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Global, regional, and national burden of neonatal disorders and subtypes attributable to air pollution from 1990 to 2021: a systematic analysis of the Global Burden of Disease Study 2021

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Abstract

Background Exposure to air pollution is associated with the development of numerous neonatal diseases (NDs). This study aimed to evaluate the worldwide changes in the burden of NDs attributable to air pollution from 1990 to 2021.

Methods The 2021 Global Burden of Disease Study (GBD) reported neonatal deaths attributable to air pollution and the associated age-standardized rates and disability-adjusted life years (DALYs). To assess the global burden of NDs and the subtypes, age-standardized DALY rates (ASDARs) and age-standardized death rates (ASDRs) were employed. The estimated annual percentage change (EAPC) was used to track global and regional temporal trends from 1990 to 2021. Spearman's rank correlation coefficients were applied to evaluate the relationship between the sociodemographic index (SDI), ASDARs, and ASDRs for NDs. The slope inequality index and concentration index were derived from health inequality analyses to measure international disparities. Finally, frontier analysis were employed to determine optimal burden for NDs at corresponding SDI levels.

Results In 2021, the air pollution-related NDs resulted in 496,966 deaths and 44,737,311 DALYs worldwide. The burden for NDs showed a decreasing trend globally in past three decades. Neonatal preterm birth was the most severe subtype of NDs in 2021. With the global and regional increase in the SDI, the ASDR and ASDAR for five NDs subtypes have decreased. Significant absolute and relative income disparities in the burden of DALYs and mortality due to NDs were observed worldwide. Frontier analysis indicated inverse correlations between the ASDR/ASDAR and SDI, with the Solomon Islands, a low SDI country, showing the smallest overall differences.

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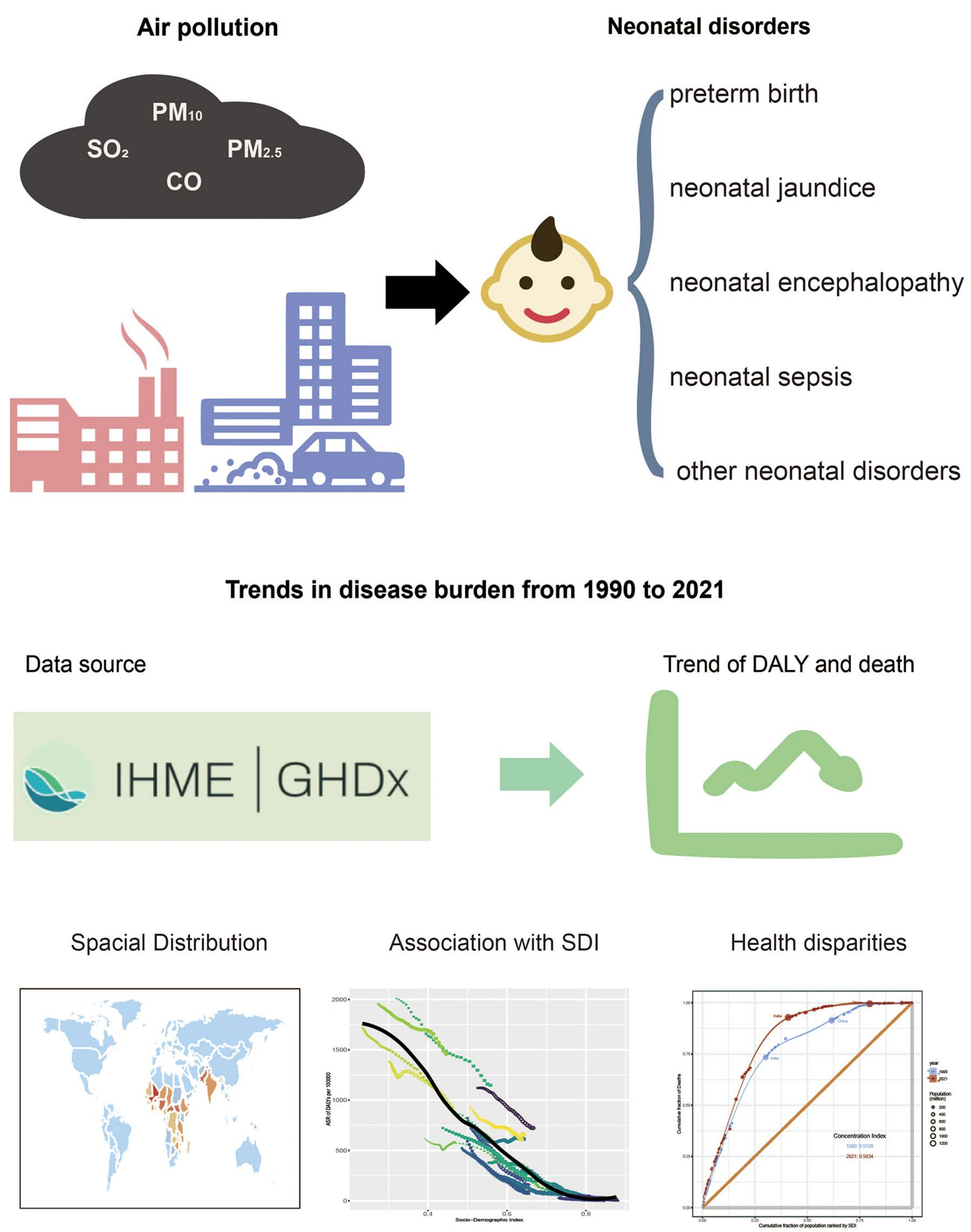
Conclusion Although the burden of air pollution-induced NDs has decreased, it remains a significant public health concern, with regional disparities. More nuanced policies and preventive measures are needed to reduce the burden of NDs.

Graphical abstract



Keywords Air pollution, Neonatal diseases, Death, Disability-adjusted life years, Solomon Islands

Introduction

As the future of a nation, the health of children is pivotal in societal progress and development [1–3]. Over the past few decades, economic and medical advancements have substantially improved newborn health, resulting in a reduced incidence of neonatal diseases (NDs) [4, 5]. However, with the rapidly economic development, the health impact of air pollution on children has become increasingly concerning. According to the Global Burden of Disease Study 2021 (GBD 2021), air pollution was a major contributor to the global disease burden in 2021, accounting for 8.0% of total disability-adjusted life years (DALYs), and was identified as the second leading risk factor for neonatal deaths worldwide [6]. In 2021, air pollution was associated with an estimated 496,966 neonatal deaths globally, only inferior to behavioral risk factors (1,482,668 deaths) [6, 7]. Substantial evidence has demonstrated a strong association between air pollution exposure and neonatal disorders. Ambient particulate matter, particularly $PM_{2.5}$, can impair respiratory function in children and increase the risk of severe neonatal respiratory distress, thereby contributing to elevated neonatal mortality [8]. During pregnancy, exposure to air pollutants may disrupt fetal development, leading to adverse birth outcomes such as low birth weight (LBW) and preterm birth [9, 10]. These outcomes may result from the transplacental penetration of particulate matter, which can bind to placental proteins or lipids, induce oxidative stress, and alter DNA methylation patterns—mechanisms linked to neonatal conditions including PTB, LBW, and congenital anomalies [11, 12]. In addition, the metallic components of air pollution can generate reactive oxygen species, serving as key mediators of oxidative damage and systemic inflammatory responses [9].

Given the heightened vulnerability of neonates to environmental exposures—particularly in the context of accelerating industrialization—the health consequences of air pollution warrant urgent global attention. Thus，it is critical to comprehensively assess the burden of neonatal disorders attributable to air pollution at both global and regional scales. However, existing studies have primarily focused on individual neonatal conditions using GBD data from 1990 to 2019, lacking comprehensive analyses across various subtypes of neonatal disorders [13–15]. Moreover, disparities in socioeconomic development among countries affect investments in healthcare infrastructure and environmental governance—factors that contribute to international inequities in disease burden. To date, most studies have examined country-specific patterns, such as in China or India, without fully addressing the complex cross-national heterogeneity or the temporal influences of socioeconomic development on disease burden [16, 17]. These limitations hinder a comprehensive understanding of the global burden of neonatal disorders attributable to air pollution.

Utilizing data from the GBD2021, this study aimed to achieve three main objectives: (1) to conduct a detailed and comprehensive quantitative assessment and trend analysis of the global and regional burden of NDs caused by air pollution; (2) to evaluate the regional burden differences of NDs related to air pollution across areas with different levels of social development; and (3) to estimate the minimum achievable disease burden at corresponding level of socioeconomic development in various countries and forecast the global burden trends of five ND subtypes over the next decade, offering guidance for developing disease prevention and control policies in different countries and regions.

Methods

Overview and data sources

This study presents a secondary analysis of the GBD2021 data, detailing the global, national, and regional impacts of air pollution-related NDs and their subtypes in 2021 and their trends from 1990 to 2021. The mortality rate and disability-adjusted life years (DALYs) for NDs were obtained from the GBD 2021 dataset (available at https://vizhub.healthdata.org/gbd-results/). The dataset encompasses the annual disease burden of 371 diseases across 204 countries and territories since 1990, including their associated risk factors [6, 18]. We extracted data on NDs and five of their subtypes from 1990 to 2021, including neonatal preterm birth, hemolytic disease and other neonatal jaundice, neonatal sepsis, and other neonatal infections, neonatal encephalopathy due to birth asphyxia and trauma, and other neonatal disorders. We analyzed estimates of deaths and DALYs in addition to their corresponding 95% uncertainty intervals (95% UIs). The analysis included global data, 21 GBD regions, and 204 countries and territories. Additionally, we incorporated the sociodemographic index (SDI), a metric developed by GBD researchers to gauge the socioeconomic status of a region. The SDI integrates per capita income, educational attainment, and fertility rates into a single index ranging from 0 to 1, reflecting the socioeconomic health and developmental progress of a region or country [19].

Definitions

Data on the burden of NDs attributable to air pollution in this study were obtained from the GBD 2021 and are publicly available through the GBD results tool (https://vizhub.healthdata.org/gbd-results/). The approach in GBD to estimating air pollution exposure has been described previously study [7]. Briefly, it integrates multiple data sources—including WHO databases, meteorological data, ground monitoring, population distribution, and satellite measurements—to generate population-weighted average exposure levels at the regional scale using the GEOS-Chem chemical transport model and Bayesian hierarchical modeling. In accordance with the GBD2021, the specific causes of NDs were categorized into five subtypes: neonatal preterm birth (NPB), hemolytic disease and other forms of neonatal jaundice (HD), neonatal sepsis and other neonatal infections (NS), neonatal encephalopathy resulting from birth asphyxia and trauma (NE), and other neonatal disorders (OND). Age-standardized death rates (ASDRs) indicate the number of deaths per 100,000 individuals across all age groups, whereas the age-standardized DALYs rate (ASDAR) accounts for both the years lived with disability and the years of life lost due to premature mortality per 100,000 people, standardized for age.

Statistical analysis

Burden description

This study examined the ND burden from 1990 to 2021 by analyzing the ASMRs and ASDRs per 100,000 population across 21 GBD regions and 204 countries. The findings are depicted through world maps and composite line charts. Additionally, the burden of the five ND subtypes is represented using bar charts.

Trend analysis

The estimated annual percentage change (EAPC) served as a metric to delineate the evolving burden of NDs and their subtypes across global and regional dimensions. The EAPC quantified the annual rate of change over a defined period, as derived from a linear regression analysis. A negative EAPC signified a decreasing trend, whereas a positive EAPC denoted an increasing trend. A bar chart was used to visually represent the temporal dynamics of five neonatal diseases across 21 GBD regions spanning from 1990 to 2021.

Correlation analysis

The SDI served as a comprehensive indicator of the economic development level within a region or country. An elevated SDI signified superior socio-economic conditions and improved health outcomes. We categorized the 204 countries and regions into four quartiles based on their SDI values: low (0–0·454743), lower-middle (0·454743–0·607679), upper–middle (0·607679–0·689504), high (0·689504–0·805129), and very high (0·805129–1). We employed Spearman's rank correlation coefficients to assess the correlation between the SDI and ND metrics, specifically the ASDRs and ASDARs.

Inequality analysis

Disparities in the ND burden across nations were quantified using the slope inequality index (SII) and the health inequality concentration index (HCI). The SII measures absolute health disparities between the most and least advantaged subgroups within a population, incorporating socioeconomic factors, such as education and wealth, through a weighted regression analysis. Conversely, the HCI is a relative inequality measure that reflects the concentration of health indicators within either disadvantaged or advantaged groups. The SII was determined by regressing ASDRs and ASDARs for NDs against the income-related social status scale. The HCI was derived from the area between the Lorenz curve and the line of equality, plotting the cumulative proportion of ASDRs and ASDARs against the ordered cumulative population distribution by the SDI. A negative HCI value signified a higher burden in countries with a lower SDI, while a positive value indicated a higher burden in countries with a higher SDI. The magnitude of health inequality is directly proportional to the absolute value of the SII and HCI.

Frontier analysis

Frontier model was constructed using data on age-standardized disability-adjusted life year rates (ASDAR) and age-standardized death rates (ASDR) from 1990 to 2021, with the SDI as the predictor. We applied locally weighted scatterplot smoothing (LOESS) and local polynomial regression with varying smoothing spans (0.3, 0.4, and 0.5) to generate frontier curves. Frontier curve represents the minimum achievable burden (namely the optimal or ideal burden level) at corresponding level of socioeconomic development as measured by SDI. For each country and region, the gap between the observed ASDAR and ASDR in 2021 and the estimated frontier values was calculated based on their SDI, to evaluate the potential for reducing the burden of NDs. Frontier analysis, by incorporating national SDI levels, not only reveals spatiotemporal trends in disease burden but also helps to identify the gap between a country's current burden and the theoretically achievable lower burden, given its level of socioeconomic development. According to frontier analysis, we aimed to pinpoint countries and regions with the most significant discrepancies, specifically: (1) the 15 countries exhibiting the greatest divergence from the optimal level across all nations; (2) the five countries with the burden of NDs closest to ideal levels among those with a relatively low SDI (SDI<0·5); and (3) within high SDI countries (SDI>0·85), the five countries with the largest deviation from the ideal standard.

ARIMA model

The Auto-Regressive Integrated Moving Average (ARIMA) model is a widely used technique in epidemiology for forecasting time-series data. The ARIMA model is specified by three parameters: p (autoregressive), d (differencing), and q (moving average). We utilized the autocorrelation function (ACF) and partial autocorrelation function (PACF) to determine the three parameters. Then, Model selection was based on the Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), and the coefficient of determination (R^2). Lower AIC and BIC values indicate better model parsimony and likelihood of representing the true data structure, whereas a higher R^2 reflects improved goodness of fit. Residuals were tested for white noise using the Ljung-Box Q test, ACF, and PACF. Once validated, the model was used to forecast the burden of NDs attributed to air pollution from 2022 to 2032.

Data analysis and visualization were conducted using R Studios 4.3.3, with a two-tailed p-value of $<0{\cdot}05$ deemed to indicate statistical significance. The R packages used in this study are as following: dplyr, ggplot2, reshape2, readxl, ggpubr, ggh4x, ggsci, magrittr and grid.

Results

The graphical abstract can see in Supplementary material Figure S1.

Global, regional, and National burden of NDs 1990–2021

In 2021, air pollution was estimated to have caused 496,966 neonatal deaths worldwide (95% UI: 419,486 to 580,880), with an ASDR of 8·03 per 100,000 live births (6·78 to 9·39). NDs attributed to environmental pollution resulted in 44,737,311 DALYs globally (37,766,690 to 52,293,054), with an ASDAR of 723·6 per 100,000 people (610·39 to 845·18). Among the 21 GBD regions, the highest ASDR was observed in Western Sub-Saharan Africa (16·23; 95% UI: 13·84 to 18·82), followed by South Asia (12·75; 95% UI: 10·41 to 15·54) and Eastern Sub-Saharan Africa (12·65; 95% UI: 9·93 to 15·61). The top three regions regarding the ASDR were also Western Sub-Saharan Africa (1460·55), South Asia (1148·1), and Eastern Sub-Saharan Africa (1138·43) (Table 1). Among the 204 countries assessed, Mali, Nigeria, the Central African Republic, and Pakistan had the outstanding ASDR and ASDAR for NDs in 2021 (Fig. 1A, B).

Between 1990 and 2021, the global ASDR for NDs attributed to air pollution decreased annually by 1·53 per 100,000, from 12·45 to 8·03. The EAPC was – 1·53% (95% UI: – 1·63 to – 1·43). The global ASDAR decreased from 1,120·38 per 100,000 in 1990 to 723·06 in 2021, with an EAPC of – 1·53% (95% UI: – 1·63 to – 1·43) (Table 2; Fig. 2). Regionally, Eastern Europe (EAPC = – 6·92%) and Central Europe (EAPC = – 6·82%) experienced the most pronounced declines in ASDRs and ASDARs. At the national level, Belarus exhibited the steepest reduction in ASDRs and ASDARs, with an EAPC of – 9·73% (Supplementary material Table S1).

In summary, from 1990 to 2021, both the ASDR and ASDAR for NDs due to air pollution exhibited a downward trend worldwide. Interetingly, the burden of NDs were higher in males than females (Fig. 2).

Burden of the five ND subtypes

In 2021, the leading causes of neonatal mortality were NPB, HD, NS, OPD, and NE, with the following respective number of deaths: 227,616, 7,258, 54,026, 155,361, and 52,436. The corresponding ASDRs were 3·68, 0·12, 0·87, 2·51, and 0·85 per 100,000 population. Globally, the number of DALYs and the ASDARs for these conditions were 20,494,978 (331·25), 680,206 (10·99), 4,861,948 (78·57), 13,980,139 (225·97), and 4,472,004 (76·29) per 100,000 people, respectively (Tables 1 and 2). As depicted in Fig. 3, NPB and NE were found to be significant contributors to the ND burden across the 21 GBD regions, with a particular concentration in Western Sub-Saharan Africa, South Asia, and Eastern Sub-Saharan Africa. In these 21 GBD regions, the death and DALY rates, along with the corresponding age-standardized criteria, for NE were slightly higher than for NPB. However, in the remaining 19 regions, NPB had higher death and DALYs, in addition to the age-standardized rates, than the other four subtypes.

As shown in Fig. 4, the burden of HD in Australasia has seen the most substantial reduction in the past three decades, with EAPCs for deaths and DALYs of – 10·62% and – 9·99%, respectively. The most notable decrease in the burden of NE was observed in Eastern Europe, with EAPC values of – 8·93% for deaths and – 8·92% for DALYs. Central Europe experienced significant reductions in NS, with an EAPC of – 7·26% for deaths and – 7·24% for DALYs, whereas ONDs had an EAPC of – 6·92% for deaths and – 6·91% for DALYs. The most pronounced decline in NPB was noted in Tropical Latin America, with an EAPC of – 7·52% for both deaths and DALYs. Between 1990 and 2021, a significant decrease in the incidence of the five ND subtypes was observed in Andean Latin America, Central Europe, East Asia, Eastern Europe, Southern Latin America, Tropical Latin America, and Western Europe. Globally, the ASDR and ASDAR of NPB (EAPC = – 1·73), HD (–3·52), NS (–0·96), NE (–1·15), and OND (–1·77) all exhibited significant reductions. Concurrently, the global ASDARs for these five NDs subtypes have decreased (Table 2); however, NE is increasing in the Caribbean, while NS is rising in the Caribbean and Central Asia, and ONDs are increasing in the Caribbean, Central Asia, and Australasia (Supplementary material Table S2).

Association between the NDs subtypes burden and SDI

In 2021, approximately 247,443 neonatal deaths were attributed to air pollution in low-SDI regions, with an ASDR of 14·33. Additionally, approximately 22,272,985 DALYs were lost due to NDs in these regions, with

Table 1 Mortality from air pollution-related neonatal diseases and changes from 1990 to 2021

Characteristics	Number of deaths cases No. *102 (95% UI),1990	ASDR per 100,000 No. (95% UI),1990	Number of deaths cases No. *102 (95% UI),2021	ASDR per 100,000 No. (95% UI),2021	ASDR-EAPC
Global	7967 [7291–8627]	12.45 [11.39–13.48]	4969.66 [4194.86-5808.8]	8.03 [6.78–9.39]	-1.53 [-1.63 to-1.43]
Cause					
Neonatal preterm birth	3991 [3602–4445]	6.24 [5.63–6.94]	2276.16 [1891.6-2714.67]	3.68 [3.06–4.39]	-1.73 [-1.8to-1.66]
Hemolytic disease and other neonatal jaundice	231 [194–291]	0.36 [0.3–0.45]	75.28 [58.19–99.21]	0.12 [0.09–0.16]	-3.52 [-3.69to-3.35]
Neonatal sepsis and other neonatal infections	706 [611–811]	1.1 [0.96–1.27]	540.26 [453.71-640.84]	0.87 [0.73–1.04]	-0.96 [-1.09to-0.84]
Other neonatal disorders	856 [601–1070]	1.34 [0.94–1.67]	524.36 [367.64-655.88]	0.85 [0.59–1.06]	-1.77 [-1.94to-1.61]
Neonatal encephalopathy due to birth asphyxia and trauma	2183 [1906–2530]	3.41 [2.98–3.95]	1553.61 [1291.04-1872.56]	2.51 [2.09–3.03]	-1.15 [-1.32to-0.98]
GBD region					
Oceania	7 [5–10]	6.9 [5.08–9.08]	13.27 [8.72–18.08]	6.46 [4.25–8.81]	-0.21 [-0.4 to -0.01]
Central Asia	39 [31–49]	4.18 [3.32–5.15]	25.85 [18.86–34.95]	2.63 [1.92–3.56]	-1.5 [-1.81 to -1.2]
Southeast Asia	583 [516–658]	9.85 [8.71–11.11]	197.55 [158.42–240.24]	3.66 [2.94–4.45]	-3.26 [-3.42 to -3.1]
East Asia	727 [609–848]	6.33 [5.31–7.39]	49.32 [39.62–60.87]	0.89 [0.72–1.1]	-6.33 [-6.83 to -5.82]
Eastern Europe	30 [25–36]	2.12 [1.74–2.51]	2.43 [1.79–3.16]	0.28 [0.21–0.37]	-6.92 [-7.34 to -6.5]
High-income Asia Pacific	4 [3–7]	0.47 [0.27–0.73]	0.52 [0.35–0.73]	0.09 [0.06–0.13]	-4.93 [-5.32 to -4.54]
Central Europe	27 [23–31]	3.3 [2.84–3.78]	2.14 [1.63–2.67]	0.42 [0.32–0.53]	-6.82 [-7.08 to -6.55]
Australasia	0 [0–1]	0.29 [0.04–0.69]	0.23 [0.03–0.54]	0.13 [0.02–0.31]	-1.91 [-2.22 to -1.59]
Western Europe	16 [14–20]	0.74 [0.61–0.88]	3.41 [2.38–4.68]	0.17 [0.12–0.24]	-4.54 [-4.59 to -4.49]
Southern Latin America	14 [8–21]	2.69 [1.49–4.06]	2.52 [1.06–4.08]	0.68 [0.28–1.1]	-4.61 [-4.91 to -4.31]
High-income North America	15 [12–18]	0.68 [0.54–0.82]	3.73 [2.58–4.96]	0.19 [0.13–0.25]	-3.85 [-4.07 to -3.64]
Caribbean	34 [26–43]	7.83 [6.06–9.98]	25.99 [17.93–34.6]	6.81 [4.7–9.07]	-0.22 [-0.39 to -0.04]
Andean Latin America	51 [40–64]	9.13 [7.09–11.36]	10.14 [6.45–15.25]	1.7 [1.08–2.56]	-5.24 [-5.57 to -4.91]
Central Latin America	139 [118–162]	5.8 [4.93–6.77]	25.35 [18.5-33.32]	1.35 [0.99–1.78]	-4.62 [-4.8 to -4.44]
Tropical Latin America	106 [89–122]	6.56 [5.51–7.57]	14.58 [10.39–19.17]	0.88 [0.63–1.16]	-6.36 [-6.68 to -6.03]
Western Sub-Saharan Africa	929 [842–1021]	21.72 [19.68–23.88]	1381.53 [1178.78-1602.59]	16.23 [13.84–18.82]	-0.8 [-0.88 to -0.72]
South Asia	3670 [3256–4085]	22.33 [19.82–24.86]	1929.89 [1575.49-2351.77]	12.75 [10.41–15.54]	-1.76 [-1.84 to -1.68]
Central Sub-Saharan Africa	189 [147–243]	15.36 [11.97–19.77]	201.91 [142.55-271.44]	9.45 [6.67–12.7]	-1.23 [-1.46 to -1]
Eastern Sub-Saharan Africa	819 [725–910]	19.1 [16.9-21.22]	829.44 [651.08-1023.94]	12.65 [9.93–15.61]	-1.22 [-1.33 to -1.11]
Southern Sub-Saharan Africa	80 [66–95]	10.31 [8.44–12.3]	57.09 [43.53–74.68]	7.3 [5.57–9.56]	-1.07 [-1.18 to -0.96]
North Africa and Middle East	319 [266–372]	8.03 [6.71–9.37]	98.96 [77.03-124.32]	2.35 [1.83–2.95]	-3.75 [-4.11 to -3.38]
High SDI	64 [54–74]	1.06 [0.89–1.23]	11.16 [9.15–13.16]	0.23 [0.18–0.27]	-4.69 [-4.82 to -4.57]
High-middle SDI	375 [324–434]	4.27 [3.69–4.94]	40.53 [33.07–47.89]	0.72 [0.59–0.85]	-5.88 [-6.18 to -5.58]
Low SDI	2210 [2022–2408]	20.88 [19.1-22.74]	2474.43 [2041.43-2933.31]	14.33 [11.82–16.99]	-1.07 [-1.15 to -1]
Low-middle SDI	3593 [3201–3998]	19.38 [17.27–21.57]	1951.63 [1606.05-2363.73]	10.46 [8.61–12.67]	-1.99 [-2.08 to -1.89]
Middle SDI	1721 [1566–1897]	8.59 [7.82–9.47]	489.21 [410.46–578.3]	3.19 [2.68–3.78]	-3.19 [-3.37 to -3]

GBD2021: Global Burden of Disease Study 2021, UI: uncertainty interval, NDs: neonatal diseases, SDI: sociodemographic index, DALYs: disability-adjusted life years, ASR: age-standardized rate

an ASDAR of 1289·97. The disease burden associated with NDs caused by air pollution was disproportionately higher in areas with a low SDI. Notably, the most significant reduction in ASDRs and ASDARs was observed in high–middle SDI regions, with an EAPC of −5·88 for both metrics (Tables 1 and 2). From 1990 to 2021, across the 21 GBD regions, ASDR and ASDAR for NDs and their five subtypes decreased as the SDI increased, demonstrating a significant negative correlation with SDI (Fig. 5). Between 1990 and 2021, globally and in South Asia, Southeast Asia, and Southern Saharan Africa, the ASDRs and ASDARs for air pollution-related NDs remained above expected levels based on the SDI. In contrast, the burden in the Caribbean was initially

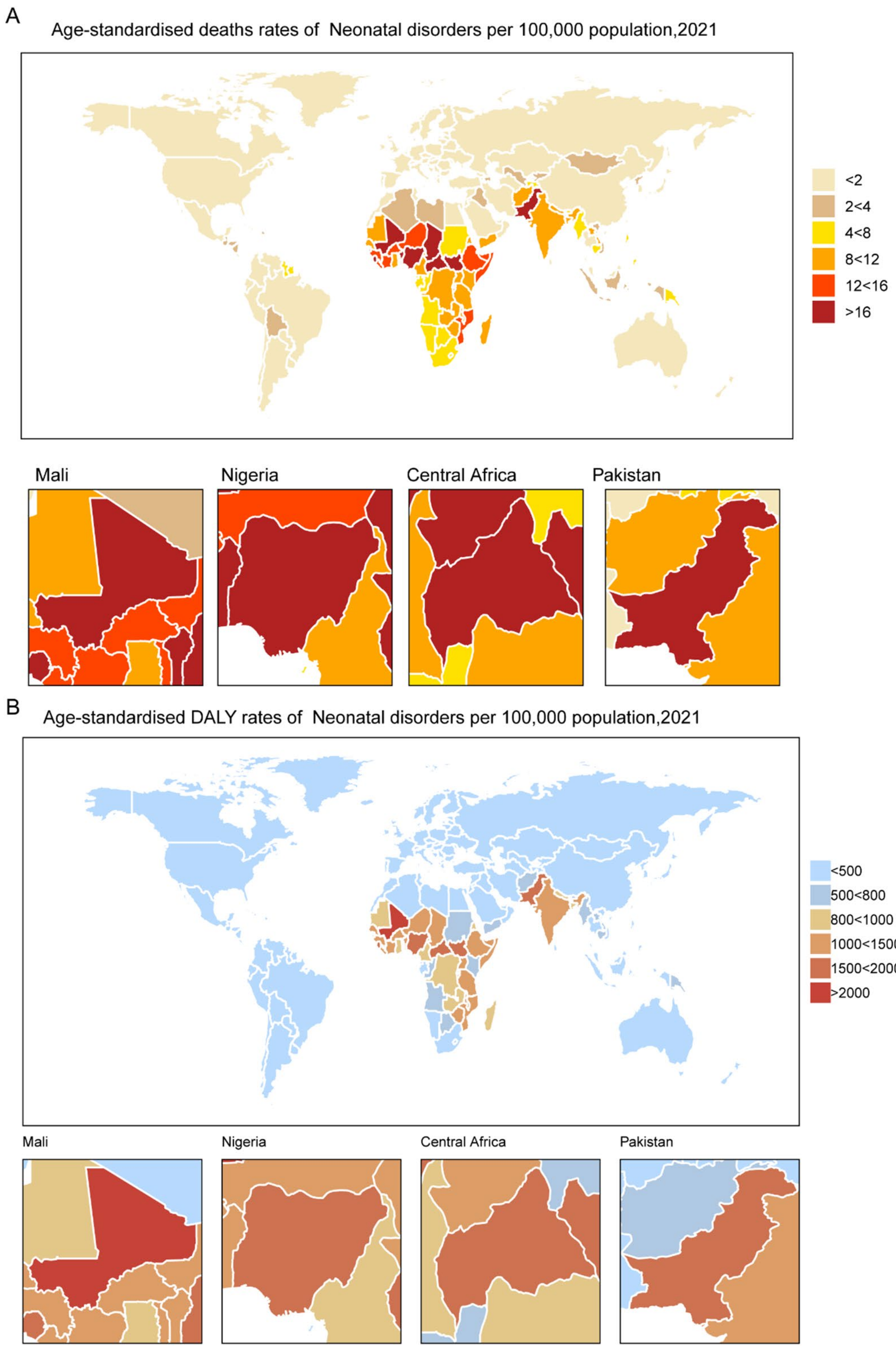


Fig. 1 Age-standardized rates (ASRs) for deaths and disability-adjusted life years rates (DALYs) for neonatal diseases in 204 countries worldwide

lower than expected but gradually increased above the expected levels (Fig. 5A, B). For HD, the burden has been consistently higher than the expected SDI levels globally and in South Asia over the past three decades; however, in Western Sub-Saharan Africa, the burden has been lower than expected since 2013 (Fig. 5C, D). In high-income Asia-Pacific regions, the burden of NE in East Asia has gradually declined in recent years, falling below

Table 2 DALY from air pollution-related neonatal diseases and changes from 1990 to 2021

Characteristics	Number of DALY cases No. *102 (95% UI),1990	ASR-DALY per 100,000 No. (95% UI),1990	Number of DALY cases No. *102 (95% UI),2021	ASR-DALY per 100,000 No. (95% UI),2021	EAPC-DALY
Global	717,105 [656233–776547]	1120.38 [1025.34-1213.25]	447373.11 [377666.9-522930.54]	723.06 [610.39-845.18]	-1.53 [-1.63 to -1.43]
Cause					
Neonatal preterm birth	359,336 [324329–400145]	561.4 [506.76–625.1]	204949.78 [170383.42-244355.07]	331.25 [275.38-394.95]	-1.73 [-1.8to-1.66]
Hemolytic disease and other neonatal jaundice	20,770 [17455–26190]	32.49 [27.3-40.96]	6802.06 [5267.41-8953.49]	10.99 [8.51–14.47]	-3.51 [-3.68to-3.34]
Neonatal sepsis and other neonatal infections	63,545 [55028–73026]	99.4 [86.07-114.19]	48619.48 [40833.1-57671.76]	78.57 [65.98–93.19]	-0.96 [-1.09to-0.84]
Other neonatal disorders	77,064 [54138–96297]	120.41 [84.61-150.43]	47200.4 [33098.87-59025.8]	76.29 [53.49–95.4]	-1.77 [-1.93to-1.61]
Neonatal encephalopathy due to birth asphyxia and trauma	196,390 [171495–227629]	306.68 [267.81-355.51]	139801.39 [116179.5-168501.73]	225.97 [187.79-272.36]	-1.15 [-1.32to-0.98]
GBD region					
Oceania	669 [493–881]	621.04 [457.44-817.45]	1194.27 [784.99-1627.31]	581.73 [382.39-792.64]	-0.21 [-0.4 to -0.01]
Central Asia	3555 [2819–4372]	376.71 [298.68-463.28]	2327.42 [1698.46-3145.96]	236.82 [172.8-320.15]	-1.5 [-1.81 to -1.2]
Southeast Asia	52,503 [46432–59216]	886.42 [784.06-999.85]	17782.33 [14261.78-21621.63]	329.59 [264.31-400.78]	-3.26 [-3.42 to -3.1]
East Asia	65,409 [54825–76355]	570.06 [477.81-665.48]	4441.62 [3567.76-5481.58]	80.36 [64.54–99.19]	-6.32 [-6.83 to -5.81]
Eastern Europe	2745 [2248–3246]	191.05 [156.46-225.95]	219.24 [161.16-285.05]	25.38 [18.65–33.01]	-6.92 [-7.34 to -6.5]
High-income Asia Pacific	405 [235–623]	42.62 [24.72–65.51]	47.02 [31.9-65.78]	8.21 [5.56–11.49]	-4.92 [-5.32 to -4.53]
Central Europe	2456 [2114–2807]	297.29 [255.88-339.86]	192.41 [146.81-240.76]	38.18 [29.12–47.78]	-6.82 [-7.08 to -6.55]
Australasia	40 [5–94]	26.32 [3.57–61.68]	20.47 [2.99–48.72]	11.89 [1.74–28.31]	-1.91 [-2.22 to -1.59]
Western Europe	1476 [1229–1764]	66.27 [55.15–79.19]	307.52 [214.51-421.51]	15.58 [10.86–21.35]	-4.54 [-4.59 to -4.49]
Southern Latin America	1228 [683–1851]	242.11 [134.55-364.96]	227.28 [95.75-367.52]	60.97 [25.66–98.62]	-4.61 [-4.91 to -4.31]
High-income North America	1348 [1064–1629]	61.35 [48.41–74.12]	335.86 [232.83-446.13]	17.21 [11.93–22.87]	-3.85 [-4.07 to -3.64]
Caribbean	3044 [2356–3879]	705.1 [545.64-898.36]	2339.63 [1614.01-3114.24]	613.4 [423.16-816.49]	-0.22 [-0.39 to -0.04]
Andean Latin America	4624 [3589–5753]	821.96 [638.05-1022.65]	913.44 [581.38-1373.13]	153.54 [97.7-230.84]	-5.24 [-5.57 to -4.91]
Central Latin America	12,505 [10628–14608]	522.01 [443.65-609.82]	2283.2 [1666.2-2999.72]	121.68 [88.81-159.89]	-4.62 [-4.8 to -4.44]
Tropical Latin America	9512 [7995–10971]	590.44 [496.32–681]	1313.42 [936.17-1725.44]	79.37 [56.58-104.25]	-6.35 [-6.68 to -6.03]
Western Sub-Saharan Africa	83,596 [75764–91926]	1954.97 [1771.71-2149.44]	124345.2 [106105.72-144232.06]	1460.55 [1246.2-1694.11]	-0.8 [-0.88 to -0.72]
South Asia	330,353 [293120–367723]	2010.43 [1783.91-2237.83]	173751.89 [141864.1-211685.28]	1148.1 [937.41-1398.69]	-1.76 [-1.84 to -1.68]
Central Sub-Saharan Africa	17,009 [13256–21898]	1382.54 [1077.66-1779.47]	18174.31 [12832.45-24430.16]	850.38 [600.47-1143.03]	-1.23 [-1.46 to -1]
Eastern Sub-Saharan Africa	73,724 [65228–81933]	1718.83 [1520.99–1910]	74659.26 [58608.91-92164.21]	1138.43 [893.73-1405.35]	-1.22 [-1.33 to -1.11]
Southern Sub-Saharan Africa	7204 [5899–8592]	927.98 [759.85-1106.73]	5138.7 [3918.37-6721.23]	657.5 [501.38-859.97]	-1.07 [-1.18 to -0.96]
North Africa and Middle East	28,682 [23958–33457]	723.09 [604.1-843.47]	8912.95 [6940.56-11195.04]	211.68 [164.79-265.91]	-3.74 [-4.11 to -3.38]
High SDI	5757 [4828–6681]	95.68 [80.23-111.05]	1005.28 [825.01-1185.97]	20.28 [16.65–23.93]	-4.69 [-4.81 to -4.57]
High-middle SDI	33,755 [29179–39047]	384.34 [332.26–444.6]	3651.15 [2979.53-4314.64]	64.81 [52.88–76.6]	-5.88 [-6.18 to -5.57]
Low SDI	198,955 [182009–216767]	1879.09 [1719.05-2046.94]	222729.85 [183759.57-264026.23]	1289.97 [1064.27-1529.2]	-1.07 [-1.15 to -1]

Table 2 (continued)

Characteristics	Number of DALY cases No. *102 (95% UI),1990	ASR-DALY per 100,000 No. (95% UI),1990	Number of DALY cases No. *102 (95% UI),2021	ASR-DALY per 100,000 No. (95% UI),2021	EAPC-DALY
Low-middle SDI	323,388 [288125–359863]	1744.86 [1554.68-1941.68]	175696.09 [144599.65-212761.89]	941.85 [775.15-1140.54]	-1.99 [-2.08 to -1.89]
Middle SDI	154,909 [140933–170706]	773.47 [703.71-852.33]	44047.41 [36965.39-52057.22]	287.58 [241.35–339.9]	-3.18 [-3.37 to -3]

EAPC: estimated annual percentage change

the expected levels (Fig. 5E, F). The incidence of NPB has further exhibited a declining trend globally, especially in Western Sub-Saharan Africa, Eastern Sub-Saharan Africa, North Africa, Middle East, and Southern Sub-Saharan Africa over the past three decades. Despite this, the rates remained considerably higher than the anticipated levels based on the SDI (Fig. 5G, H). NS in South Asia has increasingly surpassed the projected SDI levels (Fig. 5I, J). In recent years, the prevalence of ONDs in Central Sub-Saharan Africa, the Caribbean, Central Asia, and Central Europe has surpassed expected levels, necessitating the development of targeted policies and interventions. Overall, it is evident that the burden of NDs has significantly decreased globally and across the 21 GBD regions with an increase in the SDI. However, disparities persist between the burden of air pollution-related NDs and their subtypes in each region and expected SDI-based levels. Regional health authorities should consider the correlation between national economic development and the burden of ND subtypes when devising health management strategies.

Health inequality across countries

Since the ND burden was found to be highly correlated with the SDI, we conducted a detailed analysis to explore health disparities. Our analysis revealed significant absolute and relative income disparities in the DALY and the mortality burden of NDs worldwide (Fig. 6). The ND burden is predominantly found in regions with a low SDI. A comparative analysis of data from 1990 to 2021 indicates a reduction in health disparities. Figure 6A illustrates that the DALY rate gap between low- and high-SDI countries narrowed from 4054·795 in 1990 to 1448·897 in 2021, while the CI for DALYs increased from 0·5129 in 1990 to 0·5834 in 2021. The SII for neonatal DALYs indicated an increase in inequality among countries with moderate SDI levels (Fig. 6B). The mortality CI shifted from − 0·5129 in 1990 to − 0·5834 in 2021, and the SII improved from − 45·24,857 in 1990 to − 16·09583 in 2021 (Fig. 6C, D). These findings suggest a positive reduction in the unequal burden of NDs from 1990 to 2021.

Frontier analysis

Figure 7 depicts an inverse correlation between the SDI and both the ASDAR and ASDR for NDs. Notably, As SDI increased over time, both the age-standardized disability-adjusted life year rates (ASDAR) and age-standardized death rates (ASDR) of NDs showed a declining trend, indicating an overall reduction in burden with socioeconomic development. The results of our frontier analysis indicated that among the countries and territories with a lower SDI, the Solomon Islands exhibited the most ideal levels of DALYs and deaths from NDs attributed to air pollution. Mali, South Sudan, Nigeria, Sierra Leone, Pakistan, Benin, Guinea, Bissau, Guinea, Côte d'Ivoire, Comoros, Ethiopia, Lesotho, Gambia, and India are the 15 countries that exhibit suboptimal control over the burden of NDs associated with air pollution. Among the low and middle SDI countries, the burden of NDs in the Solomon Islands, Somalia, Niger, Vanuatu, and Bhutan is closest to the ideal curve. Similarly, among high SDI countries, Taiwan (Province of China), the United Kingdom, the Republic of Korea, the Netherlands, and Germany still have considerable potential for improvement in controlling their national burden of NDs.

Predicting the prevalence of NDs

The forecast results for the ASDARs of NDs from 2022 to 2032 are shown in Fig. 8. Based on the prediction results, the global burden of HD (Fig. 8A), NPB (Fig. 8C), and OND (Fig. 8E) are expected to show a downward trend over the next decade, although the decline in the OND burden will be relatively mild. In contrast, the ASDR and ASDAR caused by NE are predicted to continue to rise from 2022 to 2032 (Fig. 8B). Interestingly, among all subtypes of NDs, the global trends of the ASDR and ASDAR for NS are expected to remain relatively stable over the next decade (Fig. 8D).

Discussion

This study conducted a secondary analysis of the GBD2021 data to systematically assess the distribution and trends of air pollution-related NDs and their subtypes from 1990 to 2021. It also examined health disparities among countries and aimed to establish the ideal minimum mortality rates and DALYs for NDs in each nation. The findings revealed a substantial decrease in mortality and DALYs for air pollution-related NDs and their subtypes worldwide between 1990 and 2021; however, the primary burden continues to be concentrated in

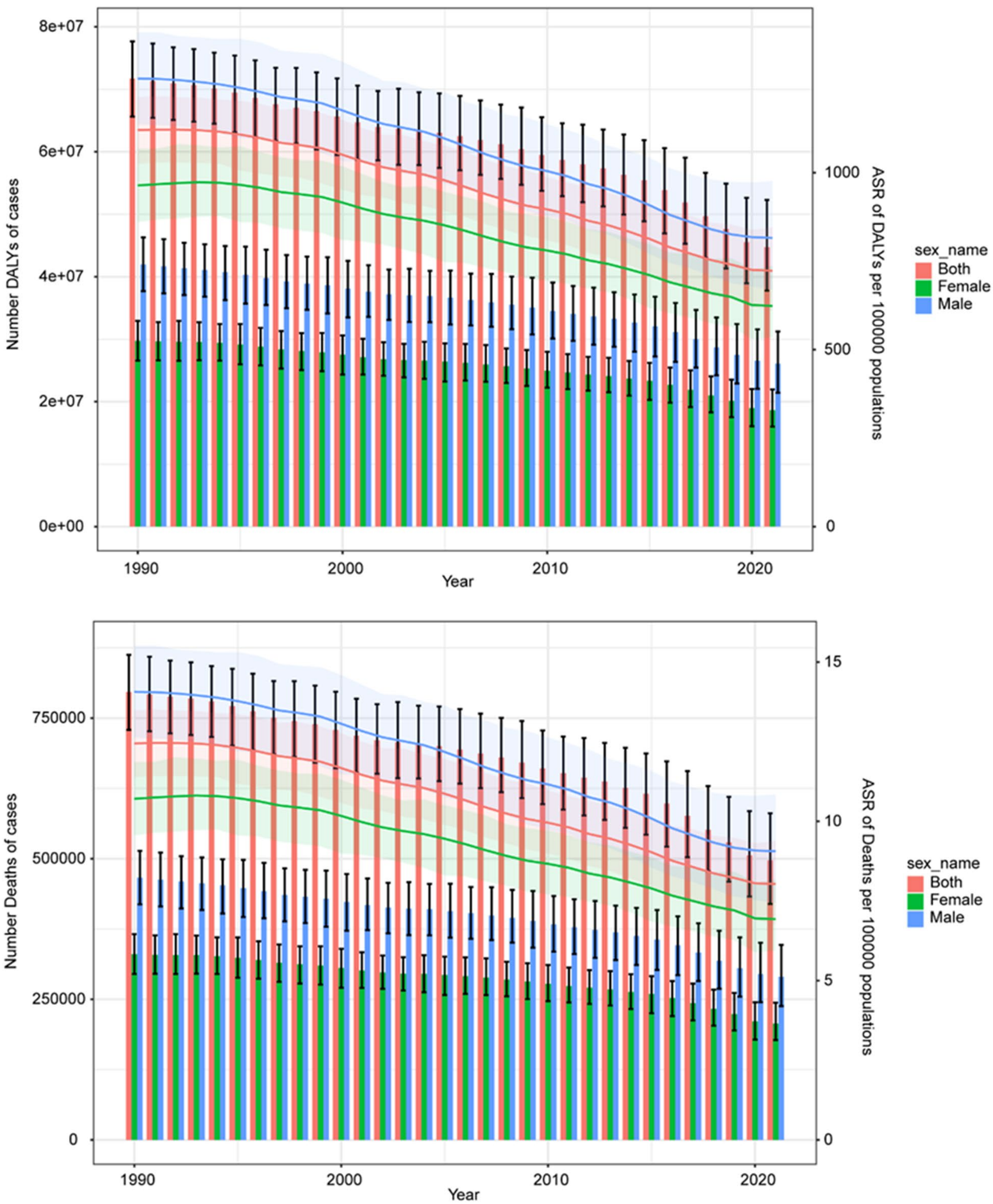


Fig. 2 Time trend of the number of cases and disability-adjusted life years (DALYs) caused by air pollution-related neonatal diseases from 1990 to 2021

low SDI regions, including Mali, Nigeria, Central African Republic, and Pakistan [20]. Considering the high prevalence of NDs in populous Asia and Africa, these regions must formulate policies and strategies to further mitigate the impact of NDs. Additionally, the study identified a notable gender disparity in the global burden of NDs, with males exhibiting a significantly higher burden than females. The mechanisms contributing to this variation

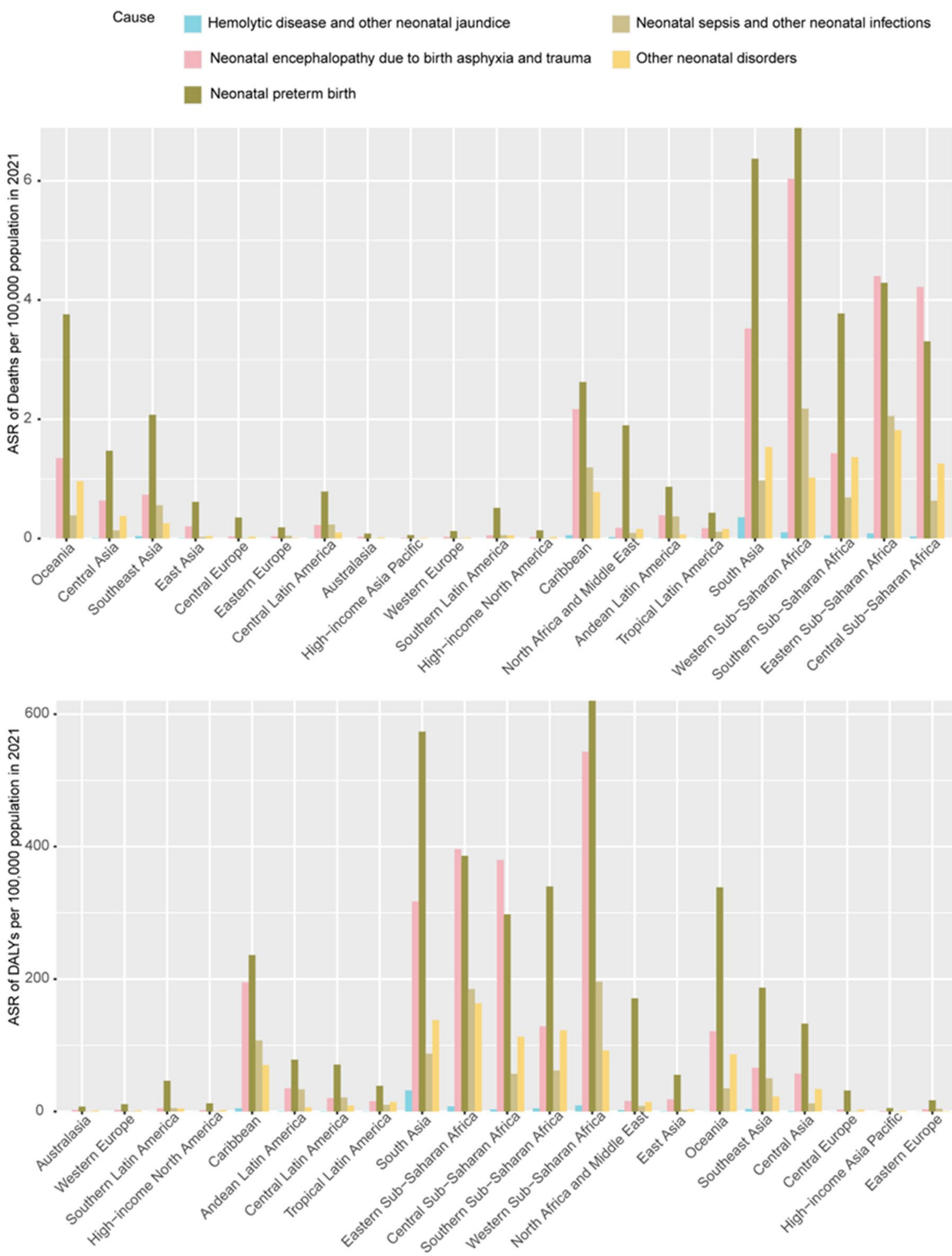


Fig. 3 Age-standardized rates (ASRs) for deaths and disability-adjusted life years rates (DALYs) for five neonatal disease subtypes in 21 Global Disease Burden (GBD) regions

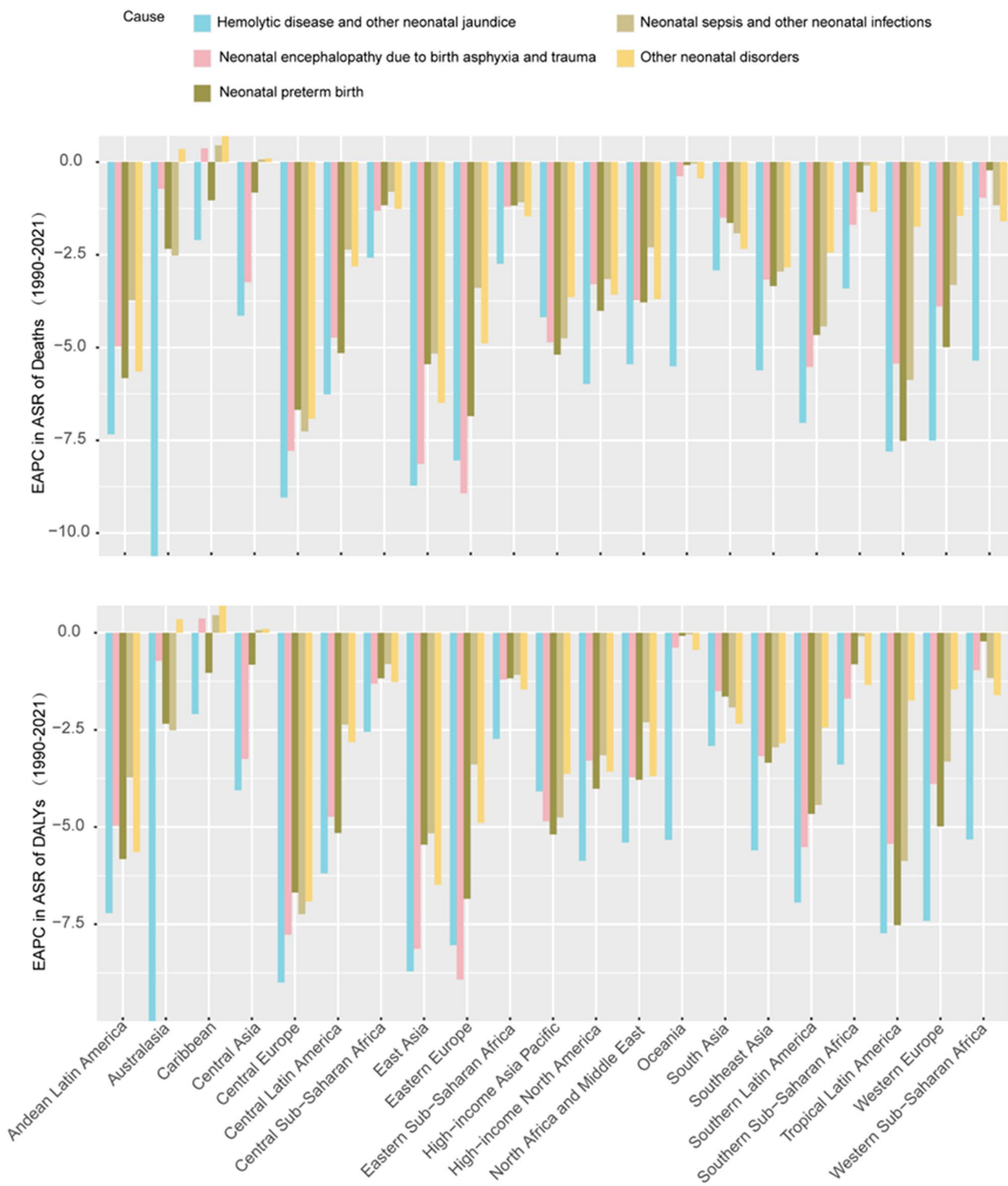


Fig. 4 Estimated annual percentage changes (EAPCs) in age-standardized rates (ASRs) for deaths and disability-adjusted life years rates (DALYs) for five neonatal disease subtypes in 21 Global Disease Burden (GBD) regions

are not yet fully understood. This disparity might be attributed to the fact that male infants grow more rapidly and demand a greater oxygen supply than female infants, rendering them more vulnerable to the effects of air pollution [21–23], or may be influenced by genetic susceptibility to air pollutant [24].

Among the five subtypes of NDs, NPB constitutes a substantial proportion of the ND burden, particularly in

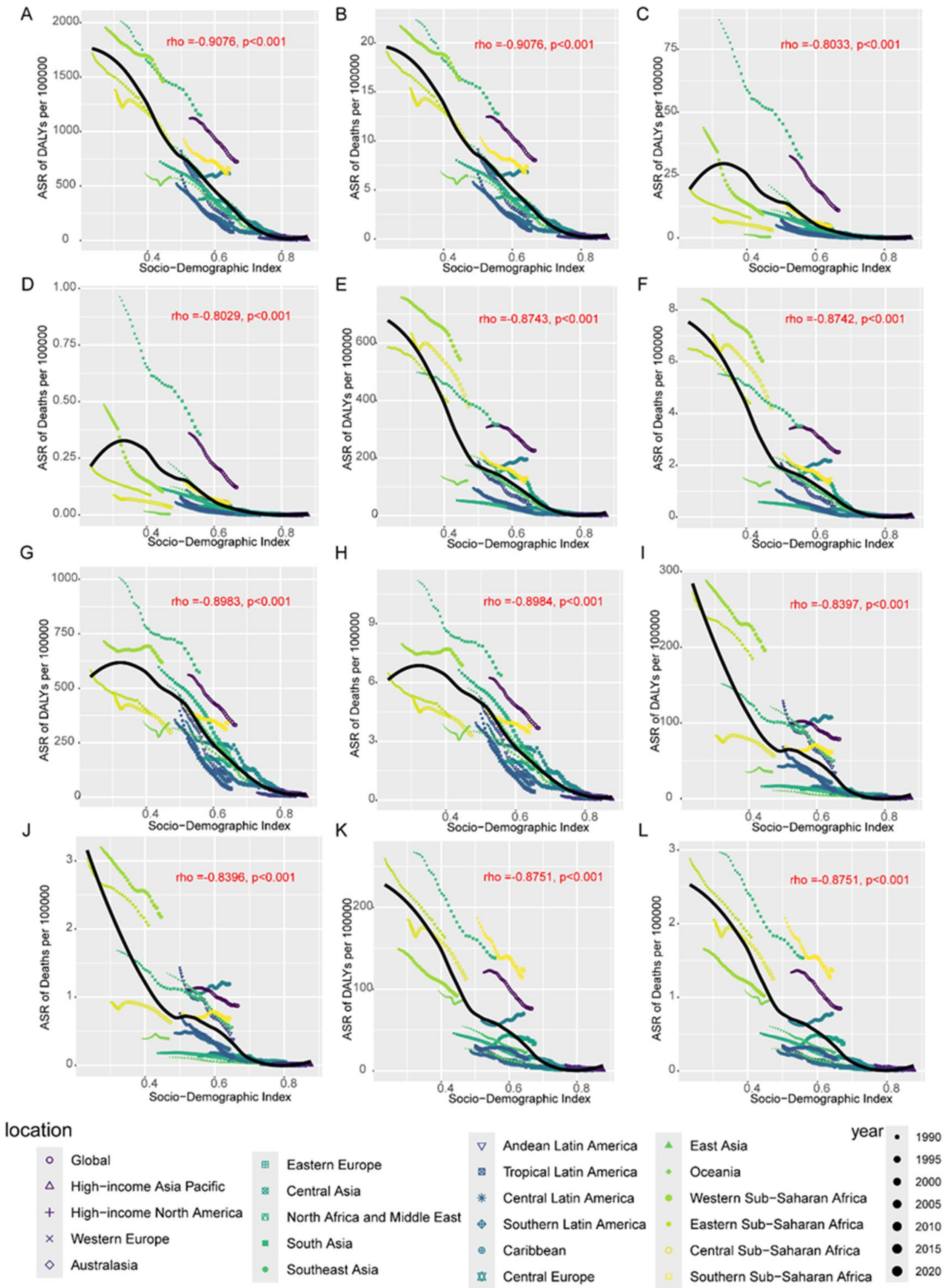


Fig. 5 Age-standardized rates (ASRs) for death due to neonatal diseases (NDs) and their subtypes and the relationship between disability-adjusted life years (DALYs) and the socioeconomic index (SDI). **A**, **B**) NDs. **C**, **D**) Hemolytic disease and other neonatal jaundice. **E**, **F**) Neonatal encephalopathy due to birth asphyxia and trauma. **G**, **H**) Neonatal preterm birth. I, J) Neonatal sepsis and other neonatal infections. **K**, **L**) Other neonatal disorders

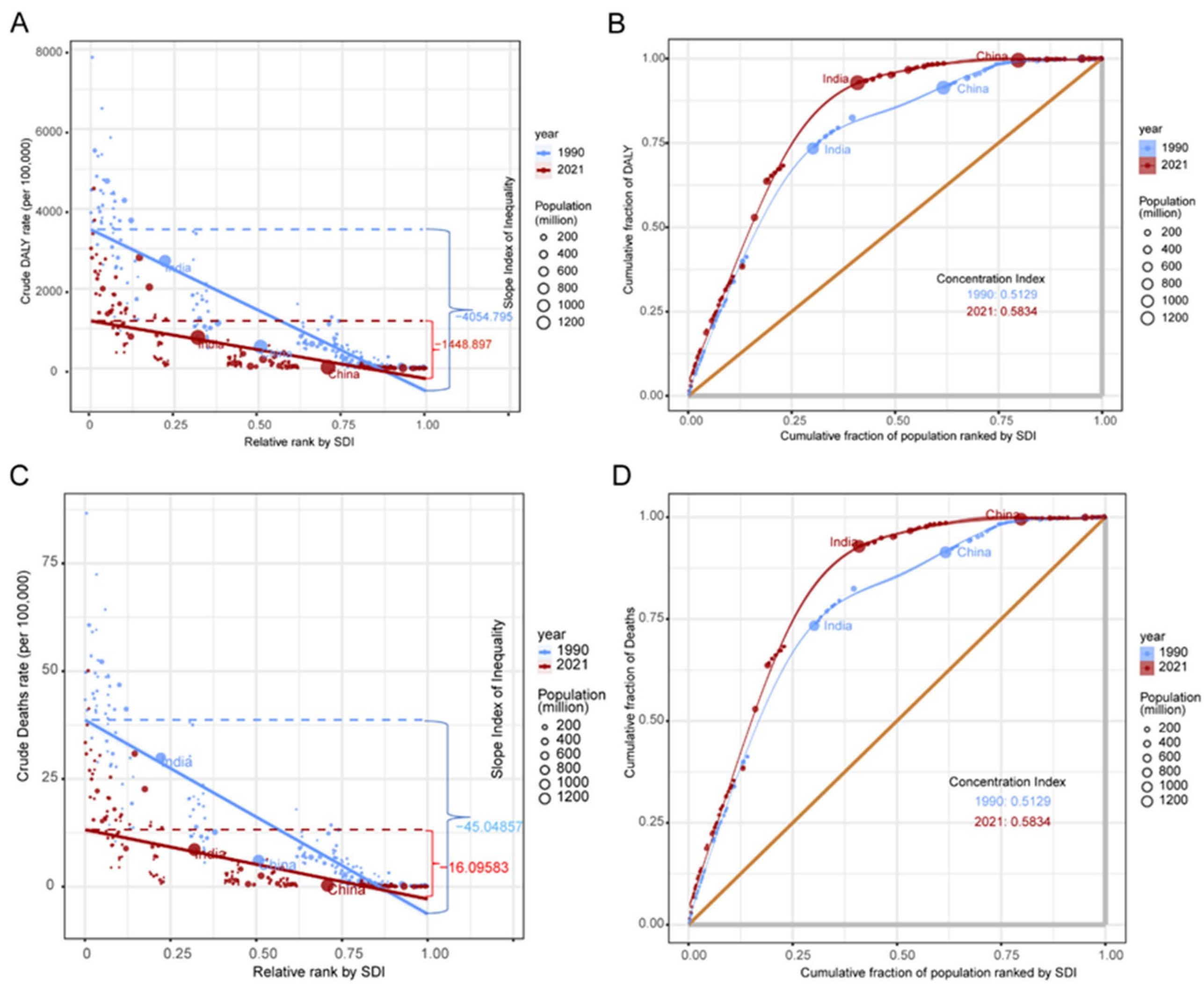


Fig. 6 Health inequality regression and concentration curves for disability-adjusted life years (**A** and **B**) and mortality (**C** and **D**). SDI, sociodemographic index

regions with lower SDI scores, such as Africa and South Asia. Indoor air pollution resulting from cooking with unclean fuels and indoor smoking is a significant contributor to the elevated incidence of NPB in these areas [25, 26]. In Nigeria, the use of unclean cooking fuels by pregnant women has been associated with an increased risk of stillbirth [27]. With improved access to maternal and prenatal care, a notable reduction in the global burden of NPB has been observed in both developed and developing nations [28, 29]. Therefore, local government initiatives to promote prenatal care, implement prenatal care programs, and reduce exposure to air pollution can contribute to alleviating the burden of NPB. Policymakers should prioritize the prevention and management of NPB when developing relevant health policies and interventions.

Air pollution includes both ambient and indoor sources [30]. One study based on the GBD2019 data analyzed the ND burden attributable to environmental and household particulate matter. There was an inverted V-shaped relationship between DALYs and the SDI for NDs caused by ambient air pollution, whereas a strong negative correlation existed for those related to indoor air pollution [16]. We utilized the latest GBD dataset to analyze the global and regional burden of NDs attributable to air pollution, thereby enhancing our understanding of its significant impact to some extent. Our study found that the global and regional burdens of air pollution-related NDs and their subtypes were highly negatively correlated with the SDI. In countries with low-to-medium SDI levels, increased air pollution exposure, higher concentrations of harmful air pollutants, and reduced investment in air quality management and healthcare are likely to result in new air pollution-related diseases [31]. Conversely, in countries with higher SDI levels, effective air quality management may result in a lower burden of air

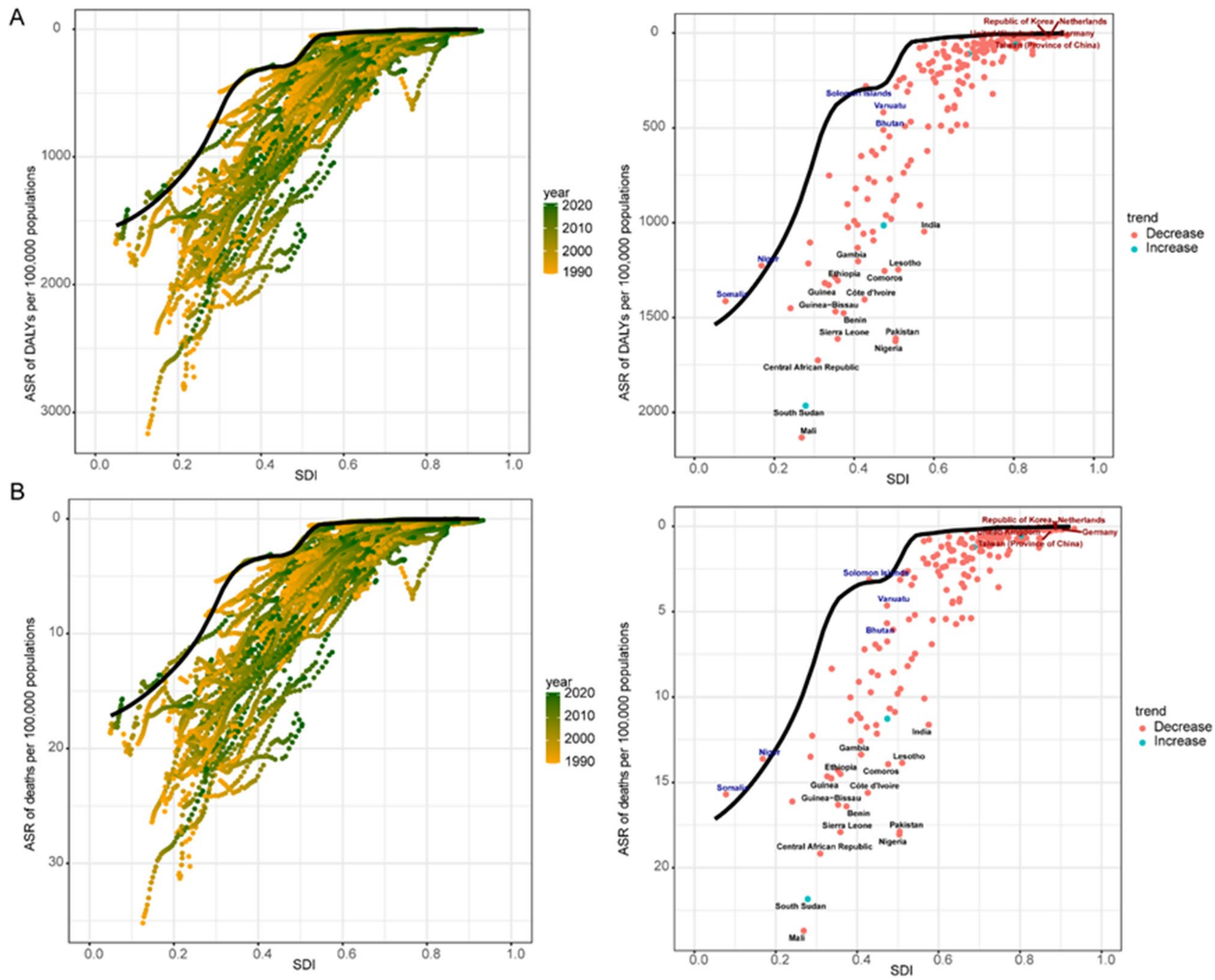


Fig. 7 Frontier analysis involving the sociodemographic index (SDI) and neonatal diseases in 2021. The frontier is shown as a solid black line, with each country or region represented by a dot. As SDI increased over time, both the age-standardized disability-adjusted life year rates (ASDAR) and age-standardized death rates (ASDR) of NDs showed a declining trend, indicating an overall reduction in burden with socioeconomic development. The five countries closest to the fitted line (ideal level) are labelled blue in the lower SDI countries, the five countries furthest from the fitted line are labelled red in the higher SDI countries, and the 15 countries furthest from the fitted line are labelled black in all countries

pollution-related NDs than in developing nations [32, 33]. Thus, developing countries should enhance air quality management to accelerate social development, including stricter industrial dust control, improved energy consumption structures, and regulated exhaust emissions, thereby mitigating health impacts on pregnant women and newborns.

Our inequality analysis revealed that while health inequalities in the burden of NDs due to air pollution decreased from 1990 to 2021, they continued to increase in low- and middle-income SDI countries. This disparity may stem from inadequate healthcare and economic development in underdeveloped countries coupled with escalating air pollution [34, 35]. Notably, PM2·5, caused by air pollution, increases the risk of mortality and disease burden among local infants by increasing NPB, further intensifying global development inequalities [16]. Frontier analysis revealed substantial potential for reducing the burden of NDs across countries, particularly in those with low SDI, where a large gap remains between the actual and optimal burden levels. The Solomon Islands, despite high climate hazards and limited source [36], had an actual burden level closely close to the minimum achievable burden for its current level of socioeconomic development. It may be attributed to effective resource allocation systems and heightened awareness of environmental protection and neonatal care. The Solomon island government had implemented numerous policies aimed at the protection and management of environmental resources, including the rapid deployment of renewable energy, construction of the Tina River Hydropower, innovative forest management, and

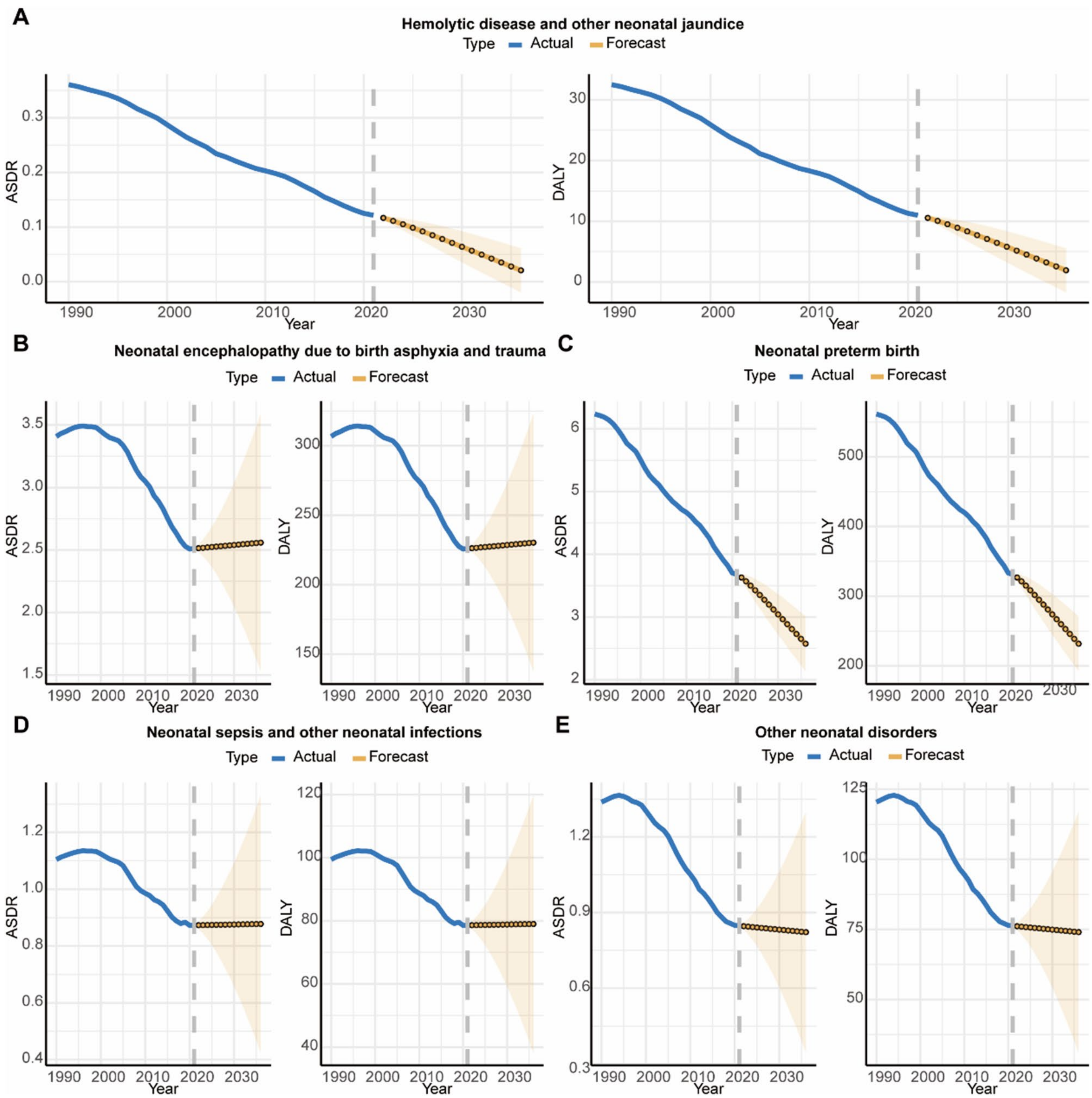


Fig. 8 Prediction of age standardized death rate (ASDR) and disability-adjusted life years (DALYs) of five neonatal disease subtypes using ARIMA models

participation in international cooperation, such as the National Action Plan on Ship Emissions [37, 38]. These initiatives have improved local air quality and boosted local incomes. The environmental protection strategies for the Solomon Islands offer valuable lessons for countries and regions struggling with air quality management. In addition, to strengthen the management of neonatal disorders, the Early Essential Newborn Care (EENC) program was launched, which improved the professional capacity of healthcare providers and contributed to a reduction in neonatal mortality to some extent [39]. Other low-income countries may benefit from critically adapting the Solomon Island's experiences in environmental protection, resource optimization, and healthcare investment based on their own national contexts, which could help reduce the burden of disease.

Limitations and future perspectives

This study has some limitations. First, the heterogeneity in the GBD2021 data is unavoidable. Our analysis was based directly on the GBD database, using data on NDs attributable to air pollution. Despite the strengths of the

GBD framework in offering standardized and comprehensive estimates, it does not account for all possible confounding variables. Factors such as maternal health, prenatal care access, and other environmental exposures may not be fully adjusted, potentially impacting the precision and validity of our results. Future studies could consider stratified analyses focusing more on these potential confounders. Additionally, the development of more advanced algorithms to mitigate the impact of confounding is important. Next, our research is based solely on GBD data, therefore, incorporating additional databases may improve the accuracy of this study. Lastly, we were unable to elucidate the underlying mechanisms responsible for the higher burden of air pollution–related neonatal disorders observed in males compared with females. Current research in this area remains limited. Further investigation into the biological and environmental mechanisms underlying this sex-based disparity may have important implications for improving neonatal health. In addition, regions with low SDI should increase investments in environmental governance, improve the efficiency of resource allocation, and enhance health care investment to reduce health disparities related to disease burden.

Conclusion

In conclusion, although we observed a reduction in the burden of NDs over the past three decades, it continues to be substantial in low- and middle-income countries. Furthermore, although health disparities between countries have diminished, regional inequalities within countries persist. Improving air quality could further reduce the disease burden among neonates. The Solomon Islands's achievements in environmental protection and the management of ND burdens provide a model that other developing nations could adopt.

Abbreviations

GBD2021	Global Burden of Disease Study 2021
UI	Uncertainty interval
NDs	Neonatal diseases
NPB	Neonatal preterm birth
NE	Neonatal encephalopathy due to birth asphyxia and trauma
NS	Neonatal sepsis and other neonatal infections
OND	Other neonatal diseases
HD	Hemolytic disease and other neonatal jaundice
SDI	Sociodemographic index
DALYs	Disability-adjusted life years
EAPC	Estimated annual percentage change
ASDR	Age-standardized death rates
ASDAR	Age-standardized disability-adjusted life years
CI	Concentration index
SII	Slope inequality index
ARIMA	Auto-Regressive Integrated Moving Average

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

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Author contributions

Yan Li：Conceptualization，Data curation，Software，Writing– original draft，Validation，Writing– review & editing. Rongjie Ye：Methodology，Software，Validation，Visualization，Writing– original draft. Shuqi Yang：Software，Validation，Visualization，Writing– review and editing. Hao Yu: Visualization，Writing– review and editing. Boqian Yu：Investigation, Writing– review & editing. Jing Feng：Validation, Writing– review & editing. Quan Yuan：Conceptualization, Formal analysis，Project administration, Supervision, Writing– review & editing.

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Data availability

All data in this study are publicly available through the GBD 2021 portal, please visit the Global Health Data Exchange at https://ghdx.healthdata.org/gbd-2021.

Declarations

Ethics approval and consent to participate

Ethics approval is exempted for this study.

Patient consent for publication

Not applicable.

Provenance and peer review

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Competing interests

The authors declare no competing interests.

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