Medycyna Pracy 2014;65(6):799–818

http://medpr.imp.lodz.pl/en
http://dx.doi.org/10.13075/mp.5893.00054
REVIEW PAPER

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HEALTH EFFECTS OF OCCUPATIONAL EXPOSURE TO CRYSTALLINE SILICA IN THE LIGHT OF CURRENT RESEARCH RESULTS

ZDROWOTNE SKUTKI NARAŻENIA ZAWODOWEGO NA KRYSTALICZNĄ KRZEMIONKĘ W ŚWIETLE WYNIKÓW AKTUALNYCH BADAŃ

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Abstract

Crystalline silica is commonly found in the work environment. Possible health effects of occupational exposure continue to be the subject of extensive research. The aim of this paper was to analyze the recent findings concerning the health effects of exposure to crystalline silica, taking into account different levels of exposure. This work is based on the relevant information from the papers retrieved from the following databases: EBSCO, Scopus, ScienceDirect, and Web of Science, using the following keywords: crystalline silica, quartz, health effects. The review of the results confirms the multi-faceted harmful effects of crystalline silica. Prolonged occupational exposure, apart from silicosis and non-cancer respiratory diseases, may also result in the development of lung cancer, and autoimmune and chronic kidney diseases, the pathogenesis, which has not been completely explained yet. The exposure to the crystalline silica at concentrations close to the current occupational exposure limit value does not exclude the risk of the following pathologies: silicosis, lung cancer, other lung diseases and renal diseases. It is not feasible to completely eliminate the crystalline silica dust from the work environment. The best way to reduce the health effects of the exposure is to minimize the concentrations of silica dust. Further progress in clarifying the true mechanisms of interaction between silica dust and lung cells, the determination of the importance of surface properties of the silica particles in the pathogenic processes and explaining the effects of co-morbid dust in the work environment may help to prevent the harmful effects of silica dust. Med Pr 2014;65(6):799–818

Key words: crystalline silica, quartz, silicosis, health effects, lung cancer, occupational exposure

Streszczenie

Krystaliczna krzemionka powszechnie występuje w środowisku pracy. Możliwe zdrowotne skutki zawodowego narażenia są nadal przedmiotem wielu badań. Celem niniejszej pracy była analiza aktualnych wyników badań dotyczących zdrowotnych skutków narażenia na krystaliczną krzemionkę, z uwzględnieniem różnych poziomów ekspozycji. Podstawę opracowania stanowiły publikacje zawarte w bazach: EBSCO, Scopus, ScienceDirect oraz Web of Science, znalezione z użyciem słów kluczowych: crystalline silica, quartz, health effects. Przegląd wyników badań potwierdza wielokierunkowe szkodliwe działanie krystalicznej krzemionki. W następstwie długotrwałej zawodowej ekspozycji, oprócz krzemicy płuc i nienowotworowych chorób układu oddechowego, może rozwijać się rak płuca, a także choroby o niewyjaśnionej ostatecznie patogenezie – choroby autoimmunizacyjne i choroby nerek. Ekspozycja na krystaliczną krzemionkę występującą w zakresie stężeń zbliżonych do obecnie obowiązujących wartości dopuszczalnych nie wyklucza ryzyka wystąpienia następujących patologii: krzemicy, raka płuca, innych chorób płuc oraz chorób nerek. Wyeliminowanie pyłu krystalicznej krzemionki ze środowiska pracy jest praktycznie niemożliwe, a głównym sposobem ograniczania zdrowotnych skutków narażenia nadal pozostaje jego minimalizowanie. Ważnym elementem zapobiegania szkodliwemu działaniu krzemionki może być dalszy postęp w dokładnym wyjaśnieniu mechanizmów interakcji pyłu krzemionkowego z komórkami, ustalenie znaczenia właściwości powierzchniowych cząstek w patogenezie oraz dokładne poznanie interakcji z pyłami współwystępującymi w środowisku pracy. Med. Pr. 2014;65(6):799–818

Słowa kluczowe: krystaliczna krzemionka, kwarc, krzemica, skutki zdrowotne, rak płuca, narażenie zawodowe

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Received: 2014, March 7, accepted: 2014, April 23

INTRODUCTION

Silicon dioxide (SiO_2) commonly known as silica, is one of the most ubiquitous chemical compounds in the world. Quartz, one of the crystalline forms of silica, represents a very frequent component of the natural environment. It represents 12% of the Earth's crust, occurs in almost all types of rocks and is an important raw material. Cristobalite is an another form of crystalline silica, which rarely occurs in nature, but in the industrial conditions, it may be formed as a result of thermal transformations of other forms of crystalline silica, kaolinite, clay minerals or amorphous silica, if they are subjected to the temperature higher than 800°C (1,2).

Siliceous materials are extensively used in construction, for the production of glass, ceramics, foundry molds and cores, metallic silicon, silicium iron, sodium silicate, organosilicon compounds, refractory products, friction and filter materials and fillings. Quartz crystals are used in optical and electrical instruments (2).

Crystalline silica is one of the most common factors harmful to health in the work environment, particularly in mining and extractive industries, fuel and energy production, metallurgical plants, ceramic products industry, house-building and construction industries, refractory industry, as well as in the chemical industry, glass manufacture, agriculture and horticulture (1). Adverse effects of crystalline silica in humans are associated with the accumulation of respirable dust in the alveoli and health effects of the exposure include: silicosis and its complications connected with bacterial or fungal infections, other non-cancer respiratory diseases (e.g., chronic obstructive pulmonary disease), lung cancer, cancers located outside the respiratory system, autoimmune and chronic kidney diseases (3). Although the adverse effects of crystalline silica have been known for a long time, the research aiming at explaining the determinants of the known pathologies as well as at detecting the yet unknown long-term effects of exposure to this factor still continues.

The aim of this study was to analyze the current findings concerning the health effects of exposure to crystalline silica in the workplace, taking into account the different levels of exposure.

MATERIAL AND METHODS

The present work uses English-language publications collected in the following databases: EBSCO, Scopus, ScienceDirect, and Web of Science, and found using the keywords: crystalline silica, quartz, health effects, silicosis, lung cancer. In the case of lung cancer as an effect of exposure to crystalline silica, selection of literature was limited mainly to the works containing the results of meta-analyzes and pooled analyzes. The bulk of the accumulated literature was published over the years 2000–2012; but some publications important for the studied problems were published in the years 1985–1999. Recent publications by the International Agency for Research on Cancer (IARC), the American Conference of Governmental Industrial Hygienists (ACGIH) and the National Institute for Occupational Safety and Health (NIOSH) have been also included in the analysis.

RESULTS

Silicosis

Silicosis is a result of deposition of silica dust particles with a diameter less than 10 μm in the alveoli and terminal bronchioles. There are 3 types of silicosis, namely: acute silicosis, accelerated silicosis and chronic silicosis.

Acute silicosis (silicoproteinosis, silicolipoproteinosis) develops as a result of exposure to very high (probably up to 100 mg/m^3) concentrations of crystalline silica within a period ranging from a few weeks to 4 years. The resultant pathological changes are characterized by hypertrophy and hyperplasia of type II pneumocytes, which under the influence of dust produce excessive amounts of proteins and surfactant, leading to silica-induced lipoproteinosis. The progression of the disease is very rapid, resulting in a considerable impairment of gas exchange in the lungs. The radiographic image usually does not show the changes typical of other forms of silicosis (3–5).

Accelerated silicosis is a result of exposure to crystalline silica at concentrations of several tens mg/m^3 over a period of several years. It develops after 4–10 years and is characterized by a clinical image similar to chronic silicosis, but with a higher pathological progression, while the fibrotic changes in the lung may be more irregular and more dispersed (3,4,6). At present, this form of silicosis is mainly encountered in developing countries, among the miners employed in small mines, and its risk is estimated to amount to 30–50% after about 3–5 years of exposure (6).

Chronic silicosis is the most common form of silicosis. The disease develops after at least 10 years of exposure to relatively low levels of crystalline silica. It is understood that the deposition in the lung of 1–3 g respirable crystalline silica is sufficient to initiate the development of this form of pneumoconiosis (5,7), and the morbid process may progress even after cessation of the exposure (1,8). The pathogenesis of silicosis has not been yet completely elucidated. The major contributor is the direct impact of particulate matter on the macrophages and other cells of the alveoli. The development of pathological changes is a series of successive inflammatory processes, immune and fibrotic reactions leading to the formation of nodular (focal) or diffused pulmonary fibrosis (3–5). The diagnosis of silicosis is based primarily on radiological examination, and observed changes are classified according to the criteria set by the International Labour Organisation – ILO 2002 (9).

The research on the incidence of silicosis in the people exposed to crystalline silica has continued for several decades and the results have been published in several review papers (3,10–12). Table 1 shows the results of epidemiological studies on the risk of silicosis published during the recent 25 years, involving large exposed groups.

Studies by Park et al., Steenland et al., and Rosenman et al. have shown that the higher-than-acceptable risk of developing silicosis, assumed to be 1×10^{-5}–1×10^{-3}, is associated with virtually every exposure to respirable crystalline silica (22–24). The value of the risk associated with a 45-year exposure, assuming 85-year lifetime, is 0.2–0.5% in the case of exposure to very low levels – about 0.01 mg/m^3 (the dose: 0.45 mg/m^3×years) and 2–3% in the case of exposure to concentrations close to 0.02 mg/m^3 (the dose: 0.9 mg/m^3×years) (22).

The risk associated with cumulative exposure to about 1–2 mg/m^3×years is estimated to range from 1% to 20% (median: 5%) (16,19,22,23,26). In the case of higher doses, from 4 to 6 mg/m^3×years, corresponding to 40 years of exposure to crystalline silica concentration equal to 0.1–0.15 mg/m^3, the risk of silicosis ranges from several per cent to several ten percent (15,16,26). The highest cumulative exposure of over 6 mg/m^3×years involves the risk of 8–77% (the average around 40%) (17–19,23). The differences in the level of the risk of silicosis estimated in various studies may be caused by several factors:

- The adopted criterion for diagnosing the silicosis-related changes in the radiographic image of the lungs (shading category 1/0, 1/1, 2/1 or ≥ 2/1 according to the ILO 2002 (9)) (15,16,18,22–24).
- Erroneous estimation of exposure in the people with silicosis, especially in the cases of people exposed decades earlier (27).
- Different time of observation of the exposed people; silicosis is often diagnosed after more than 30 years of latency and many years after retirement (8,18,28).

The results of the studies on mortality due to silicosis (Table 2) are more coherent than the results of the studies on the incidence of the disease, although silicosis is rarely the direct cause of death (27). Hedlund et al. and Mannetje et al. have found that the risk of death from exposure to respirable crystalline silica at doses below 2 mg/m^3×years is close to 1%, while it has been found to be slightly higher if the dose exceeded 2 mg/m^3×years (27,28). The standardized mortality ratios (SMRs) due to silicosis resulting from intense exposure may reach very high values ranging

Table 1. The risk of silicosis based on the results of the epidemiological studies
Tabela 1. Ryzyko pylicy krzemowej w oparciu o wyniki badań epidemiologicznych

References Piśmiennictwo	Study, country Badanie, państwo	Exposure to respirable crystalline silica (RCS) Narażenie na działanie respirabilnej krystalicznej krzemionki	Degree of radiological changes in the lungs according to the ILO classification 2002 (9) Stopień zmian radiologicznych w płucach wg klasyfikacji Międzynarodowej Organizacji Pracy z 2002 r. (9)	Results of the risk assessment Wyniki oceny ryzyka
Graham et al. / / i wsp. 1991 (13)	a cross-sectional study of 972 granite quarry workers, USA / badanie przekrojowe w grupie 972 pracowników kopalni granitu, Stany Zjednoczone	average level of concentration / średni poziom stężenia: 0.06 mg/m^3	cat. / kat. ≥ 1/0	0.7%, abnormalities that have been observed in X-ray films may be related to smoking / nieprawidłowości zaobserwowane na zdjęciach rentgenowskich mogą mieć związek z paleniem papierosów
Love et al. / / i wsp. 1999 (14)	a cross-sectional study of 1 934 heavy clay factories workers, Great Britain / / badanie przekrojowe w grupie 1 934 pracowników fabryk wyrobów ceramicznych, Wielka Brytania	97% of all quartz concentrations / / 97% wyników pomiarów stężenia kwarcu: < 0.4 mg/m^3	cat. / kat. ≥ 1/0 cat. / kat. ≥ 2/1	risks /ryzyko [%]: 1.4 0.4

Table 1. The risk of silicosis based on the results of the epidemiological studies – cont.
Tabela 1. Ryzyko pylicy krzemowej w oparciu o wyniki badań epidemiologicznych – cd.

References Piśmiennictwo	Study, country Badanie, państwo	Exposure to respirable crystalline silica (RCS) Narażenie na działanie respirabilnej krystalicznej krzemionki	Degree of radiological changes in the lungs according to the ILO classification 2002 (9) Stopień zmian radiologicznych w płucach wg klasyfikacji Międzynarodowej Organizacji Pracy z 2002 r. (9)	Results of the risk assessment Wyniki oceny ryzyka	
Miller et al. / / i wsp. 1998 (15)	a follow up study of 547 men worked in colliery, Great Britain / długofalowe badanie 547 mężczyzn, którzy pracowali w kopalni węgla, Wielka Brytania	concentration / stężenie [mg/m^3]:	cat. / kat. ≥ 2/1	risks [%] after 15 years of exposure / ryzyko [%] po 15 latach narażenia:	
		0.02		0.26	
		0.04		0.50	
		0.10		5.00	
Muir et al. / / i wsp. 1989 (16)	a follow up study of 2 109 workers from gold and uranium mines, Canada / / długofalowe badanie 2 109 pracowników kopalni złota i uranu, Kanada	concentration / stężenie [mg/m^3] / cumulative exposure [mg/m^3×years] / skumulowane narażenie [mg/m^3×liczba lat]:	cat. / kat. ≥ 1/1	cumulative risks / skumulowane ryzyko [%] [M (95% CI)]:	
		0.05/2		0.4 (0.2–0.8)	
		0.10/4		1.2 (0.7–2.1)	
		0.15/6		2.4 (1.4–3.9)	
		0.20/8		3.8 (2.2–6.5)	
Cherry et al. / / i wsp. 1998 (17)	a cohort study of 1 080 men employed in pottery, refractory and sandstone industries, Great Britain / badanie kohortowe 1 080 mężczyzn zatrudnionych w zakładach produkujących wyroby ceramiczne, materiały ogniotrwałe i przy obróbce piaskowca, Wielka Brytania	cumulative exposure [mg/m^3×years] / / skumulowane narażenie [mg/m^3×liczba lat]:	cat. / kat. ≥ 1/0	risks: non-smokers / ryzyko dla osób niepalących [%]:	risks: smokers / ryzyko dla osób palących [%]
		< 2		0	0
		2–3.999		0.9	1.8
		4–5.999		2.9	6.3
		≥ 6		9.3	16.3
Graham et al. / / i wsp. 2001 (8)	a cross-sectional study of 600 retired granite workers, USA / / badanie przekrojowe w grupie 600 emerytowanych pracowników kopalni granitu, Stany Zjednoczone	initialy concentration / narażenie początkowe > 0.1 mg/m^3; 1940–1954: 0.05–0.06 mg/m^3, but about 10–15% samples exceeded 0.1 mg/m^3 / ale ok. 10–15% próbek przekraczało 0,1 mg/m^3; cumulative exposure [mg/m^3×years] / / skumulowane narażenie [mg/m^3×liczba lat]:	cat. / kat. ≥ 1/0	risks / ryzyko [%]:	
		< 4		5.7	
		> 4		25.9	

Hnizdo et al. / / i wsp. 1993 (18)	a cohort study of 2 235 white South African gold miners, RPA / badanie kohortowe w grupie 2 235 białych pracowników kopalni złota, Republika Południowej Afryki	exposure / narażenie: 24–40 years / lat; cumulative exposure [mg/m³×years] / / skumulowane narażenie [mg/m³×liczba lat]:	cat. / kat. ≥ 1/1	cumulative risks / skumulowane ryzyko [%]:			
		9		25			
		12		53			
		15		77			
Chen et al. / / i wsp. 2005 (19)	a follow up study of 4 547 pottery workers, 4 028 tin miners, 14 427 tungsten miners, China / badanie długofalowe 4 547 pracowników zakładów ceramicznych, 4 028 pracowników kopalni cyny, 14 427 pracowników kopalni wolframu, Chiny	employed in exposure at least 1 year / / co najmniej 1 rok pracy w warunkach narażenia / cumulative exposure [mg/m³×years] / skumulowane narażenie [mg/m³×liczba lat]:	Chinese radiological criteria similar to cat. 1/1 / Chińskie kryteria radiologiczne podobne do kat. 1/1	risks / ryzyko [%]:			
		2.43		tin miners / pracownicy kopalni cyny: 21.2			
		3.25		tungsten miners / pracownicy kopalni wolframu: 19.5			
		6.37		pottery workers / pracownicy zakładów ceramicznych: 17.3			
Buchanan et al. / / i wsp. 2003 (20)	a follow up study of 371 Scottish coal miners, Great Britain / badanie długofalowe 371 szkockich pracowników kopalni węgla, Wielka Brytania	exposure for 15 years to concentrations < 1 mg/m³ / 15-letnie narażenie przy stężeniu < 1 mg/m³; concentration / stężenie [mg/m³] / cumulative exposure [mg/m³×years] / / skumulowane narażenie [mg/m³×liczba lat]:	cat. / kat. ≥ 2/1	prediction of risks [%] of silicosis 15 years after exposure ends as a function of 15 years spent in concentration < 1 mg/m³ and additional months in concentration of 2 mg/m³ / przewidywane ryzyko [%] pylicy krzemowej 15 lat od zaprzestania pracy w warunkach narażenia, która trwała 15 lat przy stężeniu < 1 mg/m³ i dodatkowych miesiącach pracy przy stężeniu 2 mg/m³			
				0 months / / miesięcy	4 months / / miesiące	8 months / / miesięcy	12 months / / miesięcy
		0.02/0.3		1.00	4.48	17.88	50.26
		0.04/0.6		1.26	5.58	21.53	56.02
		0.06/0.9		1.58	6.93	25.70	61.62
		0.08/1.2		1.98	8.59	30.36	66.93
		0.10/1.5		2.49	10.58	35.46	71.84
		0.20/3.0		7.50	27.36	63.61	89.03
		0.30/4.5		20.52	54.51	84.76	96.27
Churchyard et al. / i wsp. 2004 (21)	a cross-sectional study of 520 black gold miners (aged > 37 years), RPA / badanie przekrojowe w grupie 520 czarnoskórych pracowników kopalni złota (w wieku > 37 lat), Republika Południowej Afryki	average duration of exposure / średni okres narażenia: 21.8±5.3 years / lat; average concentration / średnie stężenie: 0.053±0.015 mg/m³; cumulative exposure: 1.15±0.43 mg/m³×years / skumulowane narażenie: 1,15±0,43 mg/m³×liczba lat	cat. / kat. ≥ 1/1	prevalence of silicosis [%]: 18.3–19.9 (depending of reader of chest radiographs) / występowanie pylicy krzemionkowej [%]: 18,3–19,9 (w zależności od osoby odczytującej zdjęcia rentgenowskie klatki piersiowej)			

Table 1. The risk of silicosis based on the results of the epidemiological studies – cont.
Tabela 1. Ryzyko pylicy krzemowej w oparciu o wyniki badań epidemiologicznych – cd.

References Piśmiennictwo	Study, country Badanie, państwo	Exposure to respirable crystalline silica (RCS) Narażenie na działanie respirabilnej krystalicznej krzemionki	Degree of radiological changes in the lungs according to the ILO classification 2002 (9) Stopień zmian radiologicznych w płucach wg klasyfikacji Międzynarodowej Organizacji Pracy z 2002 r. (9)	Results of the risk assessment Wyniki oceny ryzyka	
Park et al. / / i wsp. 2002 (22)	a follow up study of 2 342 diatomaceous earth mining and processing workers, USA / badanie długofalowe 2 342 osób pracujących przy pozyskiwaniu i przetwórstwie ziemi okrzemkowej, Stany Zjednoczone	concentration / narażenie [mg/m^3] / cumulative exposure [mg/m^3×years] / / skumulowane narażenie [mg/m^3×liczba lat]:	cat. / kat. ≥ 1/0	excess lifetime risks [%] resulting from up to 45 years exposure, estimated at age of 85 / dodatkowe całożyciowe ryzyko [%] wynikające z maks. 45 lat narażenia, wartość oszacowana dla wieku 85 lat:	
		0.001/0.045		0.16	
		0.005/0.225		0.78	
		0.010/0.45		1.60	
		0.020/0.90		3.10	
		0.050/2.25		7.50	
		0.10/4.50		14.00	
		0.200/9.00		26.00	
Steenland et al. / / i wsp. 1995 (23)	a cohort study of 3 330 gold miners, USA / badanie kohortowe w grupie 3 330 pracowników kopalni złota, Stany Zjednoczone	cumulative exposure [mg/m^3×years] / / skumulowane narażenie [mg/m^3×liczba lat]:	cat. / kat. ≥ 1/1	cumulative risks / skumulowane narażenie [%]:	cumulative risks adjusted for age / skumulowane narażenie z uwzględnieniem wieku [%]:
		0–0.2		0.002	0.002
		0.2–0.5		0.005	0.005
		0.5–1.0		0.022	0.017
		1.0–2.0		0.064	0.060
		2.0–3.0		0.245	0.167
		3.0–4.0		0.534	0.403
		> 4.0		0.844	0.678

Rosenman et al. / / i wsp. 1996 (24)	a cross-sectional study of 1 072 current and retired workers in automotive foundry, USA / badanie przekrojowe w grupie 1 072 obecnych i emerytowanych pracowników odlewni motoryzacyjnej, Stany Zjednoczone	time-weighted average of silica concentration / średnia ważona stężenia krzemionki [mg/m^3]:	cat. / kat. ≥ 1/0	OR (95% CI) – adjusted for cigarette smoking race and silica exposure at another job / z uwzględnieniem palenia papierosów, rasy i narażenia na działanie krzemionki w innej pracy:	
				after 20 years exposure / / po 20 latach narażenia:	after 40 years exposure / / po 40 latach narażenia:
		0.01		1.04 (1.02–1.15)	1.08 (1.05–1.11)
		0.05		1.20 (1.12–1.30)	1.45 (1.25–1.68)
		0.10		1.45 (1.25–1.68)	2.10 (1.56–2.82)
		0.15		1.74 (1.40–2.17)	3.04 (1.96–4.72)
		0.20		2.10 (1.56–2.82)	4.40 (2.45–7.93)
		0.25		2.53 (1.75–3.65)	6.38 (3.06–13.30)
		0.30		3.04 (1.96–4.72)	9.24 (3.83–22.31)
Hughes et al. / / i wsp. 1998 (25)	a cohort study of 1 809 workers in the diatomaceous earth industry, USA / / badanie kohortowe w grupie 1 809 pracowników przemysłu zajmującego się pozyskiwaniem ziemi okrzemkowej, Stany Zjednoczone	cumulative exposure [mg/m^3×years] / / skumulowane narażenie [mg/m^3×liczba lat]:	cat. / kat. ≥ 1/0	cumulative risks / skumulowane ryzyko [%]:	
		≤ 2		1.1	
		> 2		3.7	
				estimated RR (95% CI) adjusted for age / RR (95% CI) z uwzględnieniem wieku:	
		≤ 1		1.00	
		1.1–3.0		4.4 (1.7–11.1)	
		3.1–6.0		20.2 (8.2–49.7)	
		> 6.0		40.4 (16.1–101.3)	
Kreiss et al. / / i wsp. 1996 (26)	a cross-sectional study of 100 miners from Leadville, aged ≥ 40 years, USA / / badanie przekrojowe w grupie 100 pracowników kopalni w Leadville w wieku ≥ 40 lat, Stany Zjednoczone	average concentration / średnie stężenie [mg/m^3]:	cat. / kat. ≥ 1/0	risks / ryzyko [%]:	
		0.025–0.05		13	
		0.06–0.10		34	
		> 0.10		75	

ILO – International Labour Organization / Międzynarodowa Organizacja Pracy.
M – mean / średnia; OR – odds ratio / iloraz szans; RR – relative risk / ryzyko względne, CI – confidence interval / przedział ufności.

from 20 to over 500 (29–32). In a study conducted by Marinaccio et al. it has been also found that the level of that ratio depended on gender; it was significantly higher in women than in men (31).

The abovementioned data indicate that the most important factor in the occurrence of silicosis is the cumulative exposure to respirable crystalline silica and the time of the 1st exposure (18,23,25,26,28). Hnizdo et al. have indicated that the relationship between the risk of silicosis and the dose up to 4 mg/m^3×years is linear; at higher doses, the risk of silicosis increases in a manner similar to an exponential function (18). Multiple increase in the risk was also noted for the doses exceeding 2 mg/m^3×years followed by additional several months of exposure to crystalline silica at concentrations higher than 2 mg/m^3 (20). Yet another factor increasing the risk of developing silicosis consists in the exposure to freshly fractured silica dusts produced during crushing, grinding or pulping siliceous materials (3,33). The modification of the surface properties of such particles by coal mine dusts or clay dusts, i.e., minerals, which cause occlusion of the silica particles, as well as aluminum salts and metallic iron, can lead to reduction of biological activity of crystalline silica (34). It is believed that the weaker fibrotic effect of such dusts results in reducing the risk of silicosis among the workers employed in factories manufacturing ceramic products (14,19) and in coal mines (15).

The relationship between silicosis and tobacco smoking has not been fully resolved. The results suggesting additive effect of both factors may be biased by an error resulting from an incorrect interpretation of non-specific radiographic changes in the lungs of smokers (35).

Systemic silicosis (extrapulmonary silicosis)

Silicotic patients happen to develop silicotic-like nodules in organs other than lungs. It is believed that these changes occur as a result of the transportation of the respirable dust with blood and/or lymph beyond the respiratory system, mainly to the liver, spleen, pancreas or bone marrow. Other factors, such as immune responses, are also suspected of being involved in the development of those changes (36,37).

Complications of silicosis

Silicosis may be complicated by severe bacterial or fungal infections, developing as a result of the impairment of macrophage phagocytic function by the crystalline silica dust. In the relevant literature, silicotuberculosis

Table 2. The risk of death from silicosis based on the results of the epidemiological studies
Tabela 2. Ryzyko zgonu spowodowane pylicą krzemową w oparciu o wyniki badań epidemiologicznych

References Piśmiennictwo	Study, country Badanie, państwo	Exposure to respirable crystalline silica (RCS) Narażenie na działanie respirabilnej krystalicznej krzemionki	The risk of death from silicosis Ryzyko zgonu spowodowanego pylicą krzemową	
Hedlund et al. / / i wsp. 2008 (28)	a mortality study of 7 729 miners identified from company's personal record; Swedish miners had worked for at least 1 year between 1923 and 1996, died between 1952 and 2001 / badanie umieralności w grupie 7 729 pracowników kopalni wg danych z akt osobowych; szwedzcy pracownicy kopalni pracujący przez co najmniej 1 rok w latach 1923–1996, którzy zmarli w latach 1952–2001	concentration / stężenie [mg/m^3] / cumulative dose [mg/m^3×years] / dawka skumulowana [mg/m^3×liczba lat]:	mortality rate crude per 100 000 person-years / surowy wskaźnik umieralności na 100 000 osobolat	mortality rate adjusted to year of birth and attained age per 100 000 person-years / współczynnik umieralności z uwzględnieniem roku urodzenia i osiągniętego wieku na 100 000 osobolat
		< 0.02/ < 0.9 (M = 0.4)	9.7	18.7
		0.02–0.07/1–2.9 (M = 1.8)	24.6	32.8
		0.07–0.11/3–4.9 (M = 3.9)	117.0	117.0
		0.11–0.16/5–6.9 (M = 5.9)	154.0	129.0
		> 0.16/ > 7 (M = 8.3)	224.0	140.0

Mannetje et al. / / i wsp. 2002 (27)	pooled 6 cohort studies: 2 342 diatomaceous earth workers, USA; 1 026 granite workers, Finland; 5 408 granite workers, USA; 4 027 industrial sand workers, USA; 3 348 gold miners, USA; 2 213 gold miners, Australia / analiza zbiorcza 6 badań kohortowych: 2 342 pracowników zajmujących się pozyskiwaniem ziemi krzemionkowej, Stany Zjednoczone; 1 026 pracowników kopalni granitu, Finlandia; 5 408 pracowników kopalni granitu, Stany Zjednoczone; 4 027 pracowników kopalni piasku, Stany Zjednoczone; 2 213 pracowników kopalni złota, Australia	cumulative exposure [mg/m^3×years] / / skumulowane narażenie [mg/m^3×liczba lat]:	mortality rate per 100 000 person-years / wskaźnik umieralności na 100 000 osobolat:	RR (95% CI) – adjusted for age / / z uwzględnieniem wieku:
		0–0.99	4.7	1.00 (referent)
		0.99–1.97	26.9	3.39 (1.42–8.08)
		1.97–2.87	58.4	6.22 (2.56–15.12)
		2.87–4.33	67.4	9.40 (3.71–23.80)
		4.33–7.12	61.1	13.69 (5.04–37.180)
		7.12–9.58	90.6	22.64 (7.88–65.100)
		9.58–13.21	83.2	23.97 (8.05–71.32)
		13.21–15.89	144.7	40.25 (13.25–122.3)
		15.89–28.10	73.6	25.11 (8.09–77.91)
		> 28.10	233.6	63.63 (19.87–203.8)
Steenland et al. / / i wsp. 2001 (29)	a study of mortality due to lung cancer among 4 269 industrial sand plants workers, USA / badanie umieralności z powodu raka płuca wśród 4 269 pracowników kopalni piasku, Stany Zjednoczone	average length of employment: 9 years; average concentration: 0.05 mg/m^3 / średni okres zatrudnienia: 9 lat; średnie stężenie: 0,05 mg/m^3	SMR (95% CI): 66.3 (33.1–118.7)	
Graham et al. / / i wsp. 2004 (30)	a study of mortality of 2 539 granite industry workers, hired before 1940, and who had died by the end of 1996, USA / badanie umieralności w grupie 2 539 pracowników zakładów obróbki granitu zatrudnionych przed 1940 r., którzy zmarli przed końcem 1996 r., Stany Zjednoczone	concentration to 1955 / stężenie do roku 1955: 0.2–0.6 mg/m^3; concentration after 1955 / stężenie po roku 1955: 0.05–0.06 mg/m^3	SMR (95% CI): 20.55 (15.39–26.87)	
Marinaccio et al. / / i wsp. 2006 (31)	a study of mortality of 14 098 men and 831 women with silicosis, living in 1980 and who died before 2000, Italy / / badanie umieralności w grupie 14 098 mężczyzn i 831 kobiet chorych na pylicę krzemową, którzy żyli w 1980 r. i zmarli przed 2000 r., Włochy	no data on exposure / brak danych dotyczących narażenia	SMR (95% CI) for men / dla mężczyzn: 21.73 (20.58–22.94) SMR (95% CI) for women / dla kobiet: 536.75 (380.04–758.08)	
Scarselli et al. / / i wsp. 2011 (32)	a cohort study of 2 034 men compensated for silicosis between 1943 and 1986, alive in 1987 and resident in Latium, mortality follow-up was from 1987 to 2006, Italy (Latium) / badanie kohortowe w grupie 2 034 mężczyzn otrzymujących odszkodowanie z tytułu pylicy krzemowej w latach 1943–1986, którzy żyli w 1987 r. i mieszkali w Lacjum, uzupełniające dane dot. umieralności z lat 1987–2006, Włochy (Lacjum)	no data on exposure / brak danych dotyczących narażenia	SMR (95% CI): 261.27 (228.11–299.26)	

SMR – standardized mortality ratio / standaryzowany wskaźnik zgonu.
Other abbreviations as in Table 1 / Pozostałe skróty jak w Tabeli 1.

is the most frequently reported complication, while mycobacteriosis, nocardiasis, cryptococcosis (torulosis) are considerably less frequent (3). The analysis of the death certificates of the silicotic patients living in Tuscany and Lazio, Italy, showed a significant increase in mortality due to infectious diseases to the SMR = 3.11 (95% CI: 1.38–7.01) (31,32). In a study of mortality due to tuberculosis in the silicotic workers, the SMR values ranging from 2.89 (95% CI: 2.20–3.80) to 10.47 (95% CI: 4.24–25.85) (31,32,38) were observed, and the mortality odds ratio (OR) for silicotuberculosis as compared to a non-silicotic control group amounted to 39.5 (95% CI: 16.9–92.4) (39). The human immunodeficiency virus (HIV) infection in the patients with pulmonary silicosis additionally increases the risk of developing tuberculosis (40). The odds of developing silicotuberculosis increase in proportion to the time of exposure (38) and the dose of respirable crystalline silica (30).

Other frequent non-infection-related complications of silicosis include enlargement of the right ventricle of the heart (cor pulmonale) and the progressive right ventricular circulatory failure (3).

Other non-malignant respiratory diseases

The workers exposed to crystalline silica suffer also from the following diseases: chronic obstructive pulmonary disease (COPD), chronic bronchitis and emphysema (3). Studies on the relationship between exposure to silica and the occurrence of the COPD and chronic bronchitis are difficult to conduct and evaluate, as tobacco smoking is the major cause of these diseases. An additional factor complicating the study of this relationship is the fact that the particle size fraction responsible for the development of diseases located in the bronchial tree, and in the thoracic fraction, is different from that involved in the development of silicosis and pulmonary cancer.

Park et al. (22) who studied the workers mining and processing diatomite has estimated that the risk of developing lung diseases other than cancer, pneumoconiosis and pulmonary inflammation increases in proportion to the dose of dust, and ranges from 0.11% at a dose of 0.045 mg/m^3× years to 19% at a dose of 9–10 mg/m^3×years. The risk of death from these diseases, estimated using the SMR, is significantly higher after a long, 20-year-long period of exposure and its value ranges from 1.47 (95% CI: 1.30–1.66) to 3.91 (95% CI: 3.49–4.37) (30–32,38). An increased risk of death (SMR) due to chronic obstructive pulmonary disease in the workers exposed to silica reported by Scarselli et al. (32) and Calvert et al. (39) is as follows: 1.43 (95% CI: 1.14–1.79) and OR = 4.38 (95% CI: 3.39–5.67). Those values were not confirmed by Marinaccio et al. whose SMR was equal to 0.79 (95% CI: 0.71–0.87) (31). Similarly, in the case of chronic bronchitis, higher SMR values amounting to 1.52 (95% CI: 1.19–1.94) were estimated in Scarselli studies (32), which were not confirmed by Marinaccio et al. (SMR = 0.84 (95% CI: 0.75–0.94)) (31).

Crystalline silica is not considered a factor that may contribute to the development of asthma (3). Epidemiological studies have failed to demonstrate a relationship between the frequency of fatal cases due to asthma (30–32) or emphysema (30) and exposure to silica.

Lung cancer

Lung cancer belongs to the most common tumors diagnosed in the general population, and its major risk factor is tobacco smoking. A significant risk is also related to factors of occupational origin. The International Agency for Research on Cancer (IARC) in 1997 decided that there was sufficient evidence in the case of humans for carcinogenicity of inhaled crystalline silica in a form of quartz and cristobalite from occupational sources, and included them into group 1 – carcinogenic to humans (1). In 2009, the Working Group, after reviewing the results of the available studies confirmed this classification, specifying lung as the only target organ (41).

The mechanism of carcinogenicity of crystalline silica is not completely explained. Borm et al. (42) after analyzing more than 200 publications in this field has concluded that the most likely hypothesis for carcinogenicity of crystalline silica is its secondary genotoxic effect resulting from its potent pro-inflammatory activity. Exposure to crystalline silica may result in the development of all major histological types of lung cancer, such as squamous cell carcinoma, adenocarcinoma and small cell carcinoma (43,44).

Quantitative estimation of the risk of lung cancer attributable to occupational exposure to quartz and cristobalite obtained in the meta-analysis of the results of many epidemiological studies is shown in the Table 3. Research conducted in the people occupationally exposed to crystalline silica indicates that the relative risk (RR) ranges from 0.97 (95% CI: 0.68–1.38) among the non silicotic subjects to 3.27 (95% CI: 1.32–8.2) among the silicotic only (50) and the SMR from 1.2 (95% CI: 1.1–1.3) to 2.15 (95% CI: 1.63–3.66) (this data were not adjusted for smoking) (45,51).

Table 3. The risk of lung cancer due to occupational exposure to respirable crystalline silica (RCS) in meta-analysis studies
Tabela 3. Ryzyko zachorowania na raka płuca z powodu narażenia na działanie respirabilnej krystalicznej krzemionki (RCS) w metaanalizach badań epidemiologicznych

References Piśmiennictwo	Study Badanie	Results Wyniki			
Steenland et al. / / i wsp. 2001 (45)	a nested case-control analysis of 10 cohort studies – US: diatomaceous, granite, industrial sand, gold mine; China: pottery, tin and tungsten mine; Finnish: granite; South Africa and Australia: gold mine / badanie gniazdowe kliniczno-kontrolne na podstawie obserwacji 10 kohort – pracownicy: Stany Zjednoczone: kopalni ziemi okrzemkowej, granitu, piasku przemysłowego, złota; Chiny: przemysłu ceramicznego, kopalni cyny i wolframu; Finlandia: kopalni granitu; Republika Południowej Afryki i Australia: kopalni złota	quintiles of average concentration / / kwintyle średniego stężenia [mg/m^3]:	OR (95% CI):	quintiles of cumulative exposure / kwintyle skumulowanego narażenia [mg/m^3×days]:	OR (95% CI):
		< 0.07	1.0	< 0.4	1.0
		0.07–0.21	1.4 (1.1–1.7)	0.4–2.0	1.0 (0.85–1.3)
		0.21–0.41	1.6 (1.3–2.0)	2.0–5.4	1.3 (1.1–1.7)
		0.41–1.36	1.6 (1.2–2.0)	5.4–12.8	1.5 (1.2–1.9)
		> 1.36	1.7 (1.2–2.3)	> 12.8	1.6 (1.3–2.1)
Kurihara et al. / / i wsp. 2004 (46)	a meta-analysis of 17 cohort studies: granite, stone and slate quarry workers, gold, lead and zinc miners, diatomaceous earth mining and processing factory workers, foundry workers, sand, ceramic and refractory workers, construction workers / metaanaliza 17 badań kohortowych w grupie: osób pracujących przy obróbce granitu i kamienia oraz pracowników kopalni łupków, złota, ołowiu i cynku; osób pracujących przy pozyskiwaniu i przerobie ziemi okrzemkowej; pracowników odlewni, piaskowni i zakładów ceramicznych; pracowników zakładów produkujących materiały ogniotrwałe, pracowników budowlanych	RR (95% CI): 1.29 (1.20–1.40)			
	a meta-analysis of 13 case-control studies: iron-cupper, tin and tungsten miners, quarry workers, ceramic, sandstone and refractory workers, foundry workers, paper and various workers / / metaanaliza 13 kliniczno-kontrolnych badań przypadków w grupie: pracowników kopalni miedzi, cyny i wolframu, pracowników kamieniołomów, pracowników zakładów produkujących wyroby ceramiczne, obrabiających piaskowiec oraz produkujących materiały ogniotrwałe, pracowników odlewni, pracowników zakładów papierniczych i innych	RR (95% CI): 1.42 (1.22–1.65)			
	a pooled analysis of 17 cohort studies and 13 case-control studies / zbiorcza analiza 17 badań kohortowych i 13 badań kliniczno-kontrolnych przypadków	RR (95% CI): 1.32 (1.23–1.41)			
Cassidy et al. / / i wsp. 2007 (43)	a case-control study conducted in 15 areas in 6 countries: 1 in Romania and Russia, 2 in Poland, 3 in Slovakia and Czech Republic, 5 in Hungary, 1 in United Kingdom / kliniczno-kontrolne badania przypadków przeprowadzone na 15 obszarach w 6 krajach: 1 w Rumunii i Rosji, 2 w Polsce, 3 na Słowacji i w Czechach, 5 na Węgrzech, 1 w Wielkiej Brytanii	duration of exposure [years] / / czas trwania narażenia [w latach]:	20-year lag period / 20-letni okres opóźnienia [OR (95% CI)]:	cumulative exposure [mg/m^3×h] / / skumulowane narażenie [mg/m^3×godz.]:	20-years lag period / / 20-letni okres opóźnienia [OR (95% CI)]:
		0–2	1.25 (0.87–1.80)	0–9	1.07 (0.77–1.50)
		3–5	1.06 (0.75–1.50)	9–35	1.06 (0.75–1.49)
		6–14	1.44 (1.05–1.97)	35–200	1.47 (1.04–2.06)
		> 14	1.73 (1.26–2.39)	> 200	2.08 (1.49–2.90)
		overall / razem: OR (95% CI): 1.37 (1.14–1.65)			

Table 3. The risk of lung cancer due to occupational exposure to respirable crystalline silica (RCS) in meta-analysis studies – cont.
Tabela 3. Ryzyko zachorowania na raka płuca z powodu narażenia na działanie respirabilnej krystalicznej krzemionki (RCS) w metaanalizach badań epidemiologicznych – cd.

References Piśmiennictwo	Study Badanie	Results Wyniki			
Olsson et al. / / i wsp. 2011 (47)	multicenter 15 case-control studies: 3 in Czech Republic, 5 in Hungary, 2 in Poland, 3 in Slovakia, 1 in Romania and 1 in Russia / 15 wieloośrodkowych, kliniczno-kontrolnych badań przypadków: 3 w Czechach, 5 na Węgrzech, 2 w Polsce, 3 na Słowacji, 1 w Rumunii i 1 w Rosji	OR (95% CI): in men / u mężczyzn: 1.31 (1.08–1.58) in women / u kobiet: 2.69 (1.20–6.04)			
Vida et al. / / i wsp. 2010 (44)	a pooled analysis of 2 case-control studies in Canada (persons diagnosed with lung cancer) / / zbiorcza analiza 2 badań kliniczno-kontrolnych przeprowadzonych w Kanadzie (osoby, u których zdiagnozowano raka płuca)	smoking level [cigarette–years] / / palenie papierosów [papierosolata]:	unexposed / brak narażenia [OR (95% CI)]:	non–substantial exposed / / nieznaczny stopień narażenia [OR (95% CI)]:	substantial exposed / znaczne narażenie [OR (95% CI)]:
		0	1	1.28 (0.52–3.17)	2.25 (0.59–8.56)
		> 0 to < 400	2.19 (1.28–3.76)	3.20 (1.51–6.77)	3.67 (0.95–14.14)
		≥ 400 to < 1000	6.91 (4.40–10.85)	6.70 (4.01–11.40)	9.49 (4.68–19.24)
		≥ 1000	16.9 (10.87–26.28)	23.20 (14.41–37.36)	26.93 (15.16–47.84)
Lacasse et al. / / i wsp. 2009 (48)	a meta-analysis of 4 cohort studies (sand and diatomaceous earth industry and no specific industry), 3 case-control studies (stone, quarrying, mining, ceramic industry and foundry), 2 nested case-control studies (sand workers, aluminum foundries) / metaanaliza 4 badań kohortowych (pracownicy zatrudnieni przy wydobyciu piasku i ziemi okrzemkowej i w innym przemyśle), 3 badań kliniczno-kontrolnych (pracownicy zakładów kamieniarskich, kamieniołomów, górnictwa, przemysłu ceramicznego i odlewni), 2 badań gniazdowych kliniczno-kontrolnych (pracownicy kopalni piasku i odlewni aluminium)	cumulative exposure [mg/m^3/year] / / skumulowane narażenie [mg/m^3/liczba lat]:	RR (95% CI):		
		1.0	1.22 (1.01–1.47)		
		6.0	1.84 (1.48–2.28)		
		the risk of lung cancer is plateaus at a level exposure > 6 mg/m^3×year / ryzyko zachorowania na raka płuca nie zwiększa się przy narażeniu > 6 mg/m^3×rok			
Erren et al. / / i wsp. 2009 (49)	a meta-analysis of 9 cohort studies: mining, quarry, refractory trick, ceramic, diatomaceous earth, foundry and miscellaneous industry / metaanaliza 9 badań kohortowych w grupach osób pracujących w: górnictwie, kamieniołomach, przemyśle materiałów ogniotrwałych, ceramicznym, przy uzyskiwaniu ziemi okrzemkowej, w odlewniach i innym przemyśle	in non-silicotic / u osób bez pylicy krzemowej [RR (95% CI)]: 1.2 (1.1–1.34)			
	a meta-analysis of 2 case-control studies: ceramic and miscellaneous industry / / metaanaliza 2 badań kliniczno-kontrolnych wśród: pracowników przemysłu ceramicznego i innego	RR (95% CI): 1.0 (0.7–1.3)			
	a pooled analysis of 9 cohort studies and 2 case-control studies / zbiorcza analiza 9 badań kohortowych i 2 badań kliniczno-kontrolnych	not smoking adjusted / bez uwzględnienia palenia [RR (95% CI)]: 1.2 (1.1–1.4) smoking adjusted / z uwzglednieniem palenia [RR (95% CI)]: 1.0 (0.8–1.3)			
Kurihara et al. / / i wsp. 2004 (46)	11 cohort studies: miners, slate quarry and diatomaceous earth workers, ceramic workers and silicotic patients / 11 badań kohortowych wśród: pracowników kopalni łupków i osób pracujących przy uzyskiwaniu ziemi okrzemkowej, produkcji wyrobów ceramicznych oraz chorych na pylicę krzemową	from silicosis / spowodowane pylicą krzemową [RR (95% CI)]: 2.49 (2.08–2.99)			
	5 case-control studies: gold miners, ceramic and silica factory workers, lung cancer patients / / 5 badań kliniczno-kontrolnych w grupach: pracowników kopalni złota, osób pracujących przy produkcji materiałów cermicznych oraz w zakładach przerabiających krzemionkę	from silicosis / spowodowane pylicą krzemową [RR (95% CI)]: 1.89 (1.45–2.48)			

	a meta-analysis of 6 cohort studies (miners, slate quarry and diatomaceous earth workers, ceramic and other workers expose to silica) and 2 case-control studies (ceramic workers and lung cancer patients) / metaanaliza: 6 badań kohortowych wśród pracowników kopalni, osób pracujących przy wydobyciu łupków i uzyskiwaniu ziemi okrzemkowej, produkcji wyrobów ceramicznych oraz pracowników innych zakładów, w których byli narażeni na działanie krzemionki; 2 badań kliniczno-kontrolnych wśród osób pracujących przy produkcji wyrobów ceramicznych oraz chorych na raka płuca	from silicosis in smokers / spowodowane pylicą krzemową u osób palących [RR (95% CI)]: 4.47 (3.17–6.30) from silicosis in non-smokers / spowodowane pylicą krzemową u osób niepalących [RR (95% CI)]: 2.24 (1.46–3.43)
Pelucchi et al. / / i wsp. 2006 (50)	11 cohort studies / 11 badań kohortowych	in silicotic patients / u pacjentów chorych na pylicę krzemową [RR (95% CI)]: 1.69 (1.32–2.16)
	24 cohort studies / 24 badania kohortowe	in patients with silicosis undefined status / u pacjentów bez uwzględu na występowanie pylicy krzemowej [RR (95% CI)]: 1.25 (1.18–1.33)
	1 cohort study / 1 badanie kohortowe	in patients without silicosis / u pacjentów, którzy nie chorują na pylicę krzemową [RR (95% CI)]: 1.19 (0.87–1.57)
	total cohort studies / wszystkie badania kohortowe	total / ogółem [RR (95% CI)]: 1.34 (1.25–1.45)
	1 case-control study / 1 badanie kliniczno-kontrolne	in silicotic patients / u pacjentów chorych na pylicę krzemową [RR (95% CI)]: 3.27 (1.32–8.2)
	13 case-control studies / 13 badań kliniczno-kontrolnych	in patients with silicosis undefined status / u pacjentów bez uwzględu na występowanie pylicy krzemowej [RR (95% CI)]: 1.41 (1.18–1.70)
	1 case-control study / 1 badanie kliniczno-kontrolne	in patients without silicosis / u pacjentów, którzy nie chorują na pylicę krzemową [RR (95% CI)]: 0.97 (0.68–1.38)
	total case-control studies / wszystkie badania kliniczno-kontrolne	total / ogółem [RR (95% CI)]: 1.41 (1.18–1.67)
Lacasse et al. / / i wsp. 2005 (51)	a meta-analysis of 4 case-control studies (silicosis patients) / metaanaliza 4 badań kliniczno-kontrolnych wśród pacjentów chorych na pylicę krzemową	OR (95% CI): 1.70 (1.15–2.53)
Kurihara et al. / / i wsp. 2004 (46)	a meta-analysis of 5 case-control studies: miners, ceramic workers, workers exposed to silica / / metaanaliza 5 badań kliniczno-kontrolnych wśród: pracowników kopalni, osób pracujących przy produkcji wyrobów ceramicznych, pracowników narażonych na działanie krzemionki	in lung cancer patients – all with silicosis/ u chorych na raka płuca i pylicę krzemową [RR (95% CI)]: 1.89 (1.45–2.48)
	a meta-analysis of 6 cohort studies (miners, slate quarry workers, silica brick workers, other workers expose to silica), 2 case-control studies (ceramic workers and lung cancer patients) / / meatanaliza 6 badań kohortowych wśród pracowników kopalni, osób pracujących przy wydobyciu łupków, produkcji cegły silikatowej oraz innych pracowników narażonych na działanie krzemionki; 2 badań kliniczno-kontrolnych wśród osób pracujących przy produkcji wyrobów ceramicznych oraz chorych na raka płuca	non-silicotic subjects with silica exposure / u osób, które nie zachorowały na pylicę krzemową, a które były narażone na działanie krzemionki [RR (95% CI)]: 0.96 (0.81–1.15)
Steenland et al. / / i wsp. 2001 (45)	a pooled analysis of 9 cohort studies – US: diatomaceous, granite, industrial sand, gold mine; China: pottery, tin and tungsten mine; Finnish: granite; Australia: gold mine / zbiorcza analiza 9 badań kohortowych – zatrudnieni w: Stany Zjednoczone: kopalniach ziemi okrzemkowej, granitu, piasku przemysłowego, złota; Chiny: przemyśle ceramicznym, kopalniach cyny i wolframu; Finlandia: kopalni granitu; Australia: kopalni złota	lung cancer / rak płuca [SMR (95% CI)]: 1.2 (1.1–1.3)

Table 3. The risk of lung cancer due to occupational exposure to respirable crystalline silica (RCS) in meta-analysis studies – cont.
Tabela 3. Ryzyko zachorowania na raka płuca z powodu narażenia na działanie respirabilnej krystalicznej krzemionki (RCS) w metaanalizach badań epidemiologicznych – cd.

References Piśmiennictwo	Study Badanie	Results Wyniki
Lacasse et al. / / i wsp. 2005 (51)	a pooled analysis of 27 cohort studies: mining, tunneling, quarring, refraktory trick industry, foundries, stone, glass and ceramic workers (all was silicosis patients) / zbiorcza analiza 27 badań kohortowych: wśród pracujących w górnictwie, przy drążeniu tuneli, w kamieniołomach, przy produkcji materiałów ogniotrwałych, w odlewniach, hutach szkła, w przemyśle kamieniarskim oraz przy produkcji materiałów ceramicznych (wszyscy chorzy na pylicę krzemową)	SMR (95% CI) for lung cancer (all with silicosis) / dla raka płuca (u osób chorych na pylicę krzemową): after adjustment for smoking (4 cohort studies) / po uwzględnieniu palenia (4 badania kohortowe): 1.60 (1.33–1.93) after exclusion of smokers (10 cohort studies) / po wyłączeniu osób palących (10 badań kohortowych): 1.52 (1.02–2.26) after exclusion of underground miners (24 cohort studies) / po wyłączeniu pracowników kopalni pracujących pod ziemią (24 badania kohortowe): 2.47 (1.76–3.48) total / ogółem: 2.45 (1.63–3.66)

Abbreviations as in Tables 1 and 2 / Skróty jak w Tabelach 1 i 2.

The increased risk of lung cancer due to exposure to quartz and cristobalite depends primarily on:

- Silicosis diagnosis and the time elapsed since the diagnosis (1,10,33,46,50); RR or odds ratio (OR) of the lung cancer patients with silicosis is the highest, ranging from 1.7 (95% CI: 1.15–2.53) to 3.3 (95% CI: 1.32–8.2), while an increased risk was not recorded in the exposed groups without pathological changes in radiological image of the lung, and this increase was not significant and did not exceed the value of 1.19 (95% CI: 0.87–1.57) (44,46,49–51),
- Cumulative exposure to respirable crystalline silica and the maximum intensity of exposure (1,3,29,33,43,45,48); in the case of exposure to small doses – up to about 1–2 $mg/m^3 \times$years – the risk of lung cancer was not increased or the recorded increase was at the border of statistical significance (29,48), while in the case of higher exposure levels the RR or OR adopted values about 2.0 (29,43–45,48). According to Steenland et al. and Lacasse et al., the growing trend of the risk in response to higher cumulative exposure levels continues until about 6 $mg/m^3 \times$years, above which there is no further increase (45,48).

Just like silicosis, gender is another factor that may affect the level of cancer risk. In the studies by Olsson et al., OR of lung cancer in women exposed to silica was 2-fold higher than in men (47). Lung cancer risk is probably not dependent on the source of exposure or forms of crystalline silica (43). Interaction between the two risk factors for lung cancer i.e., tobacco smoking and exposure to silica has not been explained. The risk estimated among the silica-exposed tobacco smokers is several times higher as compared with the risk in the exposed non-smokers (44). The character of interaction between tobacco smoking and exposure to silica can be described as being somewhere between additive and multiplicative (43,46).

Comparison of the RR or OR values for different lung carcinogens in work environments seems to indicate that crystalline silica appears to be a weaker carcinogen than soluble nickel, arsenic, cadmium and chromiumVI (33,45,46).

Cancers other than lung cancer

People who are occupationally exposed to crystalline silica, apart from having an elevated frequency of lung cancer were found to be at a higher risk of other cancers, such as stomach, liver, esophageal, pancreatic, intestinal, bone, pharyngeal, skin, brain and kidney

cancer (1,3,39). However, epidemiological studies have not definitively proven a relationship between exposure to crystalline silica and the occurrence of tumors at locations other than the lung (3,41).

Autoimmune diseases

Activation of the immune system by crystalline silica deposited in the alveoli is linked with an increased risk of autoimmune diseases in the silica-exposed patients: systemic sclerosis (scleroderma), rheumatoid arthritis or Caplan's syndrome, systemic lupus erythematosus, systemic vasculitis (3,39,52–55). Elevated frequencies were also recorded for sarcoidosis, dermatomyositis, dermatopolymyositis, autoimmune hemolytic anemia (3,39,52).

The pathogenesis of autoimmune diseases in the patients exposed to silica has not been yet completely explained. Based on experimental results, it is believed that crystalline silica may show an adjuvant effect by non-specifically enhancing the immune response to the dust, and triggering or enhancing the development of the quoted diseases (39,52,54).

The frequency of those diseases may be also affected by genetic susceptibility and some environmental factors, such as the relationship between the observed number of cases of rheumatoid arthritis and the geographic latitude of the habitats of the silica-exposed people (53). The development of scleroderma seems to result also from silica directly penetrating the skin of the exposed people (3). The increased incidence of arthritis and systemic rheumatoid sclerosis in the patients diagnosed with silicosis has been confirmed by epidemiological studies (3,39,52,54).

In contrast, the relationship between exposure to crystalline silica and other autoimmune diseases is not obvious, although some studies reported increased OR of the development of these diseases in the exposed people (39,56).

Chronic kidney diseases

Chronic renal disease observed in an increased number of cases among the workers exposed to crystalline silica is supposed to be associated with 3 possible mechanisms of their development: deposition in the kidneys of immune complexes resulting from the inflammatory processes taking place in the lungs; disorders of the immune system leading to autoimmunization; or direct nephrotoxicity of the silica transported by blood from alveoli to the kidneys (3,39,57–59).

Harmful effects of crystalline silica are associated with a variety of chronic kidney diseases, including glomerulonephrititis and end-stage kidney diseases. The results of epidemiological studies on the relationship between exposure and various pathological changes in the kidneys are not clear (11,38,39,58,59). The risk of chronic kidney disease assessed by Steenland et al. (11) based on pooled analyses of the results of three cohorts was increased in proportion to the exposure to crystalline silica; the OR in the upper quartile of cumulative silica exposure above 1.67 mg/m^3×years was 3.93 (95% CI: 1.31–11.76), and the SMR for all the exposed was 1.41 (95% CI: 1.05–1.85).

In a recent case-control study, the OR of the development of chronic renal disease in the exposed people was equal to 1.40 (95% CI: 1.04–1.89) and was also dependent on the dust dose; in a group of less exposed people the OR was 1.20 (95% CI: 0.77–1.86), and in the longer exposure group it was 1.76 (95% CI: 1.14–2.71). Similar values of the OR were assessed for renal insufficiency, 1.74 (95% CI: 1.05–2.87) and for end-stage kidney diseases, 1.75 (95% CI: 0.76–4.01) although the latter value was not statistically significant (59).

Health effects in the context of the current limit values

For silicosis (a critical effect of exposure to respirable crystalline silica, also essential for the possibility of secondary development of lung cancer), the NOAEL (No Observed Adverse Effect Level) has not been established (60). Occupational exposure limit values for crystalline silica are currently set at levels which do not eliminate, although significantly restrict, the risk of adverse health effects.

In a large number of countries in Europe and worldwide, the hygienic standards for this harmful agent are at the level recommended by the NIOSH (3) and the European Commission SCOEL (Scientific Committee on Occupational Exposure Limits) (60), i.e., 0.05 mg/m^3 or 2-fold higher – 0.1 mg/m^3.

Epidemiological studies of the exposed people show that exposure to 0.05 mg/m^3 (Table 4) is associated with the risk of silicosis ranging from about one to several percent (16,22,26), one percent additional risk of lung cancer (45) and a few percent risk of other respiratory (excluding infectious) diseases (22).

Exposure to quartz and cristobalite at a concentration of 0.1 mg/m^3 causes silicosis development in at least 1 (to several dozen) percent of people (16,22,23,57) and other pulmonary diseases (except cancer) in 10% of the exposed people (22). In this exposed group, the additional risk of death from both pneumoconiosis

Table 4. The risk of health effects of exposure to respirable crystalline silica (RCS) at concentrations close to the current limit values
Tabela 4. Ryzyko wystąpienia skutków zdrowotnych związanych z narażeniem na respirabilną krzemionkę krystaliczną (RCS) występującą w stężeniu zbliżonym do obowiązujących wartości dopuszczalnych

Exposure to RCS Narażenie na działanie RCS			Risk of health effects or subgroup Ryzyko skutków zdrowotnych albo podgrupy		References Piśmiennictwo
concentration stężenie [mg/m³]	duration [years] czas narażenia [w latach]	cumulative exposure [mg/m³×years] skumulowane narażenie [mg/m³×liczba lat]	ILO cat. / kat. ILO (9)	%	
				risks of silicosis / ryzyko zachorowania na pylicę krzemową	
0.025–0.05	40	1.00–2.00	> 1/0	13.0	Kreiss et al. / i wsp. 1996 (26)
0.05	40	2.00	> 1/1	0.4	Muir et al. / i wsp. 1989 (16)
0.05	45	2.25	> 1/0	7.5	Park et al. / i wsp. 2002 (22)
0.05–0.1	40	2.00–4.00	> 1/0	34.0	Kreiss et al. / i wsp. 1996 (26)
0.05–0.1	40	2.00–4.00	> 1/1	2.0–11.0	Chen et al. / i wsp. 2005 (19)
0.10	45	4.50	> 1/0	14.0	Park et al. / i wsp. 2002 (22)
0.10	40	4.00	> 1/1	1.2	Muir et al. / i wsp. 1989 (16)
0.10	45	4.50	> 1/1	35.0	Steenland and / i Brown 1995 (23)
0.10	45	4.50	> 1/1	47.0–77.0	Steenland 2005 (57)
				excess lifetime risk of lung disease other than cancer and infectious diseases / / dodatkowe całożyciowe ryzyko zachorowania na choroby płuc inne niż rak czy choroby zakaźne	
0.05	45	2.25	–	5.4	Park et al. / i wsp. 2002 (22)
0.10	45	4.50	–	10.0	
				excess lifetime risk of lung cancer / / dodatkowe całożyciowe ryzyko zachorowania na raka płuca	
0.05	40	2.00	–	1.3	Steenland et al. / i wsp. 2001 (45)
0.10	40	4.00	–	1.7	Steenland et al. / i wsp. 2001 (29)
				excess lifetime risk of end–stage renal disease / dodatkowe całożyciowe ryzyko wystąpienia schyłkowej niewydolności nerek	
0.10	45	4.50	–	5.1	Steenland 2005 (57)
				risk of death from silicosis / ryzyko zgonu z powodu pylicy krzemowej	
0.025–0.05	45	1.12–2.25	–	0.6 (at the age of 75 years) / (w wieku 75 lat)	Steenland 2005 (57)
0.05	45	2.25	–	0.6 (at the age of 65 years) / (w wieku 65 lat)	Mannetje et al. / i wsp. 2002 (27)
0.06–0.1	45	2.70–4.70	–	1.9 (at the age of 75 years) / (w wieku 75 lat)	Steenland 2005 (57)
0.10	45	4.50	–	1.3 (at the age of 65 years) / (w wieku 65 lat)	Mannetje et al. / i wsp. 2002 (27)
				excess risk of death from lung cancer / / dodatkowe ryzyko zgonu z powodu raka płuca	
0.10	45	4.50	–	1.7	Steenland 2005 (57)
				excess risk of death from renal disease / / dodatkowe ryzyko zgonu z powodu niewydolności nerek	
0.10	45	4.50	–	1.8	Steenland 2005 (57)

ILO – International Labour Organization / Międzynarodowa Organizacja Pracy.

and lung cancer is almost 2% (27,57). The risk of death from one of the renal diseases, a category heretofore rarely considered as the effect of exposure to crystalline silica, reaches a similar value (57).

All of the above values of the risks associated with exposure to quartz and cristobalite exceed the threshold of acceptable risk, i.e., 0.1%.

CONCLUSIONS

The review of the results of this research on the health effects of exposure to respirable crystalline silica confirms its multi-faceted harmful effects. In addition to the diseases developing at the places of respirable dust deposition, i.e., silicosis and its complications, lung cancer and other non-neoplastic respiratory diseases, exposure to respirable crystalline silica may be responsible for the development of diseases in other organs, such as kidneys, as well as systemic diseases, such as systemic silicosis, autoimmune diseases (systemic sclerosis, rheumatoid arthritis, systemic lupus erythematosus, systemic vasculitis).

The prevalence of harmful health effects of respirable crystalline silica mainly depends on the concentration of the dust in the air in the workplace and the exposure time. Prolonged, a 40- to 45-year exposure, even at exposure levels close to the current limit values of 0.05–0.1 mg/m^3, does not exclude, but significantly reduces, the risk of developing silicosis, lung cancer and other non-malignant respiratory and renal diseases.

Complete elimination of crystalline silica dust from the work environment is not feasible, and the main way to reduce adverse health effects of the exposure is to minimize exposure and the use of personal respiratory protection in situations when concentrations of particulate matter cannot be reduced. Further studies on the influence of the surface characteristics of particles of crystalline silica in their interactions with cells, investigations into mechanisms and carcinogenic potential of silica and its interaction with tobacco smoke, and comorbid dusts in the work environment could contribute to more effective protection of the health of the exposed workers.

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