GLOBAL SURGERY DIVISION

DEPARTMENT OF SURGERY

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UNIVERSITY OF CAPE TOWN

PREVALENCE OF BABIES BORN WITH NEURAL TUBE DEFECTS AND GEOSPATIAL MAPPING OF THERAPEUTIC SERVICES: A SYSTEMATIC REVIEW

A Dissertation Submitted to the

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Plagiarism Declaration

I, ANDRE YVAN ZOLO OSSOU, affirm that the content of this dissertation is entirely my own original work (except as acknowledged), and no portion of it has been, is being, or will be submitted for another degree at this university or any other institution. I grant the university permission to reproduce any part of the contents for research purposes in any form.

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Declaration of Any Conflicting Interests

The authors declare not having any conflicting interest(s).

Dedication

I dedicate this work to my mother, MINKOULOU MARIE PAUL. Thank you for your constant and unfailing love and support.

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Acronyms and Abbreviations

Acronym/Abbreviation	Description
AFR	African Region
AMR	Region of the Americas
CASP	Critical Appraisal Skills Programme
DRC	Departmental Research Committee
EMR	Eastern Mediterranean Region
EUR	European Region
GIS	Geographic Information Systems
HICs	High-Income Countries
LMICs	Low- and Middle-Income Countries
MeSH	Medical Subject Headings
NTDs	Neural Tube Defects
SEAR	South East Asian Region
WHO	World Health Organization
WPR	West Pacific Region

Glossary

CASP (Critical Appraisal Skills Programme)	A tool used for assessing the quality and validity of research studies.
DRC: Departmental Research Committee	A committee within a department or organization responsible for overseeing research-related matters and decision-making.
GIS: Geographic Information Systems	A technology used for capturing, managing, analyzing, and visualizing geographically referenced information.
LMICs: Low- and Middle-Income Countries	Countries with relatively lower income levels compared to high-income countries.
MeSH: Medical Subject Headings	A controlled vocabulary used for indexing and searching biomedical literature.
NTDs: Neural Tube Defects	A group of congenital malformations affecting the development of the neural tube in embryos, leading to conditions such as spina bifida and anencephaly.
Global Surgery	A multidisciplinary field dedicated to improving access to surgical care worldwide
Telemedicine	The use of technology, such as video conferencing, for remote medical consultations and healthcare delivery.
Environmental Determinants	Factors in the environment, such as nutrition and pollution, that contribute to health conditions.
Prevalence	The proportion of a population that has a particular condition or characteristic at a given time
Access Disparities	Differences in the availability and accessibility of healthcare services.

Resource Allocation	The process of distributing resources, such as funds and personnel, to achieve specific goals.
International Collaboration	Cooperation and knowledge sharing between organizations and professionals from different countries.
Data-Driven Decision-Making	Making informed decisions based on data analysis.
Monitoring and Evaluation	Continuous assessment of the progress and impact of programs or initiatives.
Community Engagement	Involving communities in healthcare planning, education, and decision-making
Neurosurgical Interventions	Surgical procedures related to the nervous system
Physiotherapy	Rehabilitation and treatment through physical methods
Environmental Initiatives	Efforts to address environmental factors that impact health
Holistic Interventions	Comprehensive approaches that consider various aspects of health and well-being
Cognitive Abilities	Mental processes such as thinking, learning, and problem-solving
Motor Abilities	Skills related to movement and physical coordination
Telemedicine Solutions	Technological approaches for remote healthcare delivery
Ground-Truthing	Systematic observation and data collection in the physical environment
Comprehensive Surgical Care	A range of surgical services and support for patients
Data-Driven Resource Allocation	Allocating resources based on data analysis

Holistic Solutions	Comprehensive approaches addressing multiple factors
GINI Coefficient	A measure of income inequality within a population
Human Resources	Personnel and healthcare professionals
Access Barriers	Obstacles preventing individuals from accessing healthcare services
Medical Intervention	Medical treatment and care
Health Care Provision	The delivery of healthcare services
Public Health	Efforts to improve the health of populations

Abstract

Introduction: Neural tube defects (NTDs) are an important global health concern with high morbidity and mortality. Enhancing access to healthcare for children born with NTDs is crucial for improving health systems and service delivery.

Methods: We conducted a systematic review to assess the global prevalence of NTDs and the accessibility of healthcare services. Our search spanned databases like PubMed, EMBASE, and Scopus, focusing on NTD prevalence, healthcare service mapping, and access barriers. We followed a standardized data extraction process, and the study is registered with PROSPERO (CRD42023425843).

Results: From 3 067 records, 65 studies met our inclusion criteria, mainly focusing on newborns. The study durations range from six months to 40 years. The NTD prevalence was between 0.4 and 215.13 per 10 000 births, with Spina Bifida, Anencephaly, and Encephalocele being the most common. The African Region was the WHO region with the highest prevalence while the Western Pacific Region had the lowest prevalence. One study used geospatial mapping to identify healthcare access barriers.

Conclusion: Our study revealed wide disparities in the prevalence rates of neural tube defects with the African region having the highest prevalence. Geospatial mapping was not used to assess access to healthcare services for children born with NTDs in almost all the studies. This underscores the global challenge of access to surgical care for children born with NTDs and the need for strengthening healthcare services in settings with high prevalences.

Keywords: Accessibility of Healthcare, Geospatial Mapping, Healthcare Disparities, Neural Tube Defects, Policy Reform

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SYNOPSIS

The study that was conducted is a systematic review on the prevalence of neural tube defects and geospatial access to NTD services.

The dissertation has been divided into 3 chapters as outlined below:

Chapter One: Is the comprehensive Systematic review proposal

Chapter Two: Is a Literature review on the topic

Chapter Three: Is the results chapter written in publication draft format

CHAPTER ONE: PROTOCOL

2.1 Background

Neurological malformations at birth impose a substantial public health burden globally, with high morbidity and mortality [1]. However, access to suitable healthcare services for affected children is often limited in many countries due to factors such as inadequate infrastructure, resource constraints, and a shortage of skilled healthcare providers [2]. Geospatial mapping of healthcare services and the prevalence of children born with neurological malformations can help to understand the accessibility and distribution of healthcare services for affected children across different regions and countries worldwide [3–6]. The mapping includes specialized healthcare centre's, trained healthcare providers, and infrastructure necessary for comprehensive care, such as advanced imaging and rehabilitation services [5–7].

Geospatial mapping is derived from Geographic Information Systems (GIS) and have been defined as the "integration of software, and hardware for capturing, sorting, analysing and displaying all forms of geographically referenced information to understand relationships trends and patterns [8].

Geospatial mapping reveals significant variation in access to healthcare services for children born with Neural tube defects (NTDs) depending on their location [9].

For the sake of this study Geospatial mapping shall interchangeably be called Ground-truthing which involves a systematic and direct observation of various attributes of the built environment [10]. In this case, Geospatial mapping/Ground truthing may include road networks, land use, destinations, hospital facilities, community centres, health care providers, rehabilitation services.

Improved geospatial mapping is essential for timely and appropriate healthcare intervention, which is critical for children's long-term outcomes, including cognitive, motor, and functional abilities [3]. A comprehensive understanding of the geospatial mapping of healthcare services and prevalence of children born with NTDs globally and in LMICs is necessary to inform future research, practice, and policy development aimed at improving access to healthcare services for this vulnerable population.

To our knowledge, a "Comprehensive geospatial mapping of healthcare services and prevalence of children born with neural tube defects" has not been done whether globally or for LMICs in particular and this is necessary to inform future research, practice in LMICs including South Africa. LMICs have vast inequalities (high GINI coefficient) and therefore ground-truthing the built environment in health care services may provide insights to better understand the ecological and environmental barriers to health care provision [11].

Therefore, a systematic review of available literature on geospatial location of healthcare services for children with Neural tube defects (NTDs) can provide a better understanding of the current state of healthcare services for this vulnerable population globally, identify gaps in access to healthcare services, and inform the development of targeted interventions to improve outcomes for the infants. Ultimately, this understanding can contribute to reducing the burden of disease of children born with neurological malformations globally and particularly in low- and middle-income countries [12].

2.2 Problem statement

Children born with congenital neurological malformations, including neural tube defects (e.g., spina bifida), brain malformations (e.g., holoprosencephaly, hydrocephalus, microcephaly), cerebral palsy, and epilepsy, face significant challenges in accessing adequate neurosurgical care globally, with pronounced disparities in low-income regions [13]. Neurosurgical interventions, neurological consultations and physiotherapy are often necessary to improve outcomes and prevent further complications. However, the geospatial distribution and accessibility of these services for this vulnerable population in low- and middle-income countries are not adequately understood, indicating a critical knowledge gap in the delivery of care.

Addressing this gap in understanding regarding the availability and accessibility of neurosurgical, neurological and physiotherapeutic services requires addressing the challenges of providing adequate care to affected infants and their families. Studies are needed to examine the barriers to access to this care and identify gaps and disparities in different regions of the world. A systematic review of the available literature on the geospatial location of these healthcare services and prevalence of babies born with neural tube defects can help address this knowledge gap and inform future research, practice, and policy development aimed at improving access to healthcare services

for this vulnerable population. The ultimate goal is to improve outcomes, reduce the burden of these conditions on affected infants and their families, and ensure equitable access to neurosurgical care globally.

2.3 Study justification

Neural tube defects (NTDs) are a significant cause of children morbidity and mortality worldwide [14]. While many countries have implemented measures to reduce the incidence of NTDs, their prevalence remains high, particularly in low- and middle-income countries. Access to neurological, neurosurgical, and physiotherapeutic services is critical in the management of children with NTDs to prevent further complications and improve outcomes [14]. However, there is a significant gap in understanding the geospatial distribution and accessibility of these services, which can negatively impact the health of affected children and their families.

This study aims to conduct a systematic review of existing literature on the prevalence of children born with NTDs and the geospatial mapping of associated neurological, neurosurgical, and physiotherapeutic services worldwide. By reviewing and synthesizing available data, the study will address the knowledge gap on the distribution and accessibility of these services, particularly in low- and middle-income countries. The review will interrogate the disparities in access to these services across geographical regions, identify innovative approaches to delivering care, and provide critical insights into the current state of healthcare services globally.

The findings of this study will be relevant to policymakers and healthcare providers worldwide, providing evidence-based recommendations to improve access to these services and reduce the burden of NTDs on affected children and their families. By contributing to the broader literature on healthcare access and geospatial mapping, this review will help inform future research, practice, and policy development, ultimately leading to better outcomes for children with NTDs and their families.

2.4 Aim

The aim of this systematic review is to determine the prevalence of children born with neural tube defects and the geospatial distribution and accessibility of associated neurological, neurosurgical, and physiotherapeutic services worldwide.

2.5 Objectives

2.5.1 Primary objective:

1. To determine the global prevalence of children born with neural tube defects and the geospatial distribution of associated neurological, neurosurgical, and physiotherapeutic services.

2.5.2 Secondary objective:

2. To investigate the disparities in access to care for children born with neural tube defects across different geographical regions.

3. To provide critical insights into the current state of healthcare services for children born with neural tube defects, which can inform future research, practice, and policy development.

2.6 Methods

2.6.1 Research Question: What is the prevalence of children born with neural tube defects and what is the geospatial mapping of associated neurological, neurosurgical, and physiotherapeutic services globally, and what are the barriers to accessing these services?

2.6.2 Search Strategy: A comprehensive search will be conducted in electronic databases including PubMed, EMBASE, Scopus, Web of Science, CINAHL, and Cochrane Library. The search will include relevant keywords and Medical Subject Headings (MeSH) terms such as "neural tube defects," "spina bifida," "anencephaly," "encephalocele," "prevalence," "geospatial mapping," "neurological services," "neurosurgical services," "physiotherapy services," "access barriers," and "healthcare services", “ground truthing,” “GIS”.

The following search term will be used:

("neural tube defects"[MeSH Terms] OR "spina bifida"[MeSH Terms] OR "anencephaly"[MeSH Terms] OR "encephalocele"[MeSH Terms]) AND ("prevalence"[MeSH Terms] OR "geospatial mapping" OR "neurological services"[MeSH Terms] OR "neurosurgical services"[MeSH Terms] OR "physiotherapy services"[MeSH Terms] OR "access barriers"[MeSH Terms] OR "healthcare services"[MeSH Terms]).

The search will be limited to studies published in English language from the year 2000 to present. Limiting the search to studies published in English language from 2000 to present ensures that the most current and relevant literature is included in the review. English is the predominant language of scientific communication, and by limiting the search to studies published in English, we reduce the risk of language bias and increase the generalizability of the findings. Additionally, limiting the search to studies published from 2000 to present ensures that the review is focused on recent literature, which is more likely to reflect current practices, policies, and healthcare systems. This improves the relevance and applicability of the findings to current clinical and public health settings.

2.6.3 Study Selection Criteria:

Inclusion Criteria:

- Studies reporting the prevalence of neural tube defects in children worldwide
- Studies reporting the geospatial location of neurological, neurosurgical, and physiotherapeutic services associated with neural tube defects worldwide
- Studies examining barriers to accessing neurological, neurosurgical, and physiotherapeutic services associated with neural tube defects in children
- Studies published in English language from 2000 to present

Exclusion Criteria:

- Studies published in languages other than English
- Studies published before 2000

- Studies not mentioning the geospatial location of healthcare services and prevalence of children born with neurological malformations
- Studies not focusing on neurosurgical care for children with congenital neurological malformations
- Studies not examining barriers to access to neurosurgical care for children with congenital neurological malformations
- Studies with incomplete or insufficient data
- Studies with low methodological quality or significant risk of bias
- Studies that do not meet the pre-defined inclusion criteria

2.6.4 Data Extraction: A standardized data extraction form will be developed to extract relevant data from the selected studies. The form will include the following information: first author, title of study, WHO Region, country investigated, study type, data source, location of data source, reported prevalence, prevalence of subtypes of NTDs reported, geospatial mapping of services, geospatial analysis of healthcare service location and patient densities, and barriers to services.

2.6.5 Quality Assessment: A modified Critical Appraisal Skills Programme (CASP) tool will be used to assess the quality of the selected studies. The tool comprises of ten questions that will be used to assess the validity, reliability, and applicability of the studies. Studies will be graded as low, moderate, or high quality based on their scores (APPENDIX 3).

2.6.6 Data Synthesis: A narrative synthesis will be employed to synthesize the selected studies' findings. This approach justifies organizing the data based on the research questions and presenting it using tables, graphs, and maps, enhancing clarity and understanding for readers. However, it's essential to note that the absence of critical data may necessitate the exclusion of some studies from the synthesis. We decided not to conduct subgroup analyses and meta-regression and this decision is justified by the nature of the research questions and the foreseen scarcity in available data. These methods are typically employed to identify and account for variations in findings across different studies. However, due to the specific research objectives and data constraints, these approaches are not deemed suitable or necessary for this synthesis.

2.6.7 Study Registration: The study has been registered on PROSPERO under the ID CRD42023425843. The registration was last edited on May 22, 2023.

2.7 Limitations

Here are some limitations specific to this systematic review:

Language bias: The review will only include studies published in English, which may limit the generalizability of the findings to populations that primarily publish in other languages.

Publication bias: The possibility of relevant studies not being published or being difficult to access may result in a biased representation of the available literature. However, we will attempt to mitigate this limitation by searching multiple databases and using additional search strategies such as citation searching.

Quality of included studies: As a systematic review, the focus will be on identifying the breadth of available literature rather than assessing the quality of individual studies. This means that some studies with weak methodology or biased results may still be included in the review. However, we will use a critical appraisal tool to evaluate the quality of the included studies and highlight any limitations or biases.

Heterogeneity of study designs: The review will include studies with different study designs, which may make it challenging to compare and synthesize findings across studies. However, we will attempt to categorize studies based on their design and methodology to facilitate comparisons.

Generalisability of findings: Due to the heterogeneity of study designs and populations included in the review, it may not be possible to generalize the findings to all settings and populations. However, we will attempt to identify common themes and patterns across the included studies to provide insights into the prevalence of neural tube defects in babies and associated healthcare services globally.

2.8 Timeline

Table 1: Gantt Chart of Activities

Activity	**Duration**	**Month**						
		April	**May**	**June**	**July**	**August**	**September-December**	**January**
Proposal submission to DRC	*½ month*							
Ethical Clearance	*½ month*							
Conduct a comprehensive search	*½ month*							
Screen the search results for relevance and eligibility using the established inclusion and exclusion criteria	*½ month*							
Extract data Synthesize the findings and develop a narrative summary of the scoping review results	*2 months*							

Data Analysis and result interpretation	*1 month*							
Drafting Thesis	*1 month*							
Implementing Draft. Thesis corrections	*3 months*							
Thesis Submission								

2.9 Ethical Consideration

Since this study will involve a review of published literature, ethical approval is not required. However, we will ensure that all data are anonymized and that no identifying information is reported in the study.

2.10 Dissemination of Findings

The findings of the study will be disseminated through publication in a peer-reviewed journal and presentations at relevant conferences. A summary of the findings will also be made available to relevant stakeholders, including policymakers and healthcare providers, to inform future research and policy development aimed at improving access to healthcare services for infants with congenital neurological malformations.

2.11 Funding

This research has not received any funding. The principal investigator will support any expenses associated with this research and if needed by the supervisor. The Mandela Rhodes Foundation scholarship funds the principal investigator's postgraduate studies. The cost of publication of the final work will be endorsed by the principal investigator with the help of the supervisors.

Any software needed for this research that is not freely made available by the University of Cape Town will be purchased by the principal investigator.

2.12 Budget Summary

Table 2: Budget Summary

ITEM	UNIT	ESTIMATED COST IN RANDS
Grammarly software subscription per year	2	4 677.28
Publication of study	1	To be determined
Provisional Total		4 677.28

CHAPTER TWO: LITERATURE REVIEW

3.1 Global Disparities in Prevalence of Neural Tube Defects and Needs for Affected Children

Neural tube defects (NTDs) represent a significant global public health concern, necessitating a comprehensive and concerted effort to address their impact [15]. The prevalence and global burden of neural tube defects were estimated in a pivotal study published by Zaganjor et al. in 2016 [16]. Zaganjor's study stands out as a comprehensive review of NTD prevalence, drawing on data collected from various countries. A key finding from that research was the notable variation in NTD prevalence across different World Health Organization (WHO) regions, with figures ranging widely: 2.1 to 124.1 per 10 000 births in the Eastern Mediterranean, 1.3 to 35.9 in Europe, 3.3 to 27.9 in the Americas, 1.9 to 66.2 in South-East Asia, and 0.3 to 199.4 in the Western Pacific. The study underscored a significant gap in data, particularly in low- and middle-income countries, it also revealed that less than half of the 194 WHO Member States had data on NTD prevalence. This variability and data scarcity highlight the challenges in understanding the global impact of NTDs and underscore the need for enhanced monitoring and reporting systems, especially in regions currently underrepresented in global data.

The prevalence of NTDs contributes to elevated levels of morbidity and mortality among affected children, underscoring the urgent need for effective preventive measures, early detection, and accessible medical services [17–19]. The existing disparage in the availability of appropriate surgical and healthcare services for infants with NTDs is a critical issue that demands attention. Bridging the gap in healthcare accessibility across diverse regions worldwide is imperative to ensure equitable and optimal outcomes for infants affected by NTDs. Achieving this requires a collaborative approach that considers socio-economic factors, healthcare infrastructure, and the implementation of tailored strategies to enhance the overall care and well-being of these vulnerable populations [20,21].

3.2 A Focus on Surgical Care for Children Affected by NTDs in Low- and Middle-Income Regions

It is imperative that attention is focused on specific challenges faced by low- and middle-income countries in providing comprehensive surgical care to children affected with NTDs [22]. In LMICs, the accessibility of specialized medical services becomes an even more pressing concern due to limited resources and infrastructure [23]. The important disparities in socio-economic conditions in these countries contribute significantly to the existing healthcare gaps, necessitating targeted initiatives to bridge these disparities [24]. Collaborative efforts between international organizations, local governments, and healthcare providers are essential to implement sustainable solutions that address the unique needs of children in LMICs [25–27]. This focus on surgical care for children with NTDs in LMICs should extend beyond immediate interventions to encompass long-term strategies, including capacity building, medical education, and community outreach. By fostering a holistic approach, we can aspire to create enduring improvements in the accessibility and quality of surgical care for children affected by NTDs in LMICs, ultimately contributing to a more equitable global healthcare landscape.

3.3 Geospatial Mapping Could Improve Surgical Services Accessibility for Children Born with Neural Tube Defects

Geospatial mapping plays a pivotal role in strengthening surgical systems by enhancing the understanding of surgical services accessibility and the prevalence of NTDs in children [3,9]. Geospatial mapping is particularly vital in LMICs where congenital neurological malformations are expected to be common [14]. This technology helps identify and overcome geographical and environmental barriers, improving the distribution and accessibility of surgical services for children with NTDs [4,7].

The technology is instrumental in pinpointing vulnerable populations that face significant challenges in accessing healthcare due to remoteness or socioeconomic disparities [3,28]. It effectively guides the allocation of resources in global surgery initiatives, ensuring they are directed towards areas with the greatest need [29]. Furthermore, geospatial mapping fosters international collaboration and the sharing of best practices, thereby enhancing the care of infants

with NTDs [30–32]. Geospatial mapping also informs policy development and advocacy, supporting increased investment in surgical infrastructure and workforce development [33]. With effective global surgery initiatives requiring community engagement and education, geospatial mapping can provide information about areas where community health workers and educational campaigns are most needed [31,32,34]. By empowering communities with knowledge about NTD prevention, early detection, and timely intervention, the global surgery community can then create a proactive approach to addressing the issue at its roots. This engagement fosters a sense of ownership and encourages communities to advocate for improved surgical care access for children born with NTDs.

3.4 Conclusion: Addressing Neural Tube Defects Globally, a Call for Collaborative Efforts and Technological Integration

The global challenge of Neural Tube Defects highlights significant disparities, particularly in low- and middle-income countries, underscoring the need for enhanced monitoring, reporting, and accessible healthcare for affected children. The variability in NTD prevalence across different regions demands a collaborative, multi-sectoral approach that addresses socio-economic, infrastructural, and educational disparities. Prioritizing surgical care in LMICs is crucial due to the exacerbated challenges posed by limited resources. This calls for a comprehensive strategy that includes capacity building, medical education, and community outreach to improve the quality and accessibility of healthcare for children with NTDs.

Geospatial mapping has emerged as a critical tool in this context due to its ability to help improve our understanding of healthcare accessibility and guide in resource allocation. It helps in identifying vulnerable populations and the barriers they face, enabling targeted interventions and international collaborations. This technology not only aids in policy development and advocacy for better surgical infrastructure and workforce development but also promotes community engagement and education on NTD prevention and care. Addressing the NTD challenge requires a coordinated, data-driven approach, blending technology, international cooperation, and community initiatives to ensure equitable and effective care for all affected children, making it a moral imperative to bridge healthcare disparities and uplift vulnerable populations globally.

CHAPTER THREE: RESULTS AND MANUSCRIPT

Title:

Prevalence of Babies Born with Neural Tube Defects and Geospatial Mapping of Therapeutic Services: A Systematic Review

Authors:

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Abstract:

Introduction: Neural tube defects (NTDs) are an important global health concern with high morbidity and mortality. Enhancing access to healthcare for children born with NTDs is crucial for improving health systems and service delivery.

Methods: We conducted a systematic review to assess the global prevalence of NTDs and the accessibility of healthcare services. Our search spanned databases like PubMed, EMBASE, and Scopus, focusing on NTD prevalence, healthcare service mapping, and access barriers. We followed a standardized data extraction process, and the study is registered with PROSPERO (CRD42023425843).

Results: From 3 067 records, 65 studies met our inclusion criteria, mainly focusing on newborns. The study durations range from six months to 40 years. The NTD prevalence was between 0.4 and 215.13 per 10 000 births, with Spina Bifida, Anencephaly, and Encephalocele being the most common. The African Region was the WHO region with the highest prevalence while the Western Pacific Region had the lowest prevalence. One study used geospatial mapping to identify healthcare access barriers.

Conclusion: Our study revealed wide disparities in the prevalence rates of neural tube defects with the African region having the highest prevalence. Geospatial mapping was not used to assess access to healthcare services for children born with NTDs in almost all the studies. This

underscores the global challenge of access to surgical care for children born with NTDs and the need for strengthening healthcare services in settings with high prevalences.

Keywords: Accessibility of Healthcare, Geospatial Mapping, Healthcare Disparities, Neural Tube Defects, Policy Reform

Introduction

Neural tube defects (NTDs) represent a global public health challenge, marked by significant morbidity and mortality rates [35]. The burden of NTDs extends beyond individual health, impacting families, healthcare systems, and societies at large [17]. Early diagnosis and timely access to specialized healthcare services are crucial for managing NTDs and improving outcomes [36]. Unfortunately, there is a recognized lack of comprehensive data on the prevalence of NTDs and the corresponding geographic distribution of healthcare services tailored to address the unique needs of infants with NTDs [6,9].

The complexities of NTDs extend beyond geographical considerations, presenting a challenge that demands a multifaceted approach to implementing effective interventions [13]. Children affected by NTDs often face barriers to receiving adequate healthcare services due to a myriad of factors, including insufficient infrastructure, resource limitations, and a shortage of skilled healthcare personnel [12,18]. Especially prevalent in low- and middle-income countries (LMICs), healthcare disparities might further compound the difficulties in ensuring accessible care for children with NTDs. Addressing the unique challenges associated with NTDs becomes imperative. The prevalence of NTDs and the barriers to healthcare access must be thoroughly understood to implement targeted interventions that account for social, economic, and cultural factors. This holistic approach is essential for decision-makers who seek to strategically allocate resources and create a framework that guarantees equitable access to healthcare services for children with NTDs, irrespective of their geographic location.

Geospatial mapping offers a comprehensive and data-driven approach to addressing the global public health challenge posed by NTDs [5,9,33,37,38]. It could empower policymakers and healthcare professionals to make informed decisions, allocate resources efficiently, and work towards reducing the burden of NTDs, particularly in regions where healthcare inequalities are most pronounced. However, there is a need to understand the utilization of this tool in the evaluation of access to healthcare facilities for children born with NTDs.

This study aimed to bridge this knowledge gap through a systematic review determining the prevalence of children born with NTDs and to assess access to healthcare through geospatial mapping.

Methods

Research Questions and Search Strategy:

The study's primary research questions pertained to the global prevalence of NTDs in children, and access to surgical services through geospatial mapping of associated neurological, neurosurgical, and physiotherapeutic services, and the identification of barriers to accessing these services. To address these questions, a comprehensive search strategy was employed across electronic databases such as PubMed, EMBASE, Scopus, Web of Science, CINAHL, and the Cochrane Library. The search included relevant keywords and Medical Subject Headings (MeSH) terms such as "neural tube defects," "spina bifida," "anencephaly," "encephalocele," "prevalence," "geospatial mapping," "neurological services," "neurosurgical services," "physiotherapy services," "access barriers," and "healthcare services", "ground truthing," "GIS".

Inclusion and Exclusion Criteria:

The study's inclusion criteria encompassed studies reporting the prevalence of neural tube defects in children, studies detailing the geospatial mapping of healthcare services associated with NTDs, and studies exploring barriers to accessing these services by children born with NTDs. We focused exclusively on English-language studies published from the year 2000 to 2023. This date range ensures that the review incorporates current and pertinent literature, minimizes language bias, and enhances the applicability of findings to contemporary healthcare systems. Studies not related to NTD prevalence, geospatial mapping of healthcare services for infants with NTDs, or barriers to accessing these services were excluded from consideration.

Data Extraction and Quality Assessment:

Two authors (YZ and DUD) reviewed and screened titles and abstracts for inclusion and exclusion criteria. A standardized data extraction form was developed to extract relevant data from the selected studies. The form included the following information: first author, title of study, WHO Region, country investigated, study type, data source, location of data source, reported prevalence, prevalence of subtypes of NTDs reported, geospatial mapping of services, geospatial analysis of healthcare service location and patient densities, and barriers to services (see APPENDIX 2 for details).

A modified Critical Appraisal Skills Programme (CASP) tool was used to assess the quality of the selected studies. The tool comprised ten questions that were used to assess the validity, reliability, and applicability of the studies. Studies were graded as low, moderate, or high quality based on their scores (see APPENDIX 3 for details).

Data Synthesis and Study Registration:

A narrative synthesis approach was employed to present study findings, organizing data around the research questions and utilizing tables, graphs, and maps to enhance clarity. The study had been registered on PROSPERO under the ID CRD42023425843, with the registration last updated on May 22, 2023 (see APPENDIX 8 for details).

Results

Studies Selection:

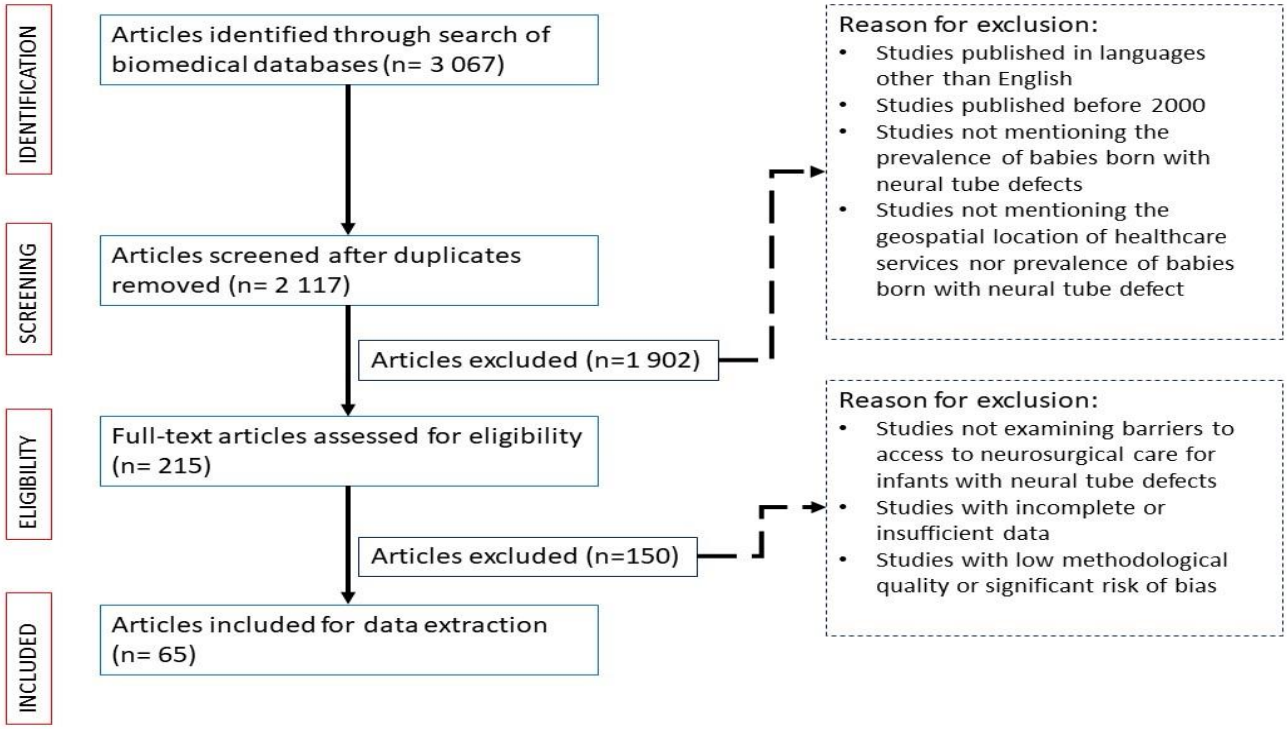

Figure 1: Studies Selection Flowchart

The database search yielded 3 067 results, of which 950 were duplicates. The 2 117 unique titles were screened for inclusion and exclusion criteria. After the initial screening, 1 902 articles were

excluded. A full-text review of the remaining 215 articles was done and 150 articles were excluded. We identified 65 unique studies that met our inclusion criteria in the final stage of review (Figure 1).

When examining the distribution of studies by World Health Organization (WHO) regions, it is noted that 18 (27.7%) studies originated from the European Region (EUR), the Western Pacific Region (WPR) contributed 15 (23.1%) studies, both the Region of Americas (AMR) and the African Region (AFR) comprised 13 (20.0%) studies each while the South East Asian Region (SEAR) accounted for 4 (6.2%) studies, and the Eastern Mediterranean Region (EMR) had 2 (3.1%) studies (Figure 2).

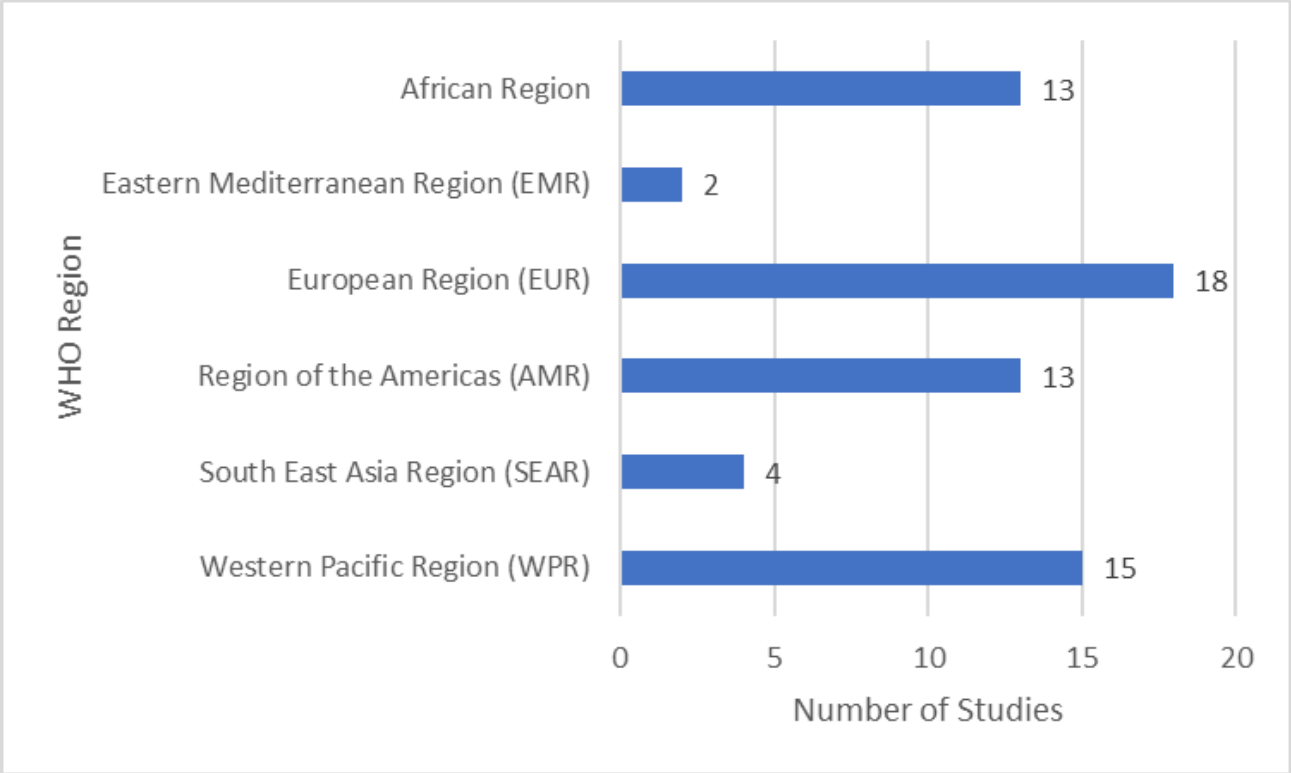

Figure 2: Studies Distribution According to WHO Regions

Characteristics and Data Extracted from Included Studies:

The data sources of the included 65 studies were as follows: Patient records (n=34, 52.3%), Regional registry (n=13, 20%), National registry (n=24, 36.9%), Self-administered questionnaires/ questionnaires (n=5, 7.69%) and Geographic Information System (GIS) Data Sources (n=1, 1.5%) (Supplementary 1).

Most (n=12, 35.3%) studies using Patient records were from the African Region (AFR), while 75% (n=18) of studies using National registries were from the European Region (n=10) and the Region of the Americas (n=8). Up to 69.2% (n=9) of studies using regional registries were from the Region of the Americas (n=5) and European Region (n=4). The only study that utilized GIS data was from the Region of the Americas (Table 3).

The study with the longest duration lasted for 40 years while the shortest study lasted for six months (see Supplementary 1 for details). Regarding the study types, 21 (32.3%) studies were cross-sectional studies and 44 (67.7%) were longitudinal studies. All the studies were descriptive studies, 36 (55.4%) studies were retrospective and 7 (10.8%) were prospective studies (see Supplementary 1 for details).

Table 3: Source of Data Per WHO Region

Data Source	Count per WHO Region						Total
	African Region (AFR)	Eastern Mediterranean Region (EMR)	European Region (EUR)	Region of the Americas (AMR)	South East Asia Region (SEAR)	Western Pacific Region (WPR)	
Patient record	12	2	8	2	4	6	34
Regional registry	1	0	4	5	0	3	13
National registry	1	0	10	8	0	5	24
Self-administered questionnaires/questionnaires	1	0	0	0	1	3	5
Geographic Information System (GIS)	0	0	0	1	0	0	1

In terms of the study population, 54 (83.1%) studies focused on newborns (aged 0 to 28 days old), 9 (13.85%) studies centered on children (aged 0 to <18 years old), 3 (4.61%) studies involved abortuses, 1 (0.15%) study examined infants (aged 0 to <5 years), 1 (0.15%) study explored stillbirths, and 13 (0.2%) studies investigated pregnant women as the study population. Additionally, 2 (3.1%) studies concentrated on postpartum women as the study population (Supplementary 1).

Concerning the inclusion criteria, the most prevalent was the age of participants (n=53, 81.5%), followed by the diagnosis of NTDs (n=32, 49.2%), the birth outcome (n=26, 40.0%), the birth period (n=20, 30.8%), the birthplace (n=16, 24.6%), the geographic location (n=9, 13.8%), the diagnosis period (n=7, 10.8%), the co-morbidities (n=2, 3.1%), the location of facility (n=1, 1.5%) and admission period (n=1, 1.5%). Six (9.2%) studies did not report their inclusion criteria (Supplementary 1).

The largest study in terms of population size was conducted in the European region (EUR). This was a 4-year longitudinal study involving 15 million children. These participants were sourced from national registries across 13 European countries: Austria, Belgium, Croatia, Denmark, France, Germany, Ireland, Italy, Malta, the Netherlands, Poland, Switzerland, and the United Kingdom. In contrast, the study with the smallest population size was a cross-sectional study in India, located in the South East Asian region (SEAR), involving just 310 children (see Supplementary 1 for details).

The lowest prevalence (0.4 per 10 000 births) was from a study in the Western Pacific Region (WPR) while the highest prevalence (215.13 per 10 000 births) was from a study in the African Region (AFR) (Supplementary 1).

Most (n=58, 89.2%) studies reported NTDs subtypes with 47 (72.3%) studies reporting Spina Bifida, 45 (69.2%) studies reporting Anencephaly, 36 (55.3%) studies reporting Encephalocele, 8 (12.3%) studies reporting Myelomeningocele, 3 (4.6%) studies reporting Meningocele, 1 (1.5%) study reporting Cephalocele and 1 (1.5%) study reporting Craniorachischisis. Only 7 (10.8%) studies did not report NTDs subtypes (Supplementary 1).

The African region had the widest prevalence range, followed by the European region and the South East Asia Region. The Eastern Mediterranean Region had the smallest prevalence range (Table 4).

Table 4: Prevalence Interval and Range per WHO Region

WHO Region	Prevalence Interval	Prevalence Range
African Region	2.02 – 215.13 per 10 000 births	213.11 per 10 000 births
Eastern Mediterranean Region (EMR)	28 – 28.7 per 10 000 births	0.7 per 10 000 births
European Region (EUR)	0.94 – 69.6 per 10 000 births	68.66 per 10 000 births
Region of the Americas (AMR)	3.2 – 14.01 per 10 000 births	10.81 per 10 000 births
South East Asia Region (SEAR)	4 – 57 per 10 000 births	53 per 10 000 births
Western Pacific Region (WPR)	0.4 – 20.1 per 10 000 births	19.7 per 10 000 births

Only 1 (1.5%) study (Eric M Delmelle et al.) reported geospatial mapping and geospatial analysis of services for babies born with NTDs. The study is a cross-sectional observational study from the Region of the Americas (AMR) published in 2013. The authors utilized Geographic Information Systems for the geospatial mapping of services and geospatial analysis of services. The results of the geospatial analysis of service location and patient density found that the average one-way travel time for families and infants during an infant's first year of life was approximately 45 minutes, covering an estimated distance of 34 miles. The study also uncovered various barriers, such as geographical constraints, that hindered families and infants from accessing healthcare services for infants with NTDs. Moreover, factors like longer travel distances and transportation availability contributed to these barriers to services for families and infants with NTDs (see Supplementary 1 for details).

Results of Syntheses:

Only 1 (1.5%) study reported factors contributing to gaps and disparities in care delivery to babies born with NTDs. This cross-sectional observational study by Eric M Delmelle et al. from the United States of America was published in 2013. The reported factors contributing to gaps and disparities in care delivery to babies born with NTDs are geographic location, availability of specialized hospitals, transportation options, and socioeconomic status (see Supplementary 2 for details). None of the studies mentioned the gaps or disparities in care delivery, interventions aimed at addressing these issues, shortages in skilled providers, or the impact of cost on access to care delivery (see Supplementary 2 for details).

Risk of Bias and Certainty of Evidence:

Out of the studies reviewed, 63 (96.9%) studies showed a moderate risk of bias, while 2 (3.1%) studies had a low risk, with both low-risk studies conducted in the Americas. These studies are important for guiding future research and policies to improve healthcare for infants with NTDs (see Supplementary 3 for details).

Discussion

Central to our findings is the range of NTD prevalence, from 0.4 per 10 000 births in the Western Pacific Region to 215.13 per 10 000 births in the African Region, which underscores the heterogeneity in NTD burden globally. Our findings are different from those observed in a systematic review published in 2016 by Zaganjor et al.[16], where the prevalence ranged from 0.3 to 199.4 per 10 000 births with the lowest and highest prevalence being from studies in the Western Pacific Region [16]. This is probably due to variations in data collection methodology between their study and our study. Our study had a more comprehensive data collection not excluding studies based on their population sizes while the Zaganjor et al excluded studies with populations sizes less than 5 000 total births, which surely excluded a lot of studies from the African Region where there is a known lack of well-structured databases including databases with over 5 000 total births [39,40]. Understanding these disparities in prevalence between regions is crucial for tailoring public health strategies and resource allocation to address the specific needs of each region and our findings reveal the need for tailored interventions in developing countries. Additionally, in our review Spina Bifida, Anencephaly, and Encephalocele emerged as the most frequently reported subtypes, emphasizing their significance in the epidemiology of NTDs. The

order of occurrence of NTDs is similar to that reported by a 2018 study estimating the global and regional prevalence of NTDs [35]. The identification of these subtypes allows for targeted preventive measures and intervention strategies, considering the distinct characteristics and risk factors associated with each subtype.

Our comprehensive analysis of the 65 studies included in this research provides valuable insights into the source of data on neural tube defects (NTDs) across diverse populations and settings. The utilization of various data sources reflects the multifaceted nature of NTDs research, with patient records being the predominant source in more than half of the studies. The inclusion of various sources of data is similar to that observed in a study published in 2018 by Hannah Blencowe et al.[35] underscoring the importance of leveraging diverse methodologies to enhance the robustness of findings and capture a holistic picture of NTDs prevalence. However, our study also reveals the fact that registries on NTDs are not adequately present in most WHO regions with most registries (National and Regional registries) found in the European Region and the Region of the Americas similar to what was observed by in 2016 by Zaganjor et al.[16]. Ensuring that all if not most countries (and WHO regions) have well established and maintained NTDs registries can help effectively curb the burden of NTDs. This is because registries will lead to a better measurement of the real burden of NTDs and facilitate the development of informed strategies aimed at reducing the observed burden of NTDs in areas with observed high prevalences of NTDs [41].

The observed significant variation in study durations highlights the necessity for extended research to understand the changing trends and patterns of NTDs [42]. It is noteworthy that we observed that studies with longer durations predominantly occurred in high income countries, likely due to more substantial research funding available in these regions. This highlights the need for more investment in NTD research in low- and middle-income countries, aligning with global health goals to reduce NTD prevalence in LMICs. Our analysis found a predominance of longitudinal studies (67.7%), highlighting the importance of long-term data for understanding NTD risk factors and effective intervention strategies. However, the reliance on descriptive studies, mainly retrospective, indicates a lack of experimental research, such as randomized controlled trials, which are vital for establishing causal links and validating interventions like folic acid supplementation. Integrating experimental methods with longitudinal research is essential for a comprehensive and effective approach to NTD management in LMICs [15,43].

Our review reveals a notable gap in the use of geospatial mapping in studies on neural tube defects (NTDs), with only one study (Eric M Delmelle et al.)[44] employing this method. The observed limited utilization of geospatial mapping despite its importance for understanding access to specialized healthcare services for infants with NTDs, highlights the need for its wider integration in future research. Insights from Eric M Delmelle et al. [53] reveal the profound potential of geospatial analysis in uncovering crucial insights into healthcare accessibility for infants with NTDs. Geospatial analysis not only provides insights into accessibility challenges, such as long travel times and transportation barriers for families of children with NTDs, but also aids in strategic healthcare planning. It can guide the placement of specialized clinics, improvement of transport infrastructure, and efficient allocation of resources, ensuring equitable access for all affected infants, especially in geographically constrained areas [7,45,45].

Another important observation emanating from our review is the marked absence of interventions specifically aimed at addressing the identified access barriers (Supplementary 2). There is a noticeable dearth of strategies designed to alleviate these barriers, whether they pertain to geographic disparities, shortages in skilled healthcare providers, or the financial burdens associated with accessing care. Whilst there is a high number of studies on prevalence to understand the burden of disease (outcome), our review highlights the gap in studies on process and structural barriers.

Limitations:

Our systematic review faces several design-related limitations. It is restricted to English-language studies published post-2000, which may exclude relevant non-English research and historical data on neural tube defects (NTDs). This restriction is particularly impactful for regions where English is not the primary language, such as parts of Africa, potentially leading to a gap in understanding the full scope of NTDs in these areas. The variability in study designs further complicates data synthesis and interpretation. Moreover, due to limitations in the available data, we were unable to fully address objective of describing access to health services. These limitations highlight the need for more inclusive research practices to capture a comprehensive view of NTD care globally.

Recommendations:

Research: Prolong and experiment – researchers should extend prevalence studies, use randomized controlled trials, and focus on geospatial mapping to understand and improve accessibility. Future research should also address the gaps in understanding the overall state of healthcare services for children with NTDs.

Practice: Tailor and optimize – Healthcare practices for children with NTDs should focus on interventions for common NTD subtypes, improve data collection methods, and strategically position clinics using geospatial analysis to address access issues identified in our study.

Policy: Reform, invest, and learn – Policy reforms are needed to address disparities in NTD care. Encouraging research investments and ensuring comprehensive, unbiased studies will aid in developing effective global strategies for NTDs. Implementing policy changes to support the establishment of NTD registries and improving access to care can help reduce the burden of NTDs globally.

Conclusion

The review shows uneven neural tube defects (NTDs) prevalence across WHO regions, highest in Africa and lowest in the Western Pacific. It notes the underuse of geospatial mapping in evaluating NTDs healthcare accessibility and the need for more studies on process and structure barriers to accessing care for children born with NTDs. Policymakers and healthcare providers are urged to develop innovative solutions, including policy reforms and awareness campaigns, to improve care for NTD-affected infants and address disparities.

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Author contribution:

YZ conceptualized the study, investigated, curated, analyzed, and visualized the data, wrote the original manuscript draft, and administered the project. MI and SM supervised the study, wrote the original manuscript draft, and administered the project. DUD assisted with article screening. All authors have read and approved the final manuscript.

Declaration of conflicts of interests:

The authors declare no conflict of interest.

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APPENDICES

APPENDIX 1: SEARCH STRATEGY

Here is an elaborate search strategy for this systematic review:

1. Relevant keywords and search terms related to the topic of the review:
    - Neural tube defects
    - Spina bifida
    - Anencephaly
    - Encephalocele
    - Prevalence
    - Epidemiology
    - Geospatial location
    - Geographical information systems
    - Ground truthing
    - Neurological services
    - Neurosurgical services
    - Physiotherapy services

2. Databases that will be searched:

- MEDLINE and PubMed
- Embase
- Cochrane Library
- CINAHL
- Scopus
- Web of Science

3. Search strategy using the identified keywords and search terms:
    a. PubMed:

("neural tube defects"[MeSH Terms] OR "spina bifida"[MeSH Terms] OR "anencephaly"[MeSH Terms] OR "encephalocele"[MeSH Terms]) AND ("prevalence"[MeSH Terms] OR "epidemiology"[MeSH Terms])

("neural tube defects"[MeSH Terms] OR "spina bifida"[MeSH Terms] OR "anencephaly"[MeSH Terms] OR "encephalocele"[MeSH Terms]) AND ("geographic mapping"[MeSH Terms] OR "geographic information systems"[MeSH Terms])

("neurological services"[MeSH Terms] OR "neurosurgical services"[MeSH Terms] OR "physiotherapy"[MeSH Terms]) AND ("neural tube defects"[MeSH Terms] OR "spina bifida"[MeSH Terms] OR "anencephaly"[MeSH Terms] OR "encephalocele"[MeSH Terms])

b. Embase:

('neural tube defect'/exp OR 'spina bifida'/exp OR 'anencephaly'/exp OR 'encephalocele'/exp) AND ('prevalence'/exp OR 'epidemiology'/exp)

('neural tube defect'/exp OR 'spina bifida'/exp OR 'anencephaly'/exp OR 'encephalocele'/exp) AND ('geographic information system'/exp OR 'geospatial mapping'/exp)

('neurological service'/exp OR 'neurosurgical service'/exp OR 'physiotherapy'/exp) AND ('neural tube defect'/exp OR 'spina bifida'/exp OR 'anencephaly'/exp OR 'encephalocele'/exp)

c. Cochrane Library:

(neural tube defect OR spina bifida OR anencephaly OR encephalocele) AND (prevalence OR epidemiology)

(neural tube defect OR spina bifida OR anencephaly OR encephalocele) AND (geospatial mapping OR geographical information systems)

(neurological services OR neurosurgical services OR physiotherapy) AND (neural tube defect OR spina bifida OR anencephaly OR encephalocele)

d. Scopus:

(TITLE-ABS-KEY ("neural tube defects" OR "spina bifida" OR "anencephaly" OR "encephalocele") AND TITLE-ABS-KEY ("prevalence" OR "epidemiology") AND TITLE-ABS-KEY ("geospatial" OR "geographical information systems") AND TITLE-ABS-KEY ("neurological services" OR "neurosurgical services" OR "physiotherapy services"))

e. Web of Science:

TS=((((("Neural Tube Defects") OR "Spina Bifida") OR "Anencephaly") OR "Encephalocele") AND (Prevalence OR Epidemiology) AND ((((("Geography") OR "Geographic Information Systems") OR "Geospatial") OR "Geographical") AND (("Neurology") OR "Neurosurgery" OR "Physical Therapy Modalities")))

f. CINAHL:

(MH "Neural Tube Defects+" OR MH "Spinal Dysraphism+" OR MH "Anencephaly+" OR MH "Encephalocele+") AND (MH "Prevalence+" OR MH "Epidemiology+")

(MH "Neural Tube Defects+" OR MH "Spinal Dysraphism+" OR MH "Anencephaly+" OR MH "Encephalocele+") AND (MH "Geographic Mapping+" OR MH "Geographic Information Systems+")

(MH "Neurological Services+" OR MH "Neurosurgical Services+" OR MH "Physiotherapy+") AND (MH "Neural Tube Defects+" OR MH "Spinal Dysraphism+" OR MH "Anencephaly+" OR MH "Encephalocele+")

4. After applying the filters, we shall including date, language, and publication type, as necessary we shall conduct a search in each identified database using the developed search strategy and record the number of results for each database.

5. We (the student investigator and a global surgery fellow at the division of global surgery, UCT) shall screen the resulting studies for eligibility, based on inclusion and exclusion criteria established for the scoping review using the software called Rayyan.

6. Extraction of relevant data from eligible studies using a standardized form and analysis of the findings to address the research objectives of the systematic review will be done.

APPENDIX 2: DATA EXTRACTION TOOL

Study Information

a. Author(s):

b. Title:

c. Journal:

d. Year of publication:

Study Design

a. Type of study:

b. Study population:

c. Inclusion criteria:

d. Exclusion criteria:

e. Study location:

f. Study period:

Prevalence of Neural Tube Defects

a. What is the reported prevalence of neural tube defects in the study population?
b. What are the most common types of neural tube defects reported in the study?
c. Are there any variations in the prevalence of neural tube defects across different regions or countries?

Availability and Accessibility of Neurosurgical Care

a. What is the reported availability of neurological, neurosurgical, and physiotherapeutic services for infants born with neural tube defects?

b. What is the definition of neurological, neurosurgical, and physiotherapeutic services used in the study?

c. What types of neurological, neurosurgical, and physiotherapeutic interventions are reported in the study?

d. Are there any variations in the availability of neurological, neurosurgical, and physiotherapeutic services across different regions or countries?

e. What are the reported barriers to accessing neurological, neurosurgical, and physiotherapeutic services for infants with neural tube defects?

f. Are there any reported innovative approaches to delivering neurological, neurosurgical, and physiotherapeutic services, such as telemedicine or task-shifting?

Geospatial Mapping of Services and Geospatial Analysis

Describe results

Geospatial Analysis of Service Location and Patient densities

Describe results

Barriers to Services

Describe results

Gaps and Disparities in Care Delivery

a. Are there any reported innovative approaches to delivering neurological, neurosurgical, and physiotherapeutic services, such as telemedicine or task-shifting?

b. What are the reported factors contributing to these gaps or disparities?

c. Are there any reported interventions to address these gaps or disparities?

Quality of Care

a. What is the reported quality of neurological, neurosurgical, and physiotherapeutic care delivered to infants born with neural tube defects?

b. Are there any reported shortages of skilled healthcare providers or other resources necessary for comprehensive care?

c. What is the reported impact of cost on access to care?

Study Limitations

a. What are the reported limitations of the study?

b. Are there any factors that may have affected the accuracy or reliability of the study's findings?

Conclusion

a. What are the main findings of the study?

b. How do these findings contribute to our understanding of the prevalence of neural tube defects and the availability and accessibility of neurological, neurosurgical, and physiotherapeutic services globally?

c. What are the implications of these findings for future research and policy development?

APPENDIX 3: CRITICAL APPRAISAL TOOL

Here is the critical appraisal tool to be used to assess the quality of articles to be included in our systematic review it is adapted from the "JBI CRITICAL APPRAISAL CHECKLIST FOR STUDIES REPORTING PREVALENCE DATA":

1. Study design: What was the study design used in the article? Was it appropriate for the research question?

2. Sampling: Was the sampling strategy clearly described and appropriate for the research question? Was there a risk of selection bias?

3. Data collection: Was the data collection method clearly described and appropriate for the research question? Was there a risk of measurement bias?

4. Data analysis: Was the data analysis method clearly described and appropriate for the research question? Was there a risk of confounding?

5. Results: Were the results presented clearly and accurately? Were the conclusions supported by the results?

6. Generalizability: Are the findings of the study generalizable to the population of interest? Were there any limitations to the study that affect generalizability?

7. Bias: Were there any sources of bias in the study that may affect the validity of the results?

8. Funding: Was the study funded by any organizations that may have influenced the results or conclusions?

Each question will be answered on a scale of 0 to 2, with 0 indicating a low risk of bias and 2 indicating a high risk of bias. The total score should be tallied up, with a higher score indicating a higher risk of bias. Articles with a score of 6 or higher may be excluded from the systematic review, while articles with a score of 4 or lower may be included. Articles with a score of 5 may be included but should be examined more closely.

APPENDIX 4: PRISMA ABSTRACT CHECKLIST

PRISMA 2020 for Abstracts checklist*

Section and topic	Item #	Checklist item
Title		
Title	1	Identify the report as a systematic review.
Background		
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.
Methods		
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.
Synthesis of results	6	Specify the methods used to present and synthesise results.
Results		
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).
Discussion		
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).
Interpretation	10	Provide a general interpretation of the results and important implications.
Other		
Funding	11	Specify the primary source of funding for the review.
Registration	12	Provide the register name and registration number.

- * This abstract checklist retains the same items as those included in the PRISMA for Abstracts statement published in 2013,54 but has been revised to make the wording consistent with the PRISMA 2020 statement and includes a new item recommending authors specify the methods used to present and synthesise results (item #6).

Figure 3: The PRISMA 2020 statement: an updated guideline for reporting systematic reviews*[46]*

APPENDIX 5: PRISMA CHECKLIST

Section and topic	Item Number	Checklist item	Location where item is reported
Title			
Title	1	Identify the report as a systematic review.	Cover page
Abstract			
Abstract	2	See the PRISMA 2020 for Abstracts checklist	x
Introduction			
Rationale	3	Describe the rationale for the review in the context of existing knowledge	2-4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses	4
Methods			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	5-6
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	4-6
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	4-6
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	4-6
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	4-6

Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	APPENDIX 2
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	APPENDIX 2
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	APPENDIX 3
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Not Applicable
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Not applicable
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	4-6
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	4-6
	13d	Describe any methods used to synthesise results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	4-6
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	4-6

	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesised results.	4-6
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	4-6
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	APPENDIX 3
Results			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	18
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	/
Study characteristics	17	Cite each included study and present its characteristics.	Supplementary 1
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Supplementary 3
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Supplementary 1 to 3
Results of syntheses	20a	For each synthesis, briefly summarize the characteristics and risk of bias among contributing studies	Supplementary 3
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Not applicable
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Not applicable

	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesised results.	Not applicable
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Supplementary 3
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Supplementary 3
Discussion			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	23 to 25
	23b	Discuss any limitations of the evidence included in the review	25
	23c	Discuss any limitations of the review processes used.	25
	23d	Discuss implications of the results for practice, policy, and future research	25 to 26
Other information			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	APPENDIX 8
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared	1 to 10
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Not applicable
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	26
Competing interests	26	Declare any competing interests of review authors.	26
Availability of data, code, and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Not applicable

APPENDIX 6: DEPARTMENTAL RESEARCH COMMITTEE APPROVAL LETTER

UNIVERSITY OF CAPE TOWN

Department of Surgery
Departmental Research Committee
A/Prof Maritz Laubscher
Groote Schuur Hospital
Observatory 7925
South Africa
Tel (021) 404 5108
Email: maritz.laubscher@uct.ac.za

9 May 2023

Dr. A ZOLO OSSOU

Department of Surgery
University of Cape Town

Dear Dr. ZOLO OSSOU

RE: Project 2023/049

PROJECT TITLE: Prevalence Of Babies Born With Neural Tube Defects And Geospatial Mapping Of Therapeutic Services: A Systematic Review

The above protocol has been reviewed by the Department of Surgery Research Committee. I am pleased to inform you that the committee approved the scientific merit of the study, and endorse the protocol for submission to the relevant ethics committee.

Although this letter serves as confirmation that the above protocol has successfully passed through the surgical DRC, respective ethics committees still require DRC chair signature before submission.

Please use the above project number in all future correspondence,

Yours sincerely

Signed by candidate

A/PROF MARITZ LAUBSCHER
CHAIR SURGICAL DRC

"OUR MISSION is to be an outstanding teaching and research university, educating for life and addressing the challenges facing our society."

APPENDIX 7: HUMAN RESEARCH ETHICS COMMITTEE APPROVAL LETTER

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room 45, E-52 Old Main Building
Groote Schuur Hospital
Observatory 7925
Email: hrec-enquiries@uct.ac.za
Website: www.health.uct.ac.za/home/human-research-ethics

10 July 2023

HREC REF NO: 471/2023

Dr A Zolo Ossou
Department of Surgery
Division of Global Surgery
Email: zlsand001@myuct.ac.za

Dear Dr Zolo Ossou

PROJECT TITLE: PREVALENCE OF BABIES BORN WITH NEURAL TUBE DEFECTS AND GEOSPATIAL MAPPING OF THERAPEUTIC SERVICES: A SYSTEMATIC REVIEW

Thank you for submitting your request to the Faculty of Health Sciences Human Research Ethics Committee.

The HREC acknowledges that the Supervisor is Professor Salome Masiwime.

The HREC note that the proposed study is a systematic review.

As the systematic review involves published literature available through publicly accessible electronic databases, research ethics review and approval is not required.

This is in accordance with Section 1.1.8 of the Department of Health's Ethics in Health Research: Principles, Processes and Structures (South African Department of Health, 2015), which states: *"Research that relies exclusively on publicly available information or accessible through legislation or regulation usually need not undergo formal ethics review. This does not mean that ethical considerations are irrelevant to the research."*

The HREC recommend that researchers refer to the PRISMA website, for the PRISMA statement and checklist, to facilitate the reporting of systematic reviews and meta-analyses. For more information, please refer to http://www.prisma-statement.org/.

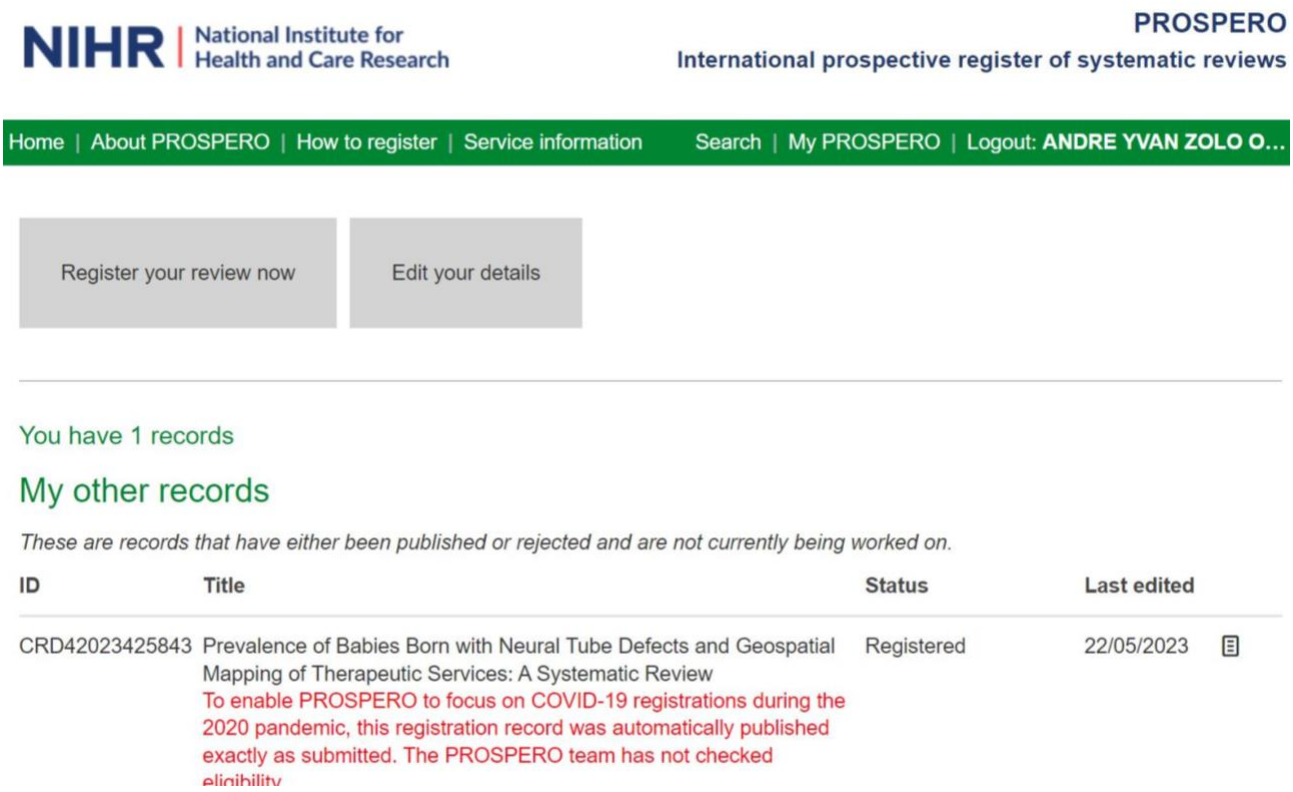
Further, fundamental ethical principles for health-related research should be considered in the objectives and methods of the systematic review. See, for example, the Declaration of Helsinki (Fortaleza, Brazil, 2013) and the Department of Health's Ethics in Health Research: Principles, Processes and Structures (South African Department of Health, 2015).

Yours sincerely

Signed by candidate

PROFESSOR MARC BLOCKMAN
CHAIRPERSON, FACULTY OF HEALTH SCIENCES HUMAN RESEARCH ETHICS COMMITTEE

APPENDIX 8: STUDY REGISTRATION ON PROSPERO



NIHR | National Institute for Health and Care Research

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ID	Title	Status	Last edited
CRD42023425843	Prevalence of Babies Born with Neural Tube Defects and Geospatial Mapping of Therapeutic Services: A Systematic Review To enable PROSPERO to focus on COVID-19 registrations during the 2020 pandemic, this registration record was automatically published exactly as submitted. The PROSPERO team has not checked eligibility	Registered	22/05/2023

APPENDIX 9: SUPPLEMENTARY MATERIALS

Supplementary 1: Characteristics of Studies, Prevalence, Geospatial Mapping of Services, Geospatial Analysis and Barriers to Access Services Reported in Studies

First Author	Country investigated	WHO Region	Type of Study			Population Type	Inclusion Criteria	Size of Population	Reported Prevalence (per 10 000 live births)	Types of NTDs reported	Study length	Data source
Birhane Alem Berihu[47]	Ethiopia (Tigray)	African Region (AFR)	Cross sectional	Descriptive	/	Newborns	Age, Birth outcome	14 903	30.13	Anencephaly Spina bifida	1 year	Patient records
Atsuo Kondo[48]	Japan	Western Pacific Region (WPR)	Cross sectional	Descriptive	/	Pregnant women and newborns	Age	311 000	8.7	Myelomeningocele Anencephaly	1 year	Patient records
Ilham M Omer[49]	Sudan (Khartoum state)	African Region (AFR)	Cross sectional	Descriptive	/	Newborns	Age	36 785	28	Myelomeningocele Anencephaly Encephalocele Meningocele	1 year	Patient records
Soressa Abebe Geneti[50]	Ethiopia (Soutwestern)	African Region (AFR)	Cross sectional	Descriptive	/	Newborns	Age	45 951	40.05	Anencephaly Spina bifid Meningomyelocele	4 years	Patient records
Mark A. Canfield[51]	United States of America (Texas)	Region of the Americas (AMR)	Cross sectional	Descriptive	/	Newborns	Age	1 800 000	6.33	Anencephaly Spina bifida	4 years	Regional Registry
R McDonnell[52]	Ireland	European Region (EUR)	Cross sectional	Descriptive	/	Newborns	Birth outcome, Nutrient supplement	274 732	10.5	Anencephaly Spina Bifida Encephalocele	2 years	Patient records

							ation, Diagnosis period					
Nóra Szabó[53]	Hungary	European Region (EUR)	Cross sectional	Descriptive	/	Newborns	Age, Diagnosis period	156 433	6.14	Myelomeningocele Anencephaly Encephalocele	11 years	National registry
Mikyong Shin[54]	United States of America	Region of the Americas (AMR)	Longitudinal	Descriptive	Retrospective	Children	Age, Geographic location, Diagnosis,	Not reported	3.2	Spina Bifida	1 year	National registry
E I Krzesinski[55]	South Africa	African Region (AFR)	Longitudinal	Descriptive	Retrospective	Newborns and abortions	Age, Diagnosis	Not reported	7.6	Anencephaly Encephalocele Spina Bifida	6 years	Patient records
Jie Liu[56]	China	Western Pacific Region (WPR)	Longitudinal	Descriptive	Retrospective	Pregnant women and Newborns	Diagnosis period, Age	1 208	12.21	Spina bifida Anencephaly Encephalocele	8 years	Patient records and Questionnaires
Shiva Bhandari[57]	Nepal	South-East Asian Region (SEAR)	Cross sectional	Descriptive	/	Pregnant women and children	Age, Birth outcome	27 201	4	Myelomeningocele Encephalocele	1 year	Patient records
María de la Paz Barboza-Argüello[58]	Costa Rica	Region of the Americas (AMR)	Cross sectional	Descriptive	/	Newborns	Age, Diagnosis, Birth period, Address	1 170	4.8	Spina bifida Anencephaly Encephalocele	25 years	National registry

M J Golalipour[59]	Iran	Eastern Mediterranean Region (EMR)	Longitudinal	Descriptive	Retrospective	Newborns	Age, Birth ooutcome	37 951	28.7	Spina bifida Anencephaly	5 years	Patient records
Kaouther Nasri[60]	Tunisia	African Region (AFR)	Longitudinal	Descriptive	Retrospective	Stillborn and Newborns	Age, Birthplace, Diagnosis, Birth period	769	2.02	Not reported	20 years	Patient records
Dania María Pastora Bucardo[61]	Nicaragua	Region of the Americas (AMR)	Cross sectional	Descriptive	/	Pregnant women and Newborns	Age, Birth outcome, Diagnosis, Diagnosis period	178 498	14.01	Spina bifida Anencephaly Encephalocele	12 years	Patient records
R. McDonnell[52]	Ireland	European Region (EUR)	Longitudinal	Descriptive	Retrospective	Newborns		225 998	10.4	Anencephaly Spina bifida Encephalocele	2 years	Patient records
B. Mahadevan[62]	India	South-East Asian Region (SEAR)	Cross sectional	Descriptive	/	Newborns	Age, Birthplace	310	57	Spina bifida Anencephaly Encephalocele Craniorachischisis	6 years	Patient records
Nem-Yun Boo[63]	Malaysia	Western Pacific Region (WPR)	Longitudinal	Descriptive	Prospective	Newborns	Age, Birthplace	263 034	4.2	Anencephaly Spina bifida Encephalocele	1 year	National registry

R E Stevenson[64]	USA	Region of the Americas (AMR)	Longitudinal	Descriptive	Prospective	Newborns	Age, Birthplace, Birth period, Diagnosis, Birth outcome	278 122	9.5	Spina bifida Anencephaly Encephalocele	6 years	Regional registry
Hayelom Kebede Mekonen[65]	Ethiopia	African Region (AFR)	Cross sectional	Descriptive	/	Newborns	Age, Birth outcome, Address	12 225	215.13*	Spinal Bifida Anencephaly Encephalocele	1 year	Patient records
S T Onrat[66]	Turkey	European Region (EUR)	Longitudinal	Descriptive	Retrospective	Newborns	Age, Birth outcome, Diagnosis period	8 631	35.9	Spina bifida Anencephaly Encephalocele Meningocele	1 year	Patient record
Philippe De Wals[67]	Canada	Region of the Americas (AMR)	Longitudinal	Descriptive	Retrospective	Newborns	Age, Birthplace, Birth outcome, Diagnosis	2 446	8.6*	Spina bifida Anencephaly Encephalocele	9 years	National registry
Jelena G Petrova[68]	Russia and Norway	European Region (EUR)	Longitudinal	Descriptive	Retrospective	Newborns	Age, Geographic location, Diagnosis	141 159 and 293 708	21.1 (Russia) and 10.8 (Norway)*	Anencephaly Spina bifida	9 years	National registry
Eric M Delmelle[44]	USA	Region of the Americas (AMR)	Cross sectional	Descriptive	/	Newborns	Age, Birth outcome, Birth Period, Geographic location	Not reported	614**	Spina bifida	9 years	National registries and Geographic Information System (GIS) Data Sources

Robert E Meyer[69]	USA	Region of the Americas (AMR)	Longitudinal	Descriptive	Retrospective	Infants	Age, Birthplace, Birth Period, Birth outcome, Diagnosis, Geographic location	Not reported	4.22	Spina bifida	4 years	Regional Registry
Carol Bower[70]	Australia	Western Pacific Region (WPR)	Longitudinal	Descriptive	Retrospective	Pregnant women and children	Not reported	Not reported	13.8	Anencephaly Spina bifida	20 years	National Registry
Molla Taye[71]	Ethiopia	African Region (AFR)	Cross sectional	Descriptive	/	Children	Age, Diagnosis	76 201	80.2	Not reported	0.5 year	Patient Records
Jane N Githuku[72]	Kenya	African Region (AFR)	Longitudinal	Descriptive	Retrospective	Children	Age, Birth period, Geographic location	6 041	3.3	Spina bifida Encephalocele	5 years	Patient Records
Dagoberto Estevez-Ordonez[73]	Honduras	Region of the Americas (AMR)	Cross sectional	Descriptive	/	Newborns	Age, Birth period, Birth outcome	123 903	13	Spina bifida Anencephaly Encephalocele	5 years	Patient records, National Registries and Regional Registries
J Rankin[74]	United Kigndom	European Region (EUR)	Longitudinal	Descriptive	Retrospective	Newborns	Age, Birthplace, Birth	Not reported	1.2	Anencephaly Spina bifida Encephalocele	12 years	Regional Registry

							period, Diagnosis					
Keewan Kim[75]	USA	Region of the Americas (AMR)	Longitudinal	Descriptive	Retrospective	Newborns	Age, Geographic location, Birth Period, Birth outcome, Diagnosis period, Diagnosis	Not reported	4.73	Anencephaly Spina bifida Encephalocele	24 years	Regional Registry
Carol Bower[76]	Australia	Western Pacific Region (WPR)	Longitudinal	Descriptive	Retrospective	Newborns	Age, Birth period, Birthplace, Diagnosis	Not reported	14.1	Anencephaly Spina bifida Encephalocele	26 years	Regional Registry
Atsuo Kondo[77]	Japan	Western Pacific Region (WPR)	Longitudinal	Descriptive	Prospective	Post partum women and newborns	Age, Birth outcome, Birthplace, Birth period	Not reported	5.5	Spina bifida	1 year	Self-administered questionnaires
Amos Olufemi Adeleye[78]	Nigeria	African Region (AFR)	Longitudinal	Descriptive	Prospective	Children	Age, Diagnosis, Birth period, Birthplace	Not reported	33**	Cephalocele Spina bifida	1 year	Patient records and Questionnaires
N Kitisomprayoonkul[79]	Thailand	South-East Asian	Longitudinal	Descriptive	Retrospective	Pregnant women	Diagnosis period, Diagnosis	Not reported	6.6	Spina bifida Encephalocele	Not reported	Patient records and Questionnaires

		Region (SEAR)										
Mohammad Jafar Golalipour [80]	Iran	Eastern Mediterranean Region (EMR)	Cross sectional	Descriptive	/	Newborns	Age, Birthplace, Birth outcome, Diagnosis	49 534	28*	Anencephaly	7 years	Patient records
K Loncarek[81]	Croatia	European Region (EUR)	Longitudinal	Descriptive	Retrospective	Newborns	Age, Birthplace, Birth outcome, Birth weight	135 451	1.6*	Anencephaly	37 years	Patient records and Regional registry
Emilia Prospero[82]	Italy	European Region (EUR)	Cross sectional	Descriptive	/	Pregnant women and newborns	Age, Birth outcome, Birth period	Not reported	18.5*	Anencephaly Myelomeningocele	2 years	Patient records
Christopher Bismarck Eke[83]	Nigeria	African Region (AFR)	Longitudinal	Descriptive	Retrospective	Children	Age, Diagnosis	7 329	83.3*	Spina bifida Encephalocele Anencephaly	3 years	Patient records
Anne Klusmann[84]	Germany	European Region (EUR)	Longitudinal	Descriptive	Prospective	Newborns	Age, Birthplace, Birth outcome, Diagnosis	Not reported	6.8	Anencephaly Encephalocele Meningomyelocele	7 years	Patient record
Annamari Nikkilä[85]	Sweden	European Region (EUR)	Longitudinal	Descriptive	Retrospective	Newborns	Age, Geographic location, Birth period,	Not reported	1.5*	Spina bifida	30 years	National Registry, regional

							Birth outcome, Diagnosis					registry and patient records
Stephen J Monteith[86]	New Zealand	Western Pacific Region (WPR)	Longitudinal	Descriptive	Retrospective	Children	Admission period, Ethnicity, Age, Geographic location	Not reported	0.75*	Encephalocele	25 years	Patient record
T J Owen[87]	Australia	Western Pacific Region (WPR)	Longitudinal	Descriptive	Retrospective	Children	Age, Diagnosis, Birth outcome, Birth period, Diagnosis	Not reported	15.66*	Spina bifida Anencephaly Encephalocele	14 years	Regional Registry
Hashem Amini[88]	Sweden	European Region (EUR)	Longitudinal	Descriptive	Retrospective	Newborns and abortions	Age, Diagnosis, Birth outcome	Not reported	6.1*	Spina bifida	5 years	National registry
Abdul-Rauf Sayed[89]	South Africa	African Region (AFR)	Longitudinal	Descriptive	Retrospective	Newborns	Age, Birth outcome, Birthplace	Not reported	9.1*	Spina bifida Anencephaly	4 years	National and Regional registries
Dominic A Harris[90]	USA	Region of the Americas (AMR)	Longitudinal	Descriptive	Retrospective	Newborns	Age, Diagnosis	Not reported	1.9	Myelomeningocele	9 years	National registry

Nilgün Çaylan[91]	Turkey	European Region (EUR)	Longitudinal	Descriptive	Retrospective	Newborns	Age, Diagnosis, Birth period, Birthplace	7 736 309	27.5*	Anencephaly Encephalocele Spina bifida	5 years	National registry
Xiaohong Li[28]	China	Western Pacific Region (WPR)	Longitudinal	Descriptive	Retrospective	Newborns	Age, Birth period, Diagnosis, Geographic location	Not reported	14*	Anencephaly Spina bifida Encephalocele	2 years	National registy
Prajkta Bhide[92]	India	South-East Asian Region (SEAR)	Longitudinal	Descriptive	Prospective	Pregnant women, Newborns	Age, Geographic location	1 822	27.44	Not reported	2 years	Patient records
Abel Gedefaw[93]	Ethiopia	African Region (AFR)	Longitudinal	Descriptive	Prospective	Pregnant women, Newborns	Age, Geographic location, Birth outcome	Not reported	63.4*	Anencephaly Spina bifida Encephalocele	0.5 year	Patient records
Joël Zlotogora[94]	Israel	European Region (EUR)	Longitudinal	Descriptive	Retrospective	Pregnant women, Newborns	Age, Admission period, Diagnosis	Not reported	24.8	Anencephaly Spina bifida	5 years	National registry
J K Morris[95]	England and Wales	European Region (EUR)	Longitudinal	Descriptive	Retrospective	Pregnant women and newborns	Not reported	969	3*	Anencephaly Spina bifida Encephalocele	40 years	National Registry

Xingguang Zhang[96]	China	Western Pacific Region (WPR)	Cross sectional	Descriptive	/	Newborns, stillbirths and abortions	Age, Birth outcome, Birth period, Geographic location	976	20.1*	Anencephaly Spina Bifida Encephalocele	3 years	Patient records and self administered questionnaires
Donghua Xie[97]	China	Western Pacific Region (WPR)	Longitudinal	Descriptive	Retrospective	Newborns	Not reported	925 413	1.74*	Anencephaly Spina bifida Encephalocele	9 years	National registries
Karin M van der Pal-de Bruin[98]	The Netherlands	European Region (EUR)	Longitudinal	Descriptive	Retrospective	Newborns	Age, Diagnosis, Facility location	Not reported	1.59*	Not reported	10 years	National registries
Samanthi Abeywardana[99]	Australia	Western Pacific Region (WPR)	Longitudinal	Descriptive	Retrospective	Pregnant women, Newborns	Age, Diagnosis, Birth outcome	Not reported	5.51*	Anencephaly Spina bifida Encephalocele	7 years	National registries
Xingdi Yang[100]	China	Western Pacific Region (WPR)	Longitudinal	Descriptive	Retrospective	Newborns	Not reported	147 817	0.4*	Not reported	2 years	Regional registry
Peter Spazzapan[101]	Slovenia	European Region (EUR)	Longitudinal	Descriptive	Retrospective	Newborns	Age, Diagnosis, Birth period	Not reported	1*	Myelomeningocele	10 years	Patient records
J Rankin[102]	United Kingdom (UK)	European Region (EUR)	Longitudinal	Descriptive	Retrospective	Newborns	Age, Diagnosis,	839 521	69.6*	Not reported	8 years	National and Regional registries

							Birth outcome					
Boris Groisman[103]	Argentina	Region of the Americas (AMR)	Cross sectional	Descriptive	/	Newborns	Age, Birthplace, Diagnosis	Not reported	14.9*	Anencephaly Encephalocele Spina bifida	3 years	National registry
Helen Dolk[104]	Austria Belgium Croatia Denmark France Germany Ireland Italy Malta Netherlands Poland Switzerland United Kingdom	European Region (EUR)	Longitudinal	Descriptive	Retrospective	Newborns	Age, Birthplace, Birth period, Diagnosis	15 000 000	0.94*	Anencephaly Encephalocele Spina bifida	4 years	National registries
Hidetoshi Mezawa[105]	Japan	Western Pacific Region (WPR)	Longitudinal	Descriptive	Prospective	Pregnant women and newborns	Not reported	101 825	6.4*	Anencephaly Encephalocele Spinal bifida	3 years	Patient records

Cara T. Mai[106]	USA	Region of the Americas (AMR)	Longitudinal	Descriptive	Retrospective	Newborns	Not reported	Not reported	7.35	Anencephaly Encephalocele Spinal bifida	4 years	National registries
M N Noraihan[107]	Malaysia	Western Pacific Region (WPR)	Cross sectional	Descriptive	/	Newborns	Age, Birth period, Co morbidities, Diagnosis, Birth outcome	34 109	12.4*	Anencephaly Spina bifida Meningocele Myelomeningocele	1 year	Patient records
Daniel Mumpe-Mwanja[108]	Uganda	African Region (AFR)	Cross sectional	Descriptive	/	Postpartum and newborns	Age, Parity, Co morbidities, Birth outcome	Not reported	10.3	Not reported	2 years	Patient records

* Studies with reported prevalence per 10 000 births,

** Studies with prevalence not reported but number of cases were reported

Supplementary 2: Reported Gaps and Disparities to Care Delivery

First Author	WHO Region	Healthcare facility	Geospatial Mapping of Services	Geospatial Analysis of Service Location and Patient Densities	Report on Barriers to Services	Reported Gaps and Disparities in Care Delivery	Factors Contributing to Gaps and Disparities	Reported Interventions to Address the Gaps and Disparities	Reported Quality of Care Delivered	Reported Shortages in Skilled Providers	Reported Impact of Cost on Access to Care
Birhane Alem Berihu	African Region (AFR)	Mekelle and Ayder hospitals; Lemelem Karl hospital; St. Mary hospital; Sihul hospital; Adigrat and Wukro hospitals and Kahsay Abera Hospital.	ND	ND	NP	NP	NP	NP	NP	NP	NP
Atsuo Kondo	Western Pacific Region (WPR)	Hospitals affiliated with the Japan Association of Obstetricians and Gynecologists (JAOG)	ND	ND	NP	NP	NP	NP	NP	NP	NP

Ilham M Omer	African Region (AFR)	NICU in Soba University and Omdurman Maternity hospitals	ND	ND	NP	NP	NP	NP	NP	NP	NP
Soressa Abebe Geneti	African Region (AFR)	Jimma Medical Centre, Shanan Gibe hospital, Limmu Genet hospital, and Agaro hospital; Mattu Karl hospital and Nekemte hospital.	ND	ND	NP	NP	NP	NP	NP	NP	NP
Mark A. Canfield	Region of the Americas (AMR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
R McDonnell	European Region (EUR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP

Nóra Szabó	European Region (EUR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
Mikyong Shin	Region of the Americas (AMR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
E I Krzesinski	African Region (AFR)	Tygerberg Academic Hospital	ND	ND	NP	NP	NP	NP	NP	NP	NP
Jie Liu	Western Pacific Region (WPR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
Shiva Bhandari	South-East Asian Region (SEAR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
María de la Paz Barboza-Argüello	Region of the Americas (AMR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP

M J Golalipour	Eastern Mediterranean Region (EMR)	Dezyani teaching hospital	ND	ND	NP	NP	NP	NP	NP	NP	NP
Kaouther Nasri	African Region (AFR)	Center for Maternity and Neonatology Wassila Bourguiba	ND	ND	NP	NP	NP	NP	NP	NP	NP
Dania María Pastora Bucardo	Region of the Americas (AMR)	N/A	ND	ND	NP	NP	NP	NP	NP	NP	NP
R. McDonnell	European Region (EUR)	National Paediatric Neurosurgical Centre	ND	ND	NP	NP	NP	NP	NP	NP	NP
B. Mahadevan	South-East Asian Region (SEAR)	Department of Pediatrics, JIPMER, Pondicherry	ND	ND	NP	NP	NP	NP	NP	NP	NP
Nem-Yun Boo	Western Pacific	/	ND	ND	NP	NP	NP	NP	NP	NP	NP

	Region (WPR)										
R E Stevenson	Region of the Americas (AMR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
Hayelom Kebede Mekonen	African Region (AFR)	Ayder Comprehensive Specialized Hospital Lemelem Karl Hospital St. Mary Hospital Sihul Hospital Adigrat Hospital Alamata Hospital	ND	ND	NP	NP	NP	NP	NP	NP	NP
S T Onrat	European Region (EUR)	Department of Pediatrics, Zubeyde Hanım Hospital for Children's and Women's Health	ND	ND	NP	NP	NP	NP	NP	NP	NP

Philippe De Wals	Region of the Americas (AMR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
Jelena G Petrova	European Region (EUR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
Eric M Delmelle	Region of the Americas (AMR)	/	Done using Geographic Information Systems	The average one-way travel time for families during an infant's first year of life was approximately 45 minutes, covering a distance of around 34 miles.	The study uncovered various barriers, such as geographical constraints, that hindered families from accessing healthcare services. Factors like longer travel distances and transportation availability contributed to these barriers.	NP	Geographic location, availability of specialized hospitals, transportation options, and socioeconomic status	NP	NP	NP	NP

Robert E Meyer	Region of the Americas (AMR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
Carol Bower	Western Pacific Region (WPR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
Molla Taye	African Region (AFR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
Jane N Githuku	African Region (AFR)	Pediatric neurosurgical center at AIC Kijabe Hospital in Kenya	ND	ND	NP	NP	NP	NP	NP	NP	NP
Dagoberto Estevez-Ordonez	Region of the Americas (AMR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
J Rankin	European Region (EUR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP

Keewan Kim	Region of the Americas (AMR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
Carol Bower	Western Pacific Region (WPR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
Atsuo Kondo	Western Pacific Region (WPR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
Amos Olufemi Adeleye	African Region (AFR)	Neurosurgical Unit in Ikeja	ND	ND	NP	NP	NP	NP	NP	NP	NP
N Kitisomprayoonkul	South-East Asian Region (SEAR)	Nakorn Chiang Mai Hospital in Chiang Mai	ND	ND	NP	NP	NP	NP	NP	NP	NP
Mohammad Jafar Golalipour	Eastern Mediterranean Region (EMR)	Dezyani Hospital in Gorgan, Northern Iran	ND	ND	NP	NP	NP	NP	NP	NP	NP

K Loncarek	European Region (EUR)	Medical Faculty of Rijeka and Institute of Public Health in Rijeka	ND	ND	NP	NP	NP	NP	NP	NP	NP
Emilia Prospero	European Region (EUR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
Christopher Bismarck Eke	African Region (AFR)	University of Nigeria Teaching Hospital (UNTH), Enugu	ND	ND	NP	NP	NP	NP	NP	NP	NP
Anne Klusmann	European Region (EUR)	Children's Hospital of Heinrich Heine University in Dusseldorf, Germany.	ND	ND	NP	NP	NP	NP	NP	NP	NP
Annamari Nikkilä	European Region (EUR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP

Stephen J Monteith	Western Pacific Region (WPR)	Auckland Hospital and Starship Children's Hospital in New Zealand	ND	ND	NP	NP	NP	NP	NP	NP	NP
T J Owen	Western Pacific Region (WPR)	Perinatal Data Collection Unit in the Public Health Division of the Department of Human Services in Victoria, Australia	ND	ND	NP	NP	NP	NP	NP	NP	NP
Hashem Amini	European Region (EUR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
Abdul-Rauf Sayed	African Region (AFR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
Dominic A Harris	Region of the	/	ND	ND	NP	NP	NP	NP	NP	NP	NP

	Americas (AMR)										
Nilgün Çaylan	European Region (EUR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
Xiaohong Li	Western Pacific Region (WPR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
Prajkta Bhide	South-East Asian Region (SEAR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
Abel Gedefaw	African Region (AFR)	Addis Ababa University Teaching Hospitals	ND	ND	NP	NP	NP	NP	NP	NP	NP
Joël Zlotogora	European Region (EUR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
J K Morris	European Region (EUR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP

Xingguang Zhang	Western Pacific Region (WPR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
Donghua Xie	Western Pacific Region (WPR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
Karin M van der Pal-de Bruin	European Region (EUR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
Samanthi Abeywardana	Western Pacific Region (WPR	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
Xingdi Yang	Western Pacific Region (WPR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
Peter Spazzapan	European Region (EUR)	Unit of Pediatric Neurosurgery, Department of Neurosurgery, University	ND	ND	NP	NP	NP	NP	NP	NP	NP

		Medical Centre Ljubljana, Ljubljana, Slovenia									
J Rankin	European Region (EUR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
Boris Groisman	Region of the Americas (AMR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
Helen Dolk	European Region (EUR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
Hidetoshi Mezawa	Western Pacific Region (WPR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP
Cara T. Mai	Region of the Americas (AMR)	/	ND	ND	NP	NP	NP	NP	NP	NP	NP

M N Noraihan	Western Pacific Region (WPR)	Maternity Hospital Kuala Lumpur (MHKL) in Malaysia	ND	ND	NP	NP	NP	NP	NP	NP	NP
Daniel Mumpe-Mwanja	African Region (AFR)	Mulago National Referral Hospital, Mengo Hospital, St. Francis Hospital Nsambya, and Uganda Martyrs Hospital Lubaga	ND	ND	NP	NP	NP	NP	NP	NP	NP

ND: Not done, NP: Not Present

Supplementary 3: Risk of Bias Analysis Using Critical Appraisal Tool and Implications of Studies Findings for Accessibility and Availability of Physiotherapeutic and Neurosurgical Services for Babies Born with NTDs

First Author	WHO Region	Score on Critical Appraisal Tool	Implications of Findings for Future Research and Policy Development for Accessibility and Availability of Physiotherapeutic and Neurosurgical Services
Birhane Alem Berihu	African Region (AFR)	5 (Moderate risk of bias)	1. Future Research: Long-term studies inform NTD outcomes, guiding policies. 2. Health System Strengthening: Improve NTD detection, management, and care through health system strengthening.
Atsuo Kondo	Western Pacific Region (WPR)	5 (Moderate risk of bias)	1. Future Research: Investigate NTD prevalence disparities, and innovative prevention approaches. 2. Policy Development: Advocate for equitable specialized care access, and improved prenatal screening.
Ilham M Omer	African Region (AFR)	5 (Moderate risk of bias)	1. Future research: Examine high prevalence factors, conduct long-term studies. 2. Policy development: Emphasize healthcare infrastructure improvement. 3. Healthcare planning: Prioritize comprehensive care, parent support, enhanced referral systems.
Soressa Abebe Geneti	African Region (AFR)	5 (Moderate risk of bias)	1. Specialized Training: Train healthcare providers in NTD diagnosis and management. 2. Regional NTD Care Centers: Establish centralized regional centers with expertise and boost NTD care capacity in selected hospitals. 3. Geospatial Mapping: Identify care access gaps for strategic facility placement. 4. Service Barriers Research: Investigate access barriers for targeted interventions 5. Government Support: Allocate resources to NTD care and prevention. 6. Monitoring and Evaluation: Regularly assess intervention effectiveness for data-driven decisions.
Mark A. Canfield	Region of the Americas (AMR)	4 (Moderate risk of bias)	1. Future Research: a. Conduct longitudinal studies to track NTD prevalence trends and risk factors over time. b. Explore environmental factors contributing to geographic NTD variation. c. Investigate genetic factors in NTDs, especially among specific ethnic groups. d. Study socioeconomic determinants, education, and healthcare access in NTD occurrence. 2. Policy Development: a. Enhance prenatal and healthcare access, especially for vulnerable populations with lower education levels. b. Address ethnic disparities through equitable healthcare access and support services. 3. Public Awareness and Education: a. Engage border-region communities to address cultural healthcare factors.

R McDonnell	European Region (EUR)	4 (Moderate risk of bias)	1. Findings: Emphasize the need for further research and policy development. 2. Goals: Address persisting NTD rates and enhance preventive strategies.
Nóra Szabó	European Region (EUR)	5 (Moderate risk of bias)	1. Future research: Explore contributing factors. 2. Policymakers: Use insights for efficient resource allocation and program strengthening. 3. Awareness campaigns: Crucial for emphasizing early intervention's importance..
Mikyong Shin	Region of the Americas (AMR)	4 (Moderate risk of bias)	1. Resource Allocation: Use prevalence data for targeted resource allocation to physiotherapeutic and neurosurgical services. 2. Targeted Interventions: Develop interventions for specific populations, addressing racial/ethnic disparities. 3. Equitable Service Delivery: Promote equitable access to services across regions and communities. 4. Interdisciplinary Collaboration: Encourage collaboration among healthcare providers for comprehensive spina bifida care. 5. Health Insurance Coverage: Advocate for insurance coverage of relevant services for affordability.
E I Krzesinski	African Region (AFR)	4 (Moderate risk of bias)	1. Future Research: Investigate rural prenatal detection rate disparities. 2. Policy Development: Enhance prenatal ultrasound and informed TOP decisions. 3. Neurosurgical Services Accessibility: Expand services in high NTD prevalence tertiary hospitals. 4. Physiotherapeutic Services Availability: Improve rehab access, especially in high-prevalence regions. 5. Interdisciplinary Collaboration: Encourage teamwork for integrated care. 6. Equitable Service Distribution: Address urban-rural care disparities.
Jie Liu	Western Pacific Region (WPR)	4 (Moderate risk of bias)	1. Future Research: a. Socioeconomic Factors: Explore impact in deprived areas. b. NTD Subtypes and Outcomes: Develop specialized care pathways. 2. Policy Development a. Specialized Facilities: Establish centers with targeted services. b. Telehealth: Implement remote consultations for underserved areas. c. Financial Support: Aid affected families d. Multidisciplinary Approach: Foster cooperation among professionals and policymakers.
Shiva Bhandari	South-East Asian Region (SEAR)	4 (Moderate risk of bias)	1. Further Research: Understand NTD factors and outcomes. 2. Evaluate Services: Assess quality and expertise. 3. Capacity Building: Train healthcare for NTDs. 4. Early Detection: Screen for timely intervention. 5. Integration: Integrate within healthcare. 6. Health Insurance: Cover NTD care. 7. Rehabilitation: Research intervention effectiveness.

María de la Paz Barboza-Argüello	Region of the Americas (AMR)	4 (Moderate risk of bias)	1. Findings Implications: a. Examine folic acid fortification's long-term impact on NTD prevalence and service demand. b. Enhance specialized care access in underserved areas. c. Assess cost-effectiveness for resource allocation. d. Sustain fortification to reduce NTD prevalence and ease healthcare burden. 2. Policy Development: a. Expand fortification to reduce NTD prevalence. b. Integrate birth defects data for better resource allocation. c. Prioritize equitable access, especially in underserved regions. d. Collaborate for evidence-based policies improving service accessibility.
M J Golalipour	Eastern Mediterranean Region (EMR)	4 (Moderate risk of bias)	1. Prevalence findings affect future research and policy for NTD services. 2. Policymakers should target interventions for demographic disparities. 3. Improve healthcare in high-prevalence areas. 4. Prioritize early detection, especially for older mothers. 5. Prepare for peak prevalence periods. 6. Promote research on prevention strategies to reduce future NTDs.
Kaouther Nasri	African Region (AFR)	4 (Moderate risk of bias)	1. Long-Term Follow-Up Studies: Conduct long-term follow-up studies on NTD patients to assess intervention effectiveness and refine treatment protocols. 2. Telemedicine and Tele-Rehabilitation: Integrate telemedicine and tele-rehabilitation services for remote care, enhancing access to expert consultations and guidance. 3. Awareness Campaigns: Implement public awareness campaigns emphasizing the importance of early prenatal care and folic acid supplementation to reduce NTD prevalence and empower informed health decisions. 4. Health Insurance Coverage: Ensure health insurance covers NTD-related services, improving affordability and access to treatment. 5. Multi-Disciplinary Care Teams: Promote collaboration among healthcare providers, including physiotherapists, neurosurgeons, and pediatric specialists, to optimize patient care through coordinated treatment plans. 6. Training and Capacity Building: Invest in healthcare professional training for NTD management through educational programs and workshops to enhance skills. 7. Research Funding: Increase funding for NTD research to support innovation in physiotherapy and neurosurgery, ultimately improving patient outcomes and quality of life.
Dania María Pastora Bucardo	Region of the Americas (AMR)	4 (Moderate risk of bias)	1. Future Research: a. Long-term Outcomes: Assess NTD individuals' quality of life and evolving healthcare needs. 2. Policy Development: a. Capacity Building: Enhance healthcare facilities and provider readiness for NTD services

			b. Regional Centers: Establish specialized hubs for centralized NTD care. c. Support Programs: Develop family support for comprehensive care. 3. Collaboration and Partnerships: a. Public-Private Partnerships: Improve resource allocation and service quality. b. International Collaboration: Share best practices to advance global NTD care.
R. McDonnell	European Region (EUR)	4 (Moderate risk of bias)	1. Further Research: Investigate factors driving increasing NTD prevalence. 2. NTD Prevalence and Impact: a. Assess long-term NTD effects on individuals and families. b. Examine economic and social burdens for resource allocation. 3. Improving Access: Prioritize physiotherapeutic and neurosurgical service access, especially in high-prevalence areas. 4. Interdisciplinary Care: a. Integrate healthcare disciplines for comprehensive NTD care, enhancing quality and outcomes.
B. Mahadevan	South-East Asian Region (SEAR)	4 (Moderate risk of bias)	1. Perform long-term follow-up studies on infants with NTDs to assess outcomes and quality of life. 2. Develop policies to improve antenatal and maternal healthcare access, especially for “unbooked” mothers. 3. Identify geographic variations in NTD prevalence for targeted resource allocation and services. 4. Foster multidisciplinary collaboration among healthcare professionals for holistic NTD care.
Nem-Yun Boo	Western Pacific Region (WPR)	4 (Moderate risk of bias)	1. Risk Factors Study: Focus on genetic, environmental, and socio-economic NTD risk factors for targeted prevention and early interventions. 2. Health Services Research: Assess physiotherapeutic and neurosurgical service availability, access, and quality across Malaysian regions for policy guidance. 3. Policy Development: Inform policies enhancing service accessibility through funding, referral networks, and professional capacity building. 4. Public Awareness: Prioritize NTD awareness and education for early detection and care access.
R E Stevenson	Region of the Americas (AMR)	4 (Moderate risk of bias)	1. Research: Encourage further research to study folic acid's impact on different NTD types and long-term effects on affected individuals requiring physiotherapeutic and neurosurgical services. 2. Policy Development: Utilize study findings for policies promoting periconceptional folic acid supplementation awareness and enhancing accessibility for women of childbearing age. 3. Service Planning: Inform resource allocation for physiotherapeutic and neurosurgical services considering potential changes in demand post-decline in NTD prevalence, optimizing service distribution for continued access.
Hayelom Kebede Mekonen	African Region (AFR)	4 (Moderate risk of bias)	1. Research: Explore factors behind high NTD prevalence in Tigray for targeted prevention strategies. 2. Research: Assess effectiveness of folic acid programs in Ethiopia for improvement. 3. Policy Development: Increase accessibility of physiotherapeutic and neurosurgical services for NTD-infants. 4. Policy Development: Enhance public awareness of prenatal care, folic acid, and early screening through community-based education programs.

S T Onrat	European Region (EUR)	4 (Moderate risk of bias)	1. Research Priorities: Investigate factors behind increased NTD incidence, including genetics, environment, and nutrition. 2. Policy Implications: Use prevalence data to evaluate and expand physiotherapeutic and neurosurgical services. 3. Healthcare Training: Develop programs to train healthcare providers in NTD-related care. 4. Support Programs: Establish comprehensive support and awareness initiatives for affected individuals and families, emphasizing preventive measures like prenatal folic acid supplementation.
Philippe De Wals	Region of the Americas (AMR)	3 (Low risk of bias)	1. Research Focus: Study highlights folic acid fortification's potential in reducing NTDs. 2. Research Opportunities: Investigate long-term effects and cost-effectiveness of fortification. 3. Policy Implications: Support continued fortification policies in Canada and similar NTD-affected countries. 4. Resource Allocation: Use findings for more efficient resource allocation for physiotherapeutic and neurosurgical services. 5. Service Accessibility: Explore ways to improve access to services, considering regional disparities and barriers.
Jelena G Petrova	European Region (EUR)	4 (Moderate risk of bias)	1. Research Focus: Study's implications for understanding NTD prevalence disparities. 2. Policy Development: Emphasize accessibility of physiotherapeutic and neurosurgical services. 3. Targeted Interventions: Create specialized clinics and allocate resources for timely care. 4. Evidence-Based Policy: Use study insights to develop strategies to reduce NTD burden and improve affected individuals' quality of life.
Eric M Delmelle	Region of the Americas (AMR)	4 (Moderate risk of bias)	1. Research Implications: Study's results highlight disparities in service access. 2. Research Focus: Investigate factors behind geographical variations in access to care. 3. Policy Development: Use findings for interventions addressing travel barriers, transportation, and equitable SB care access.
Robert E Meyer	Region of the Americas (AMR)	4 (Moderate risk of bias)	1. Accessibility and Availability of Services: a. Use findings for future policy development on physiotherapeutic and neurosurgical services. b. Anticipate service demands with changing spina bifida prevalence. c. Ensure equitable service distribution and accessibility regardless of socioeconomic status. 2. Targeted Interventions: a. Explore factors behind differential prevalence among demographic groups. b. Guide policy development with insights into disadvantaged populations. c. Tailor educational programs and improve preventive measure access. 3. Long-Term Trends and Services Planning: a. Extend research beyond 1999 to assess long-term spina bifida prevalence trends. b. Plan for sustained decline and changing specialized service demand. c. Allocate resources based on long-term trends and sustainability.
Carol Bower	Western Pacific Region (WPR)	4 (Moderate risk of bias)	1. Research Shift: Focus research on other disorders as NTD cases decrease. 2. Resource Focus: Allocate resources for evolving neurosurgical and physiotherapy needs. 3. Surveillance: Continuously monitor to ensure NTD reduction continues. 4. Health Infrastructure: Adapt robust systems to changing health demands.

Molla Taye	African Region (AFR)	4 (Moderate risk of bias)	1. Research Focus: Target access barriers to physiotherapeutic and neurosurgical services. 2. Policy Recommendations: Promote holistic care, enhance training, integrate services, raise awareness, allocate resources, and foster collaborations. 3. Goal: Improve care and outcomes for children with congenital anomalies.
Jane N Githuku	African Region (AFR)	4 (Moderate risk of bias)	1. Nationwide Surveillance: Implement a national NTD surveillance system for accurate prevalence and regional insights, guiding resource allocation, policies, and targeted interventions. 2. Equitable Access: Explore reasons for prevalence variations between provinces to inform policies ensuring fair access across regions, considering healthcare infrastructure and awareness. 3. Awareness and Education: Prioritize NTD awareness through public education, healthcare provider training, and preventive measures like folic acid supplementation. 4. Capacity Building: Strengthen capacity in existing facilities for NTD care, including professional training, facility improvement, and local provider collaboration.
Dagoberto Estevez-Ordonez	Region of the Americas (AMR)	5 (Moderate risk of bias)	1. Research Implications: Study findings impact research and policy for CNS malformation care, especially NTDs. 2. Regional Disparities: Investigate factors behind regional prevalence differences, including health literacy, folic acid awareness, prenatal care, and socio-economic conditions. 3. Policy Development: Strengthen policies for physiotherapeutic and neurosurgical service access through prenatal care improvement, folic acid promotion, and equitable service provision. 4. Geospatial Mapping: Use prevalence and service distribution mapping to identify high-burden areas and service gaps. 5. Targeted Interventions: Design interventions to address access disparities and enhance CNS malformation care management and prevention.
J Rankin	European Region (EUR)	4 (Moderate risk of bias)	1. Service Planning: Research to align services with evolving patient needs. 2. Outcome Assessment: Evaluate long-term outcomes for service improvement. 3. Equitable Access: Ensure access regardless of location or income. 4. Public Awareness: Promote early diagnosis and service awareness. 5. Collaboration: Encourage interdisciplinary care. 6. Capacity Building: Support healthcare professional training.
Keewan Kim	Region of the Americas (AMR)	2 (Low risk of bias)	1. Research Implications: Study impacts research and policy for physiotherapy and neurosurgical services. 2. Trend Understanding: Investigate factors behind changing birth defect prevalence, including environmental and genetic influences. 3. Policy Development: Formulate strategies for better service access, especially for NTD-affected populations. 4. Resource Allocation: Increase resources, healthcare professional training, and equitable service distribution. 5. Evidence-Based Policies: Emphasize evidence-based policies for children with NTDs and related health services.
Carol Bower	Western Pacific Region (WPR)	4 (Moderate risk of bias)	1. Targeted Services for High-Risk Groups: Focus on understanding barriers faced by Aboriginal populations in accessing services and develop tailored interventions. 2. Long-Term Impact Assessment: Assess how reduced NTD prevalence affects demand, quality, and accessibility of physiotherapeutic and neurosurgical services.

			3. Equitable Service Distribution: Ensure regions with historically high NTD prevalence, like Aboriginal communities, have adequate access to specialized care. 4. Healthcare Workforce Preparation: Prepare healthcare workforce for changing service needs as NTD prevalence decreases through training and planning.
Atsuo Kondo	Western Pacific Region (WPR)	4 (Moderate risk of bias)	1. Research: Investigate risk factors like anti-epileptic drugs and spina bifida connections, and explore low birth weight's impact and interventions. 2. Policy: Consider mandatory folic acid fortification due to stable prevalence. Expand physiotherapeutic and neurosurgical services, particularly in high-risk regions. Implement awareness campaigns for timely interventions.
Amos Olufemi Adeleye	African Region (AFR)	4 (Moderate risk of bias)	1. Research Implications: Highlight the need for comprehensive research on CNS congenital anomalies, especially in resource-limited settings. 2. Policy Advocacy: Use findings to advocate for increased funding and resource allocation for neurosurgical and physiotherapeutic services. 3. Policy Development: Focus on awareness campaigns, medical education improvement, and collaborations to enhance service accessibility.
N Kitisomprayoonkul	South-East Asian Region (SEAR)	4 (Moderate Risk of Bias)	1. Research: Explore Thai context for needs and outcomes. 2. Policy: Develop integrated care, resource allocation, and awareness strategies. 3. Resource Allocation: Align resources with specialized care needs. 4. Awareness/Education: Promote antenatal screening and support.
Mohammad Jafar Golalipour	Eastern Mediterranean Region (EMR)	4 (Moderate risk of bias)	1. Future Research: Investigate maternal age and consanguinity as potential risk factors for NTDs, exploring genetic and environmental influences. 2. Policy Development: Emphasize early intervention, culturally sensitive care, and resource alignment to improve service accessibility.
K Loncarek	European Region (EUR)	5 (Moderate Risk of Bias)	1. Anencephaly Rates: Inform prevention, management, and treatment planning. 2. Associated Malformations: Highlight complex care needs, warranting multi-disciplinary support. 3. Gender Distribution: Suggest potential biological factors in NTDs. 4. Resource Allocation: Indirectly guide neurosurgical and physiotherapy service accessibility based on demand.
Emilia Prospero	European Region (EUR)	5 (Moderate Risk of Bias)	1. Research: Investigate environmental triggers like water quality links for anencephaly cases. 2. Policy: Enhance NTD care policies, improve physiotherapy and neurosurgery access, and promote collaborations for early intervention and holistic care.
Christopher Bismarck Eke	African Region (AFR)	4 (Moderate risk of bias)	1. Research: Assess geographic distribution of CNS anomalies to identify high-prevalence regions for resource allocation and healthcare planning. 2. Policy Development: Enhance accessibility and availability of physiotherapeutic and neurosurgical services, especially in high-prevalence areas. 3. Healthcare Services: Integrate genetic counseling and prenatal screening to provide families with risk information and treatment options for CNS anomalies.

Anne Klusmann	European Region (EUR)	4 (Moderate Risk of Bias)	1. Research Implications: a. Study folic acid supplementation's impact on NTDs requiring physiotherapy and neurosurgery. b. Investigate if decreasing NTD incidence reduces service demand. c. Explore the link between folic acid and NTD severity. 2. Policy Implications: a. Enhance Awareness: Increase public folic acid awareness through targeted campaigns. b. Collaborative Care: Promote care collaboration for infants with NTDs, emphasizing early intervention.
Annamari Nikkilä	European Region (EUR)	5 (Moderate Risk of Bias)	1. Research Implications: a. Highlight the effectiveness of prenatal diagnosis and ultrasound screening in reducing spina bifida prevalence. b. Emphasize the need for ongoing research to enhance diagnostic techniques and accessibility. c. Suggest exploring socioeconomic factors, healthcare access, and public health campaigns in further research. 2. Policy Implications: a. Promote routine prenatal screenings and improve healthcare infrastructure. b. Address regional disparities in NTD prevalence. c. Enhance accessibility and availability of physiotherapeutic and neurosurgical services for comprehensive care.
Stephen J Monteith	Western Pacific Region (WPR)	4 (Moderate risk of bias)	1. Physiotherapy Role: Explore physiotherapy's role in addressing motor and developmental challenges related to encephalocoele. 2. Neurosurgical Access: Improve access to neurosurgical services, emphasizing timeliness and comprehensive care. 3. Equitable Healthcare: Address disparities among ethnic groups by targeting equitable access in policy efforts. 4. Long-Term Outcomes: Research long-term outcomes to inform ongoing care policies.
T J Owen	Western Pacific Region (WPR)	4 (Moderate risk of bias)	1. Research Implications: a. Understand specific requirements and challenges of NTD patients in accessing services. 2. Policy Development: a. Enhance accessibility and availability of physiotherapy and neurosurgery services for NTD individuals to improve care quality.
Hashem Amini	European Region (EUR)	5 (Moderate Risk of Bias)	1. Research Direction: Investigate improved ascertainment rates' impact on long-term health outcomes for spina bifida and cleft lip/palate individuals. Assess intervention and rehabilitation effectiveness. 2. Policy Development: Inform evidence-based policies to enhance specialized service accessibility and availability. Prioritize timely access to neurosurgery and physiotherapy for NTD individuals, improving outcomes.
Abdul-Rauf Sayed	African Region (AFR)	5 (Moderate Risk of Bias)	1. Effective Folic Acid Fortification: Demonstrates importance of evidence-based health policies. 2. Lessons for Physiotherapy and Neurosurgery: Research inspired by study may lead to innovative service accessibility interventions. 3. Population-Wide Impact: Shows how broad measures can improve public health, influencing healthcare decisions and resource allocation.

Dominic A Harris	Region of the Americas (AMR)	4 (Moderate Risk of Bias)	1. Research Guidance: Identify barriers, disparities, and innovative approaches to improve service accessibility and availability. 2. Policy Influence: Use findings on demographics, hospital practices, and costs to enhance access to physiotherapy and neurosurgery services for myelomeningocele and other neurosurgical patients.
Nilgün Çaylan	European Region (EUR)	4 (Moderate risk of bias)	1. Research Focus: Study socio-economic factors' link to NTD prevalence for targeted interventions. 2. Folic Acid Programs: Assess the impact of folic acid fortification on NTD prevalence. 3. Maternal Health and Environment: Investigate their role in NTD occurrence. 4. Policy Priority: Improve healthcare accessibility, especially in high-prevalence regions. 5. Prevention and Awareness: Strengthen preventive strategies and public health campaigns, like promoting folic acid intake, to reduce NTDs.
Xiaohong Li	Western Pacific Region (WPR)	4 (Moderate risk of bias)	1. Research Focus: Investigate factors causing NTD prevalence disparities, including environmental, socioeconomic, and healthcare access factors. 2. Service Enhancement: Guide policy for better physiotherapeutic and neurosurgical service access through infrastructure investment, workforce training, and resource allocation. 3. Targeted Policies: Tailor policies to regions with higher prevalence, ensuring resources for prevention, early diagnosis, and specialized treatment. 4. Health Education: Implement health education campaigns to raise NTD awareness and promote early intervention. 5. Collaboration: Encourage collaboration among healthcare providers, public health agencies, and stakeholders for coordinated, comprehensive NTD patient care.
Prajkta Bhide	South-East Asian Region (SEAR)	5 (Moderate Risk of Bias)	1. Targeted Policy: Address preventable conditions like anencephaly and treatable anomalies like talipes. 2. Research: Assess preconception folate supplementation programs for NTD reduction. 3. Low-Cost Interventions: Study cost-effective talipes interventions. 4. Service Integration: Prioritize integrating physiotherapeutic and neurosurgical services for accessibility. 5. Collaboration: Foster healthcare collaboration for comprehensive birth defect prevention and management.
Abel Gedefaw	African Region (AFR)	5 (Moderate Risk of Bias)	1. Research Focus: a. Assess service capacity and availability in Ethiopia. b. Evaluate healthcare professionals, facilities, and equipment. c. Explore preventive strategy effectiveness and implementation barriers. 2. Policy Emphasis: a. Address service accessibility through policies. b. Consider specialized units in healthcare facilities. c. Enhance early detection and prenatal intervention. d. Launch awareness and education campaigns. 3. Resource Allocation: a. Allocate resources for professional training. b. Invest in medical infrastructure and equipment.

Joël Zlotogora	European Region (EUR)	4 (Moderate Risk of Bias)	1. Research Focus: Assess preventive measures' impact on healthcare service demand. 2. Policy Priority: Promote preventive strategies and ensure ongoing healthcare accessibility for NTD-affected individuals. 3. Resource Allocation: Prioritize resource distribution and equitable access.
J K Morris	European Region (EUR)	5 (Moderate Risk of Bias)	1. Research Focus: a. Enhance screening methods. b. Understand long-term healthcare needs c. Assess service distribution for accessibility. 2. Policy Development: a. Implement equitable healthcare infrastructure. b. Promote early intervention through awareness campaigns. c. Formulate comprehensive long-term care policies for NTD-affected individuals.
Xingguang Zhang	Western Pacific Region (WPR)	5 (Moderate Risk of Bias)	1. Future research priorities: a. Explore specific environmental NTD factors. b. Investigate genetic and familial aspects. 2. Policy considerations: a. Expand rural prenatal care access. b. Promote maternal health education. c. Ensure physiotherapeutic and neurosurgical service availability. d. Target interventions based on identified risk factors.
Donghua Xie	Western Pacific Region (WPR)	5 (Moderate Risk of Bias)	1. Research Focus: Explore NTD prevalence and care needs within the broader birth defect population. 2. Policy Development: Use findings as an indicator for service demand. a. Improve accessibility, affordability, and service quality. b. Focus on urban areas and older mothers. c. Address birth defect and NTD challenges in Hunan Province.
Karin M van der Pal-de Bruin	European Region (EUR)	5 (Moderate Risk of Bias)	1. Research should address data limitations and enhance tracking methods. 2. Policy should promote folic acid use and evaluate service accessibility
Samanthi Abeywardana	Western Pacific Region (WPR	5 (Moderate Risk of Bias)	1. Research Focus: Study barriers to healthcare access among high-risk groups. 2. Policy Development: Improve access to NTD-related services, especially in remote areas. 3. Ongoing Monitoring: Continuously assess policy impact on NTD prevalence and healthcare access.

Xingdi Yang	Western Pacific Region (WPR)	5 (Moderate Risk of Bias)	1. Early Detection: Prioritize early detection and intervention in research. 2. Education and Awareness: Promote prenatal care awareness for early diagnosis in policies. 3. Telemedicine and Clinics: Consider telemedicine and specialized clinics in remote areas. 4. Research Collaboration: Foster collaboration among researchers, providers, and policymakers. 5. Policy Frameworks: Develop comprehensive policies for equitable access to specialized services.
Peter Spazzapan	European Region (EUR)	5 (Moderate Risk of Bias)	1. Long-Term Outcomes: Assess patients' education, vocational success, and adult medical needs. 2. Resource Allocation: Use prevalence data for accessible care resource allocation. 3. Standardized Protocols: Develop effective, consistent care protocols. 4. Patient Support: Explore holistic support for patients and families. 5. Cost-Benefit Analysis: Analyze resource allocation cost-benefit for decisions.
J Rankin	European Region (EUR)	5 (Moderate Risk of Bias)	1. Future Research: a. Study NTD-specific prevalence and regional trends. b. Investigate factors behind regional disparities. c. Assess healthcare policy changes' impact on NTD prevalence. 2. Policy Development: a. Allocate resources effectively based on prevalence. b. Enhance early detection for better outcomes. c. Implement screening programs, especially in high-prevalence regions.
Boris Groisman	Region of the Americas (AMR)	5 (Moderate Risk of Bias)	1. Targeted Interventions: Allocate resources to high NTD prevalence regions. 2. Health Infrastructure: Invest in specialized facilities. 3. Data Integration: Integrate healthcare data for better anomaly understanding and accessibility insights.
Helen Dolk	European Region (EUR)	5 (Moderate Risk of Bias)	1. Research Focus: Investigate factors influencing service accessibility in European countries. 2. Policy Development: Use findings to enhance service access, address barriers, ensure equitable regional access, and raise awareness for congenital anomalies, including NTDs.
Hidetoshi Mezawa	Western Pacific Region (WPR)	5 (Moderate Risk of Bias)	1. Service Accessibility: Urgency in improving access to physiotherapeutic and neurosurgical services. 2. Research Focus: Evaluate intervention effectiveness and develop policies for reducing the impact of congenital anomalies. 3. Policy Considerations: Policymakers should prioritize enhancing healthcare services for children with congenital anomalies.
Cara T. Mai	Region of the Americas (AMR)	5 (Moderate Risk of Bias)	1. Urgent Accessibility Needs: Emphasis on addressing accessibility and availability in healthcare services. 2. Service Expansion: Expand physiotherapeutic and neurosurgical services to meet growing demand. 3. Research Focus: Identify barriers and develop targeted policies for improved service delivery.

M N Noraihan	Western Pacific Region (WPR)	5 (Moderate Risk of Bias)	1. Resource Adjustment: Healthcare resources should align with birth defect prevalence. 2. Early Detection: Research should prioritize early detection and intervention. 3. Accessible Services: Policy should prioritize accessible physiotherapy and neurosurgery.
Daniel Mumpe-Mwanja	African Region (AFR)	4 (Moderate risk of bias)	1. Geographic Expansion: Expand surveillance to rural areas for comprehensive insights. 2. Access Improvement: Policies should enhance service accessibility, especially in high-prevalence regions. 3. Health Infrastructure: Strengthen healthcare infrastructure and provider training for NTD diagnosis and management.