Health Science Reports

WILEY

Health Science Reports
Open Access

SYSTEMATIC REVIEW OPEN ACCESS

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

Yvan Zolo | Dalle Ulrich David | Moses Isiagi | Salome Maswime

Global Surgery Division, Faculty of Health Sciences, University of Cape Town, Cape Town, Western Cape, South Africa

Correspondence: Yvan Zolo (andre.zoloossou@uct.ac.za)

Received: 19 January 2025 | **Revised:** 12 February 2025 | **Accepted:** 10 March 2025

Funding: The authors received no specific funding for this work.

Keywords: accessibility of healthcare | geospatial mapping | healthcare disparities | neural tube defects | policy reform

ABSTRACT

Background and Aims: 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 3067 records, 65 studies met our inclusion criteria, mainly focusing on newborns. The study durations range from 6 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 NTDs 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.

1 | Introduction

Neural tube defects (NTDs) represent a global public health challenge, marked by significant morbidity and mortality rates [1]. Nutritional deficiencies, including folic acid, vitamin B12, and zinc deficiencies, are risk factors for NTDs, and addressing them can help reduce the risk. The burden of NTDs extends beyond individual health, impacting families, healthcare systems, and societies at large [2]. Early diagnosis and timely access to specialized healthcare services are crucial for managing NTDs and improving outcomes [3]. 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 [4, 5].

The complexities of NTDs extend beyond geographical considerations, presenting a challenge that demands a multifaceted approach to implementing effective interventions [6]. 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 [7, 8]. 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, 9–12]. It could empower policymakers and healthcare professionals to make informed decisions, allocate resources efficiently, and work toward 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.

2 | Methods

2.1 | 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 (see Appendix 1 for details) 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.”

2.2 | Inclusion and Exclusion Criteria

The study's inclusion criteria encompassed studies reporting the prevalence of NTDs 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.

2.3 | Data Extraction and Quality Assessment

Two authors (Y.Z. and D.U.D.) 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, World Health Organization (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 Program (CASP) tool was used to assess the quality of the selected studies. The tool comprised 10 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). The study findings were presented in accordance with the PRISMA abstract checklist (refer to Appendix 4) and the PRISMA checklist (refer to Appendix 5).

2.4 | Ethics Approval

The study was approved by the Department of Surgery Research Committee (see Appendix 6) and The University of Cape Town's Human Research Ethics Committee (see Appendix 7) with reference number HREC Ref No: 471/2023.

2.5 | 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).

3 | Results

3.1 | Studies Selection

The database search yielded 3067 results, of which 950 were duplicates. The 2117 unique titles were screened for inclusion and exclusion criteria. After the initial screening, 1902 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 WHO regions, it is noted that 18 (27.7%) studies originated from the European Region (EUR), the Western Pacific Region (WPR) contributed

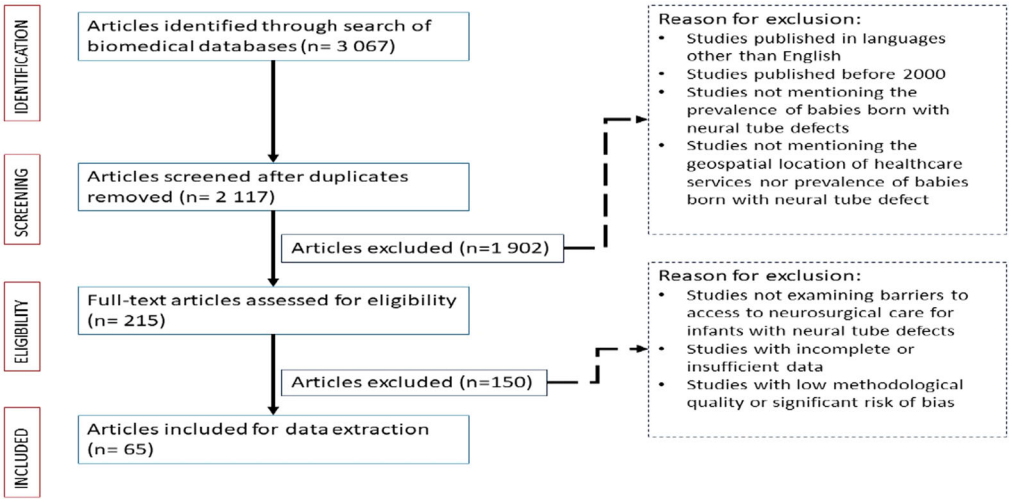

FIGURE 1 | Studies selection flowchart.

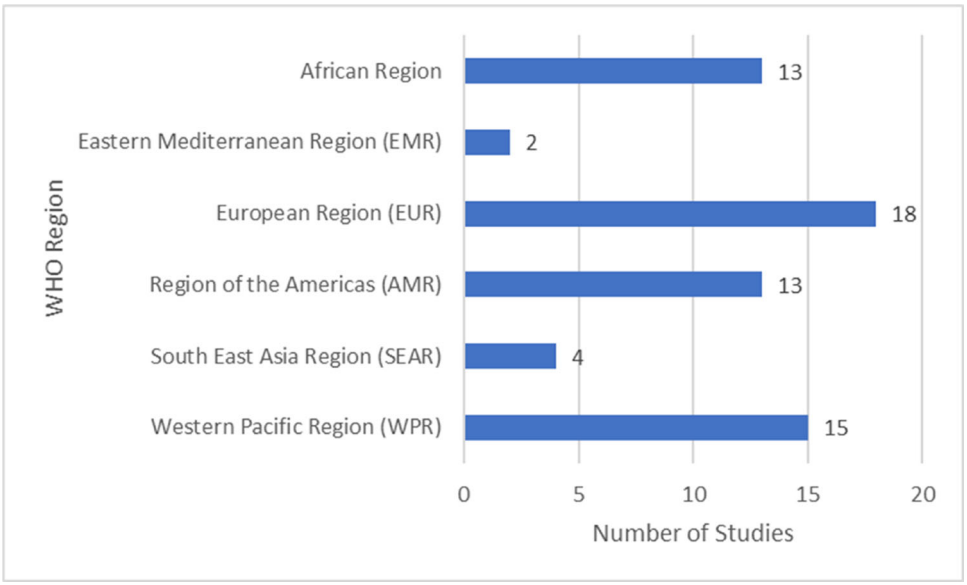

FIGURE 2 | Studies distribution according to WHO regions.

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).

3.2 | 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%) (Supporting Information S1: 1 [Appendix 9]).

Most ($n = 12$, 35.3%) studies using patient records were from the AFR, while 75% ($n = 18$) of studies using national registries were from the EUR ($n = 10$) and the AMR ($n = 8$). Up to 69.2% ($n = 9$) of studies using regional registries were from the AMR ($n = 5$) and EUR ($n = 4$). The only study that utilized GIS data was from the AMR (Table 1).

The study with the longest duration lasted for 40 years while the shortest study lasted for 6 months (see Supporting Information S1: 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 Supporting Information S1: 1 [Appendix 9] for details).

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 (Supporting Information S1: 1 [Appendix 9]).

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 comorbidities ($n = 2$, 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 (Supporting Information S1: 1 [Appendix 9]).

The largest study in terms of population size was conducted in the 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 SEAR, involving just 310 children (see Supporting Information S1: 1 [Appendix 9] for details).

The lowest prevalence (0.4 per 10,000 births) was from a study in the WPR, while the highest prevalence (215.13 per 10,000 births) was from a study in the AFR (Supporting Information S1: 1 [Appendix 9]).

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 (Supporting Information S1: 1 [Appendix 9]).

The AFR had the widest prevalence range, followed by the EUR and the SEAR. The EMR had the smallest prevalence range (Table 2).

Only 1 (1.5%) study (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 AMR published in 2013. The authors utilized GIS 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 min, 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 Supporting Information S1: 1 [Appendix 9] for details).

TABLE 1 | 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

TABLE 2 | 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

3.3 | 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 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 socio-economic status (see Supporting Information S1: 2 [Appendix 9] 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 Supporting Information S1: 2 [Appendix 9] for details).

3.4 | 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 Supporting Information S1: 3 [Appendix 9] for details).

4 | Discussion

Central to our findings is the range of NTD prevalence, from 0.4 per 10,000 births in the WPR to 215.13 per 10,000 births in the AFR, 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. [13], 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 WPR [13]. 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 population sizes less than 5000 total births, which surely excluded a lot of studies from the AFR where there is a known lack of well-structured databases including databases with over 5000 total births [14, 15]. 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 [1]. 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 study provides valuable insights into the source of data on 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 Blencowe et al. [1], 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 EUR and the AMR similar to what was observed by in 2016 by Zaganjor et al. [13]. 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 [16].

The observed significant variation in study durations highlights the necessity for extended research to understand the changing trends and patterns of NTDs [17]. 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 LMICs, 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 [18, 19].

Our review reveals a notable gap in the use of geospatial mapping in studies on NTDs, with only one study (Delmelle et al.) [20] 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 Delmelle et al. [20] 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 [21, 22].

Another important observation emanating from our review is the marked absence of interventions specifically aimed at addressing the identified access barriers (Supporting Information S1: 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.

4.1 | Limitations

Our systematic review faces several design-related limitations, primarily due to its restriction to English-language studies post-2000, which potentially excludes non-English research and historical data on NTDs. Moreover, this reliance on published studies introduces a potential publication bias, as it may overlook unpublished or less accessible studies, thereby skewing the representation of research findings. Furthermore, the variability in the designs of the included studies complicates the synthesis and interpretation of data.

4.2 | Recommendations

Research: Prolong and experiment—researchers should extend prevalence studies, use randomized controlled trials, and focus on geospatial mapping to understand and improve accessibility.

Practice: Tailor and optimize—healthcare practice for children with NTDs should target interventions for common NTD subtypes, enhance data collection methods, and strategically position clinics using geospatial analysis.

Policy: Reform, invest, and learn—there is a need to address NTD care disparities through policy reforms, encourage research investments, and gain insights from unbiased studies for effective global management strategies.

5 | Conclusion

The review shows uneven 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.

Author Contributions

Yvan Zolo conceptualized the study, investigated, curated, analyzed, and visualized the data, wrote the original manuscript draft, and administered the project. Moses Isiagi and Salome Maswime supervised the study, wrote the original manuscript draft, and administered the project. Dalle Ulrich David assisted with article screening. All authors have read and approved the final manuscript.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The authors confirm that the data supporting the findings of this study are available in the article and its supporting materials. Any additional data can be supplied upon request to the corresponding author. Yvan Zolo had full access to all the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

Transparency Statement

The lead author, Yvan Zolo, affirms that this manuscript is an honest, accurate, and transparent account of the study being reported, that no important aspects of the study have been omitted, and that any discrepancies from the study as planned (and if relevant, registered) have been explained.

References

1. H. Blencowe, V. Kancherla, S. Moorthie, M. W. Darlison, and B. Modell, "Estimates of Global and Regional Prevalence of Neural Tube Defects for 2015: A Systematic Analysis," *Annals of the New York Academy of Sciences* 1414, no. 1 (February 2018): 31–46.

2. R. Wakoya and M. Afework, "Burden of Neural Tube Defects and Their Associated Factors in Africa: A Systematic Review and Meta-analysis," *International Journal of Pediatrics* 2023 (2023): 1–22.

3. S. Getahun, S. Masresha, E. Zenebe, T. Laeke, and A. Tirsit, "Four-Year Treatment Outcomes of Children Operated for Neural Tube Defect in Addis Ababa, Ethiopia: A Retrospective Study," *World Neurosurgery* 148 (April 2021): e695–e702.

4. S. Juran, P. N. Broer, S. J. Klug, et al., "Geospatial Mapping of Access to Timely Essential Surgery in Sub-Saharan Africa," *BMJ Global Health* 3, no. 4 (August 2018): e000875, https://gh.bmj.com/content/3/4/e000875.

5. E. L. MacQuillan, A. B. Curtis, K. M. Baker, R. Paul, and Y. O. Back, "Using GIS Mapping to Target Public Health Interventions: Examining Birth Outcomes Across GIS Techniques," *Journal of Community Health* 42, no. 4 (August 2017): 633–638.

6. M. M. Simpamba, P. M. Struthers, and M. M. Mweshi, "Access to Health Care for Children With Neural Tube Defects: Experiences of Mothers in Zambia," *African Journal of Disability* 5, no. 1 (December 2016): 11, https://ajod.org/index.php/ajod/article/view/267.

7. A. Lo, D. Polšek, and S. Sidhu, "Estimating the Burden of Neural Tube Defects in Low- and Middle-Income Countries," *Journal of Global Health* 4, no. 1 (June 2014): 010402.

8. D. Atlaw, Y. Tekalegn, B. Sahiledengle, et al., "Magnitude and Determinants of Neural Tube Defect in Africa: A Systematic Review and Meta-Analysis," *BMC Pregnancy and Childbirth* 21, no. 1 (June 2021): 426.

9. P. G. Greenough and E. L. Nelson, "Beyond Mapping: A Case for Geospatial Analytics in Humanitarian Health," *Conflict and Health* 13 (November 2019): 50, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6839210/.

10. J. E. Ishii-Rousseau, S. Seino, J. Ashby, L. A. Celi, and K. B. Park, "Leveraging Data Science for Global Surgery," in *Global Cardiac Surgery Capacity Development in Low and Middle-Income Countries*, ed. J. Kpodonu (Springer International Publishing, 2022), 55–65, https://doi.org/10.1007/978-3-030-83864-5_5.

11. "What Is Geospatial Mapping?," Azuga [Internet], cited September 21, 2023, https://www.azuga.com/blog/what-is-geospatial-mapping.

12. M. K. Bakker, M. Loane, E. Garne, et al., "Accuracy of Congenital Anomaly Coding in Live Birth Children Recorded in European Health Care Databases, a EUROlinkCAT Study," *European Journal of Epidemiology* 38, no. 3 (March 2023): 325–334.

13. I. Zaganjor, A. Sekkarie, B. L. Tsang, et al., "Describing the Prevalence of Neural Tube Defects Worldwide: A Systematic Literature Review," *PLoS One* 11, no. 4 (April 2016): e0151586, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4827875/.

14. P. E. Mbondji, D. Kebede, E. W. Soumbey-Alley, C. Zielinski, W. Kouvividila, and P.-S. Lusamba-Dikassa, "Health Information Systems in Africa: Descriptive Analysis of Data Sources, Information Products and Health Statistics," supplement, *Journal of the Royal Society of Medicine* 107, no. S3 (May 2014): 34–45, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4109358/.

15. "Births and Deaths Must Be Registered in Africa," The Lancet Global Health [Internet], cited December 22, 2023, https://www.thelancet.com/journals/langlo/article/PIIS2214-109X.

16. "Disease Registries," Journal of Public Health International [Internet], cited December 26, 2023, https://openaccesspub.org/public-health-international/disease-registries.

17. B. Khoshnood, M. Loane, H. Walle, et al., "Long Term Trends in Prevalence of Neural Tube Defects in Europe: Population Based Study," *BMJ* 351 (November 2015): h5949, https://www.bmj.com/content/351/bmj.h5949.

18. A. Flores, C. Vellozzi, D. Valencia, and J. Sniezek, "Global Burden of Neural Tube Defects, Risk Factors, and Prevention," supplement, *Indian Journal of Community Health* 26, no. S1 (November 2014): 3–5, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4480200/.

19. A. J. Copp, P. Stanier, and N. D. Greene, "Neural Tube Defects: Recent Advances, Unsolved Questions, and Controversies," *Lancet Neurology* 12, no. 8 (August 2013): 799–810, https://www.thelancet.com/journals/laneur/article/PIIS1474-4422%2813%2970110-8/fulltext.

20. E. M. Delmelle, C. H. Cassell, C. Dony, et al., "Modeling Travel Impedance to Medical Care for Children With Birth Defects Using Geographic Information Systems," *Birth Defects Research Part A: Clinical and Molecular Teratology* 97, no. 10 (October 2013): 673–684.

21. "Rethinking Healthcare in Africa With Geospatial Mapping," Gavi, the Vaccine Alliance [Internet], cited September 21, 2023, https://www.gavi.org/vaccineswork/rethinking-healthcare-africa-geospatial-mapping.

22. AssetWorks, "Importance of Geospatial Data Services in Real-Time Asset Tracking [Internet]," cited September 21, 2023, https://utilitiesone.com/importance-of-geospatial-data-services-in-real-time-asset-tracking.

Supporting Information

Additional supporting information can be found online in the Supporting Information section.

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 0–2, 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

Appendix 5

PRISMA 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).

Section and topic	Item number	Checklist item	Location where item is reported
Title			
Title	1	Identify the report as a systematic review.	Page 1
Abstract			Page 1
Abstract	2	See the PRISMA 2020 for abstracts checklist.	Page 1
Introduction			Page 3
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 3
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 3–4
Methods			Page 4–5
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 4–5
Information sources	6	Specify all databases, registers, websites, organizations, reference lists, and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 4–5
Search strategy	7	Present the full search strategies for all databases, registers, and websites, including any filters and limits used.	Page 4–5
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.	Page 4–5
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.	Page 4–5
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.	Page 4–5
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 4–5
	13d	Describe any methods used to synthesize 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.	Page 4–5
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g., subgroup analysis, meta-regression).	Page 4–5
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Page 4–5

(Continues)

Section and topic	Item number	Checklist item	Location where item is reported
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Page 4–5
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Appendix 3
Results			Page 5
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.	Page 5
	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.	Supporting Information S1: 1
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Supporting Information S1: 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.	Supporting Information S1: 1 to 3
Results of syntheses	20a	For each synthesis, briefly summarize the characteristics and risk of bias among contributing studies.	Supporting Information S1: 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 synthesized results.	Not applicable
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Supporting Information S1: 3
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Supporting Information S1: 3
Discussion			Page 10
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 10–12
	23b	Discuss any limitations of the evidence included in the review.	Page 12
	23c	Discuss any limitations of the review processes used.	Page 12
	23d	Discuss implications of the results for practice, policy, and future research.	Page 13
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.	Protocol available on request
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Not applicable
Support	25	Describe sources of financial or nonfinancial support for the review, and the role of the funders or sponsors in the review.	Page 13
Competing interests	26	Declare any competing interests of review authors.	Page 13
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

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

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

PROSPERO
International prospective register of systematic reviews

Home | About PROSPERO | How to register | Service information Search | My PROSPERO | Logout: **ANDRE YVAN ZOLO O...**

Register your review now | Edit your details

You have 1 records

My other records

These are records that have either been published or rejected and are not currently being worked on.

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 eligibilty	Registered	22/05/2023