

Meta Analysis the Effects of Asbestos and Silica Dust on the Risk of Lung Cancer among Workers

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ABSTRACT

Background: Lung cancer is a cancer whose incidence increases every year and is the number one cancer cause of death in the world. One of the causes of lung cancer comes from occupational exposure in the form of asbestos dust and silica. This study aims to analyze the effect of exposure to asbestos and silica dust on the incidence of lung cancer in the working community.

Subjects and Method: This study is a meta-analysis with the following PICO, population: working society. Intervention: exposure to asbestos dust and silica dust. Comparison: not exposed to asbestos dust and silica dust. Result: lung cancer. The articles used in this study were obtained from three databases, namely Google Scholar, Pubmed, and Science Direct. The keywords to search for articles were “dust exposure” OR “silica dust exposure” OR “asbestos dust exposure” OR “occupational dust exposure” AND “lung cancer”. The articles included are full-text English with a case-control study design from 2007 to 2022. The articles were selected using PRISMA flow diagrams. Articles were analyzed using the Review Manager 5.3 application.

Results: A total of 14 case-control studies from continental Europe, America and Asia were selected for systematic review and meta-analysis. Based on 8 studies on the effect of exposure to asbestos dust on the incidence of lung cancer, the incidence of lung cancer increased 1.57 times compared to workers who were not exposed to asbestos dust (aOR= 1.57; 95% CI= 1.20 to 2.06; p= 0.001) and 9 case-control studies on the effect of exposure to silica dust showed an increase of 1.31 times the incidence of lung cancer compared to workers who were not exposed to silica dust (aOR = 1.31; 95% CI = 1.25 to 1.38; p<0.001).

Conclusion: Exposure to asbestos and silica dust increases the incidence of lung cancer in workers.

Keywords: asbestos, silica, occupational dust exposure, lung cancer.

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BACKGROUND

Lung cancer is the leading cause of cancer death worldwide, and its incidence has been increasing over the past three decades. According to the latest GLOBOCAN 2020 data, an estimated 2.2 million new cancer

cases and 1.8 million deaths, lung cancer is the second most common diagnosed cancer and the leading cause of cancer death in 2020, representing approximately one in 10 (11.4%) diagnosed cancers. and one in five die (18.0%) (Sung et al., 2021).

Lung cancer is the most frequently diagnosed malignancy 2.1 million new cases or equivalent to 11.6% of the total incidence of cancer cases in 2018 with a standard incidence rate of 22.5 years (31.5 years in men, 14.6 years in women) per 100,000 person-years worldwide in 2018. Furthermore, lung cancer was ranked first and accounted for 18.4% of total cancer deaths (equivalent to 1.8 million deaths) in 2018, with a standard age mortality rate of 18.6 (27.1 years in men and 11.2 years in women) per 100,000 people (Lin et al., 2020).

In 90% of diagnosed cases, lung cancer is associated with the consumption of tobacco derivatives. Genetic susceptibility and comorbidities also contribute to disease progression. In addition, carcinogenesis is a complex process involving the participation of hereditary and environmental risk factors, such as food, smoking, occupation and exposure to radiation and chemical agents in the environment. Carcinogen concentrations are almost always higher in the work environment than in extra work environments. According to an assessment carried out by the International Labor Organization (ILO), approximately 440,000 people died worldwide in 2005 as a result of exposure to hazardous substances in the workplace. More than 70% of them, i.e. around 315,000 people, died of work-related cancers (Gaúcha et al., 2020).

Across Europe there has been a major shift in the main source of occupational exposure to respiratory hazards, from high exposure to mineral dusts in the early 20th century in large industrial concentrations (such as coal and silica dust in the mining and metal production sectors) to low dose allergens (e.g. flour and enzymes in bakery and food processing industries) and current irritants (e.g. cleaning agents) (de Matteis et al., 2017).

The most common risk factors for lung cancer include lifestyle, environment, and occupational exposure. Asbestos exposure is one of the most recognized occupational causes of lung cancer. Workers in asbestos mining and milling, shipbuilding, construction, textiles and insulation, and auto repair are at the highest risk (Barta et al., 2019). Other occupations with an increased incidence of lung cancer include coal mining, asphalt paving with exposure to coal tar, chimney sweeping, and painting although the risk appears to be lower than asbestos and diesel exhaust (Christian et al., 2011; Guha et al., 2010; Hogstedt et al., 2013; Olsson et al., 2010). Exposure to other organics and metals that has been linked to lung cancer includes beryllium, cadmium, chromium, silica, formaldehyde, benzo[a]pyrene, nickel, hard metal dust, and vinyl chloride (De matteis et al., 2012; Guha et al., 2010; Vida et al., 2010).

With respect to occupational respiratory disease malignancies, asbestos-related diseases (especially malignant pleural mesothelioma and lung cancer) still represent a large part of the occupational cancer burden and are the leading cause of and increasing occupational respiratory disease deaths in Europe and the world (Takala, 2015). It is estimated that the asbestos-related cancer burden will peak in 2020-2030 in most European countries, depending on local asbestos extraction and use patterns (de Matteis et al., 2017).

A recent analysis of the case-control study on lung cancer, the SYNERGY Project, which uses more than 100,000 quantitative exposure measures, shows that exposure estimates are still high but that there has been a downward trend in exposure from the 1970s onwards (Peters et al., 2016). However, for some carcinogens, such as crystalline silica, exposure is known to be a major problem in certain industrial

sectors such as the construction industry (de Matteis et al., 2017; Van Deurssen et al., 2015).

The IARC considers that exposure to arsenic, inorganic arsenic compounds, beryllium, beryllium, cadmium, chromium-VI compounds, nickel compounds, asbestos (chrysotile, crocidolite, amosite, tremolite, actinolite and amphibole) and crystalline silica dust is associated with lung cancer (Rogado et al., 2020).

SUBJECTS AND METHOD

1. Study Design

This research is a systematic research and meta-analysis. The articles used in this study were obtained from several databases, namely Google Scholar, PubMed, and Science Direct between 2007 and 2021. The selection of articles was carried out using the PRISMA flow chart. The keywords to search for articles are as follows “dust exposure” OR “silica dust exposure” OR “asbestos dust exposure” OR “occupational dust exposure” AND “lung cancer”.

2. Inclusion Criteria

The inclusion criteria in this research article were: full-text article with case-control design, research subjects were workers exposed to asbestos and silica dust, research results were lung cancer, non-smokers, multivariate analysis with adjusted Odds Ratio (aOR) to measure the predicted effect.

3. Exclusion Criteria

The exclusion criteria in this research article were: articles published in languages other than English, statistical results reported in the form of bivariate analysis, articles before 2007.

4. Operational Definition of Variables

The search for articles was carried out by considering the eligibility criteria determined using the PICO model. Population:

working society. Intervention: exposure to asbestos and silica dust. Comparison: not exposed to asbestos and silica dust. Result: lung cancer.

Exposure to Asbestos and Silica Dust are asbestos and silica dust particles that are inhaled by workers at their work sites as long as the worker is working in the production process/work with a long exposure of 8 hours/day or a minimum working period of 5 years.

Lung cancer, all malignancies in the lung, includes malignancies originating from the lungs themselves (primary). In a clinical sense, primary lung cancer is a malignant tumor originating from the bronchial epithelium (bronchial carcinoma = bronchogenic carcinoma).

5. Study Instruments

This research study is guided by the PRISMA diagram and article quality assessment using the Critical Appraisal Skills Program (CASP, 2018).

6. Data Analysis

The data in the study were analyzed using the Review Manager application (RevMan 5.3). Forest plots and funnel plots were used to determine the size of the relationship and heterogeneity of the data. The fixed effects model was used for homogeneous data, while the random effects model was used for heterogeneous data across studies.

RESULTS

The article search process is carried out through several journal databases, including Google Scholar, PubMed, and Science Direct. The review process for related articles can be seen in the PRISMA flow chart in figure 1. Research related to exposure to asbestos and silica dust on the incidence of lung cancer consists of 14 articles from the initial search process yielding 1,535 articles, after the deletion

process was published articles with 54 requirements for full-text review more carry on. A total of 14 articles that met the quality assessment were included in the quantitative synthesis using a meta-analysis.

It can be seen in Figure 2 that the research articles come from three continents, namely Europe (Italy and England), Asia (Indonesia, Hong Kong and South Korea) and North America (Canada). Table 1, researchers conducted an assessment of the quality of research.

Critical Assessment for case control studies. Case-Control Study Checklist published by CASP (Critical Appraisal Skills Program):

- a. Does the case-control study clearly address the clinical problem?
- b. Did the researcher use the correct method to answer the research question?
- c. Was the case selected in the right way?
- d. Were the controls selected the right way?

- e. Is exposure measured accurately (correctly) to prevent/minimize bias?
- f. Apart from the exposure under study, has the researcher taken into account the influence of all potential confounding factors in this study?
- g. Has the researcher controlled for the influence of all potential confounding factors in the design and/or analysis of the data?
- h. How big is the exposure effect?
- i. How precise is the estimation of the exposure effect?
- j. Are the results reliable?
- k. Are the results applicable to the local (local) population?
- l. Are the results of this study compatible with other available evidence?

After assessing the quality of the study, 14 articles were divided into 2 categories according to the independent variables included in the quantitative synthesis meta-analysis using Rev-Man 5.3.

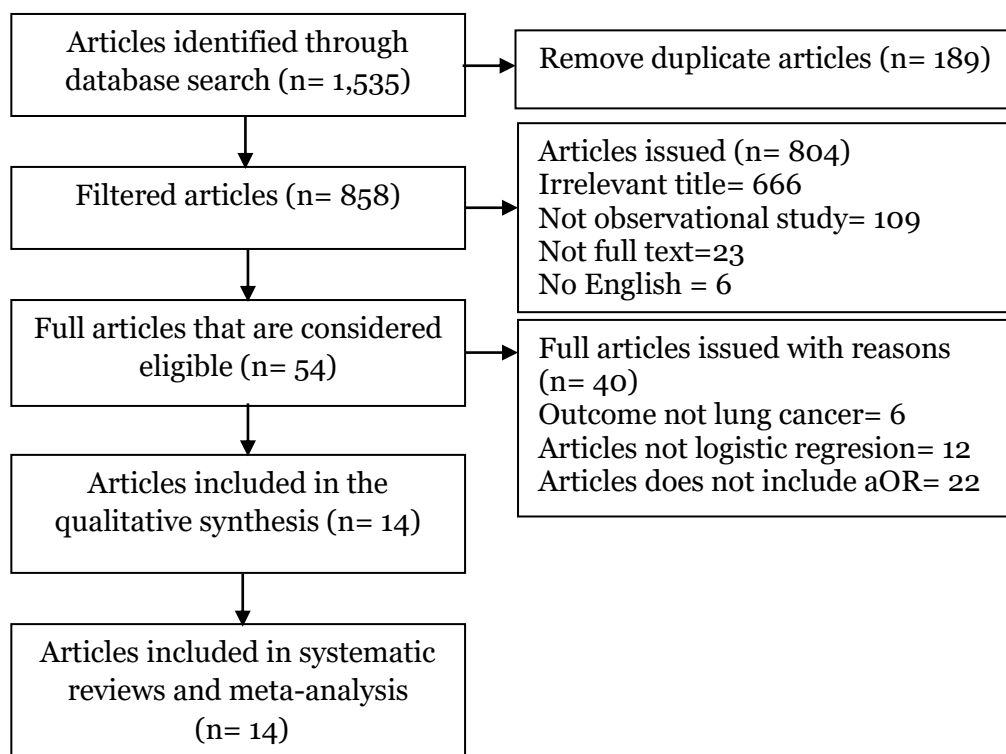


Figure 1. PRISMA Flowchart



Figure 2. Map of the study area of asbestos dust and silica dust exposure with lung cancer

Table 1. Results of Case-Control Study Quality Assessment Effect of Exposure to Asbestos and Silica Dust on Lung Cancer

Author (Year)	Criteria												Total
	1	2	3	4	5	6	7	8	9	10	11	12	
Carel et al. (2017)	2	2	2	2	2	2	2	2	1	2	2	2	23
Consonni et al. (2010)	2	2	2	2	2	2	2	2	2	2	2	2	24
Consonni et al. (2012)	2	2	1	2	2	2	2	2	2	2	2	2	23
De Matteis et al. (2012)	2	2	2	2	2	2	2	2	2	2	2	2	24
Ge et al. (2020)	2	2	2	2	2	2	2	2	2	2	2	2	24
Kachuri et al. (2014)	2	2	2	2	2	2	2	2	2	2	2	2	24
Lacourt et al. (2015)	2	2	2	2	2	2	2	2	2	2	2	2	24
Suraya et al. (2020)	2	2	2	2	2	2	2	2	2	2	2	2	24
Suraya et al. (2021)	2	2	1	2	2	2	2	2	2	1	2	2	22
Villeneuve et al. (2012)	2	2	2	2	2	2	2	2	2	2	2	2	24
Huh et al. (2021)	2	2	2	2	2	2	2	2	2	2	2	2	24
Tse et al. (2011)	2	2	2	2	2	2	2	2	2	2	2	2	24
Tse et al. (2012)	2	2	2	2	2	2	2	2	2	2	2	2	24
Vida et al. (2010)	2	2	2	2	2	2	2	2	2	2	2	2	24

Note: 2: Yes; 1: Can't tell; 0: No

Table 2. Description of the Primary Study

Author (Year)	Country	Study Design	Sample	Population	Intervention	Comparison	Outcome	aOR (CI 95%)
Carel et al. (2007)	Hungarian, English, Russian, Slovak, Polish, Roman	Case control	2,205 cases and 2305 controls	industrial worker	Exposure to asbestos dust	Not exposed to asbestos dust	Lung cancer	1.85 (1.07 to 3.21)
Consonni et al. (2010)	Italy	Case control	2,100 cases and 2,120 controls	Mining and quarry workers	Exposure to dust asbestos, arsenic, uranium, zinc, cadmium, aluminum, nickel, chromates, beryllium	Not exposed to asbestos dust	Lung cancer	0.93 (0.22 to 3.89)
De Matteis et al. (2012)	Italy	Case control	2,100 cases and 2,120 controls	Construction worker		Not exposed to asbestos dust	Lung cancer	1.76 (1.42 to 2.18)
Villeneuve et al. (2012)	Canada	Case control	1,681 cases and 2,053 controls	Mechanical workers, repairmen, plumbers, and construction worker	Exposure to asbestos dust, silica, Ni-Cr, PAH, DME	Not exposed to asbestos dust	Lung cancer	1.28 (1.02 to 1.61)
Huh et al. (2021)	South Korea	Case control	179 cases and 21,832 controls	construction worker	Exposure to asbestos dust	Not exposed to asbestos dust	Lung cancer	3.08 (1.86 to 5.11)
Suraya et al. (2020)	Indonesia	Case control	336 cases and 360 controls	Mining, industrial and loading and unloading workers	Exposure to asbestos dust	Not exposed to asbestos dust	Lung cancer	2.04 (1.21 to 3.42)
Tse et al. (2011)	Hong Kong	Case control	132 cases and 536 controls	Construction and manufacturing workers	Exposure to asbestos dust	Not exposed to asbestos dust	Lung cancer	0.99 (0.30 to 3.32)
Tse et al. (2012)	Hong Kong	Case control	1,208 cases and 1,069 controls	Construction worker	Exposure to asbestos dust, silica, wood dust, welding fume, chromium, textile dust	Not exposed to asbestos dust	Lung cancer	0.86 (0.55 to 1.36)

Table 3. Description of primary studies included in the meta-analysis of silica dust exposure on lung cancer incidence

Author (Year)	Country	Study Design	Sample	Population	Intervention	Comparison	Outcome	aOR (95%CI)
Consonni et al. (2012)	Italy	Case control	2,100 cases 2,120 controls	New handyman	Exposure to silica dust	Not exposed to silica dust	Lung cancer	1.57 (1.12 to 2.21)
De Matteis et al. (2012)	Italy	Case control	2,100 cases and 2,120 controls	Construction worker	Exposure to silica dust, asbestos, Ni-Cr, PAHs, DME	Not exposed to silica dust	Lung cancer	1.31 (1.00 to 1.71)
Ge et al. (2020)	Canada	Case control	11,978 cases, 16,477 controls	Construction workers, masons	Exposure to silica dust	Not exposed to silica dust	Lung cancer	1.30 (1.23 to 1.38)
Tse et al. (2011)	Hong Kong	Case control	132 cases and 536 controls	Manufacturing, construction workers	Exposure to silica dust, asbestos, wood dust, welding fume, chromium, textile dust	Not exposed to silica dust	Lung cancer	3.09 (1.30 to 7.37)
Tse et al. (2012)	Hong Kong	Case control	1,208 cases and 1,069 controls	Construction worker	Exposure to silica dust, asbestos, wood dust, welding fume, chromium, textile dust	Not exposed to silica dust	Lung cancer	1.75 (1.16 to 2.62)
Kachuri et al. (2014)	Canada	Case control	1,681 cases, 2052 controls	Metal processing workers, mining, quarrying, construction	Exposure to silica dust, asbestos, wood dust, welding fume, chromium, textile dust	Not exposed to silica dust	Lung cancer	1.20 (1.00 to 1.43)
Lacourt et al. (2015)	Canada	Case control	1,593 cases and 1,427 controls	Construction worker	Exposure to silica dust	Not exposed to silica dust	Lung cancer	1.20 (0.9 to 1.5)
Suraya et al. (2021)	Indonesia	Case control	340 cases and 370 controls	Construction worker	Exposure to silica dust, asbestos, wood, rock dust	Not exposed to silica dust	Lung cancer	1.90 (1.03 to 3.40)
Vida et al. (2010)	Canada	Case control	857 cases and 1,349 controls	Mining workers and masons	Exposure to silica dust, asbestos, welding fume	Not exposed to silica dust	Lung cancer	1.56 (1.09 to 2.25)

1. Exposure to Asbestos Dust on Lung Cancer

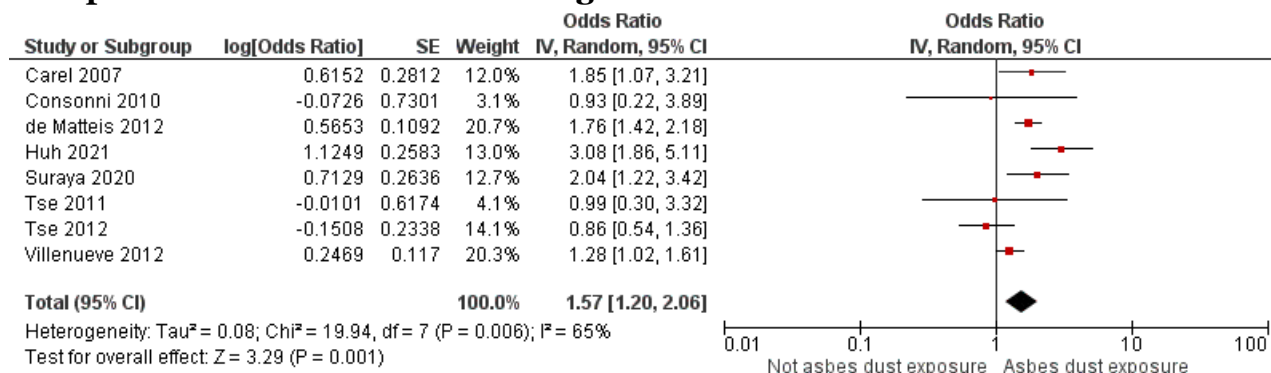


Figure 3. Forest Plot of Asbestos Dust Exposure to Lung Cancer Cases

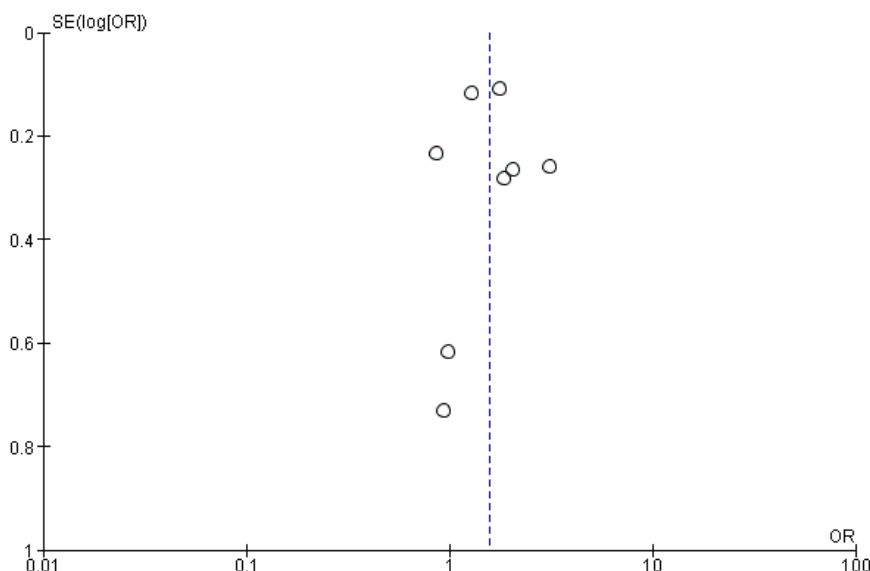


Figure 4. Funnel Plot of Asbestos Dust Exposure to Lung Cancer Cases

a. Forest plot

Based on the results of the forest plot (Figure 3), workers who were exposed to asbestos dust had a 1.57 times risk of developing lung cancer compared to workers who were not exposed to asbestos dust, and the results were statistically significant (aOR= 1.57; 95% CI= 1.20 to 2.06; p= 0.001). The heterogeneity of the research data shows I²= 65% so that the distribution of the data is declared heterogeneous (random effect model).

b. Funnel plot

The funnel plot in Figure 4 shows no publication bias as indicated by a symmetric distribution between the right and left plots. There are 4 plots on the right and 4 plots on the left. The plot on the right of the graph appears to have a standard error (SE) between 0 and 0.40. The plot on the left of the graph appears to have a standard error (SE) between 0 and 0.80.

2. Exposure of Silica Dust to Lung Cancer

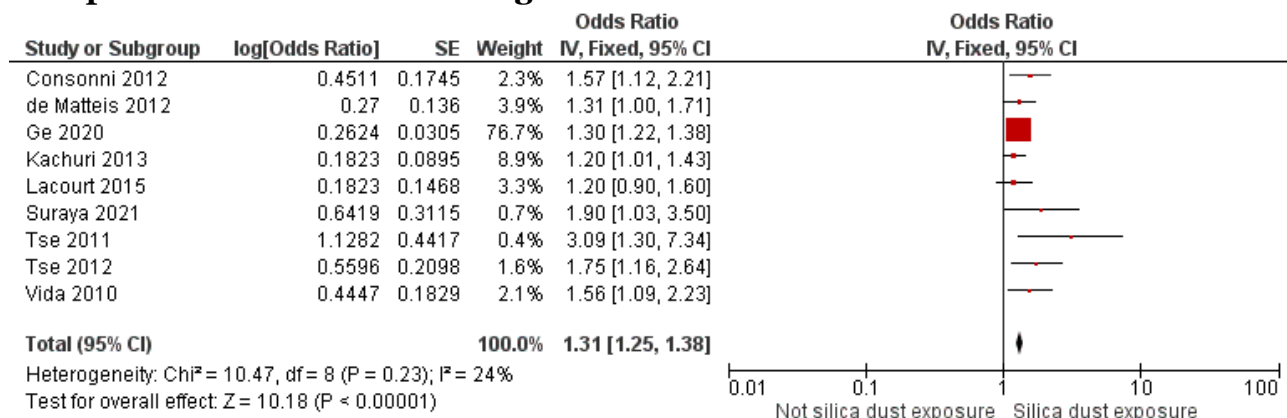


Figure 5. Forest Plot of Silica Dust Exposure to Lung Cancer Cases

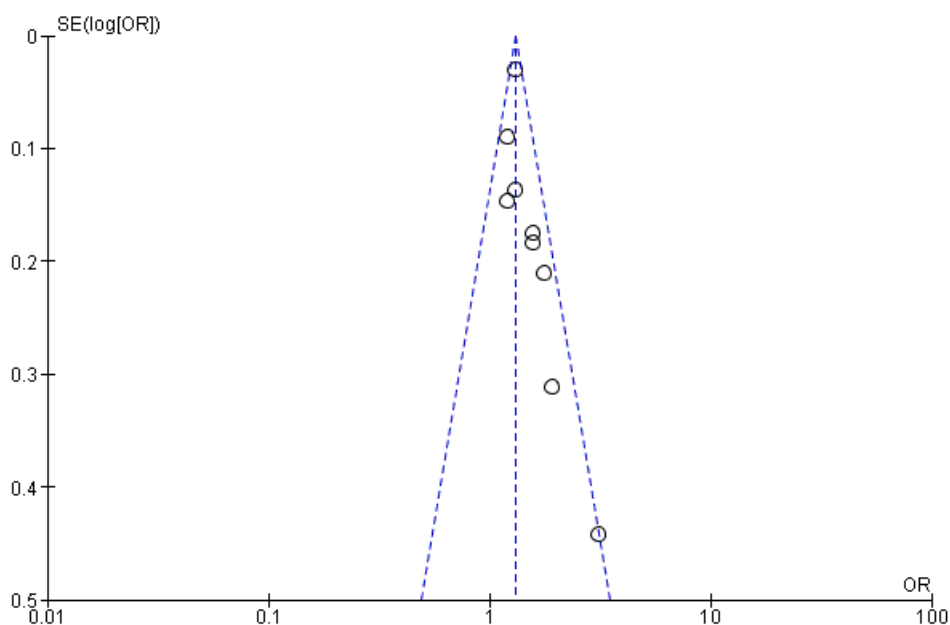


Figure 6. Funnel Plot of Silica Dust Exposure to Lung Cancer Cases

a. Forest plot

Based on the results of the forest plot (Figure 5), workers exposed to silica dust had a 1.31 times risk of developing lung cancer compared to workers who were not exposed to silica dust, and the results were statistically significant (aOR= 1.31; 95% CI= 1.25 to 1.38; p<0.001). The heterogeneity of the research data shows I²= 24% so that the distribution of the data is declared homogeneous (fixed effect model).

b. Funnel plot

The funnel plot in Figure 6 shows a publication bias characterized by an asymmetric distribution between the right and left plots. There are 5 plots on the right, 2 plot on the left, and 2 plots touching the vertical line. The plot on the right of the graph appears to have a standard error (SE) between 0 and 0.40. The plot on the left of the graph appears to have a standard error (SE) between 0 and 0.20.

DISCUSSION

This research is a systematic research and meta-analysis that raises the theme of the effect of exposure to asbestos and silica dust on the incidence of lung cancer. This systematic study and meta-analysis uses controlled research for confounding factors that can be seen from the study inclusion requirements, namely multivariate analysis, and statistical results reported by adjusted odds ratio (aOR). The combined estimate of the effect of asbestos and silica dust exposure on the incidence of lung cancer was processed using RevMan 5.3 with the generic inverse variance method.

The results of the systematic study and meta-analysis are presented in the form of forest plots and funnel plots. The forest plot provides an informational overview of each study examined in the meta-analysis, and an estimate of the overall outcome (Murti, 2018). The funnel plot shows visually the amount of variation (heterogeneity) (Akobeng, 2005 in Murti, 2018). Funnel plots show the relationship between study effect sizes and the sample sizes of the various studies studied, which can be measured in a number of different ways.

The primary studies that met the criteria regarding the effect of exposure to asbestos and silica dust on the incidence of lung cancer were 14 articles from 4 European continents, 5 from North America, and 5 from Asia.

Lung cancer is the most common cancer worldwide. Approximately 2 million people worldwide are diagnosed with lung cancer each year, of which 1.76 million die (WHO, 2022). Lung cancer is traditionally classified into two primary groups: small versus non-small cell type. This grouping was progressively defined by the use of histopathological features and immunohistochemical markers, and now break-

throughs are being made in differentiating invasive adenocarcinoma from pre-invasive lesions. Moreover, further knowledge of the molecular characteristics of lung cancer and the availability of targeted therapies have substantially influenced the classification of lung cancers (Barta et al., 2019).

The most common risk factors for lung cancer include lifestyle, environment, and occupational exposure. Workers in mining, asbestos milling, shipbuilding, construction, coal mining are at the highest risk. For some carcinogens, such as crystalline silica, this exposure is known to be a major problem in certain industrial sectors such as the construction industry (Barta et al., 2019; de Matteis et al., 2017).

1. Exposure to Asbestos Dust on Lung Cancer

A total of 8 case-control observational research articles as a source of meta-analysis of the effect of asbestos dust exposure on the incidence of lung cancer. This study showed that the results of the analysis of workers exposed to asbestos dust had a risk of developing lung cancer as much as 1.57 times compared to workers who were not exposed to asbestos dust, and the results were statistically significant (aOR= 1.57; 95% CI= 1.20 to 2.06; p= 0.001). The heterogeneity of the research data shows $I^2= 65\%$ so that the distribution of the data is declared heterogeneous (random effect model).

Exposure to asbestos dust increases the incidence of lung cancer in workers, these results are in accordance with the hypothesis. According to research Huh et al. (2021) We found that people who work in factories that produce asbestos-containing products have a higher risk of lung cancer than those who work in other locations that are not exposed to asbestos dust. The research of Suraya et al. (2020) found a significant relationship between the

duration of asbestos exposure measured in years and the risk of lung cancer, the duration of exposure can be considered as a valid proxy measure of cumulative exposure.

Although asbestos was once considered a miracle mineral, today even the word itself has unpleasant implications for all walks of life in our society. Combined in the past to more than 3,000 different industrial and consumer products, as well as in building materials and military equipment, the opportunity for exposure continues to exist in our environment. Thousands of workers and servicemen in various fields of commerce have been disabled or died from asbestos' health effects, and many more are expected to be affected in the years to come (Craighead and Gibbs, 2008)

This is supported by the research of Villeneuve et al. (2012) occupational exposure to asbestos increased the 28% risk of developing lung cancer observed among men who had been exposed to asbestos. The results of the study were in line with that of (Hardt et al., 2014) which stated that exposure to asbestos increased the incidence of lung cancer in Canada (aOR= 1.90; 95% CI 1.30 to 2.70; $p < 0.001$).

The results of this study are not in line with the research conducted by Tse et al. (2012) that asbestos reduces the incidence of lung cancer in Hong Kong (aOR= 0.86; 95% CI 0.55 to 1.36; $p < 0.05$) because of the low amount of exposure. Similar results were also found in Hong Kong (Tse et al., 2011; Tse et al., 2012).

2. Exposure to Silica Dust on Lung Cancer Incidence

A total of 9 case-control observational research articles as a source of meta-analysis of the effect of silica dust exposure on the incidence of lung cancer. This study showed that the results of the analysis of workers

exposed to silica dust had a risk of developing lung cancer as much as 1.31 times compared to workers who were not exposed to silica dust, and the results were statistically significant (aOR= 1.31; 95% CI= 1.25 to 1.38; $p < 0.001$). The heterogeneity of the research data shows $I^2 = 24\%$ so that the distribution of the data is declared homogeneous (fixed effect model).

In the research of Ge et al. (2020) silica exposure is associated with lung cancer even at low levels of exposure. According to Lacourt et al. (2015) OR for all construction workers increased the incidence of lung cancer. However, compared to other collar blue workers, there was only a slight increase in lung cancer risk for subjects who had held jobs in the construction industry.

Silica exposure is most commonly associated with silicosis, a restrictive lung disease characterized by extensive fibrosis. Despite the well-established association with silicosis, the carcinogenicity of human inhaled crystalline silica has been highly debated in the scientific literature. The International Agency for Research on Cancer (IARC) classified inhaled crystalline silica as a human carcinogen. This classification is from studies of highly exposed workers in certain industries, which reported that the risk of lung cancer tends to increase with cumulative exposure to inhaled silica, duration of exposure and peak intensity of exposure (Kachuri et al., 2014).

The results of the study were in line with those carried out by De Matteis et al. (2012) which stated that exposure to silica dust increased the incidence of lung cancer in workers in Italy (aOR=1.78; 95% CI= 1.46 to 2.18; $p = 0.000$). Other similar studies were found in Canada (Kachuri et al., 2014; Vida et al., 2010), Indonesia (Suraya et al., 2020, 2021) and in Hong Kong (Tse et al., 2011; Tse et al., 2012).

AUTHOR CONTRIBUTION

Aurina Firda Kusuma Wardani is the main researcher who selects the topic, explores and collects data. Sumardiyono and Bhisma Murti played a role in analyzing data and reviewing research documents.

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CONFLICT OF INTEREST

There is no conflict of interest in this study.

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