

Comparison of tracheal, bronchus, and lung cancer mortality after occupational cadmium exposure in china and the world

Çin ve dünyada mesleki kadmiyum maruziyetinden sonra trakea, bronş ve akciğer kanseri ölüm oranlarının karşılaştırılması

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ABSTRACT

Aim: Cadmium is a heavy metal pollutant that is a human carcinogen. Exposure occurs primarily through ingestion and inhalation.

Materials and Methods: In our study, we examined the mortality rates, Disability Adjusted Life Years (DALYs) and population-attributable fraction (%) due to cadmium exposure in China and the world for the years 2000, 2010 and 2016 using the World Health Organization (WHO) occupational disease burden application tool.

Results: In China, the mortality rate (per 100,000 of population) due to occupational cadmium exposure due to bronchus, trachea and lung cancer has not decreased over the years, and the mortality rate due to exposure is still high. According to the latest 2016 data, although the death rate (per 100,000 of population) in China (.4269) is higher than the world (.2002) average; the death rate (per 100,000 of population) was determined to be similar to Europe (.4650), but lower than the death rates in Africa (44.9514), Americas (30.0927), Eastern Mediterranean (12.5471), South-East Pacific (14.4381) and Western Pacific (201.1176) regions ($p < .05$). As a result of the comparisons made, it is seen that the number (for DALYs in 1000s) due to cadmium exposure has increased over the years (2000: 3.82, 2010: 4.95, 2016: 5.55). It was determined that the number (for DALYs in 1000s) showed significant differences over the years ($p < .05$). Mortality rates (per 100,000 of population) have been decreasing over the years (2000: 79.7906, 2010: 49.3388, 2016: 41.4298) ($p < .05$).

Conclusion: Morbidity and mortality rates due to cadmium exposure remain high due to rapidly increasing industrialization.

Keywords: Cancer, China, mortality, occupational cadmium exposure, WHO.

ÖZ

Amaç: Kadmiyum, insanlar için kanserojen olan ağır metal bir kirleticidir. Maruz kalım öncelikle yutma ve solunum yoluyla gerçekleşir.

Gereç ve Yöntem: Çalışmamızda, Dünya Sağlık Örgütü (DSÖ) mesleki hastalık yükü uygulama aracını kullanarak 2000, 2010 ve 2016 yıllarında Çin'de ve küresel düzeyde kadmiyuma maruz kalıma bağlı ölüm oranlarını, Engelliliğe Ayarlanmış Yaşam Yılları'nı (DALY) ve nüfusa atfedilebilir oranları (%) inceledik.

Bulgular: Çin'de yıllar içerisinde kadmiyuma mesleki maruz kalım nedeniyle bronş, trakea ve akciğer kanserlerine bağlı ölüm oranında (100.000 kişide) bir azalma görülmemiş olup maruz kalıma bağlı ölüm oranı hala yüksektir. En son 2016 yılı verisine göre Çin'deki ölüm oranı (100.000 kişide) (.4269) dünya ortalamasına (.2002) göre yüksek olmasına rağmen; ölüm oranının (100.000 kişide) Avrupa (.4650) ile benzer, ancak Afrika (44,9514), Amerika (30,0927), Doğu Akdeniz (12,5471), Güneydoğu Pasifik

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(14,4381) ve Batı Pasifik (201,1176) bölgelerindeki ölüm oranlarından düşük olduğu belirlendi ($p<.05$). Yapılan karşılaştırmalar sonucunda kadmiyuma maruz kalıma bağlı olarak DALY sayısının (1000'ler halinde) yıllar içerisinde arttığı görülmektedir (2000: 3,82, 2010: 4,95, 2016: 5,55). DALY sayısının (1000'ler halinde) yıllar içerisinde anlamlı farklılıklar gösterdiği belirlendi ($p<.05$). Ölüm oranları (100.000 kişide) yıllar içinde azalmaktadır (2000: 79,7906, 2010: 49,3388, 2016: 41,4298) ($p<.05$).

Sonuç: Hızla artan sanayileşme nedeniyle kadmiyuma maruz kalıma bağlı morbidite ve mortalite oranları halen yüksektir.

Anahtar Sözcükler: Çin, kanser, kadmiyuma mesleki maruz kalım, mortalite, DSÖ.

INTRODUCTION

Cadmium is found in the Earth's crust and is released by activities such as mining, alloys, high-phosphate fertilizers, battery production, fossil fuel burning, cement, electroplating and stabilization of plastics (1). Cadmium accumulates in fruits and vegetables as a result of its presence in the soil. It is taken into the body by eating these products and by consuming fish and shellfish. Exposure occurs through inhalation of cadmium in the air and absorption of cadmium through the skin (2). One of the heavy metals that is a significant carcinogen for humans is cadmium. Human exposure occurs primarily through ingestion and inhalation. Cadmium exposure can occur through environmental or occupational exposure. Recently, cadmium has been found to cause changes in human bronchial epithelium. Cadmium-related lung cancer has often been associated with occupational exposure. Metallothionein (MT), a protein with high metal-binding affinity, is thought to be responsible for the accumulation of cadmium and its long half-life. Cadmium bound to metallothionein may cause accumulation of metal in target cells and cause toxic effects (3). Metallothionein has been found to protect cells from oxidative stress and participate in the differentiation, apoptosis, and proliferation of cancer and normal cells (4). Cadmium is widely distributed in the environment through agricultural practices, natural sources and various industrial applications. Cadmium reaches the population through cadmium-contaminated beverages and foods and tobacco use (5). Cadmium can cause toxic effects and cancer in the lungs, liver, kidneys and prostate. Cadmium changes the expression of FGF2 and IL1B in the respiratory organs and causes DNA damage. It also disrupts cell junction integrity, promotes apoptosis and leads to lung cancer. Cadmium alters the expression of HMOX1 and EDN1 in the prostate, leads to abnormal protein activity and maturation, suppresses tumor suppressors and promotes apoptosis, leading to

prostate cancer (6). Environmental cadmium exposure may cause chronic obstructive pulmonary disease (COPD) (7). Bronchial, tracheal and lung cancers cause 1.8 million deaths and 2.094 million new cases worldwide each year and are important causes of morbidity and mortality. Tracheal, bronchial and lung cancers are associated with smoking, genetic variation, occupational exposure and environmental factors. Occupational exposure accounts for 25% of tracheal, bronchial and lung cancer deaths. According to the International Labour Organization, it is estimated that 2 million of the 2.5 billion workers in the world die each year from work-related accidents or occupational diseases. It has been estimated that one third of these diseases are interstitial lung diseases and respiratory tract cancers. Occupational exposure is responsible for years of life lost due to disability and cancer deaths globally (8).

MATERIALS and METHODS

Study Design

The type of research is ecological study.

Study Population

In our study, we used the World Health Organization (WHO) occupational disease burden application tool and used the available data for the years 2000, 2010 and 2016. Tracheal, bronchus and lung cancers were examined in individuals of both sexes, aged 15 years and over. We compared China with world regions.

Research Data

The research consists of data expressing cadmium exposure for the years 2000-2010-2016, in line with World Health Organization (WHO) data. The most recent available data were used. In this context, data from 184 countries were accessed and the data from these countries were categorized and analyzed regionally. The data covers 6 regions: Africa, Americas, Eastern

Mediterranean, Europe, South-East Pacific, Western Pacific. Since the Global and China are included as one region in the dataset, they are included in the analysis as separate regions. Additionally, a total of 174,420 data were obtained, 58,140 for each data period for global, China and 6 regions. The independent variables used for the study are the regions where the individuals are located, gender, year included in the sample and age. There is no data on smoking, alcohol or addictive substances in the data included in the research. Therefore, this study is limited to data reported by the World Health Organization (WHO) between 2000-2010-2016.

Statistical Analysis

In our study, we examined the mortality rates, Disability Adjusted Life Years (DALYs) by WHO, and population-attributable fraction (%) due to cadmium exposure in China and globally using the World Health Organization (WHO) occupational disease burden application tool. DALYs represent the health loss caused by fatal and non-fatal outcomes. DALYs are calculated by adding Years of Life Lost (YLL) and Years Lost Due to Disability (YLD). One year of health loss is equivalent to one DALYs (8). IBM SPSS Statistics for Windows, Version 27.0 program was used for statistical analysis. Shapiro Wilk or Kolmogorov-Smirnov tests were used to determine whether the variables were normally distributed. Normality test results of $p \geq 0.05$ were accepted as having a normal distribution. The dependent variables of the study, "number (for DALYs in 1000s)", "population-attributable fraction (%)", "rate (per 100,000 population)" were found to have skewness and kurtosis values between -1 and +1 and were normally distributed. For these reasons, independent sample t-test and ANOVA test were applied in the analyses. For all statistical analyses, $p < 0.05$ was considered significant. The research data were collected independently for each period, not as repeated measures. Therefore, the periods and people for whom data were collected are different.

RESULTS

Descriptive statistics regarding the distribution of the data are examined in Table-1.

As a result of the analysis, skewness and kurtosis values were examined and it was seen that these data values were normally distributed. Accordingly, it was concluded that there were

extreme values in the data and the distribution of the data was not normal. However, considering the condition and amount of the data, it was accepted that it showed a normal distribution. Therefore, parametric statistical techniques such as the ANOVA test and independent samples t test were applied in the analyses.

In Table-2, the data included in the study were compared in terms of year, region, gender and age according to cadmium exposure. When the descriptive statistics of the data included in the study were examined, it was determined that 33.3% of the data belonged to 2000, 33.3% to 2010 and 33.3% to 2016. So, the analyzed data were included in the study in equal percentages according to the periods. When the data in the study is examined by region, it is seen that 25.3% comes from Africa, 17.9% from Americas, 26.8% from Europe, 0.5% globally, 6.3% from the South-East Pacific, 11.3% from the Western Pacific and 0.3% from China. It was determined that 50.0% of the data were taken from women and 50.0% from men (individuals included in the study were matched in terms of gender). In terms of age, it was determined that 23.5% of the data were 15-34 years old, 23.5% were 35-54, 23.5% were 55-74 and 29.4% were 75+ years old.

Figure-1 shows the distribution of data by year, region, gender and age.

In Table-3, comparison of mortality rates due to cadmium exposure by region was analyzed using ANOVA test. As a result of the analysis;

In the study, it was determined that the number (for DALYs in 1000s) in China and the global population was higher than the regions according to the 2000 data ($F = 1472.122$; $p < .05$). China and the global were found to have lower population-attributable fraction (%) than the regions ($F = 3.020$; $p < .05$). It was determined that the rates (per 100,000 of population) in China, the European region and the global region were lower than in other regions ($F = 11.026$; $p < .05$). The study determined that, according to 2010 data, China and global numbers (for DALYs in 1000s) were higher than the regions ($F = 1340.158$; $p < .05$). China, Global, Europe region was found to have lower population-attributable fraction (%) than other regions. However, this difference was not significant ($F = .943$; $p > .05$). The decrease in mortality rates despite the increase in exposure rates can be explained by improved treatment methods, increased awareness of the disease and the impact of developing technologies. China, global and European regions were found to have

lower rates (per 100,000 of population) compared to other regions ($F=13.741$; $p<.05$). The study determined that the global and China had higher numbers (for DALYs in 1000s) than other regions according to 2016 data ($F=1289.360$; $p<.05$). Global, China and the European region were found to have lower population-attributable fraction (%) than other regions. However, this difference was not significant ($F=1.469$; $p>.05$). It was determined that the Global, China, and European regions had lower rates (per 100,000 of population) than other regions ($F=8.241$; $p<.05$). In Table-4, comparison of mortality rates due to cadmium exposure by gender when analyzed independently of the year using the Kruskal Wallis test. As a result of the analysis; When the table was examined, it was determined that there was an increase in the numbers (for DALYs in 1000s) over the years and that this increase was significant ($F=10.426$; $p<.05$). It was

determined that there was no significant change in population-attributable fraction (%) over the years ($F=.005$; $p>.05$). It was determined that there was a decrease in rates (per 100,000 of population) over the years and that this decrease was significant ($F=7.097$; $p<.05$). In Table-5, comparison of mortality rates due to cadmium exposure by gender was analyzed using independent sample t test. As a result of the analysis; When cadmium exposure is examined by year, it is seen that men have higher numbers (for DALYs in 1000s) than women according to the data of 2000, 2010 and 2016. It was also determined that women have higher population-attributable fraction (%) than men in all the periods examined. Figure-2 shows global deaths from bronchial, tracheal and lung cancer due to cadmium exposure in 2000, 2010 and 2016 (9).

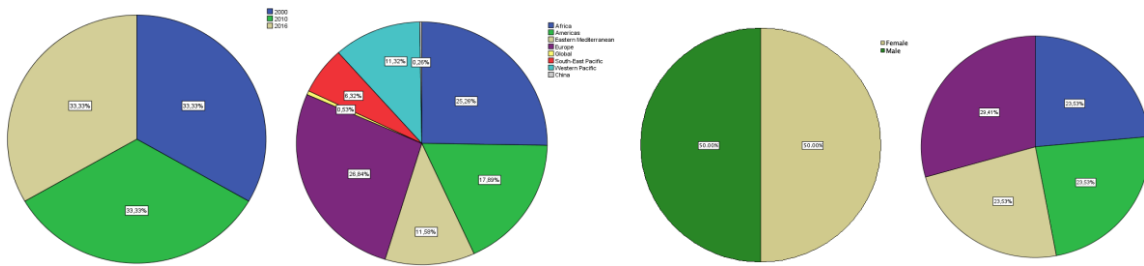


Figure-1. Distribution of data by year, region, gender and age.

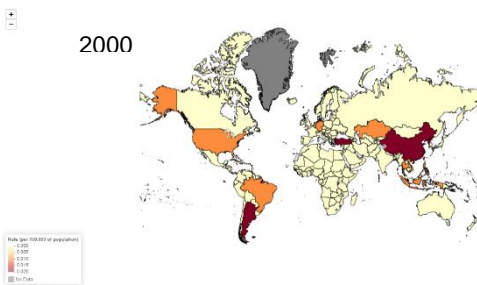


Figure-2a.

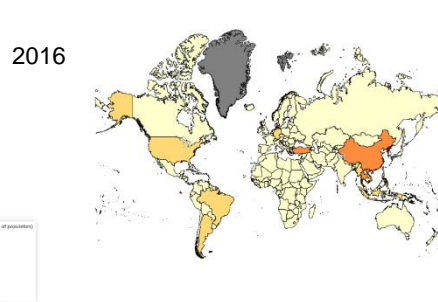


Figure-2c.

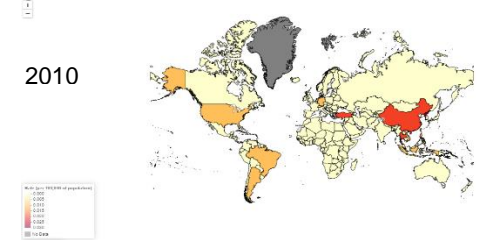


Figure-2b.

Figure-2. Maps of trachea, bronchus and lung cancer following cadmium exposure worldwide by year, according to the World Health Organization (WHO) (9).

Table-1. Descriptive statistics on the distribution of data.

	Year	n	Mean	Std. Deviation	Skewness	Kurtosis
Regions	2000	58140	3.25	1.971	.599	-.670
Regions	2010	58140	3.25	1.971	.599	-.670
Regions	2016	58140	3.25	1.971	.599	-.670

Table-2. Descriptive statistics on the data.

		n	%
Year	2000	58140	33.3
	2010	58140	33.3
	2016	58140	33.3
Regions	Africa	44064	25.3
	Americas Region	31212	17.9
	Eastern Mediterranean Region	20196	11.6
	Europe Region	46818	26.8
	Global Region	918	.5
	South-East Pacific Region	11016	6.3
	Western Pacific Region	19737	11.3
	China Region	459	.3
Gender	Female	58140	50.0
	Male	58140	50.0
Age	15-34	41040	23.5
	35-54	41040	23.5
	55-74	41040	23.5
	75+	51300	29.4

Table-3. Mortality rates due to cadmium exposure by region.

Year	Region	n	Mean	Std. Deviation	sd	F	Sig.
2000	Africa	14688	.28	1.651			
	Americas	10404	1.87	12.327			
	Eastern Mediterranean	6732	.51	2.905			
	Europe	15606	1.23	11.384	7	1472.122	.001
	Global	306	235.66	478.900			
	South-East Pacific	3672	6.26	27.765			
	Western Pacific	6426	7.02	62.449			
	China	306	117.02	229.987			
	Africa	14688	9.5233	232.94703			
	Americas	10404	119.4115	5369.02465			
	Eastern Mediterranean	6732	4.5685	165.68059			
	Europe	15606	1.6785	136.30565	7	3.020	.004
	Global	306	.0260	.03360			
	South-East Pacific	3672	6.9959	197.55515			
	Western Pacific	6426	13.4868	327.08308			
	China	306	.0429	.04070			
	Africa	14682	104.6265	2014.75309	7	11.026	.001
	Americas	10404	86.6664	2321.70351			

2010	Rate (per 100,000 of population)	Eastern Mediterranean	6732	32.4443	671.05677			
		Europe	15606	.6996	11.85368			
		Global	306	.2127	.44578			
		South-East Pacific	3654	59.4131	1206.72523			
	Number (for DALYs in 1000s)	Western Pacific	6372	274.3847	4908.11544			
		China	306	.4138	.78306			
		Africa	14688	.26	1.551			
		Americas	10404	2.09	14.372			
	Population-attributable fraction (%)	Eastern Mediterranean	6732	.73	4.423			
		Europe	15606	1.26	11.995	7	1340.158	.001
		Global	306	308.27	650.645			
		South-East Pacific	3672	8.64	39.488			
	Rate (per 100,000 of population)	Western Pacific	6426	9.61	90.681			
		China	306	163.62	342.272			
		Africa	14688	5.3314	131.60226			
		Americas	10404	131.9653	10915.07920			
Number (for DALYs in 1000s)	Eastern Mediterranean	6732	2.1277	100.69723				
	Europe	15606	.8943	64.73414	7	.943	.471	
	Global	306	.0271	.02818				
	South-East Pacific	3672	3.4167	99.41484				
2016	Rate (per 100,000 of population)	Western Pacific	6426	9.0223	218.10913			
		China	306	.0444	.04292			
		Africa	14688	67.3799	1364.82828			
		Americas	10404	42.8657	1004.41324			
	Number (for DALYs in 1000s)	Eastern Mediterranean	6732	17.4132	413.73980			
		Europe	15606	.4947	7.98013	7	13.741	.001
		Global	306	.2100	.40495			
		South-East Pacific	3672	29.7029	587.13781			
	Population-attributable fraction (%)	Western Pacific	6402	187.0512	3177.01198			
		China	306	.4586	.87457			
		Africa	14688	.29	1.802			
		Americas	10404	2.22	15.442			
	Rate (per 100,000 of population)	Eastern Mediterranean	6732	.87	5.503			
		Europe	15606	1.30	12.332	7	1289.360	.001
		Global	306	346.22	742.084			
		South-East Pacific	3672	10.64	49.052			
Number (for DALYs in 1000s)	Western Pacific	6426	10.70	103.330				
	China	306	180.88	391.136				
	Africa	14688	4.1529	105.45668				
	Americas	10404	145.9731	9733.92513				
Population-attributable fraction (%)	Eastern Mediterranean	6732	1.4779	70.57844				
	Europe	15606	1.7924	139.71430	7	1.469	.173	
	Global	306	.0282	.02824				
	South-East Pacific	3672	1.9601	56.00113				
Rate (per 100,000 of population)	Western Pacific	6426	6.7640	164.87662				
	China	306	.0455	.04347				
	Africa	14688	44.9514	1002.58209	7	8.241	.001	
	Americas	10404	30.0927	712.05445				

Rate (per 100,000 of population)	Eastern Mediterranean	6732	12.5471	330.00039
	Europe	15606	.4650	8.70233
	Global	306	.2002	.38465
	South-East Pacific	3672	14.4381	281.55184
	Western Pacific	6414	201.1176	5313.13822
	China	306	.4269	.82971

Table-4. Mortality rates due to cadmium exposure by year.

		n	Mean	SD	df	F	Sig.
Number (for DALYs in 1000s)	2000	58140	3.82	48.813	2	10.426	.001
	2010	58140	4.95	67.482			
	2016	58140	5.55	76.842			
Population-attributable fraction (%)	2000	58140	26.6867	2279.48565	2	.005	.995
	2010	58140	26.6615	4618.75503			
	2016	58140	28.6947	4119.29941			
Rate (per 100,000 of population)	2000	58062	79.7906	2187.63559	2	7.097	.001
	2010	58116	49.3388	1344.50127			
	2016	58128	41.4298	1865.55282			

Table-5. Mortality rates due to cadmium exposure by gender.

Year	Gender	n	Mean	Std. Deviation	t	df	Sig.	
2000	Number (for DALYs in 1000s)	Female	19380	1.82	20.959	-5.783	38758	.001
		Male	19380	3.94	46.645			
	Population-attributable fraction (%)	Female	19380	.6205	3.77970	6.074	38758	.001
		Male	19380	.4142	2.84094			
	Rate (per 100,000 of population)	Female	19350	78.9001	2102.18544	-.399	38698	.690
		Male	19350	87.9373	2347.44503			
2010	Number (for DALYs in 1000s)	Female	19380	2.32	28.224	-5.543	38758	.001
		Male	19380	5.14	64.949			
	Population-attributable fraction (%)	Female	19380	.5381	3.38564	5.220	38758	.001
		Male	19380	.3770	2.64371			
	Rate (per 100,000 of population)	Female	19374	50.7967	1402.99613	-.638	38740	.524
		Male	19368	60.5792	1609.65742			
2016	Number (for DALYs in 1000s)	Female	19380	2.60	32.377	-5.418	38758	.001
		Male	19380	5.74	73.728			
	Population-attributable fraction (%)	Female	19380	.5090	3.24494	4.657	38758	.001
		Male	19380	.3694	2.62175			
	Rate (per 100,000 of population)	Female	19380	44.8976	2010.31591	.297	38746	.766
		Male	19368	39.9647	1140.68326			

DISCUSSION

A retrospective cohort study found a significant risk of lung cancer in workers exposed to cadmium, with 50 to 111 lung cancer deaths per 1,000 workers exposed over 45 years (10). A meta-analysis study found that both general and occupational exposure significantly increased the risk of lung cancer (11). One study found that

cadmium is also associated with bladder, kidney, breast and pancreatic cancer, and its basic cationic portion is responsible for both carcinogenic and toxic effects (12). One study found that chronic occupational exposure to cadmium in Egyptian workers caused deterioration in different body systems (13). A meta-analysis of ten years of epidemiological data determined that low-level cadmium exposure was

a risk factor for lung cancer and total cancer (14). Cigarette smoke inhalation is a major cause of cadmium exposure. 10% of inhaled cadmium accumulates in the lungs. More than 30% of accumulated cadmium passes into the bloodstream (15). One study found that increasing serum cadmium concentration caused lung function to decrease more rapidly in COPD patients (16). In a study, it was determined that the immune system can deepen the damage it creates in our own tissue as a result of tissue damage caused by cadmium exposure (17). A study conducted in Iran found that cadmium exposure was higher in industrial workers (18). A study conducted in the Netherlands found high levels of cadmium in the blood of workers involved in the production of cadmium stabilizers and enamels, electrochemical coatings, and silver-cadmium soldering (19). A study conducted in Italy found that the workers most exposed to cadmium were glass/ceramic factory operators and jewelry/precious metal workers (20). A meta-analysis, systematic review found that cadmium exposure was associated with a 31% increase in lung cancer (21). In a study, cadmium levels in the blood of welding workers were found to be high and a significant decrease in lung function was detected (22). According to the data obtained in the study, occupational cadmium exposure is seen to cause especially trachea, bronchus and lung cancer and other organ cancers. The fact that occupational cadmium exposure significantly affects morbidity and mortality in workers is supported by studies and my own work. Our study results show that mortality rates due to cadmium exposure have decreased significantly over the years worldwide. DALYs due to cadmium exposure have increased over the years in China and the world. Mortality rates due to cadmium exposure are higher in men than in women. When the research findings are taken into consideration, it is very important to conduct health surveillance, preventive measures and periodic health checks of all employees at the workplace. In a study conducted by Byber et al. it was stated that one of the important causes of cadmium exposure was lack of information (23). In a study by Nordberg et al. it was reported that long-term exposure to cadmium causes keratin (24). It has also been observed that long-term exposure causes adverse health effects on the lungs and kidneys (25). Industrial pollution also causes high levels of cadmium exposures, mainly as a result of past emissions (26). Inhalation of

small particles vaporized during tobacco and cigarette smoking causes cadmium exposure. Therefore, active smoking is considered to be an important source of cadmium exposure. Exposure to environmental tobacco smoke also causes exposure, but not high enough to significantly affect blood cadmium levels (27).

Limitations

Since smoking is the main source of exposure, it may vary by region. However, this can be seen as a limitation of the study since the data prepared did not include information on smoking status, frequency and duration.

CONCLUSION

In conclusion, since we are in a period of accelerating industrialization, it is clear that occupational exposure to cadmium will increase even more. According to our results, although there has been a significant decrease in cadmium-related mortality worldwide over the years, the mortality rate is still high. Cadmium exposure needs to be taken seriously. It is very important for all employees to be subject to health surveillance at work, to take preventive measures and to have periodic health checks. There are very few studies examining deaths due to bronchial, tracheal and lung cancer due to cadmium exposure. Therefore, we believe that this study will be a source of inspiration for other researchers.

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