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TITILADE KEHINDE AYANDEYI TEIBO

Time series and spatial distribution of Tuberculosis in Oyo state Nigeria

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TITILADE KEHINDE AYANDEYI TEIBO

Time series and spatial distribution of Tuberculosis in Oyo state Nigeria

Dissertation presented to the School of Nursing of Ribeirão Preto, University of São Paulo, to obtain the title of Master of Science, Graduate Program in Public Health Nursing.

Line of research: Health-disease process and epidemiology

Advisor: Ricardo Alexandra Arcêncio

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DEDICATION

To **GOD-** the lover of my soul for the gift of life, for always being with me in every momentof smiles and tears.

To my Husband **John Oluwafemi Teibo**, thank you for sharing the love of God with me in the course of this journey. You were all the motivation and support system I needed.

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"Take the first step with faith. You do not necessarily have to see the entire staircase. Just begin with the first step."

Martin Luther King

ABSTRACT

TEIBO, Titilade Kehinde Ayandeyi**. Time series and spatial distribution of Tuberculosis in Oyo state Nigeria.** 2023, 132p. Dissertation (Master's), Ribeirão Preto School of Nursing, University of São Paulo, Ribeirão Preto, 2023.

The virulence of Tuberculosis (TB) in the population makes it imperative to intensify studies on the disease caused by *Mycobacterium tuberculosis*. TB most frequently affects the lungs (pulmonary TB) and may also affect other organs (extra-pulmonary TB). There are few studies on TB using spatial and temporal approaches, especially in African countries. Therefore, the aim of the present study was to describe the epidemiological profile of TB and analyze the spatial distribution and temporal trend of TB incidence and mortality in Oyo state Nigeria from 2015-2019. The study comprises TB cases reported by the Oyo State Ministry of health between 2015 and 2019. The spatial analysis technique was applied to analyze the spatial distribution of incidence and mortality rate of TB. To identify areas with spatial dependence of TB, the Gi* technique was used through the ArcGis 10.5 software. The time series analysis technique was applied to assess the behavior of TB in Oyo state over the period studied. A total of 28,680 cases of pulmonary and extrapulmonary TB and 1,131 TB deaths were reported in all local governments of Oyo state between 2015 and 2019. The highest cases rate occurred in Ibadan South west local government (334 cases per 100,000), with the single local government area (LGA) having more than 10% cases of all 33 LGAs. Ido and OluyoleLGAs were hotspot regions for TB with a 99% confidence interval. The historical series of theTB incidence rate slightly increased between 2015 to 2017, with a sharp declinefrom then until 2019, but the temporal trend for the incidence of TB in the period under study decreased. While a slight increase in the TB mortality rate throughout the analyzed period wasobserved, the temporal trend of the event between 2015 and 2019 showed an increase. Advancing knowledge by highlighting areas of risk for the occurrence of TB (hotspots) and its relationship with social and economic inequality remains fundamental to theachieving the goals of public health actions. The results of the present study contributed to the knowledge of the epidemiological profile, spatial and temporal distribution, and areas with a higher risk of tuberculosis transmission in Oyo state and Nigeria as a whole. This information allows policymakers to target hotspot areas for intervention and diseaseprevention.

Keywords: Tuberculosis, Spatial Analysis, Oyo state, Time Series, Epidemiology.

RESUMEN

TEIBO, Titilade Kehinde Ayandeyi**. Series temporales y distribución espacial de la tuberculosis en el estado de Oyo, Nigeria.** 2023, 132p. Disertación (Maestría), Escuela de Enfermería de Ribeirão Preto, Universidad de São Paulo, Ribeirão Preto, 2023.

La virulencia de la Tuberculosis (TB) en la población hace imperativo intensificar los estudios sobre la enfermedad, causada por Mycobacterium tuberculosis, la TB afecta más frecuentemente los pulmones (TB pulmonar) y puede afectar otros órganos (TB extra pulmonar). Existen pocos estudios sobre la TB que utilicen enfoques espaciales y temporales, especialmente en los países africanos. Por lo tanto, el objetivo del presente estudio fuedescribir el perfil epidemiológico de la TB y analizar la distribución espacial y la tendencia temporal de la incidencia y la mortalidad por TB en el estado de Oyo, Nigeria, entre 2015 y 2019. El estudio comprende los casos de TB notificados por el Ministerio de Salud del estado de Oyo entre 2015 y 2019. Se aplicó la técnica de análisis espacial para analizar la distribución espacial de la incidencia y la tasa de mortalidad por TB. Para identificar las áreas con dependencia espacial de la TB, se utilizó la técnica Gi* a través del software ArcGis 10.5.Se aplicó la técnica de análisis de series temporales y se utilizó para evaluar el comportamiento de la TB en el estado de Oyo a lo largo del periodo estudiado. Se verificaron 28.680 casos de TB pulmonar y extrapulmonar y 1.131 muertes por TB en todos los gobiernos locales del estado de Oyo entre 2015 y 2019. La tasa de casos más alta se registróen el gobierno local de Ibadan Suroeste (334 casos por 100.000), siendo la única área de gobierno local (AGL) con más de un 10% de casos de las 33 AGL. Las áreas de gobiernolocal de Ido y Oluyole fueron las regiones más afectadas por la tuberculosis, con un intervalo de confianza del 99%. La serie histórica de la tasa de incidencia de TB aumentó ligeramente entre los años 2015 y 2017, con un fuerte descenso desde entonces hasta 2019, pero la tendencia temporal de la incidencia de TB en el período estudiado disminuyó. Si bien se observa un ligero aumento de la tasa de mortalidad por TB a lo largo del periodo analizado también se observa que la tendencia temporal del evento entre 2015 y 2019 es creciente. Avanzar en el conocimiento destacando las áreas de riesgo para la ocurrencia de TB (hotspots) y su relación con la desigualdad social y económica sigue siendo fundamental para el logro de los objetivos de las acciones de salud pública. Los resultados del presente estudio contribuyeron al conocimiento del perfil epidemiológico, la distribución espacial y temporal ylas zonas con mayor riesgo de transmisión de tuberculosis en el estado de Oyo y en Nigeria ensu conjunto. Permite a los responsables políticos seleccionar las zonas críticas para la intervención y la prevención de la enfermedad.

Palabras clave: Tuberculosis, Análisis Espacial, Estado de Oyo, Series Temporales, Epidemiología

RESUMO

TEIBO, Titilade Kehinde Ayandeyi**. Série temporal e distribuição espacial da tuberculose no estado de Oyo, Nigéria.** 2023, 132p. Dissertação (Mestrado), Escola de Enfermagem de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, 2023.

A virulência da Tuberculose (TB) na população torna imperativa a intensificação dos estudos sobre a doença, causada pelo *Mycobacterium tuberculosis*, a TB acomete mais frequentemente os pulmões (TB pulmonar), podendo afetar outros órgãos (TB extrapulmonar). Existem poucos estudos sobre a TB com abordagens espaciais e temporais, especialmente nos países africanos. Por conseguinte, o objetivo do presente estudo foi descrever o perfil epidemiológico da TB e analisar a distribuição espacial e a tendência temporal da incidência e mortalidade da TB no estado de Oyo, na Nigéria, de 2015 a 2019. O estudo inclui casos de TB notificados pelo Ministério da Saúde do Estado de Oyo entre 2015 e 2019. A técnica de análise espacial foi aplicada para analisar a distribuição espacial da taxa de incidência e mortalidade da TB. Para identificar áreas com dependência espacial da TB, foi utilizada a técnica Gi* através do software ArcGis 10.5. A técnica de análise de séries temporais foi aplicada e utilizada para avaliar o comportamento da TB no estado de Oyo durante o período estudado. Foram registados 28 680 casos de TB pulmonar e extrapulmonar e 1 131 mortes por TB em todos os governos locais do estado de Oyo entre 2015 e 2019. A taxa mais alta de casos ocorreu no governo local do sudoeste de Ibadan (334 casos por 100.000), com a única área de governo local (AGL) tendo mais de 10% de casos de todas as 33 AGLs. As AGLs de Ido e Oluyole foram regiões de hotspot para TB com intervalo de confiança de 99%. A série histórica da taxa de incidência de TB aumentou ligeiramente entre os anos de 2015 e 2017, com um declínio acentuado desde então até 2019, mas a tendência temporal da incidência de TB no período em estudo diminuiu. Embora tenha sido observado um leve aumento na taxa de mortalidade por TB durante todo o período analisado, também podemos ver que a tendência temporal do evento entre 2015 e 2019 está aumentando. O avanço do conhecimento ao destacar áreas de risco para a ocorrência da TB (hotspots) e sua relação com a desigualdade social e econômica continua sendo fundamental para o alcancedos objetivos das ações de saúde pública. Os resultados do presente estudo contribuíram parao conhecimento do perfil epidemiológico, da distribuição espacial e temporal e das áreas com maior risco de transmissão da tuberculose no estado de Oyo e na Nigéria como um todo. Isso possibilita que os formuladores de políticas visem às áreas de maior risco para intervenção e prevenção da doença.

Palavras-chave: Tuberculose, Análise espacial, Estado de Oyo, Séries temporais, Epidemiologia.

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LIST OF ABBREVIATIONS AND ACRONYMS

USP	University of São Paulo (*Universidade de São Paulo*)
TB	Tuberculosis
EERP/USP	Ribeirão Preto School of Nursing at University of São Paulo (*Escola de Enfermagem de Ribeirão Preto da Universidade de São Paulo*)
GEOTB	Epidemiological-Operational Study Group on Tuberculosis (*Grupo de Estudos Epidemiológico-Operacional em Tuberculose*)
PAE	Teaching Improvement Program (*Programa de Aperfeiçoamento de Ensino*)
ICGEB	International Centre for Genetic Engineering and Biotechnology
FAPESP	São Paulo State Research Support Foundation (*Fundação de Amparo à Pesquisa do Estado de São Paulo*)
BMC	Biomed Central
AIDS	Acquired Immunodeficiency Syndrome
WHO	World Health Organization
PLHIV	People Living with the Human Immunodeficiency Virus
COVID-19	Coronavirus Disease 2019
TS	Time Series
SA	Spatial Analysis
GIS	Geographic Information Systems
MDGs	Millennium Development Goals
MDR	Multidrug-resistant
EHRs	Electronic Health Records
CoCoPop	Condition; Context; Population
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-

	Analyses
PRISMA-P	Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols
Q	Questions
MEDLINE	Medical Literature Analysis and Retrieval System Online
PubMed	Public/Publisher MEDLINE
LILACS	Latin American Literature in Health Sciences (*Literatura Latino-Americana e do Caribe em Ciências da Saúde*)
BVS	Virtual Health Library (Biblioteca Virtual em Saúde)
EMBASE	Excerpta Medica Database
CAFe	Federated Academic Community (*Comunidade Acadêmica Federada*)
CAPES	Coordination for the Improvement of Higher Education Personnel (*Coordenação de Aperfeiçoamento de Pessoal deNível Superior*)
DeCS	Descriptors in Health Science (*Descritores em Ciências da Saúde*)
MeSH	Medical Subject Headings
QCRI	Qatar Computing Research Institute Rayyan Systematic Review
LGAs	Local Government Areas
PHCs	Primary Health Centers
NTBLCP	National Tuberculosis and Leprosy Control Program
DOTS	Directly Observed Treatment Short Course
PTB	Pulmonary Tuberculosis
ECDC	European Centre for Disease Prevention and Control

SUMMARY

PRESENTATION

I obtained my Bachelor's degree in Biochemistry from Ladoke Akintola University of Technology in Ogbomoso, Oyo State, Nigeria. I made the decision to further my studies at the Universityof Sao Paulo (USP – *Universidade de São Paulo*), in Sao Paulo state, Brazil. This choice was driven by the university's international reputation and because they offered a program that aligned perfectly with my interests and enthusiasm: in Public Health Nursing. The topic of Tuberculosis has always held great significance for me, particularly due to its high prevalence in Africa and especially in Nigeria. This interest was further fueled by a personal experience of mine, where an acquaintance sadly lost her life to TB. As a result, studying TB became an even more compelling subject for me.

My first contact with the topic of tuberculosis occurred while I was preparing my research proposal for a Master's degree in the Ribeirão Preto School of Nursing at University of São Paulo (EERP/USP). The persistent burden of TB in Nigeria motivated me to select this subject for my research. During the application process, I identified Prof. Doctor Ricardo Alexandre Arcêncio as leader of the Epidemiological-Operational Study Group on Tuberculosis (GEOTB – *Grupo de Estudos Epidemiológico-Operacional em Tuberculose*) of the EERP/USP and chose to work with the group.

Afterward, I began my Master's research program with a systematic review of the spatial analysis and time series of TB with the aim of discovering areas that are most vulnerable to TB, then I performed an analysis of retrospective data from Oyo state Nigeria making use of Spatial analysis and Time series to locate different areas with their varying degrees of TB incidence and mortality.

I participated in events that were of great value for the improvement of the research line, enhancing my knowledge on the subject, and applying investigative methodologies and procedures for data collection and analysis. Regarding scientific activities, it is worth commenting that this growing researcher is a member of the GEOTB which is internationally recognized and I am still a member until today. The main objectives of GEOTB are as follows: to promote the production of interdisciplinary knowledge related to new technologies of proactive work, involving various social actors such as users, health professionals, workers, managers and members of organized civil society. These activities are conducted within specific socio-political, economic and cultural contexts in the healthcare system for tuberculosis control,through quantitative and qualitative approaches.

During my master's program, I had the opportunity to organize an English course with my GEOTB group members. In this course, we present and discuss scientific articles in English, an action which has greatly enhanced our language skills and scientific communication. Additionally, I participated in the Teaching Improvement Program (PAE – *Programa deAperfeiçoamento de Ensino*), where I took courses that contributed to the development of my research and teaching training. Through this program, I engaged in teaching-learning activities related to the Health-disease process subject, allowing me to facilitate enriching learning experiences and expand my knowledge. Interacting with students provided me with valuable insights into public health issues and the health-disease process.

Furthermore, I had the privilege of attending the conference "Emerging infectious diseases: biology, prevention and treatment" a workshop organized by International Centre for Genetic Engineering and Biotechnology (ICGEB). The conference took place from 07/11/2022 to 11/11/2022 in São Paulo, Brazil, and was supported by the São Paulo State Research Support Foundation (FAPESP – *Fundação de Amparo à Pesquisa do Estado de São Paulo*). Participating in this event allowed me to stay updated on the latest advancements in the field and connect with experts in the area of emerging infectious diseases.

It is noteworthy mentioning that the results obtained from my master's thesis have been submitted and are currently under review for publication, entitled "Geo-spatial hotspots of Tuberculosis in the global general population: a systematic review" to be submitted in Biomed Central (BMC) Journal.

Additionally, another research paper titled "Surveillance of Tuberculosis Incidence and Mortality through Spatial Intelligence in Oyo State, Nigeria" has been submitted to the African Health Sciences Journal. Furthermore, a portion of this research was presented at the ICGEB Workshop on Emerging Infectious Diseases: Biology,Prevention and Treatment. A Systematic Review and Meta-Analysis of Time Series and Spatial Distribution of the Incidence of Tuberculosis held at Sao Paulo in November, 2022.

Additionally, I have also submitted abstract for the Union Conference on Lung Disease. The abstract is titled "Spatiotemporal analysis of Tuberculosis Incidence in Oyo State, Nigeria 2015-2019".

In accordance with the Program's regulations, my dissertation is structured into the following sections: Introduction, Systematic Review of Literature, Objectives, Methods, Results, Discussion and Conclusion. This organization allows for a comprehensive and logical presentation of the research findings and their interpretation.

1. INTRODUCTION

Mycobacterium tuberculosis, which causes tuberculosis (TB), typically affects the lungs (pulmonary TB) but it can also affect other organs (extra pulmonary TB). The main mode of transmission is through coughing by bacilliferous individuals (individuals who have active TB), contributing to the high incidence of the disease (WHO, 2018).

TB was a leading cause of death globally until the appearance of the new coronavirus, responsible for the pandemic starting in 2020. TB is an infectious and communicable disease that primarily affects the lungs. Approximately 6 million new cases are reported annually worldwide, resulting in over one million deaths annually. The situation is further exacerbated by the emergence of drug-resistant TB outbreaks and the presence of Acquired Immunodeficiency Syndrome (AIDS). Consequently, TB remains an important global public health problem. Its relevance and magnitude of the disease can be observed through estimates provided by the World Health Organization (WHO) which indicate 8.7 million new cases and 1.4 million deaths annually (WHO, 2019).

A significant number of individuals infected with TB experience a long latency period, with a 10-15% lifetime risk of eventually developing active disease. Only about 5% of those infected progress to active TB within the first two years. The likelihood of progression is influenced by the individual's immunological status, with immunocompromised patients having a significantly higher risk MAHER et al., 2009).

Since the WHO declared TB be a global health emergency in 1993, there has been notable progress in several indicators. The most significant achievement was the reduction of global TB mortality by 45% in 2012. However, the global TB incidence rate has been decreasing at a relatively low rate of 2% per year (WHO, 2013). While only a small proportion (5–10%) of the estimated 1.7 billion people infected with *M. tuberculosis* will develop TB in their lifetime, this proportion is higher in people living with the human immunodeficiency virus (PLHIV) or those affected by risk factors such as malnutrition, diabetes, smoking and alcoholism (WHO, 2018). According to the WHO, TB is currently one of the top ten causes of death worldwide. In 2017, 10 million people fell ill with the disease and 1.6 million died from it (WHO, 2018).

The progress made over the years in reducing the burden of TB and providing essential TB services has been undermined by the COVID-19 pandemic. Despite some notable national and regional achievements, the global targets for TB are generally off track. One of the most significant effects is the substantial decrease in the number of reported new TB cases globally. This decreased from 7.1 million in 2019 to 5.8 million in 2020, a fall of 18% that brought it back to its 2012 level and far short of the roughly 10 million persons who had TBin 2020.

India, Indonesia, and the Philippines were the worst affected nations, accounting for 93% of this decline (WHO, 2021).

Reduced access to TB diagnosis and treatment has resulted in an increase in TB deaths. Best estimates for 2020 are 1.3 million TB deaths among HIV-negative people (up from 1.2 million in 2019) and an additional 214 000 among HIV-positive people (up from 209 000 in 2019), with the combined total, back to the level of 2017. Declines in TB incidence (the number of people developing TB each year) achieved in previous years have slowed almost to a halt. These impacts are forecast to be much worse in 2021 and 2022.

Other impacts include reductions between 2019 and 2020 in the number of people provided with treatment for drug-resistant TB (-15%, from 177 100 to 150 359, about 1 in 3of those in need) and TB preventive treatment (-21%, from 3.6 million to 2.8 million), and a fall in global spending on TB diagnostic, treatment and prevention services (from US$ 5.8 billion to US$ 5.3 billion, less than half of what is needed) (WHO, 2021). TB is a leading cause of mortality globally. Despite being curable, TB is still ravaging throughout the entire world.

Actions to mitigate and reverse these impacts are urgently required. The immediate priority is to restore access to and provision of essential TB services such that levels of TB case detection and treatment can recover to at least 2019 levels, especially in the most badly-affected countries.

In recent years, the discovery of infectious disease hotspots has been done using spatial-temporal cluster analysis (METRAS et al., 2012). Significant results were obtained when it was effectively applied to the identification of TB clusters (BAKER et al., 2014). According to prior research, TB is an infectious disease that spreads through the air and has a spatially and temporally heterogeneous distribution. It is thought that a better understanding of the spatial epidemiology of TB will help policymakers and other stakeholders develop effective regional prevention and control strategies (LIU et al., 2012).

Time series (TS) analysis of TB is a method used to identify and understand the patterns and trends of occurrences such as mortality and incidence of TB over time. It allows for the analysis of historical data and can be utilized to forecast future values of variables obtained from the time series research (forecasting). On the other hand, spatial analysis (SA) involves the examination of geographically aggregated TB data in relation to various risk factors such as demographic, environmental, infectious agents and socioeconomic conditions within a specific area. The combination of TS and SA in TB research provides valuable insights into the current statistical updates of the disease.

For example, by conducting TS analysis, one can examine how TB rates have changed over time and detect any significant fluctuations or trends. SA, on the other hand, allows researchers to investigate the spatial distribution of TB cases, identify high-risk areas, and understand the factors contributing to the prevalence of TB in those areas. This information is crucial for targeted interventions and resource allocation.

Considering the association between low socioeconomic status and high TB prevalence, it is important to conduct evaluations that provide a better understanding of specific areas at high risk of TB. By combining TS and SA, researchers can make informed predictions about the likelihood of TB occurrence or reoccurrence in the future. These analytical approaches contribute to a comprehensive understanding of TB dynamics and support evidence-based decision-making in TB control and prevention efforts.

Studies that aim to examine the progression of the disease's symptoms over time benefit from the usage of databases. Based on continuous data streams, such studies are able to forecast the likelihood of incidents (NAIDUS et al., 2016). Additionally, the incorporation of various factors, particularly demographic and socioeconomic variables, in health research is made possible by the use of geoprocessing techniques with geographic information systems (GIS) and spatial statistics (BAILEY et al., 2001), making it possible to generate hypotheses regarding the transmission of diseases in different populations (GUIMARAES et al., 2016). From 2000 to 2015, global and national efforts to reduce the burden of TB were focused on achieving targets set in the context of the Millennium Development Goals (MDGs). The MDGs were established by the United Nations (UN) and WHO in 2000 and targets were set for 2015 with the creation of the STOP TB strategy.

The main goals of the STOP TB strategy, which were to be achieved by 2005, were to diagnose at least 70% of new TB cases through sputum smear microscopy and cure at least 85%, and by 2015 to reduce prevalence and deaths by 50% arising from TB in relation to1990 (LONNROTH et al., 2016). A new strategy called END TB consists of three pillars: 1) Comprehensive care and prevention centered on the TB patient; 2) Bold policies and support systems (patient support); 3) Intensification of research and innovation (WHO, 2015) and aims to end the global TB epidemic, with targets to reduce TB deaths by 95% and reduce new cases by 90% between 2015 and 2035 (LONNROTH et al., 2016).

A new classification of priority countries was defined by the WHO, which took into account three epidemiological characteristics: 1) TB burden, 2) Multidrug-resistant (MDR) TB and 3) TB/HIV co-infection. This classification consists of three lists, each containing 30 countries, among which Nigeria is found in two of these lists: disease burden and TB/HIV co-infection (WHO, 2021).

The low TB case finding for both adults and children is problematic for TB control and monitoring in Nigeria. Just before the pandemic, only 104,904 TB cases were detected out of an estimated 407,000 of all TB cases expected to be detected. This indicates a treatment coverage of just 25.8 per cent and leaves a gap of 302,096 people with TB who were either undetected or detected but were not recorded (WHO, 2019).

In Nigeria, according to WHO 2019, just before the pandemic, only 104,904 TB cases were detected out of the 407,000 cases expected to be detected, making a coverage of just 25.8 per cent and a gap of 302,096 people. The country has one of the lowest case detection rates among the high TB burden countries with 117,320 (27%) of the incident cases being notified in 2019.

Regarding Nigeria's socioeconomic position, Nigeria's Human Development Index (HDI) is 0.535. In the third quarter of 2015, the labor force population in Nigeria was predicted to be 75.9 million people, with 20.7 million people unemployed. Currently, it is expected that the unemployment rate is 9.9% and the underemployment rate is 17.49%. Ages 15 to 34 are the ones with the highest rates of unemployment, while metropolitan areas have greater rates than rural ones. On the other hand, underemployment is more common in rural areas. According to the trend study, the jobless rate increased overall from 5% in 2010 to 9.9% in 2015. (UN, 2016)

In spite of Nigeria's economic progress and diversification, poverty levels have not significantly decreased. According to the 2010 Harmonized Nigeria Living Standards Survey (HNLSS), which included 112.7 million people, 69% of the population is thought to be living in poverty. The country's geopolitical zones all have varying levels of poverty, with northern regions having higher levels than southern regions and rural areas having higher levels than metropolitan areas. By all measures of poverty, the South-West has the lowest rate of poverty whereas the North-West has the highest rate measures.

In Nigeria, 61% of households have access to a more reliable source of drinking water. Pipe-borne water inside of a home; water from public taps or boreholes; protected well, spring water; bottled water; and rainwater are examples of "improved sources". A tube well or a borehole is the most typical source of drinking water (37%). Compared to rural families (49%), a higher percentage of urban households (76%) have access to a better source of drinking water. 25% of families utilize shared facilities, whereas 30% have upgraded toilets that are not shared with other households. 4596 out of 4550 households make use of an unimproved toilet facility. Twenty- nine percent (29%) of households have no toilet facility, rural households are more likely than urban households to have no toilet facility (40% versus 16%), and Households in urban areas have higher access to improved sanitation than rural areas. (UN, 2016)

These figures suggest that Nigeria did not meet its MDG target of at least 63% having improved sanitation facilities and at least 75% of the population having access to improved drinking water by 2015.

In Nigeria, 75% of men and 50% of women are literate. In urban areas, both men and women have greater literacy rates than in rural areas. 38 percent of women and 21 percent of males say they have never attended school. For both men and women, only 17% have completed elementary school. Men (62%) and women (45%) have completed at least a secondary education. Greater educational attainment is more likely for both women and men who live in metropolitan regions than for those who do not. Younger women are more likely to have attended school than older women.

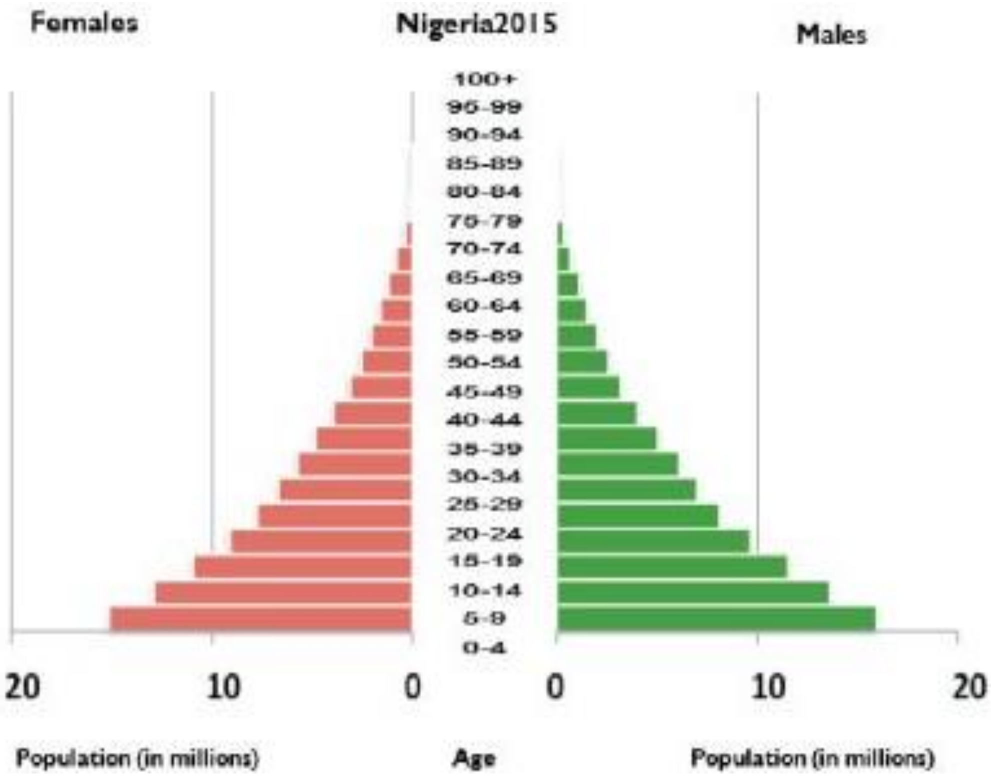
In Nigeria, women in urban regions have a median of 10.2 years of education, compared to women in rural areas who have a median of zero years. Compared to 5% of women in the South-South and South-East zones, 69% of women in the North-West zone have never attended school. (UN, 2016) Forty-five percent (45%).

Both the public and commercial sectors in Nigeria provide health services through primary, secondary, and tertiary healthcare facilities. Despite the fact that basic healthcare is the backbone of the Nigerian health system, both primary and secondary healthcare services are poorly provided for, funded, and managed.

The availability of healthcare facilities does not guarantee the accessibility of high-quality medical care. For a significant portion of the population, certain services are not typically available. Due to frequent industrial action by all healthcare provider cadres at public facilities, healthcare services are consistently disrupted. Although the private sector has been essential in making health services accessible, it has nevertheless been poorly integrated into Nigeria's healthcare system. In rural and difficult-to-reach locations in particular, many healthcare institutions are located distant from the populace. The cost of services, travel time to the medical institution, and the attitude of medical staff are the most frequent obstacles to the population's access to healthcare.

Health services are often of poor quality and do not inspire confidence in the populace. Due to this, some people are now seeking medical attention abroad or avoiding primary and secondary hospitals in favor of tertiary medical centers. Clinical guidelines are poorly followed yet there is a disproportionally high level of competence in the diagnosis and treatment of clinical disorders. Even in cases where the quality of the care provided may be excellent, service consumers' perceptions may not match the reality. These might be brought on by the unfavorable attitudes of healthcare professionals, the haziness of standards and procedures, and the ineffective application of these recommendations. (NHP, 2016)

The Health Information System (HIS) policy has been reviewed, with the vision of the policy being "Health Information System that ensures evidence-based decision making for improved health status of Nigerians" and the mission being "to produce timely, reliable and accurate data for informed policy making, programming, and resource allocation for health care" at the three tiers of government" (FMH, 2014). Despite this, Nigeria's health system and health information system continue to face a number of issues.



Source: United Nations Department of Economic and Social Affairs, Population Division [2015]. World Population Prospects: The 2015 Revision).

Some of the health policies in Nigeria include;

I. To decrease morbidity and mortality among pregnant women, newborns, and adolescents in Nigeria and to advance universal accessibility to quality reproductive and sexual health services for young people and adults at all stages of life.

II. To achieve the third sustainable development goal's targets for reducing the burden of communicable illnesses in Nigeria.

III. To achieve the third sustainable development goal's targets by considerably reducing the prevalence of non-communicable diseases in Nigeria. the burden of public health emergencies

IV. To promote the mental health and wellbeing of all Nigerians

V. To provide good oral health for all Nigerians

VI. To promote eye care services for Nigerians

VII. To improve the wellbeing of people living with disabilities so that they can have an economically productive life.

VIII. To better the nutritional status of Nigerians at all stages of life, with a special emphasis on vulnerable groups, such as pregnant women and young children.

IX. To reduce the burden of food-borne diseases in the general population

X. To reduce the burden of disease resulting from unsafe drinking water and poor sanitation

XI. Ensure proper healthcare waste management and protect human health from environmental and chemical hazards and the effects of climate change.

XII. To ensure access to gender- sensitive health services, irrespective of sexual orientation

XIII. To make Nigeria a preferred regional medical tourist destination and reverse the current trend for outward medical tourism.

XIV. Primary health care shall remain the basic philosophy and central focus for national health development.

In Nigeria, TB data is usually collected from the local government area health service, transferred to the state ministry of health and collated in the quarterly health report. The three tiers of government; (local, state and federal government). Private healthcare providers also play important roles in health service delivery. Traditional medicine, complementary medicine and alternative medicine are also on the rise in Nigeria. Only 25.15 % of the total amount spent on health care in Nigeria is paid for by the government. About 70% of the citizens' spending on health (74.85) is made up of out-of-pocket expenses to cover the cost of access to healthcare in both public and private facilities. The majority of the remaining funds that people spend on their health is used to buy expensive alternatives (OBOKOH, 2019).

Following the challenging targets set by the WHO for countries in its post-2015 strategy, definingas a vision of the future “A world free of tuberculosis: zero deaths, illness and suffering caused by the disease”. To achieve this commitment, in reference to World Tuberculosis Day – 2015, the Stop TB Partnership was launched which has been modified to End-TB strategy with 3 pillars that are patient centered and supportive of innovation and research (WHO, 2020).

This work is based on the Pilar 3, and considers some tools for surveillance of TB in territories. It is important to highlight that there are several tools used for surveillance in public health (MONKEN; BARCELLOS, 2005; MURRAY; COHEN, 2016), including:

a) Disease registries: These are databases that collect information on cases of a particular disease or condition. They can be used to monitor trends in disease incidence and prevalence, and to track outbreaks.
b) Syndromic surveillance: This involves monitoring data on symptoms and other indicators that may be associated with a particular disease or condition. For example, emergency room visits for respiratory symptoms can be monitored to detect a potentialoutbreak of influenza;
c) Laboratory-based surveillance: This involves monitoring laboratory test results for specific diseases or conditions. This can help to identify outbreaks and track thespread of disease.
d) Electronic health records (EHRs): EHRs can be used to collect and analyze data on patient demographics, diagnoses, and treatments. This information can be used to monitor disease trends and identify populations at risk;
e) Geographic information systems (GIS): GIS can be used to map the distribution of diseases and identify areas with high incidence rates. This can help to target

interventions and resources to where they are most needed.

f) Outbreak investigation tools: These include methods for conducting epidemiological investigations of outbreaks, such as case-control studies and contact tracing. These tools can be used to identify the source of an outbreak and prevent further spread of disease.

Thus, this study seeks to advance knowledge in health surveillance of territories (item e, described above) by filling a gap with regard to Time series and spatial distribution of TB in Nigeria, with the identification of hotspots and areas with high prevalence, in addition to contributing to the qualification of practices in health services and the formulation of public policies that contribute to solving the problem. Studies covering public health surveillance are essential for decision-making and the design of strategic actions aimed at mitigating problems, and their main objective is to provide information to guide these interventions and there are still few studies using these approaches in African countries, such as Nigeria, but specifically in Oyo, no studies on tuberculosis were found using space-time approaches.

2. SYSTEMATIC REVIEW OF LITERATURE

A systematic review of literature was carried out in order to identify studies that applied spatial, spatiotemporal, and time series analyses for understanding and estimating the vulnerability of territories and communities to TB, in addition to verifying the importance of the study and knowledge gaps, considering what has been produced so far.

Systematic review techniques include (I) formulating the correct question to answer (Condition; Context; Population - CoCoPop), (II) protocol development (inclusion and exclusion criteria), (III) detailed and broad literature search and (IV) abstracts screening of studies identified in the search and subsequently of the selected complete texts (Preferred Reporting Items for Systematic Review and Meta-Analysis - PRISMA) (LINARES-ESPINÓS; HERNÁNDEZ; DOMÍNGUEZ-ESCRIG, 2018).

Systematic reviews play a crucial role in establishing qualitative and quantitative relationships by utilizing the results of various studies, often through meta-analyses, to strengthen the evidence. A systematic review entails a comprehensive and reproducible summary of the findings from existing publications pertaining to a specific topic or clinical question. To enhance the rigor and transparency of scientific writing, a structured methodology is employed in conducting a systematic review.

By following a structured approach, the systematic review methodology ensures that the process is systematic, transparent, and replicable. This typically involves clearly defining the research question, specifying inclusion and exclusion criteria for studies, conducting a comprehensive search of relevant literature, appraising the quality of included studies, extracting data, synthesizing the findings, and critically assessing the overall strength of the evidence.

By adhering to these methodological steps, systematic reviews provide a robust and rigorous approach to summarize and evaluate the available evidence on a specific topic, enabling researchers and decision-makers to make informed conclusions and recommendations based on the best available evidence.

2.1. Methods used for Systematic Mapping

The protocol of this review was registered on PROSPERO (CRD42021274287). This systematic review was developed in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) (MOHER et al., 2015; SHAMSEER et al., 2015) recommendations which involved the following steps:

2.1.1. Step 1: Research Question

The research question was based on the strategy "CoCoPop" coded as "Where are the geo-spatial hotspots of tuberculosis among the general population located in any global context?", the acronym CoCoPop was used, which was structured as follows: Condition (Co) corresponding to TB; Context (Co) every global context and Population (Pop) general population. The strategy is represented in Table 1.

Table 1 - CoCoPop structure for research question.

Description	Abbreviation	Research Components
Condition	Co	Tuberculosis
Context	Co	Global Context
Population	Pop	General population

Source: Prepared by the author.

Thus, the main research question that guided this review was the following: Where are the specific territories and areas that are vulnerable to TB, identifiable by specific TB hotspots?

Secondary questions (Q) were established for a better characterization of the publications to be obtained, they include:

Q1 - Which countries have publications on geospatial analysis of TB?

Q2 - What are the most used spatial analysis techniques?

Q3 - Which studies involve association with social vulnerability?

Q4 - What is the relationship between TB cases and their specific hotspot regions?

Q5 - Are there other prominent factors that affect hotspots location?

2.1.2. Step 2: Research protocol

A research protocol was elaborated, in which all stages of the review process were established. Ecological, cross-sectional and observational studies that had in their scope the spatiotemporal analysis and geospatial analysis of TB were included in the protocol.

2.1.3. Step 3: Search for Evidence

2.1.3.1. Data base

The bibliographic databases MEDLINE (Medical Literature Analysis and Retrieval System Online) via PubMed (Public/Publisher MEDLINE) – United States National Library of Medicine – access via: https://www.ncbi.nlm.nih.gov/pubmed/; LILACS (Latin American Literature in Health Sciences (*Literatura Latino-Americana e do Caribe em Ciências da Saúde*)) via BVS (Virtual Health Library (*Biblioteca Virtual em Saúde*)) – access via: http://bvsalud.org/; EMBASE (Excerpta Medica Database) via CAFe (Federated Academic Community – *Comunidade Acadêmica Federada*) of CAPES (Coordination for the Improvement of Higher Education Personnel – *Coordenação de Aperfeiçoamento de Pessoal de Nível Superior*) journals portal – access via: https://www-periodicos-capes-gov-br.ezl.periodicos.capes.gov.br/index.php?; Scopus (SciVerse Scopus) via CAFe from CAPES journals portal; Web of Science (Web of Science Core Collection) via CAFe from CAPES journals portal; and Google Scholar – access via: https://scholar.google.com.br/?hl=pt.

2.1.3.2. Search Strategy

The search was carried out in February 2023 on PubMed, LILACS, EMBASE, Scopus (SciVerse Scopus) and Web of Science. For gray literature search, it was carried out with Google Scholar. The keywords and descriptors used for the search were identified in the Descriptors in Health Science (DeCS) and Medical Subject Headings (MeSH). The search strategies were adapted for each database using Boolean operators (OR and AND) as shown in Chart 1. In the search, language limits will not be used.

Chart 1 - Article search strategies used to carry out systematic review on geo-spatial hotspots of tuberculosis in the general population globally.

Databases	Vocabulary found/free vocabulary

MEDLINE	("tuberculosi" OR "tuberculosis"[MeSH Terms] OR "tuberculosis" OR "tuberculoses" OR "tuberculosis s" OR "tb" AND ("hotspot" OR "hotspots" OR "hot-spot" OR "hot-spot" OR ("hotspot" OR "hotspots" OR "hot-spots" OR "hot-spots" OR (("geographic" OR "geographical" OR "geographically" OR "geographics" AND ("focal" OR "focalities"[All Fields] OR "focality"[All Fields] OR "focalization"[All Fields] OR "focalized" OR "focally" OR "focals" OR "local" OR "localisation" OR "localisations" OR "localise" OR "localised" OR "localises" OR "localising" OR "localization" OR "localizations" OR "localize" OR "localized" OR "localizer" OR "localizers" OR "localizes" OR "localizing" OR "locally" OR "locals" AND 1,143 articles
	("risk"[MeSH Terms] OR "risk" OR "risk area"] OR "risk areas" OR "spatialanalysisOR "spatial interpolation" OR "spatial dependency" OR "spatial dispersion" OR "spatiotemporal analysis" OR "spatio-temporal analysis" OR"spatiotemporal patterns" OR "spatio-temporal patterns" OR "spatiotemporalepidemiology" OR "spatio-temporal epidemiology" OR "geographic information systems" OR "medical topography" OR ("geographic mapping"[MeSH Terms] OR ("geographic" AND "mapping" OR "geographic mapping" OR "georeferencing" OR "georeferenced" OR"geoprocessing"

LILACS	(tuberculose OR tuberculosis OR tb) AND (hotspot OR "hot-spot" OR "hot spot" OR hotspots OR "hot-spots" OR "hot spots" OR "geographical localization of risk" OR "risk area" OR "risk areas" OR "spatial analysis"OR "spatial interpolation" OR "spatial dependency" OR "spatial dispersion" OR "spatiotemporal analysis" OR "spatio-temporal analysis" OR "spatiotemporal patterns" OR "spatio-temporal patterns" OR "spatiotemporal epidemiology" OR "spatio-temporal epidemiology" OR "geographic information systems" OR "medical topography" OR georeferencing OR geoprocessing OR "punto alto" OR "localização geográfica de risco" OR "área de risco" OR "áreas de risco" OR "localización geográfica de riesgo" OR "zona de riesgo" OR "zonas de riesgo" OR "análise espacial" OR "interpolação espacial" OR "dependência espacial" OR "dispersão espacial" OR "análise espaço-temporal" OR "padrões espaço-temporal" OR"epidemiologia espaço-temporal" OR "análisis especial" OR "interpolación espacial" OR "dependencia espacial" OR "dispersión especial" OR "análisis espaciotemporal" OR "patrones espacio-temporales" OR "epidemiología espaciotemporal" OR "sistemas de informação geográfica" OR "sistemas de información geográfica" OR "topografia médica" OR "topografía médica" OR georreferenciamento OR georeferenciación OR geoprocessamento OR geoprocesamiento) 120 articles
EMBASE	#1 'tuberculosis'/exp OR tuberculosis OR 'tb'/exp OR tb #2 'hotspot'/exp OR hotspot OR 'hot-spot' OR 'hot spot'/exp OR 'hot spot' OR hotspots OR 'hot-spots' OR 'hot spots' OR 'geographical localization of risk' OR 'risk area' OR 'risk areas' OR 'spatial analysis'/exp OR 'spatial analysis' OR 'spatial interpolation' OR 'spatial dependency' OR 'spatial dispersion' OR 'spatiotemporal analysis'/exp OR 'spatiotemporal analysis' OR 'spatio-temporal analysis'/exp OR 'spatio-temporal analysis' OR 'spatiotemporal patterns' OR 'spatio-temporal patterns' OR 'spatiotemporal epidemiology' OR 'spatio-temporal epidemiology' OR 'geographic information systems'/exp OR

	'geographic information systems' OR 'medical topography'/exp OR 'medical topography' OR 'georeferencing'/exp OR georeferencing OR geoprocessing #3 #1 AND #2 1,415 articles
Scopus	TITLE-ABS-KEY (tuberculosis OR tb) AND TITLE-ABS-KEY (hotspot OR "hot-spot" OR "hot spot" OR hotspots OR "hot-spots" OR "hot spots" OR "geographical localization of risk" OR "risk area" OR "risk areas" OR "spatial analysis" OR "spatial interpolation" OR "spatial dependency" OR "spatial dispersion" OR "spatiotemporal analysis" OR "spatio-temporal analysis" OR "spatiotemporal patterns" OR "spatio-temporal patterns" OR "spatiotemporal epidemiology" OR "spatio-temporal epidemiology" OR "geographic information systems" OR "medical topography" OR georeferencing OR geoprocessing) 1,470 articles
Web ofScience	(TS=(tuberculosis OR tb)) AND TS=(hotspot OR "hot-spot" OR "hot spot" OR hotspots OR "hot-spots" OR "hot spots" OR "geographical localizationof risk" OR "risk area" OR "risk areas" OR "spatial analysis" OR "spatial interpolation" OR "spatial dependency" OR "spatial dispersion" OR"spatiotemporal analysis" OR "spatio-temporal analysis" OR "spatiotemporal patterns" OR "spatio-temporal patterns" OR "spatiotemporalepidemiology" OR "spatio-temporal epidemiology" OR "geographic information systems" OR "medical topography" OR georeferencing OR geoprocessing) 87 articles
GoogleScholar (Two strategies was used)	Spatiotemporal analysis tuberculosishotspots tuberculosis 200 articles

Source: Prepared by the authors.

2.1.3.3. Inclusion and Exclusion Criteria

The review includes studies which performed spatial analysis or spatiotemporal analysis of TB, regardless of the country in which it was carried out. For study selection, primary studies or gray literature were included, which intend to identify the hotspots of TB in the general population in the global context. Studies that include only latent infection with *Mycobacterium Tuberculosis* or only special populations like TB-coinfection or people deprived of liberty were not excluded.

2.1.3.4. Initial Selection

The Qatar Computing Research Institute Rayyan Systematic Review application QCRI was used to manage citations chosen from databases (OUZZANI et al., 2016). From there, we excluded duplicate publications and titles and abstracts read by two independent reviewers. In case of any doubt or disagreement between the two reviewers regarding the inclusion of any material, a third reviewer was consulted. To confirm the inclusion of selected articles, all eligible articles were read in full.

The entire search process and the eligibility process of the materials initially found and finally included were presented in a flow diagram, as recommended by the PRISMA (PAGE et al., 2021).

2.1.3.5. Final extraction and selection

Data was extracted using a standard form designed by the research team, after which an independent pair of trained reviewers compared the results and, in the event of dispute, a third reviewer was consulted. The data extraction form used was prepared according to items created in consonance by the authors, they are: Authors, Year of publication, Country of study, Purpose of study, Type of data, Type of cases, Geographical level, Spatial methods, Cluster detection methods, Statistical regression methods, Spatial error, Spatial smoothing techniques, Study period, Results, Tuberculosis hotspots, Hotspot characteristics.

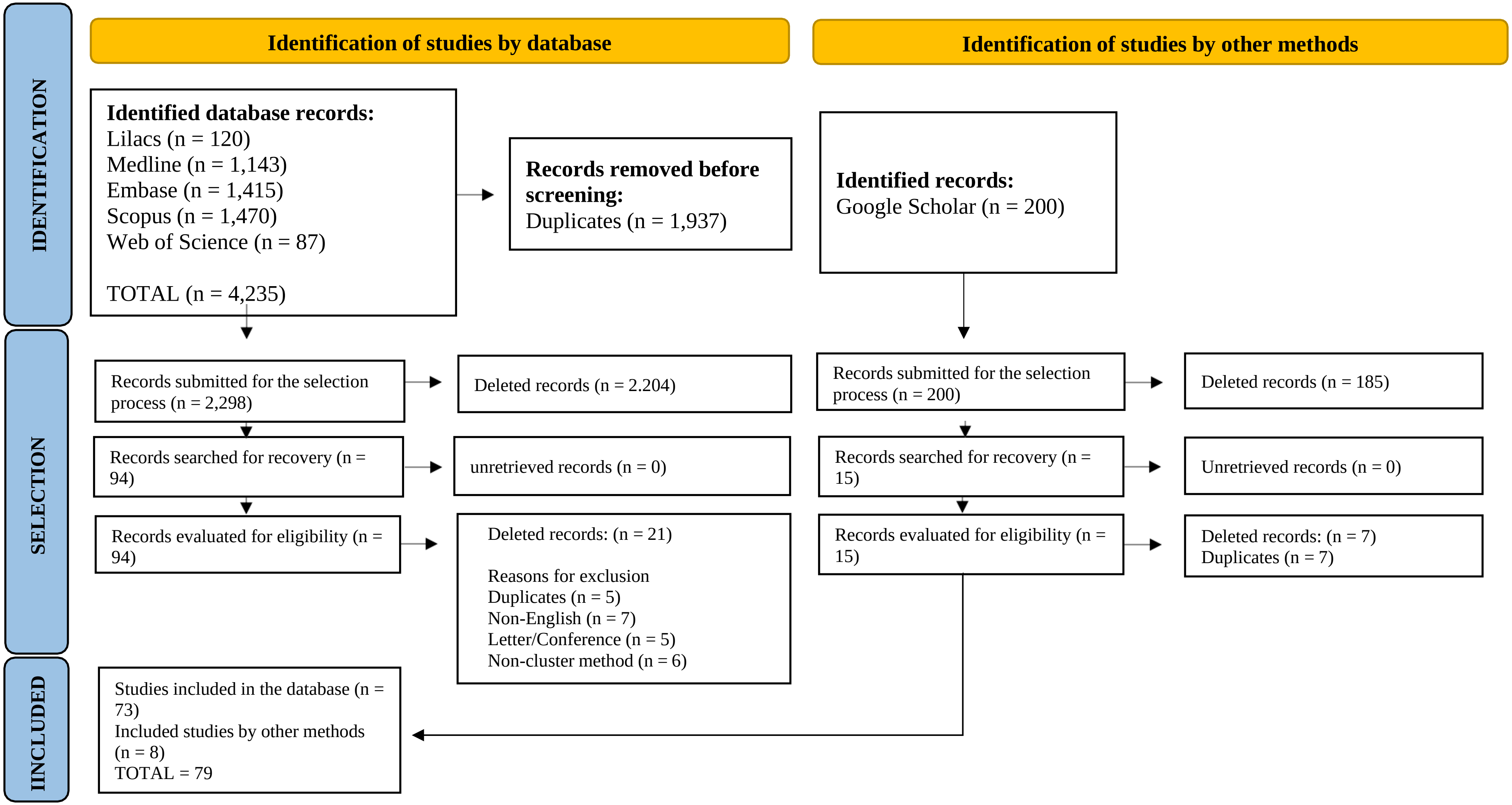
2.1.3.6. Summary of studies

The studies included in the final selection were cataloged, so that the mapping results could be better visualized and understood. A table with the summary of the final articles was built containing an identification code to facilitate reference to the studies listed throughout the text, the Study, Authors / Year of publication / Country of study, Study Objective, Study period, Data type / Geographic level, Case type, Study, Type of map, Cluster detection method, Regression statistics method, smoothing technique and results were used.

2.1.3.7. Summary of systematic mapping results

Systematic mapping was performed according to the previously described protocol. In the search carried out in the databases, 4,235 publications were found, while on Google Scholar, we found 200 articles. After the selection steps, 102 publications remained in the study but the 23 studies that did not meet the inclusion criteria after reading the full text were excluded leaving 79 studies. Figure 1 illustrates the steps followed to conduct the mapping with the respective results.

Figure 1 - PRISMA Diagram showing article selection.



Source: Modified from Page et al. (2020).

Chart 2 presents the authors and locations where the studies were carried out, which cut across Africa, North and South America and Asia. About 90% of the studies used notification data and the general study period ranged from 1982 till date. More than 50% of the study used pulmonary and extrapulmonary cases in their study.

Chart 2 - Characteristics of the studies included in the systematic review of the geo-spatial hotspots of tuberculosis in the global general population.

Study	Authors / Year of publication / Country of study	Study Objective	Study period	Data type / Geographic level	Case type
S1	RIDZUAN et al., 2021 Malaysia	Utilizing a public participatory GIS (ppgis) technique and a 5- risk scale from 1 to 5 to study the effects of lifestyle risk variables on TB cases in Shah Alam.	2017	Survey / Region	Lifestyle risk factors of TB diseases
S2	SELMANE; L'HADJ, 2021 Algeria	To create a forecasting model, define the spatiotemporal distribution, and determine the seasonal pattern oftuberculosis (TB) in Algeria.	1982 to 2019	Notification / Country	Pulmonary and extra pulmonary
S3	MESQUITA et al., 2021 Brazil	To present the geographic and epidemiological trends of TB infections between 2013 and 2018 in the Pará, Brazil, Amazonian area, Marajó Island.	2013-2018	Notification / Region	Pulmonary andextra pulmonary

S4	TANJUNG et al., 2021 Indonesia	To identify the prevalence of the pulmonary Tb risk factorsin the Kabanjahe District, Karo Regency.	Jan-Oct 2020	Survey / Region	Pulmonary andextra pulmonary
S5	YU et al., 2020 China	To evaluate the temporal and spatial distribution characteristics of PTB in Chongqing.	2011-2018	Notification / City	Only Pulmonary TB
S6	XIA et al., 2020 China	To describe the case notification rate (CNR) and determinewhat factors influence the TB pandemic.	2006 to 2015	Notification / Province	Only Pulmonary TB
S7	CHIRENDA et al., 2020 Zimbabwe	To use geospatial methods to describe the presence of hotspot transmission of TB cases in Harare city between2011 and 2012.	2011 and 2012	Notification / City	Not specified (TB cases)
S8	PEREIRA et al., 2022 Brazil	To study the temporal trend of Santa Catarina's tuberculosis incidence rate by sex from 2010 to 2019 and to define the profile of patients.	2010-2019	Notification / State Level	Not specified (New TB cases)
S10	YANG et al., 2019 China	To look into the spatiotemporal distribution of TB at the township level throughout urbanization in the brand-new urban area of Nanchang.	2010 to 2018	Notification / Region	Not specified (TB data)
S11	LI et al., 2019 China	From 2009 to 2015, investigate the spatiotemporal distribution of TB and its contributing factors in China'smainland.	2009-2015	Notification / Region	Pulmonary andextra pulmonary

S12	GEHLEN et al., 2019 Brazil	In a Brazilian city with a high TB incidence, to elucidate the prevalence of TB and its associations with the Human Development Index (HDI).	2011-2013	Notification / City	Pulmonary andextra pulmonary
S13	ZHANG et al., 2019 China	To identify the geographic distribution of tuberculosis and itsrelationship to environmental factors in mainland China.	2005-2015	Notification / Country	Pulmonary andextra pulmonary
S14	ZHANG et al., 2018 China	To investigate the factors influencing the prevalence of tuberculosis and the temporal and geographic relevance of the pulmonary tuberculosis pathogenesis.	2008-2015	Notification / Country	Only Pulmonary
S15	LIU et al., 2018 China	To examine the spatial and temporal clustering analysis of tuberculosis at the prefecture level in mainland China from 2005 to 2015.	2005-2015	Notification / Country	Pulmonary andextra pulmonary
S16	RODRIGUES et al., 2017 Brazil	To examine the geographic distribution of the endemictuberculosis from 2002 to 2011 in Rio de Janeiro State.	2002 to 2011	Notification / State	pulmonary andextra pulmonary
S17	KHAZAEI et al., 2019 Iran	To look at the regional and spatial distribution of TB in Hamadan Province from 1992 to 2013.	1992-2013	Notification / Country	Pulmonary andextra pulmonary
S18	FUSCO et al., 2017 Brazil	Analyzing the spatial distribution of patients in a municipality in the state of So Paulo and describing the	2008-2013	Notification / City	Pulmonary andextra pulmonary

		epidemiological clinical picture of tuberculosis.			
S19	MAGALHÃES etal., 2017 Brazil	To use spatial statistical models to discover pertinentsocioeconomic factors for the prevalence of the disease in order to analyze the spatial pattern of tuberculosis (TB) from 2005 to 2008.	2005-2008	Notification / Municipal	Pulmonary andextra pulmonary
S20	MOHAMMED etal., 2019 Iraq	Using geographic information science (GIS) technology to identify hotspot geographic locations with PTB incidenceand to assess spatial global autocorrelation.	2010-2016	Notification / City	Only Pulmonary
S21	CHINPONG et al., 2022 Thailand	To outline the TB incidence and mortality patterns inThailand from 2011 to 2020, including their temporal trends and geographic distribution.	2011-2020	Notification / Country	Pulmonary and extra pulmonary
S22	PUSCH et al., 2019 Germany	The locations with the highest densities of incident TB cases and variations in distribution over a ten-year period are identified in order to analyze the pattern of case distribution within the municipal limits.	2006-2015	Notification / Country	Pulmonary andextra pulmonary
S23	ANDRADE et al., 2021 Brazil	To locate the geographic areas of a Brazilian municipality that are more likely to experience tuberculosis and to have successful treatment.	2013-2018	Notification / City	Pulmonary andExtra pulmonary

S24	WANG et al., 2021 China	The Beijing-Tianjin-Hebei metropolitan agglomeration, which is a region with a high number of aging householdsand socio-economic inequality, was the focus of the firstobjective, which was to look into spatio-temporal variation inthe incidence of TB among people older than 65 years. The second goal was to look at any potential non-linear relationships between socioeconomic characteristics and the risk of TB in this aging population.	2009-2014	Notification / Region	Only Pulmonary
S25	RENGGANIS WARDANI et al., 2020 Indonesia	To examine the temporal and spatial patterns of TB clustersin Bandar Lampung, Indonesia, from 2015 to 2016, and to pinpoint the clusters' features for population density and percentage of poverty.	2015 to 2016,	Survey City	Pulmonary andextra pulmonary
S26	SATRIANI et al., 2018 Indonesia	To identify risk factors for TB illness occurrence in Barru regency and use geographic information systems (GIS) to map the geographical patterns of TB.	May-Jun 2016	Survey / City	Only Pulmonary
S27	ZUO et al., 2020 China	To track the epidemiology and spatial-temporal aspects oftuberculosis in China from 2004 to 2017.	2004- 2017	Notification / Country	Pulmonary andextra pulmonary
S28	ASEMAHAGN etal., 2021 Ethiopia	Determine whether reported cases of pulmonary tuberculosis (PTB) in the East Gojjam Zone of	2013-2019	Notification / Region	Only Pulmonary

		northwest Ethiopia are geographically and chronologically clustered.			
S29	SHOJAEI et al., 2017 Iran	To provide two cutting-edge statistical techniques, take into account the spatial distribution of tuberculosis incidence in Iran.	Not mentioned	Notification / Country	Only Pulmonary
S30	JIANG et al., 2022 China	To provide information on the spatiotemporal distributiontraits of reported BP-PTB and notified BN-PTB in NorthwestChina in order to support interventions and enhance PTB management.	2011-2018	Notification / Province	Only Pulmonary
S31	DUAN et al., 2022 China	To identify the epidemic's features and the spatiotemporal distribution of TB cases reported in Shandong Province, and to offer a scientific foundation for the creation of more potentTB prevention and control measures.	2016-2020	Notification / City	Pulmonary and intrapulmonary
S32	ROMANYUKHA et al., 2020 Russia	Moscow's high-incidence residential regions for tuberculosis will be identified utilizing spatiotemporal analysis of incidence data.	2000-2015	Notification / City	Only Pulmonary
S33	SADEQ et al., 2018 Morocco	Analyzing TB trends in Morocco, locating TB geographicalclusters, and identifying TB-related	1995-2014	Notification / Country	Only Pulmonary

		variables.			
S34	CARRASCO-ESCOBAR et al., 2020 Peru	The spatial distribution and clustering of TB cases in Lima, Peru, as well as the co-occurrence of PM2.5 and economic index clusters, were determined.	2015-2017	Notification / Country	Only Pulmonary
S35	BROOKS et al., 2022 Peru	To detect local hot areas of rates of reported tuberculosis cases using regularly gathered data, geographic information, and census data.	2013-2017	Notification / Region, District	Only Pulmonary
S36	SHAWENO et al., 2018 Ethiopia	To comprehend the geographic spread of tuberculosis from hotspots to areas in a remote area of Ethiopia that are placedat various distances from one another.	2010-2014	Notification / City	Pulmonary and Extra pulmonary
S37	GWITIRA et al., 2021 Zimbabwe	Using GIS and spatial statistics to investigate the geographical patterns of TB recurrence at the district level in Zimbabwe from 2015 to 2018 in order to identify areas at higher risk for the prioritization of control and intervention measures	2015-2018	Notification / Country	Only Pulmonary
S38	GEMECHU; DEBUSHO, 2022 Ethiopia	To evaluate the spatial clustering of concurrent TB and HIVpatients in Ethiopia at the district level.	2015-2018	Notification / Country	Pulmonary andextra pulmonary
S39	MOLLALO et al., 2019	To investigate the geographic spread of the illness and	2006-2010	Notification /	Pulmonary andextra

	USA	the viability of MLTs in TB modeling under the following suppositions (1) All reported county-level TB incidence statistics reflect the prevalence of the disease across the US, and (2) environmental and socioeconomic factors have an impact on the risk of TB infection.		Country	pulmonary
S40	IM et al., 2021 South Korea	To research TB cases in Korea from a socioeconomic andenvironmental vantage point.	2008-2016	Notification / Country	Pulmonary andExtra pulmonary
S41	GELAW et al., 2019 Ethiopia	The Amhara Region's sociodemographic characteristics ofspatial clusters were described in order to determine the spatial distribution of TB and its prevalence.	2014-2017	Notification / Region	Pulmonary andExtra pulmonary
S42	MOHIDEM et al., 2021 Malaysia	To elucidate the geographic location of TB cases in the Gombak district and their relationship to sociodemographic and environmental parameters	2013-2017	Notification / Region / District	Pulmonary andExtra pulmonary
S43	ROBSKY et al., 2020 Uganda	To ascertain, based on routinely collected data, whether small-scale geographic areas which have elevated reports of TB rates have a proportionately high risk of undiagnosed prevalent TB.	2018-2019	Notification / City (community)	Only Pulmonary
S44	LI et al., 2022	To provide evidence for the creation of more sensible public health policies, as well as for the prevention and	2010-2017	Notification / Country	Only Pulmonary

	China	reduction of TB incidence.			
S45	KHALIQ et al., 2022 Pakistan	To identify spatial-temporal TB clusters in Pakistan and comprehend patterns in TB notification throughout the country's various.	2007-2020	Notification / Region	Only Pulmonary
S46	HUANG et al., 2022 Peru	We find hotspots for local TB transmission by measuring thepairwise genomic distances between TB patient isolates as a function of geographic distance, and we contrast theselocations with high-incidence hotspots in the same regions.	2009-2012	Survey / City	Only Pulmonary
S47	BERRA et al., 2022 Brazil	To display and categorize the time series of COVID-19, TB notification, cure, treatment abandonment, and mortality; to assess the influence of the new coronavirus pandemic onthese indices in Brazil; and to assess the existence of geographical autocorrelation between TB and COVID-19.	2010-2021	Notification / City	Pulmonary andExtra pulmonary
S48	SOUSA et al., 2022 Brazil	To examine the spatial distribution of TB incidence and thefactors that influence it.	2001-2017	Notification / region	Pulmonary andExtra pulmonary
S49	PAIVA et al., 2022 Brazil	To investigate the temporal, spatial, spatial-temporal, andchronological-spatial effects of socially vulnerable individuals on the incidence of tb in Brazil from 2001	2001-2017	Notification / Country	Only Pulmonary

		to 2017.			
S50	ALMEIDA et al., 2022 Cuba	To spatially categorize children under 15 with tuberculosis inwestern Cuba between 2011 and 2015 in accordance with theevolving objectives for the eradication of the disease.	2011-2015	Notification / Region	Pulmonary andextra pulmonary
S51	LI et al., 2021 China	To identify notifiable respiratory infectious diseases' spatial distribution and epidemic traits.	2005-2014	Notification / Region	Only pulmonary
S52	ALENE et al., 2021 China	To analyze the spatial distribution of TB in Hunan Province, China, and to determine its socioeconomic, demographic,and environmental determinants.	2013 to 2018	Notification / Province	Only pulmonary
S53	DISMER et al., 2021 Haiti	To use routine TB surveillance data to conduct geographical analysis to see if there were operational geographic levels of TB transmission foci in the Ouest department from 2011 to 2016 that would help PNLT target preventative and control activities.	2011-2016	Notification / Country	Pulmonary andextra pulmonary
S54	KIANI et al., 2021 Iran	To determine the TB incidence rate's spatiotemporal patternin Iran between 2008 and 2018.	2008-2018	Notification / Country	Pulmonary andextra pulmonary
S55	GIACOMET et al., 2021 Brazil	To determine whether seasonal variation in tuberculosis occurs, to determine the temporal trend of	2001-2017	Notification / City	Pulmonary andextra pulmonary

		tuberculosis incidence following the deployment of the rapid molecular test (RMT-TB), to categorize the region according to case density and risk regions in Macapá, Amapá.			
S56	TITOSSE et al., 2020 Mozambique	Perform a space-time characterization of Maputo, Mozambique's TB prevalence.	2011-2016	Notification / Region	Pulmonary and extra pulmonary
S57	SILVA et al., 2021 Brazil	For the purpose of disease prevention, to identify spatial and spatiotemporal agglomerations of tuberculosis in a priority municipality in northern Brazil.	2009 to 2018	Notification / City	Only Pulmonary
S58	LEAL et al., 2019 Brazil	Examine the spatial distribution of new tuberculosis cases in relation to the locations of the Primary Health Care (PHC) facilities that handled the mandatory notification.	2010-2014	Notification / City	Only Pulmonary
S59	SANTOS et al., 2019 Brazil	Identify potential regions of underreporting or high transmission risk by analyzing the spatial distribution and trend of tuberculosis in the state of Alagoas from 2010 to 2015.	2010-2015	Notification / Region	Pulmonary andextra pulmonary
S60	SILVA et al., 2018	To pinpoint determinants impacting the geographic distribution and prevalence of tuberculosis in Olinda,	1991 to 2010	Notification / City	Only Pulmonary

	Brazil	Pernambuco, between 1991 and 2010.			
S61	CUI et al., 2019 China	To identify the spatiotemporal pattern of tuberculosis notification rates from 2010 to 2016 in the Guangxi Zhuang Autonomous Region of China and any potential relationships with ecological environmental factors.	2010 to 2016	Notification / Region	Pulmonary andextra pulmonary
S62	WANG et al., 2019a China	From 2010 to 2014, the spatiotemporal patterns and geographical variations of the prevalence of tuberculosis in Inner Mongolia were examined, and associated climatic factors were found.	2010 to 2014	Notification / Country	Only Pulmonary
S63	MAO et al., 2019 China	To analyze epidemic characteristics, spatial auto-correlation, and advanced space-time scan statistics to examine the dynamics of the temporal trends and spatial patterns of smearpositive PTB cases at the province level from 2004 to 2015.	2004-2015	Notification / Country	Only Pulmonary
S64	KHAZAEI et al., 2019 Iran	Investigated the spatial and geographic distribution of TB inthe province of Hamadan between 1992 and 2013.	1992-2013	Notification / Region	Pulmonary andextra pulmonary
S65	SAMADZADEH et al., 2019	To find out how TB is disseminated and where hot and cool TB areas have been in Iran's Ardabildo region	2007-2017	Notification / Region	Pulmonary andextra pulmonary

	Iran	over the past 12 years.			
S66	TADESSE et al., 2018 Ethiopia	To Identify the location, size and risk of purely spatial and spatiotemporal clusters for high occurrence of tuberculosis inthe Gurage Zone, southern Ethiopia during 2007 to 2016	2007 to 2016	Notification / Region	Pulmonary andextra pulmonary
S67	GUO et al., 2017 China	To inquire how TB differs in different regions and studyyears in terms of spatial clustering and seasonal variability.	2005-2013	Notification / Country	Only Pulmonary
S68	FAHDHIENIE et al., 2022 Indonesia	To examine if TB clusters exist in this district and their temporal pattern of distribution over the past three years(2019–2021).	2019-2021	Notification / Region	Pulmonary
S69	BIE et al., 2021 China	Use the INLA algorithm and the spatiotemporal distribution model to analyze the spatiotemporal patterns of the relative risk (RR) of tb in mainland China and the impact of seven influencing factors.	2013-2015	Notification / Country	Pulmonary andextra pulmonary
S70	MESQUITA et al., 2022 Brazil	to examine the regional and temporal dynamics of TB in the context of social inequality in northern Brazil from 2001 to 2016.	2011 and 2015	Notification / Region	Pulmonary andextra pulmonary
S71	CASTRO et al., 2018	Analyze the effectiveness of TB epidemiological	2008-2013	Notification /	Only Pulmonary

	Brazil	surveillanceand describe the social drivers of TB incidence in Manaus as well as its spatial distribution.		City	
S72	WANG et al., 2019b China	NOT MENTIONED.	2013-2016	Notification / Country	Only Pulmonary
S73	DIEFENBACH-ELSTOB et al., 2019 Papua, New Guinea	To identify TB patient clusters and characteristics linked to high rates of TB by describing the spatial distribution of the disease in the Balimo District Hospital (BDH) catchmentarea.	2013-2017	Notification / Country	Pulmonary andextra pulmonary
S74	LIMA et al., 2019 Brazil	The study's goal was to examine the regional and temporal dynamics of TB in northeast Brazil's socioeconomic inequality between 2001 and 2016.	2001-2016	Notification / Region	Only Pulmonary
S75	HUANG et al.,2017 China	Investigating the spatio-temporal dynamics of PTB cases in Zhaotong in order to produce valuable data that will aiddecision-makers in creating efficient regional prevention and control strategies.	2011-2015	Notification / Region	Only Pulmonary
S76	ZHANG et al.,2023 China	For targeted TB epidemic intervention, this study examined the temporal and spatial distribution patterns of PTB in Hubei Province.	2011-2021	Notification / City	Only Pulmonary
S77	RAO et al., 2017China	The objective of this research is to identify the spatial	2009-2016	Notification /	Only Pulmonary

		patterns of tuberculosis in the Qinghai province, which may be useful for the formulation and application of important preventative measures.		Region	
S78	DAO et al., 2022 Vietrnam	To provide an online geospatial platform that will aid healthcare professionals in data visualization, active case surveillance in the community, and spatial and temporal TB incidence prediction.	1st of January 2020to the 30th ofApril 2022.	Notification / Country	Pulmonary andextra pulmonary
S79	MILAHAM et al., 2022 Nigeria	Examined how TB Case Notification Rates, diagnoses, andcoverage vary geographically across LGAs.	2017-2019	Notification / Region	Pulmonary andextra pulmonary

Source: Prepared by the author.

Chart 3 elucidates methods used to identify the hotspots, majority used spatial scan statistic, generated thematic maps and used a specific regression model. 80% of the hotspots identified were associated with poor socioeconomic status and overcrowding.

Chart 3 - Spatial analysis methods and the results of the studies included on the systematic review of the geo-spatial hotspots of tuberculosis inthe global general population.

Study	Type of map	Cluster detectionmethod	Regression statistics method	Smoothing technique	Results
S1	Point map Thematic map Risk map	Spatial scanstatistic Outro-inverse distance weightedidw-geostatistical approach	Not mentioned	Not mentioned	TB Hotspot – located between Shah Alam hospitaland PKNS flat (0 to 0.5 risk Characteristics) TB burden not directly proportionate with lifestyle status factors factors only a minimal significant correlation occurred during geospatialanalysis.
S2	Rate map	Moran’s I, GetisOrd statistic	Not mentioned	Not mentioned	TB Hotspot –hot spots were localized in the northwest region of the country. Characteristics – Sputum positive TB changed to extra pulmonary TB with a downward trend ratio over 1982–2019.
S3	Thematic map Map of	Not mentioned	Regression models	Not mentioned	TB Hotspot – four named

	temporaltendency		(with or without including spatial terms)		municipalities had very high TB incidence. Characteristics – The strategic location of the city facilitated tourism attraction
S4	Point map Thematic map	k-NN (nearest neighbourhood test)	Regression models (with or without including spatial terms)	Not mentioned	TB Hotspot – Most cases were found in a particular village and, the TB distribution showed a trend of clustering with the nearest neighbor index established in the study. Characteristics – High proportion of underprivileged families within the population
S5	Rate map/ map oftemporal tendency	Spatial scanstatistics	Not mentioned	Not mentioned	TB Hotspot – The region southeast of Chongqing, which included three counties, had the most likely cluster.

					Characteristics - The PTB notification rates in Chongqing were not dispersed randomly. These counties and districts are the most crucial for TB control in the upcoming years because it was shown that they had an excess burden of PTB and had a higher risk of disease transmission.
S6	Thematic map	Moran's I, GetisOrd statistic	Bayesian CAR models	Fully Bayesian	TB Hotspot – Concentrated at the county level. Characteristics –TB notification rate suggested that neighboring counties were more likely to interact with each other
S7	Thematic map	Moran's I, GetisOrd statistic	Not mentioned	Not mentioned	TB Hotspot – The Harare city's west south-west region was the

					hotspot's highest point. Characteristics – Non-random TB occurrence
S8	Point Map	Not used (Timeseries study)	Prais-Winsten Regression Model	Not mentioned	TB Hotspots - Time series analysis Characteristics - reduction in TB incidence rates in Santa Catarina Yearly, there was a TB Statistically significant decline in the prevalence of tuberculosis among women
S9	Rate map	Kulldorff's scanstatistics	Not mentioned	Not mentioned	TB Hotspot – the most likely cluster of TB was in Zhenxiong county.and northeast angle of Yunnan. Characteristics – TB not randomly distributed

S10	Thematic map	Spatial scanstatistic	Not mentioned	Not mentioned	TB Hotspot – High–High cluster in Jiaoqiao and Changleng towns in the 8-years duration Characteristics –TB distribution was random across all towns from 2010 to 2018. Higher Tb rates in rural areas than in urban areas.
S11	Thematic map	None	Gwr	Spatial empirical Bayesian	TB Hotspot – The provinces of Xinjiang held the majority of the higher incidence areas. Characteristics – Obvious geographic heterogeneity
S12	Kernel density map	Moran's I, GetisOrd statistic	Not mentioned	Not mentioned	TB Hotspot – located in 4 neighborhoods; NiteróiA, Estância Velha/Olaria and Mathias VelhoB. Characteristics –TB cases showed

					heterogeneity across the 29 neighborhoods,
S13	Rate map	Moran's I, GetisOrd statistic	Geographically Weighted Regression	Not mentioned	TB Hotspot - Six high-high clusters were detected. Characteristics- Between 2005 and 2015, China's TB incidence was geographically imbalanced, with a high rate in the west and a low rate in the east.
S14	Thematic map	Morans i, getisordstatistic	Regression models (with or without	Not mentioned	High prevalence of respiratory tuberculosis and prevalence in three cities
S15	Thematic map	Kulldorff's space-time scan statistical analysis	Spatial scanstatistic	Not mentioned	TB Hotspots- was located southwest of Xinjiang Uygur Characteristics - clustering similar in each year the majority of the disease's victims.

S16	Rate map	Global moran (lisa)statistics.	Regression models (with or without including spatial terms) Multilevel poisson regression	EmpiricalBayesian	TB Hotspots - On the state's south coast, there was a notable concentration of areas with high TB incidence rates. Characteristics- Greater TB burden in large metropolitan areas
S17	Thematic map		Not mentioned	Not mentioned	TB Hotspots- risk of extra pulmonary occurrence higher in the western part Characteristics- Areas with high prevalence had effect on neighboring areas
S18	Point Map	Kernel pointdensity,	Not mentioned	Not mentioned	TB Hotspots-- The South and Southeast parts of the municipality had the largest concentration of cases.

					Characteristics - non-random distribution of TB Cluster detected in high urban areas with social vulnerability
S19	Thematic map	Morans I, Index	Multivariate regression model, spatial lag models	Fully Bayesian	TB Hotspots- The three clusters detected. Characteristics- -those who have trouble getting healthcare and are thus more disadvantaged make up the majority of the disease's victims.
S20	Map of temporaltendency	Moran's I, GetisOrd statistic	Bayesian carmodels	Spatial empirical Bayesian	TB HOTSPOTS – TB hotspots aggregated in seven quarters within Kerbala Province Characteristics - Likely presence of unknown environmental and socio-economic
S21	Rate map, thematic map,	Moran's I, GetisOrd statistic	Not mentioned	Spatial empirical	TB Hotspots- in the western

	Spatial contiguitymatrix map.			Bayesian	provinces and in the northern region Characteristics - Hotspots common along the borders with neighboring countries
S22	Point map/ Rate map/ Kernel density map	Moran's I, GetisOrd statistic	Spatial lag models	Spatial empirical Bayesian	TB Hotspots- detected in Riehl, Kalk and Mülheim Characteristics- located closer to the city Centre.
S23	Density Kernel map	Spatial scan statistic Isotonic Scanning	Not mentioned	Spatial empirical Bayesian	TB Hotspots- located in the central region of the municipality Characteristics- Areas with high demographic density and poor sanitary and socioeconomic conditions had higher TB cases
S24	Map of temporaltendency	Spatial scanstatistic	Spatial lag models	Spatial empirical	TB Hotspots- located in the northwest regions and southeast

				Bayesian	rural regions Characteristics - Decreasing temporal trend.
S25	Map of temporaltendency	Spatial scanstatistic	Spatial lag models	Spatial empirical Bayesian	TB Hotspots- the Labuhan Ratu, Kedaton, Way Halim, and Sukarame subdistricts were where the most likely cluster was discovered. Characteristics - All of the clusters shared the same social determinant traits.
S26	Point map	Not applied	Spatial lag models	NOT MENTIONED	According to the study, socioeconomic. characteristics including working, being a housewife, having a low education, smoking, and eating more conventionally

					are linked to the chance of developing tuberculosis.
S27	Rate map, Thematicmap	Moran's I, GetisOrd statistic	Regression models (with or without including spatial	Spatial empirical Bayesian	TB Hotspots- China southern region from 2004 to 2008, characteristics of this group
S31	Map of temporaltendency	Spatial scanstatistic	Not mentioned	Not mentioned	TB Hotspots- the southern region of Qingdao City and Liaocheng City, where they are concentrated. Characteristics - regional variations in temporal trends of TB prevalence.
S32	Rate map Thematic map	Spatial scanstatistic	Not mentioned	Not mentioned	TB Hotspots - In the Southern and Northern areas of the city. Characteristics - fewer adults with more schooling and lower capital toward housing

S33	Thematic map	Moran's I, GetisOrd statistic	Regression models (with or without including spatial terms)	Not used	TB Hotspots – north-west part of Morocco. Characteristics - poverty and poor housing conditions
S34	Rate map/ Thematicmap	Moran's I, GetisOrd statistic	GWR	Spatial empirical Bayesian	TB Hotspots- central-east part of Lima. Characteristics- Socio-economic and environmental risk factors of TB incidence
S35	Thematic map	Moran's I, GetisOrd statistic	Not specified	Spatial empirical Bayesian	TB Hotspots- in the eastern-central region Characteristics-TB prevalence spatial heterogeneity, underlying population care-seeking patterns, and access restrictions to diagnostic and treatment facilities.

S36	Thematic Map	Moran's I, GetisOrd statistic	Mixture models	Not mentioned	TB Hotspots- Rural Ethiopia Characteristics- Underdevelopment
S37	Rate map Thematic map	Spatial scanstatistic	Spatial lag models	Not mentioned	TB Hotspots- central, southern and western part of the country. Characteristics - congestion caused by formal and informal mining operations, excessive population.
S38	Map of temporaltendency	Moran's I, GetisOrd statistic	Not mentioned	Not mentioned	TB Hotspots- Addis Abeba, Adama, Dire Dawa, Bahir Dar, and Shashemene are among the most urbanized regions. Characteristics- urbanization and population density
S39	Rate map	Moran's I, GetisOrd statistic	Regression models	Spatial empirical	TB Hotspots- During the time of

	Thematic map		(with or without including spatial terms)	Bayesian	the research, in the continental US. Characteristics – economic factors, proportion of population of all ages in poverty economic factors, the percentage of people of all ages who are poor
S40	Rate map Thematic map	Moran's I, GetisOrd statistic	Regression models (with or without including spatial terms)	Spatial empirical Bayesian	TB Hotspots- The eastern region of Korea is where hotspots are mostly found. Characteristics - Migration
S41	Thematic map	Moran's I, GetisOrd statistic	Regression models (with or without including spatial terms)	Spatial empirical Bayesian	TB Hotspots - Mirab Armacho, Tach Armacho, Metema and Tsegede Characteristics – A weak TB control program in the area, insufficient availability of TB

					treatment and diagnosis, and poor treatment adherence.
S42	Rate map Thematic map Map of central tendency	Moran’s I, GetisOrd statistic	Regression models (with or without including spatial terms)	Spatial empirical Bayesian	TB Hotspots - prison in the southwest section of Gombak near Rawang mukim Characteristics - socioeconomic and environmental influences on TB cases.
S43	Rate map Thematic map	Spatial scanstatistic	Mixture models	Spatial empirical Bayesian	TB Hotspots- high-risk zones accounting 22%
S44	Map of temporaltendency	Moran’s I, GetisOrd statistic	GWR regression models (with or without including spatial terms)	Not mentioned	TB hotspots- located in the northwest and south Characteristics - Temperature, humidity and precipitation were related to TB incidence.
S45	Point map Rate map Thematic map	Not specified	Regression models (with or without including spatial	Not mentioned	TB Hotspots- In four districts of Punjab which are Bahawalpur, Faisalabad, Gujranwala and

	Map of temporal tendency		terms)		Lahore Characteristics - Unbalanced population socioeconomic factors
S46	Point map	Moran's I, GetisOrd statistic	Regression models (with or without including spatial terms)	Not mentioned	TB Hotspots- TB incidence and the percentage of clustered TB cases have a modest correlation. Characteristics - residents of low-transmission areas might travel often to regions where there is a high risk of contracting tuberculosis (TB), such as those where there is a high prevalence of HIV, malnutrition, or the use of biomass fuel.
S47	Rate map	Moran's I, GetisOrd statistic	Mixture models	Not mentioned	TB Hotspots- municipalities classified as High–High (high rates of COVID with high rates of

					TB). Characteristics - increasing temporal trend of the TB notification rate in the pre-pandemic period, especially in the North
S48	Thematic mapRate map	Spatial scanstatistic	GWR Regression models (with or without including spatial terms	EmpiricalBayesian	TB Hotspots - Located in Sobral, a municipality in the state's rural interior, and the metropolitan area of Fortaleza. Characteristics - The most probable cluster, which exhibits the characteristics of an urban agglomeration—constant migration between towns and greater levels of poverty—is constituted of the state's capital with the towns in the

					metropolitan region.
S49	Rate map Thematic map Map of centraltendency	Moran’s I, GetisOrd statistic spatial scan statistic	Spatial lag models	EmpiricalBayesian	TB Hotspots- Six of the 15 spatial-temporal clusters are in the state of So Paulo and spread over the northern and Southeastern regions. Characteristics - social vulnerability, low urban infrastructure and human capital,
S50	Rate map Thematic map	Not specified	Regression models (with or without including spatial terms)	Not mentioned	TB Hotspots- Not Indicated Characteristics - Not Indicated
S51	Rate map Thematic map Map of temporaltendency	Moran’s I, GetisOrd statistic spatial scan statistic	Mixture models	Spatial empirical Bayesian	TB Hotspot- Mainly in Binzhou, Liaocheng and Linyi. Characteristics - Not specified
S52	Rate map Choropleth map	Moran’s I, GetisOrd statistic	Spatial lag models Bayesian spatial	Fully Bayesian	TB Hotspots- observed in the

			Poisson regression models		western part of the province Characteristics – Climatic factors and health care access
S53	Point map Rate map Thematic map Map of temporal tendency	Moran's I, GetisOrd statistic Spatial scan statistic	Not mentioned	Not used	TB Hotspot - located near the coast of Port-au-Prince, Carrefour, Cité-Soleil, and in the northeastern quartiers of Delmas'.
S54	Rate map Thematic map Map of temporaltendency	Moran's I, GetisOrd statistic Spatial scan statistic	Not mentioned	Not mentioned	TB Hotspots- Iran's northeast and southeast have been designated as TB hotspots. Characteristics - The province has a high incidence of TB, while nearby areas have a low prevalence.
S55	Thematic map Map of temporaltendency	Moran's I, GetisOrd statistic Spatial scan statistic	Regression models (with or without including spatial	Not mentioned	TB Hotspots - Central, Northern and Southern districts

	Density kernel map		terms)		Characteristics - low Human Development Index, stilt houses, absence of sanitation, clusters of population, and large number of informal workers corroborate the spread of the disease.
S56	Map of temporal	Moran's I, GetisOrd statistic Spatial scanstatistic	Not mentioned	Not mentioned	TB Hotspot - El Salado neighborhood in the North Characteristics - low socioeconomic sphere and high poverty conditions
S57	Point map Thematic map Map of temporaltendency	Moran's I, GetisOrd statistic Spatial scan statistic	Not mentioned	Not used	TB Hotspots- 25 census sectors; the Centro, Mercadinho, Bacuri, Parque Anhanguera, Nova Imperatriz, Vila Lobão, Santa Rita neighborhoods Characteristics - lower demand

					for health services in the periphery, as well as the accentuated population agglomeration in the Central region.
S58	Rate map Thematic map Density kernel map	Moran’s I, GetisOrd statistic	Regression models (with or without including spatial terms)	Not mentioned	TB Hotspots- south and southwest of Belém Characteristics - lower socioeconomic conditions
S59	Rate map	Moran’s I, GetisOrd statistic	Regression models (with or without including spatial terms)	EmpiricalBayesian	TB Hotspots- Eastern Alagoan mesoregion Characteristics – Precarious access to health services, high degree of vulnerability and under diagnosis.
S60	Rate map Thematic map Map of temporal tendency	Not mentioned	Not mentioned	Not mentioned	TB Hotspots- In the metropolitan region of São Paulo, municipalities on the south coast

	Thesis/Dissertation				of São Paulo Characteristics - Worse socioeconomic and demographic conditions
S61	Map of temporaltendency	Moran's I, GetisOrd statistic Spatial scan statistic	Regression models (with or without including spatial terms)	EmpiricalBayesian	TB Hotspots- Centrally located in Guangxi Characteristics - Gross domestic product per inhabitant is a negative measurement of growth in socioeconomic status.
S62	Rate map Map of temporal tendency	Moran's I, GetisOrd statistic	Not mentioned	Fully Bayesian	TB Hotspots- high-high areas spread from Inner Mongolia are northeastern to the southeasterly regions. Characteristics - Due to poor economic conditions and a lack of public health resources,

					farming was the profession most at risk for TB.,
S63	Thematic map Map of temporaltendency	Moran’s I, GetisOrd statistic Spatial scan statistic	Not mentioned	Not mentioned	TB Hotspots- HH cases clusters moved toward southwest more obviously.
S64	Thematic map Map of temporaltendency	Spatial scanstatistic	Regression models (with or without including spatial terms	Not mentioned	TB Hotspots- Kabudarahang and Famenin counties. Characteristics- factors such as socioeconomic position, the environment, or medical issues such the prevalence of HIV infection, undernourishment, and diabetes
S65	Point map Rate map Thematic map	Moran’s I, GetisOrd statistic	Not mentioned	Not mentioned	TB Hotspots- the center of the province and in the north of the province Characteristics - Regular border crossings; the comparatively

					underprivileged and dense immigrant population
S66	Point map Thematic map	Moran's I, GetisOrd statistic Spatial scan statistic	Not mentioned	Not mentioned	TB Hotspots- At the edges of the geographical zone, southwest of the Abeshege District Characteristics of Hotspots - The risk of contracting TB was 4.16 times higher for persons inside this cluster than for those outside. Additionally, 11 significant secondary clusters with a high TB prevalence were found.
S67	Rate map Map of temporal tendency Density kernel map	Moran's I, GetisOrd statistic	Regression models (with or without including spatial terms)	Fully Bayesian	TB Hotspots- Northwest; Xinjiang, Qinghai, Tibet, and Yunnan and central China; Hunan. Characteristics – underdeveloped economic conditions, poor health

					care, and ignorance
S68	Rate map Map of temporal tendency Density kernel map	Moran's I, GetisOrd statistic Spatial scan statistic	Not mentioned	Not mentioned	TB Hotspots- in North Aceh District and the Heureudong Pase sub-district Characteristics – High population density facilitating transmission of TB and high level of community mobility to the capital city.
S69	Map of temporal tendency Density kernel map	Moran's I, GetisOrd statistic Spatial scan statistic	Regression models (with or without including spatial terms)	Fully Bayesian	TB Hotspots- Northwest and South China regions Characteristics - a year-round tropical marine ecosystem characterized with excessive amounts of humidity, frequent rainfall, and constant daylight.
S70	Point map Map of temporal tendency	Moran's I, GetisOrd statistic	Not mentioned	EmpiricalBayesian	TB Hotspots- Sacramenta (Fátima, Telégrafo, Sacramenta,

	Density kernel map				and Barreiro) and Guam (Jurunas, Condor, Guam, and Terra Firme). Characteristics - the most populated area of Belém, with a large concentration of households with many occupants. highest HDI
S71	Rate map Thematic map Map of temporaltendency	Moran's I, GetisOrd statistic	Regression models (with or without including spatial terms)	Not mentioned	TB Hotspots- south and west of the city Characteristics - unemployment and poor access to running water.
S72	Rate map Map of temporal tendency	Moran's I, GetisOrd statistic	Regression models (with or without including spatial terms)	Not mentioned	TB Hotspots- the western districts, mainly in Xinjiang, Tibet and Qinghai province Characteristics - located in the interior, with weak economic

					foundations, poor medical resources and low educational level of residents
S73	Point map Thematic map	Spatial scanstatistic	Regression models (with or without including spatial terms)	Not mentioned	TB Hotspots- Lower sections of the Bamu and Gama Rivers are located in the Bamu area. Characteristics - under diagnosis of TB
S74	Rate map Thematic map Map of temporaltendency	Moran’s I, GetisOrd statistic	Regression models (with or without including spatial terms)	Empirical Bayesian	TB Hotspots- in the Southeast (between 2001 and 2015) and Northeast (between 2001 and 2009) of the state. Characteristics - poor economic growth whereas there was a larger frequency in more urbanized areas between 2011 and 2015.
S75	Thematic map Map of	Moran’s I, GetisOrd statistic	Not mentioned	Not mentioned	TB Hotspotsthe core and

	temporaltendency				Wufeng regions of Zhenxiong Characteristics - inadequate care, poor treatment, or patient management.
S76	NO MAP	Moran's I, GetisOrd statistic Spatial scan statistic	Not mentioned	Not mentioned	TB Hotspots- Enshi Prefecture, southwest Hubei province Characteristics - backward economic conditions and inconvenient
S77	Thematic mapDistance map	Moran's I, GetisOrd statistic	Not mentioned	Not mentioned	TB Hotspots- southwest of Qinghai Characteristics - very low income, poorer living conditions and sanitation
S78	Rate map Thematic map	Spatial scan statistic (WebGIS)	Not mentioned	Not mentioned	TB Hotspots - southwestern part of the country. namely Ha Noi, Da Nang, and Ho Chi Minh

					City Characteristics - TB patients' movement to major cities
S79	Rate map Choropleth map	Global Moran'sIndex (Global Moran's I)	Not mentioned	Not mentioned	TB Hotspots- In Local Government Areas (Jibia, Kurfi, and Batagarawa) that are adjacent to or surround the state capital Characteristics – Due to an inadequate pattern of the Xpert facility distribution, the local government areas on the state's boundary of Sokoto State and the Niger Republic were not covered by the diagnostic services which were provided.

Source: Prepared by author.

Chart 4 displays the characteristics of the hotspots obtained from the study. Socioeconomic condition, overpopulation, climate and border-sharing all determined hotspotsclustering.

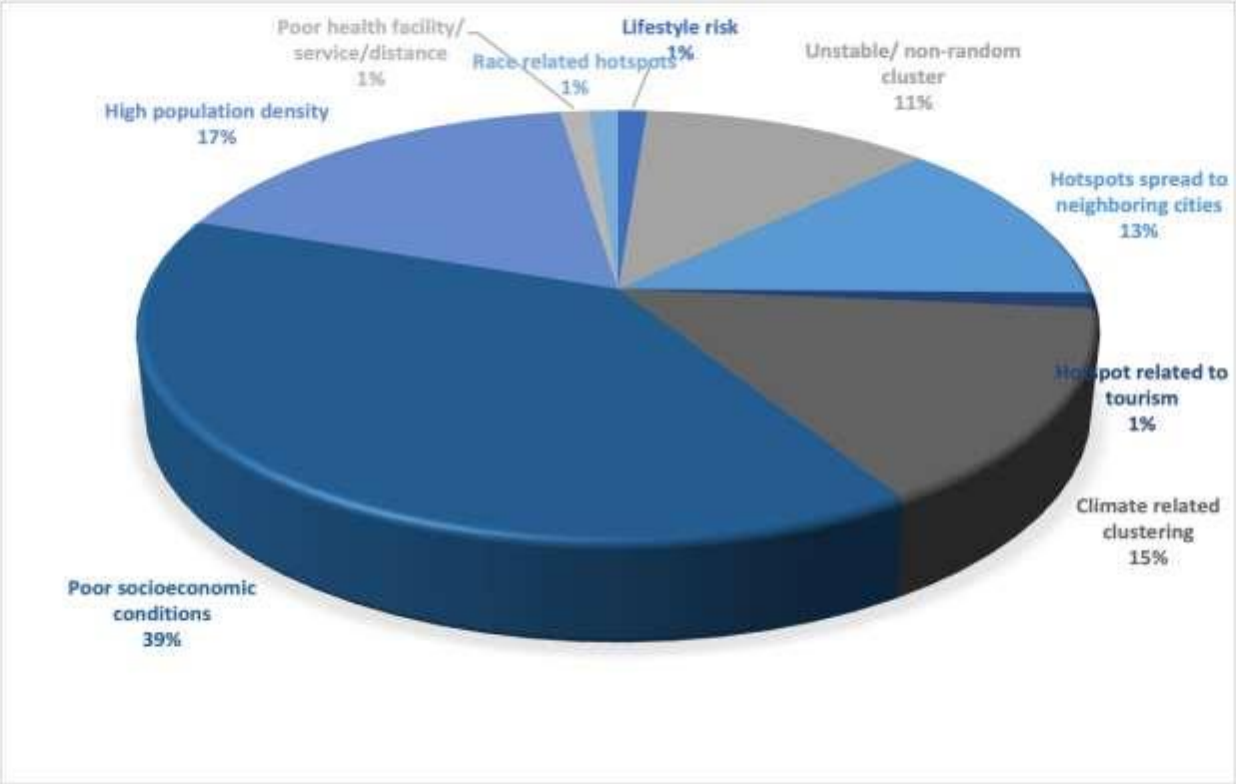
Chart 4 - Synthesis of TB hotspots characteristics throughout the world found in the studies included on the systematic review of the geo-spatial hotspots of tuberculosis in the global general population.

Hotspots Characteristics	- Lifestyle risk[1] - Unstable/ non-random cluster[2, 4, 5,7,9,19,33,63,66] - Hotspots spread to neighboring cities[3,4,6,12,18,23,29,54,63,70,76] - Hotspot related to tourism[3] - Climate related clustering[4,13,28,36,41,44,46,54,66,67,71,74,78] - Poor socioeconomic conditions[4,12,13,19,20.24,25,28,32,34,35,36,41,44,47,49,50,51,54,57,58,60,63,64,67,69,72,73,74,75, 78,79] - High population density[,17,24,39,40,50,57,58,60,61,70,72,75,76,77] - Poor health facility/ service/distance [30] - Race related hotspots[41]

Source: Prepared by author.

Figure 2 represents the TB distribution rate included in the study based on specific factors.

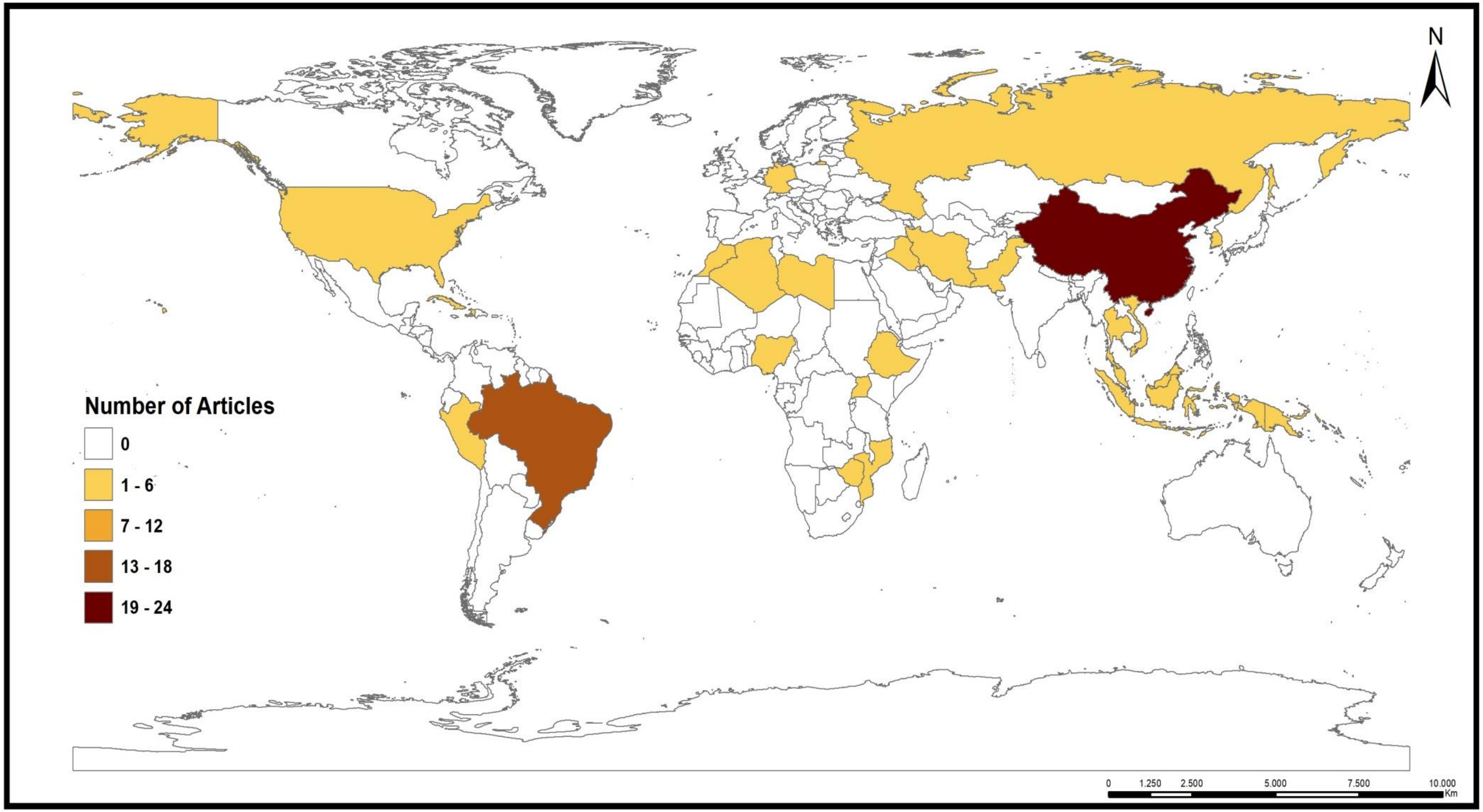
Figure 2 - Characteristics of Hotspots.



Source: Prepared by author.

Figure 3 represents the distribution of countries that performed geospatial analysis of TB included in the study.

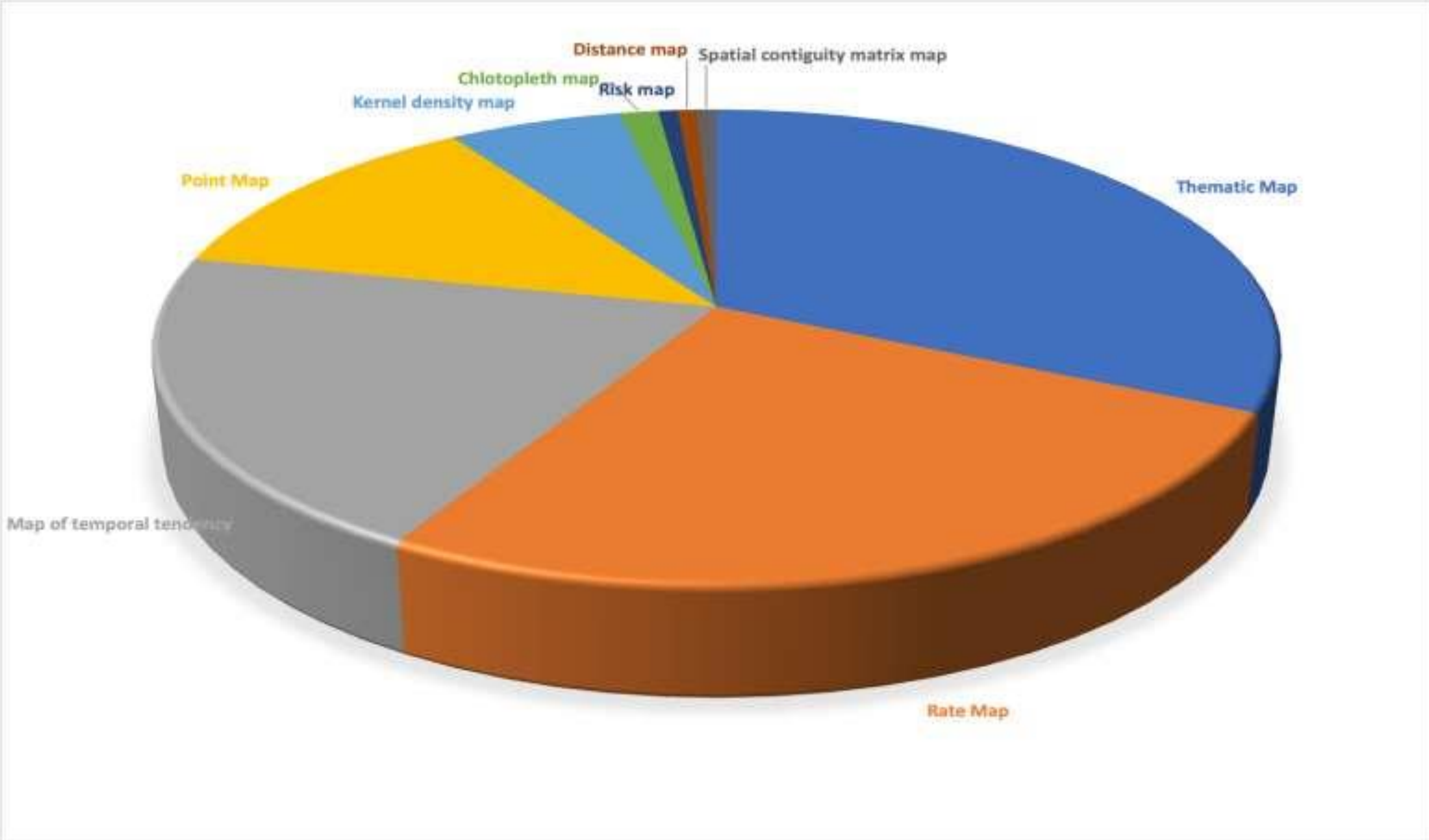
Figure 3 - Distribution of Countries included in the study.



Source: Prepared by author.

Figure 4 shows the various types of graphical maps used in each study to represent the hotspots of TB.

Figure 4 - Statistical representation of maps used in the study.



Source: Prepared by author.

The aim of this systematic review was to identify TB hotspots among the general population globally and this can contribute to reducing TB incidence and mortality and thus help channel resources and efforts to these regions (WHO, 2022). A total of 79 published articles between 1982 and 2022 which is a 40 years study period were evaluated.

To answer these questions above, out of the 79 studies, China has the highest number of studies constituting 40% of all countries that have carried out geospatial analysis of TB followed by Brazil with 23%, Iran and Ethiopia both have 6% and others 2% and 1%. Various maps were used in the various studies and the most used is the thematic map (32%), rate map (26%), map of temporal tendency (20%), and others like the kernel density map (6%).

The characteristics of the hotspots and the factors that affects hotspot's location is evident through studies related to poor socioeconomic conditions constituting (39%), followed by high population density (17%), climate related clustering (15%), hotspots spread to neighboring cities (13%), unstable and non-random cluster (11%).

From studies in China, TB hotspots was suggested to have been imported from nearby countries with a high incidence of the disease in one of the studies, in the same study, it was inferred that the high-high areas spread from the northeastern to the southeastern region, showing the way TB burdens possibly spread between territories especially those lying close to each other. The United Nations gave a supporting report about this, evidencing it isdifficult to track TB cases as it moves across borders. Chuengsatiansup et al. (2019) alsofound that TB as an epidemic was spread between the borderland of Myanmar and Thailand due to mobility of migrants and microbes.

Also, in another China-based study, it was found that the hotspot location discovered was as a result of underdeveloped economic conditions, inefficient healthcare, and a lack of awareness of essential prevention knowledge as evidenced by TB report of the World health organization, Tuberculosis is a disease closely associated with poverty and poor living conditions (WHO, 2022).

From studies in Brazil, hotspots regions discovered were among the population composed of individuals with difficulties in accessing health services and are therefore more deprived. This population is precisely the one that lives in places of difficult localization especially in the Northeastern region (LIMA et al., 2019)., this is in par with the China based study as well. The localization of TB in the Northwestern part of the country proves both socioeconomic relationship of TB with poverty as well as the specificity of TB to particular locations as evidenced by a study by Lima et al. (2019) who found out that in the period from 2010 to 2019 (prior to the COVID-19 pandemic), the country and all of its macro-regions showed an increasing temporal trend of the TB notification rate, with an emphasis on the Northern Region of Brazil.

From studies in Ethiopia, Generally, the TB hot spots in the country over the study period appeared in rural Ethiopia and in more urbanized areas such as Addis Ababa, and other parts of Northwest Ethiopia further emphasizing the localization of TB hotspots, effect of high population density and poor socioeconomic condition on TB. The study also recommended that ensuring access to TB diagnosis and treatment could aid in TB incidence diminution, improve adherence to therapy, and strengthen the community's TB control program (ALENE et al., 2017).

The result points to the presence of vulnerable populations in specific territories affecting people of specific socioeconomic status (social determinants of health). This points to specific locations having high TB prevalence and this is in support of Scholze et al. (2022) that evidenced that TB burden was associated with specific communities, evidencing three hotspots detected in the Northwest, Northcentral and Metropolitan regions. In this sense, the hotspots were concentrated in the northern region (66.7%) similar to our study.

TB is a disease prevalent among the poor and caused majorly by poor living conditions, higher in places of high population density with difficulty in accessing health services. The population being poor goes from socioeconomically bad to worse following the occurrence of TB, as the total cost of TB treatment is greater than 20% annual household income in these populations (WHO, 2022). The result of this study confirms this evidence showing that high TB incidence which reflect as clusters (hotspots) are due to low socioeconomic conditions and poor health care access.

Comprehensive care can be best given to patients through greater resource utilization, active diagnosis, and affordable medications. In addition, all of these require research to offer an informed platform for prudent use of the resources that are already available (FRICK et al., 2017). Discovery of hotspots and vulnerable populations and communities will help to put the limited resources available to optimum use. This study therefore contributes to knowledge by pointing out vulnerable populations for preferential application of TB control policy.

The second pillar of the END TB strategy focuses on bold policies and supportsystems for patients with the aim of reducing as much cost as possible for TB patients. This can be best implemented based on the knowledge of the socioeconomic status of territories, which the systematic review presents (hotspots), thereby reinforcing the third pillar in the light of improved innovation and research as we point out the vulnerability of territories and communities to Tuberculosis.

We recommend that more studies making use of spatial, temporal and spatio-temporal analysis be carried to point out territories and populations that are vulnerable to TB. Although our study aimed to analyze TB burden on a global basis, only few studies are available and have covered few parts of the globe.

3. OBJECTIVES

3.1. General Objective

To describe the epidemiological profile of TB and analyze the spatial distribution andtemporal trend of TB incidence and mortality in Oyo state Nigeria.

3.2. Specific Objectives

I. To calculate the TB incidence rate in Oyo state Nigeria between 2015 and 2019;

II. To calculate the TB mortality rate in Oyo state Nigeria between 2015 and 2019;

III. To analyze the spatial distribution of TB according to each Local government area inOyo state Nigeria from 2015 to 2019;

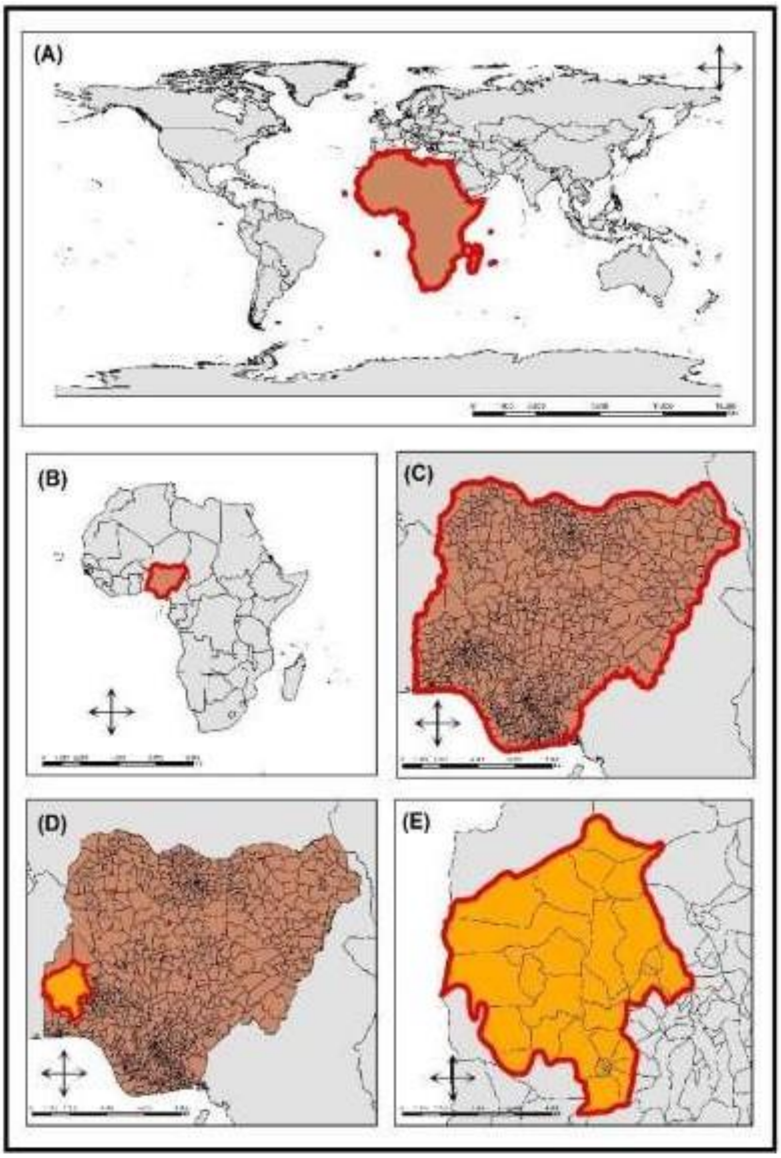
IV. To analyze the time series of TB over the time period between 2015 to 2019 in Oyostate Nigeria.

4. METHODS

4.1. Research Scenario

This is an ecological study (ROTHMAN; GREENLAND; LASH; 2008) carried out in local government areas (LGAs) in Oyo state Nigeria, southwest of Nigeria (Figure 5), using spatial and temporal analysis.

Figure 5 - Geographic location of Oyo State, Nigeria.



Source: Prepared by author.

Caption: A) Geographical location of the African continent; B) Geographical location of Nigeria; C) States of Nigeria; D) Geographic location of Oyo state, Nigeria; E) Geographic division of the LGAs of Oyo state.

Located in southwest Nigeria, Oyo State is an interior state. Ibadan, the country's third-largest metropolis and formerly the continent's second-largest city, serves as the state's capital (NENGE et al., 2019) Kwara State, Osun State, Ogun State, and the Republic of Beninall border Oyo State on its northern, eastern, and southwestern borders, respectively. The statehas an estimated population of 7,840,864; it is rated 6th in terms of population and 14th in terms of size, and has an area of about 28,454 squares. The area is located at 3.9470°E longitude and 73775°N latitude

In terms of epidemiology of TB, Nigeria ranks first in Africa. The 13th-highest state inthe nation in terms of TB prevalence is Oyo based on WHO 2021 report, with 11,817 cases diagnosed and treated and 388 cases of comorbidity with HIV (WHO, 2021) despite the 564 health facilities across the state involved in diagnosis and treating TB (OGUNTOLA, 2022)..

In Oyo state, there are over 1,729 health facilities distributed across 712 Primary Health Centers (PHCs), 46 Secondary Health Facilities, 3 Tertiary Health Centers and 968 registered private health facilities.

TB diagnosis is coordinated by the National Tuberculosis and Leprosy Control Program (NTBLCP) which is structured along the three tiers of government i.e., Federal, State and Local Government Areas (OTU, 2013). The majority of TB services are offered as apart of primary healthcare, which is then followed by secondary and tertiary care offered by governmental and commercial institutions. Consultations, tests, medications, and hospitalization care for TB are all free in the public sector. Supervised TB treatment, health education and adherence, counseling, as well as HIV counseling and testing, remain the main objectives of the NTBLCP. They continue to offer free Directly Observed Treatment Short Course (DOTS) to all people with active TB (OYEDIRAN, 2019). The Yoruba speaking ethnic group mainly inhabits the state. The climate is humid with dry and wet seasons and relatively high humidity.

4.2. Population, data sources and selection criteria

The study population consisted of TB cases and deaths notified from January 1, 2015 to December 31, 2019. Data was obtained through the Oyo state ministry of health -yearly report obtained and collated manually by the state- level health service officers. TB data is usually collected from the local government area health service, transferred to the state ministry of health and collated in the quarterly health report in Nigeria.

4.3. Variables under study

The variables studied are: gender, age, TB cases and years of study.

4.4. Research Ethics Committee

The research proposal was approved by the Oyo state ministry of health under the reference code; AD 13/479/ 4009 (ANNEX I).

4.5. Data analysis

4.5.1. Stage I - Data sorting and coding

The first thing we did was to sort the data obtained from the Oyo state ministry of health, we did this by filling in the name of each LGA in Oyo state. The next was to fill in the population of each LGA in Oyo state. The coding of data was done by assigning a number code to each LGA which we used to join the spreadsheet with the shape (map) of Oyo state. All this was done using the Excel program.

4.5.2. Stage II- Calculation of the Incidence Rate and trends

First, the incidence and mortality rates were calculated. For the calculation, we divided the number of TB cases and the number of deaths from TB by the population of each local government area in Oyo state and multiplied by the constant 100,000. Microsoft Office Professional Plus 2016 was used to perform the analysis, on Excel (Microsoft Corp., Redmond, WA, USA).

4.5.3. Stage III- Spatial analysis

To determine the existence of local spatial association between TB incidence and mortality rates, the Getis-Ord Gi* technique was used. In this analysis, there is a *z-score* for each unit of analysis. The higher the *z-score*, the more intense the clustering of high values (Hotspot), while the lower the *z-score* value, the more intense the clustering of low values or the lower occurrence of the event (Cold spot) (GETIS; ORD, 1992).

In addition to the *z score*, the analysis provides the *p-value* and the *bin* confidence level (*Gi-Bin*). *Gi-Bin* values identify statistically significant hot and cold spots. Values can range from +/-3 and reflect statistical significance with a 99% confidence level, +/-2 with a 95% confidence level, +/-1 with a 90% confidence level, and zero when the analysis unit does not show statistical significance (*p-value* > 0.05) (GETIS; ORD, 1992).

The Getis-Ord Gi* analysis and the choropleth map with the representation of areas identified with the presence of spatial association for TB incidence and mortality rates were performed using ArcGis software version 10.5.

4.5.4. Time series analysis

Finally, to verify the trend of incidence and mortality rates over the period under study, first, the rates (incidence and mortality due to TB) were calculated per year (2015 to 2019). We used the decomposition method called Seasonal-Trend by Loess (STL), which is based on a locally-based regression (CLEVELAND, 1990) to estimate the temporal tendency in the period under study. The graphics with the historical series and estimated time trendwere performed using the RStudio version 3.3.0 software (RStudio Inc., Boston, MA, USA).

5. RESULTS

During the study period, 28,680 TB cases and 1,131 TB deaths were reported. High TB incidence was seen among the male gender group, and the age group with the highest TB incidence was the age group between 35-44 years. The highest incidence rate was observed in the LGAs of Ibadan South West (334 cases/100,000 inhabitants) and the lowest rate was observed in the municipality of Surulere (9 cases/100,000 inhabitants). As for the mortality rate, the highest rate was observed in the municipality of Oyo East (19.01 cases/100,000 inhabitants) and the lowest rates were observed in the municipalities of Ibadan North, Ibarapa Central, Iwajowa and Oluyole, with no deaths from TB in the period under study, according to Figure 2.

Table 2 details, the profile of TB in Oyo state Nigeria according to age group and gender.

Table 2 - Clinical and epidemiological profile of TB cases in Oyo state Nigeria.

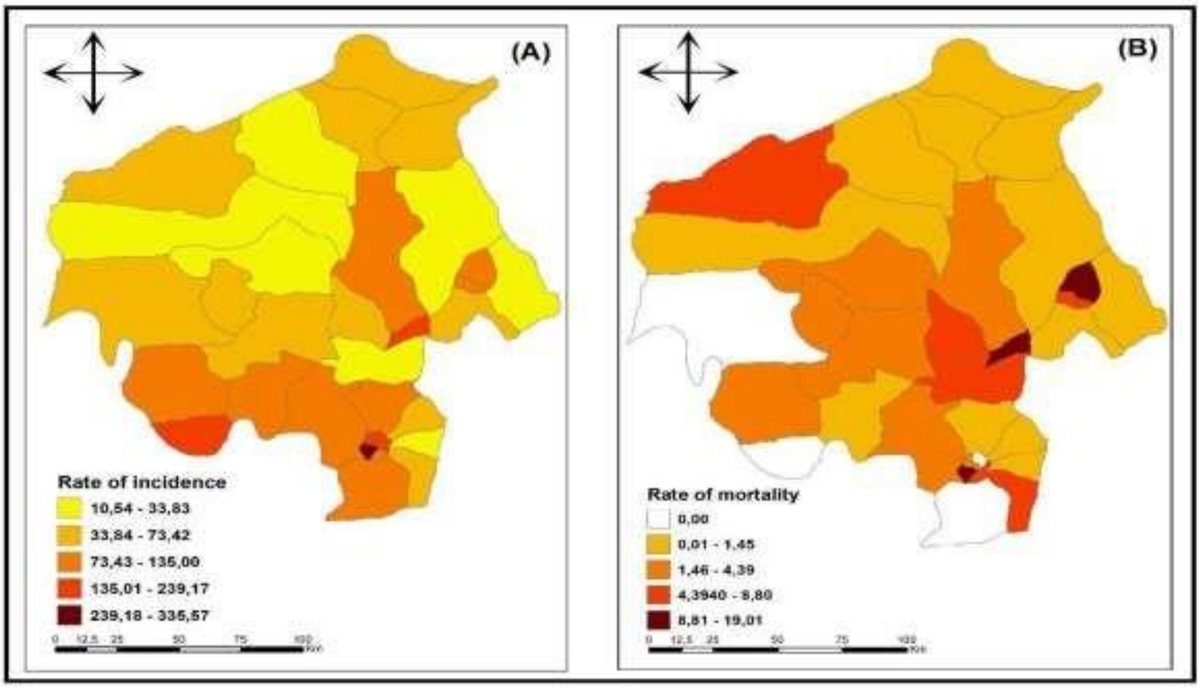
				2015					
Sex	0-4	5-15	15-24	25-34	35-44	45-54	55-64	$\geq$ 65	Total
Male	63	91	424	978	926	647	373	340	3842
Female	60	112	431	793	630	392	225	213	2856
Total	123	203	855	1771	1556	1039	598	553	6698
				2016					
Male	59	107	420	896	909	705	400	333	3829
Female	46	108	416	724	666	407	249	219	2835
Total	105	215	836	1620	1575	1112	649	552	6664
				2017					
Male	55	123	413	945	1070	759	379	341	4085
Female	60	116	404	694	703	423	214	202	2816
Total	115	239	817	1639	1773	1182	593	543	6901
				2018					
Male	58	82	401	873	1080	779	361	441	4075

Female	43	112	365	695	664	429	280	257	2845
Total	101	194	766	1568	1744	1208	641	698	6920
2019									
Male	15	30	90	209	276	206	115	129	1070
Female	18	35	83	136	197	124	78	73	744
Total	33	65	173	345	473	330	193	202	1814

Source: Prepared by author.

Figure 6 shows the rate of TB incidence and mortality in Oyo state Nigeria according to the various local government areas using the Getis-Ord Gi* technique.

Figure 6 - Distribution of tuberculosis incidence and mortality rates, Oyo - Nigeria (2015 - 2019).



Source: Prepared by author.

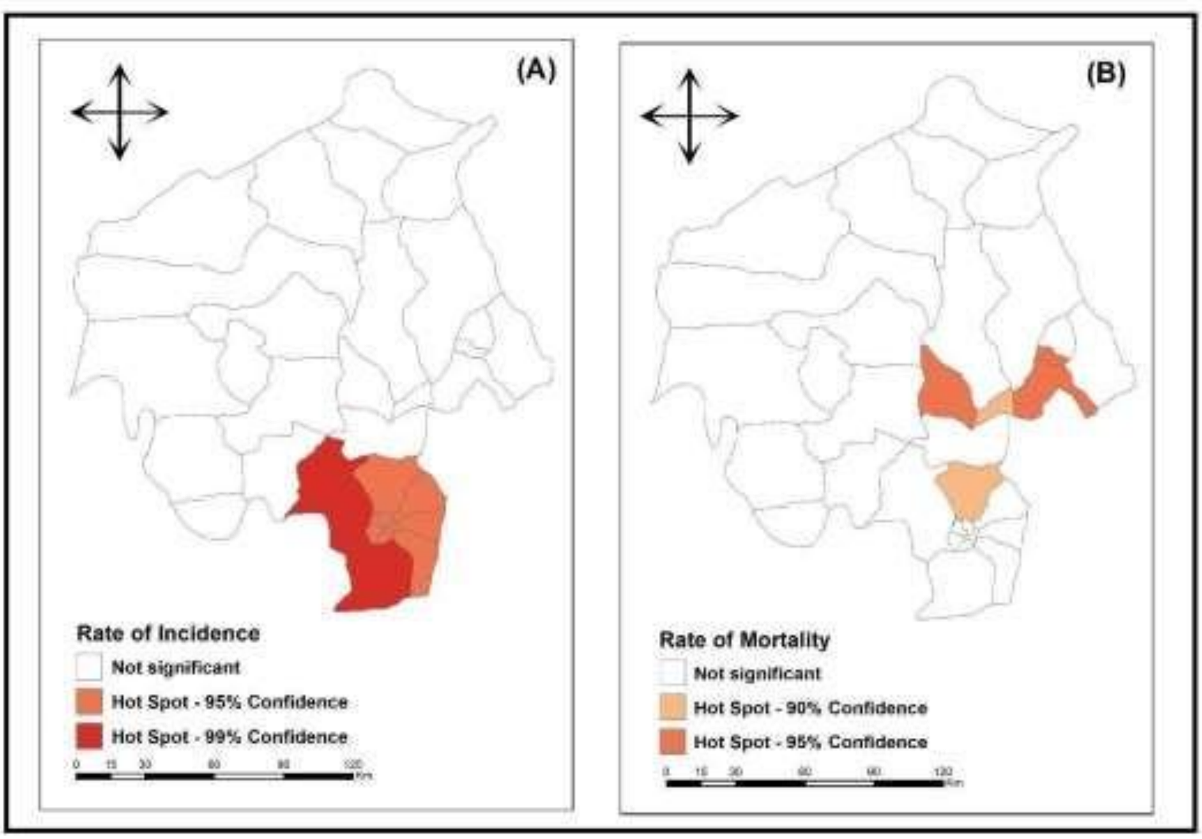
Legend: A) Distribution of tuberculosis incidence rates according to LGAs in Oyo state, Nigeria (2015 – 2019); B) Distribution of tuberculosis mortality rates according to LGAs in Oyo state Nigeria (2015 - 2019).

Using the Getis-Ord Gi* technique for TB incidence rates, 11 municipalities with spatial association were identified, with Ido and Oluyole classified as Hot Spot and presenting 99% confidence and the municipalities Akinyele, Lagelu, Egbeda, Ona -Ara, Ibadan North-West, Ibadan South-West, Ibadan South-East, Ibadan North-East and Ibadan North also classified as Hot Spot, but with 95% confidence (Figure 7-A).

As for TB mortality rates, using the Getis-Ord Gi* technique, five municipalities were identified with a spatial association for the event, with Oyo West, Ogo-Oluwa and Ogbomosho South classified as Hot Spot and presenting 95% confidence and the Oyo East and Akinyele municipalities also classified as Hot Spot, but with 90% confidence (Figure 7-B).

Figure 7 shows the specific areas with High TB hotspots through spatial association.

Figure 7 - Municipalities with spatial association for tuberculosis incidence and mortality,Oyo - Nigeria (2015 - 2019).



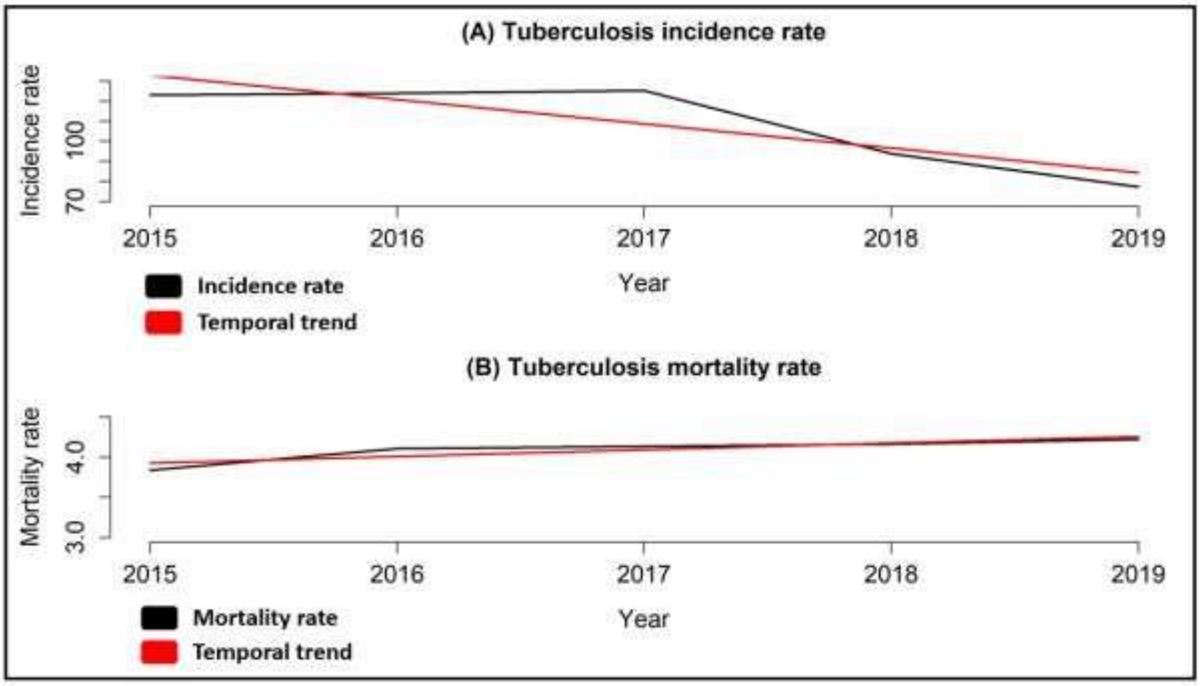
Source: Prepared by author.

Legend: A) LGAs with spatial association for tuberculosis incidence rate in Oyo state, Nigeria (2015 - 2019); B) LGAs with spatial association for tuberculosis mortality rate in Oyo state, Nigeria (2015 - 2019).

Finally, using the time series and the STL technique to estimate the temporal trend of this study, it is possible to observe in Figure 8-A that the historical series of the TB incidence rate showed a slight increase between the years 2015 to 2017, while it showed a sharp decline until 2019. It is also possible to see that the temporal trend for the incidence of TB in the period under study is decreasing. While in Figure 8-B we see a slight increase in the TB mortality rate throughout the analyzed period, we can also see that the temporal trend of the event between 2015 and 2019 is increasing.

Figure 8 shows how TB varies from one year to another during the study period.

Figure 8 - Series and time trend of tuberculosis incidence and mortality rates, Oyo - Nigeria (2015 - 2019).



Source: Prepared by author.

Legend: A) Series and time trend of tuberculosis incidence rate in Oyo state, Nigeria (2015 - 2019); B) Series and time trend of tuberculosis mortality rate in Oyo state, Nigeria (2015 - 2019).

6. DISCUSSION

To the best of our knowledge, this is the first study to report the spatial analysis and time series of TB incidence and mortality rate in recent years in Nigeria. The objective of the present study is to describe the epidemiological profile and mortality rate of the population by analyzing the spatial and temporal distribution of tuberculosis incidence in Oyo state from 2015 to 2019. It was possible to trace the epidemiological profile, analyze the spatial distribution and classify the temporal trend of the incidence of tuberculosis in Oyo state between these Periods. We observed an increase in the incidence rate of cases over the years 2015 to 2017 in almost all LGAs.

With Nigeria having an incidence rate of 219 /100,000 population in 2016 (CEIC, 2021), the LGA with the highest incidence rate from our study- Ibadan south west has a rate (334 cases/100,000 population) which is higher than that of the entire country. Being very variable and heterogonous, the LGA with the lowest rate- Surulere has 9 cases/100,000 inhabitants. This evidences the existence of risk variability within the same state. This could point to differences in class of economy and social development. For certainty, this local government area with the highest incidence rate is reputed to be the most potentially economically productive in the whole of Oyo State. The reason is not far- fetched because the bulk of the Oyo State Industries lie within this Local Government area. Ibadan South West Local Government has the largest concentration of industries and companies in the whole of Oyo State. About 50% of the Companies in the Local Government are located in Oluyole Industrial Estate while the remaining 50% spread across the Local Government area. Because of the concentration of industries, the inhabitants are highly enterprising.

The high TB incidence observed could be a result of high case notification, high level of education of residents and availability of health care facilities and high socio-economic profile of the LGA. A study developed by Nidoi et al. (2021) supports this supposition stating that; Social and economic support was mentioned as a motivator for treatment adherence, also, the wealthiest sector of their study showed significantly lower odds of having an unsuccessful treatment outcome preceded by high notification rate and high level of health service availability and adherence. This high TB incidence rate could also be linked with the high population density in these local government areas, as these two LGAs are the most densely populated urban centers in Oyo state Nigeria. This agrees with a study by Yang et al. (2022) which found the local region's pulmonary tuberculosis (PTB) notification rates were positively impacted by the total number of undergraduates and the cost of health care per person. In order to pinpoint high-risk and low-risk zones that are not evident at the state level, it is critical to survey reported TB rates within smaller geographic units owing to the degree of disparity between rates between urban and rural areas. To achieve this, using the Getis-Ord Gi* technique for TB incidence rates, we identified certain municipalities with spatial association, this generated hotspots and cold spots. Of these, Ido and Oluyole are classified as Hot Spots with 99% confidence interval. More importantly, these two LGAs share boundaries with each other (NIPOST, 2009).

Identifying specific areas within a geographical location with high or low TB loads provides insights for program planning and execution. . Analyzing geographical data collected regularly allows for the identification of regions within a community where TB cases or risk factors for transmission are concentrated. This information can assist healthcare providers in targeting screening efforts to these areas (ROBSKY et al., 2020). Additionally, identifying regions as "cold spots" may indicate areas where services are lacking and need improvement.

It is important to acknowledge that various factors contribute to spatial dependence analysis. Care-seeking behaviors of individuals in the population and access to diagnostic and treatment facilities can influence the observed spatial patterns (BROOKS et al., 2022). The quality of data and analytical approach employed may also have an impact on the spatial variation in reported TB rates. Our study forexample used data collected manually at the Primary health centers DOTS facility from each LGA and collated at the state level in a period where passive case finding was common. Therefore, it is anticipated that these registries will miss a substantial number of TB cases andpush the observed clusters toward areas that have better access to diagnostic services, in line with the rates reporting (WHO, 2021).

In males, the rate of TB cases was 15% higher than in females based on our result. Literature has established the prevalence of TB cases among males to be higher than females as seen in the research by Miller et al. (2021) who found that TB was more prevalent among adult males than among women even in a social context. Also, according to WHO (2021), higher proportion of TB cases among men is consistent with findings from prevalence surveys showing that TB disease affects men more than women and that gaps in case detection and reporting are greater among men, this could be because men tend to hide their sickness and do not frequent health facilities compared to women.

The incidence of TB varies by age group as well; the lowest TB incidence rate was seen in the 0-4 age group while the highest incidence rate was seen in the age group between 35-44. Largely, childhood TB incidence was low while incidence rate was higher among adults (age group 25-54). According to the WHO (2022), most often adults with TB who are in their prime of life. All age groups are, nevertheless, at risk. According to Zhu et al. (2018), based on their study on a population in Shenzhen, age groups 25–34 years and 15–24 years, accounting nearly 40% of total TB cases, being the age groups with the highest percentage of TB cases in their study, this corresponds with the current findings of our study. This attribute surrounding the age group could be due to the high activity rate of individuals in this age bracket in search for means of livelihood and survival.

Regarding TB mortality, Ibadan South west has the highest mortality rate over the five years, which also has the highest incidence rate as earlier states. This LGA is characterized by a relatively high development index in the entire state, which contributes to high case and mortality reporting in the state. According to the Centers for Disease Control and Prevention (2022), the ratio of social determinants of health in this population is positive. The non-medical factors that affect public health are referred to as social determinants of health (SDOH). In addition to the larger group of factors and systems influencing the quality of community life, being the conditions in which people are born, grow, work, live, and age (HACKER, 2022).

It is also possible to see that the temporal trend for the incidence of TB in the period under study is decreasing; this could be due to generally improved health care services in Oyo state. According to a study by Oladimeji et al. (2018) TB patients who visited TB facilities thought that the quality of access to care was excellent, that the attitude of the healthcare professionals was positive, that the facility's appearance was excellent; that there were many people using the facilities, and that the wait time at a facility was under 30 minutes. This is consistent with a study conducted in the United States, where enhanced hygiene helped reduce the number of TB cases in the US, though rates continued to increase in poor, crowded neighborhoods.

In addition, in the WHO European Region the TB burden as a whole is decreasing, and is down 19% overall for 2015–2019, according to the latest WHO/European Centre for Disease Prevention and Control (ECDC) report Tuberculosis surveillance and monitoring in Europe 2021 (ECDC, 2021). Also, the first milestone of the End TB Strategy is a 20% reduction in the TB incidence rate (the number of new and relapse cases per 100,000 population per year) by 2020 compared with 2015 (WHO, 2021).

While in Figure 8-B we see a slight increase in the TB mortality rate throughout the analyzed period, we can also see that the temporal trend of mortality between 2015 and 2019 is increasing.

The End TB Strategy of the WHO outlines global goals and targets for significant decreases in the annual number of TB deaths between 2016 and 2035. The first goal is a decrease of 35% from 2015 to 2020. Following plans for reductions of 90% by 2030 and 95%

by 2035, the next milestone in 2025 is a 75% decrease from 2015 levels (WHO, 2022). It is necessary to accomplish worldwide milestones and targets for reducing the number of people who contract TB each year in order to meet these targets. The slight increase in the mortality rate observed could be a sequel to this set target by the WHO in a bid to reduce the burden. Improved case reporting and surveillance would increase the number of cases reported and point out the fatality of TB for a more effective control.

It is known that TB is a disease closely related to the social determinants of health and is associated with low social class, poverty, social vulnerability and immunosuppressive diseases such as HIV can influence the appearance of the disease in which the person, in addition to having who deal with the disease itself, usually also suffer from stigma from the society in which they are inserted, usually influenced by the perception of risk or lack of knowledge about the disease on the part of the community.

TB with its symptoms and the consequent stigma doubly influence the impact on TB control, since the respiratory symptomatic person, who has a long-lasting cough, has reservations about seeking a health service for fear of the diagnosis. In addition, after the TB diagnosis has been made, given that the dread of being discovered as having the TB bacillus would make other elements of a person´s life problematic, it is more difficult to continue with the care (FAHDHIENIE; SITEPU, 2022). This behavior is observed even in countries that have a low incidence of TB, since stigma is one of the most striking characteristics when we talk about TB.

This fear of seeking medical care and consequent delay in diagnosis makes the person spend more time in the bacilliferous phase, that is, contaminating other people, and thus makes it difficult to break the TB transmission chain, in addition to being able to take the person infected to serious complications that may require hospitalization or even death due to the delay in being diagnosed and starting treatment.

A study by Junaid et al. (2021) that sought to assess Most participants in a research project on TB stigma in an urban population in Nigeria were aware that the disease was an issue in the nation. Most also had a favorable attitude toward prevention, although the levels of knowledge, attitude and practice were compatible. In addition, the same study found that knowledge reduces the stigma of TB, reinforcing the need to improve community literacy to classify the disease and this may have an impact on how people seek healthcare as well as better TB prevention, detection, and treatment outcomes.

According to the same study, about a fifth of the participants reported stigmatizing attitudes towards people with TB, stating that they did not feel compassion for them, in addition to mentioning that they could not have meals with the sick person and that people with TB should not keep their jobs and should distance themselves from other people. From these speeches, we can observe how important health education becomes, since knowledge about TB transmission could minimize the suffering of sick people, and after 15 days of treatment, the person no longer transmits the causative bacilli of TB.

Thus, in addition to the disease itself, the stigma that people with TB suffer can cause very harmful consequences in their daily lives, such as low self-esteem, insults, ridicule, self-exclusion and social exclusion, leading to a worsening of their quality of life and social status, as identified in a study conducted in Zambia.

The use of georeferencing techniques provides an overview of the areas that should be prioritized in the fight against TB in the state of Oyo and also deserve attention from the perspective of the social determinants of health in the health-disease process. The identification of areas considered at risk or with a higher concentration of TB cases is extremely important for the planning and implementation of public policies and strategic actions to prevent transmission and also timely diagnosis of the disease, with emphasis on actions to actively search for symptomatic patients breathing.

With the identification of critical areas for the analyzed event, where the risk of TB transmission is more intense, priority should be given to investigating and monitoring risk factors for TB infection in these areas, with the aim of helping TB programs. prevention in the effective control of both diseases, since the dynamics of disease transmission is not limited to political-administrative borders.

Therefore, it is important for managers at all levels of administration to focus on combat strategies aimed at early diagnosis and active search for cases. In addition, with the aim of improving the epidemiological indicators of both diseases, a necessary and effective tool is the periodic training of health professionals, not only in the biological sense, but also to understand the epidemiological and social reality of the territory in which they are inserted, so that they can understand the relationship between TB and the social determinants of health.

Regarding the limitations of the study, as it is an ecological study, we highlight the so-called ecological fallacy in which, due to the fact that aggregated variables are used, the results may not represent associations at the individual level. It is also worth highlighting the use of secondary data sources that may have incomplete data or with typing errors, in addition to considering only notified cases, so that the data considered may underestimate the number of TB cases.

Thus, it is important that managers prioritize the organization of the health care network throughout the territory in order to facilitate access and early diagnosis of TB. In addition, the importance of rapid initiation of treatment and the correct drug regimen according to the form of TB diagnosed is highlighted, which should be started as soon as possible.

In this sense, it should also be noted that the diagnosis of HIV during treatment or diagnosis of TB indicates a late diagnosis, and it is important to organize the care network to expand HIV testing. Thus, failures in early diagnosis, in the provision of actions and organization of health services are factors that can influence treatment and, consequently, coping with the disease. Measures such as public awareness of the symptoms of both diseases and availability of rapid tests are examples of strategies to minimize delays in the diagnosis of TB and HIV.

7. CONCLUSION

The results of the present study contributed to the knowledge of the epidemiological profile, the spatial and temporal distribution and areas with higher risk of tuberculosis transmission in Oyo state and Nigeria as a whole. It made it possible to policy makers to target hotspot areas for intervention and disease prevention.

The use of spatial analysis tools allowed the identification of hot and cold areas for TB incidence and mortality rates in Oyo, Nigeria, representing an important advance towards the elimination of the disease in the scenario studied.

The study also shows the temporal trend of the event, given that it follows the opposite direction to the policies aimed at eliminating TB through the End TB Strategy, thus, the attention of the health authorities becomes necessary, given that the policies and actions are not being effective, mainly in the hot areas identified in the study.

It reinforces that community involvement can be an effective mechanism to favor the diagnosis and conclusion of treatment, since raising awareness and educating populations at risk, involving family and community as a whole, can improve the indicators of the scenario under study.

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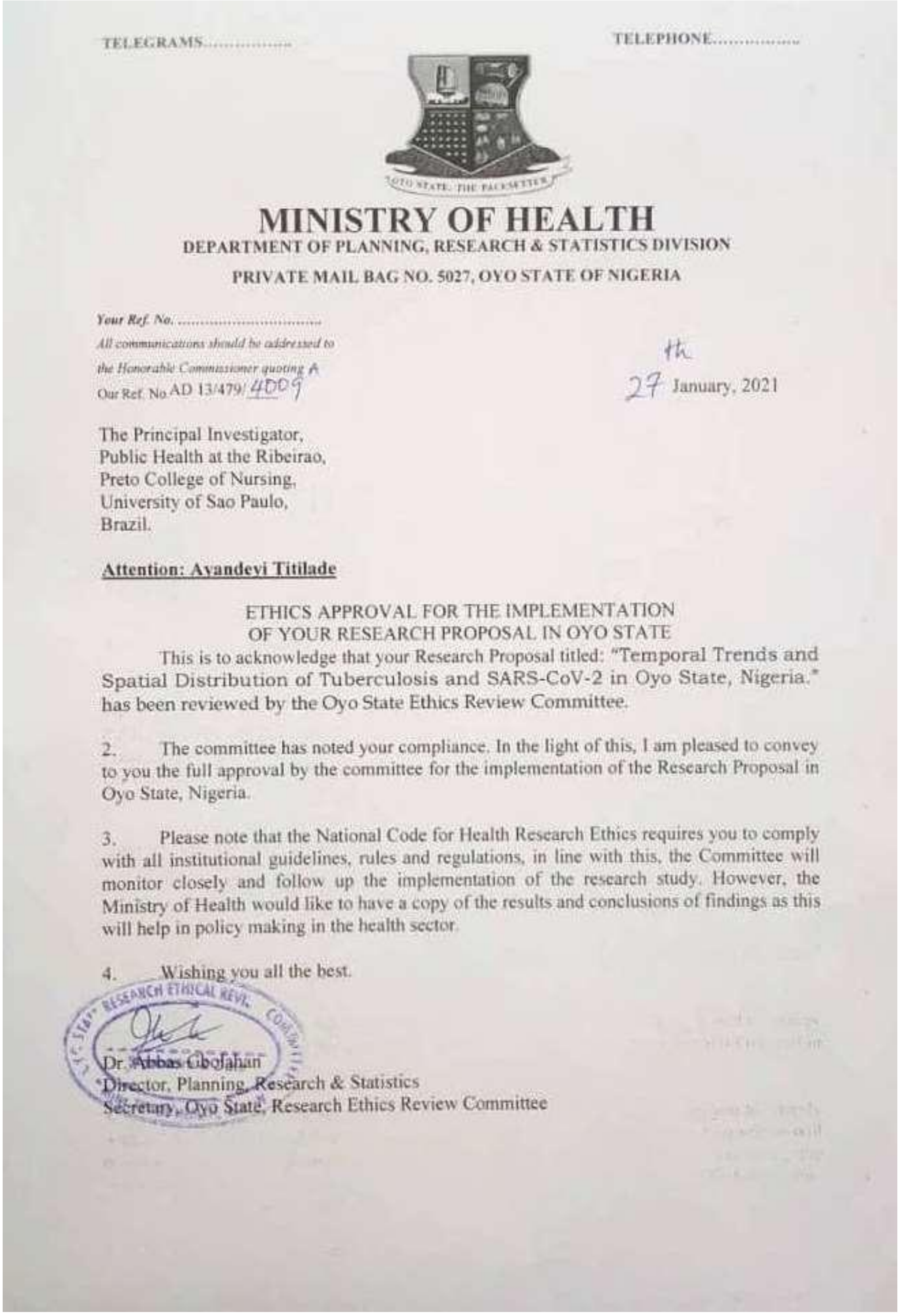
ATTACHMENTS

ANNEX I

Approval by the Research Ethics Committee of the Ministry of Health, Oyo State, Nigeria



TELEGRAMS................ TELEPHONE................

OYO STATE: THE PACESETTER

MINISTRY OF HEALTH

DEPARTMENT OF PLANNING, RESEARCH & STATISTICS DIVISION

PRIVATE MAIL BAG NO. 5027, OYO STATE OF NIGERIA

Your Ref. No. ....

All communications should be addressed to the Honorable Commissioner quoting A

Our Ref. No AD 13/479/ 4009

27th January, 2021

The Principal Investigator,
Public Health at the Ribeirao,
Preto College of Nursing,
University of Sao Paulo,
Brazil.

Attention: Ayandeyi Titilade

ETHICS APPROVAL FOR THE IMPLEMENTATION
OF YOUR RESEARCH PROPOSAL IN OYO STATE

This is to acknowledge that your Research Proposal titled: "Temporal Trends and Spatial Distribution of Tuberculosis and SARS-CoV-2 in Oyo State, Nigeria." has been reviewed by the Oyo State Ethics Review Committee.

2. The committee has noted your compliance. In the light of this, I am pleased to convey to you the full approval by the committee for the implementation of the Research Proposal in Oyo State, Nigeria.

3. Please note that the National Code for Health Research Ethics requires you to comply with all institutional guidelines, rules and regulations, in line with this, the Committee will monitor closely and follow up the implementation of the research study. However, the Ministry of Health would like to have a copy of the results and conclusions of findings as this will help in policy making in the health sector.

4. Wishing you all the best.

Dr. Abbas Gbolahan
Director, Planning, Research & Statistics
Secretary, Oyo State, Research Ethics Review Committee