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DIAGNOSIS AND MANAGEMENT OF POTENTIALLY INFECTIOUS PATIENTS WITH SUSPECTED PULMONARY TUBERCULOSIS IN A DEVELOPING COUNTRY SETTING

by

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GNZLIC001

Submitted to the University of Cape Town in fulfilment of the requirements for the degree:

Master of Science in Medicine in Public Health

Faculty of Health Sciences
University of Cape Town

August 28, 2011
Supervisor: Associate Prof. Mark Hatherill
South African Pulmonary Tuberculosis Vaccine Initiative (SATVI)
Institute of Infectious Disease and Molecular Medicine
School of Child and Adolescent Health
DECLARATION

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Thesis presented for the degree of Master of Science in Medicine in the School of Public Health and Family Medicine University of Cape Town August 2011

Supervisor: Associate Professor Mark Hatherill

This thesis is presented in fulfilment of the requirements for the degree of Master of Science in Medicine [M.Sc.(Med)] in the School of Public Health and Family Medicine, Faculty of Health Sciences, University of Cape Town. The work on which this thesis is based is original research and has not, in whole or in part, been submitted for another degree at this or any other university. The contents of this thesis are entirely my work. Wherever contributions of others are involved, every effort is made to indicate this clearly, with due reference to the literature, and acknowledgement of collaborative research and discussions. I empower the University of Cape Town to reproduce for the purpose of research either the whole or any portion of the contents in any manner whatsoever.

Licé Yulieth González-Angulo
August 2011
—I don’t want anything for me.
I only wish for the possible impossible:
A world without victims.”

The end of the Century (Poem) - José Emiliano Pacheco
ACKNOWLEDGEMENTS

I am indebted to Associate Professor Mark Hatherill, my supervisor, for all the support, constant encouragement and valuable guidance throughout this research. This work wouldn’t have been possible without his mentorship and suggestions.

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Foremost, without my parents' support, the most difficult times of this journey, would not have been possible. Moreover I deeply thank and express my profound appreciation to my husband Helge for supporting and encouraging me to pursue this degree, and for his patience as I completed this process. Finally, I wish to express my sincere gratitude to my very good friends: Angélica Muñoz-Córdoba, Brian Abel, Phiona Enid Namale, Nancy Marin-Agudelo, Gustavo Adolfo Salazar and Carlos Perez-Velez for the support, camaraderie, entertainment, and care they provided.

Thank you, everyone!
This thesis comprises two projects, which focus on simple TB control strategies that can help reduce the risk of *M. tuberculosis* transmission, and which have been summarized on two manuscripts:


The candidate wrote the research protocols for both projects, designed data collection instruments, collected the data and conducted all of the analyses for both projects under the supervision of A/Professor Mark Hatherill. The contents of this thesis are entirely the work of the candidate, and in the case of multi-authored manuscripts, constitutes work for which the candidate was the lead author. The candidate wrote and managed all drafts of the manuscript, incorporating suggestions from co-authors.
EXECUTIVE SUMMARY

DIAGNOSIS AND MANAGEMENT OF POTENTIALLY INFECTIOUS PATIENTS WITH SUSPECTED PULMONARY TUBERCULOSIS IN A DEVELOPING COUNTRY SETTING

By
Licé Yulieth González-Angulo

Background

There are 9.4 million new active TB cases each year and nearly 5,000 TB deaths occur every day—mostly in the developing world. Poor and vulnerable groups are at greater risk of infection with \( M. \) \textit{tuberculosis}, compared to the general population. Overcrowded living or working conditions, poor nutrition, and co-morbidities such as HIV/AIDS, increase the annual risk of TB infection and development of TB disease. TB can be controlled by preventing infection, and by early treatment of active disease. Rapid identification of sources of infection, early diagnostic evaluation, and completion of treatment, have been described as key elements for effective TB control. TB control efforts have focused on new diagnostics to identify patients with TB, new shorter anti-tuberculosis drug regimens, and innovative infection control technologies to reduce the risk of TB exposure. However, many of these advances are not readily implemented in resource-constrained settings, where most TB cases occur.

New effective and field-adapted interventions are needed to improve TB programme outcomes. Two projects, which focus on breaking the cycle of TB transmission in developing country settings, are reported. First, we evaluate the diagnostic yield of sputum induction, a method used to improve the collection of pulmonary specimens for the bacteriological
confirmation of TB, and which contributes to the prompt identification of paucibacillary TB cases; second, we evaluate how knowledge of TB and acceptability of patient-specific infection control measures compares between patients suspected with TB who lack TB education and patients with TB, who have received TB education; and we evaluate changes over time in patients with TB on treatment. The strategies described here may improve the diagnosis and management of potentially infectious patients with suspected pulmonary TB in a developing country setting and address major public health objectives; first, early identification and diagnosis of TB cases, with rapid treatment initiation; and second, improved, early, and intensive TB education to increase the acceptability of patient-specific infection control measures, in order to reduce TB transmission at health care facilities, and in home and work settings. These field-adapted strategies can provide long-term sustainability to TB control programmes where resources are scarce.

**Sputum Induction for Diagnosis of Tuberculosis:**
*A Systematic Review and Meta-Analysis*

Studies have assessed sputum induction for the diagnosis of active TB in patients who are unable to produce spontaneous sputum; or who have smear-negative spontaneous sputum samples; and in children with paucibacillary TB. These studies have compared sputum induction to several different comparator methods. The diagnostic yield of culture positive *M. tuberculosis* that might be expected using sputum induction under programmatic conditions is not known. Our systematic review and meta-analysis of this technique showed the following:
**Key findings**

- The diagnostic yield of sputum induction in individual studies ranged from 35% to 95%.

- *M. tuberculosis* was isolated through sputum induction in 627 cases of 975 culture-confirmed patients with TB (64%) in 17 studies.

- Sources of heterogeneity which could be attributed to within-study factors (HIV prevalence and age group) and between-study factors (comparator method) were explored by meta-regression. However, significant heterogeneity in diagnostic yield was not explained by these variables.

- The findings of this meta-analysis suggest that higher saline concentrations are not associated with better diagnostic yield in sputum induction, after adjusting for confounders.

**Conclusion**

Prospective, comparative studies of the diagnostic yield of sputum induction are needed, with rigorous definition of the study populations and standardization of technique.

**Patient-Specific Infection Control Measures for Tuberculosis in Developing Countries**

**Background**

Previous authors have demonstrated that health education should be a continuous process which starts when patients are confirmed to have pulmonary TB and continues until patients are cured. The association between knowledge of TB and acceptability of patient-specific infection control measures, and changes over time with on-going TB education have not been studies.
Key findings

The following were major findings of this study:

- Participants showed poor to moderate levels of knowledge regarding TB disease and measures to reduce TB transmission, coupled with low levels of acceptability of certain patient-specific measures, at baseline.

- Core knowledge elements, such as understanding of TB transmission showed low levels of comprehension. 54% of participants claimed to know how TB was transmitted, but some misconceptions were found in both patients suspected with TB and in newly diagnosed patients with TB. Some participants believed that TB was a hereditary disease, or that it was spread by sharing food utensils, kissing patients with TB, and living in cold areas.

- Patient-specific infection control measures that could be implemented at health care facilities and at home, showed higher levels of acceptability than infection control measures to be conducted in work settings.

- We demonstrated that acceptability of these patient-specific infection control measures increased in relation to improvements in knowledge about TB, over the course of treatment in patients with TB.

Conclusion

Public health authorities should design and implement early intensive TB education programmes to increase knowledge and acceptability of patient-specific infection control measures. These educational resources should be accessible not only for patients suspected with TB and patients with TB, but for entire communities in which TB poses a challenge.
CHAPTER OVERVIEW

Each chapter is divided into two sections. The first part comprises aspects related to sputum induction for diagnosis of TB; and the second section refers to patient-specific infection control measures for TB in developing countries.

1 INTRODUCTION

The first chapter explores how, in spite of advances in technology to improve TB diagnostics and public health measures to control the disease, TB continues to affect individuals of all ages from communities throughout the developing world. We describe the burden of TB disease and we provide the rationale for a systematic review and meta-analysis of the diagnostic yield of sputum induction. Second, we describe the rationale for a study to determine how knowledge and acceptability of patient-specific infection control measures changes over time and how implementation of infection control measures might be optimized by early, intensive TB education to newly diagnosed patients with TB.

2 LITERATURE REVIEW

In the second chapter, we present a literature review of current methods to control TB and we summarise two simple and field-adapted measures that could improve TB control in developing country settings. The first strategy is a simple and affordable method (sputum induction) to improve respiratory specimen collection and provide early diagnosis of TB, including paucibacillary TB among immunocompromised patients and children. The second strategy focuses on patient-specific infection control measures to prevent TB transmission in health care facilities, and the home and work settings.
3 Research Methodology

The third chapter describes the methods used to conduct a systematic review and meta-analysis of studies reporting the use of sputum induction for the diagnosis of pulmonary tuberculosis; second, this chapter describes a questionnaire-based study to determine the knowledge and acceptability of patient-specific infection control measures among patients suspected with TB, at the time of investigation, and among patients with TB, at baseline and at the end of treatment.

4 Results

In this section we present the results of the systematic review and meta-analysis of sputum induction for the diagnosis of pulmonary TB; and the results of the study of patient-specific infection control measures for TB.

5 Discussion

The final chapter presents a summary of the principal results and explores the implications of our observations. We highlight the clinical and public health implications of the use of sputum induction, as well as technical and epidemiologic factors that might influence the diagnostic yield of this procedure. Second, we discuss the relationship between knowledge of TB, acceptability of patient-specific infection control measures, and the implications for early, focused TB education among newly diagnosed patients.
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# ACRONYMS AND ABBREVIATIONS

<table>
<thead>
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<th>Acronym</th>
<th>Definition</th>
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<tbody>
<tr>
<td>AFB</td>
<td>Acid Fast Bacilli</td>
</tr>
<tr>
<td>AIDS</td>
<td>Acquired Immunodeficiency Syndrome</td>
</tr>
<tr>
<td>BCG</td>
<td>Bacille Calmette-Guérin</td>
</tr>
<tr>
<td>CDC</td>
<td>U.S. Centers for Disease Control and Prevention</td>
</tr>
<tr>
<td>COPD</td>
<td>Chronic Obstructive Pulmonary Disease</td>
</tr>
<tr>
<td>DOTS</td>
<td>Directly Observed Treatment, Short-course</td>
</tr>
<tr>
<td>DST</td>
<td>Drug-susceptibility testing</td>
</tr>
<tr>
<td>FOB/BAL</td>
<td>Fiberoptic bronchoscopy with Broncho-Alveolar Lavage</td>
</tr>
<tr>
<td>HEPA</td>
<td>High Efficiency Particulate Air</td>
</tr>
<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
</tr>
<tr>
<td>IPT</td>
<td>Isoniazid Preventive Therapy</td>
</tr>
<tr>
<td>M. tuberculosis</td>
<td>Mycobacterium tuberculosis</td>
</tr>
<tr>
<td>MDR-TB</td>
<td>Multidrug Resistant tuberculosis</td>
</tr>
<tr>
<td>NPIR</td>
<td>Negative pressure isolation rooms</td>
</tr>
<tr>
<td>SATVI</td>
<td>South African Tuberculosis Vaccine Initiative</td>
</tr>
<tr>
<td>TB</td>
<td>Tuberculosis</td>
</tr>
<tr>
<td>TST</td>
<td>Tuberculin Skin Test</td>
</tr>
<tr>
<td>UVGI</td>
<td>Ultraviolet germicidal irradiation</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
<tr>
<td>XDR-TB</td>
<td>Extremely Drug Resistant tuberculosis</td>
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Chapter Introduction

This chapter provides a brief historical background about tuberculosis (TB) and describes how this disease continues to present significant problems for many developing nations. This chapter also sets out the rationale for putting into practice simple and affordable TB diagnostic methods, and improving infection control strategies for patients with pulmonary TB in high TB burden settings.

1.1 Historical Background

Tuberculosis (TB) has been described as one of the most pervasive, debilitating and lethal diseases to humankind. TB has been tracked nearly as far back as humanity has been recording its history (1). The spread of TB was documented more than 5000 years ago in Egypt, and its causative agent, *Mycobacterium tuberculosis*, has been reported to have killed more people than any other microbial pathogen ever since (1).

Several tentative measures were implemented to control and cure the disease. Such methods included prolonged bedrest, sanatoria for the care of consumptives, adequate nutrition and also the implementation of collapse therapy methods (e.g., artificial pneumothorax induction and thoracoplasty) as an attempt to accelerate healing in very ill
patients (2, 3). The anti-tuberculosis drugs were widely implemented in the 1950’s and resulted in cures for 90–95% of patients (4). The Bacille Calmette-Guérin (BCG) vaccine and the standardized treatment regimen (known as directly observed treatment, short-course—DOTS) contributed to the slow drop in TB prevalence that was experienced for many years in succession (5).

Unfortunately, at the end of the 1980’s and beginning of the 1990’s TB rates began to rise globally; this could be explained due to three main factors: firstly, neglected TB control programmes; secondly, the deprived economic development of some regions and deterioration of their public health infrastructure; and lastly, the human immunodeficiency virus (HIV) infection that up to recently has driven the TB epidemic in high TB burden areas (5–8).

1.2 GLOBAL BURDEN AND PULMONARY TUBERCULOSIS CONTROL

The consequences of pulmonary TB on society are immense, in spite of advances in technology and public health measures to control the disease. Currently one third of the world’s population is infected with *M. tuberculosis*. Indeed, one person is infected with the bacteria every second. Up to 9.4 million new active TB cases are reported every year (range, 8.9 million- 9.9 million cases), with an estimated 14 million prevalent cases (range, 12 million–16 million), of which 440 000 cases are reported as multi-drug resistant cases (range, 390 000–510 000) and nearly 5000 patients with TB are estimated to die every day, mostly in the developing world (9) (See Error! Reference source not found. and Error! Reference source not found.). TB accounts for 2.5 % of the global burden of disease and it is the most common cause of death in young women, killing more women than all causes of maternal mortality combined (10).
Global burden of tuberculosis [Numbers in thousands]

<table>
<thead>
<tr>
<th>WHO Region</th>
<th>Population</th>
<th>Mortality</th>
<th>Prevalence</th>
<th>Incidence</th>
<th>HIV in Incident TB Cases (%)</th>
</tr>
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<tr>
<td>Africa</td>
<td>824401</td>
<td>430</td>
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<td>14000</td>
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</table>

Table 1. Estimated Epidemiological Burden of Tuberculosis according to WHO regions  
Source—Adapted from “Global Tuberculosis Control: WHO Report 2010”

Interventions to control pulmonary TB were sought to address three public health objectives: (1) to reduce infectiousness, (2) to decrease transmission capacity from bacilliferous patients to the rest of the community and (3) to reduce morbidity and mortality (12). These objectives were partially accomplished by increasing BCG vaccination coverage, and by providing effective TB chemotherapy. Nevertheless, controlling TB...
through BCG vaccination and treatment have not been sufficient. The current vaccine, BCG, does not provide lifelong immunity but provides unreliable protection against pulmonary TB, and it is only effective against severe forms of TB in childhood (13, 14). Moreover, TB chemotherapy has challenges: availability of drugs, availability of drug susceptibility testing (DST) to provide accurate diagnosis and effective treatment to either patients with sensible or resistant *M. tuberculosis* strains, the DOTS regimen is still six months or more and, socio-economic factors that lead patients to abandon TB treatment (15, 16).

Poor access to diagnostic services along with the low performance of current tools and strategies for the diagnosis of TB contributes to underdiagnosis of millions of infectious TB cases (17). TB control programmes in high TB burden settings may not have adequate diagnostic tools to early identify TB cases. Bacteriological confirmation of pulmonary TB has been achieved through sputum evaluation (18). However, the direct observation of the mycobacterium (smear microscopy) is affected under three circumstances: firstly some patients provide sputum samples of poor quality or scanty sputum; secondly, there is a significant number of paucibacillary cases in whom *M. tuberculosis* can not be detected. Such is the case of paediatric patients and HIV infected persons (18); and thirdly, low quality laboratory infrastructure, especially in resource-constrained settings in the developing world, hinders the bacteriological confirmation of TB.

TB control activities are not implemented universally. Under these circumstances, the diagnosis of pulmonary TB in low and middle income countries becomes difficult. patients with suspected TB are not early diagnosed, or are misdiagnosed because of the lack of accurate and affordable diagnostic tools. DST methods to determine whether strains are
resistant to TB chemotherapy are unavailable; and the measures to prevent transmission of the disease are difficult to implement.

1.3 TOOLS TO CONTROL TB

In order to interrupt TB transmission, early diagnosis and prompt treatment are considered the most effective TB control strategies (19-21). Yet, both approaches have encountered limitations, principally the detection of the bacillus in clinical specimens, which has impeded TB control due to a lack of rapid, accurate and affordable diagnostic methods, particularly in low and middle income countries (21). For instance, in high-burden settings, mainly in the developing world, sputum smear microscopy is the predominant test to diagnose patients suspected with TB (21, 22), and although different methods to increase the speed and sensitivity of acid fast bacilli (AFB) smear microscopy have been or are being developed (23, 24), these may not be available in low and middle income countries. In the case of industrialized countries, where the burden of TB is low, high-tech molecular methods and rapid culture systems have been designed to detect cases with many fewer organisms in less time (22).

Another paradoxical example of availability of resources to interrupt TB transmission in low and middle income countries and high income countries is reflected by implementation of infection prevention and TB control plans. For instance, in industrialized countries, environmental controls such as high efficiency particulate air (HEPA) filtration or sterilization methods with ultraviolet germicidal irradiation (UVGI) are used to control the transmission of M. tuberculosis TB in confined areas (25). This is not the case in poor areas where infectious patients can be easily missed, and therefore, contribute to the chain of transmission which increases the burden of disease in these areas (25).
1.3.1 TB diagnostics

1.3.1.1 The “gold” standard

TB follows a human-to-human transmission pattern. TB transmission only occurs when individuals with pulmonary TB exhale infectious droplets by speaking, laughing and sneezing and a susceptible person inhales these infectious droplets. Hence, the importance of ensuring early recognition of individuals with suspected pulmonary TB, since they are considered sources of infection. For several decades, the examination of spontaneously produced sputum samples (routine sputum) from patients suspected with TB has been the mainstay for the diagnosis of active TB (26). Smear microscopy is considered the gold standard method for the diagnosis of pulmonary TB, particularly in communities of the developing world, where 95% of TB cases and 98% of deaths occur (27). However, this technique requires approximately 10,000 mycobacteria per millilitre of sputum for a positive diagnosis (28). The yield of sputum smear microscopy depends on intrathoracic manifestations of TB disease. Hence, for patients with advanced disease, the bacteriologic yield tends to be higher, as compared to patients with mild to moderate disease, since the mycobacterial load is likely to be lower (29). The use of AFB smear is limited in children and HIV positive individuals, because of the paucibacillary nature of their disease.

![Sputum smear microscopy](image)

Figure 2. Distribution of Sputum Smear Microscopy (Acid-Fast Bacilli [AFB] among patients with TB/suspects)

Source—. Adapted from the STOP TB New Diagnostics Working Group - Strategic Plan 2006-2015 (18).
The STOP TB working group on "New Diagnostics for TB" reported that more than 50% of the TB cases are AFB smear negative (See Error! Reference source not found. above). This represents a clear public health problem. As stated by Behr et al, AFB smear negative patients are generally not diagnosed, and consequently not treated on time (30). Furthermore, it has been shown that TB transmission does occur from smear-negative patients\(^1\) (30, 31). In addition to the poor diagnostic yields (30% - 70%) of AFB smear microscopy (21), the collection of pulmonary specimens is often problematic. When collecting sputum samples, it is common to collect low quality specimens, either because patients provide excessive salivary contamination of sputum samples, or do not produce any sputum. Error! Reference source not found. summarizes some of the factors that can lead to a negative AFB smear microscopy result after the collection of a routine sputum sample.

**Limitations of collected sputum samples for smear and culture processing**

<table>
<thead>
<tr>
<th>Sputum Processing Stages</th>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sputum collection</strong></td>
<td>• Inadequate sputum sample (i.e. oropharyngeal sample)</td>
</tr>
<tr>
<td></td>
<td>• Inappropriate sputum container</td>
</tr>
<tr>
<td></td>
<td>• Sputum stored too long before microscopic examination</td>
</tr>
<tr>
<td><strong>Sputum processing</strong></td>
<td>• Faulty sampling for smear</td>
</tr>
<tr>
<td></td>
<td>• Faulty smear preparation and staining</td>
</tr>
<tr>
<td><strong>Smear examination</strong></td>
<td>• Inadequate time spent examining smear</td>
</tr>
<tr>
<td></td>
<td>• Inadequate attention to smear</td>
</tr>
</tbody>
</table>

Table 2. Factors that can lead to a negative AFB smear microscopy result on regular sputum samples

Source—Adapted from Long R. (32)

Demonstration of acid-fast bacilli in a smear made from a clinical specimen provides an initial diagnosis of mycobacterial disease, while the isolation and identification of the mycobacterium on culture provides a definite diagnosis of TB. In the case of children and HIV positive patients, current guidelines for the management of such cases have

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\(^1\) The threshold for detecting bacilli on microscopy is about 5000-10000 bacilli/mL, while the infecting dose is estimated to be fewer than ten organisms.
established that all samples need to be cultured. Even though culture requires a greater amount of sputum\(^2\), only 10 bacilli/mL are needed [in concentrated samples] for a cultured specimen to be positive, fact that confers sputum culture a higher sensitivity (70-90\%) than that of smear. Nevertheless, bacteriological confirmation of TB via culture methods is arduously long due to the mycobacterium’s slow growth rate.

1.3.1.2 Current alternative sample collection methods

Without effective, rapid and affordable diagnostic tools, the bacteriological confirmation of TB will not be established in patients in disease-endemic areas.

In the presence of factors that impede the collection of good quality specimens, different methods have been recommended as an alternative to routine sputum. For example, because of the difficulty in achieving bacteriologic confirmation in sputum smear-negative disease or paucibacillary cases, gastric lavage and fiber-optic bronchoscopy (FOB) with bronchoalveolar lavage (BAL) have been recommended as the reference diagnostic tools to collect adequate specimens and thus, improve the sensitivity of AFB smear microscopy and culture (33, 34). Both, BAL and gastric lavage have shown good results, nevertheless tolerability of the procedures and safety become an issue given that these are invasive specimen-collection methods. Moreover, there are notable resource implications for both procedures. For instance, in order to obtain gastric specimens, patients may be required to stay in hospital while two or three samples are consecutively taken. Lobato et al did demonstrate that the yield of gastric aspirates from paediatric outpatients was similar of that in hospitalized patients (35). Although the yield from gastric aspirates is relatively low, it also has been shown that when gastric lavage is done on three consecutive days, its diagnostic yield is better than that of FOB/BAL for the bacteriologic diagnosis of TB.

\(^2\) AFB smear processing requires 0.01 mL per slide. Once the sample is extended in 10,000 microscopic fields, in average, 100 to 200 fields are read, while \(M.\) \(tuberculosis\) culture requires 0.1 mL of a concentrated sample.
Although FOB/BAL has additive value in the rapid diagnosis of TB (36); however, the sensitivity of sputum or FOB/BAL microscopy for the detection of AFB is variable, ranging from 50 to 80% for three consecutive specimens (37). Moreover, this technique requires highly sophisticated equipment which is unavailable in high TB burden areas or resource-constrained settings in the developing world.

1.3.1.2.1 A simple and cost-effective method of diagnosis

Simpler and more accurate diagnostic tools must be implemented in low and middle income countries as a key resource in the fight against TB. For several years, sputum induction has been used as a method to collect respiratory specimens directly from the lungs for the macro and microscopic study of a number of respiratory pathologies. It has been implemented as a diagnostic tool to detect morphologic changes in lung carcinoma; to observe patterns of airway inflammation in asthmatics and patients with chronic obstructive pulmonary disease (COPD); and to confirm the diagnosis of Pneumocystis jiroveci pneumonia in HIV infected individuals. This method has been described as a useful tool in the diagnosis of TB, especially in paucibacillary cases. Furthermore, this diagnostic tool is suitable for resource-limited areas where bronco-alveolar or gastric lavage are not financially feasible.

1.3.2 Controlling TB transmission during diagnostic work-up of patients suspected with TB disease

In 1994, the Centers for Disease Control and Prevention (CDC) published the guidelines for preventing the transmission of pulmonary TB in health-care facilities. The guidelines were issued in response to 1) a resurgence of pulmonary TB disease that occurred in the United States in the mid-1980’s and early 1990’s; 2) the documentation of several high-profile health-care–associated (previously termed —nosocomial”) outbreaks, related to
an increase in the prevalence of TB disease and HIV co-infection; 3) lapses in infection-control practices; 4) delays in the diagnosis and treatment of persons with infectious TB disease; and 5) the appearance and transmission of multidrug-resistant (MDR) and extensively drug-resistant (XDR) *M. tuberculosis* strains. The 1994 guidelines, which considered statements issued in 1982 and 1990 about the dramatic increase in global trends of TB, presented recommendations for TB infection control based on a risk assessment process that classified health care institutions in accordance with different categories of TB risk.

### 1.3.2.1 Adoption of nosocomial / health care associated TB control measures in developing countries

TB transmission occurs in all overcrowded and poorly ventilated spaces, such as hospitals, schools, prisons, households and work places. However, the CDC guidelines for TB infection control were designed primarily for health care facilities in industrialized countries (25). By contrast, in low and middle income countries, infection control strategies as proposed by the CDC remained unachievable due to the high cost of implementation (38).

The WHO acknowledged that TB infection control was largely neglected in low and middle income countries, principally due to inappropriate allocation of resources, unclear policies, and lack of awareness of TB control (39). Consequently, the WHO designed a framework for the implementation of TB infection control measures in health-care facilities, congregate settings and households, centering attention in low and middle income countries. This framework was designed under the same principles or hierarchical levels established by the CDC: administrative, environmental and respiratory protection controls, and outlined cost-effective strategies and patient-specific measures to prevent the transmission of *M. tuberculosis* in resource-constrained settings (40).
The framework on TB infection control in health-care facilities, congregate settings and households highlighted individual and community participation as key elements the control of TB. Also, it was specified that in order for communities to help stop transmission of the disease, they should firstly understand how TB affects them and their families, and also how the disease is transmitted, cured and prevented. However, patients’ knowledge, perceptions and attitudes towards TB depends on socio-cultural and economic factors. Several studies have reported how prejudice and stigma can influence health seeking behaviour in individuals with suspected TB (41-43). Others have reported the correlation between TB knowledge and completion of chemotherapy (44, 45). Relatively little research has been conducted on the acceptability and implementation of measures to prevent the transmission of TB in community settings.

1.3.3 Need for improvement of infection control methods

TB is not exclusively a disease of the poor; however, the disease imposes a social and economic burden on individuals of all ages from communities and societies everywhere, especially in very poor populations where accurate and simpler diagnostic tools as well as infection control measures are lacking or are poorly implemented. Poverty increases the risks of TB infection and the development of TB disease, and adequate and affordable diagnostic tools could prevent delays in diagnosis in high TB burden areas, and so the implementation of simple and cost-effective infection control measures could reduce the transmission of \emph{M. tuberculosis} in at high-risk individuals and communities (46-48).

Attention has been focused on the need for the development of new and better medicines and, high-technology diagnostic systems. Despite global expenditures on TB diagnostics, large numbers of TB cases are detected late or are not detected at all. Implementation of new diagnostic methods such as molecular or biochemical technologies
might not be viable for resource-constrained settings, but without affordable, rapid and simple diagnostics, patients suspected with TB in the developing world would not be diagnosed opportune. A method such as sputum induction which certainly can improve the sensitivity of both, smear microscopy and culture, could be of practical use in disease-endemic settings and contribute to an increase in diagnosis rate, a subsequent reduction of *M. tuberculosis* transmission (*due to early administration of TB chemotherapy*) and therefore it will have a positive impact on morbidity and mortality attributed to TB.

In addition to simple diagnostic methods, adequate implementation of patient-specific and other low-cost infection control measures could reduce repetitive exposure to *M. tuberculosis*, not only in close contacts of patients with TB, but also in health care workers. Moreover, empowerment of patients with TB through on-going educational programmes to implement TB infection control measures could be more cost-effective than diagnosing and treating every new reported TB case.

In 2007, Loveday *et al* identified three major ―leakages” during patients’ journey from diagnosis to treatment completion (See Figure 3) (49). The identified ―leakages” highlight the problems and challenges that TB control programmes face during different stages of diagnosis and treatment. Initially, patients with active TB were not registered as patients with TB—total leakage of smear-positive patients with TB from the laboratory to the TB register was 58%; 31% were counted as having leaked from the system between the hospital and the clinic, and finally, 39% of all diagnosed patients who started chemotherapy, failed to complete it (49). Loveday’s study highlighted the importance of adopting measures that not only help resource-constrained areas increase TB diagnosis rates but also help control TB transmission.
The need to put into practice simple and affordable diagnostic methods and management of infection control for patients with suspected TB in high TB burden settings, prompted us to conduct two studies. The first one, to determine the diagnostic yield of sputum induction, a rapid and simple method to diagnose TB; and the second, to evaluate TB knowledge levels and acceptability of patient-specific infection control measures among newly diagnosed patients with TB.

Objectives

**Sputum Induction Project:**
• To conduct a systematic review and meta-analysis of studies reporting the use of sputum induction for the diagnosis of pulmonary tuberculosis.

**Infection Control Measures Project:**

• To conduct an observational study to determine TB knowledge and acceptability of patient-specific infection control measures among patients suspected with TB and newly TB diagnosed patients.
REFERENCE LIST


37. Diagnostic Standards and Classification of Tuberculosis in Adults and Children. This official statement of the American Thoracic Society and the Centers for Disease Control and Prevention was adopted by the ATS Board of Directors, July 1999. This statement was endorsed by the Council of the Infectious Disease Society of America, September 1999. Am J Respir Crit Care Med. 2000;161(4 Pt 1):1376-95. Epub 2000/04/14.


Chapter introduction

In the following chapter, we present a literature review on current methods to control TB. The first section describes aspects related to the collection of pulmonary specimens for the bacteriological confirmation of TB, and also, it points out characteristics of sputum induction, its utility and diagnostic yield in patients with TB, and its advantages over other diagnostic procedures. Then, the second section describes fundamental aspects on infection control in TB, and lastly, we focus on the implementation of patient-specific measures to reduce the transmission of *M. tuberculosis*.

2.1 Sputum Induction and Tuberculosis

2.1.1 Background

Collection of sputum is the simplest non-invasive procedure available to examine aetiologic agents in tracheal, bronchial and pulmonary infections as well as to evaluate cytologic and inflammatory changes in the tracheobronchial tree. However, some patients are unable to produce sputum for examination. In such cases, sputum induction is a key diagnostic procedure. This diagnostic tool allows collection of adequate samples from the lower respiratory tract in patients suspected with TB—particularly patients with
paucibacillary TB or sputum-unproductive cases, providing an opportunity for bacteriologic diagnosis and also, giving the public health authorities the opportunity to administer effective and prompt treatment to the patient.

The method was first described by Garcia et al in 1952 (1). Initially, bronchial secretions were obtain by nebulization and inhalation of sterile distilled water (1). The method was soon modified and several researchers induced sputum production by inhalation of heated hypertonic aerosols. Initially, Bickerman et al used various concentrations of hypertonic solutions ranging from 3 to 15 %, for the cytologic diagnosis of lung cancer (2, 3). Subsequently, the inhalation of sodium chloride was used to collect pulmonary specimens from patients under investigation for TB. Hensler et al and other researchers implemented sputum induction in absence of spontaneous cough, or scant sputum production (4-7).

Even though preliminary studies set the scene for the use of sputum induction in the diagnosis of pulmonary TB, particularly in paucibacillary patients with TB, its clinical use gradually declined as a result of an increased risk for nosocomial transmission of *M. tuberculosis* and the advent of bronchoscopy (8).

Collection of pulmonary secretions by inhalation of hypertonic solutions remained ideal to examine cellular and molecular markers of airway inflammation in patients with asthma and chronic obstructive pulmonary disease (COPD) (9). Interest in the technique for the diagnosis of pulmonary infections returned following the increasing number of cases with unusual infections during the beginning of the HIV epidemic in the 1990’s (10). Initially, sputum induction appeared to have value in the diagnosis of *Pneumocystis Jiroveci Pneumonia* (PJP) (11, 12). Moreover, various studies provided relevant information on the
diagnostic utility of sputum induction for confirming the presence of *M. tuberculosis* in immunocompromised individuals or paucibacillary cases (13).

2.1.2 The pulmonary effect of hypertonic solution inhalation

Hypertonic saline has been shown to have a favourable effect on mucus rheology (14). The postulated mechanism whereby inhalation of hypertonic saline improves mucociliary clearance is as follows: (a) hypertonic saline breaks the ionic bonds within the mucus gel, thereby it reduces the degree of cross-linking and entanglements and lowers the viscosity and elasticity of the mucus (15); (b) hypertonic saline also increases the ionic concentration of the airway surface fluid, causing water to be drawn into the airway lumen along its osmotic gradient, thereby it rehydrates the airway surface fluid and promotes the separation of mucus, which facilitates its expectoration; (c) hypertonic saline stimulates ciliary activity via the release of prostaglandin E\(^2\), which increases mucociliary clearance and stimulates the cough reflex (16, 17).

In order for hypertonic solutions to improve mucociliary clearance, the aerosol must be deposited correctly in the tracheobronchial tree. The effectiveness of deposition of an aerosol in the tracheobronchial tree is determined by a number of physical and physiologic factors (18, 19). Theoretically, maximum aerosol deposition on all segments of the respiratory tree would be desirable to facilitate bronchial drainage and later expectoration, and even though factors such as density and tonicity of the aerosol, temperature, volume of solution nebulized per minute, and the rate and depth of respiration, have been described as contributing factors to deposition inefficiency, particle size has been the most important determinant for the deposition of aerosol particles(18).
Particle size and aerosol density depend on the nebulization device used for hypertonic solution inhalation. Different devices, such as ultrasonic nebulizers, conventional nebulizers (or air compressors) and oxygen cylinders have been used to deliver hypertonic aerosols directly into the respiratory system. Although every device can produce a regular "mist" for inhalation, only aerosol particles in the therapeutic range of 1-10 μm in diameter will be deposited in the airway surface. Even though all of the previously mentioned devices can produce particles within that range, their size varies due to the nebulizer output (flow). Either very small particles (< 1 μm) or large particles (>10 μm) will not be properly deposited. Small particles, due to their instability and high speed, will enter the airway, remain suspended in the airstream and afterwards approximately 80 percent will be exhaled, whereas bigger particles will be deposited in the upper respiratory tract.

2.1.3 TB diagnosis in paucibacillary and sputum unproductive patients suspected with TB

In its most recent report on TB control, the World Health Organization (WHO) presented the following disaggregated estimates of the global burden of TB: 9.4 million incident cases, 14 million prevalent cases, 1.3 million deaths among HIV-negative people, and 0.4 million deaths among HIV-positive people. Moreover, 57% of global notifications were sputum smear-positive (2.6 million cases) whereas the remaining 43% were reported as sputum smear-negative patients (2.0 million cases) (20). The latter represents a clear challenge for the early detection of patients suspected with TB, especially in developing countries, which account for 95% of all estimated cases worldwide (20, 21).
The microscopic examination of routine sputum for *M. tuberculosis* is still the reference standard test for TB diagnosis (22). However, in sputum smear-negative patients (commonly paucibacillary and sputum-unproductive cases), FOB/BAL and gastric lavage have been suggested as the most optimal diagnostic tools (23). However, the use of these diagnostic tools faces two major limitations: on the one hand, resource-constrained settings in the developing world may not have the health care facilities supplied with materials and instruments to collect specimens via FOB/BAL and gastric lavage; and on the other hand, the diagnostic yield of such alternative diagnostic tools has been reported to be of equal or lower to that of sputum induction.

The use of sputum induction for establishing a diagnosis in patients with suspected smear-negative pulmonary TB has been previously studied. Parry *et al* for example, investigated the yield of this procedure and concluded that sputum induction was a useful technique for improving the case detection rate of patients suspected with TB in resource-limited settings (24).

2.1.3.1 Hypertonic inhaled solutions for the diagnosis of tuberculosis

The clinical utility of sputum induction provides a real alternative to FOB and BAL in the diagnosis of pulmonary TB. Moreover, sputum induction has been reported to be as effective as, or superior to, gastric lavage or FOB for diagnosis of TB (23, 25). As a matter of fact, this method has been shown to have a better diagnostic yield than spontaneous sputum and gastric aspirates (25) and several studies have also demonstrated that the yield of one induced sputum—as a primary diagnostic modality for paucibacillary cases—is at least equivalent to that of one bronchoscopy with BAL (26, 27). The yield of sputum induction is

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3 Routine sputum (also known as spontaneous sputum) is understood as a sputum specimen which is provided by an individual in whom TB—or any other respiratory infection is suspected. This specimen is usually provided by the patient in a spontaneous (sometimes self-provoked) cough without medical or pharmacological assistance.
further increased when multiple pulmonary specimens are obtained, with reported mycobacterium identification rates by smear microscopy of 91% to 98%, and 99% to 100% by culture, significantly higher than with bronchoscopy alone (27).

Several authors have evaluated not only the clinical utility of the procedure but also its tolerability by patients suspected with TB and safety. Kawada et al found sputum induction to be better than gastric aspiration in patients suspected with TB (28, 29). Anderson et al reported that the diagnostic yield of sputum induction is as good as FOB for diagnosis of smear-negative pulmonary TB (23). Hatherill et al found the diagnostic yield of sputum induction in children to be equivalent to that of gastric lavage (30). Conde et al reported that sputum induction was safe, with high diagnostic yield and substantial agreement with FOB, in both HIV seronegative and seropositive patients (26). Menzies et al championed the role of induced sputum in the diagnosis of pulmonary TB and stated that, as compared to bronchoscopy, repeated induced sputum testing offers many advantages in terms of safety and cost, with at least comparable, if not greater diagnostic yield (8). However, induced sputum testing in the diagnosis of pulmonary TB carries a risk of nosocomial TB (8).

2.1.3.2 The use of sputum induction in low resource settings

Sputum induction is a potential tool for improving specimen quality and positivity rates in smear microscopy and culture techniques. Unlike routine sputum, sputum induction allows the collection of pulmonary secretions. The inhalation of saline solutions increases and liquefies the amount of pulmonary secretions while it causes a slight irritation of the
airway, promoting cough, fostering mobilization of mucus and allowing patients to expectorate satisfactory quality specimens (9).

Studies from high TB burden settings in which sputum induction has been used in patients suspected with TB who were found to be AFB smear negative have shown that this procedure is a safe, simple and cost effective method to obtain sputum in smear negative patients (10, 13, 31). Unfortunately, one of the limitations with this procedure is that up till recently, no clear protocols to carry out the procedure have been described. Technical variations to implement this method (i.e., different saline concentrations; different outputs; nebulisation times) clearly reflect the variability in the diagnostic yield of sputum induction. Current literature shows yields that range from 20% to 99%. Many factors could be causing the wide range in the yield of this procedure. For example, different saline concentration, nebulization devices (e.g., ultrasonic or venturi-type face mask nebulizers), flow rate provided during nebulization, time, patient’s position during saline administration, and others that have not been wide explored. Toubes et al compared the performance of two sputum induction methods and concluded that the collection of sputum samples with an ultrasonic device was more effective than the use of oxygen cylinders for the same purpose (32). Reported diagnostic yields are 66% and 46%, respectively. Toubes’ study has been the only report which explores other technical factors that can affect the procedure. Although saline solutions increase airway hyperactivity, the use of variable sodium chloride (NaCl) concentrations has commonly been studied in asthma and COPD, as a mean to determine safety of the procedure and in order to recommend the use of bronchodilators for patients with obstructive lung disease (9, 33). No studies to standardize the procedure have yet been conducted.
Although this method has been described as a high-risk procedure on account of infectious droplet nuclei that are expelled into the air while patients suspected with TB are coughing, it is clear that implementation of appropriate infection control measures should reduce the likelihood of transmission of *M. tuberculosis* to health care workers and other patients. In low and middle income countries, where major infrastructural or environmental changes are needed to control TB, measures such as the implementation of negative pressure isolation rooms or specific TB isolation areas can not be carried out due to their high operative costs. In 1997, Kellerman *et al* determined the costs of infection control measures at hospitals with a history of *M. tuberculosis* outbreaks and concluded that the costs associated with implementing control measures similar to those recommended by the CDC involved the largest capital outlay in health care facilities (34). Therefore, the implementation of low-cost strategies has been recommended in resource-limited settings.
REFERENCE LIST


2.2 INFECTION CONTROL IN TUBERCULOSIS

2.2.1 Risk of *M. tuberculosis* transmission

*M. tuberculosis* can be easily spread by aerosol droplets expelled by people with active disease when speaking, coughing, sneezing or singing (1). These infectious aerosol droplets contain the mycobacterium, which being only 0.5 to 7 µm in diameter, can easily be inhaled and become established in the lung parenchyma of susceptible individuals.

In a study conducted to measure the number of pathogenic organisms that could be expelled from the respiratory tract, it was determined that speaking, coughing and sneezing produce a significant quantity of mycobacterium-containing aerosols (2). Accordingly to Duguid, speaking and coughing could release between 0 to 210 and 0 to 3500 infectious particles respectively, whereas by sneezing, a bacilliferous individual could liberate from 4500 infectious particles to more than one million particles (2). Beggs *et al* studied the most significant factors that influence and/or increase the probability of TB transmission and the development of disease (3), and determined that for a susceptible individual to become infected with *M. tuberculosis* and develop disease, it was necessary to consider the following factors: quantity of infectious droplets expelled by the infectious source ⁵; virulence of the *M. tuberculosis* strain; duration of exposure and ventilation rate.

Subsequent studies estimating the infectiousness of *M. tuberculosis*, determined that the infectious dose of *M. tuberculosis* is very low, and that inhaling fewer than ten bacteria may cause TB infection and subsequent TB disease (4-6). Therefore, preventing the generation of infectious droplet nuclei by the early identification of patients suspected with

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³‡Infectious Source” refers to an individual in whom TB is highly suspected or a TB patient who is not receiving or responding to anti-tuberculosis chemotherapy.
TB and administration of effective chemotherapy can reduce the infectivity of an individual. Although the virulence of *M. tuberculosis* mostly depends on intrinsic properties of the mycobacterium, duration of contact and frequency of exposure are important factors in the transmission of TB, with the risk of infection increasing with the total time of exposure (3). If a susceptible person remains in the presence of a patient with active pulmonary TB for long enough, they will inevitably become infected, even when the concentration of infectious particles is relatively low (3). It is also probable that brief exposures to a bacilliferous source can also increase the risk of transmission if contact between a susceptible individual with an active case of TB remains frequent (7). The ability of an infected individual to transmit *M. tuberculosis* also depends on ventilation. Smear positive patients usually contain ≥ 5000 bacilli per millilitre of sputum (8). Under insufficient ventilation conditions, *M. tuberculosis* transmission would result due to dissemination of infectious droplet nuclei that remain suspended in air. Although aerosolisation of infectious particles depends upon the frequency, force, and region of the cough, simple respiratory manoeuvres (speaking; coughing; and sneezing), can produce infectious aerosols containing a large amount of bacilli. Therefore, poor ventilation conditions increase the risk of infection in households, health care facilities and other congregate settings\(^6\) with insufficient ventilation (9-11).

In health care facilities, once a TB suspect seeks medical attention, the risk of infection for health care workers and other inpatients might be diminished considerably if infection control measures (early diagnosis and treatment and specific strategies to reduce transmission) are correctly set in place. However, the risk of infection for close contacts is not reduced immediately after patients start receiving TB chemotherapy.

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\(^6\)The term congregate settings include correctional facilities and military barracks, to homeless shelters, refugee camps, dormitories and nursing homes.
2.2.2 Fundamentals of infection control

The CDC guidelines were designed when *M. tuberculosis* re-emerged as a significant nosocomial pathogen (12). Several nosocomial outbreaks of TB involved inpatients and health care workers (12, 13) late 1980s and early 1990s, and as stated by the CDC Division of Tuberculosis Elimination, the factors contributing to these outbreaks included (1) the delayed recognition of patients with tuberculosis; (2) the convergence in health care facilities of bacilliferous cases and immunocompromised patients; (3) the delayed diagnosis and initiation of effective anti-tuberculosis chemotherapy; (4) inadequate ventilation for TB isolation and (5) inadequate precautions for cough-inducing procedures in patients suspected with TB. In response to this problem, TB infection control measures aimed to ensure prompt detection, airborne precautions, and rapid diagnosis of patients suspected with TB and early treatment of patients with confirmed TB disease through the implementation of a combination of measures grouped as administrative, environmental respiratory protection, and described as follows:

2.2.2.1 Administrative controls

This first set of administrative measures intended to reduce the risk of exposing uninfected individuals to patients suspected with TB by ensuring the development of infection control policies and protocols that allow the rapid identification, diagnostic evaluation, and treatment of persons likely to have TB; also by educating and training of health care staff on TB, biosafety practices, and health care workers screening for TB infection and disease (12).
2.2.2.2 Environmental controls

The second level of the hierarchy defined by the CDC was the use of environmental controls to prevent the spread of *M. tuberculosis*, and reduce the concentration of infectious droplet nuclei in ambient air. Primary environmental controls consisted of controlling the source of infection by using local exhaust ventilation (natural and mechanical) and room air extractors to remove contaminated air to the outside. Secondary environmental controls consisted of controlling the airflow to prevent contamination of air in areas adjacent to the source and cleaning the air by using HEPA filtration, or Ultraviolet germicidal irradiation (UVGI) (12).

2.2.2.3 Respiratory protection controls

The first two control levels were designed to minimize the number of areas in which exposure to *M. tuberculosis* could occur and, therefore, minimize the number of individuals that could be exposed. However, these control levels aimed at reducing, but do not eliminate, the risk for exposure in areas in which exposure could still occur (procedure and isolation rooms). Since persons entering these areas could be exposed to *M. tuberculosis*, the third level of the hierarchy was the implementation of respiratory protective equipment in situations that posed a high risk for exposure. Therefore, health care staff working in isolation wards or who were in frequent contact with patients with TB should use high efficiency masks for protection against infection with *M. tuberculosis*. Moreover, with the implementation of a respiratory-protection program, in which health care workers were instructed on the correct use of respiratory protection, and in which patients received education on respiratory hygiene and cough etiquette procedures, the risk of TB exposure for other patients and health care workers was reduced (12).
2.2.3 Implementation of initial infection control measures

In a descriptive study, Blumberg et al evaluated the effectiveness of the infection control measures proposed by the CDC (13). Researchers measured the number of TB exposure episodes and tuberculin skin test (TST) conversion rates among health care workers before and after the implementation of administrative (or managerial), environmental, and personal respiratory controls. Their experience at an institution located in a high TB burden area showed that, implementation of these guidelines was effective in preventing nosocomial transmission of TB to health care workers (13).

Basu et al constructed a mathematical model to simulate TB transmission and investigated the effect of infection control measures on the epidemic trajectory of MDR TB in the rural community of Tugela Ferry, South Africa (14). They modelled the reduction of hospitalisation time for patients with TB, the implementation of rapid drug-susceptibility assays, the involuntary detention of XDR patients with TB who refused to take chemotherapy or default from treatment, improved natural ventilation by using fans and opening windows, the use of a mechanical ventilation systems, HEPA filters, UVGI and the use of N95 respirators for health care workers and surgical masks for patients with TB, as infection control measures (14). The model predicted that different combinations of the early mentioned infection control strategies could prevent almost 50% of XDR TB cases, even in resource-constrained settings. Also, emphasis was made on the importance of implementing parallel community-based programmes to reduce TB transmission within communities. Projections of the model indicated that if infection control measures were not introduced, up to 1300 cases of XDR TB were predicted to occur (14).

Although Basu et al concluded that correct implementation and combination of infection control strategies could in fact, reduce the concentration of infectious droplet
nuclei, it is evident that environmental and respiratory-protection measures such as the use of high-tech diagnostic tests, mechanical ventilation systems, HEPA filters, UVGI, and the use of N95 respirators, are not available for most low and middle income countries. Another study conducted to determine the limits of protection achievable by improvements in environmental controls, demonstrated that in cases where the concentration of infectious particles is very high (e.g., enclosed spaces, settings with air recirculation), even large ventilation rates make very little difference on infection rates (15). Nardell’s study also highlighted the importance of implementing a combined set of infection control measures (15).

Work carried out in several countries has provided evidence on effectiveness of the three-level hierarchy of control measures (12, 16, 17). However, the adoption of these guidelines faced one major challenge for the control of the epidemic in high burden countries (HBCs): A high operational cost. As a solution to this challenge, and due to the recent outbreaks of MDR-TB and XDR-TB, the WHO adapted the guidelines earlier established by the CDC and recommended a set of measures that could be implemented in congregate settings and households from resource-limited areas (18); these recommendations were based on the same hierarchy of control measures or infection control policies previously described by the CDC.

2.2.4 Patient-specific infection control measures

The WHO described the importance of community participation to reduce the transmission of TB and stated that the empowerment of the community—particularly at-risk groups—was a crucial element in TB control and urged public health authorities to create public awareness campaigns to allow populations to understand TB, its impact on communities, transmission patterns, and more importantly, to recognise that TB could be
cured and prevented. Therefore TB education and a particular set of recommendations to control TB infection in health-care facilities, congregate settings and households were recognized as a fundamental element of TB control in developing countries.

Recommended patient-specific infection control measures\textsuperscript{7} included:

- Implementation of cough etiquette and respiratory hygiene protocols, and
- Implementation of environmental practices such as:
  1. Improvement of Ventilation - Houses should be adequately ventilated, particularly rooms where people with infectious patients with TB spend considerable time (natural ventilation may be sufficient to provide adequate ventilation),
  2. Spending as much time as possible outdoors (while smear positive),
  3. Sleeping alone in a separate, adequately ventilated room, if possible (while smear positive),
  4. Spending as little time as possible in congregate settings or in public transport (while smear positive),
  5. And, in the case of children below five years of age, they should spend as little time as possible in the same living spaces as the smear positive patient.

\textsuperscript{7}Recommendations developed by the WHO and published in an evidence-based policy report for the implementation of TB infection control.
In spite of being low-cost strategies to reduce *M. tuberculosis* transmission, patient-specific infection control measures have not been well-studied. Researchers have centred their attention on documenting the risk of nosocomial transmission of *M. tuberculosis* as an occupational hazard for health care staff, mainly in industrialised countries (12, 13, 19, 20). The design and performance of isolation areas, negative pressure isolation rooms (NPIR) and respiratory wards have been well documented (17, 21, 22). The effectiveness and efficiency of high efficiency particulate air (HEPA) filtration has been evaluated for several years but natural ventilation as a strategy to improve ventilation in resource-limited settings has not been well explored.

There is clear evidence of the occupational risk of TB for health care workers in facilities or areas with a high prevalence of TB. However, close contacts of patients with TB have as much risk of acquiring *M. tuberculosis* infection and developing TB disease as health care workers in these settings do, and a higher risk than do casual contacts (23).

Few studies have given particular attention to TB education and patient-specific infection control measures in congregate settings and households. Escombe *et al* studied natural ventilation as a low-cost alternative to reduce transmission of airborne infections, especially in resource–limited settings (10, 24). Although this study was carried out in a health care facility, it provides basic information on how by implementing a low-cost strategy such as opening windows and doors, natural ventilation is maximised, and the risk of airborne TB infection (percent of susceptible persons who are infected) decreases. Escombe's study showed that in order to improve ventilation and reduce the amount of infectious droplet nuclei, opening windows and doors can work as well as a negative pressure room (10, 24).
Although improvements on natural ventilation may be sufficient to provide adequate air changes in an area with a high potential risk of TB transmission, no more studies reporting the utility and cost-effectiveness and feasibility of natural ventilation have yet been published. Moreover, although improvements in natural ventilation and the use of fans in households are a highly recommended practice for patients with TB, no studies showing the effectiveness and feasibility of these simple measures have been conducted in resource-constrained areas.

In addition, other strategies that aim at decreasing infectious aerosol particles in closed environments and reducing exposure for contacts of patients with TB include the use of face masks when available, covering mouth principally when coughing or sneezing, and spend as little time as possible with susceptible individuals (e.g., children; HIV infected individuals). The use of face masks as a means to prevent health care workers from inhaling infectious droplets has been a well-known practice for the prevention of respiratory infections. As for TB, due to the characteristic size of the mycobacterium, the use of high efficiency masks (i.e. N95 masks) is a common practice when institutions can afford the provision of such masks for their staff (25). Face masks have been recommended for patients with TB, patients with suspected TB and health care workers. However, in some facilities, high efficiency masks can not always be afforded, and as a result, institutions must decide who gets to wear them. Nettleman et al conducted a study designed to determine the cost of high-efficiency masks required in a health care facility, and the number of TB cases in employees that could potentially be prevented; the study concluded that high-efficiency masks are a costly means of trying to prevent TB, and that costs could be reduced by reusing masks or by restricting the number of health care workers allowed to have contact with potentially infectious patients (25). Therefore, the efficient applicability of this measure depends on the effective institutional infection control policies, allocation of resources for each institution, and the
burden of TB. Controlling the sources of infection by either providing patients with high efficiency masks or giving them instructions to cover their mouth when coughing, could theoretically, reduce the infectious droplets that are released and that remained suspended in the air. However, patients might not implement this measure at all times, especially in their homes, work places and health care facilities. Some of the reasons that could be contributing to this are described below:

- Patients do not feel the need for infection control measures in their homes and/or work places;
- Patients might not have a clear understanding of the importance of covering mouth with a face mask, handkerchief, or with their hands;
- Patients might be afraid of social stigma and prejudice if they are identified as patients with TB;

Previous reports have indicated that one of the major limitations in TB control programmes is the deficient educational systems (26). If patients do not understand how TB is transmitted, how the disease can affect their close contacts, and how they can help prevent TB transmission, the measures could not be implemented, and transmission will continue.

Respiratory protection strategies as well as measures to reduce exposure time (e.g., patients with TB sleeping in a room by themselves or spending less time with children) if applied correctly, could reduce the amount of infectious droplets in congregate settings and households. Under unavailability of DST for all patients with TB in resource-constrained settings, even if patients are receiving TB chemotherapy, the use of face masks or the implementation of good respiratory hygiene (cough protocols) could significantly decrease
the exposure to *M. tuberculosis* to health care providers and close contacts of patients with TB.

### 2.2.5 Gap in Infection Control

Little research and limited resources have been expended on TB infection control during the past 50 years especially the implementation of preventive and cost-effective measures in different settings other than health care facilities. There has been extensive guidance written on prevention of pulmonary TB at health care settings (3, 13, 19) but little on transmission of TB in congregate and household settings. A number of studies have addressed the health education requirements of at-risk populations and the need to increase patient’s knowledge about TB (27-29). Yet the literature reveals that, overall, the emphasis in health care has centred on TB treatment, adherence to anti-tuberculosis drugs, but not on the implementation of patient-specific measures to reduce the possibility of TB transmission to close contacts.

In spite of growing evidence that nosocomial transmission of TB is a critical factor in the epidemic HIV-associated TB and the emergence of MDR-TB and XDR-TB strains, many argue that the evidence demonstrating that community transmission is not playing an equally important role in resource-constrained settings is not available. A top priority, then, should be to obtain that evidence, so that resources will be allocated toward protecting health care workers, patients, and other occupants of congregate settings (i.e. HIV/AIDS facilities, prisons, refugee camps, etc).

In a study conducted by Jaramillo on the impact of health education on TB, it was argued that poor TB education to patients and health care workers is one of the fundamental
challenges of the current strategy of control (30). Another study conducted in Rwanda about the perception and beliefs of cough revealed that many patients, regardless of the severity of their disease, are too afraid to even seek early care (31). TB knowledge therefore, is an important contributing factor that interferes with TB control activities; particularly in infection control because in spite of the availability of some strategies such as TB chemotherapy or the feasibility of implementing patient-specific infection control measures, some patients refuse to adopt these measures because of the experienced or believed social stigma which seems to outweigh the fear of having TB (31). John et al stated that every person must participate in TB control activities and that providing basic information about TB and practical elements to control the disease in resource-limited settings must become a common practice in entire communities (32).
REFERENCE LIST


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Chapter Introduction

The following section presents the methods used to conduct a systematic review and meta-analysis of studies reporting the use of sputum induction for the diagnosis of pulmonary TB; second, it describes the steps conducted on a questionnaire-based study to determine the knowledge and acceptability of patient-specific infection control measures among patients suspected with TB, and among patients with TB at baseline and at the end of treatment.

3.1 Methods for Sputum Induction for the Diagnosis of Pulmonary TB

3.1.1 Study design

We conducted a systematic review, aiming to identify, appraise and synthesize studies reporting the yield of sputum induction in the diagnosis of pulmonary TB. Explicit methods used in systematic reviews allow researchers to produce more reliable findings that can be used in the evidence-based decision making process. In our case, presenting the summary of the yield of sputum induction would allow us to reach a conclusion on the clinical use of sputum induction as a practical and effective method for improving the collection of pulmonary specimens and establishing a bacteriological confirmation of TB.
3.1.2 Search strategy

We searched the online database of biomedical citations and abstracts, MEDLINE/PubMed using a search strategy which combined logical operators from the Boolean language (OR, AND, NOT) with a sequence of medical/clinical terms included in our PICO framework (See diagram 1). We also conducted a systematic manual search of biomedical journals and conference proceedings for relevant studies to ensure that our search included inaccurately indexed or unindexed papers, as well as to identify papers other than the ones published in high-impact journals. Unavailable electronic copies of Chest Journal and American Journal of Respiratory and Critical Care Medicine (past volumes) were searched. In addition, researchers who had experience in the use of sputum induction as an alternative method for the diagnosis of TB provided us with lists of relevant articles. Also, a fully recursive search of reference lists of the original studies was performed to find studies that were not identified by the previous searches.

P [Population]: ➔ Patients with suspected TB and/or patients with paucibacillary TB disease.

I [Intervention]: ➔ Sputum induction.

C [Comparison]: ➔ Routine expectorated sputum; gastric lavage; nasopharyngeal aspiration; or FOB with bronchoalveolar lavage.

O [Outcome]: ➔ Microbiological confirmation of pulmonary TB.


3.1.3 Inclusion and exclusion criteria

All prospective diagnostic studies that compared sputum induction using hypertonic saline (sodium chloride) solution and compared its yield to any of the following techniques were eligible for review: (1) routine expectorated sputum; (2) gastric lavage; (3) nasopharyngeal aspiration; or (4) FOB with BAL. Studies that used sputum induction with
nebulized solutions other than sodium chloride were excluded from this review; in addition, papers reporting the use of specialized induction devices (eg. Lung flute®); and studies reporting the use of sputum induction for the diagnosis of pulmonary infections other than tuberculosis were also excluded.

3.1.4 Quality assessment and data extraction

In order to minimize human error and selection bias, two reviewers examined each citation for relevance. Those deemed relevant were retrieved in full and compared each study against the selection criteria. We designed an Access® data extraction form and once both reviewers selected the eligible studies, data extraction proceeded (See Table 3); data gathered from these papers were tabulated in a summary data table. Two reviewers crosschecked the information and verified the methodological details of the sputum induction procedure as well as the exact number of cases diagnosed by culture of M. tuberculosis using sputum induction and the total number of patients diagnosed by culture of M. tuberculosis using induction of sputum and/or any of the comparator techniques listed above. In cases in which the data reported by the authors was unavailable or insufficient for the purposes of this review, we contacted authors aiming to complete our data extraction form.

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</tr>
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<td>• Year of Publication</td>
</tr>
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</tr>
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</tr>
<tr>
<td>• Nebulizer output and time</td>
</tr>
<tr>
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</tr>
<tr>
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</tr>
<tr>
<td>• Number of cases diagnosed by other procedure</td>
</tr>
<tr>
<td>• Total of TB cases confirmed by culture</td>
</tr>
</tbody>
</table>

Table 3. Summary of data extracted from each study
3.1.5 Statistical analysis

Pooled diagnostic yield and 95% confidence intervals (CI) were calculated from the raw study data. Diagnostic yield was defined as the number of TB cases diagnosed by sputum induction (numerator), divided by the total number of culture-confirmed tuberculosis cases by any technique (denominator).

3.1.6 Meta-analysis: A random effect model

The goal of a meta-analysis will often be to estimate the overall or combined effect of all the studies reporting the diagnostic yield of sputum induction. Although, the meticulous search in systematic reviews aims to bring together similar studies which can provide a general summary estimate, due to various characteristics of the papers that were selected for this study, we decided to compute a meta-analysis under the random effects model (1, 2). Included papers were assumed to be a random sample of the relevant distribution of effects, and the combined effect estimated the mean effect in this distribution.

3.1.6.1 Measuring heterogeneity and estimating its causes: Sub-group and meta-regression analyses

Sources of variation in meta-analysis include the following: random variation in outcome definition, variation between the patient groups in different studies, variation between sputum induction protocols, and variation in the way a given protocol is implemented. Selected studies showed a difference of effect across various studies. This variability commonly referred to as heterogeneity (3) and which may have been responsible for observed discrepancies in the results of included studies was also graphically and statistically measured.
We measured heterogeneity with the Cochran test (Q) which was calculated as the weighted sum of squared differences between individual study effects and the pooled effect across studies. Also, we used the F statistic to describe the percentage of variation across studies that was due to heterogeneity rather than chance. Given the fact that, selected studies gave us very different effects, we examined the reasons why effects differed across studies by subgroup and meta-regression analyses. These techniques allowed us to work out whether particular characteristics of studies were related to the yield of sputum induction. We identified four groups defined by: (1) age (adults vs. children); (2) saline concentration (<5 vs. ≥5); (3) HIV prevalence; and (4) the use of comparator methods of diagnosis (FOB with BAL). We also conducted a meta-regression analysis as an extension to the subgroup analyses in order to investigate whether particular covariates (‘potential effect modifiers’) explain any of the heterogeneity of our estimated effects between studies. It is not reasonable to assume that all of the heterogeneity is explained, and the possibility of ‘residual heterogeneity’ must be acknowledged in the statistical analysis.

3.1.7 Study duration

This systematic review and meta-analysis of the diagnostic yield of sputum induction was carried out from February 2009 to September 2010.
3.2 METHODS FOR PATIENT-SPECIFIC INFECTION CONTROL MEASURES

3.2.1 Study design

We conducted a prospective observational study to determine levels of TB knowledge among patients with suspected TB and newly TB diagnosed patients. Moreover, we determine which infection control measures for prevention of TB transmission are acceptable among patients with suspected TB and patients with TB in the Breede Valley community.

3.2.2 Data collection tool

We designed a questionnaire survey consisting of a series of questions on core knowledge about TB and patient-specific infection control measures (See Appendix 1). The questionnaire was divided into four main sections: (1) a profile (containing some demographic characteristics of the respondents such as age, gender, employment status, housing conditions) and also, some baseline questions regarding general knowledge on TB, particularly on TB transmission mode; (2) infection control measures at health care facilities; (3) infection control measures at home; and (3) infection control measures at work settings respectively.

Although the Breede Valley region has an average literacy rate of 73% (4), and most participants speak English as their second language, we decided to conduct this questionnaire survey in participants’ home language (Afrikaans and IsiXhosa) and adopted face-to-face interviews as a means to establish rapport with participants and increase participation and response rates. Both, the questionnaire and consent forms were translated by certified translators (See appendix section).
3.2.2.1 Data collection tool development

Questionnaire development and evaluation followed criteria that have been defined as important in patient satisfaction measurement. The development of the questionnaire was based on a review of the literature that included TB knowledge questionnaires and recommendations of members of infection control committees. After a process of peer-review, the questionnaire was revised and adjusted. This process was designed to ensure content validity; that the questionnaire addressed important aspects of TB knowledge and patient-specific measures to control TB in sufficient detail. The resulting questionnaire was then pilot-tested by means of semi-structured interviews with five patients with TB and five patients with suspected TB. Some of the steps in our questionnaire development are summarised in the following graph:

Diagram 2. Questionnaire development phases.

3.2.2.2 Question types

The questionnaire was structured using both, open-ended and closed-ended questions. The response options for closed-ended questions were: dichotomous, and
nominal-polychotomous questions; in some instances, participants had to answer filter and contingency questions, which were determined by their responses to some other question. Open-ended questions were numerical (discrete) variables (i.e., *How many people do you share the room with?; How many people are in the same room with you while you are working?*)

### 3.2.2.3 Validity

In order to improve and test the adequacy of our research instrument, assess the feasibility of this project, and identify logistical problems which might have occurred using proposed methods, we piloted the questionnaire. The initial assessment allowed us to determine if this research tool was valid, in other words, if the questionnaire was measuring what it intended to measure and how appropriate it was for participants. The questionnaire was tested to ten respondents whose answers were only used for evaluation purposes. After the questions were answered, we asked the respondents for any suggestions or any necessary corrections to ensure further improvement and validity of the instrument. The questionnaire was revised based on the suggestion of the respondents, and irrelevant questions were excluded. Also, vague or difficult terminologies were changed into simpler ones in order to ensure the participants’ comprehension.

Furthermore, the questionnaire was peer-reviewed by three members of the infection control committee from the Brewelskloof Hospital, two registered nurses from local TB clinics in the Breede Valley Municipality, and six academic members from the South African Tuberculosis Vaccine Initiative (SATVI).

Pre-testing the questionnaire and peer-revision helped us control both, *external* and *internal* validity. On the one hand, we addressed external validity by considering the community’s characteristics and their experience regarding TB education
and infection control practices so that our results could be generalizable. On the other hand, internal validity was improved by contacting experts who provided us with assistance in the study's design, questionnaire construction, and decisions concerning what should and should not be measured.

### 3.2.2.4 Reliability

As considered in questionnaire-based studies, the data collection tool must have the ability to produce similar or consistent results if this tool is tested several times. And although, reliability is difficult to achieve in practice, we addressed it firstly by creating a data collection tool that was simple and understandable for participants. Also, considering that reliability is more likely to be ensured when participants devote a consistent degree of concentration and interest throughout the interview process, we decided to train our research staff in how to interact with participants and how to be consistent when asking the questions.

### 3.2.3 Sample size estimation

Given that no previous research was conducted to determine TB knowledge and acceptability of patient-specific infection control measures, we drew a minimum sample size anticipating that 50% of participants had core knowledge about TB and knew some of the measures for TB control. We estimated an acceptable margin of error of 10%, if the true population proportion was 50%. We estimated a minimal sample size of 96 individuals using the formula shown below (5). However, we increased our sample to one hundred and ten individuals. The first ten participants were recruited in order to pilot our data collection instrument. The rest of the participants were divided into two groups, patients with TB and patients with suspected TB.
\[ n = \frac{Z^2 \cdot P(P - 1)}{d^2} \]

Formula: Sample Size Estimation

Note—. Characters refer to: \( n \): Sample size; \( Z \): Z Statistic for a level of confidence; \( P \): Expected prevalence or proportion; \( d \): Precision

3.2.4 Selection of participants

Participants were selected mainly from Worcester, De Doorns, and Rawsonville municipalities in the Breede River Valley. This region is located in the Western Cape province of South Africa, and has a population of about 134,271 people and an estimated TB prevalence of 1188 / 100 000 population (4). The South African Tuberculosis Vaccine Initiative (SATVI) developed a trial site to conduct clinical and epidemiological studies at the Brewelskloof Hospital. The present study was nested upon 2 SATVI studies that were enrolling adult participants with suspected and confirmed TB in the Breede Valley region [An International Multicentre Controlled Clinical Trial to Evaluate High Dose Rifapentine and A Quinolone in the Treatment of Pulmonary Tuberculosis—RIFAQUIN (REC REF 077/2007), and Diagnostic Yield Of Induced Sputum for Rapid Diagnosis of Pulmonary Tuberculosis (REC REF 263/2006)]. Participants were selected according to their TB status: Patients with TB were defined as individuals who were recently diagnosed and were participating in the RIFAQUIN trial; Patients with suspected TB were defined as individuals being screened (or under investigation) for TB and who were participating in the Sputum Induction Trial.

By the time this study was conducted, patients with suspected TB were in recent contact with the TB clinics from the area, and had not received TB education, contrary to patients with TB, who initially received TB education from health care workers at the local health facilities, and later, were in frequent contact with SATVI clinical research workers,
who were also providing participants with information about TB. The purpose of this classification into patients suspected with TB and patients with TB was to determine whether on-going contact influences levels of knowledge, with a subsequent increase in acceptability of patient-specific measures to control TB.

3.2.4.1 Inclusion criteria:

- Male and female adults (> 18 years old)
- Suspected or confirmed TB
- Ability to give informed consent
- Ability to understand and complete the questionnaire

3.2.4.2 Exclusion criteria:

- Previous TB
- Failure to obtain informed consent
- Participation in another research protocol which precludes taking part in another study.

3.2.4.3 Withdrawal:

Participants could decide to withdraw at any time, before or during the interview, without affecting their routine health care or participation in other SATVI studies.

3.2.5 Ethical considerations

Permission to carry out the two previously mentioned SATVI trials (REC REF 077/2007 and REC REF 263/2006) was obtained from respective public health authorities from the Breede Valley Municipality following all ethical and clinical requirements established to conduct research in human subjects. The current study was undertaken after that, the protocol, the questionnaire and the informed consent documents were submitted to
the University of Cape Town Research Ethics Committee (UCTREC) and later approved (See Appendixes 3 and 4). Translated versions of the consent form and questionnaire were also submitted for UCTREC approval (See official translation certificate in Appendix 5). As part of the SATVI academic team, researches had the prerogative to conduct this project at the clinical research site at Brewelskloof Hospital.

As this study required the participation of human respondents, participants’ interests were safeguarded according to the South African and International standards of Good Clinical Practice (GCP) guidelines, applicable government regulations, and institutional research policies and procedures.

The consideration of these ethical issues was necessary for the purpose of ensuring the privacy as well as the safety of the participants. In order to secure the consent of the selected participants, we communicated all important details of the study, including its aim and purpose. By explaining these important details, the respondents were able to understand the importance of their role in the completion of this study. The respondents were also advised that they could withdraw from the study even during the process. With this, the participants were not forced to participate in the research. The confidentiality of the participants was also ensured by not disclosing their names or personal information in the research. Only relevant details that helped in answering the research questions were included.

All participants in the study were provided with a consent form describing adequate information concerning the study, providing adequate opportunity for the subject to consider all options, responding to the subject's questions, ensuring that the subject has comprehended this information, obtaining the subject's voluntary agreement to participate
and, continuing to provide information as the subject or situation requires. This study and providing sufficient information for them to make an informed decision about participation.

The formal consent of a participant, using the approved consent form, was obtained before he or she proceeded to be interviewed. The consent form was signed by the participant or a legally acceptable surrogate and by the research staff member obtaining the consent.

3.2.6 Study time-points

3.2.6.1 Consenting Process

Participants being recruited for the RIFAQUIN and the Sputum Induction SATVI trials were given information about this questionnaire survey on TB knowledge and the implementation of infection control measures. Then, they proceeded to give us their consent to take part in this study. Written informed consent for participation was taken either at the participant’s home, at the local TB clinics, or at the SATVI research site (See Appendix 2).

3.2.6.2 Interviews

After informed consent was obtained, participants proceeded to be interviewed. Both groups were interviewed at baseline so that we could determine the initial levels of knowledge about TB and the acceptability of patient-specific measures. Ultimately, only patients with TB continued to be interviewed for a second time—at the end of their TB treatment—in order to determine TB knowledge and acceptability of patient-specific measures over time.

3.2.7 Data analysis

For each question, differences between proportions were compared at different time-points; initially, differences between patients with suspected TB (at the time of TB
screening) and patients with TB (at the start of TB treatment). Moreover, differences between patients with TB at the start of TB treatment and patients with TB at the end of treatment were also calculated through a before and after analysis.

In order to compare the differences between groups (patients with suspected TB versus patients with TB; Patients with TB at the start of treatment versus patients with TB at the end of treatment) and quantify the association between knowledge and acceptability of patient-specific measures for TB control, we computed the Chi-square test—or the Fisher's exact when applicable, to compare different proportions, and the association between knowledge and acceptability of patient-specific measures with different demographic variables (patients with suspected TB versus Patients with TB; patients with TB at baseline versus patients with TB at the end of treatment). Spearman's correlation analysis was applied to determine bivariate relationships between knowledge and acceptability scores. The level of statistical significance was set at 5%. The statistical package Stata® 11 was used for data analysis.

3.2.7.1 Rating scales: Knowledge and acceptability of patient-specific infection control measures

Additionally, in order to measure if there was an association between TB knowledge and acceptability of infection control measures, we constructed two analogue psychometric scales, knowledge score and acceptability score, respectively.

Core TB knowledge was determined by a score based on answers given to seven questions (TB cause; TB transmission; transmission mode; chemoprophylaxis in children; and, TB

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8 Rating scale that allows the measurement of knowledge, abilities, attitudes, and personality traits.
treatment). These questions were based on the “core TB education elements” which are described in the South African National TB control programme (6), and which should be provided on a regular basis to individuals attending TB clinics (6). As observed in the following schematic table (See Table 4), one point is given for each affirmative answer (e.g., Do you know how a person gets TB? Answer: yes), and each correct answer would also be assigned with a point (e.g., TB is transmitted by being in close contact with people who have TB”).

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</table>

Table 4. Schematic representation of core TB knowledge score

Answers were categorised as poor knowledge and acceptable knowledge depending on the total of points obtained by each participant. A perfect score for knowledge would be 28 points. Poor knowledge was defined by scores ≤ 12 points; acceptable knowledge was delimited as a score > 12 points.

The acceptability score was created on the same basis as the knowledge score. The sections about infection control measures at health care facilities, home and workplaces comprised a total of 14 questions, which along with their attributes” gave us a total of 18 points for a perfect score. Low acceptability of patient-specific measures was then delimited by a score ≤ 10 points; and satisfactory acceptability was delimited by a score > 10.
3.2.8 Study Duration

This study was conducted between October 12 2009 and May 12 2011.


Chapter Introduction

This chapter comprises two sections which cover (1) the results of the systematic review and meta-analysis of sputum induction for TB diagnosis; and (2) results from the prospective observational study of TB infection control measures in the Breede Valley community.

4.1 Sputum Induction: A Cost-Effective Method to Improve TB Diagnosis

4.1.1 Study selection

A total of 90 publications were identified by a combined search in an electronic database and also by examining relevant reference lists and consultation with experts. Forty-one papers were selected and reviewed (See detailed study selection flow gram in Figure 4). After revision, only 17 studies were included in the review. Selected studies comprised a total sample of 3,988 participants and study sample sizes ranged from 28 to 1,869 individuals (median $n=129$, IQR 94 - 189). The number of participants diagnosed with culture-positive TB ranged from 7 to 138 individuals (median $n=20$, IQR 15 – 48). 29% of studies were conducted in children and 47% were either conducted in high HIV prevalence areas, or researchers reported a HIV sero-prevalence greater than 10% among participants. The majority of studies (65%) were conducted in low and middle income countries. Sputum
induction was performed using saline concentrations ranging from 3% to 20% (median 3%, IQR 3 - 10), using a variety of ultrasonic nebulizers, conventional air compressors or by providing hypertonic saline nebulisation via O₂ cylinders.

**Study Selection Process**

![Flow chart of the study selection process](image)

*Figure 4. Flow chart of the study selection process*
4.1.2 Publication bias

We explored the potential for publication bias using a funnel plot. The funnel plot was plotted using proportions *versus* standard error (See Figure 5). The graphical analysis showed no evidence of publication bias. We complemented the funnel plots by using the Eggers test as a bias indicator (Egger bias test = -1.75 [95% CI = -4.8 - 1.3] \( p = 0.24 \))

![Publication Bias Assessment](image)

*Figure 5. Symmetrical funnel plot in the absence of Publication Bias*

4.1.3 Sputum induction and comparison procedures

Among the selected studies, 35% of the articles compared sputum induction to gastric lavage, 24% compared sputum induction to FOB, 6% compared sputum induction to spontaneous expectorated sputum, 17% compared sputum induction to other invasive procedures (including the string test, lymph node biopsy, and nasopharyngeal aspiration), and finally 18% of the studies compared three diagnostic procedures (sputum induction, spontaneous sputum, and FOB in one publication; and sputum induction, gastric lavage, and FOB in the other) (See Table 5).
### Studies’ Characteristics

<table>
<thead>
<tr>
<th>Citation</th>
<th>Study Population</th>
<th>Category of TB Suspect</th>
<th>Sample Size</th>
<th>HIV Prevalence</th>
<th>Saline</th>
<th>Comparator Procedures</th>
<th>Total SI Samples</th>
<th>Total Comparator Samples</th>
<th>TB Diagnosis by SI</th>
<th>TB Diagnosis by Comparator</th>
<th>Total TB Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hensler [1961]</td>
<td>Adults</td>
<td>$S_{NEG}/S_{UNPROD}$</td>
<td>28</td>
<td>0</td>
<td>10</td>
<td>GL</td>
<td>3</td>
<td>3</td>
<td>19</td>
<td>14</td>
<td>20</td>
</tr>
<tr>
<td>Beck [1962]</td>
<td>Adults</td>
<td>$S_{NEG}/S_{UNPROD}$</td>
<td>62</td>
<td>0</td>
<td>10</td>
<td>SS</td>
<td>NS¹</td>
<td>NS¹</td>
<td>138</td>
<td>84</td>
<td>153</td>
</tr>
<tr>
<td>Yue [1967]</td>
<td>Adults</td>
<td>$S_{NEG}/S_{UNPROD}$</td>
<td>189</td>
<td>0</td>
<td>10</td>
<td>GL</td>
<td>NS¹</td>
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<td>138</td>
<td>84</td>
<td>153</td>
</tr>
<tr>
<td>Anderson [1995]</td>
<td>Adults</td>
<td>$S_{NEG}/S_{UNPROD}$</td>
<td>92</td>
<td>0</td>
<td>3</td>
<td>FOB</td>
<td>1</td>
<td>1</td>
<td>20</td>
<td>19</td>
<td>26</td>
</tr>
<tr>
<td>Zar [2000]</td>
<td>Children</td>
<td>$S_{ALL}$</td>
<td>142</td>
<td>100</td>
<td>5</td>
<td>GL</td>
<td>1</td>
<td>2</td>
<td>15</td>
<td>9</td>
<td>16</td>
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<td>Conde [2000]</td>
<td>Adults</td>
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<td>10</td>
<td>3</td>
<td>FOB</td>
<td>1</td>
<td>1</td>
<td>94</td>
<td>103</td>
<td>143</td>
</tr>
<tr>
<td>McWilliams [2002]</td>
<td>Adults</td>
<td>$S_{NEG}/S_{UNPROD}$</td>
<td>129</td>
<td>0</td>
<td>3</td>
<td>FOB</td>
<td>3</td>
<td>1</td>
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<td>GL</td>
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<td>3</td>
<td>51</td>
<td>38</td>
<td>62</td>
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<tr>
<td>Vargaz [2005]</td>
<td>Adults</td>
<td>$S_{NEG}/S_{UNPROD}$</td>
<td>212</td>
<td>76</td>
<td>20</td>
<td>ST</td>
<td>1</td>
<td>1</td>
<td>9</td>
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<td>15</td>
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<tr>
<td>Iriso [2005]</td>
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<td>126</td>
<td>49</td>
<td>3</td>
<td>PLNB</td>
<td>1</td>
<td>1</td>
<td>30</td>
<td>6</td>
<td>36</td>
</tr>
<tr>
<td>Brown [2007]</td>
<td>Adults</td>
<td>$S_{NEG}/S_{UNPROD}$</td>
<td>140</td>
<td>0</td>
<td>3</td>
<td>GL / FOB</td>
<td>3</td>
<td>3/1</td>
<td>42</td>
<td>37</td>
<td>54</td>
</tr>
<tr>
<td>Schoch [2007]</td>
<td>Adults</td>
<td>$S_{ALL}$</td>
<td>101</td>
<td>0</td>
<td>3</td>
<td>FOB / SS</td>
<td>2</td>
<td>1/2</td>
<td>27</td>
<td>28</td>
<td>33</td>
</tr>
<tr>
<td>Owens [2007]</td>
<td>Children</td>
<td>$S_{ALL}$</td>
<td>94</td>
<td>47</td>
<td>3</td>
<td>NPA</td>
<td>NS¹</td>
<td>NS¹</td>
<td>19</td>
<td>21</td>
<td>24</td>
</tr>
<tr>
<td>Ganguly [2008]</td>
<td>Adults</td>
<td>$S_{NEG}/S_{UNPROD}$</td>
<td>52</td>
<td>0</td>
<td>3</td>
<td>FOB</td>
<td>NS¹</td>
<td>NS¹</td>
<td>7</td>
<td>5</td>
<td>20</td>
</tr>
<tr>
<td>Morse [2008]</td>
<td>Adults</td>
<td>$S_{ALL}$</td>
<td>140</td>
<td>81</td>
<td>20</td>
<td>GL</td>
<td>NS¹</td>
<td>NS¹</td>
<td>48</td>
<td>13</td>
<td>57</td>
</tr>
<tr>
<td>Hatherill [2009]</td>
<td>Children</td>
<td>$S_{ALL}$</td>
<td>1869</td>
<td>2</td>
<td>5</td>
<td>GL</td>
<td>2</td>
<td>2</td>
<td>108</td>
<td>127</td>
<td>191</td>
</tr>
<tr>
<td>Bell [2009]</td>
<td>Adults</td>
<td>$S_{NEG}/S_{UNPROD}$</td>
<td>111</td>
<td>68</td>
<td>3</td>
<td>FOB / GL / SS</td>
<td>NS¹</td>
<td>NS¹</td>
<td>13</td>
<td>26</td>
<td>18</td>
</tr>
</tbody>
</table>

**Table 5.** Description of Studies included in the Meta-Analysis

**Note.**—“Category of TB Suspect” differentiates studies that included all patients with suspected TB ($S_{ALL}$) from those that pre-screened only smear negative ($S_{NEG}$) and/or sputum unproductive ($S_{UNPROD}$) participants. “NS¹” Refers to included studies in which the total of samples per procedure was not clearly specified.

**Procedure Acronyms:** GL Gastric Lavage; FOB Fiber-optic bronchoscopy with bronchoalveolar lavage; NPA Nasopharyngeal Aspiration; PLNB Pleural or Lymph Node Biopsy; SS Spontaneous Sputum.
4.1.4 Sputum induction diagnostic yield

*M. tuberculosis* was isolated in 975 (24%) of the 3,988 participants. Microbiological diagnosis of TB was established through sputum induction in 627 cases (64% of all culture-confirmed TB diagnoses). Figure 6 shows the Forest plot of diagnostic yield with 95% CI for each study. Diagnostic yields for sputum induction ranged from 35% to 95% (median 79%), with pooled diagnostic yield of 74% (95% CI 65 to 81%).

**Sputum Induction Diagnostic Yield**

![Forest plot of diagnostic yield with 95% CI for each study.](image)

Diagnostic Yield of Sputum Induction among all the studies: **Heterogeneity tests**: Cochran Q = 115.29 (df = 16) \( P < 0.0001 \) Moment-based estimate of between studies variance = 0.12 \( I^2 \) (inconsistency) = 86% (95% CI 79% to 90%). **Pooled proportion** = 74 (95% CI 65 - 81).

Inspection of the above forest plot showed that the sputum induction diagnostic yield was inconsistent across the outcomes reported by each study; Statistical tests to determine
variability showed was substantial heterogeneity in study results: $X^2 (df=16) = 115$, $P < 0.0001$, $I^2 = 86\%$ (95% CI 79% to 90%). Further analyses were conducted to explore the possible sources of this variability via sub-group and meta-regression analyses.

### 4.1.5 Exploring sources of heterogeneity

#### 4.1.5.1 Sub-Group Analyses

Sub-group analyses of diagnostic yield by age category, concentration of nebulized saline, HIV prevalence, and use of FOB as the comparator method, were displayed in separate Forest plots (See Figures 7a, 7b, 8a, 8b, 9a, 9b, 10a, and 10b). Summary estimates are shown in Table 6.

<table>
<thead>
<tr>
<th>Category</th>
<th>Pooled Estimate (%)</th>
<th>Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Overall Yield</strong></td>
<td>74</td>
<td>(65-81)</td>
</tr>
<tr>
<td><strong>Adults vs. Children</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults</td>
<td>71</td>
<td>(60-81)</td>
</tr>
<tr>
<td>Children</td>
<td>79</td>
<td>(62-92)</td>
</tr>
<tr>
<td><strong>Saline Concentration</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saline Concentration &lt;5</td>
<td>73</td>
<td>(63-82)</td>
</tr>
<tr>
<td>Saline Concentration ≥5</td>
<td>75</td>
<td>(59-89)</td>
</tr>
<tr>
<td><strong>HIV Prevalence</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High HIV Prevalence</td>
<td>78</td>
<td>(69-86)</td>
</tr>
<tr>
<td>Low HIV Prevalence</td>
<td>69</td>
<td>(54-83)</td>
</tr>
<tr>
<td><strong>Use of Fiber-Optic Bronchoscopy (FOB)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No use of FOB</td>
<td>81</td>
<td>(70-90)</td>
</tr>
<tr>
<td>Use of FOB</td>
<td>58</td>
<td>(38-77)</td>
</tr>
</tbody>
</table>

Table 6. Diagnostic Yield of Sputum Induction by sub-groups.

The pooled diagnostic yields for adults and children were not significantly different: 71% (95% CI 60% to 81%) and 79% (95% CI 62% to 92%) respectively. However, the confidence intervals were wide and significant heterogeneity was observed [adults: $X^2(df=11) = 73$, $P < 0.0001$, $I^2 = 85\%$ (95% CI 75% to 89.8%); Children: $X^2(df=4) = 38$, $P <$
0.0001, $F = 89\% \ (95\% \ CI \ 77\% \ to \ 94\%)$. Age category was not significantly associated with diagnostic yield in univariate analysis ($p = 0.354$).

*Sputum Induction Diagnostic Yield: Adults vs. Children.*

![Figure 7a. Sputum Induction in Adults](image)

Diagnostic Yield of Sputum Induction by Subgroup Analysis according age groups: Adults (a): **Heterogeneity tests**: Cochran $Q = 73.36 \ (df = 11) \ P < 0.0001$ Moment-based estimate of between studies variance $= 0.13$ I$^2$ (inconsistency) $= 85\% \ (95\% \ CI = 75\% \ to \ 90\%)$ **Pooled proportion** $= 71 \ (95\% \ CI = 60 - 80)$. 
Diagnostic Yield of Sputum Induction by Subgroup Analysis according age groups: Children (b):

**Heterogeneity tests:** Cochran $Q = 37.6$ (df = 4) $P < 0.0001$ Moment-based estimate of between studies variance $= 0.17$ I² (inconsistency) = 89% (95% CI = 77% to 94%). **Pooled proportion** = 0.79 (95% CI = 0.61 - 0.92).

Studies using saline concentrations < 5% demonstrated pooled diagnostic yield of 72% (95% CI 63% to 82%), compared to 75% (95% CI 59% to 89%) for studies that used concentrations ≥ 5%. Significant heterogeneity was also found in each subgroup [saline concentration <5%: $X^2$(df=9) = 56, $P < 0.0001$, I² = 84% (95% CI 71% to 90%); and saline concentration ≥ 5%: $X^2$(df=6) = 47, $P < 0.0001$, I² = 88% (95% CI 76% to 92%)].

Saline concentration was positively associated with diagnostic yield in univariate analysis, although results were not statistically significant ($p = 0.517$).
Sputum Induction Diagnostic Yield: Nebulized Saline Concentration.

Figure 8a. Sputum Induction with Saline Concentrations < 5%

<table>
<thead>
<tr>
<th>Study</th>
<th>Diagnostic Yield (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yue [1967]</td>
<td>0.90 (0.84, 0.94)</td>
</tr>
<tr>
<td>Anderson [1995]</td>
<td>0.77 (0.56, 0.91)</td>
</tr>
<tr>
<td>Conde [2000]</td>
<td>0.66 (0.58, 0.74)</td>
</tr>
<tr>
<td>McWilliams [2002]</td>
<td>0.48 (0.29, 0.68)</td>
</tr>
<tr>
<td>Irso [2005]</td>
<td>0.83 (0.67, 0.94)</td>
</tr>
<tr>
<td>Brown [2007]</td>
<td>0.78 (0.64, 0.88)</td>
</tr>
<tr>
<td>Owens [2007]</td>
<td>0.79 (0.58, 0.93)</td>
</tr>
<tr>
<td>Garguly [2008]</td>
<td>0.35 (0.15, 0.59)</td>
</tr>
<tr>
<td>Morse [2008]</td>
<td>0.84 (0.72, 0.93)</td>
</tr>
<tr>
<td>Bell [2009]</td>
<td>0.72 (0.47, 0.90)</td>
</tr>
<tr>
<td>Combined</td>
<td>0.73 (0.63, 0.82)</td>
</tr>
</tbody>
</table>

Figure 8b. Sputum Induction with Saline Concentrations ≥ 5%

<table>
<thead>
<tr>
<th>Study</th>
<th>Diagnostic Yield (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hensler [1961]</td>
<td>0.95 (0.75, 1.00)</td>
</tr>
<tr>
<td>Beck [1962]</td>
<td>0.88 (0.47, 1.00)</td>
</tr>
<tr>
<td>Zar [2000]</td>
<td>0.94 (0.70, 1.00)</td>
</tr>
<tr>
<td>Zar [2005]</td>
<td>0.88 (0.77, 0.95)</td>
</tr>
<tr>
<td>Vargaz [2005]</td>
<td>0.53 (0.27, 0.79)</td>
</tr>
<tr>
<td>Schoch [2007]</td>
<td>0.52 (0.34, 0.69)</td>
</tr>
<tr>
<td>Hatherill [2009]</td>
<td>0.56 (0.48, 0.63)</td>
</tr>
<tr>
<td>Combined</td>
<td>0.75 (0.59, 0.89)</td>
</tr>
</tbody>
</table>

Diagnostic Yield of Sputum Induction by Subgroup Analysis according to Salinity: Saline Concentration <5%
(a): Heterogeneity tests: Cochran Q = 56.55 (df = 9) \( P < 0.0001 \) Moment-based estimate of between studies variance = 0.09 \( F \) (inconsistency) = 84% (95% CI = 71% to 90%) Pooling proportion = 73 (95% CI = 63 - 82).
(b): Cochran Q = 47.94 (df = 6) \( P < 0.0001 \) Moment-based estimate of between studies variance = 0.19 \( F \) (inconsistency) = 88% (95% CI = 76% to 92%) Pooling proportion = 75 (95% CI = 59 - 89).
Pooled diagnostic yield did not differ in studies conducted in high HIV prevalence populations compared to low HIV prevalence study populations: 75% (95% CI 65% to 84%) versus 71% (95% CI 55% to 85%), respectively. There is considerable between-study variability in each subgroup [high HIV prevalence: $X^2(df=8) = 47, P < 0.0001, I^2 = 83\%$ (95% CI 67% to 89%); and low prevalence: $X^2(df=7) = 60, P < 0.0001, I^2 = 88\%$ (95% CI 79% to 92%)]. HIV prevalence was not significantly associated with diagnostic yield in the univariate analysis ($p = 0.358$).

**Sputum Induction Diagnostic Yield: HIV Prevalence**

![Sputum Induction Diagnostic Yield: HIV Prevalence](image)

Diagnostic Yield of Sputum Induction by Subgroup Analysis according to HIV Prevalence: High HIV prevalence (a): **Heterogeneity Tests**: Cochran $Q = 21.97 (df = 7) P < 0.0026$ Moment-based estimate of between studies variance = 0.05 $I^2$ (inconsistency) = 68% (95% CI = 12% to 83%). **Pooled proportion** = 0.78 (95% CI = 0.69 - 0.86).
Diagnostic Yield of Sputum Induction by Subgroup Analysis according to HIV Prevalence: Low HIV prevalence (b): Heterogeneity Tests: Cochran $Q = 89.93$ (df = 8) $P < 0.0001$ Moment-based estimate of between studies variance = 0.20 $I^2$ (inconsistency) = 91% (95% CI = 86% to 94%) Pooled proportion = 69 (95% CI = 54 - 82).

The diagnostic yield of sputum induction in studies that did not use FOB as the comparator method was higher than those which included this procedure: 81% (95% CI 69 – 90%) versus 58% (95% CI 37 – 77%) respectively.
**Sputum Induction Diagnostic Yield: Use of Fiber-optic Bronchoscopy (FOB) as the comparator method.**

**Figure 10a. Sputum Induction Studies without FOB**

- Hensler [1961]: 0.95 (0.75, 1.00)
- Beck [1962]: 0.88 (0.47, 1.00)
- Yue [1967]: 0.90 (0.84, 0.94)
- Zar [2000]: 0.94 (0.70, 1.00)
- Zar [2005]: 0.87 (0.76, 0.94)
- Vargaz [2005]: 0.53 (0.27, 0.79)
- Irso [2005]: 0.83 (0.67, 0.94)
- Owens [2007]: 0.79 (0.58, 0.93)
- Morse [2008]: 0.84 (0.72, 0.93)
- Hatheril [2009]: 0.55 (0.48, 0.63)
- Combined: 0.81 (0.70, 0.90)

**Figure 10b. Sputum Induction Studies in comparison to FOB**

- Anderson [1995]: 0.77 (0.56, 0.91)
- Conde [2000]: 0.34 (0.27, 0.43)
- McWilliams [2002]: 0.48 (0.29, 0.68)
- Brown [2007]: 0.78 (0.64, 0.88)
- Schoch [2007]: 0.82 (0.65, 0.93)
- Ganguly [2008]: 0.21 (0.13, 0.30)
- Bell [2009]: 0.72 (0.47, 0.90)
- Combined: 0.58 (0.38, 0.77)

Diagnostic Yield of Sputum Induction by Subgroup Analysis according to the use of Fiberoptic Bronchoscopy. Studies reporting no use of FOB (a): **Heterogeneity Tests**: 78.03 (df = 9) \( P < 0.0001 \); Moment-based estimate of between studies variance = 0.15; \( I^2 \) (inconsistency) = 89% (95% CI = 81% to 92.1%). **Pooled proportion** = 81 (95% CI = 69 - 90). Studies reporting the use of FOB (b): **Heterogeneity Tests**: Cochran Q = 93.51 (df = 6) \( P < 0.0001 \); Moment-based estimate of between studies variance = 0.28; \( I^2 \) (inconsistency) = 93.6% (95% CI = 90% to 96%). **Pooled proportion** = 58% (95% CI = 37 - 77).
4.1.5.2 Univariate and Meta-Regression Analysis

Univariate regression analysis demonstrated no significant associations between diagnostic yield and HIV prevalence (p=0.37), or age category (p=0.35). Use of FOB as the comparator method was associated on average with 22% reduction in the diagnostic yield of sputum induction (95% CI 2 – 42%), p=0.036, compared to studies that did not use FOB, in the univariate analysis. However, interpretation of this association was confounded by use of 3% saline in all studies using FOB as the comparator method. A meta-regression analysis including the covariates “Saline concentration”, “Study Population”, “Use of FOB” and “Study HIV Prevalence” was conducted in order to examine all possible confounders that might conceal the effect these covariates on the yield of sputum induction. HIV prevalence and age category had no effect on the model and were excluded. The meta-regression model confirmed that FOB usage (p=0.21) and saline concentration (p=0.31) were not independently associated with changes in diagnostic yield of sputum induction (See Figure 11).

![Figure 11. The Effects of Saline Concentration and FOB Use on Diagnostic Yield.](image-url)
4.2 TB Knowledge, TB Infection Control and Acceptability of Patient-Specific Measure to Reduce TB Transmission

4.2.1 Participants Demographic Profile

We recruited one hundred and ten adults with suspected and confirmed TB, who were participants in on-going community studies. Ten participants were interviewed to pilot and validate the questionnaire (See appendix 1). The remaining 100 participants, 50 patients with TB and 50 patients with suspected TB, were interviewed. Demographic data are presented as follows:

<table>
<thead>
<tr>
<th>Variable and Attribute(s)</th>
<th>Patients with suspected TB (%)</th>
<th>Patients with TB (%)</th>
<th>Total</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Language:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IsiXhosa</td>
<td>10 (20)</td>
<td>12 (24)</td>
<td>22</td>
<td>0.629</td>
</tr>
<tr>
<td>Afrikaans</td>
<td>40 (80)</td>
<td>38 (76)</td>
<td>78</td>
<td></td>
</tr>
<tr>
<td><strong>Gender:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Females</td>
<td>28 (56)</td>
<td>19 (38)</td>
<td>47</td>
<td>0.071</td>
</tr>
<tr>
<td>Males</td>
<td>22 (44)</td>
<td>31 (62)</td>
<td>53</td>
<td></td>
</tr>
<tr>
<td><strong>Age (median)</strong></td>
<td>33 years (18-54)</td>
<td>33 years (19-54)</td>
<td></td>
<td>0.526</td>
</tr>
<tr>
<td><strong>Housing Conditions</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total people in home:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 5 people</td>
<td>20 (40)</td>
<td>24 (48)</td>
<td>44</td>
<td>0.42</td>
</tr>
<tr>
<td>&lt; 5 people</td>
<td>30 (60)</td>
<td>26 (52)</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>Total people/room (median)</td>
<td>2 people (2-9)</td>
<td>2 people (2-7)</td>
<td></td>
<td>1.000</td>
</tr>
<tr>
<td>Sleep alone</td>
<td>11 (22)</td>
<td>7 (14)</td>
<td>18</td>
<td>0.298</td>
</tr>
<tr>
<td><strong>Working Status:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Currently working</td>
<td>29 (58)</td>
<td>27 (54)</td>
<td>56</td>
<td>0.687</td>
</tr>
<tr>
<td>Working indoors</td>
<td>14 (48)</td>
<td>7 (26)</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Working outdoors</td>
<td>15 (52)</td>
<td>20 (74)</td>
<td>35</td>
<td>0.084</td>
</tr>
</tbody>
</table>

Table 7. Demographic Data

Table 7 summarizes descriptive information from the 100 participants enrolled in this study. All participants were living in the Breede Valley River community when the interviews were conducted. Seventy-eight percent (78%) of the recruited participants were Afrikaans speakers while the remaining 22% were IsiXhosa speakers. There was a similar gender distribution among participants, 53% males and 43% females. No differences were found in the age distribution between patients with TB and patients with suspected TB.
Although no statistical differences were found between patients with suspected TB and patients with TB, housing or living conditions reflected overcrowding conditions among both groups. 44% of all participants responded that they were living with more than 5 individuals in their homes. A significant proportion of participants (82%) confirmed that there were more than 2 individuals per room, whereas only 18% of the participants slept alone; 29% of the participants responded that they were sharing their room only with children; 24% responded that they were sleeping in the same room as both adults and children; and 29% were sharing a room only with other adults (See Figure 12).

![Distribution of contacts who sleep in the same room with TB patients and TB Suspects](image)

**Figure 12. Sleeping Conditions**

Only 56% of the participants were working. Taking into account that the risk of transmitting TB is higher when the proximity of contact increases, we asked the participants whether they were working indoors or outdoors. 21% of the participants were working

---

Overcrowding is defined as households which don’t have at a minimum number of rooms equal to: one room for the household; one room per couple in the household; one room for each single person aged 18 or more; one room per pair of single people of the same gender between 12 and 17 years of age; one room for each single person between 12 and 17 years of age and not included in the previous category; and one room per pair of children under 12 years of age.
indoors and the remaining 35% out of all participants worked outdoors. Patients with TB who were working indoors (7%) were in contact with median 15 co-workers, whereas the median number of co-workers in the case of patients with suspected TB was 8 (Patients suspected with TB, range 1 - 84 co-workers; patients with TB, range 6 - 50 co-workers).

We also gathered information regarding “cough status”. Eighty-seven percent (87%) of the participants were coughing before seeking medical attention. In total, 18% of the participants stated to have been coughing for less than 2 weeks. More patients with suspected TB had been coughing for 2 weeks compared to patients with TB. There were no significant differences in relation to cough duration of two weeks or more before seeking medical attention. However, patients with TB were more likely to report that they were coughing for more than 4 weeks when they sought medical care (See Figure 13).

**Figure 13.** Coughing and seeking medical attention
4.2.2 Baseline knowledge among participants

Patients’ responses to questions regarding core knowledge elements about transmission of TB such as: what is TB?, what causes it?, how is TB transmitted?, who is more susceptible to developing TB disease?, what measures can be taken to limit TB transmission?, and the implementation of chemoprophylaxis for children, showed no major differences between patients with TB versus patients with suspected TB at baseline (See Table 8).

Only 57% of all respondents reported that they knew the cause of TB. When these participants were asked to specify their answer, 32% of respondents attributed causes other than “Germs”. Participants reported that TB was caused by: drinking alcohol (5%), uncleanliness (5%), smoking (12%), the use of drugs (4%), and that it was passed down through generations (6%). Only 25% of the participants agreed that TB was caused by a micro-organism. Surprisingly, more patients with suspected TB knew that TB was a microbial disease as compared to patients with TB (p-value 0.003) (See Table 8).

Ninety-five percent of the participants reported that TB could be transmitted to other people. A small difference was found between patients with suspected TB (45%) and patients with TB (50%) when asked about TB transmission: Patients with TB were more aware that TB follows a human-to-human transmission pattern (p-value 0.022). However, only 54% of the participants confirmed that they knew how the disease was transmitted. Participants reported that TB could be transmitted through sharing food utensils; by kissing; and even by living in low-temperature areas. Only 20% and 26% of patients with TB and patients with suspected TB, respectively, reported that TB was transmitted by being in close contact with an infectious source case (See Table 8).
When participants were asked whether children would require chemoprophylaxis (isoniazid preventive therapy [IPT]) if they were exposed to TB, most participants (93%) agreed. However, knowledge of which particular group of children require IPT was low among patients with TB and patients with suspected TB. For instance, 75% of participants believed that all children would require IPT after exposure to *M. tuberculosis* (See Table 8).

Less than half of the participants reported that TB transmission could be stopped or reduced once an effective treatment regimen is started. Neither groups reported a clear understanding of when TB chemotherapy starts to lower the bacillary load (See Table 8).
<table>
<thead>
<tr>
<th>General Information on Tuberculosis</th>
<th>Patients with suspected TB (%)</th>
<th>Patients with TB (%)</th>
<th>Total n = 100</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do you know the cause of TB?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>32(32)</td>
<td>25(25)</td>
<td>57</td>
<td>0.157</td>
</tr>
<tr>
<td>Generations</td>
<td>2(2)</td>
<td>3(3)</td>
<td>5</td>
<td>1.000</td>
</tr>
<tr>
<td>Germs</td>
<td>19(19)</td>
<td>6(6)</td>
<td>25</td>
<td>0.003*</td>
</tr>
<tr>
<td>Uncleanliness</td>
<td>2(2)</td>
<td>3(3)</td>
<td>5</td>
<td>1.000</td>
</tr>
<tr>
<td>Smoking</td>
<td>5(5)</td>
<td>7(7)</td>
<td>12</td>
<td>0.538</td>
</tr>
<tr>
<td>Toxic Substances</td>
<td>2(2)</td>
<td>2(2)</td>
<td>4</td>
<td>1.000</td>
</tr>
<tr>
<td><strong>Do you think TB can be passed on to other people?</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults</td>
<td>45(45)</td>
<td>50(50)</td>
<td>95</td>
<td>0.022*</td>
</tr>
<tr>
<td>Young children</td>
<td>5(5)</td>
<td>9(9)</td>
<td>14</td>
<td>0.249</td>
</tr>
<tr>
<td>Elderly people</td>
<td>11(11)</td>
<td>10(10)</td>
<td>21</td>
<td>0.806</td>
</tr>
<tr>
<td>Co-Workers</td>
<td>3(3)</td>
<td>6(6)</td>
<td>9</td>
<td>0.487</td>
</tr>
<tr>
<td>HIV/AIDS Patients</td>
<td>4(4)</td>
<td>5(5)</td>
<td>9</td>
<td>1.000</td>
</tr>
<tr>
<td>All above mentioned</td>
<td>26(26)</td>
<td>30(30)</td>
<td>56</td>
<td>0.420</td>
</tr>
<tr>
<td>Not sure</td>
<td>7(7)</td>
<td>9(9)</td>
<td>16</td>
<td>0.585</td>
</tr>
<tr>
<td><strong>How a person does get TB?</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sharing food utensils</td>
<td>29(29)</td>
<td>25(25)</td>
<td>54</td>
<td>0.422</td>
</tr>
<tr>
<td>Kissing people</td>
<td>3(3)</td>
<td>6(6)</td>
<td>9</td>
<td>0.487</td>
</tr>
<tr>
<td>Living or being in close contact with people</td>
<td>6(6)</td>
<td>4(4)</td>
<td>10</td>
<td>0.505</td>
</tr>
<tr>
<td>Living in or moving to cold areas</td>
<td>26(26)</td>
<td>20(20)</td>
<td>46</td>
<td>0.229</td>
</tr>
<tr>
<td><strong>Do young children need chemoprophylaxis therapy once exposed to MTB?</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Children &lt; 5 years</td>
<td>4(4)</td>
<td>10(10)</td>
<td>14</td>
<td>0.084</td>
</tr>
<tr>
<td>Children &gt; 5 years</td>
<td>1(1)</td>
<td>2(4)</td>
<td>3</td>
<td>0.558</td>
</tr>
<tr>
<td>All HIV(+) children</td>
<td>1(1)</td>
<td>0(0)</td>
<td>1</td>
<td>1.000</td>
</tr>
<tr>
<td>All children</td>
<td>38(38)</td>
<td>37(37)</td>
<td>75</td>
<td>0.817</td>
</tr>
</tbody>
</table>

**Table 8.** Difference in core TB knowledge between patients with suspected TB and patients with TB from the Breede Valley Community, Worcester, 2011.

**Note**—Statistical significance [p<0.05] is marked with an asterisk.
### General Information on Tuberculosis

<table>
<thead>
<tr>
<th>Do you know when a TB patient usually stops transmitting the disease?</th>
<th>Patients with suspected TB (%)</th>
<th>Patients with TB (%)</th>
<th>Total n = 100</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First day of treatment</strong></td>
<td>18(18)</td>
<td>23(23)</td>
<td>41</td>
<td>0.309</td>
</tr>
<tr>
<td><strong>&gt; 2 weeks</strong></td>
<td>3(3)</td>
<td>6(26)</td>
<td>9</td>
<td>0.487</td>
</tr>
<tr>
<td><strong>2nd month</strong></td>
<td>2(2)</td>
<td>2(2)</td>
<td>4</td>
<td>1.000</td>
</tr>
<tr>
<td><strong>Complete a course of anti-TB treatment</strong></td>
<td>12(12)</td>
<td>12(12)</td>
<td>24</td>
<td>1.000</td>
</tr>
</tbody>
</table>

**Note.** Statistical significance [p<0.05] is marked with an asterisk.

<table>
<thead>
<tr>
<th>Do you know some measures to control tuberculosis?</th>
<th>Patients with suspected TB (%)</th>
<th>Patients with TB (%)</th>
<th>Total n = 100</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Use facemask during transportation to a hospital or clinic</strong></td>
<td>14(14)</td>
<td>14(14)</td>
<td>28</td>
<td>1.000</td>
</tr>
<tr>
<td><strong>Use facemask in a hospital or clinic</strong></td>
<td>17(17)</td>
<td>17(17)</td>
<td>34</td>
<td>1.000</td>
</tr>
<tr>
<td><strong>Cover his/her mouth when coughing and/or sneezing in a hospital or clinic</strong></td>
<td>24(24)</td>
<td>16(16)</td>
<td>40</td>
<td>0.102</td>
</tr>
<tr>
<td><strong>Cover his/her mouth when coughing and/or sneezing at home or at work</strong></td>
<td>24(24)</td>
<td>15(15)</td>
<td>39</td>
<td>0.065</td>
</tr>
<tr>
<td><strong>Be separated from other patients and requested to wait in a separated area</strong></td>
<td>11(11)</td>
<td>11(11)</td>
<td>22</td>
<td>1.000</td>
</tr>
<tr>
<td><strong>Sleep in a room alone, or avoid sleeping in a room with small children</strong></td>
<td>17(17)</td>
<td>12(12)</td>
<td>29</td>
<td>0.271</td>
</tr>
<tr>
<td><strong>Open house windows to the outside air</strong></td>
<td>20(20)</td>
<td>12(12)</td>
<td>32</td>
<td>0.086</td>
</tr>
<tr>
<td><strong>Use fans for moving air to the outside</strong></td>
<td>13(13)</td>
<td>8(8)</td>
<td>21</td>
<td>0.220</td>
</tr>
<tr>
<td><strong>Complete their course of anti—TB treatment</strong></td>
<td>27(27)</td>
<td>14(14)</td>
<td>41</td>
<td>0.008*</td>
</tr>
</tbody>
</table>

**Note.** Statistical significance [p<0.05] is marked with an asterisk.

<table>
<thead>
<tr>
<th>Do you know why measures to control tuberculosis are important?</th>
<th>Patients with suspected TB (%)</th>
<th>Patients with TB (%)</th>
<th>Total n = 100</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prevention for HCW</strong></td>
<td>17(17)</td>
<td>15(15)</td>
<td>32</td>
<td>0.668</td>
</tr>
<tr>
<td><strong>Prevention at home/close contacts</strong></td>
<td>26(26)</td>
<td>20(20)</td>
<td>46</td>
<td>0.229</td>
</tr>
<tr>
<td><strong>Prevention at work</strong></td>
<td>17(17)</td>
<td>15(15)</td>
<td>32</td>
<td>0.668</td>
</tr>
</tbody>
</table>

**Note.** Statistical significance [p<0.05] is marked with an asterisk.
Only 49% of the participants reported they knew of measures to control TB. A higher proportion of patients with suspected TB claimed to know of patient-specific measures to help reduce TB transmission (30%), compared to patients with TB (19%). However, answers regarding implementation of patient-specific measures such as: (1) use of facemasks during transportation to a hospital or clinic; (2) use of facemasks in a hospital or clinic; (3) covering the mouth at a health care facility; (4) covering the mouth at home or at work; (5) separation from other patients, (6) sleeping alone, or avoiding sleeping in a room with small children; (7) opening house windows to the outside air; and (8) the use of fans for moving air to the outside, showed no significant difference between patients with suspected TB and patients with TB (See Figure 14). On the other hand, when participants were asked about treatment as an infection control measure, more patients with suspected TB (27%) acknowledged that TB chemotherapy was a means to reduce transmission of the disease, compared to patients with TB (14%).

**Figure 14.** Difference in baseline knowledge about infection control measures among patients with suspected TB and patients with TB.
When participants were asked if they knew of any methods to reduce the transmission of *M. tuberculosis*, more patients with suspected TB than patients with TB reported that they knew of such infection control measures (patients with TB: 60% patients with suspected TB compared to 38% Patients with TB). However, when participants were questioned about which measures could reduce TB transmission, a greater proportion of patients with suspected TB believed that by completing a course of anti-TB treatment, TB transmission could be prevented, compared to patients with TB (*p*-value 0.008). Also, 23% and 30% of patients with TB and patients with suspected TB, respectively, reported that they knew why these TB infection control measures were important. Most participants reported that the prevention measures were aimed at preventing transmission of TB at home. 52% of patients with suspected TB reported that these measures were essential to prevent family members from developing infection, compared to 40% of patients with TB (See Figure 15).

**Figure 15.** Participants' perceptions on protection of infection control measures

![Distribution of knowledge about who these infection control measures will protect](image-url)
Participants reported that they had received information about TB from different sources: Health care facilities, other patients with TB, family, friends, at work, on the radio and also on T.V. (See Figure 16). Although most participants said that they received information from health care workers, no significant differences were found when between patients with suspected TB and patients with TB, except that more patients with suspected TB received information at their work place as compared to patients with TB.

![Distribution of source of knowledge among participants](image)

**Figure 16.** Difference on baseline knowledge about infection control measures among patients with suspected TB and patients with TB from the Breede Valley Community, Worcester, 2011.

*p* = 0.476  
*p* = 0.505  
*p* = 0.220  
*p* = 0.461  
*p* = 0.025  
*p* = 0.0401  
*p* = 1.000

4.2.2.1 Acceptability of infection control measures at a health care facility

When participants were asked about infection control measures at health care facilities, there seemed to be a high level of acceptability for these precautions. Eighty-nine percent (89%) of the participants were willing to use facemasks in health care facilities. Similar levels of acceptability of such measures were found among patients with TB and patients with suspected TB (48% and 41% respectively). Participants who
disagreed with the use of facemasks highlighted that they did not understand the importance of this measure. No differences were found between patients with suspected TB and patients with TB when participants were asked whether they were prepared to cover their mouth with a handkerchief or tissue while at health care facilities. The only measure at health care facilities that many participants were reluctant to participate in was isolation and/or separation from other patients (48%). Patients with suspected TB and patients with TB who did not agree with the implementation of this measure reported that they would not like to be separated from other patients, and the fear of rejection or TB stigma influenced their decision (See Table 9).
<table>
<thead>
<tr>
<th>Infection Control Measures at Health Care Facilities</th>
<th>Patients with suspected TB (%)</th>
<th>Patients with TB (%)</th>
<th>Total</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use facemask in health care settings? Y/N</td>
<td>41 (41)</td>
<td>48 (48)</td>
<td>89</td>
<td>0.025*</td>
</tr>
<tr>
<td>If no, why?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uncomfortable</td>
<td>3 (3)</td>
<td>1 (1)</td>
<td>4</td>
<td>0.617</td>
</tr>
<tr>
<td>Not important</td>
<td>5 (5)</td>
<td>0 (0)</td>
<td>5</td>
<td>0.056</td>
</tr>
<tr>
<td>TB stigma</td>
<td>1 (1)</td>
<td>1 (1)</td>
<td>2</td>
<td>1.000</td>
</tr>
<tr>
<td>Cover mouth when coughing and/or sneezing in a health care setting? Y/N</td>
<td>48 (48)</td>
<td>50 (50)</td>
<td>98</td>
<td>0.495</td>
</tr>
<tr>
<td>If no, why?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No handkerchief or tissue</td>
<td>2 (2)</td>
<td>0 (0)</td>
<td>2</td>
<td>0.495</td>
</tr>
<tr>
<td>Complete a course of anti—TB treatment? Y/N</td>
<td>50 (50)</td>
<td>50 (50)</td>
<td>100</td>
<td>-</td>
</tr>
<tr>
<td>Be separated from other patients? Y/N</td>
<td>32 (32)</td>
<td>36 (36)</td>
<td>68</td>
<td>0.391</td>
</tr>
<tr>
<td>If no, why?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do not like being separated from others</td>
<td>9 (9)</td>
<td>6 (6)</td>
<td>15</td>
<td>0.401</td>
</tr>
<tr>
<td>TB stigma</td>
<td>7 (7)</td>
<td>5 (5)</td>
<td>12</td>
<td>0.538</td>
</tr>
<tr>
<td>HIV stigma</td>
<td>3 (3)</td>
<td>5 (5)</td>
<td>8</td>
<td>0.715</td>
</tr>
</tbody>
</table>

Table 9. Infection control measures at health care facilities among patients with suspected TB and patients with TB

Note—Statistical significance [p<0.05] is marked with an asterisk.
4.2.2.2 Acceptability of infection control measures at home

Certain measures to control the transmission of TB in the home were acceptable to most participants. Precautions such as covering the mouth with a handkerchief and/or tissue, opening house windows to the outside, and being isolated at home, were accepted by most participants. No significant differences were found between groups (See Table 10). Even though more than 50% of the participants considered that these patient-specific measures were feasible, the use of facemasks at home, the use of fans to increase ventilation, as well as sleeping in a room by themselves or avoiding sleeping in a room with small children were less acceptable. Patients with TB were more accepting of the use of facemasks compared to patients with suspected TB. Sixty-five percent (65%) of the participants who were willing to use isolation at home as a method to reduce the transmission of \textit{M. tuberculosis} to their families, reported that this was feasible in their homes, whereas 20% reported that even though they were willing to be isolated, isolation was not feasible at their homes. Only 15% of all participants reported that they were not willing to be isolated at home (See Table 10).
<table>
<thead>
<tr>
<th>Infection Control Measures at Home</th>
<th>Patients with suspected TB (%)</th>
<th>Patients with TB (%)</th>
<th>Total n = 100</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cover mouth with a handkerchief/tissue when coughing and/or sneezing?</td>
<td>50 (50)</td>
<td>49 (49)</td>
<td>99</td>
<td>1.000</td>
</tr>
<tr>
<td>If no, why?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV stigma</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>1</td>
<td>1.000</td>
</tr>
<tr>
<td>Cover mouth with facial mask when coughing and/or sneezing?</td>
<td>21 (21)</td>
<td>33 (33)</td>
<td>54</td>
<td>0.016*</td>
</tr>
<tr>
<td>If no, why?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Forget</td>
<td>8 (8)</td>
<td>2 (6)</td>
<td>10</td>
<td>0.046*</td>
</tr>
<tr>
<td>Not interested</td>
<td>9 (9)</td>
<td>0 (0)</td>
<td>9</td>
<td>0.003*</td>
</tr>
<tr>
<td>No facial mask with me all the time</td>
<td>17 (17)</td>
<td>12 (12)</td>
<td>29</td>
<td>0.271</td>
</tr>
<tr>
<td>Secret</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>1</td>
<td>1.000</td>
</tr>
<tr>
<td>TB stigma</td>
<td>5 (5)</td>
<td>0 (0)</td>
<td>5</td>
<td>0.056</td>
</tr>
<tr>
<td>HIV stigma</td>
<td>5 (5)</td>
<td>3 (3)</td>
<td>8</td>
<td>0.715</td>
</tr>
<tr>
<td>Sleep in a room by oneself or avoid sleeping in a room with small children?</td>
<td>33 (33)</td>
<td>35 (35)</td>
<td>68</td>
<td>0.668</td>
</tr>
<tr>
<td>If no, why?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not necessary</td>
<td>4 (4)</td>
<td>7 (7)</td>
<td>11</td>
<td>0.338</td>
</tr>
<tr>
<td>Not enough rooms</td>
<td>10 (10)</td>
<td>9 (9)</td>
<td>19</td>
<td>0.799</td>
</tr>
<tr>
<td>Secret</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>1</td>
<td>1.000</td>
</tr>
<tr>
<td>Family rejection</td>
<td>3 (3)</td>
<td>1 (1)</td>
<td>4</td>
<td>0.617</td>
</tr>
<tr>
<td>Open house windows to the outside?</td>
<td>43 (43)</td>
<td>46 (46)</td>
<td>89</td>
<td>0.338</td>
</tr>
<tr>
<td>If no, why?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not necessary</td>
<td>1 (1)</td>
<td>1 (1)</td>
<td>2</td>
<td>1.000</td>
</tr>
<tr>
<td>No windows</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>1</td>
<td>1.000</td>
</tr>
<tr>
<td>Cold</td>
<td>3 (3)</td>
<td>3 (3)</td>
<td>6</td>
<td>1.000</td>
</tr>
<tr>
<td>Security</td>
<td>2 (5)</td>
<td>0 (0)</td>
<td>2</td>
<td>0.495</td>
</tr>
</tbody>
</table>

**Table 10.** Infection control measures at home among patients with suspected TB and patients with TB

*Note—*. Statistical significance [p<0.05] is marked with an asterisk.
### Infection Control Measures at Home

<table>
<thead>
<tr>
<th>Infection Control Measures at Home</th>
<th>Patients with suspected TB ((n = 50))</th>
<th>Patients with TB ((n = 50))</th>
<th>Total ((n = 100))</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use fans if possible for moving air to the outside?</td>
<td>30 (30)</td>
<td>29 (29)</td>
<td>59</td>
<td>0.839</td>
</tr>
<tr>
<td>If no, why?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not important</td>
<td>8 (8)</td>
<td>8 (8)</td>
<td>16</td>
<td>1.000</td>
</tr>
<tr>
<td>No fans</td>
<td>10 (10)</td>
<td>13 (13)</td>
<td>23</td>
<td>0.476</td>
</tr>
<tr>
<td>Cannot afford it</td>
<td>3 (3)</td>
<td>1 (1)</td>
<td>4</td>
<td>0.617</td>
</tr>
<tr>
<td>Isolation at home?</td>
<td>42 (42)</td>
<td>43 (43)</td>
<td>85</td>
<td>0.779</td>
</tr>
<tr>
<td>Isolation is feasible</td>
<td>31 (31)</td>
<td>34 (34)</td>
<td>65</td>
<td>0.529</td>
</tr>
<tr>
<td>Willing to do it, but not feasible</td>
<td>11 (11)</td>
<td>9 (9)</td>
<td>20</td>
<td>0.617</td>
</tr>
<tr>
<td>If not willing, why?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physically impossible to be isolated</td>
<td>6 (6)</td>
<td>6 (6)</td>
<td>12</td>
<td>1.000</td>
</tr>
<tr>
<td>It won’t work</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>1</td>
<td>1.000</td>
</tr>
<tr>
<td>Family won’t allow</td>
<td>1 (1)</td>
<td>1 (1)</td>
<td>2</td>
<td>1.000</td>
</tr>
</tbody>
</table>

Cont. Table 10. Infection control measures at home among patients with suspected TB and patients with TB.
4.2.2.3 Acceptability of infection control measures at work

Infection control measures at work had a relatively high level of acceptability among participants at baseline. Sixty-five percent (65%) of all participants would be willing to stop working until they have completed 2 weeks of treatment, or until smear microscopy is negative. The majority of patients who did not agree with this measure stated that they would not receive any income. TB and HIV stigma were not contributing factors to participants’ decision. 98% of the participants stated that they would be more willing to cover their mouth with a handkerchief or tissue at work, compared to 58% who would prefer to use a facemask (See Table 11).
<table>
<thead>
<tr>
<th>Infection Control Measures at Work</th>
<th>Patients with suspected TB (%)</th>
<th>Patients with TB (%)</th>
<th>Total</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stop working until you have completed 2 weeks of treatment, or longer?</td>
<td>32 (32)</td>
<td>33 (33)</td>
<td>65</td>
<td>0.834</td>
</tr>
<tr>
<td>If no, why?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not so sick</td>
<td>7 (7)</td>
<td>9 (9)</td>
<td>16</td>
<td>0.585</td>
</tr>
<tr>
<td>No compensation</td>
<td>10 (10)</td>
<td>8 (8)</td>
<td>18</td>
<td>0.795</td>
</tr>
<tr>
<td><strong>TB stigma</strong></td>
<td>1 (1)</td>
<td>1 (1)</td>
<td>2</td>
<td>1.000</td>
</tr>
<tr>
<td><strong>HIV stigma</strong></td>
<td>2 (2)</td>
<td>2 (2)</td>
<td>4</td>
<td>1.000</td>
</tr>
<tr>
<td>Cover mouth with a handkerchief/tissue when coughing and/or sneezing?</td>
<td>48 (48)</td>
<td>50 (50)</td>
<td>98</td>
<td>0.495</td>
</tr>
<tr>
<td>If no, why?</td>
<td>2 (2)</td>
<td>0 (0)</td>
<td>2</td>
<td>0.495</td>
</tr>
<tr>
<td><strong>TB stigma</strong></td>
<td>2 (2)</td>
<td>0 (0)</td>
<td>2</td>
<td>0.495</td>
</tr>
<tr>
<td>Cover mouth with facial mask when coughing and/or sneezing? Y/N</td>
<td>25 (25)</td>
<td>33 (33)</td>
<td>58</td>
<td>0.105</td>
</tr>
<tr>
<td>If no, why?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Forget</td>
<td>6 (6)</td>
<td>0 (0)</td>
<td>6</td>
<td>0.027*</td>
</tr>
<tr>
<td>Not interested</td>
<td>7 (7)</td>
<td>1 (1)</td>
<td>8</td>
<td>0.059</td>
</tr>
<tr>
<td>No facial mask all the time</td>
<td>12 (12)</td>
<td>9 (9)</td>
<td>21</td>
<td>0.461</td>
</tr>
<tr>
<td>Secret</td>
<td>3 (3)</td>
<td>2 (2)</td>
<td>5</td>
<td>1.000</td>
</tr>
<tr>
<td><strong>TB stigma</strong></td>
<td>3 (3)</td>
<td>0 (0)</td>
<td>3</td>
<td>0.242</td>
</tr>
<tr>
<td><strong>HIV stigma</strong></td>
<td>3 (3)</td>
<td>3 (9)</td>
<td>6</td>
<td>1.000</td>
</tr>
</tbody>
</table>

Table 11. Infection control measures at work among patients with suspected TB and patients with TB

Note—Statistical significance [p<0.05] is marked with an asterisk.
4.2.2.4 Relationship between baseline knowledge and acceptability of infection control measures

No major differences were found between patients with suspected TB and patients with TB neither in knowledge nor in acceptability of field-adapted measures to prevent TB transmission. At baseline, only 33% of the participants (15% patients with TB; 18% patients suspected with TB) had an adequate understanding of core TB knowledge (i.e. what TB is, how TB is transmitted, the causative agent, and essential infection control measures—covering mouth, improve ventilation, complete TB treatment). Eighty percent (80%) of all participants agreed to implement some TB prevention measures. However, more than half of the individuals in each group disagreed with the implementation of patient-specific measures.

Core knowledge and acceptability of TB infection control measures at baseline

![Diagram showing relationship between baseline TB knowledge and acceptability of infection control measures among patients with suspected TB and patients with TB.](image)

**Figure 17.** Relationship between baseline TB knowledge and acceptability of infection control measures among patients with suspected TB and patients with TB
Neither differences in level of knowledge (p-value 0.523) nor differences in acceptability of patient-specific infection control measures (p-value 0.134) were found between patients with suspected TB and patients with TB. When we quantified the relationship between core TB knowledge and the acceptability of these measures at baseline (See Figure 17), we did not find any significant correlation (Spearman correlation-coefficient 0.003 p = 0.9980).

4.2.3 Knowledge of patients with TB at the end of treatment

Patients with TB were interviewed for a second time. Nine percent (9%) of all participants who were recruited at baseline could not attend the second interviews and therefore 82 paired-interviews were analyzed.

Knowledge about TB and infection control measures increased significantly over time, between start and end of treatment, under research conditions. There was a 32% increase in the proportion of participants who stated that they knew what the cause of TB was, and a 41% increase in participants who agreed that TB was caused by a microorganism. 44% of respondents, who, at baseline, stated that they did not to know how TB is transmitted, reported that they knew how a person can get TB, at the second interview. When participants were asked to specify how TB was transmitted, an increase of 54% of participants reported that only by being in close contact with an infectious source, other individuals could get TB. Most participants believed that children require IPT once exposed to *M. tuberculosis*, but there was no change over time. After receiving education under research conditions, most participants reported that they knew when a TB patient usually stops transmitting the disease (32% increase in response rate). Measures such as using facemasks, covering the mouth in health care facilities, opening house windows to
the outside air and completing anti-TB treatment were more often recognized as measures to reduce the transmission of TB at the end of participant’s follow-up, compared to baseline. An increase of 41% in a positive response over time was found when participants were asked whether they knew the importance of these measures. A higher proportion of participants responded that these preventive methods helped to reduce TB transmission for health care workers (56%), home contacts (66%) and co-workers (54%), compared to baseline (See Table 12).
<table>
<thead>
<tr>
<th>Knowledge &amp; Perceptions about Tuberculosis</th>
<th>Baseline (%) [n = 41]</th>
<th>End Treatment (%) [n = 41]</th>
<th>Absolute Diff (%)</th>
<th>Confidence Interval</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Do you know the cause of Tuberculosis (TB)?</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>23 (28)</td>
<td>36 (44)</td>
<td>32↑</td>
<td>13.21 - 36.46</td>
<td>0.001*</td>
<td></td>
</tr>
<tr>
<td>Germs /Other causes</td>
<td>6 (7)</td>
<td>25 (30)</td>
<td>41↑</td>
<td>5.38 - 56.82</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td><strong>How a person gets TB? Y/N</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19 (23)</td>
<td>37 (45)</td>
<td>44↑</td>
<td>24.51 - 48.66</td>
<td>&lt;0.001*</td>
<td></td>
</tr>
<tr>
<td>Sharing food utensils</td>
<td>5 (6)</td>
<td>6 (7)</td>
<td>2</td>
<td>−10.79 - 13.69</td>
<td>1.000</td>
</tr>
<tr>
<td>Kissing people</td>
<td>3 (4)</td>
<td>9 (11)</td>
<td>15↑</td>
<td>−1.03 - 19.39</td>
<td>0.07</td>
</tr>
<tr>
<td>Living or being in close contact with people</td>
<td>14 (17)</td>
<td>36 (44)</td>
<td>54↑</td>
<td>33.81 - 58.41</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Living in or moving to cold areas</td>
<td>6 (7)</td>
<td>10 (12)</td>
<td>9</td>
<td>−5.89 - 18.27</td>
<td>0.289</td>
</tr>
<tr>
<td><strong>Do you think tuberculosis can be passed on to other people?</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>41 (50)</td>
<td>41 (50)</td>
<td>—</td>
<td>—</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Adults</td>
<td>8 (10)</td>
<td>4 (5)</td>
<td>10</td>
<td>−5.89 - 18.27</td>
<td>0.289</td>
</tr>
<tr>
<td>Young children</td>
<td>8 (10)</td>
<td>5 (6)</td>
<td>7</td>
<td>−8.81 - 18.66</td>
<td>0.508</td>
</tr>
<tr>
<td>Elderly people</td>
<td>5 (6)</td>
<td>4 (5)</td>
<td>2</td>
<td>−8.62 - 10.91</td>
<td>1.000</td>
</tr>
<tr>
<td>Co-Workers</td>
<td>5 (6)</td>
<td>3 (4)</td>
<td>5</td>
<td>−8.11 - 13.37</td>
<td>0.688</td>
</tr>
<tr>
<td>HIV/AIDS Patients</td>
<td>4 (5)</td>
<td>4 (5)</td>
<td>0</td>
<td>−13.38 - 13.38</td>
<td>1.000</td>
</tr>
<tr>
<td>All above mentioned</td>
<td>24 (29)</td>
<td>29 (35)</td>
<td>12</td>
<td>−8.50 - 27.93</td>
<td>0.302</td>
</tr>
<tr>
<td>Not sure</td>
<td>8 (10)</td>
<td>6 (7)</td>
<td>5</td>
<td>−11.59 - 18.46</td>
<td>0.754</td>
</tr>
<tr>
<td><strong>Do young children need treatment?</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40 (49)</td>
<td>41 (50)</td>
<td>2</td>
<td>−2.32 - 2.44</td>
<td>1.000</td>
<td></td>
</tr>
<tr>
<td>Who? Children &lt;5 and HIV /All children</td>
<td>7 (9)</td>
<td>4 (5)</td>
<td>8</td>
<td>−7.34 - 16.22</td>
<td>0.4531</td>
</tr>
<tr>
<td><strong>Do you know when a TB patient usually stops transmitting the disease?</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21 (26)</td>
<td>34 (41)</td>
<td>32↑</td>
<td>11.24 - 40.25</td>
<td>0.002*</td>
<td></td>
</tr>
</tbody>
</table>

*Table 12.* Difference in core TB knowledge among patients with TB at the beginning and at the end of treatment

*Note*: Statistical significance [p<0.05] is marked with an asterisk.
### Knowledge & Perceptions about Tuberculosis

<table>
<thead>
<tr>
<th>#</th>
<th>Knowledge &amp; Perceptions about Tuberculosis</th>
<th>Baseline (%)</th>
<th>End Treatment (%)</th>
<th>Absolute Diff (%)</th>
<th>Confidence Interval</th>
<th>P- Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>Do you know some measures to control tuberculosis? Y/N</td>
<td>16 (20)</td>
<td>33 (40)</td>
<td>41†</td>
<td>18.41 - 52.98</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>17</td>
<td>Use facemask during transportation to a hospital or clinic</td>
<td>11 (13)</td>
<td>26 (32)</td>
<td>36†</td>
<td>13.99 - 48.10</td>
<td>0.002*</td>
</tr>
<tr>
<td>18</td>
<td>Use facemask in a hospital or clinic</td>
<td>14 (17)</td>
<td>24 (29)</td>
<td>25†</td>
<td>0.87 - 40.33</td>
<td>0.041*</td>
</tr>
<tr>
<td>19</td>
<td>Cover his/her mouth when coughing and/or sneezing in a hospital or clinic</td>
<td>13 (16)</td>
<td>23 (28)</td>
<td>24†</td>
<td>0.87 - 40.34</td>
<td>0.041*</td>
</tr>
<tr>
<td>20</td>
<td>Cover his/her mouth when coughing and/or sneezing at home or at work</td>
<td>12 (15)</td>
<td>19 (23)</td>
<td>17</td>
<td>−6.07 - 34.69</td>
<td>0.167</td>
</tr>
<tr>
<td>21</td>
<td>Be separated from other patients and requested to wait in a separated area</td>
<td>8 (10)</td>
<td>13 (16)</td>
<td>12</td>
<td>−7.25 - 25.94</td>
<td>0.267</td>
</tr>
<tr>
<td>22</td>
<td>Sleep in a room by him/herself or avoid sleeping in a room with small children</td>
<td>9 (11)</td>
<td>19 (23)</td>
<td>24†</td>
<td>2.07 - 38.27</td>
<td>0.031*</td>
</tr>
<tr>
<td>23</td>
<td>Use fans if possible for moving air to the outside</td>
<td>6 (7)</td>
<td>14 (17)</td>
<td>19</td>
<td>−1.86 - 33.35</td>
<td>0.077</td>
</tr>
<tr>
<td>24</td>
<td>Complete their course of anti—TB treatment</td>
<td>11 (13)</td>
<td>30 (37)</td>
<td>46†</td>
<td>22.90 - 57.87</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>25</td>
<td>Do you know why measures to control tuberculosis are important? Y/N</td>
<td>16 (20)</td>
<td>33 (40)</td>
<td>41†</td>
<td>20.10 - 50.02</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>26</td>
<td>Prevention for HCW</td>
<td>10 (12)</td>
<td>23 (28)</td>
<td>32†</td>
<td>8.29 - 45.65</td>
<td>0.007 *</td>
</tr>
<tr>
<td>27</td>
<td>Prevention at home/close contacts</td>
<td>13 (16)</td>
<td>27 (33)</td>
<td>34†</td>
<td>10.43 - 48.09</td>
<td>0.004*</td>
</tr>
<tr>
<td>28</td>
<td>Prevention at work</td>
<td>10 (12)</td>
<td>22 (27)</td>
<td>30†</td>
<td>9.09 - 37.81</td>
<td>0.004*</td>
</tr>
</tbody>
</table>

Continued Table 12. Difference in core TB knowledge among patients with TB at the beginning and at the end of treatment

Note—Statistical significance [p<0.05] is marked with an asterisk.
4.2.3.1 Acceptability of infection control measures at a health care facility at baseline and end of treatment

The majority of all participants accepted infection control measures at health care facilities. No significant differences were observed when we compared to the baseline, due to the high levels of acceptability of infection control measures in health care facilities at baseline (See Table 13).
<table>
<thead>
<tr>
<th>Infection Control Measures at Health Care Facilities</th>
<th>Baseline (%) <em>n = 41</em></th>
<th>End Treatment (%) <em>n = 41</em></th>
<th>Absolute Diff (%)</th>
<th>Confidence Interval</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use facemask HC settings? Y/N</td>
<td>39 (48)</td>
<td>41 (50)</td>
<td>5</td>
<td>-3.34 - 4.88</td>
<td>0.5</td>
</tr>
<tr>
<td>If no, why?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uncomfortable</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>2</td>
<td>-2.32 - 2.44</td>
<td>1.000</td>
</tr>
<tr>
<td>TB stigma</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>2</td>
<td>-2.32 - 2.45</td>
<td>1.000</td>
</tr>
<tr>
<td>Cover mouth when coughing and/or sneezing in a health care setting? Y/N</td>
<td>41 (50)</td>
<td>41 (50)</td>
<td>-</td>
<td>-</td>
<td>N/A</td>
</tr>
<tr>
<td>Complete a course of anti—TB treatment? Y/N</td>
<td>41 (50)</td>
<td>41 (50)</td>
<td>-</td>
<td>-</td>
<td>N/A</td>
</tr>
<tr>
<td>Be separated from other patients? Y/N</td>
<td>28 (34)</td>
<td>26 (32)</td>
<td>5</td>
<td>-15.71 - 23.61</td>
<td>0.804</td>
</tr>
<tr>
<td>If no, why?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do not like being separated from others</td>
<td>5 (6)</td>
<td>6 (7)</td>
<td>2</td>
<td>-12.64 - 15.94</td>
<td>1.000</td>
</tr>
<tr>
<td>TB stigma</td>
<td>5 (6)</td>
<td>6 (7)</td>
<td>2</td>
<td>-12.64 - 15.95</td>
<td>1.000</td>
</tr>
<tr>
<td>HIV stigma</td>
<td>5 (6)</td>
<td>5 (6)</td>
<td>0</td>
<td>-12.64 - 15.96</td>
<td>1.000</td>
</tr>
</tbody>
</table>

Table 13. Infection control measures at health care facilities among patients with TB at the beginning and at the end of treatment
4.2.3.2 Acceptability of Infection Control Measures at Home at baseline and end of treatment

There were no major changes between start and end of treatment in the acceptability of measures such as covering the mouth, and being isolated at home. Both measures had a high level of acceptability before and after exposure to TB education. However, measures such as using facemasks at home \( (p = 0.023) \), opening windows to the outside \( (p = 0.023) \) and, use of fans to improve ventilation \( (p = 0.023) \), were more likely to be acceptable by participants at the end of treatment. On the other hand, although there was a small increase in the number of participants who were willing to be isolated, no significant difference was found between baseline and end of treatment (See Table 14).
<table>
<thead>
<tr>
<th>Infection Control Measures at Home</th>
<th>Baseline (%) n = 41</th>
<th>End Treatment (%) n = 41</th>
<th>Absolute Diff (%)</th>
<th>Confidence Interval</th>
<th>P- Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cover mouth with a handkerchief/tissue when coughing and/or sneezing?</td>
<td>41 (50)</td>
<td>40 (49)</td>
<td>2</td>
<td>-2.32 - 2.44</td>
<td>1.000</td>
</tr>
<tr>
<td>If no, why? HIV stigma</td>
<td>0 (0)</td>
<td>1 (1)</td>
<td>3</td>
<td>-2.32 - 2.45</td>
<td>1.000</td>
</tr>
<tr>
<td>Cover mouth with facial mask when coughing and/or sneezing?</td>
<td>26 (32)</td>
<td>35 (43)</td>
<td>22 †</td>
<td>2.89 - 30.49</td>
<td>0.023*</td>
</tr>
<tr>
<td>If no, why? Forget</td>
<td>2 (2)</td>
<td>1 (1)</td>
<td>2</td>
<td>-5.94 - 7.19</td>
<td>1.000</td>
</tr>
<tr>
<td>No facial mask with me all the time</td>
<td>10 (12)</td>
<td>2 (2)</td>
<td>22 †</td>
<td>2.68 - 24.27</td>
<td>0.022*</td>
</tr>
<tr>
<td>TB stigma</td>
<td>0 (0)</td>
<td>1 (1)</td>
<td>2</td>
<td>-2.32 - 2.44</td>
<td>1.000</td>
</tr>
<tr>
<td>HIV stigma</td>
<td>3 (4)</td>
<td>3 (4)</td>
<td>0</td>
<td>-8.44 - 8.44</td>
<td>1.000</td>
</tr>
<tr>
<td>Sleep in a room by oneself or avoid sleeping in a room with small children?</td>
<td>28 (34)</td>
<td>33 (40)</td>
<td>12</td>
<td>-4.39 - 20.72</td>
<td>0.18</td>
</tr>
<tr>
<td>If no, why? Not necessary</td>
<td>5 (6)</td>
<td>2 (2)</td>
<td>7</td>
<td>-5.28 - 12.07</td>
<td>0.375</td>
</tr>
<tr>
<td>Not enough rooms</td>
<td>7 (9)</td>
<td>4 (5)</td>
<td>7</td>
<td>-7.16 - 15.82</td>
<td>0.453</td>
</tr>
<tr>
<td>Family rejection</td>
<td>1 (1)</td>
<td>2 (2)</td>
<td>2</td>
<td>-2.32 - 2.44</td>
<td>1.000</td>
</tr>
<tr>
<td>Open house windows to the outside?</td>
<td>37 (45)</td>
<td>40 (49)</td>
<td>22 †</td>
<td>2.07 - 38.27</td>
<td>0.031*</td>
</tr>
<tr>
<td>If no, why? Not necessary</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>2</td>
<td>-2.32 - 2.44</td>
<td>1.000</td>
</tr>
<tr>
<td>Cold</td>
<td>3 (4)</td>
<td>1 (1)</td>
<td>5</td>
<td>-5.97 - 9.63</td>
<td>0.625</td>
</tr>
<tr>
<td>Use fans if possible for moving air to the outside?</td>
<td>23 (28)</td>
<td>32 (39)</td>
<td>22 †</td>
<td>4.68 - 26.71</td>
<td>0.012*</td>
</tr>
<tr>
<td>If no, why? Not important</td>
<td>8 (10)</td>
<td>3 (4)</td>
<td>12</td>
<td>-0.53 - 12.20</td>
<td>0.063</td>
</tr>
<tr>
<td>No fans</td>
<td>9 (11)</td>
<td>5 (6)</td>
<td>10</td>
<td>-7.44 - 21.13</td>
<td>0.344</td>
</tr>
<tr>
<td>Cannot afford it</td>
<td>1 (1)</td>
<td>1 (1)</td>
<td>0</td>
<td>-4.76 - 4.76</td>
<td>1.000</td>
</tr>
<tr>
<td>Isolation at home?</td>
<td>37 (45)</td>
<td>39 (48)</td>
<td>5</td>
<td>-5.97 - 9.63</td>
<td>0.625</td>
</tr>
<tr>
<td>Isolation isn't a problem</td>
<td>28 (34)</td>
<td>30 (37)</td>
<td>5</td>
<td>-11.59 - 18.46</td>
<td>0.754</td>
</tr>
<tr>
<td>Willing to be isolated at home</td>
<td>9 (11)</td>
<td>9 (11)</td>
<td>0</td>
<td>-15.26 - 15.26</td>
<td>1.000</td>
</tr>
<tr>
<td>If not willing, why?</td>
<td>4 (5)</td>
<td>2 (2)</td>
<td>5</td>
<td>-5.97 - 9.63</td>
<td>0.625</td>
</tr>
</tbody>
</table>

Table 14. Infection control measures at home among patients with TB at the beginning and at the end of treatment

Note—Statistical significance [p<0.05] is marked with an asterisk.
4.2.3.3 Acceptability of infection control measures at work at baseline and end of treatment

Few participants reported changes in acceptability of implementation of infection control measures at work at the end of treatment. Small absolute differences were found when patients were asked about the implementation of measures, such as stop working for at least 2 weeks, or until smear results were negative, or even the use of facemasks at work. All participants reported that they were willing to cover their mouths with a handkerchief or tissue when coughing and/or sneezing (See Table 15).
<table>
<thead>
<tr>
<th>Infection Control Measures at Work</th>
<th>Baseline (%)</th>
<th>End Treatment (%)</th>
<th>Absolute Diff (%)</th>
<th>Confidence Interval</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stop working until you have completed 2 weeks of treatment, or longer?</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If no, why?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not so sick</td>
<td>26 (32)</td>
<td>31 (38)</td>
<td>12</td>
<td>-4.39 - 20.72</td>
<td>0.18</td>
</tr>
<tr>
<td>No compensation</td>
<td>8 (10)</td>
<td>5 (6)</td>
<td>7</td>
<td>-8.81 - 18.66</td>
<td>0.508</td>
</tr>
<tr>
<td>TB stigma</td>
<td>8 (10)</td>
<td>5 (6)</td>
<td>7</td>
<td>-8.81 - 18.66</td>
<td>0.508</td>
</tr>
<tr>
<td>HIV stigma</td>
<td>1 (1)</td>
<td>2 (2)</td>
<td>2</td>
<td>-2.32 - 2.44</td>
<td>1.000</td>
</tr>
<tr>
<td><strong>Cover mouth with a handkerchief/tissue when coughing and/or sneezing?</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>41 (50)</td>
<td>41 (50)</td>
<td>-</td>
<td>-</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td><strong>Cover mouth with facial mask when coughing and/or sneezing?</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If no, why?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not interested</td>
<td>27 (33)</td>
<td>33 (40)</td>
<td>15</td>
<td>-1.03 - 19.39</td>
<td>0.070</td>
</tr>
<tr>
<td>No facial mask all the time</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>2</td>
<td>-2.32 - 2.44</td>
<td>1.000</td>
</tr>
<tr>
<td>Secret</td>
<td>7 (9)</td>
<td>1 (1)</td>
<td>15</td>
<td>-1.03 - 19.39</td>
<td>0.07</td>
</tr>
<tr>
<td>TB stigma</td>
<td>1 (1)</td>
<td>2 (2)</td>
<td>2</td>
<td>-5.94 - 7.19</td>
<td>1.000</td>
</tr>
<tr>
<td>HIV stigma</td>
<td>0 (0)</td>
<td>4 (5)</td>
<td>10</td>
<td>-2.00 - 9.76</td>
<td>0.125</td>
</tr>
<tr>
<td><strong>Table 15.</strong> Infection control measures at work among patients with TB at the beginning and at the end of treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
4.2.3.4 Relationship between knowledge and acceptability of infection control measures at the end of treatment

The proportion of participants with an acceptable level of knowledge increased by 42% between the start and end of treatment (p = 0.0005). Moreover, acceptability of these patient-specific measures increased from 54% to 76% (p = 0.0225). The increase in knowledge was associated with a significant increase in acceptability of TB infection control measures (Spearman correlation-coefficient 0.5288 p = 0.0033) (See Figure 18).

**Figure 18.** Relationship between TB knowledge and acceptability of infection control measures at the end of treatment
DISCUSSION

Chapter Introduction

This research provides an insight into two simple and cost-effective strategies for TB control in developing countries. Below we discuss how both strategies—sputum induction, a simple method to identify potentially TB infectious patients and on-going TB education—can be implemented in low income countries. Moreover, we emphasize the implications of these strategies for TB control in resource-constrained areas.

5.1 Evaluation of the Diagnostic Yield of Sputum Induction

In response to the critical need for new and accurate TB diagnostic tools, researchers have made remarkable progress in development of new and better TB diagnostics. However, in an era of increasing multi-drug resistance, it remains important to obtain good quality sputum specimens from patients with suspected TB for mycobacterial culture and drug sensitivity testing (1). Cost effective sample collection methods such as sputum induction may be implemented in high TB burden and resource-constrained areas.

We conducted the first systematic review and meta-analysis of the diagnostic yield of sputum induction. The strengths of the study include the comprehensive search strategy; duplicate and independent study selection; quality assessment and data extraction; and the
use of meta-regression analysis. It is particularly important that potential sources of heterogeneity are examined in a meta-analysis showing high levels of inconsistency in yield. Sources of variability that could be attributed to within-study factors (eg. participant selection) and between-study factors (study design and conduct) are explored by meta-regression.

This evaluation of studies reporting the utility of sputum induction as a simple method to identify potentially TB infectious patients showed that, sputum induction is likely to detect between 65 to 81% of culture-confirmed TB cases under study conditions, regardless of age group or HIV prevalence in the study population. We might have expected the comparative diagnostic yield of sputum induction to be greater among studies reporting paucibacillary disease, such as paediatric studies and those with high HIV prevalence in the study population, but no such effect was observed. We found that use of bronchoscopic lavage as a comparison method was associated with, on average, 22% lower diagnostic yield from sputum induction, compared to studies that did not employ FOB; second, we observed that use of 3% saline nebulisation for sputum induction was a significant confounder in studies using FOB. However, we have demonstrated by meta-regression analysis that neither saline concentration nor FOB usage were independently associated with diagnostic yield from sputum induction.

5.1.1 Saline Concentration

The optimal saline concentration for sputum induction is not known. It has been suggested that higher nebulised saline concentrations might have a greater osmotic effect on airway secretions (2, 3), increasing the volume of the induced sputum sample, and thereby increasing the diagnostic yield. Our group has shown that nebulised 5% saline is both safe
and tolerable, with minimal physiologic changes, when used for sputum induction among adults investigated for PTB in an ambulatory setting (4). However, others have suggested that higher nebulised saline concentrations might be associated with greater risk of airway reactivity and higher rates of adverse events during the procedure (5). The findings of this meta-analysis suggest that higher saline concentrations are not associated with better diagnostic yield in sputum induction after adjusting for confounders. We suggest that the safety and diagnostic yield of low nebulised saline concentrations, perhaps even 0.9% saline, should be studied prospectively in an effort to minimize adverse events.

5.1.2 Comparative Procedures

We have shown that the observed reduction in sputum induction diagnostic yield in those studies using FOB as the comparator method is confounded by use of lower saline concentration (3%) in this group. Studies using invasive diagnostic techniques might be more likely to include smear-negative or sputum-unproductive individuals, leading to selection bias towards lower yield. It is also possible that, if FOB were better at detecting paucibacillary culture-positive TB cases than sputum induction, the observed yield of this procedure relative to the total number of culture-confirmed cases would be lower in studies reporting FOB data. However, some studies have shown that the yield of sputum induction is equal to, or even better than that of FOB, which is consistent with our finding that FOB usage was not independently associated with lower diagnostic yield (6-8).

5.1.3 Standardization of Sputum Induction

Observed variability might also be explained by unreported differences in the sputum induction technique and lack of standardization. Technical factors that affect density of the aerosol and particle size, such as the nebulisation device, might also affect deposition of the
saline solution in the tracheobronchial tree and diagnostic yield of the procedure. The selected studies used a broad range of nebulisation devices and oxygen cylinders with different flow outputs, which would have directly affected nebulised particle size and airway deposition. However, there were limited data on the number of IS samples required, the optimum volume of the sample for mycobacterial culture, devices, the timing of specimen collection, and other technical factors. Therefore reporting of these important data was inconsistent, incomplete, and did not allow meaningful analysis. Other potential sources of heterogeneity include severity of pre-existing lung disease, inclusion bias towards paucibacillary TB disease, and other patient-specific characteristics that might explain the presence of outliers in this analysis.

5.1.4 Limitations

Several limitations of this meta-analysis must be considered. The literature search was restricted to three sources, including one electronic database; additional references recommended by experts in the field; and published reference lists and reviews. One reviewer conducted the primary search to screen for citations, which might have introduced study selection bias, although two reviewers conducted the secondary search and quality assessment of papers identified by the primary screening. Another limitation that affects this meta-analysis is the lack of a gold standard diagnostic comparator group in the reported studies. Although some diagnostic methods, such as FOB, are believed to provide better diagnostic accuracy than others, it is clear that none of the reported comparator methods are sufficiently sensitive to define the population with true TB disease with 100% accuracy. It follows that surrogate measures must be used to infer sensitivity, as others have done using percentage diagnostic yield, which utilizes all culture-confirmed TB cases as the denominator (9, 10). As noted above, few studies documented key technical aspects of the
sputum induction procedure and reporting of this important information was often inconsistent.

5.1.5 Conclusion

Sputum induction has been widely used for the diagnosis of pulmonary TB and it has shown to have a superior diagnostic yield to other invasive methods such as gastric lavage and FOB. Our study has demonstrated that *M. tuberculosis* can be isolated in nearly three-quarters of suspected cases using sputum induction for sample collection. In resource-poor countries, sputum induction would be an ideal diagnostic tool for TB diagnosis, as it is a low-cost technique and more feasible than invasive procedures, since it does not require hospitalization. However, despite the advantages—such as the lower risk of occupational exposure compared to bronchoscopy (11), excellent acceptability by patients (12), cost (7), and safety—that other authors have shown, and due to the variability found in this meta-analysis, we recommend further prospective, comparative studies of the diagnostic yield of sputum induction. These studies should standardize the sputum induction methodology for the initial investigation of suspected TB cases.

In the following section, we will discuss the implications of our findings about knowledge of TB and infection control measures, and acceptability and willingness to implement patient-specific infection control measures, in patients with suspected TB and patients with TB who at the beginning of treatment; second, we discuss the potential for early intensive TB education to replicate the gains in knowledge and acceptability that we have shown by the end of a course of TB treatment.
5.2 IMPLEMENTATION OF INFECTION CONTROL MEASURES

In developing countries, the force of TB transmission increases due to overcrowding, social deprivation, poverty and other factors that contribute to immunosuppression, such as HIV infection (13-15). It is clear that better field-adapted and cost-effective infection control measures are urgently needed in highly endemic settings (16). The DOTS strategy promoted by the WHO endorses education for patients with TB, household members and other close contacts as a simple community-based approach to help reduce the proportion of previously uninfected individuals who are newly infected each year and are at risk of developing TB disease (16).

The effect of health education for patients with TB has primarily been studied to determine how TB education influences adherence to TB treatment (17-19). Several authors have stated that well-informed patients are more likely to adhere to a treatment protocol and to undertake appropriate preventive measures for their families (18, 20). We report the first study of knowledge and attitudes to TB in relation to the acceptability and implementation of patient-specific infection control measures, including environmental and respiratory protection measures. One of the activities carried out by TB control programmes is to provide TB information when patients start treatment. Although education to patients with TB and their family members should be provided at baseline and reinforced continuously throughout treatment, implementation may not be optimal under field conditions. After interviewing patients with suspected TB and newly diagnosed patients with TB, our study revealed limited knowledge about TB and a low degree of acceptability of patient-specific measures for TB control, immediately after individuals have had initial contact with health care providers. Gender and the role of cultural characteristics (e.g., Xhosa-speaking versus Afrikaans-speaking participants) did not play a role in knowledge and acceptability of
patient-specific infection control measures. In our study, patients on TB treatment, who had received some limited TB education at diagnosis, did not show greater core knowledge about TB and preventive measures, compared to patients with suspected TB, who had not received any information or education. However, we have shown that with on-going education and experience of diagnostic procedures and a course of TB treatment, patients with TB showed increased knowledge of TB and infection control measures over time. Furthermore, the increase in knowledge was associated with a significant increase in the acceptability of patient-specific measures.

5.2.1 Core TB knowledge

No major differences were found at baseline between patients with suspected TB and patients with TB, except for a slightly higher proportion of patients with suspected TB who reported that TB was caused by a micro-organism and highlighted anti-TB treatment as the most important infection control measure. In general, TB knowledge among participants was found to be poor to moderate. Only 57% of the participants reported that they knew the cause of TB and only 25% knew that TB was caused by a micro-organism. Although most participants (95%) reported awareness about who was more likely to get TB, there was no clarity about the risk that TB poses for young children and HIV-positive patients. This is of particular importance from a public health perspective, since the risk of disease progression is mainly determined by the age (21) and immune-compromise —the risk of developing TB is between 20 and 37 times greater in HIV infected individuals (22). Therefore, the lack of recognition that other susceptible individuals might develop TB once exposed to an infectious patient at home or in work settings, hinders the acceptance and implementation of specific measures that might reduce transmission in overcrowded spaces occupied by small children or HIV-positive individuals.
Fifty-four percent of the participants claimed to know how TB was transmitted, although some misconceptions were found in both groups. Some participants believed that TB was a hereditary disease, or that it spread by sharing food utensils, kissing patients with TB, and living in cold areas. As has been highlighted by many authors, lack of knowledge of the modes of TB transmission leads to misconceptions about preventive measures and encourages people to consider alternatives for their TB care (23-25). Yadav et al evaluated knowledge levels and attitudes of sand-stone quarry workers in Jodhpur towards tuberculosis and reported that only 1.6% knew that tuberculosis was caused by germs and 45.2% respondents had the misconception that TB was a hereditary disease (26).

These initial findings were surprising. One might expect that core TB knowledge among patients with TB would be at least moderate, since they had received some information regarding TB at the time of diagnosis and initiation of TB treatment. Other studies evaluating knowledge levels among patients with suspected TB and newly diagnosed patients with TB have also shown low overall knowledge among participants (27-29).

5.2.2 Acceptability of patient-specific infection control measures

The patient-specific infection control measures considered in this study were adapted from the infection control hierarchy endorsed by the CDC and the WHO (16, 30). Covering the patient’s mouth with a facemask, handkerchief, and tissues; completing a course of anti-TB treatment; cohorting and isolation; opening windows to the outside and the use of fans to improve ventilation, are “field-adapted” measures intended to reduce the risk of exposing uninfected individuals to M. tuberculosis. Initially, nearly half of the participants reported that they knew of some TB infection control measures. The most well-recognized infection control measures were wearing facemasks at health care facilities;
covering the mouth with a handkerchief or tissue at a hospital or clinic; and completing TB treatment. Other potential measures, such as wearing facemasks during transportation to a hospital or clinic; covering the mouth when coughing/sneezing at work; being separated from other patients; sleeping alone; and other environmental [field-adapted] measures were less well-known to participants. Field-adapted environmental and respiratory protection measures presented moderate levels of acceptability among patients with suspected TB and patients with TB.

5.2.3 Patient-specific environmental control Measures

5.2.3.1 Completing TB treatment

Initially, when participants were asked if they considered TB treatment a measure to control TB, a significant difference was found between each group. Patients with suspected TB were more likely to recognize completion of chemotherapy as an infection control measure, compared to patients with TB. However, when participants were asked if they would complete a course of anti-TB treatment, so that they could be cured, all participants agreed they would do so. It is not clear why more patients with suspected TB, who have never received anti-TB treatment, believed that TB transmission can be reduced by adhering to chemotherapy, compared to patients with TB. Health care systems should explore the reasons why patients default treatment (e.g., patients begin to feel better; lack of knowledge on the benefits of completing treatment; adverse effects of TB drugs; duration of treatment) and emphasize the family and community benefits of TB treatment completion.

5.2.3.2 Cohorting

In general, patient-specific measures that could be implemented at health care facilities, or at home, presented higher levels of acceptability, compared to the same
infection control measures in work settings. However, it should be noted that measures related to cohorting or isolation, whether at health care facilities, at home, or at work, showed lower acceptability rates than other patient-specific measures that did not involve separation from others. We assume that one of the reasons why patients are reluctant to apply these measures might be related to rejection. The fear of the stigma of isolation and other psychosocial factors might have had an impact on the willingness of patients to accept such measures. Kelly *et al* stated that stigma of isolation is related to two other themes, separation from family and avoidance by the community (31). It was not surprising therefore, that patients chose to avoid infection control practices that might reveal their TB disease status, but also have significant psychosocial implications for them and their families. Patients might decide to keep their TB status a secret for fear of being shunned (either as a TB patient, HIV patient or both). It appears that increased education and incentives would be needed for patients to accept cohorting and isolation, regardless of the setting. The alternative, given the increasing incidence of drug resistant TB, is that compulsory or statutory cohorting and isolation measures might need to be considered, if interventions to improve acceptability fail.

**5.2.3.3 Leave of absence from the work place**

Sixty-five percent (65%) of all participants reported that they would be willing to stop working until their AFB smear status became negative, although only 56% of participants were working at the time the interviews were conducted. Only 36% of participants who were currently working affirmed that they would stop working if they were asked to do so. Lack of compensation and loss of wages were two major factors influencing participants not to accept this measure. However, providing employees the right to stop working, until smear negativity is confirmed, is not a current health policy in South Africa. However, a recommendation to inform employers about patients’ TB status, requesting
permission to be absent from work, might be given to patients attending health care facilities at the time of diagnosis.

5.2.3.4 Improving ventilation

Eighty-nine percent (89%) of participants in this study reported that they were willing to open house windows to the outside, so that natural ventilation could help remove infectious particles. A small proportion of our patients were not willing to implement this measure, mainly due to the prevailing climatic conditions. Forty-one percent (41%) of participants were not willing to use fans, either because they did not have access to a fan, or because they did not understood the importance of this measure.

5.2.3.5 Patient-specific respiratory protection

5.2.3.5.1 The use of facemasks, handkerchiefs or tissues

A reduction in the burden of airborne droplet nuclei containing *M. tuberculosis* may be achieved by controlling the number of particles released by the sources of infection – usually undiagnosed, untreated, or partially treated patients with TB. At baseline, most of our participants were willing to cover their mouths to reduce the risk of TB transmission to others. Wearing facemasks at health care facilities showed a high acceptance rate (89%). However, the acceptability of facemask usage decreased by 35% at home and by 31% in work settings. Use of facemasks might not be affordable for use at all healthcare facilities in developing countries. Therefore, participants were asked about covering their mouth with handkerchiefs or tissues as a practical alternative.
The majority of subjects considered covering the mouth with a handkerchief or tissues as an acceptable option for implementation. A small proportion of participants reported that using facemasks was not feasible, since they did not understand the importance of this measure. This situation was observed in both groups and reflects that, even though educational material is provided when patients are investigated, diagnosed, and treated in programmatic circumstances, the educational process around TB infection control measures needs to be strengthened.

5.2.4 Acceptability of patient-specific infection control measures at the end of TB treatment

Mohamed et al states that health education is a continuous process, which starts when patients are being investigated for TB, continues after their diagnosis has been confirmed, and ends once patients are cured and complete treatment. Similar to the findings of other authors, who investigated levels of knowledge and practices among newly TB diagnosed patients (19, 32-34), our study showed low baseline levels of knowledge regarding TB disease and measures to reduce transmission, coupled with low levels of acceptability of certain patient-specific measures. However, after on-going contact with treating staff, personal experience, observation, and education, over the course of TB treatment, we could demonstrate that acceptability of these patient-specific measures increased in parallel with improvements in knowledge about TB at the end of treatment.

Some infection control measures were considered acceptable by a high proportion of patients, even at baseline; For instance, the use of face masks at health care facilities; Cover the mouth when coughing and/or sneezing; complete anti-TB treatment; cover the mouth
with a handkerchief or tissue at home; and, open windows to the outside were practices that most patient were willing to implement. The most acceptable infection control measures were those to be implemented at health care facilities, with the exception of isolation. Patients did not feel comfortable being separated from others while waiting in health care facilities, neither at the start nor at the end of treatment. However, a high proportion of participants (85%) were willing to be isolated at home, both at baseline and at the end of treatment. Acceptability of other patient-specific measures to be implemented at home increased at the end of treatment. The use of face masks, isolation, and the use of fans at home particularly showed a higher suitability among participants.

5.2.5 Factors that could affect TB knowledge and acceptability of infection control measures

5.2.5.1 Participants’ educational level, TB knowledge, and acceptability of infection control measures

We recognize that educational level may be a determining factor for an increased understanding and acceptability of any measures to control the disease (25, 34). Previous studies have shown that people with higher educational levels tend to accept and implement more preventive measures, compared to individuals with a lower educational background. At the end of treatment, participants considered isolation at home, the use of facemasks, and other practices to improve ventilation at home (opening house windows; and the use of fans) as feasible infection control measures. We can infer that on-going education provided by clinic staff and research workers over time had a positive effect on TB knowledge, and on the perceptions of participants regarding the acceptability and implementation of infection control measures.
5.2.5.2 Stigma

We know that TB is a highly stigmatized disease (35-38). However, contrary to what we were expecting, stigma or fear to rejection did not contribute significantly to participants’ decision whether or not to accept infection control measures. The Breede Valley area has one of the highest incidence rates of TB in South Africa (518 per 100 000) (39). The high prevalence in this community may be the reason why stigma seemed not to play a significant role in our participants’ decisions to practice these patient-specific measures. Communities with lower prevalence of TB might be more concerned by potential stigma, which might result in lower rates of acceptability of measures that clearly identify a TB patient to other members of the community.

5.2.5.3 Social desirability bias

We understand that when interviewing participants, we must take into account the possibility of a tendency of respondents to reply in a manner that we would consider “favourable” (40). We acknowledge that some of our participants might have overreported “good behaviour” or underreported “bad behaviour”, in relation to the acceptability of patient-specific infection control measures. We tried to mitigate the effects of social desirability bias, firstly by training our clinical research workers in the conduct of in-depth interviews and secondly, by ensuring confidentiality according to ethical research standards, and by creating a stable relationship with our research staff.

5.2.6 Limitations of this research

There were some potential limitations of our study. First, a major limitation of this research was the low-power statistics because of the small number of participants enrolled to this study. Although the estimated sample size was achieved, we acknowledge that the final
estimation was drawn on the basis of participants’ availability and recruitment rates of the
nest trials.

One of the challenges in health education is that the quality and amount of
information provided to patients depends on the knowledge, perceptions and attitudes of
providers. In this case, information was provided by health care staff from public health
facilities and by clinical research workers under study conditions. In both cases, these
providers have been trained to educate patients. However, public health institutions in
developing countries face overcrowded conditions and in many cases, the quality and
duration of interaction between health care providers may be insufficient for a complete and
satisfactory educational dialogue. As revealed in our evaluation of knowledge and
acceptability of infection control measures at baseline, both groups, patients with suspected
TB and patients with TB had similar levels of knowledge, even though patients with
suspected TB had not received any TB education from health care facilities prior to
diagnosis. We were not able to evaluate the quality of information that health care staff from
public health facilities might be providing to patients in the interim, between baseline and
end of treatment. Therefore, our findings (increased acceptability of some patient-specific
measures as knowledge increased) might not be replicable in settings in which health care
staff or other patients with TB might be providing inaccurate information, or demonstrating
inadequate infection control practices. For example, a study reporting knowledge, attitudes
and practices among health care workers in Iraq established that, although TB knowledge
among health care workers might be high, by contrast, their infection control practices were
suboptimal (41). Further, Hashim et al showed that only 38.2% of health care workers from
primary care centres in Iraq handled suspected TB cases correctly (41).

Moreover, when waiting at a health care facility, patients are surrounded by other
patients with TB who may have different sources of information, of varying accuracy. For
instance, patients with TB in this study were in frequent contact with research staff, but also with other patients with TB with their own opinions about TB, transmission and prevention. Therefore, it is clear that under programmatic conditions, levels of knowledge and acceptability of these infection control measures might vary according to the specific clinic setting and patient population. The findings of our study, in which on-going TB education was provided under research conditions, may represent an ideal situation that may not be achievable under programmatic conditions in many low-resourced health care settings.

5.2.7 Implications for policy

This research presents an opportunity for TB control programmes to strengthen measures to decrease TB transmission. TB still ranks as one of the leading causes of death in low and middle-income countries and many of these deaths might have been prevented by more effective infection control measures. The dynamics of TB transmission vary according to the socio-economic status of families, and communities. Poorer communities face social conditions that predispose them to develop TB disease once exposed to *M. tuberculosis*, whereas wealthier communities, with well-established health policies and financial resources, are able to contain transmission. New policies have advocated the use of isolation, or even short term incarceration, as well as other "environmental" practices to reduce TB transmission (42). However, in resource-constrained areas, public health authorities face (a) a lack of accurate, accessible diagnostic tools, which delays confirmation of infectious cases; (b) overcrowded health care facilities, in which patients with TB mix with other patients, increasing the risk of nosocomial TB transmission to other patients and health care staff; and (c) lack of personnel in health care facilities, which hampers the quality of information and educational support to patients. These factors amplify the risk of exposure to *M.*
tuberculosis, and increase the possibility of developing TB disease, particularly for close contacts of patients with TB and health care workers.

The ―National Infection Prevention and Control Policy for TB, MDR-TB and XDR-TB‖, published by the South African Department of Health, suggests that patients who are identified as TB suspects on screening must be given advice on respiratory hygiene and cough etiquette; provided with a facemask or tissues to cover their mouths and noses; and separated from other patients and requested to wait in a separate area. Our findings showed that patients are reluctant to be isolated in health care facilities, although they are more willing to be isolated at home. Increased emphasis on home-based care could help reduce nosocomial transmission of TB, by removing the infectious source case from the enclosed hospital environment. Clearly, the implementation of effective isolation at home must be followed by implementation of other measures to protect household members from incident TB: first, adequate TB treatment must be provided and health care institutions must promote adherence to TB chemotherapy; second, education about optimal infection control measures must also be provided to family members and community members, to create a strong support network for patients with TB. The risk of transmitting the disease to close contacts might also be reduced if patients are equipped with high efficiency (N95) masks to use at home, especially during the first weeks after treatment has been initiated.

The mission of public health is to fulfil society's interests and to foster practices and behaviours that assure populations stay healthy. Governmental bodies would need to interact and work synergistically in order to create appropriate policies to protect the rights of patients with TB, while ensuring that communities are not at risk of developing TB infection and subsequent TB disease due to bad or inexistent infection control practices.
5.2.8 Conclusion

Baseline knowledge about TB pathogenesis and TB infection control measures was poor to moderate among patients with suspected TB and patients with TB, although the latter had received TB education and information after their diagnosis was confirmed. Acceptability of patient-specific infection control measures increased over time, in parallel with increased knowledge of TB pathogenesis. Public health authorities should design and implement early intensive TB education programmes to increase knowledge and acceptability of patient-specific infection control measures. These educational resources should be accessible not only for patients with suspected TB and patients with TB, but for entire communities in which TB poses a challenge. Information given to patients with TB needs to be constantly reinforced.
REFERENCE LIST


GLOSSARY

**Administrative controls**: Defined as managerial or administrative measures that guide work practices to reduce significantly the risk of TB transmission by preventing the generation of droplet nuclei. These include early diagnosis, prompt isolation or separation of infectious patients with TB, prompt initiation of appropriate anti-tuberculosis treatment.

**Droplet nuclei**: Microscopic particles that are estimated at 1-5 microns in diameter and are produced when a person coughs, sneezes, shouts or sighs. Such particles may remain suspended in the air for hours.

**Environmental control measures**: Measures that can be used in high-risk areas to reduce the concentration of droplet nuclei in the air (e.g., maximizing natural ventilation or controlling the direction of airflow).

**Health care associated infection (nosocomial or hospital-associated infection)**: An infection acquired in a health care facility by a patient, health care worker, or a visitor to a health care facility, who was in the facility for a reason other than that infection.

**High Efficiency facemasks (N95)**: Mask prevents the spread of microorganisms by providing a high filtration capacity, and at least can filter 95% of airborne particles.

**Infection prevention and control**: Specific measures and work practices that reduce the likelihood of transmitting *M. tuberculosis*. 
Mucociliary Clearance: Refers to the mechanical elimination of fluid, bacteria, and particulates from the respiratory tract, relying on the close coordination of ciliary function, airway surface fluid secretion, and mucin secretion.

Natural ventilation: Defined as natural air movement to achieve dilution and air exchange in an area with free-flow of ambient air (e.g. through the open windows).

Personal protective equipment: This refers to items specifically used to protect the health care worker from exposure to body substances or from droplet or airborne organisms. Personal protective equipment includes gloves, aprons, gowns, caps, masks and protective eye wear.

Respirators: A special type of closely fitted mask with the capacity to filter particles 1 micron in size to protect from inhaling infectious droplet nuclei.

Ultraviolet germicidal irradiation (UVGI): An environmental control measure to kill or inactivate micro-organisms like *M. tuberculosis* through exposure to UVGI.
Appendix 1: Questionnaire  [English Version]

TUBERCULOSIS INFECTION CONTROL PROJECT

Questionnaire No: __________________________

Interviewer: __________________________

Date: DD/MM/YYYY

Language: __________________________

Age: __________________________

TB Status:

☐ TB Suspect  ☐ TB Patient

If TB patient, please specify:

☐ 1st Month  ☐ 6th Month

1. Do you know the cause of Tuberculosis (TB)?
   a. Yes
   b. No

If yes, please specify what the most important cause of TB is:
   a. Tuberculosis is a disease that is passed through generations
   b. Tuberculosis is a disease that is caused by drinking alcohol
   c. Tuberculosis is a disease that is caused by smoking
   d. Tuberculosis is a disease that is caused by lack of cleanliness
   e. Tuberculosis is a disease that is caused by witchcraft
   f. Tuberculosis is a disease that is caused by germs
   g. Tuberculosis is a disease that is caused by inhaling toxic substances
   h. Other: _______________________________________________________________________________________________

2. Do you know how a person gets TB?
   a. Yes
   b. No

If yes, please specify:

Please, select all that apply:
   a. TB is transmitted by sharing food utensils with people who are ill from tuberculosis
   b. TB is transmitted by kissing people who are ill from tuberculosis
   c. TB is transmitted by living or being in close contact with people who have tuberculosis (by one person to another)
   d. TB is transmitted by living in or moving to cold areas

3. Do you think that tuberculosis can be passed on to other people?
   a. Yes
   b. No

If yes, please specify who are more likely to get tuberculosis?

Please, select all that apply:
   a. Adults
   b. Young children
   c. Elderly people
   d. Co-Workers
   e. HIV/AIDS Patients
   f. All above mentioned
   g. None
4. Do young children need treatment to stop getting TB once they have been exposed to the disease in their house?
   a. Yes
   b. No

If yes, please specify what children must receive treatment to prevent them to get TB?

Please, select all that apply:
   a. Children under the age of 5
   b. Children over 5 years of age
   c. All HIV positive children
   d. All children

5. Do you know when a TB patient usually stops transmitting the disease?
   a. Yes
   b. No

If no, please go to question number 8.

If yes, please specify:

Please, mark an X on the appropriate answer:
   a. On the first day after they start receiving treatment
   b. After 2 weeks on treatment
   c. After 2 months of treatment
   d. Once treatment is completely over

6. For how long were you coughing before you sought medical attention for this illness?
   a. Not at all
   b. Less than two weeks
   c. More than two weeks
   d. More than four weeks
   e. More than six weeks

7. Do you know some measures to control tuberculosis?
   a. Yes
   b. No

If yes, please specify which ones you know:

Please, select all that apply:
   a. A Person with TB must use facemask during transportation to a hospital or clinic
   b. A Person with TB must use facemask in a hospital or clinic
   c. A Person with TB must cover his/her mouth when coughing and/or sneezing in a hospital or clinic
   d. A Person with TB must cover his/her mouth when coughing and/or sneezing at home or at work
   e. A Person with TB must be separated from other patients and requested to wait in a separated area
   f. A Person with TB must sleep in a room by him/herself or avoid sleeping in a room with small children
   g. A Person with TB must open house windows to the outside air
   h. A Person with TB must use fans if possible for moving air to the outside
   i. A Person with TB must complete their course of anti—TB treatment
   j. Other(s): _______________________________________________________________________________

8. Do you know why measures to control tuberculosis are important?
   a. Yes
   b. No

If yes, please specify:

Please, select all that apply:
   a. These measures are important to prevent persons with TB from spreading germs so that health care workers are not infected
   b. These measures are important to prevent persons with TB spreading germs so that close contacts (family and/or people who you live with) do not get infected
c. These measures are important to prevent persons with TB from spreading germs so that people who work with you do not get infected

9. From where did you get your information about TB and TB control measures?

Please, select all that apply:

a. Health Care Workers (Hospital, TB Clinics, etc)
b. Other patients (e.g., in waiting areas)
c. Family
d. Friends
e. Work
f. Radio
g. Television

10. Which of the following measures/instructions do you consider acceptable for health care settings (hospital or clinic)?

10.1 Use facemask during transportation and stay in a health care setting?

a. Yes
b. No

If not acceptable, why so? Please select all that apply:

a. Because the mask itself is uncomfortable
b. Because you are not sure why it’s important to use a facemask all the time
c. Because people are going to think that you have tuberculosis and they might avoid you
d. Because people are going to think that you are HIV positive and they might avoid you

10.2 Cover mouth when coughing and/or sneezing in a health care setting?

a. Yes
b. No

If not acceptable, why so? Please select all that apply:

a. Because you forget to do it
b. Because you are not be interested in covering your mouth
c. Because you might not have a handkerchief or tissue to cover all the time
d. Because people in the hospital are going to think that you have tuberculosis and they might avoid you
e. Because people in the hospital are going to think that you are HIV positive and they might avoid you

10.3 Complete a course of anti—TB treatment?

a. Yes
b. No

If not acceptable, why so? Please select all that apply:

a. Because the health care centre is too far away from home and you can not afford transport to go there
b. Because you have been told that TB treatment is very long
c. Because you have to go to work
d. Because you do not like taking pills
e. Because the pills make you sick

10.4 Be separated from other patients and requested to wait in a separate area?

a. Yes
b. No

If not acceptable, why so? Please select all that apply:

a. Because you do not like the idea of being separate from others
b. Because people are going to think that you have tuberculosis and they might avoid you
c. Because people are going to think that you are HIV positive and they might avoid you

11. Which of the following measures/instructions do you consider acceptable and doable for household settings (home)?
11.1 Cover mouth with a handkerchief/tissue when coughing and/or sneezing?
   a. Yes
   b. No

If not acceptable, why so? Please select all that apply:

Please, select all that apply:
   a. Because you forget to do it
   b. Because you might not be interested in covering your mouth
   c. Because you might not have a handkerchief or tissue to cover all the time
   d. Because you do not want your family to find out that you might be sick
   e. Because people are going to think that you have tuberculosis and they might avoid you
   f. Because people are going to think that you are HIV positive and they might avoid you

11.2 Cover mouth with facial mask when coughing and/or sneezing?
   a. Yes
   b. No

If not acceptable, why so? Please select all that apply:

Please, select all that apply:
   a. Because you forget to do it
   b. Because you might not be interested using a mask
   c. Because you might not bring the facial mask with me all the time
   d. Because you do not want your family to find out that you might be sick
   e. Because people are going to think that you have tuberculosis and they might avoid you
   f. Because people are going to think that you are HIV positive and they might avoid you

11.3 Sleep in a room by oneself or avoid sleeping in a room with small children?
   a. Yes
   b. No

If not acceptable, why so? Please select all that apply:

Please, select all that apply:
   a. Because you think this is not necessary
   b. Because there are not enough rooms and we have to share
   c. Because you do not want your family to find out that you might be sick
   d. Because your family is going to think that you have an infectious disease and they may get sick because of you

11.4 Open house windows to the outside?
   a. Yes
   b. No

If not acceptable, why so? Please select all that apply:

Please, select all that apply:
   a. Because you think this is not necessary
   b. Because there are not windows in your house
   c. Because it is cold and because of security reasons (i.e., robbers can get into your house)

11.5 Use fans if possible for moving air to the outside?
   a. Yes
   b. No

If not acceptable, why so? Please select all that apply:

Please, select all that apply:
Please, select all that apply:

a. Because you do not know why that is important
b. Because there are no fans at home
c. Because you can not afford a fan

12. What instructions do you consider acceptable to follow at work?

12.1 Stop working until you have completed 2 weeks of treatment, or longer if your sputum is still positive for TB

a. Yes
b. No

If not acceptable, why so? Please select all that apply:

Please, select all that apply:

a. Because you are not so sick that you cannot work
b. Because if you do not go to work, you will not be compensated
c. Because if you do not go to work, your colleagues and co-workers will think that you have TB and they are going to avoid you
d. Because if you do not go to work, your colleagues and co-workers will think that you are HIV positive and they are going to avoid you

12.2 Cover mouth with a handkerchief/tissue when coughing and/or sneezing?

a. Yes
b. No

If not acceptable, why so? Please select all that apply:

Please, select all that apply:

a. Because you forget to do it
b. Because your colleagues/co-workers are going to think that you have tuberculosis and they might avoid you
c. Because your colleagues/co-workers are going to think that you are HIV positive and they might avoid you

d. Because you do not want your colleagues/co-workers to find out that you might be sick
e. Because people are going to think that you have tuberculosis and they might avoid you
f. Because people are going to think that you are HIV positive and they might avoid you

12.3 Cover mouth with facial mask when coughing and/or sneezing?

a. Yes
b. No

If not acceptable, why so? Please select all that apply:

Please, select all that apply:

a. Because you forget to do it
b. Because you might not be interested using a mask
c. Because you might not bring the facial mask with you all the time
d. Because you do not want your colleagues/co-workers to find out that you might be sick
e. Because people are going to think that you have tuberculosis and they might avoid you
f. Because people are going to think that you are HIV positive and they might avoid you

g. All the above mention

13. Is it acceptable that health care workers use facemasks during the consultation?

a. Yes
b. No

If acceptable, why so? Please select all that apply:

a. Because you understand that they must protect themselves
b. Because you understand that they are protecting you from passing you a disease, if they are sick
c. All the above mention

If not acceptable, why so? Please select all that apply:

a. You feel that there is a communication barrier between you and the health care worker (i.e. Sister and/or doctors) because they are using facemasks
b. You feel that they are worried and avoid you because they can pick something up from you (catch the disease) if they do not cover
c. You think that other people might assume that health care workers are protecting themselves from you because you are going to transmit them either TB or other disease

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14. **Tuberculosis Control at Home / Work**

14.1 Number of people in your house?
   a. 5 or more people at home
   b. Less than 5 people at home

14.2 Number of people per room in your house?
   a. More than 2 people per room
   b. Less than 2 people per room

14.3 Do you sleep by yourself in a room?
   a. Yes
   b. No

14.4 How many people do you share the room with? ____________________________________________________________

If answer to question 14.3 is yes, please specify who do you share the room with? Select all that apply:

a. Children younger than 5 years
b. Children age 5 years and older
c. Young adults
d. Elderly people

15. How would you feel about isolation at home (i.e., sleeping in a room by yourself) until you can no longer spread the disease to others? ?
   a. You have no problem with this
   b. This will not be easy for you but you are willing to try it out
   c. You are definitely not willing to do this

   If you are definitely not willing (c), please specify why:
   a. It's not physically possible to do this in your home (e.g., too few rooms)
   b. You do not believe that this will help
   c. Your family will not allow this

16. Are you working?
   a. Yes
   b. No

If yes, please specify:
   a. Indoors
   b. Outdoors

And if indoors, please specify:

   a. How many people are in the room with you while you are working? ____________________________________________

   b. How do you get to work most of the time?
   Please, mark an X on the appropriate answer:
   a. Taxi
   b. Bus
c. Train
d. Bicycle
e. Car
f. Motorbike
g. Walk
Appendix 1: Questionnaire  
[Afrikaans Version]

**TUBERKULOSE-INFEKSIEBEHEER-PROJEK**

**Vraelysnommer:**  
**Onderhoudsoordegter:**  
**Datum:** DD/MM/JJJ  
**Taal:**  
**Ouderdom:**  
**TB-status:**

1. **Weet u wat Tuberkulose (TB) veroorsaak?**
   
   c. Ja  
   d. Nee  
   
   Indien ja, spesifieer asseblief wat die belangrikste oorsaak van TB is:
   
   i. Tuberkulose is 'n siekte wat oorgeërf word  
   j. Tuberkulose is 'n siekte wat deur die gebruik van alkohol veroorsaak word  
   k. Tuberkulose is 'n siekte wat deur rokery veroorsaak word  
   l. Tuberkulose is 'n siekte wat deur 'n gebrek aan higieene veroorsaak word  
   m. Tuberkulose is 'n siekte wat deur toordery veroorsaak word  
   n. Tuberkulose is 'n siekte wat deur inaseming van giftige stowwe veroorsaak word  
   o. Ander:  

2. **Weet u hoe 'n persoon TB kry?**
   
   c. Ja  
   d. Nee  
   
   Indien ja, spesifieer asseblief:
   
   e. TB word oorgedra deur eetgerei te deel met mense wat met tuberkulose siek is  
   f. TB word oorgedra deur mense wat met tuberkulose siek is, te soen  
   g. TB word oorgedra saam met mense wat met tuberkulose siek is, of in noue kontak te wees met mense wat met tuberkulose siek is (van een persoon na 'n ander)  
   h. TB word oorgedra deur in koue areas te woon of na sulke areas toe te verhuis  

3. **Dink u dat tuberkulose aan ander mense oorgedra kan word?**
   
   c. Ja  
   d. Nee  
   
   Indien ja, spesifieer asseblief watter mense meer waarskynlik is om tuberkulose op te doen?
   
   Kies asseblief almal wat van toepassing is:
   
   i. Volwassenes  
   j. Jong kinders  
   k. Bejaardes  
   l. Medewerkers  
   m. MIV/VIGS-pasiënte  
   n. Al bogenoemde  
   o. Niemand nie
4. Het jong kinders behandeling nodig om te keer dat hulle TB opdoen nadat hulle by hul tuiste aan die siekte blootgestel is?
   c. Ja
   d. Nee

   Indien ja, spesifiseer asseblief watter kinders behandeling moet ontvang om te keer dat hulle TB kry?

   Kies asseblief almal wat van toepassing is:
   e. Kinders onder die ouderdom van 5 jaar
   f. Kinders oor die ouderdom van 5 jaar
   g. Alle MIV-positiewe kinders
   h. Alle kinders

5. Weet u wanneer 'n TB-pasiënt gewoonlik ophou om die siekte oor te dra?
   c. Ja
   d. Nee

   Indien nee, gaan asseblief oor na Vraagnommer 8.

   Indien ja, spesifiseer asseblief:

   Merk asseblief die gepaste antwoord met ‘n X:
   e. Op die eerste dag nadat hulle begin het om behandeling te ontvang
   f. Na 2 weke van behandeling
   g. Na 2 maande van behandeling
   h. Wanneer die behandeling heeltemal klaar is

6. Vir hoe lank het u gehoes totdat u mediese aandag vir hierdie siekte gaan soek het?
   a. Glad nie
   b. Minder as twee weke
   c. Meer as twee weke
   d. Meer as vier weke
   e. Meer as ses weke

   Algemene Maatreëls / Instruksies vir die Beheer van Tuberkulose

6. Ken u party van die maatreëls vir die beheer van tuberkulose?
   c. Ja
   d. Nee

   Indien ja, spesifiseer asseblief watter maatreëls u ken.

   Kies asseblief almal wat van toepassing is:
   j. ‘n Persoon met TB moet ‘n gesigmasker gedurende vervoer na ‘n hospitaal of kliniek gebruik
   k. ‘n Persoon met TB moet ‘n gesigmasker in ‘n hospitaal of kliniek gebruik
   l. ‘n Persoon met TB moet sy/haar mond bedek wanneer hy/sy in ‘n hospitaal of kliniek hoes en/of nies
   m. ‘n Persoon met TB moet sy/haar mond bedek wanneer hy/sy by die huis of by die werk hoes en/of nies
   n. ‘n Persoon met TB moet van ander pasiënte afgesonder word en versoek om ‘n in aparte area te wag
   o. ‘n Persoon met TB moet alleen in ‘n kamer of slaap, of slaap in ‘n kamer met klein kinders vermy
   p. ‘n Persoon met TB moet oop huisvensters na buitekant toe hê
   q. ‘n Persoon met TB moet van ander pasiënte afgesonder word en versoek om ‘n in aparte area te wag
   r. ‘n Persoon met TB moet sy/haar kursus van anti-TB-behandeling klaarmaak
   a. Ander: __________________________________________________________

7. Weet u waarom maatreëls vir die beheer van tuberkulose belangrik is?
   c. Ja
Kies asseblief almal wat van toepassing is:

d. Hierdie maatreëls is belangrik om te keer dat persone met TB die kieme versprei, sodat gesondheid-sorgwerkers nie die infeksie kry nie

e. Hierdie maatreëls is belangrik om te keer dat persone met TB die kieme versprei sodat mense naby hulle (familie en/of mense met wie hulle saamwoon) nie die infeksie kry nie

f. Hierdie maatreëls is belangrik om te keer dat persone met TB die kieme versprei sodat mense met wie hulle saamwerk nie die infeksie kry nie

9. Waar het u u inligting oor TB en die beheermaatreëls gekry?

Kies asseblief almal wat van toepassing is:

h. Gesondheidsorgwerkers (Hospitala, TB-klinieke, ens.)
i. Ander pasiënte (bv. in wagareas)
j. Familie
k. Vriende
l. Werk
m. Radio
n. Televisie

10. Watter van die volgende maatreëls/instruksies beskou u as aanvaarbaar vir gesondheidsorginstellings (hospitala of klinieke)?

10.1 Gebruik ’n gesigmasker gedurende vervoer en bly in ’n gesondheidsorginstelling?

c. Ja
d. Nee

Indien nie aanvaarbaar nie, waarom nie? Kies asseblief almal wat van toepassing is:

f. Omdat die masker self ongemaklik is
g. Omdat u nie seker is waarom dit belangrik is om te alle tye ’n gesigmasker te dra nie
h. Omdat mense gaan dink dat u tuberkulose het en u dalk sal vermy
i. Omdat mense gaan dink dat u MIV-positief is en u dalk sal vermy
j. Omdat mense gaan dink dat u tuberkulose het en u dalk sal vermy

10.2 Bedek mond wanneer mens hoes en/of nies in ’n hospitaalopset?

c. Ja
d. Nee

Indien nie aanvaarbaar nie, waarom nie? Kies asseblief almal wat van toepassing is:

f. Omdat mens vergeet om dit te doen
g. Omdat u nie daarin belangstel om u mond te bedek nie
h. Omdat mens sakdoek of snesie byderhand het en u nie taai daarom nie
d. Nee

10.3 Voltooi kursus van anti-TB-behandeling?

c. Ja
d. Nee

Indien nie aanvaarbaar nie, waarom nie? Kies asseblief almal wat van toepassing is:

f. Omdat die gesondheidsorgsentrum te ver is van u huis af is en u nie kan bekostig vervoer daarheen te neem nie
g. Omdat u vertel is dat TB-behandeling baie lang vat
h. Omdat u moet gaan werk
i. Omdat u nie daarvan hou om pille te drink nie
j. Omdat die pille mens siek laat voel

10.4 Afgesonder wees van ander pasiënte en versoek word om in ’n aparte area te wag?

c. Ja
d. Nee

Indien nie aanvaarbaar nie, waarom nie? Kies asseblief almal wat van toepassing is:

d. Omdat u nie hou van die idee om van ander mense afgesonder te wees nie
e. Omdat mense gaan dink dat u tuberkulose het en hulle u dalk sal vermy
f. Omdat mense gaan dink dat u MIV-positief is en hulle u dalk sal vermy
11. Watter van die volgende maatreëls/instruksies beskou u as aanvaarbaar en doenbaar in 'n huishoudelike opset (by die huis)?

11.1 Bedek die mond met 'n sakdoek/snesie wanneer mens hoes en/of nies?

   c. Ja
   d. Nee

Indien nie aanvaarbaar nie, waarom nie? Kies asseblief almal wat van toepassing is:

Kies asseblief almal wat van toepassing is:

   g. Omdat mens vergaat om dit te doen
   h. Omdat u dalk nie daarin belangstel om u mond te bedek nie
   i. Omdat mens dalk nie altyd 'n sakdoek of snesie byderhand het om mens se mond te bedek nie
   j. Omdat u nie sou wou hê u familie moet uitvind dat u dalk siek is nie
   k. Omdat mense dalk gaan dink dat u tuberkulose het en u dalk sal vermy
   l. Omdat mense dalk gaan dink dat u MIV-positief is omdat u u mond bedek en u dalk sal vermy

11.2 Bedek die mond met 'n gesigsmasker wanneer mens hoes en/of nies?

   c. Ja
   d. Nee

Indien nie aanvaarbaar nie, waarom nie? Kies asseblief almal wat van toepassing is:

Kies asseblief almal wat van toepassing is:

   h. Omdat mens vergeet om dit te doen
   i. Omdat u dalk nie daarin belangstel om 'n gesigsmasker te gebruik nie
   j. Omdat mens dalk nie altyd 'n gesigsmasker met jou saamdra nie
   k. Omdat u nie sou wou hê u familie moet uitvind dat u dalk siek is nie
   l. Omdat mense dalk gaan dink dat u tuberkulose het en u dalk sal vermy
   m. Omdat mense dalk gaan dink dat u MIV-positief is omdat u u mond bedek en u dalk sal vermy

11.3 Alleen in 'n kamer slaap, of slaap in 'n kamer met jong kinders vermy?

   c. Ja
   d. Nee

Indien nie aanvaarbaar nie, waarom nie? Kies asseblief almal wat van toepassing is:

Kies asseblief almal wat van toepassing is:

   e. Omdat u meen dat dit nie nodig is nie
   f. Omdat daar nie genoeg kamers in u huis is nie en almal moet deel
   g. Omdat u nie sou wou hê u familie moet uitvind dat u dalk siek is nie
   h. Omdat u familie gaan dink dat u 'n aansteeklike siekte het en dat hulle as gevolg van jou mag siek word

11.4 Oop huisvensters na buite toe?

   c. Ja
   d. Nee

Indien nie aanvaarbaar nie, waarom nie? Kies asseblief almal wat van toepassing is:

Kies asseblief almal wat van toepassing is:

   d. Omdat u meen dat dit nie nodig is nie
   e. Omdat daar geen vensters in u huis is nie
   f. Omdat dit koud is
   g. Weens sekeriteitsredes (bv. rowers kan in jou huis kom)

11.5 Gebruik waaiers indien moontlik om die lug buitentoe te waai

   c. Ja
   d. Nee

Indien nie aanvaarbaar nie, waarom nie? Kies asseblief almal wat van toepassing is:

Kies asseblief almal wat van toepassing is:

   d. Omdat u nie weet waarom dit belangrik is nie
   e. Omdat daar geen waaiers in u huis is nie
12. Watter instruksies beskou u as aanvaarbaar by die werk?

12.1 Ophou werk totdat u 2 weke van behandeling voltooie het, of langer u nog positief is vir TB
   a. Ja
   b. Nee

Indien nie aanvaarbaar nie, waarom nie? Kies asseblief almal wat van toepassing is:

   g. Omdat u nie so siek is dat u nie werk toe kan gaan nie
   h. Omdat u nie betaal sal word as u nie werk toe gaan nie
   i. Omdat u van die werk af wegbly, u kollegas en medewerkers gaan dink dat u TB het en u gaan vermy
   j. Omdat u van die werk af wegbly, u kollegas en medewerkers gaan dink dat u MIV-positief is en u gaan vermy

12.2 Bedek die mond met 'n sakdoek/snesie wanneer mens hoes en/of nies?
   a. Ja
   b. Nee

Indien nie aanvaarbaar nie, waarom nie? Kies asseblief almal wat van toepassing is:

   d. Omdat u sal vergeet om dit te doen
   e. Omdat u kollegas/medewerkers gaan dink dat u tuberkulose het en u dalk sal vermy
   f. Omdat u kollegas/medewerkers gaan dink dat u MIV-positief is en u dalk sal vermy

12.3 Bedek die mond met 'n gesigsmasker wanneer mens hoes en/of nies?
   a. Ja
   b. Nee

Indien nie aanvaarbaar nie, waarom nie? Kies asseblief almal wat van toepassing is:

   g. Omdat u sal vergeet om dit te doen
   h. Omdat u nie wil hé dat u kollegas/medewerkers moet uitvind dat u dalk siek is nie
   i. Omdat mense gaan dink dat u tuberkulose het en u dalk sal vermy
   j. Omdat mense gaan dink dat u MIV-positief is en u dalk sal vermy

13. Is dit aanvaarbaar vir gesondheidsorgwerkers om gesigsmaskers gedurende konsultasies te dra?
   a. Ja
   b. Nee

Indien dit aanvaarbaar is, waarom? Kies asseblief almal wat van toepassing is:

   d. Omdat u verstaan dat hulle hulself moet beskerm
   e. Omdat u verstaan dat hulle u beskerm teen 'n siekte wat hulle kan oordra as hulle siek is
   f. Beide van bovengenoemde

Indien dit nie aanvaarbaar is nie, waarom nie? Kies asseblief almal wat van toepassing is

   a. U voel dat daar 'n kommunikasieblok tussen u en die gesondheidsorgwerker is (d.w.s. Susters en/of dokters) omdat hulle gesigsmakser dra
   b. U voel dat hulle bekommernis is en u vermy omdat hulle h siekte by u kan aaneensteek as hulle nie toemaak nie
   c. U dink dat ander mense mag aanvaar dat gesondheidsorgwerkers hulself teen u beskerm omdat u TB of 'n ander siekte aan hulle gaan oordra
14. Tuberkulose-beheer by die Huis / Werk

14.1 Aantal mens in u huis?
   c. 5 of meer mense by die huis
   d. Minder as 5 mense by die huis

14.2 Aantal kamers in u huis?
   c. Meer as 2 mense per kamer
   d. Minder as 2 mense per kamer

14.3 Slaap u alleen in 'n kamer?
   c. Ja
   d. Nee

14.4 Met hoeveel mense deel u 'n kamer?

_______________________________________

Indien u antwoord op 14.4 ja is, spesifiseer asseblief met wie u die kamer deel? Kies almal wat van toepassing is:
   e. Kinders onder 5 jaar oud
   f. Kinders van 5 jaar en ouer
   g. Jong mense
   h. Bejaardes

15. Hoe sou u voel oor isolasie by die huis (d.w.s. alleen in 'n kamer slaap) totdat u nie meer die siekte aan ander mense kan versprei nie?
   d. U het geen probleem hiermee nie
   e. Dit sal nie vir u maklik wees nie, maar u is gewillig om dit te probeer
   f. U is beslis nie gewillig om dit te doen nie

Indien u beslis nie gewillig is nie (c), spesifiseer asseblief waarom nie:
   d. Dit is nie fisies moontlik om dit by my huis te doen nie (bv. te min kamers)
   e. U glo nie dat dit sal help nie
   f. U familie sal dit nie toelaat nie

16. Is u werksaam?
   c. Ja
   d. Nee

Indien ja, spesifiseer asseblief:

   c. Binnenshuis
   d. In die buitelug

   a. Hoeveel mense is in dieselfde kamer saam met u terwyl u werk?

_______________________________________

b. Hoe kom u meestal by die werk?

Merk asseblief die toepaslike antwoord met 'n X:
   h. Taksi
   i. Bus
   j. Trein
   k. Fiets
   l. Motor
   m. Motorfiets
   n. Stap
Appendix 1: Questionnaire
[IsiXhosa Version]

UMSEBENZI WOLAWULO LOMOSULELEKO WESIFO SEPHEPHA

Inombolo yoluhluko
lwemibuzo:
Umntu obuza imibuzo:
Umla:
Ulwimi:
Ubudala:
Isimo seTB:

☐ TB Suspect  ☐ TB Patient

If TB patient, please specify:
☐ 1st Month  ☐ 6th Month

1. Uyasazi ukuba isifo sephepha (iTB) sibangelwa yintoni?
   e. Ewe
   f. Hayi

Ukuba ewe, nceda uchaze ukuba ngowuphi oyena nobangela ubalulekileyo we-TB:
   q. Isifo sephepha sisifo esifunyanwa ngezizukulwana
   r. Isifo sephepha sisifo esibangelwa ukusaya utywala
   s. Isifo sephepha sisifo esibangelwa kukutshaya
   t. Isifo sephepha sisifo esibangelwa kukungacoceki
   u. Isifo sephepha sisifo esibangelwa kukuthakathwa
   v. Isifo sephepha sisifo esibangelwa ziintsholongwane
   w. Isifo sephepha sisifo esibangelwa kukubizwa
   x. Okunye:

2. Uyayazi ukuba umntu usifumana njani isifo sephepha, i TB?
   e. Ewe
   f. Hayi

Ukuba ewe, nceda uchaze:

Nceda, khetha konke okufanelekileyo:
   i. I-TB igqithiselwa komnye umntu ngokwabelana ngamacephe nezinye izinto yokuyana nabantu abagula sisifo sephepha
   j. I-TB igqithiselwa komnye umntu ngokuphuza abantu abagula sisifo sephepha
   k. I-TB igqithiselwa komnye umntu ngokuhlala okanye ukuba kunjela kakhulu nabantu abanesifo sephepha (omnye ukuya komnye)
   l. I-TB igqithiselwa komnye umntu ngokuhlala okanye ukuthathela kwindawo ezibandayo

3. Ucinga ukuba isifo sephepha singabosulela abanye abantu?
   e. Ewe
   f. Hayi

Ukuba ewe, nceda uchaze ukuba ngoobani abangabanesifo sephepha lula?

Nceda, khetha konke okufanelekileyo:
   q. Abantu abadalala
   r. Abantu abangacoceki
   s. Abantu abagugileyo
   t. Abantu osebenza nabo
   u. Abaguli abane-HIV/AIDS
   v. Bonke abakhankanywe ngasentla
   w. Akho bantu
   x. Andiqinisekanga
4. Ingaba abantwana abancinane kufuneka bafumane unyango ukunqanda ukuba bangayifumani iTB xa sele beveziwe kwesi sfo ekhayeni labo?
   e. Ewe
   f. Hayi

_Ukuba ewe, nceda uchaze ukuba ngabaphi abantwana abafanele ukufumana unyango ukubathintela ukufumana i TB?_

Nceda, khetha konke okufanelekileyo:
   i. Abantwana abangaphantsi kweminyaka e-5 ubudala
   j. Abantwana abangaphenzi kweminyaka e-5 ubudala
   k. Bonke abantwana abane-HIV
   l. Bonke abantwana

5. Uyayazi ukuba umguli one-TB uyeka nini ukosulela ngesi sifo?
   e. Ewe
   f. Hayi

_Ukuba hayi, nceda uye kumbuzo 8._

_Ukuba ewe, nceda uchaze:_

Nceda, uphawule ngo-X kwipendulo efanelekileyo:
   i. Kusuku lokuqala emva kokuba beqala ukufumana unyango
   j. Emva kweveeki ezi-2 kunyango
   k. Emva kweenyanga ezi-2 kunyango
   l. Xa sele lugqityiwe unyango

6. Ubukohohlela ixesha elingakanani phambi kokuba ufune unyango lwesi sigulo?
   f. Bendingakhohleli
   g. Ngaphantsi kweveeki ezimbini
   h. Ngaphezu kweveeki ezimbini
   i. Ngaphezu kweveeki ezine
   j. Ngaphezu kweveeki ezintandathu

7. Uyawazi amanye amanyathelo olawulo lwesifo sephepha?
   e. Ewe
   f. Hayi

_Ukuba ewe, nceda uchaze ngawaphi owaziyo:_

Nceda, khetha konke okufanelekileyo:
   s. Umntu one-TB kufanele asebenzise imaski yokugquma ubuso xa esisiwa esibhedlele okanye eklini
   t. Umntu one-TB kufanele asebenzise imaski yokugquma ubuso xa esibhedlele okanye eklini
   u. Umntu one-TB kufanele agqume umlomo wakhe xa ekhothola naxa/okanye xa ethimla esibhedlele okanye eklini
   v. Umntu one-TB kufanele agqume umlomo wakhe xa ekhothola naxa/okanye xa ethimla ekhaya okanye emsebenzini
   w. Umntu one-TB kufanele ohlulwe kwabanye abaguli acelwe ukuba alinde kwindawo eyodwa yokulinda
   x. Umntu one-TB kufanele alale kwigumbi yedwa okanye akuphephe ukulala kwigumbi elinabantwana abancinane
   y. Umntu one-TB kufanele avule lifestile zendlu ezivulela ngaphandle
   z. Umntu one-TB kufanele asebenzise ifeni xa enako ukukhuphela ngaphandle umoya
   aa. Umntu one-TB kufanele alugqibe unyango lwakhe le-TB
   b. Okunye: _________________________________________________________________________________

8. Uyayazi ukuba kutheni amanyathelo olawulo lwesifo sephepha ebalulekile?
   e. Ewe
   f. Hayi
Ukuba ewe, nceda uchaze:

Nceda, khetha konke okufanelekileyo:

\( g. \) La manyathelo abalulekile ukuthintelaabantu abane-TB banganwenisi iintsholongwane ukuze abasebenzi kwezempilo bangosuleke

\( h. \) La manyathelo abalulekile ukuthintelaabantu abane-TB banganwenisi iintsholongwane ukuze abantu abakufutshane naye (*usapho kunye/okanye abantu ohlala nabo*) bangosuleke

\( i. \) La manyathelo abalulekile ukuthintelaabantu abane-TB banganwenisi iintsholongwane ukuze abantu abasebenza nawe bangosuleke

9. Ulufumene phi ulwazi onalo malungu ne-TB namanyathelo olawulo lwe-TB?

Nceda, khetha konke okufanelekileyo:

\( o. \) Kubasebenzi kwempilo (Esibhedele, kwikliniki ze-TB, njil-njil)

\( p. \) Abanye abaguli (umz., kwindawo zokulinda)

\( q. \) Usapho

\( r. \) Abahlulo

\( s. \) Emsebenzini

\( t. \) Kunomathotholo

\( u. \) Kum bona-kude

10. Ngawaphi kula manyathelo/kule miyalelo oyithatha njengeyamakelekileyo kwindingo zokongi wa kwempilo (esibhedele okanye ekliniti)?

\( 10.1 \) Sebenzisa imaski yokugguma ubuso xa umuntu esisiwa naxa ehlala kwindingo yempilo?

\( e. \) Ewe

\( f. \) Hayi

Ukuba akwamakelekanga, njani njala? Nceda, khetha konke okufanelekileyo:

\( i. \) Kuba yona imaski avengi umuntu aziwe ekbhulekile

\( j. \) Kubasebenzi kule kuthi kubalulekile ukusebenza imaski uguymi ubuso Jombok ixesha

\( k. \) Kubasebenzi kule kuthi kubalulekile ukusebenza imaski unesipho kungaba yale bangahambela kude kunawe

\( l. \) Kubasebenzi kule kuthi kubalulekile ukusebenza imaski unesipho kungaba yale bangahambela kude kunawe

\( 10.2 \) Gquma umlomo xa kukuholwele naxa/okanye kuthimiyo kwindingo yokongi wa kwempilo?

\( e. \) Ewe

\( f. \) Hayi

Ukuba akwamakelekanga, njani njala? Nceda, khetha konke okufanelekileyo:

\( k. \) Kubasebenzi kule kuthi kubalulekile ukusebenza imaski uguymi ubuso Jombok ixesha

\( l. \) Kubasebenzi kule kuthi kubalulekile ukusebenza imaski unesipho kungaba yale bangahambela kude kunawe

\( m. \) Kubasebenzi kule kuthi kubalulekile ukusebenza imaski unesipho kungaba yale bangahambela kude kunawe

\( n. \) Kubasebenzi kule kuthi kubalulekile ukusebenza imaski unesipho kungaba yale bangahambela kude kunawe

\( o. \) Kubasebenzi kule kuthi kubalulekile ukusebenza imaski unesipho kungaba yale bangahambela kude kunawe

\( 10.3 \) Gqiba unyango olulwa ITB?

\( e. \) Ewe

\( f. \) Hayi

Ukuba akwamakelekanga, njani njala? Nceda, khetha konke okufanelekileyo:

\( k. \) Kubasebenzi kule kuthi kubalulekile ukusebenza imaski uguymi ubuso Jombok ixesha

\( l. \) Kubasebenzi kule kuthi kubalulekile ukusebenza imaski unesipho kungaba yale bangahambela kude kunawe

\( m. \) Kubasebenzi kule kuthi kubalulekile ukusebenza imaski unesipho kungaba yale bangahambela kude kunawe

\( n. \) Kubasebenzi kule kuthi kubalulekile ukusebenza imaski unesipho kungaba yale bangahambela kude kunawe

\( o. \) Kubasebenzi kule kuthi kubalulekile ukusebenza imaski unesipho kungaba yale bangahambela kude kunawe

\( 10.4 \) Ukohlulwa kwabanye abaguli ucelwe ukuba ulinde kwindingo eyodwa yokulinda?

\( e. \) Ewe

\( f. \) Hayi

Ukuba akwamakelekanga, njani njala? Nceda, khetha konke okufanelekileyo:

\( g. \) Kubasebenzi kule kuthi kubalulekile ukusebenza imaski uguymi ubuso Jombok ixesha

\( h. \) Kubasebenzi kule kuthi kubalulekile ukusebenza imaski unesipho kungaba yale bangahambela kude kunawe

\( i. \) Kubasebenzi kule kuthi kubalulekile ukusebenza imaski unesipho kungaba yale bangahambela kude kunawe

\( j. \) Kubasebenzi kule kuthi kubalulekile ukusebenza imaski unesipho kungaba yale bangahambela kude kunawe

\( k. \) Kubasebenzi kule kuthi kubalulekile ukusebenza imaski unesipho kungaba yale bangahambela kude kunawe

\( l. \) Kubasebenzi kule kuthi kubalulekile ukusebenza imaski unesipho kungaba yale bangahambela kude kunawe

\( m. \) Kubasebenzi kule kuthi kubalulekile ukusebenza imaski unesipho kungaba yale bangahambela kude kunawe

\( n. \) Kubasebenzi kule kuthi kubalulekile ukusebenza imaski unesipho kungaba yale bangahambela kude kunawe

\( o. \) Kubasebenzi kule kuthi kubalulekile ukusebenza imaski unesipho kungaba yale bangahambela kude kunawe

\( 10.5 \) Ukuhlanganisele abanye abaguli ucelwe ukuba ulinde kwindingo eyodwa yokulinda?

\( e. \) Ewe

\( f. \) Hayi

(TB Infection Control Project: Questionnaire, Version No. 3 (2009.06.27). English (Xhosa translation by Yolanda Giyose)
11. Ngawaphi kula manyathelo alandelayo/kule miyalelo elandelayo oyithatha njengeyamkelekileyo nenako ukwenzelwa ekhaya?

11.1 Ukugguma umlomo ngetshefu/ithishu xa ukhohlela naxa.okanye xa uthimla?
   e. Ewe
   f. Hayi

Ukuba akwamkelekanga, njani njalo? Nceda, khetha konke okufanelekileyo:

Nceda, khetha konke okufanelekileyo:
   m. Kuba uyalibala ukukwenza oku
   n. Kuba ungathi ungbali namdla yokugquma umlomo
   o. Kuba kungenzenza ungbabini itshfu okanye uthemba yokugquma maxa onke
   p. Kuba awufuni usapho lucinge ukuba ungaba uyagula
   q. Kuba abantu baza kucinga ukuba unesifo sephetha yaye bangahambela kude kunawe
   r. Kuba abantu baza kucinga ukuba une-HIV yaye bangahambela kude kunawe

11.2 Gquma umlomo ngemaski yokugquma ubuso xa ukhohlela kunye/or uthimla?
   e. Ewe
   f. Hayi

Ukuba akwamkelekanga, njani njalo? Nceda, khetha konke okufanelekileyo:

Nceda, khetha konke okufanelekileyo:
   n. Kuba uyalibala ukukwenza oku
   o. Kuba ungathi ungbali namdla yokugquma umlomo
   p. Kuba ungangazi nemaski yokugquma ubuso lonke ikesha
   q. Kuba awufuni usapho lufumanise ukuba ungaba uyagula
   r. Kuba abantu baza kucinga ukuba unesifo sephetha yaye bangahambela kude kunawe
   s. Kuba abantu baza kucinga ukuba une-HIV yaye bangahambela kude kunawe

11.6 Ukulala wedwa egumbini okanye ukuphepha ukulala ezumbini nabantwana abasebancinane?
   e. Ewe
   f. Hayi

Ukuba akwamkelekanga, njani njalo? Nceda, khetha konke okufanelekileyo:

Nceda, khetha konke okufanelekileyo:
   i. Kuba ucinga oku akwomunye
   j. Kuba akuko magumbi aneleyo yaye kufanele sabelane ngemaski
   k. Kuba awufuni usapho lwakho lufumanise ukuba ungaba uyagula
      Kuba usapho lwakho lwazi kucinga ukuba unesifo esosulelayo, yaye bangagula ngenxa yakho

11.7 Vula iifestile ekhaya eziphumela ngaphandle?
   e. Ewe
   f. Hayi

Ukuba akwamkelekanga, njani njalo? Nceda, khetha konke okufanelekileyo:

Nceda, khetha konke okufanelekileyo:
   h. Kuba ucinga oku akwomfuneko
   i. Kuba akuko zifestile endlwini yakho
   j. Kuba kusinga tamagama versatshu zokhuseleko (o.k.k.t., ootsotsi bangangena endlwini yakho)

11.8 Sebenzisa ifeni ukuba oko kuyakwazeka ukusambisa umoya ukuya phandle?
   e. Ewe
   f. Hayi
Ukuba akwamkelekanga, njani njalo? Nceda, khetha konke okufanelelekiyo:

g. Kuba awuyazi ukuba kutheni kuhululekile oku
h. Kuba akukho zifeni ekhaya
i. Kuba awunako ukuzithengela ifeni

14. Yeypiphi imiyalelo oyithatha ngathi yamnelelelele ukuba uyllandele emsebenzini?
12.1 Yeka ukusebenza de uqobo iiveke ezi-2 zonyango, okanye ngaphezulu ukuba isikhohlalela sakho sisabonakalisa ubukho be-TB

e. Ewe
f. Hayi

Ukuba akwamkelekanga, njani njalo? Nceda, khetha konke okufanelelekiyo:

12.3 Gquma uumlomo ngentshefu/ithishu xa ukhohlela naxa/okanye xa uthimla?

e. Ewe
f. Hayi

Ukuba akwamkelekanga, njani njalo? Nceda, khetha konke okufanelelekiyo:

15. Kwamkelekile ukuba abasebenzi kwezempilo basebenzise imaski zokugquma ubuso xa bebonana nabaguli?

a. Ewe
b. Hayi
17. Ulawulo lxesifo sepepha ekhaya/emsebenzini

14.1 Inani labantu endlwini yakho?
e. Ba-5 okanye ngaphezulu abantu ekhaya
f. Bangapantsi kwe-5 abantu ekhaya

14.2 Inani lamagumbi endlwini yakho?
e. Bangapezulu kwe-2 abantu kwigumbi ngalinye
f. Bangaphantsi kwe-2 abantu kwigumbi ngalinye

14.3 Ulaia wedwa egumbini?
e. Ewe
f. Hayi

14.4 Wabelana ngegumbi nabantu abangaphi? ______________________________________________________________

Ukuba impendulo yombuzo 14.3 ngu ewe, nceda ucaze ukuba wabelana nabani ngegumbi? Khetha konke okufanelekileyo:

i. Abantwana abangaphantsi kweminyaka e-5 ubudala
j. Abantwana aba-5 ngaphezulu
k. Abantu abadala abasebatsha
l. Abantu abagugileyo

18. Ungaziva njani ngokuhlaliswa wedwa ekhaya (umz. Ukulaliswa egumbini wedwa) de ube awusenako ukubosulela abanye abantu ngesifo?
g. Awunangxaki noku
h. Oku akusayi kuba lula kuwe, kodwa uyafula ukuzama
i. Awufuni kwaphela ukwenza oku

Akuba awufuni ngokushemekileyo (c), nceda uchaze ngoba:
g. Akukwazi lokwena oku ekayeni lam (umz., amagumbi ambalwa kakhulu)
h. Awukholela ukuba oku kuya kunceda
i. Usapho lwako alusayi kukuvumela oku

19. Uyasebenza?
e. Ewe
f. Hayi

Ukuba ewe, nceda uchaze:
e. Ngaphakati
f. Ngaphandle

Yaye ukuba phakathi, nceda uchaze:

a. Bangaphi abantu abakwigmibi elinye naye xa usebenza? __________________________________________

b. Uya ngantoni emsebenzini unini lwenxesa?
Nceda, phawula ngo-X kwimpendulo efanelekileyo:
o. Nge-Taxi
p. Ibhasi
q. Uloliwe
r. I-Bicycle
s. Imoto
t. isithuthuthu
U. Hamba
PARTICIPANT INFORMATION AND CONSENT FORM

Protocol Title: "Knowledge and acceptability of measures for control of tuberculosis transmission in the Breede Valley community"

The following information will tell you about the study and your part in it. Please read carefully and feel free to ask any questions.

This is a research study being done by the South African TB Vaccine Initiative (SATVI), Institute of Infectious Disease and Molecular Medicine, University of Cape Town Medical School, Anzio Rd, Observatory, Cape. The team members in charge of the study are Mark Hatherill, Senior investigator and Yulieth Gonzalez-Angulo, MPH student within SATVI.

Background
Tuberculosis (TB) is a common infectious disease caused by a bacteria (Mycobacterium tuberculosis), which most commonly affects the lungs (pulmonary TB) but it can also affect any organ in our body. Tuberculosis has been a serious threat to public health for many years and practices have been implemented to prevent the spread of TB infection.

These infection control measures have an important place in TB control and we would like to know what is known about TB and infection control measures in the Breede Valley community. We would also like to know how people who are being, or who have been tested for TB, feel about these infection control measures. We would like to know whether or not they would be acceptable to people and whether people would agree to co-operate with infection control measures.

Participant’s contribution
One hundred and ten (110) people will take part in this study, of whom half (55) will have been diagnosed with TB already and half will be having tests for TB for the first time. You have been invited to participate in this study because either you are being, or have been tested for TB, as part of another SATVI study. This does not necessarily mean that you do have TB, but you will have had some clinical tests for TB and you may be waiting for the results. You may have taken part in some infection control measures already.

You may choose not to take part in this study and you must know that it would not make any difference to the health care that you would normally receive, or to your participation in other research studies. You can leave the study at any time. You will not pay any penalty or lose any benefits you have earned if you say no.

Participant’s Responsibilities
In this study, no diagnostic tests will be done, but your time and willingness to answer some questions during an interview are needed. Your involvement in this study is limited to 1 session where you will be interviewed for about 30 minutes or less about infection control measures for TB. Participants who are being tested for TB for the first time will have one interview. Participants who have already been diagnosed with TB at the time of the first interview will undergo a second concise interview about TB infection control measures once their treatment is completed.
Participant’s Benefits
Your participation in the study is completely voluntary and you will not receive any direct benefits for your participation in this study. However, your contribution by sharing this information with us would help our understanding of people’s knowledge about the measures for control of TB.

Participant’s Compensation
No compensation or incentive would be given to you for your participation in this study, nor would you have to pay for your participation in this project.

Participant’s Risks
As this study is an interview, there are no medical or health risks, or potential adverse effects. While the topics raised during the questionnaire are quite generic and general, you are free to leave if at any point should you become uncomfortable.

Participant’s Privacy
Your answers will be kept confidential among the study staff. Your information will be kept in an electronic database using a coded number that will not be directly traceable to you. All participants will remain anonymous in the final reporting of the findings.

Contact Information for Questions or Concerns
You will receive a copy of this consent form if you agree to take part. The study has been approved by the Research Ethics Committee, Faculty of Health Sciences, University of Cape Town. If you have any concerns about your rights as a research participant, you should contact the secretary of the research ethics committee at the Faculty of Health Sciences on (021) 406-6492.

If at any time, you have questions or concerns about this study or are injured as a result of participation in this study you should contact:

Researchers:
Dr. Mark Hatherill, Principal Investigator, and Ms. Yulieth González-Angulo, MPH student. South African TB Vaccine Initiative (SATVI), Institute of Infectious Disease and Molecular Medicine, University of Cape Town School of Public Health and Family Medicine, Health Sciences Faculty Anzio Rd, Observatory, Cape Town, South Africa. Telephone (27) 21 404 7622; E-mails: Mark.Hatherill@uct.ac.za and Yulieth.Gonzalez-Angulo@uct.ac.za
Consent to take part in this Study

I have read and understood this consent form, the contents of which have been explained to me. My questions have been answered and I voluntarily agree to take part in the research described in this consent form.

Date

Name of study participant (please print)

Signature: participant

Name of study personnel taking consent (please print)

Signature: study personnel

Interpreter used (tick only if applicable)

Witness used (tick only if applicable; tick one below to describe witness)

☐ Study personnel

☐ Independent/impartial person

Name of witness (please print)

Signature of witness

Date
Deelnemernummer: ______________

INSTEMMINGSVORM

Protokoltitel: “Kennis en aanvaarbaarheid van maatreëls vir die beheer van oordrag van tuberkulose in die Breede Vallei-gemeenskap”

Die volgende inligting gaan u vertel van die studie en u rol daarin. Lees dit asseblief noukeurig deur en vrae gerus enige vrae.

Hierdie is ’n navorsingstudie wat deur die Suid-Afrikaanse TB-vaksien-inisiatief (SATVI), die Instituut van Infektiewe Siektes en Molekülêre Medisyne, Universiteit van Kaapstad se Mediese Skool, Anzio-weg Obervatory, Kaapstad uitgevoer word. Die spanlede in beheer van die studie is dr. Mark Hatherill, Senior Ondersoeker, en Yulieth Gonzalez-Angulo, MPH-student by SATVI.

Agtergrond
Tuberkulose (TB) is ’n algemene aansteeklike siekte wat deur bakterieë (Mycobacterium tuberculosis) veroorsaak word en wat meestal die longe (pulmonêre TB) aantas, maar ook enige ander orgaan in die liggaam kan affekteer. Tuberkulose is al vir baie jare ’n ernstige bedreiging vir openbare gesondheid, en prakteky is in plek gestel om die verspreiding van TB-infeksie te voorkom.

Hierdie infeksiebeheermaatreëls speel ’n belangrike rol by die beheer van TB, en ons wil graag vasstel wat mense in die Breede Vallei-gemeenskap weet van TB en die infeksiebeheermaatreëls. Ons wil graag weet hoe mense wat vir TB getoets word, of reeds vir TB getoets is, oor hierdie infeksiebeheermaatreëls voel. Ons wil ook graag uitvind of dit vir mense aanvaarbaar is, al dan nie, en of mense sou ooreenkom om met die infeksiebeheermaatreëls saam te werk.

Deelnemer se bydrae
Een honderd en tien (110) mense gaan aan hierdie studie deelneem, waarvan die helfte (55) reeds met TB gediagnoseer en die ander helfte TB-toetse vir die eerste keer sal ondergaan. U word genooi om aan hierdie studie deel te neem omdat u nou vir TB getoets word, of al in die verlede reeds as deel van ’n ander SATVI-studie vir TB getoets is. Dit beteken nie noodwendig dat u TB het nie, maar u het dalk sekere kliniese toetse vir TB gehad en mag tans die resultate afwag. U mag alreeds aan sekere infeksiebeheermaatreëls deelgeneem het.

U kan kies om nie aan hierdie studie deel te neem nie, en u moet besef dat dit geen verskil sal maak aan die gesondheidsorg wat u normaalweg sou ontvang nie, of aan u deelname aan ander navorsingstudies nie. U kan te enige tyd die studie verlaat. As u “nee” sê, sal dit geen benadeling vir u inhou nie, of verlies van enige voordele wat u verdien nie.

Deelnemer se verantwoordelikhede
Geen diagnostiese toetse gaan in hierdie studie uitgevoer word nie, maar u tyd en gewilligheid om enkele vra gedurende ’n onderhoud te beantwoord, word benodig. U betrokkenheid by hierdie studie is beperk tot 1 sessie, waartydens u onderhoud vir omtrent 30 minute of minder oor infeksiebeheermaatreëls vir TB met u gevoer sal word. Deelnemers wat vir die eerste keer vir TB getoets word, sal een onderhoud hê. Deelnemers wat ten tye van die onderhoud reeds met TB gediagnoseer is, sal ’n tweede kort onderhoud oor TB-infeksiebeheermaatreëls hê wanneer hulle behandeling voltooi is.
Deelnemer se voordele
U deelname aan hierdie studie is heeltermals vrywillig en u sal geen regstreekse voordele weens u deelname aan hierdie studie geniet nie. U bydrae, deur hierdie inligting met ons te deel, sal ons egter help om mense se kennis van die maatreëls vir die beheer van TB beter te verstaan.

Vergoeding aan deelnemer
Geen vergoeding of aansporing sal vir u deelname aan hierdie studie voorsien word nie, maar u sal ook nie vir u deelname aan hierdie projek hoef te betaal nie.

Risiko’s vir deelnemer
Aangesien hierdie studie ’n onderhoud behels, is daar geen mediese of gesondheidsrisiko’s of potensiële nadelige effekte nie. Hoewel die onderwerpe wat gedurende die vraelys geopper word generies en van ’n algemene aard is, staan dit u vry om te enige tyd die onderhoud te staak indien u ongemaklik begin voel.

Deelnemer se privaatheid
U antwoorde sal deur die studiepersoneel vertroulik gehou word. U inligting sal in ’n elektroniese databasis bewaar word, met gebruik van ’n gekodeerde nommer wat nie regstreeks na u terugherlei kan word nie. Alle deelnemers sal in die finale verslagdoening van die bevindings naamloos bly.

Kontak-inligting vir vrae of kwellinge
U sal ’n afskrif van hierdie instemmingsvorm ontvang indien u tot deelname instem. Die studie is deur die Etiiese Navorsingskomitee, Fakulteit Geneeskunde,Universiteit van Kaapstad goedgekeur. As u enige kwellinge het oor u reëte as ’n navorsingsdeelnemer, kan u in aanraking kom met die sekretaris van die Etiiese Navorsingskomitee, Fakulteit Geneeskunde, by (021) 406-6492.

As u te enige tyd enige vrae of kwellinge oor hierdie studie het, of as u as gevolg van deelname aan hierdie studie ’n besering opdoen, moet u in aanraking kom met:

Navorsers:
Dr. Mark Hatherill, Hoofondersoeker, en me. Yulieth González-Angulo, MPH-student by die Suid-Afrikaanse TB-vaksien-inisiatief (SATVI), Instituut van Infectiewe Siektes en Molekulêre Medysyne, Universiteit van Kaapstad se Skool van Openbare Gesondheid en Familiegeneeskunde, Fakulteit Geneeskunde, Anzio-weg Observoty, Kaapstad, Suid-Afrika. Telefoon (27) 21 404 7622
E-posadressee: Mark.Hatherill@uct.ac.za en Yulieth.Gonzalez-Angulo@uct.ac.za
**Instemming tot Deelname aan hierdie Studie**

Ek het hierdie instemmingsvorm, die inhoud waarvan vir my verduidelik is, deurgelees en verstaan. My vrae is beantwoord en ek kom vrywillig ooreen om aan die navorsing wat in hierdie instemmingsvorm beskryf word, deel te neem.

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- ☐ Tolk gebruik *(merk slegs indien van toepassing)*
- ☐ Getuie gebruik *(merk slegs indien van toepassing; merk een hieronder om getuie te beskryf)*
  - ☐ Studiepersoneellid
  - ☐ Onafhanklike/Onpartydige persoon

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Inombolo yomthathi nxaxheba ____________

ULWAZI LOMTHATHI NXAXHEBA NEFOMU YOKUNIKA IMVUME.

Isihloko seNkqubo yoPhando: “Ulwazi nokuvumeleka kwamanyathelo olawulo lokosulela ngesiyo sephpha kulantu lwase-Breede Valley”

Olu lwazi lulandelayo luya kukuxelela malunga nophando nenxaxheba oya kuyithatha kulo. Nceda ufunde ngononophelo yaye uzive ukhululekile ukuba ubuze nayiphi imibuzo.

Olu laphando lwesemfuna-lwazi olwenziwa yi-South African TB Vaccine Initiative (SATVI), Institute of Infectious Disease and Molecular Medicine, University of Cape Town Medical School, Anzio Rd, Observatory, Cape. Amalungu eqela elongamele olu phando ngu Gqr. Mark Hatherill, Umphandi oyintlolo no-Yulieth Gonzalez-Angulo, umfundi we-MPH kw-SATVI.

Intsusa
Isifo sephpha (iTB) sisifo esixhaphakileyo esosulelayo esibangelwa yintsholongwane eyi-bacteria (i-Mycobacterium tuberculosis), edla ngokuchaphazela kakhu kuimiphunga (i-Tb yemiphunga) kodwa ingakwashaphazela naliphi na eliney ilungu lomzimba wethu. Isifo sephpha ibe lugrogriso olukhulu kwezempilo kawonke-wonke iminyaka eliqela ngoku yaye inkqubo zokuthintela ukumweni komosuleleko we-TB zibekiwe.


Igalelo lomthathi nxaxheba
Ngabantu abalikhulu elineshumi (110) abaya kuthatha inxaxheba kolu phando, isiqingatha sabo (55) esiya kuba sele sikhonywe ngokuba ne-TB nesinye isiqingatha esiya kwenzwiwa ukuvumayo i-lo-TB okokusala. Umeniyewe ukuba uqathetha inxaxheba kolu phando kuba ukuvumayo elokanye ukhe wawavanyelwa iTB, njengenxaleny e yolunye uphando lw-SATVI. Oku akuthethi ukuba unayo iTB, kodwa umlele ukuba ukhe weniwa uqathetha luhleleyo uTH-iTB ekliniki, yaye ungaba usalinde iziphumo. Ungaba kanti sele wakhe wathatha inxaxheba kumanyathelo olawulo lomosuleleko.

Ungakhetha ukungathathi nxaxheba kolu phando yaye kufanele wazi ukuba akusayi kwenzwiwa mahluco kukongiwa kwempilo yakho obuya kukufumana kakade, okanye ekuthatheni kwakhe inxaxheba kolunye uphando lwesemfuna-lwazi. Ungalushiya uphando nanini na. Awusayi kuhlalwa nasiphi na isohlwane okanye ulehekelwe nazo naphe sihlozi obungaba uzifumene kakade ukuba uthi hayi.

Uxanduva lomthathi nxaxheba
Kolu phando, akusayi kwenzwiwa luwaxhaya lokuchona isigolo, kodwa kufunwa ixesha lakho nokufuna kwakho ukuphendula imibuzo ethile ngeshe eshloliwano-nxakhe. Ukubandakanye kwakho kolu phando luphelele kwekheshe e-1 apho kuya kudlwiano-nxakhe naye ihe ngeshe elinganemizulu engama-30 okanye ngaphantsi malunga namanyathelo olawulo lomosuleleko we-TB. Abathathi nxaxheba abavusuphakala nasele bebevutheni njengabanayo iTB ngeshe eshloliwano-nxakhe lokuqala bay xa kodwa nodlwiano-nxakhe.
lesibini olufutshane malunga namanyathelo olawulo lomosuleleko we-TB about xa unyango lwabo lugqityiwe.

Iinzuzo zomthathi nxaxheba
Ukuthatha kwakho inxaxheba kolu phando kukuqithandela ngokuphelelelo yaye awusayi kufumana izinto ngezinto oya kuyifumana ngenxa yokuthatha inxaxheba kolu phando, yaye awusayi kuhambe; e; a ukuthatha inxaxheba kulo msebenzi.

Ubungo kumthathi nxaxheba
Nanjengoko olu phando lulululwane-ndlebe, akukho bunego bonayengo okanye bempilo, okanye iziphumo eziscaleleni ezingathi zibe kwena. Naxa izikhloko eziphakanyiswayo ngexesha loluulhu lwemibuzo iyimibuzo ngento zonke ejikelele, ukhululekile ukuba uhambe ukuba nanini na uziva ungakhululekanga.

Imfihlelo yomthathi nxaxheba

Ulwazi loqhagamshelwano lwemiBuzo okanye ezikuKhathazayo
Uya kufumana ikopi yale fomu yokunika imvume ukuba uyavuma ukuthatha inxaxheba. Olu phando luvunyelwe yiKomiti yezeNgobo kuPhando (iResearch Ethics Committee), kwi-Faculty of Health Sciences, e-University of Cape Town. Ukuba ukhathazekile ngamalungelo akho njengomthathi inxaxheba kuphanmdo, kufanele uqaghamekhulwele lewekomiti yezeNgobo kuPhando kwi-Faculty of Health Sciences kwenzintera (021) 406-6492.

Ukuba nanini na, unemibuzo okanye kukho okukukhathazayo malunga nolukho phando okanye wonzakele ngenxa yokuthatha inxaxheba kolu phando, kufanele uqaghamekhulwele:

Nabaphandla:
Gqr. Mark Hatherill, Umphandla oyInkoko no Ms. Yulieth González-Angulo, umfundi we MPH kwi-South African TB Vaccine Initiative (SATVI), Institute of Infectious Disease and Molecular Medicine, University of Cape Town School of Public Health and Family Medicine, Health Sciences Faculty Anzio Rd, Observatory, Cape Town, South Africa. Umxweka (27) 21 404 7622 ii-E-mail: Mark.Hatherill@uct.ac.za no Yulieth.Gonzalez-Angulo@uct.ac.za
IMVUME YOKU THATA INXAXHEBA KOLU PHANDO

Ndiyifundile ndaza ndayiqonda le fomu yokunika imvume, eziqulatho ndizicaciselweyo. Imibuzo yam iphendulile yeaye ndiyavuma ngokuzithandela ukuthatha inxaxheba kuphando oluchazwe kule fomu yokunika imvume.

DD/MM/YYYY
Umhla

_______________________________________________________________________________
Igama lomthathi nxaxheba kuphando (nceda uprinte)

_______________________________________________________________________________
Isandla somthathi nxaxheba

_______________________________________________________________________________
Igama lomsebenzi kuphando othatha imvume (nceda uprinte)

_______________________________________________________________________________
Isandla somsebenzi kuphando othatha imvume

☐ Kusetyenziswe itoliki *(korekisha kuphela ukuba kunjalo)*

☐ Kusetyenziswe ingqina *(korekisha kuphela ukuba kunjalo; korekisha le ingezantsi ukuchaza ingqina)*

☐ Umsebenzi kuPhando

☐ Umntu ozimeleyo/ongenakhethe

_______________________________________________________________________________
Igama lengqina *(nceda uprinte)*

_______________________________________________________________________________
Isandla sengqina
Appendix 3: UCT Research Ethics Committee Approval Letter

13 August 2009

REC REF: 202/2009

R M Hatherill
SATVI
IIDMM

Dear Dr Hatherill

PROTOCOL TITLE: 09-001
KNOWLEDGE AND ACCEPTABILITY OF THE MEASURES FOR CONTROL OF TUBERCULOSIS TRANSMISSION IN THE BREEDE VALLEY COMMUNITY.

Thank you for your letter to the Research Ethics Committee dated 07 August 2009.

It is a pleasure to inform you that the Ethics Committee has noted and approved the following documents with reference to the above mentioned study:

- Participant information and Consent form, version 2.0 dated 18 July 2009.
- Questionnaire, version 3.0 dated 27 June 2009.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, HSF HUMAN ETHICS
Appendix 4: Questionnaire and consent form submission to the UCT Research Ethics Committee

The Chairperson
Research Ethics Committee
Faculty of Health Sciences
University of Cape Town

Dear Professor Blockman

Re: SUBMISSION OF QUESTIONNAIRE AND CONSENT FORM TRANSLATIONS:

Study Title: KNOWLEDGE AND ACCEPTABILITY OF MEASURES FOR CONTROL OF TUBERCULOSIS TRANSMISSION IN THE BREEDE VALLEY COMMUNITY

Protocol Date: Version 2.0 dated 13 July 2009

Principal Investigator: Dr. Mark Hatherill

Study area: TB Infection Control

UCTREC Ref: 202/2009

Thank-you for your approval letter dated 13 August 2009.

Appended, for your records and acknowledgment, please find the Afrikaans and Xhosa translations of the following documents:

- Questionnaire, Version 3.0 dated 27 June 2009
- Participant information and consent Form, Version 2.0 dated 8 July 2009
- Certificate of translation (PLB), dated 30 March 2010

Please do not hesitate to contact me should you require any further detail.

Yours sincerely

Ashley Veldsman
Regulatory Affairs Manager
TO WHOM IT MAY CONCERN

This is to certify that the translations of the following documents from English into Afrikaans and IsiXhosa for the South African Tuberculosis Vaccine Initiative (SATVI) have been executed by this bureau and, as such, are true and accurate versions of the original documents as presented to the translators indicated below.

- **Participant Information & Informed Consent Form**, Version No. 2 dated 8 July 2009
- **Tuberculosis Infection Control Project: Questionnaire**, Version No. 3 dated 27 June 2009

Afrikaans translator: Wima Maartens
IsiXhosa translator: Yolanda Giyose

Signed: ........................................

WIMA MAARTENS

Date: 30 March 2010
Sputum Induction for Diagnosis of Tuberculosis: A Systematic Review and Meta-Analysis

Yulieth Gonzalez-Angulo BSc(RT)\textsuperscript{1,3}, Charles Shey Wiysonge MD\textsuperscript{2,3}, Hennie Geldenhuys MFamMed\textsuperscript{1,3}, Willem Hanekom FCPaed\textsuperscript{1,3}, Hassan Mahomed MMed\textsuperscript{1,3}, Gregory Hussey FFCH\textsuperscript{1,3}, Mark Hatherill MD\textsuperscript{1,3}

\textsuperscript{1}South African Tuberculosis Vaccine Initiative (SATVI), \textsuperscript{2}Institute of Infectious Disease & Molecular Medicine, \textsuperscript{3}School of Child & Adolescent Health, University of Cape Town, Cape Town, South Africa.

Correspondence to:
Associate Prof. Mark Hatherill, South African TB Vaccine Initiative (SATVI), Wernher Beit Building N2.10, Faculty of Health Sciences, University of Cape Town, Anzio Road, Observatory, Cape Town, 7925, South Africa
Telephone: (+27) 21 404 7618
Fax: (+27) 21 406 6081
E-mail: Mark.Hatherill@uct.ac.za

Financial Support: YG is the recipient of a SATVI Masters Scholarship and MH and WH are supported by NIH grant [1R01AI075603-01].

Potential conflicts of interest: All authors: no conflicts.

Keywords: Sputum induction, Saline, Tuberculosis, Diagnosis, Meta-Analysis.

Running Head: Sputum Induction for the Diagnosis of Tuberculosis
ABSTRACT

Background: Sputum induction (SI) has been proposed as the optimal sample collection method for patients with paucibacillary tuberculosis (TB).

Methods: Studies reporting culture of Mycobacterium tuberculosis from SI were reviewed. A random-effects meta-analysis of diagnostic yield (numerator M. tuberculosis SI culture-positive cases; denominator all culture-positive cases) was conducted. Diagnostic yields (95% confidence intervals, CI) were displayed as Forest plots. Heterogeneity was evaluated using Chi-squared and I-squared tests and meta-regression analysis.

Results: Ninety publications were screened, 28 full-text papers reviewed, and 17 analyzed. Collectively, n = 627 SI culture-positive cases among n = 975 culture-confirmed TB cases were reported. Diagnostic yield of SI ranged from 35% to 95%. Pooled diagnostic yield was 74% (CI 65-81%), with significant heterogeneity (p<0.0001, \( I^2 = 86\% \)). There were no statistically significant differences in yield between sub-groups defined by HIV prevalence or age. Univariate analysis demonstrated that use of fiber-optic bronchoscopy (FOB) as the comparator method was associated with 22% reduction (CI 2-42%) in diagnostic yield of SI. However, after adjustment for confounding, meta-regression analysis showed that FOB usage (p=0.21) and saline concentration (p=0.31) were not independently associated with diagnostic yield.

Conclusion: Sputum induction will detect approximately three-quarters of M. tuberculosis culture-positive cases under study conditions. Significant heterogeneity in diagnostic yield was not explained by HIV prevalence, age, or use of fiber-optic bronchoscopy as the comparator method. The use of a particular nebulized saline concentration for sputum induction cannot be recommended on the basis of this meta-regression analysis.
INTRODUCTION

Early diagnosis to reduce the period of infectivity is considered one of the most effective TB control strategies. However, isolation of *M. tuberculosis* is difficult in children, HIV co-infected people, and others with paucibacillary disease (1-3). Failure to confirm the presence of *M. tuberculosis* at first presentation may contribute to ongoing disease transmission. It follows that strategies to improve bacteriologic confirmation of pulmonary TB by optimization of sputum collection are of great importance for control of the epidemic.

Gastric lavage and fiber-optic bronchoscopy (FOB) with lavage have been regarded as the optimal diagnostic procedures in persons with paucibacillary TB (4-7). However, these methods are relatively invasive and not always accessible in TB-endemic settings (8). Sputum Induction (SI) is a non-invasive procedure that allows sputum to be obtained from patients who are unable to expectorate, or who produce insufficient sputum. SI has been reported to be as effective as, or superior to, gastric lavage or FOB for diagnosis of TB (9, 10). Kawada *et al* found SI to be better than gastric aspiration in TB suspects (11). Anderson *et al* reported that the diagnostic yield of SI is as good as FOB for diagnosis of smear-negative pulmonary tuberculosis (PTB) (12). Hatherill *et al* found the diagnostic yield of sputum induction in children to be equivalent to that of gastric lavage (13). Conde *et al* reported that SI was safe, with high diagnostic yield and substantial agreement with FOB, in both HIV seronegative and seropositive patients (14).

Interpretation of the usefulness of SI in clinical and programmatic settings is difficult, due to the heterogeneous patient populations and wide variation in techniques that have been reported (15). Published SI guidelines have not tackled this methodological heterogeneity; since they were developed primarily for the study of airway inflammation
in asthma, and recommendations vary widely - for example, the concentration of nebulized saline ranges from 0.9 to 7% (15-18). It follows that risk-benefit and cost-benefit ratios for SI in a national TB control programme are difficult to estimate. We conducted a systematic review and meta-analysis of factors affecting the percentage diagnostic yield of SI (numerator *M. tuberculosis* SI culture-positive cases; denominator all culture-positive cases) in order to inform clinical and programmatic guidelines for TB diagnosis.

**METHODS**

**Search strategy**

We performed a systematic literature search to identify relevant studies in an electronic database; personal reference collections of experts; reference lists of papers of interest; working group reports; and published review articles. Studies published in English or Spanish were searched for through PubMed. Search terms included “Sputum Induction”, “Induced Sputum”, “Inducción de Secresiones”, “Esputo Inducido” “Tuberculosis”, “TB” and “PTB”. All prospective diagnostic studies that compared SI using a saline (sodium chloride) solution, in addition to any of the following techniques were eligible for review: (1) routine expectorated sputum; (2) gastric lavage; (3) nasopharyngeal aspiration; or (4) FOB with bronchoalveolar lavage. Studies that used nebulized solutions other than saline; specialized induction devices (eg. Lung flute®) (19); studies that did not use SI or a comparative diagnostic technique in all patients; and studies that reported pulmonary infections other than tuberculosis, were excluded.

**Study selection and quality assessment**

Two authors (YG and MH) developed the search strategy and one author (YG) conducted the primary systematic search for all studies meeting the pre-determined inclusion criteria. Titles and abstracts of eligible studies identified by the primary search were
screened. Study quality assessment and data extraction were conducted if a study met all inclusion criteria and no exclusion criteria. Data were extracted using a standardized data collection tool and entered into a Microsoft® Access database. A second reviewer (MH) cross-checked study eligibility, quality assessment, and data extraction, for validity and consistency. Full-text papers of the identified citations were reviewed by both the primary and secondary reviewers to select the final study set. Disagreement between the two reviewers at each stage was resolved by discussion until consensus was reached.

Data extraction

The following data were extracted from each study: 1) first author, year of publication, and journal; 2) country where the study was conducted; 3) study design; 4) study population; 5) methodological details of the SI procedure (if available), including saline volume and concentration, and nebulizer output and duration; 6) complications of the SI procedure; 7) number of cases diagnosed by culture of *M. tuberculosis* using SI; and 8) total number of patients diagnosed by culture of *M. tuberculosis* using SI and/or any of the comparator techniques listed above.

Data analysis

Percentage diagnostic yield, defined as the number of tuberculosis cases diagnosed by SI (numerator), divided by the total number of culture-confirmed tuberculosis cases by any technique (denominator), with 95% confidence intervals, was calculated for each study. Cochran’s Q test was used to assess statistical heterogeneity in yield between studies, with p-value ≤ 0.1 indicating significant heterogeneity. Inconsistency across studies was quantified using the I-square statistic (20). Potential causes of heterogeneity were investigated by stratification into subgroups and by fitting a meta-regression model to explain heterogeneity in terms of study-level covariates. Sub-group stratification included age category of participants (children or adults); saline concentration (<5% or ≥ 5%
saline); HIV prevalence in the study population (high or low); and use of a bronchoscopic comparator technique (FOB with lavage). For the purposes of this analysis, study HIV prevalence ≥ 10% was defined as high (21). Diagnostic yields, statistical tests for heterogeneity, and Forest plots were analysed using StatsDirect Software, Version 2.7.8 [StatsDirect Limited; http://www.statsdirect.com]. Considering the extent of variability between the studies, and based on the a priori assumption that each study estimated a different diagnostic yield, a random effect (8) meta-regression analysis was performed to assess independent associations with diagnostic yield of SI, after adjustment for potential confounding by saline concentration, HIV prevalence, age category, and FOB use, using Stata® 11.0 [StataCorp LP].

RESULTS

Literature search and study selection

Figure 1 summarises the search strategy and selection of studies for inclusion in the meta-analysis. A total of 78 citations were obtained from PubMed and 12 papers from other sources. Forty-eight papers which did not meet the inclusion criteria were excluded after screening of titles and abstracts and, of the remaining 42 publications, one published in Japanese was excluded. The full text of each of the 41 papers was reviewed, and 24 were excluded on the basis of: (1) publication reporting extra-pulmonary TB; (2) use of nebulisation solutions other than saline; or (3) study design that did not incorporate a comparator technique. The remaining 17 studies were included in the meta-analysis.

All 17 studies were cross-sectional (Table 1) and recruited a total of 3,988 participants. Publication dates ranged from 1961 to 2009. The studies differed in population (patient selection), sample size, and SI methodology. Study sample sizes ranged from 28 to 1,869 individuals (median n=129, IQR 94 - 189) and the number of participants diagnosed with
culture-positive TB ranged from 7 to 138 individuals (median n=20, IQR 15 – 48). Twenty nine percent of studies were conducted in children and 47% were either conducted in high HIV prevalence areas, or researchers reported a HIV sero-prevalence greater than 10% among participants. The majority of studies (65%) were conducted in low and middle income countries. SI was performed using saline concentrations ranging from 3% to 20% (median 3%, IQR 3 - 10), using a variety of ultrasonic nebulizers or conventional air compressors, and varying duration of saline nebulization (data incomplete). Eight studies (47%) compared SI to gastric lavage(13, 22-26), six studies (35%) to FOB(12, 14, 27-29), three studies (18%) to spontaneous expectorated sputum(29-31), three studies (18%) compared SI to other invasive procedures, including the string test, lymph node biopsy, and nasopharyngeal aspiration(32-34), and two studies (12%) compared three diagnostic procedures (SI, spontaneous sputum, and FOB in one publication (31); and SI, gastric lavage, and FOB in the other (9)).

**Diagnostic yield**

*M. tuberculosis* was isolated in 975 (24%) of the 3,988 participants. Microbiological diagnosis of TB was established through SI in 627 cases (i.e. 64% of all culture-confirmed TB diagnoses). **Figure 2** shows the Forest plot of diagnostic yield with 95% CI for each study, as well as the pooled diagnostic yield and 95% CI. Diagnostic yields for SI ranged from 35% to 95% (median 79%), with pooled diagnostic yield of 74% (95% CI 65 to 81%). However, there was substantial heterogeneity in study results: $X^2$ (df=16) = 115, $P < 0.0001$, $I^2$ 86% (95% CI 79% to 90%). Sub-group analyses of diagnostic yield by age category, concentration of nebulized saline, HIV prevalence, and use of FOB as the comparator method, are displayed in separate Forest plots in **Figures 3-6**, and summary estimates are shown in **Table 2**.
**Meta-Regression: Exploring sources of Heterogeneity**

Univariate regression analysis demonstrated no significant associations between diagnostic yield and HIV prevalence (p=0.37), or age category (p=0.35). Use of FOB as the comparator method was associated on average with 22% reduction in the diagnostic yield of SI (95% CI 2 – 42%), p=0.036, compared to studies that did not use FOB, in the univariate analysis. However, interpretation of this association was confounded by use of 3% saline in the studies also using FOB as the comparator method (Figure 7). A meta-regression analysis was conducted to adjust for potential confounding effects of FOB usage, saline concentration, HIV prevalence, and age category on diagnostic yield as the outcome variable. HIV prevalence and age category had no effect on the model and were excluded. The meta-regression model demonstrated that FOB usage (p=0.21) and saline concentration (p=0.31) were not independently associated with changes in diagnostic yield of SI.

**DISCUSSION**

This meta-analysis of SI for diagnosis of pulmonary TB has shown that, although diagnostic yield in individual studies may range from 35% to 95%, SI is likely to detect between 65 – 81% of culture-confirmed TB cases under study conditions, regardless of age group or HIV prevalence in the study population. We might have expected the comparative diagnostic yield of SI to be greater among studies reporting paucibacillary disease, such as pediatric studies and those with high HIV prevalence in the study population, but no such effect was observed. We found that use of bronchoscopic lavage as a comparison method was associated with, on average, 22% lower diagnostic yield from SI, compared to studies that did not employ FOB; second, we observed that use of 3% saline nebulization for SI was a significant confounder in studies using FOB.
However, we have demonstrated by meta-regression analysis that neither saline concentration nor FOB usage were independently associated with diagnostic yield from SI.

This is the first reported meta-analysis of the diagnostic yield of SI and the strengths of the study include the comprehensive search strategy; duplicate and independent study selection; quality assessment and data extraction; and the use of meta-regression analysis. It is particularly important that potential sources of heterogeneity are examined in a meta-analysis showing high levels of inconsistency in yield. Sources of variability that could be attributed to within-study factors (eg. participant selection) and between-study factors (study design and conduct) are explored by meta-regression.

The optimal saline concentration for SI is not known. It has been suggested that higher nebulized saline concentrations might have a greater osmotic effect on airway secretions (35), increasing the volume of the induced sputum sample, and thereby increasing the diagnostic yield. Our group has shown that nebulized 5% saline is both safe and tolerable, with minimal physiologic changes, when used for SI among adults investigated for PTB in an ambulatory setting (36). However, others have suggested that higher nebulized saline concentrations might be associated with greater risk of airway reactivity and higher rates of adverse events during the procedure (37). The findings of this meta-analysis suggest that higher saline concentrations are not associated with better diagnostic yield in SI after adjusting for confounders. We suggest that the safety and diagnostic yield of low nebulized saline concentrations, perhaps even 0.9% saline, should be studied prospectively in an effort to minimize adverse events.

Observed variability might also be explained by unreported differences in SI technique and lack of standardization. Technical factors that affect the density of aerosol and
particle size, such as nebulization devices (jet or ultrasonic nebulizer), might also, affect deposition of the saline solution in the tracheobronchial tree, and the diagnostic yield of the procedure. The selected studies used a broad range of nebulization devices and oxygen cylinders with different flow outputs, which would have directly affected nebulized particle size and airway deposition. Other potential sources of heterogeneity include severity of pre-existing lung disease, inclusion bias towards paucibacillary TB disease, and other patient-specific characteristics that might explain the presence of outliers in this analysis. However, reporting of these important data was inconsistent, incomplete, and did not allow a more in-depth analysis.

We have shown that the observed reduction in SI diagnostic yield in those studies using FOB as the comparator method is confounded by use of lower saline concentration (3%) in this group. Studies using invasive diagnostic techniques might be more likely to include smear-negative or sputum-unproductive individuals, leading to selection bias towards lower yield. It is also possible that, if FOB were better at detecting paucibacillary culture-positive TB cases than SI, the observed yield of SI relative to the total number of culture-confirmed cases would be lower in studies reporting FOB data. However, some studies have shown that the yield of sputum induction is equal to, or even better than that of FOB, which is consistent with our finding that FOB usage was not independently associated with lower diagnostic yield (9, 12, 14).

Several limitations of this meta-analysis must be considered. The search was restricted to three sources, including one electronic database, additional references recommended by experts in the field, and the published reference lists and reviews. One reviewer conducted the primary search to screen for citations, which might have introduced study selection bias, although two reviewers conducted the secondary search and quality assessment of papers identified by the primary screening. Another limitation that affects
this meta-analysis is the lack of a gold standard diagnostic comparator group in the reported studies. Although some diagnostic methods, such as FOB, are believed to provide better diagnostic accuracy than others, it is clear that none of the reported comparator methods are sufficiently sensitive to define the population with true TB disease with 100% accuracy. It follows that surrogate measures must be used to infer sensitivity, as others have done using percentage diagnostic yield, which utilizes all culture-confirmed TB cases as the denominator (13, 25). As noted above, few studies documented key technical aspects of the SI procedure and reporting of this important information was often inconsistent. Prospective, comparative studies of the diagnostic yield of SI are needed, with rigorous definition of the study populations and standardization of technique.

**Conclusion:** Sputum induction will detect approximately three-quarters of *M. tuberculosis* culture-positive cases under study conditions, among children and adults, regardless of HIV prevalence. However, the significant heterogeneity demonstrated in this meta-analysis indicates that diagnostic yield in certain study populations may differ significantly from this estimate. The observed variability in diagnostic yield cannot be attributed to differences in HIV prevalence, or age category of the study population. Use of FOB as the comparator method was associated with lower diagnostic yield in the univariate analysis, but interpretation of this effect was confounded by use of lower nebulized saline concentration in the same studies. FOB use and saline concentration were not independently associated with diagnostic yield and therefore, the use of a particular nebulized saline concentration cannot be recommended on the basis of diagnostic yield. We suggest that additional technical, clinical, and epidemiologic factors that might influence the diagnostic yield of sputum induction should be evaluated in prospective studies.
AUTHOR CONTRIBUTIONS

Y. Gonzalez-Angulo contributed to the design of the study, data collection, data analysis, and wrote the final manuscript; C. Wiysonge contributed to the design of the study, data analysis, and writing the manuscript; H. Geldenhuys contributed to writing the manuscript; W. Hanekom contributed to writing and editing the manuscript; H. Mahomed contributed to writing and editing the manuscript; G. Hussey contributed to writing and editing the manuscript; M. Hatherill contributed to the design of the study, data analysis, and writing of the final manuscript.
Reference List


### Table 1: Detailed description of studies included in the meta-analysis.

<table>
<thead>
<tr>
<th>Citation</th>
<th>Country</th>
<th>Study Population</th>
<th>Category of TB Suspect</th>
<th>Sample Size</th>
<th>Study HIV Prevalence (%)</th>
<th>Saline</th>
<th>Comparator Procedures</th>
<th>Total SI Samples</th>
<th>Total Comparator Samples</th>
<th>TB Diagnosis [by SI]</th>
<th>TB Diagnosis [by Comparator]</th>
<th>Total TB Diagnosis</th>
</tr>
</thead>
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<tr>
<td>Hensler , 1961 (12)</td>
<td>US</td>
<td>Adults</td>
<td>S\textsubscript{NEG}/S\textsubscript{UNPROD}</td>
<td>28</td>
<td>0</td>
<td>10</td>
<td>GL</td>
<td>3</td>
<td>3</td>
<td>19</td>
<td>14</td>
<td>20</td>
</tr>
<tr>
<td>Beck, 1962 (13)</td>
<td>US</td>
<td>Adults</td>
<td>S\textsubscript{NEG}/S\textsubscript{UNPROD}</td>
<td>62</td>
<td>0</td>
<td>10</td>
<td>SS</td>
<td>NS\textsuperscript{†}</td>
<td>NS\textsuperscript{†}</td>
<td>8</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>Yue , 1967 (23)</td>
<td>US</td>
<td>Adults</td>
<td>S\textsubscript{NEG}/S\textsubscript{UNPROD}</td>
<td>189</td>
<td>0</td>
<td>10</td>
<td>GL</td>
<td>NS\textsuperscript{†}</td>
<td>NS\textsuperscript{†}</td>
<td>138</td>
<td>84</td>
<td>153</td>
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<td>Anderson , 1995 (12)</td>
<td>Canada</td>
<td>Adults</td>
<td>S\textsubscript{NEG}/S\textsubscript{UNPROD}</td>
<td>92</td>
<td>0</td>
<td>3</td>
<td>FOB</td>
<td>1</td>
<td>1</td>
<td>20</td>
<td>19</td>
<td>26</td>
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<td>Zar, 2000 (24)</td>
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<td>Children</td>
<td>All</td>
<td>142</td>
<td>70</td>
<td>5</td>
<td>GL</td>
<td>1</td>
<td>2</td>
<td>15</td>
<td>9</td>
<td>16</td>
</tr>
<tr>
<td>Conde , 2000 (14)</td>
<td>Brazil</td>
<td>Adults</td>
<td>All</td>
<td>251</td>
<td>17</td>
<td>3</td>
<td>FOB</td>
<td>1</td>
<td>1</td>
<td>94</td>
<td>103</td>
<td>143</td>
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<tr>
<td>McWilliams, 2002 (27)</td>
<td>NZ</td>
<td>Adults</td>
<td>All</td>
<td>129</td>
<td>0</td>
<td>3</td>
<td>FOB</td>
<td>3</td>
<td>1</td>
<td>26</td>
<td>1</td>
<td>27</td>
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<tr>
<td>Zar , 2005 (25)</td>
<td>SA</td>
<td>Children</td>
<td>All</td>
<td>250</td>
<td>38</td>
<td>5</td>
<td>GL</td>
<td>3</td>
<td>3</td>
<td>51</td>
<td>38</td>
<td>62</td>
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<tr>
<td>Vargaz, 2005 (12)</td>
<td>Peru</td>
<td>Adults</td>
<td>S\textsubscript{NEG}/S\textsubscript{UNPROD}</td>
<td>212</td>
<td>100</td>
<td>20</td>
<td>ST</td>
<td>1</td>
<td>1</td>
<td>9</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>Iriso, 2005 (13)</td>
<td>Uganda</td>
<td>Children</td>
<td>All</td>
<td>126</td>
<td>49</td>
<td>3</td>
<td>PLNB</td>
<td>1</td>
<td>1</td>
<td>30</td>
<td>6</td>
<td>36</td>
</tr>
<tr>
<td>Brown, 2007 (9)</td>
<td>UK</td>
<td>Adults</td>
<td>S\textsubscript{NEG}/S\textsubscript{UNPROD}</td>
<td>140</td>
<td>4</td>
<td>3</td>
<td>GL / FOB</td>
<td>3</td>
<td>3 / 1</td>
<td>42</td>
<td>37</td>
<td>54</td>
</tr>
<tr>
<td>Schoch, 2007 (31)</td>
<td>Switzerland</td>
<td>Adults</td>
<td>All</td>
<td>101</td>
<td>0</td>
<td>3</td>
<td>FOB / SS</td>
<td>2</td>
<td>1 / 2</td>
<td>27</td>
<td>28</td>
<td>33</td>
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<tr>
<td>Owens, 2007 (34)</td>
<td>UK</td>
<td>Adults</td>
<td>S\textsubscript{NEG}/S\textsubscript{UNPROD}</td>
<td>94</td>
<td>47</td>
<td>3</td>
<td>NPA</td>
<td>NS\textsuperscript{†}</td>
<td>NS\textsuperscript{†}</td>
<td>19</td>
<td>21</td>
<td>24</td>
</tr>
<tr>
<td>Ganguly, 2008 (28)</td>
<td>India</td>
<td>Adults</td>
<td>S\textsubscript{NEG}/S\textsubscript{UNPROD}</td>
<td>52</td>
<td>0</td>
<td>3</td>
<td>FOB</td>
<td>NS\textsuperscript{†}</td>
<td>NS\textsuperscript{†}</td>
<td>7</td>
<td>5</td>
<td>20</td>
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<tr>
<td>Morse, 2008 (26)</td>
<td>Botswana</td>
<td>Adults</td>
<td>All</td>
<td>140</td>
<td>81</td>
<td>20</td>
<td>GL</td>
<td>NS\textsuperscript{†}</td>
<td>NS\textsuperscript{†}</td>
<td>48</td>
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<td>57</td>
</tr>
<tr>
<td>Hatherill, 2009 (13)</td>
<td>SA</td>
<td>Children</td>
<td>All</td>
<td>1654</td>
<td>2</td>
<td>5</td>
<td>GL</td>
<td>2</td>
<td>2</td>
<td>108</td>
<td>127</td>
<td>194</td>
</tr>
<tr>
<td>Bell, 2009 (28)</td>
<td>Malawi</td>
<td>Adults</td>
<td>S\textsubscript{NEG}/S\textsubscript{PRODUCT}</td>
<td>111</td>
<td>68</td>
<td>3</td>
<td>FOB / GL / SS</td>
<td>NS\textsuperscript{†}</td>
<td>NS\textsuperscript{†}</td>
<td>13</td>
<td>26</td>
<td>18</td>
</tr>
</tbody>
</table>

Note: ‘Category of TB Suspect‘ differentiates studies that only included TB suspects that were smear negative and sputum productive (S\textsubscript{NEG}/S\textsubscript{PRODUCT}) or smear negative and sputum unproductive (S\textsubscript{NEG}/S\textsubscript{UNPROD}) at pre-screening from studies that included all smear negative TB suspects. ‘NS\textsuperscript{†}‘ Refers to included studies in which the total of samples per procedure was not clearly specified.

**Country Abbreviations:** SA South Africa; NZ New Zealand; UK United Kingdom; US United States.

**Procedure Acronyms:** FOB Fiber-optic bronchoscopy with bronchoalveolar lavage; GL Gastric Lavage; NPA Nasopharyngeal Aspiration; PLNB Pleural/Lymph Node Biopsy; SS Spontaneous Sputum, ST String test.
Table 2: Diagnostic yield of sputum induction by sub-group.

<table>
<thead>
<tr>
<th>Category</th>
<th>Pooled Estimate (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults vs. Children</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults</td>
<td>71</td>
<td>(60-81)</td>
</tr>
<tr>
<td>Children</td>
<td>79</td>
<td>(62-92)</td>
</tr>
<tr>
<td>Saline Concentration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saline Concentration &lt;5</td>
<td>73</td>
<td>(63-82)</td>
</tr>
<tr>
<td>Saline Concentration ≥5</td>
<td>75</td>
<td>(59-89)</td>
</tr>
<tr>
<td>HIV Prevalence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High HIV Prevalence</td>
<td>78</td>
<td>(69-86)</td>
</tr>
<tr>
<td>Low HIV Prevalence</td>
<td>69</td>
<td>(54-83)</td>
</tr>
<tr>
<td>Use of Fiber-Optic Bronchoscopy (FOB)</td>
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<td></td>
</tr>
<tr>
<td>No use of FOB</td>
<td>81</td>
<td>(70-90)</td>
</tr>
<tr>
<td>Use of FOB</td>
<td>58</td>
<td>(38-77)</td>
</tr>
<tr>
<td>Overall Yield</td>
<td>74</td>
<td>(65-81)</td>
</tr>
</tbody>
</table>
**FIGURE LEGENDS**

**Figure 1:** Flow chart of the study selection process.

- Publications identified through PubMed search: **n=78**
  - Studies recommended by tuberculosis experts: **n=12**
  - Studies excluded: **n=48**
    - Reasons:
      - Not Pulmonary TB
      - Other TB
      - Other Pulmonary Disease
      - No Sputum Induction
      - No Sodium Chloride
  - Studies retrieved for more detailed evaluation: **n=42**
    - Studies withdrawn (Language): **n=1**
    - Potential studies included in the meta-analysis: **n=41**
      - Studies withdrawn (Methods): **n=24**
        - Reasons:
          - No comparison procedure
          - Retrospective analysis of clinical records
  - Studies with usable information, full text review included in the Meta-Analysis: **n=17**
Figure 2: Sputum Induction Diagnostic Yield – All Studies.

Diagnostic Yield of SI among all the studies: Heterogeneity tests: Cochran $Q = 115.29$ (df = 16) $P < 0.0001$ Moment-based estimate of between studies variance = 0.12 I² (inconsistency) = 86% (95% CI = 79% to 90%). Pooled proportion = 74 (95% CI = 65 - 81).
Figure 3: Sputum Induction Diagnostic Yield: Adults vs. Children.

Diagnostic Yield of SI by Subgroup Analysis according Age Groups:  

Adults (a): **Heterogeneity tests:** Cochran Q = 73.36 (df = 11) P < 0.0001 Moment-based estimate of between studies variance = 0.13 I² (inconsistency) = 85% (95% CI = 75% to 90%) **Pooled proportion** = 71 (95% CI = 60 - 80).  

Children (b): **Heterogeneity tests:** Cochran Q = 37.6 (df = 4) P < 0.0001 Moment-based estimate of between studies variance = 0.17 I² (inconsistency) = 89% (95% CI = 77% to 94%) **Pooled proportion** = 79 (95% CI = 61 - 92).
Figure 4: Sputum Induction Diagnostic Yield: Nebulized Saline Concentration.

**Figure 4a. Sputum Induction with Saline Concentrations < 5%**

- Yue [1967] 0.90 (0.84, 0.94)
- Anderson [1995] 0.77 (0.56, 0.91)
- Conde [2000] 0.66 (0.58, 0.74)
- McWilliams [2002] 0.48 (0.29, 0.68)
- Iriso [2005] 0.83 (0.67, 0.94)
- Brown [2007] 0.78 (0.64, 0.88)
- Owens [2007] 0.79 (0.58, 0.93)
- Ganguly [2008] 0.35 (0.15, 0.59)
- Morse [2008] 0.84 (0.72, 0.93)
- Bell (1) 0.72 (0.47, 0.90)
- Combined 0.73 (0.63, 0.82)

**Figure 4b. Sputum Induction with Saline Concentrations ≥ 5%**

- Hensler [1961] 0.95 (0.75, 1.00)
- Beck [1962] 0.88 (0.47, 1.00)
- Zar [2000] 0.94 (0.70, 1.00)
- Zar [2005] 0.88 (0.77, 0.95)
- Vargaz [2005] 0.53 (0.27, 0.79)
- Schoch [2007] 0.52 (0.34, 0.69)
- Hatheui [2009] 0.56 (0.48, 0.63)
- Combined 0.75 (0.59, 0.89)

Diagnostic Yield of SI by Subgroup Analysis according to Salinity: Saline Concentration <5% (a):

**Heterogeneity tests:** Cochran Q = 56.55 (df = 9)  P < 0.0001 Moment-based estimate of between studies variance = 0.09 P (inconsistency) = 84% (95% CI = 71% to 90%)  **Pooled proportion** = 73 (95% CI = 63 - 82). Saline Concentration ≥ 5% (b): Cochran Q = 47.94 (df = 6)  P < 0.0001 Moment-based estimate of between studies variance = 0.19 P (inconsistency) = 88% (95% CI = 76% to 92%)  **Pooled proportion** = 75 (95% CI = 59 - 89).
Figure 5: Sputum Induction Diagnostic Yield: HIV Prevalence.

**Diagnostic Yield of SI by Subgroup Analysis according to HIV Prevalence:**

- **High HIV prevalence (a):**
  - Heterogeneity Tests: Cochran Q = 21.97 (df = 7) $P < 0.0026$
  - Moment-based estimate of between studies variance = 0.05 $I^2$ (inconsistency) = 68% (95% CI = 12% to 83%).
  - Pooled proportion = 78 (95% CI = 69 - 86).

- **Low HIV prevalence (b):**
  - Heterogeneity Tests: Cochran Q = 89.93 (df = 8) $P < 0.0001$
  - Moment-based estimate of between studies variance = 0.20 $I^2$ (inconsistency) = 91% (95% CI = 86% to 94%).
  - Pooled proportion = 69 (95% CI = 54 - 82).

---

**Figure 5a. Sputum Induction in High HIV Prevalence Studies**

- Zar [2000] 0.94 (0.70, 1.00)
- Conde [2000] 0.66 (0.58, 0.74)
- Zar [2005] 0.88 (0.77, 0.95)
- Vargaz [2005] 0.53 (0.27, 0.79)
- Irigo [2005] 0.83 (0.67, 0.94)
- Owens [2007] 0.79 (0.58, 0.93)
- Morse [2008] 0.84 (0.72, 0.93)
- Bell [2009] 0.72 (0.47, 0.90)
- Combined 0.78 (0.69, 0.86)

**Figure 5b. Sputum Induction in Low HIV Prevalence Studies**

- Hensler [1961] 0.95 (0.75, 1.00)
- Beck [1962] 0.88 (0.47, 1.00)
- Yue [1967] 0.90 (0.84, 0.94)
- Anderson [1995] 0.77 (0.56, 0.91)
- McWilliams [2002] 0.48 (0.29, 0.68)
- Brown [2007] 0.78 (0.64, 0.88)
- Schoch [2007] 0.52 (0.34, 0.69)
- Ganguly [2008] 0.35 (0.15, 0.59)
- Hatherill [1] 0.56 (0.48, 0.63)
- Combined 0.69 (0.54, 0.83)
Figure 6: Sputum Induction Diagnostic Yield: Use of Fiber-optic Bronchoscopy (FOB) as the comparator method.

Diagnostic Yield of SI by Subgroup Analysis according to the use of Fiberoptic Bronchoscopy. Studies reporting no use of FOB (a): Heterogeneity Tests: 78.03 (df = 9) $P < 0.0001$; Moment-based estimate of between studies variance = 0.15; $I^2$ (inconsistency) = 89% (95% CI = 81% to 92.1%). Pooled proportion = 81% (95% CI = 69 - 90). Studies reporting the use of FOB (b): Heterogeneity Tests: Cochran Q = 93.51 (df = 6) $P < 0.0001$; Moment-based estimate of between studies variance = 0.28; $I^2$ (inconsistency) = 93.6% (95% CI = 90% to 96%) Pooled proportion = 58% (95% CI = 37 - 77).
All FOB studies reported using a 3% saline concentration. After the model is adjusted for FOB use, the yield of SI decreased, revealing the confounding effect of saline concentration and FOB use on diagnostic yield.
KNOWLEDGE AND ATTITUDES TOWARDS PATIENT-SPECIFIC INFECTION CONTROL MEASURES FOR TUBERCULOSIS

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Keywords: Tuberculosis, Infection control.

Running Head: Patient-specific infection control measures.

ABSTRACT

Context/Introduction: Knowledge and acceptability of patient-specific infection control measures to reduce transmission of Mycobacterium tuberculosis has not been adequately studied in developing countries.

Setting: Breede Valley region, South Africa.
Design: Prospective questionnaire-based study to determine the knowledge and acceptability of patient-specific infection control measures after frequent contact with health care workers. 100 participants were consecutively interviewed (50 TB suspects; 50 newly diagnosed TB patients). TB patients underwent a second interview at the end of treatment.

Results: At baseline, patients on TB treatment, who had received TB education at diagnosis, did not show higher levels of TB knowledge and preventive measures, compared to TB suspects, who had not received any TB education at screening. Acceptability of patient-specific infection control measures to be conducted at health care facilities was higher compared to acceptability for measures to be conducted at home and at work, except for cohorting and/or isolation. At the end of TB treatment, TB patients increased their knowledge of TB and showed higher acceptability levels towards patient-specific infection control measures over time.

Conclusion: Knowledge and acceptability of patient-specific infection control measures for TB increases over time with frequent contact with health care workers. In order to increase acceptability and adherence to patient-specific measures to reduce TB transmission, public health authorities must design and implement effective health education programmes for newly diagnosed TB patients. These programmes should focus on knowledge and empowerment of TB at diagnosis, the point of entry to the TB programmes.
INTRODUCTION
Early diagnosis and treatment of tuberculosis (TB) infectious cases have been considered the most effective control strategies to reduce TB transmission [1-3]. However, efforts to improve TB case identification and treatment compliance, have only partially improved this major public-health problem [4, 5]. The burden of TB dramatically declined in industrialized countries during the past century, even prior to the introduction of TB chemotherapy [6]. This decline in TB rates was attributed to reduction in the degree of effective contact between individuals [7], in other words, a decrease in the number of individuals in contact with each infectious case [7]. This reduction in effective contact was attributed to improvements in social conditions, nutrition, and isolation of infectious cases [7, 8].

Strategies to reduce TB transmission were further outlined in 1994 by the Centres for Disease Control and Prevention (CDC) [9]. Strategies such as patient isolation and cohorting, artificial ventilation, ultra-violet lighting, cough protocols, and respiratory protection for health care workers were implemented in industrialized countries to minimize air-bone TB contact bacilli, mainly in health care facilities [10, 11]. TB control efforts made considerable progress in countries in which rigorous implementation of measures to control infection, lowered the risk of tuberculosis among health care workers [12-14]. However, implementation of these same practices have not been feasible in developing countries due to financial constraints, and limited structural and human resource capacity [15].

South Africa has one of the highest TB notification rates in the world, with almost 1% of the population developing TB disease every year [16], despite of a well-
formulated National Strategic Plan for TB control [17], delay in starting TB treatment and low case-finding rates may contribute to on-going transmission in South Africa. Therefore, it is important to apply field-adapted infection control measures concurrently with chemotherapy.

Patient-specific infection control measures have been suggested for resource-limited areas, including cough protocols; cohorting and/or isolation; improvement of ventilation at home; and, staying away from work until at least two weeks of treatment has been completed [2, 18]. However, the success of any infection control measures that rely on patient adherence hinges on the degree to which these measures are accepted by patients in the community. Knowledge and acceptability of patient-specific measures to control TB transmission have not been studied in developing countries with high TB burden.

The aim of this study was to determine baseline TB knowledge levels among TB suspects and newly diagnosed TB patients and establish which patient-specific measures for control of TB transmission were acceptable, in a South African community with high TB incidence rates; second, we aimed to determine if knowledge and acceptability of patient-specific infection control measures improved with on-going TB education over time.

**Patients and Methods**

We conducted a prospective questionnaire-based study to determine knowledge and acceptability of patient-specific TB infection control measures, (October 2009 - May 2011). A total of one hundred participants were recruited from Worcester, De
Doorns, and Rawsonville TB clinics in the Breede River Valley. This region is located in the Western Cape province of South Africa and has a population of about 134,271 people and an estimated TB prevalence of 1188 / 100 000 population [19].

Participants were classified based on their status, as (i) TB suspects or (ii) TB patients. TB patients were defined as individuals who were newly diagnosed and starting treatment for pulmonary TB for the first time; moreover, TB patients had already received TB education from health care workers (at diagnosis). TB suspects were defined as individuals undergoing TB investigation and who had not received TB. Participants were eligible for inclusion if they were a TB suspect or a TB patient, status, aged ≥18 years old, and with the ability to give informed consent and to understand and complete the survey questionnaire.

Data Collection
A questionnaire was designed based on recommendations of local infection control specialists, and modified after the pilot study with TB suspects and TB. The questionnaire was based upon WHO recommendations for TB infection control in health-care facilities, congregate settings and households [2]. The questionnaire comprised questions about (1) core TB knowledge; and patient-specific infection control measures at (2) health care facilities; (3) at home, and finally at (4) work settings. Participants’ TB knowledge was determined through six basic questions about the disease (TB cause; TB transmission; transmission mode[s]; chemoprophylaxis for children; TB treatment; and, TB infection control measures). The remaining sections of the questionnaire aimed to determine acceptability of patient-specific measures to help reduce TB transmission among TB patients and their close contacts. Information was collected at two different time-points. TB
patients and TB suspects were both interviewed at baseline. Subsequently, once TB patients had ended their treatment, a second interview was conducted.

**Data analysis**
The Chi-square test—or the Fisher’s exact when applicable—was used to compare proportions (TB suspects versus TB patients; TB patients at baseline versus TB patients at the end of treatment). A scoring system was used to assess levels of TB knowledge and acceptability. One point was accrued for every correct answer and none for an incorrect one. Spearman’s correlation analysis was applied to determine bivariate relationships between knowledge and acceptability scores. The level of statistical significance was set at 5%. Stata® 11 was used for data analysis.

**RESULTS**
Twenty-two percent of participants were IsiXhosa speakers ($n = 22$); 78% were Afrikaans speakers ($n = 78$). 47% of participants were women ($n = 47$), and 53% men ($n = 53$); 44% of participants, at the time that the first interview was conducted, were living with 5 or more people in their houses ($n = 44$); 74% of participants confirmed that there were more than two individuals per room ($n = 74$). 9% of confirmed TB patients were sharing a room with children under the age of 5 ($n = 5$); 6% of them were sharing a room with children older than 5 years ($n = 6$), and 10% of TB patients were sharing a room with other adults and children altogether ($n = 10$). Only 18% of the participants slept alone ($n = 18$); 56% of our participants were working when the first interview was conducted ($n = 56$). At baseline, there were no important differences in terms of demographic characteristics between TB suspects and TB patients (See Table 1).

**Core TB knowledge**
**TB cause and transmission**

No major differences were found between TB suspects and patients in terms of core TB knowledge. However, in both groups, participants had poor to moderate levels of knowledge about TB. Only 57% of all respondents reported that they knew the cause of TB \( (n = 57) \), although only 25% of these respondents \( (n = 25) \) confirmed that TB was caused by a micro-organism. The remaining participants \( (n = 75) \) had misconceptions regarding the cause of TB. 5% of participants reported that TB was caused by drinking alcohol \( (n = 5) \); 5% attributed TB to uncleanliness \( (n = 5) \); 12% to smoking \( (n = 12) \); 4% to the use of drugs \( (n = 4) \); and, 6% believed that TB was a hereditary disease \( (n = 6) \). Surprisingly, more TB suspects \( (n = 19) \) knew that TB was a microbial disease as compared to TB patients \( (n = 6) \) \( (p \text{-value 0.003}) \). 95% of the participants reported that TB could be transmitted to other people \( (n =) \). TB patients \( (n = 50) \) as compare to TB suspects \( (n = 45) \) were more aware that TB follows a human-to-human transmission pattern \( (p\text{-value 0.022}) \). However, only 54% of all participants reported that they knew how TB was transmitted \( (n = 54) \). Participants confirmed that TB could be transmitted through sharing food utensils \( (n = 9) \); by kissing \( (n = 10) \); and even by living in low-temperature areas \( (n = 15) \). Only 20% and 26% of TB patients \( (n = 20) \) and TB suspects \( (n = 26) \), respectively, reported that TB was transmitted by being in close contact with a TB patient (See Table 2).

**TB treatment and TB transmission**

Less than half of the participants \( (n = 41) \) reported that TB transmission could be stopped or reduced once that an effective treatment regimen is started. Neither TB
patients nor TB suspects had a clear understanding of when TB chemotherapy starts to lower the bacillary load. 4% of participants \((n = 4)\) responded that, a TB patient usually stops transmitting TB on the first day of treatment; 4% reported that TB treatment was effective in reducing \(M.\) \textit{tuberculosis} transmission after 2 months on TB chemotherapy \((n = 4)\), and 24% of participants \((n = 24)\) said that TB transmission stops after treatment has been completed.

\textit{Knowledge about infection control measures}

When participants were asked if they knew of any methods to reduce the transmission of \(M.\) \textit{tuberculosis}, only 49% of the participants \((n = 49)\) reported that they knew of measures to control TB. A higher proportion of TB suspects \((30\%; n = 30)\) claimed to know of patient-specific measures to help reduce TB transmission \((p\text{-value 0.028})\) compared to TB patients \((19\%; n = 19)\). However, answers regarding implementation of patient-specific measures such as: (1) use of facemasks during transportation to a hospital or clinic; (2) use of facemasks in a hospital or clinic; (3) covering the mouth at a health care facility; (4) covering the mouth at home or at work; (5) separation from other patients, (6) sleeping alone, or avoiding sleeping in a room with small children; (7) opening house windows to the outside air; and (8) the use of fans for moving air to the outside, showed no significant difference between TB suspects and TB patients. On the other hand, a greater proportion of TB suspects \((n = 27)\) believed that by completing a course of anti-TB treatment, TB transmission could be prevented, compared to TB patients \((n = 14)\) \((p\text{-value 0.008})\).
Acceptability of infection control measures

Acceptability of infection control measures at health care facilities
There was a high level of acceptability of patient-specific infection control measures among TB suspects and TB patients. For instance, all participants were willing to complete anti-TB treatment as a means to prevent TB transmission, and 89% of the participants \( (n = 89) \) were willing to use facemasks in health care facilities—more TB patients \( (n = 48) \) than TB suspects \( (n = 41) \) were willing to implement such measure \( (p\text{-value } 0.025) \). TB patients and TB suspects showed similar levels of acceptability for cough protocols while at a health care facility. The measure that many participants were reluctant to implement at health care facilities was isolation and/or separation from other patients. TB suspects and TB patients who did not agree with the implementation of this measure reported that they would not like to be separated from other patients, and the fear of rejection or TB stigma influenced their decision (See table 3).

Acceptability of infection control measures at home
Measures to control TB transmission at home were in general, acceptable to most participants. Cough protocols, opening of house windows to improve ventilation, and isolation at home, were accepted by most participants. No significant differences were found between TB suspects and TB patients (See table 3). The use of facemasks at home \( (n = 54) \), the use of fans to increase ventilation \( (n = 59) \), as well as sleeping in a room by themselves or avoiding sleeping in a room with small children \( (n = 68) \) were less acceptable. TB patients \( (n = 33) \) were more accepting of these facemasks compared to TB suspects \( (n = 21) \) (See table 3). 65% of the
participants who were willing to use isolation at home as a method to reduce the transmission of *M. tuberculosis* to their families, reported that this was feasible in their homes, whereas 20% reported that even though they were willing to be isolated, isolation was not feasible at their homes. Only 15% of all participants reported that they were not willing to be isolated at home.

*Acceptability of infection control measures at work*

Infection control measures at work had a relatively high level of acceptability among participants at baseline. 65% of all participants would be willing to stop working until they have completed 2 weeks of treatment, or until smear microscopy was negative (*n* = 65). The majority of patients who did not agree with this measure stated that they would not receive any income (*n* = 18). TB and HIV stigma were not contributing factors to participants’ decision. 98% of participants stated that they would be more willing to cover their mouth with a handkerchief or tissue at work (*n* = 98), compared to 58% who would prefer to use a facemask at their workplace (*n* = 58) (See table 3).

**TB Knowledge and acceptability of infection control measures at the end of treatment**

Among the initial group of TB patients who were interviewed at baseline, only 82% (*n* = 41) TB patients completed a second interview. Knowledge about TB and TB infection control measures increased significantly over time, between start and end of treatment, under research conditions. There was an increase from 23 to 36 in the number of participants who stated that they knew the cause of TB (increase in
response rate of 32%), and a 41% increase in the total of participants who agreed that TB was caused by a micro-organism (6 to 25). 44% of respondents, who, at baseline, stated that they did not know how TB is transmitted, reported that they knew how a person can get TB, at the second interview (increase in response rate from 19 to 37 individuals). When participants were asked to specify how TB was transmitted, an increase of 54% of participants reported that only by being in close contact with an infectious source, other individuals could get TB (14 to 36). At baseline most participants ($n = 93$) believed that children require IPT once exposed to $M. tuberculosis$, but there was no change over time. At the end of treatment, most participants also reported that they knew when a TB patient usually stops transmitting the disease. Measures such as using facemasks, cough protocols in health care facilities, opening house windows to improve ventilation and completing anti—TB treatment, were more often recognized as measures to reduce the transmission of TB at the end of participant’s follow-up, compared to baseline. A higher proportion of participants responded that these preventive methods helped to reduce TB transmission for health care workers (56%), home contacts (66%) and co-workers (54%), compare to baseline (See tables 4 & 5).

**DISCUSSION**

We report the first study of knowledge and attitudes to TB in relation to the acceptability and implementation of patient-specific infection control measures (environmental and respiratory protection measures). After interviewing TB suspects and newly diagnosed TB patients, our study revealed limited basic knowledge about TB and a low degree of acceptability of patient-specific measures for TB control,
immediately after individuals have had initial contact with health care providers. In our study, patients on TB treatment, who had received some TB education at diagnosis, did not reflect higher levels of TB knowledge and preventive measures, compared to TB suspects, who had not received any information or education. However, we have shown that with on-going education and experience, TB patients had increased knowledge of TB and infection control measures. Furthermore, we could observe that TB knowledge and acceptability of patient-specific infection control measures for TB increased over time (See figures 1 & 2). Similar to the findings of other authors who investigated levels of knowledge and practices among newly diagnosed TB patients [20-23], our study initially showed fairly low levels of knowledge regarding the disease and measures to reduce its transmission, coupled with moderate levels of acceptability of certain patient-specific measures. However, after contact with clinical research workers and personal on-going education, we could demonstrate that, the acceptability of these patient-specific measures increased in parallel with improvements in knowledge about TB.

Turning to the results for attitudes towards patient-specific infection control measures for TB, at baseline we found that patients were much more comfortable and more willing to implement such practices at health care facilities compared to households and work settings. And although participants seemed to know that TB chemotherapy was a way to stop transmission and were eager to complete anti-TB treatment, they ignored when the infectiousness of TB patients declines. In addition, it was clear that measures involving cohorting or isolation at health care facilities were not acceptable for a vast proportion of participants. We could speculate that these findings of fear to isolation may be due in part to patients’ perspectives and
experiences of stigmatization and social rejection. However, participants’ acceptance or perceptions on self-isolation (at home) increased over time. We also found that acceptability of measures that could “reveal” the TB status of patients such as the use of facemasks at home, increased significantly over time.

As revealed in our evaluation of knowledge and acceptability of infection control measures at baseline, both groups, TB suspects and TB patients had similar levels of knowledge, even though TB suspects had not received any type of information from health care facilities. Yet, we could not evaluate the quality of information that health care staff from public health facilities might be providing to patients. Therefore, our findings (increased acceptability of some patient-specific measures as knowledge increased) might not be replicable in resource-challenged health care settings. A study reporting knowledge, attitudes and practices among health care workers in Iraq, established that although TB knowledge among health care workers might be high, by contrast, infection control practices were poor [24]. Hashim et al showed that only 38.2% of health care workers from primary care centres in Iraq handled suspected TB cases correctly [24]. In this study, participants had frequent contact with health care providers under strict research conditions; this situation may therefore represent an ideal condition. However, this may not be achievable under programmatic conditions in many low-resourced health care settings. We were aware that social desirability bias is an important limitation of questionnaire-based studies and that it might have affected the validity of our research findings. Although we demonstrated that acceptability of patient-specific infection control measures increases in relation to improvements in knowledge about TB over the course of treatment in TB patients after constant contact with health care
workers, and even though we tried to mitigate the effects of SDB, we acknowledged that some of our participants could have overreported “good behaviour” or underreported “bad behaviour” in relation to the acceptability of patient-specific infection control measures.

One of the challenges in health education is that, the quality and amount of information provided to patients depends on the knowledge, perceptions and attitudes of providers. In this case, information was provided by health care staff from public health facilities and by clinical research workers under strict research conditions. In both cases, these providers have been trained to educate patients. However, public health institutions in developing countries face overcrowding conditions and in many cases, the quality and duration of interaction between health care providers may be insufficient for a complete and satisfactory educational dialogue.

However, this research presents an opportunity for TB control programmes to strengthen measures to decrease TB transmission. New policies emphasize the use of isolation or even short term incarceration, as well as other “environmental” practices to reduce TB transmission [25-27]. However, in resource-constrained areas, public health authorities face (a) a lack of accurate diagnostic tools, which delays confirmation of infectious TB cases; (b) overcrowded health care facilities in which TB patients mix with other patients, increasing the risk of nosocomial TB transmission to other patients and health care staff; and (c) lack of personnel in health care facilities, hampers the quality of information and educational support to patients [28-31]. These factors amplify the risk of exposure to M. tuberculosis, and
increase the possibility of developing TB disease, particularly for close contacts of TB patients and health care workers.

The “National Infection Prevention and Control Policy for TB, MDR-TB and XDR-TB” published by the South African Department of Health states that patients who are identified as TB suspects at screening must be given advice on respiratory hygiene/cough etiquette, provided with a facemask or tissues to cover their mouths and noses, and then be cohorted separately from other patients. Our findings showed that patients are reluctant to be isolated in health care facilities although they are more willing to be isolated at home. Increased emphasis on home-based care could help reduce nosocomial transmission of TB. Clearly, the implementation of effective isolation at home must be followed by the implementation of other measures: firstly, health care institutions must promote adherence to TB chemotherapy; secondly, education about infection control measures must also be provided to family members and other community members to create a strong support network for TB patients. The risk of transmitting the disease to close contacts might also be reduced if patients are equipped with high efficiency (N95) masks to use at home, especially during the first weeks after treatment has been initiated.

**Conclusion**

Baseline knowledge about TB and TB infection control measures was poor to moderate among both TB suspects and TB patients, although the latter had received TB education after their diagnosis was confirmed. However, acceptability of patient-specific infection control measures increases in relation to improvements in TB knowledge over time. In order to increase acceptability of patient-specific infection
control measures, public health authorities must design and implement early intensive TB education programmes to increase knowledge of TB and TB infection control measures. These educational resources should be accessible not only for TB suspects and TB patients, but for entire communities in which TB poses a challenge.
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REFERENCE LIST


Table 1. Demographic Data

<table>
<thead>
<tr>
<th>Variable &amp; Attribute (s)</th>
<th>TB Suspects (%)</th>
<th>TB Patients (%)</th>
<th>Total</th>
<th>P-Value</th>
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<td>12 (24)</td>
<td>22</td>
<td>0.629</td>
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<td>40 (80)</td>
<td>38 (76)</td>
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<td>Females</td>
<td>28 (56)</td>
<td>19 (38)</td>
<td>47</td>
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<td>Males</td>
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<td><strong>Age (median)</strong></td>
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<td>0.526</td>
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<td>33 years (18-54)</td>
<td>33 years (19-54)</td>
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<tr>
<td><strong>Housing Conditions</strong></td>
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<tr>
<td>Total people in home:</td>
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</tr>
<tr>
<td>≥ 5 people</td>
<td>20 (40)</td>
<td>24 (48)</td>
<td>44</td>
<td>0.42</td>
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<tr>
<td>&lt; 5 people</td>
<td>30 (60)</td>
<td>26 (52)</td>
<td>56</td>
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<td>Total people/room (median)</td>
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<td>Sleep alone</td>
<td>11 (22)</td>
<td>7 (14)</td>
<td>18</td>
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<td>Currently working</td>
<td>29 (58)</td>
<td>27 (54)</td>
<td>56</td>
<td>0.687</td>
</tr>
<tr>
<td>Working indoors</td>
<td>14 (48)</td>
<td>7 (26)</td>
<td>21</td>
<td>0.084</td>
</tr>
<tr>
<td>Working outdoors</td>
<td>15 (52)</td>
<td>20 (74)</td>
<td>35</td>
<td></td>
</tr>
</tbody>
</table>
Table 2. Baseline TB knowledge among TB suspects and newly diagnosed TB patients

<table>
<thead>
<tr>
<th>General Information on Tuberculosis</th>
<th>TB Suspects (%) $n = 50$</th>
<th>TB Patients (%) $n = 50$</th>
<th>Total $n = 100$</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do you know the cause of TB?</td>
<td>32(32)</td>
<td>25(25)</td>
<td>57</td>
<td>0.157</td>
</tr>
<tr>
<td><strong>Germs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you think TB can be passed on to other people?</td>
<td>45(45)</td>
<td>50(50)</td>
<td>95</td>
<td>0.022*</td>
</tr>
<tr>
<td>How a person does get TB?</td>
<td>29(29)</td>
<td>25(25)</td>
<td>54</td>
<td>0.422</td>
</tr>
<tr>
<td>Do young children need chemoprophylaxis therapy once exposed to MTB?</td>
<td>44(44)</td>
<td>49(49)</td>
<td>93</td>
<td>0.112</td>
</tr>
<tr>
<td>Do you know when a TB patient usually stops transmitting the disease?</td>
<td>18(18)</td>
<td>23(23)</td>
<td>41</td>
<td>0.309</td>
</tr>
<tr>
<td>Do you know some measures to control tuberculosis?</td>
<td>30(30)</td>
<td>19(19)</td>
<td>49</td>
<td>0.028*</td>
</tr>
<tr>
<td><strong>Complete their course of anti—TB treatment</strong></td>
<td>27(27)</td>
<td>14(14)</td>
<td>41</td>
<td>0.008*</td>
</tr>
<tr>
<td>Do you know why measures to control tuberculosis are important?</td>
<td>30(30)</td>
<td>23(23)</td>
<td>53</td>
<td>0.161</td>
</tr>
</tbody>
</table>
Table 3. Acceptability of patient-specific measure at baseline

<table>
<thead>
<tr>
<th></th>
<th>TB Suspects (%)</th>
<th>TB Patients (%)</th>
<th>Total (%)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 50</td>
<td>n = 50</td>
<td>n = 100</td>
<td></td>
</tr>
<tr>
<td><strong>Infection Control Measures at Health Care Facilities</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use facemask in health care settings? Y/N</td>
<td>41 (41)</td>
<td>48 (48)</td>
<td>89</td>
<td>0.025*</td>
</tr>
<tr>
<td>Cover mouth when coughing and/and sneezing in a health care setting? Y/N</td>
<td>48 (48)</td>
<td>50 (50)</td>
<td>98</td>
<td>0.495</td>
</tr>
<tr>
<td>Complete a course of anti-TB treatment? Y/N</td>
<td>50 (50)</td>
<td>50 (50)</td>
<td>100</td>
<td>-</td>
</tr>
<tr>
<td>Be separated from other patients? Y/N</td>
<td>32 (32)</td>
<td>36 (36)</td>
<td>68</td>
<td>0.391</td>
</tr>
<tr>
<td><strong>Infection Control Measures at Home</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cover mouth with a handkerchief/tissue when coughing and/and sneezing?</td>
<td>50 (50)</td>
<td>49 (49)</td>
<td>99</td>
<td>1.000</td>
</tr>
<tr>
<td>Cover mouth with facial mask when coughing and/and sneezing?</td>
<td>21 (21)</td>
<td>33 (33)</td>
<td>54</td>
<td>0.016*</td>
</tr>
<tr>
<td>Sleep in a room by oneself or avoid sleeping in a room with small children?</td>
<td>33 (33)</td>
<td>35 (35)</td>
<td>68</td>
<td>0.668</td>
</tr>
<tr>
<td>Open house windows to the outside?</td>
<td>43 (43)</td>
<td>46 (46)</td>
<td>89</td>
<td>0.338</td>
</tr>
<tr>
<td>Use fans if possible for moving air to the outside?</td>
<td>30 (30)</td>
<td>29 (29)</td>
<td>59</td>
<td>0.839</td>
</tr>
<tr>
<td><strong>Infection Control Measures at Work</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stop working until you have completed 2 weeks of treatment, or longer?</td>
<td>32 (64)</td>
<td>33 (66)</td>
<td>65</td>
<td>0.834</td>
</tr>
<tr>
<td>Cover mouth with a handkerchief/tissue when coughing and/and sneezing?</td>
<td>48 (96)</td>
<td>50 (100)</td>
<td>98</td>
<td>0.495</td>
</tr>
<tr>
<td>Cover mouth with facial mask when coughing and/and sneezing? Y/N</td>
<td>25 (50)</td>
<td>33 (66)</td>
<td>58</td>
<td>0.105</td>
</tr>
</tbody>
</table>
Table 4. Baseline TB knowledge among at the end of treatment

<table>
<thead>
<tr>
<th>Knowledge &amp; Perceptions about Tuberculosis</th>
<th>Baseline (%) n = 41</th>
<th>End Treatment (%) n = 41</th>
<th>Absolute Diff (%)</th>
<th>Confidence Interval</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do you know the cause of Tuberculosis (TB)?</td>
<td>23 (56)</td>
<td>36 (88)</td>
<td>32†</td>
<td>13.21 - 36.46</td>
<td>0.001*</td>
</tr>
<tr>
<td>Do you think tuberculosis can be passed on to other people?</td>
<td>41 (100)</td>
<td>41 (100)</td>
<td>—</td>
<td>—</td>
<td>N/A</td>
</tr>
<tr>
<td>How a person gets TB? Y/N</td>
<td>19 (46)</td>
<td>37 (90)</td>
<td>44†</td>
<td>24.51 - 48.66</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Do young children need treatment?</td>
<td>40 (98)</td>
<td>41 (100)</td>
<td>2</td>
<td>-2.32 - 2.44</td>
<td>1.000</td>
</tr>
<tr>
<td>Do you know when a TB patient usually stops transmitting the disease?</td>
<td>21 (51)</td>
<td>34 (83)</td>
<td>32†</td>
<td>11.24 - 40.25</td>
<td>0.002*</td>
</tr>
<tr>
<td>Do you know some measures to control tuberculosis? Y/N</td>
<td>16 (39)</td>
<td>33 (80)</td>
<td>41†</td>
<td>18.41 - 52.98</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Do you know why measures to control tuberculosis are important? Y/N</td>
<td>16 (39)</td>
<td>33 (80)</td>
<td>41†</td>
<td>20.10 - 50.02</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Infection Control Measures at Health Care Facilities</td>
<td>Baseline (%)</td>
<td>End Treatment (%)</td>
<td>Absolute Diff (%)</td>
<td>Confidence Interval</td>
<td>P-Value</td>
</tr>
<tr>
<td>-----------------------------------------------------</td>
<td>--------------</td>
<td>-------------------</td>
<td>-------------------</td>
<td>---------------------</td>
<td>---------</td>
</tr>
<tr>
<td>Use facemask HC settings?</td>
<td>39 (95)</td>
<td>41 (100)</td>
<td>5</td>
<td>-3.34 - 4.88</td>
<td>0.5</td>
</tr>
<tr>
<td>Cover mouth when coughing and/sneezing in a health care setting?</td>
<td>41 (100)</td>
<td>41 (100)</td>
<td>-</td>
<td>-</td>
<td>N/A</td>
</tr>
<tr>
<td>Complete a course of anti—TB treatment?</td>
<td>41 (100)</td>
<td>41 (100)</td>
<td>-</td>
<td>-</td>
<td>N/A</td>
</tr>
<tr>
<td>Be separated from other patients?</td>
<td>28 (68)</td>
<td>26 (63)</td>
<td>5</td>
<td>-15.71 - 23.61</td>
<td>0.804</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Infection Control Measures at Home</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cover mouth with a handkerchief/tissue when coughing and/sneezing?</td>
<td>41 (100)</td>
<td>40 (98)</td>
<td>2</td>
<td>-2.32 - 2.44</td>
<td>1.000</td>
</tr>
<tr>
<td>Cover mouth with facial mask when coughing and/sneezing?</td>
<td>26 (63)</td>
<td>35 (85)</td>
<td>22</td>
<td>2.89 - 30.49</td>
<td>0.023*</td>
</tr>
<tr>
<td>Sleep in a room by oneself or avoid sleeping in a room with small children?</td>
<td>28 (68)</td>
<td>33 (80)</td>
<td>12</td>
<td>-4.39 - 20.72</td>
<td>0.18</td>
</tr>
<tr>
<td>Open house windows to the outside?</td>
<td>37 (90)</td>
<td>40 (98)</td>
<td>24</td>
<td>2.07 - 38.27</td>
<td>0.031*</td>
</tr>
<tr>
<td>Use fans if possible for moving air to the outside?</td>
<td>23 (56)</td>
<td>32 (78)</td>
<td>22</td>
<td>4.68 - 26.71</td>
<td>0.012*</td>
</tr>
<tr>
<td>Isolation at home?</td>
<td>37 (90)</td>
<td>39 (95)</td>
<td>5</td>
<td>-5.97 - 9.63</td>
<td>0.625</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Infection Control Measures at Work</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Stop working until you have completed 2 weeks of treatment, or longer?</td>
<td>26 (63)</td>
<td>31 (76)</td>
<td>12</td>
<td>-4.39 - 20.72</td>
<td>0.18</td>
</tr>
<tr>
<td>Cover mouth with a handkerchief/tissue when coughing and/sneezing?</td>
<td>41 (100)</td>
<td>41 (100)</td>
<td>-</td>
<td>-</td>
<td>N/A</td>
</tr>
<tr>
<td>Cover mouth with facial mask when coughing and/sneezing?</td>
<td>27 (66)</td>
<td>33 (80)</td>
<td>15</td>
<td>-1.03 - 19.39</td>
<td>0.070</td>
</tr>
</tbody>
</table>
Core knowledge and acceptability of TB infection control measures at baseline

Figure 1. Relationship between baseline TB knowledge and acceptability of infection control measures among TB suspects and TB patients
Core knowledge and acceptability of TB infection control measures at the end of treatment

Figure 2. Relationship between TB knowledge and acceptability of infection control measures at the end of treatment