Clinical Epidemiology

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Global, Regional, and National Burden of Ischemic Heart Disease Attributable to 25 Risk Factors and Their Summary Exposure Value Across 204 Countries With Different Socio-Demographic Index Levels, 1990–2021: A Systematic Fixed-Effects Analysis and Comparative Study

Juntao Tan[1], Min Xue[2], Huanyin Li[3], Yang Liu[3], Yuxin He[4], Jing Liu[5], Jie Liu[1], Luojia Tang[6], Jixian Lin[3]

[1]College of Medical Informatics, Chongqing Medical University, Chongqing, 400016, People's Republic of China; [2]Department of Respiratory, Minhang Hospital, Fudan University, Shanghai, 201101, People's Republic of China; [3]Department of Neurology, Minhang Hospital, Fudan University, Shanghai, 201101, People's Republic of China; [4]Department of Medical Administration, Affiliated Banan Hospital of Chongqing Medical University, Chongqing, 401320, People's Republic of China; [5]Department of Nursing, Minhang Hospital, Fudan University, Shanghai, 201101, People's Republic of China; [6]Emergency Department of Zhongshan Hospital, Fudan University, Shanghai, 200032, People's Republic of China

Correspondence: Jixian Lin, Department of Neurology, Minhang Hospital, Fudan University, Shanghai, 201101, People's Republic of China, Email linjixian@fudan.edu.cn; Luojia Tang, Emergency Department of Zhongshan Hospital, Fudan University, Shanghai, 200032, People's Republic of China, Email tang.luojia@zs-hospital.sh.cn

Clinical Epidemiology downloaded from https://www.dovepress.com/
For personal use only.

Background: A systematic relational assessment of the global, regional, and national Ischemic heart disease (IHD) burden and its attributable risk factors is essential for developing more targeted prevention and intervention strategies.

Methods: The GBD 2021 comparative risk assessment framework was employed to evaluate stroke burden attributable to environmental, behavioral, metabolic, and dietary risk factors, and a total of 25 risk factors were included. Specifically, we used the joinpoint regression model, decomposition analysis, and systematic fixed-effects analysis to reveal the global, regional, and national burden of IHD attributable to these 25 risk factors and their exposure value across 204 countries and territories with different socio-demographic index (SDI) levels from different perspectives.

Results: Joinpoint regression revealed similar trends in summary exposure value (SEV) and attributable burdens for 25 IHD risk factors. From 1990 to 2021, SEV rankings increased for 12/25 risk factors, decreased for 10/25, and remained unchanged for 3/25. Decomposition analysis indicated that from 1990 to 2021, low SDI countries experienced the most significant increase in IHD burden attributable to 25 risk factors due to population growth, while upper-middle and high SDI countries were most affected by population aging, and high SDI countries demonstrated the greatest reduction in IHD burden attributed to epidemiological changes. Panel data analysis elucidated the impact of SEV, SDI, and quality-of-care index (QCI) on attributable IHD burden.

Conclusion: This study emphasizing the critical role of risk factor control. Tailored interventions and exploration of country-specific factors are crucial for effectively reducing the global IHD burden.

Keywords: ischemic heart disease, disease burden, risk factors, socio-demographic index, systematic fixed-effects analysis

Introduction

Cardiovascular diseases, particularly ischemic heart disease (IHD), constitute a formidable challenge to global health systems in the 21st century. As a leading contributor to mortality and morbidity worldwide, IHD accounted for approximately 182 million 9.14 million quality-adjusted life years (QALYs) and deaths globally in 2019, exerting a profound impact on both individual well-being and societal resources.[1]

Received: 4 December 2024
Accepted: 3 February 2025
Published: 20 February 2025

© 2025 Tan et al. This work is published and licensed by Dove Medical Press Limited. The full terms of this license are available at https://www.dovepress.com/terms.php and incorporate the Creative Commons Attribution – Non Commercial (unported, v3.0) License (http://creativecommons.org/licenses/by-nc/3.0/). By accessing the work you hereby accept the Terms. Non-commercial uses of the work are permitted without any further permission from Dove Medical Press Limited, provided the work is properly attributed. For permission for commercial use of this work, please see paragraphs 4.2 and 5 of our Terms (https://www.dovepress.com/terms.php).

The etiology of IHD is intricately linked to a constellation of modifiable risk factors. Recent epidemiological studies have elucidated that a significant proportion of the global IHD burden is attributable to well-defined risk factors. These include, but are not limited to, hypertension, dyslipidemia, diabetes mellitus, tobacco use, and obesity.[2] The population attributable fractions (PAFs) associated with these risk factors underscore the considerable potential for disease prevention.[3] Notably, the prevalence and intensity of exposure to these risk factors within populations exhibit a strong correlation with IHD incidence rates. Preliminary modeling suggests that comprehensive strategies aimed at mitigating these risk factors could potentially avert a substantial proportion of IHD events within a relatively short timeframe.[4,5]

Economic analyses have revealed a striking disparity between healthcare expenditures allocated to managing IHD-related complications and those directed towards primary prevention and risk factor control.[6] This misalignment of resources suggests that a paradigm shift towards preventive strategies could yield significant economic benefits and alleviate the burden on healthcare systems. The landmark INTERHEART study further reinforced this notion by demonstrating that approximately 90% of the attributable risk for acute myocardial infarction is associated with nine potentially modifiable risk factors.[7] This finding underscores the critical importance of public health interventions targeting these risk factors.

The burden of IHD is further compounded by demographic transitions occurring globally. Population growth and aging have contributed substantially to the increasing prevalence of IHD, albeit with varying impacts across different regions and socioeconomic strata.[8] Many nations have witnessed a surge in IHD-related DALYs, attributable not only to an expanding population base but also to a shifting age structure skewed towards older demographics.[9]

Disparities in IHD burden are starkly evident when comparing countries across the economic spectrum. Low- and middle-income countries (LMICs) bear a disproportionate share of global IHD morbidity and mortality, with the rate of increase in disease burden outpacing that observed in high-income countries (HICs).[10] This inequity may be partially attributed to variations in the quality and accessibility of acute cardiac care, as well as differences in the implementation of preventive strategies.[11]

To quantify and compare these disparities, researchers have employed metrics such as the Socio-Demographic Index (SDI) and the quality-of-care index (QCI). The SDI serves as a valuable tool for stratifying populations based on socioeconomic factors, enabling the identification of variations in risk factor prevalence and disease burden across diverse contexts.[3] This stratification facilitates the development of tailored health interventions that address the specific needs of different populations. Complementarily, the QCI provides insight into the performance of healthcare systems in managing IHD. High-quality care, as reflected by superior QCI scores, has been associated with reduced mortality rates, extended life expectancy, improved quality of life, and decreased disease incidence.[12]

In light of these complex interactions between risk factors, demographics, socioeconomic conditions, and healthcare quality, our study aims to elucidate the multifaceted determinants of IHD burden. We employ a decomposition analysis to quantify the contributions of population growth and aging to the changing landscape of IHD. Furthermore, we utilize panel analysis models to examine the relationships between the intensity of attributable IHD burden (adjusted for demographic effects) and key variables including risk factor summary exposure values (SEVs), national SDI, and QCI. Additionally, leveraging longitudinal data spanning several decades, we construct fixed-effects models to capture country-specific factors that influence IHD burden. This comprehensive approach allows us to explore the impact of both measurable indicators and less tangible country-specific characteristics on the evolving patterns of IHD burden globally.

Methods

Overview

Data from the 2021 GBD study was obtained via the Global Health Data Exchange (GHDx) query tool (https://vizhub.healthdata.org/gbd-results/). The 2021 GBD study assessed 371 diseases and injuries along with 88 risk factors.[13] The methodological framework for data acquisition, processing, and analysis in the 2021 GBD study has been thoroughly documented in prior publications. Informed consent forms were not required as the GBD utilizes deidentified aggregate data. In the GBD classification system, diseases and injuries are organized into four levels of causes. IHD is classified as a level 3 cause under noncommunicable diseases (level 1) and cardiovascular diseases (level 2). In this study, we extracted the annual number of cases, their corresponding 95% uncertainty intervals (UIs), and age-standardized rates (ASRs) for the prevalence, incidence, DALYs, and deaths associated with IHD from the GBD 2021 dataset.

Definition

The GBD database encompasses 204 countries or territories, categorized by the quintiles of the socio-demographic index (SDI).[14] The SDI regional classification can be obtained from the Institute for Health Metrics and Evaluation (https://ghdx.healthdata.org/search/site/SDI). The SDI ranges from 0 to 100, reflecting a country's overall social and economic development by integrating per capita income, total fertility rate (for those under 25), and average education level (for those aged 15 and above).

Risk Factors

GBD risk factors are categorized into four levels, ranging from Level 1, which is the broadest category (environmental, behavioral, dietary, and metabolic), to Level 4, which is the most specific (such as household air pollution from solid fuels).[15] In this study, 25 risk factors were included in risk estimation for IHD. Specifically, Risk factors for IHD include environmental risks, ie ambient particulate matter pollution, household air pollution from solid fuels, high temperature, low temperature, and lead exposure; Behavioral risks, ie low physical activity, smoking, and secondhand smoke; Dietary risks, ie diet low in fruits, diet low in vegetables, diet low in whole grains, diet high in red meat, diet high in processed meat, diet high in sugar-sweetened beverages, diet low in fiber, diet low in polyunsaturated fatty acids, diet high in sodium, diet low in legumes, diet low in nuts and seeds, and diet low in seafood omega-3 fatty acids; Metabolic risks, ie high fasting plasma glucose, high LDL cholesterol, high systolic blood pressure, high body-mass index, and kidney dysfunction. Our analysis incorporated data on IHD-related DALYs and deaths attributable to these factors, stratified by region to highlight geographical variations. Additionally, the age-standardized SEV summarizes the population's exposure distribution to these 25 risk factors.

Statistics

We utilized the joinpoint regression model (JRM) to analyze the time trends of IHD-attributable risk factors and the time trends of SEV for each attributable risk factor from 1990 to 2021.[16] We then computed the average annual percent change (AAPC). The AAPC was calculated as the weighted average of the slope coefficients of the JRM, with weights corresponding to the duration between each pair of connecting points within a predetermined time interval.[17] This weighted average was subsequently converted into a percentage change. The advantage of JRM lies in its ability to assess the statistical significance of changes across different time periods, thereby reducing the subjectivity inherent in traditional trend analysis when interpreting linear trends.

We performed a decomposition analysis to comprehensively understand the factors influencing changes in DALYs and deaths due to IHD from 1990 to 2021, considering population, aging, and epidemiological change. Additionally, we conducted a decomposition analysis to elucidate the epidemiological changes associated with each IHD-attributable risk factor over consecutive two-year periods.

Finally, we explored the relationship between country-level indicators (SDI, SEV, and QCI) and the epidemiological changes of each ihd-attributable risk factor over two consecutive years using panel data analysis.[18] In this study, we derived four secondary indicators from six main indicators to comprehensively evaluate the quality of care parameters: (1) mortality to incidence ratio, (2) prevalence to incidence ratio, (3) mortality to incidence ratio, and (4) years of life lost to years lived with disability ratio. We employed principal component analysis (PCA) to aggregate these four indicators into separate components, with the first component extracted from PCA being QCI.[19] The QCI score ranges from 0 to 100, where 100 represents the highest quality of care in the sample.[20] A fixed-effects model was utilized in this study to reduce the likelihood of multiplicity in the constructed model and to provide a more conservative estimate. The fixed effects were used as the standard for comparing the burden of IHD and its attributable risk factors across different countries. World maps were generated based on quintiles of effect values from 204 countries and territories, and Sankey plots were used to depict the relationships between various regions and the fixed effects quintiles of DALYs and deaths.

https://doi.org/10.2147/CLEP.S510347

All statistical analyses were conducted using R software (version 4.3.3). A p-value of less than 0.05 was considered statistically significant.

Results

Overall IHD Burden

In 2021, there were 31.87 million (95% UI 26.28–38.27) incident IHDs and 254.28 million (221.45–295.49) prevalent IHDs, 188.36 million (177.04–198.15) DALYs due to IHD, and 8.99 million (8.26–9.53) deaths from IHD (Table 1). Although the ASR of IHD deaths, DALYs, prevalence, and incidence declined from 1990 to 2021, the absolute number of died, remained disabled, survived, or new IHD from IHD substantial increased. The results of the decomposition analysis revealed that population growth and aging were the main catalysts for the absolute number of IHD-related deaths, DALYs, prevalence, and incidence (Figure 1). We also found that whether IHD-related deaths, DALYs, prevalence, or incidence, the region with the best control of percent change of epidemiology change was high SDI, while the region with the worst control of percent change of epidemiology change was Low-middle SDI (Figure 1). In addition, the burden of IHD still mainly attributed to risk factors (Table S1). Specifically, in 2021, all risk factors contribute 91.67% (88.44% to 93.36%) and 92.27% (88.88% to 93.95%) of the IHD deaths and DALYs, respectively.

Global Exposure to Risk Factors

Figure 2 shows the trends in risk exposure for each risk factor included in this study globally over two time intervals: the entire study period from 1990 to 2021. Figure 2A and B illustrate the distribution of SEVs for various risk factors across different SDI regions in 1990 and 2021, respectively.Based on this figure, we can divide risks into three groups according to the changes in global SEV rankings in 1990 and 2021: increases group (ambient particulate matter pollution, high temperature, low physical activity, diet high in sugar-sweetened beverages, diet high in red meat, diet high in sodium, diet low in whole grains, diet low in fruits, high fasting plasma glucose, high systolic blood pressure, high LDL cholesterol, and high body-mass index), declines group (household air pollution from solid fuels, lead exposure, smoking, secondhand smoke, diet high in processed meat, diet low in vegetables, diet low in fiber, diet low in legumes, diet low in nuts and seeds, and diet low in seafood omega-3 fatty acids), and the remainder risks with no changes (low temperature, diet low in polyunsaturated fatty acids, and kidney dysfunction). Figure 2C shows how SEV exposure trends and percentage change of SEV has led to marked changes in risk rankings from 1990 to 2021. In 1990, the top five risk factors of SEVs were diet low in polyunsaturated fatty acids (78.22), diet low in seafood omega-3 fatty acids (49.24), high LDL cholesterol (46.78), lead exposure (46.70), and diet low in fruits (45.33). By 2021, all of these factors have shown varying degrees of decline in SEVs. The top five risk factors of SEVs in 2021 were diet low in polyunsaturated fatty acids (75.64), high LDL cholesterol (45.30), diet low in whole grains (43.75), diet low in fruits (40.90), and diet high in sodium (39.97). Other notable shifts include the large increase in percentage change of SEV and rank for high body-mass index, high fasting plasma glucose, and high temperature, and high systolic blood pressure.

IHD Burden Attributable to Risk Factors

In 2021, the five leading specific risk factors contributing to IHD deaths were high systolic blood pressure (4692.86 thousand [3799.89–5515.76] attributable deaths; 56.94% [51.99–61.99] of all IHD deaths]), high LDL cholesterol (2709.81 thousand [1803.80–3683.80]; [32.88% [24.68–41.40]), ambient particulate matter pollution (1729.55 thousand [1212.50–2286.98]; 20.98% [16.59–25.70]), kidney dysfunction (1398.57 thousand [976.44–1778.40]; 16.97% [13.36–-19.99]), and smoking (1346.29 thousand [1143.83–1571.73]; 16.33% [15.65–17.66]; Table S2). The five leading specific risk factors contributing to IHD DALYs were high systolic blood pressure (93.96 million [75.57–110.79] attributable DALYs; 54.06% [48.03–59.51] of all IHD DALYs]), high LDL cholesterol (66.75 million [47.51–86.99]; [38.40% [30.19–46.72]), ambient particulate matter pollution (36.52 million [25.54–48.13]; 21.01% [16.23–25.85]), smoking (35.48 million [30.53–40.70]; 20.42% [19.40–21.86]), and diet low in whole grains (27.13 million [16.85–36.70]; 15.61% [10.71–19.71]; (Table S3).

Table 1 Absolute Number and Age-Standardised Rates per year of Incident and Prevalent IHDs, Deaths From IHD and DALYs Due to IHD in 2021, and Percentage Change Globally for 1990–2021, by SDI Regions

	Incidence (95% UI)		Deaths (95% UI)		Prevalence (95% UI)		DALYs (95% UI)	
	2021	**Percentage Change, 1990–2021**	**2021**	**Percentage Change, 1990–2021**	**2021**	**Percentage Change, 1990–2021**	**2021**	**Percentage Change, 1990–2021**
Global								
Absolute number, millions	31.87 (26.28 to 38.27)	101.55% (99.42 to 103.02)	8.99 (8.26 to 9.53)	67.53% (62.79 to 71.34)	254.28 (221.45 to 295.49)	126.69% (122.75 to 135.02)	188.36 (177.04 to 198.15)	58.07% (54.55 to 60.51)
Age-standardised rate, per 100,000 people	372.9 (307.95 to 444.19)	−11.12% (−12.28 to −10.83)	108.73 (99.6 to 115.38)	−31.57% (−32.77 to −30.2)	2946.38 (2572.69 to 3424.32)	1.43% (−0.13 to 5.43)	2212.16 (2075.54 to 2327.61)	−28.81% (−30.03 to −27.77)
High SDI								
Absolute number, millions	3.99 (3.38 to 4.71)	5.88% (5.22 to 6.1)	1.39 (1.22 to 1.49)	−19.63% (−23.51 to −17.17)	34.23 (30.15 to 39.2)	35.58% (34.7 to 38.64)	23.55 (21.45 to 24.74)	−26.43% (−29.27 to −24.76)
Age-standardised rate, per 100000 people	195.63 (164.52 to 231.53)	−43.05% (−43.43 to −43.12)	58.45 (52.18 to 61.92)	−62.91% (−63.81 to −62.22)	1671.6 (1475.88 to 1910.43)	−26.42% (−26.97 to −24.76)	1134.02 (1053.56 to 1186.53)	−61.16% (−61.87 to −60.48)
High-middle SDI								
Absolute number, millions	7.87 (6.46 to 9.45)	85.6% (82.25 to 87.61)	2.45 (2.22 to 2.65)	52.69% (45.23 to 59.67)	63.83 (55.67 to 74.56)	107.59% (103.69 to 116.51)	44.54 (41.13 to 48.04)	32.69% (27.38 to 38.42)
Age-standardised rate, per 100000 people	404.44 (331.92 to 480.98)	−12.6% (−14.17 to −11.96)	127.5 (115.03 to 137.72)	−34.26% (−36.83 to −31.35)	3217.58 (2814.34 to 3742.18)	0.63% (−1.52 to 4.49)	2301.49 (2122.97 to 2482.46)	−35.89% (−38.21 to −33.14)
Middle SDI								
Absolute number, millions	10.5 (8.57 to 12.7)	187.27% (185.67 to 188.89)	2.81 (2.56 to 3.02)	170.57% (162.1 to 174.79)	85.37 (73.61 to 100.12)	205.84% (199.39 to 215.97)	61.24 (56.96 to 65.53)	130.87% (126.79 to 133.49)
Age-standardised rate, per 100000 people	403.84 (330.37 to 481.69)	5.12% (4.75 to 5.5)	118.71 (107.23 to 127.8)	−6.57% (−9.4 to −5.31)	3226.3 (2806.67 to 3798.24)	12.48% (11.07 to 17.35)	2351.21 (2174.84 to 2514.63)	−9.34% (−11.13 to −8.41)
Low-middle SDI								
Absolute number, millions	7.29 (6.12 to 8.7)	133.37% (128.68 to 137.78)	1.83 (1.7 to 1.96)	143.6% (143.24 to 144.12)	55.2 (48.04 to 63.65)	156.74% (152.42 to 163.04)	46.06 (42.69 to 49.49)	122.77% (122.06 to 123.78)
Age-standardised rate, per 100000 people	515.6 (433.64 to 614.95)	−3% (−3.57 to −1.55)	142.1 (131.3 to 151.87)	0.79% (0.41 to 1.19)	3941.42 (3448.94 to 4577.03)	6.03% (4.76 to 9.31)	3138.58 (2912.65 to 3360.62)	−2.58% (−2.7 to −2.24)
Low SDI								
Absolute number, millions	2.19 (1.81 to 2.67)	118.14% (116.16 to 121.92)	0.49 (0.45 to 0.54)	115.67% (112.83 to 121.42)	15.42 (13.31 to 17.82)	132.92% (125.69 to 139.55)	12.78 (11.57 to 14.12)	106.27% (103.05 to 112.42)
Age-standardised rate, per 100000 people	444.61 (362.9 to 537.75)	−5.68% (−6.09 to −5.51)	116.41 (105.21 to 127.69)	−2.59% (−3.59 to −0.98)	3162.53 (2763.3 to 3679.6)	2.01% (−0.04 to 5.81)	2464.12 (2235.87 to 2725.2)	−7.67% (−8.16 to −5.31)

Notes: Absolute numbers in millions, age-standardised rates per 100000 people and percentage change are presented to two decimal places.
Abbreviations: UI, uncertainty interval; SDI, socio-demographic index; DALY, disability adjusted life-year.

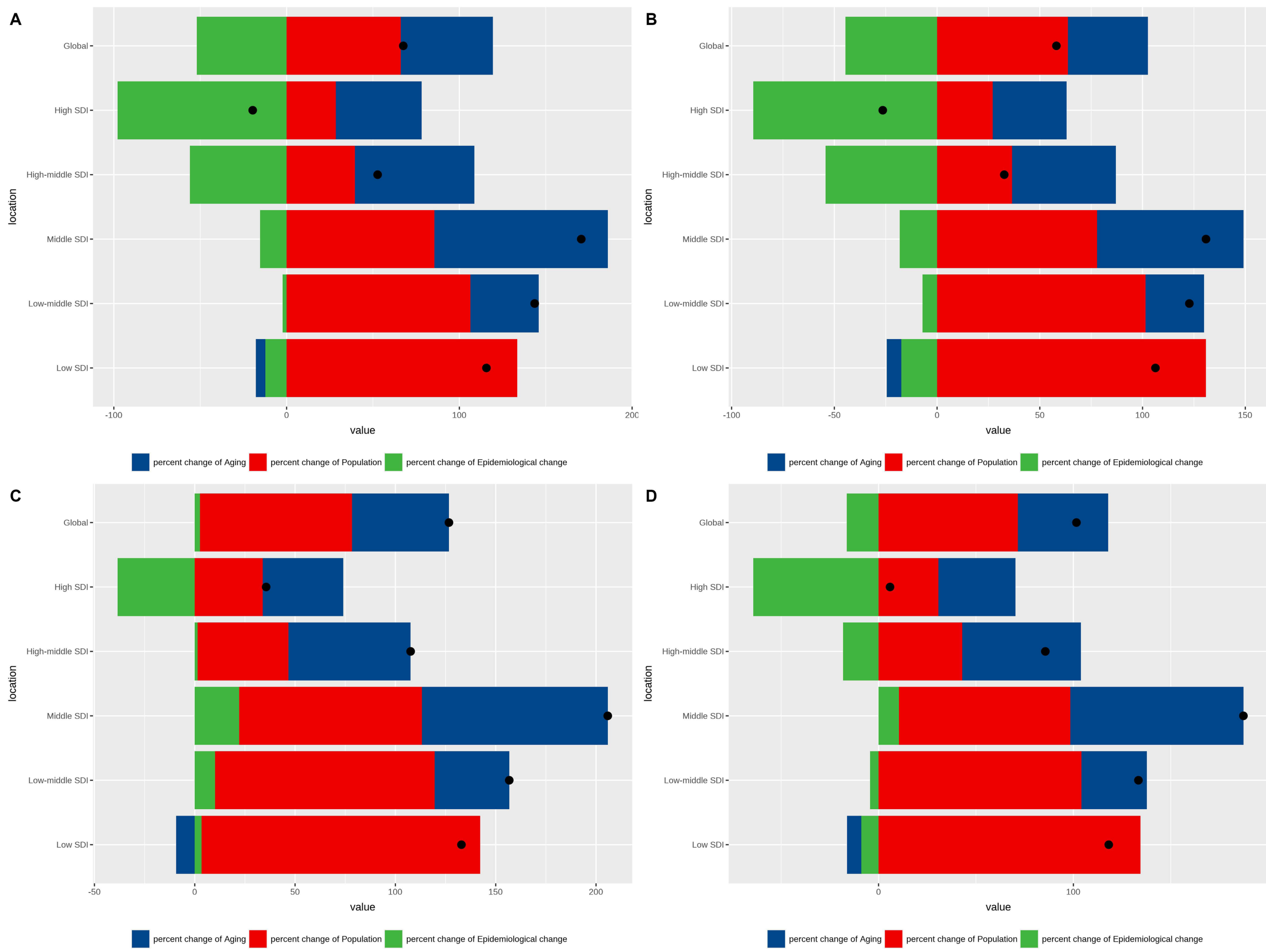

Figure 1 Changes in deaths, DALYs, prevalence, and incidence of IHD according to aging, population growth and epidemiological change from 1990 to 2021. (**A**) deaths. (**B**) DALYs. (**C**) prevalence. (**D**) incidence.
Abbreviation: DALYs, disability-adjusted life years.

Figures 3 and 4 respectively illustrate the deaths and DALYs risk factor burden of IHD in 2021, along with the proportion of burden of different SDI regions in each risk factor. High systolic blood pressure, high LDL cholesterol, and ambient particulate matter pollution rank among the top three risk factors of deaths and DALYs burden, with the proportion of risk burden of high systolic blood pressure even exceeding 50% (Figures 3A and 4A). For the risk burden of deaths, High SDI, High-middle SDI, Middle SDI, and Low-middle SDI have the highest burden proportions in diet high in processed meat (58.68%), diet high in red meat (39.29%), ambient particulate matter pollution (40.50%), and household air pollution from solid fuels (48.85%), respectively (Figure 3B). While for the risk burden of DALYs, the distribution of the highest risk burden proportion in each SDI region is consistent with the distribution of deaths risk burden (Figure 4B).

The pattern of risk-factor-attributable burden varied considerably by SDI and over time, as shown in Figure 5 and Figures S1–S5, which includes arrows plots for global combined and for five SDI regions (High SDI, High-middle SDI, Middle SDI, Low-middle SDI, and Low SDI). These figures illustrate specific risk factors at Level 4 of the risk factor hierarchy. Figure 5 demonstrates how trends in risk exposure and underlying changes in disease numbers and rates have led to marked changes in risk rankings from 1990 to 2021. In 1990, the leading risk factors were high systolic blood pressure, high LDL cholesterol, and smoking, all of which have changed hardly in terms of percentage of attributable deaths and rank by 2021 (Figure 5A). The leading risks in 2021 were high systolic blood pressure, high LDL cholesterol, and ambient particulate matter pollution. Other notable shifts include the large increase in percentage of attributable

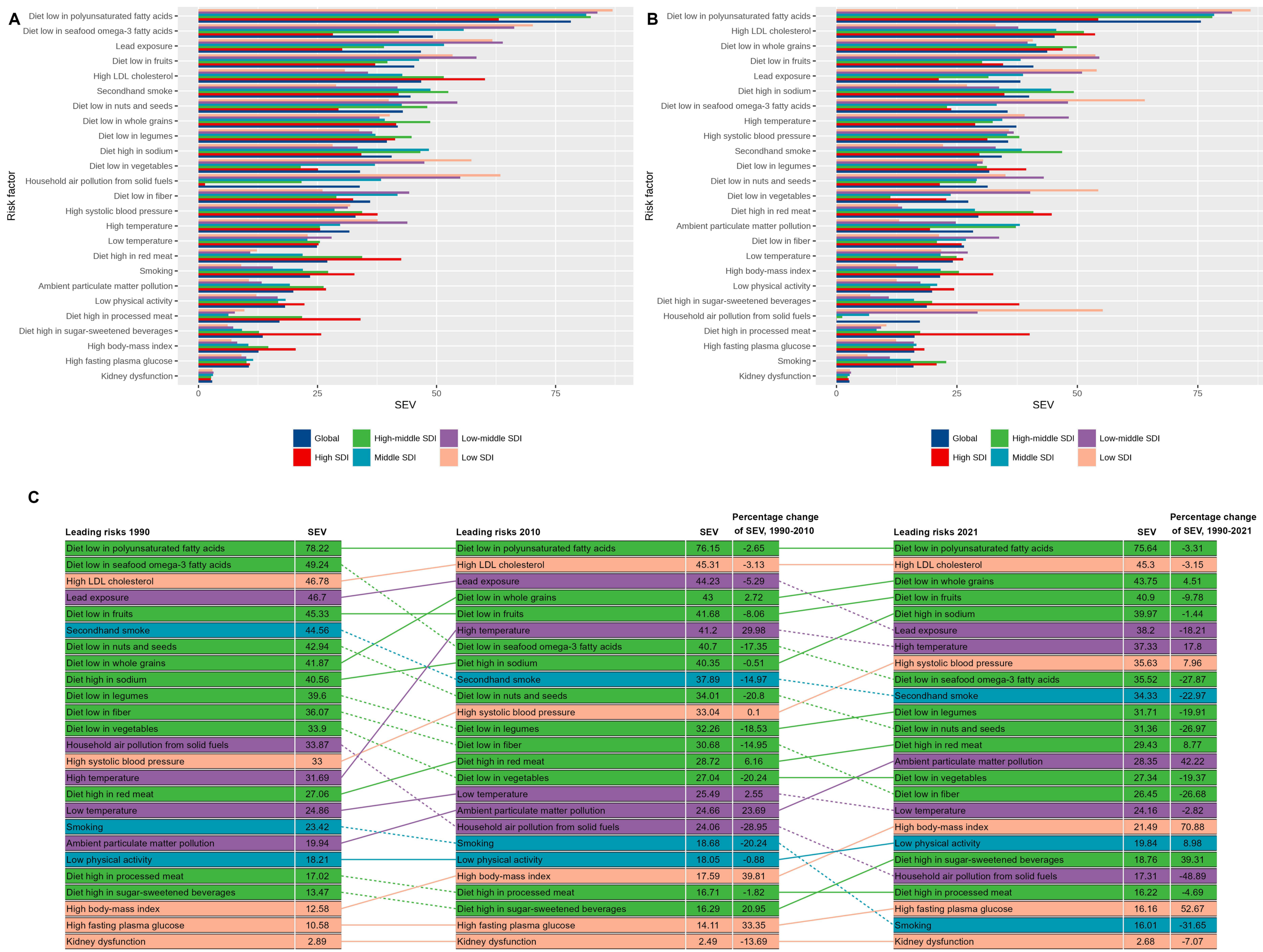

Figure 2 The SEV distribution of various risk factors. (**A**) Distribution of SEV in 1990. (**B**) Distribution of SEV in 2021. (**C**) The changes in global SEV rankings in 1990 and 2021.
Abbreviation: SEV, summary exposure value.

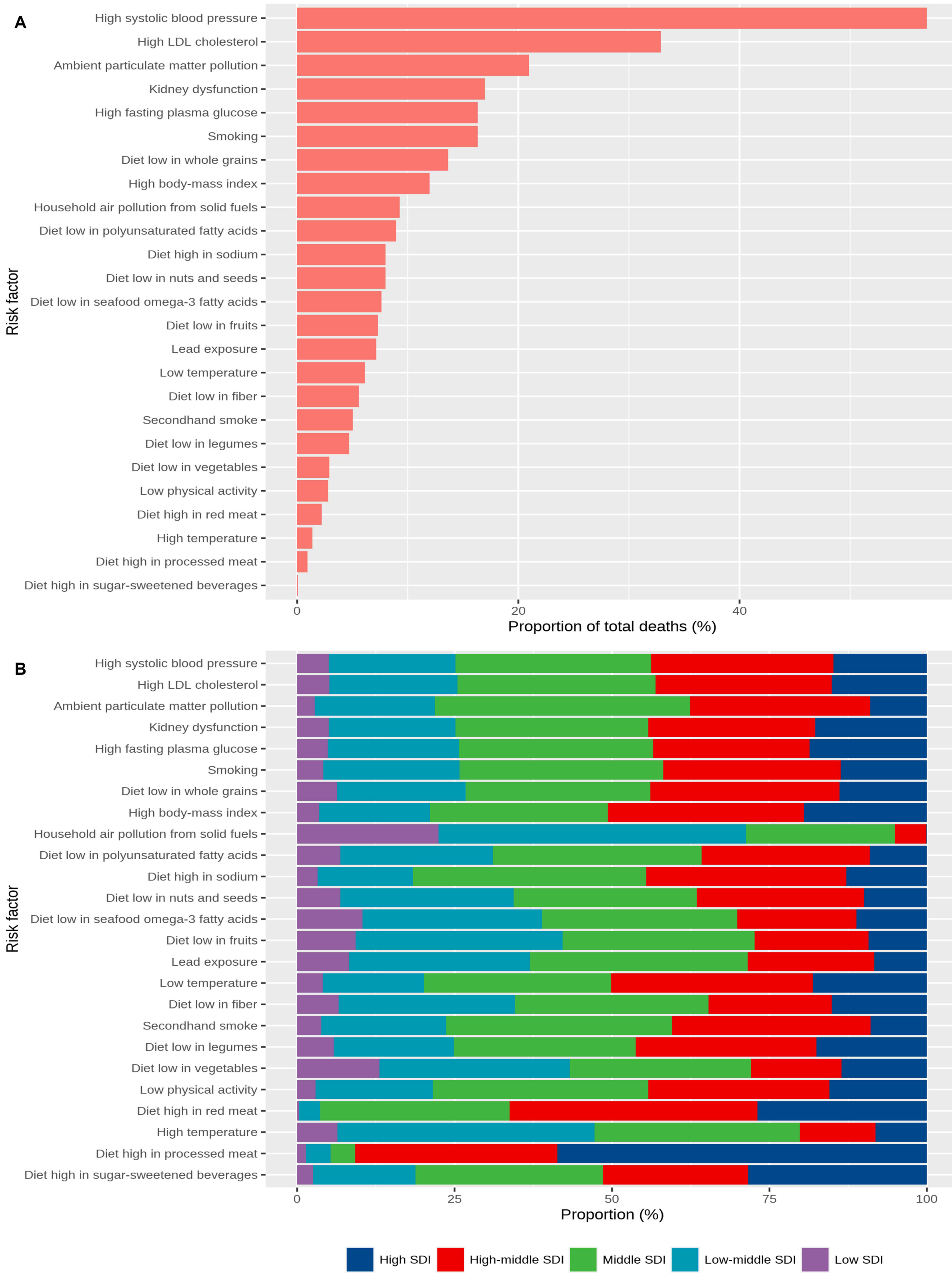

Figure 3 The deaths risk factor burden of IHD in 2021. (**A**) The proportion of attributable risk factors for IHD related deaths. (**B**) The proportion of risk factor burden of deaths of different SDI regions in each risk factor.
Abbreviation: SDI, sociodemographic index.

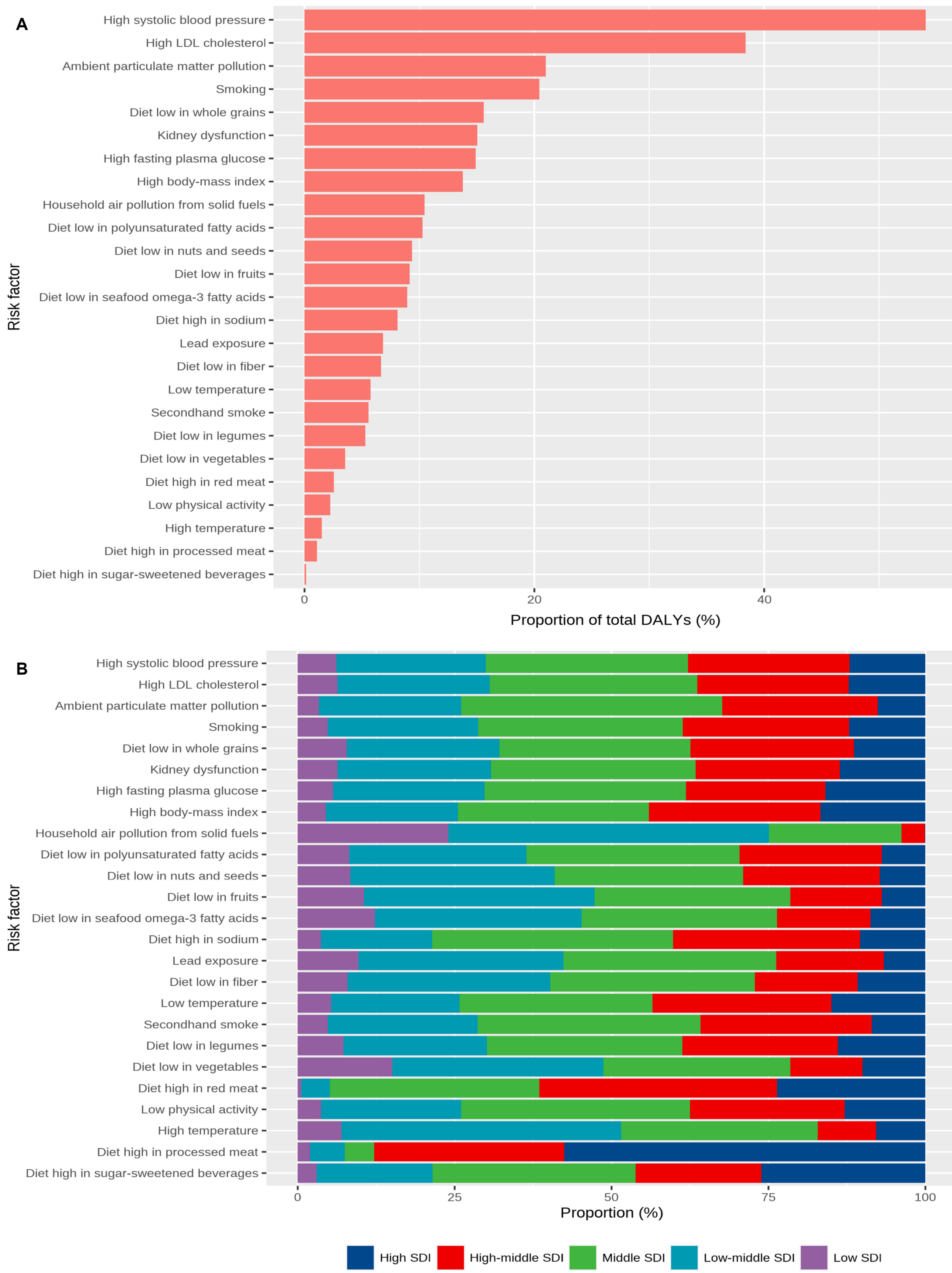

Figure 4 The DALYs risk factor burden of IHD in 2021. (**A**) The proportion of attributable risk factors for IHD related DALYs. (**B**) The proportion of risk factor burden of DALYs of different SDI regions in each risk factor.

Abbreviations: DALYs, disability-adjusted life years; SDI, sociodemographic index.

https://doi.org/10.2147/CLEP.S510347

https://doi.org/10.2147/CLEP.S510347

A

Leading risks 1990	Percentage of deaths, 1990
High systolic blood pressure	57.16
High LDL cholesterol	36.03
Smoking	20.66
Ambient particulate matter pollution	17.03
Kidney dysfunction	16.6
Diet low in whole grains	15.02
Household air pollution from solid fuels	14.44
High fasting plasma glucose	11.38
Diet low in nuts and seeds	10.35
Diet low in seafood omega-3 fatty acids	10.03
High body-mass index	9.8
Diet low in polyunsaturated fatty acids	8.89
Diet low in fruits	8.32
Diet low in fiber	7.53
Diet high in sodium	7.31
Low temperature	6.53
Diet low in legumes	6.2
Secondhand smoke	5.76
Lead exposure	5.57
Diet low in vegetables	3.78
Diet high in red meat	2.8
Low physical activity	2.52
Diet high in processed meat	2.36
High temperature	0.65
Diet high in sugar-sweetened beverages	0.08

Leading risks 2010	Percentage of deaths, 2010	Percentage change in number of deaths, 1990–2010	Percentage change in the ASR of deaths, 1990–2010
High systolic blood pressure	56.88	36.66	-23.15
High LDL cholesterol	33.65	28.26	-25.66
Ambient particulate matter pollution	18.4	48.36	-17.12
Smoking	18.08	20.16	-27.52
Kidney dysfunction	16.74	38.5	-24.53
High fasting plasma glucose	14.73	77.66	0.66
Diet low in whole grains	14.29	30.64	-24.18
Household air pollution from solid fuels	13.35	26.98	-23.82
High body-mass index	11.06	54.96	-10.34
Diet low in polyunsaturated fatty acids	8.98	38.64	-18.94
Diet low in nuts and seeds	8.81	16.94	-31.82
Diet low in seafood omega-3 fatty acids	8.72	19.4	-30.3
Diet high in sodium	7.84	47.26	-14.43
Diet low in fruits	7.66	26.51	-25.24
Lead exposure	6.96	71.67	0.71
Low temperature	6.49	36.52	-22.44
Diet low in fiber	6.41	17.01	-32.94
Secondhand smoke	5.44	29.54	-24
Diet low in legumes	5	10.58	-36.07
Diet low in vegetables	2.98	8.33	-36.4
Low physical activity	2.64	43.62	-21.72
Diet high in red meat	2.35	15.25	-32.49
Diet high in processed meat	1.51	-12.3	-47.44
High temperature	1.37	189.18	69.57
Diet high in sugar-sweetened beverages	0.08	38.64	-19.07

Leading risks 2021	Percentage of deaths, 2021	Percentage change in number of deaths, 1990–2021	Percentage change in the ASR of deaths,1990–2021
High systolic blood pressure	56.94	64.58	-33.84
High LDL cholesterol	32.88	50.75	-36.04
Ambient particulate matter pollution	20.98	103.52	-18.39
Kidney dysfunction	16.97	68.87	-35.22
Smoking	16.33	30.63	-41.48
High fasting plasma glucose	16.33	137	-4.77
Diet low in whole grains	13.66	50.3	-36.19
High body-mass index	11.96	101.62	-14.99
Household air pollution from solid fuels	9.26	5.9	-53.77
Diet low in polyunsaturated fatty acids	8.94	66.18	-28.8
Diet high in sodium	7.99	80.63	-24.25
Diet low in nuts and seeds	7.99	27.5	-45.32
Diet low in seafood omega-3 fatty acids	7.61	25.43	-46.3
Diet low in fruits	7.3	45.06	-36.52
Lead exposure	7.16	112.61	-10.05
Low temperature	6.13	55.2	-36.92
Diet low in fiber	5.57	22.19	-48.48
Secondhand smoke	5.03	44.21	-37.92
Diet low in legumes	4.72	25.78	-47.18
Diet low in vegetables	2.91	27.08	-45.47
Low physical activity	2.82	84.72	-29.63
Diet high in red meat	2.2	29.87	-44.15
High temperature	1.36	245.08	48.1
Diet high in processed meat	0.94	-33.89	-70.7
Diet high in sugar-sweetened beverages	0.08	78.18	-22.37

B

Leading risks 1990	Percentage of DALYs, 1990
High systolic blood pressure	53.1
High LDL cholesterol	41.21
Smoking	25.78
Diet low in whole grains	17.09
Household air pollution from solid fuels	16.68
Ambient particulate matter pollution	16.3
Kidney dysfunction	14.64
Diet low in nuts and seeds	12.09
Diet low in seafood omega-3 fatty acids	11.77
High body-mass index	10.75
Diet low in fruits	10.37
Diet low in polyunsaturated fatty acids	10.27
High fasting plasma glucose	10.15
Diet low in fiber	8.83
Diet high in sodium	7.48
Diet low in legumes	6.88
Secondhand smoke	6.67
Low temperature	6.28
Lead exposure	5.85
Diet low in vegetables	4.46
Diet high in red meat	3.23
Diet high in processed meat	2.78
Low physical activity	2.03
High temperature	0.73
Diet high in sugar-sweetened beverages	0.1

Leading risks 2010	Percentage of DALYs, 2010	Percentage change in number of DALYs, 1990–2010	Percentage change in the ASR of DALYs, 1990–2010
High systolic blood pressure	53.6	34.8	-19.97
High LDL cholesterol	39.4	27.68	-22.07
Smoking	22.87	18.49	-26.46
Ambient particulate matter pollution	18.16	48.78	-11.82
Diet low in whole grains	16.39	28.03	-21.68
Kidney dysfunction	14.79	34.88	-21.32
Household air pollution from solid fuels	14.77	18.29	-26.22
High fasting plasma glucose	13.11	72.54	2.61
High body-mass index	12.6	56.55	-4.95
Diet low in polyunsaturated fatty acids	10.36	34.76	-17.18
Diet low in nuts and seeds	10.32	14.02	-29.94
Diet low in seafood omega-3 fatty acids	10.19	15.6	-28.87
Diet low in fruits	9.6	23.6	-23.35
Diet high in sodium	8.03	43.37	-12.92
Diet low in fiber	7.69	16.3	-29.07
Lead exposure	6.88	57.05	-3.37
Secondhand smoke	6.15	23.16	-24.01
Low temperature	6.1	29.61	-21.9
Diet low in legumes	5.56	7.81	-34.27
Diet low in vegetables	3.54	6.17	-34.68
Diet high in red meat	2.8	15.85	-29.23
Low physical activity	2.05	34.99	-21.67
Diet high in processed meat	1.78	-14.54	-47.15
High temperature	1.54	180.5	73.2
Diet high in sugar-sweetened beverages	0.11	42.71	-11.92

Leading risks 2021	Percentage of DALYs, 2021	Percentage change in number of DALYs, 1990–2021	Percentage change in the ASR of DALYs,1990–2021
High systolic blood pressure	54.06	59.61	-30.2
High LDL cholesterol	38.4	46.1	-31.96
Ambient particulate matter pollution	21.01	102.06	-10.85
Smoking	20.42	24.15	-40.92
Diet low in whole grains	15.61	43.19	-33.19
Kidney dysfunction	15.04	61.03	-31.29
High fasting plasma glucose	14.91	130.37	-0.49
High body-mass index	13.76	100.71	-7.69
Household air pollution from solid fuels	10.44	-1.85	-53.86
Diet low in polyunsaturated fatty acids	10.27	56.84	-26.48
Diet low in nuts and seeds	9.36	21.34	-42.77
Diet low in fruits	9.16	38.54	-33.51
Diet low in seafood omega-3 fatty acids	8.92	18.87	-43.93
Diet high in sodium	8.1	69.71	-23.61
Lead exposure	6.82	82.82	-16.58
Diet low in fiber	6.64	17.92	-44.36
Low temperature	5.73	42.97	-35.94
Secondhand smoke	5.58	31.29	-38.16
Diet low in legumes	5.27	20.05	-44.44
Diet low in vegetables	3.52	23.88	-41.65
Diet high in red meat	2.54	23.32	-42.27
Low physical activity	2.24	73.4	-27.71
High temperature	1.51	222.36	51.5
Diet high in processed meat	1.09	-38.46	-70.92
Diet high in sugar-sweetened beverages	0.12	81.29	-11.8

Figure 5 Leading Level 4 risks by attributable deaths and DALYs, 1990–2021. (**A**) deaths. (**B**) DALYs.
Abbreviation: DALYs, disability-adjusted life years.

deaths and rank for diet high in sodium, high body-mass index, and high temperature. From 1990 to 2021, the top three risk factors with the largest percentage change in number of DALYs were high temperature (222.36%), high fasting plasma glucose (130.37%), and ambient particulate matter pollution (102.06%), while the top three risk factors with the largest percentage change in the ASR of DALYs were diet high in processed meat (−70.92%), household air pollution from solid fuels (−53.86%), and high temperature (51.50%) (Figure 5B). Notably, high temperature was the only risk factor that shows a positive percentage change in the ASR of DALYs. Figures S1–S5 respectively illustrate the changes in terms of percentage of attributable deaths and DALYs and rank of all these risk factors across five SDI regions.

Environmental Risks

Joinpoint regression analysis revealed that the global change in SEV of ambient particulate matter pollution showed an upward trend from 1990 to 2015 and a downward trend from 2015 to 2021 (APC = −1.86%; 95% CI: −2.46% to −1.26%) (Figure 6A). The overall trend in the ASRs of deaths (AAPC = −0.70%; 95% CI: −1.05% to −0.36%) and DALYs (AAPC = −0.41%; 95% CI: −0.79% to −0.04%) were minor from 1990 to 2021 (Figure 6B and C). From 1990 to 2021, aging, population growth and epidemiological change accounted for 59.20%, 72.52%, and −28.21% of the global increase in IHD related Deaths, and 45.32%, 71.71%, and −14.96% of the global increase in IHD related DALYs, respectively (Figure 6D and G). Whether deaths or DALYs, most Low SDI countries and territories were concentrated in the level 5-fixed effects interval, while the 1-level fixed effects interval mainly comprised Middle SDI countries and territories (Figure 6E and H). The top five countries and territories with the best fixed effects of deaths were Russian Federation, United States of America, Germany, United Kingdom, and Italy, while Russian Federation, United States of America, Germany, United Kingdom, and Iran (Islamic Republic of) were the top five countries and territories with the best fixed effects of DALYs (Figure 6F and I). The detailed results of the remaining environmental risks (household air pollution from solid fuels, high temperature, low temperature, and lead exposure) were presented in Figures S6–S9.

Behavioral Risks

Among behavioral risks, the risk factor burden of IHD was mainly attributed to smoking. Similarly, SEV (AAPC = −1.22%; 95% CI: −1.24% to −1.21%), the ASR of deaths (AAPC = −1.72%; 95% CI: −1.89% to −1.55%), and ASR of DALYs (AAPC = −1.69%; 95% CI: −1.85% to −1.53%) were all exhibited global downward trends (Figure 7A–C). From 1990 to 2021, aging, population growth and epidemiological change accounted for 37.51%, 58.79%, and −65.68% of the global increase in IHD related deaths, and 29.28%, 57.18%, and −62.32% of the global increase in IHD related DALYs, respectively (Figure 7D and G). Interestingly, whether deaths or DALYs, most low SDI countries and territories were concentrated in the level 1-fixed effects interval, while most high SDI countries and territories were concentrated in the level 5-fixed effects interval (Figure 7E and H). The top five countries and territories with the best fixed effects of deaths were United States of America, India, Brazil, Myanmar, and Bangladesh, while India, United States of America, Brazil, China, and Myanmar were the top five countries and territories with the best fixed effects of DALYs (Figure 7F and I). The detailed results of the remaining behavioral risks (low physical activity and secondhand smoke) were presented in Figures S10 and S11.

Dietary Risks

Among dietary risks, the risk factor burden of IHD was mainly attributed to diet low in whole grains. The overall trend in SEV was minor from 1990 to 2021 (AAPC = 0.14%; 95% CI: 0.13% to 0.15%) (Figure 8A). For the ASR of deaths, diet low in whole grains showed the most notable decline during the 2003–2007 period (APC= −2.50%; 95% CI: −3.32% to −1.68%), while for the ASR of DALYs, diet low in whole grains showed the most notable decline during the 1994–1998 period (APC= −2.29%; 95% CI: −3.16% to −1.40%) (Figure 8B and C). From 1990 to 2021, aging, population growth and epidemiological change accounted for 45.79%, 62.74%, and −58.22% of the global increase in IHD related deaths, and 32.91%, 60.80%, and −50.51% of the global increase in IHD related DALYs, respectively (Figure 8D and G). Figure 8E and H shown the correspondences between different SDI regions and fixed effects quintiles of deaths and DALYs, respectively. The top five countries and territories with the best fixed effects of deaths were United States of America, Russian Federation, Afghanistan, Morocco, and Turkey, while Russian Federation, United States of America, Turkey, Morocco, and Afghanistan were the top five countries and territories with the best fixed effects of

https://doi.org/10.2147/CLEP.S510347

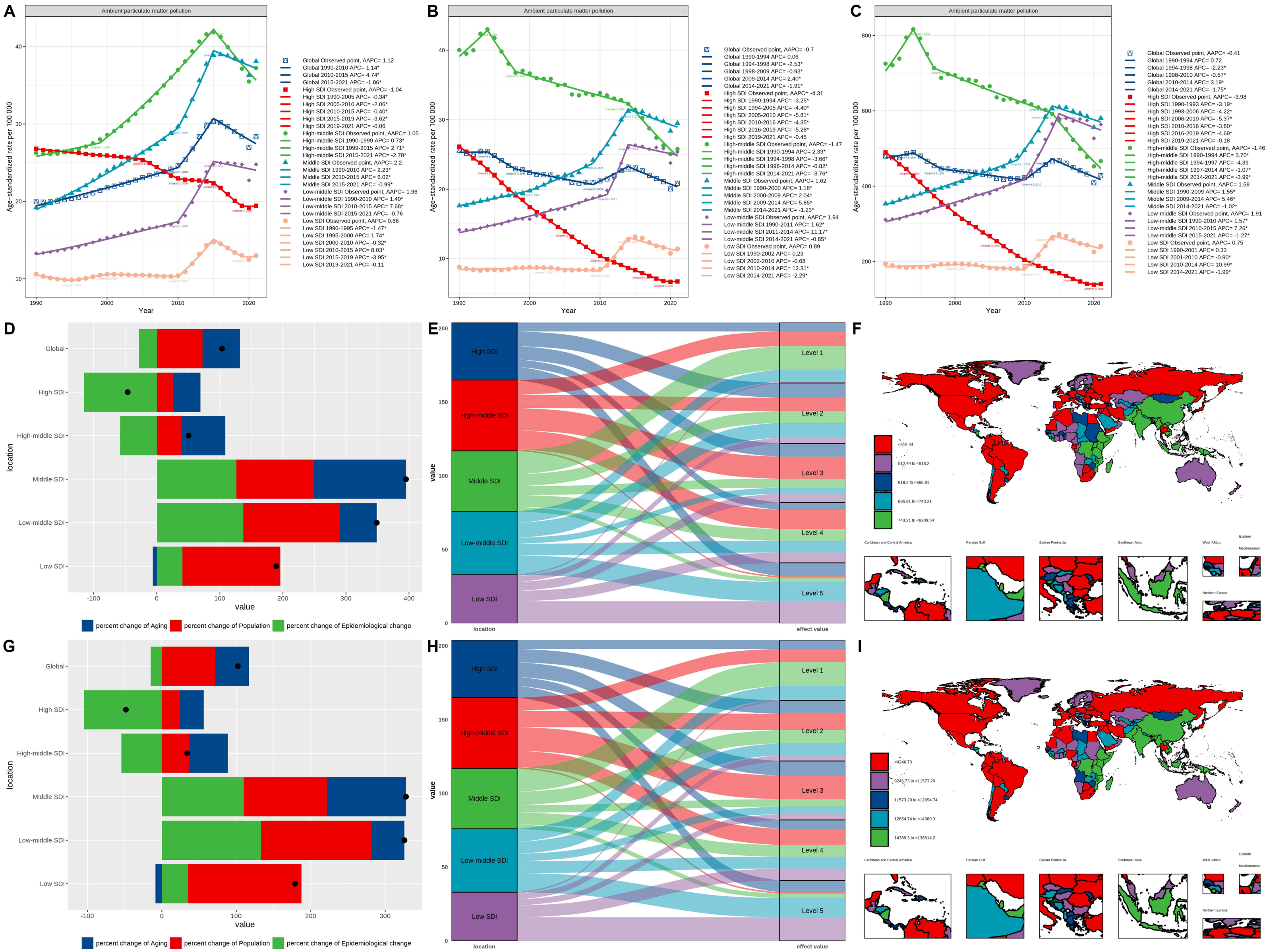

Figure 6 Summary of analysis results for ambient particulate matter pollution. (**A**) The joinpoint regression analysis on SEV. (**B**) The joinpoint regression analysis on the ASR of deaths. (**C**) The joinpoint regression analysis on the ASR of DALYs. (**D**) Changes in deaths according to aging, population growth and epidemiological change from 1990 to 2021. (**E**) Changes in DALYs according to aging, population growth and epidemiological change from 1990 to 2021. (**F**) The correspondence between different regions and fixed effects quintiles of stroke related deaths. (**G**) The correspondence between different regions and fixed effects quintiles of stroke related DALYs. (**H**) The fixed-effects of deaths of 204 countries and territories. (**I**) The fixed-effects of DALYs of 204 countries and territories.

Abbreviations: SEV, summary exposure value; ASR, age-standardized rate; DALYs, disability-adjusted life years.

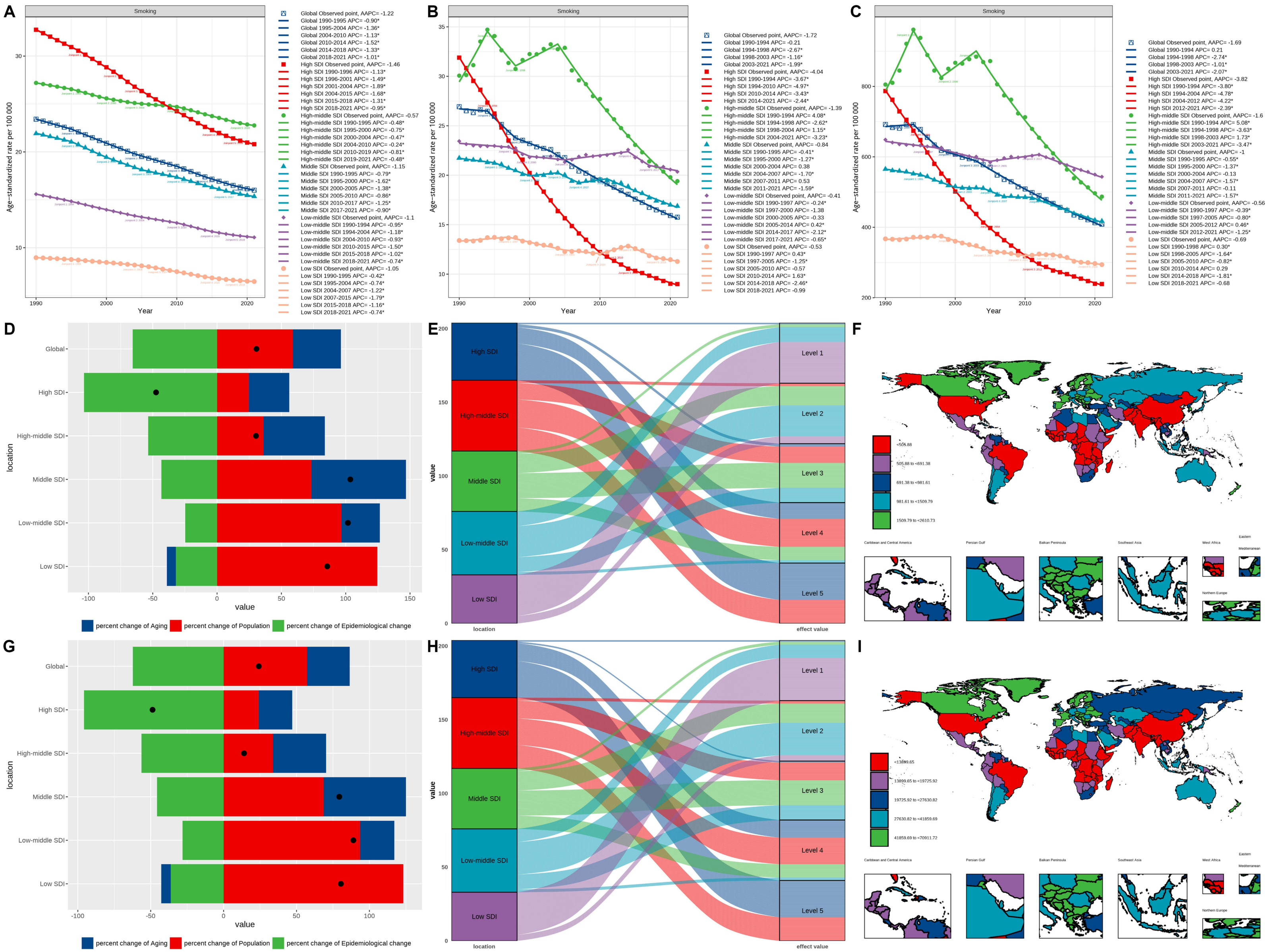

Figure 7 Summary of analysis results for smoking. (**A**) The joinpoint regression analysis on SEV. (**B**) The joinpoint regression analysis on the ASR of deaths. (**C**) The joinpoint regression analysis on the ASR of DALYs. (**D**) Changes in deaths according to aging, population growth and epidemiological change from 1990 to 2021. (**E**) Changes in DALYs according to aging, population growth and epidemiological change from 1990 to 2021. (**F**) The correspondence between different regions and fixed effects quintiles of stroke related deaths. (**G**) The correspondence between different regions and fixed effects quintiles of stroke related DALYs. (**H**) The fixed-effects of deaths of 204 countries and territories. (**I**) The fixed-effects of DALYs of 204 countries and territories.

Abbreviations: SEV, summary exposure value; ASR, age-standardized rate; DALYs, disability-adjusted life years.

https://doi.org/10.2147/CLEP.S510347

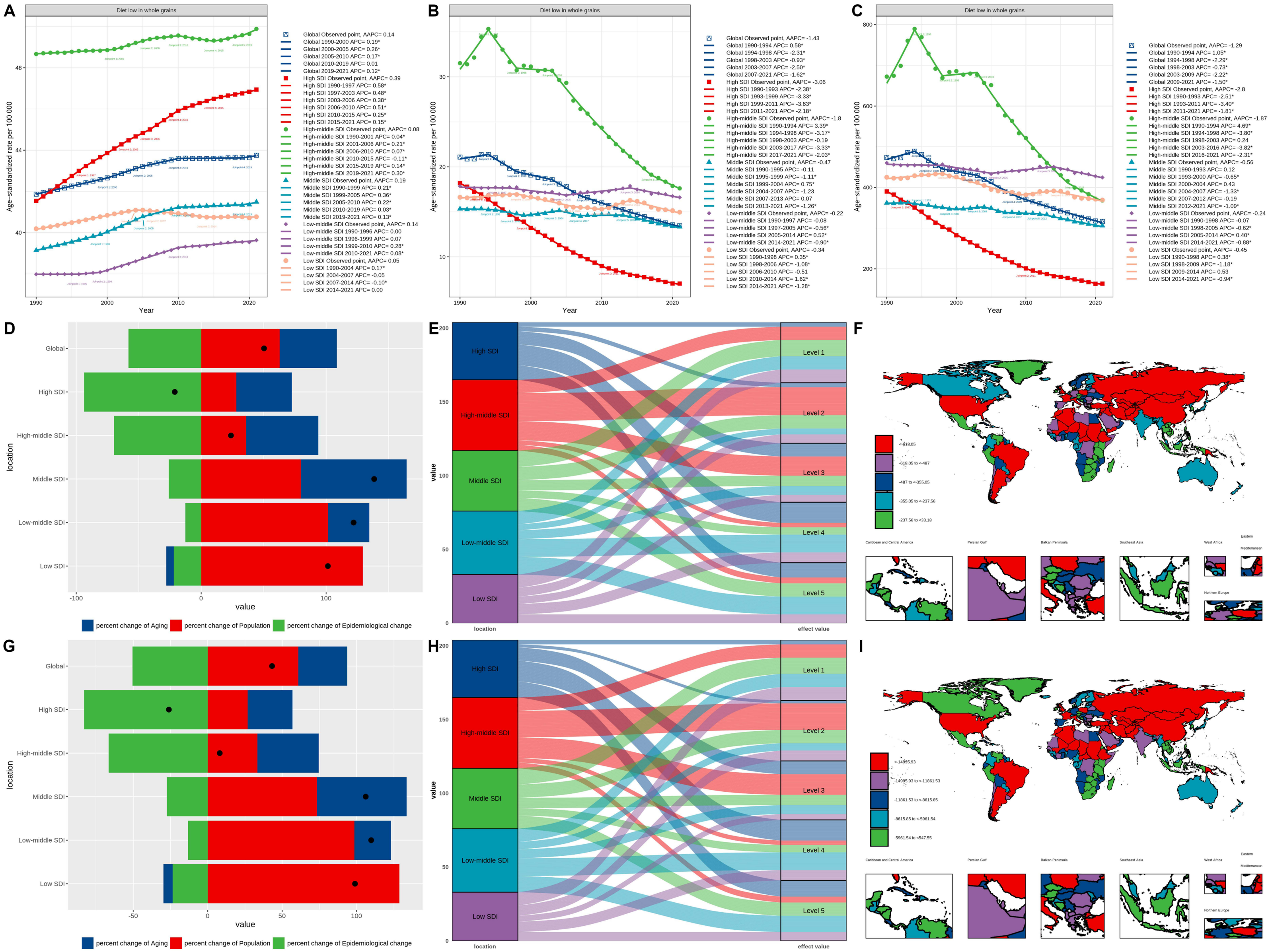

Figure 8 Summary of analysis results for diet low in whole grains. (**A**) The joinpoint regression analysis on SEV. (**B**) The joinpoint regression analysis on the ASR of deaths. (**C**) The joinpoint regression analysis on the ASR of DALYs. (**D**) Changes in deaths according to aging, population growth and epidemiological change from 1990 to 2021. (**E**) Changes in DALYs according to aging, population growth and epidemiological change from 1990 to 2021. (**F**) The correspondence between different regions and fixed effects quintiles of stroke related deaths. (**G**) The correspondence between different regions and fixed effects quintiles of stroke related DALYs. (**H**) The fixed-effects of deaths of 204 countries and territories. (**I**) The fixed-effects of DALYs of 204 countries and territories.

Abbreviations: SEV, summary exposure value; ASR, age-standardized rate; DALYs, disability-adjusted life years.

DALYs (Figure 8F and I). The detailed results of other dietary risks (diet low in fruits, diet low in vegetables, diet high in red meat, diet high in processed meat, diet high in sugar-sweetened beverages, diet low in fiber, diet low in poly-unsaturated fatty acids, diet high in sodium, diet low in legumes, diet low in nuts and seeds, and diet low in seafood omega-3 fatty acids) were shown in Figures S12 and S22.

Metabolic Risks

In fact, taken together, metabolic risks were the most associated with IHD burden among the four categories of risks. High systolic blood pressure has the highest proportion of risk factor burden of deaths and DALYs risk burden among all 25 risk factors. Joinpoint regression analysis revealed that the global change in SEV of high systolic blood pressure showed a downward trend from 1997 to 2002 (APC = −0.14%; 95% CI: −0.21% to −0.08%) and an upward trend from 2002 to 2021 (Figure 9A). The ASR of deaths (AAPC = −1.31%; 95% CI: −1.50% to −1.12%), and ASR of DALYs (AAPC = −1.15%; 95% CI: −1.31% to −0.99%) were all exhibited global downward trends (Figure 9B and C). From 1990 to 2021, aging, population growth and epidemiological change accounted for 54.70%, 65.69%, and −55.81% of the global increase in IHD related deaths, and 42.66%, 64.16%, and −47.21% of the global increase in IHD related DALYs, respectively (Figure 9D and G). Whether deaths or DALYs, most low SDI countries and territories were concentrated in the level 1-fixed effects interval, while most high SDI countries and territories were concentrated in the level 5-fixed effects interval (Figure 9E and H). The top five countries and territories with the best fixed effects of deaths were United States of America, Germany, Russian Federation, United Kingdom, and Japan, while United States of America, Russian Federation, Germany, United Kingdom, and Brazil were the top five countries and territories with the best fixed effects of DALYs (Figure 9F and I). The detailed results of the remaining metabolic risks (high fasting plasma glucose, high LDL cholesterol, high body-mass index, and kidney dysfunction) were presented in Figures S23–S26.

IHD Attributable to All Risk Factors

In total, the absolute number of all risks-attributable deaths from 5.37 million (95% UI 5.08–5.56) in 1990 to 8.99 million (95% UI 8.26–9.53) in 2021, a 67.41% increase from 1990 to 2021, while the absolute number of all risks-attributable DALYs from 119.16 million (95% UI 114.55–123.45) in 1990 to 188.36 million (95% UI 177.04–198.15) in 2021, a 58.07% increase from 1990 to 2021. From 1990 to 2021, aging, population growth and epidemiological change accounted for 52.87%, 65.64%, and −53.29% of the global increase in IHD related deaths, and 39.31%, 63.46%, and −46.01% of the global increase in IHD related DALYs, respectively (Figure 10A and B). Whether DALYs or deaths, most low SDI countries and territories were concentrated in the level 1-fixed effects interval, while most high SDI countries and territories were concentrated in the level 5-fixed effects interval (Figure 10C and D). The top five countries and territories with the best fixed effects of deaths were United States of America, Russian Federation, Germany, United Kingdom, and Brazil, while United States of America, Russian Federation, Germany, China, and United Kingdom were the top five countries and territories with the best fixed effects of DALYs (Figure 10E and F). The top five countries and territories with the worst fixed effects of deaths were Ukraine, San Marino, Monaco, India, and Indonesia, while Ukraine, San Marino, Monaco, Luxembourg, and Iceland were the top five countries and territories with the worst fixed effects of DALYs (Figure 10E and F).

Discussion

This study provides a comprehensive analysis of the SEV of 24 risk factors and the attributable burden of IHD across 204 countries and regions from 1990 to 2021. Although the mortality rates, DALYs, prevalence, and incidence rates related to IHD declined from 1990 to 2021, the absolute numbers significantly increased, primarily due to population growth and aging. In 2021, IHD burden decreased across all SDI regions, with the most significant progress observed in high SDI areas. Risk factors continue to be the primary contributors to IHD mortality and DALYs, accounting for 91.67% and 92.27%, respectively. Globally, the trends in risk factor exposure from 1990 to 2021 indicate a duality of progress and challenges. Certain risk factors, such as household air pollution and smoking, have significantly decreased, likely due to improvements in SDI. In contrast, other factors, particularly dietary and metabolic issues like high body mass index and

https://doi.org/10.2147/CLEP.S510347

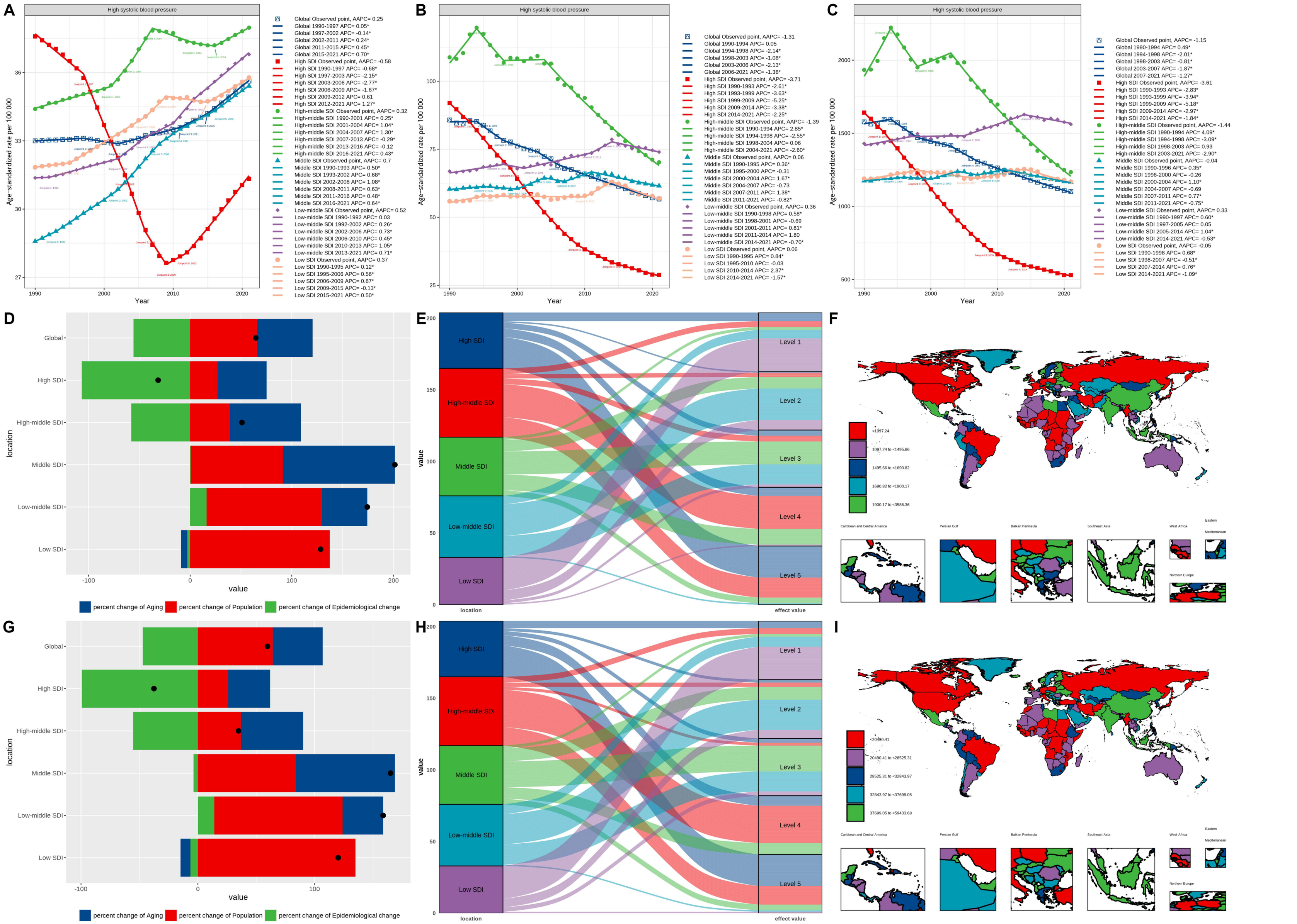

Figure 9 Summary of analysis results for high systolic blood pressure. (**A**) The joinpoint regression analysis on SEV. (**B**) The joinpoint regression analysis on the ASR of deaths. (**C**) The joinpoint regression analysis on the ASR of DALYs. (**D**) Changes in deaths according to aging, population growth and epidemiological change from 1990 to 2021. (**E**) Changes in DALYs according to aging, population growth and epidemiological change from 1990 to 2021. (**F**) The correspondence between different regions and fixed effects quintiles of stroke related deaths. (**G**) The correspondence between different regions and fixed effects quintiles of stroke related DALYs. (**H**) The fixed-effects of deaths of 204 countries and territories. (**I**) The fixed-effects of DALYs of 204 countries and territories.

Abbreviations: SEV, summary exposure value; ASR, age-standardized rate; DALYs, disability-adjusted life years.

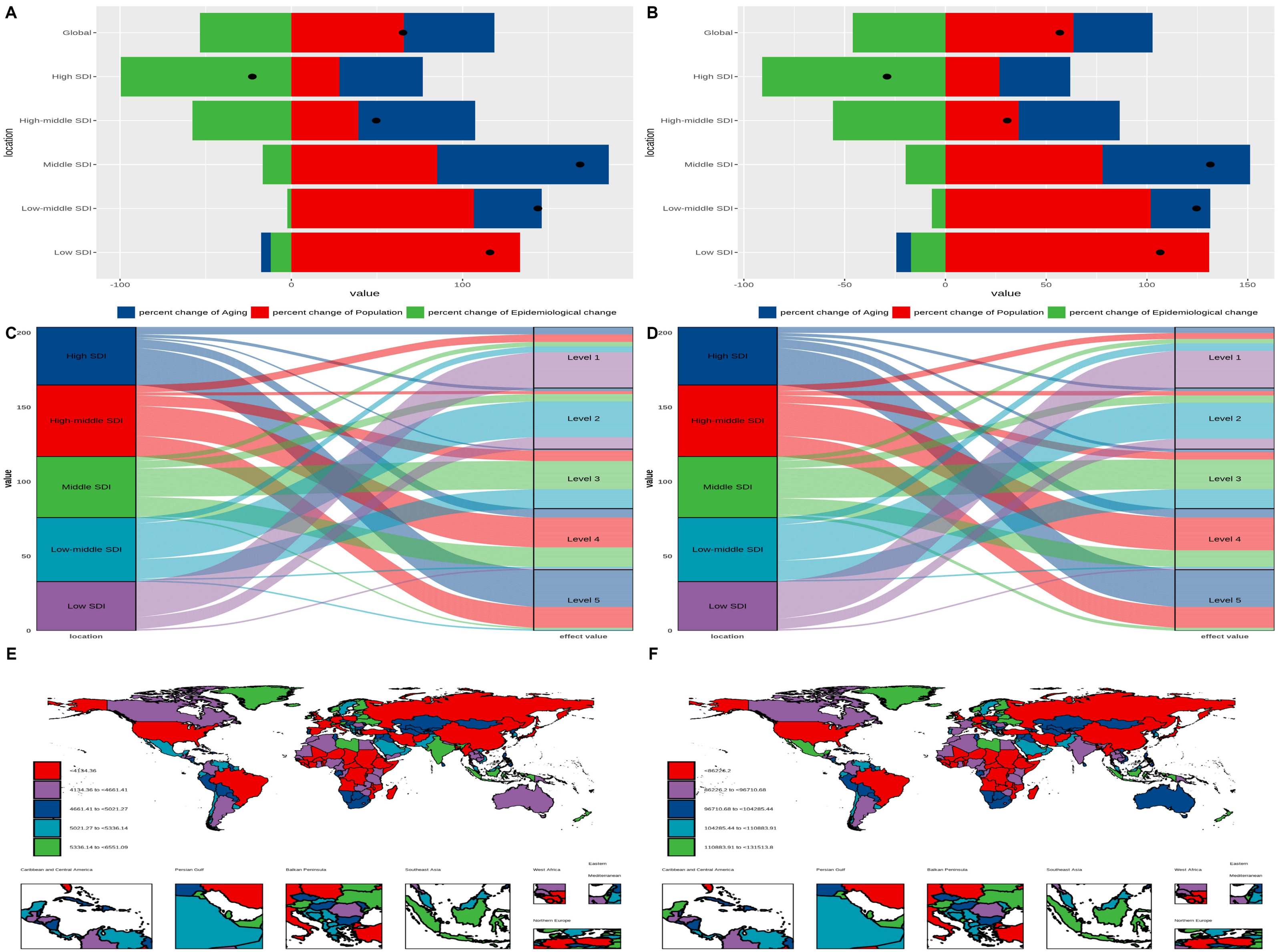

Figure 10 Summary of analysis results for all risk factors. (**A**) Changes in deaths according to aging, population growth and epidemiological change from 1990 to 2021. (**B**) Changes in DALYs according to aging, population growth and epidemiological change from 1990 to 2021. (**C**) The correspondence between different regions and fixed effects quintiles of stroke related deaths. (**D**) The correspondence between different regions and fixed effects quintiles of stroke related DALYs. (**E**) The fixed-effects of deaths of 204 countries and territories. (**F**) The fixed-effects of DALYs of 204 countries and territories.

Abbreviation: DALYs, disability-adjusted life years.

https://doi.org/10.2147/CLEP.S510347

sugar-sweetened beverage consumption, have surged at concerning rates, emphasizing the urgent need for enhanced public health interventions. During the same period, the DALYs associated with IHD were influenced by the complex interactions of various risk factors. High temperature, high fasting plasma glucose, and ambient particulate matter pollution were found to significantly increase DALYs, while household air pollution and dietary factors led to a notable decrease in these years. In 2021, the most impactful risk factors contributing to DALYs related to IHD included high systolic blood pressure, high LDL cholesterol, ambient particulate matter pollution, smoking, and a diet low in whole grains. This underscores the critical roles of metabolic, dietary, behavioral, and environmental risks in the IHD burden.

Environmental Risks

The study demonstrates a positive correlation between SEV for environmental particulate pollution and the burden of IHD across different Socio-Demographic Index (SDI) levels. In countries with high SDI, SEV have significantly declined from 1990 to 2021, highlighting substantial improvements in governance and developmental policies. However, many low and middle SDI countries are experiencing rising exposure rates, largely attributable to the accelerated pace of industrialization and urbanization.[21,22] In terms of IHD burden from particulate pollution, high SDI countries have consistently maintained the lowest levels, while upper-middle SDI countries have shown a steady reduction since 1990, reflecting advances in healthcare. In contrast, countries with medium and low SDI levels are witnessing an increase in both exposure rates and disease burden, underscoring the persistent challenge of balancing environmental pollution control with public health initiatives.[23]

The study indicates that household air pollution and lead exposure, along with their burden on IHD, are inversely correlated with the SDI levels of countries. This downward trend is observed across all SDI groups. However, countries with low and lower-middle SDI levels continue to experience higher exposure rates and health burdens, posing ongoing significant challenges.[24,25]

Similarly, high-temperature exposure and its burden on IHD are also inversely correlated with SDI levels. While fluctuations in exposure and disease burden are seen across all SDI groups, there is no clear upward or downward trend. Countries with low and lower-middle SDI levels are at greater risk of high-temperature exposure and its associated IHD burden, which is closely related to geographical factors.[26] Tropical and subtropical regions—typically countries with lower SDI levels—face higher risks of heat exposure, whereas temperate and polar regions (including some countries with medium SDI levels) are more vulnerable to cold exposure. In contrast, the risk of cold exposure remains relatively low in both high and low SDI countries, suggesting that the relationship between climate change and geographical location significantly affects the disparities among countries with varying SDI levels.[27]

Behavioral Risks

Smoking, secondhand smoke exposure, and their attributable burden on IHD are positively correlated with SDI levels across countries, yet show a decreasing trend across all SDI groups. In high SDI countries, secondhand smoke exposure rates have significantly declined and are only slightly higher than those in low SDI countries, likely due to the implementation of robust tobacco control policies.[28] Furthermore, the IHD burden from smoking and secondhand smoke is lowest in high SDI countries, reflecting their substantial advantages in the prevention and control of IHD.[29] Upper-middle SDI countries also demonstrate a preventive advantage, with a significant reduction in the IHD burden from smoking and secondhand smoke, now lower than that of middle SDI countries.[30]

The prevalence of low physical activity is also positively correlated with SDI levels across countries, with an increasing trend in all SDI groups. As economies grow, the incidence of low physical activity tends to rise, possibly due to lifestyle changes and socio-cultural factors. In terms of the IHD burden, high SDI countries experience the lowest burden from low physical activity, while other countries show a positive correlation between IHD burden and SDI levels.[31] However, across all SDI groups, the IHD burden due to low physical activity has decreased. This suggests that despite higher lifestyle-related risk factors in high SDI countries, their advanced healthcare resources and effective health interventions may have successfully mitigated the IHD burden.[32]

Dietary Risks

Studies indicate that high sodium diets, high consumption of sugar-sweetened beverages, diets low in legumes, and high intake of red and processed meats are positively correlated with the SDI levels of countries. However, compared to other nations, high SDI countries exhibit significantly lower IHD burdens attributable to these dietary factors, reflecting their superior disease treatment capabilities.[33]

In terms of trends, high sodium intake has remained relatively stable across all SDI countries, yet the overall IHD burden attributable to sodium has declined, likely due to improvements in treatment.[34] Although global consumption of sugar-sweetened beverages continues to rise, the IHD burden associated with these beverages has decreased in high middle and high SDI countries, while it has continued to increase in other regions, underscoring the disparities in healthcare services and health interventions between nations.[35] In high middle and high SDI countries, red and processed meat consumption remains relatively high, but the attributable IHD burden has significantly declined, suggesting an increased awareness of dietary health. In contrast, exposure rates and IHD burdens in middle and lower SDI countries have shown no significant changes, likely due to lower industrialization and less diverse dietary patterns.[36]

Additionally, low intake of fruits and vegetables, low consumption of seafood omega-3 fatty acids, and polyunsaturated fatty acids are generally negatively correlated with SDI levels, as is the IHD burden, highlighting global health inequities. This suggests that lower SDI countries need to enhance control of these dietary risk factors.[37]

There is no clear correlation between diets low in nuts and seeds, low in fiber, and low whole grain diets with SDI levels. However, both exposure rates and attributable IHD burdens remain lower in high SDI countries, indicating their advantages in prevention and treatment. The exposure rates and IHD burdens associated with low intake of nuts, seeds, and fiber have been decreasing, suggesting that efforts to improve dietary habits are showing success. Although the exposure rates for low whole grain diets are rising, the associated IHD burden continues to decline, signaling an overall positive trend.[33]

Metabolic Risks

High fasting plasma glucose, high LDL cholesterol, high systolic blood pressure, and high body-mass index are positively correlated with the Socio-Demographic Index (SDI) levels of countries, as is the attributable burden of ischemic heart disease (IHD). However, the burden of IHD attributable to these factors remains lowest in high SDI countries, reflecting the superior treatment capabilities of these nations.[38] Similar patterns have been observed in other rapidly developing economies like India and Brazil, though China's unique healthcare system and demographic transition present distinct challenges in managing these cardiovascular risk factors.

In terms of trends, high fasting plasma glucose and high body-mass index have shown an upward trajectory, with the IHD burden remaining constant in lower and lower-middle SDI countries, while declining in high middle and high SDI countries, indicating the treatment advantage in more developed nations and underscoring the need for stronger prevention efforts in less developed countries.[31,39,40] Except for high SDI countries, where exposure to high LDL cholesterol is declining, other nations are experiencing increases. Nevertheless, the attributable IHD burden has decreased in high middle and high SDI countries, while remaining stable in others, suggesting overall improvements in treatment but also emphasizing the need for enhanced prevention strategies.[41] Systolic blood pressure exposure is generally rising, yet the attributable IHD burden is decreasing, which reflects advancements in treatment while highlighting the ongoing need for better prevention efforts.[10]

The prevalence of kidney dysfunction is inversely correlated with SDI levels, as is the burden of IHD, indicating persistent health inequities.[42] Although the trend in kidney dysfunction remains relatively stable, the declining IHD burden in upper-middle and high SDI countries suggests improved control, likely due to enhanced public health interventions.

Population Growth and Aging

Between 1990 and 2021, decomposition analysis revealed that the increase in IHD burden in low SDI countries was primarily driven by population growth. Low SDI countries generally have higher fertility rates and younger population structures, leading to a rapid expansion of the potential patient base. This suggests that as these populations age into the high-risk period for IHD, the burden could increase significantly in the coming years.[43] Therefore, public health policies should focus on reproductive health and education in these countries to reduce future health burdens.

During the same period, the increase in IHD burden due to population aging was most prominent in high middle and high SDI countries between 1990 and 2021. This demographic shift has particularly affected women in China, who face unique cardiovascular challenges post-menopause and often have different healthcare-seeking behaviors than men. The fundamental cause of this trend lies in demographic shifts: declining fertility rates and improved healthcare conditions have extended life expectancy, increasing the proportion of elderly individuals.[9] As IHD incidence rises significantly with age, this trend is especially pronounced in middle SDI countries. The urban-rural divide in healthcare access remains a critical challenge in China, with rural areas having limited access to advanced diagnostic tools and preventive services compared to urban centers. Hence, long-term public health planning, which anticipates aging trends and allocates healthcare resources accordingly, will be crucial in addressing future health challenges.

The reduction in IHD burden through prevention and control measures is most evident in high SDI countries. This can be attributed to a higher level of health awareness and a deeper understanding of IHD risk factors and preventive strategies among the population in these nations. Furthermore, high SDI countries generally possess advanced medical technologies and resources, facilitating more effective prevention and treatment of IHD.[1]

Panel Data Models

The GBD study offers a comprehensive framework for analyzing the relationship between exposure to risk factors and attributable burden. By employing relative risks (RRs) and PAFs, GBD links risk factor exposure directly to health outcomes, supporting our hypothesis that variations in exposure rates can influence attributable burdens.

The GBD's standardized methods, which cover 204 countries and territories, provide a reliable foundation for international comparisons of risk factor exposure and disease burden. Notably, the use of age-standardized rates in these estimations mitigates the impact of differing age demographics, ensuring that cross-national comparisons are both valid and meaningful.

Additionally, incorporating the SDI and QCI as control variables is well-justified. These indices serve as proxies for national development and healthcare infrastructure, allowing for a more nuanced analysis of how countries manage risk factors by accounting for underlying disparities in development and healthcare systems.

The Fixed Effects Model

The fixed effects model in this analysis indicates that after controlling for SDI, QCI, and risk factor exposure, countries with lower SDI present relatively stronger fixed effects for IHD-attributable burden, whereas higher SDI nations show weaker fixed effects. This finding challenges the conventional expectation that higher SDI is associated with superior health outcomes. Nevertheless, before adjusting for these variables, high-SDI countries exhibited a lower IHD-attributable burden, underscoring the significance of SDI, QCI, and risk factors in shaping IHD outcomes while also hinting at additional influential factors.

The fixed effects model captures the impact of each nation's unique, relatively stable attributes on IHD burden, demonstrating the need to account for factors beyond traditional health metrics. Factors such as stress, pace of life, and environmental adaptation are not included in the GBD database but are essential to consider in cardiovascular health. Although lower SDI countries might experience greater economic strain, the fast-paced lifestyles and occupational stress prevalent in high SDI countries could exert a more detrimental effect on cardiovascular health.[44] Moreover, populations in low SDI countries may possess physiological adaptations to certain environmental stressors, indirectly reducing IHD risk, an ability that may have diminished in high SDI populations over time.[45]

Furthermore, Low SDI countries may possess higher genetic diversity, potentially providing some protective genetic variations against IHD, while populations in high SDI countries may have undergone genetic homogenization.[46] Additionally, low SDI countries have seen unexpected successes in implementing public health policies, whereas high SDI nations often face diminishing returns as they near theoretical limits in improving public health indicators.[47] In this context, low SDI countries can effectively leverage the experiences of their high SDI counterparts to adopt public health policies more rapidly and cost-effectively. Furthermore, the ease of scaling innovative policies allows these nations to leapfrog developmental stages, directly integrating more advanced technologies and strategies.[48]

The study investigates the differences in the IHD attributable burden across multiple countries after accounting for known factors such as risk exposure, SDI, QCI, population aging, and growth. It highlights the potential influence of geographical factors on the IHD burden. By comparing countries with high IHD burdens—Ukraine, San Marino, Monaco, Luxembourg, and Iceland—with countries with lower burdens such as the United States, Russia, Germany, China, and the United Kingdom, several conclusions were drawn.

Low-burden countries (eg, the United States, Germany, and the United Kingdom) benefit from extensive geographic diversity, which provides residents with a broader range of healthy lifestyle options and mitigates the negative effects of social unrest and psychological stress, thereby reducing the IHD burden.[49] In contrast, high-burden countries (eg, Ukraine, San Marino, Monaco, Luxembourg, and Iceland) face limitations due to smaller geographic areas, leading to less diverse lifestyles, while socioeconomic instability and high occupational stress contribute to increased psychological pressure, potentially elevating IHD risk.[43] The experiences of high-burden countries suggest that geographic constraints and increased social pressure elevate IHD risks. In contrast, geographic diversity and social stability offer effective buffers in low-burden countries. Therefore, public health policies should account for the geographic and social environmental differences across countries to develop more targeted strategies for cardiovascular disease prevention and intervention.

This study, through stratified analysis, found that low SDI countries exhibit relatively better fixed effects regarding several risk factors associated with ischemic heart disease (IHD). These factors include high fasting plasma glucose, elevated LDL cholesterol, high systolic blood pressure, household air pollution from solid fuels, high temperatures, lead exposure, smoking, secondhand smoke, low physical activity, insufficient fruit intake, low dietary fiber intake, low seafood omega-3 fatty acids, and low polyunsaturated fatty acid intake. In contrast, high SDI countries show better fixed effects concerning diet-related risk factors, such as low vegetable intake, high processed meat consumption, and high intake of sugar-sweetened beverages. Given these findings, it is crucial to develop targeted intervention measures specific to the SDI levels of different countries. In high SDI countries, public health policies should focus on controlling traditional risk factors such as hypertension, diabetes, and smoking. In low SDI countries, improving dietary structures by reducing the consumption of red meat, processed meats, and sugary drinks, while increasing vegetable intake, will help further reduce the burden of IHD and other cardiovascular diseases.

This study also highlights the importance of considering country-specific risk factors in addition to conventional socio-economic and healthcare quality indicators when assessing national IHD burdens. These factors may act independently or interact, shaping the unique burden of IHD in each country. Therefore, future research should further investigate these country-specific risk factors to better understand the global distribution of IHD burden and to inform the development of more targeted prevention and intervention strategies.

Strengths and Limitations

The key strengths of this study are evident in several aspects. First, it utilized a joinpoint regression model to thoroughly analyze the exposure rates and attributable burdens of 24 IHD risk factors, revealing trends and exploring their correlations with the SDI, providing a comprehensive view of the dynamic changes in IHD risk factors. Second, the study applied decomposition analysis to evaluate changes in IHD burden across countries with varying SDI levels from 1990 to 2021, quantifying the contributions of population growth and aging to these changes, offering crucial evidence for developing targeted IHD prevention strategies. Third, panel data analysis was employed to assess the impact of risk factor exposure rates, SDI, and the QCI on the attributable burden of IHD. This approach not only identified the relative significance of these factors but also revealed country-specific effects by controlling for them, providing a novel perspective for identifying determinants of IHD burden globally. Finally, the integration of multiple analytical methods presents a holistic framework for understanding the complexity of IHD risk factors, advancing scientific knowledge of the global IHD burden while offering empirical foundations for targeted public health interventions.

However, this study has several limitations. First, while the GBD study provides high-quality data, the potential for measurement errors and estimation biases cannot be entirely excluded, which may affect the precision of the findings.

Additionally, although fixed-effects models were employed to identify unique determinants of IHD burden across countries, these models do not specify the nature of these determinants, requiring more in-depth, country-specific analyses. In the decomposition analysis, changes in IHD attributable burden between consecutive years were modeled using risk factor exposure rates, SDI, and QCI as independent variables, yet the time lag between risk factor exposure and disease onset could influence the accuracy of the model. Despite these limitations, trends in risk factor exposure generally aligned with trends in IHD-attributable burden, which is consistent with the Comparative Risk Assessment method used by the GBD database. Collectively, these observations substantiate the inferences drawn from the panel analysis model, providing a rationale for its validity.

Conclusions

This study demonstrates a continuous decline in the burden of IHD, including major risk factors, from 1990 to 2021, which correlates with a reduction in exposure to most of these risk factors. These findings underscore the critical importance of managing risk factors to alleviate the global burden of IHD. The research also highlights the urgent need to address rapidly growing risk factors, such as high body mass index and sugar-sweetened beverage consumption, in addition to major contributors to IHD burden like high systolic blood pressure, high LDL cholesterol, ambient particulate matter pollution, and smoking.

An analysis of the correlation between risk factors and SDI indicates that prevention strategies for IHD must be tailored to a country's level of development. Developing countries should prioritize risk factors positively correlated with SDI to avoid the "develop first, treat later" dilemma faced by more developed nations. Conversely, low SDI countries must address risk factors that negatively correlate with SDI to mitigate health disparities.

The impact of population dynamics on the IHD burden varies significantly depending on a country's stage of development. Low SDI countries face challenges associated with population growth, necessitating the strengthening of primary healthcare infrastructure, while upper-middle and high SDI countries must enhance IHD prevention and rehabilitation services for the elderly to address the challenges of an aging population.

Stratified analysis of country effect values highlights the necessity of formulating strategies based on specific contexts. High SDI countries should focus on managing traditional risk factors such as hypertension, diabetes, and smoking. In contrast, low SDI countries should improve dietary habits by limiting the intake of red meat, processed meats, and sugar-sweetened beverages while increasing vegetable consumption. Furthermore, it is essential to explore and address the unique factors contributing to IHD in each country. Such a differentiated and personalized strategy will significantly contribute to efforts aimed at reducing the global burden of IHD.

Data Sharing Statement

GBD study 2021 data resources were available online from the Global Health Data Exchange (GHDx) query tool (http://ghdx.healthdata.org/gbd-results-tool).

Ethic Statement

Our study utilized the publicly accessible Global Burden of Disease Study 2021. According to Article 32 of the Measures for Ethical Review of Research in Life Sciences and Medicine Involving Human Beings, research involving human data or biological samples in life sciences and medicine may be exempt from ethical review if it does not harm individuals, nor involves sensitive personal or commercial information. This exemption aims to ease the burden on researchers and support research involving humans, provided the data is legally obtained or publicly available without interfering with public behavior. Following consultation with the institutional review board of Minhang Hospital, Fudan University, Shanghai, China, ethical approval was deemed unnecessary for our study.

Acknowledgments

We extend our gratitude to the contributors of the Global Burden of Diseases, Injuries, and Risk Factors Study 2021 for their invaluable work.

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 study was funded by the Projects of High-level Key Physicians of Minhang District Health Committee (2020MZYS11), Shanghai Municipal Health Commission Medical Special Project (202240231), Medical Engineering Joint Fund of Fudan University (yg2022-32), Chongqing medical scientific research project (Joint project of Chongqing Health Commission and Science and TechnologyBureau) (2024QNXM017), Scientific and Technological Research Program of Chongqing Municipal Education Commission (KJQN202300454), and Banan District Science and Technology Bureau of Chongqing Municipality (BNWJ202300106).

Disclosure

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

References

1. Roth GA, Mensah GA, Johnson CO, et al. Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2019: update From the GBD 2019 Study. *J Am College Cardiol*. 2020;76:2982–3021.
2. Bays HE, Taub PR, Epstein E. Ten things to know about ten cardiovascular disease risk factors. *Am J Prevent Cardiol*. 2021;5:100149. doi:10.1016/j.ajpc.2021.100149
3. Collaborators G 2021 RF. Global burden and strength of evidence for 88 risk factors in 204 countries and 811 subnational locations, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet*. 2024;403(10440):2162–2203. doi:10.1016/S0140-6736(24)00933-4
4. Ss K, Matsushita K, Sang Y, et al. Development and Validation of the American Heart Association's PREVENT Equations. *Circulation*. 2024. doi:10.1161/CIRCULATIONAHA.123.067626
5. Arnett DK, Khera A, Blumenthal RS. ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: part 1, Lifestyle and Behavioral Factors. *JAMA Cardiol*. 2019;4(10):1043–1044. doi:10.1001/jamacardio.2019.2604
6. HJ Bolnick, AL Bui, A Bulchis, et al. Health-care spending attributable to modifiable risk factors in the USA: an economic attribution analysis. *Lancet Public Health*. 2020;5(10):e525–e535. doi:10.1016/S2468-2667(20)30203-6
7. Yusuf S, Hawken S, Ôunpuu S, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Available from: https://www.thelancet.com/journals/lancet/article/PIIS0140-67360417018-9/abstract. Accessed Sept 22, 2024.
8. Roth GA, Forouzanfar MH, Moran AE. Demographic and Epidemiologic Drivers of Global Cardiovascular Mortality. *N Engl J Med*. 2015;372(14):1333–1341. doi:10.1056/NEJMoa1406656
9. Cheng X, Yang Y, Schwebel DC, et al. Population ageing and mortality during 1990–2017: a global decomposition analysis. *PLoS Med*. 2020;17(6):e1003138. doi:10.1371/journal.pmed.1003138
10. Safiri S, Karamzad N, Singh K. Burden of ischemic heart disease and its attributable risk factors in 204 countries and territories, 1990–2019. *Eur J Prevent Cardiol*. 2022;29(2):420–431. doi:10.1093/eurjpc/zwab213
11. Owolabi MO, Thrift AG, Mahal A, et al. Primary stroke prevention worldwide: translating evidence into action. *Lancet Public Health*. 2022. 7(1):e74–e85. doi:10.1016/S2468-2667(21)00230-9
12. Mohammadi E, Ghasemi E, Azadnajafabad S. A global, regional, and national survey on burden and Quality of Care Index (QCI) of brain and other central nervous system cancers; global burden of disease systematic analysis 1990–2017. *PLoS One*. 2021;16(2):e0247120. doi:10.1371/journal.pone.0247120
13. M Naghavi. Global burden of 288 causes of death and life expectancy decomposition 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):2100–2132. doi:10.1016/S0140-6736(24)00367-2
14. Cousin E, Bb D, Stein C, et al. Diabetes mortality and trends before 25 years of age: an analysis of the Global Burden of Disease Study 2019. Available from:: https://www.thelancet.com/journals/landia/article/PIIS2213-8587(21)00349-1/fulltext. Accessed Sept 29, 2024.
15. Ong KL, Stafford LK, McLaughlin SA, et al. Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet*. 2023;402(10397):203–234. doi:10.1016/S0140-6736(23)01301-6
16. Kim H-J, Fay MP, Feuer EJ, Midthune DN Permutation tests for joinpoint regression with applications to cancer rates. Available from: https://onlinelibrary.wiley.com/doi/10.1002/(SICI)1097-0258(20000215)19:3<335::AID-SIM336>3.0.CO;2-Z. Accessed Sept 29, 2024.
17. Akhtar S, Al-Abkal J, Alroughani R. Joinpoint Regression Analysis of Trends in Multiple Sclerosis Incidence in Kuwait: 1980–2019. *Neuroepidemiology*. 2020;54(6):472–481. doi:10.1159/000511205
18. Bretó C, Ionides EL, King AA. Panel Data Analysis via Mechanistic Models. *J Am Stat Assoc*. 2019;115(531):1178–1188. doi:10.1080/01621459.2019.1604367

19. Aminorroaya A, Ghasemi E, Shabani M. Global, regional, and national quality of care and burden of ischemic heart disease, 1990 to 2017: results from the GBD study 2017. *Eur Heart J*. 2020;41:ehaa946.3560. doi:10.1093/ehjci/ehaa946.3560
20. Aminorroaya A, Yoosefi M, Rezaei N. Global, regional, and national quality of care of ischaemic heart disease from 1990 to 2017: a systematic analysis for the Global Burden of Disease Study 2017. *Eur J Prevent Cardiol*. 2022;29(2):371–379. doi:10.1093/eurjpc/zwab066
21. Jia Y, Lin Z, He Z. Effect of Air Pollution on Heart Failure: systematic Review and Meta-Analysis. *Environ Health Perspect*. 2023;131(7):076001. doi:10.1289/EHP11506
22. Cohen AJ, Brauer M, Burnett R. Estimates and 25-year trends of the global burden of disease attributable to ambient air pollution: an analysis of data from the Global Burden of Diseases Study 2015. *Lancet*. 2017;389(10082):1907–1918. doi:10.1016/S0140-6736(17)30505-6
23. Lim S, Bassey E, Bos B. Comparing human exposure to fine particulate matter in low and high-income countries: a systematic review of studies measuring personal PM2.5 exposure. *Sci Total Environ*. 2022;833:155207. doi:10.1016/j.scitotenv.2022.155207
24. Dang P, Tang M, Fan H, Hao J. Chronic lead exposure and burden of cardiovascular disease during 1990–2019: a systematic analysis of the global burden of disease study. *Front Cardiovasc Med*. 2024;11:1367681. doi:10.3389/fcvm.2024.1367681
25. jj F, Qp N, Mm B, et al. Mapping development and health effects of cooking with solid fuels in low-income and middle-income countries, 2000–18: a geospatial modelling study. Available from:. https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(22)00332-1/fulltext. Accessed Sept 28, 2024.
26. Alahmad B, Khraishah H, Royé D, et al. Associations Between Extreme Temperatures and Cardiovascular Cause-Specific Mortality: results From 27 Countries. *Circulation*. 2023;147:1:35–46. doi:10.1161/CIRCULATIONAHA.122.061832
27. Zhang J-D, Cheng X-F, Min S-H. Burden of non-communicable diseases attributable to high temperature in a changing climate from 1990 to 2019: a global analysis. *BMC Public Health*. 2024;24(1):2475. doi:10.1186/s12889-024-19947-z
28. Zhai C, Hu D, Yu G. Global, regional, and national deaths, disability-adjusted life years, years lived with disability, and years of life lost for the global disease burden attributable to second-hand smoke, 1990–2019: a systematic analysis for the Global Burden of Disease Study. *Sci Total Environ*. 2023;862:160677. doi:10.1016/j.scitotenv.2022.160677
29. Smith CE, Hill SE, Amos A. Impact of population tobacco control interventions on socioeconomic inequalities in smoking: a systematic review and appraisal of future research directions. *Tob Control*. 2021;30(e2):e87–95. doi:10.1136/tobaccocontrol-2020-055874
30. Yousuf H, Hofstra M, Tijssen J. Estimated Worldwide Mortality Attributed to Secondhand Tobacco Smoke Exposure, 1990–2016. *JAMA Network Open*. 2020;3(3):e201177. doi:10.1001/jamanetworkopen.2020.1177
31. Dai H, Alsalhe TA, Chalghaf N, Riccò M, Bragazzi NL, Wu J. The global burden of disease attributable to high body mass index in 195 countries and territories, 1990–2017: an analysis of the Global Burden of Disease Study. *PLoS Med*. 2020;17(7):e1003198. doi:10.1371/journal.pmed.1003198
32. Luo Y, Liu J, Zeng J, Pan H. Global burden of cardiovascular diseases attributed to low physical activity: an analysis of 204 countries and territories between 1990 and 2019. *Am J Prev Cardiol*. 2024;17:100633. doi:10.1016/j.ajpc.2024.100633
33. Rostami R, Moradinazar M, Moradi S. Impact of dietary risk on global ischemic heart disease: findings from 1990–2019. *Sci Rep*. 2024;14(1):18012. doi:10.1038/s41598-024-69089-w
34. Wang K, Jin Y, Wang M. Global cardiovascular diseases burden attributable to high sodium intake from 1990 to 2019. *J Clin Hypertens*. 2023;25(9):868–879. doi:10.1111/jch.14717
35. Wang L, Ma N, Wei L Global burden of ischemic heart disease attributable to high sugar-sweetened beverages intake from 1990 to 2019. Available from: https://www.nmcd-journal.com/article/S0939-47532300094-7/abstract. Accessed Sept 28, 2024.
36. Looker KJ, Booton R, Begum N. Global burden of ischemic heart disease associated with high red and processed meat consumption: an analysis of 204 countries and territories between 1990 and 2019. *BMC Public Health*. 2023;23(1):1–15. doi:10.1186/s12889-022-14670-z
37. Parajára MC, Colombet Z, Machado ÍE. Mortality attributable to diets low in fruits, vegetables, and whole grains in Brazil in 2019: evidencing regional health inequalities. *Public Health*. 2023;224:123–130. doi:10.1016/j.puhe.2023.08.028
38. Hu W, Zhai C, Sun H. The global burden of disease attributable to metabolic risks in 204 countries and territories from 1990 to 2019. *Diabetes Res Clin Pract*. 2023;196:110260. doi:10.1016/j.diabres.2023.110260
39. Z Li, Y Yang, X Wang, et al. Comparative analysis of atherosclerotic cardiovascular disease burden between ages 20–54 and over 55 years: insights from the Global Burden of Disease Study 2019. *BMC Med*. 2024;22:1–12. doi:10.1186/s12916-023-03187-w
40. Shen N, Liu J, Wang Y. The global burden of ischemic heart disease attributed to high fasting plasma glucose: data from 1990 to 2019. *Heliyon*. 2024;10(5):e27065. doi:10.1016/j.heliyon.2024.e27065
41. Du H, Shi Q, Song P. Global Burden Attributable to High Low-Density Lipoprotein-Cholesterol From 1990 to 2019. *Front Cardiovasc Med*. 2022;9:903126. doi:10.3389/fcvm.2022.903126
42. Yu Y, Zhang M, Tang Y. Global disease burden attributable to kidney dysfunction, 1990–2019: a health inequality and trend analysis based on the global burden of disease study. *Diabetes Res Clin Pract*. 2024;215:111801. doi:10.1016/j.diabres.2024.111801
43. Xi J-Y, Lin X, Hao Y-T. Measurement and projection of the burden of disease attributable to population aging in 188 countries, 1990–2050: a population-based study. *J Glob Health*. 2022;12:04093. doi:10.7189/jogh.12.04093
44. Osborne MT, Shin LM, Mehta NN, Pitman RK, Fayad ZA, Tawakol A. Disentangling the Links Between Psychosocial Stress and Cardiovascular Disease. *Circ Cardiovasc Imag*. 2020;13(8):e010931. doi:10.1161/CIRCIMAGING.120.010931
45. Münzel T, Sørensen M, Gori T. Environmental stressors and cardio-metabolic disease: part I–epidemiologic evidence supporting a role for noise and air pollution and effects of mitigation strategies. *Eur Heart J*. 2017;38(8):550–556. doi:10.1093/eurheartj/ehw269
46. Choudhury A, Aron S, Botigué LR. High-depth African genomes inform human migration and health. *Nature*. 2020;586(7831):741–748. doi:10.1038/s41586-020-2859-7
47. Thomson K, Hillier-Brown F, Todd A, McNamara C, Huijts T, Bambra C. The effects of public health policies on health inequalities in high-income countries: an umbrella review. *BMC Public Health*. 2018;18(1):869. doi:10.1186/s12889-018-5677-1
48. Zarulli V, Sopina E, Toffolutti V, Lenart A, Goli S. Health care system efficiency and life expectancy: a 140-country study. *PLoS One*. 2021;16(7):e0253450. doi:10.1371/journal.pone.0253450
49. Mason A, Lee R. Network members of the N. Six Ways Population Change Will Affect the Global Economy. *Popul Dev Rev*. 2022;48(1):51–73. doi:10.1111/padr.12469

Clinical Epidemiology

Dovepress
Taylor & Francis Group

Publish your work in this journal

Clinical Epidemiology is an international, peer-reviewed, open access, online journal focusing on disease and drug epidemiology, identification of risk factors and screening procedures to develop optimal preventative initiatives and programs. Specific topics include: diagnosis, prognosis, treatment, screening, prevention, risk factor modification, systematic reviews, risk & safety of medical interventions, epidemiology & biostatistical methods, and evaluation of guidelines, translational medicine, health policies & economic evaluations. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use.

Submit your manuscript here: https://www.dovepress.com/clinical-epidemiology-journal