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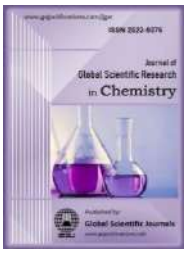

Study Into How Heavy Metal Exposure Increases The Chance Of Developing Lung Cancer

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ABSTRACT

Heavy metals (HMs) are elements with a high atomic number, whose entry through natural and human activities causes pollution of water, soil, and air sources. HMs can increase Physical problems, concerns about its effects on health and the environment. The aim of this study was to investigate an increased risk of lung cancer due to exposure to heavy metals. In this narrative review study, the first literature search was performed with three hundred and seventy articles were retrieved based on PubMed, Elsevier, Web of science, Spring, and Google Scholar databases from 1989 to 2022. In this study, according to databases 370 articles were retrieved. In final stage literature, there is a notable lung cancer because of exposure to heavy metals. 22 papers based on abstract and article text filtered. In the next stage, 17 studies were screened after review and 13 full-text articles entered into the analysis process. Finally, 10 articles were selected in this study. **Result** this study showed that the toxicity of heavy metals depends on the chemical properties, dose, and route of exposure to the substances, as well as the age, gender, and nutritional status of the exposed people. It depends on pollutants and genetics. Heavy metals can accumulate in body organs, and lower levels of these metals also act as systemic poisons and cause multiple damages to different tissues of the body. One of the most important effects and disorders of heavy metals can be the effect on the central and peripheral nervous system, the effect on the skin, the effect on the hematopoietic system, the effect on the cardiovascular system, damage to the kidneys, and accumulation in the tissues, and carcinogenesis.

1. Introduction

Heavy metals are one of the phrases that is known all over the world as one of the important processes that threaten human health (1, 2). The smoke caused by smoking, drinking water containing heavy metals, forest fires, indoor air pollution and food contaminated with heavy metals have become fundamental issues today (3, 4). The number of risks to human health is increasing day by day (5, 6). One of the main concerns is the presence of heavy metals and other trace elements in tobacco smoke, which can be transmitted through smoke and condensation from smoke. Lead, arsenic, chromium, nickel, and cadmium are usually associated with adverse effects on human health (7). The filters in cigarettes have removed these elements to some

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extent. The environmental pollution caused by cigarettes is caused by exhaled smoke and environmental smoke iscaused by cigarettes (8). The environmental smoke caused by cigarettes can have a high concentration of heavy metals that can cause thedeposition of high concentrations of heavy metals in the depth of lung tissue (9, 10). Lead and cadmium elements with a long half-life (10 to 12 years) accumulate in body tissues and fluids. Biomonitoring studies have shown that non-smokers have lower levels of lead and cadmium in their bodies than smokers(11). It should be mentioned in these studies that the bioaccumulation of heavy metals has been shown due to the exposure of smokers (12). Heavy metals such as lead are involved effective in various biochemical processes in the human body, including the activation of cell death pathways and calcium metabolism that play a role in carcinogenesis (13, 14). Among many people in developing countries use biomass fuels such as wood and coal to provide household energy, and these materials are often used in simple gas stoves, which causes an incomplete combustion process (13, 15, 16). As a result, residents of houses, including women and children, are daily exposed to a high concentration of indoor air pollution (17). Carbon monoxide, nitrogen oxides, sulfur oxides, polycyclic organic substances, including benzopyrene, formaldehyde, and particles, including indoor air pollutants (18). The particles in indoor air pollution include PM_{10} and $PM_{2.5}$ particles, which penetrate deep into the lungs and cause damage to this sensitive organ (19, 20). It shows the acute respiratory disease caused by indoor air pollution, which is the most important cause of death of preschool children in developing countries (17, 21, 22). Also, the increase in infant and perinatal mortality, pulmonary tuberculosis, low birth weight, cancer, cataracts, lung, nasopharynx, and larynx cancer is caused by biomass smoke, especially coal (23, 24). Climate change causes an increase in the growth rate, tree movements, changes in forest species collections, an increase in the occurrence of fires, an increase in storm damage, an increase in insects, and an increase in severe drought (25, 26). Pathogenic factors In addition to increasing temperature, several climatic and non-climatic factors play a role in determining the frequency of fire, including sources of ignition, characteristics of vegetation, humidity, wind, topography, fuel load, and policies (27, 28). At present, research on the effects of forest fire smoke on health is limited. Smoke from fires contains particles and polycyclic aromatic hydrocarbons, which are polycyclic aromatic hydrocarbons(29, 30). Result different study reported that can contain substances such as benzopyrenes, which are carcinogenic (30, 31). The aim of this study was to investigation of the increased risk of lung cancer due to exposure to heavy metals.

2. Evidence Acquisition

2.1. Eligibility criteria and search strategy

In this narrative review study, the first literature search was performed with three hundred and seventy articles retrieved based on PubMed, Science Direct, Web of Science, Springer, and Google Scholar databases. English language was used for a review of the epidemiological literature. Identify all relevant studies published 1989-2022. In the final stage of literature, there is a notable health effect (increased risk of lung cancer) because of exposure to heavy metals. The query results according to different databases showed in Table 1.

Table 1: Search terms and query results.

Term	*Science Direct*	*Google Scholar*	*Springer*	*Web of Science*	*PubMed*	*Unique results*
Lung Cancer	**27**	**36**	**12**	**7**	**10**	**92**
Risk Assessment	**19**	**18**	**10**	**4**	**8**	**59**
Heavy Mental	**21**	**9**	**6**	**11**	**10**	**57**
Carcinogenic	**9**	**36**	**5**	**21**	**4**	**75**
Air Pollutants	**10**	**32**	**23**	**16**	**6**	**87**
Total	**86**	**131**	**56**	**59**	**38**	**370**

2.2. Eligibility criteria

'Lung Cancer', 'Risk Assessment', 'Heavy Mental', 'Carcinogenic', and 'Air Pollutants' were used as in this study Medical Subject Heading (MeSH). In this narrative review study the time search of studies limited in the range of 1989 to 2022. According reported different center of health exposure to heavy metals can increased risk of lung cancer. PubMed, Elsevier, Web of science, Spring, and Google Scholar were databases used to for searched in our study. According to studies published in journals and searches including articles in PubMed database 38 articles, Science Direct received 86 articles, Web of Sciences database 59 articles, springer database 56 articles and 131 articles in the Google Scholar search engine.

2.3. Study selection

According to the criteria mentioned above, after an initial screening of the 370 titles publications. 22 papers based on abstract and article text filtered. In the next stage, 17 studies were screened after review and 13 full-text articles entered into the analysis process. Deletion of 6 articles and deletion of 3 articles during the secondary studies, finally 10 articles entered the analysis process. Identify all relevant studies published 1989-2022. The how to prepare studies and the selection process articles based on PRISMA flow diagram showed in **Figure 1**.

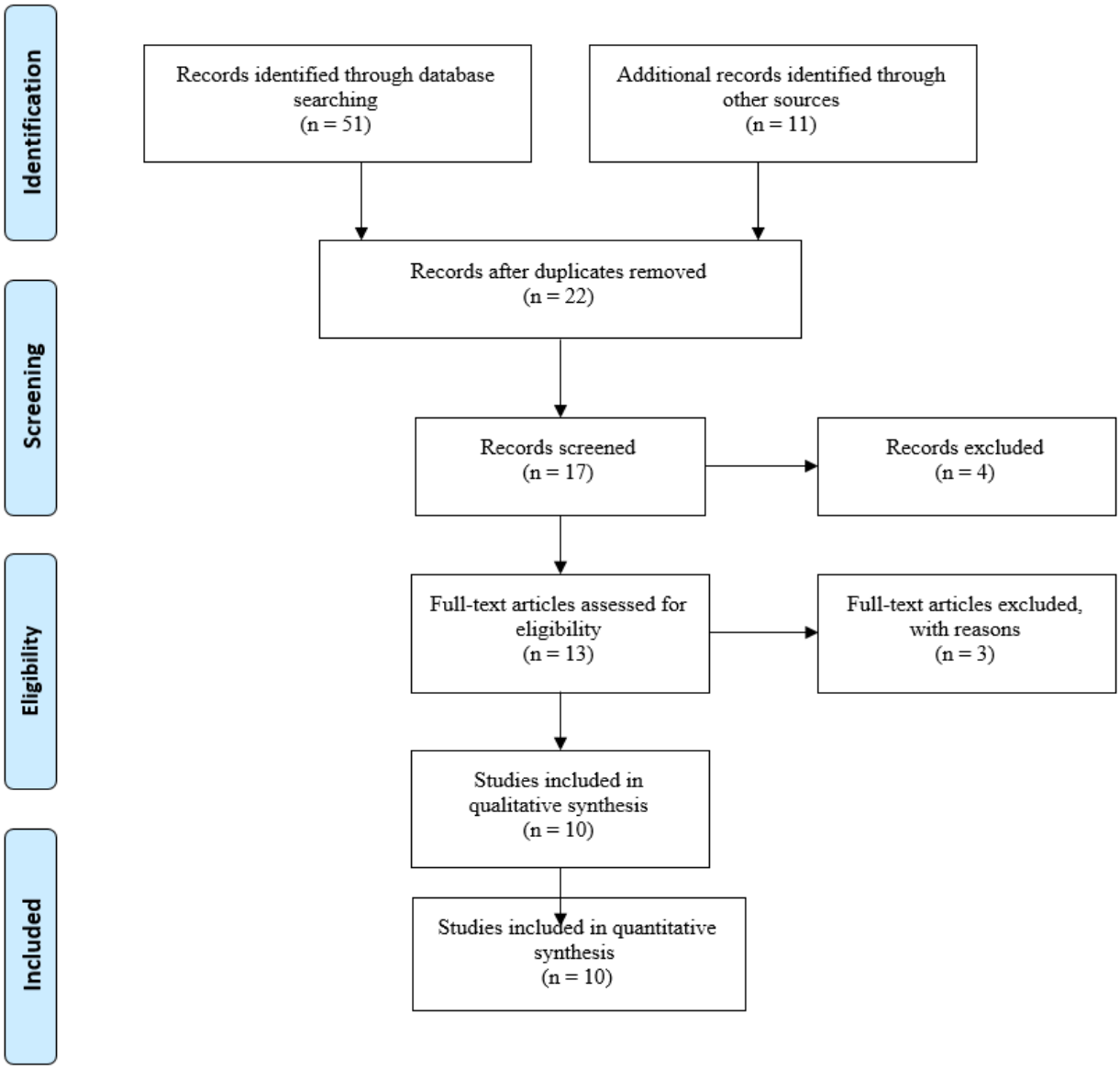

Figure 1: Representation of the search strategy based on PRISMA flow diagram

2.4. Extraction of the data

Data from selected publications were extracted and documented in the EXCEL spreadsheet.

2.5. Ethical approval

According to the national guidelines, studies such as this do not require individual consent.

3. Results and Discussion

3.1. Sources of heavy metals in the environment

During recent decades, especially in industrialized societies various pollutants enter the environment. One of these pollutants, which has become a global problem, is heavy metals (32). Heavy metals are considered stable and long-lasting environmental pollutants, because they cannot be decomposed through chemical or biological processes in nature like organic pollutants (33, 34). These metals in small amounts are naturally necessary for the body and the environment, but in higher concentrations brought into the environment by human activities, they bring many environmental risks (32, 35). Sources resulting from human activities that mainly cause the entry of heavy metals into the environment are: metal mining, agricultural industries, metallurgical industries, electronic industries, battery manufacturing and industrial effluents (36). The complications and disorders they cause can be seen in all organs and various factors, including the type of metal, are involved in them. Among their most important disorders and complications, we can mention carcinogenesis, effect on the central and peripheral nervous system, effect on the skin, effect on the hematopoietic system, effect on the cardiovascular system, damage to the kidneys, and accumulation in the tissues (37). **Figure 2** showed the Sources of heavy metals in the environment.

Figure 2: Sources of heavy metals in the environment

3.2. Investigating the effects of heavy elements on human health

Cadmium:

Cadmium is found in a large number of electronic compounds, phosphate fertilizers, pigments and alloys, and pure refined petroleum products (38). Also, cadmium can cause lung cancer and obstruction in people with kidney transplants (39)(40). Trace metals can also cause osteoporosis in smokers (41).

Chromium:

Chromium is found in large amounts in aquatic environments (42). Low levels of chromium can cause ulcers and skin irritation, but high amounts of chromium can cause damage to the nervous system, kidneys, and liver of humans (43).

Copper:

Copper is naturally present in the piping system, which is added to storage tanks to control the growth of algae. Copper is one of the essential elements for human life in such a way that its deficiency causes anemia, kidney, liver, stomach, and intestinal disorders(44) (45).

Arsenic:

Arsenic is used in tanning, textile industries, dyeing, detergents, and laundry detergents. It is also found in small amounts in herbicides, insecticides, and fungicides(46). Consumption of drinking water containing arsenic can cause cancer and long-term skin damage. The duration and blood pressure will increase(47).

Lead:

Lead can enter through air, soil, water, and dust. Children are usually more sensitive to lead than adults(48). High levels of lead in the human body can cause biological effects, including hemoglobin synthesis, effects on the stomach, He has kidney, and intestine, nerve damage, joints, and reproductive system(49).

Mercury:

The main source of mercury in the environment includes volcanoes, industrial processes, and diagenesis in the earth's crust. It is also used in the pharmaceutical and dental industries(50). Mercury is a poison that can cause inflammation of the gums and psychological effects due to its effect on the central nervous system(51).

Nickel:

Nickel can accumulate in water environments. Low amounts of nickel are needed for red blood cells, and moderate amounts can cause mild poisoning, and high amounts can cause skin irritation, weight loss, and kidney and liver damage(52).

Selenium:

Selenium can be accumulated in the tissues of the body and cause an increase in volume and problems such as damage to the central nervous system, damage to the kidney and liver, thinning of hair, and loosening of nails(53). Small amounts of selenium are necessary for the human body. Too much of it can cause fatigue and damage to the central nervous system(54).

3.3. Effects of heavy metals on the human body

High amounts of heavy metals in the body can accumulate in bones, brain, kidneys, and liver and disrupt their function. Heavy metals are carcinogenic and affect the body's ability to produce red and white cells (4). Every heavy metal affects a part or parts of the body. Some heavy metals are more toxic or even some forms of heavy metals are more dangerous than other forms (55). For example, exposure to an inorganic compound of heavy metal will have different effects compared to its organic form. The age group that bears the greatest risk of exposure to heavy metals are fetuses and children, and small amounts of heavy metals in fetuses and children can reduce their mental and physical development and damage their brains and organs. to be Heavy metals can be transferred directly from the mother to the fetus, and some can enter the baby's body through breast milk. **Figure 3** showed the effects of heavy metals on the fetus and children.

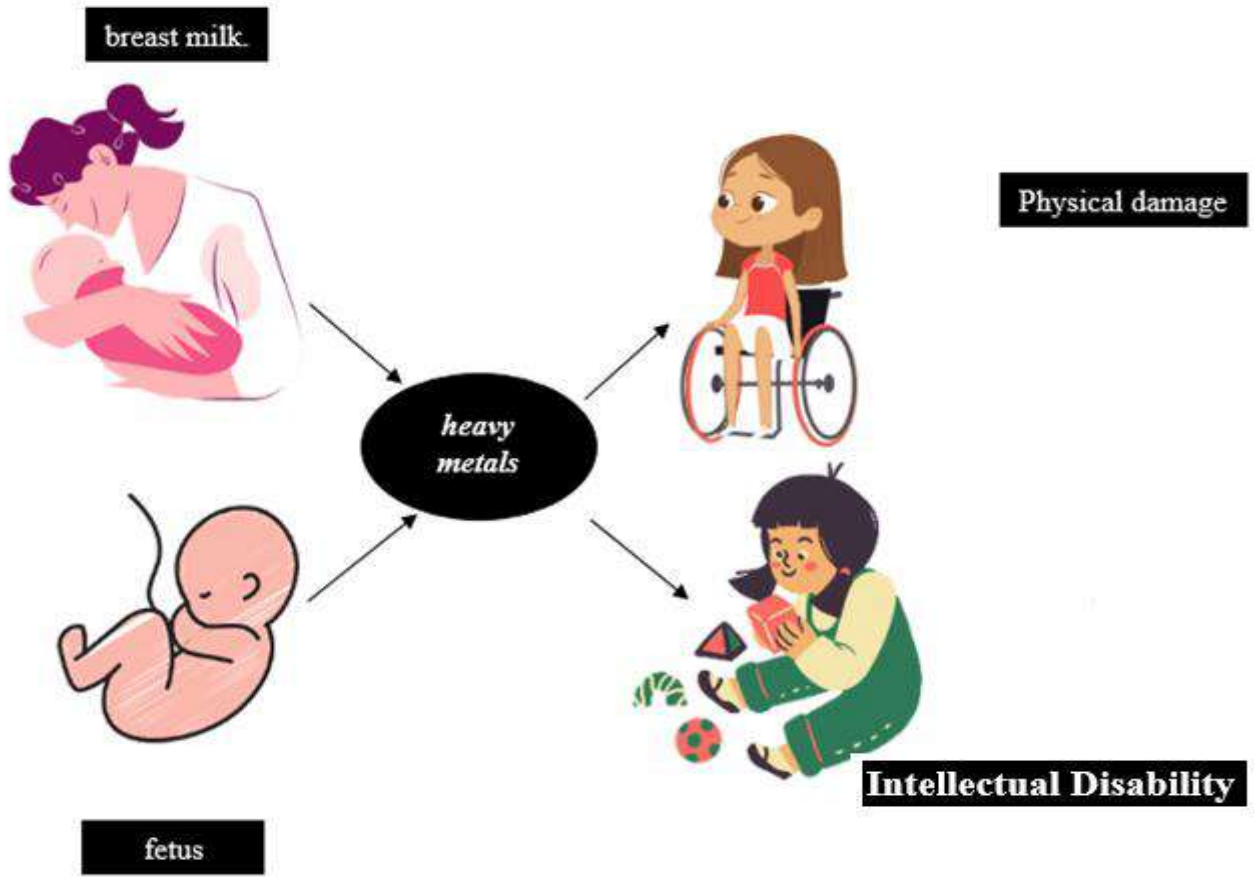

Figure 3: Effects of heavy metals on the fetus and children

3.4. Carcinogenic effects of heavy metals

Air quality is one of the most important issues related to people's health and the environment(56). In such a way low air quality can be a great risk to the health of people and the environment, and also causes the spread of lung, cardiovascular and respiratory cancers(57). Suspended particles include PM_{10} and $PM_{2.5}$ particles, PM_{10} particles are considered one of the most important air pollutants, whose excessive concentration or long-term exposure can have severe toxic effects on humans and the environment(58). The sources of production of PM_{10} particles include natural and artificial phenomena, which include the combustion of fossil fuels, the emission of greenhouse gases from vehicles, the known industrial activities of energy production, and the natural phenomena can be mentioned heavy metals are not metabolized and accumulate in organs and tissues such as bones, joints, muscles and fat and cause various diseases from These to include Alzheimer's and various types of cancer (59, 60).

Evaluation of long-term exposure to heavy metals includes carcinogenicity, mutagenicity and genotoxicity. Standard genotoxicity tests consist of bacterial gene mutation assays (the Ames test) of a mutation in laboratory mammals or chromosome damage assays (61). Carcinogenic potential in animals and extrapolation of cancer risk to humans can be performed using a 2-year chronic bioassay in a rodent model. Many "hot spot" mutations in the p53 gene are not associated with single carcinogens, but may reflect the effects of multiple genotoxic agents and should be suitable for bioregulatory mixtures (62). Other mutations are associated with oxidative stress and thus may reflect intracellular oxidative stress caused by xenobiotics or viruses (63). Possible carcinogens include non-genotoxic carcinogens. Cell transformation assays are based on the examination of phenotypic changes (morphology, colony-forming ability, or growth rate) (64). The last of these, the gap junction intercellular communication method, is based on the disruption of intercellular exchange between molecules of molecular weight less than It is

through gap junctions of adjacent cells that leads to abnormal cell growth. These assays include practical techniques for screening non-genotoxic carcinogens and tumor promoters, but need to be standardized and validated (65). The effects of heavy metals in increased lung cancer express in Figure 4.

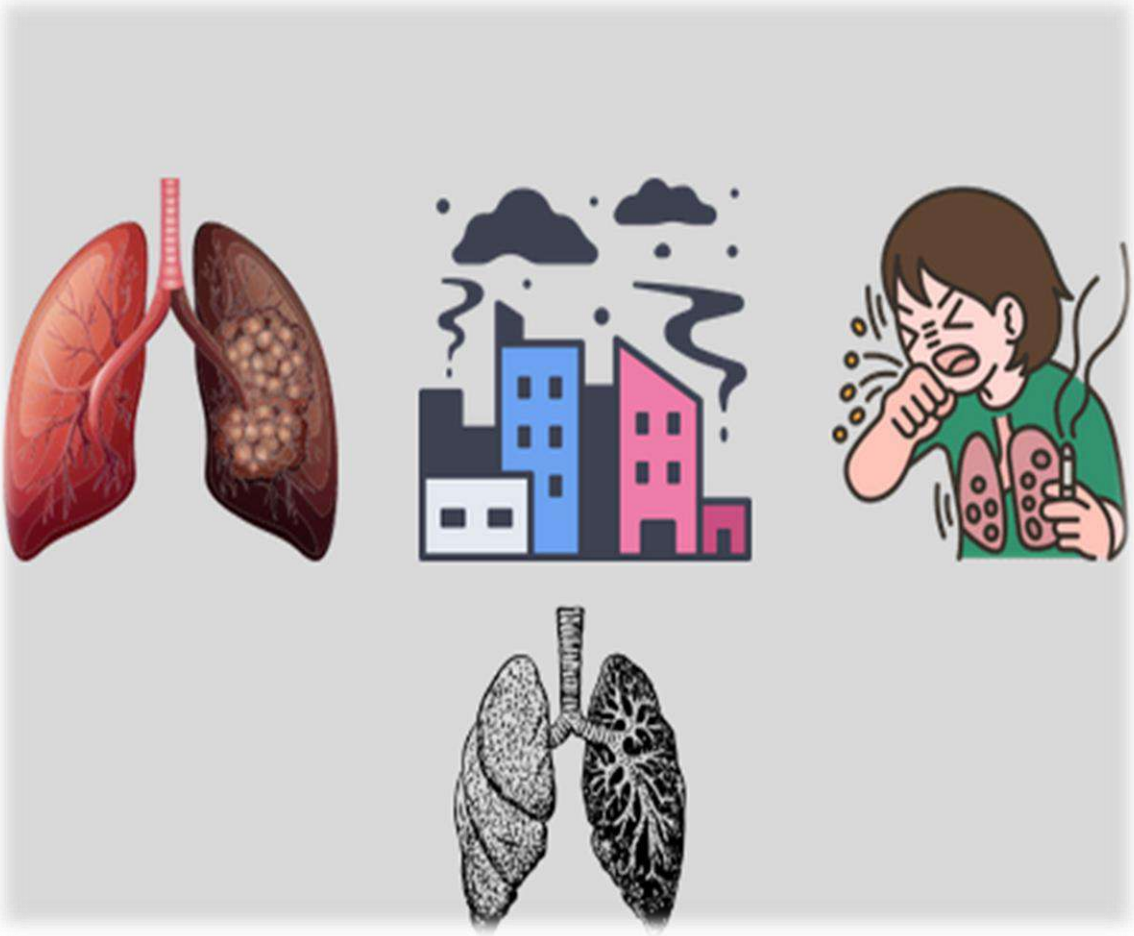

Figure 4: Effects of heavy metals in increased lung cancer

4. Conclusion

According result of in this study, exposure to heavy metals can causes different cancers and especially increased risk of lung cancer. Result of different studies have shown that exposure to pollutants due to the entry of heavy metals into the food cycle and its entry into the body through inhalation, eating contaminated food, and drinking contaminated water can have many dangerous effects on human health, including increasing the incidence of cancer, especially having anabortion, lung cancer, respiratory problems, and liver cancer.

Calculates epidemiological studies to estimate all of the possibilities, angles, and factors that affect how carcinogenicity indices were calculated negative effects due to pollutants on human, animal, and environmental health. It be should noted that the main activities that suggested for decrease health endpoint including reducing fossil fuels especially diesel fuel and using more gas in industries, reducing the use of private cars, developing the public transport fleet, using more hybrid and electric cars, increasing the green space per capita in cities, preventing the change of use of forest lands and cutting trees, the use of new equipment and technologies, reducing the consumption of agricultural pesticides, increasing public awareness of the dangerous effects of heavy metals, the use of organic materials and ultimately reducing the release of pollutants, especially

heavy metals, into the environment (water, soil and air).

5. Declarations

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Authors Contributions

All authors contributed to the design and data analysis and assisted in the preparation of the final version of the manuscript. All authors read and approved the final version of the manuscript.

Informed consent:

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Ethical approval

The conducted research is not related to either human or animal use

Disclosure statement

No potential conflict of interest was reported by the authors.

Consent to Participate

'Not applicable' for that specific section.

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