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Original Article

Burden of cardiovascular disease attributable to lead exposure in China: a comprehensive analysis of data from 1990 to 2019

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Abstract: Objective: To analyze the burden of cardiovascular disease (CVD) caused by lead pollution exposure in China from 1990 to 2019. Methods: Utilizing data from the Global Burden of Disease 2019 (GBD 2019), this research examines the changes in the number of CVD deaths, deaths rates, disability-adjusted life years (DALYs) and DALY rates, as well as their age-normalization rates, due to lead pollution exposure in China from 1990 to 2019. Joinpoint was used to estimate average annual percentage of change (AAPC) and reflect the time change trend of the burden of CVD caused by lead pollution exposure in China, the world and different socio-demographic index (SDI) regions. Results: The age-standardized mortality rate and age-standardized DALY rate showed a decreasing trend in China from 1990 to 2019, with an average annual decrease of -1.17% (95% confidence interval (CI): -3.49~-3.14, P<0.05) and -1.90% (95% CI: -2.04~-1.75, P<0.05), respectively. In 2019, age-standardized CVD mortality and DALY rates attributed to lead exposure in China were higher than those in the global, high-SDI, medium-high SDI and moderate SDI regions. In 2019, 5.94% of CVD deaths in China were caused by lead exposure. Compared to 1990, the number of attributable deaths and mortality increased by 0.73% and 0.44%, respectively, and the attributable DALY and DALY rates increased by 30.04% and 8.22%, respectively. From 1990 to 2019, the mortality rate and DALY rate of males were higher than those of females, and the mortality rate and DALY rate increased with the increase of age, reaching the highest in the age group of 70 years and above. Conclusion: In 2019, the standardized death rate of CVD and the standardized DALY rate attributed to lead pollution exposure in China were higher than those in the global regions with high SDI, medium-high SDI and medium SDI. The findings highlight demographic disparities in CVD deaths and DALYs attributable to lead exposure, with males and the elderly identified as high-risk groups.

Keywords: Lead exposure, cardiovascular diseases, disability-adjusted life years, disease burden, air pollution

Introduction

Due to the high corrosion resistance, low melting point and good plasticity, lead is widely used in cable, chemical and battery industries. However, lead is a major environmental pollutant and one of the oldest known occupational pollutants worldwide. Populations can ingest environmental lead via food, water, air and soil, at different degrees. It has been reported that in some countries leaded paint and aviation fuel such as gasoline are still the remarkable sources [1]. Another study showed that in United States, lead-based coating is the major source of exposure [2]. Although the environmental source of lead has been obviously reduced, low-level lead exposure remains a remarkable global public health concern in many countries. Overall, there is a need to identify the lead exposure sources and their actions to enable the implementation of precise and effective regulation measures.

The lead toxicity is cumulative, and prolonged exposure has been linked to several adverse effects on human health [3], including increased risk of cardiovascular disease (CVD) [4]. Nowadays, CVD is a leading cause of death and disease burden in China, with 3.975 million deaths in total in 2016, accounting for 41.1%

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of all deaths [5]. The incidence of CVD is related to some risk factors, among which the role of lead warrants further investigation. The burden of CVD attributable to lead exposure has not been thoroughly recognized and considered in China.

This study utilized the latest data from global burden of disease (GBD) 2019, dividing the age, period and cohort by gender, to explore the potential trends of death rates and disability-adjusted life years (DALYs) rates of CVD attributed to lead exposure from 1990 to 2019 in China. The results of this study would extend and enhance the previous findings and provide a more targeted basis for promoting the CVD control strategies development and environmental improvement.

Methods

Sources of data

We used the GBD 2019 data on deaths and DALY of CVD attributable to lead exposure in China and Global in this study. The GBD 2019 project was conducted by the Institute for Health Metrics and Evaluation (IHME) and aimed to evaluate the global, regional and national burden of diseases, injuries, and the associated risks. The GDB 2019 evaluated the diseases burden attributable to 87 risk factors and 369 diseases in 204 countries and regions worldwide [6]. The GBD 2019 database published on the official website of IHME was adopted. The GBD 2019 estimated the burden of disease in China using data from multiple sources, including Chinese Center for Disease Control and Prevention Death Cause Network Reporting System, the China Maternal and Child Health Monitoring System, the National Disease Monitoring System, China Cancer Registration Data, Hong Kong and Macao death cause data, and other published and unpublished reports [7]. The details on the methodology are available at http://ghdx.healthdata.org/gbd-results-tool and https://vizhub.Healthdata.org/gbd-compare.

The socio-demographic index (SDI) is a multifactor detection of socioeconomic development that incorporates three key components: the total fertility rate for people under the age of 25, educational attainment for those aged 15 and above, and lag-distributed income per capita. The scale of SDI ranges from 0 to 1, where 0 represents least developed and 1 indicates the most developed. According to the SDI level, countries are divided into the following five quintiles: low, low-middle, middle, middle-high and high SDI.

Analysis of population attributable factor (PAF), mortality and DALY in patients with CVD

This study evaluated time trends of mortality through age-standardized mortality rates and relative changes in the percentage of death between 1990 and 2019. The global age-standardized population data obtained from the GBD 2019 were used to estimate the age-standardized mortality rates. The mortality population was divided into three age groups (15-49, 50-69 and 70+ years), with the proportion of mortality calculated in each group. The age-standardized DALY and the relative change percentage of DALY between 1990 and 2019 were used to evaluate the time trends of DALY in this study. The detailed methods for the calculation of mortality and DALY are elaborated in previous studies [8]. The PAF indicated that exposure to risk factors posed harm to all humans [9]. Based on the comparative risk assessment (CRA) theory, the counterfactual analysis methods were used. Under the assumption that the exposure levels of other risk factors remained unchanged, the target population's lead pollution exposure level and the theoretical minimum risk exposure level were compared, to estimate the proportion of the overall disease burden in the target population caused by lead pollution exposure [10, 11].

Statistical analysis

The number of deaths, mortality rates, DALY, and DALY rates were used to describe the disease burden of CVD attributed to lead pollution exposure in different gender and age groups in China. The Joinpoint regression program software (version 4.7.0.0) was used to perform trend analysis. The logarithmic linear regression model was used to calculate the average annual percentage change (AAPC) and its 95% CI, and the trends were also analyzed [12]. *P* values <0.05 were considered statistically sig-

Table 1. The trend of age-standardized rates of deaths and DALY in China, Global and different SDI regions from 1990 to 2019

Regions	Age-standardized rates of deaths			Age-standardized DALY rates		
	1990	2019	AAPC	1990	2019	AAPC
China	22.62	16.17	-1.17 (-1.32~-1.01)	480.44	276.26	-1.90 (-2.04~-1.75)
Global	13.89	10.8	-0.88 (-0.92~-0.83)	318.54	216.8	-1.32 (-1.39~-1.25)
High SDI	5.56	2.09	-3.31 (-3.49~-3.14)	105.43	35.88	-3.65 (-3.75~-3.55)
Middle-high SDI	10.7	7.58	-1.18 (-1.44~-0.92)	228.98	133.84	-1.83 (-2.05~-1.62)
Middle SDI	19.33	14.83	-0.93 (-1.09~-0.77)	421.22	269.92	-1.54 (-1.66~-1.43)
Low-middle SDI	24.32	20.9	-0.47 (-0.58~-0.36)	565.51	420.2	-0.98 (-1.12~-0.83)
Low SDI	23.59	21.25	-0.38 (-0.48~-0.28)	542.49	431.12	-0.80 (-0.91~0.68)

Note: DALY: disability-adjusted life years; AAPC: average annual percentage of change; SDI: socio-demographic index.

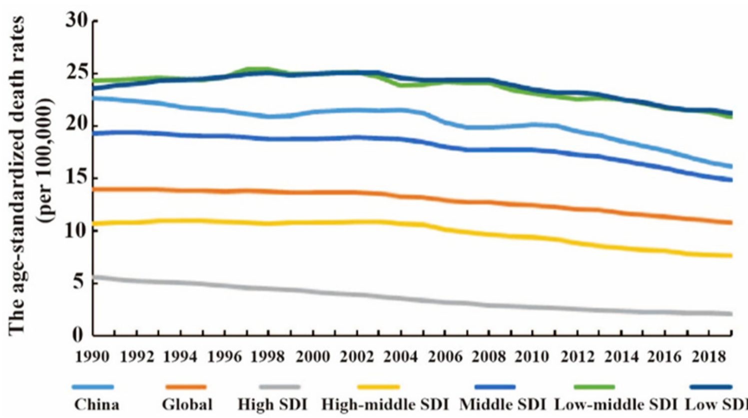

Figure 1. The tread in age-standardized death rates attributed to lead exposure in China, Global and different SDI regions from 1990-2019. Note: SDI: socio-demographic index.

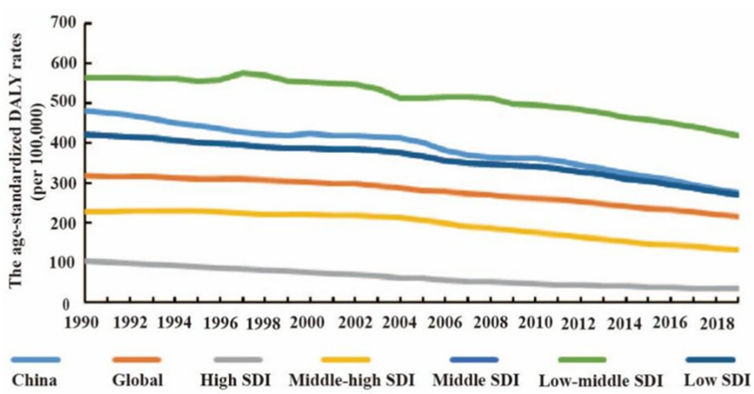

Figure 2. The tread in age-standardized DALY rates attributed to lead exposure in China, Global and different SDI regions from 1990-2019. Note: DALY: disability-adjusted life years; SDI: socio-demographic index.

nificant. R software version 3.6.3 was used to analyze the collected data.

Results

Cardiovascular disease burden attributable to lead exposure in China, global and different SDI regions from 1990 to 2019

As shown in **Table 1** and **Figures 1**, **2**, the age-standardized mortality rate and DALY rate of CVD attributed to lead exposure in China, Global and different SDI regions showed a decreasing trend from 1990 to 2019, and the mortality rate and DALY rate of CVD attributed to lead pollution exposure in China in 2019 were higher than those in Global, high SDI, middle-high SDI and middle SDI regions. The mortality rate in China decreased from 22.62/100,000 in 1990 to 16.17/100,000 in 2019, with an average annual decrease of -1.17% (95% CI: -3.49~-3.14, $P<0.05$), and the DALY rate decreased from 480.44/100,000 in 1990 to 276.26/100000, with an average annual decrease of -1.90% (95% CI: -2.04~-1.75, $P<0.05$). The reductions in these rates in China exceeded those observed globally and in regions with middle SDI, low-middle SDI and low SDI.

Table 2. The trends of CVD deaths attributed to lead exposure in China from 1990 to 2019

Age/years	Year	PAF (%)	The Number of deaths (per 10,000)			The deaths rate (per 1/100,000)		
			Male	Female	Total	Male	Female	Total
15-49 years	1990	7.27	1.14	0.44	1.57	3.29	1.36	2.35
	2000	6.64	1.21	0.49	1.70	3.16	1.36	2.28
	2010	5.42	1.06	0.26	1.32	2.60	0.67	1.65
	2019	3.47	0.56	0.12	0.67	1.51	0.33	0.93
	Rate of change (%)	-0.52	-0.51	-0.73	-0.57	-0.54	-0.75	-0.60
50-69 years	1990	8.01	4.70	2.17	6.88	58.96	29.26	44.64
	2000	8.12	4.93	1.86	6.79	49.89	20.12	35.51
	2010	7.46	5.18	1.83	7.01	38.32	13.98	26.36
	2019	6.39	5.14	1.79	6.94	27.88	9.73	18.81
	Rate of change (%)	-0.20	0.09	-0.17	0.01	-0.53	-0.67	-0.58
70 years and above	1990	5.47	4.07	3.19	7.26	246.62	146.83	189.89
	2000	5.98	6.41	4.37	10.78	259.85	144.50	196.32
	2010	6.07	9.84	6.21	16.04	275.05	148.65	206.96
	2019	5.95	12.05	7.57	19.62	244.73	128.90	181.73
	Rate of change (%)	0.09	1.96	1.37	1.70	-0.01	-0.12	-0.04
Entire population	1990	6.48	9.91	5.80	15.72	16.24	10.12	13.28
	2000	6.62	12.55	6.72	19.27	18.72	10.67	14.82
	2010	6.36	16.08	8.29	24.37	23.02	12.45	17.86
	2019	5.94	17.75	9.48	27.23	24.49	13.59	19.15
	Rate of change (%)	-0.08	0.79	0.63	0.73	0.51	0.34	0.44

Note: CVD: cardiovascular disease; PAF: population attributable factor.

The trends in CVD deaths attributed to lead exposure in China from 1990 to 2019

In 2019, 5.94% of CVD deaths in the Chinese population aged 15 years and above were caused by lead exposure, totaling 272,300 deaths with a mortality rate of 19.15/100,000. This represents an increase of 0.73% in the number of deaths and 0.44% in the mortality rate compared to 1990. Analysis of the number and mortality rate of CVD deaths attributed to lead exposure from 1990 to 2019 showed that there was an increasing trend with age, reaching a peak in the group aged ≥70 years, and the number and mortality rate of CVD in males were significantly higher than those in females, as shown in **Table 2**.

The trends in DALY of CVD attributed to lead exposure in China from 1990 to 2019

In 2019, the DALY of CVD attributed to lead exposure in China was 5.2723 million years, with an attributable DALY rate of 370.68/100,000. Among them, the attributable DALY and its rate for males were 3.5959 million years and 496.11/100,000, respectively, while those for females were 1.6764 million years and 240.33/100,000, respectively. It was found that the attributable DALY and its rate of males were significantly more than those of females. Compared with 1990, the attributable DALY and its rates in 2019 increased by 30.04% and 8.22% respectively, and both of them showed an upward trend with age, reaching the peak in the group aged ≥70 years, as shown in **Table 3**.

Discussion

The high levels of lead exposure and its adverse influences on human health have become a significant public health concern since the 1990s, drawing increased attention to reduce lead exposure [13]. According to GBD 2019 study, although overall lead exposure has declined, the decrease has been slower in low- and middle-income countries and developing countries compared to high-income countries, with lead exposure remaining high in develop-

Table 3. The trends in DALY of CVD attributed to lead exposure in China from 1990 to 2019

Age/years	Year	DALY (per 100,000)			DALY rates (per 1/100,000)		
		Male	Female	Total	Male	Female	Total
15-49 years	1990	57.23	22.82	80.05	165.68	70.64	119.75
	2000	60.23	25.35	85.58	157.16	69.86	114.7
	2010	51.33	13.74	65.07	125.91	34.98	81.3
	2019	27.14	6.43	33.57	73.42	18.33	46.58
	Rate of change (%)	-0.53	-0.72	-0.58	-0.56	-0.74	-0.61
50-69 years	1990	144.81	67.57	212.38	1814.89	909.89	1378.62
	2000	151.23	59.1	210.34	1530.98	639.94	1100.43
	2010	160.3	59.23	219.54	1185.97	453.48	826
	2019	159.6	59.31	218.91	865.06	321.68	593.45
	Rate of change (%)	0.1	-0.12	0.03	-0.52	-0.65	-0.57
70 years and above	1990	64.77	48.24	113.02	3923.79	2218.06	2954.06
	2000	100.18	64.15	164.33	4059.85	2120.11	2991.45
	2010	144.88	85.8	230.69	4051.77	2054.96	2976.15
	2019	172.85	101.89	274.75	3510.45	1735.07	2544.77
	Rate of change (%)	1.67	1.11	1.43	-0.11	-0.22	-0.14
Entire population	1990	266.82	138.63	405.45	437.27	241.73	342.53
	2000	311.64	148.6	460.24	464.9	235.83	353.91
	2010	356.52	158.77	515.29	510.54	238.32	377.63
	2019	359.59	167.64	527.23	496.11	240.33	370.68
	Rate of change (%)	34.77	20.93	30.04	13.46	-0.58	8.22

Note: CVD: cardiovascular disease; DALYs: disability-adjusted life years.

ing countries [14]. It was estimated that in 2019, lead exposure accounted for 900,000 deaths and 21,700,000 DALY worldwide, with the highest burden in development countries.

In this study, based on the data from GBD 2019, it was found that the degree of decline in the standardized mortality rate and DALY rate of CVD attributed to lead pollution exposure in China from 1990 to 2019 was more pronounced than that observed globally and regions with medium SDI, medium-low SDI and low SDI, which can be attributed to China's cessation of production and sales of motor gasoline containing lead. The Chinese government mandated that from January 1, 2000, all gasoline production enterprises had to cease the production of leaded gasoline for vehicles, and required all gasoline vehicles produced by automobile manufacturers to be suitable for using lead-free gasoline [15]. Starting from July 1, 2000, all gas stations stopped selling leaded gasoline for vehicles and switched to selling unleaded gasoline. These measures had reduced lead pollution in the atmospheric environment, greatly reducing the disease burden attributed to lead pollution exposure in China [16].

Moreover, this study showed that the death rates and DALY rates reached a peak in individuals aged over 70 years, and it was more significant in men than that in women in all age group, both in 1990 and 2019. This imply that elderly populations were more susceptible to CVD associated with high attributable deaths and DALY to lead exposure [17]. Lead exposure is also linked to long-term health issues, including an increased risk of kidney damage and hypertension [18]. Other studies also showed that the attributable age-standardized death rate and DALY were higher in men than in women [19], aligning with the results of this study.

This study showed that there were age differences in the number of CVD deaths, mortality rates, DALY, and DALY rates attributed to lead pollution exposure in China. The number of deaths, mortality rate, DALY, and DALY rates attributed to lead exposure in CVD in China from 1990 to 2019 were highest in the group aged over 70 years, with males being higher than females. This study also showed that compared with 1990, the 2019 mortality rate and DALY rate of CVD attributed to lead exposure in China were increased by 0.44% and 8.22%, respectively, while the standardized mortality rate and DALY rate of CVD were decreased by 28.51% and 42.50%, respectively, indicating that aging of population had increased the burden of cardiovascular disease caused by lead exposure. The World Population Outlook 2019 report showed that the pace of population aging in China continues to accelerate, and the proportion of elderly people would continue to rise, with the number of people aged 60 and above expected to rise from 250 million to 488 million in 2020. The gender differences in the number of CVD deaths, mortality rates, DALY, and DALY rates attributed to lead pollution exposure in China may be related to population aging, male-dominated unhealthy lifestyle habits such as smoking, as well as the weak protective awareness in the workplace and occupational differences between women and men.

Previous studies revealed that the burdens of mental retardation and cardiovascular adverse outcomes caused by lead exposure were estimated to be nearly 1% of the global disease burden [20]. As CVDs attributed to lead exposure account for a large proportion of DALY and impose a high economic burden [21], preventive measures against lead exposure are considered cost-effective to reduce the disease burden. This study found that although the age-standardized mortality rate and age-standardized DALY rate of CVD attributed to lead pollution exposure in China showed a decreasing trend from 1990 to 2019, they remain higher than those in the global, high SDI, middle-high SDI and middle SDI regions.

On the one hand, the rapid industrialization had increased the risk of environmental lead exposure in low- and middle-income countries, including lead-acid batteries, lead based coatings, metal alloys, and ceramics [22, 23]. Some studies indicated that the total lead consumption in China was currently close to 5 million tons, and the impact of lead pollution on China cannot be ignored [24]. On the other hand, other studies demonstrated that besides automobile exhaust, the previous and current industrial emissions in China were the main source of lead pollution. China's economic model has traditionally supported high-polluting industries, suggesting that industrial exposure sources could continue to harm the population long after these industries decline. Moreover, despite challenges in implementing comprehensive regulations to address vulnerabilities in lead-emitting enterprises, the persistence of the lead manufacturing industry continues to pose significant health risks [1, 23]. In some developing countries, the disease burden attributable to lead exposure remains the highest [25]. It was reported that the application of governmental actions and public health efforts for regulation of lead content and control of lead sources successfully contributed to the reduction in lead exposure [26].

Overall, the burden of CVD disease attributed to lead exposure in China remains heavy. To address this, China should continue to strengthen the control of lead pollution, standardize industrial production processes, improve production technology and prohibit excessive lead discharge [27]. At the same time, it is necessary to strengthen the protection of lead exposed workers and regularly screen for excessive blood lead levels. Besides, it is necessary to strengthen publicity and education on the sources and hazards of lead pollution [28].

This research provides the most up-to-date and comprehensive analysis of the trends and current situation concerning the burden of disease attributable to lead exposure and its related CVD in China and globally from 1990 to 2019, based on data from the Global Burden of Disease (GBD) 2019 study. However, like other GBD studies, the main limitations of the current research were caused by GBD methodologies in data collection and usage of the complex modelling strategies, which restrict our direct manipulation of the data. Moreover, the availability and quality of primary data were mainly limited by the GBD estimates, especially in regions where data completeness rates are low. The limitations of exposure measurement of the GBD 2019 research including heterogeneous patterns of data availability and less reliable methods of data collection in various regions over time are present in this study. The drawbacks of application methods for estimating lead exposure are also exist in this study. The analysis of disease burden caused by lead exposure was based on the assumption that the lead exposure had the independent effects. However, lead exposure usually coexists with other factors and interacts with them.

In conclusion, the age-standardized mortality rate and DALY rate of CVD attributed to lead exposure in China, Global and different SDI regions have decreased slowly over the past 30 years. In China, in contrast to 1990, the number of attributable deaths and its rate in 2019 were increased by 0.73% and 0.44%, respectively, while the attributable DALY and its rates were increased by 30.04% and 8.22%, respectively, reaching a peak in the group aged more than 70 years. Given the trends of CVD attributed to lead exposure in China, urgent attention and measures are required to control and reduce the source of lead exposure and its attributable burden. Moreover, the lack of reliable exposure data from China underscores the need for more studies to determine the exact burden of disease attributed to lead exposure in China.

Disclosure of conflict of interest

None.

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