A QUANTITATIVE AND QUALITATIVE STUDY TO INVESTIGATE THE EPIDEMIOLOGY OF TUBERCULOSIS AND ITS DETERMINANTS IN KHOMAS REGION, NAMIBIA

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Abstract

Namibia has the seventh highest Tuberculosis (TB) incidence rate in the world, but the disease epidemiology is not well researched. This thesis investigated the TB burden and its determinants in the country's most populous region Khomas, and empirical work was divided into four inter-related phases.

Phase one involved a Joinpoint regression analysis of trends in TB notification rates. The results showed that from 1997 to 2015, the notification rates for all forms of TB declined from 808 to 400 per 100 000 population, representing an average annual percent change of -3.9% (95% CI: -6.4 to -1.3%). Significant annual percent changes were observed for all specific types of TB.

Phase two focused on the spatial and spatiotemporal analysis of TB notifications from 2006 to 2015, using the Moran's I and scan statistics. The results showed that TB depicted a strong spatial autocorrelation, with a significant positive Global Moran's I obtained each year. The northern townships were repeatedly identified as TB hotspots, and these townships mostly had notification rates higher than the city average.

Phase three involved a comparative and descriptive cross-sectional survey with 800 participants from two townships. The results showed that participants who were unemployed, consumed alcohol frequently, stayed in overcrowded households, rarely visited healthcare services and had poor TB knowledge were significantly more likely to reside in the high TB burden township.

Phase four comprised of a thematic analysis of 14 qualitative interviews exploring TB knowledge, attitudes and practices. The results showed that perceived increased risk of TB infection was attributed to lifestyle behaviours, while the township's overall disease burden was attributed to poor sanitation, overcrowding and a lack of basic services.

In conclusion, despite the overall declining trend, the TB burden in specific townships in Khomas remains worryingly high. Focused prevention interventions are needed to heighten impact in the identified hotspots. Also, further research is needed to study the local burden in relation to internal migration and diabetes, neither of which were measured in this study.

Dedication

To my husband, Lukas, and daughter, Twapewa, for their support and unconditional love.

To all those affected by TB in one way or another, and to the memory of the ones we have lost as a result of TB.

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Acronyms

AAPC	Average Annual Percent Change
AIDS	Acquired Immunodeficiency Syndrome
APC	Annual Percent Change
ART	Antiretroviral therapy
CB DOT	Community-based Directly Observed Treatment
CNRs	Case Notification Rates
CPT	Co-trimoxazole Preventive Therapy
DOT	Directly Observed Treatment
DR-TB	Drug Resistant Tuberculosis
DTLC	District Tuberculosis and Leprosy Coordinator
EPTB	Extra Pulmonary Tuberculosis
GIS	Geographic Information Systems
GFATM	The Global Fund to fight AIDS, Tuberculosis and Malaria
HEP	Health Extension Programme
HIS	Health Information System
HIV	Human Immunodeficiency Virus
IEC	Information, Education and Communication
MDR	Multi-Drug Resistance
MoHSS	Ministry of Health and Social Services
NDHS	Namibia Demographic and Health Survey
NIP	Namibia Institute of Pathology
NSA	Namibia Statistics Agency
NTLP	National Tuberculosis and Leprosy Programme
RR	Relative Risk
TB	Tuberculosis
UK	United Kingdom
USA	United States of America
WHO	World Health Organisation
XDR	Extreme-Drug Resistance
95% CI	95% Confidence Interval

Chapter 1 : Introduction

1.1 Research background

Despite being a preventable and curable disease, Tuberculosis (TB) remains a serious public health threat, particularly in Africa and South East Asia (1). Of thirty highest TB burden countries, sixteen are on the African continent, with Namibia having the seventh highest TB incidence rate in the world (1). The disease has detrimental effects at different levels of society. For instance, at the individual level, TB not only causes significant ill health, but also takes a toll on the person's prospects in life (2-4). Moreover, due to disability and associated discrimination, it affects relationships between family members, friends and neighbours (5-7). At the family level, the disease fuels poverty in households, as it usually affects people in the most productive age groups, therefore it has a catastrophic effect on the family's income, health and nutrition (8-10). At the country level, a high TB burden can drain a country's resources (including human capital), so it is a major setback to development (11).

The fight against TB was prioritised on the global scale, after the disease was declared a global emergency in 1993 (12). This resulted in global efforts which saw the realisation of strategies such as the Stop TB strategy (13), and the currently implemented End TB strategy (14). At the 2018 United Nations high level meeting on TB in New York, world leaders committed to a political declaration aimed at ending TB by 2030 (15).

It has been emphasised that effective disease control requires the embracement of innovative approaches to intensify impact (1), and consequently, there has been increased use of Geographic Information System (GIS) techniques as well as spatial and spatiotemporal methods to study the distribution of TB (16, 17). Specifically, these techniques have been used to guide TB control interventions, by identifying TB hotspots and investigating associated risk factors (18, 19). For example, in Ethiopia, Dangisso *et al*. used spatiotemporal techniques to study the distribution of smear positive TB from 2003 to 2012 (20). In South Africa, Smith *et al*. recently utilised similar techniques to study the distribution of Multi-Drug Resistance (MDR) TB during the years 2011 to 2015 (21). Touray *et al*. used spatial techniques to study the distribution of TB during a one year period in The Gambia (22). Moreover, spatial and spatiotemporal methods have been widely utilised in other regions such as in Asia (23-25), South America (26, 27) and Europe (28-30).

Despite the use of spatial analysis techniques and their demonstrated ability to guide disease control (16-18), to the best of my knowledge, no study has been conducted to date to analyse the spatial epidemiology of TB in Namibia. Furthermore, the local modifiable factors that could explain the geographic variation of the disease burden are poorly understood. This undoubtedly leaves a critical gap for effective TB control in the country, especially when resources are limited. Gains from TB control activities could be much improved through knowledge of the spatial epidemiology of the disease, as well as an understanding of local factors influencing its distribution (19), particularly in high TB burden regions/districts in the country.

Therefore, in addressing this gap, this thesis focuses on generating local evidence about the TB burden in Namibia's most populous region, Khomas. The findings of the research presented here would be useful in improving our knowledge of the disease epidemiology, in order to improve the implementation of control and prevention interventions in the general public.

In this introductory chapter, I provide a brief background of the disease aetiology as well as an overview of its global distribution. Moreover, I give a brief background to my country, Namibia, including an overview of the national health system and the national TB burden. Furthermore, the chapter covers specific details about the rationale for my research as well as the research aims and objectives. I conclude by providing details of the geographic scale of my research and the thesis structure.

1.2. Background information about TB

1.2.1. Infection

TB is a contagious disease caused by the bacillus, *Mycobacterium tuberculosis* (1). The disease affects all parts of the body, and is referred to as pulmonary TB when it affects the lungs, or as extra-pulmonary TB when it affects other organs of the body. Pulmonary TB is the most common and most infectious form of TB (1). The numbered bullet points below details the specific clinical definitions used to categorise TB cases. TB Transmission mostly occurs when an uninfected person comes into contact with droplets from the throat or lung of a pulmonary TB infected person, when they cough or sneeze, and infection requires inhaling only a few bacteria (31). A person infected with TB bacteria may or may not develop active TB disease. This primary phase of infection is referred to as latent infection, and it is estimated that about one third of the world population is in this phase each year (32, 33).

People infected with the TB bacteria who have not yet developed TB disease are not infectious. However, they have a lifetime risk of 5-10% of developing active TB disease (1).

1. **New smear positive pulmonary TB**: This is a new TB patient with at least one positive sputum smear sample. These are patients confirmed to have at least one Acid-Fast Bacilli (AFB) present in at least one sputum sample.
2. **New smear negative pulmonary TB**: This is a TB case where there is negative AFB in the sputum sample, but a patient is put on TB treatment on the basis of clinical judgement.
3. **Extra-pulmonary TB**: This is when a person has TB involving other body organs than the lungs, such as, lymph nodes, pleural, abdomen, skin, joint and bones.

1.2.2. Symptoms and Diagnosis

Active TB disease manifests in a person through various symptoms, and the most common include a persistent cough of three or more weeks, coughing blood, chest pain, fatigue, unexplained loss of weight, fever and night sweats (1). The disease is diagnosed through methods such as rapid molecular tests, direct smear microscopy or culture growth examination (1). In both children and adults, the World Health Organisation (WHO) recommends that the initial diagnostic test should be rapid testing using an Xpert MTB/RIF assay (Cepheid, USA), which reveals results within two hours of testing (34). Testing through sputum smear microscopy requires examination of sputum samples by microscopy to observe the presence of the TB bacteria (34). Culture growth involves growing the bacteria in clinical specimens such as sputum or urine samples, and then examining whether the TB causing bacteria are present (34).

1.2.3. Treatment

TB is a treatable condition. The standard treatment length is usually six months, with the first two months classified as the initial treatment phase, and the last four months as the treatment continuation phase (34). The first line anti-TB drugs include Rifampicin, Isoniazid, Streptomycin, Pyrazinamide and Ethambutol (34). If a patient is resistant to first line drugs, the second line anti-TB drugs are administered and these include Kanamycin, Ethionamide and Levofloxacin (34). Patients resistant to the first line anti-TB drugs can be variously categorised. A mono-resistant patient is resistant to one first line drug. A multi-drug resistant patient is resistant to multiple first line drugs. An extreme drug-resistant (XDR) patient is resistant to both first and second line drugs (34). Treatment for patients on second line drugs usually takes longer, up to about two years (34).

1.2.4. Who is most at risk of Tuberculosis?

The bacillus, *Mycobacterium tuberculosis* can infect anyone (1, 35), and hence TB is a worldwide disease (36), which can manifest in people of different ages and sexes (1). However, the TB literature documents a variety of factors associated with an increased risk of infection and/or active TB disease (37). For instance, observational studies have documented that specific populations are at increased risk of TB, including homeless people (38), healthcare workers (39), immigrants (40) and prisoners (41). More importantly, it is established that the single most important risk factor for TB infection and active disease is HIV/AIDS (1). People living with HIV/AIDS are 16-27 times at greater risk of developing TB compared to HIV/AIDS negative people (42). In addition, it has been shown that increased age, poor nutrition and diabetes mellitus are other important risk factors for TB (43, 44). Furthermore, studies have also shown that the risk of TB infection and/or disease is elevated among people with low socioeconomic status, heavy alcohol drinkers and smokers (33, 45, 46).

1.3. The global epidemiology

According to the WHO, TB kills more people globally than any other infectious disease, despite being a preventable and treatable illness (1). The disease is also amongst the top ten causes of death worldwide (1). The most recent global TB epidemiological data shows that around 10 million people developed TB in 2017, and of these, 1.3 million HIV-negative and an additional 300 000 HIV-positive persons died in the same year (1). As shown in Figure 1.1, TB mostly affects South East Asia and Africa, and the latter carries the heaviest burden per capita, with an estimated incidence rate of 237 cases per 100 000 populations in 2017, higher than the global average of 133 cases per 100 000 population. The thirty highest TB burden countries accounted for 87% of all TB cases worldwide (1).

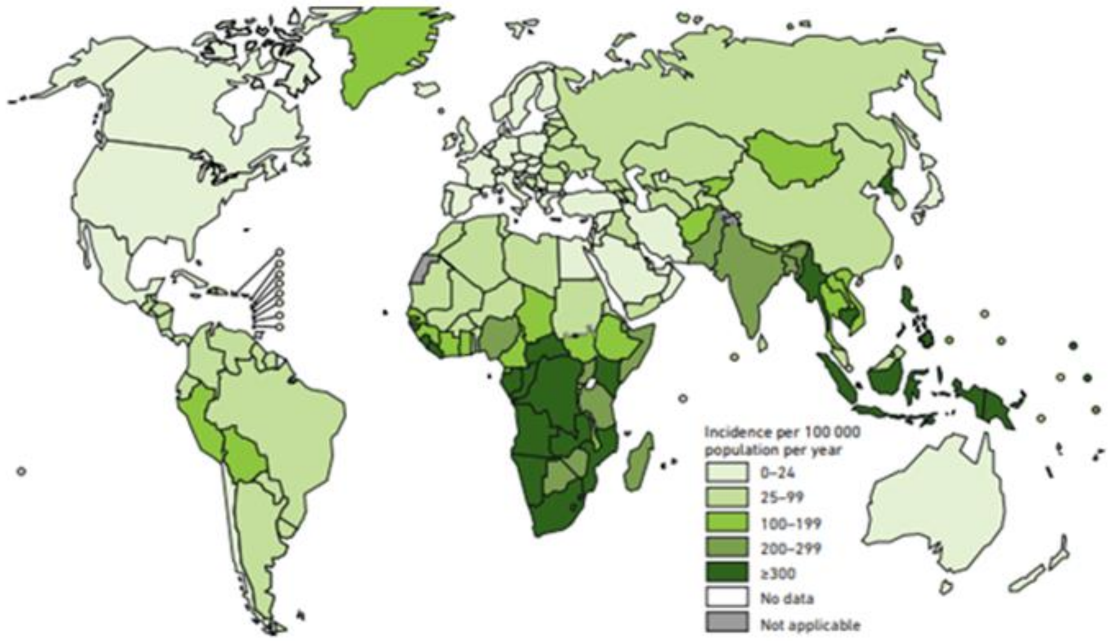


Figure 1.1 Estimated TB incidence rates, 2017 (1).

TB morbidity and mortality are nonetheless declining globally, but the progress made so far has not been sufficient enough to meet the global targets (14). In 2014, the WHO member states endorsed the End TB strategy (14), a three pillar strategic tool geared towards facilitating the fight against TB on a global scale. The strategy aims to reduce the TB burden through reducing incidence by 90% by 2035. Meeting this target requires an accelerated shift from the current 2% annual decline in global incidence to a yearly decline of 10% and 17% by the years 2025 and 2035 respectively. Therefore, key strategic components have been proposed, one of them being intensified research to heighten implementation and impact (14).

1.4. Country background

Namibia is located in the southern part of Africa, and shares a land border with South Africa, Botswana, Zambia and Angola. The Atlantic Ocean stretches down the western edge of the country, alongside the Namib Desert, from which the country's name is derived. It has a population of just over two million inhabitants, of whom 48% and 58% live in urban and rural areas, respectively (47). The pyramid in Figure 1.2 shows the country's population structure based on recent census data (47). There is a broad base, indicating a high fertility rate, but also a high mortality rate, as indicated by the narrow top. According to recent estimates, life expectancy is 65 years, a figure which shows improvement from that estimated in previous years (48).

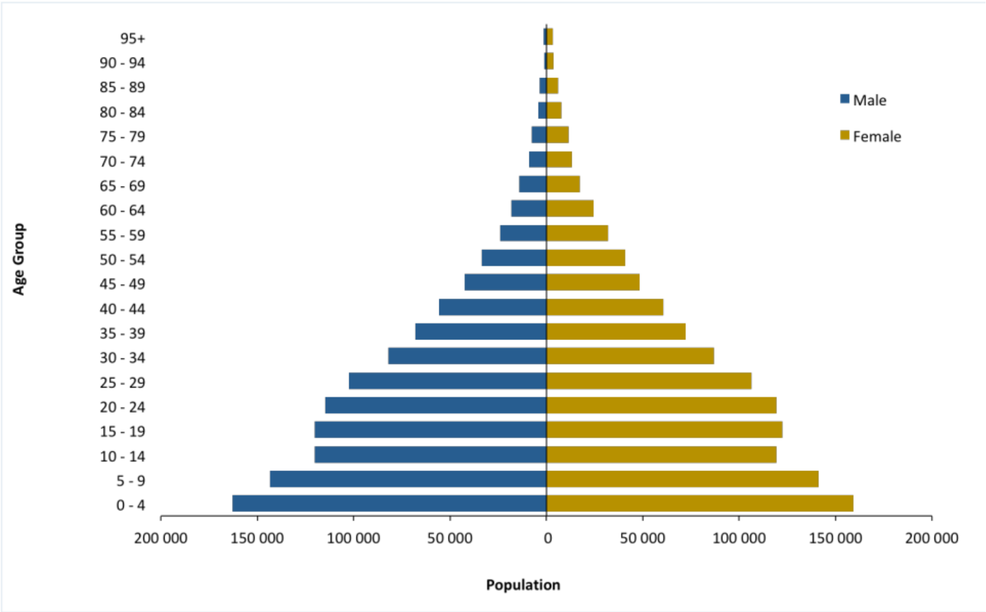


Figure 1.2 Namibia Population structure, 2016 (47).

Namibia gained independence in 1990, after first being under German colonial rule and later under South Africa apartheid rule. The country was colonised by Germany from 1884 until the end of the World War one, after which South Africa took over from 1915. Since independence, Namibia has transitioned into a full parliamentary democracy with several political parties, national and local elections are held regularly (49).

The country covers a total surface area of 824 116 km^2, and has a sparse population with one of the lowest densities in the world (50). English is the official language (49), but there are other twenty-seven languages spoken, including twenty-two indigenous and five non-indigenous languages (47). The most common language is Oshiwambo, spoken by 50% of the population (47). Recent census data shows that Namibia has a high literacy rate at 89%, but also a high unemployment rate at 37% among economically active people (51).

Both formal and informal economies are present, and the country has modern infrastructures such as roads, telecommunication and port facilities. Agriculture, tourism, and mining are the main sectors contributing to the country's GDP (49). The World Bank has classified Namibia as an upper middle income country (48). However, the country is known to have one of the highest Gini-coefficients in the world (48, 52), and this has been the case since the colonial era (50). In rural areas, where the majority of the population live, people are generally involved in subsistence farming and crop cultivation (50).

1.4.1. Overview of the Namibian health system

The Namibian government, through the Ministry of Health and Social Services (MoHSS), is mandated through a constitutional act to ensure that people in the country have the right to adequate public health and social services (49). Therefore, the government, via the public health service, is the leading health provider, and private healthcare is estimated to serve about 19% of the population (53). The MoHSS has adopted the Primary Health Care (PHC) approach, which is centred on four components namely, promotion of health, disease prevention, curative services as well as rehabilitation services (49). These components are further divided into eight specific elements, which include amongst others, provision of safe water and proper nutrition, maternal and childcare, immunisation, housing and sanitation, treatment of disease, and participation of community members in health matters (49).

Public health service activities are implemented based on a three-tier system consisting of national, regional and district levels (50). The national level is where overall planning of the MoHSS is established, in terms of finances, human resources and infrastructural planning. The fourteen regions, have respective health directorates, which oversee the implementation of activities in thirty-four health districts across the country. The latest data show that the MoHSS has 38 hospitals (including one national referral hospital and three intermediate hospitals), 43 health centres and 288 health clinics countrywide (54).

In ensuring fair access to public health facilities, treatment for TB and other diseases, including HIV/AIDS and Malaria is free at public facilities (49). The Namibia Institute of Pathology (NIP) provides all pathological services for the public health sector, and these services are funded by the government, with no cost to the patient (53). The specific tests used for TB diagnosis available at NIP include fluorescent microscopy, rapid molecular tests (Gene xpert), and liquid culture and drug susceptibility testing (53).

In 1991, the MoHSS formed the National TB and Leprosy Programme (NTLP) to coordinate the implementation of TB control activities in the country (55). Its establishment resulted in the development of the country’s first TB strategic plan in 2004 covering the period 2005-2009 (55). Since the first plan, the NTLP has facilitated the development of subsequent national strategic plans, including the second medium-term plan covering 2010-2015 and was later extended to cover 2016/17 (56). Currently, the country is implementing activities based on the third medium-term plan covering 2017/18 to 2021/22 (53). The development of the current strategic plan was informed by the national development plans (57, 58), the sustainable development goals (59), the End TB strategy (14) and the Stop TB partnership Global plan to end TB (60).

Namibia adopted the Directly Observed Treatment (DOT) strategy of the WHO during the mid-1990s and the country's first national TB treatment guidelines were developed 1995 (55). DOT was primarily established by the WHO to standardise methods of case finding, case management and reporting (61). TB activities are largely funded by the government, and to complement these efforts, there are a number of community-based TB organisations funded through international donors, mainly the Global Fund to fight AIDS, Tuberculosis and Malaria (GFATM), President's Emergency Plan for AIDS Relief (PEPFAR) and United States Agency for International Development (USAID) (53).

The NTLP produces TB reports on an annual basis (62-70). Apart from programmatic information, these reports detail the number of notified TB and treatment outcomes for TB patients notified in the preceding year. The data are summarised at national, regional and districts levels.

1.4.2. Overview of the national TB burden

In 2017, Namibia had an estimated incidence rate of 423 per 100 000 population, a mortality rate of 30 per 100 000 population among HIV negative TB patients, and a mortality rate of 31 per 100 000 population among HIV/AIDS positive TB patients (1). Nationally, TB is a well-recognised public health threat, alongside other infectious diseases such as HIV/AIDS and Malaria (53). The disease burden is however declining, with recent data showing a national case notification rate (CNR) of 394 per 100 000 population in 2016 from a peak of above 800 per 100 000 population in 2004 (53). National data show that the burden varies considerably between regions, as shown in Figure **1.3**, and urban regions contribute the largest proportion to the overall burden (53). Those in the most productive years of their lives (25-44 years) are the most affected, with the majority being male (53). HIV/AIDS is observed to be one of the key contributing factors to the TB burden in Namibia, and the national average TB and HIV/AIDS co-infection rate was 37% in 2016 (53). According to the WHO, Namibia is not classified as a high Drug Resistance (DR) TB burden country (1). However, a recent national anti-TB DR survey shows that the prevalence of MDR TB was 3.9% among new TB patients and 8.7% among previously treated TB patients (71). These data are similar to countries classified as high DR TB nations, such as Angola, Kenya and South Africa (1). Nationally, the majority of DR TB cases are recorded as rifampicin resistant, and males generally makes up the majority of those cases (53).

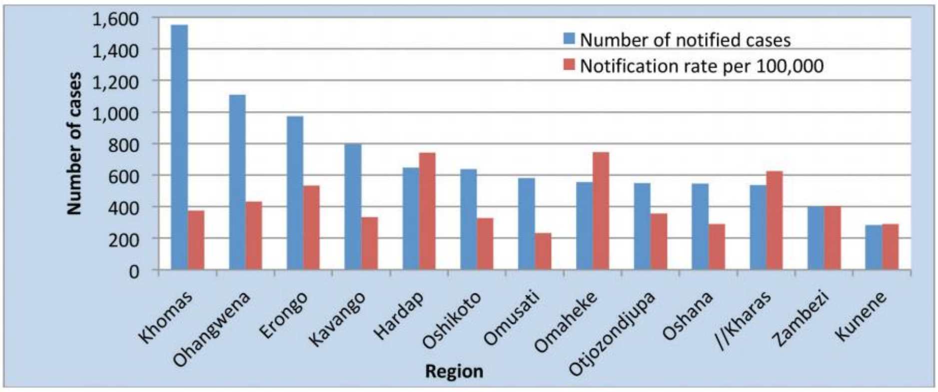


Figure 1.3 Notified all forms of TB cases by region, 2016 (53).

1.5. Justification for the research

Namibia aims to reduce the annual incidence of TB to 321 cases per 100 000 population by 2021 and to 50 cases per 100 000 population by 2035 (53). Consequently, several strategic interventions have been formulated at the national level towards reaching these targets (53). However, despite these efforts, TB epidemiological data in Namibia are only analysed and presented up to the health district level, and these districts varies considerably in terms of population size. For instance, some regions are made up of only one health district while others have more two or more districts (53). The presentation of the disease burden up to health district level implies that there is little understanding of the disease burden at the community level, which is one of the primary levels for TB transmission (72). For effective disease control, the WHO, through the global TB End strategy, recommends countries to have comprehensive knowledge of their disease burden, a component which they have termed as "know your epidemic" (14). In that strategy, it is stated that countries should "*undertake a thorough epidemiological assessment based on available national and subnational data with the objective of understanding the distribution of the burden of disease and identify geographical areas or subpopulations or sectors with especially high TB burden*" (14).

The lack of TB information at levels lower than the district in Namibia imply that the current understanding of the disease burden is not adequate. In addition, while we have an understanding of the role that HIV/AIDS may have on the disease burden at national, regional and district levels, this understanding is missing at community level. Furthermore, local knowledge of the factors concerning socio-demographic and behavioural factors which could potentially explain variations in the disease distribution, is limited. An understanding of how factors such as education, employment, housing conditions, behavioural factors (alcohol, smoking) and TB knowledge, attitude and practices (TB KAP), might guide health service planning, particularly in a resource constrained setting such as Namibia. In his paper on the social determinants of health, Marmot argues that the tackling social determinants of diseases will not only improve health conditions but is also a move towards creating social justice and meeting basic human needs (73).

TB control is possible, but requires coordinated policies, effective clinical and public health interventions and multi-sectoral approach (74). In the current strategy of the MoHSS, the need for innovative approaches to guide the control and prevention of diseases has been emphasised (75). However, utilization of innovative techniques especially regarding epidemiological research is poor. Therefore, against this background, I conducted a study, which primarily stems from the disease prevention standpoint in the general population of one of the country's most populous region, Khomas. My study provides a novel contribution to the literature concerning TB burden in this particular region. The specific aim and objectives of the study are outlined below.

1.5.1. Aim

The aim of the research presented here was to investigate the burden and determinants of TB in Khomas in recent years. Details regarding why Khomas was the focus region for my study are provided in Chapter Two, section 2.3.

1.5.2. Specific objectives

1. To describe temporal changes in trends of TB case notifications rates in Khomas.
2. To analyse the spatial and spatiotemporal distribution of TB notifications and investigate the potential occurrence of TB hotspots in Khomas.
3. To investigate population level socio-demographic factors which may explain the space-time distribution of the disease.
4. To describe temporal changes in the trends of TB notifications rates in areas identified as TB hotspots (if found).
5. To investigate individual level socio-demographic and behavioural factors which may explain the disease's spatial distribution.
6. To investigate if TB Knowledge, Attitudes and Practices (TB KAP) can explain variation in the disease distribution.

7. To explore detailed narratives about TB KAP among people residing in the high TB burden township.

1.6. Geographic scale

Out of the fourteen political regions in Namibia, (see map in Chapter Two), this thesis focuses on Khomas region. I primarily focused on one region in order to allow for detailed exploration of the disease burden within a defined setting. Given that there are variations across regions, one cannot take a generalised approach. Therefore, since the study focuses on Khomas, the findings, interpretations and suggested implications for practice are relevant in the context of the Khomas region. However, other similar urban regions in the country, and locations in similar countries could find the study findings useful.

1.7. Thesis structure

Chapter One (this chapter) presents information about the research background, disease aetiology and global epidemiology as well as background information about Namibia. The chapter also provides the rationale for the research together with the thesis aim, specific objectives and the geographic scale of the research.

Chapter Two is a brief chapter which presents an overview of the empirical work conducted during this research, as well as background information on Khomas, which is the focus location of my research.

Chapters Three to Six, constitute the main work of this thesis. These chapters detail the empirical work conducted to address the research objectives. Within each chapter, I provide an introduction, literature review, materials and methods, results, as well as a discussion of findings.

The varying nature of the methods and results obtained during each phase implied that a traditional way of structuring the thesis would have been less logical and informative. Therefore, the empirical work is written in four distinct but related chapters. Chapter Two expands on the specific work conducted during each study phase.

Chapter Seven integrates the findings concerning TB KAP. This component was studied through a cross sectional survey (Chapter Five) and through a qualitative study (Chapter Six), and hence the need for the integration of the findings. The integration exercise used the triangulation protocol proposed by Farmer *et al*. (76).

Chapter Eight concludes the thesis by offering a reminder of the study rationale and a summary of the main research findings in relation to the study objectives. The chapter also presents the thesis overarching strengths and limitations, highlights the implications of the study findings, and identifies possible areas for future research. I conclude the thesis with brief remarks as well as a reflection on the PhD journey.

Chapter 2 : Overview of the research methods

2.1.Research methodology

I utilised both quantitative and qualitative research methods to address the research objectives. The empirical work was divided into four phases described below. The temporal periods covered during phases one and two were based on data available at the time of implementing my research.

Phase one: This phase involved an analysis and description of temporal trends in TB notifications in Khomas from 1997 to 2015. Trends were analysed according to specific types of TB and, where possible, by sex and age group. This phase also involved an analysis of trends concerning TB and HIV/AIDS related indicators. The specific details of the work conducted during this phase are presented in Chapter Three.

Phase two: The second phase involved an analysis of the spatial and spatiotemporal distribution of TB notifications in Khomas during a ten-year period from 2006 to 2015. The work aimed to examine the potential occurrence of TB hotspots and to investigate population level determinants of the disease spatial distribution. Moreover, I conducted an analysis of temporal trends in TB notifications within identified TB hotspots. The specific details of this work are presented in Chapter Four.

Phase three: This phase involved a comparative cross sectional survey, conducted to investigate the individual level socio-demographic and behavioural factors which may help explain the variation of TB burden. Moreover, this phase aimed to determine whether TB Knowledge, Attitudes and Practices (TB KAP) can explain the spatial variation of the disease. The specific details of this work are presented in Chapter Five.

Phase four: The last phase of my study involved a qualitative study conducted to gather detailed narratives about TB KAP among people living in one of the high TB burden townships. Chapter Six details work conducted during this phase.

Overall, considering that my research aimed to understand the TB burden and factors which may explain its distribution, the methodology followed in this research was the best to address the study objectives. Phase one was specifically executed to provide a historical perspective of the disease burden, and to give an idea of future disease trends. Phase two was conducted to identify exactly where and when TB cases occurred and to study population level factors which may explain the variation of the disease burden among communities. Phases three and four allowed for identification of individual level modifiable factors which could be considered to reduce the disease burden. Phase four was specifically added because quantitative data alone (phases one to three), would have been insufficient to understand detailed contextual factors. As pointed out by Tashakkori and Teddlie, the utilisation of multiple research methods may improve the understanding of the phenomena under study, as the limitations of one method are balanced by the strengths of another (77). Overall, the study findings can be used to improve the design and conduct of public health interventions as far as local efforts to address TB are concerned.

2.2. Study site

Figure 2.1 show the different regions in Namibia, including Khomas which is the focus region of my research.

Figure 2.1 Geographic regions in Namibia (50).

2.2.1. Population and Geography

Located in the central part of the country, and surrounded by a rocky and mountainous area, Khomas is the region where the country's capital city, Windhoek is located. The region has a total population of 415 780 inhabitants, making it the most populous region in the country (47). Census data show that 95% of the Khomas population reside in the urban part (Windhoek city), while the remaining 5% reside in what is referred to as Windhoek rural (47). The majority of the inhabitants (68%) are aged between 15 to 59 years, while the remaining age groups are as follow, under-fives (13%), 5-14 years (16%) and over 60 years (3%) (47).

2.2.2. Socioeconomic conditions

Khomas is the administrative and main urban business region in Namibia. For this reason, it is mostly the place to which people from other parts of Namibia migrate, in search for better living conditions (78). According to census projections, the region's population is expected to increase over time, mainly due to internal migration (51). The literacy rate in the region is 97% (47) and the overall unemployment rate is 30.3% among economically active people aged 15 years and above (51). Residents engage in various types of jobs, ranging from highly and semi-skilled to unskilled work (47). About 75% of households' main sources of income is from wages/salaries, while the remaining households depend on other sources of income such as farming, other business activities, or on old-age pension and orphaned social care grants (47).

2.3. Why is there a focus on Khomas?

I focused on Khomas because it is amongst regions which consistently had CNRs higher than the national average in past years (69), although this has changed since 2015 (79). In Khomas, respiratory related diagnoses are among the top ten reasons for hospitalisation (54). In 2015, the TB and HIV/AIDS co-infection rate was 44% in Khomas compared to 40% nationally (70). The treatment success rate for all forms of TB cases was 85%, similar to the national treatment success rate. The treatment success rate for new smear positive TB cases was also similar to the national TB success rate at 88% (70). Since Khomas is the most populous region in Namibia, it consistently had the highest proportion of TB cases in the country, although per capita disease burden is higher in regions such as Hardap and Karas (53). Therefore, given that the region's population is expected to grow over the coming years (51), effective TB control within this region will have a profound effect on the overall national burden.

2.4. TB coordination in Khomas region

Khomas has only one health district, referred to as the Windhoek health district (53). In terms of public health facilities, the region is served by two hospitals, three health centres and eleven primary healthcare clinics (54). With support mainly from the GFATM, community-based TB services are coordinated by one organisation known as Penduka (80), which provides services at thirteen DOT points attached to various public health facilities in Khomas (81), three of which are community-based DOT points. Two District TB and Leprosy Coordinators (DTLCs) coordinate TB activities and data recording across all public health facilities, under the supervision of the regional health directorate office.

2.5. Ethical approval

As my research involved accessing patient level data (phase two), as well as direct contact with people (phases three and four), I had to apply for ethical approval before implementation of the study. Full ethical approval was granted by the Ministry of Health and Social services and the Khomas Regional Health Directorate (Appendix A) as well as by Newcastle University (Appendix B). All ethical issues were taken into consideration throughout the research conduct and reporting of the findings.

Chapter 3 : An analysis of temporal trends in TB notifications in Khomas

3.1. Introduction

Trend analysis involves measuring a change in a particular outcome, usually over time or space (82). An analysis of temporal trends in TB notifications can enhance our understanding of the impact of TB control interventions, to inform the implementation of current and future interventions (83). Moreover, trend analysis can help us monitor performance towards reaching national and global TB control targets (84). During the first phase of my research, I was interested in investigating and describing temporal trends in TB case notifications rates in Khomas using routine data. I investigated trends in different types of TB, and where possible by gender and age group. Furthermore, I investigated trends concerning TB and HIV/AIDS related indicators. Given that Khomas has the highest proportion of TB cases in the country, trends in this region could be used by the NTLP to inform targets in subsequent national strategic TB frameworks. Therefore, in the results section of this chapter, I present trends for Khomas alongside the national trends. The inclusion of national trends is intended to illustrate how trends in Khomas compare to national trends, but the interpretations of the study findings are focused on Khomas, as the location of my study.

In the next sections of this chapter, I provide a literature review (Section 3.2), methods (Section 3.3), results (Section 3.4) and discussion (Section 3.5) for this phase of my study.

3.2. Literature review

Several reviews have been conducted to study trends in TB notifications (85-88). However, the challenge with some of the existing reviews is that individual countries were grouped into sub-regions, and some of these studies were not comprehensive in nature (i.e. did not analyse trends by types of TB, gender or age). Recently, systematic reviews concerning trends in TB notifications have been published (89-91). These reviews were nonetheless mostly limited to specific types of TB cases (i.e. MDR cases) or involved studies confined to a specific country.

A review of individual studies not limited to any country and narrated according to the different types of TB would be more informative. Such a review would allow for comparison of trends between countries and enable identification of possible reasons for heterogeneity in trends. Therefore, before implementing phase one, I conducted a literature review of primary studies that have investigated trends in TB notifications in the general population of any country. The review presented here was not a systematic review, although I initially used search terms to identify articles and over the course of the PhD period, I included newly published studies relevant to my work. The objectives of the literature review were:

1. To critically review methods used to investigate trends in TB notifications.
2. To critically review the findings of studies in the literature and identify potential factors for heterogeneity in trends (if any).

3.2.1. Literature search

I searched for the relevant literature from electronic databases, namely, Scopus, Embase, Web of Knowledge and Google Scholar. I also obtained some of the studies through searching reference lists of identified articles. I reviewed studies that analysed trends in TB notifications for all forms of TB cases (whether pulmonary and/ or extra-pulmonary TB). Only primary studies published in peer-reviewed journals were reviewed. The actual temporal length examined in studies was not limited. All studies that exclusively analysed trends for other TB dimensions such as treatment outcomes or case detection rates were excluded from this review. In addition, I excluded multi-country studies, as well as studies conducted exclusively in high-risk congregate settings such as prisons, mines or those which solely involved MDR cases and HIV/AIDS infected TB cases.

3.2.2. Literature synthesis

In the results section of the review, I first described studies in relation to location, temporal length and unit of analysis. I subsequently provide an appraisal of the methods used for trend analysis. I followed with a section detailing the findings of studies and consequently an appraisal considering the potential factors for heterogeneity in trends. I conclude with the summary of the literature review, which also explains how my study contributes to the current literature.

3.2.3. Review results

3.2.3.1. Description of studies

Thirty-one studies were included in this review and their characteristics are summarised in detail in Appendix C. Eleven studies were from Africa (83, 92-101), ten from Asia (36, 84, 102-109), four from Europe (110-113), three from North America (114-116), two from Oceania (117, 118) and one study from South America (119).

The longest studies, which included periods over 30 years, were from Asia (103, 104) and North America (115). The shortest studies were from Africa and analysed trends for a four-year period (95, 98). The majority of the studies (n=6) analysed data for a ten-year period (83, 102, 112, 116-118).

Twenty five studies included all forms of TB cases (36, 83, 84, 92-94, 96-107, 112-116, 118, 119). Three studies exclusively analysed trends for extra pulmonary TB (110, 111, 117) and three others exclusively analysed pulmonary TB cases (95, 108, 109).

In terms of the different levels of analyses, the majority of studies (n=18) analysed national level data (36, 84, 94-97, 101, 103, 104, 106-108, 110, 112, 114, 115, 117, 119). Eight studies analysed trends for a particular district, zone or province (83, 98-100, 102, 109, 113, 118). Four studies analysed city level trends (93, 105, 116, 119), and one study analysed trends at township level (92).

3.2.3.2. Methods used for trend analysis

Statistical trend analysis methods were used in fifteen studies (36, 83, 92, 93, 99, 101, 105-111, 114, 118), whereas in sixteen studies, only rates were described over time with no application of a particular statistical test (84, 94-98, 100, 102-104, 112, 113, 115-117, 119).Various trend analysis methods exist, and these mostly involve the use of regression models (82). Regression is a measure of the direction and strength of an association between a dependent and an independent variable (120). For instance, in the reviewed studies, the dependent variable was the TB CNRs whereas the independent variable was the length of the study (in years). Studies have utilised both linear and non-linear regression models, and I will discuss below the common methods used in the reviewed literature.

3.2.3.2.1. Linear regression

Using linear regression, Pesut *et al*. and Lesic *et al*. in Serbia examined trends in different types of extra-pulmonary TB CNRs between 1993 to 2007 (110, 111). Another study from Haiti by Charles *et al*. used linear regression to study trends in all forms of TB CNRs from 2010 to 2015 (114). However, Charles *et al*. only reported absolute changes in CNRs and did not report the actual results of the regression model. In brief, linear regression is based on the assumption that the response variable has a linear relationship with the independent variable (120). Moreover, linear regression assume that the residuals, that is the level of error for each value of the response variable, are normally distributed (121). However, the challenge with these assumptions, particularly in modelling health data have been noted (82). For instance, in some cases, the application of linear regression may not be appropriate due to skewness and excess kurtosis in the data (82, 122). In addition, linear regression is sensitive to outliers (121), and one may expect outliers in TB CNRs over time, resulting from introduction of new TB control activities or changes in contextual factors. For example, the Charles *et al.* study showed that the CNRs were higher during the years 2012 and 2013 compared to other years, while the two Serbian studies clearly showed fluctuating patterns in the trends, especially from the year 2005. Hence, in these studies, the estimates from the linear regression model may have been less accurate because of the observed outliers. All the three studies did not provide details about how their data met the conditions/assumptions of linear regression.

3.2.3.2.2. Chi square test for trend

Four studies (83, 93, 99, 105) analysed trends using the Chi-square test for trend, which is also known as the Cochrane Armitage test for trend (123). In particular, Dangisso *et al*. used the Chi-square for trend to study trends in different types of TB CNRs in Sidama zone, Ethiopia, from 2003 to 2012 (83). In Uganda, Wobudeya *et al*. used the Chi-square test for trend to describe the trends for children aged 0-14 in Kampala, from 2011 to 2015 (93). Adejumo *et al*. in Lagos state, Nigeria used the same test to describe trends in TB notifications from 2011 to 2015 (99). In addition, Wu *et al*. used the same method to analyse trends in the epidemiology of TB from 1992 to 2015 in Chongqing, China (105). The Chi-square test for trend assesses whether there is a significant linear trend in the binomial proportions of a particular ordinal variable (82). However, one of the main limitations of this test is that it is not able to determine the magnitude by which the trend decreased or increased, and this is a general limitations of Chi-squared tests (123). For instance, in all four studies, trends were only described in terms of direction and significance, and not the magnitude. Furthermore, the Chi-square test for trend also assume a linear change in proportions over time, and in some of these studies, the expected linear pattern was less apparent.

3.2.3.2.3. Poisson and negative binomial regression

Two studies analysed trends using regression models for count response variables (106, 118). In particular, Gleason and colleagues in Saudi Arabia used the Poisson regression model to study trends in all forms of TB notifications rates from 2005 to 2009 (106). The Poisson regression model makes a strong assumption that there is no over-dispersion, in other words, it assumes that the mean and variance are equal (124). If there is over-dispersion in the data, other options are recommended, such as the incorporation a scale parameter in the model (82), indeed this is what Gleason *et al*. did in their study (106). Another option for modelling over-dispersed data is to use negative binomial regression, which is an extension of Poisson regression, and loosens the assumption that the mean is equal to the variance (82, 124). For example, Jones *et al*. in Australia used negative binomial regression to analyse trends in TB notifications and CNRs from 2006-2015 (118). These regression models are claimed to be a better models for count data, because they have better validity (more accurate estimates) than normal linear models (124). Moreover, these models are able to model trends over time adjusted for covariates (123). However, the disadvantage is that, they also assume that the trend is linear over time. The data presented in the two studies (106, 118) do not necessarily suggest a linear trend, hence the conclusions made in these studies may have been less accurate.

3.2.3.2.4. Joinpoint regression

Trends among studies reviewed were also described using the regression model which does not assume a linear trend over time, in particular, Joinpoint regression. For example, a recent study by Tao *et al*. used Joinpoint regression to analyse trends in pulmonary TB among children aged 0-17 in China's Shandong province, from 2005 to 2017 (109). Similarly, Joinpoint regression was used in a recent nationwide study in Japan conducted by Hagiya *et al*. to analyse trends in TB incidence from 1997 to 2016 (36). In Iran, Khazaei *et al*. used the same approach to analyse smear positive pulmonary TB CNRs from 1995 to 2012 (108). In addition, Arsang-jang *et al*. in Iran also used Joinpoint regression to study trends in different types of TB from 2001-2015 (107). Joinpoint regression examines the relationship between two variables through a segmented linear relationship, and identifies a specific point where the slope of the regression function changes (125). Unlike models which assume a linear change over time, Joinpoint regression does not assume a linear trend throughout the study period (125) but it identifies a point at which a significant change in the slope regression function occurred. Furthermore, Joinpoint can model trends in counts, rates, percentages and proportions (82). However, one of the main disadvantages of this model is that, other than through stratification, it does not allow for adjustment of covariates (82). For instance, the studies which used this model analysed trends separately by factors such as age and gender (36, 108).

3.2.3.3. Trends reported in studies

Studies examined trends for different types of TB. For instance, some studies presented trends in one type of TB (i.e. all forms of TB), whereas others examined trends in multiple types of TB (i.e. all forms of TB, smear positive TB and smear negative TB). In the narrative synthesis below, I have discussed the study findings grouped according to the different types of TB, and where possible according to gender and age groups. Studies will appear in different sections of the narrative as long as they have examined trends in a particular group.

To avoid repetition, the overall appraisal and discussion of potential factors for heterogeneity in trends is provided in the subsequent section (Section 3.2.3.4).

3.2.3.3.1. All forms of TB CNRs

Four studies reported increasing trends in all forms of TB CNRs over time (83, 92, 94, 100). In particular, Lawn *et al.* in South Africa reported a rapidly increasing and statistically significant trend from 1996 to 2004, in a peri-urban Western Cape township (92).The authors attributed the observed trend to the HIV/AIDS burden. In Ethiopia, two studies by Hammusse *et al.* in Arsi zone and Dangisso *et al.* in Sidama zone reported increasing trends in all forms of TB from 1997-2011 and 2003-2012, respectively (83, 100). Both studies attributed the increasing trends to expansion of community-based TB services in Ethiopia. Unlike the Lawn *et al*. study, the two Ethiopian studies presented trends for different types of TB. However, these studies analysed trends in zones including both urban and rural areas, and because CNRs could differ geographically, neither of them examined heterogeneity in all rates by location (rural/urban). In Zambia, a nationwide study by Mwaba *et al*. reported a progressively increasing trend in CNR from 1964 to 2000, which they attributed to the HIV/AIDS epidemic (94). Although the Zambian study had a longer temporal length, information reported is limited, as they did not disaggregate trends by age group, sex or according to different types of TB. Moreover, Mwaba *et al*. did not analyse trends statistically.

In contrast, sixteen studies reported stable or declining trends in all forms of TB CNRs over time (36, 84, 96, 97, 99, 101, 103-106, 113-116, 118, 119). A recently published study in Namibia by Kibuule *et al*. reported that from 1996 to 2004, the national CNRs increased significantly with an average of 23 per 100 000 population, and thereafter declined significantly with an average of 60 cases per 100 000 population per year until 2015 (101). They attributed the observed decline to the introduction of Community-based Directly

Observed Treatment (CB DOT) in 2005. To my knowledge, the Kibuule *et al*. study is the first effort made to statistically analyse trends in TB CNRs in Namibia, and they also used a statistical method similar to Joinpoint regression, in other words they did not assume a linear change over time. However, their study did not present the actual percent change to statistically quantity the magnitude of the observed pattern. Moreover, the Kibuule *et al*. study did not analyse temporal trends in CNR by specific types of TB or age group and sex, and their study was limited to the national level.

In Haiti, Charles *et al*. observed that national level all forms of TB CNRs increased from 2010 to 2013 and thereafter declined until 2015 (114). They attributed the increase from 2010 to 2013 to the earthquake experienced in that country in 2010. However, Charles *et al*. did not show the trends prior to the year 2010, which would have given the historical perspective of the disease burden, prior to the earthquake. In Chongqing municipality, in China, Wu *et al.* reported a trend in all forms of TB which initially increased between 1992 to 2004 and thereafter declined from 2005 until 2015 (105).Wu *et al.* attributed the initial increase to improved TB case detection, as a result of a change of policy which required reporting of all TB cases and also to expansion of DOT. In addition, they attributed the decline observed between the years 2005 to 2015, to improved public health interventions and socioeconomic improvements in the area. Wu *et al.* analysed trends using the Chi-square test for trend, hence their analysis assumed a linear trend over time, despite that there was first an increase followed by a decreasing trend.

A nationwide study conducted by Kapata *et al*. in Zambia showed that trends in CNRs increased from 1990 to 2004, and thereafter declined until the year 2010. The authors attributed the initial increase (from 1990 to 2004) to HIV/AIDS and the decline (from 2005 to 2010) to improved TB control interventions (97). In another national level Zambian study, Kapata *et al.* showed that there was a progressive decline in TB CNRs from 2004 to 2011 (96). Kapata *et al.* attributed the declining trend to improvements in TB control and treatment outcomes, rather than to HIV/AIDS burden, which according to the authors did not change profoundly during their study period. However, no statistical tests were utilised to assess the magnitude and significance of the trends reported in the two Zambian studies.

A recent study in Japan conducted by Hagiya *et al*. showed that CNRs progressively and significantly declined with an average annual percent of -6.0% per year, from 1997 to 2016 (36). The Hagiya *et al. study* also presented trends by demographics such as age and sex.

Despite the declining trend, Hagiya *et al.* nonetheless reported that, Japan is yet to meet both the national and global TB incidence targets. Reis *et al.* in Brazil reported a declining trend in CNRs between 2002-2008 in Belo city (119). In that study, Reis *et al.* showed that the CNRs peaked during the year 2003 with a rate of 55 per 100 000 population and thereafter rates declined to 38 per 100 000 population in the years 2007 and 2008. In a study from Canada, Kim *et al*. showed a declining trend in TB CNRs from 1995 to 2004 in Ottawa city (116). They documented that the trend peaked in 1996, after which a fluctuating but generally declining trend was observed until 2004. Both Reis *et al.* and Kim *et al.* did not assess the statistical significance of the trends.

In Hong Kong, Tam *et al*. showed that trends in CNRs declined between 1947 to 2015 (103). They showed a rapid decline in CNRs after introduction of the BCG vaccine in 1992. In Cuba, Marrero *et al.* reported a declining trend in nationwide CNRs from 1962 to 1997 (115). In Marrero *et al*. study, the decline was observed since the peak in 1965 and thereafter there has been a decline (albeit with fluctuations) until 1997. Another earlier nationwide study in Kuwait by Behenbani *et al.,* reported a declining trend in CNRs from 1965 to 1999 (104). In that study, the authors reported that the CNRs continually declined until 1989, since the peak in 1965. Behenbani et *al.* reported that, because of the Gulf War experienced from 1990-1991, the subsequent years (1993 to 1998) were characterised by an increase in CNRs. According to the authors, the Gulf War resulted in devastating conditions including the closure of the national TB programme. In Italy, Crimi *et al*. reported that there was an increase in TB rates from 1988 to 1996, and thereafter a decline until 2002 in Liguria City (113 89). Crimi *et al*. attributed the observed increase to immigration rather than to factors such as HIV/AIDS. Despite the long temporal periods in all these studies (104, 113, 115), the trends were not analysed statistically.

3.2.3.3.2. All forms of TB CNRs by sex

From 2010 to 2015, Charles *et al.* in Haiti documented that the TB CNRs for males were higher with an average of 160 per 100 000 population compared to the average of 144 per 100 000 population for females (114). Charles *et al*. reported that the CNRs for both sexes initially increased from 2010 then declined after the year 2013. In Lagos state Nigeria, Adejumo *et al.* showed that trends in TB CNRs were higher in males than females from 2011 to 2015, but over time, a declining trend was reported in both sexes (99). Wu *et al*. in Chongqing, China also reported high CNRs for males over time, and that rates declined significantly in both sexes from 2008 to 2015 (105). Similarly, Reis *et al.* in Brazil reported higher incidence rates for males compared to those of females (119). Reis *et al*. also observed that there was a declining trend over time, for both sexes. All these studies did not assess the statistical significance of the trends by sex. In contrast, a national study by Hagiya *et al*. in Japan (36) found that between 1997 to 2016, there was a statistically significant declining trend for both sexes, and that the trend for males declined slightly faster at an average annual of -6.2%, while the trend for female cases declined at an average of -5.7% annually. Since they used Joinpoint regression, the Hagiya *et al*. study was also able to determine specific change points in the trend for each sex.

Five studies analysed trends in TB CNRs among children by sex (96, 98, 102, 112). Ghadhir *et al*. in Kermanshah, Iran, reported that from 1996 to 2005, the CNRs in children aged 0-18 years declined from 5.02 to 4.55 per 100 000 population and from 2.85 to 1.62 per 100 000 population in females and males, respectively (102). There was no regression model applied in that study. Hetlerberg *et al*. in Denmark (112), reported that CNRs for children aged 0-14 years were slightly higher in females than in males from 2000 to 2009. The authors also reported that rates were generally stable over time, but no statistical tests were used to confirm their conclusion. Kapata *et al*. in Zambia reported CNRs which were slightly higher for males than females, but in all sexes, trends declined from 2004 to 2011 (96). Daniel *et al*. in Lagos state, Nigeria observed that CNRs were similar for male and female children aged 0-14 years between 2011 to 2014, and that rates increased steadily in both sexes (98). Although the Daniel *et al*. study provided detailed characteristics of the cases such as age and types of TB, the temporal length of their study was short, of four-years, and no statistical tests were used to describe trends.

3.2.3.3.3. All forms of TB CNRs by age group

From 2011 to 2015, Adejumo *et al.* in Lagos state, Nigeria showed an increasing trend in CNRs for the youngest age group (0-14 years), a declining trend among middle age groups (15-44 years) as well as an increasing trend in the older age groups (45+ years) (99). In Haiti, Charles *et al.* showed an increasing trend in almost all age groups from 2010 to 2015 (114). Both of these studies were conducted over a relatively short periods (five years) and did not report the significance and magnitudes of temporal trends. A study from Hong Kong, by Tam *et al.* reported a declining trend over time for age groups between 0-70 years but the observed decline was less apparent in the older groups (above 70 years) (103). Tam *et al*. explained that this might have been because the older population did not receive the BCG vaccine when they were younger. Reis *et al.*in Brazil examined CNRs for all forms of TB in all age groups, and showed a declining trends in all age groups, although the decline was less apparent in some age groups (40-59 years). Both Tam *et al.* and Reis *et al*. presented rates over time without assessing the statistical significance of the trends.

Wu *et al*. in China reported significantly declining trends for age groups 0-14 and 15-64 years but the trend for those aged 65+ years was not statistically significant (105). However, Wu *et al*. used broader age groups (0-14, 15-64 and 65+ years), and this may have masked trends which would have been observed in narrower age groups. Moreover the statistical test (Chi-square test for trend) used in Wu *et al*. could not reveal the exact magnitude of temporal changes in trends. In contrast, The Hagiya *et al*. study in Japan showed that there was a statistically significant declining trend in all age groups between 1997 to 2016 (36). In that study, trends declined with an average annual percent of -3.8%, -5.6%, -7.5% and -5.6% for age groups 0-24, 25-44, 45-64 and 65+ years, respectively.

Four studies examined trends in CNRs among children (93, 96, 98, 112). Hatlerberg *et al.* in Denmark reported stable national level CNRs for children aged 0-9 years and a fluctuating pattern for the age group 10-14 years between 2000 to 2009 (112). Recently, a Chinese study conducted by Tao *et al*. (109) among children aged 0-17 years, in seven cities in Shandong province, found a significant decrease in TB incidence between 2005 to 2017. Tao *et al*. reported that trends in CNRs declined at an average annual percent of -10.9% from 2005 to 2010 and thereafter by a rate of -0.9% per year until 2015. In Zambia, Kapata *et al*. showed that the trend for CNRs for children aged 0-14 years declined from 135 in 2004 to 69 in 2011 per 100 000 population (96). Both Hatlerberg *et al.* and Kapata *et al*. did not assess the statistical significance of trends. Wobudeya *et al.* in Kampala, Uganda showed a significant decline in trends in age group 0-4 years but not in the age group 5-14 years, but they also did not present the actual magnitudes of the observed trends. A Nigerian study by Daniel *et al.* showed an increasing trend for both children aged 0-4 and 5-14 years from 2011 to 2014. Daniel *et al.* pointed out that the increasing trend may be attributed to improved diagnostics. Considering that both Wobudeya *et al.* and Daniel *et al*. studies were conducted in urban settings, and over a similar time-period, perhaps discrepancy between them may indeed be explained by differences in contextual factors such as case ascertainment methods.

3.2.3.3.4.   Smear positive pulmonary TB CNRs

Ten studies reported trends in CNRs for smear positive pulmonary TB (83, 84, 95, 96, 99, 100, 107-109, 114). Increasing trends over time were reported in some studies. For example, Charles *et al.* in Haiti reported a steady increase in CNRs from 85.5 to 105.7 per 100 000 population from 2010 to 2015 (114). The Charles *et al.* study was conducted immediately after an earthquake in Haiti, hence the authors speculated that the aftermath of the earthquake might have resulted in more TB cases, but they reported that improved diagnostic tests were also used during the study period, indicating improvement in case detection. Adejumo *et al.* in Lagos, Nigeria reported an increasing trend from 39 in 2011 to 46 in 2015 per 100 000 population (99). Adejumo *et al*. attributed the observed trend to expansion of microscopy sites and roll out of Gene-xpert for TB diagnosis. Dangisso *et al.* in Sidama zone, Ethiopia found an increasing trend in TB CNRs from 55 to 111 per 100 000 population from 2003 to 2012(83). Similarly, another Ethiopian study by Hamusse *et al*. reported an increase from 40 to 63 per 100 000 from 1997 to 2013 (100). Both Dangisso *et al*. and Hamusse *et al.* attributed the increase to the expansion of DOT coverage, rather than a true increase in incidence. However, the statistical analyses in these studies were limited, as most of them only used the Chi-square for trend.

In contrast, other studies reported decreasing trends in CNRs for smear positive pulmonary TB. In particular, Arsang-Jang *et al*. in Iran found that CNRs declined at an average annual rate of -2.06% between 2001 to 2015 (107). Arsang-Jang *et al* attributed the decline to improvement in healthcare. Similarly, another study in Iran by Khazaei *et al*. reported a decline in smear positive TB CNRs from 15.5 to 7.1 per 100 000 from 1995 to 2012, but they did not analyse this trend statistically (108). The Noppert *et al.* study from Zimbabwe reported that national level CNRs declined from 90 to 87 per 100 000 between 2008 to 2011 (95). They found that rates initially increased from 90 in 2008 to a peak of 111 per 100 000 population in 2010, and then declined in 2011. Noppert *et al.* attributed the initial increase to improved case detection rather than to increase in incidence. However, their study period was short. Kapata *et al.* in Zambia reported a decline from 9 to 4 per 100 000 population from 2004 to 2011 among children aged less than 15 years (96). Kapata *et al*. explained that the low rates and declining trend may have been due to poor diagnostics and that the true burden of paediatric TB was underestimated. Trends were not analysed statistically in Kapata *et al*. and Noppert *et al*. studies. In Nepal, Shrestha *et al*. reported just a marginal decline from 58.9 to 55.7 per 100 000 population from 2001 to 2008 (84). Shrestha *et al*. attributed the slower decline to TB and HIV co-infection as well as to Multi-drug resistance TB. However, no data concerning the prevalence of HIV/AIDS or MDR were provided in that study to substantiate the reasons provided.

3.2.3.3.5. Smear positive pulmonary TB CNRs by sex

Six studies examined trends in CNRs for smear positive pulmonary TB by sex (83, 84, 95, 96, 99, 108). Adejumo *et al.* in Lagos state Nigeria and Dangisso *et al.* in Sidama zone Ethiopia both found increasing trends for both sexes, which were steady in the recent years of their respective study periods, however the specific magnitude of increase was not documented in the two studies (83, 99).

In contrast, Shrestha *et al.* in Nepal reported that between 2001 and 2008, CNRs for males declined slightly from 39.3 to 38.4 per 100 000 population, while the CNRs for females declined slightly from 19.5 to 17.3 per 100 000 population (84). In Zimbabwe, Noppert *et al.* reported that from 2008 to 2011, the average CNRs were 108 and 88 per 100 000 population for male and female cases, respectively. Noppert *et al.* further reported that the trend for females declined higher by 11.7% during the four-year period compared to 5.7% for males. A study of children aged 0-14 by Kapata *et al.* in Zambia, showed that rates for smear positive TB were higher in males, but trends for both sexes declined overtime (96). However, the magnitude of the decline by sex was not assessed in all the three studies (84, 95, 96). In contrast, Khazaei *et al.* in Iran reported that trends for both males and females declined significantly overtime. They also reported the trend for females declined more by -4.7% per year, compared to -3.9% per year in the trend for males from 1995 to 2012 (108).

3.2.3.3.6. Smear positive pulmonary TB CNRs by age group

Dangisso *et al*. in Ethiopia, showed an increasing trend in all seven age groups from 2003-2012(83). The authors did not employ any regression model to investigate the magnitude of trends within specific age groups. In contrast, Tao *et al*. in China reported that CNRs decreased with an average annual rate of -22.2% per year from 2005 to 2017 (109). Similarly, Khazaei *et al.* in Iran (108) reported that trends in CNR declined significantly among the groups 0-14, 15-64 and 65+, but the annual decline was lowest in the oldest age group. Shrestha *et al*. in Nepal and Noppert *et al.* in Zimbabwe showed that trends in CNRs declined among the younger age groups (44 years or less) but increased among the older age groups (45+ years) (84, 95). These two studies did not analyse trends statistically.

3.2.3.3.7. Smear negative pulmonary TB CNRs

Six studies reported trends in CNRs for smear negative pulmonary TB. In particular, Dangisso *et al.* in Ethiopia, reported an increase from 22 to 60 per 100 000 from 2003-2012 (83). Similarly, Tao *et al*. in China reported a significant increase of 5.3% per year, among children aged 0-17 years, from 2005 to 2017 (109). Tao *et al*. attributed the increase to the gradual improvement in diagnostics, while Dangisso *et al*. attributed the increase to improved heath access.

In contrast, Arsang-jang *et al.* in Iran reported a significant annual average decline of -3.56% from 2001 to 2015 (107). Arsang-jang *et al.* reported that the declining trend might be due to limited diagnosis capacity. Shrestha *et al.* in Nepal reported a decline from 39 to 35 per 100 000 population from 2001 to 2008 (84). In Zambia, Kapata *et al.* reported a progressive decline in CNRs from 80 to 34 per 100 000 from 2004 to 2011(96). Kapata *et al*. reported that the decline may be due to poor diagnostics and noted that more cases (74%) were reported in urban areas than in rural areas (26%), perhaps suggesting geographic differences in diagnostic capacity. Adejumo *et al.* in Nigeria, reported a fluctuating but generally declining trend from 38 to 24 per 100 000 population from 2011 to 2015 (99). Adejumo *et al*. cautioned that in 2015, the WHO estimated that Nigeria notified less than one fifth of the estimated TB cases, implying that the low CNRs may reflect under-reporting of TB cases. According to Adejumo *et al*. the under-reporting may be due various factors including health system challenges. However, the temporal length of this study was short to allow for a thorough understanding of the disease trends.

3.2.3.3.8. Extra-pulmonary TB CNRs

Seven studies presented trends in CNRs for extra-pulmonary TB, and of these, the CNRs were lower and reported to have increased over time in four studies (99, 110, 111, 117). In contrast, CNRs were much higher in other studies. For instance, Dangisso *et al.* in Ethiopia, reported an increase from 18 to 26 per 100 000 population from 2003 to 2012 (83). Shrestha *et al.* in Nepal, reported an increase from 21 to 25 per 100 000 population from 2001 to 2008 (84). In these studies the increasing trends were observed towards the end of the specific study periods, hence it is very likely that these increments may be attributed to advancements in TB case diagnostics or improved access to healthcare as speculated by authors.

Other studies have reported declining trends over time. In particular, Arsang-jang et *al.* in Iran, observed a significant declining trend from 2001 to 2015 (107). Kapata *et al*. reported a generally declining trend from 34 to 26 per 100 000 in Zambia from 2004 to 2011 (96). Similarly, Ghadiri *et al*. observed a decline from 2.20 to 1.11 per 100 000 population from 1996 to 2005 among children aged 0-17 years (102). Both Kapata *et al*. and Ghadiri *et al*.

attributed the trends to insufficient diagnostics and cautioned that the current CNRs may not accurately represent the true disease burden.

3.2.3.3.9. Trends in HIV/AIDS testing and prevalence rates among TB cases

Three studies examined trends in HIV/AIDS testing among TB patients, and a consistent increasing trend over time was observed in some studies (93, 105, 114). A study by Charles *et al.* in Haiti reported an increase in the percent of TB cases with known HIV/AIDS from 66.7% in 2010 to 90.2% in 2015 (114). A study by Wobudeya *et al*. conducted among children in Uganda, showed an increase in the percent of TB cases with known HIV/AIDS status from 59% in 2011 to 100% in 2015 (93). Wu *et al.* in China also reported an increase from 14.1% in 2011 to 55.7% in 2015 (105). The variation between studies may be due to differences in the time that the recommendation of testing TB patients for HIV/AIDS was introduced in countries and how it was received in a specific setting. For example, Wu *et al.* reported that the recommendation of testing all TB cases for HIV/AIDS was introduced in 2011 in their study area, which perhaps may explain the low percentages in that study.

Three studies reported trends in HIV/AIDS prevalence among TB patients, and a consistent declining trend was observed in all studies (93, 99, 114). Wobudeya *et al.* in Uganda reported a decline in prevalence from 38% in 2011 to 35% in 2015, but the decline was not statistically significant (93). In Haiti, Charles *et al.* reported a decline in prevalence from 19.9% in 2010 to 16.4% in 2015, but they did not report the statistical significance of this trend (114). Adejumo *et al.* in Lagos, Nigeria reported a decline form 21.8 % in 2011 to 19.2% in 2015, but there was also no assessment of statistical significance (99). The slow decline in Adejumo *et al*. study might be due to a short temporal period.

3.2.3.4. Appraisal: potential factors for heterogeneity in CNR trends

It is clear from the findings that there are inconsistencies in trends reported in the literature. While these trends could in fact indicate the ‘true’ magnitude of TB transmission in specific locations, the differences between studies might also be due to variations in case ascertainment methods, study time, study location, case finding methods and trend analysis methods. I will now briefly explain these factors.

3.2.3.4.1. Case ascertainment

The case definitions presented in the literature reviewed imply that all studies have classified cases according to WHO criteria, and therefore case definitions are unlikely to explain heterogeneity in the trends. However, an appropriate TB diagnosis depends on country specific laboratory strength. This is particularly true of paediatric TB, TB in the elderly and extra-pulmonary TB, where the diagnosis is generally known to be challenging (96). For example, Adejumo *et al*. in Nigeria and Charles *et al*. in Haiti reported that there was improvement in microscopy such as introduction of gene-xperts, which may explain the observed increasing trend among the younger age groups (99, 114). In contrast, Kapata *et al.* in Zambia attributed the declining trend for paediatric TB to the success of TB control efforts, but they also cautioned that limited diagnostic tests and the lack of trained healthcare workers remains a challenge to appropriate TB diagnosis in that country, particularly in rural areas (96). Similarly, in Uganda, Wobudeya reported that 82% of pulmonary TB cases in children were diagnosed clinically rather than laboratory confirmed (93). Therefore, these variations in case ascertainment methods may explain the variation in findings.

3.2.3.4.2. Time periods

Variations in trends might also be explained by differences study periods. Even though I was unable to rank studies into distinct time periods, as study periods varied between studies, I observed that the studies conducted in earlier years in African countries tended to report increasing trends (92, 94, 97). The authors mostly attributed the trends to the HIV/AIDS epidemic as well as well as to the lack of TB interventions in the earlier years. For example, the studies by Lawn *et al*. in South Africa and Mwaba *et al*. in Zambia all showed that trends increased rapidly until about mid-2000 years. In contrast, studies which included more recent years reported declining trends. For instance, a recent study by Kapata *et al*. showed that there was an increase in the trend from 1990 to 2004 and thereafter there was a progressive decline from 2005 to 2009 (97). This is similar to Kibuule *et al*. in Namibia who reported that national trends increased from 1996 to 2004, and thereafter CNRs declined until 2015. This pattern is also similar to a Chinese study, which showed an initial increase from 1992 to 2004, and later a decline until 2015 (105).

However in other recent African studies, increasing rather than decreasing trends were observed (83, 98-100). These studies perhaps also suggest that the observed declining trends in some countries (especially in high burden countries) must be interpreted with caution, as these may be due to a number of factors (i.e. poor detection and poor health access) and not necessarily true decline in the disease burden. In developed nations, the decreasing trends were mostly observed in the early years (36, 104, 115, 116, 119) and in some developed countries declines were consistent throughout the recent years (36).

3.2.3.4.3. Study Location

Variations in trends may have also been due to differences in geographic factors. It is possible that studies conducted in countries where health infrastructure is generally of good standard and have had stable economies over a period of time will have seen declining to stable trends over time. These are mostly studies conducted in developed nations, which generally reported lower rates and decreasing trends over time (36, 112, 113). In some studies, contextual factors resulted in increasing trends. For instance, the Charles *et al.* study which was conducted after an earthquake in Haiti, showed an increasing trend after the earthquake (114). According to the authors, the earthquake left millions of people in dilapidated conditions in that country. Similarly, Behenbani *et al.* in Kuwait reported an increase in CNRs after the Gulf war in 1990 to 1991(104). According to the authors, the war resulted in the closure of the TB programme. In South Africa, Lawn *et al*. reported an increase in the trend for all forms of TB and attributed it to the high rates of HIV/AIDS in that country (92). In some developed countries, TB has been attributed more to increase in immigrants rather than to local transmission (112, 113). Therefore, setting specific conditions might also influence heterogeneity in trends between studies.

3.2.3.4.5. Case finding methods

Variations in trends may also be due to specific case finding methods for TB, which may vary between countries due to differences in the capacity and performance of the TB programme, and the health sector in general. In some countries, TB is diagnosed through passive case finding whereas in others active case finding methods are employed such as screening of HIV/AIDS, screening of TB among contacts of TB patients, screening for TB at reproductive health centres and also in specific populations e.g. prisons, mines and migrants. The implementation and scale of these case-finding methods may vary between countries. For instance, two studies from Ethiopia reported that there was a rapid increase in notification rates, which they attributed to expansion of TB DOT in communities, implying that active case detection was improved in that country (83, 100). Improved healthcare access in Ethiopia as a result of community health interventions has indeed been noted in the literature (126). Similarly, Charles *et al*. reported that the increase in CNRs may have been due to active screening of TB in urban slums and centres after the earthquake in Haiti (114). In Lagos state, Nigeria, Daniel *et al*. reported that the use of improved diagnostic tests might have resulted in the increasing trend observed in their study. (98, 99). These studies which reported active case finding methods tended to report increasing trends, particularly in recent years.

3.2.3.4.6. Trend analysis methods

The different trend analysis methods used in studies may also have resulted in heterogeneity in trends. For example, some of the studies assumed a linear change over time (83, 106, 110, 111, 118), and no goodness of fit of the models were reported in these studies. In other studies, non-linear models were used (36, 107-109). Studies that used regression models which assume a linear change over time might have reported inaccurate conclusions, as CNRs showed fluctuating than a linear patterns. The usage of Joinpoint regression in other studies might have overcome that challenge (36, 107, 108). In some of the studies, conclusions were made without any statistical assessment (84, 94-98, 100, 102-104, 112, 113, 115-117, 119), and so it is possible that some of the trends reported as either increased or decreased were not statistically significant.

3.2.4. Literature review summary

In this review, I considered primary studies that reported trends in TB CNRs in several countries. I was particularly interested in reviewing the methods which have been used for trend analysis, and in reviewing the study findings to identify potential factors for heterogeneity in trends.

I found that some studies did not use statistical methods for trend analysis, but only presented CNRs over time. Among those that utilised statistical tests for trend analysis, I observed that different methods were used, involving methods that assume a linear trend over time and those that do not. I described above the common methods used among the reviewed literature, highlighting advantages and disadvantages of individual methods. For example, most of the studies presented fluctuating patterns in CNRs, hence the conclusions made in studies which utilised regression models that assume a linear trend over time may have been inaccurate (83, 106, 110, 111, 118). The approach taken in some studies may have been a better, as these studies used Joinpoint regression, which is able to determine a specific point, at which a change in the slope of the regression line occurred (36, 107, 108), and so I have also analysed and described trends in my study using Joinpoint regression. I have expanded on this regression model in the method section of this chapter (section 3.3.7.2).
In terms of the study findings, I observed that the majority of studies reported trends for all forms of TB, and only few studies have analysed trends for particular types of TB, especially concerning smear negative TB (83, 84, 96, 99, 107, 109), extra-pulmonary (96, 99, 102, 107, 110, 111, 117) and notification for TB and HIV/AIDS co-infected patients (93, 99, 105, 114).

I observed that trends varied between studies in the literature. Some studies reported increasing trends for all forms of TB over time (83, 92, 94, 100), while the majority of studies generally reported declining trends (36, 84, 96, 97, 99, 101, 103-106, 113-116, 118, 119), and in others, trends were generally stable over time (84, 102, 116). The variation in trends may reflect ‘real’ disease transmission in different settings. However, I have also explained that the heterogeneity in trends might have resulted from factors such as case ascertainment, study time, study location case finding methods or from the different trend analysis methods used.

Even though I did not conduct a systematic review, I only found two studies in the literature which specifically analysed trends in CNRs in Namibia (88, 101). One of these studies was a recently published study by Kibuule *et al*., and I have discussed the approach and findings of this study in the narrative synthesis above. Another study was a multi-national study conducted by Surie *et al*., which reported trends in TB notification in twenty three African countries (including Namibia) (88). Since Surie *et al*. was a multi-national study, its results are not included in the narrative synthesis above but I have discussed the findings of this paper in the discussion section of this chapter (Section 3.5).

In summary, given the previous work as presented in this literature review, my study aims to contribute to the literature in two ways. Firstly, to my knowledge, this is the first study to gather information regarding temporal trends in TB notifications in Khomas, and to statistically describe the magnitude of trends in Namibia. Secondly, my study will add to few studies which have analysed trends by demographic factors as well as trends in TB and HIV/AIDS related indicators.

3.3. Materials and methods

In this section, I present the methods used to describe trends in TB notifications in Khomas. As indicated earlier, I analysed trends in Khomas alongside those of the national trends. The inclusion of the national trends was to demonstrate how Khomas compare to trends nationally, given that Khomas has the highest proportion cases than other regions (53). However, the interpretations of findings primarily focuses on Khomas as the location of my study.

3.3.1. Types of TB trends analysed

3.3.1.1. Trends by types of TB

Trends in crude CNRs were analysed separately according to four types of TB: new smear positive pulmonary TB, new smear negative pulmonary TB, extra-pulmonary TB and all forms of TB.

3.3.1.2. Trends by gender and age groups

Data for TB cases were available by sex and age groups for one type of TB, the new smear positive pulmonary TB for the period 2006-2014. Therefore, I analysed trends according to these demographic factors for this group. The trends by age groups were analysed using the following age groups (0-24, 25-44 and 45+ years).

3.3.1.3. Trends for TB and HIV/AIDS related indicators

I also examined trends for TB and HIV/AIDS related indicators. The first indicator was the percent of TB patients with known HIV/AIDS status, and the second was the percent of TB cases who are HIV/AIDS positive. TB and HIV/AIDS data were available 2006 to 2015, and so analysis was limited to that period.

3.3.2. Case definitions

In line with the WHO definitions, the Namibia TB treatment guidelines define the various types of TB as follow (127):

4. **New smear positive pulmonary TB**: This is a new TB patient with at least one positive sputum smear sample. These are patients confirmed to have at least one Acid-Fast Bacilli (AFB) present in at least one sputum sample.
5. **New smear negative pulmonary TB**: This is a TB case where there is negative AFB in the sputum sample, but a patient is put on TB treatment on the basis of clinical judgement.
6. **Extra-pulmonary TB**: This is when a person has TB involving other body organs than the lungs, such as, lymph nodes, pleural, abdomen, skin, joint and bones.
7. **All forms of TB:** This category includes all new and relapse TB cases of all forms, including cases not mentioned above such as cases who returned after treatment, failure or treatment interruption, smears not done or others.

3.3.3. Source of data

During phase one, I relied on data published in the official annual TB reports of the NTLP. The temporal period for each indicator considered in this study was based on data availability during the implementation stage of my research.

3.3.4. An overview of how TB data are collected and reported to the NTLP

In Namibia, the collection and reporting of TB data is performed at different levels, consequently, the NTLP has developed several standardised paper-based data collection and reporting forms. These include but are not limited to the sputum TB register, the TB treatment card, the health facility TB register and the district TB register (127). In addition, the NTLP has an Electronic TB Register (ETR), which is simply an electronic version of the district TB register. I will expand more on the ETR in Chapter Four. The data I used during phase one were obtained from the annual reports, compiled by using the paper-based forms.

At all health facilities providing TB services, a person suspected to have TB is recorded in the TB sputum register. This register specifically captures information related to the name of the patient, sex, age, patient address, date sputum sent to the laboratory, sputum results, and date sputum results were received, turn-around time (in days), and the person who suggested the test (self or healthcare worker).

Upon receiving results, all patients diagnosed with TB are provided with individual TB treatment cards, which are kept at the health facility where they will receive TB treatment. The treatment card captures information related to patient name, age, sex, residential address, occupation, health facility, DOT preference, and DOT provider. Moreover, the TB card records information regarding classification of the TB patient, sputum smear information, body weight, HIV/AIDS testing and status, ART treatment as well as culture and drug susceptibility testing. In addition, the card records information related to treatment start and end dates and the specific medicines and dosages prescribed during both initial and continuation treatment phases. The treatment card also details patient responses regarding basic knowledge about TB, and this is assessed at different times during the treatment phase. These cards are compiled by healthcare workers.

The subsequent TB recording tool is the TB facility register, which is a summary of all notified TB patients during a month within a specific health facility. The register is compiled by healthcare workers using the TB treatment cards. The TB facility register details individual level patient information concerning the date of registration, registration number, name, sex, age, residential address, name of the health facility where individual patients receive TB treatment, date treatment started, TB classification (pulmonary or extra-pulmonary) and the category of TB patient (new, relapse, return after defaulter, return after failure). In addition, the register captures information related to patient’s sputum examination over the course of the treatment phase, the frequency of treatment collection, HIV/AIDS status, ART provision, CPT provision, DOT option, number of household contacts screened for TB, household contacts diagnosed with TB and lastly the patient’s TB treatment outcome.

Healthcare workers compile the facility registers with assistance from the field promoters attached to the various health facilities. A field promoter is a community based TB healthcare worker (chosen from the community), who is recruited by a particular community-based TB organisation to implement TB activities, such as the recording of TB data, contact screening, tracing of defaulters and providing health education in communities(80). In the case of Khomas, the field promoters are recruited and trained through Penduka, the only community-based TB organisation in the region.

The subsequent reporting form is the district TB register, which collates information recorded in the individual health facility registers. The district register has the same fields as the health facility register and is compiled by the District TB and Leprosy Coordinators (DTLCs). Each of the 34 health districts in Namibia, has at least one DTLC.

At the end of each reporting quarter, the DTLCs summarise the data in the district TB register into what is known as a TB quarterly form. This form provides the total number of TB patients notified in the preceding three month period, and these data are split according to the type of TB, the age and sex distribution (of new smear positive cases), HIV/AIDS testing and treatment outcomes. The quarterly form is compiled in conjunction with a TB and HIV/AIDS specific quarterly form, which details information about co-infected cases, including the provision or ART and Cotrimoxazole preventative therapy (CPT), and their treatment outcomes. These two-district level quarterly forms are subsequently submitted to the national level to inform the national annual TB reports. In addition, other quarterly forms submitted to the national level include the Drug Resistance TB (DR-TB) quarterly form and the district community-based TB care report.

Upon receiving the quarterly forms from all the districts, the Monitoring and Evaluation (M&E) unit of the NTLP aggregates these data for the quarter, and the four quarterly forms are consolidated to inform the annual reports at the end of each year.

Apart from programmatic information, the national annual reports detail the number of cases notified with TB (split by types of TB), as well as treatment outcomes for TB patients notified in the preceding year. The data in the reports are summarised at national, regional and districts levels. The reports also gives details about the notification of HIV/AIDS infected TB cases, provision of ART and CPT and treatment outcomes for co-infected patients. In addition, the reports include notification of DR-TB cases as well as their treatment outcomes. The age and sex disaggregation is provided for new smear positive pulmonary TB cases only.

3.3.5. Data quality

Ensuring data quality is one of the key functions of the M&E unit of the NTLP (127). Consequently, several platforms have been established at various levels, aimed at providing the opportunity for data verification before submission of data to the national level.

According to the NTLP, the DTLCs are required to conduct routine checks to verify the accuracy of transfer of information from the individual treatment cards up to the district register (127). At the end of each quarter, each region is expected to conduct a review meeting to verify the information between the various reporting registers. These meetings are usually conducted over a three days period and are attended by the DTLCs, primary healthcare supervisors, nurses from major TB facilities, environmental health officers, and representatives from the community-based TB organisations. Specifically, the regional review meetings are conducted to fulfil the following objectives (127):

1. To strengthen peer review of data collected and analysed by the individual districts
2. To compile TB, TB and HIV/AIDs, DR-TB and leprosy notification for the previous quarter.
3. To compile treatment outcome data for the previous year.
4. To harmonise district data and share information on transferred patients among districts.
5. To harmonise paper –based and ETR data.
6. To present and discuss planned and unplanned activities related to TB, TB/HIV and Leprosy.
7. To share challenges and solutions.
8. To share latest information regarding TB, TB/HIV and leprosy control.

After the regional review meetings, zonal meetings are conducted with at least two regions, and these serve the same purpose as the regional specific review meetings. The zonal meetings also allows regions to share successes and challenges and to learn from one another (127). The zonal meetings are conducted over five days, and it is only after these meetings that data are submitted to the national level. Annually, staff from national level are expected to conduct support visits in regions, guided by standardised supervision checklists, which assesses a number of aspects such as adherence to treatment guidelines, availability of information materials, laboratory related aspects, and data recording.

On an annual basis, the NTLP conducts an annual review meeting which brings together representatives from key stakeholders including community-based TB organisations. These annual meetings provide the basis for compilation of the TB annual report for the previous year (127). The meeting serves as the final opportunity for data verification before the annual report is compiled and published (127).

3.3.6. Socio-demographic background information

The socio-economic indicators for Namibia as a whole and for Khomas are provided in Table 3.1 as per census data.

Table 3.1. Socio-demographic indicators nationally and in Khomas (47)

Variable	Khomas	National
Total Population	415 780	2 324 388
Female	209 690	1 194 634
Male	206 090	1 129 754
Population in urban areas (%)	95	48
Population in rural areas (%)	5	52
Annual growth rate (%)	3.9	1.9
Population density (per sq.km)	11.3	2.8
Age composition (%)		
Under five years	13	14
5-14 years	16	23
15-59 years	68	57
60+ years	3	6
Education, 15+ years (%)		
Never attended school	5	11
Currently in school	16	18
Left school	78	71
Household conditions (%)		
Safe water	100	94
No toilet facility	25	46
Usage of electricity for lighting	64	45
Usage of wood/charcoal for cooking	7	50
Main source of income (%)		
Farming	0.3	15
Wage/salaries	75	52
Cash remittance	6	5
Business, non-farming	10	7
Old age pension	2	10

3.3.7. Statistical analysis

3.3.7.1. Calculation of TB CNRs

As data were not available by age and sex (except for one form of TB group). I was only able to analyse trends in crude CNRs during this phase. The yearly CNRs for the different types of TB were calculated using the formula below. The denominator values (population figures) were taken from the census projection reports.

$$Crude\ rate = \frac{Total\ number\ of\ notified\ \ TB\ cases\ per\ year}{Total\ \ year\ specific\ population} \quad x\ 100\ 000$$

3.3.7.2. Trend analysis using Joinpoint Regression

Before analysing the trends statistically, I plotted the CNRs on a line graph to observe the pattern for each type of TB. I observed that trends generally formed a non-linear pattern, and for that reason, I decided to use Joinpoint regression rather than using regression models which assume a linear trend over time.

In brief, Joinpoint regression is a window-based programme developed by the surveillance research unit of the U.S National Cancer Institute (128). The programme was initially developed to analyse cancer rates, but has increasingly been used to study temporal trends for other diseases, including malaria (129, 130), HIV/AIDS (131, 132). Joinpoint requires the dependent variable to take any form of numerical values such as a counts, crude rates, adjusted rates, percentages and proportions. The variable containing time periods, typically in years, is the independent variable. The programme uses permutation tests adjusted for multiple testing using Bonferroni adjustments. Significant trend change points (if any) are identified using Monte Carlo simulations (125). Joinpoint compares if the model with join points is better than the model without any join point, and the programmes allow for a maximum of nine join points within a particular trend. The number of join points to be determined is dependent on the temporal length of the study. A Joinpoint (if any) marks a point at which a significant change in the slope regression function occurred.

For my study, the variable containing the crude notification rates was the dependent variable, and the notification years was the independent variable. I kept the minimum number of permutations at the recommended default value of 4499. The maximum number of join points was set at three for the period 1997-2015, and at one for the period 2006-2014/5. The

Bonferroni adjustment was used for multiple testing and I maintained alpha for permutation tests at =0.05, to determine significance of the slope.

In the results section, I describe trends by presenting the Annual Percentage Change (APC) for the sub-periods, and the Average Annual Percentage Change (AAPC) for the entire study period, together with their confidence intervals. A trend was considered statistically significant when the p-value was less than 0.05. All analyses were based on Joinpoint regression programme version 4.6.0.0, April 2018.

3.4. Results

3.4.1. Case description and trends by types of TB

Table 3.2 shows the total number of TB cases and average CNRs from 1997 to 2015. In Khomas, 40 735 TB cases of all forms were notified. Of these, 37% were new smear positive pulmonary TB, 25% were new smear negative pulmonary TB and 18% were extra-pulmonary. The average CNR for all forms of TB was 733 (95% CI: 634-832) per 100 000 in Khomas. The average CNR was higher for new smear positive pulmonary TB (CNR=272, 95% CI: 245-299) and lower for extra-pulmonary TB (CNR=131, 95% CI: 114-147). The all forms of TB group include cases which were categorised as other types of TB (i.e. smears not done).

Table 3.2. Number of TB cases and average CNRs according to types of TB, 1997 to 2015

Type of TB	Khomas		National	
	n (%)	Average CNR (95% CI)	n (%)	Average CNR (95% CI)
New smear positive pulmonary TB	15 197 (37.3)	272 (245-299)	86 503 (35.1)	230 (215-244)
Smear negative pulmonary TB	10 198 (25.0)	193 (113-273)	76 152 (30.9)	211 (148-273)
Extra-pulmonary TB	7318 (17.7)	131 (114-147)	34 730 (14.1)	92 (81-102)
All forms of TB	40 735 (100)	733 (634-832)	246 469 (100)	660 (597-722)

Table 3.3 shows trend analysis results of the Joinpoint regression. In Khomas, the trend for new smear positive pulmonary TB CNRs increased at an annual percent of 4.1% (95% CI: 0.3% to 8.2%) from 1997 to 2004 and thereafter there was a consistent significant decline at an annual percent of -6.2% (95% CI: -7.7% to -4.3%) from 2004 to 2015. Overall, the trend for new smear positive pulmonary TB declined significantly at an annual average of -2.3% (95% CI: -3.9% to -0.6%) during the entire study period. The trend as modelled by the Joinpoint model are shown in Figure 3.1.

The trend for smear negative pulmonary TB CNRs initially declined by 14% per year from 1997 to 2000, then significantly increased by 47% per year from 2000-2004, and subsequently declined by 28% annually between 2004-2015. The overall trend for this group declined at an annual average of -13.2% (95% CI: -22.5% to -2.8%). The trend as modelled by the Joinpoint model are shown in Figure 3.2.

For extra-pulmonary TB CNRs, the trend increased by 26% per year during 1997-2000, then declined by 1.4% annually between 2000-2008, and subsequently declined significantly by -9.4 per year from 2008 to 2015. The whole period trend declined by -0.6% per year but this was not a significant decline. The trend as modelled by the Joinpoint model are shown in Figure 3.3.

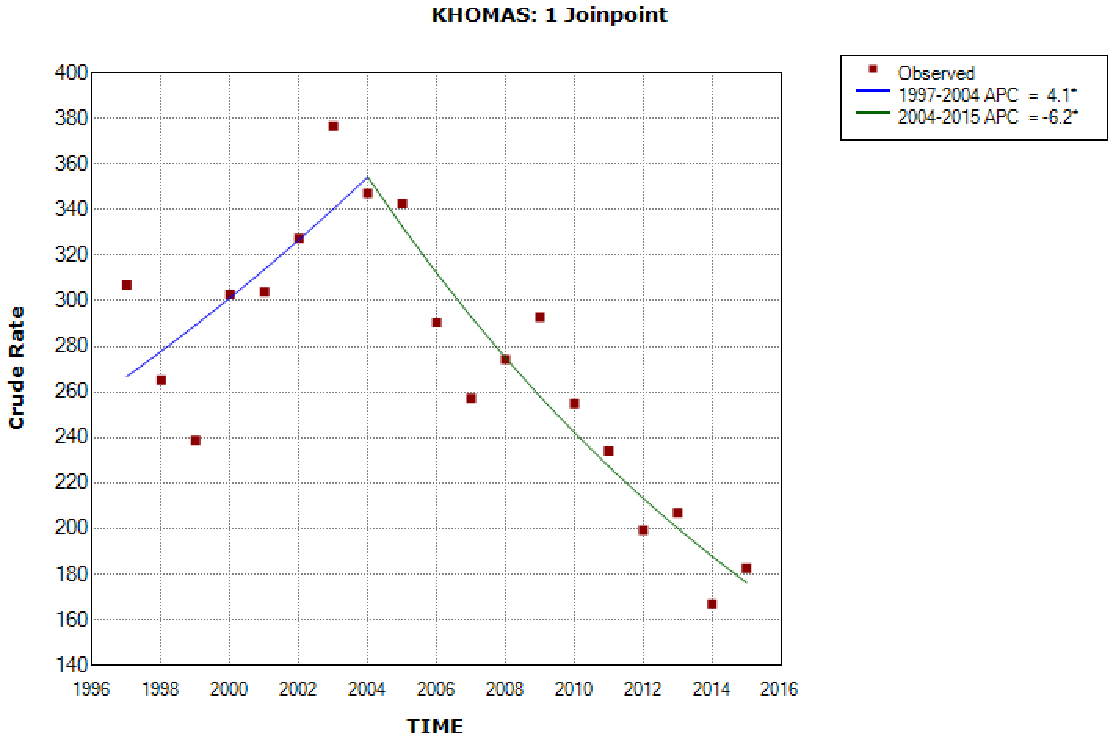
For all forms of TB, CNRs initially declined by 12% (95% CI: -29.0% to 7.8%) per year from 1997 to 1999, then increased significantly at an annual percent of 13.3% (95% CI: 6.8% to 20.7%) from 1999 to 2004 and subsequently declined consistently and significantly at an annual rate of -9.3% (95% CI: -10.4% to -8.1%). The entire period average annual percent change was -3.9% (95% CI: -6.4% to -1.3%). The trend as modelled by the Joinpoint model are shown in Figure 3.4.

Table 3.3: Joinpoint regression results for trends in CNRs by type of TB, 1997 to 2015

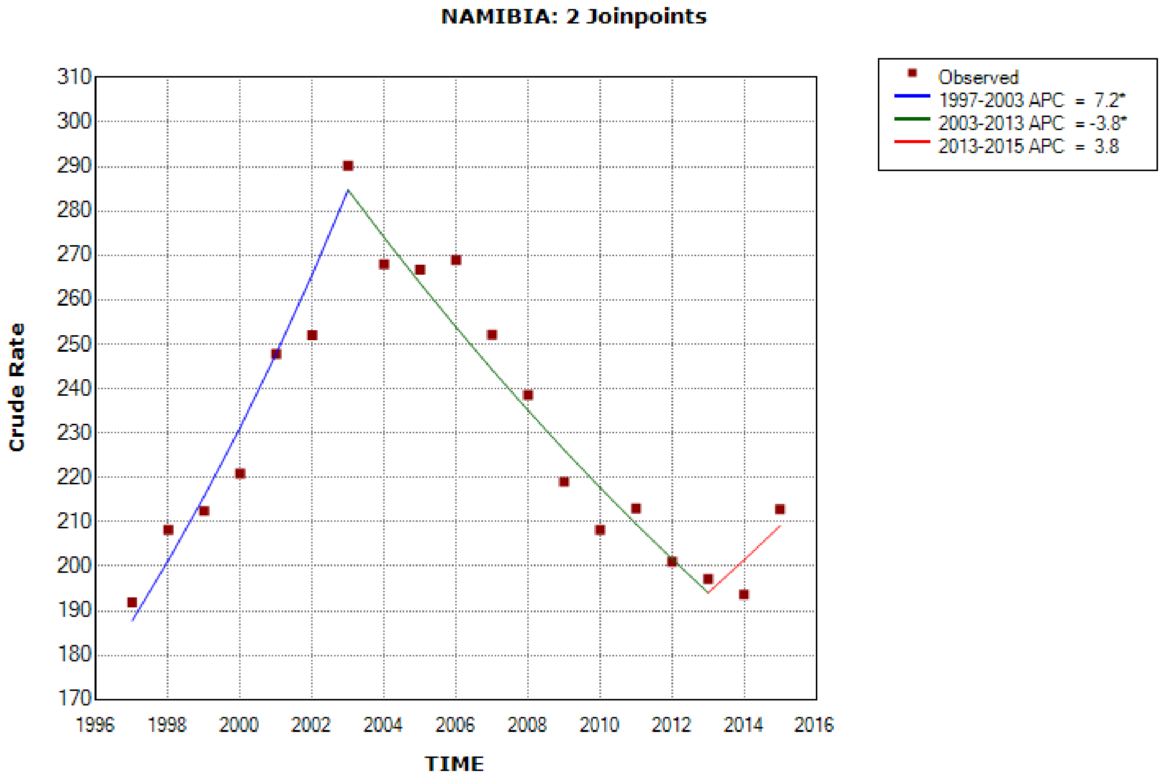
Type of TB	KHOMAS					NATIONAL				
	Sub-period	APC (95% CI)	p-value	1997 to 2015 Average APC (95% CI)	p-value	Sub-period	APC (95% CI)	p-value	1997 to 2015 Average APC (95% CI)	p-value
New smear positive pulmonary TB	1997-2004	4.1 (0.3 to 8.2)	p<0.05	-2.3 (-3.9 to -0.6)	p<0.05	1997-2003	7.2 (5.3 to 9.1)	p<0.05	0.6 (-0.6 to 1.8)	p=0.3
	2004-2015	-6.2 (-7.9 to -4.3)	p<0.05			2003-2013	-3.8 (-4.6 to -2.9)	p<0.05		
						2013 -2015	3.8 (-5.8 to 14.4)	p=0.8		
Smear negative pulmonary TB	1997-2000	-14.1 (-48.2 to 42.2)	p=0.5	-13.2 (-22.5 to -2.8)	p<0.05	1997-2006	2.5 (-3.0 to 5.3)	p=0.1	-8.7 (-15.2 to -1.7)	p<0.05
	2000-2004	47.4 (2.0 to 113.0)	p<0.05			2006 -2009	-40.8 (-62.0 to -7.8)	p<0.05		
	2004-2015	-28.3 (-33.7 to -22.3)	p<0.05			2009-2015	-4.7 (-14.2 to 5.9)	p=0.3		
Extra-pulmonary TB	1997-2000	26.3 (0.5 to 58.8)	p<0.05	-0.6 (-4.6 to 3.6)	p=0.8	1997-2004	1.0 (-2.3 to 4.3)	p=0.5	-0.7 (-3.9 to 2.5)	p=0.7
	2000-2008	-1.4 (-5.6 to 2.9)	p=0.5			2004-2007	20.1 (-1.0 to 45.7)	p=0.1		
	2008-2015	-9.4 (-13.6 to -4.9)	p<0.05			2007-2015	-8.9 (-10.9 to -6.9)	p<0.05		
All forms of TB	1997-1999	-12.5 (-29.0 to 7.8)	p=0.2	-3.9 (-6.4 to -1.3)	p<0.05	1997-2005	3.5 (2.0 to 5.0)	p<0.05	-2.3 (-3.1 to -1.5)	p<0.05
	1999-2004	13.3 (6.8 to 20.1)	p<0.05			2005 -2015	-6.7 (-7.7 to -5.7)	p<0.05		
	2004-2015	-9.3 (-10.4 to -8.1)	p<0.05							

APC: Annual Percent Change
AAPC: Average Annual Percent Change
CI: Confidence Interval

Figure 3.1. Trends in Smear positive pulmonary TB CNRs (per 100 000 population) in Khomas and nationally, 1997-2015

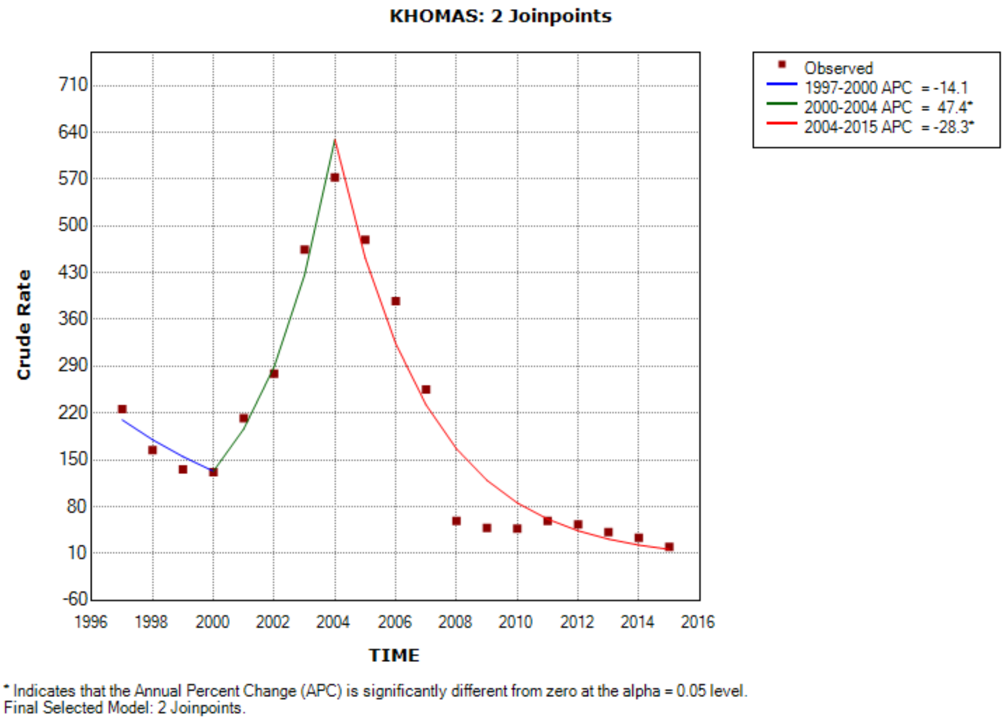


* Indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level.
Final Selected Model: 1 Joinpoint.



* Indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level.
Final Selected Model: 2 Joinpoints.

Figure 3.2. Trends in Smear negative pulmonary TB CNRs (per 100 000 population) in Khomas and nationally, 1997-2015



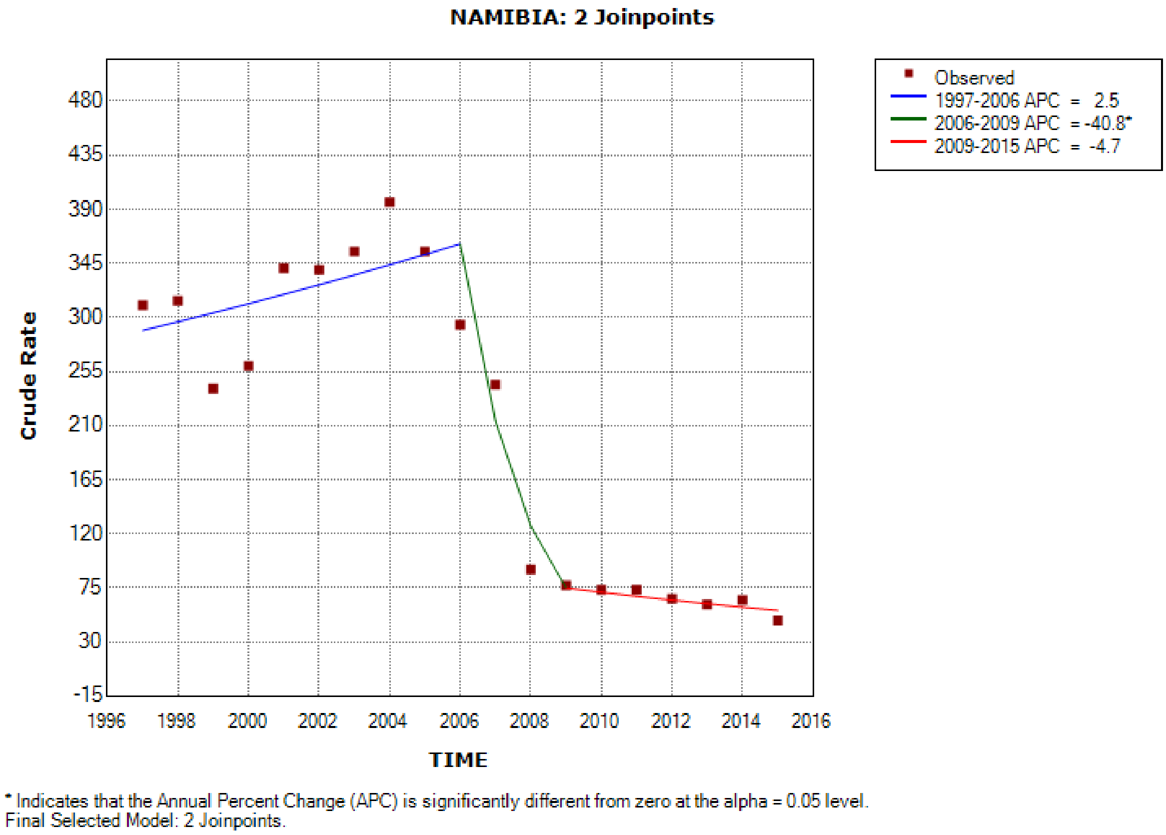
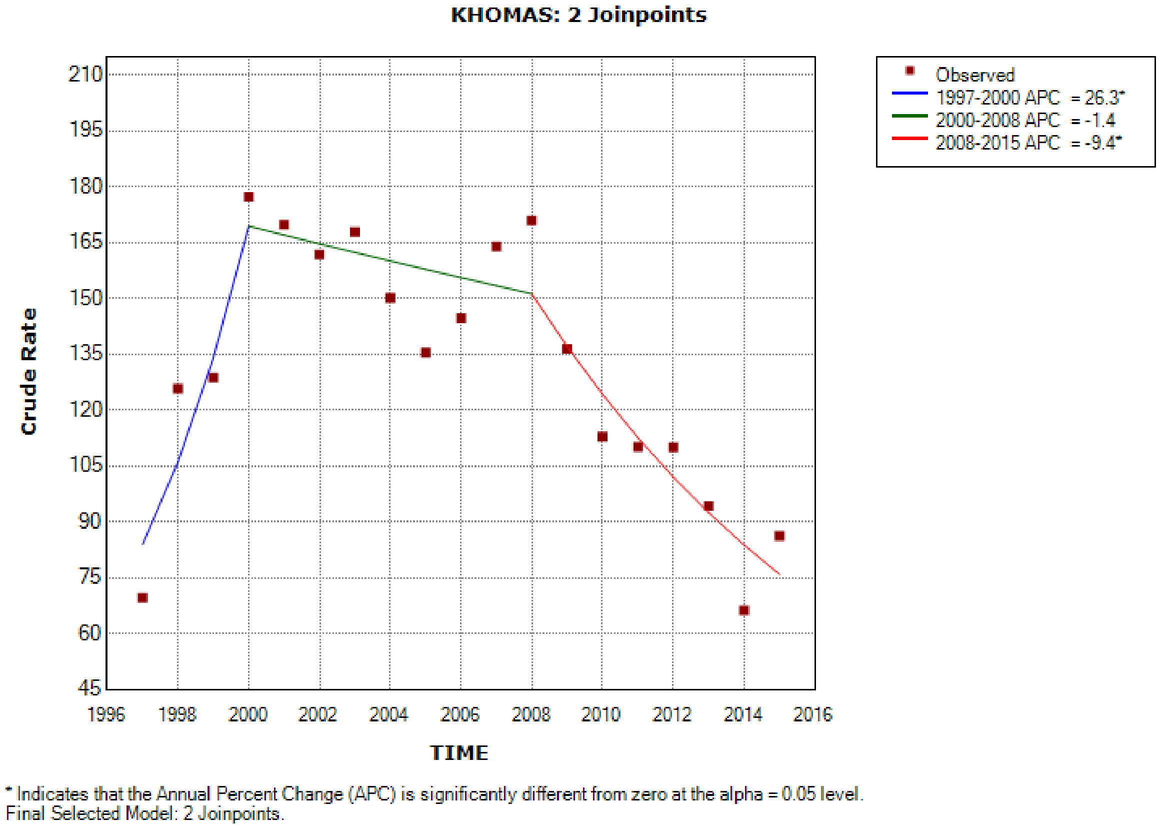


Figure 3.3. Trends in Extra-pulmonary TB CNRs (per 100 000 population) in Khomas and nationally, 1997 -2015



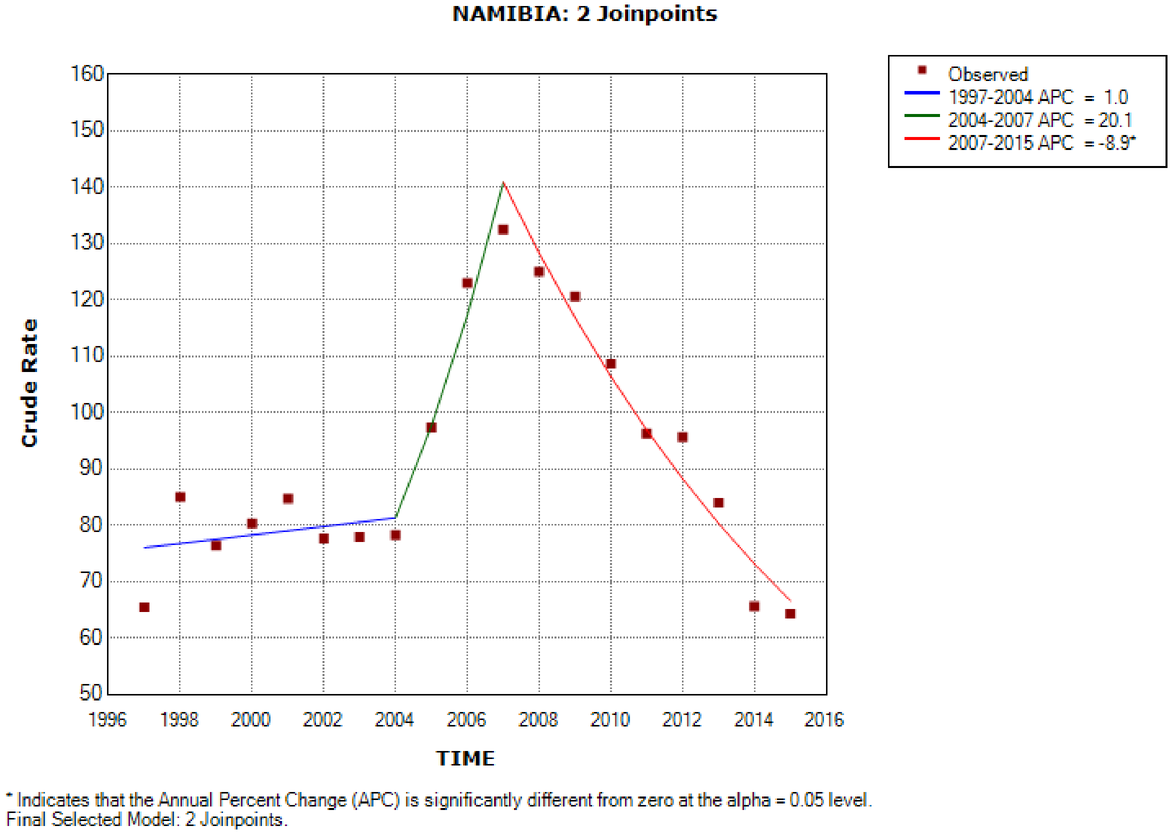
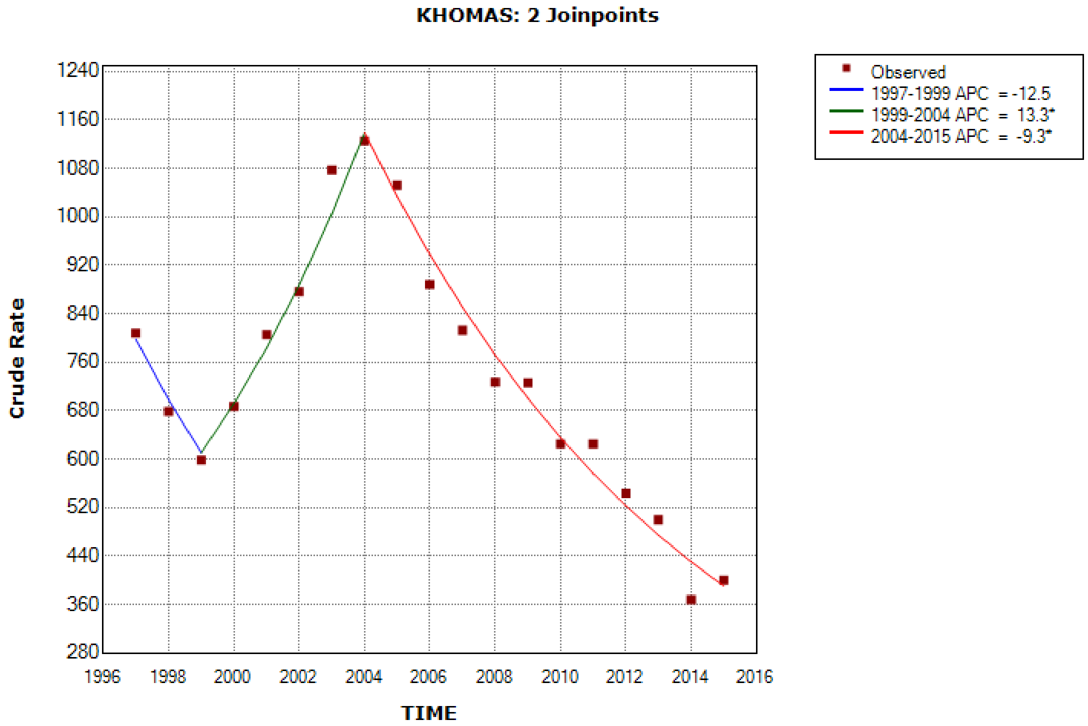
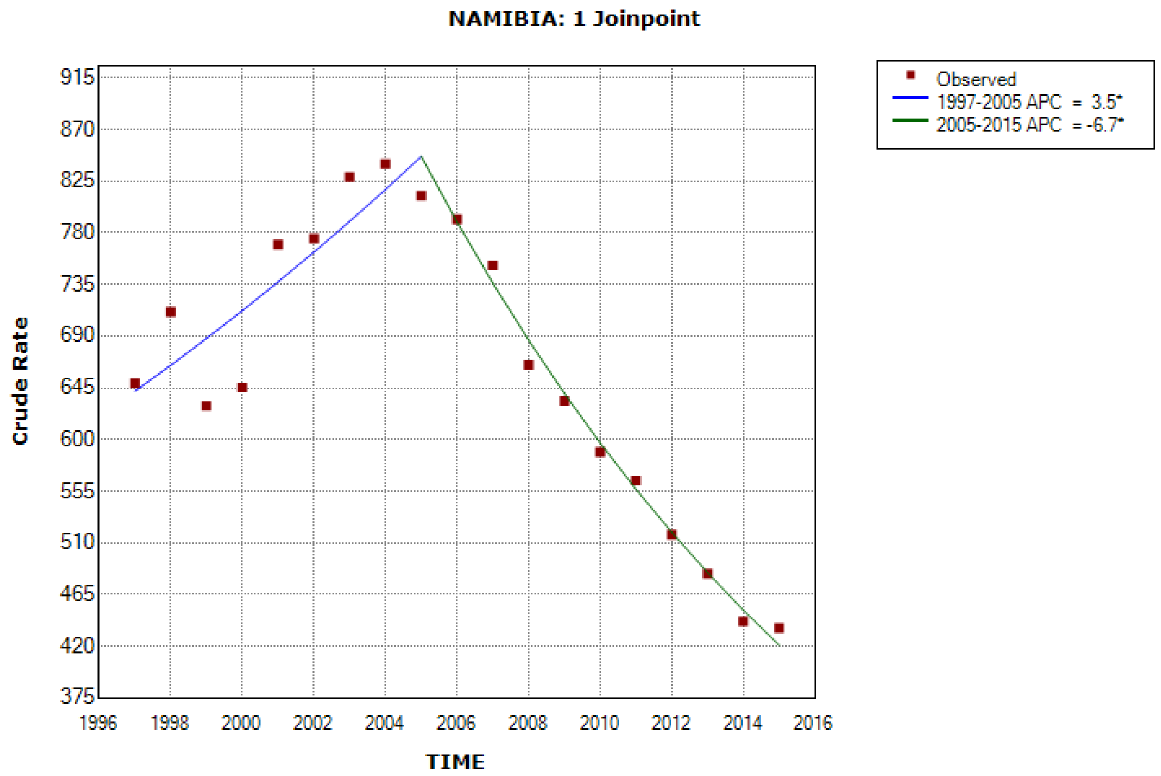


Figure 3.4. Trends in all forms of TB CNRs (per 100 000 population) in Khomas and nationally, 1997-2015



* Indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level.
Final Selected Model: 2 Joinpoints.



* Indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level.
Final Selected Model: 1 Joinpoint.

3.4.2. *Case description and trends for new smear positive pulmonary TB CNRs by sex*

Table 3.4 shows the number and average CNRs for new smear positive pulmonary TB by sex from 2006 to 2014. In Khomas, 7229 new smear positive pulmonary TB cases were notified. Of these, 4578 (63%) were males and 2651 (37%) were females. The average CNR was 310 (95% CI: 274-346) for males and 175 (95% CI: 148-203) for females per 100 000 population.

Table 3.4: Number and average CNRs for smear positive pulmonary TB by sex, 2006-2014

Gender	**Khomas**		**National**	
	n (%)	**Average CNR (95% CI)**	**n (%)**	**Average CNR (95% CI)**
Male	4578 (63.3)	310 (274-346)	23 970 (57.11)	252 (233-272)
Female	2651 (36.7)	175 (148-203)	18 001 (42.89)	193 (167-218)

Table 3.5 shows the Joinpoint regression results for trends in CNRs for new smear positive pulmonary TB by sex from 2006 to 2014. In Khomas, the trend declined consistently and significantly at an annual rate of -5.6% (95% CI: -7.7% to -3.4%) for males and at an annual change of -6.5% (95% CI: -10.9% to -1.9%) for females. There were no specific change points in trends observed for all sexes in Khomas. The trends as modelled by the Joinpoint model are shown in Figure 3.5 for Khomas and Figure 3.6, nationally.

Table 3.5: Joinpoint regression results for trends in CNRs for new smear positive TB by sex, 2006 to 2014

Type of TB	KHOMAS					NATIONAL				
	Sub-period	**APC (95%CI)**	**p-value**	**2006 to 2014 Average APC (95%CI)**	**p-value**	**Sub-period**	**APC (95%CI)**	**p-value**	**2006 to 2014 Average APC (95%CI)**	**p-value**
Male	-			-5.6 (-7.7 to -3.4)	p<0.05	2006-2008 2008-2014	-12.4 (-12.9 to -1.7) -0.2 (-2.2 to 1.9)	p<0.05 p=0.8	-3.4 (-5.6 to -1.1)	p<0.05
Female	-			-6.5 (-10.9 to -1.9)	p<0.05	-			-5.7 (-8.2 to -3.1)	p<0.05

APC: Annual Percent Change
AAPC: Average Annual Percent Change
(-) means no join point observed, hence only AAPCs presented for that trend.

Figure 3.5. Trends in smear positive pulmonary TB CNRs (per 100 000 population) by sex in Khomas, 2006-2014

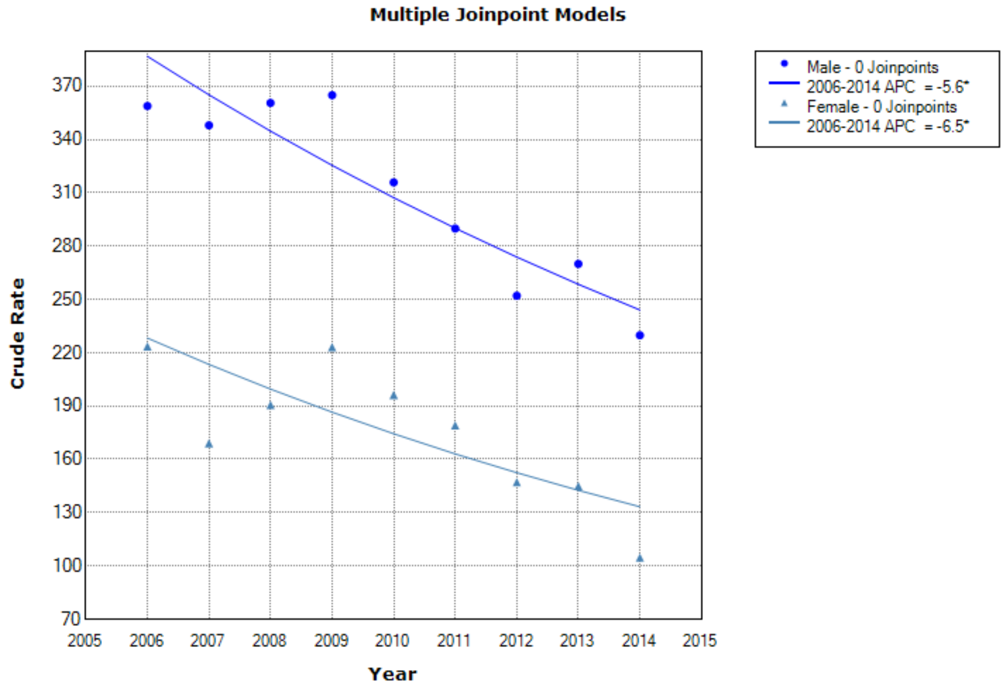
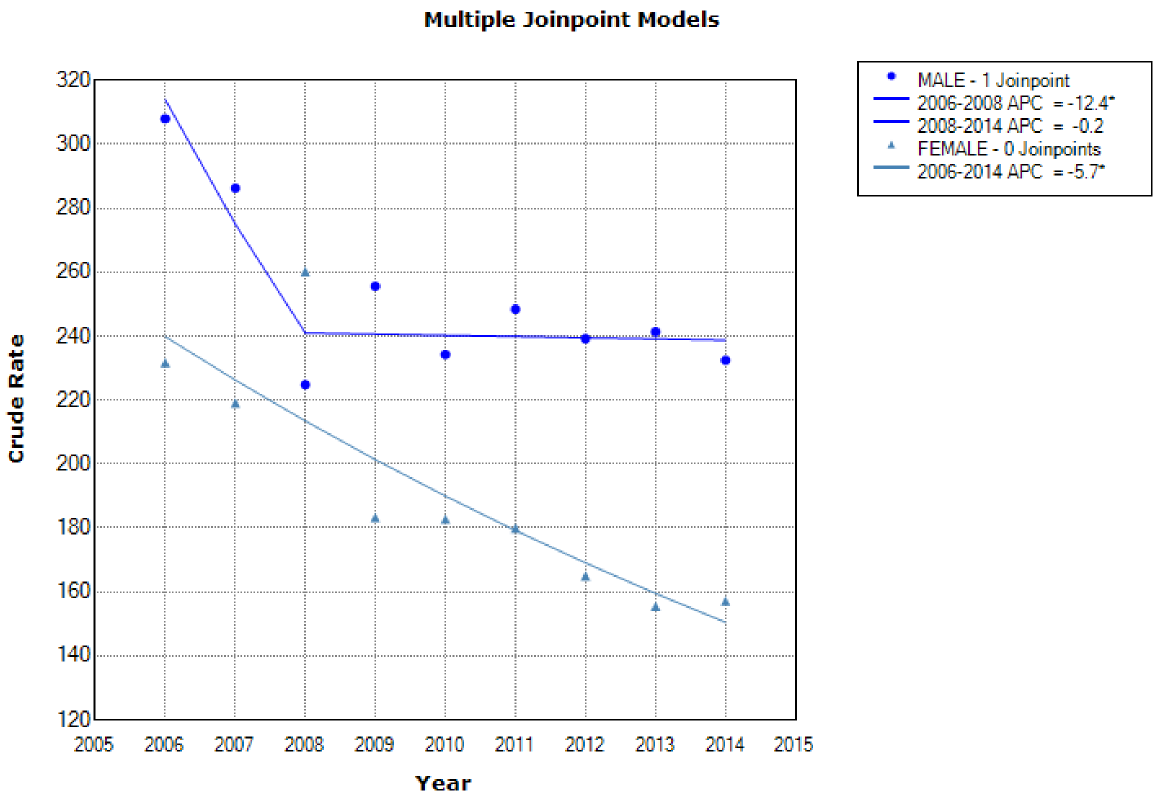


Figure 3.6. Trends in smear positive pulmonary TB CNRs (per 100 000 population) by sex nationally, 2006-2014



3.4.3. Case description and trends for new smear positive pulmonary TB by age group

Table 3.6 shows the number and average CNRs for age group specific new smear positive pulmonary TB from 2006 to 2014. In Khomas, out of 7229 notified TB cases, the majority, 4809 (67%) were aged 25 to 44 years. The average CNR was highest in the age group 25-44 years, at 417 (95% CI: 364-469) per 100 000 population. The younger age group had the lowest CNR, at 86 (95% CI: 79-94) per 100 000 population.

Table 3.6: New smear positive TB cases and average case notification rates by age group, 2006 to 2014

Age group	Khomas		National	
	n (%)	**Average CNR (95%CI)**	**n (%)**	**Average CNR (95%CI)**
0-24	1284 (17.8)	86 (79-94)	8324 (19.8)	75 (72-78)
25-44	4809 (66.5)	417 (364-469)	24465 (58.3)	488 (438-539)
45+	1136 (15.7)	318 (260-377)	9182 (21.9)	323 (295-351)

Table 3.7 shows result from the Joinpoint regression model indicating trends in age group specific CNRs for new smear positive pulmonary TB. In Khomas, the trend for the younger age group, 0-24 years, declined consistently throughout the nine years period at annual change of -2.4% (95% CI: -5.8% to 1.1%), but this trend did not meet statistical significance. The trend for age group 25-44 years declined significantly and consistently at an annual rate of -6.1% (95% CI: -8.6% to -3.6%).

For age group 45+ years, Joinpoint identified that there was an increasing trend (but not significant) at a rate of 10.2% (95%CI: -7.1% to 30.7%) from 2006 to 2009. From 2009 to 2014, the CNRs declined significantly at a yearly rate of -14.4% (95%CI: -20.6% to -7.7%). The overall average annual percent change in the trend was -5.9% (95% CI: -11.0% to -0.5%) for the oldest age group. The trends as modelled by the Joinpoint model are shown in Figure 3.7 for Khomas and Figure 3.8, nationally.

Table 3.7: Joinpoint regression results for trends in CNRs for new smear positive pulmonary TB by age group, 2006 to 2014

Age groups	KHOMAS					NATIONAL				
	Sub-period	**APC (95%CI)**	**p-value**	**2006 to 2014 Average APC (95%CI)**	**p-value**	**Sub-period**	**APC (95%CI)**	**p-value**	**2006 to 2014 Average APC (95%CI)**	**p-value**
0-24		-		-2.4 (-5.8 to 1.1)	p=0.1	2006-2009 2009-2014	-5.7 (-10.4 to -0.9) 1.2 (-1.1 to 3.6)	p<0.05 p=0.2	-1.4 (-3.1 to 0.2)	p=0.1
25-44		-		-6.1 (-8.6 to -3.6)	p<0.05		-		-5.2 (-6.1 to -4.1)	p<0.05
45+	2006 -2009 2009-2014	10.2 (-7.1 to 30.7) -14.4 (-20.6 to -7.7)	p=0.2 p<0.05	-5.9 (-11.0 to -0.5)	p<0.05		-		-4.3 (-5.4 to -3.2)	p<0.05

APC: Annual Percent Change
AAPC: Average Annual Percent Change
(-) means no join point observed, hence only AAPCs presented for that trend.

Figure 3.7. Trends in smear positive pulmonary TB CNRs (per 100 000 population) by age group in Khomas, 2006-2014

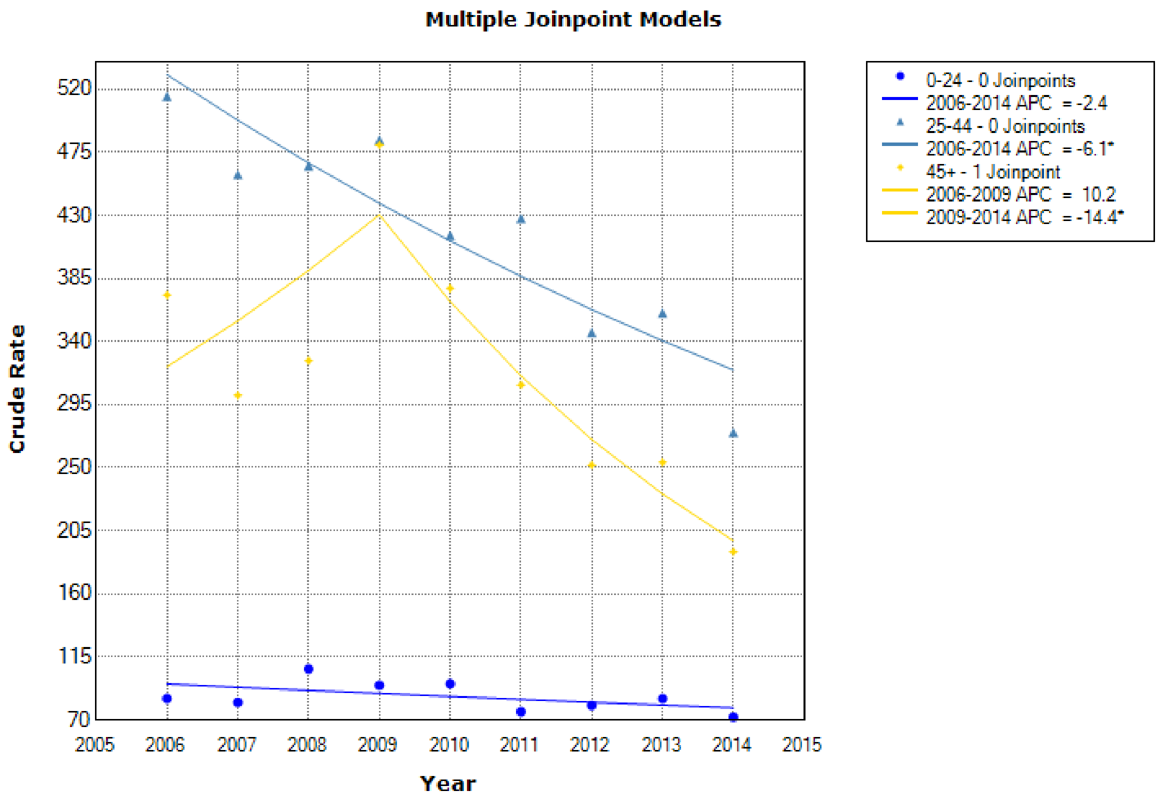
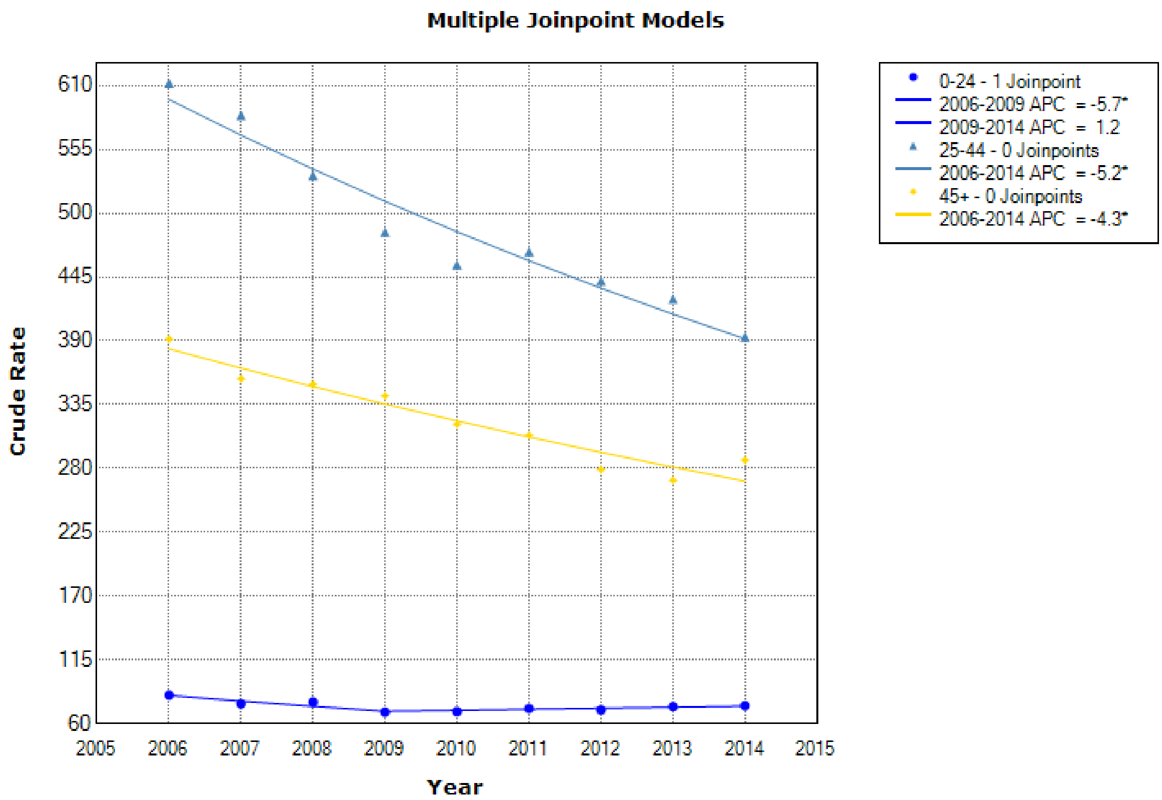


Figure 3.8. Trends in smear positive pulmonary TB CNRs (per 100 000 population) by age group nationally, 2006-2014



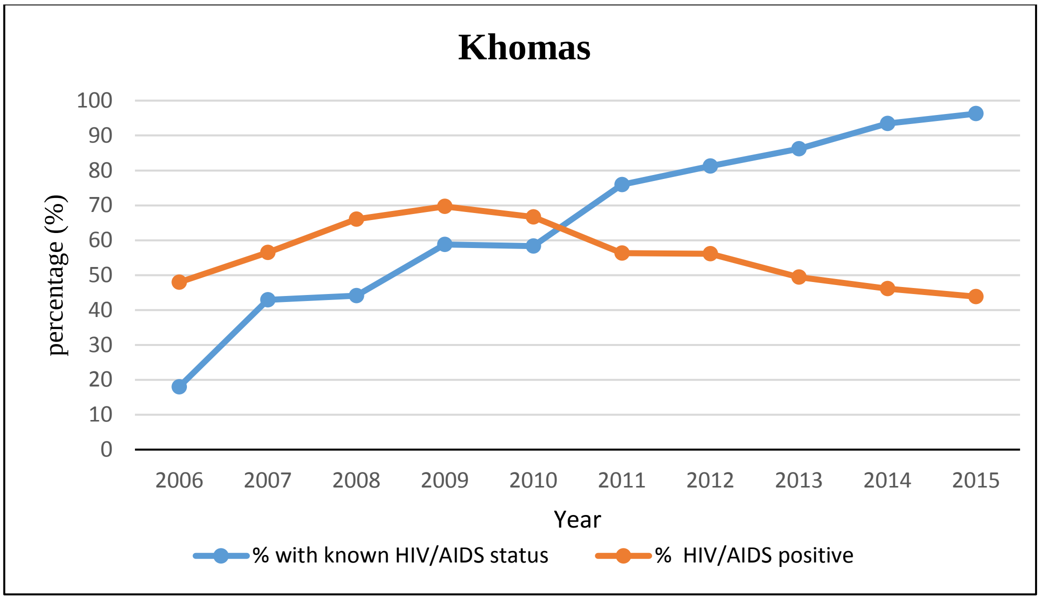
3.4.4. Case description and trends of TB and HIV/AIDS indicators, 2006-2015

Table 3.8 shows the number and average percentage of TB cases with known HIV/AIDS status and those found to be HIV/AIDS positive from 2006 to 2015. In Khomas, 12 812 (62%) cases of 20 788 notified all forms had a known HIV/AIDS status, of which 56% were HIV/AIDS positive. Figure 3.9 shows the year specific rates for known status, as well as the HIV/AIDS prevalence among TB cases.

Table 3.8: All forms of TB cases by HIV/AIDS testing and prevalence, 2006 to 2015

Indicator	**KHOMAS**		**NATIONAL**	
	N (%)	**Average rates (95%CI)**	**N (%)**	**Average rates (95%CI)**
All forms of TB cases	20 788 (100)	622 (508-735)	124 214 (100)	587 (499-676)
Number with known HIV/AIDS status	12 812 (62)	66 (49-82)	89 645 (72)	75 (60-90)
Number HIV/AIDS positive	7149 (56)	56 (50-62)	46 055 (51)	52 (46-58)

Figure 3.9: HIV/AIDS testing and prevalence rates among TB cases, 2006 to 2015



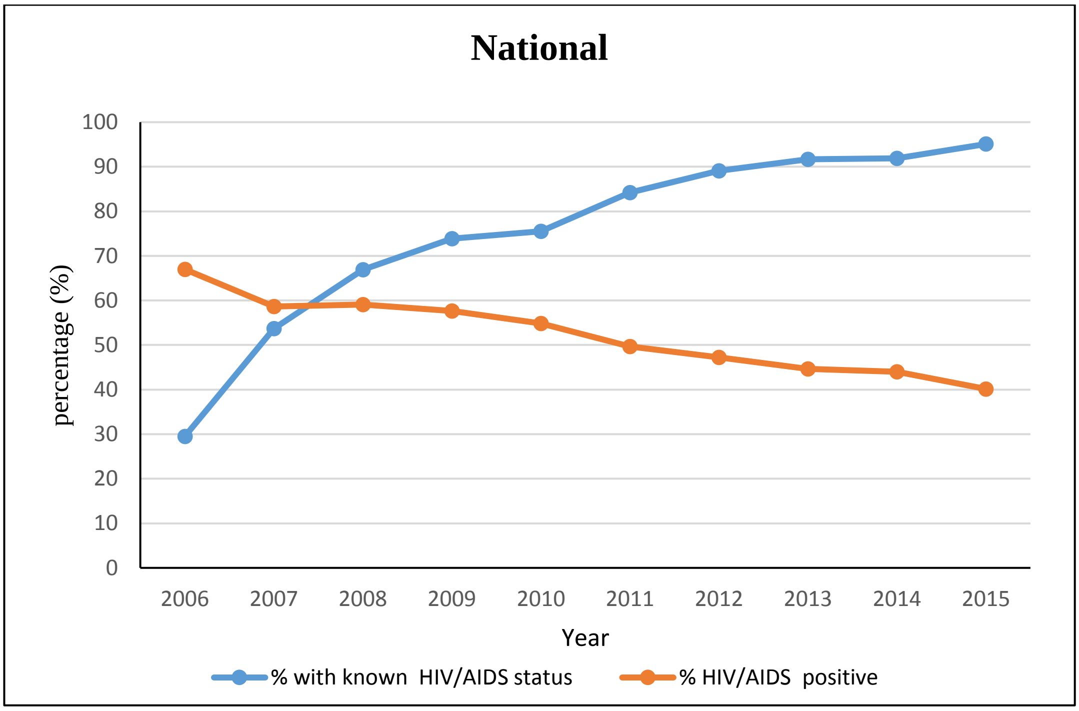


Table 3.9 shows Joinpoint regression results concerning trends in TB and HIV/AIDS related indicators. In Khomas, the trend in the percentage of TB cases with known HIV/AIDS status increased significantly by 20.3% (95% CI: 3.3% to 40.1%) from 2006 to 2011, and thereafter declined by 5.9% per year (95% CI: -0.8% to 13.1%). The overall annual percent change from 2006 to 2015 was 13.7% (95%CI: 6.2% to 21.7%), and this was a statistically significant trend.

Concerning HIV/AIDS prevalence, the percent of TB cases co-infected with HIV/AIDS increased significantly at an annual change of 11.6% (95% CI: 1.7% to 22.4%) from 2006 to 2009. Thereafter, the trend declined significantly at an annual change of -8.0% (95% CI: -10.1% to -5.9%). However, the overall period trend declined but not significantly -1.9% (95% CI: -4.5% to 0.7%).

Table 3.9: Joinpoint regression results for trends concerning TB and HIV/AIDS indicators, 2006 to 2015

Variable	KHOMAS					NATIONAL				
	Sub-period	**APC (95%CI)**	**P-value**	**AAPC 2006-2015 (95%CI)**	**p-value**	**Sub-period**	**APC (95%CI)**	**P-value**	**AAPC, 2006-2015 (95%CI)**	**p-value**
% with known HIV/AIDS status	2006-2011 2011-2015	20.3 (3.3 to 40.1) 5.9 (-0.8 to 13.1)	p<0.05 p=0.1	13.7 (6.2 to 21.7)	p<0.05	2006-2009 2009-2015	26.2 (4.6 to 52.4) 3.5 (1.0 to 6.1)	p<0.05 p<0.05	10.6 (5.3 to 16.2)	p<0.05
% HIV/AIDS positive	2006 -2009 2009-2015	11.6 (1.7 to 22.4) -8.0 (-10.1 to -5.9)	p<0.05 p<0.05	-1.9 (-4.5 to 0.7)	p=0.1	-			-5.1 (-5.9 to -4.3)	p<0.05

APC: Annual Percent Change
AAPC: Average Annual Percent Change
(-) means no join point observed, hence only AAPCs presented for that trend

3.5. Discussion

3.5.1. Summary of main findings

To the best of my knowledge, this is the first study in Namibia to statistically describe trends in CNRs by types of TB and for TB and HIV/AIDS related indicators. The focus was on Khomas, but I also showed national trends to demonstrate how the region compare to trends nationally. The remaining part of this section will primarily provide a discussion of the results in Khomas.

Significant change points in trends were observed for all types of TB examined. The trend for new smear positive pulmonary TB increased significantly by an annual rate of 4.1% from 1997 to 2004, and it significantly declined from 2004 to 2015 at a rate of -6.2% per year. The trend for smear negative pulmonary TB declined by -14% per year from 1997 to 2000, then increased significantly by 47% per year from 2000-2004 and then it declined significantly by an annual change of -29% from 2004 to 2015. The trend for extra-pulmonary TB increased significantly by an annual change of 26% from 1997 to 2000, then it declined by -1.4% from 2000 to 2008, and again declined significantly at a rate of -9.4% from 2008 to 2015. The trend for all forms of TB CNRs decreased by -13% from 1997-1999, then it increased significantly by 13% per year from 1999 to 2004 and thereafter it declined significantly a rate of -9% between 2004 -2015.

From 2006 to 2014, the trends for smear positive pulmonary TB declined significantly in both sexes, but in terms of age groups, significant declines over time were observed for the older age groups (25-44 and 45+) but not for the younger age group (0-24).

From 2006 to 2015, the trend in percentage of TB patients with a known HIV/AIDS status increased significantly at an annual average of 13.7%. Over time, there was no significant decline in the trend for the percentage of TB patients who were HIV/AIDS positive (AAPC: -1.9%, 95% CI: -4.5% to 0.7%), but a significant declining trend was observed in the recent years between 2009 -2015 at an annual rate of -8.0% (95% CI: -10.1% to -5.9%).

3.5.2. Strengths

One of the strengths of my study is that it utilised TB data collected and published in the official reports of the NTLP, and so the analysis is based on data as captured by the NTLP. As explained previously, The NTLP enhances the quality of data through verification platforms established at district, regional and zonal levels. These platforms enable for regions to verify data, before they are submitted and consolidated at the national level (127). A further strength of my study is that it had a long temporal period of 19 years in total, and this allowed for the presentation of a longer historical perspective of the disease burden. Moreover, my study was able to analyse trends in TB notifications for different types of TB groups, and where possible by gender and age groups, as well as analyse trends for TB and HIV/AIDS indicators, this has not been done before in Namibia, and so the study results would be useful in that regard. I used the Joinpoint regression programme to analyse and describe trends, and this allowed for detailed understanding of the temporal patterns. In other words, the change points presented in this research together with their annual percent changes would not have been obtained, had I used models such as linear regression, Poisson or negative binomial, both of which assume a linear trend over time.

3.5.3. Limitations

The study presented here also has several limitations. Firstly, analyses were based on data which generally include TB cases diagnosed in public health facilities, and so the extent to which these data include cases diagnosed in private health facilities is unclear. It is reported that about 19% access private healthcare (53). However given that TB treatment is free in the public sector facilities, one would expect the few cases to be treated in the private sector.

Secondly, it is possible that these data mostly include cases diagnosed through passive case finding (that is a person presenting with symptom at health facilities rather than detected through active screening). Therefore, the data presented here are likely to be an underestimation of the true disease burden. There was no TB prevalence survey conducted during the study time period, and hence the true burden at the time was not measured. However the current WHO reports consistently showed high estimated incidence rates at national level compared to the notification rates, suggesting gaps in case detection (1, 133). In 2017, the NTLP conducted a nationally representative TB prevalence survey for the first time, the results expected from that study would allow an opportunity to determine the true burden of the disease in the population. At the time of writing this thesis, the prevalence survey results were not published.

A further limitation is that, I was only able to analyse notifications by sex and age for one type of TB group (smear positive pulmonary TB), this is because the NTLP does not provide the sex and age information for all other cases of TB in their annual reports. The quarterly reports submitted to the national level only disaggregated age and sex for new smear positive pulmonary TB. Also, the fact that I could only analyse trends by sex and age group for new until 2014 is because, in 2015, the NTLP only reported the age and sex information at the national level and not for respective regions. Continuous omission of key information in the NTLP annual reports will affect the timely usage and analysis of the disease burden. I would also like to mention that, in this study, I concentrated on trends in TB notifications, future studies are required to analyse other TB components such as treatment outcomes.

3.5.4. Interpretation and comparison with the literature

3.5.4.1. CNRs for all forms of TB

My study showed that the trend for all forms of TB CNRs in Khomas is primarily characterised by two patterns, similar to that of the national trend. Specifically, the results show that the trend significantly increased by an annual rate of 13% between the years 1999 to 2004, then declined significantly by 9% per year from 2004 to 2015. Two factors may explain the observed pattern. Firstly, the increase observed prior to 2005 coincides with the period where estimates from the United Nations shows a large number of people with HIV/AIDS in Namibia (134). HIV/AIDS is known as the single most important risk factor for TB (1), and so it is unsurprising that the period characterised by a large number of people living with HIV/AIDS is also characterised by an increasing trend in CNR. There was no data for HIV/AIDS prevalence by region in Namibia until in 2013 when the MoHSS measured HIV/AIDS prevalence in the Namibia Demographic and Health Survey (NDHS) (49). The results of that survey showed a prevalence of 11.9% in Khomas and 16.4% nationally for people aged 15-49. In 2017, the MoHSS conducted another nationwide survey which measured the HIV/AIDS prevalence in the general public. The results of that survey are yet to be released, and would allow an opportunity to observe how the prevalence changed over time. The results expected from the two national level surveys (the TB prevalence survey and the recent HIV/AIDS survey) might also present an opportunity to model trends of HIV/AIDS associated TB at regional level.

Another aspect which might explain the increasing trend prior to 2005 is the lack of community based DOT (CB DOT). A recently published study by Kibuule *et al*. revealed that the CNRs in Namibia increased significantly prior to the introduction of CB DOT (101). This may have been a true increase because the lack of CB DOT implied that there was inadequate monitoring of TB patients outside health facilities and there was inadequate health education interventions in the community and no tracing of those who interrupt or default treatment. All these are factors which could influence further disease (135, 136).

The observed decline after 2005 may therefore be attributed to improved coverage of antiretroviral therapy (ART) among people living with HIV/AIDS (PLHIV), and this may have made a significant impact on reducing HIV/AIDS associated TB. Kibuule *et al*. showed that the CNRs at national level declined in the period when ART coverage gradually increased. A multi-country study by Surie *et al.* showed that in Namibia, the trend for TB CNRs declined at a median annual average change of -7.6% among people who are HIV/AIDS positive and by -0.1% among HIV/AIDS negative people (88). In Khomas, data from the annual reports show that the CNR for TB patients who were HIV/AIDS positive declined from 275/100 000 in 2008 to 171/100 000 in 2014 (64, 79). These data may therefore suggest reductions in HIV/AIDS associated TB. In future, it is worth conducting a study aimed at quantifying the regional level temporal changes in CNRs in relation to ART coverage in the general population, by using routine TB and HIV/AIDS programme data.

As noted by Kibuule *et al*., the introduction and expansion of community-based TB services in Namibia after 2005 may explain the declining trend observed from 2004 to 2015 (101). Community-based TB services include DOT, the provision of nutritional supplements, TB education sessions in communities, tracing TB patients who interrupt TB treatment, TB screening for TB patient household members and establishing income generating projects for TB patients (80). These activities may therefore have improved treatment outcomes, and improved TB awareness among the general public.

The trend for all forms of TB observed in my study is generally consistent with those reported in other studies. For example a study conducted in Zambia by Kapata *et al.* showed that the rates for all forms TB initially increased between 1990-2004 and then declined from 2005 to 2010 (97). Another study conducted in China by Wu *et al*. showed that trends initially increased from 1992-2005 and then declined from 2005 to 2015 (105). A recent study in Japan showed that trends in CNRs declined consistently at an average rate of -6.0% (95% CI -6.8% to -5.2%) per year from 1997 to 2016 (36). In my study the average annual decline was -3.9% in Khomas and -2.3 nationally. Although the time period in the Japanese study is similar to that of my study, the difference is that trends in my study initially increased, then declined in the recent years, whereas the trends in Japanese consistently declined throughout the period. This may explain the high annual rates observed in the Japanese study.

The bell-shaped trend observed in my study is inconsistent with those reported in some studies. For example, Lawn *et al*. in South Africa showed that trends in all forms of TB CNRs increased significantly from 1996 to 2004 (92). In Zambia, Mwaba *et al*. showed that trends increased throughout the period from the years 1964 to 2000(94). The inconsistency between my study and Lawn *et al.* and Mwaba *et al*. could be due to differences in the study period, with my study covering a more recent period. Indeed, in contrast to Mwaba *et al*. findings, a recent study from Zambia showed that trends in CNRs declined during the period from 2004 to 2011(96).

However, declining trend reported in my study in the recent years (from 2004 to 2015) is different to those observed in more recent studies. For example a recent zone-level study in Ethiopia by Dangisso *et al.* showed that the CNRs for all forms of TB were almost stable from 2003 to 2010, and rapidly increased from 2010 to 2012 (83). Similarly, another Ethiopian study observed that there was an increasing trend in CNRs in Arsi Zone from 1997 to 2011(100). According to the authors of the two Ethiopian studies, the increase in CNRs (which mostly occurred in the most recent years of their study periods) was due to improved access to health services through the Health Extension Programme (HEP) implemented in Ethiopia, rather than a true increase in incidence (137). In Haiti, the Charles *et al.* study conducted after the earthquake reported that an increase in CNRs may have resulted from active screening of people in slums and camps and also introduction of newer diagnostic tools (114). In Namibia, it is reported that about a third of TB cases are undiagnosed every year and therefore not reported to the NTLP (53), although case detection data by region are not available at present. However, the MoHSS started with the introduction of gene-xperts between 2013-2014, and I indeed observed that in Khomas the CNR for the year 2015 increased compared to that of 2014, which might have been due to improved diagnostics, and so it would be interesting to monitor CNRs in regions using gene-xperts beyond the year 2015, to observe the impact of the recently introduced diagnostics equipment.

3.5.4.2. CNRs for smear positive pulmonary TB

I observed that the trend for new smear positive pulmonary TB increased significantly by an annual rate of 4.1% between 1997 to 2004, and thereafter declined significantly by -6.2% per year until 2015. And the reasons I explained above could explain this trend. The observed trend for this type of TB is consistent with those observed in some countries. For instance, Wu *et al.* showed that there was an increase in the trend for smear positive pulmonary TB from 1992 to 2004, and then a decline from 2005 to 2015, but Wu *et al*. did not give the exact magnitude of the decline (105). In Iran, Arsang-jang showed that CNRs for smear positive TB declined at an average of 2.06% per year from 2001-2015 (107).

The trend observed in my study are not consistent with those observed in other studies. In particular, Charles *et al*. in Haiti showed that CNRs increased gradually from 85.5 to 105 per 100 000 population (114). In other studies, Dangisso *et al*. in Sidama showed that trends increased, especially in the recent years (83, 100). In Nigeria, Adejumo showed that trends in Lagos increased from 39 to 46 per 100 000 during the years 2011 to 2015 (99). The increasing trends observed in these studies were attributed to improved diagnostics and active case finding methods. In my study, the fact that trends in smear positive CNRs increased in 2015 both in Khomas and nationally compared to the previous year (2014), suggest that the same pattern observed in these studies may actually be the case in Namibia.

3.5.4.3. CNRs for smear positive pulmonary TB by sex

I found that the CNRs for new smear positive pulmonary TB in Khomas were significantly higher in males compared to females. This is despite the fact that the HIV/AIDS prevalence in the general population is slightly higher in females (12.2%) than males (11.6%) (49). The overall male to female ratio was 1.9:1, which is similar to ratios obtained in other studies (83, 84, 95, 99). The predominance of male TB cases may be explained by behavioural factors. For example, results of the recent NDHS show that in Khomas region, 64.3% of men reported that they have consumed alcohol in their lives compared to 52.9% of women. Furthermore, 13.7% reported that they drank five or more drinks per day of drinking compared to 6.7% of women. The survey also shows that 17.1% of men in Khomas smoked cigarettes compared to 4.6% of women (49). At present, the NTLP does not capture behavioural risk factors for TB, and so observational studies are required to assess the extent to which these factors influence the TB epidemiology in Namibia.

From 2006 to 2014, I found that there was a significant declining trend at an annual average of 6% and 7% for CNR for males and females respectively, and this is consistent with results from other studies, although in some studies the difference by sex was large. For example, Shrestha *et al*. reported an average annual decline of 2% and 11% among males and females during a nine year period in Nepal (84). Similarly, Noppert *et al*. reported a decline of 6% and 12% in CNRs for males and females respectively during a four year period in Zimbabwe (95). The fact that these two studies reported a large decline for females compared to the decline for males, perhaps suggest differences in health access. It could also perhaps indicate a slow trend and high prevalence of TB risk factors in men in those countries. In my study, the percent declines were similar by sex, and this is consistent with the findings of Khazaei and colleagues Iran, who reported a significant average annual percent decline of 4% and 5% among males and females respectively (108). I found that trends in CNRs for both males and females declined significantly in Khomas as well as nationally from 2006 to 2014. In Khomas, trends for both genders declined at a consistent annual percent change (no join points, meaning that that was no significant change in the trend). At the national level, the trend for female also declined at a consistent annual percent change, whilst the trend for males showed a significant change in the trend, having declined by -12.4% from 2006 to 2008 and then levelled off at an annual percent decline of -0.2% from 2008 to 2014. Although this change in the trend for males might be a chance result, this pattern could also be attributed to differences in risk factors between males and females. For example, data from the past two recent national demographic and health surveys (for years 2006 and 2013) (49, 138) shows a high percentage of males who smoked cigarettes, being 20.9% in 2006 and 18.6% in 2013, compared to the percentage of women who smoked cigarettes which was low in both surveys, being 5.3% in 2006 and 4.2% in 2013. These national surveys also showed that knowledge concerning TB transmission increased more in women (from 75.3% in 2006 to 85.5% in 2013) compared to that of males (from 76.6% in 2006 to 81.3% in 2013). Other risk factors such as heavy alcohol consumption and diabetes were not measured in the 2006 survey, but in the 2013 study, data shows that these specific risk factors were more prevalent in men than in women (49). Taken altogether, it can be speculated that the levelling of the trend during the recent years might be due to a high and slow declining prevalence of TB risk factors in the male population. However at the moment, there is limited data to fully support this argument, and so detailed analyses concerning trends for TB risk factors in relation to the TB CNRs are needed in future.

3.5.4.4. CNRs for smear positive pulmonary TB by age group

I found that the CNRs for smear positive pulmonary TB were highest in the age group 25-44 years, followed by 45+ years. The dominance of TB in these age groups might be because in Khomas region the HIV/AIDS prevalence among both men and women is highest in the age groups between 25-49 years, furthermore, these are also the age groups characterised by high percentages of heavy alcohol consumption and smoking (49). The high rates observed in the age groups 25-49 years in my study are similar to those of Noppert *et al*. in Zimbabwe (95), Dangisso *et al*. in Ethiopia (83) and Shrestha *et al*. in Nepal (84).

I observed a significant decline in the trend for CNRs in age groups from 25+ years , but the trend for the younger group (0-24 years) was not significant. However, caution must be taken when interpreting these trends as they are for smear positive pulmonary TB only, and do not reflect the burden as measured by all forms of TB. It is possible that the observed results may have been due to lack of power, as the numbers were smaller, given that children (e.g. younger than 15 years) are generally rarely diagnosed with sputum smear positive TB. With improvements in diagnostics, such as the use of gene-xperts in Namibia (53), further studies are required to accurately analyse paediatric TB epidemiology. A Chinese study reported that trends for smear positive pulmonary TB among cases aged 0-17 years declined significantly by 22.2% during the period 2005 to 2012 (109). Shrestha and colleagues in Nepal reported a decline from 0-44 years but they did observed an increase in the older age groups (84). Shrestha *et al*. suggested a possible age shift in TB occurrence in Nepal in the future. I found that there was a significant change in the trend for the oldest age group (45+ years) in Khomas having declined at an annual percent change of -10.2% from 2006 to 2009 and thereafter by -14.4% from 2009 to 2014. At the national level, a, significant change in the trend was observed for the youngest age group (0-24 years), having declined at an annual percent change of -5.7% from 2006 to 2009 and thereafter the trend increased slightly by 1.2% from 2009 to 2014, but this increase was not significant. These may also be chance results, or alternatively the results suggest that there were differences in TB risk factors by age groups. At present, region specific data (concerning TB risk factors) in the demographic health surveys are not split by age or gender (49, 138), hence there is need to further explore differences in the prevalence of TB risk factors by age and sex, particularly in high burden regions such as Khomas, and so my study provides a good baseline for future studies.

3.5.4.5. CNRs for smear negative pulmonary TB

I observed that the CNRs for smear negative pulmonary TB initially decreased by 14% from 1997 to 2000, then increased significantly by 47% per year between 2000 to 2004 and thereafter declined significantly by an annual change of -29% between 2004- 2015. In the earlier years, my data mostly showed that more cases were classified as smear negative during than smear positive. This may have been due to limited microscopic equipment’s in the earlier years, which possibly imply that the increase from 2000 to 2004 might indicate true increase in transmission but the possibility of misdiagnosis cannot be ruled out. Improvement in diagnostics and trained health care workers over time (such that more cases were now classified as smear positive) may explain the rapid decline in the trend from this indicator after 2004. Another possible reason for the decline may be due to a change in clinical practice, as cases with no smear results were previously classified as smear negative, but this was changed and such cases are now reported as smear not done (127).

The declining trend I observed is consistent with what was found in other studies. A study in Iran found that CNRs for smear negative TB declined by -3.6% per year from 2001 to 2015, (107). Adejumo *et al*. in Lagos Nigeria showed that trends declined from 38 to 23 per 100 000 population from 2011 to 2015 (99). In Nepal, Shrestha *et al*. showed that CNRs declined from 39 to 35 per 100 000 population during 2000 to 2008 (84). The trend in my study is not in agreement with that reported in Tao *et al.'s* study in China where they reported that CNRs for smear negative TB increased between 2005 to 2017, and they attributed the increase to improved diagnostics (109). Similarly, in Ethiopia, Dangisso *et al*. and Hamusse *et al*. both reported increasing trends in CNRs for smear negative TB, and attributed the increase to improvement in diagnostics (83, 100).

3.5.4.6. CNRs for extra-pulmonary TB

I found that in Khomas, the trend for extra-pulmonary TB increased significantly by an annual change of 26% between 1997-2000, then declined by -1.4 between 2000-2008, and subsequently declined significantly at an annual change of -9.4% between 2008-2015. The initial increase may have been due to true increase, but could also have resulted from misdiagnosis of cases in the past resulting from poor diagnosis. Since extra-pulmonary TB is known to be common in people living with HIV/AIDS (139), the decline observed in the recent years (2008 to 2015) may have resulted from the reduction in HIV/AIDS associated TB. The declining trend is similar to what was observed by Arsang-jang *et al*. in Iran, where they documented a decline of -3.4 per year between 2001 to 2015(107). The differences in the magnitudes might be due to the fact that the rates in Arsang-jang *et al*. were generally low over time, whereas in my study, I observed high and fluctuating rates. This discrepancy between countries perhaps suggest differences in case ascertainment methods or variations in prevalence and trends in TB risk factors.

The declining trend in my study is not consistent with what was observed in other studies. For instance, Adejumo in Nigeria reported low but increasing trend from 1.6 to 2.2 per 100 000 population during the years 2011 to 2015 (99). Shrestha *et al*. in Nepal showed that trends increased from 25 to 21 per 100 000 population during the years 2001 to 2008 (84). Dangisso *et al*. showed that trends increased from 18 to 26 per 100 000 population from 2003 to 2012 (83). Adejumo *et al*. suggested that the increase may be due to improvements in diagnosis of TB (99), while others suggested it may be due to improved access (83). In my study, I observed that the CNRs increased from 66 in 2014 to 86 in 2015 per 100 000 population, and this may be due to the use of gene-xperts in Khomas.

3.5.4.7. Trends concerning TB and HIV/AIDS related indicators

I found that the percentage of TB cases with known HIV/AIDS status increased from 18% in 2006 to 96% in 2015, representing a significant increase of 14% per year. The rapid increase in testing may be attributed to the guideline which recommends that all TB cases be tested for HIV/AIDS (127, 134). Similarly, patients under HIV/AIDS care are screened for TB during their routine treatment monitoring visits (53). Other studies have also documented an increase in percent of TB patients with known HIV/AIDS status over time (93, 105, 114). In particular, Charles *et al*. showed that an increase from 67% in 2010 to 90% in 2015 (114). Wu *et al*. reported an increase from 14% in 2011 to 56% in 2015 (105) and in Wobudeya *et al*. found that rates rose from 59% in 2011 to 100% in 2015 (93). Since the period examined was similar among those studies, the differences in proportion may suggest variation between countries regarding the time and scale integration of TB and HIV/AIDS services.

In my study, the percentage of TB cases infected with HIV/AIDS declined from 48% in 2006 to 44% in 2015, but this decline was not statistically significant when considering the whole period from 2006 to 2015. However, from 2009 to 2015 a statistically significant decline at an annual average of -8.0% was observed. In Namibia, HIV/AIDS patients are provided with Isoniazed Preventative Therapy (IPT) for at least nine months, to prevent occurrence of TB, this might explain the reduction in the percent of co-infected patients (134). Since the decline in HIV/AIDS prevalence was minimal (from 48-44%), yet the TB CNRs for all forms declined rapidly from 889 in 2006 to 400 in 2015 per 100 000 population, suggest the role that other factors might influence the TB burden in the region. Using the NDHS data, there is need to quantity the attributable risk of other factors to the epidemiology of TB in Namibia.

Other studies have also observed marginal declines in TB and HIV/AIDS co-infection rates. For instance Charles *et al.* reported a decline from 20% in 2010 to 16% in 2015 (114). Adejumo *et al.* the reported a significant decline from 21.9% in 2011 to 19.2% in 2015 (99).

Wobudeya *et al.* also observed a decline from 38% to 35% but this was not statistically significant. Wobudeya *et al.* further showed that HIV/AIDS prevalence among TB cases varies by age groups (93). During phase one, it was not possible to analyse TB and HIV/AIDS by age or sex, however it is documented that the general public's knowledge of HIV/AIDS and uptake of HIV/AIDS testing services differs by sex, locality and age group (49). The analysis conducted during phase two permitted the examination of TB and HIV/AIDS related indicators by sex, as I will show in the next chapter.

In summary, Namibia aims to have a reduction of 34% in the incidence rate between 2015 and 2022 (53). According to the results of my study, the trend in CNRs declined significantly at an annual average of -9.3% and -6.7% in Khomas region and nationally, respectively between 2004 to 2015. Given that Khomas contributes the majority of cases to the national burden, if the declining trend in Khomas continues beyond the year 2015, achievement of that target might be indeed possible. The End TB strategy (140) targets a reduction in TB incidence of 20%, 50%, 80% and 90% by years 2020, 2025, 2030 and 2035 respectively. The annual percent decline presented in my study for all forms of TB CNRs at a national level seems to suggest that Namibia is doing its part in ensuring that this collective global target is achieved. However, trends in Namibia must be interpreted with caution, because not all cases may be detected, and those diagnosed in private health clinics might not have been reported. Studies conducted in other countries have shown increasing trends in TB CNRs after introduction of improved diagnostics and more intensive community based-health services (83, 98, 114). In the current national TB strategy (53), there are eight TB specific strategies including improved testing of presumptive TB cases, improved treatment outcomes, infection control and data recording. However, in line with the End TB strategy (140), there is a need for the TB programme to consider other strategies such as improved case finding through continuous systematic screening of at risk groups (prisons, TB contacts) and through integration of TB services within other programmes such as maternal and child health services. Moreover, the TB programme needs to be strengthened to find innovative ways of engaging local communities and also to mobilise involvement and support from the private sector, so that TB is seen not only as a health issue but also a societal issue. In addition, the TB programme should mobilise resources and liaise with local academic institutions in conducting much needed epidemiological research, to allow for better understanding of the local changing disease epidemiology, and to subsequently guide control interventions.

Chapter 4 : An analysis of the spatial and spatiotemporal distribution of TB notifications in Khomas

4.1. Introduction

Results from phase one showed that the trend for all forms of TB CNRs in Khomas declined significantly from 2004 to 2015. The TB and HIV/AIDS co-infection rate also marginally declined, although only not significantly from 48% in 2006 to 44% in 2015. In order to further enhance our understanding of TB in the region, I conducted a study to investigate the spatial and spatiotemporal distribution of notified TB cases in Windhoek, which contains 95% of Khomas's total population (51). Work conducted during phase two specifically aimed to investigate the potential occurrence of TB hotspots and population level socio-demographic determinants of the disease distribution. In addition, the study aimed to investigate the temporal changes of TB notifications as well as TB and HIV/AIDS indicators in identified TB hotspots (if found). A hotspot/cluster refers to an area with greater clustering of a particular event at a particular time (141). In several countries, TB hotspots have been associated with various area level factors such as population density (26), socioeconomic conditions (24), household overcrowding (27) and HIV prevalence (28).

In the subsequent sections, I present a literature review (Section 4.2), methods (Section 4.3), results (Section 4.4) and a discussion of the findings (Section 4.5).

4.2. Literature review

Globally, a wealth of primary studies analysed the spatial and/or spatiotemporal distribution of TB notifications. However, few studies have been conducted to review the methods and evidence documented in the literature. Recently, Shaweno *et al*. and Rosli *et al*. both conducted a systematic review of studies which used spatial and spatiotemporal analysis methods used to investigate the TB burden (16, 18). Their review involved many studies which were not limited to any country. However, one of these reviews included studies that focused on multiple dimensions (i.e. notification and treatment outcomes), making it difficult to synthesise the evidence (16). Moreover, both reviews did not present in detail the population level determinants for the disease distribution.

A review which focuses on studies that analysed the spatial or spatiotemporal distribution of TB notifications, and which also examines population level determinants of the disease distribution would make a meaningful contribution to the TB literature, and so this literature review was conducted for that purpose. Although I did not undertake a systematic review, I initially used search terms to locate studies in the literature, and over the course of the PhD period, new studies were added based on relevance. The specific objectives of this review were:

1. To critically review the spatial or spatiotemporal analysis methods used to study the distribution of TB notifications in the general population.
2. To critically review population level socio-demographic determinants of the disease distribution, and identify potential factors for inconsistencies in study findings (if any).

4.2.1. Literature search

I searched for relevant literature from Scopus, Embase, Web of Knowledge and Google Scholar. Some studies were obtained through reading reference lists of obtained articles. Studies were included if they analysed the spatial or spatiotemporal distribution of TB notifications for either pulmonary or extra-pulmonary TB in the general population. I only reviewed primary studies published in peer-reviewed journals and in English. I included studies regardless of location and their spatial/spatiotemporal period. Studies were not reviewed if they exclusively analysed the distribution of other TB dimensions such as TB mortality or other treatment outcomes. Moreover, articles were not reviewed if they exclusively reported the distribution of specific TB cases such as MDR, relapse TB or those conducted in congregate settings.

4.2.2. Literature synthesis

In the results section of the review, I first describe the studies in relation to their location, spatiotemporal length and unit of analysis. I subsequently present and critically appraise the methods studies have used for spatial or spatiotemporal analysis. I follow with a narrative summary detailing specific socio-demographic factors studied in relation to TB distribution. This was followed by an appraisal documenting the potential factors for inconsistencies in the literature. I conclude the review with a brief summary, which also explains how my study contributes to the current body of knowledge.

4.2.3. Review results

4.2.3.1. Description of studies

Forty-six studies were reviewed and are summarised in detail in Appendix D. The majority of studies (n=17) were conducted in Asian countries (23-25, 142-155), fourteen studies were from South America, mainly from Brazil (26, 27, 156-167), eight from Africa (20, 22, 168-173) and six from Europe (28-30, 141, 174, 175) and one from North America (176).

The spatiotemporal length varied greatly between studies, with the longest being twenty years (1991 to 2010) in a Brazilian study (157), followed by a Singaporean study covering seventeen years (1995 to 2011) (153). Two studies, one from Cameroon (169) and another from The Gambia (22) were conducted over just one year.

Twenty four studies analysed data at county, provincial, district or zonal levels (22-26, 28, 30, 141, 142, 144, 146-148, 150, 152-155, 160, 167, 168, 173-175). In the remaining twenty two studies, analyses were based on neighbourhoods or lower level census tracts (20, 27, 29, 143, 145, 149, 151, 156-159, 161-166, 169-172, 176).

4.2.3.2. Spatial and/or spatiotemporal analysis methods

Of the reviewed studies, seven only produced maps of disease rates without the use of a particular statistical method for spatial or spatiotemporal analysis (24, 25, 147, 149, 152, 165, 171). Although a map is usually the first step to examine the disease distribution, depicting disease maps without statistical analysis is a practice criticised, as the development of a map can entirely dependent on what the researcher wants to show (177). Therefore, to avoid subjective conclusions, the majority of studies have used statistical methods for spatial or spatiotemporal analysis (20, 22, 23, 26-30, 141, 142, 144-146, 148, 150, 151, 153-174, 176). I will now discuss the common methods used in the literature highlighting the strengths and weaknesses of individual methods.

4.2.3.2.1. Moran's I statistics

Twelve studies exclusively used Moran's I statistics for spatial analysis (26, 27, 158-163, 167, 170, 173, 176). For instance, in Brazil, Harling and Castro used the Global and Local Moran's I statistics to study the spatial distribution of TB in Brazil from 2002 to 2009 (26). In Morocco, Sadeq and Bourkadi recently used the Global and Local Moran's I statistics to study the distribution of TB from 2011 to 2014 (173). In Sheka zone, Ethiopia, Shaweno *et al*.

used the Global Moran's I to describe the geographic distribution of TB from 2010 to 2014 (170). The concept of Moran's I is based on Tobler's first law of geography which states that "everything is related to everything else, but near things are more related than distant things" (178). The Global Moran's I statistic is used to assess the spatial autocorrelation of an attribute across the study region (179, 180). Spatial autocorrelation refers to the spatial relationship of the same attribute across different spatial locations (179) The Global Moran's I is an inferential statistics based on the null hypothesis which states that the outcome being investigated is randomly distributed across the study region (179). The advantage of the Global statistic is that it can be used to assess the presence, strength and direction of the spatial autocorrelation, and the results can be adjusted for multiple testing (179).

The Local Moran's I is based on the same concept as the global test, but instead of analysing the pattern across the entire region, it is used to study the pattern within specific locations (180). The Local Moran's I is known to have power to detect highly localised disease hotspots over a large area and can detect outliers (177). The advantage of the Moran's I statistics is also that results can be adjusted for multiple testing. However, a limitation of these statistics is that they are not able to analyse spatiotemporal analysis, in other words they cannot simultaneously assess the occurrence of an attribute in terms of both space and time (142). For instance in all the studies highlighted above, spatial analyses were conducted separately for each year. In addition, Moran's indices are not suitable for small samples (that is datasets with few locations) (169). Furthermore, depending on the defined spatial relationship between areas, Moran's Indices may ignore non-adjacent areas. In other words the statistics may ignore locations sharing no land boarders with other locations (177).

4.2.3.2.2. Getis &Ord's G statistic for local clustering*

Some studies used Global Moran's Index to study the spatial autocorrelation and they analysed local clustering using either Local Moran's I or Getis & Ord's G* statistic or both (23, 145, 146, 168). For instance, Alene *et al*. in Ethiopia and Wubuli *et al*. in China used Global Moran's I to detect the overall spatial distribution of TB, and subsequently used both the Local Moran's I and Getis & Ord's G* statistic to identify hotspots (23, 168). In other Chinese studies, Liu *et al*. and Guo *et al*. used Global Moran to study the distribution of TB, but for identification of hotspots, they only used Getis & Ord's G* statistic (145, 146). Similar to the Local Moran's I statistics, the Getis Ord's G* statistics is also based on the null hypothesis which states that there is complete randomness of an attribute across locations (179). The difference between the two statistics is that Getis Ord's G* statistics provides further information about the stability and intensity of the identified cold/hotspots by revealing the Z score as well as the varying confidence levels at which cold/hotspots were identified (23). However, Getis Ord's G* statistic is also not able to perform spatiotemporal analysis and not suitable for small samples. For example, Guo *et al.*'s study involved only 31 province's in China (146), and they only used the Global Moran's I and Getis & Ord's G* statistics for spatial analysis, both of which are necessarily not appropriate for small samples (few locations). Therefore, in that study, the use of other methods such as scan statistics would have been useful to validate results.

4.2.3.2.3. Kulldorff's scan statistics

Fourteen studies exclusively used scan statistics to study the distribution of TB notifications in various countries (22, 28, 30, 141, 142, 148, 151, 154-157, 164, 169, 174). Unlike Local Moran's I and Getis & Ord's G*statistics, scan statistics can be used to determine the presence of spatial, temporal or spatiotemporal clusters of an attribute across geographical locations (181). For example, in Cameroon, Yakam and colleagues utilised purely spatial scan statistics to analyse the distribution of pulmonary TB in Doula over a one year period (169). A study conducted by Nunes *et al*. in Portugal, used space-time scan statistics to investigate the spatiotemporal distribution of new cases of TB from 2000 to 2004 (141). Touray *et al*. and Tiwari *et al*. utilised both the purely spatial and space-time scan statistics to study the distribution of TB notification in The Gambia and in India (22, 155). One of the advantages of scan statistics is that they are able to study the distribution of an attribute simultaneously across time and space and can adjust for multi-testing (181). Moreover, scan statistics can detect the primary clusters and subsequent clusters (i.e. second, third clusters) and are able to adjust for covariates (177). This method has also the advantage of producing the relative risk of the disease for each identified cluster. Also, scan statistics is a preferred spatial analysis method of identifying clusters in less populated regions (182). However, the disadvantage of this methods is that it is prone to revealing clusters that are larger than they are in reality (171, 183) and cannot detect global clustering like the Global Moran's I.

Given that individual methods have limitations, the use of two or more methods for data analysis has been encouraged(20, 184), and indeed of the studies reviewed, some used either Local Moran's Index or Getis & Ord's G*statistics together with scan statistics (20, 143, 150). In particular, Dangisso *et al*. used the Getis & Ord's G*statistic as well as purely spatial and space-time scan statistics to analyse the local distribution of smear positive pulmonary TB cases in Sidama, Ethiopia, from 2003 to 2013 (20). In China, Wang *et al.* also utilised Getis

& Ord's G*statistic and the space-time scan statistics identify local clusters of TB in Linyi city from 2005 to 2010 (143). Hassarangsee and colleagues used Local Moran's I and the purely spatial scan statistics to study local clusters of TB from 2004 to 2008 in Si Sa Ket province, Thailand (150).

4.2.3.2.4. K-function method

K-function is used to detect spatial autocorrelation across the study region (185, 186). Similar to the Global Moran's I, the statistic is also based on the null hypothesis that the attribute is randomly distributed in space. The K- function method uses distances between locations in order to calculate the intensity of cases and determine the distance at which clustering was greatest (186). For example in a Singaporean study by Das *et al*., K- function method was used to analyse the spatial distribution of TB between 1995 to 2011 (153). Munch *et al*. in South Africa used the same method to study the degree of clustering of pulmonary TB from 1993 to 1998 in two Cape Town suburbs (172). The K-Function method has an advantage of allowing researchers to examine the statistical significance of the disease distribution across a range of defined distance values simultaneously, hence avoiding the problem of multiple testing (185, 187). One of the major limitation of the method is that it required a pre-defined number of bandwidth to calculate the relative risk, and the usage of different bandwidth may results in different results (185).

4.2.3.2.5. the k-nearest neighbours method

Two studies used the k-nearest neighbours method for hot spot analysis (166, 172). In particular, Munch *et al*. in South Africa used the K-Function method to assess global clustering and subsequently used the k-nearest neighbour algorithms to identify hotspots (172). Fusco used the k-nearest neighbour algorithms method to study local clustering of TB in Sao Paulo from 2008 to 2013(166). The k-nearest neighbour method is used to detect both the global clustering and to identify local clusters (186). When detecting hotspots, kernel intensity uses a range of defined distance values simultaneously, hence it is known to be flexible in that regard than scan statistics (186). However the drawback of this method is that the choice of the distance value (k) can be biased (188). For example, Fusco *et al*. considered a radius of 1000 metres between cases, but they did not provide a justification for using that value.

4.2.3.2.6. The Besag and Newell method

One study used the Besag and Newell method to detect local clustering. In Particular, Álvarez-Hernández *et al*. utilised the Global Moran's Index to determine the overall pattern of TB in Hermosillo city in Mexico between 2009 to 2010, and subsequently the used Local Moran's I and the Besag and Newell method to identify local clusters (176). The Besag and Newell is a spatial analysis methods developed by Besag and Newell to identify clusters (189). As with the Getis Ord's G* and scan statistics, the Besag and Newell method also has an advantage of producing estimates for the identified clusters (182), but its disadvantage is that it does not correct for multiple testing (189). Moreover, according to Costa and Assuncao (182), the Besag and Newell method requires setting several parameters which can influence results, and so it is argued that the results of this method are more subjective compared to those produced by other methods such as scan statistics. For example, Álvarez-Hernández *et al*. highlighted that one of their study limitations was regarding the parameter settings, and for that reason they suggested the use of other spatial analysis methods, particularly scan statistics, to validate their results.

4.2.3.3. Socio-demographic determinants of the spatial distribution

Of the studies reviewed, several have investigated population level determinants of the disease distribution, and so I have critically reviewed the findings from studies in the narrative section below. I was particularly interested in the association concerning measures of education, employment, population density, household overcrowding and HIV/AIDS prevalence. The studies assessed multiple factors, and so they will appear on different sections of the review as long as they have examined that particular factor.

To avoid repetition, an appraisal concerning the potential factors underlying inconsistencies in between studies are provided in the subsequent section (section 4.2.3.4).

4.2.3.3.1. Measures of education at population level

Nine studies reported a quantitative association between education related measures and TB notification/incidence rates (24, 27-29, 146, 156, 158, 163, 168). In particular, Alene *et al.* in North Gonder, Ethiopia used Poisson regression to analyse the distribution of 2240 new paediatric TB cases notified between 2013 to 2016 (168). Alene *et al.* found that high paediatric TB incidence was positively associated with high percentage of illiterate people (RR=1.47; 95% CI: 1.02-2.06). Magalhaes and Medronho in Rio de Janeiro, Brazil used linear regression to analyse notified TB cases from 2005 to 2013 (163). They found that there was a positive association between high TB rates and high proportion of illiterate people in the population. Similarly, Harling *et al.* analysed notified TB cases in Fortaleza city, Brazil from 2007 to 2014 (158). Harling *et al.* reported that the high TB burden was negatively associated with high percent of literate people during the years 2007-2014 (RR=0.59; 95% CI: 0.44-0.80). Alene *et al.* speculated that a high proportion of illiterate people suggest poor knowledge about TB transmission and protective measures (168).

In other studies, the association between measures of education and TB burden was not established (24, 27, 29, 146, 156, 159), although the lack of association in some of these studies may have been due to methodological issues. For example the de Abreu *et al.* study which was conducted in Divinopolis, Brazil may have been under powered as it had a relatively small number of TB cases (n=309) (156). A study from Brazil by Castro *et al.* in Manaus municipality from 2008 to 2013 also reported no association between the percentage of illiterate population aged at least 18 years and TB burden(27). However, in that study, only municipalities with quality surveillance TB data were included, and so the lack of association may have been due to a selection bias, as areas with poor surveillance data could have been those with a high TB burden. The authors did not provide further details about the excluded areas.

Another study from Rio de Janeiro by Pereira *et al*. found no association between the percent of people aged above 15 years who were illiterate and incidence of TB (159). The Pereira *et al*. study was conducted in Rio de Janeiro just like the Magalhaes and Medronho study (163). Since Pereira *et al*. study was conducted at neighbourhood level whilst Magalhaes and Medronho study was conducted an census tract, the difference in findings may suggest the effect that that the spatial unit of scale on results. A study by Pang *et al*. in Hong Kong also found no association between the percent of population with lower education level and TB rates (24). The lack of association may be due to the fact that, in that study both the dependent and independent variables were transformed through ranking, hence there is possibility that information may have been lost as a result of the transformation.

In summary, the majority of studies reported evidence which suggests that there is no association between TB burden and measures of education at population level. However this may have been due to methodological issues as highlighted above and also summarised later in section 4.2.3.4.

4.2.3.3.2. Population level unemployment rate

Six studies examined the association between the TB rates and unemployment rate (27-29, 168, 172, 175). In particular, Kiestemann *et al.* in Cologne Germany used Poisson regression to analyse 2903 TB from 1986 to 1997 (29). They reported a positive association between high TB incidence rates and high unemployment rates. Castro *et al.* in Manaus, Brazil, reported that the risk of TB increased about seven times per unit increase of unemployment rate, defined as the proportion of people aged 18 year or older who were unemployed (27). In addition, Munch *et al.* in South Africa used Poisson regression to analyse 1128 cases notified from 1993 to 1998 in two Cape Town suburbs (172). They reported a weak but statistically significant positive association between the high percentage of unemployed people and high TB incidence (RR=1.02; 95% CI: 1.01-1.02). Their weak association may have been due to few TB cases analysed, implying lack of power.

Sousa *et al.* used national data for TB cases notified from 2002 to 2012 in Portugal (175). They reported that an increase of 1000 unemployed persons per 100 000 population was significantly associated with one TB case per 100 000 population. In contrast, another Portuguese study by Couceiro *et al*. found that unemployment rate and TB burden were positively correlated during their univariable analysis, but the association was not maintained in their multivariable analysis (28). The inconsistency between the two Portuguese studies may be because they were conducted at different spatial scales. However, the conflicting results may also be because Couceiro *et al*. adjusted for immigration which according to them is a driving factor for TB in Portugal, whereas Sousa *et al.* did not adjust for immigration. Alene *et al.* in Ethiopia adjusted for a number of factors in the Poisson regression and found no association between TB incidence and unemployment rate (168). The definition of unemployment used in Alene *et al.* study may have been a problem as those classified as unemployed included children as young as 10 years old, and so this may have underestimated the unemployment rate in areas which may have high TB rates and also high percentage of young population, and this is expected in developing country such as Ethiopia.

In summary, I found that the majority of studies which examined the association between TB and unemployment rate at population level generally produced consistent evidence suggesting that employment is a risk factor for TB burden. The increased risk is attributed to poor socio-economic conditions of unemployed people such as poor nutrition, poor access to healthcare (175). However, the results of some studies may have been due to unmeasured confounding.

4.2.3.3.3. Measures of household size

Seven studies examined the association between household overcrowding and TB burden (26-28, 158, 159, 163, 168). A neighbourhood level study in Manaus, Brazil, reported a positive association between TB incidence and average number of people per room (27). A study by Couceiro *et al.* in Portugal also reported a positive association between high incidence of pulmonary TB and high percentage of overcrowded accommodations in populations (28). Pereira *et al.* in Brazil found a positive association between high TB notification rates and average household crowding, defined as proportion of households with two or more people per sleeping room (159). In their nationwide study, Harling and Castro study in Brazil also reported a positive association between TB notification rates and the percentage of household with more than 2 people per bedroom (26). However the reported association in Harling and Castro study (IRR=1.37; 95%CI: 1.35-1.39) may have been confounded by socio-economic variables such as education and unemployment rates which were not measured in their study.

In other studies, the association between household overcrowding and TB distribution was not established. For example an Ethiopian based study by Alene *et al*. found no association between TB burden and the average number of people per household (168). Similarly, both Harling *et al.* in Fortaleza, and Magalhaes and Medronho in Rio de Janeiro found no association between measures of household overcrowding and TB notification rates (158, 163). The difference between studies have been due to the differences in measures of household overcrowding. For example, some studies used average household size and others used average people per sleeping room. Studies that used average people per room tended to report a significant associations compared to those that used average household size.

In summary, of studies which documented an association between TB burden and measures of household size, the majority reported evidence suggesting that household size at population level is a risk factor for TB. In some studies it is explained that overcrowding at household level increase greater contact between people and therefore likelihood of TB transmission (27, 159).

4.2.3.3.4. Area level population density

Eleven studies analysed the association between area level population density and TB burden. Of these, only one Brazilian study by Rodrigues *et al*. found a weak but significant association, suggesting that increase in population density is a risk factor for TB burden (160).

However in that study, the association found may have been overestimated since there was no adjustment for socio-economic confounders (160).

The majority of studies reported no significance relationship between population density and TB burden. In particular, a study conducted in Doula, Cameroon, based on 2132 cases, found that there was no association between area level population density and TB incidence rate (169). Using linear regression, Silva *et al.* in Brazil analysed new notified TB cases between 2002 to 2012 and reported that there was no association between TB rates and census tract level population density (156). In Hong Kong, Pang *et al*. analysed 17 294 cases georeferenced to 400 district constituency areas and found no association between population density per kilometre square and TB notification rate (24). Pang *et al*. study adjusted for a number of family, ethnic and socioeconomic variables. Two Brazilian studies by Harling *et al*. in Fortaleza city (158) and Castro *et al.* in Manaus (27) also found no associations between TB rates and area level population density.

In China, Guo *et al*.'s study based on 9 597 884 TB cases notified between 2005 to 2013, across 31 provinces, found an association at univariable level, which was not maintained in their multivariable analysis (146). Similarly, Shaweno *et al*. conducted a study based on 1683 cases notified from 2010 to 2014 in Sheka, Ethiopia, and found the association between TB incidence rate and population density at univariable level, but this was not maintained at multivariable stage (170). In South Africa, Much *et al.* in Cape Town used Poisson regression and found no association between census enumeration area population density and TB case load (172). Similarly, as study in Morocco (173) and another in Germany (29) also found no effect of population density on TB notification rates.

In summary evidence from the majority of studies imply that population density is not a risk factor for TB burden. The majority of studies found the association at univariable level, but this association was not maintained at multivariable level, and this highlights the importance of adjustment of confounders.

4.2.3.3.5. HIV/AIDS prevalence

Two studies in Portugal by Couceiro *et al.* and Sousa *et al* (28, 175) both reported an increase in the risk of TB incidence with a unit increase in AIDS incidence per 100 000 population. In contrast, two studies from Brazil conducted by Harling *et al.* and Harling and Castro found no association between AIDS incidence and TB distribution (26, 158). There were some similarities in terms of units of scale and time period between these four studies, and all of them adjusted for a number of confounders (i.e. socio economic variables). The fact that the Portuguese studies found an association while the Brazilian studies not find an association, may perhaps be due to differences in setting specific HIV/AIDS burden. In Morocco, Sadeq and Bourkadi, found that one area (eastern part) high rates of TB were associated with high AIDS incidence rates but this was not observed to be the case in another area (western area) (173). In Ethiopia, Shaweno *et al.* found that there was no association between TB and HIV/AIDS co-infection rates and TB incidence (170). The differences between studies may also have been due to the different statistical test used. For example, some studies used regression models for count response variables (26, 158), other studies used linear regression (28, 170, 175) while in the Moroccan study, Kendal tau correlation test was used to assess associations (173).

In summary, the evidence related to area level HIV/AIDS burden and TB burden as documented in the reviewed studies is inconsistent. This may have been due to the fact that only few studies reviewed assessed this relationship, but the differences may also have to variations in HIV/AIDS burdens or the different statistical tests used.

4.2.3.4. Study appraisal: potential factors for heterogeneity in evidence

Studies reported inconsistent findings regarding population level socio-demographic determinants of the spatial distribution. The variation in the findings may partly be explained by the use of varying exposure variable definitions, statistical analysis, confounding, study location and units of analysis. I will now discuss these factors below.

4.2.3.4.1. Varying definitions of exposure variables

The inconsistencies in the literature may be due to the different definitions used for exposure variables, particularly concerning education level and household overcrowding. For instance, with regards education level, Alene *et al*. used the percentage of people aged 5 or older who never attended school (168). Castro *et al*. used the percentage of people aged at least 18 years who could not read or write (27). In China Pang *et al*. used the percent of population with elementary education or no education (24). In terms of household overcrowding , two studies used the average people per household (163, 168), four studies used people per sleeping room (26, 27, 158, 159). Studies which used average people per room all reported an association with TB burden (27, 158, 159), whereas those that reported average household size did not find an association (163, 168).

There was generally consistency between studies concerning the association between TB rates and employment status and population density. For example, four studies which reported the relationship between unemployment and TB burden used the unemployment rate as an independent variable (27, 29, 172, 175), and these studies produced consistent findings showing that a high unemployment rate is associated with a high a high TB burden. Similarly, studies that examined the relationship between population density and TB defined the population density in a similar way, and they generally revealed findings which suggested that the association between population density and TB rates is due to unmeasured confounding.

4.2.3.4.2.   Sample size and statistical analyses

Another possible reason for the inconsistency between studies may be due to the fact that analysis in some studies were based on few cases, and these studies generally tended to report no associations. In addition, the inconsistencies may have resulted from the use of different statistical methods, and not all studies reported how the assumptions of the regression models were met. Some of the studies modelled the relationship using linear regression models (24, 28, 159, 163), whereas other models for count response variables , specifically the Poisson regression (27, 146, 160, 168, 176) and negative binomial regression (26, 158).

4.2.3.4.3.   Confounding

Confounding is a general problem for observational studies. All these studies conducted explanatory analysis, in other words there was no main predictor variable, but all variables were treated at independent variables. However, in some studies, multivariable analysis were based on few variables only, implying that associations found may have been due to unmeasured confounding. This may possibly be due to the lack of population level data at the considered units of analyses.

For instance, a study conducted by Rodriquez *et al*. only considered the following variables in their multilevel Poisson model, sex, age group, diagnostic year and population density (160). Similarly a study conducted in Mexico only included five variables in their multivariable analysis (Income level, education, housing quality, overcrowding and car availability) (176). In Morocco, Sadeq and Bourkadi only considered the following variables in their multivariable analysis, living area, mean temperature, mean rainfall, population density and AIDS notification rate (173). Studies conducted in other countries such as South Africa (172), Brazil (156, 162), China (23) and Ethiopia (170), have also only considered few variables in their analyses, and so it is possible that some of the associations found may have been due to unmeasured confounding.

In contrast, multivariable analysis in other studies were based numerous factors in their multivariable analysis. For instance, in a study from Ethiopia, Alene and colleagues considered a number of variables related to population migration, schooling, urbanicity, unemployment, household crowding, population density, kitchen location, usage of charcoal, wood, dung, temperature and rainfall (168). Similarly, a study from Brazil, Magalhaes and Medronho considered a number of variables including household size, family income, the proportion of head of household income, average income of head of family, the proportion of illiterate people; proportion of households with water supply, proportion of households with bathroom/sanitation and sewage connection, the proportion of households with garbage collection, and race and the proportion of people who live alone (163). In Portugal, Sousa and colleagues considered variables such as the proportion of working population aged 15-64, proportion of elderly >65 years, the proportion of unemployed, the proportion of existing inmates, prison overcrowding, HIV notification rate, use of alcohol, the proportion of physicians/surgeons and medical appointments (175). These studies which included numerous potential confounders may have produced more convincing results, than those were analyses were based on few variables.

4.2.3.4.4. Study location and units of analysis

It is possible that the contextual factors which vary between locations might explain the inconsistencies observed in the literature. The prevalence of risk factors such as HIV/AIDS, unemployment rate and environmental conditions or availability of basic services like schools and health services will vary between countries and over-time. For example, two studies from Brazil conducted during a similar period reported conflicting results with regards to the effect of illiteracy rate on the TB burden (27, 158). Similarly, two studies conducted in Portugal reported conflicting results regarding the effect of unemployment rate of the TB burden (28, 175).

The inconsistencies between studies may also be due to the varying units of analysis used in the literature. For example in Brazil studies conducted at national level found an association between education and TB burden (26, 158, 163), whereas studies conducted at lower levels did not establish this relationship in Brazil (27, 160). In addition, two studies conducted at lower level reported an association between population density and TB burden, whereas those conducted at the national level in other countries did not establish this association (24, 146, 173). According to Waller and Gotway, associations may differ when tested at different levels of analysis (modifiable area unit problem)(190), and ecological studies conducted at broader levels may tend to hide associations than those conducted at finer, lower levels (26).

4.2.4. Literature review summary

This literature review considered studies that analysed the spatial and/or spatiotemporal distribution of TB. The aim was to critically review the methods used to analyse the distribution of TB. Moreover, the review aimed to examine the findings concerning selected population level socio-demographic determinants for the TB distribution.

In terms of the methods used to study the disease spatial and/or spatiotemporal distribution, I found that studies used varying methods including Moran's Indices, scan statistics, K-function, k-nearest neighbours methods and Besag and Newell. I have highlighted some of the advantages and disadvantages of the individual methods. For example, studies which exclusively used Local Moran's Index for identifying clusters were limited as they could not provide information to describe the intensity of clusters and to conduct space-time analysis. Studies which used Getis & Ord's G*statistic were able to provide the intensity of clusters, but these studies unable to conduct space-time analyses. Studies which used the scan statistics were able to overcome that challenge these challenges, although some may have produced clusters that are larger than in reality. Studies which used K -function, k- nearest neighbours methods and the Besag and Newell methods may have produced biased findings as these methods require careful consideration of parameters, and therefore are prone to revealing subjective conclusions. For my own study, I used the Global Moran's I to determine the disease distribution across the entire region. To examine local clustering, I found kulldorff's scan statistics more appropriate to answer my study questions, especially since it produces the relative risk of the disease for each cluster identified. In attempt to validate my study findings, I also used Local Moran's I statistics to study local clustering. I have further expanded on these spatial methods in the method section of this chapter.

With regards to population level determinants of the disease distribution, I observed inconsistencies in the findings, particularly concerning measures of education level, household overcrowding and HIV/AIDS prevalence. While the individual study results may be true reflecting situations in specific settings, I have explained how the inconsistencies might have resulted from the use of different exposure definitions as well as variations in sample sizes, statistical tests, confounding, study location and units of analysis.

In summary, given the previous work presented in this review, this phase of my study aims to contribute to the literature in two ways. Firstly, this is to the best of my knowledge the first study to statistically examine the spatial and spatiotemporal distribution of TB in Namibia and to identify population level factors which may explain the disease distribution. Secondly, my study will provide further information about the temporal trends in the identified TB hotpots (if found).

4.3. Data and methods

4.3.1. Source of data

Data used during phase two were obtained from the Electronic TB Register (ETR). The ETR is an electronic version of the district TB register and has been in existence since 2006 (68). The ETR permits for the analysis of specific cohorts of TB cases and provides an opportunity to check for inconsistencies in the data (68). The transfer of information from the paper based district register to the ETR is a primary function of the District TB and Leprosy Coordinators (DTLCs). The ETR contains patient level TB information regarding the type of TB, TB/HIV/AIDS co-infection, treatment outcome and drug resistance. To date, the NTLP has achieved 100% coverage of the ETR across all health districts, and it is documented that there is generally good data completeness in the ETR in relation to the paper-based registers. However, in some districts, updating the ETR remains a challenge, and as data from paper based registries are not captured electronically in a timely manner (68). At present, the national annual reports are still produced based on the paper based reports, but over time it is envisaged that ETR will become the primary source of reporting (53).

TB cases diagnosed from 2006 to 2015 were considered in my study, as these were the available electronic data at the time of data collection (September 2016). I obtained the following information for each patient, year of notification, sex, age, residential address, type of TB (whether pulmonary or extra-pulmonary) and HIV status (positive, negative or unavailable). In the results section of this chapter, I have provided information regarding the completeness of the specific fields.

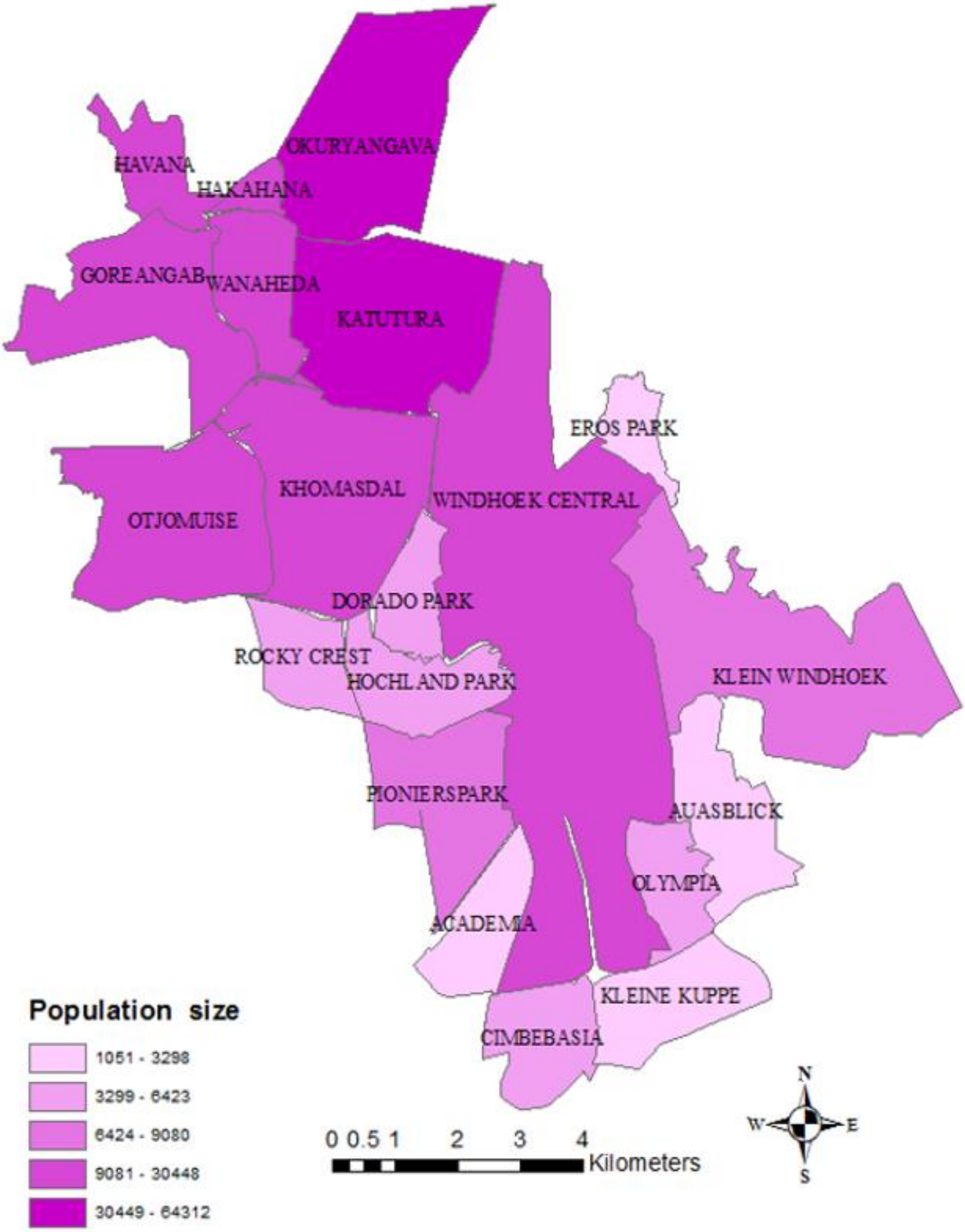
I made efforts to determine if the ETR include data for TB cases diagnosed in private healthcare facilities. In Namibia, private healthcare serves about 19% of the country's total population (53). The discussions I had with the DTLCs in Khomas as well staff from the national TB programme revealed that such cases are included in ETR because TB cases are referred from private to public services for free treatment and DOT. However, I did not find evidence to substantiate this claim, and thus could not quantify how many cases were referred from private healthcare during my study period.

4.3.2. Geocoding cases to Windhoek township areas

The unit of analysis for my study is the township level. As can be seen from Figure 4.1, the study included twenty main residential townships in Windhoek. According to the 2011 census, the median population size was 8055 for the townships. Because of the relatively small populations for two townships, Prosperita (n=114) and Lafrenz (n=36), these townships were merged with neighbouring townships. In particular, Prosperita was merged with Cimbebasia while Lafrenz was merged with Katutura. Auasblick had the smallest population (n=1051), while Katutura had the largest (n=64 312).

The patient's residential address was used to allocate cases to the respective township areas. Township hard copy maps with street names as well as shapefiles were obtained from Windhoek municipality. There were some challenges in geocoding cases to specific township areas, as the recording of the residential address in the ETR was not uniform. For example, some cases only had residential addresses indicated by a street name, without an indication of the township name. I therefore spent some time (from July to October 2016) to appropriately geocode all TB cases, one at a time. I also received assistance from staff at Windhoek municipality in instances where I could not locate specific streets (i.e. to identify the townships where some streets belonged, because not all streets were included in hard copy maps).

Figure 4.1. Population size for township areas in Windhoek according to 2011 census data



4.3.3. Inclusion and exclusion criteria

All forms of TB cases with a valid Windhoek residential address, and diagnosed with TB from 2006 to 2015 were eligible for inclusion in this study.

The study excluded all TB cases notified outside the timeframe (i.e. diagnosed in 2016), or those that had addresses belonging to other areas outside Windhoek. Furthermore, cases from prisons and those with missing or incomplete addresses were excluded. The exact number of inclusions and exclusions are shown in the results, Section 4.5.1.

4.3.4. Township level socio-demographic/economic data

I obtained census township level socio-demographic data from the Namibia Statistics Agency (NSA). Township populations for the years 2001 and 2011 were used to estimate total population for years before (2006-2010) and after (2012-2015) the 2011 census. ***Table 4.1. Socio-demographic variables analysed during phase two***Table 4.1 provides the definitions of specific socio-demographic variables considered.

Table 4.1. Socio-demographic variables analysed during phase two

Variable	**Definition**
Total population	Total number of people living in the township.
Average household size	The average number of people per household. A household is defined as a group of people, related or unrelated, who live in the same dwelling unit and share or have common catering arrangements (51).
School enrolment rate	Population aged 15 years above who had completed fulltime attendance at any regular public or private educational institution (51). This variable included people who have completed primary, secondary or tertiary education.
Unemployment rate	Economically active people aged 15 years and above who were unemployed (51)
Population density	The average number of people per square meter. The township area in square meters was calculated from township polygons in ArcGIS

4.3.5. Statistical analyses

4.3.5.1. Calculating crude and standardised CNRs

For each township, I calculated the year specific CNRs per 100 000 population using the formula below:

$$\textit{Crude rate} = \frac{\textit{Total number of notified TB cases per year}}{\textit{Total year specific population}} \times 100\,000$$

For age and sex standardised rates, I used the indirect standardisation method to minimise unstable rates which may have resulted because of the small numbers of cases and population size in some townships. The indirect standardisation method is preferred (over direct standardisation) in a situation where there are small numbers (150). Age and sex TB notification rates for Windhoek as a whole were applied to the age and sex population structure of the respective townships. The standardisation process resulted in the calculation of Standardised Morbidity Ratios (SMRs) for each township per year, and so I have presented these in the results section.

To investigate the spatial autocorrelation, for each year, the distribution of age and sex standardised rates was assessed by using the Global Moran's I. As described in Section 4.2.3.2, this index assesses the spatial dependence of the same variable across neighbouring locations. A score ranging between -1 to 1 is the assigned to describe the spatial distribution. When Moran's I is positive, it means that the neighbouring areas have attribute values that are similar, while a negative index score indicates that neighbouring locations have differing attribute values. An index around zero suggests a random pattern. I used the Queen's contiguity method to describe the spatial relationship between townships, and this imply that townships were classified as neighbours as long as they shared a common boundary or vertices (191). This spatial relationship was preferred considering that the townships varied in both sizes and shapes. I also raw standardised the rates in order to ensure that the township sizes did not affect the results.

To determine if there were TB hotspots, two methods were used as a way to validate the results, given the strengths and weaknesses in individual methods.

The first was the Local Moran's I, which classifies locations into five codes: High-High, Low-Low, High-Low, Low-High and not significant. A High-high code indicates a hotspot, which means the specific location has significantly higher values of an attribute and its surrounding locations have higher values. A Low-low code indicates a cold spot, which implies that a specific location has lower values of an attribute similar to its neighbouring locations. A High-Low code or Low-High code indicate an outlier, which means that that a specific location has values significantly higher (High-Low) or lower (Low-High) compared to its neighbouring locations. The significance of both Global and Local Moran's I statistics are based on Monte Carlo permutations tests (180), and results were adjusted for multiple testing. All analyses using the Moran's indices were conducted using Spatial Statistics Tool toolbox in ArcGIS version 10.5.

The second method used to identify hotspots was scan statistics using SaTScan software. SaTScan is a window based programme designed to analyse the spatial, temporal or spatiotemporal distribution, and to test their statistical significance (181). It can be used to model both discrete and continuous data (181). The software uses scan statistics to analyse the distribution of an attribute within a defined geographic region, and uses Monte Carlo simulations to identify clusters. For each identified cluster, the programme assigns a likelihood ratio based relative risk (RR) and a p-value (181). A p-value less than 0.05 indicates that the area in the scan window had a significantly higher risk than areas outside (indicating a cluster), and the RRs are used to evaluate the risk of TB in the identified clusters.

In my study, I conducted the purely spatial scan statistics and space-time scan statistics based on the discrete Poisson probability model. These were conducted as I wanted to observe the disease not just spatially, but also in terms of both space and time. I aggregated the data at township level and used sex and age as covariates. The three files required by SaTScan (cases, population and geographic files) were prepared for the analysis. Scan circles of various circular window sizes were executed to identify the most likely clusters. To avoid arbitrary choice of the maximum geographic cluster size, I used the default parameter which sets the maximum size of the spatial window as 50 percent of the population at risk. Similar settings have been used in other studies (20, 22, 151). The p-value used to assess the significance of the clusters were determined through 999 Monte Carlo simulations, and I reported the most likely clusters for each year from 2006 to 2015.

I further used scan statistics for retrospective space-time analysis of TB clusters. As has been done in similar studies (20, 143, 151), the minimum temporal cluster size was set at one year, while the maximum cluster size was set at 50 percent of the study period. All scan statistics analysis were performed in SaTScan version 9.4.4.

The association between the distribution of TB burden and population level socio-demographic factors was assessed using negative binomial regression with a log link function. I used the negative binomial after determining that the Poisson regression was not an appropriate model due to over-dispersion (variance greater than the mean). In the regression model, the response variable was the TB counts stratified according to age and sex. The independent variables were (average house size, percent who had attended school, percent unemployed and population density). The logarithm of township population size was used as an offset variable. The Relative Risks (RRs) were produced, indicating the change in the TB notification rate for every unit increase in each of the exposure variables. Associations were considered to be statistically significant if p-values were lower than 0.05. Negative binomial regression models were conducted in STATA version 15.0 (StataCorp LLC, 2017).

Temporal changes in trends of CNRs in identified TB hotspots were identified using Joinpoint regression (which I have described in detail in Chapter Three, see section 3.3.7.2). I analysed trends in age-sex adjusted notification rates and trends by sex and age group. Furthermore, I analysed trends in TB and HIV/AIDS related indicators at township level.

4.5. Results

4.5.1. Sample description

The ETR showed that there were 20 804 TB cases diagnosed in Khomas from 2006 to 2015. Of these, 1114 (5%) were excluded from the analysis as they had residential addresses outside Windhoek. Furthermore, 1284 (6%) were excluded as they had missing or incomplete residential addresses which could not be allocated to a specific township. Consequently, the final study sample was made up of 18 406 (88%) cases.

Of the 18 406 cases, 11 289 (61%) were male and 7117 (39%) were female. The age distribution was as follows, 0-4 years (6%), 5-14 years (4%), 14-24 years (12%), 25-34 years (32%), 35-44 years (28%), 45-54 years (12%), 55-64 years (4%) and 65+ years (2%). A total of 14 586 (79%) were pulmonary TB cases, and 3820 (21%) were extra-pulmonary TB. In addition, 14 649 (80%) were new cases and the remaining 3757 (20%), were re-treatment cases. Only 11 032 (60%) cases had a recorded HIV/AIDS status.

4.5.2. Crude and standardised CNRs

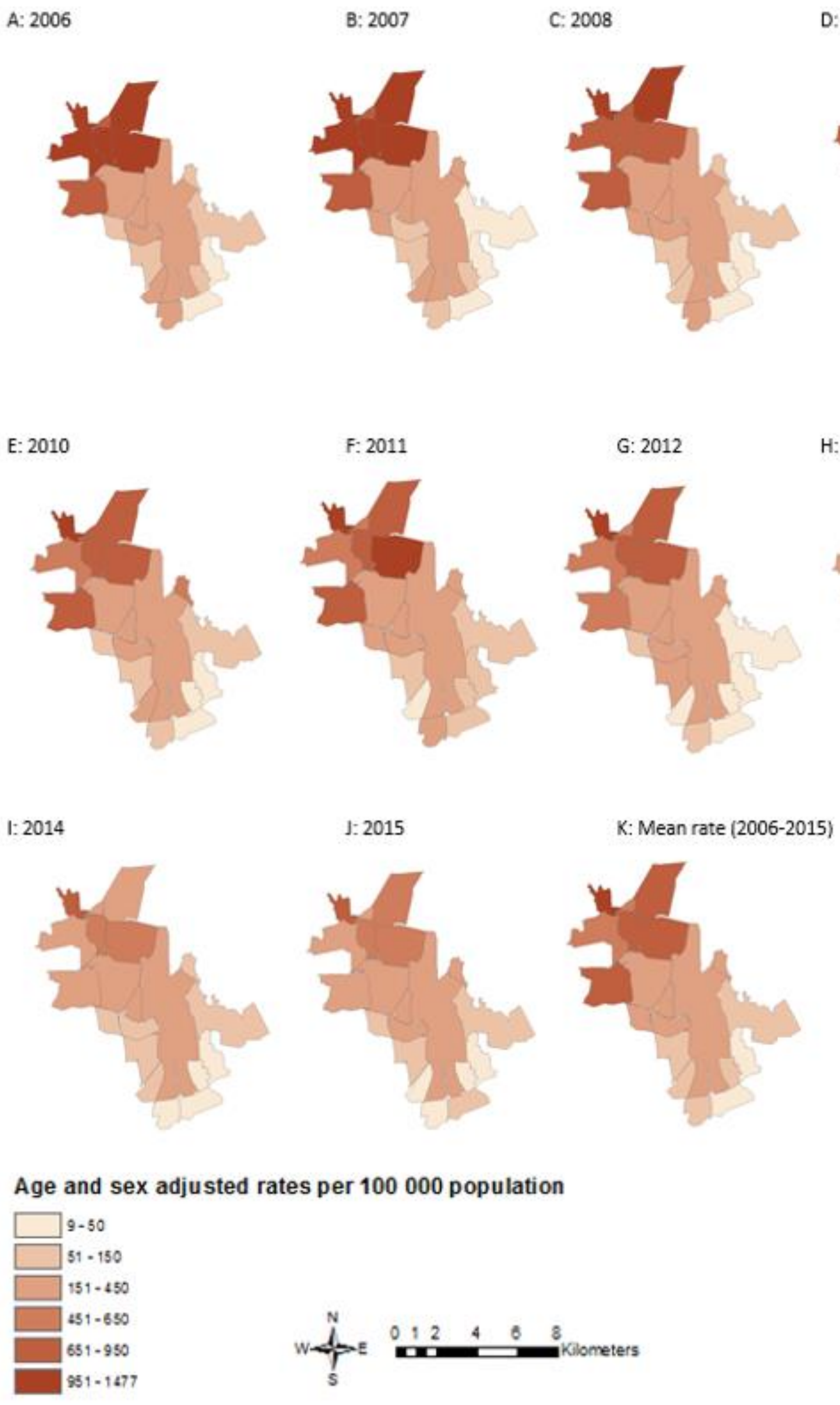
From 2006 to 2015, TB in Windhoek was mostly prevalent in the northern townships, Goreangab, Havana, Hakahana, Okuryangava, Wanaheda and Katutura. As per 2011 census, these townships constituted 64% of Windhoek's total population. As can be seen from Table 4.2, the crude mean rates ranged from 9 cases in Auasblick to 1295 per 100 000 in Havana. The age-sex standardised rates also ranged from 9 in Auasblick to 1128 per 100 000 population in Havana. There was significant heterogeneity in the mean crude and standardised rates across the townships (p values <0.001).

Table 4.2: Crude and standardised CNRs per 100 000 population by township, 2006 to 2015

Location	**Crude mean rate (95%CI)**	**Age and sex standardised mean rate (95%CI)**
Academia	118 (73-164)	121 (75-167)
Auasblick	9 (0-28)	9 (0-22)
Cimbebasia	141 (83-199)	133 (79-189)
Dorado Park	216 (173-259)	224 (179-269)
Eros Park	226 (155-297)	211 (145-278)
Goreangab	647 (484-810)	648 (485-811)
Hakahana	621 (537-705)	578 (500-657)
Havana	1295 (1085-1503)	1128 (945-1311)
Hochland Park	175 (144-207)	182 (149-215)
Katutura	734 (614 – 853	812 (680-944)
Khomasdal	291 (250-332)	305 (262 -347)
Kleine Kuppe	36 (13-61)	33 (11-54)
Kleine Windhoek	71 (49-93)	61 (42-80)
Okuryangava	858 (696-1038)	823 (650-997)
Olympia	60 (32-88	53 (28-78)
Otjomuise	670 (497-842)	691 (514-869)
Pioniersaprk	113 (54-217)	115 (96-134)
Rocky crest	168 (119-217)	173 (123-223
Wanaheda	724 (616 -832)	762 (649-875)
Windhoek central	337 (289-385)	328 (281-375)

The year specific age and sex standardised CNRs are shown in Figure 4.2 below. Havana had the highest notification rates throughout the study period. The graphs however show that over time, the density of TB cases declined in specific townships, indicated by a reduction in townships classified as having CNRs above 650 per 100 000 population in 2013-2015.

Figure 4.2. Age and sex standardised CNRs



4.5.3. Standardized Morbidity Ratios (SMRs)

Table 4.3 shows the year specific SMRs for each township. Havana had the highest SMRs across all the years, and the ten-year mean SMR was highest in Havana (average SMR=1.72). Other townships such as Katutura, Okuryangava, Otjomuise and Wanaheda also had high SMRs, particularly from 2006-2010. However, the SMRs in the majority of townships declined over time, when comparing the figures for year 2015 to those of 2006.

Table 4.3. Standardized Morbidity Ratios (SMRs) of TB in Windhoek, 2006 to 2015

Location	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Academia	0.29	0.28	0.20	0.33	0.33	0.06	0.06	0.12	0.12	0.06
Auasblick	0	0	0	0	0	0.14	0	0	0	0
Cimbebasia	0.41	0.11	0.29	0.35	0.16	0.30	0.21	0.16	0	0.04
Dorado Park	0.32	0.32	0.28	0.33	0.60	0.38	0.32	0.17	0.30	0.40
Eros Park	0.18	0.42	0.14	0.39	0.69	0.35	0.36	0.26	0.16	0.28
Goreangab	1.53	1.56	1.23	1.22	0.98	0.94	0.87	0.51	0.75	0.46
Hakahana	0.99	1.07	1.02	1.07	1.04	0.87	0.86	0.75	0.55	0.60
Havana	2.16	2.25	1.98	2.03	1.69	2.07	1.60	1.09	1.16	1.18
Hochland Park	0.38	0.13	0.35	0.30	0.32	0.32	0.29	0.19	0.19	0.29
Katutura	1.54	1.53	1.44	1.53	1.23	1.49	1.21	0.83	0.76	0.82
Khomasdal	0.47	0.45	0.57	0.51	0.59	0.55	0.46	0.48	0.27	0.30
Kleine Kuppe	0	0.06	0	0	0.05	0.16	0.08	0.07	0	0.09
Kleine Windhoek	0.14	0.06	0.12	0.15	0.09	0.11	0	0.05	0.09	0.12
Okuryangava	1.69	1.93	1.46	1.55	1.31	1.25	1.17	0.80	0.68	0.71
Olympia	0.12	0.21	0.06	0.12	0	0.09	0.03	0.09	0.06	0.03
Otjomuise	1.43	1.34	1.35	1.57	1.39	1.12	0.88	0.50	0.47	0.49
Pioniersaprk	0.15	0.13	0.16	0.23	0.19	0.19	0.27	0.18	0.14	1.11
Rocky crest	0.23	0.56	0.36	0.20	0.22	0.33	0.19	0.22	0.13	0.21
Wanaheda	1.47	1.62	1.38	1.11	1.28	1.14	1.12	0.86	0.81	0.83
Windhoek central	0.44	0.66	0.60	0.56	0.55	0.57	0.54	0.45	0.33	0.31

4.5.4. Spatial autocorrelation

Results of the Global Moran's I are shown in Table 4.4. The results show that TB depicted a strong spatial autocorrelation, with a significant positive Global Moran's Index obtained during each year from 2006 to 2015. The Global Moran's I was high across all the years and it was highest in 2006.

Table 4.4: Global spatial autocorrelation for all forms of TB notification rates in Windhoek, 2006 to 2015

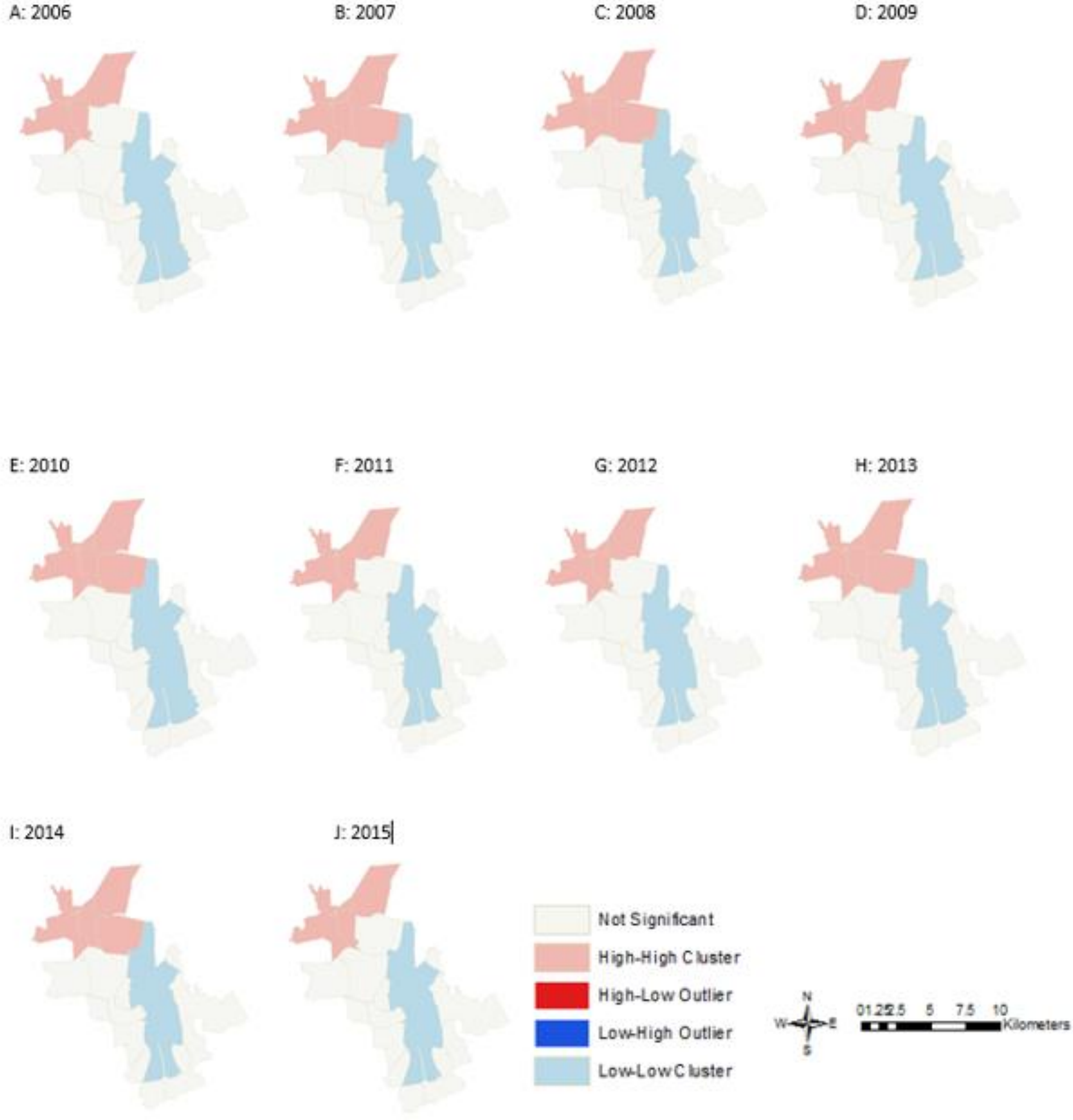
Year	Global Moran's Index	Z-value	p-value	Interpretation
2006	0.6305	4.755	p<0.001	Not random
2007	0.6222	4.703	p<0.001	Not random
2008	0.6153	4.646	p<0.001	Not random
2009	0.5416	4.152	p<0.001	Not random
2010	0.5868	4.419	p<0.001	Not random
2011	0.5071	4.043	p<0.001	Not random
2012	0.6032	4.593	p<0.001	Not random
2013	0.6321	4.776	p<0.001	Not random
2014	0.6151	4.794	p<0.001	Not random
2015	0.5923	4.624	p<0.001	Not random

4.5.5. Identification of TB hotspot/clusters

4.5.5.1. Using the Local Moran's I statistic

Results from the Local Moran's I are shown in Figure 4.3. The townships with similar and higher rates of TB included Havana, Goreangab, Hakahana, Wanaheda, Okuryangava and Katutura. Katutura was identified as a high TB burden township in five years, whereas all other townships were identified as TB hotspots throughout years.

Figure 4.3. TB hotspots identified through the Local Moran's Index, 2006 to 2015



4.5.5.2. Using Scan statistics

4.5.5.2.1. Purely spatial analyses

The purely spatial scan statistics identified the most likely clusters of TB consisting of Windhoek townships with high rates of TB, adjusted for age and sex of the population, and there are presented in Table 4.5. The most likely significant clusters generally included five townships, Goreangab, Wanaheda, Havana, Hakahana and Okuryangava, although the pattern varied slightly across the study period. Across all the 10 years, Havana was identified in a cluster eight time while Wanaheda and Okuryangava were both identified seven times. Hakahana was identified five times, Goreangab three times and Katutura two times. In the most recent year, 2015, the risk of TB was significantly higher in Havana compared to other areas (RR= 2.05; p<0.001).

Table 4.5: The most likely clusters in Windhoek from a purely spatial analysis of all forms of TB, 2006- 2015

Cluster years	Cluster areas	Observed cases	Expected cases	Annual cases/100000	Relative risk	p-value
2006	Goreangab, Wanaheda, Havana, Hakahana, Okuryangava	1249	1000.05	1058.70	1.60	< 0.001
2007	Goreangab, Wanaheda, Havana, Hakahana, Okuryangava	1413	1111.65	1125.40	1.72	< 0.001
2008	Katutura, Wanaheda, Okuryangava	1202	998.78	981.6	1.50	< 0.001
2009	Katutura, Okuryangava	1146	911.36	1041.1	1.26	< 0.001
2010	Hakahana, Okuryangava, Wanaheda, Havana	947	767	888.20	1.46	< 0.001
2011	Havana	247	127.55	1413.40	2.06	< 0.001
2012	Hakahana, Okuryangava, Wanaheda, Havana	900	716.02	803.60	1.50	< 0.001
2013	Hakahana, Okuryangava, Wanaheda, Havana	664	531.22	585.0	1.48	< 0.001
2014	Goreangab, Wanaheda, Havana	375	256.79	618.30	1.65	< 0.001
2015	Havana	164	85	840.80	2.05	< 0.001

4.5.5.2.2. Space-time analyses

Simultaneously assessing the disease distribution spatially and temporally, SaTScan identified that the most likely significant TB space-time cluster included five townships Havana, Goreangab, Hakahana, Wanaheda and Okuryangava, and this cluster was identified during the period 2006-2010 with a relative risk of 1.76 (Table 4.6).

Table 4.6: Clusters in Windhoek identified through a space and time analysis of all forms of TB cases, 2006 to 2015

Clusters detected	Period	Cluster areas	Observed cases	Expected cases	Annual cases/100 000	Relative risk	p-value
1	2006-2010	Goreangab, Wanaheda, Havana, Hakahana, Okuryangava	6211	4134.74	1003.0	1.76	< 0.001
2	2007-2011	Eros Park, Katutura	2754	2030.10	907.50	1.42	< 0.001
3	2006-2010	Otjomuise	394	266.29	988.0	1.49	< 0.001

4.5.6. Population level determinants of TB burden in Windhoek

Table 4.7 shows results from the negative binomial regression concerning the association between TB burden and township level socio-demographic variables. In the multivariable analysis, the TB CNRs decreased by 4% for every unit increase in the percentage of people with formal education (RR=0.96, 95% CI: 0.93-0.99). Moreover, the CNRs increased by 6% for every unit increase in the percentage of economically active people unemployed (RR=1.06, 95% CI: 1.04-1.09).

Table 4.7: Population level socio-demographic determinants of TB distribution in Windhoek

Variable	Model 1*			Model 2**		
	RR	95% CI	p-value	RR	95% CI	p-value
Average household size	1.32	1.19 to 1.47	p<0.001	1.27	0.95 to 1.71	p=0.104
School enrolment rate	0.91	0.90 to 0.91	P<0.001	0.96	0.93 to 0.99	p=0.024
Unemployment rate	1.08	1.07 to 1.08	p<0.001	1.06	1.04 to 1.09	p<0.001
Population density	2.02	1.88 to 2.15	p<0.001	0.90	0.80 to 1.01	p=0.070

*Model adjusted for year of TB diagnosis. ** Adjusted for year of TB diagnosis, percentage of male population and all variables in the table. RR: rate ratio; CI: confidence interval.

4.5.7. *Trends in CNRs for townships identified in clusters*

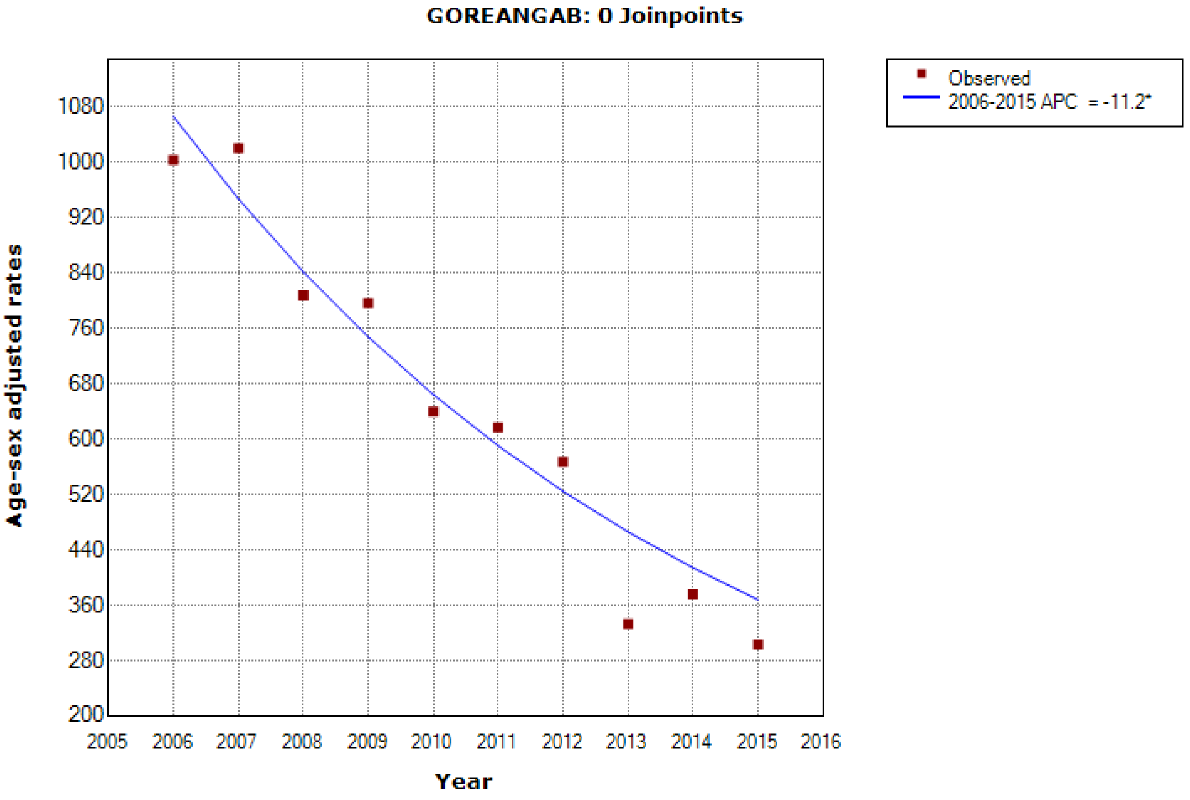
Table 4.8 shows results of Joinpoint regression indicating trends in crude and age-sex standardised CNRs. From 2006 to 2015, the standardised CNRs in Windhoek city as whole declined significantly at an annual average of -9.3% (95%CI: -13.6% to -4.9%). In all townships, trends in both crude and standardized CNRs declined significantly over time. Goreangab had the highest annual percent decline of -11.2% (-13.8% to -8.5%). Havana and Hakahana had the lowest average annual percent changes, being -6.2% (95%CI: -9.7% to -2.6%) in Havana and -6.3% (95%CI: -9.5% to -3.1%) in Hakahana. The graphs below Figure 4.4 show that specific join points were observed in the trends for Hakahana, Katutura and Windhoek city as a whole.

Table 4.8: Joinpoint regression results in trends of CNRs for all forms of TB by township, 2006 to 2015

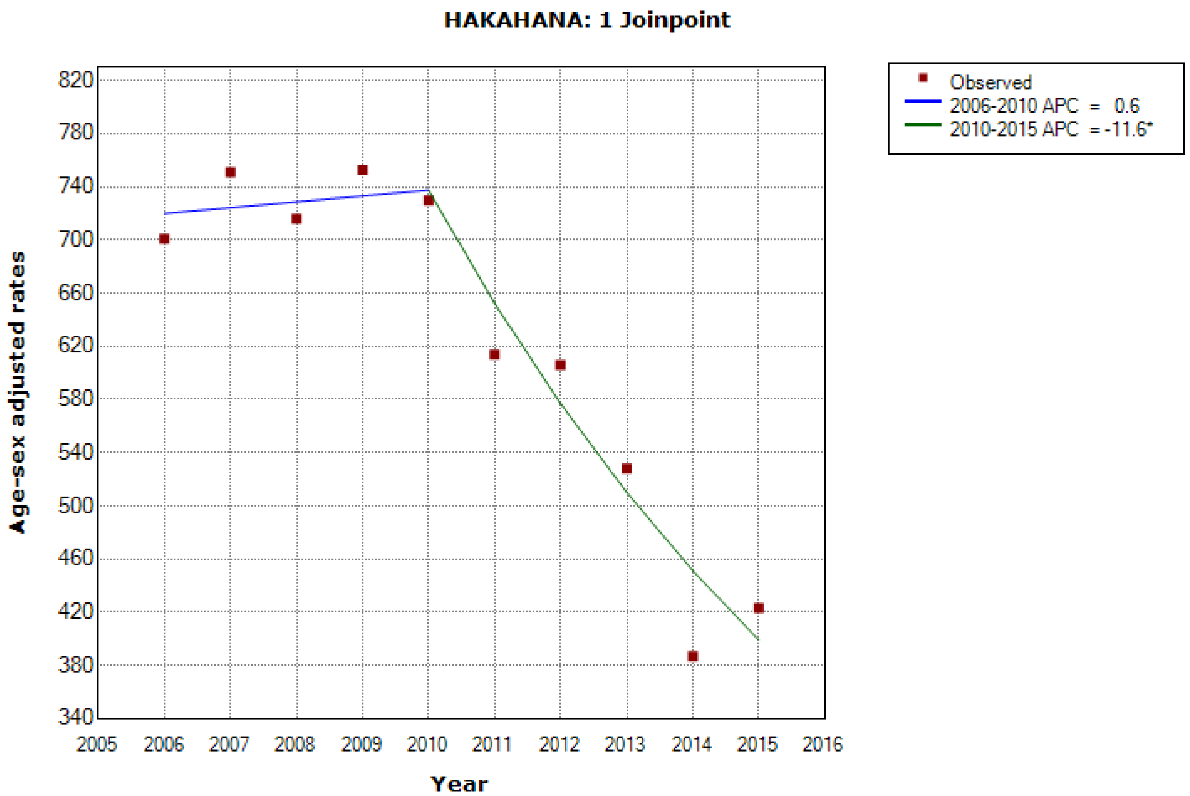
Location	*AAPC (95% CI) (crude CNR)	*AAPC (95% CI) (standardised CNR)
Goreangab	-12.8 (-15.3 to -10.2)	-11.2 (-13.8 to -8.5)
Hakahana	-6.4 (-10.1 to -2.6)	-6.3 (-9.5 to -3.1)
Havana	-7.6 (-10.9 to -4.2)	-6.2 (-9.7 to -2.6)
Katutura	-7.4 (-10.9 to -3.7)	-8.3 (-13.4 to -3.0)
Okuryangava	-10.5 (-13.3 to -7.5)	-9.3 (-12.5 to -5.9)
Wanaheda	-7.2 (-9.3 to -4.9)	-7.1 (-9.3 to -4.8)
Windhoek city as a whole	-9.3 (-13.6 to -4.9)	-9.5 (-14.1 to -4.5)

*All p-values statistically different from zero ($p<0.05$)
AAPC: Average Annual Percent Change

Figure 4.4. Trends in age-sex adjusted rates (per 100 000 population) by township, 2006-2015

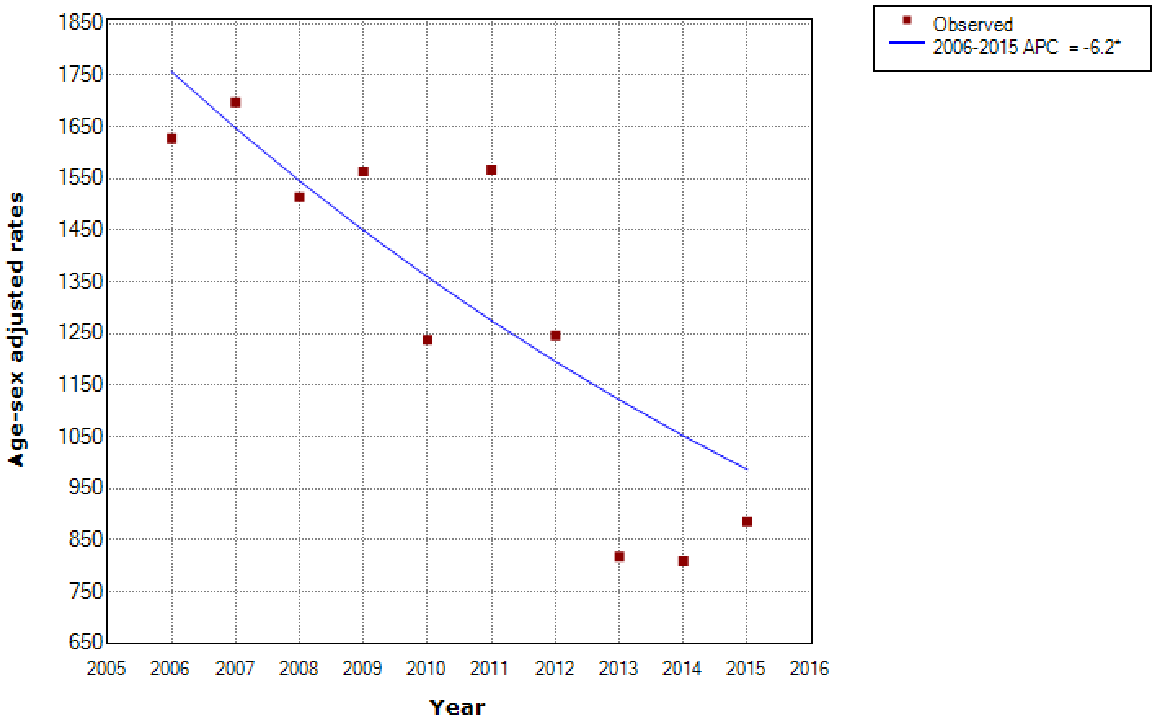


* Indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level.
Final Selected Model: 0 Joinpoints.



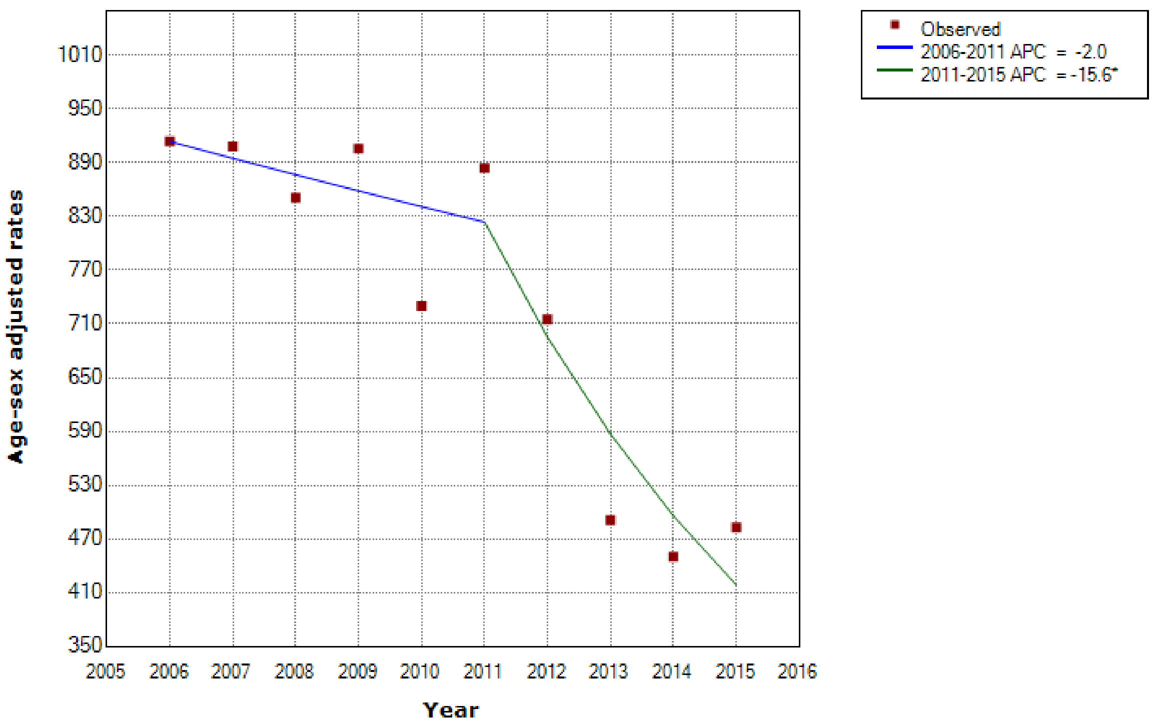
* Indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level.
Final Selected Model: 1 Joinpoint.

HAVANA: 0 Joinpoints

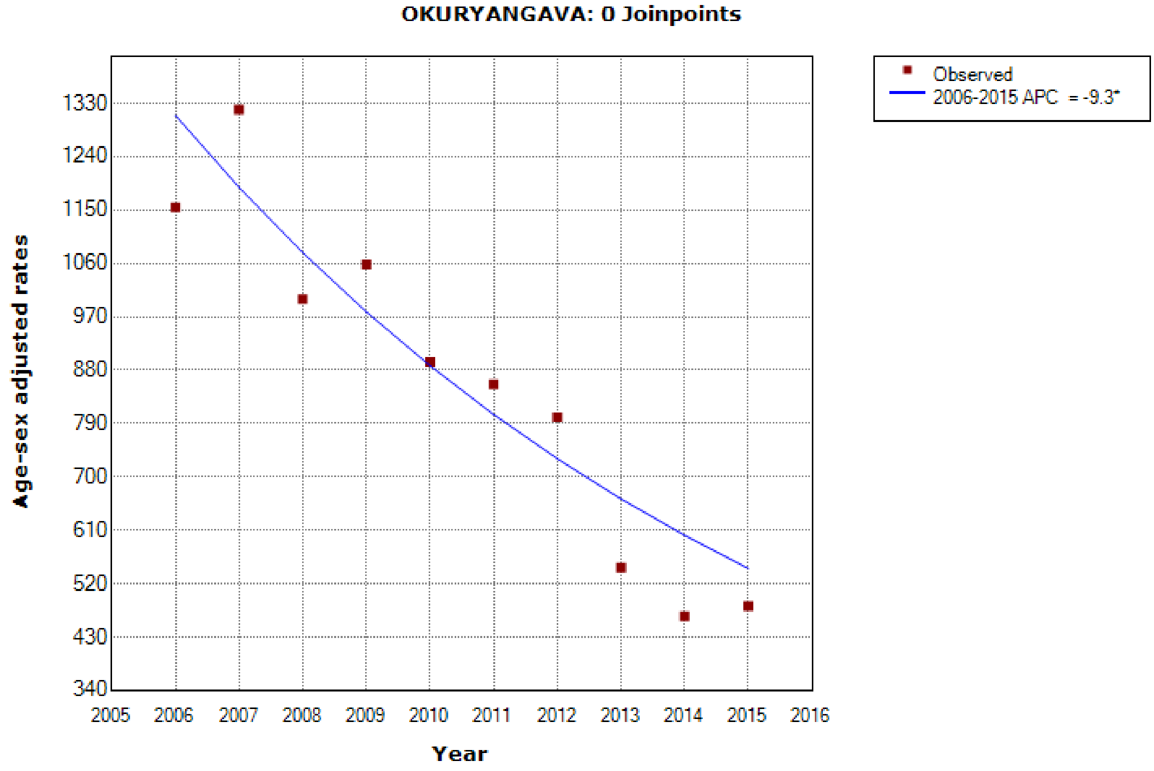


* Indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level.
Final Selected Model: 0 Joinpoints.

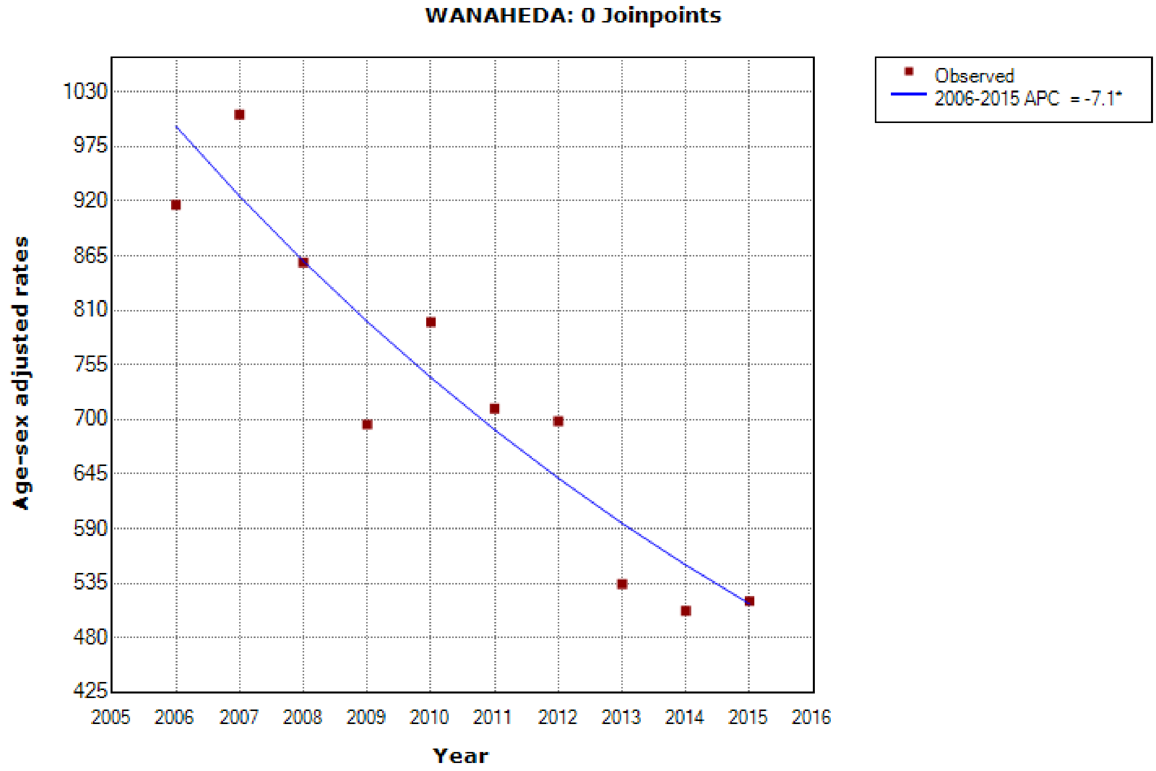
KATUTURA: 1 Joinpoint



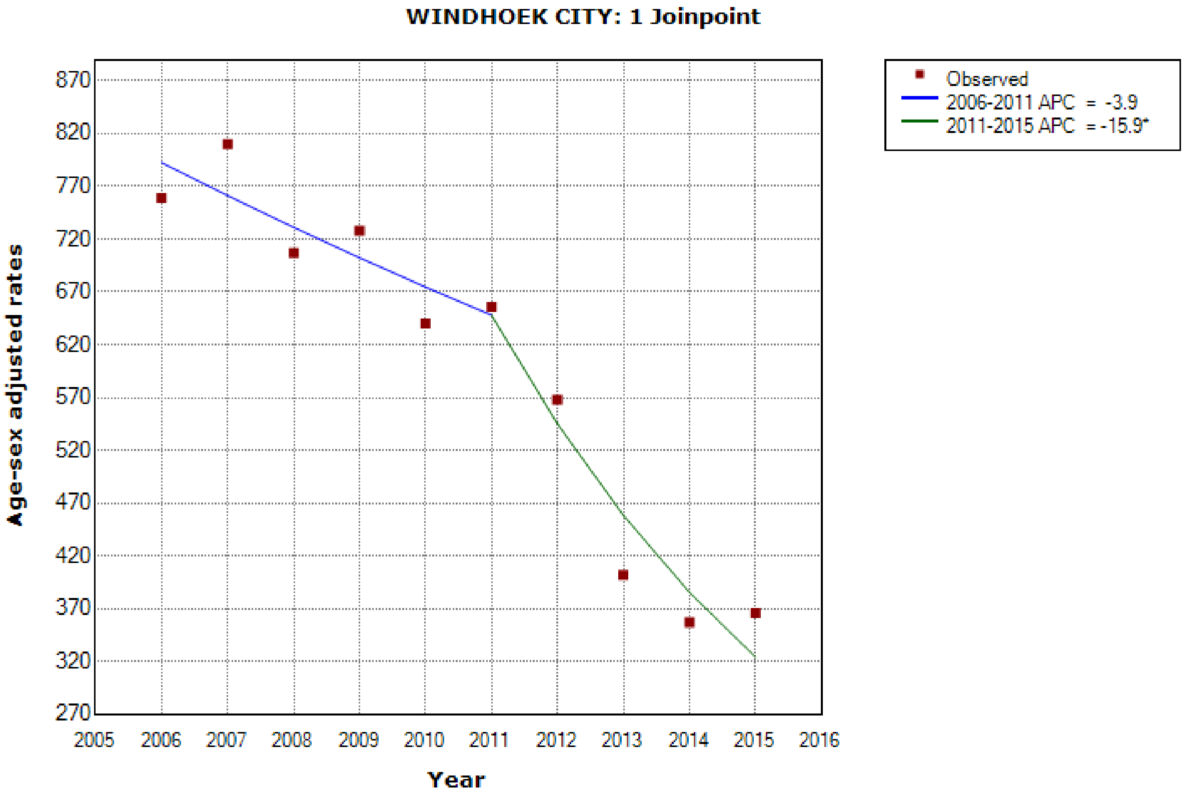
* Indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level.
Final Selected Model: 1 Joinpoint.



* Indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level.
Final Selected Model: 0 Joinpoints.



* Indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level.
Final Selected Model: 0 Joinpoints.



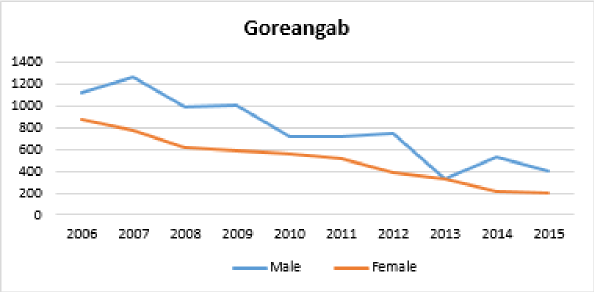
* Indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level.
Final Selected Model: 1 Joinpoint.

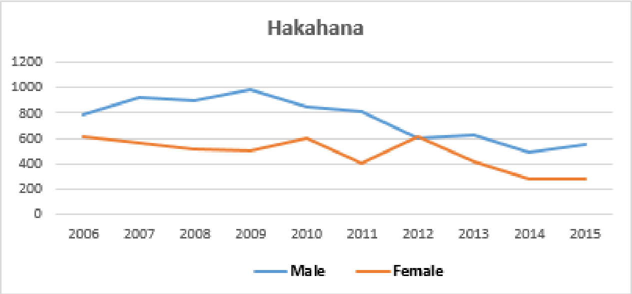
4.5.8. Sex specific CNRs for townships identified in clusters

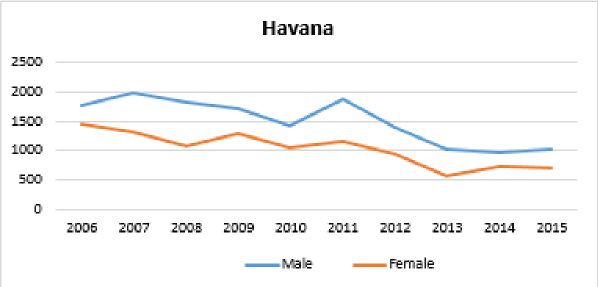
The sex specific CNRs are shown in Figure 4.5 below. In Windhoek as a whole, the average CNRs were 748 (95% CI: 620-876) and 456 (95% CI: 372-540) per 100,000 population for males and females, respectively. Havana had the highest average CNRs of 1501 (95% CI: 1258-1743) and 1034 (95% CI: 855-1215) per 100,000 population for males and females, respectively.

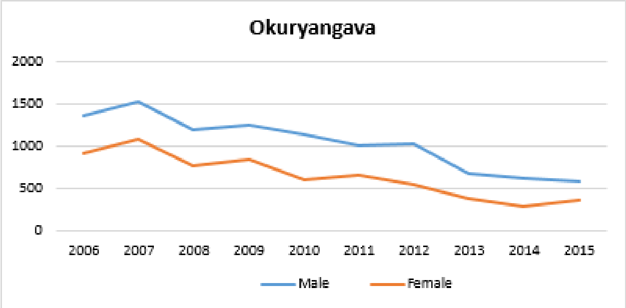
In all the selected townships, and Windhoek as a whole, the rates were higher in males than in females. However, the gap appears to be narrowing over time.

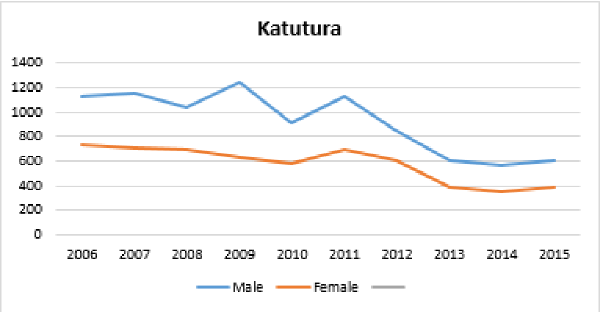
Figure 4.5. Sex specific CNRs (per 100 000 population) at township level, 2006-2015

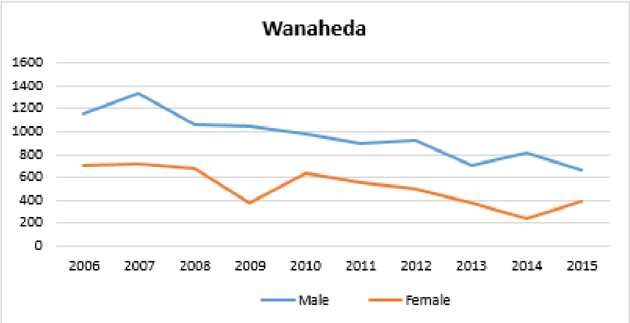


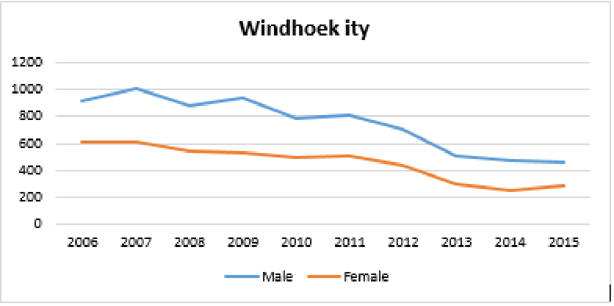












Analyses of trends in CNRs by sex are shown in Table 4.9. The CNRs in Windhoek as a whole declined for both sex, with an annual average of -9.8% (95% CI: -14.4% to -4.8%) for females and 9.1% (95% CI: -13.4% to -4.6%) for males.

Goreangab and Okuryangava had sex specific annual declines higher than those of Windhoek as a whole, whilst Hakahana, Havana, Katutura, and Wanaheda had annual sex specific rates below the city average.

Table 4.9. Joinpoint regression results for trends in sex specific CNRs by township, 2006 to 2015

Location	**FEMALE**	**MALE**
	AAPC (95% CI)*	**AAPC (95% CI)***
Goreangab	-15.0 (-18.5 to -11.2)	-11.7 (-15.6 to -7.7)
Hakahana	-6.5 (-11.5 to -1.1)	-5.6 (-10.6 to -0.2)
Havana	-8.0 (-11.3 to -4.5)	-7.4 (-11.0 to -3.7)
Katutura	-7.2 (-10.6 to -3.6)	-7.5 (-11.5 to -3.4)
Okuryangava	-12.1 (-15.5 to -8.6)	-9.5 (-12.4 to -6.6)
Wanaheda	-8.2 (-12.9 to -3.3)	-6.3 (-8.4 to -4.2)
Windhoek city as a whole	-9.8 (-14.4 to -4.8)	-9.1 (-13.4 to -4.6)

*All p-values statistically different from zero ($p<0.05$)
AAPC: Average Annual Percent Change

4.5.9. Trends in percent of TB cases by age group

The age group specific average annual percent declines in the percent of notified cases by age group are shown in Table 4.10. Overall, trends in the percentage of notified TB cases in Windhoek declined at an annual average of -10.0%, -9, 0% and -5.3% per year for age groups 0-24, 25-44 and 45+, respectively. However, the trend for the oldest group was not significant. Trends declined significantly in both age groups in Goreangab, Havana and Katutura, although only Goreangab had average annual declines higher than those of Windhoek for all age groups.

Table 4.10. Joinpoint regression results for trends in percent of cases by age group, 2006 to 2015

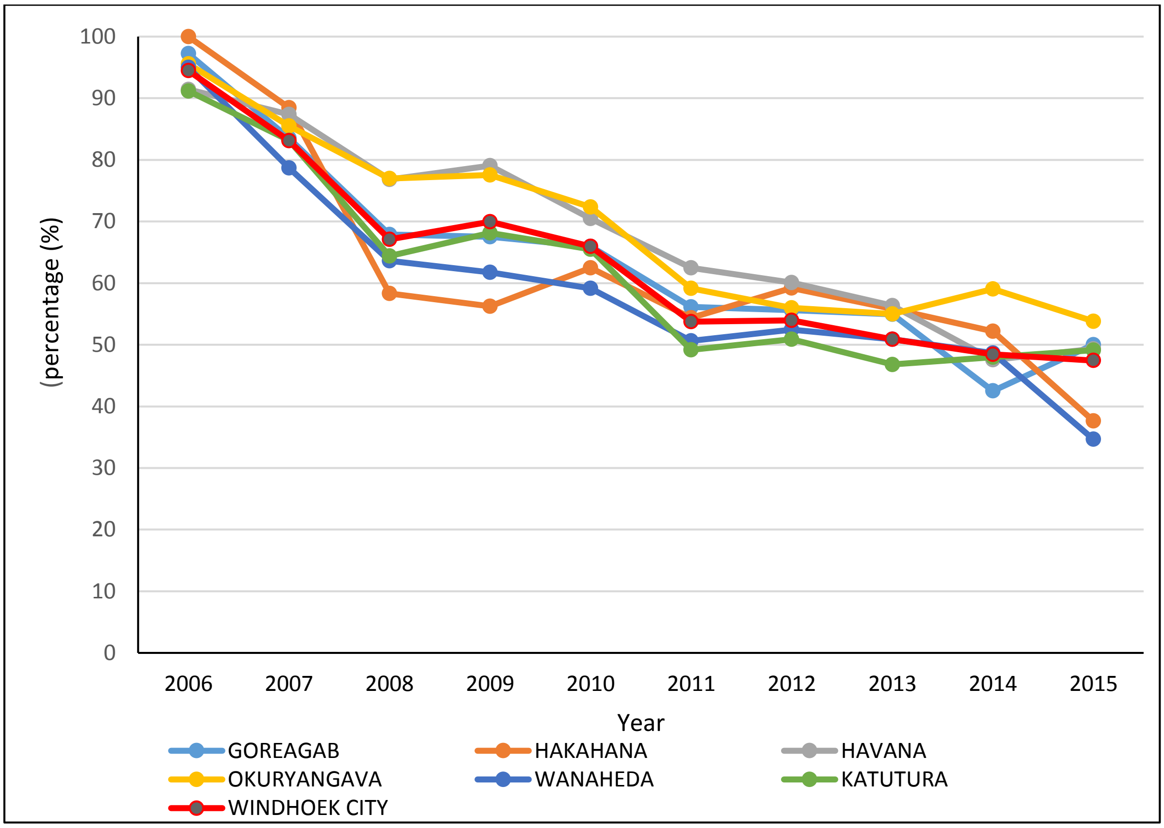
Location	**0-24 years**	**25-44 years**	**45+ years**	
	AAPC (95% CI)*	**AAPC (95% CI)***	**AAPC (95% CI)**	**p-value**
Goreangab	-14.7 (-17.2 to -12.1)	-12.4(-15.7 to -8.9)	-10.5 (-17.2 to -3.2)	p<0.05
Hakahana	-6.0 (-11.6 to -0.0)	-7.0 (-11.3 to -2.6)	-7.6 (-18.0 to 4.1)	p=0.2
Havana	-8.5 (-13.2 to -3.6)	-7.9 (-12.7 to -2.8)	-6.6 (-10.7 to -2.2)	p<0.05
Katutura	-9.6 (-13.8 to -5.1)	-7.0 (-10.3 to -3.5)	-5.4 (-10.0 to -0.6)	p<0.05
Okuryangava	-12.2 (-15.7 to -8.6)	-11.5 (-15.0 to -8.0)	-3.8 (-9.0 to 1.6)	p=0.1
Wanaheda	-8.7 (-15.5 to -1.4)	-7.3 (-10.3 to -4.3)	-5.1 (-12.2 to 2.6)	p=0.2
Windhoek city as a whole	-10.0 (-12.8 to -7.7)	-9.0 (-14.1 to -3.6)	-5.3 (-11.4 to 1.2)	p=0.1

*All p-values statistically different from zero (p<0.05)
AAPC: Average Annual Percent Change

4.5.10. Trends concerning TB and HIV/AIDS related indicators

Figure 4.6 shows the yearly HIV/AIDS prevalence rate among TB cases with known HIV/AIDS status. The co-infection rates significantly declined in all townships. The co-infection rates were generally highest in Okuryangava and Havana townships. In 2015, only Hakahana and Wanaheda had co-infection rates lower than 40%, below the city average.

Figure 4.6 Percent of TB cases co-infected with HIV/AIDS, 2006 to 2015



The sex specific HIV/AIDS prevalence among TB cases with known status are shown in Figure 4.7. In both townships, HIV/AIDS prevalence were generally higher in female TB cases compared to male cases, however trends in both genders declined over time.

Figure 4.7. Sex specific HIV/AIDS prevalence among TB cases with known HIV/AIDS, 2006-2015

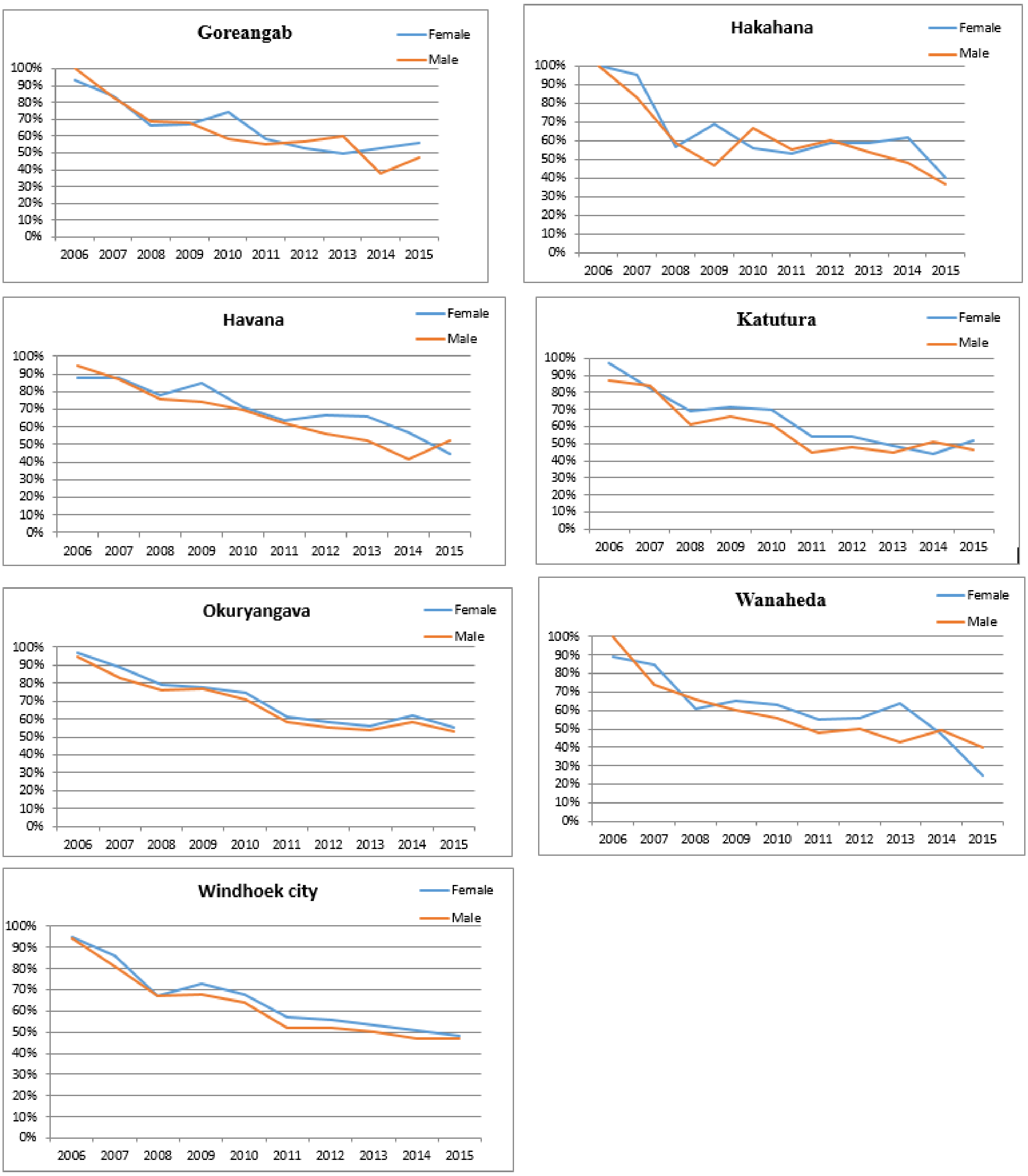


Table 4.11 shows the township level trends in the percentage of TB cases with known HIV/AIDS status and in the percentage of TB and HIV/AIDS co-infected cases. In all townships significant increase in cases with known HIV/AIDS status and significant decline in HIV/AIDS prevalence rate in TB cases (with known HIV/AIDS status) were observed.

Table 4.11. Joinpoint regression results indicating trends in for TB and HIV/AIDS indicators by township, 2006 to 2015

Location	**Known status**	**HIV/AIDS prevalence**
	AAPC (95% CI)*	**AAPC (95% CI)***
Goreangab	9.7 (5.1 to 14.4)	-8.5 (-10.0 to -6.9)
Hakahana	8.1 (2.1 to 14.4)	-9.7 (-12.7 to -6.5)
Havana	7.7 (2.2 to 13.6)	-6.7 (-7.4 to -6.0)
Katutura	9.9 (4.0 to 16.2)	-8.1 (-9.5 to -6.7)
Okuryangava	8.5 (3.7 to 13.6)	-6.7 (-7.8 to -5.7)
Wanaheda	9.9 (5.2 to 14.8)	-9.6 (-11.4 to -7.8)

*All p-values statistically different from zero ($p<0.05$)
AAPC: Average Annual Percent Change

4.6. Discussion

4.6.1. Summary of main findings

In this study, I used the spatial and spatiotemporal analysis methods to investigate the distribution of TB in Windhoek. To the best of my knowledge, this is the first epidemiological study to document the township level TB burden, and population level socio-demographic determinants in Windhoek.

Using data obtained from the NTLP electronic TB registry, I found that TB depicted a strong spatial autocorrelation, with a significant positive Global Moran's Index obtained for each year from 2006 to 2015. The Local Moran's I and Kulldorff's scan statistics identified that townships in the northern part of the city, namely Wanaheda, Havana, Hakahana, Okuryangava, Katutura and Goreangab, were hotspots for TB disease although this varied by year. I found that high TB rates were positively associated with high unemployment rates (RR=1.06, 95% CI: 1.04 to 1.09) and negatively associated with high school enrolment rates (RR=0.96, 95% CI: 0.93 to 0.99). Of the six townships identified as hotspots, I found that, overall, trends in CNRs declined significantly over time, in both genders but not in all age groups. Moreover, I found that there was a significant increase in the percent of TB cases with known HIV/AIDS status and a significant decline in the percent of HIV/AIDS prevalence among TB cases in the selected townships. However the co-infection rates still remains high, because for the most recent year (2015), only Hakahana and Wanaheda had co-infection rates lower than the city average.

4.6.2. Strengths

One strength of my study is that it analysed the region level TB epidemiology, and so the study results may be used to inform TB prevention activities in the identified hotspots and to inform hypotheses in future studies. A further strength of my study is that analyses were based on data obtained from the ETR, and so it is likely to have included most of the notified TB cases in the region, including those that were not included in the annual reports of the NTLP. For instance, the NTLP annual reports (produced using paper-based TB registers) shows that there were 20 788 all forms of TB cases notified in Khomas from 2006 to 2015. That figure is slightly lower than what was captured in the ETR (n=20 804) during the same period. The fact that ETR has a higher number of cases compared to what was reported in the official reports is however expected, because ETR is continuously updated, and hence it include cases which were not reported on time to the NTLP (68). In 2012, the NTLP conducted a nationwide comparison of data in the two systems and their results confirmed the marginal difference between the ETR and the paper based system (68). However, the comparison made was documented at national level only and not at region or district. Future work may be needed to assess the completeness of the ETR at regional level and determine the extent to which the ETR can serve as a primary reporting repository for TB within specific regions.

In this study I used data on 18 406 (88%) cases which had a valid residential address belonging to townships in Windhoek. This proportion could be high because not all TB cases in the ETR had addresses belonging to Khomas. In terms of the specific fields, none of the 18 406 cases had missing information regarding sex, age, year of diagnosis and category of patient (pulmonary or extra-pulmonary). However, only 11032 (60%) cases had a recorded HIV/AIDS status. The incomplete data regarding HIV/AIDS imply that the data reported here must be interpreted with caution.

A further strength of my study is that I used the indirect standardisation method to calculate age and sex standardised CNR for each township. This method was applied as some of the townships had smaller numbers of cases and population sizes, and so I needed to use a method which will minimise the occurrence of unstable rates (150). Furthermore, this study used both the Local Moran's statistics and Scan statistics to identify TB hotspots. The similar results obtained through the two methods confirm the reliability of my study results. The use of two or more spatial analyses methods has been encouraged, as no single method is classified as gold-standard (184).

4.6.3. Limitations

The study also had several limitations. Some cases were excluded from the study because of missing or incomplete residential addresses. In addition, at the time of data collection for my study, there was no information in the ETR regarding whether cases of TB were identified through passive or active case finding methods. It is therefore not clear whether cases reported in the ETR represent an accurate measure of the TB burden in the community. For example, my study would have missed all the TB cases who never presented themselves to health facilities, or those who had presented themselves but were not appropriately diagnosed, or those appropriately diagnosed but never captured in the ETR. The extent of the missed cases is not known currently, as case detection rates are not estimated at regional level. As observed in other studies (163), it is possible that those with missing cases were from areas identified as TB hotspots, in which case the results of my study are an underestimation the true disease burden. Furthermore, the findings of my study should be interpreted with the caveat that people who may have TB and accessed healthcare in private sector may have not been recorded in the ETR, and these people may have been from the high socioeconomic townships. However, despite these caveats, the ETR should have captured the majority of cases diagnosed in the public sector (the largest healthcare provider in the country), and so the study results provides useful findings regarding the occurrence of the disease at township level.

I was unable to study the disease distribution in relation to the prevalence of TB risk factors, for example alcohol consumption or smoking, diabetes. Such township data are currently unavailable from the census office and also in the ETR. I was only able to study the disease in relation to TB and HIV/AIDS co-infection, although these data were only available for 60% of cases considered in the analysis. Also because of incomplete information, I could not analyse the TB distribution according to types of TB in this study.

Since this was an ecological analysis, the findings regarding the socio-demographic determinants of TB cannot be interpreted at an individual level (ecological fallacy) and they do not imply a causal relationship. Further studies are needed to investigate individual level determinants of TB in the region to inform prevention interventions.

4.6.4. Interpretation and comparison with the literature

In my study, I analysed 88% of notified TB cases and included reported cases of all ages in order to provide a comprehensive view of the occurrence of TB in Windhoek. This proportion is similar to those of other studies in Africa. For instance, in Doula, Cameroon, Nana Yakam and colleagues analysed 84% of the notified TB cases over a one year period (May 2011 to April 2012(169). In the Gambia, Touray *et al*. analysed 80% of all notified cases in Greater Banjul also notified over one year period (March 2007 to February 2008) (22). In other countries`, the proportion analysed was much higher`, for example Shaweno *et al*. reported that they analysed all cases with TB notified from 2010 and 2014 in Sheka Zone, Ethiopia. Another Ethiopian study involving children aged 5 years also reported that all TB cases notified from 2013-2016 were included in their analysis (168). In other African countries, analysis were based on lower proportions compared to my study. For example, in Madagascar, Randremanana *et al*. were only able to analyse 73% of notified cases from 2004 to 2006 in Antananarivo (171). In South Africa, Munch *et al.* analysed 76% of TB cases notified in two townships in South Africa between 1993-1998 (172). The differences between studies in terms the proportion of cases analysed might suggest variation in the quality of country specific TB data. However, these variations might also be due to differences in time, as studies that included almost 100% of cases were those conducted in more recent years, suggesting improvement in the quality of data captured by national TB programmes over time.

In my study, I found that the townships in the northern part of Windhoek, namely Havana, Wanaheda, Katutura, Hakahana, Okuryangava, and Goreangab were identified as TB hotspots, although the exact locations varied by year. The Local Moran's I and scan statistics identified similar locations as TB hotspots, and this is consistent with findings from other studies. In particular, a study in Thailand which included cases notified from 2004 to 2006 in Si Sa Ket province found that the Local Moran's I and scan statistics produced similar results (150). Since my study is the first attempt to understand the TB burden at township level in Windhoek, it is worth to conduct further analysis in future using other methods such as Bayesian disease mapping which are known to be better at identifying disease hotspots by incorporating theoretical knowledge in the modelling process to determine biological parameters and processes (192), and so results of my study would be useful in guiding parameter settings (provision of theoretical knowledge) in such future studies.

The identification of these townships as hotspots is nonetheless unsurprising given that these are areas generally characterised by low socio-economic characteristics, poor sanitation and limited basic services. Furthermore, these townships are characterised by overcrowding resulting mainly from internal migration. The study results show that TB in Windhoek is related to unequal urban development and differences in socio-economic characteristics. Despite the introduction of Community-based Directly Observed Treatment (CB DOT), the findings of my study suggest that the TB burden within communities remains unacceptably high. The crude and age-sex standardised rates in townships such as Havana and Okuryangava imply that TB remains a serious public health threat in communities. Focused interventions are needed in the identified hotspots to heighten disease control impact. Lawn *et al*. in South Africa also showed high rates of TB at the township level (92). It is however important to note that Lawn *et al*. study was conducted during the era of high HIV/AIDS prevalence and low ART coverage, whereas my study still shows high rates of TB in the era when ART coverage is claimed to have reduced HIV/AIDS associated TB (88).

In this study, I found that high TB CNRs were positively associated with higher unemployment rates and negatively associated with higher school enrolment rates. TB is known to be a multi-factorial disease resulting from the interplay of various factors which facilitate infection or disease progression (172). For example, compared to the unemployed, employed people have better living conditions such as better housing, better nutrition, access to health services, access to information e.g. TV, radio, newspapers. In addition, educated people may have better TB knowledge (168). The concentration of TB in townships with people from lower socio economic backgrounds in Windhoek is similar to that found studies in the literature. For instance, TB burden was significantly associated with high unemployment rates (27, 29, 172, 175), high illiteracy level (158, 163, 168) and household overcrowding (26-28, 159). Other studies have reported a positive association with other measures of low socio-economic status (22, 157, 172).

One unexpected findings of my study is the magnitude of TB occurrence in Windhoek's most affluent townships. All townships in my study reported at least one case in at least one year, although in townships such as Auasblick, Kleine Kuppe, Olympia, the numbers were extremely low with some years recording zero cases. However, the finding that TB generally occurred even in affluent parts of the city suggests that TB control efforts should not neglect these townships, bearing in mind that priority should be given to the most affected townships.

Among the studies reviewed, none specifically studied temporal trends in the identified TB hotspots. Nonetheless, my study found that temporal trends in CNRs declined significantly in all the identified TB hotspots although the magnitude of the decline was lower than the city average in some townships, specifically Havana, Hakahana and Wanaheda. These results suggest that containing the disease in Windhoek requires more targeted efforts particularly in those townships.

I observed significant declines in all sexes in all townships, however, my results suggest that the declining trend for all forms of TB CNRs appears to be a function of declining rates among the younger age groups, but not in the older age groups. This pattern was observed at city level and within most of the identified hotspots. In contrast, a nationwide study in Brazil found that rates declined in older age groups rather than in the younger age groups (26). They indicated that the expectation is that TB control efforts would result in reduction in infections among young people faster than in old people (whose TB may be a result of a previously acquired infection)(26). If that is true, then the results at township level and in Windhoek as a whole are encouraging and shows progress made in reducing recent transmission. However, my study cannot distinguish whether TB cases in these townships were due to recent transmission or reactivation, but an earlier molecular epidemiological study conducted in Namibia showed that out of 214 smear positive TB patients from Windhoek, the majority of cases (55%) had unique strains while 45% had strains which were not unique. The fact that the majority of cases had unique strains suggest that these cases may not have been due to recent transmission (193). However, that study was conducted over a decade ago and did not provide information by age and sex. There is thus a need for further studies to define the current molecular epidemiology of the disease in Khomas region with a spatial component. On the other hand it is also important to note that the less declining trend in the older age group might have been due to small numbers, and so future studies are required to further understand the epidemiology of TB in order age groups in Windhoek.

My study found that the HIV/AIDS prevalence declined in all the hotspots, but the co-infection is still high in townships such as Havana and Okuryangava, and these are some of the townships which had below city average declining rates. These results evidently suggest that HIV/AIDS remains a major defining factor for the epidemiology of TB in the region, and there is need to strengthen TB and HIV/AIDS services at community level. However, the HIV/AIDS prevalence in the general population at township level remains unknown, hence spatial epidemiological studies using HIV/AIDS programme data are required to define the township specific burden.

My study observed that the TB and HIV/AIDS co-infection rates was generally higher among females compared to males, in all townships. This is despite the fact that the TB CNRs are higher in males than in females. These findings suggest that while HIV/AIDS remains an important factor for TB, studies are needed to investigate other factors, such as socio-demographic and behavioural factors which could be influencing the occurrence of TB disease. For example, in other countries, TB rates were associated with internal migration (168). Furthermore, the literature has also established the relationship between TB and diabetes (194), an association which is reported to be directional (195). In a recent population level demographic and health survey, it was reported that nationally 5.6% of women and 6.7% of men aged 35 - 64 years were classified as having a fasting plasma glucose of 7mmol/L or higher, or indicated that they were taking medication for diabetes at the time of the survey (49). In Khomas, the figures were 6.3% for women and 7.3% for men (49). A comprehensive understanding of the factors influencing the disease occurrence would enable targeted efforts required to reach the national target of 50 cases per 100 000 population by 2035.

Chapter 5 : An analysis of individual level determinants of the spatial distribution of TB in Khomas

5.1. Introduction

Results from phase two showed that there was heterogeneity in the distribution of TB across the townships, with northern townships repeatedly identified as TB hotspots. Furthermore, the results showed that high rates of TB were positively associated with higher unemployment rates and negatively associated with higher school enrolment rates. However, the limitation of these results is that other risk factors (i.e. socio-demographic and behavioural) were not considered in the multivariable analysis, due to unavailability of such data at township level. Furthermore, the results obtained in phase two were determined through an ecological analysis, and so they cannot necessarily be interpreted at the individual level. Therefore, given these limitations, I conducted a subsequent study to investigate the individual level factors which might explain the spatial distribution of the TB burden in Windhoek.

Specifically, phase three aimed to describe the characteristics (socio-demographic and behavioural factors) of people from a high TB burden township in relation to those of people from a low TB burden township. Moreover, the study aimed to determine whether TB knowledge, attitudes and practices could explain the spatial pattern of the disease.

In the subsequent sections of this chapter, I present the literature review (Section 5.2), methods (Section 5.3), results (Section 5.4) and a discussion of the findings (Section 5.5).

5.2. Literature review

The literature review for this phase was divided into three parts, and the first involved studies that documented the individual level socio-demographic and behavioural factors for TB disease. The second part considered studies that investigated individual level risk factors for TB hotspots, in other words factors which might explain the disease spatial distribution. The third part comprised of studies that analysed TB knowledge, attitudes and practices in the general population. After all the three literature review sections, an overall summary is provided which also explains how my study will contribute to the current TB literature.

5.2.1. *Part one: A review of individual level socio-demographic and behavioural factors for TB*

Worldwide, hundreds of studies have been conducted to assess the individual level risk factors for TB disease, alongside several systematic reviews (33, 43, 46, 196). To understand how specific factors are related to TB disease as reported within specific countries, I conducted a review of primary studies which documented a quantitative association between TB disease and selected socio-demographic factors (education, employment, household overcrowding and nutritional status) or behavioural factors (alcohol consumption and smoking). This was not a systematic review, but I used search terms at first to locate the relevant literature. The specific objective of the review was:

1. To critically review the findings of studies which quantified an association between TB and socio-demographic or behavioural risk factors, and to identify sources of inconsistencies in the findings (if any).

5.2.1.1. Literature search

Articles were searched for in electronic databases, namely Scopus, Embase and Web of Knowledge. Primary studies focusing on either pulmonary or extra-pulmonary TB among people of all ages and sexes were included. I have not reviewed primary studies solely conducted in specific high-risk congregate settings such as prisons or those which exclusively involved specific high-risk populations such as healthcare professionals, HIV/AIDS positive people or household contacts of TB cases. In addition, I have not reported evidence from studies that exclusively analysed risk factors for TB recurrence or for specific cases of TB such as MDR TB.

5.2.1.2. Literature synthesis

Since studies used varying measures of exposure variables and different populations, it was not possible to provide a quantitative summary, and therefore I provided a narrative summary but also presented tables showing the associations reported in individual studies.

5.2.1.3. Review results

Twenty-one studies were reviewed, and are summarised in detail Appendix E. Eleven studies were from Africa (197-207), six from Asia (208-211), two from North America (212, 213), one from South America (214) and one from Europe (215).

A number of studies assessed multiple factors, and so these will be included in the various sub-sections of the narrative synthesis, which is summarised according to the specific factors examined.

To avoid repetition, an appraisal of studies regarding sources of heterogeneity in findings is provided in the subsequent section (Section 5.2.1.4).

5.2.1.3.1. Employment status

The association between employment status and TB was assessed in eleven studies as shown in Table 5.1. Three of these studies reported that unemployment is a risk factor for TB (204, 213, 216). After adjusting for district TB unit of enrolment, Tiemersma *et al.* in Vietnam reported that the risk of TB in people who had no jobs was, OR=4.30, 95% CI: 1.18-15.6, while for the self-employed this was OR=1.86, 95% CI: 1.07-3.24 (216). Case control studies by Ladefoged *et al.* in Greenland (213) and by Lienhardt *et al.* (204) also reported similar findings. However these studies also reported results which were not adjusted for confounders. In two studies, associations reported may have been under or overestimated, due to the potential misclassification of participants according to exposures. In particular, Ladefoged *et al.* reported that students were classified as employed, whereas Tiemersma *et al.* reported that housewives and retired people were excluded from the unemployed.

Interestingly, two studies conducted in Malawi (199, 201) reported an increased risk of TB for people involved in professional/salaried or skilled jobs compared to those involved in farming. The authors explained that their results suggest that jobs other than farming might be associated with increased risk of TB transmission, through social mixing, travelling (in crowded minibuses) or working in indoor crowded environments (201). However, although these two studies adjusted for confounders such as age, sex, HIV, they did not adjust for behavioural factors such as smoking and alcohol consumption. Since cases were diagnosed through passive case finding method in rural settings, it is possible that their results may have occurred due to a selection bias. In other words, one cannot rule out the possibility that TB cases who participated in the study were those from better socio-economic backgrounds, because of better access to healthcare services.

Six studies reported no significant association between employment and TB disease (198, 202, 203, 207, 209, 215). The lack of association reported in four case control studies (203, 207, 209, 215) may have been due to small sample sizes.

In summary, out of the eleven studies which reported an association between employment status and TB disease, three found that unemployment is a risk factor for TB, while two reported opposite results. Six studies found no significant associations. However, the findings of some studies were not entirely convincing due to methodological issues such as the ones explained above.

Table 5.1: Studies which analysed the association between employment status and TB disease

ID		Variable categories	Reported association OR (95%CI).	Adjustment of confounders
1	Odone *et al*., 2013(201) Country: Malawi	Farmer/fisherman Not working/child/retire/casual Manual/trade/small business Salaried/large business	1 0.89 (0.7-1.13) 1.44 (1.11-1.88) 1.46 (1.06-2.01)	Adjusted age, sex, HIV, area, calendar year, distance to closest health centre, distance to district hospital
2	Boccia *et al*., 2011(207) Country: Zambia	Employed Self-employed Unemployed	1 0.7 (0.3-1.5) 0.9 (0.4-2.0)	Adjusted for age group, area of residence and household Socioeconomic position
3	Crampin *et al*., 2004 (198) Country: Malawi	Farmer/Fisherman Unskilled Skilled mannual +clerical Manegerial/adminstration	1 1.3 (0.6-2.7) 0.8 (0.6-1.2) 0.5 (0.3-1.0)	Adjusted for age, sex, area and HIV
4	Glynn *et al*., 2000 (199) Country: Malawi	Farmer Other Unknown	1 2.9 (1.4-6.0) 1.9 (0.75-4.6)	Adjusted for age, sex, housing , HIV and schooling
5	Hill *et al*., 2006 (202) Country: The Gambia	Unemployed Unskilled worker Skilled worker Professional Other	2.70 (0.56-12.94) 1 0.65 (0.24-1.71) 0.22 (0.03-1.72) 1.17(0.38-3.61)	Electric /gas cooker; ceiling, wall type, floor type, number of windows, crowding index, exposure to TB in household
6	Karim *et al*., 2012 (209) Country: Bangladesh	Working mothers	2.65 (0.56-12.50)	Age, gender, education, family composition, household overcrowding, household condition, type of kitchen, location of kitchen, contact with people outside family
7	Ladefoged *et al*., 2012(213) Country: Greenland	Social funds Workers/at school	4.08 (1.71-9.76)	Unadjusted
8	Lienhardt *et al*., 2005(204) Multi-site study: (The Gambia, Guinea Bissau and Guinee Conakry	unemployed unskilled mannual farmer skilled mannual non-mannual professional	1.20 (0.86-1.67) 1 5.78.96 (1.89-17.67) 1.91 (1.44-2.54) 1.21 (0.85-1.71) 1.20 (0.69-2.10)	Unadjusted
9	Ngadaya *et al*., 2006 (203) Country: Tanzania	Housewife Employed/Sel-employed	1.9 (0.85-4.25) 1	No association at univariable analysis
10	Tiemersma *et al*., 2013(216) Country: Vietnam	Has no job Self-employed	4.30 (1.18-15.6) 1.86 (1.07-3.24)	Adjusted for district TB unit of enrolment

11	Tocque *et al.*, 2001(215) Country: England	Working	0.72 (0.42-1.21)	No association at univariable analysis

5.2.1.3.2. Education level

Thirteen studies presented in Table 5.2 investigated the association between education level and TB disease. Of these, three found that low education is a risk factor for TB (206, 214, 216). In particular, Tiemersma *et al.* in Vietnam found that people with college or university level education were less likely to have TB compared to those with primary or less education (216). Steven *et al.* in Brazil reported that illiterate children aged 7-19 were approximately four times more likely to have TB compared to literate children (OR=3.62, 95% CI:1.08-12.07). The results of the Steven *et al.* study were adjusted for sex, contact history of TB, relation to household head, smoking, and piped water (214). In Ethiopia, Tesema *et al.* found that illiterate people were about three times more likely to have active TB compared to people with secondary or higher education level (OR=3.3, 95% CI:2.24-4.95) (206). Tesema *et al.* adjusted for kitchen location, TB contact history, presence of ceiling, presence of windows, and people per sleeping room. However, none of the three studies adjusted for HIV/AIDS infection, which is a potential risk factor for TB (1) and is also related with education level (217). Therefore, one cannot rule out that those with low education may have been those affected with HIV/AIDS.

Ten studies found no significant association between TB and education level (198, 199, 201-204, 207-210). The lack of association in some studies may have been due to small sample sizes (203, 207-209). However, even in those studies with reasonably large samples, the association between education level and TB was not established (198, 201, 204). These studies suggest that the relationship between education level and TB may be confounded by other factors.

In summary, three out of thirteen studies reported an association between education level and active TB disease. These studies all found that people with low literacy were at increased risk of TB compared to literate people. However not all confounders were considered in these studiers. Ten other studies did not establish this association, this may have been due to small sizes in some studies, but it might also suggest that effect of education level on TB only exist when important confounders such as HIV/AIDS infection are not taken into account.

Table 5.2: Studies which analysed the association between education level and TB disease

ID		Variable categories	Reported association OR (95%CI).	Adjustment of confounders
1	Odone *et al.*, 2013 (201) Country: Malawi	**Schooling** None 1-5 5-8 Secondary	 1 0.74 (0.53-1.03) 0.73 (0.52-1.02) 0.69 (0.43-1.09)	Adjusted age, sex, HIV, area, calendar year, distance to closest health centre, distance to district hospital
2	Boccia *et al.*, 2011 (207) Country: Zambia	Being illiterate **Highest education grade** 1-4 5-7 8-9 10-12 College	1.4 (0.5-3.8) 1 2.1 (0.6-6.6) 1.8 (0.5-6.3) 0.7 (0.2-3.9) 3.6 (0.6-21.2)	Adjusted for age group, area of residence and household Socioeconomic position
3	Crampin *et al.*, 2004 (198) Country: Malawi	None Primary 1-5 Primary 6-8 Secondary /Tertiary	1 1.5 (0.8-2.8) 1.2 (0.7-2.4) 1.3 (0.7-2.7)	Adjusted for age, sex, area and HIV
4	Glynn *et al.*, 2000 (199) Country: Malawi	None 1-5 primary 6-8 primary Secondary unknown	1 2.0 (0.89-4.3) 1.0 (0.38-2.8) 1.7 (0.42-6.6) 1.6 (0.49-5.2)	Adjusted for age, sex, housing , HIV and occupation
5	Hill *et al.*, 2006 (202) Country: The Gambia	**Years of schooling** none 1-4 5-8 >8	 1 0.65 (0.26-1.62) 1.07 (0.52-2.22) 0.60 (0.30-1.22)	No association at univariable analysis
6	Karim *et al.*, 2012 (209) Country: Bangladesh	Primary and above education Literate mothers	0.32 (0.10-1.00) 1.62 (0.86-3.05)	Age, gender, mother employment status education, family composition, household overcrowding, household condition, type of kitchen, location of kitchen, contact with people outside family
7	Ngadaya *et al.*, 2006 (203) Country: Tanzania	Primary >Primary education	1.6 (0.46-5.46)	No association at univariable analysis
8	Lienhardt et al., 2005 (204) Multi-site study: (The Gambia, Guinea Bissau and Guinee Conakry	**Schooling** No 1-5 >5	 1 1.08 (0.79-1.46) 0.96 (0.76-1.21)	No association at univariable analysis
9	Shalini *et al.*, 2015 (208) Country: India	Illiterate Literate Primary Seocndary Higher secondary and above	 Chi square test =3.812 df=4 p- value 0.4320	No association at univariable analysis

ID		Variable categories	Reported association OR (95%CI).	Adjustment of confounders
10	Tiemersma et al., 2013(216) Country: Vietnam	Primary school or less Secondary school Continued education after secondary College or university	1 0.29 (0.06-1.54) 1.92 (1.07-1.90) 0.29 (0.05-1.52)	Adjusted for district TB unit of enrolment
11	Tipayamongkholgul *et al*., 2005 (210) Country: Thailand	**Fathers education** Elementary Secondary Vocational degree Bachelor degree or higher **Mothers education** Elementary Secondary Vocational degreee Bachelor degree or higher	 0.73 (0.33-2.07) 0.75 (0.30-1.88) 0.39 (0.09-1.65) 1 0.23 (0.28-1.33) 0.74 (0.30-1.98) 2.39 (0.49-11.61) 1	No association at univariable analysis
12	Stevens *et al*., 2014 (214) Country: Brazil	**Literacy** Yes No	 1 3.62 (1.08-12.07)	Sex, Contact history of TB, relation to household head, smoking, piped water,
13	Tesema *et al*., 2015 (206) Country: Ethiopia	Illiterate Primary Secondary or above	3.3 (2.24-4.95) 0.85 (0.54-1.35) 1	Kitchen position, TB contact history, presence of ceiling, presence of windows, people per sleeping room

5.2.1.3.3. Alcohol consumption

Eleven studies shown in Table 5.3 assessed the relationship between alcohol consumption and TB disease. Six of them reported that increased alcohol consumption is a risk factor for TB (198, 206, 208, 211, 213, 216). In particular, Tiemersrma *et al.*, Tesema *et al.* and Shalini *et al*. all reported that people who consumed alcohol had a significant increase of TB compared to those who never drank alcohol, but all these studies did not adjusted for confounders (206, 208, 216). In the Kolappan *et al*. study from India and the Ladefoged *et al.* study from Greenland (211, 213), an increased risk of TB among people who consumed alcohol compared to those who never consumed or seldom drinkers was reported. Moreover, in another study by Crampin *et al.* from Malawi, it was reported that ex-drinkers were two times more likely to have TB disease compared to those who never drank alcohol (OR=2.3, 95% CI: 1.3-4.1). When they analysed by sex, Crampin *et al.* found that women who were ex-drinkers were about five times more likely to have TB compared to women who never drank alcohol (OR=5.3, 95% CI: 1.4-19.8), but this was not reported amongst men (198). However, the results reported amongst women in the Crampin *et al.* study may have occurred by chance as the number of women in the several categories of alcohol consumption were small (hence the wide confidence intervals).

A large scale study in India by Oxlade *et al.* reported no association between alcohol consumption and TB disease, after adjusting for a number of confounders including smoking, indoor air pollution, low body mass index, HIV/AIDS status, diabetes status, gender, age, household density (218). However, in that study, TB disease was self-reported, and so the lack of association may have been due to report bias. In a Brazilian study conducted by Steven *et al.*, the lack of association may have resulted from the fact that 80% of participants were all considered as non-drinkers (214). An association between alcohol consumption and TB was also not established in other studies (202, 207, 215).

In summary, out of the eleven studies which reported association between alcohol consumption and TB, six reported evidence suggesting that alcohol consumption is a risk factor for TB, whereas five others did not report an association. The study results were nonetheless unconvincing due to methodological issues.

Table 5.3: Studies which analysed the association between alcohol consumption and TB disease

ID		Variabble categories	Reported association OR (95%CI).	Adjustment of confounders
1	Oxlade *et al.*, 2012 (218) Country: India	Alcohol use daily	1.36 (0.73-2.55)	Adjusted for smoking, chewing tobacco, indoor air pollution, low BMI, HIV status, Diabetes status, gender, age, household density, family member with insurance, rural dwelling, smoking other than tobacco/cigarettes, frequent intake of meat, frequent fresh produce intake
2	Boccia *et al.*, 2011 (207) Country: Zambia	Alcohol abuse	1.6 (0.9-3.1)	Adjusted for age group, area of residence and household Socioeconomic position
3	Crampin *et al.*, 2004 (198) Country: Malawi	**Both gender** Never Ex drinker ≤ 1 per week ≥ 1 per week **Men** Never Ex drinker ≤ 1 per week ≥ 1 per week **Women** Never Ex drinker ≤ 1 per week ≥ 1 per week	 1 2.3 (1.3-4.1) 0.6 (0.4-1.0) 1.2 (0.7-2.1) 1 1.5 (0.7-3.2) 0.3 (0.2-0.7) 0.6 (0.3-1.3) 1 5.3 (1.4-19.8) 0.4 (0.2-1.1) 1.5 (0.4-4.8)	Association for both gender adjusted for: age, sex, area of residence, HIV status Gender specific association adjusted for : age, sex, area of residence, HIV status marital status, household possessions score, family/household contact with TB, other known contact with TB, BCG scar

ID		Variabble categories	Reported association OR (95%CI).	Adjustment of confounders
4	Hill *et al*., 2006 (202) Country: The Gambia	Never Current/past	1 2.05 (0.79-5.32)	No association at univariable analysis
5	Kolappan *et al*., 2007 (211) Country: India	**Alcohol staus** Non-Alcoholic Alcoholic	 1 1.5 (1.2-2.0)	Adjusted for age, gender and smoking
6	Ladefoged *et al*., 2012 (213) Country: Greenland	**Alcohol use** Seldom Often	 1 3.06 (1.07-8.73)	Ethnicity, town, water supply, access to flushing toilet, access to bathroom, smoking, immune suppressive treatment; Food (tradition Vs Western)
7	Shalini *et al*., 2015 (208) Country: India	**Alcohol consumptiom** Yes No	Chi square test =5.057 df-1 p-value 0.0245	Unadjusted
8	Tesema *et al*., 2015 (206) Country: Ethiopia	**Alcohol drinking** Yes No	 1 0.346 (0.232-0.514)	Unadjusted
9	Tiemersma *et al*., 2013 (216) Country: Vietnam	**Alcohol** Yes No	 1.82(1.16-2.85) 1	Adjusted for district TB unit of enrolment
10	Stevens *et al*., 2014 (214) Country: Brazil	**Alcohol use** No Yes	 1 0.99 (0.60-1.61)	No association at univariable analysis
11	Tocque *et al*., 2001 (215) Country: England	Drink >30 units per week	1.33 (0.67-2.66)	No association at univariable analysis

5.2.1.3.4. Smoking

Fourteen studies summarised in Table 5.4 below investigated the association between smoking and TB disease, and eight of these reported significant associations showing that smoking is a risk factor for TB disease (197, 204, 208, 210, 211, 213, 215, 216). A UK based study by Tocque *et al*. reported that people who smoked for at least 30 years were about 2 times more likely to have TB (215). In Vietnam, Tiermersma *et al*. reported similar results indicating that people who ever smoked were 2 times more likely to have TB compared to those who never smoked (216). Tiermersma *et al*. also showed that an increase in the number of cigarettes smoked was associated with increased risk of TB. Both Tiermersma *et al*. and Tocque *et al.* did not adjust for confounders. Two hospital based studies by Ladefoged *et al*. and Tipayamongul *et al.* respectively reported an increased risk of TB among smokers and children who stayed close to people who smoke (210, 213). Although these two studies were hospital-based studies they did not adjust for possible underlying clinical conditions, which may have been related with TB and smoking. In a multi-site their study, Lienhardt *et al.* found that current smokers were at an increased risk of TB compared to never smokers (OR=2.03, 95% CI: 1.22-3.39) (204). The Lienhardt *et al.* study adjusted for a number of confounders such as alcohol, asthma, HIV/AIDS, exposure to a TB case and socioeconomic variables. Similarly, Ladefoged *et al.* in Greenland and Kollapan *et al.* in India also found similar results suggesting a high risk of TB among smokers (211, 213).

Six studies reported no association between smoking and TB (198, 201, 202, 207, 214, 218). The lack of association in Oxlade *et al*. study may have been due to a possible report bias since TB status was self-reported (218), while small sample sizes may have affected potential associations in other studies (201, 202, 214).

In summary, the results from reviewed studies are inconsistent. Eight studies reported evidence showing that smoking is a risk factor for TB, while six did not establish this association. There were methodological issues noted in most of the studies as highlighted above.

Table 5.4: Studies which analysed association between smoking and TB disease

ID		Variable categories	Reported association OR (95%CI).	Adjustment of confounders
1	Oxlade *et al.*, 2012 (218) Country: India	Smoking cigrettes	0.77 (0.56-1.06)	Adjusted for smoking, chewing tobacco, indoor air pollution, low BMU, HIV status, Diabetes status, gender, age, household density, family member with insurance, rural dwelling, smoking other than tobacco/cigarettes, frequent intake of meat, frequent fresh produce intake
2	Odone *et al.*, 2013 (201) Country: Malawi	**Ever smoked** No Yes	 1 0.85 (0.68-1.06)	Adjusted for age, sex, area and calendar period
3	Boccia *et al.*, 2011 (207) Country: Zambia	Cigarette smoking	1.5 (0.6-3.3)	Adjusted for age group, area of residence and household Socioeconomic position
4	Crampin *et al.*, 2004 (198) Country: Malawi	Men Never Ex smoker 5/per day >5/per day	 1 1.6(0.7-3.2) 0.9 (0.5-1.7) 1.3 (0.7-2.4)	Adjusted for age, sex, area and HIV
5	Hill *et al.*, 2006 (202) Country: The Gambia	**Smoker in the past 6 months** No Yes	 1 1.88 (0.83-4.26)	Adjusted for ethnic group, Occupation, crowding index, presence of ceiling, household TB contact
6	Kolappan *et al.*, 2007 (211) Country: India	 Non-Smoker Smoker	Prevalenxe Odds ratios (POR) 1 2.1 (1.7-2.7)	Adjusted for age, gender and alcohol
7	Ladefoged et al., 2012 (213) Country: Greenland	Smoker Previous smoker Never smoker	2.83 (1.23-6.53) 1.84(0.72-4.69) 1	Ethnicity, town, water supply, access to flushing toilet, access to bathroom, alcohol, immune suppressive treatment; Food (tradition Vs Western)
8	Lienhardt et al., 2005 (204) Multi-site study: (The Gambia, Guinea Bissau and Guinee Conakry	Never Past current	1 1.53 (1.11-2.10) 2.03 (1.22-3.39)	Adjusted for sex, HIV infection, marital status, History of asthma, family TB history, number of adults in household, ownership of house
9	Shalini *et al.*, 2015 (208) Country: India	**Present smoker** Past smoker Non-smoker	 Chi square test =13.769 df=2 P value 0.00102	Unadjusted
10	Tiemersma *et al.*, 2013 (216)	Ever smoked tobbaco Currently smokes tobbaco Cigarretes smoked per day,	2.13 (1.32-3.44) 0.82 (0.47-1.43) 1.92 (1.32-2.79)	Adjusted for district TB unit of enrolment

ID		Variable categories	Reported association OR (95%CI).	Adjustment of confounders
	Country: Vietnam			
11	Tipayamongkholgul *et al*., 2005 (210) Country: Thailand	**Passive smoking** No Not close Close/very close	 1 0.54 (0.25-1.16) 9.31 (3.14-29.58)	Adjusted for age, average number of persons per room and frequency of illness
12	Stevens *et al.*, 2014 (214) Country: Brazil	**Smoking** No Yes	 1 1.58 (0.62-4.02)	Sex, Contact history of TB, relation to household head, literacy, piped water,
13	Tocque *et al*., 2001(215) Country: England	Smoked for at least 30 years	2.3 (1.2-4.2)	Unadjusted
14	Tulu *et al*., 2014 (197) Country: Ethiopia	**Smoking cogarettes** Yes No	 3.90 (1.20-12.40) 1	Residence, age, marital status, living situation, family size, active TB patient contact, HIV status

5.2.1.3.5. Household overcrowding

Ten studies presented in Table 5.5 analysed the relationship between household level overcrowding and TB, and eight of these reported findings suggesting that overcrowding is a risk factor for TB (197, 200, 204, 206, 208, 210, 212, 218). However the results reported in some of the studies were not adjusted for potential confounders (208, 212). Lienhardt *et al.* and Tipayamongkholgul *et al.* reported that the risk of TB increased with an increase in the number of people in the household (204, 210). However, the Tipayamongkholgul *et al.* study had a relatively small sample size, and so their results might have occurred by chance, as indicated by wide confidence intervals. The Tulu *et al.* study in Ethiopia reported that people in houses with more than five people were at an increased risk of TB infection compared to those in houses with five or less people (OR=4.10, 95% CI: 1.60-10.80) (197), but their study also had a small sample. A cross sectional study by Gustafson *et al*. in Guinea Bissau reported that people in houses with three or more people were at an increased risk of TB compared to people living in houses with two or less people (200). The sample size for the Gustafson *et al*. study was reasonable but they did not adjust for socioeconomic variables such as education and employment, which are related to both household over-crowding and TB. A study based on a nationally representative sample found that in India found that an increase in the number of people per sleeping room was associated with an increased risk of TB (218). The association is that study may have been underreported given that TB disease was self-reported, particularly if people from poor socioeconomic backgrounds underreported their TB diagnosis.

Two studies found no association between household overcrowding and TB disease (209, 213). In particular, Ladefoged *et al.* in Greenland adjusted for a number of potential confounders and found no association between the number of people in the household and TB. However, the binary classification of overcrowding (< 1 person per room versus >1 per room) in Ladefoged *et al.* study may have been the main cause of the lack of association in this study (213). The Karim *et al.* study from Bangladesh also found no association between people per sleeping room and TB disease, but their study also had a small sample (209).

In summary, among the studies reviewed, evidence regarding household overcrowding and TB disease has been consistent, with the majority of studies indicating that household overcrowding is associated with an increased risk of TB. Only two out of the ten studies found no significant associations. I have nonetheless observed methodological limitations in most studies.

Table 5.5: Studies which analysed the association between household overcrowding and TB disease

ID		Variable categories	Reported association OR (95%CI).	Adjustment of confounders
1	Oxlade *et al*., 2012 (218) Country: India	Household density (rooms for sleeping/people sleeping	1.08 (1.03-1.14)	Adjusted for smoking, chewing tobacco, indoor air pollution, low BMU, HIV status, daily alcohol use , Diabetes status, gender, age, family member with insurance, rural dwelling, smoking other than tobacco/cigarettes, frequent intake of meat, frequent fresh produce intake
2	Chitoor *et al*., 2013 (212) Country: Mexico	Overcrowding	0.214 (0.071-0.649)	Unadjusted
3	Gustafson *et al*., 2004 (200) Country: Guinea Bissau	**Adults in household** 1-2 3-4 5-8 >8 **Children in household** 0 1-2 3-4 ≥5	 1 1.67(1.15-2.42) 1.68 (1.09-2.57) 1.86 (1.04-3.31) 1 0.72 (0.50-1.04) 0.57 (0.38-0.86) 0.51 (0.32-0.80)	Adjusted for age, sex, ethnic group, living area, type of household, child crowding, presence of ceiling, quality of foundation. Adjusted for age, sex, ethnic group, living area, type of household, adult crowding, presence of ceiling, quality of foundation

ID		Variable categories	Reported association OR (95%CI).	Adjustment of confounders
4	Karim *et al*., 2012 (209) Country: Bangladesh	More than two persons per room	2.32 (0.81-6.64)	More than 14 years of age, sex, education level, mother literacy, mother employment, family composition, household condition, in house kitchen vent, kitchen position, duration of TB contact in household, contact with TB person outside family
5	Ladefoged et al., 2012 (213) Country: Greenland	**Person per room** >1 ≤1	 1.41(0.92-2.16) 1	No association at univariable analysis
6	Lienhardt et al., 2005 (204) Multi-site study: (The Gambia, Guinea Bissau and Guinee Conakry	**Adults in household** 1-5 6-10 >10	 1 1.37 (1.03-1.82) 2.80 (1.71-4.57)	Sex, HIV infection, smoking, history of asthma, marital status family history of TB, ownership of house,
7	Shalini *et al*., 2015 (208) Country: India	Overcrowding	 Chi square test =5.864 df=2 P value 0.01545	Unadjusted
8	**Tesema *et al*., 2015 (206)** **Country: Ethiopia**	**Persons per household** ≤4 >4 **Room space per person** <4 ≥4	 1 1.309 (2.07-4.61) 3.11 (2.09-4.63) 1	Education, Kitchen position, TB contact history, presence of ceiling, presence of windows
9	Tipayamongkholgul *et al*., 2005 (210) Country: Thailand	**Average number of persons per room** 1 person or less 1.1-2.9 persons 3-4.9 persons 5 persons or higher	 1 1.04 (0.34-3.22) 1.44 (0.46-4.57 11.18 (2.35-53.20)	Adjusted for age, frequency of illness, passive smoking
10	Tulu *et al*., 2014 (197) Country: Ethiopia	**Family size** ≤5 >5	 1 4.10(1.60-10.80)	Residence, age, marital status, living situation, smoking cigarette, active TB patient contact, HIV status

5.2.1.3.6. Nutrition related variables

The association between nutrition related measures and TB was assessed in six studies summarised in Table 5.6. Four of these reported significant associations suggesting that poor nutrition is a risk factor for TB (206, 212, 213, 218). In particular, Ladefoged *et al.* in Greenland and Oxlade *et al*. in India found that people with low BMI were at an increased risk of TB disease compared to those with normal BMI (213, 218). However, neither study adjusted for socio-economic confounders such as education and employment which are risk factors for TB and related to nutrition (219, 220). This was the same limitation in a Mexican case control study by Chitoor *et al.* which found that people who felt that their nutritional intake was of poor quality were at an increased risk of TB compared to those who viewed their nutrition to be of good quality (212). Similarly, Tesema *et al.* in Ethiopia reported that people who indicated that they consume fewer than three meals a day were about seven times more likely to have TB compared to those who had more than three meals a day (206). However, both Chitoor *et al.* and Tesema *et al.* reported unadjusted associations, and so the associations found may be due to unmeasured confounders.

A Zambian by Boccia *et al*. found no association between TB disease and frequency of meals consumed per day (207), while a study in Thailand also reported no association between nutrition status and TB (210).

In summary the evidence regarding nutritional status and TB disease is not convincing as studies that found that poor nutrition is a risk factor for TB (n=4) did not adjust for potential confounders and those that reported no association (n=2) were smaller studies. The inconsistent results might be due to methodological issues or because of the small number of studies which documented this association.

Table 5.6: Studies which analysed the association between food consumption and TB disease

ID		Variable categories	Reported association OR (95%CI).	Adjustment of confounders
1	Oxlade *et al*., 2012 (218) Country: India	Low BMI	3.71 (2.84-4.83)	Adjusted for smoking, chewing tobacco, indoor air pollution, HIV status, Diabetes status, gender, age, household density, family member with insurance, rural dwelling, smoking other than tobacco/cigarettes, frequent intake of meat, frequent fresh produce intake
2	Boccia *et al.*, 2011 (207) Country: Zambia	≤2 meals a day	1.3 (0.6-2.6)	Adjusted for age group, area of residence and household Socioeconomic position
3	Chitoor *et al*., 2013 (212) Country: Mexico	Poor nutritiom Good nutrition	10.70 (3.021-37.897) 1	Unadjusted
4	Ladefoged et al., 2012 (213) Country: Greenland	**BMI** Underweight (<18.5) Normal (18.5-24.9) Overweight(25-29.9) Obese (≥30)	 26.06(6.08-111.8) 1 0.27 (0.16-0.46) 0.06 (0.02-0.21)	Unadjusted

5	Tesema *et al*., 2015 (206) Country: Ethiopia	**Meal frequncy** < 3 meals a day ≥3 meals a day	 7.184 (5.003-10.316) 1	Unadjusted
6	Tipayamongkholgul *et al*., 2005 (210) Country: Thailand	**Nutrition staus** Normal Malnutrition (moderate) Malnutrition (severe)	 1 0.73 (0.32-1.69) 1.66 (0.59-4,75)	No association at univariable analysis

5.2.1.4. Appraisal: factors for the inconsistency in the literature

It is clear that the studies reviewed reported inconsistent findings with regards to the individual level socio-demographic or behavioural factors for TB. The differences in results may partly be due to methodological issues especially with regards to sample size, confounding and selection bias. I will now briefly discuss these elements below.

5.2.1.4.1. Sample size

In research, a large sample size is known to increase the statistical power of the study to find associations (if they exist). Therefore, studies with smaller sample sizes have reduced statistical power and are prone to report chance results. For example, some of the studies were generally small in sizes (207, 210, 212, 216), and these they tended to report non-significant results or weak associations, as suggested by wide confidence intervals. However, in some large studies (198, 218), associations related to certain variables were also not determined, and this suggest the effect of other aspects such as confounding or bias.

5.2.1.4.2. Confounding

Observational studies in general suffer from the issue of confounding. However, in some of the studies, researchers attempted to adjust for a number of factors to provide more convincing association. For example, Tesema *et al*. and Tiemersrma *et al*. both reported significant associations between alcohol consumption and TB disease, but none adjusted for confounders (206, 216). Similarly, Kolappan *et al*. reported an increased risk of TB disease among people who consume alcohol after adjusting for only age, sex and smoking (211). In contrast, Oxlade *et al*. did not establish this association after adjusting for various potential factors (such as smoking, chewing tobacco, indoor air pollution, low BMI, HIV status, Diabetes status, gender, age, household density) (218). Similarly, Crampin *et al*. did not report an association between TB and alcohol consumption by gender after adjusting for various confounders including age, sex, area of residence, HIV status marital status, household possessions score, family/household contact with TB, other known contact with TB, BCG scar (198). The lack of associations in these studies thus suggest that the results reported in studies which found association might be due to unmeasured confounders.

5.2.1.4.3. Selection Bias

The inconsistencies reported in studies may also have been due to a potential selection bias. For example in some studies, cases were recruited based on passive case finding methods, implying that some people may not have participated due to health access issues. For instance, two studies conducted in a rural village in Malawi reported no association rather unexpected results concerning the risk of TB and socio-economic variables (198, 201). One of these studies found that employed people were at increased risk of TB compared to the farmers (201). In addition, a case control study involving children aged 7 to 19 years found no association between measures of socio-economic background education, employment, household overcrowding (209). In that study both cases and controls were recruited at hospitals therefore it is also possible that these are children who might generally have better access to healthcare.

5.2.2. Part two: A review of individual level risk factors for the disease spatial distribution

I only found few studies which analysed the individual level risk factors for TB hotspots, and the findings of the most relevant studies are critically discussed below.

Recently, Huang *et al*. in China conducted a cross-sectional survey to assess biological, behavioural, socio-economic and local environmental aspects which might explain the TB distribution between towns in Zhaotong province (221). In their study, patients were consecutively recruited over a five months period and were classified according to whether a patient resided within or outside TB clusters (the TB clusters were determined using SaTScan). The Huang *et al*. study involved 1508 TB cases, out of which 813 cases were from cluster areas and 695 cases were not. Their multivariable logistic regression, which used location as an outcome binary variable (whether from cluster or not), found that history of bronchitis, living in an urban area and using coal as the main cooking fuel was associated with TB clustering. That study also found that not smoking, using electricity and low BMI were protective factors. However, the findings of this study were based on patients and not in people from the general population, therefore the generalisability of the study findings is questionable. Also, Huang *et al.* study included people mostly from the poor socio-economic backgrounds (farmers and migrant workers), and so it is questionable whether their results apply to cases from better socio-economic backgrounds. The authors did not give detail about the total number of cases notified during the period as well as some characteristics of those who did not consent to participate.

In Madagascar, Rakotosamimanana *et al*. conducted a study to assess the risk factors for TB hotspots in Antananarivo (222). In their study, neighbourhoods were divided into three groups, areas identified in principal TB clusters, areas in secondary cluster and areas outside clusters. The authors then conducted a survey among TB patients residing in each of the three groups. Their study found that there was no significant differences in the responses concerning education level, TB knowledge before treatment, or their attitudes since the diagnosis. In addition, the study found that the majority of TB patients from neighbourhoods identified in principal clusters had a contact with TB relative before their own diagnosis. Moreover, they reported that the majority of TB patients from areas outside clusters did not inform anyone about their diagnosis. Apart from the fact that the Rakotosamimanana *et al*. study was also based on information observed from TB patients, there were also other limitations. For instance, their study involved a relatively small number of patients (n=80). In fact the authors indicated that the majority of patients (especially from the cluster areas) refused to participate. Also their study did not assess differences in behaviours such as smoking, alcohol or health seeking behaviour. However one impressive effort form this study is that they also assessed whether TB KAP among the general population could explain the disease spatial distribution, but that was done through a qualitative study using focus groups.

In Connecticut, U.S, a recent study by Mullins *et al*. (223) also used logistic regression to study the characteristic of people infected with latent TB infection and TB patient according to whether they lived in a TB cluster or not. The study involved 9701 cases diagnosed with latent TB infection as well as 365 TB cases from 2010 to 2014. They found that being male, younger, black, foreign born and those who reported recent arrival in the U.S were significantly more likely to reside in the clusters. For TB patients, they reported that being male, black, non-Hispanic origin were more likely to reside in TB clusters. This study however reported results which were not adjusted for confounders.

In one study from the U.S, Oren *et al*. analysed routinely collected TB data to identify the characteristics of patients residing in cities with decreasing TB rates (224). Their study involved 42 448 patients diagnosed from 2000 to 2007 in 48 U.S cities (19 with declining rates and 29 with stable rates). The study reported that patients aged above 25 years, of black race, foreign born, HIV/AIDS positive and had history of non-injecting drug use were significantly more likely to be residents of a city with a decreasing TB rate. Furthermore, TB patients who reported excess use of alcohol and had been diagnosed in a correctional facility were significantly less likely to be from cities with decreasing rates. Although this study assessed a number of variables, the classification of cities according to decreasing rates may have been less informative. It could have been better if they had classified TB patients according to clusters as was done in the Huang *et al*. and Rakotosamimanana *et al*. studies.

5.2.3. Part three: A review of TB Knowledge, Attitudes and Practices (TB KAP)

This section considered studies that quantitatively analysed TB KAP in the general population. The specific objectives of this review were:

- To critically review the study findings.
- To critically review the methods used to investigate TB KAP in the general population.

5.2.3.1. Literature search

Studies were obtained from Web of Knowledge, Scopus, and Google Scholar as well as through reading reference lists of identified studies. I was mostly interested in studies conducted in developing countries, particularly in Africa. Studies were not reviewed if they exclusively assessed TB KAP in specific groups such as TB patients, healthcare workers or HIV/AIDS infected people.

5.2.3.2. Literature synthesis

In the narrative synthesis below, I present the findings of studies grouped according to specific components. Studies have analysed multiple components of TB KAP, and so they will be included in the various sub-sections of the review.

To avoid repetition (since studies will be repeated across the components of the review), an overall appraisal of the methodologies used in studies is provided in the subsequent sections 5.2.3.3 and 5.2.3.4.

5.2.3.3. Review findings

Twenty studies were reviewed and these are summarised in detail in Appendix F. Four studies were from Ethiopia (135, 225-227) and there were two each from Nigeria (228, 229), Malaysia (230, 231), China (232, 233) and Pakistan (234, 235). One study was from each of the following countries South Africa (236), Lesotho(237), Tanzania (238), Uganda (35), Libya (239), India (240), Vietnam (241) and the Philippines (242).

5.2.3.3.1. TB sources of information

Studies reported similar results concerning the common sources of TB information, although few reported different results, and this suggest differences in socio-economic characteristics. In a predominantly rural state in Nigeria, Uchenna *et al.* reported that the most common sources of TB information mentioned by their participants were radio (60.0%), community members (29.8%), television (17.1%), family members (16.5%) and healthcare workers (15.5%) (228). Similarly, a Ugandan study by Obuku *et al*. conducted in three urban slums in Kampala reported that the most common sources of TB information were radio (50.0%) and healthcare workers (25.5%) (35). A large study from Inner Mongolia, China by Ma *et al.* found that the main communication channels were TV programmes (65.6%) and personal sources (47.2%) (232). Similarly, a Malaysian study by Salleh *et al.,* which mostly involved people with lower education level (67%), found that the most common sources of TB information were TV and radio (31.5%), health talk (19.0%), health workers (16.0%), friends (16.3%), family members (12.5%) and the internet (4.9%) (230).

In Libya, Mukhtar *et al*. conducted a study which mostly involved participants from urban areas with higher education level, and reported that most of their participants mentioned TV (44.7%), family members (24.2%) and healthcare workers (18.9%) as the main sources of TB information (239). Surprisingly, a rural based Vietnamese study by Hoa *et al.*, which mostly involved people with lower education level, who were mostly farmers, found that the most common sources of TB were TV (64.6%) and friends/relatives (42.7%). Hoa *et al.* also reported that the commonly suggested sources of TB information were TV (70.4%), loudspeakers (55.1%), community meetings (26.5%), Radio (25.0%); newspapers (11.2%), poster (9.7%), and health workers (8.1%) (241). Similarly, a Pakistani study by Mushtaq *et al.* which mostly involved people from rural areas (60%), reported that the most common sources of TB information mentioned were TV (69.4%), health care workers (43.6%), newspapers (17.7%), and friends (11.8%) (234). Although these studies involved people from rural areas, the participant characteristics reflected better socioeconomic background. For example, in Hoa *et al*. study, the majority of people were categorised as having above average economic background, and in Mushtaq *et al*. study, the majority of participants were classified as having at least secondary level (high school) education. These characteristics perhaps explains the mentioned sources of information such as TV, which in general is associated with better living condition, particularly in rural settings.

5.2.3.3.2. Knowledge about TB symptoms

The findings of studies shows that there is good understanding of the disease symptoms, although this varied between studies. A recent nationwide study from Lesotho by Luba *et al*. reported that a cough of several weeks (55.5%), night sweating (38.1%) and loss of appetite (22.8%) as the most common TB symptoms (237). In that study, the majority of participants were from rural areas (67%), but most people had at least primary level education. Gelaw reported through a nationwide study from Ethiopia found that 71.4% knew that a persistent cough was a common symptom of TB. Other known symptoms of TB were weight loss (34.94%) and poor appetite (12%) (226). The Gelaw *et al*. study also involved participants who were mostly from rural areas, but compared to Luba *et al.*, a high proportion of participants in Gelaw's study had no education. Therefore the fact that only 55% of participants in Lesotho mentioned a persistent cough as a symptom of TB compared to 71% in Ethiopia is somehow surprising, especially considering that Lesotho has a high TB burden compared to Ethiopia (1). These findings might suggest differences in TB health education interventions between the two countries.

The findings from studies conducted within specific communities (not nationally representative) were also generally similar, although the proportions varied, perhaps due to differences in disease knowledge between countries. For example, in the Uchenna *et al.* study, the most common symptoms mentioned were a longer cough (61.5%), weight loss (50.0%), coughing blood (32.3%), and difficulty breathing (12.9%)(228). Salleh *et al.* reported that the most commonly reported TB symptoms were a persistent cough (93.1%), haemoptysis (85.3%), tiredness (79.4%), chest pain (77.5%), weight loss (69.6%), shortness of breath (67.6%), loss of appetite (67.6%), fever (63.7%) and night sweats (23.5%)(230). Obuku *et al.* in Uganda found that the common symptoms were a long lasting cough (46.8%), any cough (46.4%), weight loss (33.4%), chest pain (27.6%) and coughing up blood (20.5%) (35).

Hoa *et al.* found that the most common symptoms were a cough of more than two weeks (92.0% women; 93.2% men); fever (33.1% women, 41.3 men) and loss of weight (17.4% women and 20.7% men) (241). In Pakistan, Mushtaq *et al.* found that their participants mostly mentioned a cough of more than three weeks (43.1%), haemoptysis (52.6%), fever (49.2%), weight loss (45.7%) and chest pain (24.9%) (234). Mushtaq *et al.'s* findings are similar to those of another Pakistani study conducted by Gilani and Khurram (235). In Ethiopia, Mesfin *et al.* conducted a study which mostly involved participants from rural areas and the majority were illiterate, they found that coughing (71.5%), loss of weight (66.5%) and night sweats

(33.3%) were the most common disease symptoms mentioned by their participants (135). In contrast, a study in Ethiopia by Bati *et al*. which also mostly involved participants from rural areas (with the majority classified as illiterate) reported that only 9% of their participants mentioned a cough a common symptom of TB. The majority of participants in that study mentioned haemoptysis (60%) and chest pain (30%). Bati *et al*. also presented their results by specific locations, but they did not analyse differences statistically (227).

5.2.3.3.3. Knowledge of modes of TB transmission

The findings concerning modes of transmission were also similar between studies, and coughing was mentioned as the most common mode of TB transmission. However the proportions also varied between studies. For example, the Salleh *et al.* study reported that the most commonly mentioned modes of TB transmission were coughing (91.2%), sneezing (73.5%), spitting (50.0%), talking (27.5%), and laughing (19.6%)(230). Mushtaq *et al.* reported that 63.4% identified coughing and sneezing as a mode of transmission followed by sharing utensils (44.2%) and sharing food (32%) (234). The Tolossa *et al*. study reported that cough (59.3%), sharing cups (35.6%) and sharing feeding materials (16.8%) were the most commonly mentioned modes of transmission among participants in their study (225). In Mesfin *et al.*, the common modes of transmission were cough (62.5%), drinking raw milk (35.7%), eating together (40.3%), sleeping together (54.4%), touching (30.8%) and mother to child during birth (33.2%)(135). In India, a nationwide study by Sreeramareddy *et al.* found that 55.5% knew about correct transmission modes but also identified that 26.8% of their participants did not know (240). In another nationwide study in Ethiopia, Gelaw reported that only 49.9% of men and 61.8% knew the correct modes of transmission (226). However, Gelaw did not analyse differences by sex statistically.

In some studies, the majority of participants mentioned that TB transmission is mostly through the air, but coughing or sneezing were not explicitly mentioned. For example, Obuku *et al.* reported that the majority of participants (54.3%) said TB was transmitted through the air, sharing utensils (45.6%) and sharing meals (19.8%) (35). The Uchenna *et al.* study reported that the majority of participants (49.0%) thought TB is transmitted through contact with someone with TB and in that study, 30% of participants knew that TB is an airborne infection (228). Hoa *et al.* reported that 65.7% of women and 77.9% men said TB is transmitted through the air (241). In contrast, Mukhtar *et al*. from Democratic Republic of Congo reported that most of their participants believed that TB is transmitted through sexual contact (79.2%), infected blood transfusion (62.1%) and drinking un-boiled milk (58.4%)

(239). The variation between studies might have resulted from differences in how the questions were phrased. For example in the Mukhtar study, participants were only required to indicate yes or no to the following transmission modes (sexual transmission from infected person to his/ her partner, by kissing an infected person, drinking un-boiled milk and infected blood transfusion).

5.2.3.3.4. TB treatment

In the Uchenna *et al.* study which mostly involved participants from rural areas, the participants knew that TB is a treatable disease, although there were some reported misconceptions. In particular, they found that 96.3% of their participants knew it is a curable disease and 90.5% mentioned it was cured by medication/drugs. The authors further reported that 5.6% of their participants said native drugs could cure TB, while 4.6% mentioned it can be cured by modern medication and native drugs, while 2.2% said TB could be cured by prayer (2.2%) (228).

In other studies, the majority of participants knew that TB is a treatable disease, but in some studies the proportion of those who knew about free treatment was low. For example, Mushtaq *et al.* reported that 92% of their participants knew that TB was treated at government facilities but only 48.8% knew that treatment was free (234). Obuku *et al.* reported that 85.1% of their participants said the disease is curable, 69.4% said it is cured by specific drugs and 80% of participants said TB is cured at government facilities. Moreover, Obuku *et al.* reported that 35% of participants said TB treatment is free, 32.2% said it is expensive and 25.3% said they did not know about TB treatment costs (35). Ma *et al.* found that 85.1% believed that TB could be partly or completely cured. Moreover Ma *et al.* reported that 57.5% of their participants knew about free diagnostic and treatment (232). Hoa *et al.* reported 69.6% of women and 80.2% of men knew that TB is a curable disease. Also they reported that 45.3% women and 57.0% men knew that TB treatment was free of charge (241). Gelaw found that 84.4% knew that TB could be treated (226), and this was similar to results from another Ethiopian study by Tolossa *et al*. (225). Wang *et al.* in China found that 42.8% of their participants did not know whether TB treatment is free and 39.2% indicated that it is free. In addition, Wang *et al.* reported that 73.6% of participants indicated that TB was a curable disease and 16.4% said it was curable only sometimes (233). It is surprising that even studies conducted in high burden countries such as China and Pakistan, a relatively high proportion of participants of did not know about the cost of TB treatment, perhaps this suggest the use of other treatment facilities such as the private sector or the use of traditional remedies.

5.2.3.3.5. Perceptions about TB

Few studies, quantitatively assessed perceptions about TB disease, and these were mostly studies that used questions from the WHO TB KAP questionnaire (243). The majority of these studies reported that TB was viewed as a common and serious disease. In particular, Mushtaq *et al.* reported that 63.4% of their participants considered TB to be a fatal disease and 54.2% said it was a common problem in Pakistan (234). Mushtaq *et al*. reported that these responses differed statistically according to income and education, but not housing. In another Pakistani study, Gilani and Khurram reported that some participants thought that TB would have a negative impact on future employment (38%), getting married (40%), having children (37%) and maintaining social contacts (39%) (235). In the Wang *et al.* study from China, it was reported that 71.8% (including 71.7% men and 71.9% women) regarded it as a severe disease and 68.1% (69.5% men and 66.8% women) regarded it as a disease which can seriously affect the ability to work (233). In Ethiopia, Tolossa *et al.* reported that only 55.4% of their participants thought that TB is a very serious disease and that 40.2% said it was a common problem in the study area. In addition, Tolossa *et al*. study reported that only 52.9% participants indicated that they could get TB (225). In contrast, Salleh et *al*.in Malaysia reported that only 1% of their participants felt that they were at high risk of TB and 17% said that other people (apart from their family members) were at higher risk of TB (230). The views in the Malaysian study, might be because of a less disease burden since the country is not classified as a high TB burden country.

5.2.3.3.6. Reactions to a TB diagnosis

In terms of reactions to a TB diagnosis, studies documented varying attitudes, which suggest differences in TB knowledge, but also differences in the level of TB stigma in specific settings. For instance, the Salleh *et al.* study found that 31.1% of their participants said they would not feel embarrassed if they had TB (230). Hoa *et* al.'s study which mostly involved participants from rural areas in Vietnam found that 43% of their participants said they would be afraid if they got TB (241). In Ethiopia, Tolossa *et al*. found that the majority of their participants (69.3%) would be afraid if diagnosed with TB, and 18.5% said they would feel sad and hopeless (225). The Mushtaq *et al.* study reported that 76.3% of their participants would be embarrassed once diagnosed with TB while 39.5% would feel hopeless (234).

5.2.3.3.7. Disclosing a TB diagnosis

Only a few studies, assessed perceptions about disclosing a TB diagnosis. In particular, in a nationwide study from India, Sreeramareddy *et al*. reported 15.6% of their participants would keep a TB diagnosis a secret in their families (240). This is consistent with findings from another nationwide study in Ethiopia, where Gelaw found that 76.5% would not keep a TB diagnosis a secret (72.1% of women and 81.3% of men) (226). The findings of those two studies are also consistent with those reported in a rural based study in China, where Wang *et al*. reported that 12.8% of women and 10.9% of men would keep TB diagnosis a secret (233).

5.2.3.3.8. Individual level attitudes towards TB patients and practices

Few studies assessed participants' attitudes towards TB patients, and the proportions reported in studies varied, perhaps also due to differences in disease burden and local understanding. In particular, Salleh *et al.* in Malaysia found that 10% of their participants said they would mingle with a person with TB (230). Ma *et al.* in China reported that 32.1% of their participants would support and not discriminate against their neighbours with TB (232). The Tolossa *et al*. study reported that the majority of their participants would have no particular feeling towards a person with TB (42.4%) and 39.0% said they would feel compassion and a desire to help a person with TB. Mushtaq *et al.* study, 72.2% said they would support their family members with TB, 19.7% of participants would be friendly but avoid them and 8.1% would hate them (234). Uchenna *et al.* in Nigeria reported that 47.0% of their participants said they would eat with a person with TB, 96.1% would care for a relative with TB, 92.1% would accommodate a person with TB and 95.6% would shake hands or hug a person with TB (228). In contrast, another study from Nigeria by Anochie *et al*. reported that most of their participants would not prefer to live in the same household with a TB patient (93.8%), share food with them (95.4%) or have physical contact (97.0%) (229). The two Nigerian studies had similar sample sizes, but the Anochie *et al*. study was conducted in a rural community while the Uchenna *et al.* study involved participants from both rural and urban areas. However, Uchenna *et al*. did not find statistical differences by location regarding the specific responses about attitudes towards TB patients.

5.2.3.3.9. Community attitudes towards TB patients and practices

Two studies quantified perceptions about how TB patients are viewed in communities. In particular, Mushtaq *et al*. in Pakistan reported that 47.9% of their participants believed that TB patients were victimised, 32.2% said people were friendly towards TB patients but avoided them, and 19.9% said the community was supportive of TB patients (234). Mushtaq *et al*. study involved people from both rural and urban areas, but they did not assess differences by location. In the Tolossa *et al*. study the majority of participants (51.7%) indicated that people in their community would support a person with TB, while 31.5% were unsure about how people in their community would react towards a TB patient (225). Hoa *et al.* found that 48.7% of women and 35.1% of men said TB is associated with stigma (241), but that study did not assess specific questions to quantify the level of stigma.

5.2.3.3.10. Health seeking behaviours

Studies which assessed practices about healthcare services reported similar results suggesting good health seeking behaviours. In particular, Uchenna *et al.* reported that 91% of their participants would visit a healthcare service once they suspected that they had TB (228). Uchenna *et al.* also reported that a significant proportion of participants (9%) would engage in self-medication. In Ethiopia, Tolossa *et al*. found that 71.0% of their participants would visit a health facility if they suspected TB, while 32.2% would pursue self-treatment (225). Tolossa *et al.* study presented findings by gender, but these were not analysed statistically. Mushtaq *et al.* reported that the majority of respondents (95.3%) would go to health clinics/hospitals if they had symptoms of TB. The Mushtaq *et al*. further reported that 72.8% would go to hospital as soon as they realised they had TB symptoms, 16.9% would go when symptoms lasted for 3-4 weeks, 3.8% would go when treatment on their own does not work, and 1.0% would not go to a health facility (234). In the Philippines, Portero Navio *et al*. reported that 49.7% of participants would seek medical advice if they were showing TB symptoms, 33.4% would not seek medical care and 16.9% would self-treat (242). The differences between studies suggest variation in health access, treatment options and perhaps trust in health care systems.

5.2.3.3.11. Proportion of participants with good/low knowledge

An appraisal of how studies measured the proportion of either good or low TB knowledge is provided in Section 5.2.3.4. In general studies reported similar proportions of participants with good knowledge. In particular, the Mushtaq *et al.* study in Pakistan reported that 43% of their participants had good TB knowledge (234). Mesfin *et al.* in Ethiopia recorded that 53% of their participants had moderate TB knowledge (135). Their finding is similar to those reported in two other Ethiopian studies, where the proportion of those with high TB knowledge was 54.4% in the Tolossa *et al.* (225) and 57.6% in the Bati *et al*. study (227). In their nationwide study from India, Sreeramareddy *et al.* (240) reported that 55.5% of their participants had correct TB knowledge, and this is similar to the proportion of 55.9% reported in the Gelaw's national level Ethiopian study (226). The Luba *et al*. nationwide study in Lesotho documented that 59.9% of their participants had good TB knowledge (237). In Uganda, Obuku *et al.* found that 49.7% of participants had moderate to high TB knowledge (35).

5.2.3.3.12. Determinants of TB knowledge

In the Mesfin *et al.* study, poor TB knowledge was associated with being female, illiterate and living in a rural area (135). In the Uchenna *et al.* study, the factors associated with TB knowledge, attitudes or practices were education, literacy, and religion (228). In their nationwide in India, Sreeramareddy *et al.* found that good TB knowledge was associated with being male, Hindu, Muslim, believing that TB can be cured, education level, wealth quintile and listening to the radio (240). In Lesotho, Luba *et al*. found that sex, age, educational level, formerly married or cohabitated, mass media exposure and occupation were associated with knowledge of TB (237). In Uganda, Obuku *et al.* found that older age and residential area were the factors associated with high TB knowledge scores, while the lack of formal education, unemployment and never testing for HIV were significant factors for poor TB knowledge scores (35). In the Gelaw's study, those with no access to newspapers and radio had lower TB knowledge (226). In Vietnam, Hoa *et al.* found that being male, married, aged younger than 55 years, not a farmer, having a high education and socio-economic were associated with increased TB knowledge scores (241). Mushtaq *et al.* found that good knowledge was significantly associated with high education level, high income and good housing (234). This is similar to the results reported in the Tolossa *et al*. study from Ethiopia (225). However none of these studies adjusted for health care seeking behaviours, which might also influence TB knowledge.

5.2.3.3. An appraisal of the methods used to investigate TB KAP

5.2.3.3.1. Participant recruitment and sample size

As expected, all the studies were cross-sectional survey, with participants recruited from the general public. In the majority of studies (35, 135, 225, 227-229, 231, 232, 234-236, 241), households were selected randomly and participants were recruited through household visits. However, not all authors commented on how well their final samples represented the targeted communities. In two studies, participants were recruited from the general places frequented by people in the target communities (239, 242). In one of these studies, the authors indicated that their sample characteristics reflected those of the targeted population (242). Three studies used secondary data collected through nationally representative demographic health surveys (226, 237, 240). However, the challenge with three large scale studies is that they were limited in scope.

Sample sizes varied between studies, and in the majority the sample sizes were determined statistically (35, 135, 225, 227-230, 234, 241), but in some there was no mention of how sample sizes were determined (231, 233, 235, 238, 242). Apart from studies which used national level samples (226, 237, 240), some studies had relatively small samples. For example, a study from South Africa only involved 80 participants (236), Salleh *et al*. from Malaysia had a sample of 102 participants (230), and similarly, Haasnoot *et al*. in Tanzania had a sample of 105 participants (238).

5.2.3.3.2. Study questionnaire

Three studies utilised questions taken from the WHO guiding questionnaire on assessing TB KAP (35, 225, 234), but the majority of studies did not use the WHO questionnaire (135, 226-229, 230 , 231-233, 235-237, 239-242). However, in some studies, the authors reported they used questions taken from other validated assessment tools (135, 228, 231, 233, 242).

5.2.3.3.3. Analysis of KAP data by demographic factors

The majority of studies investigated TB KAP in samples comprised of both urban and rural areas (135, 225-228, 232, 234, 235, 239-241). This combination might not be a good, given that TB KAP could differ by residence. Only one study from Enugu state, Nigeria by Uchenna *et al*. assessed statistical differences by location (228), and indeed they showed statistical differences by location in some components. Some studies were conducted exclusively in urban areas (35, 236, 242). For example, a Uganda study by Obuku *et al.* (35) assessed TB KAP in Kampala, but the content of that study was limited as they only analysed TB knowledge and not attitudes and practices. In the Philippines, a study by Portero Navio *et al*. was also conducted in urban settings, but they also only reported mostly on knowledge, and healthcare seeking behaviour (242). Similarly, a South African urban-based study by Promtussananon and Peltzer (236) only assessed TB knowledge questions and that study also had a relatively small sample of 80 participants.

Despite the fact that TB KAP may vary by demographic factors such as age and sex, the majority of the studies did not analyse differences in TB KAP by these demographic factors

(35, 135, 226, 228, 230, 232, 234, 238, 240, 242). For example, three large studies from Ethiopia, India and Lesotho (226, 237, 240), and community based Ethiopian studies (225) all presented TB KAP results by sex, but neither assessed the statistical significance of the results. In contrast, Wang *et al.* in China presented results by sex, yet only assessed statistical differences by sex for one component of TB KAP (233). Furthermore, a study from Vietnam by Hoa *et al*. analysed the statistical differences by sex, but the comprehensiveness of this study was limited, as they only focused on TB knowledge and not on TB attitudes and practices (241).

Another study from South Africa by Promtussananon and Peltzer analysed age differences, but their study also focused on components of TB knowledge (cause, risk reduction and treatment) and the sample size for this study was small (236). Similarly, the Anochie *et al.* study from Nigeria analysed age differences but only for two questions related to the cause and preventive measures (229). In Libya, Mukhtar *et al.* analysed statistical differences by age, sex and other socio-demographic factors(239), but similar to Promtussananon and Peltzer and Anochie *et al*., they only focused on TB knowledge questions and not on attitudes and practices.

5.2.3.4. An appraisal of how studies determined proportion with good or poor TB knowledge

Eleven studies assessed the proportion of good or poor TB knowledge (35, 225-228, 232, 234, 235, 237, 240, 241). In particular, Mushtaq *et al.* used nine questions and classified participants who correctly answered six or more questions as having good TB knowledge (234). However, the authors did not provide details about the exact questions used. Two studies used nationally representative surveys but in those studies, the prevalence of good knowledge was assessed using only one question about TB transmission. (226, 240), and so the level of good knowledge might have been overestimated in those studies. In contrast, another study from Lesotho assessed the prevalence of correct knowledge using several questions taken from various components including: TB symptoms, transmission and treatment (237). This is similar to four community based studies (35, 225, 227, 241). Nevertheless, these studies did not assess knowledge with a question on TB and HIV/AIDS co-infection, and so it possible that the prevalence of correct knowledge was overestimated. Uchenna *et al.* (228), Ma *et al.* (232) and Gilani and Khummar (235), all assessed the prevalence of correct knowledge separately concerning specific questions. Hence, in these three studies it is not possible to determine the prevalence of comprehensive knowledge.

5.2.4. Literature review summary

This section contained a literature review divided into three parts. The first part involved studies which quantified an association between TB and selected socio-demographic and behavioural factors. The aim was to enable an understanding of how factors at individual level have been related to TB disease. The findings showed that there are inconsistencies in the literature, particularly regarding variables such as education level, alcohol consumption and smoking. I have explained how factors such as sample size, confounding and bias might have influenced these inconsistencies.

The second part comprised of studies that assessed the individual level factors for the spatial distribution of TB. Although I did not conduct a systematic review, a search of the literature revealed that few studies have investigated individual level risk factors for TB hotspots. The three studies I found assessed the individual factors using information collected from patients and not from the general population (221, 222), and so the generalisability of the findings of these studies to the general population is questionable.

The third part focused on studies which quantitatively measured TB KAP in the general population. I found that studies generally produced similar findings, although there were differences in proportions, suggesting variation in sample characteristics and perhaps the differences in the magnitude of the disease burden between studies. I found that the majority of were based on reasonable sample sizes, and some studies were based on nationally representative sample (226, 237, 240), However, only a few studies have used the WHO for assessing TB KAP (35, 225, 234), and only few statistically analysed TB KAP by demographic factors.

Eleven studies measured the prevalence of either good or poor TB knowledge. Studies generally produced similar results, but some may have overestimated the prevalence, because not all relevant components of the disease were assessed (35, 225, 227, 237, 241). In some studies, prevalence was only established through the use of one question (228, 232, 235).

Therefore, considering the existing literature, my study aim to contribute to the literature in three different ways. Firstly, the study is the first to document factors (risk factors and TB KAP) which might explain the spatial distribution of TB in Khomas. Secondly, my study will take a different approach by using data collected from the general public data rather than in

TB patients. Thirdly, my study will statistically compare TB KAP in two specific locations with a dissimilar disease burden and also analyse gender and age differences.

5.3. Materials and methods

5.3.1. *Study design*

This was a comparative and descriptive community-based cross-sectional survey conducted in the general population of two townships in Windhoek from November 2016 to April 2017. The specific survey methods are outlined in the sections below.

5.3.2. *Study questionnaire*

An interviewer-administered questionnaire (Appendix G) was used to collect data for this study. The questionnaire collected data on participants' socio-demographic and behavioural characteristics as well as TB knowledge, attitudes and practices (TB KAP). The interviewer administered questionnaire ensured that all questions were answered and that interviewees were clear about the questions being asked.

I adapted the WHO questionnaire designed to assess TB KAP (243). As the WHO questionnaire did not include certain questions on socio-demographic and behavioural characteristics which were of interest to my study, I included additional questions taken from other validated assessment tools, such as the WHO prevalence survey guiding handbook (244), the WHO alcohol use disorders identification test (245), the Household Food Insecurity Access Scale questionnaire (246) and the Namibia Demographic and Health Survey (49).

For TB knowledge, attitudes and practices questions, I primarily used the WHO questionnaire as it was. In brief, the WHO questionnaire is comprised of six sections. The first section collects demographic data such as age, sex, education and employment status. The second section gathers information about health seeking behaviour, specifically, where people access healthcare and how often. The third section collects information about TB knowledge and awareness, and the knowledge questions include TB symptoms, modes of transmission, prevention and treatment. Section four focuses on TB attitudes and care seeking behaviours. The questions ask about personal views on risk infection, reaction after TB diagnosis, and care seeking behaviours. Section five gathers information about TB attitudes and related stigma, specifically attitudes towards TB patients as well as knowledge about TB and HIV/AIDS co-infection. Section six focuses on information about preferred sources of TB information.

With regards to demographics, I also added questions which assessed the following information marital status, how long they lived in the area, number of people in household, sleeping pattern, type of fuel used for cooking, location of kitchen, and food availability. Concerning behavioural information, I added questions about alcohol consumption and smoking.

In terms of TB KAP, the additional questions required participants to rate their overall TB knowledge (little, average, a lot) and whether the participant would prefer to keep a TB diagnosis in his/her house a secret or not (yes, no, unsure). Those who said yes where asked to say why. I also asked information about the conduct of current TB campaigns.

The final study questionnaire was primarily based on multiple-choice questions, and a few open ended questions. Multiple questions have the advantage of reducing guessing or "I don't know" answers. The majority of questions on TB KAP required participants to give simple answers (yes, no or I do not know). Responses to open-ended questions were categorised into nominal categories during analysis. The survey was conducted in English or in Oshiwambo, depending on the respondent's preference. People that could not speak these two languages were excluded.

5.3.3. *Pilot study*

A pilot study was conducted in October 2016 involving participants who resided in two purposively selected townships, Academia and Katutura, chosen to represent townships with a low and high TB burden, respectively. Given that the questionnaire had questions taken from validated assessment tools, the key purpose of the pilot study was mainly to assess the appropriateness of the recruitment method planned for the main survey. Moreover, the pilot study was conducted to highlight resources needed for the main survey, i.e. logistical arrangements such as time, human resources. I recruited pilot study participants from the main shopping complexes in each of the two townships, and the study involved a small sample size of thirty people from each township (n=60), and so no statistical inferences were made from these data.

The pilot study demonstrated that the method of recruiting participants from public places had potential to be successful, but not in affluent townships. For example, before the pilot study was implemented in Academia, I had to change locations four times because of poor recruitment in affluent townships with a low TB burden namely, Auasblick, Kleine Kuppe, Kleine Windhoek and Olympia.

Moreover, I found that public places allowed for a mixed sample in terms of age, sex and social class, and public places ensured security for myself as a lone researcher and the participants.

5.3.4. Implementation of the main survey

5.3.6.1. Selection of townships

This survey aimed to investigate individual level factors for TB hotspots in Windhoek, and so the townships for the main cross-sectional study were selected based on the disease burden revealed during phase two (see Chapter 4, Section 4.5.2). Hochland Park was chosen as a low TB burden area and Havana was chosen as it had the highest TB burden. Table 5.7 show the socio-demographic census data for the two townships. The unit of analysis were people aged 18 years and above, who resided in these townships for a minimum period of six months.

Table 5.7 Socio-demographic characteristics of selected townships for the main survey according to 2011 Census

Variable	Havana	Hochland Park
Total Population	15882	6423
Gender composition (%)		
Female	56	52
Male	44	48
Age composition (%)		
Under five years	13	7
5-14 years	13	13
15-59 years	73	73
60+ years	1	5
Average household size	2.9	3.7
Annual growth rate	4.1	0.7
School enrolment, 15+ years (%)		
None or incomplete primary	26	4
Primary or higher	71	95
Labour conditions 15+ years (%)		
Economically active unemployed	42	11

5.3.6.2. Sample size

Minitab was used to calculate the study sample size. I followed the approach of calculating the sample size to compare differences between two population proportions. A type 1 error of 5%, and a prevalence of 50% for individual exposure variables was assumed. Fifty percent is the recommend proportion when there are no specific data to be used (247). After inputting these parameters in Minitab, a final sample of 387 per area was chosen at a power level of 80%. In the end, a sample size of 400 participants (after rounding to the nearest hundred) was expected in each township stratified by sex and age groups (18-30; 31-40; 41-50; over 50 years).

5.3.6.3. Training of research assistants

I recruited two research assistants to assist with data collection. As part of orientation, I spent two days going through the survey questionnaire with them, and piloting the questionnaire amongst three thee of us. The orientation process was not challenging, as these were university graduates, who already had a basic understanding of research and had previously conducted their own research project as part of their undergraduate studies.

On the first day of data collection, each research assistant firstly interviewed two participants in my presence. This was specifically done as part of quality assurance, to ensure that the research assistants were implementing the survey as expected.

5.3.6.4. Participant recruitment

Study participants were recruited from a shopping areas in each township. This method has been used in other similar studies (239, 242) and I have provided the justification and critically discussed the pros and cons of this recruitment method in the discussion, Section 5.5.3. In Hochland Park, the study was conducted at a complex, which contains Spar supermarket, a pharmacy, post office and some small shops. In general, Spar is a reputable yet affordable supermarket in Namibia especially among the middle class people such as those residing in Hochland Park. In Havana, the study was conducted in the open market which is the central place where there is a taxi rank, shops, bars, and it is where people gather to buy their basic needs, entertainment and business.

On a typical data collection day, the research team (myself and the two research assistants) went to one township and each of us individually invited people to participate in the study.

People who indicated that they were residents of the selected townships and were willing to partake in the study were provided with more detail about the study objectives, and at this point we dealt with questions participants had about the research. Participants were subsequently provided with a consent form to sign before commencement of the interview, however some participants declined to sign, and so we only required them to provide verbal consent.

There were no material or monetary incentives given to participants, and this was made clear during the introduction of each interview, to rule out any expectation. However, at the end of each interview, we thanked respondents for their time and responses and also offered them the opportunity to ask any related questions. We then provided answers where possible, and in instances where we could not answer questions, we referred participants to organisations, where they could obtain appropriate answers. Some of the participants enjoyed discussing or sharing their detailed experiences about TB, and when this happened, we did not abruptly end the discussion but rather accommodated such discussions, as a way of showing respect and being thankful to respondents for their time. We recruited participants until the sample size in each area was reached.

5.3.6.5. Data storage

It was my responsibility to ensure that at the end of each data collection day, all questionnaires were carefully stored to make sure there was no damage or misplacement and for data protection purposes. Data were first entered in SPSS and then imported to STATA for analysis.

5.3.6.6. Statistical analysis

The analysis conducted during this phase followed the approach used in similar studies (221-223). I first observed differences in the socio-demographic characteristics of participants from the two townships were initially studied using the Chi square test or Fisher’s exact test, when cross tabulation cells contained counts less than five. As in other studies, I then used logistic regression to describe the socio-demographic characteristics of people from Havana. Logistic regression was used because the dependent variable was binary (whether a participant was or was not from Havana). I conducted univariable analysis and subsequently multivariable analysis including all exposure variables which were statistically significant ($p<0.05$) at univariable level. I then used the backward elimination method to remove variables which were not significant, based on the likelihood ratio test. Variables with greater p-values (p-value >0.05) were removed one at a time, until the model contained only significant variables (p value <0.05). The goodness of fit for the final model was checked using the Hosmer Lemershow goodness of fit test. For all the variables included in the final model, I used the likelihood ratio test to determine whether associations found differed according to sex or age group.

With regards to TB KAP, I assessed differences in TB KAP using the Chi square test or Fisher's exact test (when cross tabulation cells contained counts less than five). This analysis aimed to examine whether there were differences in the responses of participants according to where they lived.

Since Havana was the township with the highest TB burden, I limited the analysis to participants from this township in order to test whether there were differences in participant's responses according to sex or age group. This was also done using the Chi square test or Fisher's exact test.

In my study, determining participants' level of TB knowledge was based on correct answers given to the questions listed below, which covered different dimensions of TB including TB symptoms, modes of transmission, prevention, treatment and TB/HIV co-infection. These questions have been previously used to determine TB knowledge in similar studies (35, 226, 234, 240, 242).

1. Is a cough of three weeks or more a common symptom of TB? (answers: yes, no, don't know)
2. Can TB be transmitted through air when a person coughs or sneezes? (answers: yes, no don't know)
3. Can a person avoid spreading TB through cough hygiene (covering mouth)? (answers: yes, no, don't know)
4. Can TB be cured? (answers: yes, no, don't know)
5. How can TB be cured? (answers: medication from clinic, traditional healer, home resting without medication, praying, others, don't know)
6. What is your opinion about the cost of TB treatment at public facilities? (answers: free, reasonably priced, expensive, very expensive)
7. Are people living with HIV/AIDS at increased risk of TB? (answers: yes, no, don't know)

A code of one was given for each correct answer, while a zero code was given for each incorrect answer or don't know response, as has been done in previous studies (135, 225, 227). Based on the responses given to the seven questions, a score ranging from 0- 7 was calculated, indicating the number of questions correctly answered. I followed the approach of a similar study by Abebe and colleagues (248), by grouping the scores into 25th, 50th and 75th percentiles corresponding to low, moderate and high TB knowledge level respectively. This allowed for separation of participants with low or some knowledge of TB from those with a high TB knowledge.

As the response variable had three categories (low, moderate or high), I used ordinal logistic regression to study the effect of socio-demographic variables on the participants' level of TB knowledge. The socio-demographic variables considered in my study were informed by the literature and included age, gender, place of residence, marital status, and duration of stay in area of residence, frequency of visiting healthcare services, education level, employment status and whether participants reported receiving TB information at the time of the study through sources such as radio, TV, healthcare workers and pamphlets. Ordinal logistic regression holds the assumption that the coefficients that describe the relationship between the categories of the response variables are the same (referred to as proportional odds assumption) (249), and so in the final adjusted model, I used the Brant test to determine whether this condition was met.

I chose ordinal logistic regression over multinomial logistic regression, as I wanted to take into consideration the ordered categories of the response variable (low, moderate and high), and this regression model was the preferred option in similar studies (35, 248).

In addition, I performed further sensitivity analyses using binary logistic regression. Here I re-categorised the response variable into a binary outcome using a different cut-off point, with the purpose of comparing the results with those obtained from ordinal logistic model. I initially observed the distribution of the score variable (ranging from 0-7) and found that the mean and median values were both around a score of 6. The ideal approach would have been to categorise the responses variable using a cut-off point of 6 as mean or median value as has been done in other studies (135, 225). However, I considered that this was somewhat of a strict rule in the case of my study, as only participants who answered 6 or all 7 questions correctly were going to be considered as having good knowledge, and the rest were going to be taken as having insufficient knowledge. Therefore I felt it appropriate to use the alternative approach used in similar studies (242, 250) whereby the cut-off point was 50%. This means that participants who answered at least 50% of questions correctly were considered to have good knowledge, whereas below 50% was taken as having insufficient knowledge. Since the sensitivity analysis was only performed as a supporting element, the interpretation of the study findings (section **Error! Reference source not found.**) are based on the ordinal logistic regression model.

All analyses were conducted in STATA version 15.0 (StataCorp LLC, 2017), and a p-value less than 0.05 indicated statistical significance.

5.4. Results

5.4.1. Sample description

In total, 400 participants from each township were interviewed, 200 (50%) men and women in each township, and stratified according to age groups (18-30; 31-40; 41-50; over 50 years). The participants' characteristics are shown in Table 5.8 according to area of residence. The majority of participants from Havana were single (71.3%), while majority in Hochland Park were married (49.3%). Among the participants from Havana, 27.8% had lower education level compared to 1.5% from Hochland Park. The majority of participants from Havana were unemployed (50.2%), while in Hochland Park the majority were employed (61.0%). The prevalence of self-reported TB diagnosis in the overall sample was 7.0%, with 10.5% from Havana and 3.3% from Hochland Park. Furthermore, 18.3% of Havana participants consumed alcohol more frequently compared to 3.8% of Hochland Park participants. With regards to smoking, 3.8 % of Havana participants were current smokers compared to 11.8% of Hochland Park participants.

Table 5.8. Characteristics of participants who took part in the main survey according to area of residence

Variable	Havana, n (%)	Hochland Park, n (%)
Marital status		
Single	285 (71.3)	194 (48.5)
Married	109 (27.5)	197 (49.3)
Divorced or Widowed	6 (1.5)	9 (2.3)
Duration of stay in area		
6 months to 1 year	62 (15.5)	18 (4.5)
More than 1 year to 3 years	70 (17.5)	70 (17.5)
More than 3 years	268 (67.0)	312 (78.0)
Frequency of visiting health services		
Often (one or more per year)	326 (81.5)	329 (82.3)
Sometimes (less than once per year but twice in the past five years)	38 (9.5)	60 (15.0)
Rarely (once in the past five years)	36 (3.6)	11 (2.8)
Employment status		
Employed	76 (19.0)	244 (61.0)
Self-employed	123 (30.8)	67 (16.8)
Unemployed	201 (50.2)	89 (22.3)
Education level		
No school/primary	111 (27.8)	6 (1.5)
High school and beyond	289 (72.3)	394 (98.5)
Ever had TB		
Yes	42 (10.5)	13 (3.3)
No	358 (89.5)	387 (96.8)
Exposure to TB in household (excluding those who stay alone)		
Yes	42 (11.2)	15 (3.9)
No	334 (88.8)	366 (96.1)
TB in extended family		
Yes	199 (49.8)	168 (42.0)
No	201 (50.3)	232 (58)
Alcohol consumption		
Never	154 (38.5)	189 (47.3)
Monthly or less	25 (6.3)	89 (22.3)
2 to 4 times a month	68 (17.0)	91 (22.8)
2 to 3 times a week	80 (20.0)	16 (4.0)
4 or more times a week	73 (18.3)	15 (3.8)
Smoking status		
Never smoked	378 (94.5)	341 (85.3)
Currently smoke	15 (3.8)	47 (11.8)
Past smoker	7 (1.8)	12 (3.0)
Sleeping pattern in household		
Everyone sleeps alone in their bedroom	83 (20.8)	87 (21.8)
2 -3 people sharing a room	196 (49.0)	308 (77.0)
4 or more people sharing a room	121 (30.3)	5 (1.3)
At least one window for each room in the house		
Yes	42 (10.5)	398 (99.5)
No	358 (89.5)	2 (0.5)

5.4.2. Univariable analysis

Table 5.9 show the results from the univariable logistic regression conducted to investigate the socio-demographic and behavioural characteristics of participants from Havana. The results show that study participants who were unemployed participants were significantly more likely to be from Havana, compared to those in formal employment (OR=7.25, 95% CI: 5.07-10.38). Moreover, those who had a lower education level were significantly more likely to be from Havana, compared to those with higher education level (OR=25.2, 95% CI: 10.9-58.2).

Survey participants who rarely visited healthcare services were more likely to be from Havana, in contrast to those who often visited healthcare services (OR=3.30, 95% CI: 1.65-6.60). Participants who consumed alcohol more than 2-3 times per week were significantly more likely to be from Havana, in contrast to those who never consumed alcohol (OR=6.1, 95% CI: 3.44-10.93). Moreover, those who consumed alcohol four or more times a week were significantly more likely to be from Havana than those who never consumed alcohol (OR=5.97, 95% CI: 3.29 - 10.83).

Table 5.9 Unadjusted Odds Ratio describing sociodemographic and behavioural characteristics of participants from Havana

Variable	OR (95%CI)	Likelihood ratio p –value
Employment status		
Employed	1	p<0.001
Self-employed	5.89 (3.98-8.74)	
Unemployed	7.25 (5.07-10.38)	
Education level		
No school/primary	25.2 (10 .9-58.2)	p<0.001
High school or beyond	1	
Frequency of visiting health services		
Often (one or more per year)	1	
Sometimes (less than once per year but twice in the past five years)	0.64 (0.41-0.99)	p=0.001
Rarely (once or never in the past five years)	3.30 (1.65-6.60)	
Duration of stay in area		
6 months to 1 year	3.44 (1.85-6.41)	p<0.001
More than 1 year to 3 years	0.88 (0.59-1.24)	
More than 3 years	1	
Marital status		
Single	1	p<0.001
Married	0.38 (0.28-0.51)	
Divorced or widowed	0.45 (0.16-1.30)	
Ever had TB		
Yes	3.49 (1.84-6.61)	p<0.001
No	1	
Exposure to TB in household		
Yes	3.07 (1.67-5.64)	p=0.001
No	1	
TB in extended family		
Yes	1.37 (1.03-1.81)	p=0.028
No	1	
Number of people in household ***(per one person increase)***	1.18 (1.12-1.25)	p<0.001
Maximum number of people sleeping in the same bedroom		
Everyone sleeps alone in their bedroom	1	
2 -3 people sharing a room	0.67 (0.47-0.95)	p<0.001
4 or more people sharing a room	25.37 (9.87-65.17)	
Location of cooking place		
In a room used for living/sleeping	0.73 (0.55-0.99)	p=0.039
In a separate room or outdoor	1	
Had lack of food in house due to lack of money		
Yes	20.12 (14.03-28.87)	p=0.001
No	1	
How often food lacking in house due to lack of money		
Often (more than ten times in a month)	54.13 (7.40-396.23)	p<0.001
Sometimes (three to ten times in a month)	5.12 (2.58-10.15)	
Rarely (once or twice a month)	1	
Alcohol consumption		
Never	1	
Monthly or less	0.34 (0.21-0.56)	
2 to 4 times a month	0.92 (0.63-1.34)	p<0.001
2 to 3 times a week	6.14 (3.44-10.93)	
4 or more times a week	5.97 (3.29-10.83)	
Alcohol consumption on a day drinking		
1 or less *(e.g. just a glass)*	1	p<0.001
2 to 4 bottles	2.26 (1.47-3.46)	
5 or more bottles	3.25 (1.91-5.52)	
Smoking status		
Never smoked	1	p<0.001
Current/past smoker	0.34 (0.20-0.56)	
Where do you mostly smoke		
Inside the house	1.04 (0.32-3.36)	p=0.947
Outside the house	1	
Any other person smoking at home		
Yes	0.45 (0.29-0.68)	p=0.001
No	1	
Where household member mostly smoke		
Inside the house	1.01 (0.39-2.65)	p=0.972
Outside the house	1	

5.4.3. Multivariable analysis

Statistically significant results from multivariate analysis using the backward elimination method are shown in Table 5.10. Participants who had the following characteristics were more likely to be from Havana than those in reference categories. Self-employed (OR=4.42, 95% CI: 1.97-9.91), unemployed (OR=3.61, 95% CI: 1.87-6.97), rarely visited healthcare services (OR=5.74, 95% CI: 1.12-29.39) and had been in the township for six months to a year (OR=4.87, 95% CI 1.53-15.42). Furthermore, they consumed alcohol frequently (OR=8. 31, 95% CI: 2.68-25.72), experienced lack of food due to lack of money (OR=9.02, 95% CI: 5.02-16.18) and had a TB person in household (OR=5.04, 95% CI: 1.50-16.94).

Table 5.10. Adjusted Odds Ratio describing sociodemographic and behavioural characteristics of participants from Havana

Variable	OR (95%CI)	Likelihood ratio test p – value
Employment status		
Employed	1	p=0.001
Self-employed	4.42 (1.97-9.91)	
Unemployed	3.61 (1.87-6.97)	
Frequency of visiting health services		
Often	1	p=0.003
Sometimes	0.34 (0.15-0.80)	
Rarely	5.74 (1.12-29.39)	
Duration of stay		
6 months to 1 year	4.87 (1.53-15.42)	p=0.006
More than 1 year to 3 years	1.29 (0.62-2.26)	
More than 3 years	1	
Household TB contact		
Yes	5.04 (1.50-16.94)	p<0.001
No	1	
Alcohol consumption		
Never	1	p<0.001
Monthly or less	0.25 (0.09-0.66)	
2 to 4 times a month	1.06 (0.49-2.28)	
2 to 3 times a week	9. 02 (3.23-2.15)	
4 or more times a week	8. 31 (2.68-25.72)	
Smoking status		
Never smoked	1	p=0.001
Current/past smoker	0.12 (0.04-0.35)	
Household member smoking		
Yes	0.22 (0.09-0.50)	p=0.002
No	1	
Lack of food in house due to lack of money		
Yes	9.02 (5.02-16.18)	p<0.001
No	1	
Sleeping pattern		
No one shares	1	p<0.001
2-3 people sharing	0.72 (0.35-1.41)	
4 or more people	13.62 (3.69-50.34)	

The likelihood ratio test showed that the relationship between each of the variable in Table 5.10 and the dependent variable did not differ by sex (all p-values >0.05). However the test showed that some associations varied by age group, and so the results are presented separately according for these association by age group as shown in Table 5.11.

In terms of employment, the odds of residing in Havana were higher for people aged above 40 compared participants aged 18-40 years. For alcohol consumption, the odds of being from Havana were higher among participants aged 18-40 compared to those above 40.

Table 5.11. Adjusted odds ratio describing socio-demographic and behavioural characteristics of participants from Havana

Variable	**18-40 years**		**Above 40 years**	
	Adjusted OR (95% CI)	**p-value**	**Adjusted OR (95% CI)**	**p-value**
Employment				
Employed	1		1	
Self-employed	5.03 (1.51-16.75)		6.78 (1.96-23.49)	
Unemployed	2.36 (0.96-5.80)	p=0.022	11.13 (3.15-39.37)	p<0.001
Alcohol consumption				
Never	1		1	
Monthly or less	0.26 (0.07-1.00)		0.11 (0.02-0.59)	
2 to 4 times a month	1.09 (0.41-2.94)		0.93 (0.23-3.75)	
2 to 3 times a week	26.62 (5.41-131.09)	p<0.001	2.80 (0.45-17.23)	p=0.024
4 or more times a week	28.71 (4.90-168.24)		1.98 (0.40-9.65)	

5.4.4. Assessing differences in TB Knowledge Attitudes and Practices (TB KAP)

5.4.4.1. Sources information and TB knowledge

Table 5.12 show the participants' responses related to the current sources of TB information and suggested/preferred sources of TB information. Among participants from Havana, 11.5% received TB information through newspapers compared to 29.5% from Hochland Park (p<0.001). In addition, 61.4% of participants from Havana received TB information through radio in contrast to 48.8% from Hochland Park (p<0.001). Moreover, 14.8% of Havana participants received TB information through television compared to 41.8% from Hochland Park (p<0.001).

With regards to the preferred/suggested sources of TB information, significant differences were also observed. For instance, 83.3% of Havana participants preferred radio as a source of TB information compared to 62.5% from Hochland Park (p<0.001). In addition, 25.0%, 15.0%, 52.0% and 11.0% of participants from Havana preferred television, billboard/barouches, healthcare workers and family members, respectively, in contrast to 62.0%, 48.0%, 45.0% and 20.0%, respectively from Hochland Park.

Table 5.12. Responses regarding sources of TB information according to area of residence

	Variable	**Havana**	**Hochland Park**	**p-value**
Current source of TB information	**Newspapers**			
	Yes	78 (11.5)	118 (29.5)	
	No	322 (80.5)	282 (70.5)	p<0.001
	Radio			
	Yes	244 (61.0)	195 (48.8)	p<0.001
	No	156 (39.0)	205 (51.2)	
	Television			
	Yes	59 (14.8)	167 (41.8)	p<0.001
	No	341 (85.3)	233 (58.3)	
	Billboards/brochures/pamphlets			
	Yes	54 (13.5)	67 (16.8)	p=0.200
	No	346 (86.5)	333 (83.3)	
	Health care workers			
	Yes	174 (43.5)	156 (39.0)	p=0.196
	No	226 (56.5)	224 (61.0)	
	Family members			
	Yes	37 (9.3)	33 (8.3)	p=0.617
	No	363 (90.8)	367 (91.8)	

	Variable	Havana	Hochland Park	p-value
	Religious leaders			
	Yes	4 (1.0)	2 (0.5	p=0.412
	No	396 (99.0)	398 (91.8)	
Preferred\Suggested source of TB information	**Newspapers**			
	Yes	159 (39.8)	162 (40.5)	p=0.829
	No	241 (60.3)	238 (59.5)	
	Radio			
	Yes	333 (83.3)	250 (62.5)	p<0.001
	No	67 (16.8)	150 (37.5)	
	Television			
	Yes	100 (25.0)	248 (62.0)	p<0.001
	No	300 (75.0)	152 (38.0)	
	Billboards/brochures/pamphlets			
	Yes	76 (19.0)	193 (48.3)	p<0.001
	No	324 (181.0)	207 (51.7)	
	Health care workers			
	Yes	208 (52.0)	179 (44.8)	p=0.040
	No	192 (48.0)	221 (55.3)	
	Family members			
	Yes	44 (11.0)	78 (19.5)	p=0.001
	No	356 (89.0)	322 (80.5)	
	Religious leaders			
	Yes	9 (2.3)	10 (2.5)	p=0.816
	No	391 (97.8)	390 (97.5)	

5.4.4.2. TB symptoms

Regarding the common TB symptoms (Table 5.13), significant differences were obtained. In particular, 64.8% of participants from Havana indicated that a persistent cough was a symptom of TB compared to 93.3% from Hochland Park (p<0.001). Furthermore, 17.0%, 24.8%, 53.3% of Havana participants respectively mentioned that severe headache, persistent fever and chest pain were common symptoms of TB in contrast to 30.0%, 45.0% and 31.8% from Hochland Park who mentioned the same symptoms.

Table 5.13. Responses related to TB symptoms according to area of residence

	Variable	Havana	Hochland Park	p-value
TB symptoms	**Rash**			
	Yes	21 (5.3)	12 (3.0)	p=0.110
	No	379 (94.8)	388 (97.0)	
	Persistent cough			
	Yes	259 (64.8)	373 (93.3)	p<0.001
	No	141 (35.3)	27 (6.8)	
	Coughing blood			
	Yes	158 (39.5)	160 (40.0)	p=0.885
	No	242 (60.5)	240 (60.0)	
	Severe headache			
	Yes	68 (17.0)	120 (30.0)	p<0.001
	No	332 (83.0)	280 (70.0)	
	Nausea			
	Yes	36 (9.0)	32 (8.0)	p=0.612
	No	364 (91.0)	368 (92.0)	
	Unexplained weight loss			
	Yes	231 (57.8)	228 (57.7)	p=0.830
	No	169 (42.3)	172 (43.0)	
	Persistent fever			
	Yes	99 (24.8)	180 (45.0)	p<0.001
	No	301 (75.3)	220 (55.0)	
	chest pain			
	Yes	213 (53.3)	127 (31.8)	p<0.001
	No	187 (46.8)	273(68.3)	
	Shortness of breath			
	Yes	119 (29.8)	86 (21.5)	p=0.008
	No	281 (70.3)	314 (78.5)	
	Ongoing fatigue			
	Yes	104 (26.0)	70 (17.5)	p=0.004
	No	296 (74.0)	330 (82.5)	

5.4.4.3. Modes of transmission and prevention

Regarding the common modes of transmission (Table 5.14), significant differences were also observed. Specifically, 5.5% of Havana participants said that TB is transmitted through a handshake compared to 19.5% from Hochland Park (p<0.001). In addition, 82.3% and 3.5% of participants from Havana, respectively said that TB is transmitted through the air when someone coughs/sneezes or when touching items in public, compared to 97.8% and 27.3% of Hochland Park who indicated the same transmission modes.

In terms of TB prevention, I found that 6.0%, 82.3% and 3.5% of Havana participants respectively thought that TB can be prevented by avoiding a handshake, covering mouth when coughing and closing windows at home, compared to 29.0%, 95.5% and 0.3% of Hochland Park participants who indicated the same preventative methods.

Table 5.14. Responses regarding modes of transmission and prevention according to area of residence

	Variable	Havana	Hochland Park	p-value
Transmission mode	**Through handshake**			
	Yes	22 (5.5)	78 (19.5)	p<0.001
	No	378 (94.5)	322 (80.5)	
	Though air when			
	coughing/sneezing	339 (84.8)	383 (95.8)	p<0.001
	Yes	61 (15.3)	17 (4.3)	
	No			
	Through sharing kitchen utensils			
	Yes	260 (65.0)	269 (67.3)	p=0.501
	No	140 (35.0)	131 (32.8)	
	Through touching items in the			
	public	83 (20.8)	109 (27.3)	p=0.031
	Yes	317 (79.3)	291 (72.8)	
	No			
Ways of prevention	**Avoid handshake**			
	Yes	24 (6.0)	80 (20.0)	p<0.001
	No	376 (94.0)	320 (80.0)	
	Cover mouth when coughing			
	Yes	329 (82.3)	382 (95.5)	p<0.001
	No	71 (17.8)	18 (4.5)	
	Avoid sharing kitchen utensils			
	Yes	248 (62.0)	266 (66.5)	p=0.184
	No	152 (34.0)	134 (33.5)	
	Washing hands			
	Yes	104 (26.0)	113 (28.2)	p=0.474
	No	296 (74.0)	287 (71.8)	
	Closing windows at home			
	Yes	14 (3.5)	1 (0.3)	p=0.001
	No	386 (96.5)	399 (99.8)	
	Good nutrition			
	Yes	104 (26.0)	82 (20.5)	p=0.066

	Variable	Havana	Hochland Park	p-value
	No	296 (74.0)	318 (79.5)	
	Praying Yes No	 32 (8.0) 368 (92.0)	 39 (9.8) 362 (90.3)	 p=0.384

5.4.4.4.Perceptions of TB treatment

Table 5.15 shows that there were no significant differences in responses to whether TB is a curable disease and how it is cured, and the majority of participants from both townships indicated that TB is a curable condition. However, a significant difference was noted in participants' responses on TB treatment costs at public facilities. Among the participants from Havana, 60.8% said that TB treatment was free of charge, compared to 52.8% from Hochland Park and 16.5% of participants from Havana said they knew the treatment costs, compared to 29.8% of participants from Hochland Park (p<0.001).

Table 5.15. Responses related to TB treatment according to area of residence

Variable	Havana	Hochland Park	p-value
Can TB be cured Yes No Don't know/unsure	 391 (97.8) 6 (1.5) 3 (0.8)	 389 (97.3) 4 (1.0) 7 (1.8)	 p=0.450
How can TB be cured Through medication from clinic/hospital Traditional healer Home resting without medication Praying Others don't know	 383 (95.8) 2 (0.5) 3 (0.8) 1 (0.3) 1 (0.3) 10 (2.5)	 388 (97.0) 1 (0.3) 1 (0.3) 0 (0) 1 (0.3) 9 (2.3)	 p=0.789
What do you think is the cost of TB treatment at public facilities Free of charge Reasonably priced Expensive Don't know	 243 (60.8) 86 (21.5) 5 (1.3) 66 (16.5)	 211 (52.8) 58 (14.5) 12 (3.0) 119 (29.8)	 p<0.001

5.4.4.5. Perceptions of the TB burden and risk of infection

Significant differences were observed in responses concerning views about the TB burden and risk of infection (Table 5.16). For example, 67.0% of Havana participants thought that TB was a common disease in Windhoek in contrast to 50.7% from Hochland Park (p<0.001). Among participants from Havana, 41.8% knew a person with TB at that time, compared to 26.3% from Hochland Park (p<0.001).

The proportion of participants who indicated that they were at risk of TB was similar between the two townships but it was significantly higher among participants from Havana (94.3%) compared to 90.5% from Hochland Park (p=0.046). The majority of participants in each township indicated that they were at risk of getting TB because everyone was at risk of infection. However, the proportion of those who said this was lower among Havana participants (48.3%) compared to 77.8% of Hochland Park participants (p<0.001). The proportion of participants who stated that they would visit healthcare services as soon as they noticed TB symptoms was similar in the two townships although it was significantly lower in Havana (66.5%) compared to 70.3% of Hochland Park participants (p=0.046).

In addition, 92.8% of Havana participants expressed that their community members were at risk of getting TB compared to 11.3% from Hochland Park (p<0.001). The majority of participants from both townships mentioned that their community members were at risk as most of them drank alcohol or smoked. However, this proportion was slightly higher among participants from Havana (51.8%), compared to 45.0% from Hochland Park. When participants were asked about the risk of TB in persons living with HIV/AIDS, 60.3% of participants from Havana thought such people were at risk of getting TB, compared to 94.3% from Hochland Park (p<0.001).

Table 5.16: Participants' views about the magnitude of TB burden and risk perceptions

Variable	Havana	Hochland Park	p-value
How serious is TB			
Very serious	351 (87.8)	337 (84.3)	
Somewhat serious	39 (9.8)	45 (11.3)	p=0.223
Not serious	10 (2.5)	18 (4.5)	
How common it is in Windhoek			
Very common	268 (67.0)	203 (50.7)	p<0.001
Average	89 (22.3)	70 (17.5)	
Not common	43 (10.8)	127 (31.8)	
Who is most at risk of getting TB			
Everyone	225 (56.3)	180 (45.0)	p<0.001
Poor people	0 (0)	32 (8.0)	
People who drink alcohol /smoke	143 (35.8)	102 (25.5)	
People living with HIV/AIDS	14 (3.5)	63 (15.8)	
Drug users	10 (2.5)	3 (0.8)	
Homeless or others	8 (2.0)	20 (5.0)	
Do you currently know someone with TB			
Yes	167 (41.8)	105 (26.3)	p<0.001
No	233 (58.3)	295 (73.8)	
Do you think you are at risk of getting TB			
Yes	377 (94.3)	362 (90.5)	p=0.046
No	23 (5.8)	38 (9.5)	
Why do you think you are at risk of getting TB			
Everyone can get it	193 (48.3)	311 (77.8)	
I stay at crowded places	23 (5.8)	6 (1.5)	
I/a family member had TB in the past	42 (10.5)	8 (2.0)	p<0.001
My environment is dirty	13 (3.3)	0 (0)	
I drink alcohol or smoke	48 (12.0)	17 (4.3)	
Other reasons	58 (14.5)	20 (5.0)	
How soon you will go to hospital if you have TB symptoms			
When treatment on my own does not work	5 (1.3)	11 (2.8)	p=0.044
When symptoms last for 3-4 weeks	116 (29.0)	104 (26.0)	
As soon as possible	266(66.5)	281 (70.3)	
I would not go to hospital	13 (3.3)	4 (1.0)	
Are people in your community at risk of getting TB			
Yes	371 (92.8)	45 (11.3)	p<0.001
No	29 (7.2)	355 (88.8)	
Why do you think people in your community are at risk of TB			
Very dirty environment	122 (32.9)	0	
People drink alcohol or smoke	192 (51.8)	45 (100)	p<0.001
People share utensils like cups	3 (0.8)	0	
Many people have TB	3 (0.8)	0	

Very crowded environment	51 (13.7)	0	
Are people living with HIV/AIDS at increased risk of TB			
Yes	241 (60.3)	377 (94.3)	
No	79 (19.8)	14 (3.5)	p<0.001
Don't' know	80 (20.0)	9 (2.3)	

5.4.4.6. Practices and attitudes towards persons infected with TB

Table 5.17 shows participants' responses on practices and attitudes toward persons with TB, and significant differences were observed. Of Havana participants, 42.3% stated that they would feel embarrassed or afraid if diagnosed with TB compared to 38.3% from Hochland Park, also 6.5% of participants from Havana expressed that they would be surprised if diagnosed with TB, compared to 38.8% from Hochland Park (p<0.001).

Among participants from Havana, 85.0% said they would feel compassion with a person with TB in contrast to 69.5% of participants from Hochland Park (p<0.001). Moreover, the majority of participants from Havana (51.0%) thought that most people in their community would give support to a person with TB, but among participants from Hochland Park, this thought was only expressed by 11.3% (p<0.001). Moreover, 30.0% of Havana participants reported they would keep TB in their household a secret compared to 37.3% of participants from Hochland Park (p=0.003).

Table 5.17: Attitudes and practices towards TB patients

Variable	**Havana**	**Hochland Park**	**p-value**
How would you react if you were told you had TB			
Fear and embarrassed	169 (42.3)	153 (38.3)	
Surprised	26 (6.5)	155 (38.8)	p<0.001
Take it as normal disease	205 (51.2)	92 (23.0)	
Attitudes towards TB patients			
Compassion	340 (85.0)	278 (69.5)	p<0.001
Compassion but fear	49 (12.3)	105 (26.3)	
I have no particular feeling	11 (2.8)	17 (4.0)	
How do you think a person with TB is treated in your community			
Many people will reject him/her	135 (33.8)	302 (75.5)	p<0.001
People will be friendly but try to avoid her	54 (13.5)	53 (13.3)	
People will be supportive	204 (51.0)	45 (11.3)	
Others	7 (1.8)	0	

Would you keep TB in your family a secret			
Yes	121 (30.0)	149 (37.3)	p=0.003
No	264 (66.0)	248 (62.0)	
Unsure	15 (4.0)	3 (0.8)	
Why would you keep it a secret			
People will gossip	89 (73.6)	97 (65.1)	p=0.136
People will discriminate	32 (26.4)	52 (34.9)	

5.4.4.7. Perceptions on the state of TB knowledge

Responses towards perceived state of TB knowledge are shown in Table 5.18. More than half of participants from Havana (53.8%) said that they had poor TB knowledge, compared to 35.5% from Hochland Park. Moreover, 11.8% of participants from Havana said they had good knowledge about TB compared to 25.0% from Hochland Park.

Table 5.18. Perceptions on level of TB knowledge

Variable	**Havana**	**Hochland Park**	p-value
Do you feel well informed about TB			p=0.420
Yes	141 (35.3)	152 (38.0)	
No	259 (64.8)	248 (62.0)	
How would you rate your TB knowledge			
Poor	215 (53.8)	143 (35.5)	
Average	138 (34.5)	157 (39.3)	p<0.001
Good	47 (11.8)	100 (25.0)	
Do you wish to get more TB information			
Yes	388 (97.0)	382 (95.5)	p=0.328
No	12 (3.0)	18 (4.5)	
Ever seen or attended a TB campaign in the area			
Yes	24 (6.0)	3 (0.8)	p<0.001
No	376 (94.0)	397 (99.83	

5.4.5. Sub-group analysis of TB KAP in Havana

5.4.5.1. Sex differences

In the sub-group analysis of participants from Havana, the Chi square or Fisher exact tests showed that there were no sex differences in the responses given to the majority of variable presented above, except for two variables shown in Table 5.19.

The results shows that 51.5% of female participants from Havana received TB information from healthcare workers compared to 35.5% of male participants ($p<0.001$). Among female participants 58.5% reported low TB knowledge compared to 49.0% of males. Furthermore, 7.5% of female participants reported good TB knowledge compared to 16.0% of male participants ($p=0.020$).

Table 5.19: Observed sex differences among participants from Havana

Variable	Female	Male	p-value
Health care workers			
Yes	103 (51.5)	71 (35.5)	p=0.001
No	97 (48.5)	129 (64.5)	
How would you rate your TB knowledge			
Low	117 (58.5)	98 (49.0)	p=0.020
Average	68 (34.0)	70 (35.0)	
Good	15 (7.5)	32 (16.0)	

5.4.5.2. Age differences

Table 5.20 shows TB KAP responses where there were differences by age group. In terms of current sources of TB information, 23.5% of participants aged 18 to 40 received TB information from newspapers in contrast to 15.5% of those aged above 40 years. The majority (52.0%) of participants aged 40 or above received TB information from healthcare workers compared to 35.0% of participants aged 18-40.

More participants (31.5%) aged 18-40 preferred receiving TB information through television compared to 18.5% of participants above 40 years. Furthermore, 61.0% participants aged above 40 preferred receiving information from healthcare workers compared to 43.0% of those aged 18-40.

The majority of participants (92.0%) aged above 40 thought TB was a serious disease compared to 83.5% of those aged 18-40. Moreover, 4.5% of participants aged 18-40 did not know how TB is treated compared to 1.0% of participants aged above 40. Approximately 5% of participants aged 18-40 had no particular feeling towards persons with TB, compared to 1.0% among those aged above 40. The majority (59.0%) of participants aged above 40 reported poor TB knowledge compared to 48.5% of participants age 18-40.

Table 5.20: Observed age differences in TB KAP among participants from Havana

Component	Variable	18-40	Above 40	Chi-square p-value
Current source of TB information	**Newspapers**			
	Yes	47 (23.50)	31 (15.50)	
	No	153 (76.5)	169 (84.5)	p=0.043
	Health care workers			
	Yes	70 (35.0)	104 (52.0)	p<0.001
	No	130 (65.0)	96 (48.0)	
Preferred sources on TB information	**Television**			
	Yes	63 (31.50)	37 (18.50)	P=0.003
	No	137 (68.5)	163 (81.50)	
	Health care workers			
	Yes	86 (43.0)	122 (61.0)	p<0.001
	No	114 (57.0)	78 (39.0)	
Mode of transmission	**Through sharing kitchen utensils**			
	Yes	120 (60.0)	140 (70.0)	p=0.036
	No	80 (40.0)	60 (30.0)	
	Through touching items in the public			
	Yes	29 (14.50)	54 (27.0)	
	No	171 (85.5)	146 (73.0)	p=0.002
TB burden in Windhoek and risk of infection	**How serious is TB**			
	Very serious	167 (83.5)	184 (92.0)	
	Somewhat serious	25 (12.5)	14 (7.0)	p=0.023
	Not serious	8 (4.0)	2 (1.0)	
	Who is most at risk of getting TB			
	Everyone	104 (52.0)	121 (60.5)	p=0.015
	Poor people	0 (0)	0 (0)	
	People who drink alcohol /smoke	71 (35.5)	72 (36.0)	
	People living with HIV/AIDS	12 (6.0)	2 (1.0)	
	Drug users	7 (3.5)	3 (1.5)	
	Homeless or others	6 (3.0)	2 (1.0)	
	Why do you are at risk of getting TB			
	Everyone can get it	90 (47.4)	103 (55.1)	
	I stay at crowded places	17 (9.0)	6 (3.2)	

	I/a family member had TB in the past My environment is dirty I drink alcohol or smoke Other reasons	13 (6.8) 6 (3.2) 28 (14.7) 36 (19.0)	29 (15.5) 7 (3.7) 20 (10.7) 22 (11.8)	p=0.005
	Are people in your community at risk of getting TB Yes No	192 (96.0) 8 (4.0)	179 (89.5) 21 (10.5)	p=0.012
TB treatment	**How can TB be cured** Through medication from clinic/hospital Traditional healer Home resting without medication Praying Others don't know	186 (93.0) 2 (1.0) 2 (1.0) 0 (0) 1 (1.0) 9 (4.5)	197 (98.5) 0 (0) 1 (1.0) 1 (1.0) 0 (0) 1 (1.0)	p=0.008
Practices and attitudes	**Attitudes towards TB patients** Compassion Compassion but fear I have no particular feeling	166 (83.0) 24 (12.0) 10 (5.0)	174 (87.0) 25 (12.5) 1 (1.0)	p=0.023
Perceptions on state of TB	**How would you rate your TB knowledge** Low Average Good	97 (48.5) 85 (42.5) 18 (9.0)	118 (59.0) 53 (26.5) 29 (14.5)	p=0.002

5.4.6. Assessing the effects of socio-demographic variables on the level of TB knowledge

Overall, 216 (27.0%), 322 (40.3%) and 262 (32.8%) were categorised as having low, moderate and high TB knowledge, respectively, but this differed significantly according to area of residence (Chi Square p-value <0.001). In Havana, 170 (42.5%), 157 (39.3%) and 73 (18.3%) were categorised as having low, moderate and high TB knowledge, respectively. In Hochland Park 46 (11.5%) 165 (41.3%) and 189 (47.3) were categorised as having low, moderate and high TB knowledge, respectively.

Table 5.21 shows the results of the ordinal logistic regression analysis describing the association between several socio-demographic factors and TB knowledge levels. In the univariable analysis, the following characteristics were significantly associated with increased relative odds of having a high TB knowledge score: older age (OR=1.40, 95%CI: 1.08-1.81), being married (OR=1.92, 95%CI: 1.47-2.52), staying for longer duration in the residential area (OR=1.61, 95%CI: 1.05-2.49). On the other side, the following characteristics were significantly associated with reduced relative odds of having a high TB knowledge score: male sex (OR= 0.73, 95% CI: 0.56-0.94), residing in Havana (OR=0.21, 95%CI: 0.16-0.28), rarely visiting healthcare facilities (OR=0.30, 95%CI: 0.17-0.53), lower education level (OR=0.35, 95%CI: 0.24-0.51), self-employed (OR=0.36, 95%CI: 0.26-0.51), unemployed (OR=0.34, 95%CI: 0.25-0.46) , self-employed and not receiving any TB information at the time (OR=0.46, 95%CI: 0.31-0.69).

In the multivariate model (adjusted or all variables in the table), the following variables were independent variables significantly associated with reduced relative odds of having a high TB knowledge score: residing in Havana (OR= 0.30, 95%CI: 0.21-0.42; p<0.001), rarely visited healthcare services (OR=0.46, 95%CI: 0.25-0.84; p=0.012), self-employed (OR=0.57, 95%CI: 0.40-0.83; p=0.003), unemployed (OR=0.62, 95%CI: 0.44-0.87; p=0.006) and having received no TB information at the time of the study (OR=0.50, 95%CI: 0.33-0.76; p=0.001). The Brant test indicated a non-significant p-value (Chi square= 16.0; p-value = 0.245) for the full adjusted model, suggesting that the proportional odds assumption was not violated.

Table 5.21 Univariable and multivariable Ordinal logistic regression analysis of the association between TB knowledge level (low, medium and high) and socio-demographic determinants

Variable	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Gender				
Female	1		1	
Male	0.73 (0.56-0.94)	p=0.016	0.78 (0.60-1.03)	p=0.082
Age				
18-40	1		1	
≥ 41	1.40 (1.08-1.81)	p=0.010	1.33 (0.99-1.79)	p=0.061
Place of residence				
Hochland Park	1		1	
Havana	0.21 (0.16-0.28)	p<0.001	0.30 (0.21-0.42)	p<0.001
Marital status				
Single	1		1	
Married	1.92 (1.47-2.52)	p<0.001	1.25 (0.91-1.71)	p=0.173
Divorced or Widowed	0.81 (0.32-2.06)	p=0.660	0.61 (0.22-1.68)	p=0.338
Duration of stay in Area				
6 months to 1 year	1		1	
More than 1 year to 3 years	1.68 (1.01-2.79)	p=0.045	1.99 (0.58-1.70)	p=0.974
More than 3 years	1.61 (1.05-2.49)	p=0.030	0.93 (0.58-1.48)	p=0.744
Frequency of health access				
Often *(one or more per year)*	1		1	
Sometimes *(less than once per year but twice in the past five years)*	1.06 (0.71-1.58)	p=0.785	1.11 (0.73-1.69)	p=0.621
Rarely *(once in the past five years)*	0.30 (0.17-0.53)	p<0.001	0.46 (0.25-0.84)	p=0.012
Education				
No school/Primary	0.35 (0.24-0.51)	p<0.001	0.73 (0.48-1.11)	p=0.139
High school or beyond	1		1	
Employment				
Employed	1		1	
Self-employed	0.36 (0.26-0.51)	p<0.001	0.57 (0.40-0.83)	p=0.003
Unemployed	0.34 (0.25-0.46)	p<0.001	0.62 (0.44-0.87)	p=0.006
Currently receives TB info				
Yes	1		1	
No	0.46 (0.31-0.69)	p<0.001	0.50 (0.33-0.76)	p=0.001

Table shows socio-demographic variables associated with either increased or reduced relative odds of having high TB knowledge level.

Changing the cut-off point for good TB knowledge to reflect those who answered at least 50% of questions correctly showed that as a whole, 757 (94.6%) participants had good TB knowledge while 43 (5.4%) participants had low TB knowledge. These proportions however differed significantly by area, whereby in Havana, 370 (92.5%) had good TB knowledge, but this proportion was slightly higher in Hochland Park, being 387 (96.8%).

Table 5.22 shows results of the logistic regression model indicating the determinants of good TB knowledge. In the univariable analysis, place of residence, frequency of accessing healthcare, education level, and receiving information on TB were the significant predictors of good TB knowledge. However, in the multivariable model, only the level of education level and whether participants received TB information were significant determinants of good TB knowledge. The results showed that participants with a lower education level were less likely to have good TB knowledge compared to those with a high level of education (OR=0.31, 95%CI: 0.17-0.85; $p=0.021$). Participants who reported that they received no TB information at the time of my study were significantly less likely to have good TB knowledge (OR=0.25, 95%CI: 0.13-0.52; $p<0.001$).

Table 5.22 Binary logistic regression of socio-demographic determinants of good TB knowledge

Variable	Unadjusted OR (95% CI)	LR p-value	Adjusted OR (95% CI)	LR p-value
Sex				
Female	1		1	
Male	0.58 (0.31-1.09)	p=0.083	0.66 (0.34-1.31)	p=0.235
Age				
18-40	1		1	
≥ 41	0.71 (0.38-1.32)	p=0.272	0.58 (0.28-1.20)	p=0.161
Place of residence				
Hochland Park	1		1	
Havana	0.41 (0.21-0.81)	p=0.007	0.62 (0.26-1.46)	p=0.270
Marital status				
Single	1		1	
Married	1.11 (1.58-2.14)		1.17 (0.55-2.39)	
Divorced or Widowed	0.37 (0.08-1.74)	p=0.475	0.42 (0.07-2.40)	p=0.500
Duration of stay				
6 months to 1 year	1		1	
More than 1 year to 3 years	2.50 (1.13-5.51)		2.59 (0.80-8.32)	
More than 3 years	2.53 (0.97-8.27)	p=0.087	2.52 1.04-6.10)	p=0.138
Frequency of health access				
Often *(one or more per year)*	1		1	
Sometimes *(less than once per year but twice in the past five years)*	0.52 (0.23-1.18)		0.55 (0.22-1.36)	
Rarely *(once in the past five years)*	0.32 (0.12-0.81)	p=0.044	0.40 (0.15-1.09)	p=0.148
Education				
No school/Primary	0.26 (0.14-0.50)		0.39 (0.17-0.85)	
High school or beyond	1	p<0.001	1	p=0.021
Employment				
Employed	1		1	
Self-employed	0.80 (0.36-1.78)		1.19 (0.48-2.93)	p=0.886
Unemployed	0.79 (0.39-1.61)	p=0.771	1.22 (0.53-2.77)	
Currently receives TB info				
Yes	1		1	
No	0.19 (0.10-0.36)	p<0.001	0.25 (0.13-0.52)	p<0.001

5.5. Discussion

5.5.1. Summary of main findings

Multivariable analysis of this comparative, descriptive cross sectional survey showed that participants with the following characteristics were more likely to be residents of the high TB burden, Havana: self-employed, unemployed, exposed to TB in households, consumed alcohol more frequently, experienced lack of food due to lack of money, rarely visited healthcare services and lived in the township for a shorter period. In most cases, the observed associations did not differ by sex, but significant differences were observed by age concerning employment status and alcohol consumption.

In terms of TB KAP, the survey found that there were significant differences between responses from participants from Havana and those from Hochland Park. The sub-analysis of responses from participants from Havana showed that there were mostly no sex differences, but significant differences by age were observed. The survey found that the proportion of participants with good knowledge was significantly lower (57.5%) among participants from Havana in contrast to 88.5% of participants from Hochland Park. In this study, education level and frequency of visiting healthcare services were the factors associated with good TB knowledge.

5.5.2. Strengths

To my best knowledge, this is the first study attempting to understand the individual level factors to explain the distribution of TB in Windhoek. Unlike other studies in the literature (221-223), this study collected individual level information from the general population rather than from TB patients, and so the study results will be useful from the perspective of TB control in the general public, especially in the high TB burden township, Havana. A further strength of my study is that I defined independent variables based on the definitions from validated assessment questionnaires such as WHO TB prevalence questionnaire, AUDIT questionnaire and nutrition assessment questionnaires. This will allow for comparison of the study findings with similar studies in the literature. In my study I also assessed various components of TB KAP. I was able to study differences between two specific locations as well as to examine differences by sex and age. Unlike studies in the literature, I determined the prevalence of good knowledge based on questions cutting across many dimensions of TB.

5.5.3. Limitations

The study has several limitations. Firstly, the characteristics of participants from Havana were compared to those of participants from Hochland Park, which is not the township with the lowest TB burden in the city. Therefore, if characteristics between people residing in Hochland Park differ from those residing in Auasblick (the township with the lowest TB burden in the city), then the results observed in this study are likely to be an underestimation of the true differences. However, according to census data, the socioeconomic indicators of people residing in Hochland Park are very similar to those from Auasblick. For example, the percentage of people aged 15 who had attended formal education was 96% in Auasblick and 95% in Hochland Park. Furthermore, the unemployment rate among economically active population was 6% in Auasblick and 11% in Hochland Park. Therefore, the findings might have been obtained if the study was conducted in Auasblick, instead of Hochland Park.

Another limitation of my study is that the participants in each township were recruited from local shopping areas, and I am unable to determine whether the samples truly represented the target populations. However, the sample characteristics was similar to the pattern of the census data. While recruiting participants from people from public places allowed for a mix sample in terms of sex, age, social class, the study would have excluded the participation of residents who do not attend the local shopping areas for one reason or another (e.g. home-bound disabled people). If the characteristics of those people differed from those of people who frequented these places, then this would have an impact on the study results. Given this caveat, the results of my study should be taken as descriptive rather than representing true differences between these townships, however, the results still provide a solid starting point to understanding the spatial epidemiology of TB burden in Windhoek.

The places where participants were recruited from were the main shopping areas in these townships (with each shopping area having amenities generally matching the living standards of people in the township). In comparison to the literature, most studies were based on participants recruited through household visits, (35, 135, 225, 227-229, 231, 232, 234-236, 241), however in my case, a random selection of houses in a township such as Havana was not possible as there are no formal house numbers and the houses are not built in an orderly way. In addition, a high refusal rate when visiting houses in affluent townships in Windhoek (i.e. Hochland Park) have been noted during national studies from credible organisations such as the Namibia Statistics Agency (251). Moreover, safety is also compromised when conducting household visits as a lone researcher, as at one time, the NSA reported an incident where one respondent pulled out a gun and chased NSA researchers' away (252). Therefore the method I took for my study was suitable under these circumstances and also considering the resources (time, finances) available to me at the time, and I do recognise the need for further research to confirm these findings.

It is also important to indicate that my study was not conducted in a controlled environment (i.e. a household). Whether the participant was from the selected township, their age range and duration of stay in the township was not in any way validated.

Another limitation of the study is that report of bias, which is a limitation of observational studies in general. Some participants may have reported their characteristics based on what is desired socially i.e. under reported their smoking or alcohol consumption. If the report bias differed by area of residence, then the results obtained in this study have been an underestimation of the difference, particularly if the majority of participants from Havana under-reported their behaviours.

A further limitation of this study is that because of sensitiveness of some information, I did not take into account the presence of conditions such as HIV/AIDS and diabetes which are known as important risk factors for TB disease (1, 43). In future, it is worth studying TB alongside the prevalence of these conditions among the general public.

5.5.4. Interpretation and comparison with the literature

5.5.4.1. Socio-demographic and behavioural determinants

My study revealed that participants from the high TB burden township were significantly more likely to be self-employed (mostly as street vendors) or unemployed, a finding which supports the hypothesis that the unemployed are at high risk of TB disease. Lack of formal employment may suggest low living standards, which may affect the ability to have better nutrition and household conditions as well as access to information. Indeed in my study, the participants who experienced lack of food due to lack of money as well as those who were from houses with four or more people sleeping in one bedroom were more likely to be from Havana. These are all favourable conditions for TB, given that the disease results from an interplay of various factors to facilitate infection and disease (218). Several case control studies have reported an increasing risk of TB infection or disease among the employed (201, 204, 213, 216). In addition, studies have reported high risk of TB among people from crowded households (197, 200, 204, 206, 218) and those with poor nutrition (206, 212, 213, 218). A descriptive study conducted among TB patients in Windhoek, showed that they had low socio-economic status and were form poverty stricken areas in Windhoek (253). However, that study was strictly done among TB patients, did not assess behavioural factors and presented no quantitative associations. Here I have showed that most of the factors associated with TB disease (socio-demographic and behavioural factors) are significantly present in participants from the general public of a high TB burden area compared to those from a low TB burden area. These findings suggest need for targeted TB control interventions in the wider public of the townships most affected by the disease.

My study showed that participants who consumed alcohol more frequently were more likely to reside in Havana, a finding which supports the hypothesis that frequent alcohol consumption is a risk factor for TB infection or disease. Several observational studies have documented an increased risk of TB disease among people who consumed alcohol frequently (198, 211, 213, 216). The literature offers two reasons why frequent alcohol consumers can be at higher risk for TB. It is documented that alcohol has a significant inhibitory effect on cell mediated immunity, which facilitates TB infection among exposed (254). It has also been theorised that frequent alcohol consumption might be taken as a proxy for frequenting social places such as bars, resulting in increased TB exposure through socialisation (255). Given their circumstances (i.e. being unemployed), many people in Havana generally gather at bars at the local market, therefore it is possible that the high TB burden in the area could also result through social mixing coupled with poor immunological defence from poor nutrition. The finding that people who had TB contact within their household were more likely to be from Havana is therefore not surprising, and is consistent with findings from Rakotosamimanana *et al*. who showed that patients who were from the principal cluster were significantly more likely to have had a household member with TB before they got TB (222). Various cross-sectional and case-control studies have shown that people who had a household member significantly at higher risk of contracting TB (198, 210, 214).

In my study, participants who reported that they utilised healthcare services less frequently were more likely to reside in Havana. This can be used as a proxy measure of poor healthcare seeking behaviour. Poor or delayed health seeking behaviours prolongs the time a person is infectious (256) and therefore may results in more disease transmission (257). In Namibia, TB information is mostly found at health facilities (through posters and pamphlets), and so the finding that the majority of Havana participants rarely utilised healthcare services could also explain why a significant number of them had poor TB. Poor TB knowledge has been linked with further TB transmission (258). During phase two, I found that the TB burden in Havana is higher in the male population than females, and phase three results showed that, of Havana participants, the proportion of females who visited TB healthcare services more frequently was significantly higher than that of males. Moreover, more females than males from Havana received TB information through healthcare workers and radio. These results suggest poor knowledge of TB among men, which may partly the high disease burden.

My study revealed that participants who stayed in a township for a shorter period were more likely to be residents of Havana. This finding highlights an important aspect of internal migration and health, which perhaps, too often, has received little attention in TB control and public health in general in Namibia. It is possible that the high TB burden experienced in these townships could be because of reactivation of a previously acquired infection rather than recent transmission in the township. A study from Zambia reported that people who lived anywhere else in the last few years were significantly more likely to have TB (207). In a recent study from Songjiang in China, Shen and colleagues showed that TB notification rates were higher among internal migrants compared to local residents (259). As suggested by the census data, Havana is one of the townships in Windhoek where the majority of people from poor socio-economic backgrounds reside upon migrating to the city, Therefore, it is possible that, given the conditions in that township, the high burden could also be as a result of the reactivation of previous infections rather than recent transmission. As far as TB control is concerned, these results suggest need for molecular epidemiologic studies to assess the impact of internal migration on the epidemiology of TB. An earlier study in Windhoek showed that most of the patients had strains which did not belong to TB clusters, suggesting that their TB is not a result of recent transmission (193). However, that study was conducted over a long time ago and its results may not reflect the current TB epidemiology.

5.5.4.2. TB KAP

Significant differences in TB KAP were observed between participants from Havana and Hochland Park. I will now discuss results from Havana in relation to the literature.

5.5.4.2.1. Sources of TB information

I found that the majority of participants from Havana, 61.0%, mentioned that radio was their current source of TB information. This finding suggest that radio remains the most affordable mass media platform of communication among people of low socioeconomic background. This result is consistent with what was found in studies from other developing countries, including in Nigeria (228) and Uganda (35). In their study, Salleh *et al.* in Malaysia reported that the most common source of TB information was radio and TV (31.8%) (230). The low proportion reported in Salleh *et al.* might be because they combined radio and television as one source. The results from my study as well as those from studies by Hoa *et al*. (241) and Uchenna *et al*. (228) showed that the proportion of participants who mentioned radio as a source of information differed remarkably from the proportion who mentioned television. The majority of participants from Havana (83.3%) preferred to get TB information through radio. This finding is different from Hoa *et al.* study, where the majority of participants preferred TV as a source of information (70.4%), and in that study radio was only suggested by (25.0%) (241). The difference between my study and that of Hoa *et al*. might be due to differences in the socio-economic characteristics of the study participants.

Surprisingly, I found that TB specific campaigns were rarely conducted in Havana, and only 6% of the participants indicated that they had seen, heard of or attended a TB campaign in Havana in the past 12 months, prior to the survey. Furthermore, I found that 35.3% of participants from Havana said their knowledge of TB was poor and 97.0% indicated that they were willing to learn more about TB. The fact that the majority of participants from both townships indicate interest to learn more about TB should encourage the NTLP to mobilise resources both locally and internationally to improve the conduct (in terms of both frequency and scope and nature) of mass media events such as campaigns and radio messages.

5.5.4.2.2. TB symptoms, modes of transmission and treatment

I found that 64.8% of participants from Havana indicated that a cough of at least three weeks is one the most common TB symptoms, and this was significantly lower than the proportion among Hochland Park participants. The inability to recognise the disease symptoms may result in delays in care seeking and lack of treatment may result in further disease transmission (225). The proportion observed in my study is similar to the 61.5% reported in the Uchenna *et al.* study in Nigeria (228) and is higher than the 46.8% which was reported in the Obuku *et al.* study in Uganda (35). Two studies from Ethiopia (135, 226) reported higher proportions of participants who mentioned a persistent cough as a common symptom of TB.

In particular, Mesfin and colleagues conducted a study in rural and urban areas in Ethiopia, and reported a proportion of 71.5% (135). Similarly, in a national-scale study, Gelaw reported a proportion of 71.4%. Gelaw also found that the proportion differed by sex (226), which was not the case in my study. The variation between studies may highlight variations in local understanding of the disease.

In my study I found the majority (84.8%) of participants from Havana mentioned that TB is transmitted through the air when a person coughs or sneezes. Awareness of the modes of transmission will aid good practices such as covering mouth when coughing or sneezing. The finding from my study finding is slightly lower than the finding of 91.2% reported by Salleh *et al*. in Malaysia (230), but it is higher than the results of Mesfin *et al.*, Ma *et al.* and Mushtaq *et al*. who reported that 62.3%, 63.3% and 63.4%, respectively, knew that TB can be transmitted through the air when coughing (135, 232, 234). Uchenna *et al.* reported that only 30% of their participants knew the correct mode of transmission, and they showed that the proportion was significantly lower among rural based participants (228).

I found that almost all participants from Havana (97.3%) knew that TB is a curable disease. Being aware that a disease is curable may encourage adherence to medications, knowing that a complete cure is possible. The proportion obtained in my study is higher than the 85.1% reported in Ma *et al*. (232)and Obuku *et al.* (35)studies as well as the 84.4% reported in Gelaw (226). Wang *et al*. in China reported that only 73.5% of their study mentioned that TB is a curable disease (233). Perhaps the low proportion in the Wang *et al.* study might be because their study was conducted earlier than most of the other studies reviewed, and TB knowledge has perhaps improved over time. I found that the majority (95.8%) of participants from Havana were aware that TB can be cured with specific drugs given at health facilities. This finding is consistent with the proportion of 90.5% reported in the Uchenna et *al.* study (228) and higher than what was found in Mesfin et *al.* and Obuku *et al* (35, 135).

In my study, I found that 60.8% of participants from Havana were aware that TB treatment is free at public facilities. This proportion is low and may imply that some people in Havana do not seek healthcare because of envisaged treatment costs. However, the finding from my study is similar to the 57.5% reported in the Ma *et al.* study (232), but higher than the findings of Wang *et al.* and Obuku *et al.* (35, 233). In my study, only 16.5% did not know about the costs of treatment of TB in public facilities, a finding which is lower than what was reported in the Obuku *et al.* study, where it was found that 25.3% of their participants did not know about the costs of TB treatment (35).

5.5.4.2.3. Perceptions about TB burden and risk of infection

I found that 87.8% and 67.0% of participants from Havana respectively indicated that TB is a very serious disease and that it is a common disease in Windhoek. Mushtaq *et al*. reported that 63% and 54% of their participants thought that TB is a serious disease and a common problem, respectively. Mushtaq *et al*. also observed that the responses to these questions differed significantly by education and income levels (234). In my study I did not analyse differences by education or income but found that the responses concerning the seriousness of TB significantly differed by age group. Concerning who is most at risk of getting TB, the majority of participants from Havana indicated that anyone (56.3%), people who smoke and drink alcohol (35.8%) and People Living With HIV/AIDS (PLWHA) (3.5%). In other studies, the proportion slightly differed from my results. For example, Obuku *et al*. reported that their participants mentioned anyone (68.7%), PLWHA (19.5%) and alcoholics (12.7%) (35). In the Mushtaq *et al*. study, participants reported that people at risk of TB include anyone (72.3%), the poor (28.5%) and PLWHA (1.4%) (234). Compared to other studies, the lower finding in my study that anyone could get TB should be a concern to the NTLP. This is because it suggest that there may be people in Havana who believe that they cannot get TB because they do not drink alcohol or smoke, and people with such a belief might delay accessing healthcare, even in the presence of TB symptoms. For example, 6% of participants from Havana said they were not at risk of getting TB. Among those that said they were at risk of getting TB, less than half (48.3%) said everyone is at risk of TB. The majority of participants attributed the risk of infection to specific factors such as alcohol consumption, smoking, a dirty environment and HIV/AIDS. In a community such as Havana were the disease notification rates are worryingly high, these risk perceptions should be taken seriously by the NTLP.

5.5.4.2.4. TB related practices and attitudes towards persons infected with TB

I found that 42.3% of participants from Havana indicated that they would be afraid and feel embarrassed if diagnosed with TB. This finding may suggest the extent of the stigma associated with a TB diagnosis. It has been reported in some studies that some TB patients experience self-isolation because of embarrassment associated with TB (7). In the Mushtaq *et al.* study (234), the proportion of participants who indicated the same feeling was lower (23.7%) than the finding from my study, which may suggest variation in attitudes and knowledge towards TB between countries. In my study, 85% of participants from Havana said they would feel compassion and support a person with TB, while 12.3% indicated that they would reject them or hate them. Moreover, I found that 51% of participants thought that their community members would be supportive to a person with TB, while 33.8% thought a person with TB would be rejected in their community. These findings suggest the level of TB associated discrimination which may be faced by TB patients in the community. Studies have shown that discrimination towards TB patients can lead to delayed health seeking behaviours among TB suspects, as well as treatment abandonment among TB patients (257). The Ma *et al*. study reported that 52.5% of participants indicated that their community members would keep away from the TB patient, while 32.1% said they would provide support for a TB patient (232). Mushtaq *et al.* showed that the majority of their participants (47.9%), thought that in their communities a person with TB would be rejected (234).

In my study, I found that 30% of participants from Havana would keep a TB diagnosis in their houses a secret. Sreeramaddy *et al*. reported that only 15.6% said they would keep TB diagnosis a secret (240). Hoa and colleagues reported that more women (12.1%) than men (10.9%) would keep a TB diagnosis a secret (241). However, in my study and in Sreeramaddy *et al*. study (240), sex differences were not significant. Gelaw reported that 23.5% of their participants would hide a TB diagnosis, and in their study the proportion was 27.9% among women and 18.8% among men (226). The proportions reported by Gelaw may be lower as it is unclear if all 23.5% would keep it a secret, or whether some indicated unsure or don't know. For instance, in my study, I found that 4% of participants from Havana were unsure whether to keep it a secret or not.

5.5.4.2.5. Proportion and determinants of good TB knowledge

In my study, the proportion of Havana participants with high TB knowledge was 18.3%. This proportion is statistically significantly lower than that of participants from Hochland Park. Poor TB knowledge threatens successful TB control (35, 227), as it influences further TB transmission, through delays in health seeking behaviours resulting from inability to recognise the TB symptoms, or ways of prevention (135). Data from my study thus suggest the need for targeted TB health education interventions (i.e. campaigns) in Havana, the most affected suburb in Windhoek. In Uganda, Obuku and colleagues in Uganda found that the proportion of participants with a high TB knowledge was 49.7% (35). Two Ethiopian studies showed that that the proportion of participants with moderate to good knowledge was above 50% (135, 226). However the challenge with most of the studies in the literature (35, 135, 226, 240) is that questions used to determine TB knowledge level did not include a component on TB and HIV/AIDS, despite the fact that HIV/AIDS is a major risk factor for TB (260). Also, unlike my study, many of these studies only categorised their response variable into a binary variable (i.e. low/high knowledge level), and so it is possible that there has been a loss of information in some of the studies.

In my study, I identified that participants who were males, resided in Havana, rarely visited healthcare services, self-employed, unemployed and those who received no information about TB were less likely to have high scores of TB knowledge. The finding that males were less likely to have a high TB knowledge compared to females is consistent with results from the most recent national demographic survey, which showed that the proportion of females with correct TB knowledge was higher among women aged 15-49 compared to men (49). The results of my study also correspond with those from a nationwide study from Lesotho (237), which showed that females had a two-fold increased odds of having good TB knowledge. However, some studies have reported conflicting results (135, 227), while others have reported that gender was not a significant factor in relation to TB knowledge (225, 242). In Namibia, there is evidence that more men than women engage in risky behaviours such as alcohol consumption and smoking (49) and males make up the majority of reported TB cases (53). There is thus a need for the national TB programme to find ways of reaching the male population with appropriate TB messages.

Results from my study also showed that participants from Havana were less likely to have high TB knowledge compared to those from Hochland Park. This could be due to differences in socio-economic conditions, which makes it difficult for some people in Havana to access health related information. For instance, Mesfin and colleagues in Ethiopia demonstrated that differences in TB knowledge according to place of residence were associated with literacy levels (135). The findings from my study show the need for the national programme to tailor their control interventions to priority communities such as Havana, and ensure that people in communities are reached with TB messages. Many studies in the literature have shown than TB knowledge differed by rural/urban (135, 226, 227), but in my study I have also demonstrated that these differences in knowledge are apparent even within one locality (i.e. within an urban area), and so the need for more localised community specific studies cannot be over-emphasized. My study further showed that participants who rarely visited healthcare services had low TB knowledge. Similarly, I found that participants who received no TB information (from sources such as radio, TV, posters, healthcare workers and so forth) at the time of my study were less likely to have high TB knowledge. In addition, and consistent with other studies (35), I found that self-employed/unemployed participants were less likely to have high TB knowledge. Gelaw and colleagues in Ethiopia also showed that health seeking behaviours were associated with the level of TB knowledge (226). In my study, both the ordinal and binary logistic regression models showed that receiving TB information (from various sources) was associated with high TB knowledge level, and these results reinforces the need for the national TB programme to consider innovative approaches to creating TB awareness, particularly in hard-hit yet resource limited communities such as Havana.

Chapter 6 : A qualitative study of TB Knowledge, Attitudes and Practices among the general public of Havana

6.1.Introduction

Results from phase three showed significant differences in various components of TB Knowledge, Attitudes and Practices (TB KAP) between participants from Havana and Hochland Park. These results prompted the need for further research to investigate TB KAP in detail within the Havana community. It is well known quantitative studies are unable to explore in-depth narratives about the phenomena under study (77). Therefore, phase four was an attempt to qualitatively explore detailed narratives about TB KAP among the community members. To the best of my knowledge, no study has been conducted to date to assess TB KAP in the general population of this community.

In the subsequent sections of this chapter, I present a literature review (Section 6.2), methods (Section 6.3), results (Section 6.4) and a discussion of the findings (Section 6.5).

6.2. Literature review

To inform the conduct of my study, this section details a literature of primary studies that qualitatively explored TB KAP in the general population. At the end of this section, I provide a summary of the review which also explains how my study will contribute to the current TB literature. The specific objectives of the literature review were:

- To critically review the findings reported in these studies.
- To critically review the methods used to qualitatively study TB KAP in the general public.

6.2.1. Literature search

This was not a systematic review but I first used search terms to identify studies in databases. I searched for published peer reviewed articles from Web of Knowledge and Scopus, but some studies were obtained through reference lists of articles obtained. I was particularly interested in studies conducted in similar countries (e.g. African countries or developing nations). The focus was on studies conducted in the general population, and so studies that exclusively assessed TB KAP in specific groups such as TB patients, family members of TB patients and healthcare workers were excluded from this review.

6.2.2. Literature synthesis

I started by presenting a narrative review detailing the study findings, and this was followed by an appraisal of the methods which have been used to explore TB KAP.

6.2.3. Description of reviewed studies

Nine studies were reviewed and they are summarised in detail Appendix H. Studies were conducted in different countries including Uganda (261), Democratic Republic of Congo (7), Kenya (2), Ghana (3), Malawi (262),Tanzania (61), Vietnam (5), Bangladesh (263) and Serbia (264).

6.2.4. Review results

Studies have assessed multiple components of TB KAP, and so are included in the various sub-sections of the narrative.

6.2.4.1. TB knowledge

In most studies, the narratives from participants showed good understanding of TB, but some misconceptions were also reported. For example, a study conducted by Vukovic *et al.* in Serbia reported that participants thought that TB was transmitted through saliva, family members with the same blood type, and hand shaking (264). An earlier study from Kenya by Liefooghe *et al.* also reported that participants believed TB was inherited within families, and this was mentioned alongside other causes such as sharing sleeping rooms and kitchen utensils, drinking local alcohol, smoking and even bewitchment (2). The belief that TB is an inherited disease also emerged in the Mangesho *et al*. study in Tanzania (61). In Uganda, Buregyeya *et al.* reported that only one of their participants thought that TB was caused by bacteria, as the majority narrated that TB was caused by smoking, sharing food and performing heavy manual work (i.e. making bricks) (261). Working hard and having a low living standards were some of the causes reported in another study by Long et *al.* in Vietnam (5). In contrast to Buregyeya *et al.*'s study, a recent study from Malawi, Nyasulu and colleagues reported that there was a good understanding of the germ theory among their participants, although there were misconceptions including that TB was caused by smoking, alcohol and having sex were reported (262). Both Buregyeya *et al.* and Nyasulu *et al.* reported that some of their participants thought that TB and HIV/AIDS were synonymous (261, 262).

The narratives presented in studies show that there was a good understanding of TB symptoms. For instance, participants in the Buregyeya *et al.* study narrated that TB manifests through a persistent cough, weight loss and coughing blood (261). Buregyeya *et al.* however reported that a small number of participants confused TB with asthma. In Kenya, Liefooghe *et al.* also reported that their participants had good knowledge of the disease symptoms, which included coughing, weight loss, chest pain and fatigue (2). A Bangladeshi study by Bam *et al.* found that a cough was the main symptom of TB, and in addition, they reported that more women than men knew the correct TB symptoms (263).

With regards to TB treatment, the findings in studies show that participants had good knowledge of TB treatment, although incorrect beliefs were presented in some studies. For instance, a study from the Democratic Republic of Congo conducted by Bennstam *et al.* reported that participants had doubts in the health care system regarding appropriate TB diagnosis and treatment (7). In addition, the Bennstam *et al.* study found that some participants believed that TB recovery was uncertain (7). Similarly, in the Liefooghe *et al.* study, there were also mixed feelings about the curability of TB, and some participants thought that TB was cured only when diagnosed early (2). In contrast, the Buregyeya *et al.* in Uganda found that participants believed that TB was a curable disease, particularly when one adheres to treatment instructions (261).

6.2.4.2. Perceptions concerning risk of infection

Two studies documented views on risk of infection and both studies reported that responses varied among participants. In particular, Bam *et al.* in Bangladesh reported that some of their participants thought that they were not at risk of TB (263). According to the authors, this was attributed to a number of aspects including that there were very few people with TB in the area, the area was clean and people ate healthy food (263). In contrast, A Malawian study by Nyasulu *et al*. reported that the majority of participants in their study thought they were at risk of infection because TB can infect anyone through breathing in contaminated air (262). The differences between the studies might be due to geographical differences as the Bam *et al.* study was conducted in an urban setting whereas Nyasulu *et al*. study was from a rural area.

6.2.4.3. Stigma and discrimination

The narratives concerning TB associated stigma and discrimination were also mentioned in some studies. For instance, the Bam *et al.* study, documented that participants thought their community members keep a distance from those suffering from TB (263). Bennstam *et al.* found that TB related stigma remains with a TB patient even after they have been cured (7). For example, the authors documented that people who had TB found it difficult to establish social relationships such as marriages because of their TB history. In other words, the chance of a younger person who had TB getting married was unlikely (7). Moreover they found that TB associated shame and isolation inflicted suicidal thoughts in TB patients, as they were treated as abnormal and people avoided them (7). Some participants in the Liefooghe *et al.* study believed that a person who had TB was never going to be the same again (2).
In Ghana, Dodor and Kelly found that the majority of participants would not marry a person who had TB, because of fear of infection and belief that the children born by that person might be infected (3). Moreover, participants in that reported that they would not select a person with TB to represent the community in any capacity, because they feared that person would spread the disease during interactions with other people (3). Nyasulu *et al.* reported that one of their participants shared that he was forced to divorce his wife after she was diagnosed with TB (262). According to participants in the Liefooghe *et al.* study, TB diagnosis was reported to be feared both within a household and in the community (2). The results from these studies suggest that TB is still a highly stigmatised disease.

6.2.4.4. Access and utilisation of healthcare service

A number of studies reported participants' views concerning healthcare access and uptake. For instance, Liefooghe *et al.* found that there was a strong belief in seeking healthcare from traditional healers, particularly when there had been no improvement in the patient' s conditions (2). Moreover, Liefooghe *et al.* reported that some of their participants believed that medications given by traditional healers were less cumbersome and more easily accessible than modern TB medicines (2). In a study by Nyasulu *et al.*, some of the factors hammering timely healthcare seeking were the fear of being diagnosed with HIV/AIDS, being told to give up pleasurable habits such as alcohol consumption, smoking, and having sex (262). The belief in traditional healers indicated in the Liefooghe *et al.* but not in the Nyasulu *et al.* could be because is more recent and perhaps the use of traditional remedies has changed.

In the Buregyeya *et al.* study, some participants reported that people delayed seeking healthcare because of reasons such as fear of being labelled as sick, a lack of money and the trust in traditional medication (261). In fact, Buregyeya *et al.* reported that there was a belief that TB could be cured by a combination of modern medicine as well as medicines given by traditional healers (261). They also found that the pill burden, treatment duration as well as fear of being diagnosed with HIV/AIDS were other factors which discouraged people from seeking healthcare at health facilities (261). Similarly, in the Bam *et al.* study, participants discussed that although TB treatment centres and doctors were available, financial constraints was one of the factors that affected access to healthcare (263). The participants in a the Long *et al.* reported that the financial burden resulting from TB can have a huge impact at family level, because the treatment process requires frequent travelling to health centres and the pressure to buy quality food for the TB patient (5).

6.2.4.5. An appraisal of methodologies used to qualify TB KAP

6.2.4.3.1. Target population

Except for three studies conducted in Bangladesh (263), Serbia (264) and Tanzania (61), all other studies explored TB KAP among groups of participants comprised of both TB patients and TB free participants. While this method may have allowed researchers to obtain different perspectives of TB KAP, the narratives from the two groups of participants were combined in all the studies, making it difficult to differentiate the TB KAP of the general public from those that of TB patients. By virtue of being a TB patient, one would expect that their TB KAP would be different, perhaps better from that of the public as noted in the Nyasulu *et al*. study from Malawi (262).

6.2.4.3.2. Location

In some of the studies (2, 5, 7, 262) TB KAP was assessed among groups of participants made up of people from rural and urban areas, but none of these studies discussed findings by locations. It has been documented that TB KAP differs according to whether the area is rural or urban (35, 228). In the Tanzanian study which was conducted in a primarily rural setting, the authors presented the study findings according to specific locations, however, this was only done for TB knowledge but not on attitudes and practices (61). Combining the narratives of people from both areas may have under or overrepresented the views of participants in specific locations, and this will affect the implementation of setting specific TB health education interventions.

6.2.4.3.3. Data collection method

Five studies used data collected through focus group discussions (2, 5, 7, 61, 264). Focus groups are defined as groups of participants gathered to discuss a common topic from the participant's individual perspectives (265). Focus groups offers a wide range of advantages including that they are able to gather information from a large number of participants in less time, compared to one to one interviews (265), and they also allow for some sort of consensus and information synthesis during a common discussion(266). However, the use of focus groups on a disease like TB may have some limitations given the stigma, sensitiveness and shame attached to the disease (2, 3, 7). It is possible that some participants may have hidden perceptions which they would have discussed had other methods been used. Moreover, some may have agreed to the views of others when they would have disagreed in private (267). In as much as some researchers have attempted to gather a homogenous group of participants by grouping them according to sex, age or socioeconomic background (5, 7, 264), group interactions can be inhibiting for some participants (268), and discussions can be dominated by outspoken personalities (269).

One study conducted in Bangladesh by Bam *et al*. (263) used data collected through semi-structured one to one interviews. Green and Thorogood explained that, interviews are informal discussions between two people, in which one takes the role of interviewer and the other interviewee (270). Green and Thorogood further explained that semi-structured interviews are based on a set of questions, but the discussion is flexible to accommodate new information related topic as it emerges (270). According to Milena *et al*., interviews are considered to be the best approach for gathering personal opinions and experiences (269). However, a disadvantage is that one to one interviews can be time consuming, compared to focus groups (271). Milena *et al*. nonetheless stressed that one to one interviews can enhance confidence and relaxation, which allows participants to share and express deeper experiences and interpretations than would be expected in focus groups (269).

In three studies (3, 261, 262), data were collected through both focus groups and one to one interviews, but none presented integrated findings (or at least reported that integration was done). It has been emphasised that when two or more methods are used to study a phenomenon, the results must be integrated to enhance better understanding (272). I will discuss the concept of integration in more detail in Chapter 7.

6.2.5. Literature review summary

In terms of the study findings, it is important to note that the findings of these studies can only be discussed in the context of their settings, given the qualitative nature of the studies. However, similar findings were generally reported. For example, in all the studies, participants demonstrated good knowledge of TB, although there were clear misconceptions, including that TB was an inherited disease (2, 61), caused by HIV/AIDS, smoking and alcohol (261, 262). Correct knowledge about TB symptoms and treatment was reported in all studies, but some incorrect beliefs about treatment evident (2), while in other studies there were doubts about the successful treatment of TB in the healthcare system (7). Views about TB related stigma were also expressed, and in some of the studies TB was reported to be a much stigmatised disease (2, 3, 7). With regards to healthcare seeking behaviours, participants' uptake of healthcare services was generally good, although factors such as the lack of money, stigma use of traditional healers and poor access were reported as impeding factors to the timely utilisation of healthcare services (5, 261, 262).

In terms of the methods, I found that despite that TB KAP differs according to location (228), most studies combined the narratives of participants from different locations (rural and urban). Moreover studies combined the narratives of TB KAP of people in the general public with those of TB patients. Some studies exclusively used focus groups to study TB KAP, and this may not have been appropriate, as TB is a stigmatised disease (7). Three studies used both focus groups and one to one interviews, but these studies did not integrate the findings.

No study was found to have qualitatively assessed TB KAP in the general population of a specific community in Namibia. The only studies I found were conducted exclusively among TB patients (81, 273), and I have discussed the findings of these studies in the discussion section of this chapter. Therefore, having reviewed previous work, my study aims to contribute to the literature in two ways. Firstly, this is to the best of my knowledge the first study to explore TB KAP in the general community of Havana. Secondly, the study was preceded by a cross sectional survey in the same community, and so it enabled for the integration of findings.

6.3. Materials and methods

I conducted a qualitative study between August and September 2017 to explore TB KAP among residents of Havana. The study methods are outlined in the sections below.

6.3.1. Philosophical framework

Qualitative researchers are concerned with understanding the way people give meaning to their world, through the narratives of their lived experiences, perceptions and interpretations of a particular phenomenon (274). My study was designed from the phenomenological standpoint, to provide a rich description of TB KAP as presented by people living in a high burden TB area, Havana. Phenomenology is a philosophical approach focused on understanding people's lived experiences or perceptions of the things in their surroundings, and the framework originated from the intellectual thinking of a German philosopher, Edmund Husseri (1859-1938) (275). According to Lopez and Willis, there are two classical phenomenological approaches, each with its philosophical principles. The first is the descriptive (eidetic) approach, concerned with describing people's experiences based on their subjective information. The second is the interpretative (hermeneutic) approach, focused on interpreting human experiences based on contextual factors and not merely what was said (276).

My research is primarily based on the principles of descriptive phenomenology. Polit and Beck explained that descriptive phenomenology aims to answer the question "what do we know as persons" (277). Furthermore, Green and Thorogood pointed out that descriptive phenomenology is mostly suitable when little is known about a topic or community (278). For my research, I considered that the descriptive approach was appropriate, as little is currently known about TB KAP in the general public of Havana.

6.3.2. Study sample, target population and recruitment method

In qualitative research, the purpose of sampling is not to achieve statistical representation, but rather to select study subjects who will provide "rich" insights to the subject under investigation (279). The target population for my study were people aged 18 or older who had resided in Havana for a minimum period of six months. Purposive sampling was used to select participants through house-to-house visits, and I had no prior relationship with any of the participants. In total, fourteen interviews were conducted with seven men and seven women.

6.3.3. Method of data collection

One to one interviews were the preferred choice of data collection for my study because of two reasons. Firstly, the phenomenon of interest was TB, which may be a sensitive issue to some of the participants, and hence there is the potential for stigma when disclosing individual TB perceptions and experiences when in a group. Secondly, interviews were thought to allow for direct conversations with residents of Havana, in an attempt to obtain a wealth of data concerning individual opinions, rather than a group consensus. It is the individual views that were central to my research. I used semi-structured interviews, which as discussed in Section 6.2.4.5 provide the flexibility to follow up on ideas and probe for further responses as necessary (280).

6.3.4. Interview settings

Interviews were conducted at participants' homes in Havana. Conducting in-depth interviews at home was considered appropriate to allow for relaxed and detailed discussions with the study participants. Moreover, it was thought to be the best method of limiting interruptions when recording the conversations on a digital recorder. Each interview lasted no more than an hour and the interviews were conducted to data saturation. Given that households in Havana are not built in an orderly manner, I attempted to visit different parts of Havana during recruitment to avoid recruiting participants from only one part of the community.

6.3.5. Study topic guide

I designed the topic guide myself with the help of my supervisors. The discussions of my qualitative study were grouped into five main areas as shown in the study's topic guide (Appendix I). In the first section, participants were asked to narrate how they understood TB, by describing its causes, symptoms, mode of transmission and treatment. Second two focused on opinions concerning personal risk of infection. Section three explored views about the general risk of TB infection in the community. Section four focused on views related to TB stigma and discrimination. The last section explored health seeking behaviours.

6.3.6. Pilot study

A pilot study is a small-scale study aimed to identify weaknesses and problems before the actual data collection (281). My pilot study was specifically conducted to test the clarity and appropriateness of questions in the topic guide as well as to prepare my qualitative interviewing skills. Pilot interviews included three interviews with Havana residents selected on a purposive basis (two males and one female), and I had no prior relationship with any of them. A discussion was held with each of the pilot study participants regarding the questions asked, the sequence of questions, the interview duration and my interviewing style. No significant changes were made to the topic guide after the pilot interviews. The feedback provided by the participants mainly concerned my interviewing approach, i.e. that I appeared too serious, making the interview appear too formal, or that I was at times too fast when asking questions. This kind of feedback helped me to prepare for the main study. The pilot study discussions were not included in the final analysis.

6.3.7. Interview process

I visited Havana community mostly over the weekends, and some days after 5pm on weekdays to recruit participants. These were considered to be the best times to conduct interviews, as this is usually the time when people are home. In each household, I introduced myself as a student and briefed members about the purpose of my visit. To put household members at ease, I had to mention from the beginning that the research was targeted at any household in Havana, and that having visited that particular house did not mean that house was at increased risk of TB. It was also made clear that I was not going to test people for TB or take any sputum or blood samples.

After the introduction, household members were asked if there was a person meeting the required demographic characteristics (in terms of age and sex). If there was no person with those characteristics, I thanked the household members and proceeded to another house. If there was a person with those characteristics who was willing to be interviewed, I reiterated the study's aims and objectives to that person, and indicated that the interview was going to be recorded on a digital recorder, and that no details would be taken to make that person identifiable. The person was then asked to give consent, which was audio recorded during the interview. I allowed participants an opportunity to ask any questions (if they required further clarity) before we commenced the interview. I did not encounter difficulties in terms of managing emotions or anger or extreme discomfort during the execution of all interviews. After the interview was done, I thanked the participant and welcomed any discussion or question they had about TB or my research. I also saw this as an opportunity to correct some of the misconceptions about TB which I had noted during the interview. In some houses, this discussion was very interesting and it even involved other household members not interviewed.

6.3.8. Transcription

Interviews were mainly conducted in the common local language, Oshiwambo, and were transcribed verbatim in English. I conducted interviews and transcribed all of them myself. A sample of transcribed interviews was shared with my supervisors. The transcribing process involved replaying the recording several times to capture the participant's exact words. The back and forth process was nonetheless advantageous, as it allowed me to connect with the contents of each interview.

6.3.9. Data analysis

According to Gibbs (282), there are two important practical stages involved in analysing qualitative data. The first involves creating awareness of the kind of data to be described, and stage two involves the practical application of a particular method to analyse such data. Therefore, I implemented these stages in my study. The preliminary analysis stage was more of a reflection stage and was conducted during the data collection process, before the interviews were transcribed. It involved replaying the recording of each interview and taking note of important things from the discussion. This informal analysis not only prepared me for the main analysis, but also served to identify aspects that needed further probing in subsequent interviews.

The second stage involved the application of thematic analysis as a method of generating knowledge from the interview data. This stage was implemented after all the interviews were transcribed. It has been emphasised that there must be a systematic approach when analysing qualitative data (283). I therefore followed the six steps outlined by Braun and Clark(284), which are: (1) familiarisation with the data, (2) generation of initial codes, (3) searching for themes, (4) revision of themes, (5) defining and naming themes and (6) producing the report.

Each interview transcript was read several times and reference was made to the reflection notes I made during the preliminary analysis stage. Initial coding was carried out and comparisons were made across the interview transcripts, and this resulted in the identification and naming of themes. Although the steps above imply a sequential form of data analysis, the actual analysis for this study involved a back and forth process, which was nonetheless necessary to ensure that I had grasped the content of each interview, as well as to ensure that the interpretations I made from the data (i.e. theme identified) represented the participants' voices. The guidance for analysing phenomenological studies (285)as well as the fifteen-point checklist for conducting thematic analysis proposed by Braun and Clark (284)were used to guide the actual data analysis process for my study. The specific aspects of Braun and Clark are presented in Table 6.1.

In the results section of this chapter, I present the final themes together with supporting quotations from participants.

Table 6.1. Checklist for good thematic analysis (284)

Transcription	1.	The data have been transcribed to an appropriate level of detail, and the transcripts have been checked against the tapes for 'accuracy'.
Coding	2.	Each data item has been given equal attention in the coding process.
	3.	Themes have not been generated from a few vivid examples (an anecdotal approach) but, instead, the coding process has been thorough, inclusive and comprehensive.
	4.	All relevant extracts for all each theme have been collated.
	5.	Themes have been checked against each other and back to the original data set.
	6.	Themes are internally coherent, consistent, and distinctive.
Analysis	7.	Data have been analysed – interpreted, made sense of - rather than just paraphrased or described.
	8.	Analysis and data match each other – the extracts illustrate the analytic claims.
	9.	Analysis tells a convincing and well-organised story about the data and topic.
	10.	A good balance between analytic narrative and illustrative extracts is provided.
Overall	11.	Enough time has been allocated to complete all phases of the analysis adequately, without rushing a phase or giving it a once-over-lightly.
Written report	12.	The assumptions about, and specific approach to, thematic analysis are clearly explicated.
	13.	There is a good fit between what you claim you do, and what you show you have done – i.e., described method and reported analysis are consistent.
	14.	The language and concepts used in the report are consistent with the epistemological position of the analysis.
	15.	The researcher is positioned as *active* in the research process; themes do not just 'emerge'.

6.3.10. Reflecting on the quality of the study findings

According to Flick (286), quality from the perspective of a qualitative researcher involves self-judging the extent to which the study findings can be trusted, and whether the methods as well as overall research procedures were appropriate. In this study, I judged the trustworthiness of the findings using the criteria proposed by Licoln and Guba (287), based on the following four elements:

1. Credibility - confidence in the truth of findings,
2. Transferability – showing that the findings have applicability in other contexts,
3. Dependability – showing that the findings are consistent and can be repeated,
4. Confirmability– a degree of neutrality, or the extent to which study findings are shaped by respondents, and not researcher bias, motivation and interests.

To ensure the credibility of the study findings, this qualitative study was preceded by a cross-sectional survey which quantitatively assessed TB KAP among participants from the same community. Using the two methods allowed an opportunity to assess the truthfulness of the results through an integration process whose results are presented in Chapter 7. With regards to transferability, I have provided comprehensive details about the methods followed during the execution of this study. Providing detailed descriptions of the study methods will enable other researchers to replicate the study's processes (288). To enhance dependability, I was guided by suggested steps of analysing qualitative data. In terms of conformability, this study was designed from the descriptive phenomenological standpoint, a school of thought which favours the researcher's objectivity. I followed the guidance provided by Hycner (285) to ensure that my preconceptions were put aside as much as possible and that the findings reflect the participants' voices.

6.4. Results

6.4.1. Participant demographics

Fourteen interviews were conducted, consisting of seven men and seven women. Table 6.2 gives the brief context of each interview.

Table 6.2. Characteristics of participants for the qualitative interviews and context of interview

Id	Sex	Age	Brief notes about the interview
1	Female	41-50	I found the participant inside her house. I introduced myself and the study objectives and she agreed to participate. This was an easy interview and rapport was easily established from the beginning. The children sat quietly near her listening to their mother as she narrated her story.
2	Male	18-30	The participant was outside his house together with his family. After I introduced myself and the purpose he agreed to participle but cautioned that if it is a difficult interview he will have to end it. This was not really a good interview as the participant was not very elaborative, and I was somehow put in an awkward position trying to get elaborative answers from him.
3	Male	41-50	I found the participant outside his house with his wife and a friend. After I introduced myself and the study, he agreed to participate and we commenced the interview while the two ladies were listening without saying a word. Rapport was also easily established during this interview.
4	Female	41-50	I found the participant alone outside of her house reading a newspaper. She agreed to participate in the study after I introduced myself and explained the study objectives. I enjoyed this interview, as the participant did not rush me and was very friendly.
5	Female	18-30	I found husband and wife in their house. I introduced the study and invited the wife to participate. She agreed and we commenced with the interview while her husband sat quietly listening to the discussions. Rapport was not very easily established during the interview as the wife appeared to be uncomfortable with her knowledge of TB.
6	Male	41-50	I found the participant cleaning his shoes outside his house. He agreed to participate after I briefed him on the research objectives. Rapport was established very easily and the participant appeared very comfortable talking to me and discussing about TB.
7	Female	31-40	I found the lady and her kids cooking outside their house. The lady agreed to participate in the study after I introduced myself and the research objectives. Rapport was established early on during the

			interview and the participant showed huge interest in the topic. I mostly enjoyed this interview because of the elaborative answers that she gave and the interest shown on the topic.
8	Female	18-30	I found the participant outside the house with her friend. This was an easy interview with a friendly lady who also appeared very comfortable throughout the interview.
9	Male	18-30	The participant was his house when I approached him. He agreed to participate after I introduced myself and the study purpose. Rapport was easily established although some of his responses were short and he was not really keen to elaborate more.
10	Male	31-40	I found the couple in their house and after I briefed them and invited the man to participate, he agreed. The wife listened to the interview without saying a word although her husband kept looking at her as for support I suppose, which the wife gave through head nodding throughout the interview. Rapport was easily established and the husband felt comfortable throughout the interview but kept some of his responses short.
11	Male	31-40	I found the man inside his house. I introduced myself and the study and I invited him to participate. This was not really an easy interview as the man appeared to be uncomfortable throughout the discussion.
12	Female	31-40	I found the participant outside her home doing laundry. After I approached her and introduced the study she agreed to participate. Rapport was easily established and I enjoyed this interview as the lady was very elaborative and demonstrated interest in the study.
13	Male	Over 60	I found the man sitting outside his house with his family. I introduced myself and the study and invited him to participate. He agreed to participate and we commenced with the interview. He was elaborative but kept asking if I was about to finish with my questions. Despite the rush, I enjoyed this interview.
14	Female	Over 60	I found the participant outside the house with her grandchildren. She agreed to participate after I introduced the study objectives. Rapport was easily established and I also really enjoyed this interview as the lady seemed very comfortable talking to me and she gave detailed answers.

6.4.2. Description of the study themes

The findings of my study are grouped into four themes, and the first theme is *the exact cause of TB may not be clearly understood but symptoms and treatment are*. This theme summarises views concerning what people know about TB, specifically in terms of its cause, symptoms, mode of transmission and treatment.

The second theme is *situational drivers*. This theme captures participants' narratives about their perceived risk of TB infection and their justification of the factors which either increased or decreased their risk of infection.

The third theme is *the duty of care*, which involves issues related to how participants narrated a TB diagnosis in relation to the wellbeing of people in close proximity (e.g. family, friends and neighbours). This theme also captures participants' opinions concerning the relationship between community members on disclosing a TB diagnosis.

The fourth theme is *lack of health education sessions and basic services*. It captures discussions regarding participants' take on the quality and quantity of existing community based TB control activities and their opinions concerning services which have direct effects on the wellbeing of community members, in addition, the theme also captures participants' narratives about their health-seeking behaviours.

Each theme is presented in turn below and supporting quotations from the interview transcripts are provided to corroborate findings.

6.4.3. Study results

6.4.3.1. Theme one: The exact cause of TB may not be clearly understood but symptoms and treatment are

Participants recounted their knowledge of TB in varying breadth and depth. I assessed basic TB knowledge in relation to four subsections, namely, cause of TB, modes of transmission, common symptoms and treatment. Taken together, narratives from participants showed that there was a general lack of understating of the exact cause of TB. In contrast, discussants demonstrated better understanding of the modes of transmission, disease symptoms and treatment. Each subsection under this theme is presented below.

6.4.3.1.1. The cause of TB

Participants' narratives on the cause of TB suggested that TB is a multidimensional condition. The participants specifically described the causes of TB in various ways ranging from biological, behavioural and environmental causes. The most common narratives expressed were that TB is caused by risky behaviours, mostly alcohol abuse and smoking. Interestingly, when some participants narrated these causes of TB, they mostly did this by referring to other people, using words such as "they" or "some people", implying that they themselves do not engage in these risky behaviours.

> *It is when they drink too much alcohol, and smoking. Those things are not needed, as a person can get TB if they are consuming those things* [Participant 10, male].
>
> *Some of the people are drinking, and TB is coming from alcohol. TB is also coming from dust, smoking, garbage and car fumes* [Participant 12, female].

Some participants articulated that unhygienic environmental conditions were responsible for TB infection, and this was mostly the view of women.

> *Just to say that even when I am sitting here, if you look around there, there is rubbish and water is poured there, and it is used as a toilet by small children, so that smell can diffuse and get to someone and this might result in TB. There is also that thing, if you have checked, that is collecting dirty water from pipes, so that smell from there is coming to us and causing TB* [Participant 4, female].
>
> *Even the dirty water with a smell, like here in Havana we have a lot of standing water and some of the people are just throwing stuff in those waters resulting in a bad smell. So those rotten stuff are not healthy and are causing TB* [Participant 12, female].

Moreover, some participants, men specifically, reported that TB is an inheritable disease. According to these participants, certain people cannot avoid having TB, since it is a disease within their family blood.

> *What I mean is that we hear about some people born with TB or that their family has a history of TB, and even at hospitals they do ask if there is anybody in your house who has TB* [Participant 3, male].
>
> *I also heard that it could be a family disease, so there are some families with history of TB* [Participant 9, male].

Two older participants reported TB as a disease caused by HIV/AIDS, and their narratives suggested that the two diseases are inseparable.

> *TB is a disease that I think is brought by AIDS, because I heard many people who have AIDS also have TB. When a person is confirmed to have AIDS, and then they will also be tested for TB* [Participant 13, male].

> *Like for me I know because like my daughter just started with a cough, non-stop and she went to clinic here and was sent to Katutura hospital and got confirmed that she has AIDS and TB. But she just started with a cough.* [Participant 14, female].

6.4.3.1.2. Modes of transmission

On modes of TB transmission, all participants indicated that TB is spread mostly through the act of coughing, although they generally did not generally quantify the exact cough duration. During these discussions, participants emphasised the importance of covering the mouth when coughing to avoid further disease transmission.

> *Yeah, mostly when it comes to the spread, that disease is spread when there is a person who has TB, who is for instance coughing, without holding their mouth, that way the person can spread TB* [Participant 1, female].

One female participant articulated that some of the people do not cover their mouths when coughing or sneezing, even when surrounded by other people. According to her, some people may even become angry when told to cover their mouths.

> *Because some people when you tell them to hold their mouths they cannot even understand, they just become rude, and think you hate on them* [Participant 12, female].

The majority of participants expressed that TB is also commonly transmitted when people share kitchen utensils such as cups and spoons. The participants indicated that people in the community usually drink their local alcohol, served in one big cup which many people drink from. One participant raised a concern that, in some cases, people may know that someone is sick, but this awareness does not prohibit them from sharing cups when drinking alcohol.

> *Yes, especially when we are drinking our own traditional liquor, we are just free to share the cups* [Participant 7, female].

> *Oh like here in Havana, like now you see people are drinking and sharing cups of tombo (local alcohol), some we even know that they are sick, but people just don't care, they are just sharing cups* [Participant 14, female].

It was also expressed that having sex was another way of how TB can be spread. An elderly female put it that the current way of living is not good, as people careless about their acts and consequences.

> *Here in Havana, we are too many, you can see all those houses near each other like that and there is a lot of people who are just sleeping around (having sex). And things have changed that is why even when my daughter had TB, people were not really scared because today's life is different and the way young people do things is different today…people are just at bars and they are drinking and having sex, so they don't stay in houses* [Participant 14, female].

6.4.3.1.3. Common symptoms

All participants reported that TB manifest through symptoms such as prolonged cough, chest pain and night fever. The participants generally understood that persistent cough is usually the first symptom that a person with TB will experience. In addition, one participant articulated how the disease can take a toll on one's physical appearance and body strength.

> *Well what I know is that a person with TB, their bodies are usually not okay and they cough a lot of times, so those are the things I know. What I mean is that they have thin bodies and weak bodies* [Participant 13, male].

6.4.3.1.4. Treatment

Concerning TB treatment, all participants indicated that TB is a curable disease. They further reported that the disease is treated at clinics or hospitals through modern medications. None of the participants indicated treatment at traditional healers. Many of them pointed out that successful treatment is achieved when one strictly follows clinical instructions.

> *When you follow instructions, you will be completely cured, but if you do not follow then you won't* [Participant 3, male].
>
> *What I know about TB is that it can be cured. A person is given medication then they have to take them until a stage where they will be told to stop them* [Participant 10, male].

In the narratives of some participants, reference was made to people whom they knew hah had TB, and such people had been completely cured.

> *TB can be cured, we have noticed, we know people who had TB but they are now cured and well* [Participant 1, female].

> *Well about treatment, we normally see people going to the clinic here in Havana, and get their medication, so I know that you can be treated. Because even the ones whom we knew had TB were given medication and they are now okay* [Participant 13, male].

Some of the participants emphasised hope and belief that TB is not a life sentence, also stressed that people with TB should trust that they can be cured.

> *Let me say, we need to be free, because that disease is not a deadly one, there are some more dangerous diseases. I just want to tell people if you notice that you have TB, you need to be free and get your treatment so you live your life again* [Participant 12, female].

6.4.3.2. Theme two: Situational drivers

There were mixed feelings concerning the perceived risk of TB infection. Some of the participants perceived that they were at increased risk because of their social life, which was mostly related to the way they drink alcohol with friends and their outdoor life.

> *I am at risk, because the way we are drinking here (referring to alcohol consumption), if I am thirsty and I find my friend drinking not knowing her/his health status, and then I drink from the same cup, if that person have TB, I can also get TB. For instance, if my friend has a sore on the lips and I also have, then that way we I can also get infected if the person has left saliva or blood on the cup that we are sharing* [Participant 7, female].

Some of the participants explained that the kind of environments in which they live poses a danger to their health.

> *Another thing is also the dirtiness of the environment and the location of our houses (in valleys). The surrounding is very dirty and no one takes cares of it* [Participant 7, female].

> *We are too overcrowded here and the dust is too much, even the food that we eat here is just under a lot of dust. There are no proper roads and those sorts of things* [Participant 3, male].

Two male participants' understanding was that TB is a disease that could infect anyone regardless of their behaviour and environment. These participants described TB as being a normal disease that can affect anyone at any time.

> *No, it's a normal it's a disease, can catch anytime* [Participant 2, male].

> *TB is a disease that can get to you anytime, everyone is just at risk of getting TB regardless of what* [Participant 6, male].

In contrast, a mutual thread through the narrative of participants who felt that they were not at high risk of TB infection was related to the lack or minimal indulgence in alcohol and smoking.

> *I think, I do stay away from alcohol and also smoking. Therefore, I think I have protected myself* [Participant 1, female].

> *I hardly use those things of alcohol and I do not smoke. Therefore, I believe that it is difficult for me to get TB* [Participant 10, male].

In addition, participants also pointed out that their low risk was because of a lack of proximity to a TB person, particularly in their households.

> *In addition, I also heard that sometimes if you stay with a person with TB you can also get it, but in my case I have never stayed with anyone with TB* [Participant 10, male].

> *The main thing is because we do not have TB at home, so I know I have not shared a cup at home with someone with TB. I also know that I did not go in those dirty swamps where there's dirt causing TB* [Participant 13, male].

6.4.3.3. Theme three: The duty of care

Participants presented mixed views concerning the disclosure of a TB diagnosis. The majority of participants felt it was important to share that they had a person with TB in their house when visited by friends or neighbours. They mostly emphasised that de-stigmatising the disease is one way of curbing continuous transmission. The need to protect other people from going through the same experience was strongly expressed, and this portrayed how community members valued one another's wellbeing.

> *So, say if I have a daughter with TB and she want to go to her friends from nearby houses, so you mean her friends should not know? Because if she is going to others, at least when they communicate they must not be too close to each other because she might pass on TB* [Participant 6, male].

> *It is actually dangerous if you keep it a secret. You need to tell the person so that they are able to protect themselves from getting the disease* [Participant 9, male].

One participant explained that disclosing a TB diagnosis is not only to avoid disease spread but also to avoid being blamed by neighbours, should they also become infected with TB. She said:

> *I will tell them because, if I do not tell my neighbours that I have a person with TB, if they come to my house, and tomorrow they are told that they also have TB, then if I did not tell them and they happen to find out later, then that will bring hatred between us, the person will think we infected her/him on purpose, even if maybe they have gotten it from somewhere, and not necessary from our house. But definitely the person will hate us as they will think they have picked it up from our house* [Participant 7, female].

In contrast, some participants were hesitant to reveal that they had a TB diagnosis in their households. This was positioned in the argument that social interaction will be impeded upon disclosure. Participants also explained that their unwillingness to share was not only to protect their image, but also that of the TB patient.

> *No, if they know its fine, but not for me to go and tell them that I am living with someone having TB…Just for the person I'm living with, even if my son is having TB it's not the case of going there and tell everybody that this one is sick because of what, it's not good* [Participant 2, male].

> *Yes, the patient will not be comfortable if you mention it, and that can even lead to the patient hating you because they will be wondering that if they get other disease, you will also end up mentioning it to others* [Participant 5, female].

Concerning how participants thought their neighbours or friends would react towards them following the disclosure of a TB diagnosis, some participants reported that unlike in the past, people nowadays would be supportive and have understanding of each other's conditions.

> *I think it depends on a person's understanding of TB, if a person is educated about TB, it will not change anything. But those who do not know much about TB they will have fear* [Participant 13, male].

On the other hand, some participants shared that they will experience isolation or hate from their neighbours, which according to participants is based on the fear of infection.

> *No, in my own case, I do not really know because you do not know what is in people's hearts. Because some people if they hear for instance that I have TB, they may decide not to pass by me or my house anymore like they did before. They will be scared that they may get TB* [Participant 5, female].

> *Yes if you are sick and everyone can see that, people will fear getting closer to you and the relationship between people change* [Participant 6, male].

6.4.3.4. Theme four: lack of health education sessions and basic services

The majority of the participants reported that they had never seen any TB educational information sharing sessions (i.e. campaign) being held in their community. Participants specifically attributed the poor health in the area to the notion that people are not sufficiently knowledgeable about disease prevention.

> *No we have not seen anything like that here in our neighbourhood, they need to come at tell people about TB, because some people really have no understanding at all as to how they should protect themselves for instance. They need to do sessions in the community so people will come and listen and they might get the message* [Participant 8, female].
>
> *For me I think is just that government should really do something, they only like us during election time and after that they don't do anything. They really need to come and give people information for example like we are discussing now, it must be done in the wide community because people are dying and they just don't have information* [Participant 14, female].

Participants also suggested that there is a need for educational events to be coordinated by influential people in the society, as this can enhance community members' attendance.

> *I think there is need for health education sessions in the community, mostly by people respected in the community, even nurses themselves can come from somewhere and give us information, and say this and that. That can give more information. Because if you stand up from your house and go give information, other people will question who are you to give such information and where did you get it from* [Participant 1, female].
>
> *Last month, I saw this musician, doing a campaign about male circumcision, people really attended that gathering, attendance was better in comparison with those political gathering conducted by our councillor. So maybe if they can also pass on TB information that way, it may be effective, because people like events where there is music and dancing* [Participant 14, female].

The majority of participants also complained about the absence of basic services, especially a fixed health clinic and poor sanitation.

I think there is need to redesign house plots, and put a road to minimise that dust. People are too overcrowded here as you can see the houses and health is poor here [Participant 3, male].

We do need a lot of things hear in Havana, for instance there are no toilets and it's very difficult to ease yourself as we only go in the bushes [Participant 6, male].

They need to build a clinic here in Havana, so that it will be easier for people to go there. So I think government must really do something [Participant 10, male.

We do need a clinic here in Havana as we are a lot here, even things like roads here in Havana. Because sometimes people do not like it here because we only have gravel roads with a lot of dust, that is why many of us are forever coughing and having flu constantly because we do not have a tarred road [Participant 8, female].

Even though participants indicated that there was a mobile clinic that comes to Havana, the majority were not happy with its operation. Some indicated that the growing demand from community members was not then being met by the mobile health service.

No there is no clinic, is only a mobile clinic which comes here, but it only comes some days, if it comes maybe on Monday it will come maybe on Thursday or just like that. You find that people are queuing there and they have got only the number of patients that they need to deal with per day, so the rest have to back until and wait for other days [Participant 2, male].

It is not sufficient, because sometimes they don't accommodate us all. Patients are usually a lot. And they normally just say they are taking 30-40 people for that day. Then they tell us that those who could not get help should go see health care at other clinics [Participant 8, female].

Surprisingly, the exact operation of the mobile clinic was not known by some participants. This was evident as participants' narratives revealed that they did not know the specific days when the mobile health clinic was brought to the area.

Well there is a mobile clinic that comes at the supermarket, and it comes once in a week. I just do not know exactly which days it comes but sometimes two weeks or one week can pass by without it coming [Participant 5, female].

I think it comes maybe four times in a month. I am not too sure. Sometimes it goes to the councillor's office and sometimes it goes to the school [Participant 8, female].

Regarding poor sanitation in the community, participants narrated that as an indication of poor performance on the part of the city municipality and community leaders.

> *The responsibility lies with the town municipality, it is not for us as community members to do that. Our house is very near the dirty valley. But it is the responsibility of the municipality to clean. This is because everything we use e.g. we pay the water we use daily to municipality; therefore they (municipality) should do something. And currently they are not doing anything at all, that is why you see how the environment is dirty like that* [Participant 7, female].

> *I think our councillor is not doing enough, because our environment is very dirty and no one is initiating anything so that we can clean the environment* [Participant 14, female].

However, despite that the participants mentioned a number of factors which put their health at risk. The majority reported that they did access healthcare services in a timely manner whenever they are not feeling well.

> *For me I personally just do not like it when I am not feeling well and I am just home. Even if I do not have taxi money, I will just walk to the clinic at Hakahana or Wanaheda. Those clinics are too far, but I think if you are not feeling well you just have to go* [Participant 8, female].

> *I go immediately because if I notice that I am sick and do not know what kind of disease I have, I need to go a see doctor so that they can tell what disease I have. Because if you stay with your family and you are sick is not good, because you do not know what kind of disease you are having. You need to go immediately to doctor and to get help* [Participant 12, female].

Some participants mentioned that even though they do not have a fixed clinic in Havana, and they usually do not have taxi money to go to clinics in other townships, these challenges did not prevent them from seeking healthcare.

> *If I do not have money I can just borrow from the neighbours so they can assist* [Participant 3, male].

> *If you do not have money for taxi, we usually decide to walk to Wanaheda (another suburb), but you have to go there before 6am, because if you go after 6am then you will find a long queue and you will be told that they are only treating a certain number of people during a specific day so you will be forced to come back and go tomorrow again. If you decide to go to Hakahana (another township), sometimes you may not have taxi money to go there, so you will need to come back home and see if you can get money to go elsewhere* [Participant 7, female].

6.5. Discussion

6.5.1. Summary of main findings

This chapter presented findings from fourteen qualitative interviews conducted with adult men and women in the general public of Havana. The aim was to explore participants' TB KAP, and the study captured these narratives in four themes namely: The exact cause of TB may not be clearly understood but symptoms and treatment are, situational drivers, the duty of care and the lack of health education sessions and basic services.

In this sample of participants, TB was understood to be caused by a number of factors, including smoking, alcohol consumption, a dirty environment, family relations and HIV/AIDS. Participants also believed that TB is mainly transmitted through coughing and sharing cups. The most common TB symptoms mentioned were a prolonged cough, weight loss and fatigue. Participants in this sample were aware that TB can be cured, particularly when a person adheres to treatment instructions.

Perceptions on individual and community risk of infection were attributed to how people conducted themselves socially as well as through the environment in which people lived. Some participants articulated self-control measures, while others had a view that TB infection was almost unavoidable. Moreover, participants reported the importance and ways of curbing further disease transmission within the community through disclosing a TB diagnosis. The desire and practice of de-stigmatising TB was strongly demonstrated, although not by all interviewees. Participants reported how they felt ignored when it comes to health promotion educational sessions in the area and expressed dissatisfaction about the lack of basic services. However, despite the circumstances, the majority of participants expressed that they have always managed to access healthcare in a timely manner.

6.5.2. Strengths

To the best of my knowledge, this is the first study to qualitatively assess TB KAP in the general public of Havana. The study assessed multiple components of TB to obtain breadth and depth views from people living in the most affected township. The study utilised one to one interviews as a method of data collection, therefore it allowed participants to be comfortable expressing personal opinions, which might have been under-expressed, if other methods had been used. Another strength of my study is that I followed a systematic approach of reporting the study methods from data collection and data analysis. The systematic nature of reporting the study processes will enable further studies to build on the work conducted in this study.

6.5.3. Limitations

One of the main limitations of my study is that I conducted the study and analysed data all by myself as a PhD researcher. The use of another qualitative researcher would have been beneficial to compare and validate the study findings and minimise interviewer bias. However, I prepared myself well for this study, attended qualitative training and discussed with my supervisors at each step of the research. I therefore believe that the interpretations I made from the data would have been similar to those of another researcher.

In this study, I did not include views of healthcare providers. These views would have enriched the study by providing the perspectives of those on the provider side. However, at this stage, my study aimed to capture the narratives of community members themselves and therefore in future, we may expand on this work to include the views of those who, in one way or another, have a stake in TB control in this community.

This qualitative study was conducted in Havana, and so the results can only be interpreted in the context of Havana. Further research is required to determine similarities and differences in TB KAP between people residing in different high TB burden townships in Windhoek.

6.5.4. Interpretation and comparison to the literature

My study showed that there was a general lack of understanding of the exact cause of TB. In a high burden township such as Havana, this finding suggest the need for elaborative TB education messages, which differentiate the disease risk factors from its primary cause. The emphasis that anyone can be infected with TB is needed, because wrong misconceptions about who can get TB might influence health-seeking behaviours as well as preventative efforts (225). In other words, people may have the belief that only those who drink alcohol, smoke, had family members with TB, live with HIV/AIDS can get TB. The findings of my study are consistent with what other researchers have documented. For instance, Buregyeya and colleagues in Kampala, found that only one participants was able to mentioned a germ as a cause of TB, and the rest linked TB to smoking, alcohol, HIV/AIDS and older age (261). In Tanzania, Mangesho *et al*. also observed poor knowledge about the cause of TB, and documented that participants attributed TB to various causes including smoking, alcohol consumption, overcrowding and drinking raw milk (61).

In my study, participants' narratives showed that there was good understanding of the TB symptoms as well as modes of transmission, and this is consistent with results reported in other studies (2, 261-263). A study conducted by Bam *et al.* in Dhaka, also reported that coughing was a chief symptom of TB. However, in their study, participants also mentioned that blood in the urine was a symptom of TB as well as that TB was synonymous to cancer (263). In my study, I found that only HIV/AIDS was linked to TB, and this has also been found in the Buregyeya *et al*. study in Uganda (261) as well as by Nyasulu *et al.* in Malawi (262).

Participants in my study commonly shared that TB was transmitted through coughing and sharing items such as cups and spoons. In fact, it was reported that it was very common for people in Havana to share cups especially when they are drinking their local alcohol, even with people who are known to be ill. It is therefore possible that practices such as these could be facilitating further transmission in the community. For instance, some of the people may have undiagnosed TB, or within two months of their TB treatment (meaning they are still infectious), yet they are sharing items with others. These results suggest the need for discussing with community members about practices, which even though are traditionally common, may be influencing diseases such as TB. People should be told about practicing good hygiene such as washing cups at bars before they are utilised by other people, and to encourage those with TB to avoid sharing items with other people until they have at least completed two months of treatment, at which point they are no longer necessarily considered infectious (5).

In my study, TB was commonly understood to be a curable disease, especially when a person adheres to treatment instructions. This finding concurs with those from other studies (261-263). In my study, there was no mention of trust in traditional healers or self-medication as has been shown in studies from Kenya (2) and the Democratic Republic of Congo (7). This perhaps suggest variation in cultural beliefs between countries. However, since I conducted the study exclusively in an urban area, where knowledge of TB and access to health services may be better, the findings may have been different from the perspective of people in rural areas.

Participants in my study expressed the importance of disclosing a TB diagnosis to those in close proximity with the TB patient. This practice should be encouraged in a community such as Havana, where people do live in close proximity and social mixing is common. However, the fact that not all participants were comfortable about disclosing TB suggest that this is still a stigmatised disease, and so there is a need for stigma reduction campaigns. In the Long *et al.* study from Vietnam, TB was viewed to be a death penalty (5), and in some studies conducted in Ghana (3) and in Malawi (262), it was explained that the disease can severely affect relationships such as marriage.

In my study, I did not find extreme experiences or views regarding the impact of TB on social relationships between neighbours and friends, although some participants reported that hate can manifest upon disclosing TB. The majority of participants generally expressed strong support for one another and felt that people should not be ashamed of TB because it is a curable disease. However, my results might have been similar to other studies had I included TB patients. The discrepancy between the results of my study and those of others could actually suggest that people believe TB is not a shameful disease until they experience it, at which point they then start to experience the stigma from families or community members. This should be an important finding for TB programmes, and therefore continuous education campaigns should be offered to both community members and TB patients in order to discourage medically unjustified isolation to reduce stigma. In Windhoek, a study by Kamenye *et al.* which specifically explored TB KAP among TB patients, did not report views about stigma and discrimination (273). However, a study conducted in another part of the country to determine the risk factors for treatment abandonment reported that some TB patients felt that isolation from family and community members had contributed to poor treatment adherence (81).

One of the surprising findings of my study is the lack of TB campaigns and health education sessions in Havana community. This finding can imply two main possibilities. Firstly, it may suggest weakness of the NTLP as far as their Information Education Communication (IEC) strategy is concerned and perhaps the weakness of Penduka, which is the only community based TB organisation in Windhoek. Secondly, it could be that TB knowledge promotion activities are occurring but perhaps not at a scale where they can make a meaningful impact in a high TB burden township such as Havana.

The finding that participants in this study strongly complained about lack of health services is not surprising. Despite the fact that Havana is a proclaimed township in Windhoek and is amongst townships where the majority of people with a low socio economic background live, there are no basic health services such as clinics or sewage systems. According to the participants, the mobile service which the Ministry of Health currently provides is insufficient, as not all people needing care are attended to on a particular day. The absence of a fixed clinic has implications for TB control in this township, and it is probably not wrong to speculate that some people infected with TB may go undiagnosed and are thus likely to further transmit TB within their families or surroundings, as they do not have means to reach out to health services in a timely manner. The lack of a clinic may also contribute to treatment abandonment among TB patients in this area. In the Endjala *et al* study, it was reported that distance to the nearest healthcare services, long queues at clinics and inflexible working hours were some of the factors related to treatment interruption (81). In my study, other issues raised by participants such as poor sanitation, lack of a tarred road and poorly arranged houses suggest the need for the involvement of other sectors beyond the health sector. However, these issues can only be brought to the discussion table once the NTLP strongly advocate on how other sectors can improve the public health in communities such as Havana. Hence, the community voices captured in my study would be important findings for the NTLP as far as advocacy is concerned.

Chapter 7：Systematic integration of the findings concerning TB KAP in Havana

7.1. Overview of the concept of integration

Using different research methods to study a particular phenomenon has increasingly become popular in health research (289, 290). At the centre of studies using different research methods is the concept of integration, which benefits from the combined strengths of individual methods to draw concrete conclusions concerning a particular phenomenon (291). When findings are not integrated, an opportunity to create comprehensive knowledge is missed, and findings are equivalent to those of studies which independently utilised single methods (292).

In the literature, the two terms integration and triangulation have been used interchangeably, and according to Moran-Ellis *et al.* this is problematic as it obscures the differences in the process by which various methods are brought together (integration) and the outcome of different methods (triangulation). Moran-Ellis *et al.* elaborated that integration is the actual process of merging findings, whereas triangulation in the epistemological argument of the position of the results generated (293).

The literature provides some practical examples of the how results mainly from quantitative and qualitative methods could be integrated. One method is to use a mixed method matrix, whereby researchers follow individual case responses and compare the results across other cases in the data sets to search for patterns. The mixed matrix method is however suitable in a situation where quantitative and qualitative data were obtained from the same cases (289).

Another approach in the literature is that proposed by Moran-Ellies *et al*., which is referred to as "following the thread" (293). According to the authors, this process is conducted at the analysis stage and involves the identification of a certain component in one method, and following it through across other research components. One of its criticisms is that the exact steps involved are not well detailed (289). The lack of clarity, particularly concerning the criteria for identifying threads, has the potential for making inaccurate interpretations.

Another method of integrating results from multi-methods is that of using a triangulation protocol suggested by Farmer *et al*. (76). This method was primarily developed to integrate findings obtained through multiple qualitative methods; however, it can also be applied to studies which utilised qualitative and quantitative methods (289). Farmer *et al*. discussed that there are three outcomes of findings obtained from multiple methods, and these are (1) that the results may converge, (2) results will be taken as complementary to each other or (3) that methods may produce divergent or contradictory findings. According to Farmer *et al*. their triangulation protocol can then be used to assess the level of convergence, complementarity or dissonance of findings (76).

7.2. The method used to integrate the TB KAP findings

During phase three, I conducted a cross-sectional survey which investigated TB KAP using a structured questionnaire with a sample of 400 participants from Havana. During phase four, I implemented a qualitative study, which explored TB KAP through fourteen one to one qualitative interviews. Each of the methods produced distinct findings, and therefore, rather than making conclusions from results obtained from each method, I integrated findings to generate comprehensive knowledge about TB KAP in Havana.

Of the three integration methods described above, I found the method proposed by Farmer *et al*. (76) to be more appropriate for my research. This is because, in my study the data for the cross sectional survey and from the qualitative interviews were not derived from the same participants, and so the mixed method matrix method could not be applied. In addition, I could not use the method proposed by Moran-Ellis *et al*. because it does not explain the steps involved in detail, and the lack of clarity may result in wrong findings. Therefore, I chose to use the method by Farmer *et al*., which has been explained in detail and it is explained with examples.

The process is made up of six steps as shown in Table 7.1. The first step is that of sorting, which involves the identification of sub-themes in the distinct findings of the methods being triangulated, and then collapsing them into overarching themes. The second step is that of convergence coding, which requires the identification of specific areas within the findings of each method and allocating where there is agreement, partial agreement, silence or dissonance. The third step involves producing an overall assessment of the degree of convergence between the two methods. The fourth step involves cross-checking the merged themes with the unique results of the individual method, to check for completeness and level of convergence. The fifth step requires comparing the triangulation results between researchers, and the last step involves giving feedback on the triangulation results. However, it should be noted that since I conducted the triangulation process myself as a PhD researcher, I skipped the fifth step as there was no involvement of a second researcher. However, discussing and sharing results with my supervisors served as an opportunity to obtain perspectives on my study findings besides relying on my own reflections.

The Farmer *et al*. approach enabled the assessment of the extent to which the findings I obtained from the individual methods converge, complement or contradict each other.

Table 7.1: Triangulation protocol

Step	*Activity*
1. Sorting	Sort findings from each data source or method into similarly categorized segments that address the research question(s) of interest to determine areas of content overlap and divergence.
2. Convergence coding	Identify the themes from each data source. Compare the findings to determine the degree of convergence of (a) essence of the meaning and prominence of the themes presented and (b) provincial coverage and specific examples provided in relation to each theme. Characterize the degree and type of convergence using the following typifications of concurrence (or nonconcurrence) within theme areas.
Convergence coding scheme	
Agreement	There is full agreement between the sets of results on both elements of comparison (e.g., meaning and prominence are the same, provincial coverage and specific examples provided are the same).
Partial agreement	There is agreement on one but not both components (e.g., the meaning or prominence of themes is the same, provincial coverage or specific examples provided are the same).
Silence	One set of results covers the theme or example, whereas the other set of results is silent on the theme or example.
Dissonance	There is disagreement between the sets of results on both elements of comparison (e.g., meaning and prominence are different; provincial coverage and specific examples provided are different).
3. Convergence assessment	Review all compared segments to provide a global assessment of the level of convergence. Document when and where researchers have different perspectives on convergence or dissonance of findings.
4. Completeness assessment	Compare the nature and scope of the unique topic areas for each data source or method to enhance the completeness of the united set of findings and identify key differences in scope and/or coverage.
5. Researcher comparison	Compare the assessments of convergence or dissonance and completeness of the united set of findings among multiple researchers to (a) clarify interpretations of the findings and (b) determine degree of agreement among researchers on triangulated findings. Plan for how disagreements will be handled and how final decisions on interpretations will be made.
6. Feedback	Feedback of triangulated results to research team and/or stakeholders for review and clarification.

Table taken from Farmer *et al*. (76).

7.3. Integrated findings

The triangulation process revealed five overall themes which were, Magnitude, Knowledge, Communication, Behaviour and Obstacles. These themes are shown in column one of Table 7.2 (in bold) and are presented with the specific components which were compared during the convergence coding process. The results show that overall there was generally agreement between the findings of the two research methods, as demonstrated in nineteen components. I found nine components where there was silence (implying that the component was only present in the findings of one research method). The integration of results found no specific component where there was contradiction (dissonance).

Table 7.2: Triangulation matrix showing themes identified from the cross sectional survey and qualitative interviews

Overarching themes	Agreement	Silence	Dissonance
Magnitude			
TB is a common problem in Windhoek	*		
Increased risk at individual level	*		
Increased risk of infection among people in Havana	*		
Knowledge			
Knowledge concerning the cause of TB	*		
Knowledge concerning TB symptoms	*		
Knowledge concerning modes of transmission	*		
Knowledge concerning TB prevention	*		
Knowledge concerning TB treatment	*		
Communication			
Radio		*	
Health care workers		*	
TB campaigns	*		
Interest in learning more about TB	*		
The conduct and impact of TB campaigns	*		
Usage of celebrities to promote TB health education		*	
Behaviour			
Acceptance of a TB diagnosis	*		
Positive attitude towards TB patients	*		
Individual and community attitude towards TB patients	*		
Need to disclosing TB diagnosis to family/friends	*		
Impact on social relationships upon disclosing TB diagnosis		*	
Drinking alcohol from same cups (local alcohol)		*	
Health seeking behaviour	*		
Obstacles			
Lack of hygiene in the surrounding	*		
Overcrowding	*		
Absence of fixed clinic	*		
Poor design of house plots		*	
Operation of mobile clinic not adequate		*	
Absence of a tarred road		*	
Community leaders (not doing anything to improve wellbeing)		*	
	Agreement: 19; Silence: 9; Dissonance: 0		

7.3.1. Description of overarching themes

7.3.1.1. Magnitude

This theme captured responses related to views about the burden of TB in Havana and perceived risk of infection. In both the cross-sectional survey and the qualitative interviews, TB was recognised to be a major problem in Havana. These views were reported based on direct and indirect experiences of TB disease as well on contextual factors when comparing Havana to other townships in Windhoek. The perceived high disease burden culminated in the majority of participants expressing increased risk of infection at both individual and community levels. The majority of participants reported their perceived risk of infection mostly in relation to behavioural and environmental factors rather than that TB is a disease that anyone is susceptible to.

7.3.1.2. Knowledge

This theme captured how TB was understood among participants in relation to the cause, symptoms, prevention, modes of transmission and treatment, and the link between TB and HIV/AIDS. In terms of the exact cause of TB, I found that participants' narratives suggested that TB was mainly caused by smoking and alcohol consumption. However, some of the participants in the qualitative study expressed that TB was an inheritable disease passed on through family genetics and that TB and HIV/AIDS are the same.

Participants generally showed good understanding of TB symptoms, modes of transmission, prevention and treatment. The main symptoms mentioned were, a persistent cough, weight loss and fatigue. Participants were knowledgeable that TB could be transmitted through the air when a person coughs or sneezes and through sharing kitchen utensils. TB was narrated to be a curable disease, through medications given at health facilities.

7.3.1.3. Communication

This theme captured views related to sources of TB information and ways of attracting public attention to TB education discussions. Participants in the cross-sectional survey mentioned that radio and healthcare workers were the current sources of TB information, but this did not explicitly came out of the qualitative study. In both studies, participants expressed need for TB education sessions in the community to improve knowledge. A surprising finding which came out of the two studies is that TB campaigns were rarely conducted in Havana, and the majority of participants said they had never attended or heard of such campaigns specifically in the area. In narrating how TB campaigns could be improved, participants in the qualitative study mentioned that there is need to involve local celebrities in TB campaigns as has been done with other diseases such as HIV/AIDS. According to the participants, the involvement of local celebrities would attract and improve public attention and attendance at such events.

7.3.1.4. Behaviour

This theme captured participants responses related to attitudes towards TB as a disease, as well as to those infected. The majority of participants agreed that TB was not a shameful disease and that if they are to be diagnosed with TB, most will consider it as a normal disease. Moreover, the majority also indicated that they would offer support and show compassion towards a person suffering from TB. In both studies, the majority of participants were of the opinion that community members in Havana would show support towards a TB patient. The majority of participants also indicated that they would be comfortable disclosing TB status to people in close proximity with a TB patient in their households. The qualitative study participants discussed the potential impact a TB diagnosis would have on social relationships between neighbours and friends, with the majority expressing that relationships would in general be as they were, and would not be affected by a TB diagnosis. Another component which came out of the qualitative interviews was the common practice of drinking from the same cup, particularly when drinking traditional alcohol. But despite the circumstances, the participants in both cross-sectional and qualitative interviews demonstrated good health seeking behaviours by indicating that they would reach out to health facilities should they notice that they were unwell.

7.3.1.5. Obstacles

This theme captured the views expressed with regards to contextual factors believed to pose a threat to the wellbeing of people in Havana. The majority of participants expressed that poor sanitation, overcrowding and the absence of a fixed clinic were the main obstacles to public health in Havana. The qualitative study participants also reported certain aspects including poor designs of households, the lack of tarred road and dissatisfaction with the performance of community leaders. They expressed that their community leaders were not showing any effort to improve public health and that they only seemed to care about the public during political elections. Another aspect mentioned in the qualitative interviews was that the mobile clinic brought to the community on specific days was inadequate. The participants in the qualitative interviews also mentioned that the number of days the clinic was brought to the community were inadequate and the clinic was only able to accommodate a limited number of people on a particular day, with many people being asked to go home unassisted.

7.4. Discussion

7.4.1. Summary of findings

I applied a triangulation protocol to integrate the findings concerning TB KAP in Havana. The essence at this stage was not to repeat the interpretation of the findings I have already presented and discussed in the individual empirical chapters (Chapters 5&6), but rather to obtain overarching themes after integrating the findings.

The integration of findings resulted in five overarching themes, which were, magnitude, knowledge, communication, behaviour and obstacles. The results showed that there was generally agreement between the findings concerning nineteen components and it further revealed nine components where the two methods complemented one another. Throughout the integration process, I did not find any component where there was a contradiction (dissonance).

7.4.2. Strengths

The strength of the integration process is that it provided an opportunity to synthesise the findings of the cross-sectional survey and qualitative study. The exercise was conducted to determine the level of agreement, silence and dissonance between findings obtained from distinct research methods, to produce coherent knowledge about TB KAP in the community. The fact that there was generally agreement in most of the components, and there was no apparent aspect of dissonance, increases my confidence as a researcher that the results produced are valid in the context of Havana. Areas where silence was observed could be taken as complementary given that the two methods which were integrated are different in nature. The integration exercise enabled me to discuss the implications of more succinct findings as well as to identify possible areas for future research, as shown in the next chapter.

7.4.3. Limitations

One of the main limitations of this integration exercise is that it was only conducted by one person, and hence the results are limited to my own interpretations. In addition, the five overarching themes which summarise the integrated findings were obtained from the findings of each method rather than from the actual raw data obtained during each method. Therefore, it may have left out aspects which were not captured in the results section of each method.

Another limitation of this exercise is that the nature of the cross-sectional survey and the qualitative interviews is different. For example, the questions in the cross-sectional survey were close-ended while in the qualitative study participants were free to elaborate and provide more detail about issues. Also during each study, specific questions were asked and the participants responded to specific questions based on what they were asked. It is therefore possible that areas identified as silence were due to the nature of these methods, rather than depicting real differences in the responses of the two groups of participants. In future, it would be interesting to integrate results obtained from more similar methods such as qualitative focus group interviews and one to one interviews.

7.4.4. Comparison with the literature

The studies which I reviewed during phase three (Chapter 5) and phase four (Chapter 6), were limited to either quantitative or qualitative studies, and therefore because of this inclusion criteria I cannot compare my integrated results with the findings of any of these studies. However I found that in qualitative studies multiple methods were used (i.e. FGDs and one to one interviews), but none of these studies have presented integrated results, or at least reported that the findings were integrated. A search of other studies in the literature could also not locate any particular study which has reported integrated findings of TB KAP.

Chapter 8 : Conclusion

8.1. A brief recap

Effective disease control requires comprehensive knowledge of the disease burden (14), in order to inform coordinated public health interventions (74). In Namibia, despite that TB is recognised as a public health threat (53), knowledge about the disease epidemiology is poor. Therefore, the overarching aim of this PhD study was to generate local evidence regarding the disease burden and its determinants in the country's most populous region Khomas. Since Khomas contributes the highest proportion of TB cases to the national burden (53), a reduction in TB burden in this region will have a profound effect on the overall national TB burden.

Work in my study was divided into four phases (Chapters Three to Six), and I have already provided a detailed discussion of the findings obtained within each empirical phase, in relation to other academic literature. Therefore, in this last chapter of my thesis, I only aim to provide a summary of the thesis findings in relation to the study objectives. I will then provide overarching strengths and limitations of my work, suggest implications for practice and recommend areas for future research.

8.2. Study findings in relation to objectives

The overall aim of this thesis was met by addressing seven specific objectives. The main findings for each objective are discussed in turn below.

***Objective one*:** To describe temporal trends in TB case notifications in Khomas.

In Chapter Three, I commenced with a literature review of 31 studies that have analysed trends in TB notifications in different countries. The review revealed that temporal trends in TB notifications have been studied by utilising both linear and non-linear regression models, although in some studies no particular analysis method was applied. I have discussed these methods in detail and provided a justification for the method used in my study. Trends in TB rates varied between studies and these variations could be a 'real' reflection of the setting specific disease burden but, I have also explained how the variation might have occurred as result differences in case ascertainment methods, study time, study location, case finding methods and statistical analysis methods.

After the literature review, I subsequently used Joinpoint regression to study trends in CNRs in Khomas. Trends were analysed and described according to types of TB and where possible by age groups and sex. I also analysed trends for TB and HIV/AIDS related indicators.

The results showed that from 1997 to 2015, the average CNRs for all forms of TB was 733 (95% CI: 634-832) per 100 000 population in Khomas region, having declined from 808 in 1997 to 400 per 100 000 population in 2015. The trend for all forms of TB CNRs decreased by -13% (95% CI: -29.0% to 7.8%) per year from 1997-1999, then it increased significantly by 13% (95% CI: 6.8% to 20.7%) per year from 1999 to 2004 and thereafter it declined significantly a rate of -9.3% (95% CI: -10.4% to -8.1%) per year from 2004 to 2015.

The trend for new smear positive pulmonary TB CNRs increased significantly by an annual rate of 4.1% from 1997 to 2004, and thereafter declined significantly by -6.2% per year from 2004 to 2015. The trend for smear negative pulmonary TB CNRs declined by -14% per year from 1997 to 2000, then increased significantly by 47% per year from 2000-2004 and then it declined significantly by an annual change of -28% between 2004-2015. The trend for extra-pulmonary TB CNRs increased significantly by an annual rate of 26% from 1997 to 2000, then it declined by -1.4% from 2000 to 2008, and again declined significantly at an annual rate of -9.4% from 2008 to 2015.

In terms of TB and HIV/AIDS indicators, I observed that from 2006 to 2015, the trend in the percentage of TB patients with a known HIV/AIDS status increased significantly at an annual average of 13.7% (95% CI: 6.2% to 21.7%). There was no significant change in the trend for percentage of TB patients who are HIV/AIDS positive -1.9% (95% CI: -4.5% to 0.7%). However, a significant declining trend (APC: -8.0%, 95% CI: -10.1% to -5.9%) was observed during the recent years from 2009 to 2015.

***Objective two*:** To analyse the spatial and spatiotemporal distribution of TB notifications and investigate the potential occurrence of TB hotspots in Khomas.
***Objective three*:** To investigate the population level socio-demographic factors which might explain the disease distribution within the region.
***Objective four*:** To describe temporal changes of trends in TB notifications in identified TB hotspots (if found).

In addressing the three objectives above, the work presented in Chapter Four began with a literature review of 46 studies that analysed the spatial or spatiotemporal distribution of TB notifications in different countries. The review showed that studies have used various methods including Moran's Index statistics, Kulldorff's scan statistics, Besag and Newell and K-function and k nearest neighbours' methods. I have highlighted the advantages and disadvantages of individual methods and also provided a justification for the methods used in my study. Concerning population level socio-demographic factors for the disease spatial distribution, I observed that the study results are inconsistent, and I have explained how specific factors such as the use of varying exposure variables, sample size, statistical analysis, confounding, study location and unit of analysis might have influenced the inconsistencies.

After the literature review, I then used Moran's I and scan statistics to study the spatial and spatiotemporal distribution of TB notifications in Windhoek, which contains 95% of Khomas's total population (47). I found that TB depicted a strong spatial autocorrelation, with a significant positive Global Moran's Index obtained each year from 2006 to 2015. The Local Moran's Index and scan statistics identified that townships in the northern part of the city, namely Wanaheda, Havana, Hakahana, Okuryangava, Katutura and Goreangab, were hotspots for TB disease, although this varied by year. For most of the years, Havana, Wanaheda and Okuryangava were identified repeatedly as hotspots compared to the times other townships were identified. I also found that high rates of TB were positively associated with higher unemployment rates (RR=1.06, 95% CI: 1.04 to 1.09; $p<0.001$) and negatively associated with higher school enrolment rates (RR=0.96, 95% CI: 0.93 to 0.99; $p=0.024$). Of the six townships identified as TB hotspots, I found that trends in CNRs declined significantly overall, for both sexes and for the younger age groups (0-44), but not in older age group (45+ years). A significant increase in the percent of TB cases with known HIV/AIDS status and a significant decline in the percent of HIV/AIDS prevalence among TB cases was observed across all the identified TB hotspots, although the co-infection rates in the majority of townships remains high, above the city average.

Objective five**:** To investigate individual level socio-demographic and behavioural factors which may explain the disease spatial distribution.
Objective six**:** To investigate if TB knowledge, attitudes and practices could explain variation in the disease distribution.

In addressing the two objectives above, the work presented in Chapter Five commenced with a literature review split into three parts. The first was a review of primary studies that analysed risk factors for TB disease at the individual level. The second part was a review of studies that analysed risk factors according to the distribution of the TB burden (risk factors for TB hotspots), and the third part involved studies that quantitatively analysed TB Knowledge, Attitudes and Practices (TB KAP) among the general public.

After the literature review, I then conducted a comparative descriptive cross-sectional study in two townships with a dissimilar disease burden, Hochland Park and Havana. The aim of the study was to investigate the individual level socio-demographic and behavioural characteristics of people living in the high TB burden area of Havana, which may help explain the spatial distribution of TB in Windhoek. Through multivariable analysis, my study showed that participants who had the following characteristics were significantly more likely to be from Havana compared to those in reference categories: self-employed, unemployed, had a household TB patient, from a household that had four or more people sharing a bedroom, experienced lack of food due to lack of money, consumed alcohol more frequently, rarely visited healthcare services and stayed for short period in the township.

With regards to TB KAP, my study showed that there were significant differences in most components of TB KAP between participants from the two townships. Moreover, I found that among participants from Havana, there were mostly no significant gender differences in TB KAP, but significant differences by age group were observed. Overall, 32.2% of respondents had a high level of TB knowledge, although the proportion was significantly lower among participants from Havana (18.3%) compared to participants from Hochland Park (47.3%).
In the multivariate model, characteristics significantly associated with reduced relative odds of having a high TB knowledge score were: residing in Havana, rarely visiting healthcare services, self-employed, unemployed and having received no TB information at the time of the study.

Objective seven: To explore detailed information about TB KAP among people residing in the high TB burden township.

In Chapter Six, which documented procedures for the last phase of my study, I started with a literature review of nine studies, which have qualitatively assessed TB KAP in the general population. I observed that the majority of the studies assessed TB KAP by including both TB patients and the general public, and the narratives of the two groups were not separated. I also found that the majority of studies assessed TB KAP by combining participants from rural and urban areas, despite the fact that TB KAP in these populations is different (35, 228). Another limitation of the current literature is that the majority of studies explored TB KAP using focus groups despite TB potentially being a sensitive issue, and a group discussion may limit expressions of personal feelings (269). In general, studies reported similar findings regarding TB KAP.

After the literature review, I conducted a qualitative interview study comprising of fourteen participants, to explore TB KAP in the general public of Havana. The findings of my qualitative study were captured in four themes including, *the exact cause of TB may not be clearly understood but symptoms and treatment are, situational drivers, duty of care* and *lack of health education sessions and basic services*. I found that participants in my study were knowledgeable about TB symptoms, modes of transmission, prevention, and treatment but not about the exact cause of TB. Participants expressed that TB was a problem in Havana and they mostly attributed the increased risk of TB infection to alcohol consumption, smoking, family relations and HIV/AIDS. Various community level issues were mentioned as threats to public health, and these included overcrowding, lack of a fixed clinic, lack of TB health education sessions and poor involvement of their community leaders in public health issues.

Given that I studied TB KAP using a cross-sectional survey and qualitative interview, I then used a triangulation protocol suggested by Farmer *et a*l. to integrate the study findings. The integrated results were captured into five themes including *magnitude, knowledge, communication, behaviour* and *obstacle*. There was agreement in 19 components, 9 components were identified under silence but I did not find any component where there was complete dissonance.

8.3. Overarching strengths and limitations of the study

The specific strengths and limitations for each phase of my research have already been noted within each empirical phase. Therefore, during this section, I do not intend to repeat them but rather present the overarching strengths and limitations of my work.

8.3.1. Strengths

In this research, I employed a novel methodology to investigate the burden of TB in Khomas. The research was conducted from the broad public health standpoint, in that it aimed to generate knowledge which can be used to inform community level interventions and promote the wellbeing of people in the region as far as TB control is concerned. I commenced the study by analysing and describing the disease temporal trends in order to evaluate how far we have come with TB control and to benchmark current performance to the targets in the national TB strategic plan. The subsequent use of spatial and spatiotemporal methods in phase two allowed for identification of where TB interventions could be focused in order to achieve optimal impact. I also provided further information regarding temporal trends in the identified TB hotspots. The work I conducted during phases three and four allowed me to investigate the setting specific modifiable factors for TB hotspots in the region, by collecting data from the general population rather than from TB patients as has been done in previous studies (221, 222). The inclusion of the TB KAP component in the cross-sectional survey and expanding on it during phase four added a crucial element to the understanding of the disease burden from the perspective of people's knowledge, attitudes and practices. I combined the findings of TB KAP using a triangulation protocol to arrive at a more succinct conclusion rather than interpreting the findings of the two research methods separately.

Taken together, the work conducted during this PhD programme is novel and has established useful evidence to inform both the scale and scope of TB control strategies in Khomas. Control interventions such as active case finding, design of TB education messages, conduct of TB campaigns, allocation of TB Directly Observed Treatment (DOT) points, alcohol reduction interventions and poverty reduction interventions will all benefit from evidence established in this study.

8.2.2. Limitations

My study has several limitations. One of the limitations is that analyses for the first two phases were limited to data available at the time. Moreover, the findings should be interpreted with caution, as analyses were based on data generally understood to be collected through passive case finding and the inclusion of cases diagnosed in private healthcare remains unclear. These limitations imply that the burden as presented in this study could be an underestimation of the true disease burden. As indicated previously, the results expected from the recent nationwide TB prevalence survey would provide a clear picture about the disease magnitude in the region.

Another limitation of the study is that I could not find many relevant peer reviewed articles about TB in Namibia. Therefore, during the discussion section of each of my empirical chapters, I primarily interpreted my study findings in relation to the literature based on studies from other countries.

In addition, it is important to note that, my study focused on Khomas, which is the capital region of Namibia, with living conditions which differ from those of other regions, especially the rural ones (47). Therefore, the findings of my study should only be interpreted within the context of Khomas and cannot necessarily be generalised to other regions in the country.

8.4. Implications for practice

8.4.1. Community involvement

The findings of this study have implications for TB control and prevention in various ways. Firstly, the study findings should be used to encourage community involvement in addressing TB as a common phenomenon. Bermejo and Bekui define community participation as groups of people from a defined geographic setting who are interacting to identify their needs and suggest ways to address them (294). This dialogue may result in collective efforts (i.e. community level cleaning campaigns) aimed at bringing about improvement in the wellbeing of people in the public of the most affected townships. The NTLP could strengthen these efforts through rewarding community leaders with certificates of recognition in order to attract their attention and involvement in TB control within their communities. This is important as I found that participants in the qualitative study were not satisfied with the current efforts from their leaders in enhancing public health. Community leaders hold respected positions within their communities, and so if well mobilised, they have the potential to create disease awareness within their communities and wider society (295).

8.4.2. Allocation of resources

The findings of my study could also guide resource allocation by the NTLP, for example, the planning for resources needed for mass media events (health education campaigns), the production of radio messages, establishment of DOT points and other community based interventions. Moreover, these findings may serve as an advocacy tool for the NTLP to mobilise the involvement of sectors beyond health, such as housing, urban planning and labour creation, in order for them to realise how their efforts can bring about improvement in the control of TB. TB in high burden countries requires not only strengthened healthcare interventions, but also a focus on the social determinants of the disease (296), this is because a reduction of the TB burden is not necessarily attributed to the performance of the NTLP interventions, but rather to improvements in general living conditions (297). Therefore, the results from phases three and four have highlighted some of those determinants in the context of Khomas. The NTLP could thus use such community level evidence to advocate for a multi-sectoral approach, and mobilise external resources from donor organisations such as the Global Fund, PEPFAR and KNCV.

8.4.3. Strengthening the quality of routine data

In addition, the findings of my study highlight the need for the NTLP to evaluate the usefulness of our routine data. Currently, the TB registers do not included behavioural risk factors such as smoking, diabetes and alcohol consumption. This implies that our national routine TB data are less useful in informing public health control interventions. In other countries, routine TB data include behavioural information such as smoking, alcohol consumption (158, 298). Moreover, I observed that the annual reports of the NTLP have been inconsistent in some aspects. For example in the annual report for 2015, regional data were not presented by age and sex for new smear positive pulmonary TB, as in previous years. The continuous omission of such critical information will lessen the quality of the NTLP reports with regards to the provision of timely and comprehensive picture of the disease burden within specific regions. Complete information will enable timely epidemiological research. The quality and use of TB data, particularly in monitoring disease trends over time, has been emphasised (299).

Being serious about ending TB by 2030 means the NTLP should be flexible in changing some of its practices. For instance, it needs tailor the reporting of key information in the ETR based on the set-up of individual regions. As an example, for urban areas such as Khomas, the reporting of residential address for TB cases needs to be uniformly cascaded to the street level, to allow for comprehensive epidemiological analyses of the disease occurrence. Currently, the reporting of residential address is not standardised in the ETR, and for some patients it is not even provided. Without high quality data at the local level, to guide the local response, the goal of ending TB will be jeopardised (300).

8.4.4. Target setting

Similarly, the results presented in this thesis suggest that the NTLP needs to cascade the target setting process to lower levels. Currently, TB indicators and targets only formulated at the national level and there are no specific targets set for regions or districts. This may be because TB strategic frameworks are only formulated at the national level, and there are no region or district specific TB strategic frameworks. In this thesis, I have indeed demonstrated that it is possible for us to have a better understanding of the TB epidemiology within specific regions by embracing the techniques of spatial epidemiology. Therefore, the fight against TB may be more intensified if regions are allocated specific indicator targets based on their capacity and past performance. In countries such as Tanzania, Kenya, Ethiopia and Democratic republic of Congo, it is reported that community level TB indicators are incorporated in national TB Monitoring and Evaluation (M&E) plans (301), and this is not the case in Namibia yet as the M&E plan only contains national level indicators. I strongly believe that such an approach would be a motivation for TB coordination within regions. This is because TB DTLCs, community leaders and the general population would be able to benchmark their efforts against localised targets rather than only monitoring performance nationally.

8.4.5. Changing behaviour and practices

With regards to TB KAP, the integration process identified that people in Havana were aware of the magnitude and seriousness of TB as a disease. However, the majority of people described TB infection in relation to behavioural and environmental factors rather than indicating that the disease could be contracted by anyone in contact with a TB case. These results highlight that there is need for health education using appropriate TB messages and communication modes. It has been documented that TB programmes cannot be successful if there are misconceptions regarding disease infection, transmission and treatment (302). My study has revealed that the majority of people demonstrated an interest in hearing more about TB, and this should be an encouraging result for the NTLP.

The finding that people who rarely visited healthcare facilities were more likely to be from Havana, suggest that sharing TB information at health centres (which is currently the dominating practice) may not be an effective way to reach to the public. Therefore, there is a need for concerned stakeholders to identify appropriate communication modes, as effective communication could lead not only to behaviour change at individual level but also to advocacy in the wider society (303).

In terms of behaviours, there is a need for the NTLP to make people aware of certain practices that may be fuelling further disease transmission, such as drinking traditional alcohol from the same cup/glass, which is a very common practice in a township such as Havana. Community dialogues are needed where people can discuss such matters. It has been stated that community dialogue enables a platform where affected people can gather, discuss and debate their own perspectives on a specific phenomenon (304), such as possible TB transmission through sharing cups/glasses when drinking traditional liquor. These community dialogues should also include other aspects such as health seeking behaviour, TB associated stigma. I for example, found that the percent of people who reported that they would keep a TB diagnosis secret was higher than those reported in other studies (226, 240, 241), indicating that the disease is still highly stigmatised in the community.

8.5. Areas of future research

The work conducted in this thesis has identified some research questions which could be addressed in future research to enhance further understanding of the TB burden in Khomas.

During phase one, I only focused on analysing trends in TB notifications, and so there is need for further research to analyse epidemiological trends in treatment outcomes, as well as trends concerning notifications for specific TB cases such as relapse TB, MDR, and cases infected with TB HIV/AIDS. With the recent introduction of new diagnostic tools such as gene-xperts, future studies are required to monitor trends particularly concerning paediatric TB, TB in the elderly and in HIV/AIDS patients. Other studies have shown an increase in the number of TB cases, following the introduction of diagnostic equipment (99, 114).

There is need for a collaborative study between the HIV/AIDS and the TB programmes within the ministry to examine trends in TB cases, in relation to trends of HIV/AIDS prevalence and ART coverage in Khomas. Studies have shown that areas with high ART coverage have lower TB notification rates compared to areas with low ART coverage (88). In my study I observed that CNRs in some townships such as Goreangab, had declined faster than the city average, compared to other townships such as Havana and Hakahana. Studies are thus needed to document factors which may explain the observed differences between townships, and perhaps ART coverage could be one of these.

Despite the lack of concrete data concerning diabetes prevalence in Namibia, there is a need to investigate the role that diabetes may have on the TB burden. The link between non-communicable diseases such as diabetes and infectious diseases such as TB and HIV/AIDS has been highlighted in the literature (43, 195), hence it is important to investigate co-morbidities with populations in order to integrate health services at community level.

During phase two, my study identified that the TB burden is significantly higher in townships generally characterised by internal migration. In phase three, I indeed found that people who resided in the township for a short period were significantly more likely to be from a high TB township. These results suggest the need for molecular epidemiologic studies to investigate the current transmission dynamics of TB cases and therefore quantify the possible impact of internal migration on TB epidemiology within the region. In Namibia, the TB burden is known to be higher in urban regions (53). However, it could be that the burden in urban regions is because of the reactivation of a previous infection rather than recent transmission. If true, then this implies that controlling TB in urban regions such as Khomas requires strengthened TB control efforts in rural areas from where the majority of people are migrating.

During phase three, I conducted a KAP study, which was limited to Havana (as a high TB burden township) and to Hochland Park (as a low TB burden township). Future studies could build on work presented in this thesis, and assess whether there are differences in TB KAP between participants residing in different TB hotspots to allow for tailored TB education sessions in the townships.

8.6. Concluding remarks

In this study, I implemented a novel methodology to gain an understanding of the TB burden and its determinants in Khomas. I found that the disease burden is indeed declining, and it significantly declined by a rate of 9.3% per year from 2004 to 2015. Despite the declining trend, the results of my study clearly show that the TB burden remains worryingly high within specific communities in the northern part of the city, and these results demonstrate the need for more targeted preventative interventions.

In order to achieve the national goal of reducing TB incidence to 50 per 100 000 population by 2030, there is a need for a shift in the current disease control approaches in Namibia. The need for more targeted prevention efforts and a multi-sectoral approach cannot be overemphasised, as the results of this thesis clearly show that TB occurrence is partly a matter of inequality in standards of living, and tackling such an issue is beyond the capacity and mandate of the NTLP. Nevertheless, the NTLP plays a critical role in providing the community level evidence needed to advocate for the involvement of other sectors. As we draw closer to the development of the new strategic plan for tuberculosis control, there is an urgent need to conduct further research in other regions, to guide the formulation of control strategies based on local evidence which is more useful in guiding effective health service planning.

8.7. Reflections

This research topic was entirely my idea and over the course of the PhD programme, I have designed the research with support from my supervisors and the literature. I have a keen interest in spatial epidemiology and the application of innovative techniques such as GIS study the most pressing public health threats in my country. I entirely led the research project from its inception to the write up of this thesis. When I started this programme, I was quite familiar with statistical packages such as SPSS and STATA, but this research has allowed me to learn more about other packages including ArcGIS, SaTScan and Joinpoint Regression. The focused literature reviews I conducted enabled me to have an understanding how other researchers have employed several methods regarding towards understanding the TB burden epidemiology, and I'm indeed planning to apply some of the methods to other pressing health conditions in Namibia. Moreover, coming from a mainly quantitative research background, work conducted during the PhD enabled me to learn more about, and very much appreciate qualitative research. In addition, the PhD research allowed me to improve on other aspects such as communication skills, planning, budgeting and other organisational skills. I strongly believe that the techniques and skills I have learned throughout the course of my PhD journey will undoubtedly put me in a better position as a researcher, to be able to make a significant contribution to public health research in my country and the African continent at large.

Appendix A) Ethical Approval from Namibia Ministry of Health

REPUBLIC OF NAMIBIA

Ministry of Health and Social Services

Private Bag 13198
Windhoek
Namibia

Ministerial Building
Harvey Street
Windhoek

Tel: 061 – 203 2510
Fax: 061 – 222558
E-mail: Ester.Shaama@mhss.gov.na

OFFICE OF THE PERMANENT SECRETARY

Ref: 17/3/3
Enquiries: Ms. E.N. Shaama

Date: 03rd June 2016

Ms. Anna M.N. Shifotoka
Newcastle University
Institute of Health and Society
Sir James Spence Institute
Royal Victoria Road
Newcastle upon Tyne
NE1 4LP
United Kingdom

Dear Ms. Shifotoka

Re: The spatiotemporal analysis of smear positive Tuberculosis and investigation of determinants and risk perceptions for TB infection and disease in Windhoek health district, Namibia.

1. Reference is made to your application to conduct the above-mentioned study.
2. The proposal has been evaluated and found to have merit.
3. **Kindly be informed that permission to conduct the study has been granted under the following conditions:**

3.1 The data to be collected must only be used for completion of your Doctor of Philosophy in Epidemiology/Public Health;

3.2 No other data should be collected other than the data stated in the proposal;

3.3 Stipulated ethical considerations in the protocol related to the protection of Human Subjects' information should be observed and adhered to, any violation thereof will lead to termination of the study at any stage;

3.4 A quarterly report to be submitted to the Ministry's Research Unit;

3.5 Preliminary findings to be submitted upon completion of the study;

3.6 Final report to be submitted upon completion of the study;

3.7 Separate permission should be sought from the Ministry of Health and Social Services for the publication of the findings.

Yours sincerely,

PERMANENT SECRETARY
06 JUN 2016
REPUBLIC OF NAMIBIA
MINISTRY OF HEALTH AND SOCIAL SERVICES

Andreas Mwoombola (Dr)
Permanent Secretary

Appendix B) Ethical Approval from Newcastle University

Newcastle University

Faculty of Medical Sciences

Newcastle University
The Medical School
Framlington Place
Newcastle upon Tyne
NE2 4HH United Kingdom

Anna Magdalena Nelago Shifotoka
Institute of Health & Society

FACULTY OF MEDICAL SCIENCES: ETHICS COMMITTEE

Dear Anna,

Title: The spatiotemporal analysis of smear positive Tuberculosis and investigation of determinants and risk perceptions for TB infection and disease in Windhoek health district, Namibia
Application No: 01032/2016
Start date to end date: 28 September 2015 to 28 September 2018

On behalf of the Faculty of Medical Sciences Ethics Committee, I am writing to confirm that the ethical aspects of your proposal have been considered and your study has been given ethical approval.

The approval is limited to this project: **01032/2016**. If you wish for a further approval to extend this project, please submit a re-application to the FMS Ethics Committee and this will be considered.

During the course of your research project you may find it necessary to revise your protocol. Substantial changes in methodology, or changes that impact on the interface between the researcher and the participants must be considered by the FMS Ethics Committee, prior to implementation.*

At the close of your research project, please report any adverse events that have occurred and the actions that were taken to the FMS Ethics Committee.*

Best wishes,

Yours sincerely

Kimberley Sutherland
On behalf of Faculty Ethics Committee

cc.
Professor Daniel Nettle, Chair of FMS Ethics Committee
Ms Lois Neal, Assistant Registrar (Research Strategy)

Appendix C) Description of studies reviewed during phase one

Publication	Location	Temporal length studied	Temporal analyses method	Type of TB examined	Population covered and source of information	Total cases analysed Total notified cases	Rates split by	Findings
Ghadiri *et al.*(2013)	Iran, Asia	1996-2005	Only described the pattern-no statistical analyses of trends	All forms (both Pulmonary and extra pulmonary TB)	Data for Kermanshah district. Data from medical records for rural and urban canters in district	Numerator: 150 cases aged 0-18 years Denominator not stated (not clear If only 150 children diagnosed during the period)	All children, by gender, by type of TB (pulmonary and extra pulmonary TB)	Study found that for both pulmonary and extra pulmonary TB, notification rates were higher in girls than in boys. No significant trends found
Shrestha *et al*. (2010)	Nepal, Asia	2001-2008	Only described the pattern-no statistical analyses of trends	All forms (both Pulmonary and extra pulmonary TB)	National level data, with data sourced from the Annual TB reports of the TB programme	Cases analysed: 114 322 cases of all ages reported in annual reports	Rates presented by type of TB, age group, gender,	Study reported an increase in TB rates for all forms of TB, a decline in smear positive and smear negative and increase in extra pulmonary TB
Lawn *et al*. (2006)	South Africa, Africa	1996-2004	Trend analyses conducted using the Cuzik test for trend	All forms (both Pulmonary and extra pulmonary TB)	A specific western cape township with data taken from the community TB register	Cases analysed: 968 cases of all ages Total notified cases:968	Rates analysed overall and by age	TB rates increased with a twofold from 1996 to 2004 reaching 1468/100 000.
Jones *et al*. (2017)	Australia, Oceania	2006-2015	Trend analyses conducted using the negative binomial regression	All forms (both Pulmonary and extra pulmonary TB)	Australian Capital Territory (ACT), in Australia with data sourced from the	Cases analysed: 171 cases of all ages	Rates analysed overall, by age and by place of birth	TB rates remained stable although absolute numbers increased.

					territory (ACT) notifiable disease registry			Rates were higher in foreign born
Charles *et al*. (2017)	Haiti, North America	2010-2015	Simple linear lease square regression was used to examine temporal trends	All forms (both Pulmonary and extra pulmonary TB)	National data for Haiti with data sourced from TB registry national programme	Cases analysed: 95 745 cases of all ages	Rates analysed by gender, location and age	The rates for all forms and for smear positive mostly increased during the period. Rates were higher in males and in those aged 25-44 and most of the regions had cases rates above the national average
Dangisso *et al*. (2014)	Ethiopia, Africa	2003-2012	Chi square test for trend	All forms (both Pulmonary and extra pulmonary TB)	Study covered Sidama Zone in Ethiopia with data taken from health facilities TB registers	Cases analysed: all notified 37070 cases of all ages	Rates presented by type of TB, Age, gender, urban/rural	Study found increments in the CNR for all THE TB groups studied. Rates for smear positive were higher in urban areas compared to rural. They were also high in males and those aged 25-34
Wobudeya *et al*. (2017)	Uganda, Africa	2011-2015	Chis square test for trend	All forms (both Pulmonary and extra pulmonary TB) among children aged under 15 years	Study covered Kampala city in Uganda with data taken from the district electronic TB register	Cases analysed: all notified 2333 cases of aged 0-14 years	Rates presented by division, age groups,	Study found declining rates among children during the period (a decline of 34%), with higher decline observed in those aged 0-4
Mwaba *et al*. (2003)	Zambia, Africa	1964-2000	Only described the pattern-no statistical analyses of trends	All forms (both Pulmonary and extra pulmonary TB)	National data. Study used Ministry of Health TB data	-	overall national rates which were compared to rates from neighbouring countries	Study found that rates of TB were stable during 1964 to 1984 from 90 to 113 and thereafter an exponential increase was noted from 113 in

								1984 to 512/100 000 in 2000
Pesut *et al*. (2012)	Serbia, Europe	1993-2007	Liner regression (sum of least squares)	Extra pulmonary TB	National Data sourced from the central register and from annual summaries of the Belgrade epidemiology division	Cases analysed: all notified 2858 cases of all ages	Overall rates presented and then extra pulmonary rates	Study found a significant increase in extra pulmonary rates, with an annual increase of 8.9%. Absolute number of cases were more in females than males and were mostly aged 45-64 (but these were not rates)
Tam *et al*. (2018)	Hong Kong, Asia	1995-2015	Only described the pattern-no statistical analyses of trends	All forms (both Pulmonary and extra pulmonary TB)	National Data taken from a website of the TB and Chest department in Hong Kong	Absolute numbers of TB cases not presented only notification rates	Rates presented by immigration status, age group	Rates declined overall and were found to be higher in older adults aged 75+
Behbehani *et al*. (2002)	Kuwait, Asia	1965-1999	Only described the pattern-no statistical analyses of trends	All forms (both Pulmonary and extra pulmonary TB)	National data taken from annual TB reports	Case of All ages, Absolute numbers of TB cases not presented only notification rates	Rates presented by Overall, age groups, and by citizenship	The notification rate declined from 259 to 24/100 000 population. During the last few years were highest in older people and among non-nationals
Darian-Smith *et al*. (2017)	Australia, Oceania	2006-2015	Only described the pattern-no statistical analyses of trends	Extra pulmonary TB (ocular-eye TB)	National data sourced from the ministry of health TB registry	Cases analysed: all notified 162 cases of all ages	Rates presented by Overall (all forms) and the ocular TB rates	Study reported an increase in age and sex adjusted ocular TB during the 10 year period which was dominantly in males aged 30-39

Lesic *et al.* (2010)	Serbia, Europe	1993-2007	Liner regression (sum of least squares)	Extra pulmonary TB (osteo articular-bone TB)	National Data sourced from the central register and from annual summaries of the Belgrade epidemiology division	Cases analysed: all notified 295 cases of all ages	Overall extra-pulmonary rates presented and the rates for osteo articular-bone TB	Study round that the a overall rates of extra pulmonary were increasingly significantly and so was the specific rates for osteo articular TB
Hagiya *et al*., (2019)	Japan Asia	1997 -2016	Joinpoint regression	All forms (both Pulmonary and extra pulmonary TB)	National data sourced from the ministry of health TB surveillance system	Cases analysed: all notified 42 715 cases of all ages	Rates presented overall, by gender and by age groups	Study found that rates declined overall, in both genders and in all age groups, except that the trend for age group 0-24 years was not significant during the recent sub period (2012-2016).
Hatlerberg *et al.* (2013)	Denmark, Europe	2000-2009	Only described the pattern-no statistical analyses of trends	All forms (both Pulmonary and extra pulmonary TB) aged younger than 15 years	National data for all cases of TB aged younger than 15 years. data sourced from the Department of infectious disease epidemiology	Cases analysed: all notified 323 cases of aged 0-14 years	Rates presented by age, gender	Study found that a decreasing trend in notification rates from 4.1 to 1.9/100 000, although they were fluctuations. Majority of cases were immigrant children and Danish children aged younger than 5 years
Noppert *et al.* (2015)	Zimbabwe , Africa	2008-2011	Reported absolute percentage declines (no specific temporal trend statistical testing)	New and retreatment smear positive pulmonary TB	National data sourced from Ministry of health TB programme	40 110 cases analysed out of 141 104 pulmonary (new and retreatment) cases of all ages notified	Overall rates, age and gender	Study found that the overall trend firstly increased during 2008 to 2010 then it sharply declined in 2011. The age specific trends of

						during the period. The overall all forms of TB cases were 164 535 notified		smear positive TB remained stable during the study period, however majority of cases were aged 25-44. TB was more prevalent in males and the percent decline was highest in females than in males. Urban cities were amongst provinces which had above national average CNRs
Kapata *et al.* (2013)	Zambia, Africa	2004-2011	Only described the pattern-no statistical analyses of trends	All forms (both Pulmonary and extra pulmonary TB) children aged 15 years or less	National TB data on children sourced from the National TB programme	Cases aged 0-14 years , however absolute numbers of TB cases not presented only notification rates	Rates presented by type of TB, age group	A downward trend in all forms of TB (children cases) was observed from 113 to 69/100 00 population. The downward trend was also observed in all TB types. Majority of children were from urban provinces than from rural provinces. The CNRs were higher in the all forms of TB male cases
Tao *et al.* (2019)	China, Asia	2005-2017	Joinpoint regression	Pulmonary TB cases	Data for seven cities in Sandong province	Cases involved 6283 TB cases aged 0-17 years	Rates over time analysed by type of TB. Smear positive, smear negative, relapse, new cases	Study showed a rapid decline in overall incidence from 7.62 to 3.62 per 100 000 population. Trends declined in all specific types of TB examined

								except for smear negative TB.
Wu *et al.* (2017)	China, Asia	1992-2015	Trend analyses done using the chi square test for liner trend	All forms (both Pulmonary and extra pulmonary TB) smear positive pulmonary TB	Data for Chingqing city for the years 1992-2007 were taken from the city TB annual reports while data from 2008-2015 were taken from the national TB surveillance system	Analyses based on all notified TB cases, 472 596 cases of TB (all forms) or which 264 702 smear positive cases of all ages	Rates presented Overall, Age, gender	Study found that the all forms of TB cases and the smear positive mostly increased significantly 1992 to 2005 and thereafter declined significantly. Majority of cases were males, and gender specific rates declined for both male and females
Crimi *et al.* (2005)	Italy, Europe	1986-2002	Only described the pattern-no statistical analyses of trends	All forms (both Pulmonary and extra pulmonary TB)	Data for Liguria region sourced from registries of the Ministry of Health	Case of All ages, Absolute numbers of TB cases not presented only notification rates	Overall rates presented	Study found that TB rates overall increased in the earlier ears and declined in the recent years of the study period
Daniel *et al.* (2015)	Nigeria, Africa	2011-2014	Only described the pattern-no statistical analyses of trends	All forms (both Pulmonary and extra pulmonary TB) children in	Data for Lagos state TB were sourced from the state TB and leprosy control programme	Cases analysed: all notified 2396 cases of aged 0-14 years	Overall rates, by age and gender	Study found that overall TB rates increase from 13 to 17.2/100 000 in 2014. Rates were higher
Gleason *et al.* (2012)	Saudi Arabia, Asia	2005-2009	Poisson regression used to assess trends	All forms (both Pulmonary and extra pulmonary TB)	Data sourced from the TB registry of the national TB programme	10783 cases of all ages Saudi and 9768 non-Saudis	Rates were analysed by nationality (Saudis or non –Saudis). And also presented by age	Stable rates were obtained, although rates were higher among non -Saudi compared to Saudis).
Kapata *et al.* (2011)	Zambia, Africa	1990-2010	Only described the pattern-no statistical analyses of trends	All forms (both Pulmonary and extra pulmonary TB)	Data sourced from the TB registry of	759 769 cases of all ages	Only overall rates	Study found that TB rates of TB by type of TB and gender

					the national TB programme			increased up until 2004, and thereafter decreased up until the year 2010. Majority of cases were males and more cases were aged between 25-44 years
Hamusse *et al.* (2014)	Ethiopia, Africa	1997-2011	Only described the pattern-no statistical analyses of trends	All forms (both Pulmonary and extra pulmonary TB)	Data for Arsi Zone taken from facility registers	A total of 41965 cases of all ages	Rates presented for all forms and for smear positive pulmonary TB cases	Study found that both all forms and pulmonary TB rates increased with increasing DOTS coverage
Arsang-Jang *et al.* (2017)	Iran, Asia	2001-2015	Trends analysed using Joinpoint regression	All forms (both Pulmonary and extra pulmonary TB)	National data taken from the TB programme, Iran	A total of 154 930 cases of all ages	Overall rates and by type of TB	Statistically decreasing trends between 2001 to 2015 (AAPCs) were observed overall and by type of TB group
Marrero *et al.* (2000)	Cuba, North America	1962-1997	Only described the pattern-no statistical analyses of trends	All new pulmonary and extra pulmonary cases	National data sourced from the TB registry of the national TB programme		Rates presented for all forms and for smear positive pulmonary TB cases	The study found that rates of TB decreased from 1962 to 1991, when rates dropped from 28.8 to 4.8/100 000. From 1992 to 1997, the rates increased from 5.2 to 12.2/100 000. Smear positive TB rates also had the same trend during the study period. Rates were higher among older people aged 45 and above

Kim *et al.* (2008)	Canada, North America	1995-2004	Only described the pattern-no statistical analyses of trends	All forms (both Pulmonary and extra pulmonary TB)	Ottawa city data sourced from the provincial TB registry	A total of 584 notified cases of all ages	Rates presented overall, and by nationality	Study found that rates on TB decreased from 1995 to 2004 from 8.3/100 000 to 5.8/100 000 pop. TB was more prevalent in foreign born, and the age specific rates was highest among those aged 65 and above
Reis *et al.* (2013)	Brazil, South America	2002-2017	Only described the pattern-no statistical analyses of trends	All forms (both Pulmonary and extra pulmonary TB)	Belo city data taken from provincial health information system	A total of 7590 notified cases of all ages	Rates presented overall, by age and gender	Study reported that rated declined from 43 to 34/100 000 pop. Rates were higher in males and those aged 40-59 years
Adejumo *et al.* (2017)	Nigeria, Africa	2011-2015	Chi square test for trend	All forms (both Pulmonary and extra pulmonary TB)	Lagos state with data sourced from the Lagos state TB program	A total of 44 516 notified cases of all ages	Rates presented type of TB, age groups and gender	Study found that the overall CNR increased between 2011 and 2013 and thereafter declined to 72.1/100 000 in 2015. The rates were higher in males than in females
Kibuule *et al.*, (2019)	Namibia Africa	1996 -2015	Interrupted time series analyses	All forms (both Pulmonary and extra pulmonary TB)	National data sourced from	-Absolute numbers not reported	Overall notification rates	Study found that CNR declined over time, and more sharply after introduction of Community Based DOT.
Khazaei *et al.* (2016)	Iran, Asia	1995-2012	Trends analysed using Joinpoint regression	Smear positive pulmonary TB	TB data for Iran sourced from the WHO organisation data observatory	A total of 96 579 notified cases of all ages	Overall rates (but trend analyses for the overall rates not presented), By gender and by age	Study found decreasing trends of TB rates overall and in both genders and ages,

Appendix D) Description of studies reviewed during phase two

Publication	Location	Aim	Temporal length studied	Type of TB examined	Population covered and source of information	Geographical level of analyses	Spatial/spatiotemporal analyses method	Factors considered in the analysis	Findings
Alene *et al.* (2017)	Ethiopia, Africa	To investigate spatial-temporal pattern of paediatric TB and to identify socio-economic and climatic factors associated with childhood TB incidence	July 2013- June 2016	2240 All forms of new TB cases (children under 15 years)	Data for 20 districts in North Gonder zone in Ethiopia obtained from the one TB office	District level	(1) Spatial analysis: Global and local Moran's I statistic and the Getis – Ord statistic. (2)Spatiotemporal analyses: Poisson regression	Residency; education; illiteracy rate; internal migration; economic inactivity; unemployment rate; average household size; traditional kitchen inside the house with charcoal, firewood or dung used for cooking, temperature, rainfall	Cluster areas of TB were found. Spatiotemporal distribution was associated with urbanisation, lower educational status, hi% of internal migration, high temperature, and high rainfall
Cabral Silva *et al.* (2016)	Brazil, South America	An epidemiological analysis to deepen knowledge of the profile of TB disease and its spatiotemporal dynamics	1991-2010	All forms of new TB cases	Data for Olinda) city , obtained from the Brazilian SINAN database	Census tracts (sectors) within the city	Kulldorff Scan statistics visualised in rates maps	No consideration of population level factors in the space-time analyses factors	They found a statistically significant decreasing trend in TB incidence and a reduction in the proportion of cases among primary clusters, indicating that the disease is spreading across the region.
de Abreu e Silva	Brazil, South America	To describe the epidemiologic characteristics and spatial	2002-2012	309 (94.8%) All new cases of	Data Divinopolis city , obtained from the Brazilian	Census tracts	Kulldorff Scan statistics visualised	Population density; percentage literacy; percentage of household receiving one Brazilian minimum wage or less	The study reported one statistically significant cluster and that TB was mostly present in urban census tracts. Higher population density was

et al. (2016)		distribution of new cases of TB in Divinopolis		all forms (PTB and EPTB)	SINAN database		in rates maps and kernel density maps		significantly associated with increased odds of living g in a census tract with higher density of TB cases
Harling and Castro (2013)	Brazil, South America	To characterise the spatial pattern of tuberculosis in brazil and determine relationships with social factors	2002-2009	All new cases of all forms (PTB and ETTB)	Nationwide data for 5507 municipalities , obtained from the Brazilian SINAN database	Municipality level	Global and local Moran's I statistic results depicted on rate and cluster maps	% in poverty; % urban population; race' % household with >2 people per bedroom; hospitals/100 000 people; doctors/100 000 people; % tuberculosis success rate; AIDS incidence/100 000	Spatial clusters of TB were found mostly around cities. Multivariable analyse revealed high average TB notification rates were associated with black, brown and indigenous populations, household crowding, household poverty; high population density and high % of urban population
Pereira *et al.* (2014)	Brazil, South America	To analyse the spatial distribution of risk of TB and its socioeconomic determinants in Rio de Janeiro city	2004-2006	All new cases of all forms (PTB and ETTB	Data for Rio de Janeiro city , obtained from the Brazilian SINAN database	Neighbourhood level townships	Moran's I statistic	Income, education, water supply, waste collection sewage and pop density , household size, life expectancy, adult literacy rate, school attendance and per capita income	Spatial clusters of TB were found, and TB rates were significantly associated with Income, education, pop density and household size
Venancio *et al.* (2014)	Brazil, South America	To identify spatial pattern of incidence of tuberculosis in children in the municipalities in the state of Sao Paulo	2001-2010	All cases of all forms (PTB and ETTB in children aged 0-14 years	Data for Sao Paulo state , obtained from the Brazilian SINAN database-website	Municipality level	Moran's I statistic	No statistical analyses of spatial pattern with population level factors. However the authors plotted educational level, and income on maps to compare with TB rates	Study found that there was clustering g of TB. They also found that TB surprisingly, higher rates were found in areas where many people have access to education and better living conditions
Rodrigues *et*	Brazil, South America	To analyse the spatial distribution of	2002-2011	Pulmonary TB cases	Data for Sao Paulo state , obtained from	Municipality level	Global Moran's I statistic	Sex, age group, diagnostic year, population density,	Study found some TB clusters mostly in the urban centres of Rio de Janeiro state. They also revealed that the higher risk of

al. (2014)		the TB endemic in Rio de Janeiro.			the Brazilian SINAN database				TB was significant in early 2000, in male and in the age group 40-59
Erazo *et al.* (2014)	Brazil, South America	To identify and characterise the spatial distribution patterns of TB and to examine the relationship between living conditions and TB incidence in Salvador neighbourhoods	1995-1996 and 2004-2005	10406 (96%) All new cases of all forms (PTB and ETTB	Data for Salvador city in Bahia state with data obtained from the Brazilian SINAN database	Neighbourhood level	Global and local Moran's I statistic with data presented in thematic rate maps	Income, education, crowding, sanitation and slum	Higher rates of TB occurred in areas with poor living conditions during the period 10995-1996. During 2004-2005, this association was no longer statistically significant.
Queiroga *et al.* (2012)	Brazil, South America	To analyse the spatial distribution of TB in the urban area of the city of Campina Grande	2004-2207	All new 537 (93%) cases of all forms (PTB and ETTB	data obtained from the Brazilian SINAN database	Neighbourhood level	Moran's I statistic with data	Income, education; %of households in subnormal agglomerate; % of households connected to water supply and ratio of people in household and bedrooms in households	Areas of high TB rates were found in the study and authors reported that these were mainly areas with poor living conditions. The authors also noted that some areas with good living conditions had higher rates of TB possibly due to
Magalhaes and Medronho (2016)	Brazil, South America	To analyse the spatial pattern of TB by identifying the relevant socio economic variables for the occurrence of TB	2005-2008	All new cases of all forms (PTB and ETTB	Nationwide study data obtained from the Brazilian SINAN database	Census tracts/sectors	Global and local Moran's I statistic	Average household size; Average family income; proportion of head of household with an income greater than 1 minimum was and less than 2 minimum wages; average income of head of family; proportion of illiterate people; proportion of households with water supply; proportion of households with bathroom/sanitation and sewage	Study found that there was clustering g of TB. They also found that TB surprisingly, higher with better socio economic indicators e.g. better earning of household head. They found that TB was associated with proportion of head of household with an income greater than 1 minimum was and less than 2 minimum wages; Average family income; proportion of illiterate people; average income of head of family; ; proportion of people who live alone

								connection; proportion of households with garbage collection; race, proportion of people who live alone	
Harling *et al.* (2017)	Brazil, South America	To analyse the spatial and temporal patterns of TB incidence and treatment abandonment rates in Fortaleza city and associated social and demographic factors	2007-2014	12338 (99%) All cases of all forms (PTB and ETTB	Data for Fortaleza city obtained from the Brazilian SINAN database	Neighbourhood level	local Moran's I statistic	Population size, density, % of people living in informal settlement, mean number of people per sleeping bedrooms; average household size; average income; literacy rate; proportion of people with access to services (electricity, water, garbage collection, sewage),reported AIDS cases, homicides	Study reported areas with high concentration of TB and also reported that t TB rates were negatively associated with neighbourhood level literacy, and positively with public sewage provision, homicide rates as well as proportion of people self-identifying as black
Yakam *et al.* (2013)	Cameroon, Africa	To describe the spatial distribution of pulmonary TB and association with socio economic status	May 2011-April 2012 (this was a prospective study)	2132 (84%) Adults aged (>15years) case with pulmonary TB (smear negative and EPTB cases were excluded)	Data collected as patients were diagnosed at the 20 TB diagnostic and treatment centres in Doula	Health area level in Doula	Kulldorff Scan statistics	Education level, ownership of house, type of wall material, source of drinking water, presence of modern toilet car, mobile phone, computer radio, TV, DVD, gas cooker, refrigerator, air conditioner . However the authors did not conduct actual statistical analyses	The study found significant clusters and observed that SES indicators were lower in TB patients compared to the general population. However, there was no association between SES and TB incidence of the various Has. For example the HA with the highest TB incidence had an intermediate rather than poor SES classification.

Rao *et al.* (2017)	China, Asia	To explore the spatial, temporal and space time dynamics of TB at the county level in Quinghai	2009-2016	All incident (new)cases of all forms (PTB and ETTB	Data for TB cases taken from the China Information system for disease and prevention control database	County level analysis	Kulldorff Scan statistics	No consideration of county level factors in the statistical analyses	Study found purely temporal, purely spatial and space time clusters
Wang *et al.* (2012)	China, Asia	To characterise geographic distribution pattern of TB in Linyi city	2005-2010	All cases of all forms (PTB and ETTB	Data sourced from Linyi city institute of Tuberculosis control	Town level	Global and local Moran's I statistic and Kulldorff Scan statistics	No consideration of town level factors in the statistical analyses	Study found statistically significant clusters of TB in Linyi city
Zhao *et al.* (2013)	China, Asia	To use the spatial clustering analysis of county level TB notification data to determine clustering areas of TB epidemic	2005-2011	Notification for new smear positive And notification for all forms of TB cases	Nationwide study with data sourced from the national surveillance system for notifiable infectious disease	County level	Global and local Moran's I statistic and Kulldorff Scan statistics	No consideration of town level factors in the statistical analyses	Study found statistically significant most likely clusters which were similar for both new smear positive and for all forms on TB. However the secondary clusters were different
Wubuli *et al.* (2015)	China, Asia	To use GIS to analyse the TB surveillance data for Xinjiang and to understand the geospatial characteristics	2005-2013	Analyses was done for four indicators including:	Data for Xinjiang taken from the national surveillance system for notifiable	County level	Global and local Moran's I statistic and the Getis – Ord statistic.	Population density, Proportion of males; proportion of minorities; proportion of rural population; death rate and per capita GDP	Study found statistically significant hotspots which were similar for both pulmonary TB, smear positive TB and smear negative TB. The TB incidence was associated with proportion of minorities and per capita GDP

		of TB notification rates and identify social and demographic predictors of TB incidence		Pulmonary TB cases Rates of sputum smear positive New smear positive TB And smear negative TB	infectious disease				
Liu *et al.* (2012)	China, Asia	To map the spatiotemporal distribution and hotspots of TB infection in Beijing using GIS and spatial analyses	2005-2009	All new cases of all forms (PTB and ETTB	Data sourced from Beijing city institute of Tuberculosis control	Town level	Global and local Moran's I statistic and the Getis – Ord statistic	No consideration of town level factors in the statistical analyses	Study found statistically significant hotspots. The TB incidence was associated with per capita GDP
Guo *et al.* (2017)	China, Asia	To determine the spatial clustering patterns and seasonal variations of TB across different provinces and	2005-2013	9597884 All cases of all forms (PTB and ETTB	Nationwide study with data taken from the national surveillance system for notifiable	Province level	Global and local Moran's I statistic and the Getis – Ord statistic	GDP per capita; proportion of elderly; the ratio of male to female; number of doctors per 1000 persons; number of inpatient beds per 1000 persons; proportion of people with higher education; population density	Study found statistically significant hotspots. The TB decreased with male/female ratio, and increased with proportion of elderly. TB incidence decreased with an increase per capita GDP

		years and study associated factors			infectious disease				
He *et al.* (2017)	China, Asia	To determine the distribution and variation of TB cases across time, geographic areas and socio demographic variables	2011-2015	Smear positive pulmonary TB	Data for Xinjiang with data taken from the national surveillance system for notifiable infectious disease	Region	Descriptive spatial analyses. No particular spatial analyses method used	No consideration of town level factors in the statistical analyses	Study found variations in TB incidence across regions in this province, however the variations observed were not confirmed statistically
Li *et al.* (2016)	China, Asia	To clarify the spatial and temporal distribution of TB in Beijing city	2009-2014	All forms of TB	TB data taken from the Beijing Health and population health reports published by the Beijing CDC	District level (nice intro)	Global and local Moran's I statistic and Kulldorff Scan statistics	No consideration of town level factors in the statistical analyses	Study found statistically significant hotspots.
Shaweno *et al.* (2017)	Ethiopia, Africa	To understand the geographic and temporal distribution of TB and explain likely drivers	2010-2014	1683 (97%) All forms of TB	Data for Sheka zone in Ethiopia	Kebele level , 55 kebele /neighbourhoods	Global Moran's I statistic	Health facility availability, pop density, average TB rates in adjacent kebele; TB incidence in the previous year and HIV/TB co infection	Study reported significant spatial autocorrelation in Sheka zone. They also found that TB incidence was associated with Health facility availability, average TB rates in adjacent kebele; TB incidence in the previous year
Kistemann *et al.* (2002)	Germany, Europe	To investigate inner urban strength of the association between TB and	1986-1987	All forms of new TB cases	Data for cologne obtained from municipal health authority	85 sub-districts in Cologne	Spatial heterogeneity assessed using the Chi square	Population density, living space; rooms per person, amount of dwellings per 100, amount of immigrants, amount of non-EU immigrants, amount of German	Study found spatial heterogeneity which differed by age (Younger and older). TB incidence was found to be associated with immigration, deprivation indicators, economic indicators and ethnicity

		several potential risk factors					test (modified for epidemiological purpose (Gail, 1978))	origin immigrants from eastern Europe; unemployment, amount of people receiving social income, amount of blue collar workers; amount of persons with lower educating level, and spending power	
Pang *et al.* (2010)	Hong Kong, Asia	To identify the spatial distribution of TB and explore its association with neighbourhood risk factors	2005-2007	17294 (99%) All forms of TB cases	Nationwide study Data sourced from the TB surveillance system of the Department of Health	District council constituency area	no specific spatial analyses method expect mapping crude rates and Standardized notification ratios across districts	% Unmarried population, % population with non-Hong Kong nationality, % population with non-Chinese nationality, %population with elementary education, %population with elementary occupation, % population with low monthly income, % household with low monthly income, population density	Maps of crude rates and standardised notification ratio showed that the disease was distributed unevenly in the city. Standardized notification ratios for TB were found to be associated with being non-Hong Kong born, being single and low household income
Tabatabaee *et al.* (2015)	Iran, Asia	To determine the spatial pattern of TB incidence and to evaluate TB control program indices	2006-2012	All forms of TB cases (TB incidence calculated with new cases only)	Data for all townships supervised by the Shiraz university obtained from TB register-communicable disease control	22 townships	no specific spatial analyses method expect mapping crude rates	No consideration of town level factors in the statistical analyses	Maps of crude rates showed high TB incidence in some townships e.g. Firozabad township
Yazdani Charati *et al.* (2014)	Iran, Asia	To map spatial cluster of TB in Mazandaran province in order to map	1999-2008	All forms of TB cases	Data for Mazandaran province obtained from TB registry	City level	no specific spatial analyses method expect	No consideration of city level factors in the statistical analyses	Study found that some of the cities had higher TB incidence rates than the province average rates. no gender differences observed

		when and where unusually higher concentration of new cases occurred considering gender distribution of population			centres for medical treatment in the province		mapping TB rates – although it was earlier reported that they used Moran's I		
Hassarangsee *et al.* (2015)	Thailand, Asia	To analyse spatial pattern of TB incidence in Si Sa Ket province	2004-2008	All cases of all forms (PTB and ETTB	Data were for Si Sa Ket province obtained from the province TB registry	Local authority organisation level	Global and local Moran's I statistic and Kulldorff Scan statistics	No consideration of city level factors in the statistical analyses	Study found hotspots of TB , and similar areas were identified through the Moran's I index and SaTScan
Onozuka and Hagihara (2007)	Japan, Asia	To identify when and where prevalence is high in Fukuoka prefecture	1999-2004	All cases of all forms (PTB and ETTB	Data for Fukuoka obtained from the TB surveillance system	109 census tracts	Kulldorff Scan statistics	No consideration of city level factors in the statistical analyses	Study found statistically significant hotspots for TB located mainly in the northern p**ar**t of Fukuoka
Dangisso *et al.* (2015)	Ethiopia, Africa	To assess the spatial distribution and look for spatiotemporal clustering of the disease	2003-2012	Smear positive TB cases used for spatial analysis	Data for Sidama zone obtained from the TB data registers from all health facilities in the zone	Kebele level	Global and local Moran's I statistic and Kulldorff Scan statistics	No consideration of city level factors in the statistical analyses	Study found hotspots of TB , and similar areas were identified through the Moran's I index and SaTScan
Randremanana *et al.* (2010)	Madagascar, Africa	To analyse spatial distribution of pulmonary TB	2004-2006	New cases of pulmonary TB	Data for Antananarivo city obtained from all 16 TB	Neighbourhood level	Bayesian disease mapping	No consideration of neighbourhood level factors in the statistical analyses	Study reported strong geographical heterogeneity of pulmonary TB across city neighbourhoods

		and investigate relationships with indicators in the TB registry and TB incidence rates from epidemiological data			diagnostic and treatment centres registers				
Castro *et al.* (2018)	Brazil, South America	To describe the pattern of the spatial distribution of TB incidence in Manaus and its relationship with social determinants	2008-2013	9599 (98%) New cases of pulmonary TB	Data for Manaus taken from TB epidemiological surveillance reports	Neighbourhood level	Global and local Moran's I statistic	Gini index, proportion of population vulnerable to poverty, Unemployment rate, illiteracy rate, proportion of households with running water, proportion of households connected to sewage system, proportion of suburban agglomerated households , pop density, average number of residents per room, population growth rate	Study found statistically significant clusters for TB and also that TB incidence was associated with an average number of residents per room, Unemployment rate and proportion of households connected to sewage system
Alvarez-Hernandez *et al.* (2010)	Mexico, North America	To describe the distribution of TB at the census tract level in the city of Hermosillo and identify whether the distribution is associated with low socioeconomic status	2000-2006	903 (89%) New cases of TB	Data for Hermosillo city taken from the national TB registry	census tract level-basic geo-statistical area	Moran's I statistic and Besag and Newell technique	Income level, education, housing quality, overcrowding, car availability	Study found no global spatial autocorrelation but at local level reported areas with high incidence of TB. They also found that areas with low socioeconomic statues dad an excess risk of TB

Sadeq and Bourkadi (2018)	Morocco, Africa	To examine trends in TB in Morocco and identifying TB spatial clusters and TB associated predictors	2011-2014	New cases of TB	Nationwide study with data obtained from ministry of health	Province level	Global and local Moran's I statistic	Living area (in prefecture versus living in province), annual mean rainfall, annual meal temp, AIDS incidence, population density	Study found statistically significant clusters for TB in the east and west. TB rate was associated with annual rainfall, AIDS
Kakchapati *et al.* (2014)	Nepal, Asia	To examine the spatial and temporal variation in Tb incidence in Nepal	2003-2008	All new cases of all forms (PTB and ETTB	Nationwide study with data obtained from ministry of health	District level	No specific spatial analyses method used only presented district level incidence rates	No consideration of neighbourhood level factors in the statistical analyses	There were marked variation in TB incidence across district with high rates in Terai region
Nunes (2007)	Portugal, Europe	To map spatiotemporal tuberculosis incidence in Portugal in order to when and where unusually high concentration of new cases occurred considering the gender distribution in local populations	2000-2004	New cases of TB	Nationwide data obtained from the TB control programme information system of the directorate of health	278 sub districts/ municipalities	Kulldorff Scan statistics	No consideration of sub district level factors in the statistical analyses	Study found clusters which were mostly in Oporto, Setubal and Lisbon areas

Areais *et al.* (2015)	Portugal, Europe	To identify patio-temporal municipality years notified incidence rate clusters in Portugal	2000-2010	cases of pulmonary TB	Nationwide data obtained from the TB control programme information system of the directorate of health	278 sub districts/ municipalities	Kulldorff Scan statistics	No consideration of sub district/municipality level factors in the statistical analyses	As observed in the earlier study above (Nunes, 2007), Study found clusters which were mostly in Oporto, and Lisbon areas
Couneiro *et al.* (2011)	Portugal, Europe	To characterise pulmonary TB incidence rates across municipalities in Portugal and detect potential risk areas and identify local risk factors	2004-2006	cases of pulmonary TB	Nationwide data obtained from the TB control programme information system of the directorate of health	278 sub districts/ municipalities	Kulldorff Scan statistics	AIDS incidence; % of overcrowded accommodation; % of non-standard accommodation; % of working age persons with no education; unemployment rate; % of no-qualified workers; ; % prison population % of immigrants from high PTB incidence countries ;	Study found areas with high incidence of TB than others due to high incidence and reported an association with HIV/AIDS, overcrowded accommodation and immigrant population.
Randremanana *et al.* (2011)	Madagascar, Africa	To determine whether pulmonary TB displays spatio-temporal pattern in Antananarivo neighbourhoods and whether social economic and care patient factors control this pattern factors	2004-2006	cases of pulmonary TB	Data for Antananarivo obtained from TB registers of 16 TB diagnostic and treatment centres across the city	Neighbourhood level	Kulldorff Scan statistics	Average household size; % of households with electricity, tap water, hard walls, latrine, radio, TV; % of households using gas /electricity for cooking	Study found clusters of PTB and the risk decreased with living of households with more than three cases , tap water, hard walls, and radio

Pinto *et al.* (2018)	Brazil, South America	To identify spatial and temporal clusters and variations in temporal trends clusters of TB in the immigrant population of Sao Paulo	2006-2013	New cases of TB among immigrants	Data for Sao Paulo city obtained from an online database, TB WEB	Census weighting areas	Kulldorff Scan statistics	No consideration of weighting areas level factors in the statistical analyses	Study found cluster areas with high rates of TB. They also did an analysis to compare characteristics of patients in low clusters compared to high cluster areas. And found that compared to those living in low risk clusters, high spatial clusters areas had high proportion of patients aged >30 years, indigenous population and low proportion of patients with high education level
Fusco *et al.* (2017)	Brazil, South America	To characterise the clinical epidemiological profile of TB and to analyse the spatial distribution of the cases	2008-2013	All cases of all forms (PTB and ETTB	Data for Sao Carlos city obtained from an online database, TB WEB	Street paths/postal address to generate density maps	Kernel density maps	No consideration of area level factors in the statistical analyses	The study found that the distribution of TB occurred in the non-random manner and was more concentrated in the southern part of the municipality
Roza *et al.* (2012)	Brazil, South America	To evaluate the spatial and temporal distribution of TB in Ribeirao Preto and evaluate relationship with factors of social vulnerability	2006-2010	705 All cases of all forms (PTB and ETTB	Data for Ribeirao Preto obtained from an online database, TB WEB	44 health units	Bayesian disease mapping	Income, education (see indexes described)	Bayesian model confirmed spatial variation of TB in the municipality. There was a relationship between TB rates and education and income although some of the areas with low vulnerability, high income and education also had high estimates of TB
Das *et al.* (2017)	Singapore, Asia	To analyse spatial risk of TB in Singapore and investigate geographically	1995-2011	All forms of TB cases	Nationwide Singapore, with data from T programme (STEP)	Planning area level	Inhomogeneous k-function	No consideration of area level factors in the statistical analyses	spatial variation of TB was observed across Singapore areas

		structured factors							
Munch *et al.* (2003)	South Africa, Africa	To use exploratory disease mapping to determine whether distinguishable spatial patterns in the distribution of TB patients	1993-1998	1128 (77%) All forms of bacteriologically confirmed TB cases aged 15 years or older	Data for two suburbs (Ravensmead and Uitsig) in Cape Town SA obtained from the community TB registry	39 Census enumeration area (EA)	Dot density maps	Pop density, unemployment rate, shebeens per km square	Study found hotspots mainly in the south and TB cases were associated with crowding, unemployment and number of shebeens in EA
Gomez-Barroso *et al.* (2013)	Spain, Europe	To detect spatial and spatial temporal clusters of respiratory TB in Spain	2008-2010	cases of pulmonary TB	Data reported in National epidemiological surveillance network	Municipal level	Kulldorff Scan statistics	No consideration of Municipal level factors in the statistical analyses	Study found significant clusters of TB and same areas were deterred in the purely spatial and spatiotemporal analyses
Sousa *et al.* (2016)	Portugal, Europe	To identify the main longitudinal trends in TB incidence in Portugal and association with socioeconomic and health related predictors.	2002-2012	33394 All new TB cases of all forms	Nationwide study with data taken from the Portuguese surveillance system	District level	k-function longitudinal cluster algorithm	Proportion of working population aged 15-64; proportion of elderly >65 years; proportion unemployed; proportion of existing inmates; prison overcrowding; HIV notification rate; use of alcohol; proportion of physicians/surgeons; medical appointments	Three clusters with different disease profiles were reported. HIV and unemployment were found to be positively associated with TB incidence
Touray *et al.* (2010)	The Gambia, Africa	To use GIS and spatial scan statistics to describe the spatial	2007-2008	All forms of TB cases	Data for Greater Banjul obtained from consenting TB patients at TB treatment	Settlement level	Kulldorff Scan statistics	No consideration of settlement level factors in the statistical analyses	Study found significant clusters of TB and same areas were deterred in the purely spatial and spatiotemporal analyses

		distribution of TB and identify settlements with significant clustering			centres (1145/1430)				
Huang *et al.* (2017)	China. Asia	To analyse space time dynamics of pulmonary TB cases in Zhaotong	2011-2015	All forms of PTB cases New cases of PTB cases Retreatment PTB cases	Data for Zhaotong, obtained from the Yunnan TB database (Yunnan CDC)	Town level	Kulldorff Scan statistics	No consideration of town level factors in the statistical analyses	Study found significant clusters of TB which were similar for both three indicators (all PTB, new and retreatment). The clusters were found in an area reportedly to have poor socio economic status and same
Tiwari *et al.* (2016)	India, Asia	To use GIS and spatial scan statistics to investigate statistically significant hotspots of TB in Almora district	2003-2005	All forms of TB cases	Data for Almora district obtained – source not mentioned	Region/sub-district level	Kulldorff Scan statistics	No consideration of Region/sub-district level factors in the statistical analyses	Study found significant hotspots of TB and same areas were deterred in the purely spatial and spatiotemporal analyses

Appendix E) Description of studies reviewed during phase three, part A

Publication	Location	Aim	Study design	Community based /hospital based/Both	Sample size	Source of data collection for	Risk factor variables assessed	Statistical techniques	Variables found to be significantly associated with outcome
Chittoor *et al*., 2013	Mexico, North America	To characterise socio-demographic and environmental risk factors related to TB active disease and to latent TB infection, and to identify risk factors associated with progression from latent infection to TB among people aged 15 years and above	Case control	Cases recruited from clinical settings and controls recruited from community through door to door household visits	75 cases (active TB cases) and 75 control (LTBI persons) matched by age, sex, ethnicity and neighbourhood. The TB status of both cases and controls was lab confirmed	Data collected through a questionnaire through ace to face interviews	Age gender, ethnicity, place of birth, level of education, employment status, income, type of residence, house floor, overcrowding, location of bathroom, access to portable water, mine work, use of wood for cooking, nutrition, alcohol use, drug use, needle or injection drug use, BMI, fasting glucose, Waist circumference,	Chi square test for Univariate analyses Multivariable analyses through logistic regression	TB cases were more likely to Having TB relatives, nutrition and Diabetes and not born in that study state (Chihuahua) TB cases were less likely to be from overcrowded household, injection drug users and less likely to be born in that study state (Chihuahua)
Shalini *et al*., 2015	India, Asia	To assess socio-demographic and risk factors and sputum along with sputum microscopy outcome among cough	Cross sectional	Hospital based study	A total of 225 patients who reported having a cough for two weeks. all aged from 15 years and above	Data collected through a questionnaire through ace to face interviews	Age, religion, caste, education, marital status, past history of TB, family history of TB, overcrowding, smoking, alcohol	Chi square test	Age gender, religion, area, marital status, overcrowding, and history of recent TB in family, smoking and alcohol. However these were all Univariate

		symptomatic among people aged 15 years and above				with cases and controls			analyses not multivariable analyses
Boccia et al., 2011	Zambia	To study the association between household SEP and TB	Case control	Community based	52 cases and 318 controls. Case and controls matched by area of residence and age group. The TB status of both cases and controls was lab confirmed	Data collected through a questionnaire through ace to face interviews	Gender, literacy, education level, employment status, meals per day, meal containing protein, BCG status, HIV status, cigarette smoking, indoor air pollution, migration, known contact with TB case, attending video clubs, bars, hairdressing	Univariable and multivariable analyses through logistic regression	Meals containing protein, not having BCG status, being HIV positive, known contact with TB case migration,
Tulu *et al*., 2014	Ethiopia, Africa	To determine the prevalence of smear positive TB and associated risk factors among TB suspected patients	Cross sectional	Hospital based	A total of 391 participants (response rate of 93.1%),all aged from 16 years and above	Outcome assessed through sputum examination. Risk factors assessed though questionnaire	Residence, age, sex, education, marital status, living situation (prison/homeless), family size, number of rooms, occupation, HIV previous TB infection, family history of TB, contact with TB case, smoking, alcohol consumption	Chi square test for univariate analyses Multivariable analyses through logistic regression	Age, marital status, family size, contact with TB case, smoking, HIV

Karim *et al*., 2012	Bangladesh, Asia	To identify risk factors for TB in children	Case control study	Hospital based	A total of 95 and 94 controls (children less than 18 years).	TB cases recruited from DOT centres and controls also recruited from registers of patient tested for TB and not found to have	Age, sex, child education level, mothers education level, mothers occupation, fathers occupation, family composition, persons per bedroom, household condition, ventilation status, kitchen position, in-house environment condition, contact with TB person , duration of contact with TB person	Chi square test for Univariate analyses Multivariable analyses through logistic regression	Being more than 14 years of age, better ventilated houses (protective of TB), children in contact with TB persons outside their families (reduced risk compared to those in contact with TB persons inside their households)
Crampin *et al*., 2004	Zambia, Africa	To explore risk factor for TB in relation to gender	Case control study	Community based Cases were selected from the community	598 case and 992 controls were recruited into the study matched on basis of gender and age, area of residence. all aged from 15 years and above	Participants were interviewed using a questionnaires	HIV infection, smoking, cooking exposure, pregnancy , contact with TB cases within or outside household	Logistic regression for both Univariate and multivariable analyses	HIV positivity, contact with TB cases, lack of household's possessions, previous marriage, not having a BCG scar, being an ex-drinker
Glynn *et al*., 2000	Malawi, Africa	To study the factors influencing the development of TB in the general population cohort with	Cross sectional study(study done using a subset of	Community based	Analyses were based on 11241 participants with known HIV status. all aged from 15	Participants were interviewed using a questionnaires and TB diagnosis	HIV, sex. Age group, house construction, schooling, occupation, position in household, area, population density, seen in first survey	Logistic regression for both Univariate and multivariable analyses	HIV/AIDS, older age group, occupation, house construction,

		known HIV status	individuals with known HIV status)		years and above	was lab confirmed			
Gustafson *et al*., 2004	Guinea Bissau, Africa	To study demographic, environment and socioeconomic risk factors for TB at community and household levels	Cross sectional study	Both hospital and community. (patients identified through passive and active case finding approaches)	Analyses based on 247 cases compared to total population (25189) data for population obtained from a general census. all aged from 15 years and above	Participants were interviewed using questionnaires. Data for population obtained from a general census	Sex, age, ethnic group, living area, type of household, crowding, presence of ceiling, quality of foundation and household characteristics i.e. no bathroom indoor, no kitchen indoor, poor quality roof and)	Chi square test for Univariate analyses Multivariable analyses through logistic regression	Age, sex, some ethnic groups, having more than 2 adults in the households (adult crowding), quality of foundation
Odone *et al*., 2013	Malawi, Africa	To assess the relationship between socioeconomic factors at TB in Karonga district	Case control study	Community based Cases and control recruited from Karonga district and matched based on age, se, pop density, area	1707 cases and 2678 controls. all aged from 15 years and above	Participants were interviewed using a questionnaires	Schooling, individual occupation, HOV status, smoking habit, TB contact, distance to health centre, distance to district hospital,	Logistic regression for both Univariate and multivariable analyses	Schooling, individual occupation, HIV status, TB contact,

Ladefoged *et al*., 2011	Green land, North America	To elucidate the social and lifestyle factors associated with TB	Prospective Case control	Hospital based,	146 cases and 584 controls. Case matched to controls based on sex, age and ethnicity. All ages, 4-71 years.	Participants were interviewed using questionnaires on exposures.	Age, sex, ethnicity, BMI, location, occupation, overcrowding, access to tap water, bathroom, toilet, smoking, alcohol, diet, concomitant disease, immunosuppressant treatment	Logistic regression for both Univariate and multivariable analyses	Ethnicity, living in settlement, unemployed, frequent alcohol use, immunosuppressant treatment
Tipayamongkholgul *et al*., 2005	Thailand, Asia	To determine risk factor for developing TB in BCG vaccinated children less than 15 years	Prospective Case control	Hospital based	130 cases and 130 controls. Case matched to controls based on sex, age. Controls recruited form orthopaedic department. all aged less than 15 years	Data obtained from medical record as well as interviews with parents/guardians using structured questionnaire	Father education, mother education, household income, stability of household income, birthweight, frequency of illness, underlying disease, nutritional status, history of TB patient contact, passive smoking, child bedroom ventilation, crowding in child room, average number of person per room,	Logistic regression for both Univariate and multivariable analyses	Passive smoking and crowding in household (however, no overall p values presented, on Wald p values.
Oxlade *et al*., 2012	India, Asia	To investigate the mechanisms in which poverty increases the risk of TB	Cross sectional survey (DHS data)	Community based	198 754 individuals interviewed for the India DHS. All aged from 15 years to 49 years.	Data were obtained through questionnaires, both outcome and	Smoking, tobacco use, indoor air pollution, BMI, diabetes, alcohol use, HIV, age, gender, household density, access to health	Logistic regression for both Univariate and multivariable analyses	tobacco use, indoor air pollution, low BMI, diabetes,, HIV, age, gender, household density,

						exposures were self-reported	insurance, rural/urban,		
Stevens *et al*., 2014	Brazil, South America	A study of socioeconomic and biological risk factors for Tuberculosis in children aged 7-19 years in Recife city	Case control	Community/hospital based	169 cases and 477 controls One case matched three controls based of residential area and age groups, Children aged 7-19 years	Data were obtained through questionnaires. Cases determined through medical records and control recruited from community	Age, alcohol, smoking, contact with TB person at home, relationship to head of house, born in district/or not, literacy, whether head of house was paid for work, head of house income, head of house education, in past week, having pipe water in house, number of goods in house (defined in paper),	Logistic regression for both Univariate and multivariable analyses	Sex, contact with TB in household, relation to head of household , literacy, piped water
Tiemersma *et al*., 2013	Vietnam, Asia	To assess risk factors for TB among young adults 15-34 years	Prospective case control study	Hospital based	Comparison was made between three case groups which were of interest in this study (1) TB cases aged 15-34; (2) Tb cases aged 35 years or above and (3) TB	Data on outcome were taken from medical records. Data on exposures were obtained through	HIV, chronic disease, education, occupation, housing, smoking , alcohol, drug use, residence permit status (KT status), ethnicity, place of registration, and how long person registered with KT status	Logistic regression	Male sex. Ever Smoked tobacco, cigarettes smoked per day, consumes alcohol, have a paid job, self-employed, alcohol cans per month (no overall p values given and these were unadjusted ORs)

					free persons aged 15-34 years. In this review only focused on the comparison made between TB free group and TB cases aged 15-34years	questionnaires			
Hill *et al*., 2006	The Gambia, Africa	To identify risk factors for pulmonary tuberculosis in The Gambia	Prospective Case control study	Hospital based	100 cases and 200 controls. One case matched to two controls based on 10 years age bands and sex. Both cases and controls recruited from OPD. All participants aged 15 years and above	Data were obtained through questionnaires. Both cases and controls were examined for TB to confirm TB (cases) or rule out TB (controls)	Age, sex, ethnicity, history of asthma, diabetes, history of smoking, alcohol consumption, schooling, occupation, BCG scar, gas/electric cooker, building structure/materials, occupation of head of house, any household member with TB, crowding, person per room	Logistic regression for both Univariate and multivariable analyses	Ethnicity, crowding, history of TB in household
Ngadaya *et al*., 2006	Tanzania, Africa	To determine the proportion of smear positive TB among women with a cough attending family planning and maternal	Cross sectional study	Hospital based	A sample of 749 women (out of which only 27 were smear positive). Women	Data collected through study registers at the Family planning and MCH	Age, marital status, education level, occupation, cough duration, clinic attendance, place of consultation, number of visits to any facility,	Chi square test for Univariate analyses Multivariable analyses through logistic regression	Having visited clinic before, HIV/AIDS

		child health clinics			aged 15 years and above	services. The outcome variable was lab confirmed			
Lienhardt *et al*., 2005	Three country study (The Gambia, Guinea Bissau and Guinee Conakry	To study contribution of environmental and host related factors for TB	Prospective Case control	Hospital (cases) and community (controls) based	822 cases and 816 community controls. Study had three groups: cases, household controls and thirdly community control. In this review, only results between cases and community controls were of interest. All participants aged 15 years and above	Data were obtained through questionnaires. TB in cases was lab confirmed. It's not clear in paper how TB in controls was ruled out	Sex, marital status, former TB, family history of TB, smoking, Alcohol, drug, Attaya, BCG scar, HIV status, history of worms, treatment of worms, history of asthma, treatment of asthma, Diabetes, Haemoglobin, number of people in household, number of houses in compound, number of adults in households, person per room, family history of TB, house characteristics :walls, floor, number of windows, water, electricity, latrine, waste), occupation, religion, schooling, ownership of house, ownership of (radio, bicycle, fridge, TV,	Logistic regression for both Univariate and multivariable analyses	Sex, HIV infection, smoking, marital status, history of asthma, family history of TB, number of adults in households ownership of house,

							fan, motorbike), presence of animals		
Kirenga *et al*., 2015	Uganda, Africa	To determine the prevalence of different risk factors among TB patients in Kampala	Cross sectional study	Hospital based	A total of 365 adult TB patients were examines. All participants aged 18 years and above	Data were obtained through questionnaires and TB diagnosis was lab confirmed	Poverty (defined based on daily income), overcrowding, smoking, alcohol use, HIV infection	Proportions	The prevalence found were overcrowding (57.3%), alcohol use (50.7%), HIV (41.4%), poverty (39.5), former smoker (26.3%), family history of TB (17.5%), TB contact (11.5%), diabetes (5.4%) and current smoke (1.4%)
Tocque *et al*., 2001	England, Europe	To determine risk factors for TB	Case control study	Hospital (cases) and community (controls) based	100 cases and 200 controls. One case matched to five controls based on 10 years age bands sex, postcode and ethnic origin. Cases were recruited from Liverpool city communicable disease consultants and controls	Data were obtained through questionnaires. The status of TB in both cases and controls was medically confirmed	Persons per household, migration, car ownership, access to luxury items (microwave, mobile phone, access to satellite TV), education, employment history, diet, alcohol, smoking habits,	Chi square test for Univariate analyses Multivariable analyses through logistic regression	Less likely to be born in UK, more likely to have lived with someone with TB, more likely to have had visitor from their birth country, more likely to have smoked >20 yrs, less likely to have more than one bathroom and less likely to eat dairy every week and less likely to have high blood pressure

					recruited from GP database.				
Tesema *et al*., 2015	Ethiopia , Africa	To assess environmental and host related determinants for TB in Matema district	Case – control study	Hospital (cases) and community (controls) based	218 cases and 437 controls. One case matched to two controls based on 10 years age bands sex, postcode and ethnic origin. Cases were recruited from Patients who were on TB follow up treatment at DOT centres and controls recruited from the community households.	Data were obtained through questionnaires. The status of TB in cases was medically confirmed. Controls were only excluded in they had a cough for two weeks (not lab confirmed)	Ventilation, lighting, number of household members, room size, house size, type of house, family size, solid wastes disposal, TB person in household, sanitation, window size per room, water source, sex, age, education status, occupation status, marital status, income, smoking, chewing Khat, alcohol drinking, malnutrition, Diabetes	Logistic regression for both Univariate and multivariable analyses	Education status, family size, room size per room, history of previous TB, presence of separate kitchen, contact history, house with ceiling, house with floor, house with window,
Kolappan *et al*., 2007	India, Asia	To study the association of biological and behavioural risk factors with pulmonary TB	Cross sectional study	Community based	A cross sectional survey involving 93 945 participants. The status of TB was lab	Data on smoking and alcohol (from men only)were obtained through	Age, sex, smoking (all women were treated as non-smokers), alcohol(all women were treated as non-alcohol drinkers)	Logistic regression for both Univariate and multivariable analyses	Age, sex, smoking, alcohol

					confirmed. All participants aged 15 years and above	questionnaires			

Appendix F) Description of studies reviewed during phase three, part C

Study	Location	Aim	Study design	Sample size	Data collection method statistical test	Authors conclusions
Uchenna *et al*., 2014	Nigeria	To explore knowledge, attitudes and practices, regarding TB and its determinant in urban and rural communities in Enugu state	Population based cross sectional study in Enegu state. Study involve both rural and urban	A total of 1200 people (624 women and 576 men aged 15+years) who have lived in the area for more than six months	Data collected through a pre tested questionnaires. Analysed data with Chi squared test	High awareness of TB was observed in this population. Knowledge of TB transmission was 30.0%, symptoms 61.5% and prevention (14.9%). Generally, urban dwellers had better knowledge compared to rural based respondents. TB stigma was nonetheless less among rural dwellers. The authors recommended that the design and implementation of TB behaviour change campaigns should consider socio-demographic factors.
Mesfin *et al*., 2005	Ethiopia	To assess knowledge of Tuberculosis among the general public	Community based cross sectional survey	A total of 838 (392 female and 424 males) aged 15 + years	Data collected through a pre tested questionnaires. Proportions presented.	Population demonstrates lack of TB knowledge, particularly those from rural areas.
Ma et al., 2015	China	To estimate the level of knowledge, attitudes, health seeking behaviour concerning TB in the public and to examine how those are affected by demographic, socioeconomic and	Community based cross sectional survey. Study involve both urban and rural	10581 (5358 men and 5223 female) aged 12 to 65 years who have lived in the area for more than six months	Data collected through a pre tested questionnaire. Logistic regression used for data analyses	Public awareness of TB in Inner Mongolia was higher than the national (china) target, however there were still gaps in knowledge and differences were observed by socio-demographic variables (ethnicity, occupation, regions. The authors recommended need to educational activities and further studies to monitor trends in TB Knowledge, Attitudes and Practices (KAP).)

Study	Location	Aim	Study design	Sample size	Data collection method statistical test	Authors conclusions
		policy factors in Inner Mongolia				
Salleh *et al*., 2018	Malaysia	To evaluate knowledge, attitude and practice (KAP) towards TB among the community of Kulim Municipal and also to assess factors associated with KAP	Community based cross sectional survey. Urban area	A total of 102 people (69 females and 33 male)– excluding people with TB or whose family members had TB	Data collected through a pre tested questionnaires . t-test and ANOVA used for data analyses	Authors concluded that level of knowledge in this community was moderate, while attitude towards TB was poor. They did not find any association between KAP and socio-demographic variables.
Promtussananon and Peltzer (2005)	South Africa	To investigate public perception bout causes, suggested means of risk reduction and preferred treatment of TB	Community based cross sectional survey, semi-urban area	A total of 80 (aged 11 years+) community members stratified by age and sex. Quota sampling was applied as a sampling method	Data collected through a pre tested questionnaire Analyses done through Pearson Chi Square and correlation test	Basic TB knowledge on the causes of TB was low and need to be increased mong all age groups. Misconceptions on the causes and risk reduction methods were observed. Although majority participants were aware of where to go for TB treatment, other wrong beliefs were evident Less knowledge dominated amongst teenagers, older people and men. Therefore these groups should be target for educational programs
Sreeramareddy *et al*., 2013	India	To provide estimate about prevalence of self-	A secondary analysis of the India	Participants (men 72369 and women 124385) aged 15	Data collected through a pre tested	Knowledge bout TB was very poor as only 29.7% had good TB knowledge (based on the author's operational definition of TB knowledge). Misconceptions about TB prevailed.

Study	Location	Aim	Study design	Sample size	Data collection method statistical test	Authors conclusions
		reported TBH, to assess knowledge and misconception about TB transmission and to determine determinants of correct knowledge bout TB transmission	Population Demographic and Health data. Study involve both urban and rural	years and above recruited through random sampling of households (one person per household).	questionnaires. Proportions and Logistic regression	The authors suggested strengthening of radio and TB as mass media sources of TB knowledge
Wang *et al*., 2008	China	To understand whether and to what extent people know about TB and to understand relation between people knowledge and health seeking behaviour from a gender perspective	A community based cross sectional survey in Yangzhong county. Rural based study	1083 participants (502 men and 581 women) aged 15 years or over. Participants were recruited in systematically selected households.	Data collected through a pre tested questionnaires Proportions, Chi square test, Student's t test, Kruskal Wallis test	The authors concluded that TB knowledge was still unsatisfactory in this population. Women had less knowledge on current TB policy and were less reluctant to actively seek information on TB. Women were more likely to access drug stores or village clinics while majority of men prefer seeking health care in upper level hospitals
Obuku *et al*., 2012	Uganda	To assess TB knowledge in three urban slums and determine associate socio-demographic factors	Population based cross sectional survey in Wobulenzi, Lira and Makindye. Study involve both urban and rural	1361 participants in total aged 18 years (995 men and 370 female). participants in selected areas were Systematically (every third or fifth house).	Data collected through a pre tested questionnaires. Proportions and logistic regression	The authors concluded by saying that there were deficiencies in TB knowledge in this population and that TB advocacy, communication and social mobilisation should consider the determinants of TB knowledge identified in this study

Study	Location	Aim	Study design	Sample size	Data collection method statistical test	Authors conclusions
Gelaw (2015)	Ethiopia	To identify knowledge and socioeconomic factors associate with TB knowledge and awareness among adult population	This was a secondary analyses of the Ethiopian Demographic and Health survey data (a cross sectional study) Study involve both urban and rural	The DHS included 16 515 women aged 15-49 years and 14 110 men aged 15-59 years). DHS employed a two-stage cluster sampling method. Analyses was based on people aged 15-59 years only	Data collected through a pre tested questionnaires . Logistic regression	Authors concluded that TB awareness was higher, although specific knowledge of TB components was very low. The prevalence of low TB knowledge was higher in Ethiopia, especially among females in comparison to males. TB knowledge should take into account specific groups of population with low disease knowledge. Access to mass media should be improved to allow access of TB information. TB information should reach all populations at risk of TB including in-school youths out of school, rural women, unskilled workers and the less educated.
Hoa *et al*., 2009	Vietnam	To describe TB knowledge, TB associate stigma and actions in response to TB symptoms in relation to socio-demographic factors in rural Vietnamese population. Study also obtained perspectives on appropriate TB communication	Community based cross sectional survey conducted in a rural area	A total of 12 143 participants (5069, men and 7074 women) aged from 15 years. The study villages where randomly selected based on size.	Data collected through a pre tested questionnaire. Chi square One way ANOVA,	Authors concluded that TB knowledge was not quite adequate and that social stigma on TB still prevailed. The fear and TB related stigma appeared to be experienced by women more than by men.

Study	Location	Aim	Study design	Sample size	Data collection method statistical test	Authors conclusions
		channel at community level				
Mushtaq *et al*., 2010	Pakistan	To highlight socio economic disparities regarding TB KAP	A community based cross sectional study in urban and rural Punjab province	1080 participants (826 men and 254 women) aged 20 years and above who were interviewed from randomly selected villages.	Data collected through a pre tested questionnaires. Chi square test	Level of good TB knowledge was poor. Good knowledge was associated with higher education, high income and good housing.
Tolossa *et al*., 2014	Ethiopia	To assess community TB knowledge, attitudes and practices	A community based cross sectional study in Shinile town	410 participants (206 men and 204 women) aged 18 years and above were interviewed from randomly selected villages.	Data collected through a pre tested questionnaire. Chi square Logistic regression	Authors concluded that participants had basic TB knowledge, although there were some misconceptions. They found that TB knowledge was associated with age, family income and education
Mukhtar *et al*., 2012	Libya	To assess knowledge of TB in the general public of North East Libya	A community based cross sectional study in five cities in North east Libya	1000 participants (496 men and 504 women) aged 18 years and above were interviewed	Data collected through a pre tested questionnaire. Chi square Logistic regression	Authors concluded that TB knowledge, particularly concerning TB diagnosis, transmission modes, and prevention risk factors was inadequate.

Study	Location	Aim	Study design	Sample size	Data collection method statistical test	Authors conclusions
Luba *et al*., 2019	Lesotho	To assess knowledge about TB in the public of Lesotho.	This was a secondary analyses of the Lesotho Demographic and Health survey data (a cross sectional study) Study involve both urban and rural	The DHS included 6621 women aged 15-49 years and 2626 men aged 15-59 years). DHS employed a two-stage cluster sampling method. Analyses was based on people aged 15-49 years only	Data collected through a pre tested questionnaire. Chi square Logistic regression	Authors concluded that TB knowledge was adequate although the were some misconceptions regarding specific components of TB
Noremillia and Rahman (2015)	Malaysia	To assess level of TB KAP in the community and identify modifiable factors for TB prevention	A cross sectional study conducted in Kajang district covering six residential areas (urban communities)	384 participants (169 men and 215 women) aged 18 years and above were interviewed	Study used both parametric and non-parametric tests i.e. t-test, Kruskal Wallis	Study authors concluded that reported that participants demonstrated satisfactory TB knowledge (cases, transmission, treatment) and the majority of participants demonstrated moderate practices and attitudes towards TB
Bati *et al*., 2013	Ethiopia	To assess knowledge about TB in the public of Ethiopia.	A community based cross sectional study in rural areas of Itang district, Ethiopia	422 participants (247 men and 175 women) aged 19 years and above were interviewed	Data collected through a pre tested questionnaire. Chi square Logistic regression	The authors concluded that TB knowledge was low specially regarding the causes, symptoms

Study	Location	Aim	Study design	Sample size	Data collection method statistical test	Authors conclusions
Gilani and Khurram , 2012	Pakistan	To assess TB knowledge and impact of the disease in the general public of Pakistan	A nation-wide cross sectional study in all provinces in Pakistan	2742 participants (1422 men and 1320 women) aged 18 years and above were interviewed	Data collected through a pre tested questionnaire. Chi square	Authors concluded that there were misconception on all components of TB including symptoms, transmission, diagnosis and treatment
Anochie *et al*., 2013	Nigeria	To assess level of TB knowledge and attitudes towards TB and health seeking behaviour	A community based cross sectional study in Imo state Nigeria (rural populations)	1186 participants (538 men and 648 women) aged 18 years and above were interviewed	Data collected through a pre tested questionnaire. Only frequencies presented. No statistical tests conducted	Authors in this study also concluded that there were misconception on all components of TB including symptoms, transmission.
Haasnoot *et al*., 2010	Tanzania	To assess TB Knowledge, Attitude and Practices in the general public in Tanzania	A community based cross sectional study in Simanjiro district in Tanzania (rural populations)	105 participants (69 adult population and 36 school children) aged 18 years and above were interviewed	Data collected through a pre tested questionnaire. Chi square	The authors found that TB knowledge was poor in the studied sample, especially regarding areas such as TB and HIV/AIDS. Better knowledge was observed among school going children than the general population
Navio *et al*., 2002	Philippine	To assess the role of socio-economic determinants on TB knowledge and	A community based cross sectional survey conducted in	3978 participants (1933 men and 2045 women) aged 18 years and above were interviewed	Data collected through a pre tested questionnaire.	The authors concluded that TB knowledge was poor, as shown by the low mean score value. They also found that intention to access health care was poor among people of low socio-economic backgrounds

Study	Location	Aim	Study design	Sample size	Data collection method statistical test	Authors conclusions
		health seeking behaviour	the general population of Metro Manila Philippine		Chi square Logistic regression	

Appendix G) Study questionnaire (Phase three)

TB RESEARCH QUESTIONNAIRE

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Objective: To examine risk factors and TB knowledge, attitudes and practices in Windhoek health district, Namibia

Date of interview: ___________________________

Interview location: ___________________________

Screening question: Are you 18 years of age or older? And *have you lived in this township area for at least 6 months*? **(Only people answering YES to both questions are eligible to participate)**

Note to participants*:* The answers you will provide during this interview will not be released to anyone and your name or contact detail will not be recorded on this questionnaire. Please note that your participation is voluntary and you are free to discontinue the interview at any time. Thank you for agreeing to participate, we are now ready to begin the interview.

Participant identification number		☐
SECTION 1: DEMOGRAPHIC AND GENERAL QUESTIONS		
Q1.01	**What is your age range**? *(please indicate **exact age** near the appropriate box)*	
(a)	18-30 years	☐
(b)	31-40 years	☐
(c)	41-50 years	☐
(d)	Over 50 years	☐
Q1.02	**Gender?**	
(a)	Male	☐
(b)	Female	☐
Q1.03	**What is the highest level of education you have completed?**	
(a)	No School	☐
(b)	Primary *(grade 1 to 7)*	☐
(c)	High school *(grade 8-12)*	☐
(d)	Higher/tertiary education (VTC, College, University etc)	☐

Q1.04	**Do you currently have paid employment?**	
(a)	Employed	☐
(b)	Self-employed	☐
(c)	Unemployed	☐
SECTION 2. HEALTH SEEKING BEHAVIOUR		
Q2.01	**Where do you mostly go if you are sick, or to treat a general health problem** *(tick one answer)*	
(a)	Private clinic or hospital	☐
(b)	Government clinic or hospital	☐
(c)	Traditional healer	☐
(d)	Clinic run by an nongovernmental organisation or church	☐
(e)	Other ___________________________________	☐ specify
Q2.02	**How often do you generally seek health care at a clinic or hospital** *(tick one answer)*	
(a)	Twice a year or more	☐
(b)	Once per year	☐
(c)	Less than once per year but at least twice in the past 5 years	☐
(d)	Once in the past 5 years	☐
(e)	Never in the past 5 years	☐
SECTION 3. TB KNOWLEDGE AND AWARENESS		
Q3.01	**Where do you currently hear information or learn about Tuberculosis or TB** *(tick all that are mentioned by respondent)*	
(a)	Newspapers	☐
(b)	Radio	☐
(c)	TV	☐
(e)	Billboards, Brochures, posters and other printed materials	☐
(f)	Health workers at clinics/hospitals	☐
(g)	Family, friends, neighbours and colleagues	☐
(h)	Religious leaders	☐
(i)	Teachers	☐

(j)	Other ______________________________	☐ specify
Q3.02	**In your opinion, how serious a disease is TB** *(tick one answer)*	
(a)	Very serious *(life-threatening)*	☐
(b)	Somewhat serious (not really serious)	☐
(c)	Not very serious (not life-threatening)	☐
Q3.03	**How much of a problem do you think TB is in Windhoek**	
(a)	Very serious (many TB cases)	☐
(b)	Somewhat serious (average)	☐
(c)	Not very serious (few TB cases)	☐
Q3.04	**What are the common signs and symptoms of TB?** *(Please tick all that are mentioned by respondent)*	
(a)	Rash	☐
(b)	Coughing or sneezing	☐
(c)	Cough that lasts longer than 3 weeks	☐
(d)	Coughing up blood	☐
(e)	Severe headache	☐
(f)	Nausea	☐
(g)	Weight loss	☐
(h)	Fever	☐
(i)	Fever without clear cause that lasts more than 7 days	☐
(j)	Chest pain	☐
(k)	Shortness of breath	☐
(l)	Ongoing fatigue	☐
(m)	Do not know	☐
(n)	Other____________________________________	☐ specify
Q3.05	**How can a person get TB?** *(please tick all that are mentioned by respondent)*	
(a)	Through handshake	☐
(b)	Through the air when a person with TB coughs or sneezes	☐
(c)	Through sharing dishes or eating from same plate	☐

(d)	Through touching items in public places (doorknobs, handles in transportation, etc.	☐
(e)	Do not know	☐
(f)	Other ___________________________	☐ specify
Q3.06	**How can a person prevent getting TB?** *(please tick all that are mentioned by respondent)*	
(a)	Avoid shaking hands	☐
(b)	Covering mouth and nose when coughing or sneezing	☐
(c)	Avoid sharing dishes	☐
(d)	Washing hands after touching items in public places	☐
(e)	Closing widows at home	☐
(f)	Through good nutrition	☐
(g)	By praying	☐
(h)	Do not know	☐
(i)	Other ____________________________	☐ specify
Q3.07	**In your opinion, who is most at risk of TB infection?** *(please tick only one)*	
(a)	Anybody is most at risk	☐
(b)	Poor people	☐
(c)	Homeless people	☐
(d)	Alcoholics	☐
(e)	Drug users	☐
(f)	People living with HIV/AIDS	☐
(g)	People who have been in prison	☐
(h)	Other __________________________	☐ specify
Q3.08	**Can TB be cured?**	
(a)	Yes	☐
(b)	No	☐
(c)	Don’t know/not sure	☐
Q3.09	**How can someone with TB be cured?** *(please tick all that are mentioned by respondent)*	
(a)	Herbal or traditional remedies	☐

(b)	Home rest without medicine	☐
(c)	Praying	☐
(d)	Specific drugs given at hospitals/clinics	☐
(f)	Do not know	☐
(g)	Other ____	☐ specify
SECTION 4. TB ATTITUDES AND CARE-SEEKING BEHAVIOUR		
Q4.01	**Do you think you can get TB?**	
(a)	Yes (because)____________________________________	☐ give reason
(b)	No (because)______________________________________	☐ give reason
Q4.02	**What would be your FIRST reaction if you found out that you have TB?** *(please tick one)*	
(a)	Fear	☐
(b)	Surprise	☐
(c)	Shame/Embarrassed	☐
(e)	Sadness or hopelessness	☐
(f)	Other____	☐ specify
Q4.03	**Who would you be most comfortable talking to about your illness if you had TB? (***please tick all that are mentioned by respondent)*	
(a)	Doctor or other medical worker	☐
(b)	Spouse	☐
(c)	Parent	☐
(d)	Child(ren)	☐
(e)	Other family member *(aunties, uncles, cousins etc)*	☐
(f)	Close friend	☐
(g)	No one	☐
(h)	Other ____	☐ specify
Q4.04	**What would you do if you thought you had symptoms of TB?** *(tick one answer)*	
(a)	Go to health facility	☐
(b)	Go to the pharmacy	☐

(c)	Go to traditional healer	☐
(d)	Pursue other self-treatment options (herbs etc.)	☐
Q4.05	**If you had symptoms of TB at what point would you go to the health facility?** *(please tick one answer)*	
(a)	When treatment on my own does not work *(go to Q4.07)*	☐
(b)	When symptoms that took like TB signs last for 3-4 weeks (*go to Q4.07)*	☐
(c)	As soon as I realise that my symptoms might be related to TB *(go to Q4.07)*	☐
(d)	I would not go to the doctors go to *Q4.06*	☐
Q4.06	**If you would not go the health facility, what is the reason?** *(Please tick all that are mentioned*)	
(a)	Not sure where to go	☐
(b)	Cost	☐
(c)	Difficulties with transportation /distance to clinic	☐
(d)	Do not trust the health workers	☐
(e)	Do not like the attitude of health workers	☐
(f)	Cannot leave work (overlapping work hours with health facility operating hours)	☐
(g)	Do not want to find out that something is really wrong	☐
(h)	Other ___________________________	☐ specify
Q4.07	**How expensive do you think TB diagnosis and treatment is at Government health clinics/hospitals?** *(please tick one)*	
(a)	It is free of charge	☐
(b)	It is reasonably priced	☐
(c)	It is somewhat /moderately expensive	☐
(d)	It is very expensive	☐
(e)	I don’t know	☐
Q4.08	**How expensive do you think TB diagnosis and treatment is at Private hospitals/clinics?** *(please tick one)*	
(a)	It is free of charge	☐
(b	It Is reasonably priced	☐
(c)	It is somewhat /moderately expensive	☐

(d)	It is very expensive	☐
(e)	I don't know	☐
SECTION 5. TB ATTITUDES AND STIGMA		
Q5.01	**Do you currently know people who have TB?**	
(a)	Yes	☐
(b)	No	☐
Q5.02	**In general which statement is closest to your feeling about people with TB disease?** *(tick one answer)*	
(a)	I feel compassion and desire to help	☐
(b)	I feel compassion but tend to stay away from these people(I fear them because they may infect me)	☐
(c)	It is their problem, I cannot get TB	☐
(d)	I have no particular feeling	☐
(e)	Other ______________________________	☐ specify
Q5.03	**In general, in your community, how do you think a person who has TB is usually treated?** *(tick one answer)*	
(a)	Most people reject him or her	☐
(b)	Most people are friendly but they generally try to avoid him or her	☐
(c)	The community mostly supports and helps him or her	☐
(d)	Other ______________________________	☐ specify
Q5.04	**Do you think that HIV positive people should be concerned about getting TB?**	
(a)	Yes ,WHY____	☐ give reason
(b)	No, WHY____	☐ give reason
(c)	I don't know	☐
SECTION 6. TB AWARENESS AND SOURCES OF INFORMATION		
Q6.01	**Do you currently feel well informed about TB?**	
(a)	Yes	☐
(b)	No	☐
Q6.02	**Do you wish you could get more information about TB?**	

(a)	Yes	☐
(b)	No	☐
Q6.03	**What are the THREE sources of information that you think can most effectively reach people like you with information about TB?** *(please tick the 3 most effective sources)*	
(a)	Newspapers and magazines	☐
(b)	Radio	☐
(c)	TV	☐
(d)	Billboards	☐
(e)	Brochures, posters and other printed materials	☐
(f)	Health workers	☐
(g)	Family, friends, neighbours and colleagues	☐
(h)	Religious leaders	☐
(i)	Teachers	☐
(j)	Other ______________________________	☐ specify
MY ADDITIONAL QUESTIONS **SECTION 7: GENERAL AND DEMOGRAPHIC INFORMATION**		
Q7.01	**What is you residential area?**	
(a)	Windhoek Suburb A	☐
(b)	Windhoek Suburb B	☐
Q7.02	**How long have you lived in this residential area?**	
(a)	6 months to 1 year	☐
(b)	More than 1 year to 3 years	☐
(c)	More than 3 years	☐
Q7.03	**Marital status?**	
(a)	Single	☐
(b)	Married	☐
(c)	Divorced or Widowed	☐

SECTION 8: HOUSEHOLD CHARACTERISTICS

Please answer the following questions describing your household characteristic

Q8.01	**How many people live in your house (including you)?**	
(a)	_____ (Indicate total number of household members including respondent)	
Q8.02	**Number of people sleeping in the same bedroom?**	
(a)	Every one sleeps alone in their bedroom	☐
(b)	2 -3 people sharing a room	☐
(c)	4 or more people sharing a room	☐
Q8.03	**Does your house have at least one window for each room?**	
(a)	Yes	☐
(b)	No	☐
Q8.04	**What type of fuel does your household MAINLY use for cooking?** *(Tick one answer)*	
(a)	Electricity/Gas	☐
(d)	Charcoal/Wood	☐
(f)	Agriculture crops	☐
(g)	Animal Dung	☐
(c)	Other ____	☐ Specify:
Q8.05	**Where is cooking usually done in your house?** *(tick one)*	
(a)	In a room used for living/sleeping	☐
(b)	In a separate room used as kitchen	☐
(c)	In a separate building used as kitchen	☐
(d)	Outdoors	☐
Q8.06	**In the past four weeks, was there ever no food to eat of any kind in your house, because of lack of money to buy food?**	
(a)	Yes	☐
(b)	No -(go to Q9.01)	☐
Q8.07	**How often did this happen in the past four weeks?**	
(a)	1=Rarely (once or twice in the past four weeks)	☐
(b)	2 = Sometimes (three to ten times in the past four weeks)	☐
(c)	3 = Often (more than ten times in the past four weeks)	☐

SECTION 9: BEHAVIOURAL INFORMATION

Q9.01	**How often do you have a drink containing alcohol?**	
(a)	Never *(go to Q9.04)*	☐
(b)	Monthly or less	☐
(c)	2 to 4 times a month	☐
(d)	2 to 3 times a week	☐

(e)	4 or more times a week	☐
Q9.02	**How many drinks containing alcohol do you have on a typical day when you are drinking?**	
(a)	1 or less *(e.g. just a glass)*	☐
(b)	2 to 4	☐
(c)	5 or more	☐
Q9.03	**How old were you when you first started drinking alcohol?**	
	______Years old:	
Q9.04	**Do you currently or have you ever smoked tobacco or cigarettes?**	
(a)	Never smoked (go to Q9.08)	☐
(b)	Currently smoke	☐
(c)	Smoked only in the past	☐ **Specify year stopped? _____**
Q9.05	**On average, how many cigarettes did you smoke or do you currently smoke on days that you smoke?**	
	___________________number of cigarettes per day	
Q9.06	**How old were you when you first started smoking tobacco or cigarettes?**	
	_______________________years old	
Q9.07	**If you use to smoke or you currently smoke, where do you mostly smoke?**	
(a)	Inside the house	☐
(b)	Outside the house	☐
Q9.08	**Is there another person who smokes or use to smoke in your house?**	
(a)	Yes	☐
(b)	No (go to Q9.10)	☐
Q9.09	**If yes, where does/did the person smoke?**	
(a)	Inside the house	☐
(b)	Outside the house	☐

SECTION 10: EXPERIENCES OF TB

Q10.01	**How would you rate your general TB knowledge?**	
(a)	A little	☐
(b)	Somewhat/average	☐
(c)	A lot	☐
Q10.02	**Have you ever been told by a health care worker that you have TB?**	
(a)	Yes	☐
(b)	No – *(go to Q10.06)*	☐
Q10.03	**When you were last diagnosed with TB?**	
(a)	During the last 2 years	☐
(b)	More than 2 years ago	☐
Q10.04	**Were you living in this area when you were diagnosed with TB**	
(a)	Yes	☐
(b)	No	☐Specify

Q10.05	**Were you sleeping alone in your bedroom when you had TB?**	
(a)	Yes	☐
(b)	No, with family members	☐
Q10.06	**Has anyone in your current household been diagnosed with TB?**	
(a)	Yes	☐
(b)	No – (*go to Q10.09).*	☐
Q10.07	**When was the person last diagnosed with TB ?**	
(a)	During the last 2 years	☐
(b)	More than 2 years ago	☐
Q10.08	**Was the person sleeping alone in their bedroom during the time they had TB?**	
(a)	Yes	☐
(b)	No, with family members	☐
Q10.09	**Do you know anyone among your extended family members (but not staying with you currently) who has ever been diagnosed with TB?**	
(a)	Yes	☐
(a)	No	☐

SECTION 11: STIGMA AND COMMUNITY RISK PERCEPTIONS

Q11.01	**If a member of your family got tuberculosis, would you want it to remain a secret or not?**	
(a)	Yes a secret, WHY_____________________________	☐ give reason
(b)	No, WHY NOT__________________________________	☐ give reason
(c)	Don't know/not sure	☐
Q11.02	**Do you think people in your current residential area are at risk of being infected with TB?**	
(a)	Yes, WHY_____________________________________	☐ give reason
(b)	No, WHY____________________________________	☐ give reason

SECTION 12: COMMUNITY IMPACT

Q12.01	**Has there been any TB awareness campaign(s) conducted in the last 12 months in your current residential area?**	
(a)	Yes	☐
(b)	No *(go to Q12.03)*	☐
Q12.02	**Do you think the campaign(s) conducted had potential to make an impact in your residential area?**	
(a)	Yes, WHY____	☐ give reason
(b)	No, WHY____	☐ give reason

Q12.03 Are there any other comments you would like to make?

___

Appendix H: Survey consent form

RESEARCH CONSENT FORM

Participant identification number: _______________

PROJECT TITLE: THE SPATIOTEMPORAL ANALYSIS OF TUBERCULOSIS AND INVESTIGATION OF RISK FACTORS AND RISK PERCEPTIONS FOR TB INFECTION AND DISEASE IN WINDHOEK HEALTH DISTRICT, NAMIBIA

PRINCIPAL RESEARCHER: ANNA MN SHIFOTOKA

1. I hereby confirm that I have been briefed and understood the study objectives as explained to me and was granted opportunity to ask questions and the answers provided were satisfactory.
2. I understand that I am free to withdraw from the survey at any point without providing any justification.
3. I agree to completing the questionnaire with questions aimed at assessing risk factors and risk perceptions for Tuberculosis in Windhoek
4. I am aware that for purposes of quality control, the answers I will provide in the questionnaire might be available to other members of the research (in addition to the principal researcher), and also to the ethical governing committees/structures
5. I agree to take part in the survey

Name of participant:	Signature:	Date
Name of researcher:	Signature:	Date:

Appendix I) Description of studies reviewed during phase four

Publication	Mangesho *et al*., 2007	Liefooghe *et al*., 1997	Buregyeya *et al*., 2011	Bennstam *et al*., 2004	Long et al., 2001	Vukovic *et al*., 2011	Nyasulu *et al*., 2018	Dodor and Kelly (2009)	Bam *et al*., 2014
Aim	To determine the level of TB KAP and its treatment in Mpwapwa district	To explore beliefs and knowledge about TB and to study health seeking behaviour as well as attitudes toward the disease	To explore knowledge and perceptions of TB in communities members and their health seeking behaviours in Igaga/Mayuge-Kampala	To explore and describe the underlying attitudes towards TB in	To describe the socio-economic impact of TB in Vietnam, with reverence to gender differences concerning stigma and isolation	To investigate the knowledge and beliefs about transmission, symptoms treatment about TB as well as attitudes toward TB patients among Roma community in Belgrade	To explore TB knowledge, beliefs and attitudes among community members and people diagnosed with TB in Ntcheu district	To explore attitudes and behaviours of community members towards TB	To assess the illness perception of TB and identify the facilitators and barrier of health seeking practices among the residents of Badda slum in Dhaka
Setting	Tanzania (both rural and urban communities)	Kenya (both rural and urban communities)	Uganda (urban)	Democratic republic of Congo (DRC)	Vietnam (regions including both urban and rural areas)	Serbia (Urban based study conducted in Belgrade)	Malawi	Ghana (In an urban district)	Bangladesh
Research design	Interview study (Focus Group Discussions)	Interview study (Focus Group Discussions)	Interview study (Focus groups and key informant interviews)	Grounded theory design	Interview study (16 Focus Group Discussions)	Interview study (Focus Group Discussions)	A phenomenological interview study (Focus groups and key informant interviews)	Interview study (Focus Group Discussions)	Interview study
Participants	Participants consisting of both men and women). Participants aged between 21-72 years.	Participants included people who had no TB (4 FDGS with community members) and one FDG with TB patients. 22 men and 19 women from urban and rural areas	Men and women who are caretakers of school children, adolescents, TB patients, school heads, opinion leader. Include TB patients and non-TB patients.	23 women and 26 men aged 21- 44 years. Include TB patients and non-TB patients.	Include TB patients and non-TB patients.	24 participants (9 men and 15 women) aged 19 to 55 years	(With 6-8 participants). Participants included people who never had TB and those who had TB	(With 7-12 participants). Participants included people who never had TB and those who had TB	22 participants (11 men and 11 women) aged 18 years or older
Sampling/ Recruitment method	Participant recruitment not explicitly stated.	Convenience sampling though local chiefs	Participants recruited through a purposive sampling method	Purposive sampling	Purposive sampling	Not explicitly stated	Purposive sampling	Purposive sampling	Convenience sampling

Data collection methods	6 Focus Group Discussions Each group had at least 7 participants.	5 Focus Group Discussions (with 8-13 participants).	Data were collected through FGD, and interview discussions, using pre-tested instruments.	Data were collected through eight Focus Group Discussions	Data were collected through Focus groups Discussion (with 8-10 participants per group)	Data were collected through FGD,	Data were collected through one on one interviews and Focus Group Discussions. 16 one on one interviews and 8 Focus Group Discussions	Data were collected through one on one interviews and Focus Group Discussions. 66 one to one interviews and 16 Focus Group Discussions	In-depths interviews using semi-structured interviews
Data analysis	Not explicitly stated (however it looks like they followed some steps of thematic analysis)	Not explicitly stated	Thematic content analyses	Thematic content analyses	Grounded theory analyses technique	Not explicitly stated (however it looks like they followed some steps of thematic analysis)	Inductive content analyses	Analytic approach informed by grounded theory	Not explicitly stated
Themes obtained	Paper did not divide the results section into qualitative themes. However a table was provided capturing participants discussions under the headings TB cause of infection, transmission, symptoms,	General perceptions about TB; Local terms; Recognition of early signs and symptoms; Transmission and causes of TB; Health seeking behaviour; delay is seeking appropriate treatment; Decision to seek medical attention; curability, treatment; community attitude towards TB patients	Names used for TB in the community; Beliefs about causality; who gets TB; Care seeking for TB; Factors influencing treatment choice. potential for cure; Stigma towards TB patients	TB integrated in Body and life, Isolation, Shame and Contempt, Uncertainty/Unsteadiness	Tuberculosis diagnosis-a death penalty; TB increases poverty, Isolation (within family, community); Socio economic consequences and control	Themes were similar to topic guide headings which were: Knowledge of modes of transmission; knowledge about symptoms; knowledge about treatment; opinions about most appropriate measures for TB prevention; sources of information about TB; attitudes towards TB patients	TB a very difficult disease; TB risk perceptions, the spread of TB, TB coupled with HIV; identifying TB suspects; Health system related issues and TB diagnosis; The success of medical intervention; TB is curable; TB is curable; role of complementary medicine in managing TB; Resource constraints versus real life challenges; Issues	The study results were captured under three themes which were: Fear of infection and participatory restrictions; social and physical distance; Expectations of unavoidable interactions	Local term for TB, illness perception; Health seeking practice and associated factors

							pertaining to lifestyle adaptation; Supportive role of significant others		
Conclusion	Authors stated that their participants demonstrated moderate to low knowledge of TB. Authors mentioned that participants' narratives demonstrated that TB was mainly linked to HIV/AIDS.	Authors concluded by saying that the community demonstrated good TB knowledge. TB was perceived to be a fatal disease. The importance of IEC was highlighted.	Authors concluded that there was a perception that TB suspects access health care services late, and people mostly prefer traditional healers. Factors such as lack of money for transport , heavy pill burden; health care workers attitudes, fear of HIV diagnosis, beliefs in traditional healers hindered timely access to health services. care	The community defined TB as a disease establishing distance at individual and community level. This is manifested through stigmatization and isolation. There were no gender differences in participants attitudes or stigmatization of ancestral treatments	The level of TB knowledge in this community was good,	Community members were aware of the seriousness of the disease and modes of transmission. However, misconceptions were evident. Roma community y indicated strong beliefs in Doctors.	Participants showed good practices and attitude rewards TB and indicated the presence of social support at family level for TB patients.	Author concluded that TB was a stigmatised disease. TB patients were victimised and avoided and because of their condition and these practices according to the authors may result in TB health seeking delay as a result of fear of being diagnosed or may result in treatment abandonment.	All interviewed patients seemed to have some level of knowledge but it was not adequate. Most thought they were at low or medium risk of being infected with TB. Participant's beliefs and perceptions about TB shaped their health seeking behaviours. Challenges such as lack for money for transport

Appendix J) Qualitative study topic guide

SPECIFIC OBJECTIVE:

- ✓ To explore the risk perceptions for TB infection in the general population

GENERAL AREAS TO BE EXPLORED IN THE QUALITATIVE INTERVIEWS

1. Knowledge and general feeling about the TB situation in the area
2. TB risk perception at individual level
3. Community TB risk perception
4. Views on Stigma as a result of TB
5. Health seeking behaviours

SPECIFIC OPENING QUESTIONS UNDER EACH AREA

1. Knowledge and general feeling about the TB situation in the area

- ✓ Knowledge questions:
    - Tell me more about how TB is acquired and transmitted
    - What would you say are the things that facilitates TB infection
    - What are the symptoms of TB?
    - Please tell me more about what you know about TB treatment.
- ✓ General view questions:
    - Please share with me your views of TB disease in your community
    - Based on your knowledge/experience, why would you say TB is a problem/not a problem in this area

2. TB risk perception at individual level

- ✓ Can you tell me about your views regarding your own personal risk of contracting TB?
- ✓ Why would you say you are /you are not at risk of getting TB? (Tell me about the things that you think put you at risk of TB or are protecting you from getting TB)
- ✓ Can you tell me about other things that you implement or plan to do at individual level to prevent getting TB?

3. Community TB risk perception

- ✓ What would you say about the risk of TB infection among people in Havana
- ✓ Why would you say the community is /is not at risk of getting TB? (Tell me about the things that you think predict/protective of TB in your community

- ✓ Tell me more about activities happening in your community that are aimed at providing TB education?
- ✓ What do you think can be done within your community to reduce TB infection/transmission

4. Views on Stigma as a result of TB

- ✓ What are your views on sharing with other community members that a member of your family or yourself has TB?
- ✓ Tell me more about ways of how community members might react towards a person with TB in your area?
- ✓ Based on your knowledge/ experience what you say should be done within your community to minimise any sort of the stigma attached to this disease?

5. Health seeking behaviours

- ✓ Tell me about your own health service uptake in general? (*At what point do you seek health care when not feeling well, where do you first seek treatment when ill)?*
- ✓ Tell me about the things that will encourage you to seek care /discourage you from seeking care *(is it related to knowledge, financial, family support, access and availability of health services , stigma, attitude about health services)*
- ✓ What are your general opinions on health service uptake for people in your area?
- ✓ Tell me more about what you think should be done to improve/ enhance health seeking behaviours among people in your community

Is there anything else you would like to add to what we discussed? Or perhaps something that you thought about as we were discussing?

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