Analysing the Spatial Distribution of Tuberculosis Case Notification Rates in Katsina State

Makplang James Milaham
(Nigeria)

56th Master of Public Health/International Course in Health Development
KIT (Royal Tropical Institute)
Vrije Universiteit Amsterdam (VU)
Analysing the Spatial Distribution of Tuberculosis Case Notification Rates in Katsina State

A thesis submitted in partial fulfilment of the requirement for the degree of Master of Science in Public Health

By

Makplang James Milaham (Nigeria)

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Dedication

I specially dedicate this thesis to the loving memory of my mother, Mary C. Milaham. She passed away on 22nd December 2019 due to complications related to spinal TB.
Acknowledgement

I would like to express my sincere gratitude to the Dutch Government, Ministry of Foreign Affairs and the Nuffic OKP Scholarship Fund for giving me the opportunity to study at the prestigious KIT Royal Tropical Institute.

I would like to thank the KIT ecosystem for providing me with a comfortable learning environment, memorable experiences, and an invaluable network. I am sincerely grateful to my thesis and academic advisors for their guidance and patience throughout the whole process of writing this thesis.

I especially want to thank the new and amazing friends I made in the Netherlands and my classmates. I was humbled by the immense support I got from you after the death of my mother.

I would like to express my heartfelt gratitude to my family for being my pillar throughout this learning process. Thank you for the sacrifices you made to ensure I am comfortable while I study. I love you all dearly.

Last but not least, I appreciate God for bringing me this far.
## Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tbody>
<tr>
<td>CF</td>
<td>Case Finding</td>
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<tr>
<td>CNR</td>
<td>Case Notification Rates</td>
</tr>
<tr>
<td>DOTS</td>
<td>Directly Observed Therapy Short-Course</td>
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<tr>
<td>GADM</td>
<td>Geographical Administrative Areas</td>
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<tr>
<td>GIS</td>
<td>Geographic Information System</td>
</tr>
<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
</tr>
<tr>
<td>IHVN</td>
<td>Institute of Human Virology, Nigeria</td>
</tr>
<tr>
<td>IQR</td>
<td>Interquartile Range</td>
</tr>
<tr>
<td>KNCV</td>
<td>KNCV Tuberculosis Fund (Previously known as Koninklijke Nederlandse Centrale Vereniging tot bestrijding der Tuberculose)</td>
</tr>
<tr>
<td>LGA</td>
<td>Local Government Areas</td>
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<tr>
<td>LISA</td>
<td>Local Indicators of Spatial Autocorrelation</td>
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<tr>
<td>MATCH</td>
<td>Mapping and Analysis for Tailored Disease Control and Health System Strengthening</td>
</tr>
<tr>
<td>NBS</td>
<td>Nigerian Bureau of Statistics</td>
</tr>
<tr>
<td>NGO</td>
<td>Non-Governmental Organisations</td>
</tr>
<tr>
<td>NSP-TB</td>
<td>National Strategic Plan for TB Control</td>
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<tr>
<td>NTBLCP</td>
<td>National Tuberculosis, Leprosy and Buruli Ulcer Control Program</td>
</tr>
<tr>
<td>PLHIV</td>
<td>People Living with HIV</td>
</tr>
<tr>
<td>SASCP</td>
<td>State AIDS and STI Control Program</td>
</tr>
<tr>
<td>SD</td>
<td>Standard Deviation</td>
</tr>
<tr>
<td>SDG</td>
<td>Sustainable Development Goal</td>
</tr>
<tr>
<td>STBLCP</td>
<td>State Tuberculosis, Leprosy and Buruli Ulcer Control Program</td>
</tr>
<tr>
<td>TB</td>
<td>Tuberculosis</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organisation</td>
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<td>UN</td>
<td>United Nations</td>
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### Definition of Key Terms

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
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<tbody>
<tr>
<td><strong>Active Case Finding</strong></td>
<td>A process that systematically identifies people with presumed active TB, in a predetermined target population, using tests, examinations or other procedures that can be rapidly applied (WHO, 2015).</td>
</tr>
<tr>
<td><strong>Bacteriologic Diagnostic Rate</strong></td>
<td>The proportion of TB cases diagnosed using a bacteriologic technique (Yuen et al., 2017; van Gurp et al., 2020).</td>
</tr>
<tr>
<td><strong>Case Notification Rates</strong></td>
<td>The number of TB cases notified to the national TB program per 100,000 population per year (Rood et al., 2018).</td>
</tr>
<tr>
<td><strong>Geocoordinates</strong></td>
<td>The geographic coordinates of a place or event represented using longitude and latitude (Schema, 2015).</td>
</tr>
<tr>
<td><strong>Health Facility Density</strong></td>
<td>The number of health facilities offering TB diagnostic services per 100,000 population (van Gurp et al., 2020).</td>
</tr>
<tr>
<td><strong>Notified Cases</strong></td>
<td>The number of TB cases reported to the National TB program (Uplekar et al., 2013).</td>
</tr>
<tr>
<td><strong>Positivity Yield</strong></td>
<td>The proportion of presumptive TB cases with a positive test result (Narendran and Swaminathan, 2016; van Gurp et al., 2020).</td>
</tr>
<tr>
<td><strong>Poverty Rate</strong></td>
<td>The proportion of the population living below the national poverty line (Wong et al., 2013).</td>
</tr>
<tr>
<td><strong>Presumptive TB Case</strong></td>
<td>A person any of the symptoms suggestive of active TB infection. These symptoms include cough of ≥ 2 weeks, fever, night sweat, weight loss and lymph node enlargement (Aye et al., 2018).</td>
</tr>
<tr>
<td><strong>Presumptive TB Rate</strong></td>
<td>The number of presumptive TB cases per 100,000 population.</td>
</tr>
<tr>
<td><strong>Spatial</strong></td>
<td>An adjective that describes events or occurrences related to geographical areas (Collins English Dictionary, 2020).</td>
</tr>
<tr>
<td><strong>Xpert Diagnostic Rate</strong></td>
<td>The proportion of TB cases diagnosed using Gene-Xpert MTB/RIF® machine.</td>
</tr>
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Abstract

**Introduction:** Katsina state is one of the least privileged states in Nigeria with a high poverty rate, low literacy level and an ailing health system. Despite its small population, it accounted for 4.5% of unnotified tuberculosis (TB) cases in Nigeria in 2015. It was earmarked as a high priority state along with 12 others by the National Tuberculosis Leprosy and Buruli Ulcer Control Program (NTBLCP). This study seeks to describe the spatial distribution of TB Case Notification Rates (CNR) across Local Government Areas (LGAs), find possible explanations for the patterns observed and guide the NTBLCP in finding the missing TB cases.

**Methodology:** Using 2017 to 2019 TB case finding data along with population, HIV testing, poverty rate, geocoordinates of diagnostic facilities and shapefiles, a retrospective ecological study was conducted. The data were analysed with QGIS, GeoDa and Microsoft Excel. Moran's I and LISA were used to locate and quantify hotspots. At the same time, the coverage of microscopy and Gene-Xpert facilities was assessed on QGIS using a 5km and 20km radius, respectively.

**Key Findings:** The CNR of the state and 29 of the 34 LGAs increased steadily from 2017 to 2019. Hotspots of high CNRs were also identified in 2017 (Moran’s I=0.106, p-value=0.090) and 2018 (Moran’s I=-0.020, p-value=0.370). While CNRs increased along with presumptive TB rates across most LGAs in the state over the years, the positivity yield and bacteriological and Xpert diagnostic rates decreased. Bacteriological and Gene-Xpert coverage were 78% and 49% respectively.

**Conclusion:** The results suggest that the efforts of the TB program have had some impact on the CNR; however, new approaches (e.g. the MATCH approach) need to be explored for the state to meet the NTBLCP target. Additionally, more equitable distribution of diagnostic facilities could contribute to an increase in the CNR and bacteriological diagnostic rate.

**Keywords:** Tuberculosis, Case Notification Rates, Spatial Analysis, Human Immunodeficiency Virus (HIV), Poverty and Access.

**Word Count:** 11,354
Introduction

Over the last five years, I have worked with implementing partners and various agencies of the ministry of health on HIV and TB in Nigeria. "Where are the missing cases?" is one of the most frequently asked questions by donors that is almost always not satisfactorily answered by implementing partners and government agencies. Together with the decline in funding for the TB program and the need to maximise available resources, this spurred my interest into learning Quantum Geographical Information System (QGIS) and the Mapping and Analysis for Tailored Disease Control and Health System Strengthening (MATCH) analytical framework when I got to KIT Royal Tropical Institute. I saw the need to analyse and interpret program data in a different way that provides rich and in-depth information through simple maps (i.e. outside the conventional tables and bar charts). This made me take up the challenge of writing my thesis on the spatial distribution of TB in one of the states with the highest burden of unnotified cases in Nigeria.

This thesis looks at the spatial distribution of CNR across the 34 LGAs of Katsina State over space and time and provides possible explanations for the patterns observed. Findings from the study will be disseminated to relevant government agencies, implementing partners and civil society organisations. Recommendations will also be made to the TB program based on the findings of the research. Finally, I hope this will motivate the TB program and implementing partners to adopt the MATCH framework for the routine analysis of subnational level data sets.

This study consists of five chapters: Chapter 1 provides an overview of TB, policy milestones in Nigeria, and Katsina State; Chapter 2 looks at the problem statement, justification, objectives, and methodology; Chapter 3 presents the results of the study; Chapter 4 includes a discussion of the results, and Chapter 5 concludes the research and provides recommendations.
Chapter 1: Background Information

1.1 Overview of Tuberculosis

1.1.1 Global Burden of Disease

Tuberculosis (TB), the leading cause of death globally by a single infectious agent among adults, has plagued humans for several millennia (Grosset and Chaisson, 2017; Furin, Cox and Pai, 2019; WHO, 2019a). It was declared a public health emergency by the World Health Organisation (WHO) in 1993 and has maintained that status to date with no country reported having eliminated the disease. The WHO and United Nations (UN) are committed to putting an end to the global TB epidemic and envisage zero disease, deaths and suffering by 2035 through the End TB Strategy (Nathavitharana and Friedland, 2015; WHO, 2019a). Additionally, the Sustainable Development Goals (SDGs) also seek to eliminate the disease through two targets of SDG 3—Good health and wellbeing (targets 3.3 and 3.8) and two targets of SDG 17—Partnerships for the goals (targets 17.18 and 17.19) by 2030 (UN, 2015).

Despite being a curable and preventable disease, an estimated 10 million people (57% men, 32% women and 11 children) fell ill because of TB across the globe in 2018. The disease burden varies significantly across countries with a range of 5 to 500 cases per 100,000 population and a global average of 150 cases per 100,000. Eight countries (Bangladesh, China, India, Indonesia, Nigeria, Pakistan, Philippines, and South Africa) accounted for over two-thirds of the burden of the disease. In the same year, over 1.5 million people died as a result of the infection. Over the last two decades, an estimated 58 million deaths were averted through TB diagnosis and treatment. The global incidence of TB is falling at a rate of 2% annually. However, to reach the 2020 milestone of the WHO End TB strategy, current efforts need to be doubled (WHO, 2019d).

1.1.2 Transmission, Symptoms and Diagnosis

TB is an infectious airborne bacterial disease caused by the bacilli *Mycobacterium tuberculosis*. The bacilli commonly affect the lungs (pulmonary TB); however, they can cause disease in other parts of the body in 15% of cases (extra-pulmonary TB) (Grosset and Chaisson, 2017; Houda Ben et al., 2018; WHO, 2019a). It is transmitted through the air via infectious droplets from persons with the active disease when they cough, sneeze, speak, laugh, or spit. The bacillary load of the source person, proximity to the source and duration of exposure greatly influences the transmission of the disease to uninfected persons. Most people remain asymptomatic after they get infected (latent TB/disease); however, about 10% of people develop symptoms (active TB disease), and if left untreated, TB carries around a 50% mortality rate. Cough with sputum usually characterises active pulmonary TB and at times with blood, chest pains, fever, weight loss, weakness and night sweats (Heemskerk et al., 2015; WHO, 2019d).

Many countries rely on sputum smear microscopy for the diagnosis of active pulmonary TB. Microscopy, however, has low sensitivity (detects about half of TB cases) and cannot detect drug resistance. A rapid test Gene Xpert MTB/RIF® that simultaneously detects TB and resistance to rifampicin within two hours has been recommended by WHO as the initial diagnostic test in all presumptive TB cases (Churchyard et al., 2015; WHO, 2019d). Other laboratory tests used for the detection of drug resistance include culture and drug susceptibility testing (C/DST) which assesses resistance to most anti-TB drugs; and line probe assay (LPA) which only detects resistance to rifampicin and Isoniazid (Gilpin, Korobitsyn and Weyer, 2016). Non-bacteriological methods that involve radiography (e.g. x-ray, ultrasound scan, magnetic resonance imaging and computerised
tomography scan), immunodiagnostic tests (e.g. tuberculin skin test and the interferon-gamma release assays) and clinical examination are also used to diagnose TB (Dunn, Starke and Revell, 2016; NHS, 2019).

1.1.3 TB/HIV Co-infection

Human Immunodeficiency Virus (HIV) and TB have a complex relationship that synergistically increases their prevalence, morbidity, and mortality. HIV weakens the body's immune system and has been described as a significant risk factor in the acquisition and progression of TB infection. HIV places people living with HIV (PLHIV) with latent or new TB infection at risk of developing active tuberculosis (Goldfeld and Ellner, 2007; Venketaraman, 2018). A PLHIV is estimated to have a 16–27 times greater risk of developing the disease compared to someone who is HIV-negative. Furthermore, HIV masks the signs and symptoms of TB, thus making coinfected persons a unique source of covert infection (Narendran and Swaminathan, 2016). TB is the leading cause of death among PLHIVs globally and accounted for a third of HIV/AIDS-related deaths. Over half of PLHIVs living with TB are unaware of their co-infection and are not receiving any care (Getahun et al., 2010; UNAIDS, 2019). Nigeria and 19 other countries accounted for 83% of TB and HIV co-infection globally. Low antiretroviral coverage (55%) and enrolment of PLHIVs on TB preventive therapy using the anti-TB drug isoniazid (29%) have been identified as ardent drivers of co-infection in Nigeria (AVERT, 2018).

1.1.4 TB Case Finding

TB case finding (CF) or detection is the entry point into the TB treatment cascade. It is a very crucial step in the elimination of TB. CF entails the use of a systematic approach to identifying presumptive TB cases through screening and establishing diagnosis using one or more diagnostic tests. Several strategies have been used alone or in combination with others to identify persons infected with the disease (WHO, 2015) and technology has been continuously incorporated into the process. Some notable examples of technology incorporated into this approach include the use of mathematical models, Computer-Aided Diagnosis for TB (CD4TB) and Geographic Information System (GIS).

GIS technology has yielded considerable insights into the way maps can be used in disease surveillance. GIS helps show where diseases more frequently occur and the generation of hypotheses about causes behind the spatial distribution of diseases (Eisen and Eisen, 2014). This technology has enhanced TB CF and provided vital information for targeted control efforts in different parts of the world such as The United States of America (Moonan et al., 2004), Bangladesh (Rood et al., 2018) and The Gambia (Touray et al., 2010).

1.2 TB Policy Milestones in Nigeria: From DOTS to End TB Strategy

Policies and regulations govern the prevention, diagnosis and treatment of TB as well the protection of the rights of persons with TB and groups vulnerable to the disease (Jumoke et al., 2018). In 1993, Nigeria adopted the Directly Observed Therapy Short-Course (DOTS) in a bid to eliminate TB. The DOTS strategy led to an improvement in the diagnosis of the disease using sputum smear microscopy, an increase in the number of DOTS centres and a rise in case notification (Ogbuabor and Onwujekwe, 2019). The Stop TB Partnership strategy was subsequently implemented in 2012 to build on the achievement of DOTS through expansion and enhancement of DOTS; addressing the needs of special groups (TB-HIV coinfected persons, persons with multi-drug resistant TB and other vulnerable population); health system strengthening; engaging all care providers; empowering people living with TB and their communities through partnerships; and promoting research (Nigeria Stop TB Partnership, 2012).
In conformity with the SDGs, Nigeria incorporated the End TB Strategy which is built on the pillars of bold policies and supportive systems; integrated patient-centred care and treatment; and research and innovation (WHO, 2016).

The National Strategic Plan for TB Control (NSP-TB) 2015 to 2020 aligns Nigeria with the End TB Strategy. It seeks to provide high quality, equitable and patient-centred TB preventive, diagnostic and treatment services for all Nigerians. The NSP-TB aimed at increasing the annual number of notified TB cases from 100,401 in 2013 to 625,844 by 2020; Case Notification Rates (CNR) from 57.3 cases per 100,000 in 2013 to over 287 cases per 100,000 by 2020 and increasing diagnostic facility density from a ratio of 1 facility per 109,285 population (2013) to less than 1 per 50,000(2020). The plan was designed to achieve these objectives by strategically strengthening and scaling up diagnostic facilities with particular focus on areas with a high burden of TB and inadequate diagnostic coverage (NTBLC.P, 2015).

1.3 Overview of Katsina State

Katsina State, one of the 36 states of the Federal Republic of Nigeria, is situated in the Sahel Savanah of North-Western Nigeria with a land area of 24,192 square km (Encyclopedia Britannica, 2020; Federal Republic of Nigeria, 2020). The state is relatively flat and lies within the tropics between latitude 11°00’ to 13°25N and Longitude 6°45’ to 9°05E (Katsina State Government, 2016a). It is bounded by Kano and Jigawa states to the east; Kaduna state on the South; Zamfara state on the west and shares international borders with the Republic of the Niger on the North (United Nations, 2014). It has three senatorial zones/districts (North/Daura, Central/Katsina and Southern/Funtua Zones) (Abaje et al., 2015) which are further broken down into 34 Local Government Areas (LGAs) as shown in Figure 1 below. The state capital located in Katsina LGA (Katsina State Government, 2016a). The state has an average temperature that ranges between 21°C - 30°C and two distinct climatic seasons; the rainy season which begins in May and ends in September and the dry harmattan season which lasts for about seven months of the year from October to April (Katsina State Government, 2016a).

Figure 1: Map of Katsina State showing the three zones and 34 LGAs (GADM, 2018)
The state has a population of over 7.8 million people (National Bureau of Statistics, 2018) spread across its 34 Local Government Areas (Katsina State Government, 2016b). The state constitutes mainly of the Muslim Hausa and Fulani groups and a few Maguzawas/animistic Hausas (Katsina State Government, 2016b; Encyclopedia Britannica, 2020). The state has a young population with over 48% of the population under the age of 15 years. The population consist slightly of more males (50.8%) than females (48.2%) (City Population, 2017). Over 56.4% of the state's population live below the national poverty line of 376 Nigerian Naira per day (National Bureau of Statistics, 2020) or 1.04 US Dollars per day based on the Central Bank of Nigeria exchange rate of 360.5 Nigerian Naira to 1 US Dollars on 22nd June 2020 (Central Bank of Nigeria, 2020), which is higher than the national average of 40.1% (National Bureau of Statistics, 2020). Rural dwellers account for 90% of the state's population live below the national poverty line of 376 Nigerian Naira per day (National Bureau of Statistics, 2020) or 1.04 US Dollars per day based on the Central Bank of Nigeria exchange rate of 360.5 Nigerian Naira to 1 US Dollars on 22nd June 2020 (Central Bank of Nigeria, 2020), which is higher than the national average of 40.1% (National Bureau of Statistics, 2020). Rural dwellers account for 90% of the state's population (MNCH2 Nigeria, 2020) with food and cash crop farmers and cattle rearers making up a large proportion of the state's workforce (Encyclopedia Britannica, 2020; Federal Republic of Nigeria, 2020). The state's unemployment rate was pegged at 14.3% in 2018 (National Bureau of Statistics, 2020).

Katsina state is one of the least educationally developed states in the country and has an estimated adult literacy rate of 30% which is less than half of the national average of 62% (NBS, 2016). The state has one of the least BCG (Bacille Calmette Guerin) vaccination coverage rates in the country at 29% (national BCG vaccination average coverage = 53.5%) with children of younger and uneducated mothers at a higher risk not been vaccinated against TB and other vaccine-preventable diseases (NBS, 2016).

The NTBLCP operates semi-autonomously as a unit under the Department of Public Health of the Ministry of Health. Its structure follows the three tiers of government, i.e. Federal/National, State and LGA (Refer to Annex 3 for structure of NTBLCP). The Katsina State TB, Buruli Ulcer and Leprosy Control Program (STBLCP) coordinates the activities of LGA TB control programs and collaborates with implementing partners to implement the program. The government and donors fund (e.g. Global Fund to fight AIDS, TB and Malaria and the United States Agency for International Development) the program across the states to provide free diagnostic and treatment services (NTBLCP, 2015).
Chapter 2: Problem Statement, Justification, Objectives and Method

2.1 Problem Statement

Nigeria accounted for an estimated 4.3% (429,000 cases) of TB cases globally and over 162,000 deaths were attributed to the disease in 2018. Over the past two decades, the incidence of TB has stagnated despite efforts made by the government and foreign agencies to eliminate the disease (WHO, 2019c). In 2018, only 7 million TB cases were reported globally out of an estimated 10 million new cases. Underreporting of confirmed cases and underdiagnosis (i.e. people lack access to TB services or are not diagnosed when they do) have been identified as the two significant challenges responsible for this gap. Nigeria is one of the ten countries that jointly account for 80% of this gap with 12% (360,000 TB cases) of the global unnotified/undiagnosed cases reported to be within its borders (WHO, 2019a). Furthermore, only 24% (106,533 notified cases) of cases in the country were reported in the same year despite having the highest disease burden in Africa (WHO, 2019c).

A survey conducted by the NTBLCP in 2019 revealed that 60% of TB patients live below the poverty line, with 71% of TB-affected households faced with catastrophic costs as a result of the disease (WHO, 2019b). TB disproportionately affects the poor, especially those living in resource-constrained settings (Rocha et al., 2011). Findings from several studies show that the burden of the disease rises and falls with social development (Dye et al., 2009). Poverty-related factors such as undernutrition and poor housing increase the risk of infection and progression of latent infection to active disease. Additionally, the associated cost of care and lost income can impede care, worsen impoverishment, and increase the risk of poor outcomes and recurrence despite the availability of free TB services and drugs. Furthermore, the stigmatisation of poor households affected by TB poses an additional barrier to accessing care (Rocha et al., 2011; Wingfield et al., 2014; WHO, 2019b).

Poor people do not only bear the highest risk of acquiring TB infection but also have to contend with the barrier of inequitable distribution of health facilities and human resources (Rocha et al., 2011; Oladimeji, Tsoka-Gwegweni and Udoh, 2017). The distance to health facilities has been reported in several studies to deter patients from accessing care (Mauch et al., 2011). Katsina state has inadequate facilities to cater to the needs of its populace. Additionally, the referral system within the state is barely effective as a result of the paucity of resources and the inaccessibility of receiving facilities by most people (Abubakar and Abdurrahman, 2018).

A structured laboratory network system along with new diagnostic equipment were introduced in the country as part of the National Strategic Plan 2014 (NTBLCP, 2015); however, this has been significantly limited by the uneven distribution of healthcare centres providing TB services, inadequate infrastructure and a lack of human resource (Obasanya et al., 2015). Furthermore, despite the improvements made in monitoring, evaluation and reporting of the disease, TB surveillance is still weak in Nigeria (Ogbuabor and Onwujekwe, 2019). The incorporation of mathematical models (Ogbuabor and Onwujekwe, 2019) and GIS for disease surveillance have been advocated for severally, but this is yet to be applied to TB surveillance in Nigeria.

Katsina state accounts for 4.5% of unnotified cases in the country. Together with 12 other states and the capital territory, the state accounted for over 50% of unnotified cases across Nigeria. The NTBLCP has prioritised these states and the Federal Capital Territory (FCT) for an intensified intervention package which includes: active case-finding in key populations; community...
outreaches; scale-up technologies for rapid diagnosis, public-public- and public-private partnerships to improve case-finding; and expansion of treatment capacity to meet the increased needs of the population (NTBLCP, 2015).

2.2 Justification

Potential presumptive TB patients encounter several barriers that could either hinder them from being diagnosed, treated or notified to the relevant health agencies/organisations. Firstly, patients might fail to recognise symptoms due to a lack of knowledge, misperception, or stigma (Hadley and Maher, 2000; Gosoniu et al., 2008; Stop TB Partnership, 2016). Secondly, patients might fail to seek healthcare due to transportation cost, distance to a health facility or poor perception of the quality healthcare services (Needham et al., 2004; Abebe et al., 2010; Stop TB Partnership, 2016). Thirdly, the lack of trained healthcare workers might result in a failure to recognise presumptive TB cases (Floyd et al., 2002; Stop TB Partnership, 2016). Lastly, the failure to provide high-quality diagnosis consequent to insensitive screening or diagnostic testing, the inability of the presumptive case to produce sputum, or delays encountered in between testing and diagnosis might lead to loss to follow-up (Joseph et al., 2004; Stop TB Partnership, 2016).

As with other infectious diseases, the TB epidemics varies across different regions and even between groups in a region. Spatial analysis is used widely to describe patterns of TB epidemic. Alene et al., for instance, identified hotspots in districts of areas located near international borders (Afar, Gambela, Oromiya and Somali) which are commonly characterised by poor access to health care services and a high number of immigrants (Alene et al., 2019). Similarly, Obaromi et al. found higher TB incidence rates in urban areas of a province in South Africa compared to rural areas (Obaromi, Ndege and Yongsong, 2019) while Kakchapati et al. reported higher cases notification rates in the Terai regions of Nepal compared to the mountainous areas (Kakchapati, Yotthanoo and Choonpradup, 2010).

Furthermore, Alene et al. identified HIV hotspots among TB patients in some districts (Afar, Amhara and Gambela) in Ethiopia (Alene et al., 2019) with Couceiro et al. also reporting such clusters in Porto, Portugal (Couceiro, Santana and Nunes, 2011). Existing literature also shows a higher prevalence of TB in population groups with low educational status and low socioeconomic status in Kenya (Yonge et al., 2016), Cameroon (Nana Yakam et al., 2014), Brazil (Harling and Castro, 2014), South Africa (Shaweno et al., 2018) and China (Wang et al., 2019). These studies show that TB is not evenly spread across geographical regions and even within groups in the same geographic area, therefore, control efforts should not be either.

Addressing challenges to the diagnosis and notification of TB cases requires the adoption of policies to meet local epidemic needs as well as the equitable allocation and efficient utilisation of resources. During the process of advocacy and mobilisation of resources, TB programmers need to ensure that decision-makers appreciate the impact of increasing coverage of TB services to the general population and target groups on the incidence of the disease as well as areas in the pathway that are responsible for the gaps in the program (Bakker et al., 2017). This research seeks to be a valuable tool for informed decision-making and the development of tailored interventions to increase case detection as no similar knowledge currently exists in the state. A spatial analysis of the distribution of the disease alongside the facilities providing TB services can guide the NTBLCP and other organisations on the allocation of resources for case-finding activities. Information on access to TB services, TB case notifications and treatment, can provide useful insight into where and why TB cases are "missed" by the NTBLCP surveillance systems (Rood et al., 2018).
GIS and spatial analysis have been used in several studies across Africa to describe diseases; however, only a few have focused on TB in Nigeria with none conducted in Katsina state. This study will provide better insights into case notification rates across the various LGAs in the state while addressing knowledge gaps in the patterns of TB distribution and generating hypotheses for other research that could further improve TB case finding in the state. The study could also provide insights into the planning of interventions that could improve case finding, thus, contributing to a reduction in the transmission and incidence of the disease by ensuring that target populations are adequately covered.

2.3 Objectives
The objective of this study is to analyse the spatial distribution of TB case notification rates in relation to TB diagnostic services across the 34 LGAs of Katsina State. Other (specific) objectives include:

1. To describe the trend of TB case detection across all LGAs and identify spatial clustering of TB CNR at the LGA level.
2. To assess the spatial relationship between TB notification and geographical coverage to TB diagnostic services and poverty across all LGAs.
3. To examine the spatial relationship between HIV and TB across the LGAs.
4. To disseminate findings and make recommendations to the Government, Non-Governmental Organisations (NGOs) and other relevant organisations to guide them in optimizing limited resources to increase the CNR.

2.4 Methods
2.4.1 Design
This study focuses on secondary data analysis of routinely collected TB monitoring and evaluation data. The study follows a retrospective ecological study design which allows for the (secondary) analysis of aggregate data.

This study design compares disease occurrence to other variables in a population. As such, findings from this study need to be applied cautiously at the individual level as well as smaller population units under each LGA as associations in these units could differ significantly from those observed in this study.

2.4.2 Data Collection and Collation
Quarterly facility-level TB case finding data from 2017 to 2019 across 422 health facilities supported by the Katsina STBLCP were obtained from the Katsina State Ministry of Health through Katsina STBLCP. These data were used for the calculation of Case Notification Rates (CNR) and other variables across the 34 LGAs of the state. Additionally, 2019 HIV cascade data was also acquired from the Katsina State Ministry of Health through the Katsina State AIDS and STI Control Program (Katsina SASCP).

Coordinates of health facilities providing TB diagnostic services and digital maps of the state were derived from the Nigerian Health Facility Registry (Federal Ministry of Health, 2019) and Geographical Administrative Areas (GADM) (GADM, 2018) respectively and used to visualise all collated data using GIS software. The population and population density data were acquired from the City Population (City Population, 2017), Nigerian Bureau of Statistics (NBS) and World Pop (WorldPop, 2020) respectively. Data on poverty rates across the LGAs were obtained from the World Bank Group through Energydata.info (World Bank Group, 2020).
Facility level TB and HIV data and geocordinates of the facilities were cleaned and compiled on one Excel sheet. Data on the facility level sheet were summarised according to LGAs on a second Excel sheet. Additional information such as the estimated population and poverty rate for the various LGAs were added on the second Excel sheet. Each Excel sheet was imported into the GIS software as a single file. Unique identifiers were assigned to all geographical units (LGAs), and the same code was updated on the imported Excel file containing the summarised LGA data and spatial information. Spatial information and summarised LGA data were subsequently merged and visualised on the GIS software. Facility level data was also imported into the GIS software and visualised directly. All the spatial information was visualised using WGS 1984 UTM Zone 22Scs.

2.4.3 Variables
TB CNR was selected as the primary variable for the analysis. It is defined as the number of TB cases notified to the national health authority over a period of time per 100,000 population irrespective of a patient’s previous history of TB treatment (new or relapse TB case), site of infection (pulmonary or extra-pulmonary TB case) or method of diagnosis (bacteriologically, clinically, or radiologically diagnosed TB). The CNR for each LGA was calculated by dividing the number of all TB cases in an LGA by the LGA’s population and multiplying by 100,000 (WHO, 2013a, 2018; Stop TB Partnership, 2016). The CNR provides an indication on how effective TB programs are at finding people with active TB and diagnosing them correctly as well as describing the burden of disease over time (Bakker et al., 2017).

Other variables (secondary variables) used for the analysis were selected because of the role they play in the development of an active TB infection and the availability of LGA-level data for these indicators. TB CNR was compared to the following secondary variables:

Socioeconomic Status

Low socioeconomic status is frequently described as an important determinant of TB infection. Several studies have established that people with a low socioeconomic status bear a higher risk and burden of the disease (Dye et al., 2009; Lönnroth et al., 2009; Rocha et al., 2011; Harling and Castro, 2014). Their vulnerability lies in the fact that they possess little or no capacity to negotiate for quality health services, healthy diets, good housing conditions and other basic social amenities which predisposes them to conditions that encourage the transmission of the disease.

PLHIV as a Key Population Group

Aside from people with low socioeconomic status certain groups in the population such as PLHIV (Narendran and Swaminathan, 2016), miners (Stuckler et al., 2011), migrants (Dhavan et al., 2017), children under-five years (Luzzati et al., 2017), elderly (Cheng et al., 2020), the malnourished (Chandrasekaran et al., 2017), prisoners (Dara et al., 2015) and refugees (De Vries et al., 2016) carry a significantly higher risk of acquiring TB and developing an active TB disease. PLHIVs are an important sub-group of interest because of the high mortality attributed to TB within this group and the complex synergistic relationship between TB and HIV (Goldfeld and Ellner, 2007; Getahun et al., 2010; Narendran and Swaminathan, 2016; Venketaraman, 2018).

TB Program Efforts

TB program efforts describe the performance of the program over time. The presumptive TB rate, positivity yield, bacteriological diagnostic rate, Xpert diagnostic rate and health facility density were used to assess the effort of the program in identifying presumptive and actual TB cases. Presumptive TB cases per 100,000 population gives an indication of how well TB programs can
identify presumptive cases in a population and the type of screening tool that is more appropriate for the population. Positivity yield provides some insight into the kind of population tested; a low positivity yield gives an indication that the wrong population might be tested while a yield greater than 10% might suggest that only highest risk individuals or those with advanced active TB disease are evaluated thus limiting the impact of case finding. Bacteriological diagnostic rates could provide information on over- or under-diagnosis e.g. a very high rate among children could be because of underdiagnosis of paucibacillary and extra-pulmonary disease. Lastly, facility density looks at the distribution of the facilities across the LGAs and compares it to their population to provide an idea of the burden placed on the health system of each LGA (Yuen et al., 2017).

Geographical Access TB Diagnostic Services

Access to TB, HIV and Malaria services remain low and inequitably distributed across Africa, posing a threat to the attainment of universal health coverage on the continent (WHO, 2014). High TB case notification rates have been linked to areas with better access to TB diagnostic and treatment services in Ethiopia (Dangisso, Datiko and Lindtjorn, 2015). In an ideal situation where the entire population have access to all TB services and all detected cases are reported to the National TB Program (NTP), the CNR could be equated to the incidence rate. In such a scenario, changes in the trend of the CNR will be reflected in the incidence rate provided that the efficiency of case finding remains constant (Jindal et al., 2017).

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>DEFINITION</th>
<th>SOURCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Variable:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TB Case Notification Rate</td>
<td>The number of TB cases notified to the national TB program per 100,000 population.</td>
<td>National Bureau of Statistics (NBS)/City Population and STBLCP</td>
</tr>
<tr>
<td>Socioeconomic Status:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poverty Rate</td>
<td>The percentage of the total population living below the national poverty line.</td>
<td>World Bank</td>
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<tr>
<td>PLHIV as a Key Population:</td>
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<td></td>
</tr>
<tr>
<td>New HIV Positive Cases</td>
<td>The number of new HIV positive persons identified.</td>
<td>SASCP</td>
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<tr>
<td>TB Program Effort:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presumptive TB Rate</td>
<td>The number of presumptive TB cases identified per 100,000 population.</td>
<td>NBS/City Population and STBLCP</td>
</tr>
<tr>
<td>Positivity Yield</td>
<td>The Percentage of presumptive TB cases that were diagnosed of TB irrespective of the diagnostic method.</td>
<td>STBLCP</td>
</tr>
<tr>
<td>Bacteriologic Diagnostic Rate</td>
<td>The percentage of TB cases diagnosed using a bacteriologic technique.</td>
<td>STBLCP</td>
</tr>
<tr>
<td>Xpert Diagnostic Rate</td>
<td>The percentage of TB cases diagnosed using Xpert MTB/RIF®.</td>
<td>STBLCP</td>
</tr>
<tr>
<td>Health Facility Density</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(TB Diagnosis)</td>
<td>The number of health facilities offering TB diagnostic services per 100,000 population (disaggregated into Gene Xpert and Microscopy).</td>
<td>National Bureau of Statistics (NBS)/City Population and STBLCP</td>
</tr>
</tbody>
</table>

Table 1: List of variables, their definitions, and data source

2.4.4 Analysis

Facility level TB program data for Katsina state was collated, cleaned, and summarised on a single excel sheet. CNR was calculated using the number of notified TB cases and the population of the LGA and expressed in cases per 100,000 population. The summarised facility-level data were further aggregated into an LGA level summary on a different excel sheet. Both facility level and
LGA level data were visualised using Quantum Geographical Information System (QGIS) version 3.10.2-A Coruña and analysed using GeoDa version 1.14.0 and Microsoft Excel.

**Descriptive Statistics**

Descriptive statistics were used to describe the CNR and secondary variables. The range, mean, median, interquartile range (IQR) and standard deviation were presented. CNR and variables related to program efforts were presented from 2017 to 2019. The number of units (facilities or LGAs) with missing data were also highlighted and excluded from the analysis.

Descriptive mapping was also done using QGIS to visualise CNR and all secondary variables as well as the number of presumptive and diagnosed TB cases.

**Spatial Autocorrelation**

The GeoDa software was employed for spatial analysis. The spatial autocorrelation tool, Global Moran's Index (Global Moran's I), was used to assess the overall pattern and trend of TB CNRs. Global Moran's I statistics is a correlation coefficient that assesses the extent to which the variable(s) of geographical units are similar or dissimilar. It works with the null hypothesis that the attribute being analysed is randomly distributed across all geographical units. The index is bounded by -1.0, and 1.0 with a Moran's I value of -1.0 indicating perfect dispersion, 0 indicating perfect randomness and 1.0 indicating perfect clustering (Fischer and Getis, 2010).

Additionally, Local Indicators of Spatial Autocorrelation (LISA) was used to locate and characterise clusters of geographical units with high (hot spots) and low (cold spots) TB CNR. A significance level of 5% was used for the LISA and Moran's I test.

**Coverage Analysis**

QGIS was used to estimate the proportion of the population covered by TB diagnostic services. Population density files were obtained from WorldPop and analysed with geo-coordinates of facilities providing TB diagnostic services to estimate the proportion of people covered by TB services using a 5km radius by applying a 0.045° buffer to create a 5km catchment area for each facility. The catchment areas were dissolved to avoid double counting of the population in overlapping catchment areas (e.g. populations residing within the 5km catchment area of two or more facilities). The layer was subsequently clipped to the boundaries of Katsina to discard catchment areas outside state boundaries. Similarly, Coverage of Gene Xpert MTB/RIF® facilities was calculated using a wider radius of 20km.

**2.5 Analytical Framework**

The Mapping and Analysis for Tailored Disease Control and Health System Strengthening (MATCH) analytical framework was used for this research. The MATCH framework strives to reach the 90-90-90 TB goals (reach 90% of all people with TB, reach at least 90% of the key populations and achieve at least 90% treatment success for all people diagnosed with TB) by increasing the capacity and accountability of TB programs in the planning of timely and locally tailored interventions aimed at identifying and treating people with TB. This framework encourages a move away from the "one-size-fits-all" approach to an approach that uses disaggregated geographical, temporally and demographical data along with sub-national TB data for tailored planning and monitoring of TB programs. Collated data is visualised and analysed
using QGIS software to identify program challenges and weakness (Bakker et al., 2017). See Figure 2 below for an overview of the MATCH Framework.

![Figure 2: Schematic Overview of the MATCH Analytical Framework (Bakker et al., 2017).](image)

The MATCH framework (See Figure 3) consists of two domains: "Know your local TB epidemic" and "Understand the local TB response". Knowing your local TB epidemic entails an understanding of the various underlying causes that are responsible for the variation in TB case notification rates across the regions of the country by using subnational TB data to monitor changes in the burden of the disease over time; compare subnational and local data; and evaluate the relationship between CNR, estimated disease burden and diagnostic coverage. Whereas, Understanding the local TB response maps the pathway of care (as seen in Figure 4) and highlights bottlenecks related to access to care, diagnosis and treatment (Bakker et al., 2017).

![Figure 3: The MATCH Analytical Framework (Bakker et al., 2017).](image)

The Patient pathway that the MATCH framework employs for analysis was adopted from Piot's model of healthcare access, as seen in Figure 4. Building on the knowledge that a proportion patients fail to access the next level of care due to certain barriers, Piot's model provides a framework to analyzes how patients are lost along the cascade of care from exposure to conditions that increases one's risk of acquiring an illness, the onset of symptoms, diagnosis down to treatment. The MATCH approach, on the other hand, follows the cascade but adds additional information to the data being analysed by comparing the variable(s) of a geographical area to those of its neighbours which is very useful in identifying hot and cold spots. Furthermore, this
comparison accounts for geographical dependencies which could be due to patient movement and a high level of transmission between neighbouring areas (Rood et al., 2018).

For this study, only the sections of the pyramid linked to case notification (i.e. from population to notified) as shown in Figure 4 will be used along with the MATCH framework due to the unavailability of treatment and treatment outcome data as at the time of this study. Additionally, the only key population considered in this study was PLHIVs because of unavailability of LGA level data on other key population groups such as miners, immigrants, and malnourished children. The analysis and discussion of results for this study will follow the MATCH framework. The Piot’s model will be used to analyse the TB case finding cascade and provide more information to the last step of the MATCH framework that entails mapping the pathway of care.
Chapter 3: Results

3.1 Descriptive Statistics

3.1.1 Case Notification Rates (Primary Variable)
From 2017 to 2019, case notification rates of TB in Katsina state increased from 62 to 98 cases per 100,000 population. CNRs in all LGAs have gradually increased over these years with the exception of Dutsinma, Jibia, Katsina, Kankia, Kusada and Rimi LGAs where lower CNRs were reported in 2019 compared to 2017 as shown in Figure 5. Bakori (631%, 2017 CNR=29 cases per 100,000 population), Baure (526%, 2017 CNR=21 cases per 100,000 population) and Kankara (500%, 2017 CNR=21 cases per 100,000 population) had the highest proportional increase in CNR over the past three years in the state. The number of notified cases also increased over the past three years, along with the case notification rates. Additionally, higher rates were initially reported in the North of the state, but by 2019 this shifted to the South.

In 2017, 4894 cases of TB were notified to the TB program. The highest CNR was seen in Katsina LGA (177 cases per 100,000 population) and the lowest CNR was seen in Zango LGA (15 cases per 100,000 population). The distribution of CNR across the LGAs of the state was not symmetrical and had a median of 49 cases per 100,000 population with an interquartile range (IQR) of 35 cases per 100,000 population.

In 2018, no data was reported to the TB program from Safana LGA; thus, the LGA was excluded from the analysis. Kaita had the lowest CNR (11 cases per 100,000 population) while Charanchi had the highest CNR (221 cases per 100,000 population). The distribution of the 2018 CNR across the LGAs of the state was not symmetrical and had a median of 49 cases per 100,000 population with an IQR of 43 cases per 100,000 population.

In 2019, the lowest CNRs were seen in Kusada and Sandamu LGAs (20 cases per 100,000 population) while the highest CNR was seen in Funtua LGA (232 cases per 100,000 population). The distribution of the CNR across the LGAs of the state is asymmetrical and had a median of 78. The mean and standard deviation for the CNR across the LGAs was 94 and 49.7, respectively.
<table>
<thead>
<tr>
<th>Year</th>
<th>Cases Notified</th>
<th>Mean</th>
<th>SD</th>
<th>Median</th>
<th>IQR</th>
<th>Min</th>
<th>Max</th>
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<td>33</td>
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<td>143</td>
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<td>95</td>
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<td>666</td>
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<td>177</td>
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<td>232</td>
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<table>
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<th>Year</th>
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<td>20</td>
<td>238</td>
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<td>98</td>
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</table>

*Figure 5: Summary of Case Notification Rates in Katsina State from 2017 to 2019*

The graph and map illustrate the changes in case notification rates over three years across the LGAs while the table summarises measures of central tendencies and dispersion. The table also summarises the number of notified cases across the LGAs.
3.1.2 Population, Key Population and Facility Distribution and Density

Katsina state has an estimated population of 7,832,100. The capital of the state, Katsina LGA, has the highest population and together with three other LGAs (Daura, Funtua and Kankara) they account for 17.4% of the entire state population. The state has a total of 422 health facilities supported by the STBLCP that provide TB diagnostic services across the 34 LGAs. Only 10 out of the 422 facilities providing diagnostic services offer TB diagnostic services using the Gene Xpert MTB/RIF® as shown in on the map that describes the distribution and density of diagnostic facilities in Figure 6. Katsina LGA had the highest number of diagnostic facilities (25 TB diagnostic facilities, including two Gene Xpert facilities) followed by Sabuwa and Kafur LGAs with 20 diagnostic facilities each. The facility density for the state was five facilities per 100,000 population with a range of 3 (Baure, Bindawa Daura and Musawa LGAs) to 12 (Sabuwa LGA) facilities per 100,000 population across the LGAs as shown on the table in Figure 6. Most LGAs with the lowest densities were seen along the northern international border with Niger and the western interstate border with Sokoto. Lastly, over 80% of LGAs in the state had a poverty rate of 50% or more. LGAs with some of the highest rates of poverty were seen on the southeastern part of the state along the border with Kano State.

The infographics above summarise the population estimates, health facility distribution and density and poverty rate across the 34 LGAs of Katsina. The coordinates of 23 facilities could not be obtained from the Nigerian Health Facility Registry portal and were no included in the map displaying the distribution and density of diagnostic facilities. Additionally, a facility placed under Funtua LGA by the STBLCP had coordinates outside the state.

The state has only 19 comprehensive HIV centres that manage and provide medication for PLHIVs. The geographical distribution of new HIV cases identified changed only slightly over the three years; however, a steady decrease in the number of new HIV cases was also seen across the state. Katsina, Funtua, Kankia and Daura LGAs had the highest number of HIV cases across all three years, as shown in Figure 7.
### Variable Summary

<table>
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<tr>
<th>Variable</th>
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</table>

**Figure 7: Maps and Table summarising new HIV infections from 2017 to 2019 in Katsina State**

### 3.1.3 Program Efforts

**Presumptive TB Rate and Positivity Yield:**

The number of presumptive TB cases almost doubled from 2017 to 2019 with the highest increase seen in Katsina, Kankara and Bakori LGAs. In contrast to the rising number of presumptive cases identified in the state, a decrease in the number of presumptive cases was noticed in Rimi and Kankia LGAs over the three years covered by this study. The number of new and relapse TB cases reported in the LGAs also increased steadily over the past three years from 4,894 in 2017 to 7,711 in 2019, as shown in Figure 8. The number of TB cases has consistently and dramatically increased over the past three years by over 100% in Bakori, Baure, Kankara, Zango, Mai’adua, Sabuwa, Matazu, Danja and Faskari LGAs.
The Presumptive TB rate also increased steadily from 2017 to 2019, as shown in Figure 9. The increasing trend was, however, slower in the Northern zone of the state where no LGA had over 400 presumptive TB cases per 100,000 in 2017. Daura, Zango and Sandamu LGA in the northern region had a persistent presumptive TB rate below 400 presumptive TB cases per 100,000 for the entire three years along with Charanchi in the Central zone and Danja in the Southern zone. Most of the changes seen were in the Central and Southern zones where three LGAs; Katsina, Sabuwa and Funtua had presumptive rates as high as 2,119, 1,793 and 1,623 respectively in 2019; had a steady increase that culminated with a presumptive TB rate above 1,599 presumptive TB cases per 100,000. The positivity yield, however, had an opposite trend with the yield dropping steady across the state. All LGAs had a lower yield in 2019 compared to 2017 with the exception of (Rimi,
Kankara, Matazu, Ingawa, Daura, Funtua and Danja). Three LGAs (Matazu, Dandume and Sabuwa LGAs) maintained very low positivity yields over the years.

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
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<td>464</td>
<td>780</td>
<td>670</td>
<td>260</td>
<td>2,119</td>
<td>0</td>
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</tr>
<tr>
<td>Positivity Yield</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<td></td>
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<tr>
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<td>34</td>
<td>17</td>
<td>7</td>
<td>17</td>
<td>11</td>
<td>6</td>
<td>34</td>
<td>0</td>
<td>Katsina</td>
</tr>
<tr>
<td>2018</td>
<td>33</td>
<td>17</td>
<td>7</td>
<td>15</td>
<td>10</td>
<td>6</td>
<td>39</td>
<td>1</td>
<td>Katsina</td>
</tr>
<tr>
<td>2019</td>
<td>34</td>
<td>11</td>
<td>5</td>
<td>10</td>
<td>4</td>
<td>5</td>
<td>24</td>
<td>0</td>
<td>Katsina</td>
</tr>
</tbody>
</table>

Figure 9: Maps and table summarising the presumptive TB rate and positivity yield data from 2017 to 2019 in Katsina State

In 2017, Zango LGA had the lowest rate of presumptive TB case per 100,000 population while every other LGA had less than 800 presumptive TB case per 100,000 population with exception of Funtua (1214) and Katsina LGAs (854). The state's positivity yield was 17% with the lowest yield seen in Matazu (6%) while Kafur and Mashi had the highest yield with both LGAs having a positivity rate of 34%.

In 2018, low rates of presumptive TB case per 100,000 population were seen in Kaita (52), Baure (107), Musawa (122) and Ma'adua (131) while the highest rates were seen in Katsina (1190), Batsari
(1110) and Charanchi (1051). The state's positivity yield was 14% with the lowest yield seen in Matazu (6%) and the highest yield seen in Mai'adua (39%).

Finally, in 2019, low rates of presumptive TB case per 100,000 population were seen in Danja (260), Rimi (297) and Daura (325) while the highest rates were seen in Katsina (2,119), Sabuwa (1,793) and Funtua (1,623). 71,303 presumptive TB cases were identified across the entire state out of which 56,304 clients had a bacteriological test for TB (45% Xpert Test, 55% Smear Microscopy Test and <1% TB LAMP/LF-LAM Test). The positivity yield for the entire state was 11%. Dandume, Jibia, Kusada and Sandamu had the lowest positivity yield of 5% in comparison Danja (24%), Daura (21%) and Ingawa (21%) had the highest positivity yield.

**Bacteriological and Expert Diagnostic Rates**

The proportion of TB cases diagnosed using a bacteriological method of diagnosis decreased from 51% to 44% from 2017 to 2019, as displayed in Figure 10. While the bacteriological diagnostic rates in the southern zone decreased over three years, those in the central and northern zones increased gradually. Kusada and Zango LGAs had the highest diagnostic rates in all three years, while Charanchi had the lowest rate. Additionally, the proportion of TB cases diagnosed using Gene Xpert also decreased in the southern zone over the years.
The number of presumptive cases that were tested for TB in 2017 and 2018 was not collected as part of the TB program indicators. However, out of the 31,304 presumptive TB cases that were identified in 2017, 5,015 were diagnosed with TB: 19% Xpert Test, 23% Smear Microscopy Test and 58% Clinical Diagnosis. In 2018, the number of presumptive cases increased to 35088 with a corresponding increase in the number of persons diagnosed to 5210 out of which 23% were diagnosed using Xpert test, 24% Smear Microscopy Test and 53% Clinical Diagnosis. Lastly, out of the 7,711 persons diagnosed with TB in 2019 17% were confirmed as TB cases using Gene Xpert, 27% through Smear Microscopy, <1% using TB LAMP/LF-LAM Test and 56% were diagnosed clinically.
3.2 Geographical Patterns

3.2.1 Hot Spot Analysis of TB CNR

In 2017, a cluster of low CNR (cold spots) was seen in LGAs (Baure, Zango and Ma’adua) along the north-eastern international border between the state and the Niger Republic as well as Sabuwa LGA which shares borders with Kaduna state, while clusters high CNR (hot spots) were seen in LGAs (Jibia, Kurfi and Batagarawa) which either share a border with or are in close proximity to the state capital. In contrast, Funtua LGA which had a high CNR was surrounded by LGAs with low CNR and LGAs with higher CNRs surrounded Safana LGA which had a low CNR. However, the spatial autocorrelation of CNR across the state was weak and not significant (Moran’s I: 0.106, p-value: 0.090).

In 2018, hot spots were seen around Kurfi and Batagarawa LGAs. On the other hand, Safana LGA was surrounded by LGAs with higher CNRs. This pattern was similar to that seen in 2017 but without the cold spot clusters seen around Baure, Zango, Ma’adua and Sabuwa; the high-low cluster around Funtua and the high-high cluster around Jibia. The spatial autocorrelation analysis seen in this year was showed weak dispersion; however, this was not significant (Moran’s I: -0.020, p-value: 0.370).

In 2019, hot or cold spots were seen; however, some LGAs (Faskari, Dandume and Danja) in the southern part of the state were surrounded by LGAs with higher CNRs. Additionally, these three LGAs share interstate boundaries with Kaduna. The spatial autocorrelation analysis seen in this year showed a weak but higher level of dispersion compared to 2018. However, this was also not significant (Moran’s I: -0.171, p-value: 0.080). Figure 11 summarises the results of the hot spot analysis from 2017 to 2019.

<table>
<thead>
<tr>
<th>Year</th>
<th>Moran’s I</th>
<th>P-Value</th>
</tr>
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<tbody>
<tr>
<td>2017</td>
<td>0.106</td>
<td>0.090</td>
</tr>
<tr>
<td>2018</td>
<td>-0.020</td>
<td>0.370</td>
</tr>
<tr>
<td>2019</td>
<td>-0.171</td>
<td>0.080</td>
</tr>
</tbody>
</table>

Figure 11: Summary of LISA analysis for CNR from 2017 to 2019 for LGAs in Katsina State

The maps show the spatial distribution of CNRs across LGAs in katsina state. LGAs in grey show that their CNR is not statistically significantly related to that of their neighbours. Those in dark red signify LGAs with high CNRs that are surrounded by LGAs with high CNRs (hot spot) while those in dark blue signify LGAs with low CNRs that are surrounded by LGAs with low CNRs (cold spot). The lighter shades of red represent LGAs with high CNR that are surrounded by LGAs with low CNRs and vice versa for the lighter shade of blue (spatial outliers).
3.3 Coverage Analysis

Coverage analysis using a clipped and dissolved 5km (0.045°) buffer showed that 22% of the state's population was over 5km away from a TB diagnostic facility. Kankara (25%) had the least coverage while the entire population of Katsina LGA lived less than 5km away from a TB diagnostic facility. Additionally, five LGAs (Batagarawa, Dandume, Dutsi, Sandamu and Sabuwa) all had over 90% coverage. Gene Xpert coverage, on the other hand, was analysed using a 20km radius (0.180°) buffer and showed that 49% of the state's population lived over 20km away from a Gene Xpert facility. Two LGAs (Safana and Baure) had 0% coverage and eight others had coverage of less than 25% (from <1% in Danja to 24% in Kankara). All LGAs with a Gene Xpert facility had over 75% coverage, with most of them above 90%, except Kankia LGA (71%). Furthermore, 60% of the Gene Xpert facilities are in the Central zone (two in Katsina LGA and one each in Rimi, Jibia, Dutsinma and Danmusa LGAs) while the Northern zone (one facility each in Funtua and Malumfashi LGAs) and Southern zone (One facility each in Duara and Kankia LGAs) equally share the remaining 40%. Figure 12 summarises the distribution and coverage of diagnostic facilities across the state.

Figure 12: Maps showing the proportion of the population within a 20km radius of facilities providing Gene Xpert diagnosis and 5Km radius of facilities providing TB sputum smear microscopy services
Chapter 4: Discussion

4.1 The Local TB Epidemic
The study showed that TB CNR across the LGAs of the state increased steadily from 2017 to 2019. This could be explained by the effort put by the NTBLCP to improve case notification across 13 states, including Katsina state, which accounted for over 50% of unnotified cases in 2015 (NTBLCP, 2015). Several approaches have been implemented in the state over these years in collaboration with lead implementing partner, KNCV Tuberculosis Fund (Previously known as Koninklijke Nederlandse Centrale Vereniging tot bestrijding der Tuberculose), to increase case finding as well as CNRs. Some of the notable approaches used to achieve this include Patent Medicine Vendors (PMVs) and community volunteer, contact investigators and Wellness on Wheels (WoW) or Mobile Care for TB Screening and Diagnosis (KNCV, 2020). However, despite the steady increase in CNR over the last three years, no LGA in the state has met the target of 287 notified cases per 100,000 population set by the NTBLCP in its national strategic plan in any of the three years (NTBLCP, 2015).

The hotspot analysis revealed a cluster of hotspots in 2017 and 2018; however, only a cluster of cold spots was seen in 2019. The p-values observed in all three years were not significant and no pattern was seen in the secondary variables that could clearly explain the pattern of hotspots observed. A possible explanation for the disappearance of the hotspots could be as a result of the community-based case-finding strategies which seeks to provide more diagnostic services to underserved communities.

4.1.1 CNR and Population
The maps generated in this study showed that LGAs with high population size and density were more likely to have higher CNRs through the years. This is in keeping with studies that have shown that CNRs are directly related to population size or density (Dangisso, Datiko and Lindtjørn, 2015; Okpani and Abimbola, 2015; Jibril et al., 2018; Bamgboye et al., 2019; Cheng et al., 2020). Interestingly, some LGAs (Sabuwa, Charanchi and Kurfi) with small population size and density were seen to have high CNRs which shows that TB cases relative to population size could vary greatly across regions irrespective of population size or density (Kanabus, 2019).

4.1.2 CNR and Poverty
A very weak similarity was observed in the spatial patterns of CNRs and the poverty rate across the state. Unlike the LGAs with the highest poverty rates that were seen to be lined along the state border with Kano state, the pattern of CNR over the three years had no unique observable pattern. Similarly, a negative correlation between CNR and poverty was also reported in Nigeria (Olusoji, 2016), Cambodia (Wong et al., 2013) and Bangladesh (Rood et al., 2018). This finding, however, contradicts other studies conducted in other low- and middle-income countries that have shown that poverty is linked with high TB burden or CNR (Oxlade and Murray, 2012; Nana Yakam et al., 2014; Yonge et al., 2016). However, several studies conducted in Nigeria show a correlation between poor health-seeking behaviour and poverty and could be a likely explanation for the low CNR seen in the poorest LGAs along the Kano state border (Fagbamigbe et al., 2011; Audu et al., 2014; Latunji and Akinyemi, 2018).

4.1.3 CNR and HIV
Katsina state has one of the lowest HIV prevalence's in Nigeria (0.3%) and receives less attention in comparison to other states with a higher prevalence. In contrast to most states that have at least
one comprehensive HIV treatment facility in an LGA, Katsina has only 19 comprehensive HIV treatment facilities spread across 15 LGAs out of 34 (NACA, 2019). All Gene Xpert facilities are located within health facilities with a comprehensive HIV treatment facility which could explain the higher CNRs seen in LGAs with higher numbers of new HIV cases. Additionally, studies have reported high TB CNRs in areas with a high incidence of HIV due to the synergistic roles they play in each other’s pathogenesis (Goldfeld and Ellner, 2007; Venketaraman, 2018). The synergy between these diseases and the implementation of Gene Xpert testing for all PLHIV with a current cough across comprehensive HIV treatment facilities in the country (Adeoti et al., 2017; Akanbi et al., 2017) could further explain the higher CNRs seen in these LGAs.

4.1.4 CNR and Program Efforts

While CNRs increased along with presumptive TB rates across most LGAs in the state over the years, the positivity yield, bacteriological diagnostic rate and Xpert diagnostic rate decreased. The slight increase seen between 2017 and 2018, and the spike in 2019 in the presumptive TB rates could be explained by the efforts of the STBLCP and KNCV Tuberculosis Fund in active case finding or the implementation of a more sensitive (but less specific) screening procedure (Yuen et al., 2017). Active case finding (ACF) seeks to identify and screen people with presumptive symptoms of TB in predetermined population groups using clinical examination, tests or other rapid assessments (WHO, 2013b). ACF usually includes approaches targeted at contacts of persons with active TB or mass screening of asymptomatic persons in the community and has been shown to increase the number of presumptive TB cases and CNRs in Nigeria (Adejumo et al., 2016; Stop TB Partnership, 2018) as well as other developing countries (Parija et al., 2014; Aye et al., 2018). Additionally, LGAs along the international border between the state and the Niger Republic and LGAs with high poverty rates were seen to have lower presumptive TB rates in all three years consistently compared to other LGAs. Communities along international borders as well as those with high poverty are often characterised by the paucity of diagnostic facilities (Rocha et al., 2011; Oladimeji, Tsoka-Gwegweni and Udoh, 2017; Alene et al., 2019) and could explain the pattern observed.

A framework by the Zero TB initiative asserts that a low positivity yield provides an indication that the wrong population might be tested while a yield greater than 10% suggests that only the highest risk individuals or those with more advanced active disease are evaluated or the use of screening tools with high sensitivity. A high positivity yield could also be observed at the early phase of implementation of effective active case finding strategies; however, this usually decreases over time (Yuen et al., 2017). The increase in the presumptive TB rates and TB CNR, and the decrease in positivity yield observed in this study could be attributed to the various cases finding strategies implemented by the state TB program and implementing partners, e.g. the PMV, community volunteer strategy and mobile screening and diagnostic units. These strategies employ screening tools with lower sensitivity and are targeted at populations with a high risk of TB. Their low sensitivity makes them identify a higher number of presumptive cases that turn out to be negative after being tested for TB with a diagnostic tool. Conversely, three LGAs (Matazu, Dandume and Sabuwa LGAs) maintained very low positivity yields over the years and could suggest underdetection.

In 2018, the bacteriological diagnostic rate for Africa was 65% (WHO, 2019a) which is higher than that of Katsina state and half of the LGAs in the state in 2018 and 2019. Some studies conducted in low and middle-income countries attribute low bacteriological diagnostic rates to improper documentation, improper referral, the inability of the presumptive case to produce sputum, overworked laboratory staff, stock out of the commodities required to perform the test and faulty
equipment (Mngomezulu et al., 2015; Harries and Kumar, 2018; Gidado, 2019). The decrease in bacteriological diagnostic rate over the years could be explained by an increasing number of presumptive cases accessing care in the limited diagnostic facilities whose number remained relatively unchanged over the three years.

The state's Xpert diagnostic rate for the three years (20%, 23% and 17% for 2017, 2018 and 2019 respectively) were slightly higher than the national rate of 16.8% reported in a study conducted by Gidado et al. (Gidado et al., 2019). However, despite Gene Xpert MTB/RIF® being adopted as a primary diagnostic tool for TB in Nigeria in 2016 (Gidado et al., 2019), the Xpert diagnostic rates were less than 50% in 88% of the LGAs across all three years. A possible explanation could be the burden on the Xpert facilities. Each Xpert machine has the capacity to run four samples every two hours (Churchyard et al., 2015; WHO, 2019d) for 10 hours a day and it can be estimated that an Xpert facility can perform about 1,300 tests (5 samples/day x 5days/week x 52weeks/year) every year without taking into account downtime. With the whole state having a total of 10 Xpert machines it could only run 18% (n=71,303) of samples collected from presumptive cases in 2019. This implies that the currently available facilities are overburdened and leaves clinicians with the option of a clinical diagnosis or smear microscopy which are less sensitive and specific (Harries and Kumar, 2018).

4.1.5 CNR and Diagnostic Coverage

Studies over the years show that distance significantly affects the utilisation of various healthcare services in Nigeria (Awoyemi, Obayelu and Opaluwa, 2011; Olubadewo-Joshua and Ugom, 2018). The distance to diagnostic facilities often has an inverse relationship with TB CNR. People living in areas farthest away from TB diagnostic centres are faced with the challenge of covering long distances to get to these facilities (Dangisso, Datiko and Lindtjorn, 2015). Slightly similar spatial patterns were also observed between the distribution of TB CNR and facility density and diagnostic facility coverage in this study.

Despite having 78% of the population living within 5km of a microscopy facility and an average of five facilities per 100,000 population across the state (which translates to 2.5 facilities per 50,000 and is above the target of 1 facility per 50,000 population set by the NSP-TB) microscopy facilities are inequitably distributed. An example seen was in Kankara and Katsina LGAs where both LGAs had high populations and CNRs but two extreme 5km coverage for microscopic (Kankara=25% and Katsina=100%) and different microscopy facility densities (Kankara=4 and Katsina=6 facilities per 100,000 population). Furthermore, the lack of diagnostic facilities in Kankara LGA could be hypothesized to be the cause of the low rate of bacteriological diagnosis and high rate of clinical diagnosis seen in the LGA. Clinical or empirical diagnosis of TB has a sensitivity of 16% to 44.4% and a specificity of 86.9% to 95.3% and has serious negative consequences on the individual and the health system based on a multicounty diagnostic trial conducted in some low- and middle-income countries (Vassall et al., 2011). Some of these negative consequences include exposure to the risk of adverse reaction to TB drugs, catastrophic expenditure, unnecessarily overstretching of scarce resources for health and incorrect estimation of disease burden which could lead to inequitable distribution of resources during planning (Houben et al., 2019).

The coverage of Xpert facilities was even more inequitable with the entire population of two LGAs and 75% of eight LGAs outside the 20km radius of any Xpert diagnostic facility. However, the pattern of distribution of Xpert corresponds slightly with the CNR hotspots seen in 2017. The last Xpert diagnostic site in the state was activated in 2016 (NTBLCP, 2018), and this could explain the pattern of distribution of these facilities and the CNR seen in 2017.
4.2 Understand the Local TB Response

4.2.1 Areas and Population with Limited Access
Kankara and Kurfi LGAs had the least coverage of diagnostic facilities, with both LGAs having less than 50% coverage for microscopic and Xpert diagnostic facilities. Interestingly, both LGAs had high CNRs and a decline in bacteriological diagnostic rates over the years. Other LGAs with limited coverage to both type of diagnostic facilities includes Baure, Dutsi and Mashi LGAs. Additionally, most parts of LGAs along the state’s borders with the Niger Republic and Sokoto State were not covered by available diagnostic services. A similar pattern has been observed in communities along international borders in Ethiopia (Alene et al., 2019). Additionally, the pattern of distribution of microscopy and Xpert facilities interestingly corresponds to the rate of poverty and distribution of reported new cases of HIV in the state, respectively.

4.2.2 Mapping the Pathway of Care
The efforts of the TB program and implementing partners was also reflected in the number of presumptive TB cases, those tested, diagnosed, and notified to the STBLCP. Unlike studies conducted in Nigeria (Ukwaja et al., 2016; Meribe et al., 2020) and other developing countries (Movert et al., 2013; Subbaraman et al., 2019; Subbaraman, Jhaveri and Nathavitharana, 2020) that reported losses along the pathway between diagnosed and reported cases, no losses were seen along the cascade for the state. This could be explained by either a robust surveillance system or a system with underlying data quality challenges.

4.3 Relevance of Framework
The MATCH analytical framework guided me through the analysis and interpretation of findings. It helped me to monitor the progress of the TB program and identify geographical patterns in the distribution of CNR and other variables used in the study. The framework was user friendly and aided the synthesis of valuable information in ways that can be easily understood by decision and policymakers. I, however, could not thoroughly discuss the last section of the framework as well as parts of the Piot’s framework due to the unavailability of data. I intend to routinely use the MATCH framework to routinely analyse HIV and TB data when I get back to Nigeria.

4.4 Limitations
Some limitations were encountered in this study. Firstly, the study design had two limitations. The study describes the correlation of CNRs to other variables using aggregate data but does not explain causation. As such, results from this observational study needs to be interpreted with caution. Additionally, facility coverage analysis was done only based on population coverage and did not take into account the capacity of each diagnostic facility or travel time to the facility.

Secondly, the quality of the data analysed was suboptimal as some data fields were missing, inconsistent, inaccurate, or invalid. For example, the data for an entire LGA (Safana LGA) was missing in 2018 and was excluded from the analysis for that year. Such issues were discussed with the custodians of the data; however, most of them were unresolved. LGA-level estimates of TB prevalence were also unavailable, as such a comparison between CNR and the actual burden of disease could not be made. Additionally, LGA level data on key population (e.g. miners, immigrants and malnourished children under five years) could not be obtained under the stipulated time for this study and were excluded.

Furthermore, patient-level data could not be obtained from the STBLCP due to the lengthy process of obtaining ethical clearance from the NLTBCP. Patient-level data or primary data
collected from notified TB cases would have provided more detailed information on CNRs, hotspots, and accessibility to diagnostic services.

Lastly, the HIV data set does not accurately reflect the distribution of new cases in the state as only 19 comprehensive HIV treatment facilities in 15 LGAs cater to the needs of the state’s 34 LGAs. Persons presumed to be infected with HIV and some positive cases identified at other LGAs are usually referred to and sometimes documented as new positives in LGAs with comprehensive HIV treatment facilities. Due to this, some LGAs have reported no new positive cases in some years. It is very likely that the HIV burden reported in this study is skewed to LGAs with treatment facilities and does not reflect the true burden across the LGAs. Similarly, presumptive and confirmed TB cases might access services in other LGAs outside theirs which could lead to the wrong allocation of these cases. This is a major limitation in using aggregate data.
Chapter 5: Conclusion and Recommendations

5.1 Conclusion

Despite its small population, Katsina state accounted for a significant number of unnotified cases in the country and was earmarked as a high priority state along with 12 others by the NTBLCP. Several efforts have been put by the state TB program and implementing partners to actively find the missing cases and contribute to an increase in the national case notification rate from 57.3 to 287 cases per 100,000 population by 2020. Some of the findings from this study condensed below could contribute to increasing the state and country’s CNR.

Firstly, the CNR across most LGAs as well as the state’s CNR increased steadily from 2017 to 2019. There was no statistically significant spatial clustering of CNRs across all three years. However, a few local hotspots were observed in 2017 (Jibia, Batagarawa and Kurfi LGAs). However, these hotspots reduced in 2018 (Batagarawa and Kurfi LGAs) and were no longer identified as hotspots in 2019. This suggests that initial spatial clustering of high CNR's were diluted after the statewide increase in case detection, and as such were likely the product of variation in case finding activities (passive or active) than variation in the TB burden.

Secondly, the CNR did not reflect the true local status of the epidemic because lower CNRs were observed in LGAs with the highest poverty rates. Additionally, higher CNRs were mostly observed in LGAs with high coverage of diagnostic facilities. The coverage analysis also clearly highlighted three LGAs (Kankara, Kurfi and Baure LGAs) with the poorest coverage of microscopy facilities as well as a relatively low Xpert coverage. Contrastingly, these three LGAs, unlike other LGAs (e.g. Ingawa, Musawa and Danja LGAs) with inadequate coverage all had relatively high CNRs. Additionally, 60% of Xpert facilities were concentrated in the central zone of the state which suggests the inequitable distribution (geographical) of these facilities that could hinder underserved communities from accessing care.

Thirdly, risk factors for TB, such as HIV and high population size and density, had similar spatial patterns with the CNRs. Oddly, despite the similar patterns observed between CNR and population size and density, some highly populated LGAs with very high CNRs, e.g. Kankara LGA had an extremely low facility density which could further suggest that diagnostic facilities are inequitably distributed. Also, the distribution of new HIV cases was skewed to LGAs with HIV treatment centres and highlighted a vast coverage gap in the HIV program as well.

Lastly, while CNRs increased along with presumptive TB rates across most LGAs in the state over the years, the positivity yield, bacteriological diagnostic rates and Xpert diagnostic rates decreased. This suggests that while great efforts were made to increase case detection, the diagnostic landscape may not have the capacity to keep up.

More research would be required to answer some of the hypothesis raised by this study. A more detailed study that employs a qualitative and quantitative approach using the geocoordinates of the residence of confirmed TB cases would provide detailed insights into the distribution of CNRs and where cases are more likely to be missed.
5.2 Recommendations

Poor data quality, inequitable distribution of diagnostic facilities and the high rate of clinical diagnosis were the most significant challenges identified by the study. Reflecting on these challenges, I propose the following recommendations to contribute an increase the CNR in the state while ensuring that presumptive and TB cases get the best quality of care based on national guidelines.

Firstly, the TB monitoring and evaluation (M&E) and surveillance systems urgently need to be strengthened. The relevant stakeholders needed to achieve this include: the Ministry of Health, NTBLCP, STBLCP, KNCV Tuberculosis Foundation and Institute of Human Virology. Strengthening these systems would entail the following: retraining the state program and M&E officers on data collection tools and data quality assurance processes; conducting quarterly data quality assessment across all TB diagnostic and treatment facility; training state program and M&E officers to routinely analyse TB surveillance data (using geocoordinates of the residence of confirmed TB cases) to gain a better understanding of the distribution of the disease; routine dissemination of summarised case find data and results of MATCH analysis with funders and researchers, and fostering collaboration between the stakeholders involved in the M&E ecosystem. Training activities could require some funding; however, it can be conducted at no cost if conducted during quarterly M&E meetings or routine monitoring and supervisory visits.

Secondly, the NTBLCP and STBLCP urgently need to expand the geographical coverage of microscopy and Gene Xpert diagnostic facilities. Kankara, Kurfi and Baure LGAs should be prioritised for this activity. This can be achieved by identifying facilities in underserved communities and providing them with diagnostic equipment (microscope) and laboratory commodities; training laboratory staff in identified facilities on TB microscopy and advocating for additional Gene Xpert machines from the government and funders. Significant funding from the government and donors will be required to carry out these activities. However, intensification community-based active case finding activities in LGAs with low coverage (especially Kankara, Kurfi and Baure LGAs) and strengthening of the TB diagnostic referral network could be explored as a temporary option. It is crucial also to consider key populations and population density in the process of expanding these services. Other stakeholders needed to implement this recommendation include Ministry of Health, KNCV Tuberculosis Foundation, Institute of Human Virology (IHVN), Global Fund, Stop TB Partnership, President’s Emergency Plan for AIDS Relief (PEPFAR), Centre for Disease Control and the Civil Society Organisations.

Thirdly, the NTBLCP and STBLCP need to actively enforce the new diagnostic guideline to drive down the proportion of clinically diagnosed diseases. It would require a reorientation training for clinicians on the TB diagnostic algorithm, documentation of data tools and interpretation of TB test results. Jobs aids and guidelines should be distributed to all diagnostic facilities after this training to provide them with additional guidance when offering services. Routine audits should also be conducted regularly to assess adherence to TB diagnostic guidelines. Clinical diagnosis should be made by medical doctors and strictly reserved for cases where a sample cannot be collected for a bacteriological test. All these activities are feasible but might require some funding, as such, implementing partners (KNCV Tuberculosis Fund and IHVN) could provide some assistance to ensure these activities are implemented. However, for this recommendation to be fully and successfully implemented, the coverage of diagnostic facilities needs to be improved.

Fourthly, the NTBLCP, STBLCP and implementing partners (KNCV Tuberculosis Fund and IHVN) need to encourage the use of innovative and sustainable tools and strategies in active case
finding. National and state TB program staff should be encouraged to analyse routine program data using QGIS and other open-source software to obtain additional information these data sets. Such information could provide guidance policy and decision-makers in their planning processes, allocation of resources and designing policies. Additionally, continuous quality improvement (CQI) teams should be set up at all diagnostic and treatment facilities as well as the LGA-level. The STBLCP and implementing partners should support CQI teams to design and sustainable and data-driven CQI projects and create a platform to share best practices. These approaches require little or no funds as such can be implemented with fewer challenges. Furthermore, this approach will make facility and LGA TB staff to interact more with their data and identify quality gaps while improving the services they provide.

Lastly, KNCV Tuberculosis Fund and IHVN should support the NTBLCP and STBLCP to build the capacity of their staff to conduct research and surveys. It could increase their interaction with data generated from the program and expose data quality issues. Additionally, it will provide TB program staff with the skills to interpret other researches and conduct theirs to verify or obtain information that could increase case detection. Besides, the TB program needs to strengthen collaboration with academic institutions and conduct more researches together. Collaborations like this often offer a win-win situation for both organisations as the academic institutions have access to invaluable data. At the same time, the TB program benefits considerably from the results of the research.
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RESEARCH ETHICS COMMITTEE

Contact: Meta Willems (secretary REC)
Telephone +31 (0)20 568 8514
m.willems@kit.nl

To: Makplang James Milaham
KIT ICHD Student
By E-mail: Makplang Milaham
<mmilaham@gmail.com>

Amsterdam, 19 June 2020

Subject Decision Research Ethics Committee regarding a waiver for a study on "Analysing the Spatial Distribution of Tuberculosis Case Notification Rates in Katsina State, Nigeria (S-132)"

Dear Makplang James Milaham,

The Research Ethics of the Royal Tropical Institute (REC) has reviewed your application for a waiver for a study on "Analysing the Spatial Distribution of Tuberculosis Case Notification Rates in Katsina State, Nigeria (S-132)" that was submitted on 17 June, 2020.

Your proposal has been exempted from full ethical review based on the following considerations:

1. only anonymized data at aggregate facility and LGA level will be analysed;
2. The data will be stored in a safe place only accessible for you (and possible co-researchers who you will also guide on safe storage) for the purpose of your thesis;
3. the data has been approved by the data owner being the Katsina State Ministry of Health in Nigeria;
4. It would not be feasible or practicable to ask informed consent for the participants/patients whom the data belong, while ethical clearance has been obtained from the Ethical Board at the Katsina State Ministry of Health to use the data;
5. the analysis has an important public health function;
6. the research poses no more than minimal risks to participants and does not give any rise to the disclosure of the participant’s identity.

The Committee grants this waiver provided that you inform the KIT GDPR project officer about your research for GDPR monitoring purposes.

Royal Tropical Institute
The Committee requests you to inform the REC once substantive changes to the protocol are made, important changes to the research team take place or researchers are added to the research team.

Moreover, the Committee requests you to send the final report of the research containing a summary of the study’s findings and conclusions to the Committee, for research monitoring purposes.

Please note that in case the final report is not submitted to the REC, or GDPR measurements are not taken care of sufficiently, this may have consequences for review of your next research proposal.

Wishing you success with the research,

[Signature]

Pam Baatsen
Chair of the KIT REC
Annex 2: Katsina State Ethical Clearance

MINISTRY OF HEALTH
KATSINA STATE
State Secretariat Complex IBB Way
Dandagoro, PMB 2075, Katsina

15th June, 2020

KATSINA STATE HEALTH RESEARCH ETHICAL REVIEW COMMITTEE (HREC) FULL ETHICAL CLEARANCE CERTIFICATE

Re: "Analysing the Spatial Distribution of Tuberculosis Case Notification Rates in Katsina State"

Katsina HREC assigned number: - MOH/ADM/SUB/1152/1/374
Name of principal investigator: - Maksonk James Miliahm
Address of Principal Investigator: - KT Royal Tropical Institute, Amsterdam, Netherlands.

Date of receipt of Valid Application: - 15/06/2020
Date of HREC meeting and Approval: - 16/06/2021

This is to inform you that the research described in the submitted protocol, the consent forms and other participants information materials have been reviewed and given Expedited Approval by the Katsina State Health Research Ethics Committee and accordingly by the Honorable Commissioner of Health.

Please note: this approval dates from 15/06/2019 to 16/06/2021. No recruitment of participant into this research may be conducted outside these dates.

All informed consent forms in this study must carry the Katsina HREC assigned number and the duration of the Katsina HREC approval for the study.

If there is a delay in starting the research, please inform the Katsina HREC so that starting date can be adjusted accordingly.

No changes are permitted to the research without prior approval by the Katsina HREC except in circumstances outlined in the national code of health research ethics. http://www.nhrec.net.

Katsina HREC reserves the right to conduct a compliance assessment to your research site without prior notification.

Dr. Ma'zawuya Alliu,
Director Public Health
Chairman, Katsina HREC
+234 8163292771
Annex 3: Structure of NTBLCP
(NTBLCP, 2015)