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Cause-variations in neonatal mortality across Europe and Africa; evidence from a 20-year retrospective dataset and clinical practice guidelines

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ABSTRACT

Background: Global health disparities highlight significant inequities between regions such as Africa and Europe. This present study aims to: (i) compare the trends of the leading causes of neonatal mortalities across Europe and Africa over the past two decades; (ii) analyze the impact of clinical practice guidelines on neonatal mortality trends; and (iii) explore variations in cause-specific neonatal mortality rates between the regions.

Methods: Recent mortality data (2002−2022) were extracted from the WHO database on neonatal mortality for WHO member countries. A comparative non-parametric statistical analysis was conducted on the dataset. Additionally, a scoping review of clinical practice guidelines for both continents was performed, followed by a trend analysis and interrupted time series analysis to explore the impact of these guidelines on neonatal mortality rates.

Results: We observed marked regional differences in the causes of neonatal mortality. In Africa, rates were notably high for conditions including birth asphyxia, prematurity, and infections. Europe showed lower mortality levels with more stable trends. A steady decline in European mortality was significantly associated with a higher volume of published clinical practice guidelines compared to Africa.

Conclusion: Neonatal mortality trends differ significantly between Europe and Africa, with declining rates in Europe and stable or rising rates in Africa. Regional variation in leading causes is evident. The presence of context-specific clinical guidelines is linked to improved outcomes, underscoring the need for tailored, evidence-based interventions.

1. Introduction

Neonatal mortality remains a major public health concern, with pronounced regional disparities, particularly between Europe and Africa [1–7]. The World Health Organization (WHO) estimates that 2.4 million newborn deaths occur annually, with the majority concentrated in low- and middle-income countries [8]. Despite notable improvements in Europe, many African nations continue to experience high neonatal mortality rates [2,3], largely due to systemic challenges in healthcare infrastructure, socioeconomic conditions, and access to care [9–12].

This disparity is evident in the unequal burden of infectious diseases such as lower respiratory infections (LRI), birth asphyxia and trauma (BAT), and sepsis (SEP), which disproportionately affect African countries [8]. These differences reflect not only unequal healthcare resource distribution but also divergent disease burdens, influencing resource allocation and the development of clinical practice guidelines [4,13–21].

Cultural norms, educational attainment, and political and economic stability significantly influence maternal and neonatal health outcomes [9]. In Africa, poverty and limited access to education exacerbate health risks, while in Europe, higher income levels, supportive policies, and education are associated with reduced neonatal mortality. Malaria and HIV, more prevalent in Africa, pose serious risks to newborns [5], whereas Europe has mitigated these threats through immunisation

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campaigns and effective public health strategies. Nonetheless, lower respiratory tract infections remain a concern in both regions [6,9].

Although numerous studies have examined neonatal mortality in Europe and Africa, few have combined retrospective data analysis with a review of clinical practice guidelines. Most existing research focuses on individual causes within regions, lacking direct comparative analysis [2,6,7,12,15–17,21–24]. This gap highlights the need for a comprehensive study that compares leading causes of neonatal mortality across both continents and evaluates the influence of clinical guideline trends.

The present study addresses this gap by analysing mortality causes in Europe and Africa over the past two decades, supported by a scoping review of clinical practice guidelines for neonates, infants, and childcare from 1990 to January 2025. It contrasts the two regions, emphasising global health disparities and focusing on underexplored causes such as BAT and LRI.

By integrating retrospective WHO mortality data with a scoping review, this study aims to determine whether temporal patterns in policy development align with neonatal mortality trends and to identify regional discrepancies that could inform targeted health interventions.

1.1. Aims of the study

- To compare the leading causes of neonatal mortality across European and African regions over the past two decades.
- To analyze the impact of clinical practice guidelines on neonatal mortality rate.
- To identify variations in neonatal mortality causes between the two regions, focusing on health-related causes such as birth asphyxia, trauma, and lower respiratory infections.

2. Methods

2.1. Empirical evaluation

2.1.1. Setting

Data on neonatal deaths by cause across WHO regions (Africa and Europe) were obtained from the World Health Organization's Maternal, Newborn, Child, and Adolescent Health and Ageing Database, which has been maintained since 1990. This database comprises high-quality, verified data reported by national health ministries or agencies of WHO member states, ensuring its reliability for routine monitoring. The indicator “Number of neonatal deaths by cause” captures deaths occurring within the first 28 days of life, categorised by specific causes as defined by ICD-10 codes. Primary data sources include civil registration systems with at least 80 % coverage and medical certification of cause of death. In regions lacking comprehensive civil registration data, nationally representative epidemiological studies were used, including specialised studies based on verbal autopsies and other validated methodologies. Data collection occurs biennially. The present study is therefore based on robust, high-quality data collected using evidence-based methods [25,26].

2.1.2. Data source and quality

Cause-specific neonatal mortality data for WHO member countries were obtained from the World Health Organization's Maternal, Newborn, Child, and Adolescent Health and Ageing Database. The dataset includes annual mortality rates from 2002 to 2022, covering deaths occurring within the first 28 days of life. Data are categorised by ICD-10-coded causes and derived either from complete civil registration systems or validated epidemiological models where registration data are unavailable. The unit of analysis in this study was each country's annual neonatal mortality rate by specific cause. Countries within the African and European WHO regions were included, and mortality rates per 1000 live births were recorded for causes such as birth asphyxia and trauma, prematurity, sepsis, lower respiratory infections, HIV/AIDS, congenital anomalies, diarrhoeal diseases, and others.

2.1.3. Descriptive analysis

Descriptive statistics were used to summarise cause-specific neonatal mortality data for each region. Measures included the mean, standard deviation, range, and interquartile percentiles (25th, 50th/ median, and 75th), allowing for an assessment of central tendency and dispersion. These results provided insight into the most burdensome causes and the variability of mortality patterns within and between regions.

2.1.4. Normality and variance testing

To evaluate the distributional characteristics of the data, the Shapiro–Wilk test was applied to determine whether cause-specific mortality rates followed a normal distribution in each region. Due to the prevalence of non-normally distributed variables, non-parametric methods were deemed appropriate for further analysis. Levene's test was used to assess the homogeneity of variances across causes. Both tests confirmed violations of normality and equal variance assumptions, supporting the use of non-parametric approaches.

2.1.5. Comparative analysis

Statistical differences in mortality rates among causes were assessed using the Kruskal–Wallis H test within each region. This test evaluates whether distributions differ significantly across multiple groups. Where significant results were found, pairwise comparisons were conducted using the Mann–Whitney *U* test to identify specific differences between causes. For example, comparisons were made between mortality rates due to lower respiratory infections and HIV/AIDS. All analyses were performed separately for African and European datasets using SPSS (v25) software.

2.1.6. Data visualization

To enhance interpretation of the findings, neonatal mortality data were visualized using heatmaps, with countries represented as rows and causes of death as columns. Colour gradients indicated the intensity of mortality rates. Time-trend graphs were generated to illustrate changes in the leading causes of neonatal mortality between 2012 and 2022.

Publication trends of clinical practice guidelines were plotted for both regions from 1990 to 2025, enabling assessment of alignment between policy development and mortality patterns. Additionally, an interrupted time series analysis was conducted to evaluate the potential impact of clinical practice guidelines on neonatal mortality rates. For this analysis and due to the very low numbers of CPGs from the African region, the 178 CPGs were treated as a unit without separation for the ITS analysis.

2.1.7. Methodological assumptions and limitations

This study treats each country-year as an independent observation. However, it is acknowledged that repeated annual measures from the same countries may introduce temporal correlation. Non-parametric tests such as the Kruskal–Wallis and Mann–Whitney U assume independence of observations, and this assumption may be partially violated.

While the analytical approach is appropriate for exploring broad trends in non-normally distributed data, future research should consider longitudinal or mixed-effects models to account for intra-country dependence and more accurately estimate temporal effects.

2.1.8. Summary of statistical analysis

We conducted a comparative non-parametric statistical analysis of neonatal mortality causes in Europe and Africa from 2002 to 2022. The analysis was performed using SPSS version 25, utilizing the Mann-Whitney *U* test, and Kruskal-Wallis test.

- Descriptive Statistics: We calculated the mean, median, standard deviation, range, and percentiles (50th (median), and 75th) for each mortality cause to understand the distribution and variability of the data.

- Normality and Variance Tests: The Shapiro-Wilk test was used to assess the normality of the data (supplementary file), while Levene's test evaluated the homogeneity of variances across different causes.
- Comparative Analysis: The Kruskal-Wallis' test performed to determine statistical differences in mortality rates between multiple groups. For pairwise comparisons, the Mann-Whitney U test was used to identify specific differences between causes.
- Data Visualization: Mortality rates were visualized using heatmaps, with countries as rows and causes of mortality as columns, to illustrate cause-specific mortality trends across nations.

2.2. Scoping of clinical practice guidelines for neonates and children in Africa and Europe (1st January 1990 – 31st January 2025)

The aim of the search was to provide further context for discussion and to generate hypotheses regarding the marked differences in neonatal mortality between Europe and Africa. The search was conducted on 31st February 2025 and covered studies published between 1 January 1990 and 31st January 2025. Medical Subject Headings (MeSH) terms were developed and combined using Boolean operators ('AND', 'OR'). The search strategy was adapted for each database. An example of the PubMed search string is as follows:

*((((Neonatal mortality) OR (Neonatal health)) AND (Health guidelines)) OR (Health polic)) AND (Africa)) OR (Europe)**. Filters applied included: Directory, Government Publication, Guideline, Legislation, Practice Guideline, and Technical Report, limited to the period 1990–2025.

Four databases and one international journal on health policy were searched for relevant studies. The search, conducted on 1 February 2025, yielded a total of 8018 documents. Filters were applied to include only practice guidelines, technical reports, and policy documents (see Supplementary File 1). The number of records retrieved from each source was as follows:

CINAHL (EBSCO): 17, Web of Science: 2610, PubMed: 6709, and Journal of Health Policy: 170. These results are summarised in the PRISMA flow diagram (Fig. 2).

2.2.1. Inclusion and exclusion criteria

To be included, the study must be a clinical practice or policy guideline, it targets neonates, infants or children. It targets Africa, Europe, countries within Africa and or Europe, it is published between 1990 and January 2025, the publication is done in English language, and it is a peer-reviewed study. Studies that did not meet these criteria as were as previously reviewed studies were excluded.

2.2.2. Screening and data extraction

The retrieved documents ($n = 8418$) were exported to Zotero reference manager application, where duplicates ($n = 3014$) were automatically identified and merged. A two-staged text-mining process was then conducted within Zotero. In the first phase, publications related to health policy, guidelines, or practice guidelines were identified using key terms such as *"guideline*"* and *"policy"*. This resulted in the selection of 3212 articles.

The second phase involved refining the selection to documents '3212' specifically targeting neonatal and child health. Search terms included "children/child/ childhood (child*, $n = 138$), baby/babies/ babe (bab*, $n = 5$), infant/infants (infant*, $n = 24$), neonate/neonates/ neonatal (neonat*, $n = 25$), newborn (n = 13) and under 5 ($n = 0$). This yielded a total of 205 documents. Of these ($n = 205$), 20 were identified as duplicates during the second screening, and 7 were reviews of existing guidelines. The final number of documents included in the review was 178 (see Fig. 2).

3. Results

3.1. General trends in the leading causes of neonatal mortality across the two continents from 2012 to 2022

From Fig. 1 *(a)*, a steady decline in mortality rates for most neonatal mortality causes in Europe from 2012 to 2022 is observed, particularly for lower respiratory infections (LRI). Other causes like birth asphyxia and trauma (BAT), congenital conditions (CON), and gastrointestinal diseases (OG1) also show a downward trend. Mortality from malaria (MAL), measles (MEA), HIV, and tuberculosis (TUB) remained very low throughout the period. This decline suggests sustained interventions for reducing neonatal mortality in the region.

In contrast, Fig. 1 *(b)* shows consistently high mortality rates in Africa for causes like LRI and BAT from 2012 to 2022. Preterm birth complications (PRE) and OG1 also remain high, while MAL, MEA, and TUB have lower rates. This indicates limited progress in reducing mortality due to multiple factors, both known and emerging challenges.

3.2. Descriptive statistics of the major causes of neonatal mortality across the regions

Descriptive statistics show clear regional disparities in neonatal mortality between Europe and Africa (Table 1). In Europe, preterm birth complications (PRE) and congenital conditions (CON) are the leading causes, with PRE having the highest mean (241.93). Most other causes, like HIV, malaria, and measles, show near-zero means, reflecting effective prevention. Lower respiratory infections (LRI) and gastrointestinal diseases (OG1) show moderate means with some variability.

In contrast, Africa bears a much heavier burden. PRE and birth asphyxia and trauma (BAT) dominate, with extremely high means (6578.4 and 5035.7), indicating systemic healthcare challenges. Other causes like LRI, OG1, HIV, and tetanus also show significantly higher mortality. The data highlight the need for targeted, cause-specific interventions in Africa [21,27,28].

3.3. Distribution of mortality and non-parametric statistical analysis

To assess the significance of the difference, a statistical analysis was performed. However, due to a non-normal distribution pattern evidenced the Shapiro-Wilk's normality test with p less than 0.05, a non-parametric Mann-Whitney *U* test was chosen.

The non-parametric analysis highlights significant differences in neonatal mortality causes between Africa and Europe (Table 2). Levene's and Kruskal-Wallis tests confirm high variability and statistically significant differences across all causes in both regions ($p < 0.001$). Pairwise Mann-Whitney *U* tests further reveal that nearly all cause comparisons are statistically significant, with extremely small *p*-values ($p < 0.001$), indicating distinct distributions. In Africa, causes like prematurity (PRE), birth asphyxia and trauma (BAT), and lower respiratory infections (LRI) differ markedly from others, reflecting a broad and uneven burden. Similarly, in Europe, PRE and congenital anomalies (CON) stand out significantly from lower impact causes like HIV, malaria, and measles. These findings underscore the heterogeneity in neonatal mortality patterns observed in sections 3.1 & 3.2.

3.4. Exploring the potential impact of clinical practice guidelines on the observed trends in sections 3.2–3.3

3.4.1. Total number of clinical practice guidelines published during the period of 1990 to 2025.

Identification of studies via databases

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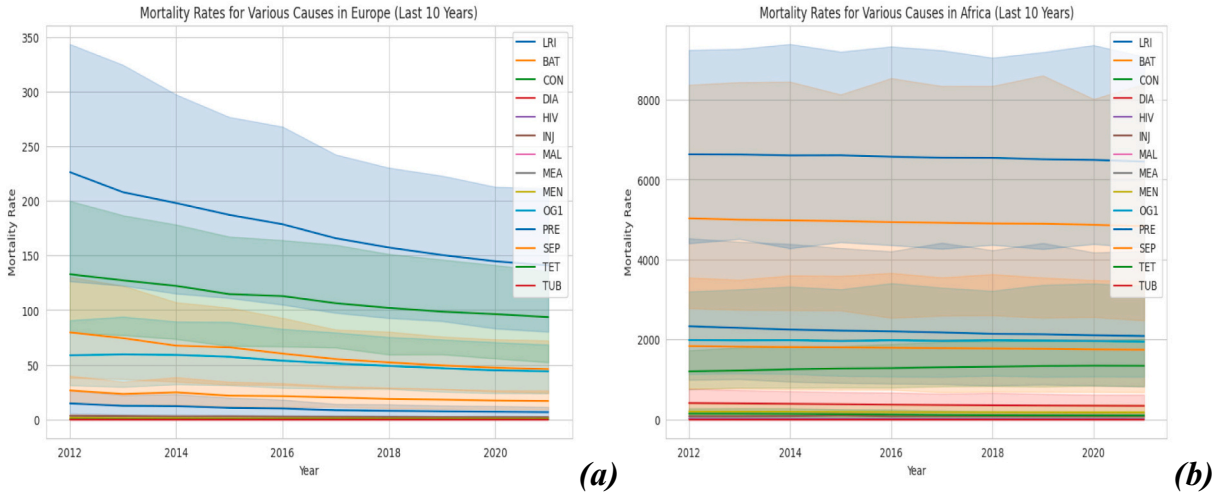

Fig. 1. (a) Trends on the leading causes of neonatal mortality among WHO European regional countries (left) for (2012−2022), (b) Trends of the major causes of neonatal mortality among WHO African regional countries (right) for the last decade (2012–2022).

Table 1
Descriptive statistics of health-related causes in Europe and Africa.

Conditions	Europe					Africa				
Causes	mean	median	std	range	75 %	mean	median	std	range	75 %
BAT	89.02	27.04	188.62	1264.76	62.67	5035.7	2853.0	10,826.0	13,258.3	1328.0
CON	137.62	58.79	203.46	1001.64	110.12	1135.1	640.4	1790.1	7224.7	400.1
DIA	0.68	0.00	3.88	31.99	0.00	419.5	140.8	1036.1	319.5	24.8
HIV	0.07	0.00	0.37	4.05	0.00	29.3	8.0	55.2	2115.0	74.6
INJ	4.86	1.27	13.57	132.20	3.28	80.6	34.4	201.9	49,235.2	2070.8
LRI	18.80	2.51	51.90	325.44	7.57	2361.1	866.4	6854.8	1.3	0.0
MAL	0.00	0.00	0.03	1.06	0.00	0.0	0.0	0.1	0.0	0.0
MEA	0.00	0.00	0.00	0.00	0.00	0.0	0.0	0.0	5385.0	168.2
MEN	1.68	0.00	5.08	35.99	0.62	212.7	60.6	653.8	29,582.8	2179.2
OG1	60.44	16.58	106.76	652.97	46.21	1982.5	1151.4	4006.7	51,261.1	8433.8
PRE	241.93	86.47	423.09	2554.10	212.64	6578.4	4649.2	8911.3	41,677.2	1597.2
SEP	27.71	7.56	48.36	252.51	22.13	1837.1	661.1	5670.4	5638.6	109.1
TET	0.17	0.00	0.82	8.37	0.00	178.4	26.2	562.5	0.0	0.0
TUB	0.00	0.00	0.00	0.00	0.00	0.0	0.0	0.0	0.0	0.0

(*continued*)

Identification of studies via databases			
Identification	Records identified from*: Total Databases (n = 8418) PubMed (n = 6709) CINAH-EBSCO (n = 17) Web of Science (n = 1518) Journal of Health policy (n = 170) ↓	→	Records removed *before screening*: Duplicate records removed (n = 3009) Records removed for other reasons (n = 2193)
Screening	Reports assessed for eligibility. (n = 3212) Records screened using text mining keywords (guideline*, policy*) ↓	→	Records excluded** (n = 5206) Did not meet text mining keywords (guideline*, policy*)
	Reports assessed for eligibility. (n = 205) Selected guideline and policy documents screened with text mining keywords; Child* (n = 138) Infant (n = 24) Neonat* (n = 25)	→	Reports excluded: (n = 3034) did not meet the MeSH terms for 'Infant' and 'Neonate keywords (n = 3014) Additional duplicates (n = 20)

(*continued on next column*)

(*continued*)

Identification of studies via databases		
	Under 5 (n = 0) Newborn (n = 13) Bab* (n = 5) ↓	
Included	Studies included in review. (n = 178)	

3.4.2. Trends in the clinical practice guideline publications between 1990 and 2025 and temporal associations in the top causes of mortality in African and Europe

The rise in clinical practice guidelines over time (Fig. 2) [8,11,22,24,28–202] coincides with declining neonatal mortality in Europe (Fig. 1 *(a)*). This inverse relationship suggests that well-disseminated and implemented clinical guidelines may impact positively to better disease management and outcomes. (See Fig. 3.)

In Africa, despite the global increase in guideline publications (fig. 3), neonatal mortality remains high. Regional narrowing of practice guidelines (9/178) (fig. 3b) for the African region further justifies the disparity. Very few clinical practice guidelines for children/ neonatal care (9/178) (Fig. 4a) were published from the African region over the last 30 years and mostly from South Africa (6/9) showing scarcity of

Table 2
Statistical analysis of neonatal mortality causes in Africa and Europe.

Non-parametric analysis for cause of neonatal death between Africa and Europe.

Cause	Test	Africa		Europe	
		Statistic	*P*-value	Statistic	P-value
All Causes	Levene	176.6434	0	222.4366	0
All Causes	Kruskal-Wallis	11,605.6	0	9270.568	0
ALRI vs BABT	Mann-Whitney U	402,539	1.82E-49	180,231	6.75E-103
ALRI vs CA	Mann-Whitney U	691,011	6.02E-05	140,589	6.99E-138
ALRI vs DD	Mann-Whitney U	935,398	1.94E-88	737,078	1.99E-201
ALRI vs HIV	Mann-Whitney U	1,159,447	2.32E-261	726,137	1.94E-171
ALRI vs Inj	Mann-Whitney U	1,100,269	1.06E-206	503,886.5	1.34E-11
ALRI vs Mal	Mann-Whitney U	1,258,137	0	756,512	2.15E-235
ALRI vs Mea	Mann-Whitney U	1,258,323	0	756,756	6.33E-236
ALRI vs M/E	Mann-Whitney U	1,024,502	3.90E-146	659,586.5	3.71E-100
ALRI vs OG1/NCD	Mann-Whitney U	589,274	0.008861	227,364	4.69E-68
ALRI vs Prem	Mann-Whitney U	323,562	2.17E-88	114,538	1.24E-163
ALRI vs Sepsis	Mann-Whitney U	694,575	2.19E-05	282,884.5	2.67E-36
ALRI vs Tet	Mann-Whitney U	1,065,948	5.82E-178	738,955	1.22E-201
ALRI vs TB	Mann-Whitney U	1,258,323	0	756,756	6.33E-236
BABT vs CA	Mann-Whitney U	898,223	1.12E-68	316,884.5	8.66E-22
BABT vs DD	Mann-Whitney U	1,072,127	5.55E-183	817,627	6.71E-292
BABT vs HIV	Mann-Whitney U	1,216,086	0	816,528	4.28E-273
BABT vs Inj	Mann-Whitney U	1,180,887	9.39E-283	731,921.5	1.55E-156
BABT vs Mal	Mann-Whitney U	1,258,884	0	825,976	0
BABT vs Mea	Mann-Whitney U	1,258,884	0	826,056	0
BABT vs M/E	Mann-Whitney U	1,141,340	5.98E-244	789,621.5	1.72E-230
BABT vs OG1/NCD	Mann-Whitney U	837,092.5	1.03E-41	487,903	1.03E-07
BABT vs Prem	Mann-Whitney U	501,336	6.97E-17	284,605	2.43E-35
BABT vs Sepsis	Mann-Whitney U	896,461	8.36E-68	581,232.5	2.68E-41
BABT vs Tet	Mann-Whitney U	1,157,649	1.30E-259	820,145	1.85E-293
BABT vs TB	Mann-Whitney U	1,258,884	0	826,056	0
CA vs DD	Mann-Whitney U	929,898	2.35E-85	826,927	7.20E-304
CA vs HIV	Mann-Whitney U	1,192,706	6.52E-295	825,802	6.11E-285
CA vs Inj	Mann-Whitney U	1,127,409	5.76E-231	761,389.5	1.03E-187
CA vs Mal	Mann-Whitney U	1,258,884	0	832,463	0
CA vs Mea	Mann-Whitney U	1,258,884	0	832,524	0
CA vs M/E	Mann-Whitney U	1,040,588	4.14E-158	806,275	3.59E-251
CA vs OG1/NCD	Mann-Whitney U	522,000	2.54E-12	579,742	1.56E-40
CA vs Prem	Mann-Whitney U	278,625	1.17E-115	364,919.5	6.56E-08
CA vs Sepsis	Mann-Whitney U	631,667	0.884749	641,242.5	5.71E-78
CA vs Tet	Mann-Whitney U	1,083,359	2.84E-192	828,166	1.47E-303
CA vs TB	Mann-Whitney U	1,258,884	0	832,524	0
DD vs HIV	Mann-Whitney U	979,410	3.93E-115	358,228.5	2.11E-23
DD vs Inj	Mann-Whitney U	870,339	1.57E-55	136,598	2.38E-181
DD vs Mal	Mann-Whitney U	1,207,907	0	449,070.5	5.94E-12
DD vs Mea	Mann-Whitney U	1,208,394	0	449,526	1.32E-12
DD vs M/E	Mann-Whitney U	769,976	5.29E-20	307,032	1.66E-51
DD vs OG1/NCD	Mann-Whitney U	289,686	1.31E-108	51,697	4.96E-273
DD vs Prem	Mann-Whitney U	127,102	5.11E-235	16,707.5	0
DD vs Sepsis	Mann-Whitney U	352,298	6.63E-73	55,290	7.23E-268
DD vs Tet	Mann-Whitney U	833,161	3.14E-40	420,055.5	0.153159
DD vs TB	Mann-Whitney U	1,208,394	0	449,526	1.32E-12
HIV vs Inj	Mann-Whitney U	418,268	4.41E-43	149,856	8.37E-150
HIV vs Mal	Mann-Whitney U	1,232,637	0	521,975	1.42E-51
HIV vs Mea	Mann-Whitney U	1,234,200	0	522,522	2.31E-52
HIV vs M/E	Mann-Whitney U	349,209	1.71E-74	352,206.5	2.10E-16
HIV vs OG1/NCD	Mann-Whitney U	72,081	8.27E-289	52,694	2.62E-254
HIV vs Prem	Mann-Whitney U	23,922	0	15,829.5	1.32E-300
HIV vs Sepsis	Mann-Whitney U	91,059	1.28E-269	55,977	6.67E-250
HIV vs Tet	Mann-Whitney U	453,517	1.99E-30	487,900.5	6.03E-18
HIV vs TB	Mann-Whitney U	1,234,200	0	522,522	2.31E-52
Inj vs Mal	Mann-Whitney U	1,257,796	0	739,835	9.06E-219
Inj vs Mea	Mann-Whitney U	1,258,323	0	740,124	2.33E-219
Inj vs M/E	Mann-Whitney U	501,004.5	5.80E-17	624,264	1.53E-73
Inj vs OG1/NCD	Mann-Whitney U	117,220.5	2.96E-244	163,576.5	2.60E-117
Inj vs Prem	Mann-Whitney U	51,451	2.0350290061258e-310	69,513.5	8.43E-214
Inj vs Sepsis	Mann-Whitney U	165,748	1.51E-200	201,468	1.71E-86
Inj vs Tet	Mann-Whitney U	631,844.5	0.875623	716,946	6.44E-179
Inj vs TB	Mann-Whitney U	1,258,323	0	740,124	2.33E-219
Mal vs Mea	Mann-Whitney U	633,930	0.004618	427,350	0.317835
Mal vs M/E	Mann-Whitney U	11,846	0	283,205	6.26E-82
Mal vs OG1/NCD	Mann-Whitney U	0	0	40,762	1.12E-296
Mal vs Prem	Mann-Whitney U	0	0	11,592.5	0
Mal vs Sepsis	Mann-Whitney U	52	0	40,772	1.16E-296
Mal vs Tet	Mann-Whitney U	42,912	0	397,319.5	1.07E-15

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Table 2 (*continued*)

Non-parametric analysis for cause of neonatal death between Africa and Europe.

Cause	Test	Africa		Europe	
		Statistic	***P*-value**	**Statistic**	**P-value**
Mal vs TB	Mann-Whitney U	633,930	0.004618	427,350	0.317835
Mea vs M/E	Mann-Whitney U	11,220	0	282,744	1.17E-82
Mea vs OG1/NCD	Mann-Whitney U	0	0	40,656	5.21E-297
Mea vs Prem	Mann-Whitney U	0	0	11,550	0
Mea vs Sepsis	Mann-Whitney U	0	0	40,656	5.21E-297
Mea vs Tet	Mann-Whitney U	42,075	0	396,858	2.33E-16
Mea vs TB	Mann-Whitney U	629,442	1	426,888	1
M/E vs OG1/NCD	Mann-Whitney U	195,979	1.64E-175	88,650	5.31E-202
M/E vs Prem	Mann-Whitney U	77,824	6.26E-283	33,157	3.46E-269
M/E vs Sepsis	Mann-Whitney U	250,490	1.27E-134	102,991.5	2.08E-185
M/E vs Tet	Mann-Whitney U	730,362	4.82E-11	542,608	1.41E-46
M/E vs TB	Mann-Whitney U	1,247,664	0	571,032	1.17E-82
OG1/NCD vs Prem	Mann-Whitney U	338,744	5.12E-80	245,847.5	3.88E-56
OG1/NCD vs Sepsis	Mann-Whitney U	734,649	7.11E-12	517,861.5	2.10E-15
OG1/NCD vs Tet	Mann-Whitney U	1,099,214	8.61E-206	805,488	9.16E-276
OG1/NCD vs TB	Mann-Whitney U	1,258,884	0	813,120	5.21E-297
Prem vs Sepsis	Mann-Whitney U	972,212	1.68E-110	674,572	1.91E-103
Prem vs Tet	Mann-Whitney U	1,192,246	1.92E-294	838,998.5	0
Prem vs TB	Mann-Whitney U	1,258,884	0	842,226	0
Sepsis vs Tet	Mann-Whitney U	1,054,186	1.31E-168	803,313	1.25E-272
Sepsis vs TB	Mann-Whitney U	1,258,884	0	813,120	5.21E-297
Tet vs TB	Mann-Whitney U	1,216,809	0	456,918	2.33E-16

Note: Extremely small p-values (e.g., < 0.001) are rounded for clarity.
Key; 'Acute lower respiratory infections': 'LRI', 'Birth asphyxia and birth trauma': 'BAT', 'Congenital anomalies': 'CON', 'Diarrhoeal diseases': 'DIA', 'HIV/AIDS': 'HIV', 'Injuries': 'INJ', 'Malaria': 'MAL', 'Measles': 'MEA', 'Meningitis/encephalitis': 'MEN', 'Other Group 1 and Other noncommunicable (neonatal and under-5 only)': 'OG1', 'Prematurity': 'PRE', 'Sepsis and other infectious conditions of the newborn': 'SEP', 'Tetanus': 'TET', and 'Tuberculosis': 'TUB'.

guidelines compares to (162/178) for Europe during the same period. Guideline implementation, access to care, and local adaptation could partly explain the observed mortality trends. The data implies that while clinical guidelines could be effective, their impact is context-and number dependent. (See Fig. 5.)

In Europe, robust health systems likely facilitated practice guideline development and uptake, [203–205]. In Africa, systemic challenges (e.g., poverty, workforce shortages, limited health infrastructure) limited the practice guideline development and effectiveness and uptake of public health interventions [21,23,29,152].

3.5. Interrupted Time Series (ITS) analysis of neonatal mortality

It summarizes the interrupted time series analysis of neonatal mortality trends in Africa, Europe, and combined (Europe and African regions) from 2000 to 2021. The analysis evaluates the impact of Clinical Practice Guidelines (CPGs) introduced around 2010, using WHO mortality data and CPG publication frequency from 1990 to 2025. The CPGs were treated together and where not separated between the regions due to the low volume of publications from the African region.

3.5.1. Africa: Pre-intervention trend

Mortality declined by approximately 2868 deaths per year ($p < 0.001$). *Immediate effect of clinical practice guidelines (CPGs):* An increase of around 6859 deaths was observed ($p = 0.047$). *Post-intervention trend:* A slight, non-significant decline of approximately 415 deaths per year ($p = 0.425$).

3.5.2. Europe: Pre-intervention trend

Mortality decreased by approximately 6752 deaths per year ($p < 0.001$). *Immediate effect of CPGs:* An increase of around 4780 deaths was recorded ($p = 0.001$). *Post-intervention trend:*

3.5.3. Combined regions

3.5.3.1. Pre-intervention trend. Mortality declined by approximately 9619 deaths per year ($p < 0.001$). *Immediate effect of CPGs (2010):* An increase of around 11,640 deaths was observed ($p = 0.025$). *Post-intervention trend:* A slight, non-significant increase of approximately 1004 deaths per year ($p = 0.201$).

Overall: Europe demonstrated a statistically significant and sustained decline in neonatal mortality following the introduction of CPGs. In contrast, Africa and the combined regions showed initial increases post-intervention—potentially reflecting improved reporting or transitional implementation challenges—followed by downward trends. However, the post-intervention slopes for Africa and the combined regions were not statistically significant, suggesting limited long-term acceleration in mortality reduction.

3.6. Bibliometric network analysis

This was done to explore the major contributors/ active players in formulating the clinical practice guidelines from the regions as presented in (fig. 5a&b), major themes of the guidelines, countries and the potential networks of the leading authors based on keyword frequencies. The network analysis was done using the VOSviewer software. The iteration frequency was set to a minimum frequency of 20 for the keyword analysis.

Fig. 5a presents a VOSviewer-generated visualization of keyword networks related to clinical practice and health policy guidelines in Europe and Africa. Node size reflects keyword frequency, while connecting lines indicate co-occurrence relationships. Six thematic clusters are identified:

Red cluster: Focused on Europe, with prominent contributions from countries such as France (24 documents), Germany (14), Finland (2), Poland (10), the United Kingdom (31), Denmark (5), Sweden (5), the Netherlands (12), and Italy (18). This cluster highlights European medical policies and interdisciplinary communication. *Blue cluster:* Centred on terms such as *female*, *pregnancy*, *treatment outcome*, and *guidelines*, reflecting themes in women's health, maternity care, and clinical recommendations from pregnancy through to postnatal care. *Green cluster*: Emphasises *risk factors*, *middle-aged*, and *age factors*, pointing to epidemiological considerations and chronic disease prevention. *Yellow cluster*: Associated with oncology, including terms such

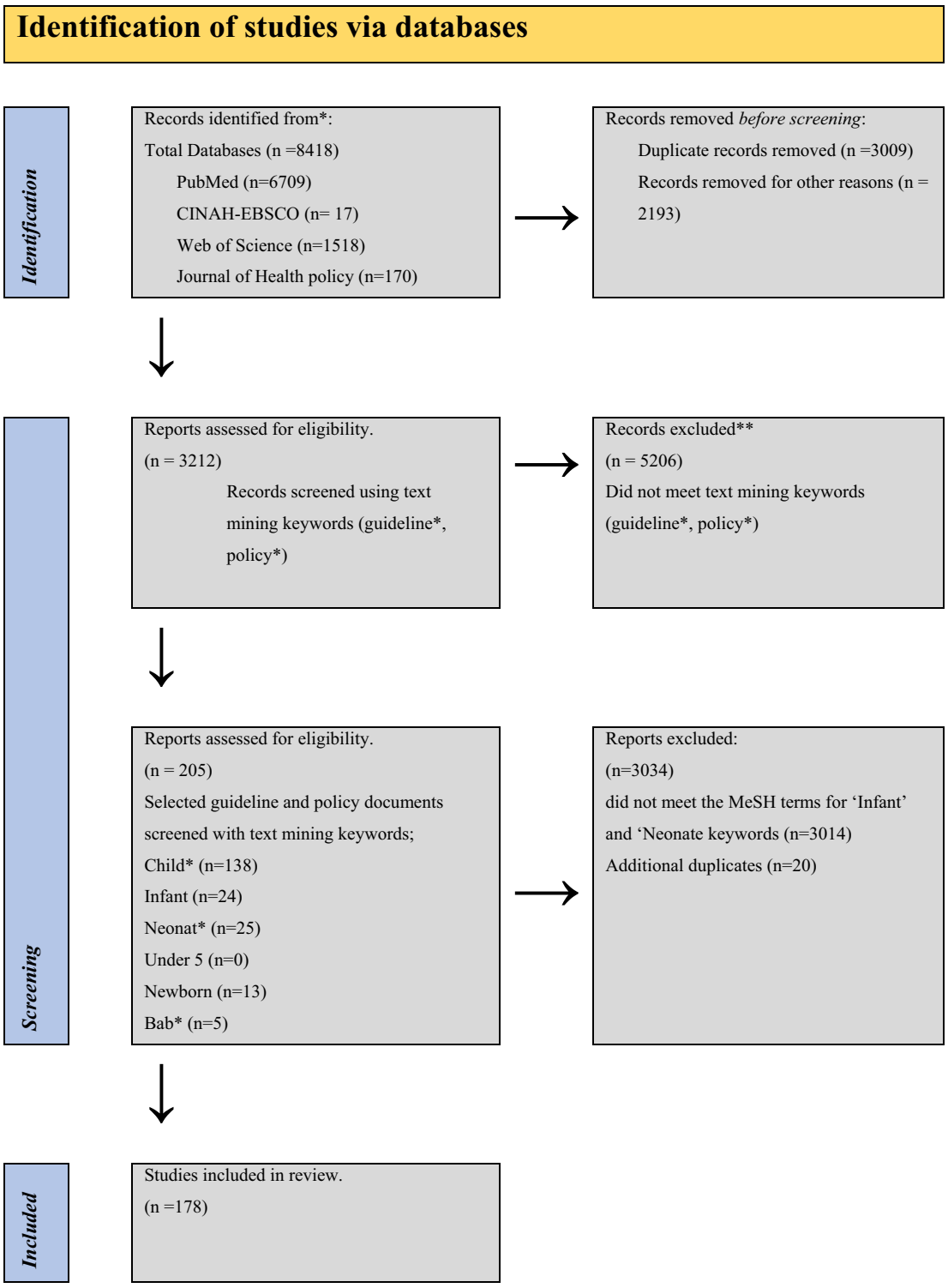

Fig. 2. The 2020 PRISMA flow diagram for the clinical practice guideline selection. http://www.prisma-statement.org/. A total of 178 guidelines were selected.

as *neoplasm staging*, *risk assessment*, and *treatment strategies*, indicating a focus on cancer research and clinical approaches. *Purple cluster*: Includes keywords such as *child*, *infant*, and *newborn*, highlighting paediatric health concerns, neonatal care, and developmental studies. *Light blue cluster*: Revolves around *consensus*, *recommendations*, and *diagnosis*, representing broader themes in clinical guideline development, best practices, and standardised medical decision-making.

Keywords related to Africa were not prominently represented in the network due to the limited number of documents (n = 9) from the region. The African contributions were dominated by South Africa (n = 6) with single entries from Tanzania Nigeria and Egypt

The co-authorship network visualization (fig. 5b) displays individual authors as nodes, with links representing collaborative relationships. Node size corresponds to network volume, while colour-coded clusters denote research groups. *Yakoub-Agha, Ibrahim* (grey cluster) emerges as a central collaborator. The red cluster (e.g., *Jensen*, *Dietrich*) and blue cluster (e.g., *Rodrigues, Anabela*, *Domingos, Nicholas*) represent active research teams. Other clusters, such as those led by *Goudswaard* (pink)

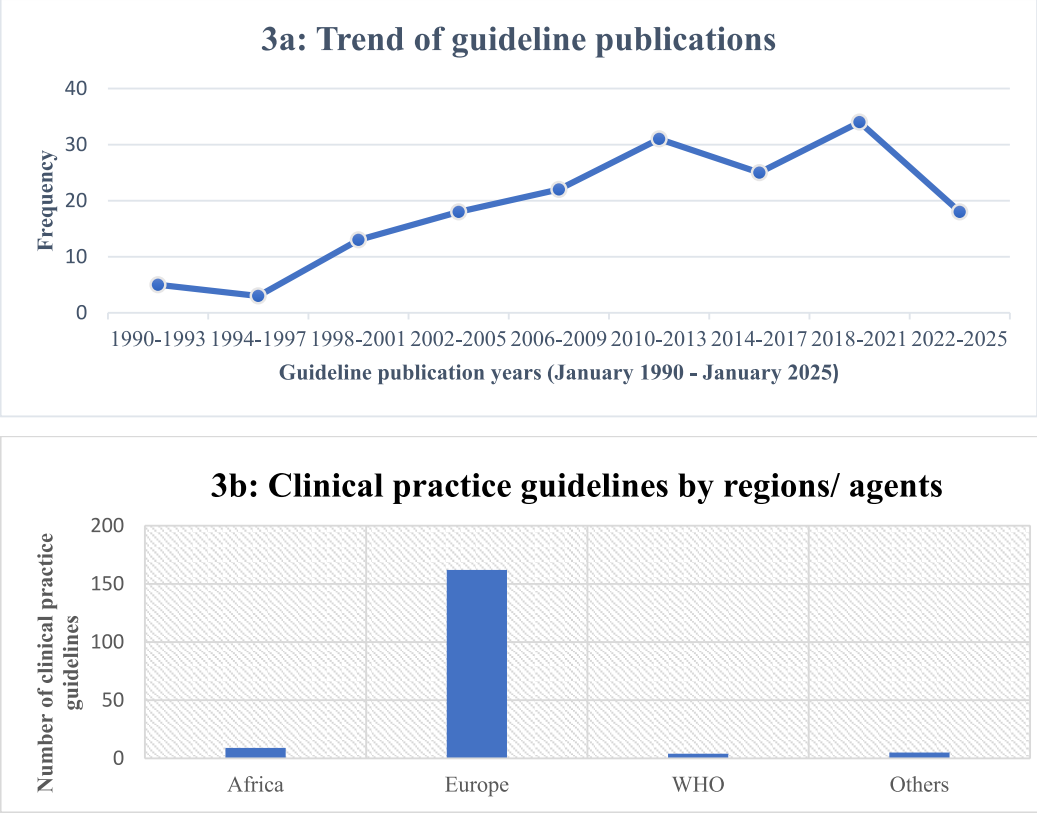

Fig. 3. a: Trends of clinical practice guideline publications from 1990 to 2025. **Fig. 3b:** Regional distribution of clinical practice guidelines (CPGs), showing high output from Europe ($n = 162$) compared to Africa ($n = 9$).

and *Nolan, Jerry* (orange), illustrate independent research circles. Overall, the network reflects the collaborative and interdisciplinary nature of clinical guideline research across regions.

4. Discussion

This study contributes to the understanding of global neonatal health disparities by examining not only the differences in mortality rates between Europe and Africa but also the structural and policy-level factors that may underpin these outcomes. While the higher burden of neonatal mortality in Africa is well established 1,3,12,42, this study adds a novel perspective by exploring the role of clinical practice guidelines (CPGs) in shaping regional health outcomes.

The stark contrast in the number of published neonatal and paediatric guidelines—162 in Europe versus only 9 in Africa—highlights a significant gap in policy infrastructure. This disparity is not merely academic but reflects broader systemic challenges. Many African countries face limitations in healthcare financing, political stability, and institutional capacity, which hinder the development, dissemination, and implementation of context-specific, evidence-based guidelines [13]. In contrast, Europe benefits from strong professional networks and established health systems that support continuous guideline development and uptake [2,12–14,18,21,23,27,28,34,152,203–207].

However, the mere presence of guidelines does not guarantee improved outcomes. In low-resource settings, even when guidelines exist, their impact may be constrained by workforce shortages, inadequate training, and weak monitoring systems [208]. These barriers impede the translation of policy into practice and contribute to persistent gaps in care quality and neonatal survival.

The limited representation of African institutions in the co-authorship network further underscores the imbalance in global health research. This lack of inclusion restricts the development of context-specific evidence and reduces opportunities for capacity-building and knowledge exchange. Strengthening regional research ecosystems and fostering equitable collaborations are essential for generating locally relevant solutions.

To further explore the temporal impact of CPGs, we employed Interrupted Time Series (ITS) analysis. The ITS results revealed distinct regional patterns in neonatal mortality trends before and after the assumed introduction of CPGs in 2010. In Europe, the post-intervention trend showed a statistically significant and sustained decline in neonatal mortality (−1419 deaths/year, $p < 0.001$), suggesting that the implementation of CPGs may have contributed to improved outcomes. This aligns with the observed increase in guideline publications and the presence of robust health systems that support their dissemination and use.

In contrast, Africa exhibited a more complex pattern. Although a pre-intervention decline in mortality was observed (−2868 deaths/year, $p < 0.001$), the immediate post-intervention period saw a statistically significant increase in deaths (+6859, $p = 0.047$), followed by a non-significant decline (−415 deaths/year, $p = 0.425$). This may reflect transitional challenges such as improved reporting, limited implementation capacity, or systemic barriers that hinder the effective use of guidelines. The low volume of CPGs from Africa (only 9 out of 178 reviewed documents) further underscores the limited policy infrastructure and research output from the region. Moreover, assuming all 178 guidelines were made available in Africa, the fact that 169 were developed outside the region suggests they may lack contextual relevance and thus be less effective.

The combined analysis of Europe and Africa showed an initial increase in mortality post-intervention (+11,640 deaths, $p = 0.025$), followed by a non-significant upward trend (+1004 deaths/year, $p = 0.201$). These findings suggest that while CPGs may have a positive impact in well-resourced settings, their effectiveness is highly context-

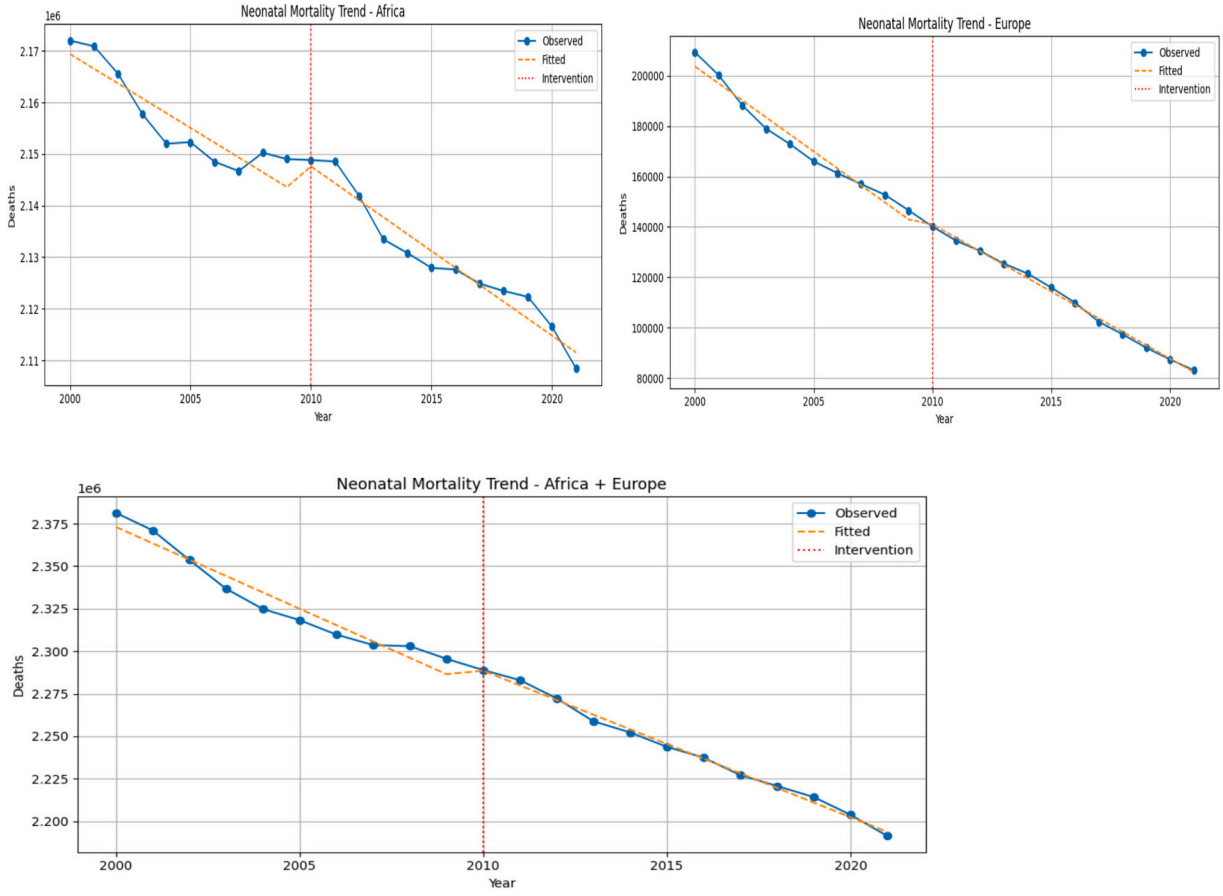

Fig. 4. Interrupted time series (ITS) analysis of neonatal mortality trends for Africa (top left), Europe (top right), and combined regions (Europe and African regions) (down left).

dependent and may be constrained in regions with weaker health systems [205].

While the association between guideline availability and improved neonatal outcomes in Europe is compelling, the present study does not claim a direct causal relationship. Rather, it emphasises the importance of viewing neonatal mortality through a systems lens—one that considers how economic conditions, governance, and institutional readiness interact with clinical care to shape outcomes [19,20]. Future research should explore these dynamics using longitudinal and implementation science approaches to better understand how guidelines influence practice in diverse contexts.

In summary, achieving the Sustainable Development Goal (SDG) 3.2 targets for neonatal mortality in Africa requires more than clinical interventions. It demands investment in health systems, policy development, and research capacity. Efforts must prioritise not only the creation of evidence-based guidelines but also the systems and structures that enable their effective implementation. Addressing these foundational issues is essential for narrowing the gap in neonatal outcomes between Africa and Europe and for achieving global health equity.

5. Limitations

This study is subject to three major limitations. First, its observational design and reliance on publicly available aggregate data limit the ability to infer causality. The observed associations between guideline volume and neonatal mortality should therefore be interpreted with caution. Second, the use of non-parametric statistical methods does not fully account for the non-independence of repeated yearly observations from the same countries, which may introduce temporal correlation. Third, the review of clinical practice guidelines did not assess the quality, contextual relevance, or implementation fidelity of the documents. As such, the presence of a guideline does not necessarily reflect its effectiveness or uptake in practice.

6. Conclusion

The present study reveals substantial regional disparities in neonatal mortality trends and causes. Europe has seen a consistent decline, primarily with linked causes like preterm birth complications and congenital anomalies. In contrast, many African countries show stable or rising mortality rates, with birth asphyxia, prematurity, and infections as leading causes. The volume and region specificity of clinical practice guidelines (CPGs) appear to be associated with improved outcomes, particularly in Europe. However, this observed relationship does not imply causality. Further research is needed to evaluate the impact of guideline implementation using longitudinal and policy evaluation methods to inform effective neonatal health strategies.

7. Recommendations

To reduce neonatal mortality and meet SDG 3.2 targets, African health systems should prioritise the development and implementation of context-specific, evidence-based clinical guidelines. This must be supported by investments in healthcare infrastructure, workforce capacity, and equitable access to essential services. Efforts should also focus on strengthening infectious disease control, expanding immunisation coverage, and improving maternal and neonatal care, including prenatal screening and neonatal intensive care services. Building institutional capacity and fostering regional research collaboration are essential for sustainable progress.

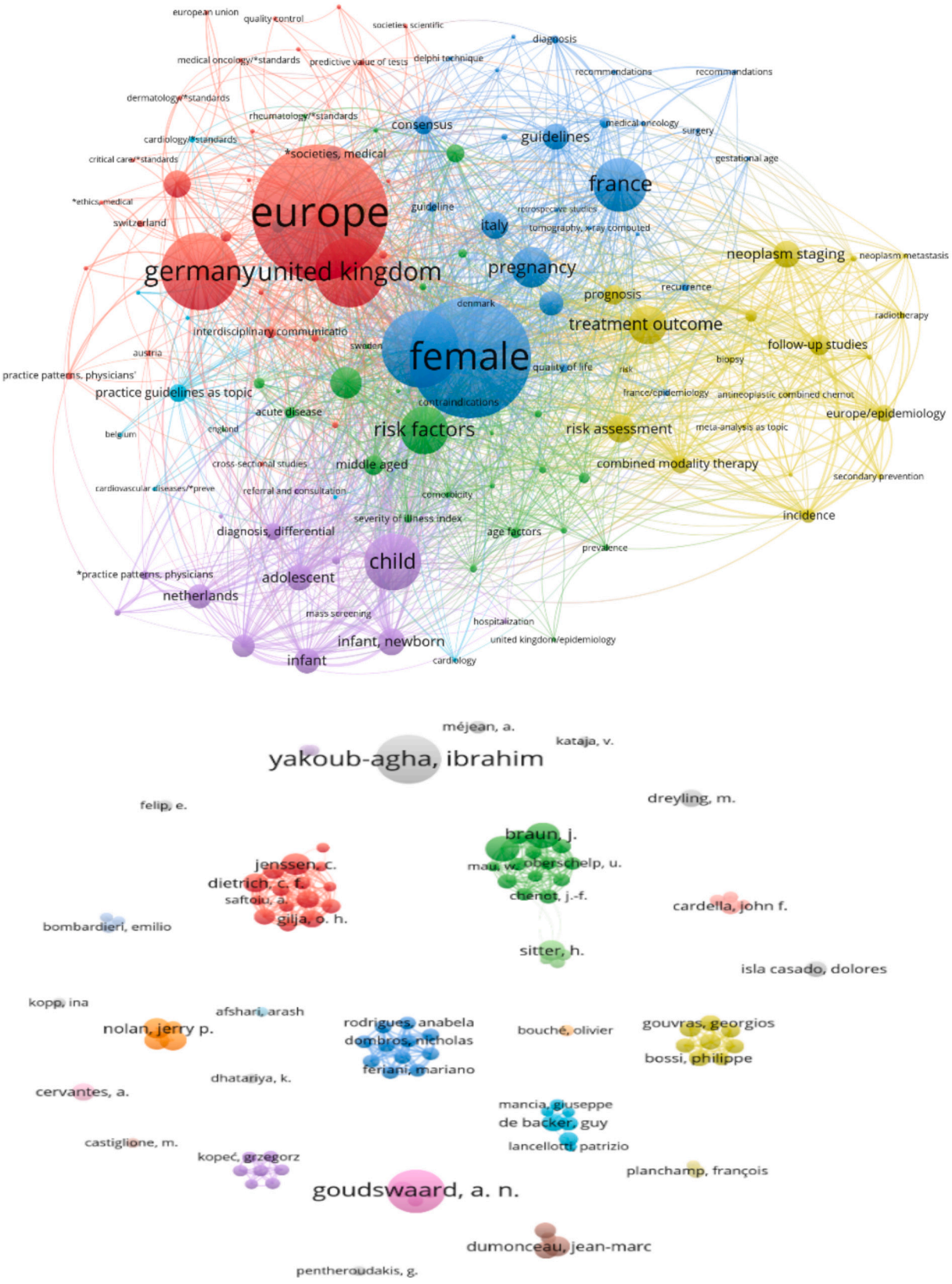

Fig. 5. a *(up): Network analysis of keywords in selected documents. 5b(down)* Co-authorship network illustrating collaborative patterns among researchers in Europe and Africa based on guideline publications.

Statement of artificial intelligence (AI) use

Microsoft Copilot was moderately used in this manuscript. It was used to perform the interrupted time series analysis (ITS) and for improving the grammar of the manuscript. The authors however reviewed the content and takes responsibility of the manuscript.

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CRediT authorship contribution statement

Frank Adusei-Mensah: Writing – review & editing, Writing – original draft, Methodology, Conceptualization. **Ahmed Ould Boudia:** Writing – review & editing, Formal analysis. **Richard Osei Agjei:** Writing – original draft. **Luqman Awoniyi:** Writing – review & editing, Writing – original draft. **Ismaila Temitayo Sanusi:** Writing – original draft. **Jussi Kauhanen:** Supervision.

Declaration of competing interest

The authors states that they have no conflicting interest towards the writing of this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dialog.2025.100272.

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