Clinical Epidemiology

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ORIGINAL RESEARCH

Burden of Carbon Monoxide Poisoning in Asian Countries From 1990 to 2021 and Its Projection Until 2030: An Analysis of the Global Burden of Disease Study 2021

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Background: Carbon monoxide (CO) poisoning represents a significant contributor to injury burden across Asia. This study seeks to assess the burden of CO poisoning in Asia from 1990 to 2021 utilizing data from the Global Burden of Disease Study (GBD) 2021.
Methods: Data on the burden of CO poisoning across 49 Asian countries were extracted from GBD 2021. The variations in burden were analyzed according to year, gender, location, age, and Socio-Demographic Index (SDI). Analyses included Joinpoint analysis to evaluate temporal trends, the age-period-cohort model to assess disease burden trends, the slope index of inequality and concentration index for assessing health disparities, frontier analysis for estimating potential outcomes based on developmental stages, and the auto-regressive integrated moving average model to predict the disability-adjusted life year (DALY) rates.
Results: During 1990–2021, the age-standardized incidence rate (average annual percent change (AAPC) = −0.83, 95% CI: −0.94 to −0.73), age-standardized mortality rate (AAPC = −2.01, 95% CI: −2.20 to −1.81), and DALY rates (AAPC = −2.39, 95% CI: −2.54 to −2.23) for CO poisoning across Asia declined. In 2021, females experienced a lower burden than males, and countries in higher latitudes bore a greater burden. The burden was more pronounced in extreme age groups, with an elevated cohort risk in the 1967–1971 birth cohort (relative risk (RR) = 1.045, 95% CI: 0.96–1.14). Health inequality analyses showed a reduction in disparities between countries with varying SDI levels. Frontier analysis identified potential improvements in reducing the burden across different countries. However, there was no notable correlation between this burden and SDI levels. The age-standardized disability-adjusted life year rate is predicted to continue declining from 2022 to 2030.
Conclusion: This study analyzes the burden of CO poisoning in Asia, revealing a decline from 1990 to 2021, with variations across countries and higher burdens in males and extreme age groups. It suggests a reduction in health inequalities and forecasts a continued decline in the burden by 2030.
Keywords: carbon monoxide poisoning, burden, trends, age-period-cohort, socio-demographic index, arima prediction

Introduction

Carbon monoxide (CO) poisoning is the leading cause of accidental poisoning and one of the most common causes of fatal poisoning globally.[1] CO is an invisible, odorless gas primarily produced by the incomplete combustion of fuels.[2,3] Common household sources include gas appliances, and the burning of wood and coal.[4–6] At low levels (0.3–1% carboxyhemoglobin, COHb), endogenous CO serves as a neurotransmitter, helping regulate inflammation, apoptosis, and cell proliferation.[7,8] However, exposure to higher concentrations of CO (≥2% COHb) impairs oxygen delivery, leading to

Received: 17 December 2024
Accepted: 8 April 2025
Published: 15 April 2025

poisoning. Clinically, CO poisoning is characterized by elevated COHb levels due to exogenous CO exposure. The severity of symptoms depends on COHb levels: mild exposure (2–10% COHb) may cause headache, fatigue, nausea, dizziness, and confusion, while severe poisoning (≥65% COHb) can lead to seizures, coma, and even death.[3,9–11]

Currently, there is no effective antidote for CO poisoning. Clinical management focuses on promptly removing patients from the exposure source and current treatments for CO poisoning involve 100% normobaric oxygen (NBO_2) and hyperbaric oxygen (HBO_2) at pressures of 2.5–3 atmospheres. Both approaches aim to accelerate the elimination of CO from the blood by increasing the oxygen pressure. However, these treatments have limitations.[10] HBO_2, in particular, carries risks of middle-ear and pulmonary injuries, as well as oxygen toxicity, especially when used in critically ill patients.[12] Some individuals may suffer from long-term neurological sequelae such as memory loss, difficulty concentrating, emotional disturbances, and impaired motor coordination, which usually occur within 20 days of CO poisoning, persist for a month or more, and can significantly reduce quality of life.[7,10,13–20] Additionally, research has shown that CO poisoning increases the risk of congestive heart failure (CHF),chronic kidney disease (CKD), and acute kidney injury (AKI), further contributing to the disease burden.[21–23] These sequelae place considerable strain on healthcare systems and families, often resulting in substantial financial costs for medical treatment, support services and rehabilitation.[24–26]

Clinical challenges and social burdens associated with CO poisoning underscore the necessity for effective prevention strategies. Implementing preventive measures can greatly lower the incidence of such poisoning[27–29] Data from the Global Burden of Disease Study (GBD) show that in 2021, the age-standardized mortality rate (ASMR) for CO poisoning in Asia (0.39, 95% uncertainty interval (UI): 0.21 to 0.48) was higher than the global average (0.37, 95% UI: 0.25 to 0.42), as well as the rates in Africa (0.11, 95% UI: 0.07 to 0.2) and the Americas (0.2, 95% UI: 0.2 to 0.21). Similarly, the age-standardized disability-adjusted life year rate (ASDR) in Asia (16.36, 95% UI: 9.02 to 19.74) surpassed both the global average (15.57, 95% UI: 11 to 17.93) and the rates in Africa (5.99, 95% UI: 3.88 to 10.21) and the Americas (9.99, 95% UI: 9.53 to 10.49) in 2021.[6] While existing studies on the burden of CO poisoning have primarily focused on global trends and individual country analyses,[6,30] there is a lack of comprehensive research on its impact in the Asian region. This gap leaves a shortage of detailed epidemiological data to inform public health policies and resource allocation for CO poisoning in Asia. Therefore, there is an urgent need for in-depth studies that examine the trends, causes, and disparities of CO poisoning across the region.

Using data from the Institute for Health Metrics and Evaluation (IHME), the purpose of this study is to evaluate the burden of CO poisoning across 49 Asian countries from 1990 to 2021. The analysis will include death rates, age-standardized incidence rates (ASIR), ASDR, ASMR, and disability-adjusted life years (DALYs). It will also examine the impact of factors such as sex, age, Socio-Demographic Index (SDI) and region. Additionally, this study will forecast future trends in the burden of CO poisoning in Asia until 2030.

Materials and Methods

Data Source

GBD 2021 conducts an in-depth assessment of the health burden of 371 diseases and injuries across 204 countries and regions from 1990 to 2021. It estimates crucial health metrics such as healthy life expectancy (HALE), years of life lost (YLLs), years lived with disability (YLDs) and DALYs, based on data from over 100,000 sources. There are three steps to prepare data for poisoning by CO. To begin with, all available data were identified and assigned to GBD causes of death.[6] Moreover, poorly defined causes were reassigned to other underlying causes of death through garbage code redistribution. Garbage code redistribution was done by age, sex, country, year, and International Classification of Diseases (ICD) system; this method is complex and variable by type of garbage code, but generally requires estimating the proportions of each group of garbage codes that should be reassigned to true underlying causes of death based on available information.[31] At last, a Bayesian noise-reduction algorithm was used to apply an adjustment to zero counts and correct for stochasticity in small populations in the cause of death data.[32] This method was implemented by cause, sex, and country, and ensured that datapoints of zero deaths were not dropped when modelling in natural logarithm or logit space. These data come from vital registration systems, censuses, household surveys, health service records, verbal autopsies, disease registries, and more. YLDs are calculated by multiplying the prevalence of disease sequelae by their disability weights, adjusting for factors like cause, year, age, sex, and location. YLLs are determined by multiplying mortality data specific to age, sex, and location by the standard life expectancy at age of death. DALYs are the sum of YLLs and YLDs. HALE calculations use YLDs per capita along with age-specific mortality rates, adjusted for factors like cause, sex, year, and location. To incorporate uncertainty, 95% UIs were created, representing the 2.5th and 97.5th percentiles from 500 model simulations. These uncertainties were factored in throughout the estimation process. The study reports counts and age-standardized rates at global, super-regional, regional, national, and subnational levels, covering seven super-regions, 21 regions, 204 countries (21 with subnational data), and 811 subnational areas for the entire period.[33] The data is publicly accessible at https://vizhub.healthdata.org/gbd-results/. We extracted and analyzed this data to explore the burden of CO poisoning.

Case Definition

CO poisoning was defined according to the ICD codes established in GBD 2021.[33] The ICD codes mapped to poisoning by CO were E862.0-E862.9, E868.0-E868.9, and E869.9 for ICD-9, and X47.0-X47.9 for ICD-10. Hence, our study only captured unintentional non-fire-related CO poisoning, and explicitly excludes intentional CO poisoning (eg, suicide) and unin-tentional fire-related CO poisoning.[6]

Asian Division

The United Nations categorizes 49 Asian countries and territories into five geographic subregions: East Asia, West Asia, Central Asia, South Asia, and Southeast Asia. These divisions consider both geographical proximity and epidemiological similarities. In our study, we examined the regional variations in the epidemiological features of CO poisoning across these Asian divisions.

Statistical Analysis

All data computations were conducted using R version 4.4.1.

EAPC (Estimated Annual Percentage Change)

The EAPC was determined using a linear model with a Gaussian distribution. This involved two main steps: (1) linear regression was performed on 31 years of data, using the equation $y=\alpha+\beta x+\epsilon$ (with y representing the natural logarithm of the rate and x the year), and (2) calculating the EAPC as $EAPC=100\times(e\beta-1)$, based on the regression parameters.

Join-Point Regression Model

Join-point regression analysis was used to examine the long-term trends in ASIR, ASMR, and ASDR by sex in Asia from 1990 to 2021. This analysis works by dividing the trend of each rate into distinct segments, or "joinpoints", fitting a straight line to each segment to estimate trends over specific periods.[34,35] Monte Carlo permutation test was used to identify the number and location of these joinpoints, with significance set at $P<0.05$. The annual percent change (APC) was calculated for each segment to quantify changes in trends. The average annual percent change (AAPC) was then computed as a geometric weighted average of the APCs, offering an overall trend measurement for the study period[36,37] The APC or AAPC greater than 0 indicated an increase in rates over time, while values less than 0 signified a decrease. To evaluate statistical significance, 95% confidence intervals (CIs) were provided for each APC and AAPC.

Age-Period-Cohort Model

The Age-period-cohort model evaluates how age, time period, and birth cohort influence health outcomes. The age effect highlights risks associated with different ages, the period effect reflects changes impacting all age groups over time, and the cohort effect examines variations in outcomes among individuals born in the same time period. This model is represented by a log-linear regression: $\log(Y_i) = \mu + \alpha *age_i + \beta *period_i + \gamma *cohort_i + \varepsilon$, where Y_i indicates the prevalence or mortality rate of CO poisoning, μ is the intercept and ε is the error term, α, β and γ are the coefficients of age, period and cohort. The intrinsic estimator (IE) method, integrated into this model, was used to determine the net effects of age, time period, and birth cohort.[38]

Measurement Health Inequalities Model

The ASDR was used to analyze inequality. Based on World Health Organization guidelines, two main measures: the Slope Index of Inequality (SII) and the Concentration Index (CI) were applied to evaluate absolute and relative income-related disparities across countries.[39] The SII represents the slope of the regression line connecting each country's ASDR for CO poisoning to its socio-economic status ranking. To adjust for the overall burden, the SII is divided by the global ASDR, producing the Relative Index of Inequality (RII). The CI assesses relative disparities in the CO poisoning burden among countries by plotting a Lorenz curve based on cumulative DALYs and population. This index ranges from −1 to 1, indicating the area under the curve. A negative CI suggests that CO poisoning is more prevalent in countries with a lower SDI.

Frontier Analysis Model

To investigate the link between CO poisoning burden and socio-demographic development, we utilized frontier analysis to formulate a model using ASDR and the SDI. Unlike traditional regression models that predict outcomes or describe linear relationships, frontier analysis accommodates the non-linear dynamics between disease burden and SDI, capturing the multifaceted factors influencing CO poisoning. This method identifies the minimum achievable ASDR for each country, relative to its developmental stage, offering a benchmark for optimal outcomes. It quantifies the difference between a nation's actual burden and its theoretical minimum, pointing out potential areas for improvement. To model the non-linear relationship between ASDR and SDI, we employed locally weighted regression (LOESS) combined with local polynomial regression, using smoothing spans of 0.3, 0.4, and 0.5 to create smooth frontier lines and enhance our understanding of this intricate relationship.[40]

Auto-Regressive Integrated Moving Average (ARIMA) Model

The ARIMA model is commonly used in both demographic and epidemiological studies to analyze time series data and forecast trends in disease patterns. We applied the ARIMA model to the 2021 GBD data, processing it through differencing to ensure the time series was stationary. The optimal model was selected based on the smallest Akaike Information Criterion (AIC) using the "auto.arima()" function. To validate the model's accuracy, we conducted a white noise test, where a residual p-value above 0.05 indicated successful validation. Lastly, the "forecast" package was used to predict the ASDR for CO poisoning, with a significance level of 0.05.

Results

Temporal Trends in Burden of CO Poisoning: 1990-2021

Table 1 illustrates the data regarding deaths and age-standardized rates (ASRs) attributed to CO poisoning in Asia from 1990 to 2021, emphasizing trends observed during this timeframe. In general, deaths caused by CO poisoning in Asia experienced a reduction of 7.12%. In 1990, the ASMR stood at 0.67 per 100,000 (95% UI: 0.50–0.91) and decreased to 0.38 per 100,000 in 2021 (95% UI: 0.20–0.46), reflecting an annual reduction of 1.64 (95% CI: 1.89–1.38). However, the burden of CO poisoning varied across different Asian countries and regions. In 2021, 28 countries reported higher death rates compared to 1990, while 21 countries had lower rates. The ASMR decreased in 46 countries, increased in one country, and remained stable in two countries. Among the countries with the highest burden, Mongolia recorded the highest ASMR in 2021, reaching 2.6 per 100,000 at 2.6 per 100,000 (95% UI: 2.03–3.56), followed by Afghanistan at 1.76 per 100,000 (95% UI: 0.61–2.69) and Kazakhstan at 1.7 per 100,000 (95% UI: 1.53–1.9). Among the 49 countries and regions in Asia, the majority exhibited a declining trend in EAPC of deaths caused by CO poisoning. The most pronounced declines were noted in the Republic of Korea (EAPC: −6.32, 95% CI: −7.0 to −5.64), followed by Kyrgyzstan (EAPC: −6.2, 95% CI: −7.6 to −4.78) and Tajikistan (EAPC: −6.2, 95% CI: −7.6 to −4.78). In contrast, Japan showed no significant trend, with an EAPC of −0.15 (95% CI: −1.18 to 0.89).

Burden of CO Poisoning by Sex and Age in Asia, 2021

In 2021, there were 12,336 male deaths (95% UI: 7118–16,380) and 5818 female deaths (95% UI: 1644–7654) due to CO poisoning. The highest number of deaths occurred in the 70–74-year age group, with 1434 deaths (95% UI: 682–1855).

Table 1 The Death Cases, Age-Standardized Mortality and Temporal Trend of Carbon Monoxide Poisoning in Asia From 1990 to 2021

Characteristics	1990		2021		1990–2021
	Deaths cases (95% UI)	**ASR per 100000 No.(95% UI)**	**Deaths cases (95% UI)**	**ASR per 100000 No.(95% UI)**	**EAPC No. (95% CI)**
Asia	18,982.70 (14,149.99 to 25,721.13)	0.67 (0.5 to 0.91)	18,153.69 (9,587.79 to 22,260.23)	0.38 (0.2 to 0.46)	−1.64(−1.89 to −1.38)
East Asia					
People's Republic of China	13,916.47 (10,116.02 to 21,131.14)	1.32 (0.96 to 2.01)	13,288.80 (6,544.45 to 17,340.25)	0.8 (0.39 to 1.03)	−1.35(−1.68 to −1.01)
Taiwan (Province of China)	47.06 (43.48 to 51.18)	0.24 (0.23 to 0.26)	85.18 (76.4 to 92.52)	0.26 (0.24 to 0.28)	−0.55(−1.04 to −0.06)
Mongolia	161.19 (85.94 to 225.23)	9.2 (4.82 to 12.32)	83.13 (64.21 to 114.6)	2.6 (2.03 to 3.56)	−5.1(−5.77 to −4.43)
Republic of Korea	573.09 (286.26 to 741.87)	1.36 (0.65 to 1.76)	129.47 (104.41 to 218.91)	0.18 (0.14 to 0.31)	−6.32(−7 to −5.64)
Democratic People's Republic of Korea	148.09 (79.89 to 255.06)	0.78 (0.43 to 1.38)	214.4 (136.91 to 379.16)	0.73 (0.46 to 1.3)	−0.15(−0.26 to −0.04)
Japan	217.42 (211.56 to 221.87)	0.16 (0.15 to 0.16)	182.36 (171.41 to 189.94)	0.11 (0.11 to 0.11)	−0.15(−1.18 to 0.89)
Southeast Asia					
Republic of the Philippines	18.68 (6.35 to 25.9)	0.03 (0.01 to 0.05)	28.67 (11.36 to 39.07)	0.03 (0.01 to 0.04)	−0.59(−0.69 to −0.49)
Socialist Republic of Viet Nam	179.78 (45.65 to 279.87)	0.34 (0.08 to 0.54)	230.72 (69.05 to 382.05)	0.22 (0.07 to 0.35)	−1.46(−1.51 to −1.41)
Lao People's Democratic Republic	4.09 (1.79 to 7.77)	0.12 (0.06 to 0.22)	4.85 (2.51 to 9.93)	0.07 (0.04 to 0.14)	−1.98(−2.08 to −1.89)
Kingdom of Cambodia	8.63 (3.59 to 15.72)	0.11 (0.05 to 0.17)	12.1 (6.48 to 22.96)	0.08 (0.04 to 0.14)	−1.08(−1.15 to −1.01)
Republic of the Union of Myanmar	130.53 (34.69 to 229.09)	0.41 (0.09 to 0.7)	112.07 (36.36 to 167.07)	0.22 (0.07 to 0.32)	−2.48(−2.64 to −2.32)
Kingdom of Thailand	25.57 (11.76 to 41.58)	0.05 (0.02 to 0.08)	36.47 (16.45 to 52.37)	0.05 (0.02 to 0.07)	−0.3(−0.51 to −0.1)
Malaysia	24.44 (13.87 to 36.3)	0.16 (0.09 to 0.23)	36.88 (24.29 to 58.55)	0.11 (0.08 to 0.18)	−1.4(−1.56 to −1.25)
Brunei Darussalam	0.59 (0.39 to 0.76)	0.26 (0.17 to 0.33)	0.56 (0.42 to 0.77)	0.12 (0.09 to 0.17)	−2.23(−2.38 to −2.07)
Republic of Singapore	2.96 (2.75 to 3.16)	0.09 (0.09 to 0.1)	0.85 (0.77 to 0.92)	0.01 (0.01 to 0.01)	−4.83(−5.58 to −4.08)
Republic of Indonesia	163.54 (42.84 to 259.83)	0.09 (0.03 to 0.15)	235.64 (73.6 to 368.9)	0.08 (0.03 to 0.13)	−0.23(−0.37 to −0.09)
Democratic Republic of Timor-Leste	0.58 (0.23 to 1.07)	0.09 (0.04 to 0.16)	0.78 (0.41 to 1.88)	0.07 (0.04 to 0.16)	−1.06(−1.43 to −0.69)
South Asia					
Federal Democratic Republic of Nepal	301.39 (131.41 to 543.42)	1.98 (0.93 to 3.18)	331.47 (199.68 to 550.95)	1.26 (0.75 to 1.98)	−1.43(−1.53 to −1.33)
Kingdom of Bhutan	0.3 (0.11 to 1)	0.06 (0.02 to 0.2)	0.25 (0.1 to 1.05)	0.03 (0.01 to 0.14)	−1.89(−2.02 to −1.76)
People's Republic of Bangladesh	132.19 (12.06 to 367.29)	0.09 (0.01 to 0.22)	63.11 (11.46 to 116.38)	0.04 (0.01 to 0.07)	−2.46(−2.68 to −2.24)
Republic of India	576.93 (122.25 to 922.95)	0.07 (0.02 to 0.11)	700.09 (166.81 to 985.39)	0.05 (0.01 to 0.07)	−1.27(−1.47 to −1.07)
Islamic Republic of Pakistan	43.91 (18.25 to 145.13)	0.05 (0.02 to 0.15)	70.59 (33.68 to 243.95)	0.03 (0.02 to 0.12)	−1.07(−1.23 to −0.92)
Democratic Socialist Republic of Sri Lanka	21.42 (8.91 to 29.18)	0.13 (0.06 to 0.18)	10.55 (6.28 to 17.86)	0.05 (0.03 to 0.08)	−4.37(−4.83 to −3.91)
Republic of Maldives	0.03 (0.01 to 0.07)	0.02 (0.01 to 0.04)	0.07 (0.04 to 0.2)	0.01 (0.01 to 0.03)	−1.65(−1.77 to −1.54)

(*Continued*)

https://doi.org/10.2147/CLEP.S512786

https://doi.org/10.2147/CLEP.S512786

Table 1 (Continued).

Characteristics	1990		2021		1990–2021
	Deaths cases (95% UI)	**ASR per 100000 No.(95% UI)**	**Deaths cases (95% UI)**	**ASR per 100000 No.(95% UI)**	**EAPC No. (95% CI)**
Central Asia					
Republic of Kazakhstan	575.81 (533.71 to 621.86)	3.71 (3.43 to 4.01)	325.91 (291.79 to 366.79)	1.7 (1.53 to 1.9)	−3.41(−4.21 to −2.61)
Kyrgyz Republic	87.47 (78.58 to 98.03)	2.32 (2.08 to 2.61)	63.84 (53.69 to 75.13)	1.03 (0.86 to 1.21)	−6.2(−7.6 to −4.78)
Republic of Tajikistan	83.54 (63.94 to 105.83)	1.82 (1.37 to 2.34)	116.5 (73.06 to 213.7)	1.24 (0.79 to 2.2)	−6.2(−7.6 to −4.78)
Republic of Uzbekistan	196.73 (174.1 to 218.35)	1.1 (0.97 to 1.22)	219.17 (185.6 to 262)	0.65 (0.55 to 0.77)	
Turkmenistan	26.09 (23.69 to 29.11)	0.83 (0.74 to 0.9)	18.01 (14.24 to 22.49)	0.36 (0.28 to 0.44)	−6.06(−7.48 to −4.63)
West Asia					
Islamic Republic of Afghanistan	206.87 (78.92 to 347.94)	2.32 (0.91 to 3.65)	426.97 (156.95 to 659.84)	1.76 (0.61 to 2.69)	−0.98(−1.16 to −0.8)
Republic of Iraq	47.43 (27.62 to 63.97)	0.3 (0.19 to 0.41)	58.38 (32.26 to 82.84)	0.16 (0.09 to 0.23)	−2.22(−2.4 to −2.04)
Islamic Republic of Iran	686.06 (346.44 to 901.16)	1.35 (0.72 to 1.78)	477.89 (300.76 to 569)	0.54 (0.35 to 0.64)	−2.73(−3.08 to −2.38)
Syrian Arab Republic	48.89 (31.68 to 66.05)	0.45 (0.31 to 0.58)	38.14 (23.33 to 52.22)	0.29 (0.18 to 0.4)	−1.08(−1.3 to −0.85)
Hashemite Kingdom of Jordan	35.71 (23.42 to 45.47)	1.16 (0.77 to 1.51)	45.42 (34.44 to 59.88)	0.42 (0.32 to 0.56)	−3.74(−4.05 to −3.42)
Lebanese Republic	3.55 (1.73 to 5.28)	0.14 (0.07 to 0.2)	4.54 (2.69 to 5.8)	0.07 (0.04 to 0.1)	−1.86(−1.95 to −1.76)
State of Israel	3.53 (3.07 to 3.93)	0.07 (0.06 to 0.08)	2.71 (2.43 to 2.95)	0.03 (0.02 to 0.03)	−2.33(−2.75 to −1.91)
Palestine	3.57 (2.07 to 5.05)	0.22 (0.13 to 0.31)	4.78 (2.86 to 6.34)	0.12 (0.07 to 0.15)	−1.95(−2.09 to −1.82)
Kingdom of Saudi Arabia	84.96 (53.04 to 120.18)	0.67 (0.44 to 0.96)	166.78 (104.5 to 237.23)	0.42 (0.28 to 0.58)	−1.21(−1.43 to −0.99)
Kingdom of Bahrain	1.44 (1 to 1.9)	0.38 (0.26 to 0.48)	2.36 (1.72 to 3.02)	0.18 (0.13 to 0.22)	−2.89(−3.07 to −2.71)
State of Qatar	3.66 (2.65 to 5.35)	1.16 (0.86 to 1.67)	9.71 (6.89 to 14.12)	0.39 (0.29 to 0.54)	−3.44(−3.94 to −2.94)
State of Kuwait	13.4 (12.16 to 14.99)	0.9 (0.82 to 1)	14.65 (12.26 to 17.48)	0.34 (0.29 to 0.4)	−3.43(−4.14 to −2.72)
United Arab Emirates	8.92 (5.17 to 13)	0.61 (0.35 to 0.88)	17.6 (11.74 to 24.74)	0.25 (0.16 to 0.34)	−2.1(−2.35 to −1.84)
Sultanate of Oman	1.37 (0.73 to 2.09)	0.09 (0.05 to 0.14)	1.42 (0.93 to 1.97)	0.04 (0.02 to 0.05)	−2.45(−2.62 to −2.29)
Republic of Yemen	127.5 (36.78 to 236.91)	1.16 (0.41 to 2.02)	228.29 (67.67 to 412.16)	0.87 (0.26 to 1.55)	−1.11(−1.24 to −0.99)
Georgia	51.96 (46.4 to 57.66)	0.89 (0.79 to 0.98)	28.36 (24.51 to 32.58)	0.63 (0.54 to 0.72)	−4.83(−6.53 to −3.11)
Republic of Armenia	22.99 (17.89 to 27.64)	0.7 (0.54 to 0.84)	14.91 (12.58 to 17.45)	0.4 (0.34 to 0.47)	−5.54(−7.02 to −4.04)
Republic of Turkey	369.82 (264.87 to 640.95)	0.71 (0.53 to 1.23)	349.1 (250.26 to 444.01)	0.41 (0.29 to 0.52)	−1.12(−1.47 to −0.76)
Republic of Cyprus	3.01 (2.05 to 4.14)	0.43 (0.28 to 0.61)	2.33 (1.8 to 2.98)	0.14 (0.11 to 0.17)	−3.78(−3.89 to −3.67)
Republic of Azerbaijan	68.59 (49.33 to 89.63)	1.02 (0.74 to 1.33)	57.72 (38.94 to 83.9)	0.51 (0.35 to 0.74)	−3.58(−4.08 to −3.09)

Abbreviations: ASR, agestandardized mortality rate; EAPC, estimated annual percentage change; UI, uncertainty interval.

Among males, the 50–54-year age group (931 deaths, 95% UI: 476–1335) recorded the greatest number of deaths. Among females, the highest number of deaths occurred in the 70–74-year age group (537 deaths, 95% UI: 139–753). (Figure 1A). Overall, males experienced a greater number of deaths across all age groups compared to females, with the exception of individuals aged 90 years and above. The most pronounced disparity between sex was found in the 30–34-year age group, where male deaths totaled 916, significantly exceeding the 283 deaths among females. (Figure 1A).

As shown in Figure 1B, the ASMR for males was 0.52 per 100,000 (95% UI: 0.30–0.70), while for females, it was 0.26 per 100,000 (95% UI: 0.07–0.34) in 2021. The highest mortality rate (MR) was observed in the 85–89-year age group (3.236 per 100,000, 95% UI: 1.631–4.114). The highest male MR occurred in the same age group (4.918 per 100,000, 95% UI: 2.657–6.685), while the highest female MR occurred in the 90–94-year age group (2.281 per 100,000, 95% UI: 0.632–3.134). In every age group, the MR was higher for males than for females, with the largest gender difference in the 85–89-year age group (4.918 for males vs 2.192 for females) In every age group, males exhibited higher MRs than females, with the most significant gender disparity observed in the 85–89-year age group (4.918 for males vs 2.192 for females). (Figure 1B).

The ASIR for males was 6.09 per 100,000 (95% UI: 4.38–8.07), and for females, it was 5.77 per 100,000 (95% UI: 3.97–8.00). The highest incidence rate occurred in the 95+ age group (24.77 per 100,000, 95% UI: 13.83–39.16). Both males and females showed similar trends in incidence by age (Figure 1C).

Regarding the ASDR, the rate for males was 22.29 per 100,000 (95% UI: 13.02–29.22), while for females, it was 10.21 per 100,000 (95% UI: 3.33–13.01). The highest ASDR occurred in the 85–89-year age group (33.23 per 100,000, 95% UI: 17.41–41.88). The highest male ASDR was also in the 85–89-year age group (49.98 per 100,000, 95% UI: 27.35–67.53), for females, the peak ASDR occurred in the 80–84-year age group (23.71 per 100,000, 95% UI: 6.97–32.25). Similar to the ASMR, the ASDR was consistently higher for males than for females across all age groups. The most substantial gender difference was found in the 85–89-year age group (49.98 for males vs 22.85 for females) (Figure 1D).

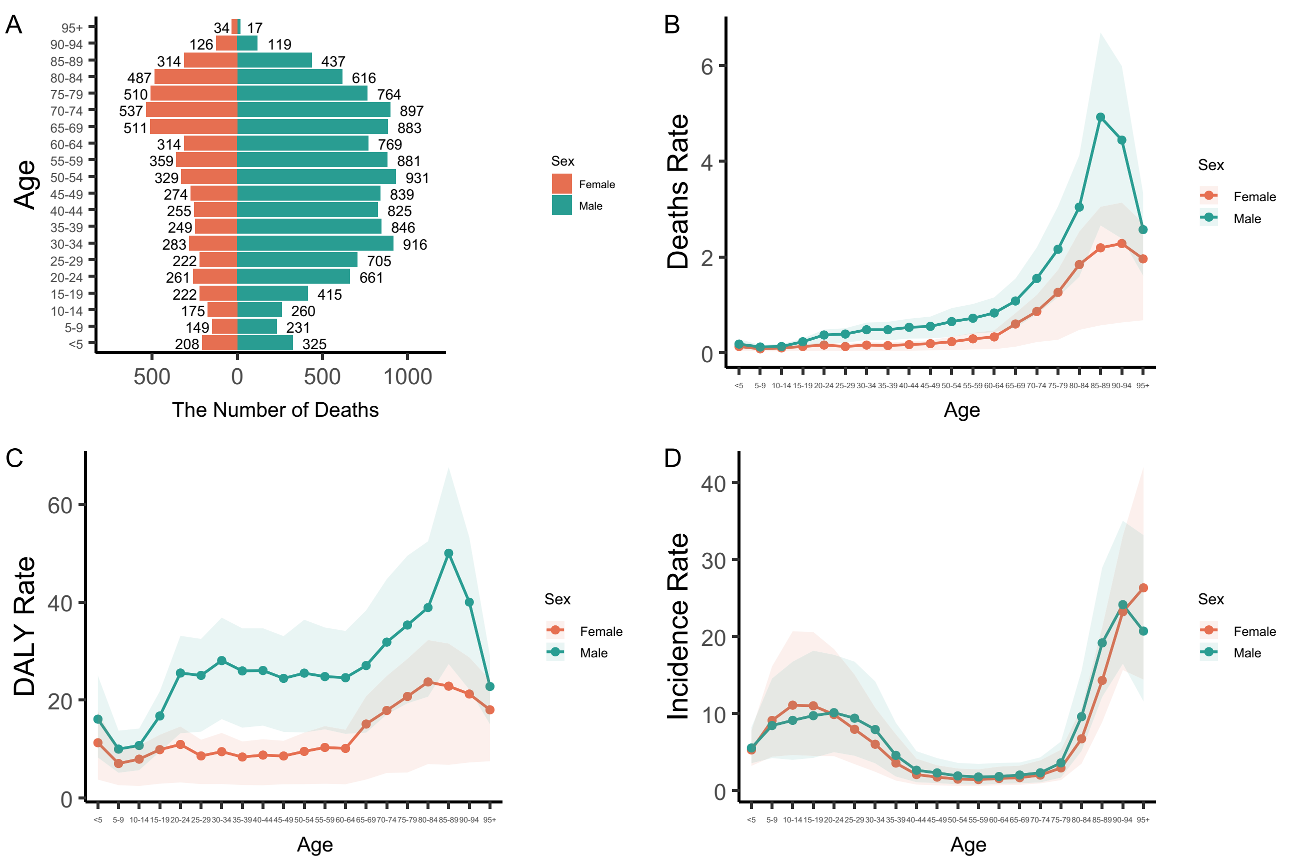

Figure 1 Age-specific deaths (**A**), ASMR (**B**), ASIR (**C**), and ASDR (**D**) due to CO poisoning in the Asian level, by sex, 2021.

Burden of CO Poisoning by Country in Asia, 2021

In 2021, the countries with the highest CO poisoning crude incidence rates (CIR) per 100,000 people were Mongolia (27.48, 95% UI: 19.86–36.97), Kazakhstan (26.99, 95% UI: 19.72–35.56), and Kyrgyzstan (17.43, 95% UI: 11.66–25.39). These findings highlight the need for enhanced prevention measures in these nations. In contrast, the countries with the lowest CIR were India (1.82, 95% UI: 1.07–2.81), Thailand (1.89, 95% UI: 1.17–2.85), and Bangladesh (2.12, 95% UI: 1.22–3.28) (Figure 2A).

Regarding CO poisoning crude mortality rates (CMR), Mongolia (2.49, 95% UI: 1.92–3.44), Kazakhstan (1.72, 95% UI: 1.54–1.94), and Afghanistan (1.37, 95% UI: 0.50–2.11) had the highest CMR in 2021, as shown in Figure 2B. The countries with the lowest mortality rates were the Maldives (0.01, 95% UI: 0.01–0.04), Singapore (0.01, 95% UI: 0.01–0.02), and the Philippines (0.03, 95% UI: 0.01–0.03).

When analyzing the EAPC in CMR, the countries showing the slowest rates of decline were North Korea (−0.15, 95% CI: −0.26 to −0.04), Japan (−0.15, 95% CI: −1.18 to 0.89), and Indonesia (−0.23, 95% CI: −0.37 to −0.09) (Figure 2C). This indicates a relatively slow reduction in mortality rates in these regions, suggesting a need for increased medical investment and policy attention. Conversely, Turkmenistan (−6.06, 95% CI: −7.48 to −4.63), Kyrgyzstan (−6.2, 95% CI: −7.6 to −4.78), and South Korea (−6.32, 95% CI: −7 to −5.64) experienced the highest decreases in CMR over the past 32 years, as illustrated in Figure 2C.

Long-Term Trends in the Burden of CO Poisoning in Asia

The trends in the incidence and ASIR of CO poisoning in Asia are presented in Figure 3. Between 1990 and 2003, both the number of cases and ASIR were slightly higher for females than for males. However, from 2004 to 2008, the incidence rate for males surpassed that of females, although their ASIR remained lower. In the years that followed, both the number of cases and the ASIR for males continued to exceed those of females. From 1990 to 2009, the incidence and ASIR for both genders increased, peaking in 2010 before declining in subsequent years. By 2021, the ASIR was 6.39 (95% UI: 4.64–8.48) per 100,000 population for males and 6.18 (95% UI: 4.24–8.68) per 100,000 for females (Figure 3).

Join-Point Analyses of the Burden of CO Poisoning by Sex in Asia

Figure 4 illustrates the APC in the ASDR, ASMR, and ASIR for CO poisoning in Asia from 1990 to 2021. The ASDR for males showed a significant decline over this period, with an AAPC of −2.27 (95% CI: −2.47 to −2.08). A similar trend was demonstrated a notable decrease during this period, with an AAPC of −2.27 (95% CI: −2.47 to −2.08). A comparable trend was observed in females (AAPC = −2.73, 95% CI: −3.13 to −2.33) and in both sexes combined (AAPC = −2.39, 95% CI: −2.54 to −2.23) (Figure 4A).

For the ASMR, both the combined-sex group (AAPC = −2.01, 95% CI: −2.20 to −1.81) and females (AAPC = −2.24, 95% CI: −2.43 to −2.06) showed a notable decline. However, the decrease was less pronounced in males (AAPC = −1.85, 95% CI: −2.05 to −1.65) (Figure 4B).

The ASIR for males demonstrated an increasing trend from 2002 to 2010 (APC = 1.48, 95% CI: 1.26 to 1.71), followed by a decline in subsequent years.

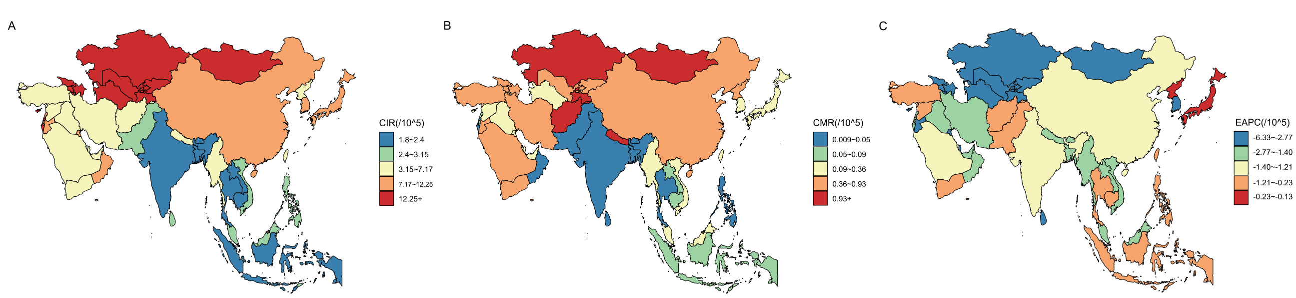

Figure 2 The Asian map of CIR (**A**), CMR (**B**), and EAPC of MR (**C**) per 100,000 population of CO poisoning in 2021, by country.

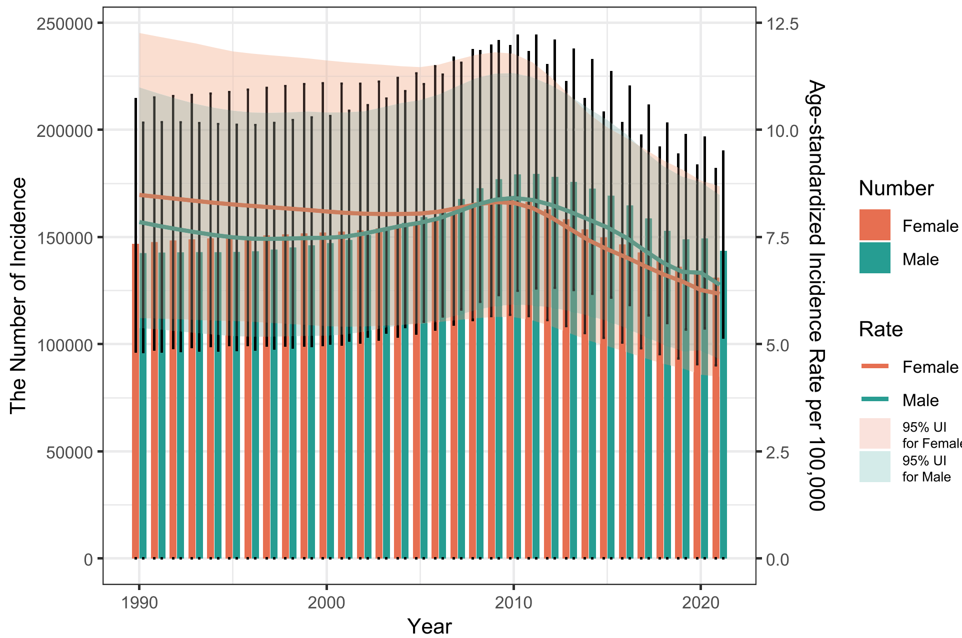

Figure 3 Trends from 1990 to 2021 in number and ASIR of CO poisoning at the Asian level. The light-green shaded area represents the 95% UI for the male ASIR, and the light-Orange shaded area represents the 95% UI for the female ASIR.

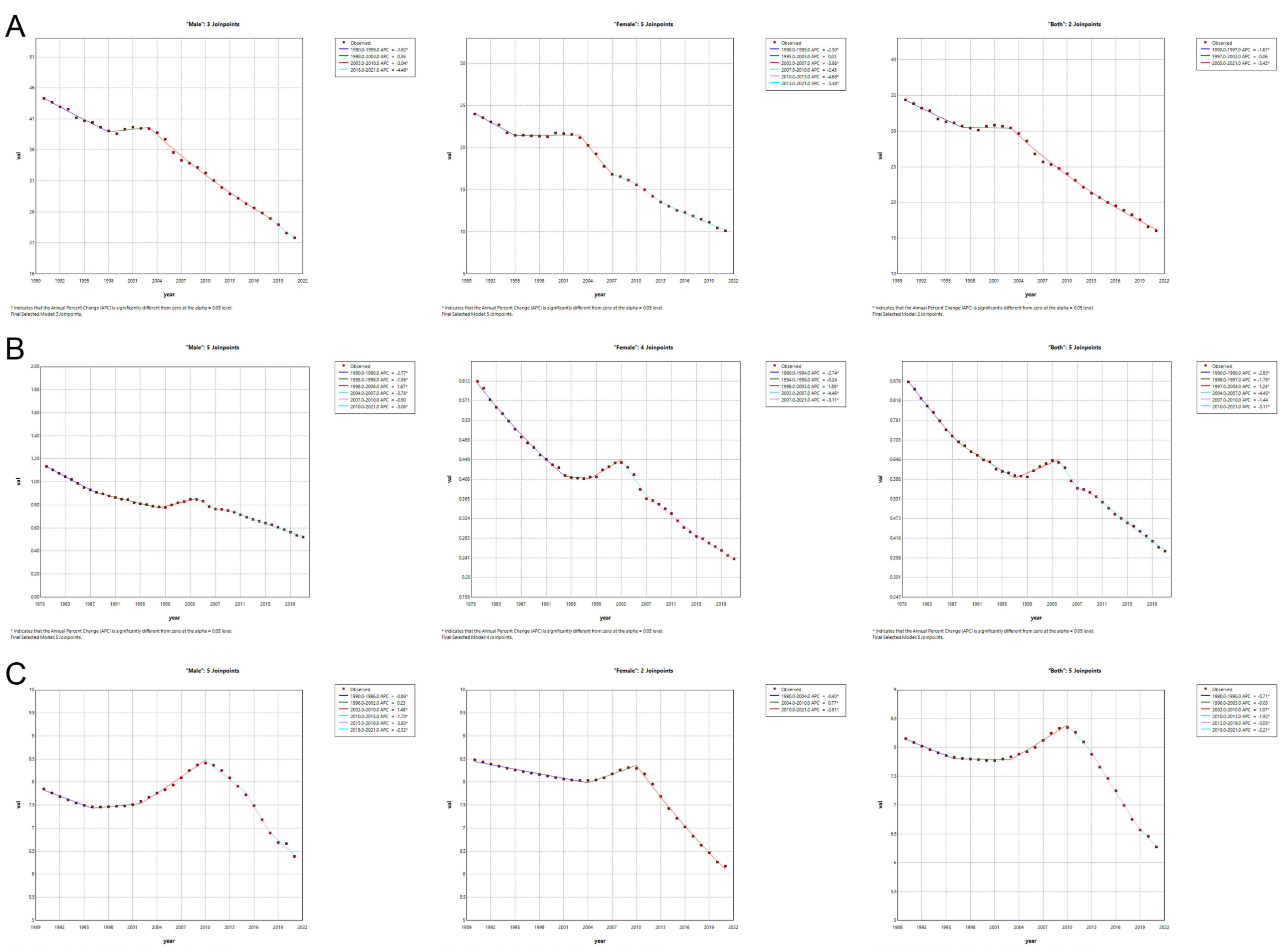

Figure 4 Join-point analyses of ASDR (**A**), ASMR(**B**) and ASIR(**C**) of CO poisoning are conducted for males, females, and both sexes in Asia over the period from 1990 to 2021.

From 1990 to 2021, the male ASIR decreased at an average annual rate of −0.63 (95% CI: −0.83 to −0.44). A similar decline was noted for both sexes combined (AAPC = −0.83, 95% CI: −0.94 to −0.73). In females, the ASIR remained relatively stable from 1990 to 2010, before decreasing significantly between 2010 and 2021 (AAPC = −2.81, 95% CI: −2.89 to −2.74). The overall AAPC for females from 1990 to 2021 was −1.04 (95% CI: −1.10 to −0.98) (Figure 4C).

Age-Period-Cohort Analysis of the Burden of CO Poisoning in Asia

Figure 5 illustrates the Age-period-cohort model effects on the incidence rate of CO poisoning. The incidence began to decline in individuals aged 20–24 years, reaching its lowest point between 55–60 years, before rising again in older age groups. Notably, the incidence rates were higher in the 15–19 and 90–94 age groups compared to others (Figures 5A and B).

Period-based trends showed a relatively stable incidence among middle-aged groups, while both younger and older age groups experienced an upward trend (Figure 5C). The relative risk (RR) remained steady, fluctuating around the baseline ratio without significant deviation. Analysis of birth cohort effects revealed that CO poisoning incidence was higher in both earlier and later birth cohorts compared to the middle cohorts. The risk was significantly elevated in the cohort born between 1967 and 1971 (RR cohort: 1.045, 95% CI: 0.957–1.141), while it was notably lower in the early cohort (born 1902–1906) (RR cohort: 0.346, 95% CI: 0.137–0.87) and the recent cohort (born 2017–2021) (RR cohort: 0.648, 95% CI: 0.567–0.741) (Figure 5D).

The Relationship Between the Burden of CO Poisoning and the SDI in Asia

Figure 6 illustrates the relationship between the SDI and the burden of CO poisoning, as indicated by DALYs. In 1990, the SII for DALYs per 100,000 population was 18.30 (95% CI: −26.61 to 80.33), which decreased to −4.78 (95% CI: −30.27 to 8.96) in 2021 (Figures 6A and B). This trend indicates a diminishing correlation between the crude DALY rate

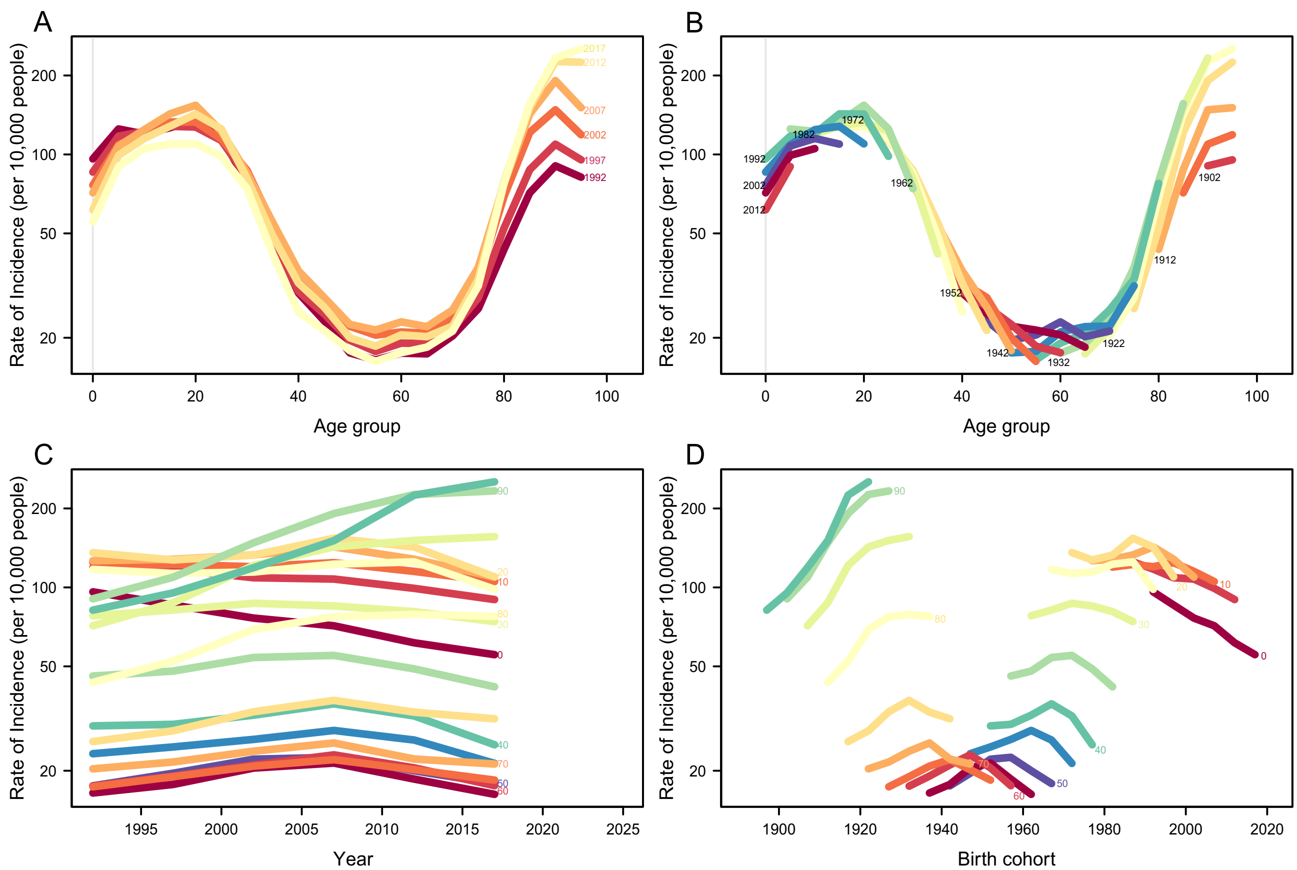

Figure 5 Trends of age-specific (**A** and **B**), period-based(**C**) and cohort-based(**D**) variation of CO poisoning incidence rate in Asia.

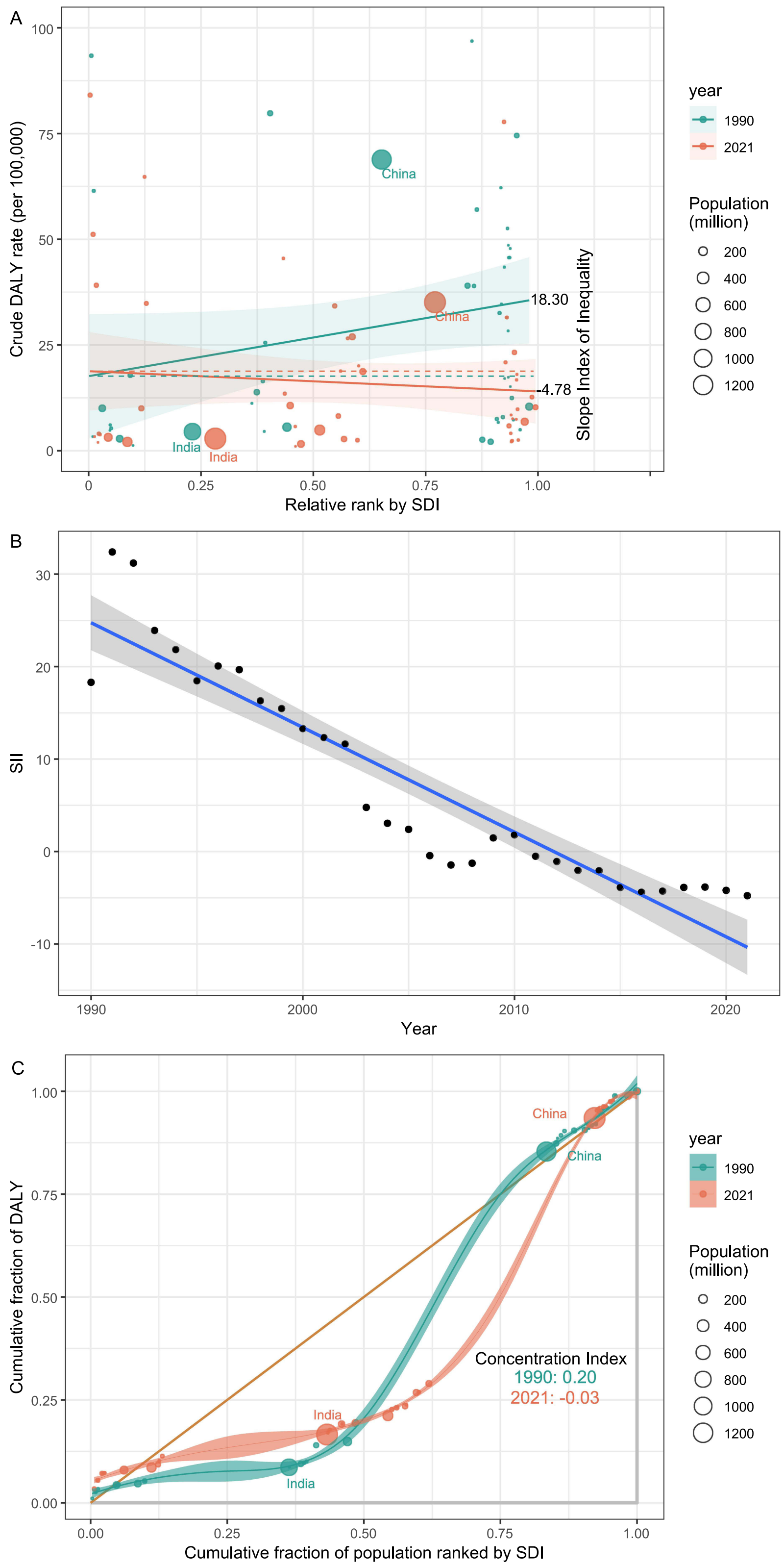

Figure 6 The analysis includes three key components: (**A**) the SII for income-related health inequality in both 1990 and 2021, (**B**) the trend of the SII across the period from 1990 to 2021, the blue line represents the trend of the SII from 1990 to 2021, the black scatter points depict the observed SII values for specific years, and the grey shaded area indicates the 95% CI around the trend line, and (**C**) an assessment of relative income-related health inequality in the burden of CO poisoning in Asia in 1990 and 2021 through the use of concentration curves and the CI.

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and SDI, indicating a decrease in the inequality of the age-standardized burden of CO poisoning between high- and low-income countries in Asia (Figure 6B). Additionally, Figure 6A shows a significant decline in the crude DALY rate (per 100,000 population) in China from 1990 to 2021, suggesting that government measures have effectively reduced the burden of CO poisoning. From 1990 to 2021, the CI for DALYs in Asia also decreased significantly, from 0.20 to −0.03, indicating a reduction in health inequities across the region (Figure 6C). Despite this progress, the inequality between high- and low-income countries in terms of CO poisoning remains a persistent issue in Asia.

From 1990 to 2021, frontier analysis based on the ASDR and SDI was conducted to assess the potential for improvement in the ASDR for CO poisoning, considering national and regional development levels frontier analysis was performed using the ASDR and SDI to evaluate the potential for improvements in the ASDR for CO poisoning, taking into account the levels of national and regional development (Figures 7A and B). Figure 7A presents a scatter plot illustrating the relationship between SDI and ASDR across Asian countries and regions. Data points positioned away from the frontier line indicate a higher-than-expected ASDR for CO poisoning given the level of SDI development, suggesting opportunities for improvement. In contrast, points near the frontier line represent countries that have effectively reduced ASDR relative to their SDI level. This analysis underscores the influence of socio-demographic factors on health outcomes and helps identify regions that may benefit from targeted interventions. This analysis identified 15 countries and territories with the greatest potential for improvement in their ASDR (effective difference range: 118.02–18.62), including Mongolia, Afghanistan, Kazakhstan, Tajikistan, Nepal, Kyrgyzstan, Yemen, China, North Korea, Uzbekistan, Georgia, Iran, Azerbaijan, Jordan, and Saudi Arabia (Figure 7B). Notably, low-SDI countries such as Timor-Leste, Bhutan, Bangladesh, Laos, and Cambodia, as well as high-SDI countries like Singapore, Japan, South Korea, and Taiwan (Province of China), showed significant improvement potential. The frontier analysis highlights that, despite having limited resources, low-SDI countries such as Bhutan and Bangladesh have achieved significant success in controlling the burden of CO poisoning (Figure 7B).

Figure 8 illustrates the relationship between ASMR and SDI across Asian countries, showing a higher ASMR in low-SDl regions. The trend indicates a potential decrease in ASMR with increasing SDl. However, the Spearman correlation coefficient ($\rho = -0.068$, $p = 0.645$) suggests no significant correlation between ASMR and SDI levels.

Prediction of CO Poisoning DALY Rates in Asia

The predicted trends for the ASDR of CO poisoning indicate a decline across all groups from 2022 to 2030. By 2030, the ASDR for males is projected to decrease to 15.31, for females to 6.06, and for both sexes combined to 10.70. This represents a 33.33% reduction in the combined-sex ASDR compared to 16.05 in 2021 (Figure 9).

Discussion

CO poisoning ranks among the most prevalent fatal poisonings globally.[11,40] It can lead to numerous long-term neurological consequences and elevate the risk of other diseases.[7,10,13–18,21–23] In 2021, Asia's ASMR for CO poisoning exceeded the global average. Despite this, there has been limited systematic analysis of the burden of CO poisoning in Asia. The research aims to fill that gap by analyzing the epidemiological trends and contributing factors, providing valuable data to guide policy development for CO poisoning prevention and improving patient outcomes.

Our findings indicate that in 2021, Asia recorded 18,153.69 (95% UI: 9587.79 to 22,260.23) CO-related deaths. The ASMR was 0.38 per 10,000 people (95% UI: 0.20 to 0.46). Between 1990 and 2021, the EAPC of ASR per 10,000 was −1.64 (95% CI: −1.89 to −1.38). Join-point analysis showed consistent downward trends in ASIR (AAPC = −0.83, 95% CI: −0.94 to −0.73), ASMR (AAPC = −2.01, 95% CI: −2.20 to −1.81) and ASDR (AAPC = −2.39, 95% CI: −2.54 to −2.23) from 1990 to 2021. This downward trend likely indicates the success of public health measures, including the expanded use of hyperbaric oxygen therapy and improvements in treatment.[41] To gain a deeper understanding of the factors affecting CO poisoning trends across various Asian nations, further research is crucial.

We also analyzed CIR and CMR across various Asian countries. In 2021, Mongolia (27.48 per 100,000, 95% UI: 19.86–36.97), Kazakhstan (26.99 per 100,000, 95% UI: 19.72–35.56), and Kyrgyzstan (17.43 per 100,000, 95% UI: 11.66–25.39) had the highest CIRs. Mongolia (2.49, 95% UI: 1.92–3.44), Kazakhstan (1.72, 95% UI: 1.54–1.94), and Afghanistan (1.37, 95% UI: 0.50–2.11) had the highest CMRs. These higher rates may be attributed to harsh climates

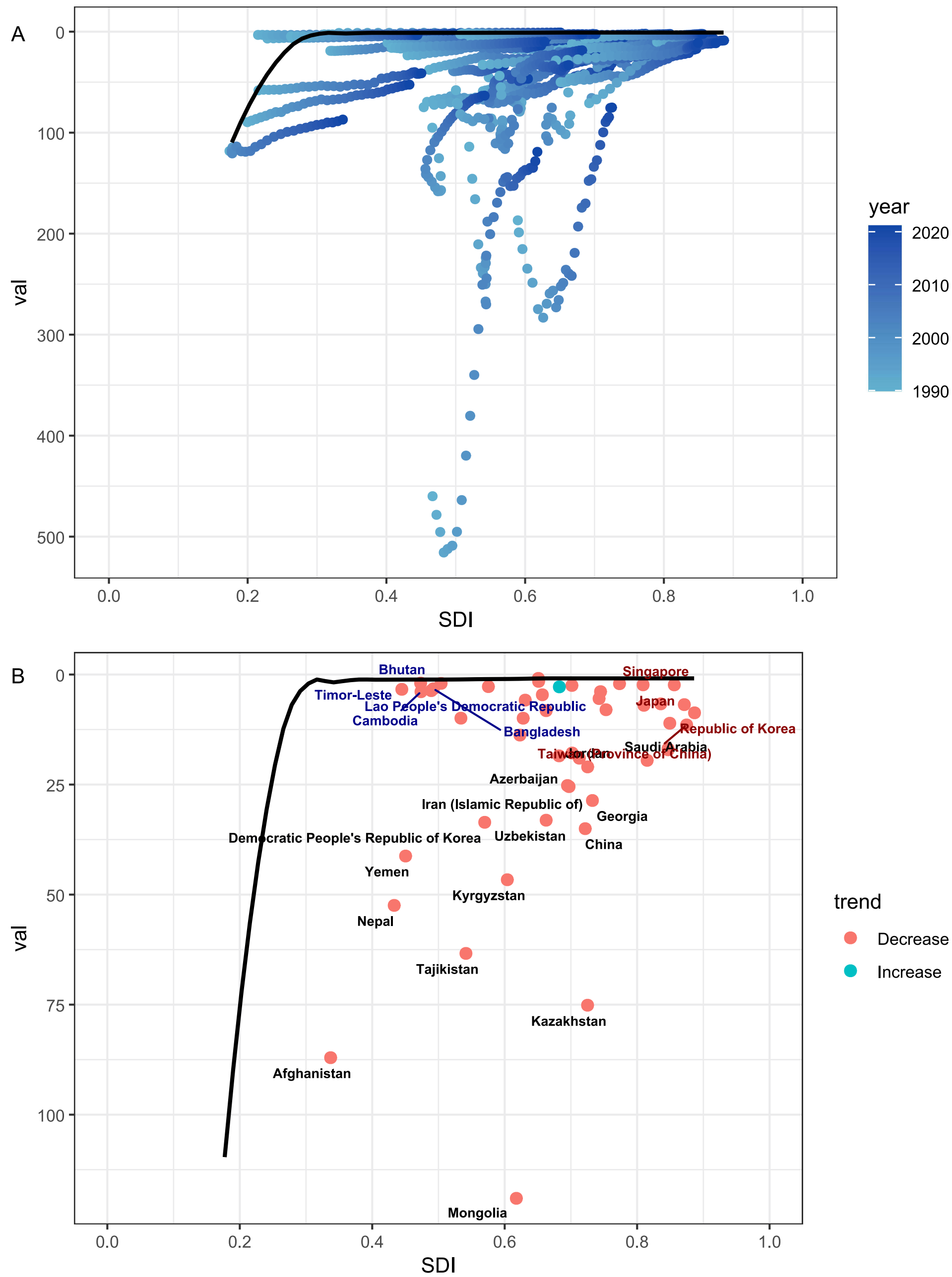

Figure 7 Frontier analysis investigates the association between the SDI and ASDR for CO poisoning across countries and territories in Asia. In Figure A, a gradient from light blue (1990) to dark blue (2021) illustrates the progression of years, with the frontier line depicted in black. In Figure B, each point represents an individual country or territory in 2021. Additionally, the 15 countries and territories with the most substantial deviations from the frontier are highlighted in black for emphasis. Blue signifies low-SDI countries with the smallest deviation from the frontier, while red indicates high-SDI countries with the largest deviations. The color of the dots also reflects the direction of ASDR change from 1990 to 2021, with Orange dots representing a decrease and the green dot indicating an increase.

with long, cold winters, which increase reliance on indoor heating systems that are often poorly ventilated or malfunctioning. Additionally, the use of alternative heating methods during power outages, such as portable generators and charcoal grills, further elevates CO exposure.[2] Given the geographical and climatic challenges, especially in rural areas, governments face increased demands to address these risks. In these regions, transitioning to cleaner fuels may not be immediately feasible, so short-term solutions, such as improving home ventilation, are recommended.[5,42,43] Public health campaigns highlighting the dangers of indoor cooking and heating could contribute to a decrease in poisoning cases. Moreover, CO poisoning can be prevented through the effective use of CO alarms.[44,45] Regular maintenance and timely replacement are crucial to ensure that these alarms provide early warnings when needed.[46] Governments can promote the

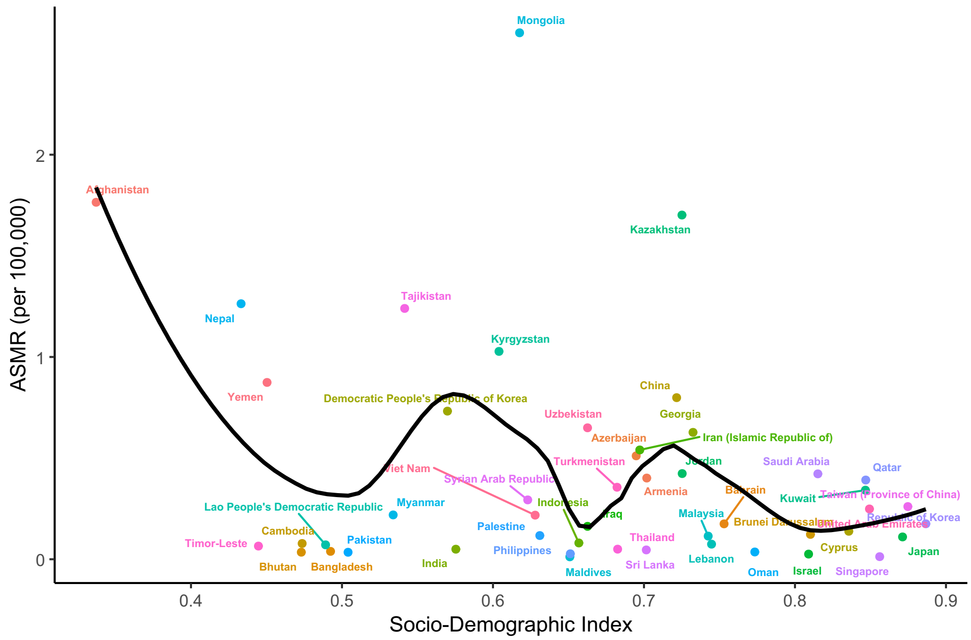

Figure 8 ASMR due to CO poisoning for Asian countries and territories by SDI, 1990–2021.

installation of residential CO alarms through legislation and supportive policies, helping to reduce the incidence of CO poisoning in the region.[47]

Our study highlights variations in CO poisoning burden across age and gender. In 2021, the ASMR was 0.26 (95% UI: 0.07–0.34) for females and 0.52 (95% UI: 0.30–0.70) for males. Similarly, the ASIR was 5.77 (95% UI: 3.97–8.00) for females and 6.09 (95% UI: 4.38–8.07) for males, while the ASDR was 10.21 (95% UI: 3.33–13.01) for females and 22.29 (95% UI: 13.02–29.22) for males. These figures indicate a significantly higher burden among males, possibly due to the following reasons. Males might be more likely to inadvertently put themselves at risk of CO poisoning when operating machinery, using fuel-burning appliances (eg, grilling), or being exposed in the workplace.[48–50] Additionally, alcohol use increases the risk of CO poisoning due to reduced inhibitions and poor decision making. Individuals under the influence of alcohol might also be less likely to recognize early symptoms of CO poisoning.[48,51] Some studies suggest that estrogen might offer females some protection against hypoxia-related injuries, which could partly explain the lower burden among women.[52–55] A few studies have also found that females have an ability to eliminate CO more rapidly, leading to better prognosis after poisoning.[56,57] The incidence of CO poisoning varied across age groups, decreasing from 20–24 years, reaching a low between 55–60 years, and then increasing in later years. Notably, the 15–19 and 90–94 age groups exhibited elevated incidence rates. This trend might be linked to a lack of awareness among adolescents and slower response times in the elderly. Furthermore, in Asia, the highest mortality rate is in the 85–89 age group (3.236, 95% UI: 1.631–4.114), likely due to existing health conditions exacerbating vulnerability.[58,59]

The SDI is a key indicator of regional development. In this study, we examined the relationship between SDI and the burden of CO poisoning across Asia. Our findings showed that countries with lower SDI values had significantly higher ASMR for CO poisoning. This disparity can be attributed to factors related to economic structures. In low-SDI countries, widespread use of solid fuels like wood and coal for cooking and heating, along with inadequate ventilation, increases the risk of CO exposure and poisoning.[60] Moreover, limited access to healthcare often results in delayed or insufficient diagnosis and treatment.[60] Additionally, low public awareness of CO risks and preventive measures contributes to higher incidence rates.[61] In contrast, high-SDI countries benefit from stricter safety regulations, such as mandatory CO detectors, and more effective enforcement of policies aimed at reducing exposure.[62] Despite these patterns, our analysis found no significant correlation between ASMR and SDI levels across the studied countries (Spearman correlation, p=0.645). This unexpected result can be attributed to several factors. The sources of CO exposure vary widely across regions. In low-SDI countries, exposure mainly results from solid fuel use, while in high-SDI countries, industrialization

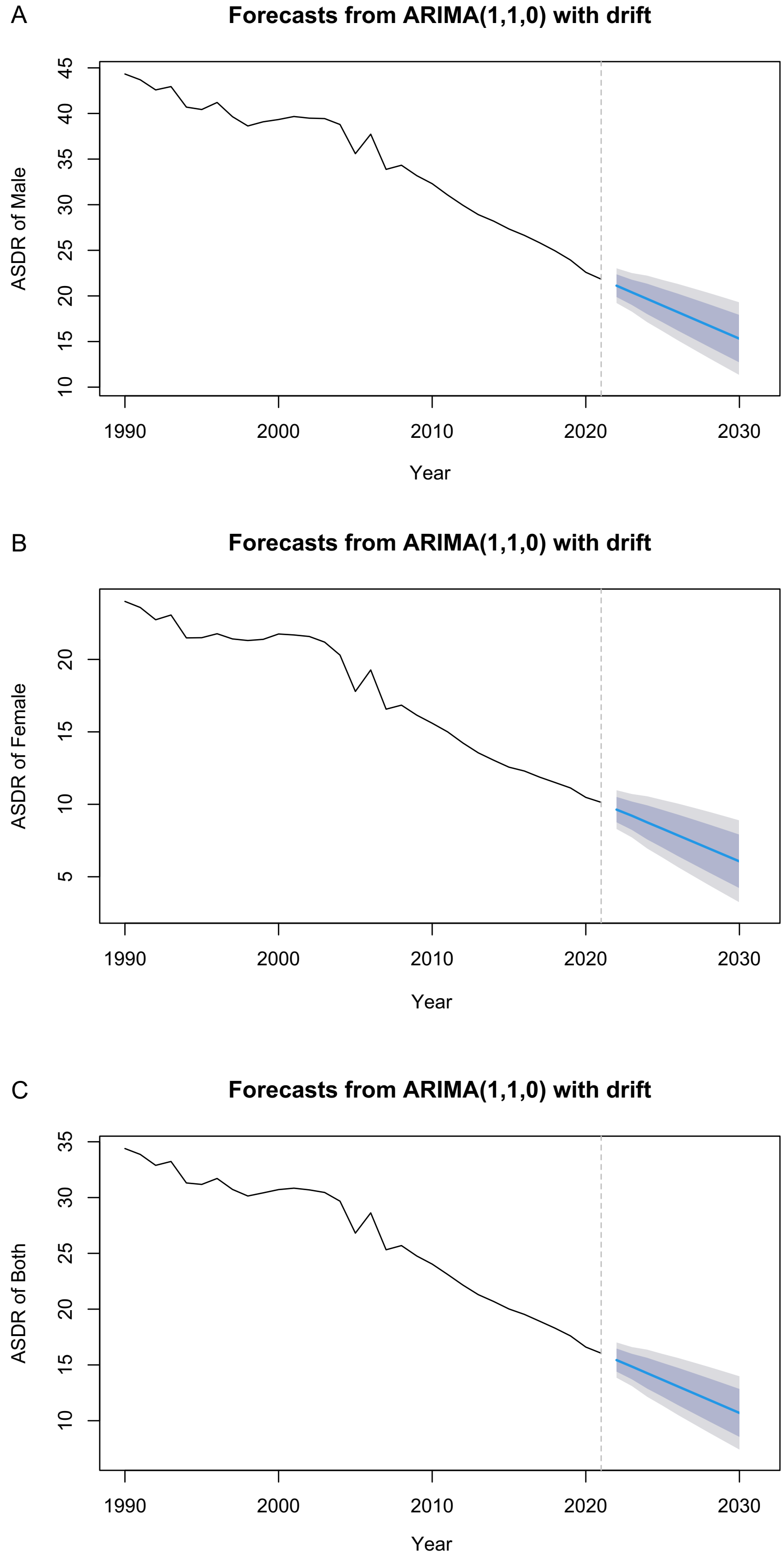

Figure 9 Predicted trends in ASDRs of CO poisoning from 2022 to 2030, by sex. (**A**) ASDR of Male; (**B**) ASDR of Female; (**C**) ASDR of Both. The black lines represent the true trend during 1990 to 2021. The blue line illustrates the projected trend, while the grey-shaded region represents the 95% CI for the predicted values. The grey-dotted vertical line separates the data into observed values (1990–2021) and forecasted values (2022–2030).

and traffic-related pollution are more prominent. Such differences in exposure sources may obscure the expected relationship between SDI and mortality. Additionally, underdeveloped healthcare systems and limited diagnostic resources in low-SDI countries could lead to underreporting or misclassification of CO poisoning cases, particularly among older populations. This may result in an underestimation of mortality rates, weakening the observed correlation.[63] Furthermore, high-SDI countries often have larger elderly populations, who are more vulnerable to CO poisoning due to age-related health issues and comorbidities. This demographic factor may reduce the effectiveness of advanced healthcare systems and preventive measures, further diluting the association between SDI and CO poisoning mortality.[64] Differences in SDI may also contribute to health inequalities reflected in DALYs. Our analysis showed that the SII for DALYs decreased from 18.30 (95% CI: −26.61 to 80.33) in 1990 to −4.78 (95% CI: −30.27 to 8.96) in 2021. This suggests a decrease in the gap in the age-standardized burden of CO poisoning between high- and low-income nations. To further analyze these trends, we conducted a frontier analysis using ASDR and SDI to identify potential areas for improvement in handling CO poisoning across different developmental contexts. The analysis demonstrated a narrowing gap between current burdens and optimal levels according to SDI from 1990 to 2021. This progress may be attributed to recent public health initiatives by Asian governments aimed at reducing CO poisoning.

Using the ARIMA model, we forecast a decline in ASDR across all groups from 2022 to 2030, with rates for males, females, and combined sexes expected to decrease to 15.31, 6.06, and 10.70, respectively, by 2030. This represents a 33.33% decrease for both sexes compared to 2021.

However, the study has limitations. It cannot fully account for discrepancies in health data across different Asian countries. It is also subject to ecological fallacy and constraints inherent in the age-period-cohort model: the linear dependency among age, period, and cohort (Cohort = Period - Age) prevents unique estimation of their independent effects. Methods like the IE impose implicit constraints that are hard to verify. If true effects do not meet these constraints, estimates become biased. IE's constraints also depend on the number of age, period, and cohort categories, leading to inconsistent results. Without prior theoretical justification, age-period-cohort models risk producing misleading conclusions, as estimates are sensitive to arbitrary constraints and data structures.[38] In addition, because the data are from GBD 2021, it has methodological limitations. The lack of data in many countries limits the accurate estimation of CO poisoning mortality, resulting in the reliance on covariates and regional data, which may produce bias. In the absence of a detailed autopsy or evidence, underreporting or overstatement of deaths remains a concern, especially in areas with weak vital registration systems.[33] Future research should address data limitations by improving data collection, enhancing vital registration systems, and standardizing ICD coding across countries. For age-period-cohort model ecological fallacies, developing methods that incorporate external theoretical information or alternative constraints could mitigate bias. Additionally, exploring hybrid models that combine age-period-cohort frameworks with machine learning techniques may improve estimation accuracy. Researchers should also focus on capturing within-country variations and risk factors to better reflect real-world complexities. Collaborative efforts to share high-quality, detailed data globally are essential to overcome these challenges and provide more reliable insights into age, period, and cohort effects.

Conclusion

This study thoroughly examines the epidemiological trends and determinants of CO poisoning in Asia from 1990 to 2021. In 2021, Asia's ASMR for this poisoning surpassed the global average, emphasizing the necessity for focused public health actions. Our findings indicate a general decline in CO poisoning rates from 1990 to 2021, reflecting the effectiveness of comprehensive public health interventions. Governments have mitigated the risk of CO exposure by promoting clean energy alternatives to traditional high-emission fuels. Concurrently, public education campaigns have raised awareness about CO concentration monitoring alarms and safety precautions against poisoning. Advances in medical treatment, including the widespread use of hyperbaric oxygen therapy, have significantly improved the survival rates and outcomes for poisoning patients. However, notable regional differences in the burden remain, with higher rates observed in countries with colder, longer winters, underscoring the need for region-specific strategies. The study also reveals a higher burden among males, likely due to greater exposure risks and biological factors, such as the protective effect of estrogen in females. Moreover, the incidence is elevated in both younger and older age groups, highlighting the necessity for targeted educational initiatives and safety measures. Although no significant link was identified between the

SDI and the burden of CO poisoning, countries with a lower SDI showed higher ASMR, suggesting economic factors like occupational exposure play a role. The narrowing gap between actual and optimal burden levels based on SDI suggests improvements in public health policies. Finally, the ARIMA model predicts a continued decline in CO poisoning burden in Asia by 2030, offering optimism for future public health outcomes.

Non-Standard Abbreviations and Acronyms

AAPC, average annual percent change; APC, annual percent change; ARIMA model, auto-regressive integrated moving average model; ASDR, age-standardized disability-adjusted life year rate; ASIR, age-standardized incidence rate; ASMR, age-standardized mortality rate; ASRs, age-standardized rates; CI, Concentration Index; CIR, crude incidence rate; CMR, crude mortality rate; CO, carbon monoxide; DALY, disability-adjusted life years; EAPC, estimated annual percentage change; GBD, Global Burden of Disease Study; HALE, healthy life expectancy; ICD, International Classification of Diseases; IE, intrinsic estimator; RR, relative risk; SDI, Socio-Demographic Index; SII, Slope Index of Inequality; UI(s), 95% uncertainty interval(s); YLDs, years lived with disability; YLLs, years of life lost.

Ethic Statement

Our study is based on the publicly available GBD 2021. After consultation with the medical ethics committee of Zhongnan Hospital of Wuhan University, it was considered that the study met the standard of exemption from ethical review specified in Article 32, paragraph 1 and paragraph 2, of the measures for ethical review of life sciences and medical research involving humans (issued by the National Health Commission of China on February 27, 2023). Article 32 stipulates that under the following circumstances, the use of human information data or biological samples for life science and medical research involving humans, which will not cause harm to humans, or which does not involve sensitive personal information or commercial interests, can be exempted from ethical review, so as to reduce the unnecessary burden of scientific researchers and promote the conduct of life science and medical research involving humans. It also stipulates that if the research is conducted using legally obtained public data or data generated through observation, and does not interfere with public behavior, it can be exempted from ethical review.

Acknowledgments

We acknowledge the Global Burden of Disease Study 2021 for providing open access to the database.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This research was funded by the Department of Finance of Hubei Province under the Hospital Discipline Capacity Building Project, grant number [YYXKNLJS2024013].

Disclosure

The authors report no conflicts of interest in this work.

References

1. Liu F, Jiang X, Zhang M. Global burden analysis and AutoGluon prediction of accidental carbon monoxide poisoning by Global Burden of Disease Study 2019. *Environ Sci Pollut Res Int*. 2022;29(5):6911–6928. doi:10.1007/s11356-021-15895-y
2. Iqbal S, Clower JH, Hernandez SA, Damon SA, Yip FY. A review of disaster-related carbon monoxide poisoning: surveillance, epidemiology, and opportunities for prevention. *Am J Public Health*. 2012;102(10):1957–1963. doi:10.2105/AJPH.2012.300674
3. Raub JA, Mathieu-Nolf M, Hampson NB, Thom SR. Carbon monoxide poisoning--a public health perspective. *Toxicology*. 2000;145(1):1–14. doi:10.1016/S0300-483X(99)00217-6

4. Graber JM, Macdonald SC, Kass DE, Smith AE, Anderson HA. Carbon monoxide: the case for environmental public health surveillance. *Public Health Rep*. 2007;122(2):138–144. doi:10.1177/003335490712200202
5. Rupert DJ, Poehlman JA, Damon SA, Williams PN. Risk and protective behaviours for residential carbon monoxide poisoning. *Inj Prev*. 2013;19 (2):119–123. doi:10.1136/injuryprev-2012-040339.
6. Moberg ME, Hamilton EB, Zeng SM. Global, regional, and national mortality due to unintentional carbon monoxide poisoning, 2000-2021: results from the Global Burden of Disease Study 2021. *Lancet Public Health*. 2023;8(11):e839–e849. doi:10.1016/S2468-2667(23)00185-8.
7. Weaver LK. Clinical practice. Carbon monoxide poisoning. *N Engl J Med*. 2009;360(12):1217–1225. doi:10.1056/NEJMcp0808891.
8. Bansal S, Liu D, Mao Q, Bauer N, Wang B. Carbon monoxide as a potential therapeutic agent: a molecular analysis of its safety profiles. *J Med Chem*. 2024;67(12):9789–9815. doi:10.1021/acs.jmedchem.4c00823.
9. Centers for Disease Control. Carbon monoxide intoxication--a preventable environmental health hazard. *MMWR Morb Mortal Wkly Rep*. 1982;31 (39):529–531.
10. Rose JJ, Wang L, Xu Q, et al. Carbon monoxide poisoning: pathogenesis, management, and future directions of therapy. *Am J Respir Crit Care Med*. 2017;195(5):596–606. doi:10.1164/rccm.201606-1275CI
11. Gozubuyuk AA, Dag H, Kacar A, Karakurt Y, Arica V. Epidemiology, pathophysiology, clinical evaluation, and treatment of carbon monoxide poisoning in child, infant, and fetus. *North Clin Istanb*. 2017;4(1):100–107. doi:10.14744/nci.2017.49368
12. Rose JJ, Nouraie M, Gauthier MC, et al. Clinical outcomes and mortality impact of hyperbaric oxygen therapy in patients with carbon monoxide poisoning. *Crit Care Med*. 2018;46(7):e649–e655. doi:10.1097/CCM.0000000000003135
13. Eichhorn L, Thudium M, Jüttner B. The diagnosis and treatment of carbon monoxide poisoning. *Dtsch Arztebl Int*. 2018;115(51–52):863–870. doi:10.3238/arztebl.2018.0863
14. Ning K, Zhou YY, Zhang N, Sun XJ, Liu WW, Han CH. Neurocognitive sequelae after carbon monoxide poisoning and hyperbaric oxygen therapy. *Med Gas Res*. 2020;10(1):30–36. doi:10.4103/2045-9912.279981
15. Choi IS. Carbon monoxide poisoning: systemic manifestations and complications. *J Korean Med Sci*. 2001;16(3):253–261. doi:10.3346/jkms.2001.16.3.253
16. Zhang Y, Wang T, Wang S, et al. Gray matter atrophy and white matter lesions burden in delayed cognitive decline following carbon monoxide poisoning. *Hum Brain Mapp*. 2024;45(5):e26656. doi:10.1002/hbm.26656.
17. Endo T, Suzuki J, Ikeda R, Katori Y. Sensorineural hearing loss due to acute carbon monoxide poisoning. *J Int Adv Otol*. 2023;19(5):435–439.
18. Zhang Y, Wang T, Wang S, et al. Early gray matter atrophy and neurological deficits in patients with carbon monoxide poisoning. *Neuroradiology*. 2023;65(2):245–256. doi:10.1007/s00234-022-03041-5.
19. Weaver LK, Hopkins RO, Chan KJ, et al. Hyperbaric oxygen for acute carbon monoxide poisoning. *N Engl J Med*. 2002;347(14):1057–1067. doi:10.1056/NEJMoa013121
20. Jasper BW, Hopkins RO, Duker HV, Weaver LK. Affective outcome following carbon monoxide poisoning: a prospective longitudinal study. *Cogn Behav Neurol*. 2005;18(2):127–134. doi:10.1097/01.wnn.0000160820.07836.cf
21. Huang TL, Tung MC, Lin CL, Chang KH. Risk of acute kidney injury among patients with carbon monoxide poisoning. *Medicine (Baltimore)*. 2021;100(38):e27239. doi:10.1097/MD.0000000000027239
22. Wei KY, Liao CY, Chung CH, et al. Carbon monoxide poisoning and chronic kidney disease risk: a nationwide, population-based study. *Am J Nephrol*. 2021;52(4):292–303. doi:10.1159/000515383
23. Huang CC, Chen TH, Ho CH, et al. Increased risk of congestive heart failure following carbon monoxide poisoning. *Circ Heart Fail*. 2021;14(4): e007267. doi:10.1161/CIRCHEARTFAILURE.120.007267
24. Jones SJ, Horton A, Brunt H, Shankar G. Preventing carbon monoxide poisoning. *BMJ*. 2019;366(l4613). doi:10.1136/bmj.l4613
25. Ran T, Nurmagambetov T, Sircar K. Economic implications of unintentional carbon monoxide poisoning in the United States and the cost and benefit of CO detectors. *Am J Emerg Med*. 2018;36(3):414–419. doi:10.1016/j.ajem.2017.08.048
26. Iqbal S, Law HZ, Clower JH, Yip FY, Elixhauser A. Hospital burden of unintentional carbon monoxide poisoning in the United States, 2007. *Am J Emerg Med*. 2012;30(5):657–664. doi:10.1016/j.ajem.2011.03.003
27. Gordon BS, Malecki KMC, Camponeschi J, LeCaire TJ, Creswell PD, Schultz AA. For submission to the journal of community health: carbon monoxide awareness and detector use in the state of Wisconsin. *J Community Health*. 2024;49(1):1–7. doi:10.1007/s10900-023-01235-3
28. Christensen GM, Creswell PD, Theobald J, Meiman JG. Carbon monoxide detector effectiveness in reducing poisoning, Wisconsin 2014-2016. *Clin Toxicol (Phila)*. 2020;58(12):1335–1341. doi:10.1080/15563650.2020.1733592
29. Wheeler-Martin K, Soghoian S, Prosser JM, et al. Impact of mandatory carbon monoxide alarms: an investigation of the effects on detection and poisoning rates in New York city. *Am J Public Health*. 2015;105(8):1623–1629. doi:10.2105/AJPH.2015.302577
30. Cui P, Jin Y, Feng H, Li Z, Ding S, Li Y. Burden of carbon monoxide poisoning in China, 1990-2019: a systematic analysis of data from the global burden of disease study 2019. *Front Public Health*. 2022;10:930784. doi:10.3389/fpubh.2022.930784.
31. Johnson SC, Cunningham M, Dippenaar IN, et al. Public health utility of cause of death data: applying empirical algorithms to improve data quality. *BMC Med Inform Decis Mak*. 2021;21(1):175. doi:10.1186/s12911-021-01501-1
32. Vos T, Lim SS, Abbafati C, et al. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet*. 2020;396(10258):1204–1222. doi:10.1016/S0140-6736(20)30925-9
33. Ferrari, A.J., Santomauro, D.F., Aali, A., et al. Global incidence, prevalence, years lived with disability (YLDs), disability-adjusted life-years (DALYs), and healthy life expectancy (HALE) for 371 diseases and injuries in 204 countries and territories and 811 subnational locations, 1990-2021: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet*. 2024;403(10440):2133–2161. doi:10.1016/S0140-6736(24) 00757-8
34. He H, Liang L, Han D, Xu F, Lyu J. Different trends in the incidence and mortality rates of prostate cancer between China and the USA: a joinpoint and age-period-cohort analysis. *Front Med Lausanne*. 2022;9:824464. doi:10.3389/fmed.2022.824464
35. Luo LS, Luan HH, Wu L, et al. Secular trends in severe periodontitis incidence, prevalence and disability-adjusted life years in five Asian countries: a comparative study from 1990 to 2017. *J Clin Periodontol*. 2021;48(5):627–637. doi:10.1111/jcpe.13447
36. Al Hasan SM, Saulam J, Kanda K, et al. Temporal trends in apparent energy and macronutrient intakes in the diet in Bangladesh: a joinpoint regression analysis of the FAO's food balance sheet data from 1961 to 2017. *Nutrients*. 2020;12(8):2319. doi:10.3390/nu12082319

37. Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. *Stat Med*. 2000;19 (3):335–351. doi:10.1002/(SICI)1097-0258(20000215)19:3<335::AID-SIM336>3.0.CO;2-Z.
38. Luo L. Assessing validity and application scope of the intrinsic estimator approach to the age-period-cohort problem. *Demography*. 2013;50 (6):1945–1967. doi:10.1007/s13524-013-0243-z
39. Hosseinpoor AR, Bergen N, Schlotheuber A. Promoting health equity: WHO health inequality monitoring at global and national levels. *Glob Health Action*. 2015;8(1):29034. doi:10.3402/gha.v8.29034
40. Xie Y, Bowe B, Mokdad AH, et al. Analysis of the Global Burden of Disease study highlights the global, regional, and national trends of chronic kidney disease epidemiology from 1990 to 2016. *Kidney Int*. 2018;94(3):567–581. doi:10.1016/j.kint.2018.04.011
41. Zhou YY, Liu W, Yang YJ, Lu GD. Use of hyperbaric oxygen on flaps and grafts in China: analysis of studies in the past 20 years. *Undersea Hyperb Med*. 2014;41(3):209–216.
42. King ME, Damon SA. Attitudes about carbon monoxide safety in the United States: results from the 2005 and 2006 healthStyles Survey. *Public Health Rep*. 2011;1(26 Suppl 1(Suppl 1)):100–107. doi:10.1177/00333549111260S113
43. Popiołek I, Popiołek L, Marchewka J, et al. Knowledge about carbon monoxide poisoning among medical and non-medical students living in Kraków - questionnaire study. *Folia Med Cracov*. 2021;61(3):21–31. doi:10.24425/fmc.2021.138948
44. Hampson NB, Weaver LK. Residential carbon monoxide alarm use: opportunities for poisoning prevention. *J Environ Health*. 2011;73(6):30–33.
45. Hampson NB, Courtney TG, Holm JR. Should the placement of carbon monoxide (CO) detectors be influenced by CO's weight relative to air? *J Emerg Med*. 2012;42(4):478–482. doi:10.1016/j.jemermed.2011.03.015
46. Ryan TJ, Arnold KJ. Residential carbon monoxide detector failure rates in the United States. *Am J Public Health*. 2011;101(10):e15–17. doi:10.2105/AJPH.2011.300274
47. Vural A, Dolanbay T, Ozçelik M, et al. Biochemical parameters and clinical outcomes of carbon monoxide poisoning in special groups: children, pregnant women, and the elderly. *Eur Rev Med Pharmacol Sci*. 2024;28(11):3711–3724. doi:10.26355/eurrev_202406_36376
48. Sircar K, Clower J, Shin MK, Bailey C, King M, Yip F. Carbon monoxide poisoning deaths in the United States, 1999 to 2012. *Am J Emerg Med*. 2015;33(9):1140–1145. doi:10.1016/j.ajem.2015.05.002
49. Henn SA, Bell JL, Sussell AL, Konda S. Occupational carbon monoxide fatalities in the US from unintentional non-fire related exposures, 1992-2008. *Am J Ind Med*. 2013;56(11):1280–1289. doi:10.1002/ajim.22226
50. Dos Santos E, Villa A, Garnier R, Dufayet L, Langrand J. Surveillance and analysis of occupational carbon monoxide poisoning in the Paris region. *Ann Work Expo Health*. 2017;61(8):986–993. doi:10.1093/annweh/wxx063
51. Yoon SS, Macdonald SC, Parrish RG. Deaths from unintentional carbon monoxide poisoning and potential for prevention with carbon monoxide detectors. *JAMA*. 1998;279(9):685–687. doi:10.1001/jama.279.9.685
52. Feldman RD, Limbird LE. GPER (GPR30): a Nongenomic Receptor (GPCR) for steroid hormones with implications for cardiovascular disease and cancer. *Annu Rev Pharmacol Toxicol*. 2017;57(1):567–584. doi:10.1146/annurev-pharmtox-010716-104651
53. Lin J, Steenbergen C, Murphy E, Sun J. Estrogen receptor-beta activation results in S-nitrosylation of proteins involved in cardioprotection. *Circulation*. 2009;120(3):245–254. doi:10.1161/CIRCULATIONAHA.109.868729
54. Rostron BL, Wang B, Liu ST. Waterpipe or hookah-related poisoning events among U.S. Adolescents and young adults. *J Adolesc Health*. 2019;64 (6):800–803. doi:10.1016/j.jadohealth.2018.12.021
55. Wang M, Smith K, Yu Q, Miller C, Singh K, Sen CK. Mitochondrial connexin 43 in sex-dependent myocardial responses and estrogen-mediated cardiac protection following acute ischemia/reperfusion injury. *Basic Res Cardiol*. 2019;115(1):1. doi:10.1007/s00395-019-0759-5
56. Huijun H, Qiang S, Dazhi G, et al. Sex differences may affect the severity of poisoning and prognosis after carbon monoxide poisoning: a retrospective study. *Undersea Hyperb Med*. 2016;43(3):207–215.
57. Zavorsky GS, Tesler J, Rucker J, Fedorko L, Duffin J, Fisher JA. Rates of carbon monoxide elimination in males and females. *Physiol Rep*. 2014;2 (12):e12237. doi:10.14814/phy2.12237
58. Long J, Sun Y, Zhao J, Liu J, Peng X. Temporal trends of carbon monoxide poisoning mortality at the global, regional and national levels: a cross-sectional study from the Global Burden of Disease study, 1990 and 2017. *BMJ Open*. 2021;11(11):e053240. doi:10.1136/bmjopen-2021-053240
59. Harper A, Croft-Baker J. Carbon monoxide poisoning: undetected by both patients and their doctors. *Age Ageing*. 2004;33(2):105–109. doi:10.1093/ageing/afh038
60. Global Burden of Disease Study 2019. Global burden of 87 risk factors in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet*. 2020;396(10258):1223–1249. doi:10.1016/S0140-6736(20)30752-2
61. Smith KR, Bruce N, Balakrishnan K, et al. Millions dead: how do we know and what does it mean? Methods used in the comparative risk assessment of household air pollution. *Annu Rev Public Health*. 2014;35(1):185–206. doi:10.1146/annurev-publhealth-032013-182356
62. Hampson NB, Weaver LK. Carbon monoxide poisoning: a new incidence for an old disease. *Undersea Hyperb Med*. 2007;34(3):163–168.
63. Roth GA, Abate D, Abate KH, et al. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2018;392(10159):1736–1788. doi:10.1016/S0140-6736(18)32203-7
64. Vural A, Dolanbay T. Early and late adverse clinical outcomes of severe carbon monoxide intoxication: a cross-sectional retrospective study. *PLoS One*. 2024;19(8):e0301399. doi:10.1371/journal.pone.0301399