	
Exposure history						
Worked in health before	13	3%	6	3%	7	3%
Community contact with TB patient	54	12%	35	17%	19	8%
Direct contact with TB patient	163	37%	N/A		163	69%

Table 5.3 Trainee (n=236) placement in areas with high risk of exposure to TB

	Medical undergraduates			Nursing undergraduates		
	N	%	Average Days (95% CI)	N	%	Average Days (95% CI)
Postings						
Medicine ward	140	100%	100 (95-105)	95	99%	34 (24-43)
Pulmonary ward	140	100%	19 (16-21)	14	15%	26 (23-29)
Pulmonary OPD	132	94%	27 (23-32)	N/A	N/A	N/A
DOTS clinic	15	11%	2 (0.6-3.7)	3	3%	1.5 (0-7.8)

Table 5.4 Activities of nursing trainees with known/suspected pulmonary TB patients (n=96)

	5 times or less (%)	6 times or more (%)	No, can't recall
Activities	12.5	0.0	87.5
Sputum sample collection	9.4	0.0	90.6
Chest physiotherapy	7.3	1.0	91.7
Bronchoscopy	8.3	4.2	87.5
Insertion of NG tube	15.6	3.1	81.3
Oral suctioning	10.4	2.1	87.5
Tracheostomy care	11.5	3.1	85.4
Tracheostomy suctioning	5.2	6.3	88.5
Endotracheal tube suctioning	0.0	0.0	0.0

Table 5.5 Participation rates and prevalence of positive TST (≥10mm) across medical and nursing programs

Program	Total n	Tested n (%)	Positive TST* n	Prevalence (95% CI)
BSc Nursing Year 1	100	62 (62%)	1	1.6% (-1.5, 4.7)
BSc Nursing Year 3	94	55 (59%)	1	1.8% (-1.7, 5.3)
Dip Nursing Year 1	56	**		
Dip Nursing Year 3	42	41 (98%)	1	2.4% (-2.4,7.2)
MBBS Semester 3	234	145 (62%)	7	4.8% (1.3,8.3)
MBBS Semester 7	237	140 (59%)	13	9.3% (4.4,14.1)
Overall	763	443	23	5.1% (3.1,7.2)

* Positive tuberculin skin test (TST) defined as induration size of ≥10 mm or more

**Participants from Diploma Nursing Year 1 program excluded to low (n<5) participation rate.

Table 5.6 Predictors of TST induration size among medical and nursing trainees, Manipal

		TST Induration size (TST mm)					
Characteristics	n	b	95% CI	P	adj b*	95% CI	P
Sex							
Male	132	Ref			Ref		
Female	307	**-0.68**	(-1.24, -0.11)	0.02	-0.41	(-1.00,0.17)	0.17
Age (years)	443	0.10	(-0.08, 0.28)	0.27	0.06	(-0.17, 0.29)	0.59
BMI (kg/m2)	437	0.04	(-0.02, 0.10)	0.17	0.01	(-0.05, 0.07)	0.75
Clinical status							
Pre-clinical years	207	Ref			Ref		
During clinical years	236	-0.03	(-0.55, 0.49)	0.90	-1.89	(-7.30, 3.52)	0.49
Self-reported exposures							
Clinical settings	443	0.15	(-0.39, 0.69)	0.59	-0.02	(-0.80, 0.77)	0.97
Community settings	443	0.12	(-0.67, 0.91)	0.77	0.16	(-0.64, 0.95)	0.70
Health history							
BCG self-reported	443	**-0.78**	(-1.45, -0.11)	0.02	**-0.75**	(-1.43, -0.08)	0.03
BCG scar observed	357	0.29	(-0.44, 1.03)	0.43	0.18	(-0.55, 0.91)	0.63
Past TST testing*	398	1.22	(-0.14, 2.58)	0.08	0.96	(-0.42, 2.33)	0.17
Past TB assessment*	420	0.35	(-1.04, 1.74)	0.62	0.63	(-0.77, 2.03)	0.38
Medicine posting	443	-0.02	(-0.54, 0.50)	0.95	0.95	(-4.50, 6.39)	0.73
Pulmonary posting	443	**0.74**	(0.20, 1.28)	0.01	**1.42**	(0.66, 2.19)	0.00
DOTS posting	443	-0.86	(-2.17, 0.46)	0.20	-1.27	(-2.61,0.07)	0.06
Program category							
BSc Nursing year 1	62	Ref			Ref		
BSc Nursing year 3	55	-0.68	(-1.67, 0.32)	0.19	-1.69	(-7.14, 3.75)	0.54
Dip Nursing year 3	41	-0.69	(-1.78, 0.39)	0.21	-1.65	(-7.22, 3.92)	0.56
MBBS Semester 3	145	0.29	(-0.53, 1.10)	0.49	0.29	(-0.53, 1.11)	0.50
MBBS Semester 7	140	0.75	(-0.07, 1.57)	0.07	-0.74	(-6.40, 4.92)	0.80
Socio-economic Status							
Low	45	Ref			Ref		
Middle-low	86	-0.05	(-1.06, 0.97)	0.93	-0.53	(-1.58, 0.53)	0.33
Middle-high	43	1.19	(0.01, 2.36)	0.05	0.30	(-0.98, 1.57)	0.65
High	247	0.48	(-0.41, 1.38)	0.29	-0.53	(-1.60, 0.54)	0.33
Indian nationality	442	-0.53	(-1.39, 0.31)	0.21	-0.46	(-1.30, 0.38)	0.29
Indian born	440	**-0.92**	(-1.77, -0.08)	0.03	-0.74	(-1.59, 0.11)	0.09
Karnataka resident	430	-0.40	(-0.96, 0.16)	0.16	-0.07	(-0.65, 0.52)	0.82

*Adjusted for exposure to clinical status, self-reported clinical exposure, posting in pulmonary medicine, posting in general medicine

Table 5.7 Predictors of TST positivity among medical and nursing trainees, Manipal

		Tuberculin Skin Test Positivity					
Characteristics	n	OR	95% CI	P	aOR*	95% CI	P
Sex							
Male	132	Ref			Ref		
Female	307	0.54	(0.23, 1.26)	0.16	0.63	(0.26, 1.49)	0.29
Age (years)	443	1.13	(0.89, 1.43)	0.32	0.85	(0.53, 1.35)	0.49
BMI (kg/m2)	437	1.02	(0.93, 1.12)	0.67	1.01	(0.91, 1.11)	0.91
Clinical status							
Pre-clinical years	207	Ref			Ref		
During clinical years	236	1.69	(0.70, 4.07)	0.24	0.31	(0.04, 2.49)	0.27
Self-reported exposures							
Clinical settings	443	**2.34**	(1.00, 5.47)	0.05	1.28	(0.43, 3.76)	0.66
Community settings	443	1.56	(0.51, 4.76)	0.44	1.98	(0.63, 6.26)	0.24
Health history							
BCG self-reported	443	0.61	(0.23, 1.59)	0.31	0.50	(0.18, 1.34)	0.17
BCG scar observed	357	1.16	(0.38, 3.55)	0.80	1.01	(0.33, 3.15)	0.98
Past TST testing*	398	2.89	(0.61, 13.68)	0.18	2.12	(0.43, 10.36)	0.35
Past TB assessment*	420				1.16	(0.14, 9.42)	0.89
Medicine posting	443	1.70	(0.71, 4.11)	0.23	0.31	(0.04, 2.54)	0.28
Pulmonary posting	443	**3.11**	(1.31, 7.36)	0.01	**3.11**	(1.31, 7.36)	0.01
DOTS posting	443	1.08	(0.14, 8.47)	0.94	0.61	(0.08, 4.97)	0.65
Program category							
BSc Nursing year 1	62	Ref			Ref		
BSc Nursing year 3	55	1.13	(0.07, 18.50)	0.93	0.493895	(0.02, 14.65)	68.3%
Dip Nursing year 3	41	1.52	(0.09, 25.09)	0.77	1.055946	(0.05, 20.94)	97.2%
MBBS Semester 3	145	3.09	(0.37, 25.70)	0.30	3.094203	(0.37, 25.70)	0.296
MBBS Semester 7	140	6.24	(0.80, 48.83)	0.08	0.809497	(0.02, 30.33)	0.909
Socio-economic Status							
Low		Ref			Ref		
Middle-low	45	0.78	(0.13, 4.83)	0.79	0.589062	(0.09, 3.79)	0.577
Middle-high	86	2.21	(0.38, 12.71)	0.38	1.200691	(0.19, 7.73)	0.847
High	43	1.29	(0.28, 5.89)	0.74	0.722608	(0.14, 3.70)	0.696
Indian nationality	247	0.53	(0.17, 1.63)	0.27	0.553324	(0.18, 1.73)	0.308034
Indian born	440	0.39	(0.14, 1.11)	0.08	0.429195	(0.15, 1.23)	0.116602
Karnataka resident	430	0.83	(0.32, 2.17)	0.70	0.93023	(0.35, 2.46)	0.884237

**Adjusted for posting in pulmonary medicine

6 Results: Manuscript 2

Tuberculosis infection control knowledge, attitudes and practices among medical interns and post-graduate residents in South India

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Background: Healthcare workers and patients in high burden countries such as India are vulnerable to Hospital-associated tuberculosis. While the World Health Organization and the government of India have developed guidelines for TB infection control in hospital-settings, it is unclear how healthcare trainees engage with infection control in their practice.

Objective: This survey evaluated the baseline knowledge and attitudes, and practices of trainees in medicine with respect to TB infection control and examined how personal characteristics, experience knowledge and attitudes relate to self-reported practices.

Methods: Between August-October 2015 interns and post-graduate residents in medicine associated with Kasturba Medical Hospital in two cities, Manipal and Mangalore, India participated in a cross sectional survey. The structured, self-administered, validated questionnaire consisted of 52-items. Data were analyzed using multivariable logistic regression.

Results: 486 participated in the study, consisting 34% of medical interns and 66% of medical post-graduates. Mean knowledge score for transmission routes and symptoms was 81% (95% CI 80-82), mean knowledge score for TB transmission risk factors was 67% (95% CI 66-69), and mean score for knowledge of infection control 50% (95% CI 49-52). More willingness to be screened for TB infection was associated with greater overall knowledge (OR 1.1, 95% CI 1.05-1.18) and being a post-graduate (aOR 1.93, 95% CI 1.04-3.61). Greater N95 mask usage when working with TB patients was reported among those who believed that N95 masks should be worn (aOR 2.311, 95% CI 1.48-3.61) and those who received praise from their supervisors (aOR 1.88, 95% CI 1.15-3.05).

Conclusions: We identified poor knowledge regarding TB infection control. Factors such as orientation training and supervisor engagement were associated with attitudes and practices conducive to TBIC. On the other hand poor knowledge and past healthcare experience were associated with attitudes and practices not conducive to TBIC. Overall we were able to simply a complex web of covariates that influence self-reported trainee TBIC behaviour.

Keywords: Infection control, tuberculosis, health education

6.1.1 INTRODUCTION

One-quarter of the world's incident tuberculosis (TB) cases each year, an estimated 2.3 million, occur in India (Central TB Division, 2014). Hospital settings provide a milieu in which TB can be transmitted from patients to other patients and healthcare workers. The use of administrative controls, environmental controls and personal protection equipment has been recommended by the World Health Organization (WHO) and India's national airborne infection control (AIC) guidelines (India Ministry of Health and Family Welfare, 2010; World Health Organization, 2009). Nevertheless, young trainees in India have very high rates of conversion to TB due to high exposure in their early years of clinical practice (Pai & Christopher, 2011). A number of factors including poor implementation of infection control practices, including failure to follow protocols when dealing with TB suspects, lack of or failure to use personal protection equipment may facilitation nosocomial infections (Pai et al., 2006).

Systematic investigation of literature investigating knowledge, attitudes and practices (KAP) toward TB and TB infection control among healthcare trainees in India identified 12 studies, largely focused on knowledge of TB. While the Revised National Tuberculosis Control Program (RNTCP) is integrated into the medical curriculum in India, studies identified gaps in knowledge of RNTCP guidelines. Kutare et al. (2012) reported that among interns very few could correctly identify modes of TB transmission (18.8%) and cough for three weeks as a symptom of TB (38.2%). M. Basu and Das (2014) found that around two-thirds (65.4%) of interns were able to identify droplets as a mode of TB transmission and a similar number recognized two weeks of cough as a symptom of TB. Mehta et al. (2012) found that only 21% of interns and post-graduates knew that you could be sputum-negative and still carry infectious pulmonary TB.

Nalabothu and Menon (2014) examined knowledge of MDR/XDR TB, and found among medical post-graduates less than half (42.8%) could correctly define MDR-TB, and even fewer (25.7%) XDR-TB correctly. (Rupali & Gautam, 2014) similarly found that less than 40% had correct knowledge regarding MDR-TB etiology and diagnostics. Kulkarni et al. (2013) conducted a semi-structured cross-sectional survey among medical students in Mangalore, India focusing on broad infection control practices, with a small portion focused on TB. They found the majority knew about cough hygiene for patients (86.6%), and sputum collection standards (81.3%). They also reported that the majority of students knew that healthcare workers should wear a mask to protect themselves (80%), however, it was unclear what was meant by a "mask" (i.e. surgical or N95 masks). Baveja and Dalal (2012) investigating mask use among medical students found that only 6% knew N95 masks are appropriate for protection against TB. Baveja and Dalal (2012) found that although a significant portion (90%) of students expressed fear regarding TB transmission from a coughing patient; in general TB risk perception and management were poor among medical students.

These studies however had several notable limitations. Only 1 study focused specifically on infection control, and among undergraduate medical students only (Kulkarni et al., 2013), and only 3 studies, two of which were components of the same study, examined attitudes and practices, again, among undergraduate medical students only (Baveja & Dalal, 2012; Emili et al., 2001; Emili et al., 2002). The questionnaires used across studies were not standardized and often not validated. Sample sizes were highly variable ranging from 36 to 268 participants. The objective of this study was to include a broader population of young physicians, and investigate several dimensions of TB infection control.

6.1.2 METHODS

Study setting

The study was conducted in Manipal University/Kasturba Medical Hospitals in Manipal and Mangalore in the South Canara region of Karnataka, India in August-October 2015.

Study population

All medical trainees in internship programs, and post-graduates enrolled in community medicine, general medicine, microbiology, pediatrics, pulmonary medicine, otorhinolaryngology (ENT), general surgery, orthopedics, and obstetrics and gynecology were eligible to participate in the study. Other inclusion criteria included being age 18 or more and giving consent to participate. For analytical purposes we estimated a minimum sample size using the finite population correction factor of 260 for a confidence limit of 95% on question items assuming a chance response.

Recruitment of participants

The vast majority of participants were recruited immediately after various clinical classes where many trainees would be in one place. Smaller groups were recruited during their clinical postings. This was both to minimize the challenges of recruiting participants during their clinical postings, including minimization of interference with their work, as well to ensure that testing conditions were standardized. Participants were given brief instructions about the purpose of the study, and asked to mark the consent form attached to the front of the anonymous questionnaire if they wish to be enrolled in the study. They then had 15-30 minutes to complete the questionnaire.

Instrument construction

The self-administered study instrument (Appendix 4) was prepared in English which is the language of instruction and work at the university and hospital. Questions were developed based on national and international guidelines, or adapted from previous questionnaire (for a full list of sources see (Appendix 5).

Personal characteristics

Two questions asked regarding demographics (age, gender), 5 regarding general occupation characteristics, 7 regarding past exposure to tuberculosis infection, including number of patients interacted with in one and workplace orientation. We examined workplace orientation rather than education based on feedback during the pre-test session that it would be difficult to recall general education with any degree of precision, and also the population of post-graduates would be coming from relatively diverse educational backgrounds.

Knowledge of TBIC

Nineteen questions assessed knowledge. The first two were designed as multiple choice questions focusing on transmission routes and symptoms. Another 8 true/false questions focused on transmission risk factors. The last 9 true/false questions focused on knowledge regarding tuberculosis infection control. Each correct answer was assigned one point and each wrong answer no point. Scores were summed to obtain a total knowledge score, and scores for each of the subsections.

Attitudes towards TBIC

Nine Likert questions were posed on attitudes to capture the following underlying constructs perceived risk and obligation, personal protection, and administrative resources and patient management. The 5-point Likert ranged from strongly agree to strongly disagree. For analysis purposes, the results could justifiably be dichotomized with "strongly agree and agree" coded as agree and versus "neither agree or disagree, disagree, and strongly disagree" coded as disagree.

Practices towards TBIC

Nine Likert questions assessed TBIC practices, capturing the following underlying constructs: Peer, administrative practices, patient management, education, and personal protection. The 4-point Likert scale ranged from always, most times, few times to never. The scale was not collapsed further, and for analysis it was treated as an ordinal outcome.

One follow-up practice question probed decision-making behind a reported practice (wearing of masks). Eight pre-selected options drawn from literature and experts were given, and trainees were also given a line to fill out their own their own reason. They were then asked to select on a Likert scale ranging from strong-weak, how strongly a given factor influenced their decision to not wear an N95 mask when appropriate. For analysis purposes, the answers were dichotomized with "strong to semi strong" coded as strong and "moderate to weak" coded as weak. Open-ended answers were qualitatively analyzed. The strength of each option on the decision to not wear a mask was examined using descriptive data.

Interventions for TBIC

Based on pre-testing and review of literature, a set of eight TBIC measures that could potentially be implemented in a healthcare setting were identified. The designed question asked individuals to rank the measures based on what they considered would make the best impact in their work setting. We used the word 'best' based on pre-testing as it denoted quality and was inclusive of a range of beliefs that may go into such a ranking, versus 'most' which denotes quantity. While in the original design, each individual was intended to only select one measure as their first choice, one as second and one as third-- reflecting the order in which they should be prioritized-- some selected more than one choice as their first, second or third ranked measure. These results were included as we believe it does not compromise the interpretation of results.

Instrument validity

The instrument was validated using consultation with experts and pre-testing with six non-medical and ten medical trainees respectively to ensure there was ease of comprehension and test for potential problems. The first round of testing on non-medical students lead to the modification of several question, the second round of testing on medical students allowed for minor typographical corrections.

Ethical considerations

Participation in the study was voluntary and personal information was collected anonymously and maintained anonymous for analysis purposes. This project was reviewed and approved by the ethics committees in Manipal University Manipal and Mangalore.

Statistical Analysis

Descriptive

Anonymous data was entered in Epi Info 7 software (CDC, Atlanta, GA), encrypted, and analyzed using Stata 12 (Stata Corporation, College Station, TX). Personal characteristics and responses to questions regarding knowledge, attitudes and practices were reported using stacked bar graphs. Likert scale responses were dichotomized and reported descriptively in tables. All analysis examined differences between trainees in internship and post-graduate programs, and generally significant associations were reported.

Inferential

Association between personal characteristics and knowledge was examined using univariable analysis, with the exception of investigation and treatment for TB which was entered in a multivariable model allowing for an interaction term between the two. Association between personal characteristics, as determinants, and responses to questions regarding attitude and practices as outcomes was examined using multivariate analysis. In order to obtain a true estimate, adjustment co-variates for generalized linear models and logistic models were identified using backward stepwise selection. A model with the full set of personal characteristics was created, and ran for each outcome. Any co-variate with a a Wald statistic $p \leq 0.05$ was kept and used as overall adjustment covariates.

Association between knowledge, attitudes, and practices was examined using two methods. In the first method, overall knowledge and specific subsets of knowledge were linked as determinants to dichotomized attitude outcomes using logistic regression (unadjusted) and Likert scale practices using ordered logistic regression (unadjusted). Attitudes were linked as determinants to practices using Likert scale practices using ordered logistic regression, in a multivariable model where all attitudes were adjusted for one another to disentangle the true effect. The odds ratios (OR) and adjusted odds ratios (aOR) were reported using a schematic.

Network

In the second method, network analysis was used as a technique to examine correlation structures as describe by Shiratori et al. (2014). Here all pertinent covariates (34) were correlated using Spearman's rank correlation coefficient and any relationship with a Spearman P-value<0.01 was extracted. Each individual co-variate was then entered as a node SocNetV 2.0 Software (Kalamaras, 2014). Relationships between nodes were equally weighted. Betweenness Centrality (BC) scores were calculated. These scores describe the centrality of each node showing which co-variate exerts most power as an intermediary in the network, considering only geodesic paths (Kalamaras, 2014). The network schematic and correlation structures between covariates were reported.

6.1.3 RESULTS

Characteristics of the study population

A total population of 798 internship year and post-graduate residents (PGs) in across nine specified departments working in Kasturba Hospital in Manipal and Mangalore were eligible to participate in the study. In total 486 (61%) participated across both campuses, although participation rates were variable across the two cities, Manipal at 71.4% and Mangalore at 47.9%. As well participation rates were variable depending on professional status, with 98.1% of PGs in Manipal participating, versus 34.4% of interns in Mangalore. However, among PGs, participation rates did not vary significantly depending on the year of the program (p=0.52) (Table 6.1). Data regarding non-respondents was not collected; however, many who did not participate could not be reached due to being dispersed in hospitals or remote postings as the time.

All respondents declared their profession as either PG (n=321) or intern (n=165). However, the number of respondents varied across all other questions. The majority of participants, 64.2%, were between the ages of 23-26 years. 45.9% of participants were female. PG specialties in general varied significantly by size, with some specialties such as MD General Internal Medicine being significantly larger than others. Although rates of participation varied across specialties, with some programs being as small as 4-10 individuals and others 120, we examined the distribution of the number of respondents which followed program sizes. Among PGs, 29.3% reported having worked in healthcare prior to their enrollment. Among these individuals 44.1% had worked in healthcare for 1 year or more (Table 6.2).

TB exposure among the participants

Among participants, more than half (54%) reported seeing 41 or more patients in one week. 12% of participants reported that they had received no orientation for their current workplace, and another 30% had received orientation that did not cover safety precautionary measures for respiratory diseases including TB (Table 6.3). The proportion of people having received orientation was similar among interns (62%) and PGs (56%). Among those PGs enrolled in MD programs between 75%-100% reported having received some health safety orientation regarding respiratory diseases, with the exception of those in MD Paediatrics. Among PGs enrolled in MS programs and MD Paediatrics between 26.2%-56.8% reported having received health safety orientation regarding respiratory diseases (data not shown).

Nearly a quarter (22.8%) of all participants reported having had tuberculin skin test (TST) in the past, and nearly a fifth (19.9%) reported having been investigated for TB in the past. 12.4% reported having had an immediate family diagnosed with TB, and 6.4% reported having being diagnosed and treated for TB themselves with proportions being nearly equal among interns (6.7%) and PGs (6.2%) (Table 6.3). Proportions for these exposure variables did not vary significantly across professions, with the exception of TST testing, where 31.5% of interns versus 19.9% of PGs reported having been tested ($p<0.01$).

Level of the knowledge of the trainees

Two multiple choice questions assessed basic knowledge regarding transmission and signs and symptoms of TB. The first multiple choice question was focused on pulmonary TB transmission routes. The average score on this question was 76.4% (95% CI 75.2-77.6). While the majority of individuals correctly identified airborne droplets (93.6%) and spitting (69.1%) as major ways pulmonary TB can be spread from person to person, only 19.7% correctly identified that TB can be transmitted through talking or singing. The great majority (85.6%-92.6%)

correctly identified that pulmonary TB is not transmissible via the sharing of utensils, handshake and physical touch, blood, or sexual contact (Figure 6.1). The second multiple choice was to identify signs and symptoms of TB. The average score on this question was 82.% (95% CI 81.6, 83.9). The majority of individuals were able to identify correctly key signs and symptoms such as cough for >2 weeks (96.1%), fever (91.36%), weight loss (87.5%).

Another 17 true/false questions tested knowledge regarding five domains (Table 6.4). Individuals were generally able to correctly answer questions regarding risk factors. Overall average knowledge score was 75% (95% CI 73-76), knowledge scores for transmission routes and symptoms was 81% (95% CI 80-82), knowledge scores for TB transmission risk factors was 67% (95% CI 66-69), and scores for knowledge of infection control 50% (95% CI 49-52) (Figure 6.2). Knowledge of transmission risk was patchy however, as for example 47.7% said that children are more likely than adults to be infectious. Among PGs, answers to questions showed significant variations depending on specialty though not in a consistent manner. For example, for the aforementioned question, among general medicine (n=90) only 26.7% answered this question correctly, whereas in paediatrics (n=44) 45.6% answered the question correctly.

In contrast to knowledge regarding TB, knowledge regarding tuberculosis infection control was less among participants. In the domain of environmental infection control measures, 41.8% incorrectly selected that airborne infection isolation rooms have *positive* pressure relative to other parts of facilities. Only 8.6 % correctly identified that those involved in care of TB patients need to wear protective masks for the entire first two weeks of treatment. Similarly 53.7% incorrectly reported that surgical mask can prevent protection by filtering out TB droplet nuclei. Only 38.7% correctly identified that N95 masks do not work fine if wet or with visible dirt. 22.2% reported that wetness and dirt did not affect the mask, and 39.1% indicated that they did not know.

Association demographic variables and overall knowledge scores was assessed (Table 6.5). Being a post-graduate was associated with 4% score increase (95% CI 1,6) compared to interns. For PGs, Being in MD Paediatrics was associated with 11% score decrease (95% CI 3,18) compared to those in MD Community Medicine. For PGs, working in healthcare settings for 1-2 years inclusive was associated with 9% score decrease (95% CI 3,15) compared to those who had worked for less than 1 year. A small model was created consisting of training program (intern, PG) and four clinical history variables, with an interaction term between being investigated for and treated for TB. Here having been assessed for TB disease, but not having been diagnosed and treated-- was a positive predictor for knowledge with a score increase of 3% (95% CI 0, 6). Having being assessed and diagnosed was a negative predictor for knowledge with a score decrease of 4% (95% CI -8, 0).

Attitude of trainees toward TBIC

The attitudes and practices of trainees towards infection control were assessed using nine five-scale Likert questions (Figure 6.3). The questions were collapsed into a dichotomous levels of agreement (strongly agree, agree) and disagreement (neutral, disagree and strongly disagree) (Table 6.6). A quarter of participants indicated that they have a low risk of acquiring TB from their patients (23.0%) and a fifth indicated that they would not be very worried if they got TB disease (21.4%). With respect to patient management choices, the vast majority (79.0%) expressed support for isolating those with TB from others. Examining attitudes towards personal protection, 62.6% indicated that they believe that they should always wear N95 masks when exposed to TB suspects and patients, but 59.9% indicated that they believe there is limited availability of masks for their use. A large majority 78.0% indicated their willingness to be screened for TB infection and disease regularly. In practicing infection control, 67.7% indicated that their supervisors would praise them for practicing infection control, but 39.5% indicated that they find themselves too busy to practice infection control daily.

A number of attitudes strongly correlated with one another (Table 6.7). Those who believed that they had a low risk of acquiring TB from their patients also were more likely to not be worried if they were to get TB disease (OR 7.65, 95% CI 4.67-12.51) and less likely to believe that patients should be isolated (OR 0.57, 95% CI 0.33-0.98). Those who stated that one should always wear a N95 masks when exposed to TB patients also believed in isolating TB patients (OR 3.11, 95% CI 1.84-5.25). Those who stated that their supervisor would praise them for practicing infection control were more likely to be willing to be screened for TB infection

(OR 3.09, 95% CI 1.84-5.18). Those who reported being too busy to practice infection control also reported limited availability of masks for healthcare use (OR 2.29, 95% CI 1.51-3.45).

Various personal characteristics were associated with expressing certain attitudes (Table 6.8). Post-graduates were less likely than interns to believe they have a low risk of acquiring TB from their patients (aOR 0.40, 95% CI 0.23-0.70), and more likely to be willing to be screened for TB infection and disease (aOR 1.93, 95% CI 1.04-3.61). Having some infection control orientation was associated with reduced belief in having a low risk of acquiring TB from patients (aOR 0.10, 95% CI 0.01-0.85), increased odds of being worried if infected with TB (aOR 2.12, 95% CI 1.27-3.56), less odds of reporting limited availability of masks (aOR 0.44, 95% CI 0.28-0.68) and greater odds of reporting confidence in one's TB knowledge (aOR 1.70, 95% CI 1.13-2.55). Those who reported having been treated for TB in the past had greater odds of reporting that they would not be very worried if they get TB disease (aOR 2.91, 95% CI 1.18-7.17) and reporting that they found themselves too busy in daily practice to practice infection control (aOR 2.48, 95% CI 1.04-5.92).

Overall knowledge and individual knowledge components were significantly associated with attitudes (Figure 6.6). Those with higher overall knowledge regarding TB were less likely to believe that they had a low risk of acquiring TB infection (OR 0.83, 95% CI 0.78-0.88), less likely to report not being worried if they got TB disease (OR 0.86, 95% CI 0.81-0.91), and less likely to report being too busy in daily activities to practice infection control (OR 0.94, 95% CI 0.90-0.99). Greater overall knowledge was also associated with more willingness to be screened for TB infection (OR 1.1, 95% CI 1.05-1.18) and believing that suspects and proven TB cases should be isolated from others (OR 1.07, 95% CI 1.00-1.14). In a multivariable model adjusting for the sub-domains of knowledge, a supportive attitude toward isolation protocols was significantly associated with knowledge of TB infection control measures only (Figure 6.6). Overall knowledge score was not significantly associated with confidence of knowledge.

Self-reported practice of trainees

Nine Likert scale questions were used to determine the self-reported practice of trainees in clinical settings (Figure 6.4). Responses were dichotomized for descriptive purposes (Table 6.9) and evaluated with respect to adherence with international infection control guideline. 64.4% indicated that they never or few times collect sputum samples to identify TB suspects in waiting rooms around other patients. Nearly half reported that patients with known TB are separated from HIV patients. The majority do tell coughing patients to follow cough hygiene practices. However, other practices were more risky. 68.3% reported that in outpatient they see patients with cough according to the general token system and not a streamlined queue. 52.7% reported that they never or few times see patients in a well-ventilated room. For personal protection, 60.1% reported that they never to very few times wear a mask when caring for patients with TB, 46.1% reported the same for when they work with MDR or XDR-TB suspects and patients.

We investigated the association between personal factors with self-reported practice (Table 6.10). Post-graduates were more likely than interns to report that their co-workers practice infection control (aOR 1.81, 95% CI 1.15-2.83), to see patients in a well-ventilated room (aOR 1.75, 95% CI 1.12-2.73) and to tell patients to follow cough hygiene (aOR 3.06, 95% CI 1.97-4.74). Among PGs, some specialities had lower odds of reporting viewing patients in well-ventilated rooms including MD pulmonary medicine (aOR 0.09, 95% CI 0.01-0.84) when compared to MD community medicine. Having received some infection control orientation was correlated with safe practices across board including seeing patients in a well-ventilated room (aOR 1.76, 95% CI 1.21-2.58), telling patients to follow cough hygiene procedure (aOR 1.48, 1.03-2.13), and wearing an N95 mask when caring for patient with suspected or active pulmonary TB (aOR 2.02, 95% CI 2.38-2.97) and MDR-TB (aOR 1.88, 95% CI 1.28-2.75).

The association between knowledge score and attitude items with practice items was examined (Figure 6.6). Greater overall knowledge score was associated with decreased odds of reporting the risky practice of collecting sputum samples around other patients (OR 0.94, 95% CI 0.90-0.98). However a higher knowledge score was largely correlated with lower odds of reporting safe practices including seeing patients in a well-ventilated room (OR 0.94, 95% CI 0.90-0.99), wearing an N95 mask when caring for TB suspects or patients (OR 0.94, 95% CI

0.90-0.98), and reporting that co-workers practice TB infection control strategies (OR 0.93, 95% CI 0.89-0.98). By contrast those with confidence in their knowledge had higher odds of reporting seeing patients in a well-ventilated room (aOR 1.62, 95% CI 1.07-2.45) and that their co-workers practiced TB infection control (aOR 1.95, 95% CI 1.27-2.99).

Reporting that one was too busy in daily activities to practice infection control was significantly associated with risky infection control activities including reduced odds of wearing a mask for TB suspects (aOR 0.54, 95% CI 0.36-0.81) and patients and MDR-TB suspects and patients (aOR 0.55, 95% CI 0.37-0.82). They were also less likely to report receiving education about infection control measures (aOR 0.59, 95% CI 0.40-0.87) and observing co-workers practicing TB infection control (aOR 0.65, 95% CI 0.43-0.99).

N95 mask usage

In addition to the above mentioned, several other attitude variables were significantly associated with wearing masks for protection against TB infection. Reporting that one had a low risk of acquiring TB from patients was associated with the safe practice of wearing an N95 mask (aOR 2.35, 95% CI 1.43-3.86) but also risky practice of collecting sputum samples in waiting rooms around other patients (aOR 1.83, 95% CI 1.11-3.04). Those who believed that N95 masks should be worn were more likely to wear them for TB suspects and patients (aOR 2.311, 95% CI 1.48-3.61) and MDR-TB suspects and patients (aOR 2.29, 95% CI 1.47-3.60). Having a supervisor praise one was correlated with increased odds of reporting N95 mask use when working with TB patients and suspects (aOR 1.88, 95% CI 1.15-3.05) and MDR-TB suspects and patients (aOR 1.72, 95% CI 1.06, 2.80).

We reported the strengths of influence of various factors on the decision to not always wear an N95 mask when a participant knew it was appropriate (Figure 6.5). The strength of influence was dichotomized into strong-somewhat strong and moderate-very weak (Table 6.11). The strongest influences on the decision to not wear an N95 mask were a lack of access to N95 mask (60.3%), but also by perceiving it to be impossible to protect oneself all the time (44.9%) and superiors that do not wear N95 masks (42.6%). On the contrary, 59.3% indicated that not viewing N95 as necessary for infection control only had a neutral or weak influence on their decision, and similarly 51.2% indicated that physical discomfort wearing an N95 mask was also a neutral to weak influencer.

Priority areas for infection control

We examined TB control measured perceived to make the best impact in their given work setting (Table 6.12). 64.8% of all respondents ranked a single factor as first, second or third, whereas 35.2% ranked multiple factors as first, second or third. Comparing interventions that were ranked versus those not ranked, overall educational interventions were the most popular with 50.8% and 50.6% of respondent considering them as a priority. On the other hand, only 25.7% of the total ranked environmental controls, 35.8% administrative support and 37.9% greater monitoring and infection quality control.

Examining interventions most considered as most important (first ranked): 34% considered more education and training of patients to be the top priority, 28% considered a widely-distributed TB infection control plan to be top priority, and 27% more education and training of medical and support staff. Fewer considered the following as top priorities: more available protective devices, 20%, more appropriate management of TB suspects, 20%, greater monitoring and infection quality control, 19%, and administrative support for infection control procedures, 17%. Only 13% of those surveyed considered more environmental controls as a top priority.

Betweenness centrality of co-variates

Using network analysis the betweenness centrality that covariates, treated as nodes, exert within a network of relationships deemed to be significant using Spearman's rank correlation (Figure 6.7). The top mediators between nodes, i.e. points that most often connect between others, were identified to be the practice "I wear an N95 mask when caring for patients with suspected or active TB infection" (betweenness centrality score, BC 0.09), and the attitudes "If I get TB disease I would not be very worried" (BC 0.08) and "I would be willing to be screened for TB infection and disease regularly" (BC 0.07).

6.1.4 DISCUSSION

Summary

This study identified major gaps in knowledge, especially in the areas of TB infection control that could leave trainees vulnerable to TB infection. The effective implementation of these measures in part depends on trainees' knowledge of TBIC, attitudes and practices towards TBIC. Medical colleges play a critical role in ensuring that graduates are appropriately trained in infection control practices (Dubey & Bhuarya, 2014).

Overall knowledge was stronger among post-graduates than interns, however experience in healthcare settings among post-graduates was linked to reduced knowledge scores. Trainees generally recognized symptoms well, and scored high in this area, for example 96.1% recognized cough for >2 weeks as a symptoms. This was higher than the 64.5% reported by (M. Basu & Das, 2014), and 18.8% reported by (Kutare et al., 2012) among India interns. Still some gaps, for example only 20% correctly identified that TB can be transmitted through talking or singing. The knowledge of risk factors and transmission risk was very variable, and strong or weak particularly among certain sub-specialties of post-graduates. Knowledge of TBIC was generally poor, particularly with respect to the use of personal protection equipment such as N95 masks.

We had hypothesized that experience-- be it academic or clinical or personal would influence knowledge scores. While being a post-graduate was associated with score increase, experience in healthcare wasn't. Interestingly, those who had been assessed for TB but were negative scored higher, but those who had been assessed and treated for TB scored lower. There may be reverse causality here, whereby a lower knowledge individual may be at higher risk of TB. Although, the only way to confirm this would be to assess knowledge status prior to diagnosis. When examining attitudes, those who reported having been treated for TB in the past also expressed less worry regarding getting TB disease in the future and reported being too busy to practice infection control.

Overall knowledge was associated with better attitudes, but not with greater confidence in one's own knowledge. Only the latter was significantly influenced by whether one had had some infection control orientation. Interestingly, overall higher knowledge was associated with slightly lower odds of reporting safe practices, whereas being confident in knowledge of TB was associated with higher odds of reporting some safe practices. Given that this is self-reported practices, it is plausible that individuals with higher knowledge actually use more stringent criteria when evaluating their own practices. It is therefore essential to evaluate practices using objective measures.

One of the strongest associations with negative attitudes and risky infection control practices was reporting that one was too busy in daily activities to practice infection control. While individuals who saw 21 or more patients were more likely to report this attitude, those who had undergone some infection control orientation had significantly reduced odds of reporting this attitude. This highlights that even if orientation does not alter knowledge in the long-term, it may be associated with fostering positive norms and attitudes towards infection control among healthcare workers.

Examining attitudes with respect to masks, those who believed that masks should be worn were more likely to wear them. However, nearly three-quarter reported that they do not always wear a mask when caring for TB patients. The reasons for not wearing a mask were similar to finding from other studies. For example, a study in Uganda reported that 28.7% of nurses and interns didn't wear masks because it was not common practice (Kamulegeya et al., 2013), here 39.7% reported not wearing a mask because no one else in their department wears it. Past studies in India found that In examining mask use as a critical aspect of personal protection against pulmonary TB, the role of personal experiences, the presence of resources, and the role of peers, supervisors and institutions was highlighted Baveja and Dalal (2012).

Several background and institutional factors stood out as been significant in exerting influence over knowledge, attitudes and perceptions. These included having some orientation which was generally associated with factors conducive to better TBIC. We also found that supervisors play an important role in reinforcing or undermining TBIC by modifying attitudes through praise, and modifying practices through the example of their own practices, for example by wearing protective masks when working with TB patients. Finally past experience in health systems and larger patient loads were generally attributed to factors not conducive to good TBIC. For the former, it is plausible that experience in the health system may lead to installation of poor TBIC habits that carry on when postgraduates return to their studies. For the latter, high patient loads may create challenges in managing resources efficiently to ensure that one is protected.

Network analysis examined strong intermediaries between all background, knowledge, attitude and practice factors. These intermediaries may serve as both points of intervention, and to measure the effectiveness of various interventions. The attitudes of not being worried in case of TB disease, and willingness to be screened were central attitude mediators in the network. In practices, wearing an N95 masks was found to be a central network mediator. It is therefore feasible that interventions that can directly modify these nodes might have widespread influence in the network of co-variates.

These findings operate within a conceptual model of TB infection risk factors and TB infection control in healthcare settings (**Error! Reference source not found.**). This model expands the TBIC model proposed by the World Health Organization. Here, the proximal outcome is TB infection susceptibility of healthcare workers and trainees and the distal outcome latent TB infection and progression to disease. The proximal outcome is mediated at the level of the institution and the individual. Institutional factors such as environmental context ('engineering controls' such as cross ventilation) can directly affect susceptibility. Other institutional factors such as educational context mediate susceptibility through acting on the individual. As illustrated in the model, factors at each level interact with each other. Each point in this model represents a place where interventions could be implemented in order to reduce susceptibility to TB infection among trainees.

Such interventions may include workshops and training session which as described in our study may impact self-reported attitudes and practices. Bogam and Sagare (2011) conducted a workshop training post-graduates in RNTCP, and found improvements in knowledge scores. Giri and Phalke (2013) conducted a workshop for final year med students and looked at definitions of

MDR-TB. They found that before the workshop only 39% could correctly define MDR-TB while after this number had risen to 95.3%. Other interventions may not directly on improving knowledge, but changing hospital culture which may affect attitudes and practices.

Strengths

This survey addressed many dimensions of TB infection control, and allowed for investigation of how knowledge, attitudes and practices interact. In that respect it is a strong and concrete point for gauging individual-level barriers to infection control in this setting. There was a number of methodological strengths associated with this study. The instrument was tested and validated at three levels--first with local experts, then with a non-study population, then confirmed with a pilot test on a portion of the study population. The physical questionnaire was structured as a twelve-page booklet to both facilitate ease of use and also minimize flipping back and forth between questions and modifying answers according to past answers. Surveys were conducted anonymously, which likely increased participation and minimized response bias, as trainees did not perceive any potential personal repercussions for answering truthfully. The vast majority of surveys were conducted under standard testing conditions after classes or in group rooms. These conditioned allowed for accurate assessment of knowledge, which would have been very difficult to assess if trainees had the opportunity to conduct the surveys on their own or communicate with one another.

Findings from this study powerfully detected subtle relationships between various factors. They suggest that one must be extremely cautious to make any directional claims with respect to knowledge attitudes and practices. For example reporting the attitude that one had a low risk of acquiring TB from patients was associated with wearing N95 masks. An attitude that minimizes risk would be unlikely to reinforce safe practice. However, a safe practice may actually be creating and reinforcing a well-justified reassurance that risk has been minimized. Another example was those treated for TB scored lower on knowledge. It may very well be that poor knowledge placed these individuals at high risk for infection and progression to disease.

Limitations

A number of limitations were also associated with this study. Our sampling method was purposive sampling of specialties that are likely to encounter TB patients and not representative of all eligible interns and post-graduates. We sought to capture as much of the population as possible, however, some eligible individuals may not have been attending classes, or might have been posted in locations in the hospital with really busy schedules (e.g. ICU or emergency departments) or remote areas that we were unable to access. We had a participation of 61% across both campuses, with one campus more over-represented, post-graduates, and certain post-graduate specialties more over-represented. We do not have any information regarding individuals who could not or chose not to participate in the study. It is for instance possible that individuals who perceived themselves to be low knowledge opted to not participate. Therefore, selection bias is a possibility and limits the external validity of the study and our ability to generalize the results to the entire population of interns and post-graduates.

While our survey was validated via pre-testing, it was not formally assessed for reliability which may affect internal validity. In particular, while we attempted to be as clear as possible, terms such as 'training' retain a degree of ambiguity. The questionnaires were completed over the course of one and a half month; however, we did not anticipate exchange of responses as surveys were conducted in separate departments over two cities, as well the majority of questions focused on personal attitudes and practices. With respect to questions referring to self-reported practice there may be recall bias and social desirability bias, although we sought to minimize the latter by conducting the surveys anonymously.

Conclusions

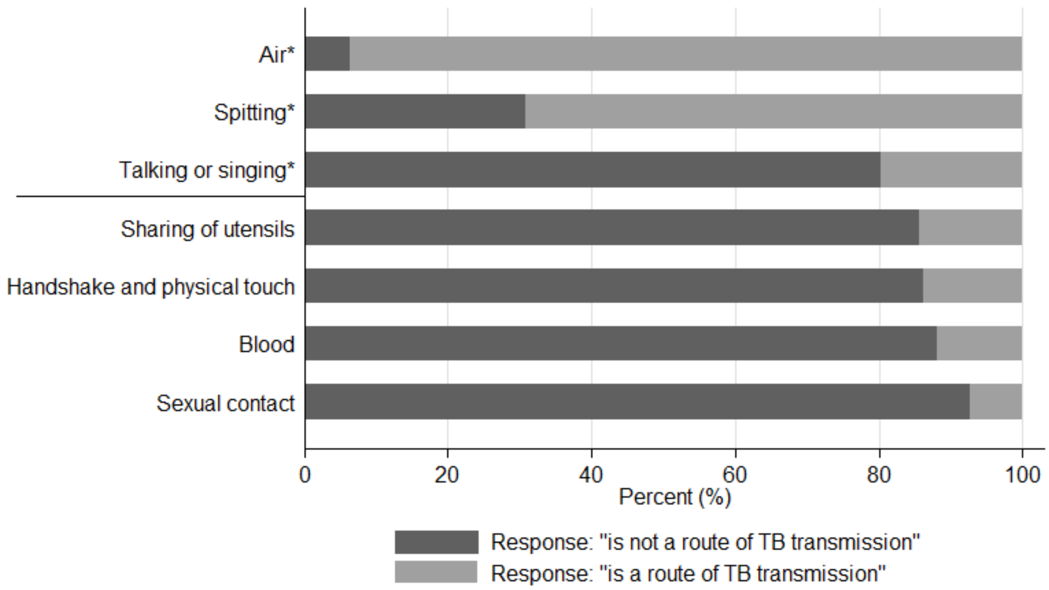
This study assessed knowledge, attitudes and practices towards infection control among healthcare trainees and early-career physicians. We found a number of significant multi-directional relationships that may regulate how TBIC is practiced by trainees. These relationships can target using interventions at the level of institutions, environments and individuals. The instrument developed as a part of this study is adaptable for use in other contexts for assessment of TBIC among healthcare trainees. Particularly, the instrument may be useful for pre-post studies focusing on interventions to improve TBIC attitudes and practices among trainees.

Acknowledgment

We thank the Manipal University and affiliate hospitals in Manipal and Mangalore for giving us permission to undertake this study, and departments across both institutions for providing us with access to trainees. The results of this study will be disseminated to institutions in Mangalore and Manipal to guide in development of future policy and interventions to reduce risk of TB infection among interns and post-graduates. This study was funded through the Dr TMA Pai Endowment Chair at Manipal University.

6.1.5 TABLES AND FIGURES

Figure 6.1 Participant knowledge regarding transmission routes which allow TB to spread from person to person



*Valid modes of pulmonary TB transmission: through airborne droplets, spitting, talking/singing

Figure 6.2 Knowledge scores for interns and post-graduates

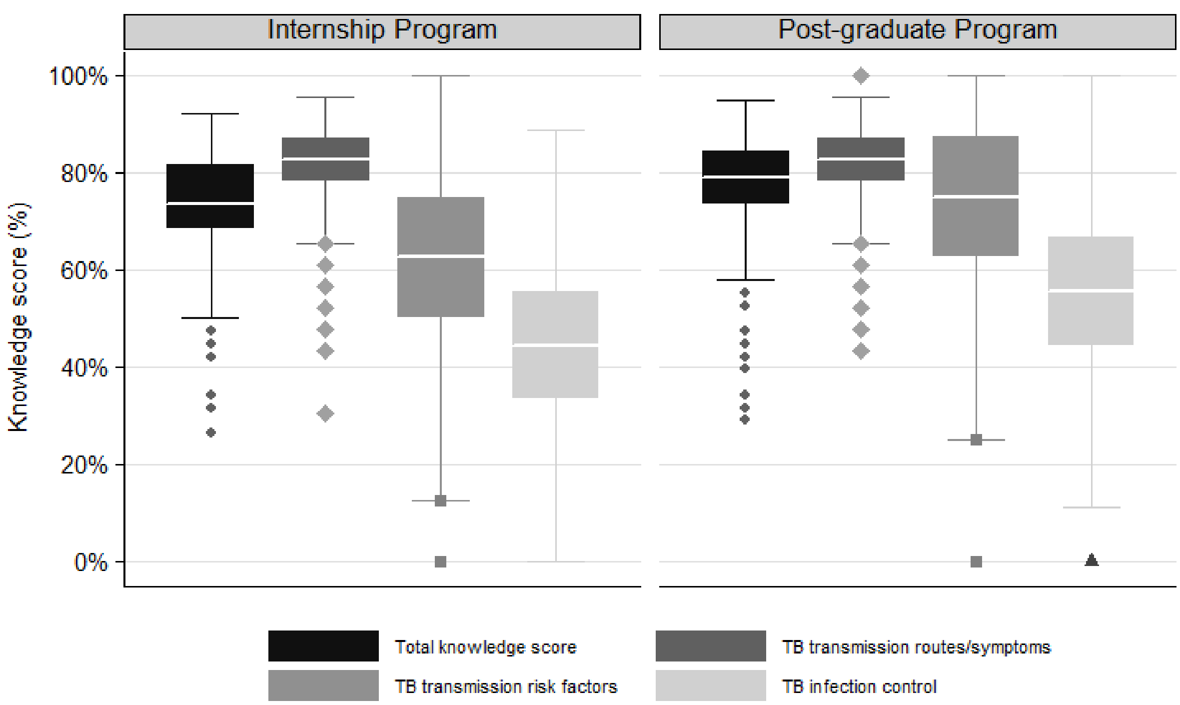


Figure 6.3 Attitudes regarding TB infection control reported by internship year and postgraduate medical trainees in Manipal and Mangalore, India

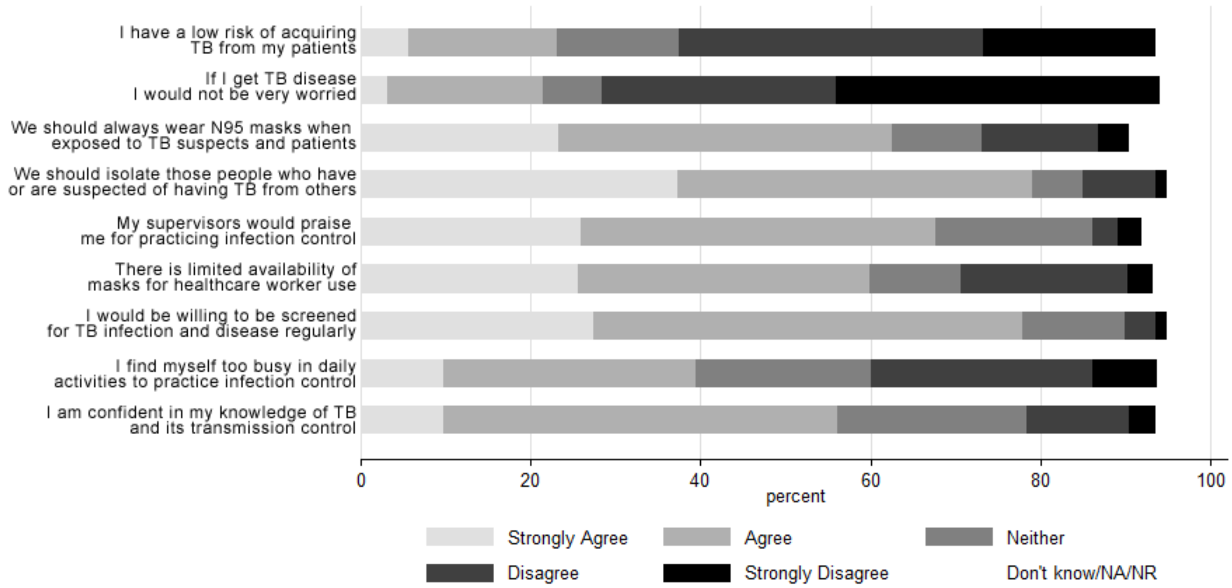


Figure 6.4 Self-reported TB infection control practices by internship year and postgraduate medical trainees in Manipal and Mangalore, India

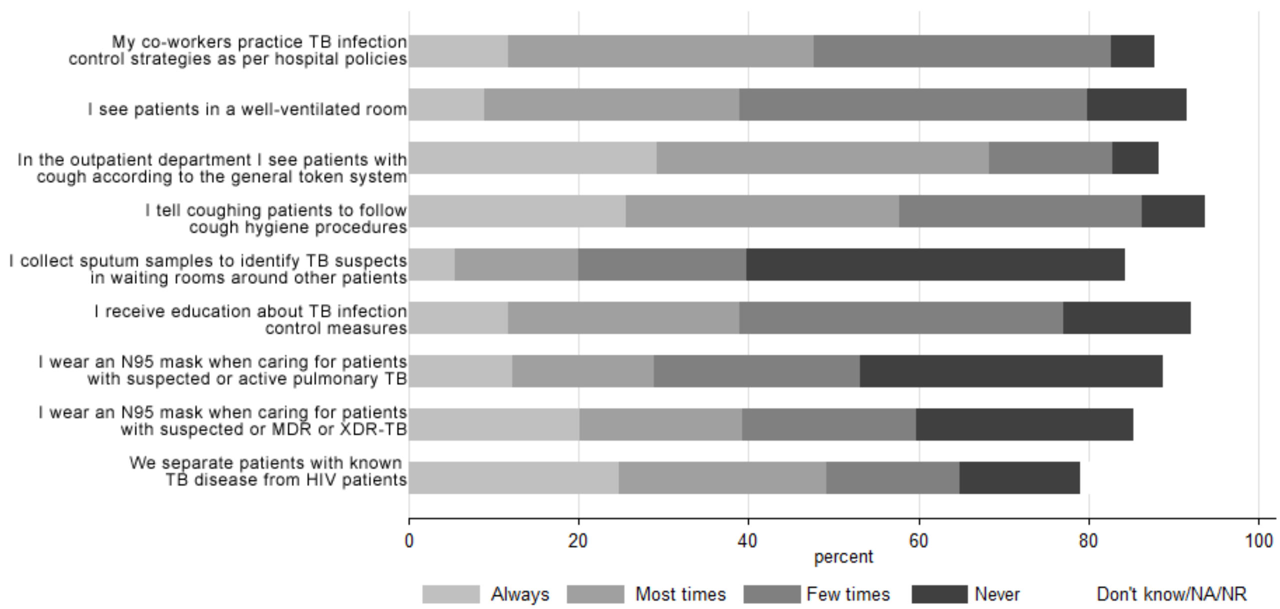


Figure 6.5 Strength of influence of various factors on the decision to not always wear an N95 mask when the -participant knows it is appropriate

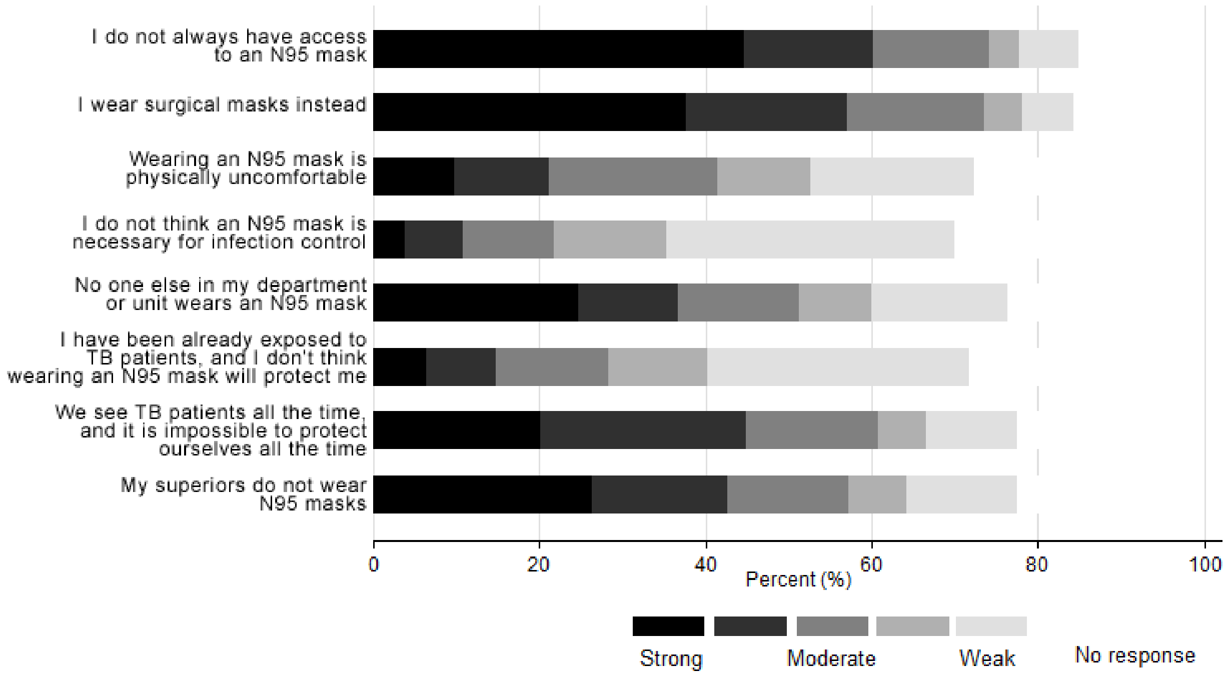
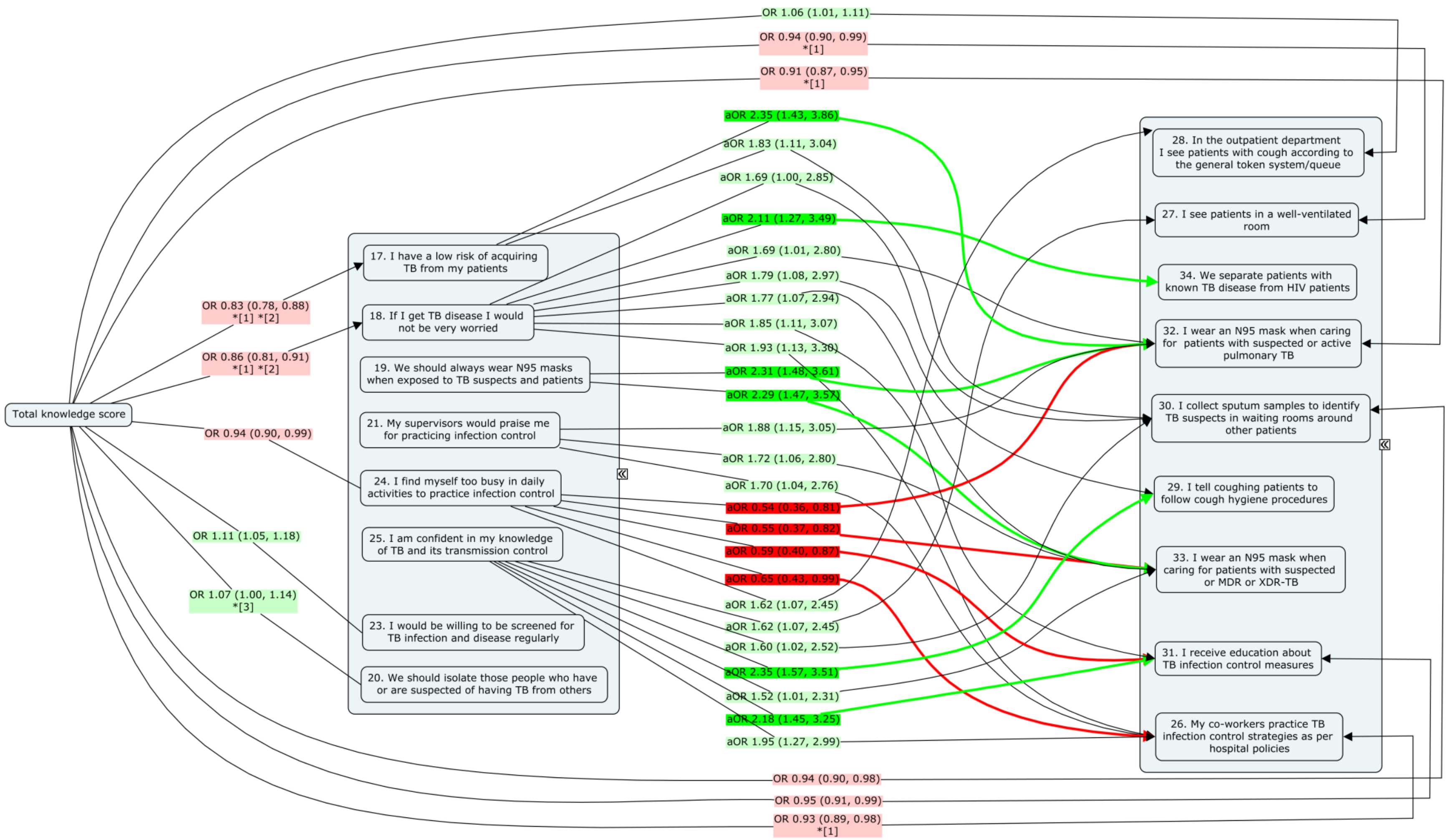


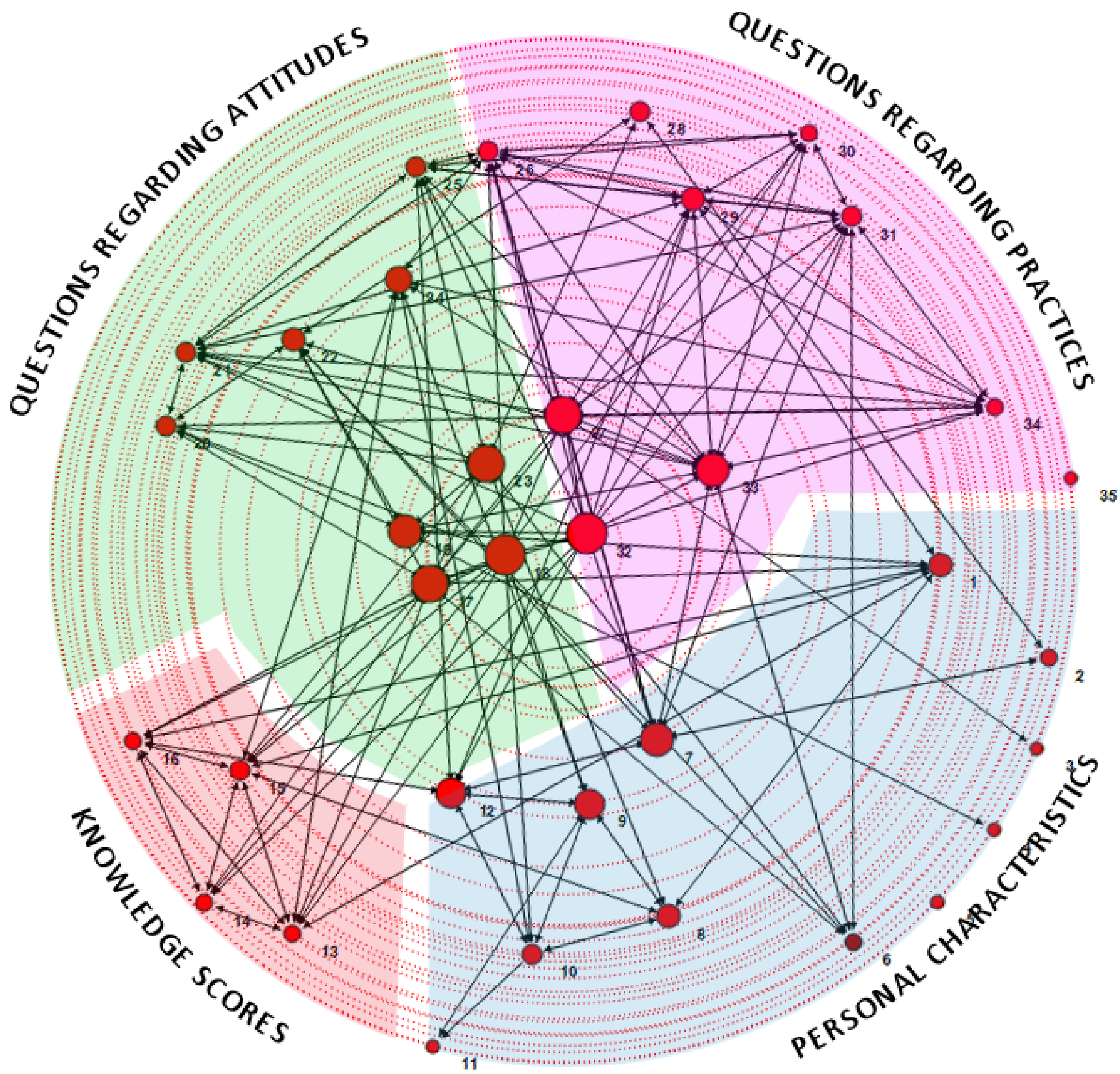
Figure 6.6 Association of infection control-practices with knowledge and attitudes



Note: OR reported unadjusted, aOR adjusted using a multivariable model containing all attitude variables as co-factors

*Multivariable analysis of three knowledge categories suggested prominent exertion influence of knowledge type [1] TB transmission routes and symptoms [2] TB transmission risk factors [3] TB infection control measures on overall OR

Figure 6.7 Between centrality network analysis of covariates in personal characteristics, levels of knowledge, attitudes, and self-reported practices



*Relationships between nodes represent spearman rank correlation with significance $p < 0.01$

Table 6.1 Participation rates for medical trainees surveyed in Kasturba Hospitals in Manipal and Mangalore, India (n=486)

	Total	Participants	(%)
Post-graduates (n=321) †			
Manipal campus	206	202	(98%)
Mangalore campus	187	116	(62%)
Program year 1	130	106	(82%)
Program year 2	129	100	(78%)
Program year 3	134	111	(83%)
Interns (n=165) †			
Manipal campus	210	95	(45%)
Mangalore campus	195	67	(34%)

† *No location information for 3 PGs and 3 interns*

Table 6.2 Demographic characteristics medical trainees surveyed in Kasturba Hospitals in Manipal and Mangalore, India (n=486)

Characteristics	**n**	**%**
Total	486	
Gender (N=451)		
Male	244	54.1
Female	207	45.9
Age (N=463)		
18-22 years	32	6.9
23-26 years	297	64.2
27 years or more	134	28.9
Institution campus (N=480)		
Manipal	297	61.6
Mangalore	183	38.4
Profession (N=486)		
Intern	165	34
Post-graduate	321	66.1
PG Specialty (N=316)		
MD Community medicine	9	2.8%
MD General medicine	90	28.0%
MD Microbiology	18	5.6%
MD Paediatrics	44	13.7%
MD Pulmonary medicine	4	1.2%
MS ENT	10	3.1%
MS General surgery	43	13.4%
MS Orthopedics	50	15.6%
MS Ob/Gyn and DGO	45	14.0%
Undeclared	8	2.5%

PG Program year (N=317)		
1st year	106	33.44
2nd year	100	31.55
3rd year	111	35.02
PG in healthcare before	93	29.3
Past history in healthcare (N=93)		
Less than 1 year	52	55.9
1-2 years inclusive	32	34.4
3-4 years	4	4.3
5 years or more	5	5.4

Table 6.3 Self-reported past exposure of medical trainees to TB infection and TB infection control in clinical and non-clinical settings

	n	%
Number of patients seen each week (n=466)		
5 or fewer	37	7.9
6-10	27	5.8
11-20	37	7.9
21-40	113	24.3
41 or more	252	54.1
Past training including TB (n=438)		
0.5 hour or less	94	21.5
0.5-1 hour	77	17.6
1-2 hours	30	6.9
2 hours or more	54	12.3
Did not receive information/training	131	29.9
Did not have an orientation	52	11.9
TB exposure (486 total)		
Tested with TST	111	22.84
Investigated for TB	97	19.9
Treated for TB	31	6.4
Family contact	60	12.4

Table 6.4 Participant knowledge in five domains of TB infection and infection control

Knowledge	Correct (%)	Incorrect (%)	Don't know/ NR
Risk-factors			
15.1. Those with HIV are more likely than those without HIV to develop active TB (T)	**91.2**	3.5	5.3
15.2. Those who have been vaccinated with BCG will not develop active TB (F)	**86.4**	6.0	7.6
15.3. A single infection with TB gives lifetime immunity (F)	**86.0**	6.0	8.0
Transmission			
15.4. Children are more likely than adults to be infectious (F)	32.3	**47.7**	20
15.5. Patients with pulmonary and extra pulmonary TB are equally infectious (F)	**76.5**	15.2	8.2
15.6. Patients with drug-resistant TB may be infectious even after receiving treatment (T)	**64.8**	23.7	11.5
15.7. Patients with smear-negative TB are not infectious (F)	**61.1**	27	11.9
15.8. TB cough droplets containing bacteria settle on the ground within minutes of expiration (T)	41.6	**29.4**	29
Environmental controls			
16.1. Airborne infection isolation rooms have positive pressure relative to other parts of the facility (F)	21.2	**41.8**	37
16.2. Mechanical air circulation systems (e.g. fans) are always more effective than natural ventilation (e.g. open windows) for infection control (F)	**58.0**	18.9	23
Administrative controls			
16.3. A patient suspected for TB must be isolated in a different room from other patients while waiting for diagnosis (T)	**72.0**	19.5	8.4
Personal protection			
16.4. Protective masks need to be worn by those involved in care of TB patients for the entire first two weeks of treatment (T)	8.6	**81.9**	9.5
16.5. Surgical masks worn by TB patients reduce TB droplet nuclei from being spread (T)	**79.8**	12.1	8
16.6. Surgical masks worn by healthcare workers filter out TB droplet nuclei and prevent infection (F)	32.9	**53.7**	13.4
16.7. Surgical masks should be given to TB patients only after diagnosis (F)	**75.5**	13	11.5
16.8. N95 masks work fine even if wet or with visible dirt (F)	38.7	**22.2**	39.1
16.9. N95 masks work fine even when not completely fitted (e.g. in heavily-bearded) (F)	**67.5**	10.3	22.2

Table 6.5 Association between personal characteristics and knowledge

	Total knowledge score*		Transmission risk factors		TB Infection control	
	b	95% CI	B	95% CI	b	95% CI
Training program						
Internship	Ref					
Post-graduate	**0.04**	**(0.01, 0.06)**	**0.07**	**(0.03, 0.11)**	**0.08**	**(0.04, 0.12)**
Postgraduate speciality						
MD Community med.	Ref					
MD General med.	0.05	(-0.03, 0.13)	0.00	(-0.13, 0.14)	**0.17**	**(0.04, 0.30)**
MD Microbiology	0.05	(-0.04, 0.14)	0.03	(-0.13, 0.19)	**0.19**	**(0.03, 0.34)**
MD Paediatrics	**-0.11**	**(-0.18, -0.03)**	**-0.17**	**(-0.31, -0.02)**	0.00	(-0.14, 0.14)
MD Pulmonary med.	0.10	(-0.03, 0.23)	0.05	(-0.19, 0.28)	**0.23**	**(0.00, 0.46)**
MS Orthopedics	0.04	(-0.04, 0.12)	0.00	(-0.14, 0.14)	**0.15**	**(0.02, 0.29)**
MS Ob/Gyn	0.05	(-0.03, 0.13)	-0.01	(-0.15, 0.14)	**0.19**	**(0.05, 0.33)**
HCW experience	-0.02	(-0.05, 0.01)	-0.01	(-0.06, 0.04)	**-0.05**	**(-0.10, 0.00)**
HCW experience length						
Less than 1 year	Ref					
1-2 years inclusive	**-0.09**	**(-0.15, -0.03)**	**-0.14**	**(-0.24, -0.04)**	**-0.11**	(-0.21, -0.02)
Clinical history						
Tuberculin skin tested	**-0.03**	**(-0.05, -0.01)**	**-0.05**	**(-0.10, -0.01)**	**-0.06**	**(-0.10, -0.01)**
Investigated for TB	0.00	(-0.02, 0.03)	-0.03	(-0.07, 0.02)	0.01	(-0.03, 0.06)
Treated for TB	**-0.07**	**(-0.11, -0.03)**	-0.05	(-0.12, 0.02)	**-0.08**	**(-0.15, -0.01)**
**Investigated/TB-	**0.03**	**(0.00, 0.06)**				
**Investigated/TB+	**-0.04**	**(-0.08, 0.00)**				
Family with TB	-0.03	(-0.06, 0.00)	-0.04	(-0.09, 0.02)	-0.01	(-0.07, 0.04)

Note: only demographics significantly associated with outcomes displayed in table
*Total knowledge score includes knowledge of modes of transmission, symptoms, transmission risk factors and TB infection control
**Adjusted estimate from multivariable model (including training program, and four clinical history variables) with interaction term for investigation for TB and treatment for TB

Table 6.6 Dichotomized responses to questions on attitudes toward TB infection control

Question item regarding attitudes	Agree* (%)	Disagree* (%)	Don't know/NR
17. I have a low risk of acquiring TB from my patients	23.0	**70.6**	6.4
18. If I get TB disease I would not be very worried	21.4	**72.6**	6.0
19. We should always wear N95 masks when exposed to TB suspects and patients	**62.6**	28.0	9.5
20. We should isolate those people who have or are suspected of having TB from others	**79.0**	15.8	5.1
21. My supervisors would praise me for practicing infection control	**67.7**	24.3	8.0
22. There is limited availability of masks for healthcare worker use	**59.9**	33.3	6.8
23. I would be willing to be screened for TB infection and disease regularly	**78.0**	16.9	5.1
24. I find myself too busy in daily activities to practice infection control	39.5	**54.3**	6.2
25. I am confident in my knowledge of TB and its transmission control	**56.2**	37.4	6.4

*Note: responses on a 5-point Likert scale have been dichotomized (agree=strongly agree, agree/ disagree= neutral, disagree, strongly disagree)

Table 6.7 Correlation matrix for attitude items

	Q17	Q18	Q19	Q20	Q21	Q22	Q23
Q18	OR 7.65 (4.68, 12.51)						
Q19							
Q20	OR 0.57 (0.33, 0.98)		OR 3.11 (1.84, 5.25)				
Q21		OR 2.53 (1.37, 4.65)		OR 2.43 (1.44, 4.09)			
Q22			OR 2.60 (1.70, 3.97)				
Q23			OR 2.07 (1.24, 3.47)	OR 2.07 (1.16, 3.67)	OR 3.09 (1.84, 5.18)		
Q24	OR 1.62 (1.05, 2.51)	OR 1.88 (1.20, 2.95)				OR 2.29 (1.51, 3.45)	
Q25	OR 1.59 (1.00, 2.52)	OR 2.34 (1.43, 3.84)			OR 2.55 (1.65, 3.95)		OR 1.82 (1.11, 2.96)

Note: Only significant relationships reported. 95% CI reported below odds ratios (OR). See table 6.6 for list of items associated with codes.

Table 6.8 Associations between personal characteristics and attitudes

Outcome attitude	Determinant	aOR*	95% CI	p	*Reference*
I have a low risk of acquiring TB from my patients	Post-graduate	0.40	(0.23, 0.70)	0.00	*Intern*
	MD General medicine	0.06	(0.01, 0.30)	0.00	*MD Comm Med*
	MD Microbiology	0.10	(0.01, 0.85)	0.03	*MD Comm Med*
If I get TB disease I would not be very worried	Some infection control orientation	2.12	(1.27, 3.56)	0.00	*No infection control orientation*
	Treated for TB	2.91	(1.18, 7.17)	0.02	
We should always wear N95 masks when exposed to TB suspects and patients	PGY 2	0.46	(0.23, 0.92)	0.03	*PGY 1*
	PGY 3	0.41	(0.20, 0.83)	0.01	*PGY 1*
	MS ENT	0.05	(0.00, 0.64)	0.02	*MD Comm Med*
We should isolate those people who have or are suspected of having TB from others	MD General medicine	8.85	(1.80, 43.57)	0.01	*MD Comm Med*
	MD Microbiology	12.39	(1.04, 148.03)	0.05	*MD Comm Med*
	MS Obstetrics and gynecology	12.54	(2.02, 77.90)	0.01	*MD Comm Med*
	MS Orthopedics	7.23	(1.35, 38.78)	0.02	*MD Comm Med*
My supervisors would praise me for practicing infection control	Immediate family with TB	2.36	(1.02, 5.45)	0.05	
	MD Microbiology	12.04	(1.01, 143.47)	0.05	*MD Comm Med*
	MS General surgery	13.38	(2.07, 86.31)	0.01	*MD Comm Med*
	MS Ob/Gyn	5.42	(1.03, 28.66)	0.05	*MD Comm Med*
	Age of 23 to 26 years	2.39	(1.05, 5.47)	0.04	*Age of 18 to 22 years*
	Age of 27 years or greater	3.14	(1.28, 7.70)	0.01	*Age of 18 to 22 years*
There is limited availability of masks for healthcare worker use	21 or more patients	2.71	(1.61, 4.56)	0.00	*<21 patients seen per week*
	Some infection control orientation	0.44	(0.28, 0.68)	0.00	*No infection control orientation*
I would be willing to be screened for TB infection and disease regularly	21 or more patients seen per week	2.39	(1.33, 4.31)	0.00	*<21 patients seen per week*
	Female	2.16	(1.19, 3.92)	0.01	*Male*
	Post-graduate	1.93	(1.04, 3.61)	0.04	*Intern*
I find myself too busy in daily activities to practice infection control	Immediate family with TB	2.08	(1.13, 3.83)	0.02	
	Treated for TB	2.48	(1.04, 5.92)	0.04	
I am confident in my knowledge of TB and its transmission control	Some infection control orientation	1.70	(1.13, 2.55)	0.01	*No infection control orientation*

*All OR adjusted for age and infection control orientation
Note: Only significant relationships reported.

Table 6.9 Dichotomized responses to questions regarding TB infection control practices

Question item regarding practices	Always/ most times* (%)	Never/ few times* (%)	Don't know/ NR
26. My co-workers practice TB infection control strategies as per hospital policies	**47.7**	40.1	11.7
27. I see patients in a well-ventilated room	38.9	**52.7**	8.9
28. In the outpatient department I see patients with cough according to the general token system/queue	**68.3**	20.0	29.2
29. I tell coughing patients to follow cough hygiene procedures	**57.8**	36.0	25.5
30. I collect sputum samples to identify TB suspects in waiting rooms around other patients	20.0	**64.4**	5.4
31. I receive education about TB infection control measures	38.9	**53.3**	11.7
32. I wear an N95 mask when caring for patients with suspected or active pulmonary TB	28.8	**60.1**	12.1
33. I wear an N95 mask when caring for patients with suspected or MDR or XDR-TB	39.3	**46.1**	20.2
34. We separate patients with known TB disease from HIV patients	**49.2**	29.8	24.7

*Note: responses on a 4-point Likert scale have been dichotomized

Table 6.10 Association between personal characteristics and self-reported practices

Outcome attitude	Determinant	aOR*	95% CI	p	*Reference*
My co-workers practice TB infection control strategies as per hospital policies	MD Paediatrics	5.73	(1.14, 28.87)	0.03	*MD Comm medicine*
	Post-graduate	1.81	(1.15, 2.83)	0.01	*Intern*
	Some infection control orientation	1.84	(1.25, 2.73)	0.00	*No infection control orientation*
I see patients in a well-ventilated room	PGY 2	0.50	(0.28, 0.91)	0.02	*PGY 1*
	PGY 3	0.38	(0.21, 0.70)	0.00	*PGY 1*
	3-4 years inclusive in HCW	8.41	(1.02, 69.12)	0.05	*Less than 1 year in HCW*
	MD Pulmonary medicine	0.09	(0.01, 0.84)	0.03	*MD Comm medicine*
	MS ENT	0.13	(0.02, 0.87)	0.04	*MD Comm medicine*
	Post-graduate	1.75	(1.12, 2.73)	0.01	*Intern*
	Some infection control orientation	1.76	(1.21, 2.58)	0.00	*No infection control orientation*
In the outpatient department I see patients with cough according to the general token system/queue	3rd year or more	2.04	(1.09, 3.84)	0.03	
	MS Obstetrics and gynecology	0.15	(0.02, 0.96)	0.04	*MD Comm medicine*
	Age of 23 to 26 years	0.43	(0.20, 0.94)	0.03	*Age of 18 to 22 years*
	Age of 27 years or greater	0.37	(0.16, 0.85)	0.02	*Age of 18 to 22 years*
I tell coughing patients	HCW experience	1.79	(1.05, 3.05)	0.03	*No HCW experience*

to follow cough hygiene procedures	Post-graduate	3.06	(1.97, 4.74)	0.00	*Intern*
	Some infection control orientation	1.48	(1.03, 2.13)	0.03	*No infection control orientation*
I collect sputum samples to identify TB suspects in waiting rooms around other patients	Investigated for TB	0.56	(0.33, 0.96)	0.04	
	HCW experience	1.94	(1.07, 3.50)	0.03	*No HCW experience*
	Tuberculin skin tested	0.56	(0.34, 0.94)	0.03	
I receive education about TB infection control measures	Some infection control orientation	3.89	(2.62, 5.79)	0.00	*No infection control orientation*
I wear an N95 mask when caring for patients with suspected or active pulmonary TB	Some infection control orientation	2.02	(1.38, 2.97)	0.00	*No infection control orientation*
I wear an N95 mask when caring for patients with suspected or MDR or XDR-TB	Some infection control orientation	1.88	(1.28, 2.75)	0.00	*No infection control orientation*
We separate patients with known TB disease from HIV patients – No associations					

*All OR adjusted for age and infection control orientation

Table 6.11 Dichotomized strength of influence on the decision to not wear an N95 mask, dichotomized by Strong to somewhat strong vs. Moderate to weak

Potential factors influencing decision to wear an N95 mask	Strong	Neutral, weak	No response
I do not always have access to an N95 mask	**60.3**	24.7	15.0
I wear surgical masks instead	**57.0**	27.4	15.6
Wearing an N95 mask is physically uncomfortable	21.2	**51.2**	27.6
I do not think an N95 mask is necessary for infection control	10.7	**59.3**	30.0
No one else in my department or unit wears an N95 mask	36.6	39.7	23.7
I have been already exposed to TB patients, and I don't think wearing an N95 mask will protect me	14.8	**57.0**	28.2
We see TB patients all the time, and it is impossible to protect ourselves all the time	**44.9**	32.7	22.4
My superiors do not wear N95 masks	**42.6**	35.0	22.4

Table 6.12 Trainees' ranking of infection control measures with best impact on work setting

Infection control interventions in hospital settings	Rank 1 %	Rank 2 %	Rank 3 %	Not ranked
More education of patients (through posters etc.)	**33.5**	9.9	7.4	49.2
More education and training of medical/support staff	**26.5**	13.8	10.3	49.4
A widely-distributed TB infection control plan	**27.8**	7.0	7.0	58.2
More appropriate management of TB suspects	19.8	9.7	12.1	58.4
Greater monitoring and infection quality control	19.3	7.2	11.3	62.1
Greater monitoring and infection quality control	19.3	7.2	11.3	62.1
More available protective devices (masks, etc.)	19.8	7.4	11.3	61.5
Administrative support for infection control procedures	17.1	11.5	7.2	64.2
More environmental controls (ventilation, irradiation, etc.)	12.6	5.3	7.8	74.3

7 Discussion and Recommendations

7.1 Summary

The objective of this thesis was to investigate latent TB infection among healthcare trainees, and knowledge, attitudes and practices with respect to TB infection control. To assess prevalence our study enrolled medical and nursing students, in whom we could far more reliably assess clinical exposures than the highly heterogeneous intern and post-graduate populations. To assess knowledge, attitudes and practices regarding TB infection control in clinical settings we enrolled interns and post-graduates in medicine who are fully embedded in hospital settings. Compared to medical and nursing students, their responses gave us more insight regarding practical strengths and barriers in TBIC. We were able to achieve the following:

1. We established the baseline prevalence of latent LTBI in undergraduate medical and nursing students with various degrees of exposure to clinical settings in Kasturba Hospital, Manipal University, India. We found that the prevalence of LTBI infection was variable between medical and nursing students, with an overall 5.1% (95% CI 3.1-7.2). However, being posted in pulmonary medicine ward and pulmonary out-patient departments was associated with both an increase in TST induration size (b=1.42mm, 95% CI 0.66, 2.19) and increased odds of TST positivity (aOR 3.11, 95% CI 1.31, 7.36).
2. We established the baseline knowledge, attitudes and practices towards TB infection control among internship and post-graduate medical students working in clinical settings in Manipal and Managlore, India. We identified generally good knowledge regarding routes of transmission, but poor knowledge regarding TB infection control. Factors such as orientation training and supervisor engagement were associated with attitudes and practices conducive to TBIC. On the other hand poor knowledge and past healthcare experience were associated with attitudes and practices not conducive to TBIC. Overall we identified a complex web of covariates that influence self-reported trainee TBIC behaviour.

Our findings show a somewhat lower prevalence of LTBI than the prevalence estimated by R. Joshi et al. (2006) for students in low to middle-income countries of 12%. In the Indian context, this is also much lower than the prevalence measured by D. J. Christopher et al. (2011) in Christian Medical College (CMC) and hospital in Vellore, Tamil Nadu where a prevalence of 47.8% and ARTI of 7.8% was found among nursing college trainees. The implications of these findings are two-fold: First, TB transmission may simply be less of a problem in Manipal than other places. For example, the hospital in Vellore, India where the D. J. Christopher et al. (2011) conducted their study is larger than Kasturba Hospital in Manipal, and receives patients from all over the Tamil Nadu state. It's possible that by virtue of their location, healthcare workers in Manipal are simply exposed to less volume of TB patients than they would be elsewhere.

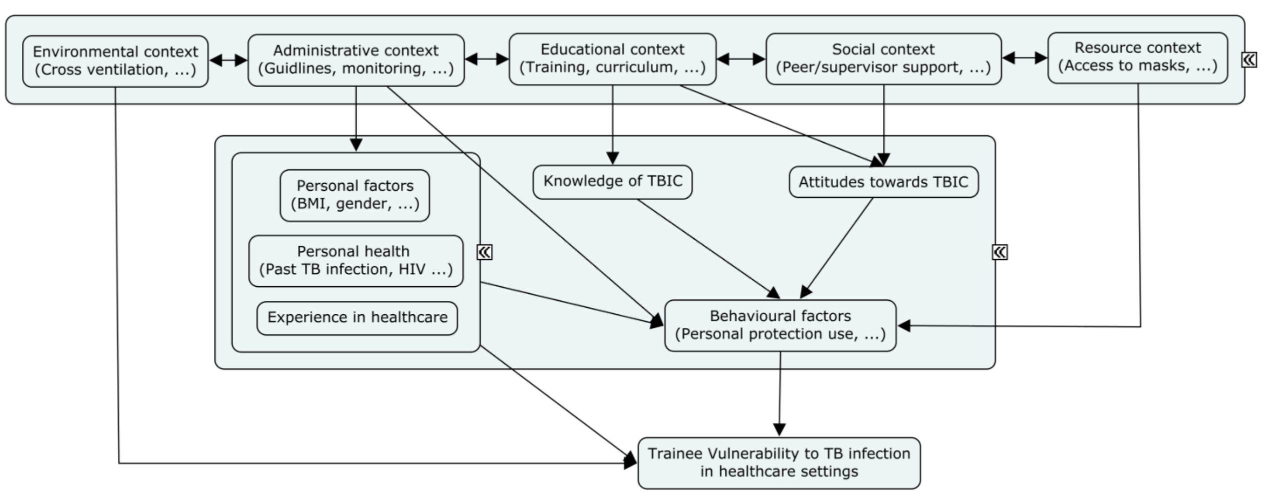
Second, the estimation of the prevalence and risk may be underestimated due to the characteristics of the study population and design limitations. The students in this setting generally have a high socio-economic status, which may lead to lower baseline exposures to TB disease prior to enrollment. The population we examined were young trainees before and after two years of exposure to clinical settings. The practical exposure to clinical settings may actually be highly limited for students since they are largely observing and not actively engaging in procedures, compared to doctors, nurses and allied health professionals. Another factor that must be considered is that we actually observed higher LTBI prevalence among senior medical undergraduate trainees versus junior pre-clinical trainees. However, the confidence intervals overlapped and the difference in proportions could not be considered significant. With greater participation rates, it is possible that we would have greater power to detect any differences.

For these reasons, the implications of this study must be considered carefully. While prevalence is low, we cannot confidently say that TB transmission is not a concern in Manipal. Our findings showed that students who had been in pulmonary clinics and out-patient departments were more likely to have larger TST reaction sizes, and to test positive for LTBI. This suggests that the hospital environment presents risks to students. The impact of this may not be entirely detectable or pronounced as it would be in places with larger volumes of patients, but with the rise of DR-TB, place-based gaps are points of vulnerability that cannot be overlooked or underestimated.

These gaps are made evident in our second study investigating TB infection control as understood and practiced by early-career clinicians. Here we found serious points of vulnerability that could render healthcare trainees and practitioners susceptible to TB infection. These findings operate within a conceptual model of TB infection risk factors and TB infection control in healthcare settings (Figure 7.1). This model expands the TBIC model proposed by the World Health Organization (World Health Organization, 2009). Here, the proximal outcome is TB infection susceptibility of healthcare workers and trainees and the distal outcome latent TB infection and progression to disease. The proximal outcome is mediated at the level of the institution and the individual.

Institutional factors such as environmental context (e.g. 'engineering controls' such as cross ventilation) can directly affect susceptibility. Other institutional factors such as educational context mediate susceptibility through acting on the individual. As illustrated in the model, factors at each level interact with each other. Even in an environment where the patient load and potential environmental exposures is low, issues such as poor education, improper administrative workflow, and lack of access to resources can exacerbate the effect of small exposures. The implications of this study really emphasize how each of these elements may be creating opportunities and imposing constraints on how healthcare trainees and workers practice TBIC.

Figure 7.1 A model for TB infection control gaps in healthcare settings and potential points for intervention



7.2 Strengths and limitations

This work contributes to literature focusing on TB infection and barriers to infection control among healthcare trainees. Each manuscript presented as part of this study had strengths and limitations associated with it.

Our prevalence study had a large number of participants. However, we had an overall participation rate of 64.1%, excluding a program that did not choose to participate this rate would be 69.2%. We also used a comprehensive questionnaire combined with administrative data to identify exposures and risk factors for TB. While exposure in clinical settings for medical students could be confirmed in part using administrative records, for direct clinical exposures and community exposures we relied on student recall and thus anticipate some recall bias.

Our KAP study similarly had a large number of participants. However, overall we had a participation rate of 61% of all eligible participants across both campuses. Relative to the total eligible participant population, one campus was over-represented, and post-graduates and certain post-graduate specialties were also over-represented. The instrument developed was tested and validated at three levels: first with local experts, then with a non-study population, then confirmed with a pilot test on a portion of the study population. The physical questionnaire was structured as a twelve-page booklet to both facilitate ease of use and also minimize flipping back and forth between questions and modifying answers according to past answers. Surveys were conducted anonymously, which likely increased participation and minimized response bias, as trainees did not perceive any potential personal repercussions for answering truthfully.

7.3 Generalizability and implications

Our study on prevalence study did not show a high prevalence of TB which was inconsistent with past studies in India. This finding may be due to the unique context of the study, due to limited exposure of the population, or other study limitations. For this reason, the results of study have limited generalizability beyond their immediate context. However, consistent with past studies we did find that certain hospital locations may put HCWs and trainees at risk. While this link cannot be established strongly without a longitudinal study, review of literature suggests that partial infection control measures may leave healthcare workers vulnerable particularly in areas where many infectious individuals are present, and should be addressed.

Our study on knowledge, attitudes and practices may have findings that are more generalizable to the broader population of medical trainees and early career physicians. This is in part because post-graduates enrolled in the study represent a relatively diverse population coming from across India. However, its generalizability is also limited by the fact that the study took place in two very similar private institutions that are well-resourced. Nevertheless the findings from the study highlight new ways that future studies can be conducted and analyzed to examine knowledge, attitudes and practice surveys, moving beyond descriptive analysis to exploring relationships and mediators that could be viable as points of intervention.

This project was conducted in association with the creation of a new international collaboration center between Manipal University, India and McGill University, Canada. In that respect, the project contributed to the building of links with investigators across the two countries, and facilitated a collaborative translational approach to conducting research that will benefit both communities.

7.4 Future directions for research

There is currently a dearth of knowledge regarding the prevalence of TB infection among trainees in India and TBIC among trainees. While these studies contribute to building knowledge, given the limitations identified above, the results are not necessarily generalizable. Longitudinal studies in more diverse institutions will provide more meaningful numerators and help quantifying the extent of the issue and identifying gaps that can be targeted. Given the place-based nature of nosocomial infections, the use of new spatial analysis tools to identify hotspots of infection in hospitals based on environmental and behavioral risk factors will be interesting to explore in future studies.

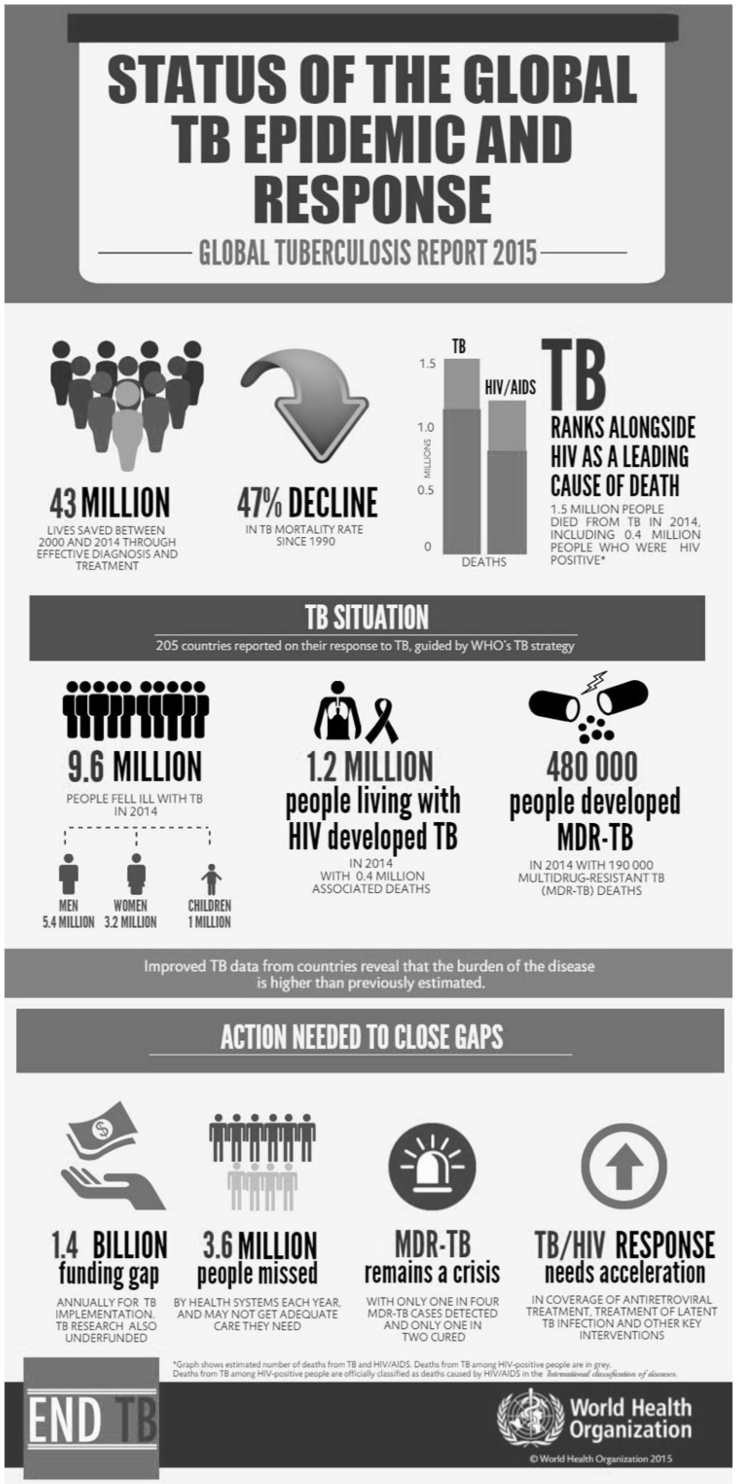
Both studies relied on self-reported exposures and self-reported practice. Future studies, especially longitudinal studies, should consider integrating audits and ethnographical approaches in order to objectively ‘see’ student interacts in healthcare settings, and how they interact with their environment. Such objective measures would be a powerful way of identifying ‘hidden’ exposures, assessing the accuracy of self-reported practices, and measuring true modifications to behaviour as a consequence of any interventions intended to modify behavior. Current knowledge, attitudes and practices literature on TB infection control has major shortcomings including a lack of strong tools. We hope that the survey instrument developed as a part of this study can be adopted by future studies for baseline measures or to examine effectiveness of TBIC interventions.

7.5 Conclusions

Tuberculosis is a public health crisis in India and across the world, and those working in the frontlines of healthcare are vulnerable to the infection. While the ‘End TB’ mission seeks to effectively eliminate TB in the next 20 years, the rise of multidrug resistance portents great difficulties in the road ahead. Teaching hospitals are an environment where with the right tools in place, infections can be monitored and new infections prevented through effective TB infection control. As well they are uniquely positioned to instill good TBIC practices in future practitioners. These studies have contributed to broader efforts worldwide to better understand nosocomial TB infection, and work towards reducing risk to both future patients seeking care and the future generation of healthcare workers.

8 Appendices

Appendix 1 Summary of status of the global TB epidemic and response
Source: Global Tuberculosis Report 2015 (World Health Organization, 2015b)



Appendix 2 Selection process for literature on knowledge, attitudes and perceptions

Search strategy
A systematic search strategy was used between 1st February 2015 to 1st March 2016 to identify pertinent articles. Databases including Embase (1996-2016), Global Health (1973-2016), Medline (1946-2016), and Allied and Complementary Medicine (1985-2016) were searched. Keywords in combination with boolean operators were used focusing on tuberculosis, health personnel and KAP surveys (Appendix - Table 1).

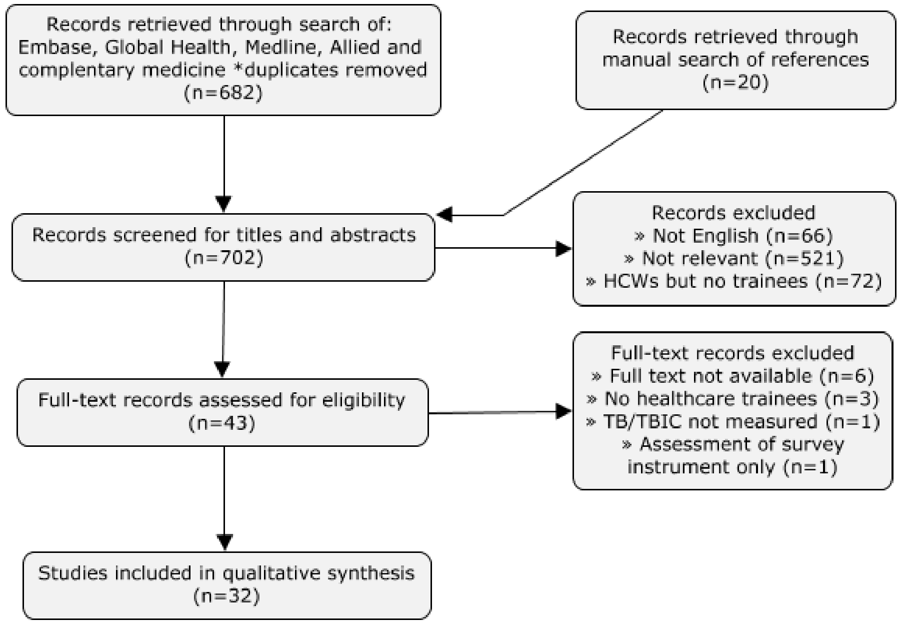
Selection strategy
Following deduplication 616 articles were identified. Articles titles were examined to identify all articles pertaining to healthcare workers and trainings. Excluding criteria included articles not in Enlish, articles not relevant to the subject of interest, articles pretaining to specific practices such as diagnostic and referral patterns as well as specific contexts such as prisons (n=90). Key manuscripts identified were read in full, and another 22 pertinent articles were identified and retrieved through the manual search of bibiliographies. Abstracts were then examined to only select studies that focused on or explicitly included healthcare trainees including undergraduate students, clerkship trainees, and postgraduate resident doctors (Appendix - Figure 1).

Analysis process
Studies identified (n=38) were divided by context— high burden versus low burden countries. Information about each study including methodology, results and conclusions was then abstracted. The studies included in the study will be assessed qualitatively and narratively synthesized. This analysis procedure was chosen as while studies report numeric results often in the form of population frequencies, the questionnaires used for the studies are not standardized. However, qualitative synthesis of the studies will allow for the examination of common emerging themes drawn out by study authors as part of their analysis.

Appendix - Table 1 Keywords and boolean operators used in combination for Medline database

Keywords for target disease	Latent Tuberculosis/ or Extensively Drug-Resistant Tuberculosis/ or Tuberculosis/ or Mycobacterium tuberculosis/ or Tuberculosis, Multidrug-Resistant/ or tuberculosis.m_titl.
Keywords for target population	Health Personnel/ or Allied Health personnel/ or Caregivers/ or Physicians/ or Medical Staff, Hospital/ or Nurses/ or Nurses' Aides/ or Nurse Practitioners/ or Students, Medical/ or Students, Nursing/ or Personnel, Hospital/ or ((healthcare or health) and (worker or student or trainee or professional)).m_titl.
Keywords for target measures	Health Knowledge, Attitudes, Practice/ or Knowledge/ or Attitude/ or Awareness/ or Perception/ or Practice/ or Intention/ or Behavior/ or Risk Assessment/ or (knowledge or attitude* or practice*).m_titl.

Appendix - Figure 1 Selection strategy used for studies included in narrative review



Appendix 3 Manuscript 1 sample data collection form for medical students

STUDY ID# |____|____|____|____| **Date ____/____/2015**

TUBERCULOSIS STUDY QUESTIONNAIRE FOR MEDICAL TRAINEES

Thank you for agreeing to participate in this research study. The purpose of this study is to examine tuberculosis prevalence and exposures in health care trainees at Kasturba Hospital. This interview will take about 20 minutes. We appreciate your cooperation.

<u>Instructions to Student</u>

1. Write clearly in **black** or **blue** pen.
2. Complete as much of the form as you can prior to the interview.
3. If your answer is **"no"** or **"unknown"** or **"don't want to answer",** please make sure you tick this box.
4. If you have any questions you cannot complete, **bring any relevant information** to the interview, and the interviewer can assist.

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4. If you have any questions you cannot complete, **bring any relevant information** to the interview, and the interviewer can assist.

Part 1: Professional profile

1. Which semester of the MBBS program are you enrolled in? ☐3rd semester ☐ 7th semester

2. When did you first enroll in KMC? ☐☐/☐☐/☐☐ (YY/MM/DD)

3. Have you worked or trained in the healthcare sector before? ☐ yes ☐ no ***if no go to PART 2**

4. What is **the total length of time** you have been a health care worker? ☐☐ years ☐☐ months

5. If you have worked in healthcare at other places, please give details:

   A. **Employer/organization**:_________________________________ Job title: _______________________

   Length of Employment ☐☐ years ☐☐ months

   What percentage of your time did have potential contact with sputum positive, pulmonary TB patients (within conversational distance)_________________%.

   B. **Employer/organization**:_________________________________ Job title: _______________________

   Length of Employment ☐☐ years ☐☐ months

   What percentage of your time did have potential contact with sputum positive, pulmonary TB patients (within conversational distance)_________________%.

   C. **Employer/organization**:__________________________________ Job title: ______________________

   Length of Employment ☐☐ ss ☐☐ months

   What percentage of your time did have potential contact with sputum positive, pulmonary TB patients (within conversational distance)_________________%.

Part 2: Potential for TB exposure in hospital

Since you began your current medical program:

1. Have you been posted in the following hospital wards:

Medicine	☐ no	☐ yes	If yes, the total duration _________ days
Surgery	☐ no	☐ yes	If yes, the total duration _________ days
OBG	☐ no	☐ yes	If yes, the total duration _________ days
Pediatrics	☐ no	☐ yes	If yes, the total duration _________ days
Pulmonary Medicine	☐ no	☐ yes	If yes, the total duration _________ days
Others? _______________________			total duration _________ days

2. Have you ever been posted in the adult isolation ward?

☐ no ☐ yes If yes, the total duration _____ days

3. Have you ever been posted in Intensive Care?

☐ no ☐ yes If yes, the total duration _________days

4. Have you ever been posted in the Emergency Department?

☐ no ☐ yes If yes, the total duration _________days

5. Have you ever been posted to Pulmonary Out Patient Department (OPD) or Medicine OPD?

☐ no ☐ yes If yes, the total duration _________days

6. Have you ever been posted to a DOTS clinic?

☐ no ☐ yes If yes, the location _________________

If yes, the total duration _________days

7. Have you ever had direct contact (within a conversational distance) with a patient with sputum-smear positive, pulmonary tuberculosis?

☐ no ☐ yes ☐ yes, but don't know if sputum positive ☐ don't know

If yes, the total duration _____________________________

8. Is there any other information you wish to share regarding your exposure or potential exposure to TB in clinical settings during your studies?

☐ no ☐ yes If yes, please detail: ____

____

____

____

Part 3: Potential for TB exposure in the community

1. **Outside of the hospital environment**,(eg. at home, high school), have you ever:

A. Stayed together in a room with someone with pulmonary TB? ☐ yes ☐ no ☐ unknown
B. Lived in a household or family with someone with pulmonary TB? ☐ yes ☐ no ☐ unknown
C. Attended a class (school/college) with someone with pulmonary TB? ☐ yes ☐ no ☐ unknown
D. Socialized as friends/acquaintances with someone with pulmonary TB ☐ yes ☐ no ☐ unknown

2. If the answer is YES to anyone of the above, provide more details:

	1A	1B	1C	1D
Was the person sputum smear positive? **Yes/no/don't know**				
When did you spend time with this person? **(year 20XX)**				
How much time did you spend with this person? **(days)**				
How often did you spend time with this person? **(hours per week)**				

If more than one person in any category please note here: ________________________________

3. **Within the hospital community/hostel**, have you ever:

A. Stayed together in a room with someone with pulmonary TB? ☐ yes ☐ no ☐ unknown
B. Lived on the same floor as with someone with pulmonary TB? ☐ yes ☐ no ☐ unknown
C. Worked together in the same dept with someone with pulmonary TB? ☐ yes ☐ no ☐ unknown
D. Attended a class (school/college) with someone with pulmonary TB? ☐ yes ☐ no ☐ unknown
E. Socialized as friends/acquaintances with someone with pulmonary TB? ☐ yes ☐ no ☐ unknown

4. If the answer is YES to anyone of the above, provide more details:

	3A	3B	3C	3D	3E
Was the person sputum smear positive? **Yes/no/don't know**					
When did you spend time with this person? **(year 20XX)**					
How much time did you spend with this person? **(days)**					
How often did you spend time with this person? **(hours per week)**					

If more than one person in any category please note here: ________________________________

Part 4: History of TB assessment and disease

1. Have you ever been **assessed** for TB disease in the past? ☐ yes ☐ no ☐ unknown

2. Have you ever been **treated** for TB disease in the past/currently? ☐ yes ☐ no ☐ unknown

***If "no" or "unknown", go to PART 5**

3. If previously diagnosed with TB disease give type: ☐ Pulmonary ☐ Extra-pulmonary ☐ Unknown

4. If previously diagnosed with TB disease give results of:

   a. Sputum smear ____ Date_____/_____/_____

   b. Sputum Culture _______________________________________ Date_____/_____/_____

   c. CXR ____ Date_____/_____/_____

   d. Biopsy____Date_____/_____/_____

5. If previously treated for TB disease, give details of Treatment

Drug name and dose	Date Started	Date Completed	Length of Treatment

Part 5: BCG Vaccination

1. BCG history:

☐ not vaccinated

☐ vaccinated at birth

☐ vaccinated after birth Give year if known yy☐☐

☐ multiple vaccinations, give years

____

☐ vaccination status unknown

***Do not complete: to be completed by interviewer**

2. BCG scar (inspect both shoulders):

Right side:	Left side:
☐ present	☐ present
☐ absent	☐ absent
☐ uncertain	☐ uncertain

Part 6: Previous Tuberculin Skin Tests (Mantoux)

1. Ever had TST in the past? ☐ yes ☐ no ☐ don't know	2. If yes, when was the most recent TST: yy☐☐/ mm☐☐/ dd☐☐	3. Previous TST result: ☐ positive (mm) ___ ☐ negative ☐ not read ☐ don't know	4. Place/Provider of previous TST: ___________________________
5. Have you ever had an adverse event after TST? ☐ yes ☐ no ☐ don't know	6. If yes, what adverse event? ☐ immediate reaction ☐ blistering ☐ ulceration ☐ scar formation ☐ other: ________________	7. Ever received any treatment for latent TB infection? ☐ yes ☐ no	8. If yes, what treatment: Drug name__________________ Dose _________________ Length of Treatment___________

Part 7: Clinical Risk Factors

1. Have you ever had a HIV test? ☐ yes ☐ no ☐ unknown/don't want to answer

2. If tested, date of most recent HIV test: mm☐☐/yy☐☐

Result: ☐ positive ☐ negative ☐ unknown/don't want to answer

3. Do you have any ongoing medical illnesses: ☐ no ☐ yes: If yes, please detail ________________________

4. Have you had any major surgery? ☐ no ☐ yes: If yes, please detail ________________________________

5. Do you have any of the following immunocompromising medical/surgical conditions?

☐ no ☐ yes ☐ don't want to answer

If yes, specify: ☐ diabetes ☐ renal failure ☐ leukemia/lymphoma
☐ cancer chemo/radio ☐ silicosis ☐ gastrectomy or intestinal bypass
☐ rheumatoid arthritis/SLE/other connective tissue diseases ☐ sarcoidosis

6. Write the names of medications you are currently taking:

____

7. Have you had a viral illness in the last week? ☐ no ☐ yes:
If yes, please detail _______________________________

8. Have you received any live viral vaccines within the last four weeks? ☐ no ☐ yes:
If yes, please detail _______________________________

Part 8: Current Symptoms

Do you have any of the following symptoms now?

A. Fever	☐ yes	☐ no	duration: ____________________	days or weeks
B. Cough	☐ yes	☐ no	duration: ____________________	days or weeks
C. Coughing up blood	☐ yes	☐ no	duration: ____________________	days or weeks
D. Night sweats	☐ yes	☐ no	duration: ____________________	days or weeks
E. Weight loss	☐ yes	☐ no	kg/time: ___________________	days or weeks
F. Enlarged Lymph nodes	☐ yes	☐ no	duration: ____________________	days or weeks
G. Loss of appetite	☐ yes	☐ no	Describe ___________________________________	

Part 9: Sociodemographic data

1. Date of Birth: mm☐☐/yy☐☐
2. Nationality: ___________________________
3. Country of birth: _______________________
4. State of permanent residence: _____________________
5. Gender: ☐ male ☐ female
6. Educational status: What was the highest level of education you **completed prior** to beginning your **current** medical training?
   - ☐ Class XII (+ 2)
   - ☐ Diploma
   - ☐ Bachelor/ BSc
   - ☐ Masters/MSc
   - ☐ Other: Give details ____________________________

Socio Economic Status of family/household:

7. Average household monthly income of family:

- ☐ < Rs. 10,000 (USD $157)
- ☐ Rs 10,001 – 30, 000 (USD $157-480)
- ☐ Rs 30, 001 – 50,000 (USD $480-785)
- ☐ Rs 50, 001 – 70,000 (USD $785-1099)
- ☐ Rs 70, 001 – 90,000 (USD $1099-1400)
- ☐ > Rs 90,001 (USD $1400)
- ☐ Do not want to respond

8. Does your family own
   - a) a house: ☐ yes ☐ no
   - b) a car: ☐ yes ☐ no
   - c) motorbike/scooter: ☐ yes ☐ no

9. **Father's** educational status (highest level completed):

- ☐ No schooling
- ☐ Primary school (class I-V)
- ☐ High school (class VI-IX)
- ☐ Class X completed
- ☐ Class XI or XII
- ☐ Diploma/Bachelor's degree
- ☐ Master's or higher degree
- ☐ Other: ____________________________

10. Your **father's** current occupational status:

- ☐ Professional
- ☐ Skilled worker
- ☐ Shop Owner/ Farm Owner
- ☐ Unskilled worker/manual labor
- ☐ Retired/pensioner
- ☐ Unemployed
- ☐ Homemaker
- ☐ Other: _____________________________________
- ☐ Not alive
- ☐ Do not want to respond

11. **Mother's** educational status (highest level completed):

- ☐ No schooling
- ☐ Primary school (class I-V)
- ☐ High school (class VI-IX)
- ☐ Class X completed
- ☐ Class XI or XII
- ☐ Diploma/Bachelor's degree
- ☐ Master's or higher degree
- ☐ Other: ____________________________

12. Your **mother's** current occupational status:

- ☐ Professional
- ☐ Skilled worker
- ☐ Shop Owner/ Farm Owner
- ☐ Unskilled worker/manual labor
- ☐ Retired/pensioner
- ☐ Unemployed
- ☐ Homemaker
- ☐ Other: _____________________________________
- ☐ Not alive
- ☐ Do not want to respond

****END – PLEASE GIVE FORM TO MEDICAL INTERVIEWER****

TO BE COMPLETED BY MEDICAL INTERVIEWER

Interviewer Initials

____

PART 10: Physical details

Current Weight ___________________ kg. Current Height _______________cms.

Part 11: TB disease history (Refer to PART 4)

******These questions from PART 4 only need answering if the student has current OR previous TB, in this case DO NOT PROCEED TO PART 13******

1. Refer to Q2 and Q5 Classification of Previous/Current Tuberculosis **Treatment**

☐ Untreated
☐ Treatment in progress
☐ Failed to complete treatment
☐ Treatment completed
☐ Unknown

2. Refer Q2 and Q5 and **ask student about outcome**

Classification of Previous TB Treatment **Outcomes** (As per TB guidelines)

☐ Cured
☐ Defaulted [reason for default:____]
☐ Moved (transferred) out
☐ Treatment complete
☐ Treatment failed

If the above cannot be ascertained, please seek information to assist in contacting the facility where treatment was given.

Health Care Facility where treatment given____

Part 12: Medical history (Refer to PARTS 5-7)

******Please assess what the student has recorded regarding medical/surgical conditions and current medication and then answer the following questions.*****

1. **Refer to PART 5 Q2:** complete inspection
2. **Refer to PART 6 Q3:** Has trainee received a previous tuberculin (Mantoux) test?

   ☐ Yes** ☐ No ☐ Unknown

   ****IF YES AND POSITIVE USING STUDY CRITERIA DO NOT PROCEED TO PART 13.**
3. **Refer to PART 7 Q1-5:** Is there an immune compromising medical or surgical condition?

   ☐ Yes ☐ No ☐ Unknown
4. **Refer to PART 7 Q6:** Does this list of medicines include those likely to compromise the immune system?

   ☐ Yes ☐ No ☐ Unknown
5. **Refer to PART 7 Q7-8:** Has trainee had a viral illness in the last 1 week OR a live viral vaccine in the last 4 weeks?

   ☐ Yes** ☐ No ☐ Unknown

   ****IF YES AND RELEVANT DO NOT PROCEED TO PART 13 AND RESCHEDULE APPOINTMENT.**

Part 13: Study TST

1st Step

1. Study TST #1 performed?
   - ☐ yes
   - ☐ no
   - ☐ unknown

2. Date **administered**: dd☐☐/mm☐☐/yy☐☐

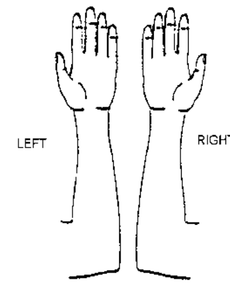
   Time: ☐☐ : ☐☐ AM / PM

3. Administered by (initials): ____________

4. PPD brand: ___
   Lot #: __________

5. Site of TST#1:
   - ☐ Left forearm
   - ☐ Right forearm

   Mark exact spot ➔



TST reading

6. TST #1 result: ☐ ☐ (mm induration)

   ☐ did not return for reading

7. Date **read**: dd☐☐/mm☐☐/yy☐☐

   Time: ☐☐ : ☐☐ AM / PM

8. **Read by (initials):** ____________

9. Adverse events:
   - ☐ none
   - ☐ immediate reaction
   - ☐ blistering
   - ☐ ulceration
   - ☐ scar formation
   - ☐ other: _____

10. **Final TST interpretation (after 1-step testing)** (≥5mm or ≥10mm depending on medical risk factors):
    - ☐ positive
    - ☐ negative
    - ☐ not determined

Part 14: Referral

1. Does this health care trainee need referral to the department of medicine? ☐ yes ☐ no

2. If yes, date on which trainee was referred: dd☐☐/mm☐☐/yy☐☐

3. Reason for referral:
   ☐ Latent tuberculosis ☐ Active tuberculosis ☐ Other: ______________________________

Part 15: Consultation 2nd reading

1. Consultation 2nd reading (blind):

☐☐mm induration Read by (Initials) _______

*Please enter study TST result for participant.
*If a difference >3mm or crossing threshold of 10mm please request a third evaluator.

Part 16: 72 hour reading (if applicable)

☐☐mm induration Read by (Initials) _______

Date read: dd☐☐/mm☐☐/yy☐☐

Time read: ☐☐ : ☐☐ AM / PM

Date ____/____/2015 (dd/mm/yy)

Protocol title: Tuberculosis infection among healthcare trainees in South India
Hospital: Kasturba Hospital, Manipal

Principal Investigator: Dr. Kavitha Saravu
Designation: Professor of Medicine and Unit Chief, Med 7B +91 9448107636

NON-PARTICIPANT INFORMATION

PLEASE NOTE: If you have previously undergone TST or previously been assessed for or diagnosed with TB **you are eligible** to participate in the study, you will simply complete the questionnaire but not undergo the TST portion.

We understand that you do not wish to participate in this study, but we are asking you to provide us with some **voluntary**, **anonymous** information. This will help us understand better those who participate in the study and those who do not.

☐ I do not wish to complete this non-participant information form.

1. What is your gender?

☐ male ☐ female ☐ don't want to answer

2. What is your age?

☐☐years ☐ don't want to answer

3. Have you ever undergone a TST?

☐ yes & tested negative (____/____ mm/yy) ☐ yes & tested positive (____/____ mm/yy) ☐ no

☐ unknown/don't want to answer

4. Have you ever been treated for TB disease in the past/currently?

☐ yes (_____ yy) ☐ no ☐ unknown/don't want to answer

Appendix 4 Manuscript 2 knowledge, attitudes and practices questionnaire

Knowledge, attitudes and practices regarding tuberculosis infection control (TBIC) among recent medical graduates in Karnataka, South India

SURVEY PARTICIPANT INFORMATION

Please read the enclosed information carefully, and ask any questions you may have from the questionnaire distributor.

Purpose of the study

India has the world's highest burden of tuberculosis (TB) with 2-2.3 million incident cases each year. Healthcare workers are routinely exposed to TB. We invite you to participate in this **anonymous self-administered questionnaire** investigating how recent medical graduates perceive and engage with hospital-based TB infection control efforts by measuring knowledge, attitude and practices relating to TB infection control.

Participation

Questionnaires will be distributed to recent medical graduates, including interns and post-graduates working in select departments across Kasturba Hospitals in Manipal and Mangalore. Participation is completely voluntary and you can withdraw at any time before or during the completion of the questionnaire.

Risks and benefits

We do not anticipate any personal costs or benefits: academic or social, financial, or physical associated with your participation in this survey.

Confidentiality

This questionnaire has been approved by the ethics committee at Manipal University.

The questionnaire will be completed and collected anonymously. It does not require or collect any personal information, and individualized data from respondents will not be published to ensure complete anonymity. Aggregate results from this survey may be presented at meetings or published in journals.

Dissemination of results

The aggregate results from this survey will be disseminated to the university programs and hospitals to take under consideration as future infection control programs are developed and implemented.

Who to contact in case of any questions

If you experience any issues, or have any concerns, please contact principal investigator Dr. Kavitha Saravu, Professor of Medicine and unit Chef, Med 7B, KMC Manipal +91 9448107636.

PARTICIPANT CONSENT FORM

Please tick each box to proceed:

1. I confirm that I have read the enclosed information sheet for the survey. I have understood the information and have received responses to my questions to my satisfaction. ☐
2. I understand that my participation is voluntary and I can refuse to answer any questions or withdraw from the survey at any time. ☐
3. I agree to participate in this survey. ☐

Date: (YY/MM/DD) __ __ / __ __ / __ __

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INSTRUCTIONS

- This questionnaire contains 52 items.
- It will take 15-20 minutes to complete.
- The data collected on this questionnaire is completely anonymous so we appreciate complete answers reflecting your true knowledge, attitudes and practices.
- If a question does not apply to you or you don’t know the answer, please check “Not applicable” or “Don’t Know.”
- To select an answer make a tick mark ✓ in the box indicated. If you make an error, please indicate so by crossing the incorrect answer out and circling the correct answer.
- Unless otherwise indicated, please only tick one box.
- For some questions more than one option may be correct.

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GENERAL OCCUPATIONAL CHARACTERISTICS

1. What is your profession in the hospital?

☐ Intern ***>> go to question 5***
☐ Post-graduate

2. If you are a post-graduate, what specialty are you enrolled in?

☐ MD Community medicine
☐ MD General medicine
☐ MD Microbiology
☐ MD Paediatrics
☐ MD Pulmonary medicine
☐ MS ENT
☐ MS General surgery
☐ MS Orthopedics
☐ MS Obstetrics and gynecology

3. If you are a post-graduate, what program year are you in?

☐ 1st year
☐ 2nd year
☐ 3rd year or more

4. If you are a post-graduate, after MBBS graduation and before entering the PG program, did you work in healthcare?

☐ Yes ***>> go to question 4a***
☐ No

4a. If yes, for how long?

☐ Less than 1 year
☐ 1-2 years inclusive
☐ 3-4 years inclusive
☐ 5 years or more

PAST EXPOSURE TO TUBERCULOSIS INFECTION

5. On average, how many patients you interact with in a week?

☐ 5 or fewer
☐ 6-10
☐ 11-20
☐ 21-40
☐ 41 or more
☐ Does not apply

6. In the orientation for your current workplace did you receive information/training regarding safety precautions for respiratory infections (including TB)?

☐ 0.5 hour or less
☐ 0.5-1 hour
☐ 1-2 hours
☐ 2 hours or more
☐ Did not receive information/training regarding respiratory infections
☐ Did not have an orientation
☐ Don't know

Please answer yes or no to the following questions.

	Yes	No	Don't know
7. Have you ever had a tuberculin skin test (TST/Mantoux) in the past?	☐	☐	☐
8. Have you ever been **investigated** for pulmonary or extrapulmonary TB disease in the past (including via chest X-ray in association with symptoms)?	☐	☐	☐
9. Have you ever been **treated** for pulmonary or extrapulmonary TB before?	☐	☐	☐

	Yes	No	Don't know
10. Has anyone in your immediate family been diagnosed or treated for TB in the past?	☐	☐	☐
11. Have you ever participated in a TB research project as an investigator?	☐	☐	☐

KNOWLEDGE REGARDING PULMONARY TB TRANSMISSION

12. Please tick all ways TB can be spread from person to person.

- ☐ Through air
- ☐ Through sexual contact
- ☐ Through blood
- ☐ Through handshake and physical touch
- ☐ Through sharing of utensils
- ☐ Through talking or singing
- ☐ Through spitting
- ☐ Other (please list): ______________________________
- ☐ Don't know

13. Please tick all the signs and symptoms of TB.

- ☐ Chest pain
- ☐ Cough for >2 weeks
- ☐ Cough with blood
- ☐ Diarrhea
- ☐ Dizziness
- ☐ Fever
- ☐ Psychosis
- ☐ Loss of appetite
- ☐ Memory loss
- ☐ Nausea
- ☐ Night sweats
- ☐ Ongoing fatigue
- ☐ Pain with Urination
- ☐ Rash
- ☐ Severe headache
- ☐ Weight loss
- ☐ Don't know
- ☐ Others (please list): ______________________________________

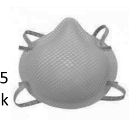
Please tick one box indicating if a statement is true or false.

	True	False	Don't know
14. Those with HIV are more likely than those without HIV to develop active TB	☐	☐	☐
15. Those who have been vaccinated with BCG will not develop active TB	☐	☐	☐
16. A single infection with TB gives lifetime immunity	☐	☐	☐
17. Children are more likely than adults to be infectious	☐	☐	☐
18. Patients with pulmonary and extra pulmonary TB are equally infectious	☐	☐	☐
19. Patients with drug-resistant TB may be infectious even after receiving treatment	☐	☐	☐
20. Patients with smear-negative TB are not infectious	☐	☐	☐
21. TB cough droplets containing bacteria settle on the ground within minutes of expiration	☐	☐	☐

KNOWLEDGE REGARDING TUBERCULOSIS INFECTION CONTROL

Please tick one box for each statement indicating if true or false.

	True	False	Don't know
22. Airborne infection isolation rooms have positive pressure relative to other parts of the facility	☐	☐	☐
23. A patient suspected for TB must be isolated in a different room from other patients while waiting for diagnosis	☐	☐	☐
24. Protective masks need to be worn by those involved in care of TB patients for the entire first two weeks of treatment	☐	☐	☐

Surgical Mask  N95 Mask 

	True	False	Don't know
25. Surgical masks worn by TB patients reduce TB droplet nuclei from being spread	☐	☐	☐
26. Surgical masks worn by healthcare workers filter out TB droplet nuclei and prevent infection	☐	☐	☐
27. Surgical masks should be given to TB patients only after diagnosis	☐	☐	☐
28. N95 masks work fine even if wet or with visible dirt	☐	☐	☐

	True	False	Don't know
29. N95 masks work fine even when not completely fitted (e.g. in heavily-bearded)	☐	☐	☐
30. Mechanical air circulation systems (e.g. fans) are always more effective than natural ventilation (e.g. open windows) for infection control	☐	☐	☐

INFECTION CONTROL PROGRAM PERCEPTIONS AND ATTITUDES

Please tick one box which represents your opinion.

	Strongly agree	Agree	Neither agree or disagree	Disagree	Strongly disagree	Don't know
31. I have a low risk of acquiring TB from my patients	☐	☐	☐	☐	☐	☐
32. If I get TB disease I would not be very worried	☐	☐	☐	☐	☐	☐
33. We should always wear N95 masks when exposed to TB suspects and patients	☐	☐	☐	☐	☐	☐
34. We should isolate those people who have or are suspected of having TB from others	☐	☐	☐	☐	☐	☐

	Strongly agree	Agree	Neither agree or disagree	Disagree	Strongly disagree	Don't know
35. My supervisors would praise me for practicing infection control	☐	☐	☐	☐	☐	☐
36. There is limited availability of masks for healthcare worker use	☐	☐	☐	☐	☐	☐
37. I would be willing to be screened for TB infection and disease regularly	☐	☐	☐	☐	☐	☐
38. I find myself too busy in daily activities to practice infection control	☐	☐	☐	☐	☐	☐
39. I am confident in my knowledge of TB and its transmission control	☐	☐	☐	☐	☐	☐

40. Which three (3) TB control measures would make the best impact in your work setting? Tick and rank 1 (most important),2,3.

☐ ___ A widely-distributed TB infection control plan
☐ ___ Administrative support for infection control procedures
☐ ___ Greater monitoring and infection quality control
☐ ___ More education of patients (through posters etc.)
☐ ___ More education and training of medical and support staff
☐ ___ More appropriate management of TB suspects
☐ ___ More environmental controls (ventilation, irradiation, etc.)
☐ ___ More available protective devices (masks, etc.)

INFECTION CONTROL PRACTICES

Please tick one box which represents your practices.

	Always	Most times	Few times	Never	Don't know	Not applicable
41. My co-workers practice TB infection control strategies as per hospital policies	☐	☐	☐	☐	☐	☐
42. I see patients in a well-ventilated room	☐	☐	☐	☐	☐	☐
43. In the outpatient department I see patients with cough according to the general token system/queue	☐	☐	☐	☐	☐	☐
44. I tell coughing patients to follow cough hygiene procedures	☐	☐	☐	☐	☐	☐
45. I collect sputum samples to identify TB suspects in waiting rooms around other patients	☐	☐	☐	☐	☐	☐
46. I receive education about TB infection control measures	☐	☐	☐	☐	☐	☐

	Always	Most times	Few times	Never	Don't know	Not applicable
47. I wear an N95 mask when caring for patients with suspected or active pulmonary TB	☐	☐	☐	☐	☐	☐
48. I wear an N95 mask when caring for patients with suspected or MDR or XDR-TB	☐	☐	☐	☐	☐	☐
49. We separate patients with known TB disease from HIV patients	☐	☐	☐	☐	☐	☐

50. If you do not always wear an N95 mask when appropriate, why? Tick your reason(s) and, only for items ticked, how strongly they influence your overall decision.

	Strong → Weak
☐ I do not always have access to an N95 mask	O------O------O------O------O
☐ I wear surgical masks instead	O------O------O------O------O

	Strong → Weak
☐ Wearing an N95 mask is physically uncomfortable	O------O------O------O------O
☐ I do not think an N95 mask is necessary for infection control	O------O------O------O------O
☐ No one else in my department or unit wears an N95 mask	O------O------O------O------O
☐ I have been already exposed to TB patients, and I don't think wearing an N95 mask will protect me	O------O------O------O------O
☐ We see TB patients all the time, and it is impossible to protect ourselves all the time	O------O------O------O------O
☐ My superiors do not wear N95 masks	O------O------O------O------O
☐ Other: ______________________	O------O------O------O------O

GENERAL DEMOGRAPHIC CHARACTERISTICS

51. What is your age?

☐ 18 to 22 years
☐ 23 to 26 years
☐ 27 years or greater
☐ Prefer not to disclose

52. What is your gender?

☐ Male
☐ Female
☐ Do not identify as either or prefer not to disclose

YOU HAVE REACHED THE END OF THIS SURVEY.

THANK YOU FOR YOUR PARTICIPATION.

KINDLY RETURN BOOKLET TO SURVEY DISTRIBUTOR.

FOR INTERNAL USE ONLY

Consent obtained: ☐ Yes ☐ No

Initials of questionnaire collector: ________

Date: (YY/MM/DD) __ __ / __ __ / __ __

Questionnaire number: __ | __ | __ | __ | __

Appendix 5 Manuscript 2 KAP questionnaire question item sources

Question #	Adapted from/modified from
#1-11, 14-16, 18, 20-21, 24, 27, 30, 35-40, 42-43, 45, 51-52	*None*
#17, 19, 22, 25-26, 33-34, 50	Centers for Disease Control and Prevention (2013)
#12, 13	Ferreira Junior, Oliveira, and Marin-Léon (2013)
#12, 28, 41, 44, 46-47	Kanjee, Catterick, Moll, Amico, and Friedland (2011)
#23, 29, 31-32	Tenna et al. (2013)

*For questions refer to KAP questionnaire in Appendix 4

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