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Quartz, Silicosis and Lung Cancer: Meta-analysis of the Epidemiological Studies

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■ Goal

Planning effective measures to prevent lung cancer among persons exposed to quartz

Background

- **1997: IARC classifies quartz as carcinogenic to humans.**
- **1999: German Research Society (DFG) and German Commission for Maximum Workplace Concentrations (MAK) classify quartz dust as carcinogenic to humans.**



■ Reservations

- **Reservations in the classification by the IARC**
- **No international agreement on the possible classification of quartz dust and on the effects of further exposure (confounders, bias)**
- **Some of the study results are contradictory.**



■ Planning preventive measures

- **Specific questions:**
In cases of quartz exposure, are there exceptionally high incidences of lung cancer linked to
 - silicosis and/or
 - smoker status?
- **How many persons are affected?**
- **Not the general question:**
Does exposure to quartz cause cancer?

■ Overview and summary

- ... of findings on possible associations between quartz dust exposure, silicosis, smoking and lung cancer
- The latest, complete findings



■ **Meta-analysis**

Epidemiological studies on lung cancer in relation to

- **Quartz dust exposure**
- **Silicosis**
- **Smoking**

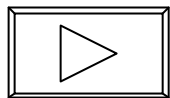


■ Implementation of the meta-analysis

- 1. Worldwide literature search
→ 330 publications on the subject**
- 2. Selection of the most recent publications
→ 157 studies**
- 3. Comparison of the publications with 35 reviews/
meta-analyses**
- 4. Consideration of studies that take account of
silicosis and smoker status (N = 16)**

■ Summary of the studies

- 1. Overview and quantitative summary of the studies without weighing of study quality (results available, see advance publication in BIA-Report 2/2001)**
- 2. Analysis and summary with weighing of study quality (initial results)**
- 3. Attempted (post hoc) adjustment for smokers (initial results)**



Quartz, Silicosis, Smoking and Lung Cancer

Relative lung cancer risk for smokers and non-smokers

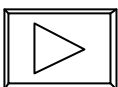
Author	S	Silicotics			
		Smokers		Non-smokers	
		N _{LC}	RR (95%-CI)	N _{LC}	RR (95%-CI)
Zambon, 1987	Co	54	2.11 (1.62-2.75)	4	0.79 (0.21-2.01)
Infante-R., 1989	Co	44	4.84 (4.16-5.71)	0	0 (0-2.51)
Rubino, 1990	P	38	1.74 (1.32-2.15)	10	1.58 (0.85-2.95)
(Chiyotani, 1990)	Co	33	5.41 (4.60-6.22)	4	2.22 (0.73-3.71)
Amandus, 1991b	Co	9	2.17 (0.99-4.12)	1	0.53 (0.01-2.95)
Carta, 1991	Co	7	4.11 (2.1-8.1)	4	0.69 (0.3-1.8)
Chia, 1991	Co	8	2.16 (0.93-4.25)	1	1.30 (0.03-7.22)
Partanen, 1994	Co	25	6.67 (4.32-9.90)	1	0.44 (0.01-2.42)
Amandus, 1995	Co	n.r.*	3.4 (2.0-5.3)	n.r.*	1.7 (0.5-3.9)
Dong, 1995	Co	21	2.34 (1.45-3.58)	12	2.13 (1.10-3.72)
Rosenman, 1995	P	10	1.82 (1.18-2.81)	4	1.48 (0.43-2.86)
Wang, 1996	Co	72	2.57 (2.0-3.3)	32	2.09 (1.4-3.0)
Oksa, 1997	Co	9	6.1 (2.8-11)	0	1.1 (0-3.5)
(Ebihara, 1998b)	Co	26	3.88 (2.64-5.70)	9	2.87 (1.49-5.50)
Mastrangelo, 1988	CC	48	19.7 (5.1-89.7)	2	5.3 (0.5-43.5)
Lagorio, 1990	CC	15	7.09 (2.47-20.32)	0	0 (0-11.20)
Hnizdo, 1997	NCC	14	19.66 (5.7-67.77)	1	4.1 (0.3-52.3)
Mean rel. risk	Co		2.82 (2.06-3.85)		1.27 (0.81-2.00)
Homogeneity P			P _{Hom} < 0.00001		P _{Hom} = 0.0057
Mean rel. risk	CC		10.48 (3.96-27.73)		2.21 (0.27-18.18)
Homogeneity P			P _{Hom} = 0.2592		P _{Hom} = 0.2447

* n.r. = not reported

Quartz, Silicosis, Smoking and Lung Cancer

Relative lung cancer risk for smokers and non-smokers

Author	S	Non-silicotics			
		Smokers		Non-smokers	
		N _{LC}	RR (95%-CI)	N _{LC}	RR (95%-CI)
Zambon, 1987	Co				
Infante-R., 1989	Co				
Rubino, 1990	p				
(Chiyotani, 1990)	Co				
Amandus, 1991b	Co	106	1.67 (1.36-2.02)	5	0.24 (0.08-0.57)
Carta, 1991	Co				
Chia, 1991	Co				
Partanen, 1994	Co				
Amandus, 1995	Co				
Dong, 1995	Co	21	1.20 (0.74-1.83)	7	0.85 (0.34-1.75)
Rosenman, 1995	P				
Wang, 1996	Co				
Oksa, 1997	Co				
(Ebihara, 1998b)	Co				
Mastrangelo, 1988	CC	85	10.4 (2.9-44.4)	1	1.3 (0-13.8)
Lagorio, 1990	CC	15	2.16 (0.84-5.59)	3	1.9 (0.4-10.2)
Hnizdo, 1997	NCC	54	7.74 (2.76-21.73)	2	1.0 (Reference)
Mean rel. risk	Co		1.51 (1.12-2.03)		0.47 (0.13-1.61)
Homogeneity P			P _{Hom} = 0.1597		P _{Hom} = 0.0505
Mean rel. risk	CC		4.38 (0.95-20.26)		1.83 (0.39-8.46)
Homogeneity P			P _{Hom} = 0.0551		P _{Hom} = 0.8825



■ Summary (part 1)

- **Statistical summary is possible as all studies take the general population as the reference population.**
- **Compared to the general population (smokers and non-smokers), enhanced risks with statistical significance are only perceived among smokers.**
- **Reservations about interpretation:
From the comparison with the general population (i.e. smokers and non-smokers mixed),**
 - **the risks of exposed smokers may be overestimated, and**
 - **the risks of exposed non-smokers may be underestimated.**

■ Summary of the studies

- 1. Overview and quantitative summary of the studies without weighting of study quality (results available, see advance publication in BIA-Report 2/2001)**
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Quartz, Silicosis, Smoking and Lung Cancer

■ Evaluation of exposure in 16 examined studies

Publication	Trade/profession of exposed persons	Evaluation of exposure based on				
		Profession/trade	Job description	Duration of employment	Period of exposure	Semi-quantitative or quantitative dimensions
Amandus, 1991a	Mining	--	No	Yes	Yes	No
Amandus, 1995	Various	No	No	No	No	No
Carta, 1991	Mining, quarrying	No	No	Yes*	No	Yes
Chia, 1991	Quarrying	--	No	Yes	No	No
Chiyotani, 1990	Various	Yes*	Yes*	Yes	No	No
Dong, 1995	Refractory industry	--	No	(Yes)	No	No
Hnizdo, 1997	Mining	--	No	Yes	No	Yes
Infante-Rivard, 1989	Various	Yes	No	Yes	Yes	No
Lagorio, 1990	Clays/quarrying	Yes	Yes	Yes	No	No
Mastrangelo, 1988	Various	Yes	No	Yes	No	No
Oksa, 1997	Various	No	No	No	No	No
Partanen, 1994	Various	Yes	No	No	No	No
Rosenman, 1995	Various	No	No	Yes	No	No
Rubino, 1990	Various	Yes	Yes	Yes	No	No
Wang, 1996	Various	Yes	No	Yes	No	No
Zambon, 1987	Various	Yes	No	Yes	No	No

* In the nested case control study



Quartz, Silicosis, Smoking and Lung Cancer

■ Available data on smoking in the 16 studies

Reference	Data source	Information in %	Proportion of smokers			Reference data
			Active	Ex	Never	
Amandus, 1991a	During study, 1959-61	>99	71	11	18	Smokers/non-smokers combined; sufficient for comparison of silicosis and non-silicosis sufferers
Amandus, 1995	Medical examinations, information on smoking available since 1964	64	67		33	Smokers/non-smokers combined; sufficient for reference group: Miners (or) and CWP miners (coal)
Carta, 1991	Hospital records; survey at the time of referral	100	50	15	35	Smokers/non-smokers combined
Chia, 1991	Register data	100	84		16	Smokers/non-smokers combined
Chiyotani, 1990	Hospital records; survey at the time of referral	>99	54	35	11	Smokers/non-smokers combined
Dong, 1995	Not Known	Not Known	N.K.	NK	N.K.	Probably smokers/non-smokers combined
Hnizdo, 1997	Questionnaire, 1968-72; checked against medical file	100	69	20	12	-

(Table continued)

Quartz, Silicosis, Smoking and Lung Cancer

■ Available data on smoking in the 16 studies

(Continued)

Reference	Data source	Information in %	Proportion of smokers*			Reference data
			Active	Ex	Never	
Infante-Rivard, 1989	Register data; status at time of compensation	75	50	43	7	Smokers/non-smokers combined
Lagorio, 1990	Survey of relatives	100	76**		24**	Non-exposed non-smokers
Mastrangelo, 1988	Hospital records	100	92		8	-
Oksa, 1997	Hospital records, 1977-85	100	34	49	18	Smokers/non-smokers combined
Partanen, 1994	Random sample of 304 silicosis cases in 1970 questionnaire	37	37	49	14	Smokers/non-smokers combined
Rosenman, 1995	Telephone survey (cases/relatives)	Not Known	NK	NK	NK	Smokers/non-smokers combined; anticipated number from survey
Rubino, 1990	Compensation files	>66	NK		NK	Smokers/non-smokers combined; corrected anticipated values
Wang, 1996	Questionnaire	Not Known	NK	NK	NK	Smokers/non-smokers combined
Zambon, 1987	Compensation files; survey when filing for compensation.	93	80	8	13	Smokers/non-smokers combined

■ Summary (part 2)

1. Persons exposed to quartz dust without contracting silicosis

No epidemiological evidence for an association between quartz dust exposure and lung cancer

■ Summary (part 2)

2. Persons exposed to quartz dust who contract silicosis

Causal association between quartz dust exposure and lung cancer is not epidemiologically substantiated by these studies.

- Models:**
- **Silicosis causes lung cancer directly or**
 - **Silicosis serves as a marker for:**
 - (high) exposure
 - individual sensitivity
 - smoking

But a statistical relationship is evident ($RR \approx 2$).

■ Summary (part 2)

3. The effect of smoking must be taken into account when interpreting the results.

Comparable results on the effect of smoking with quartz exposure are supplied by a study by P. Morfeld and K. Lampert (Saarbergbau):

- **Smokers contract pneumoconiosis more frequently (OR: 3.6; 95%-CI: 2.7-5)**
- **Lung cancer deaths in study only observed among smokers (among non-smokers: 0 observed cases from 11 expected)**

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Quartz, Silicosis, Smoking and Lung Cancer

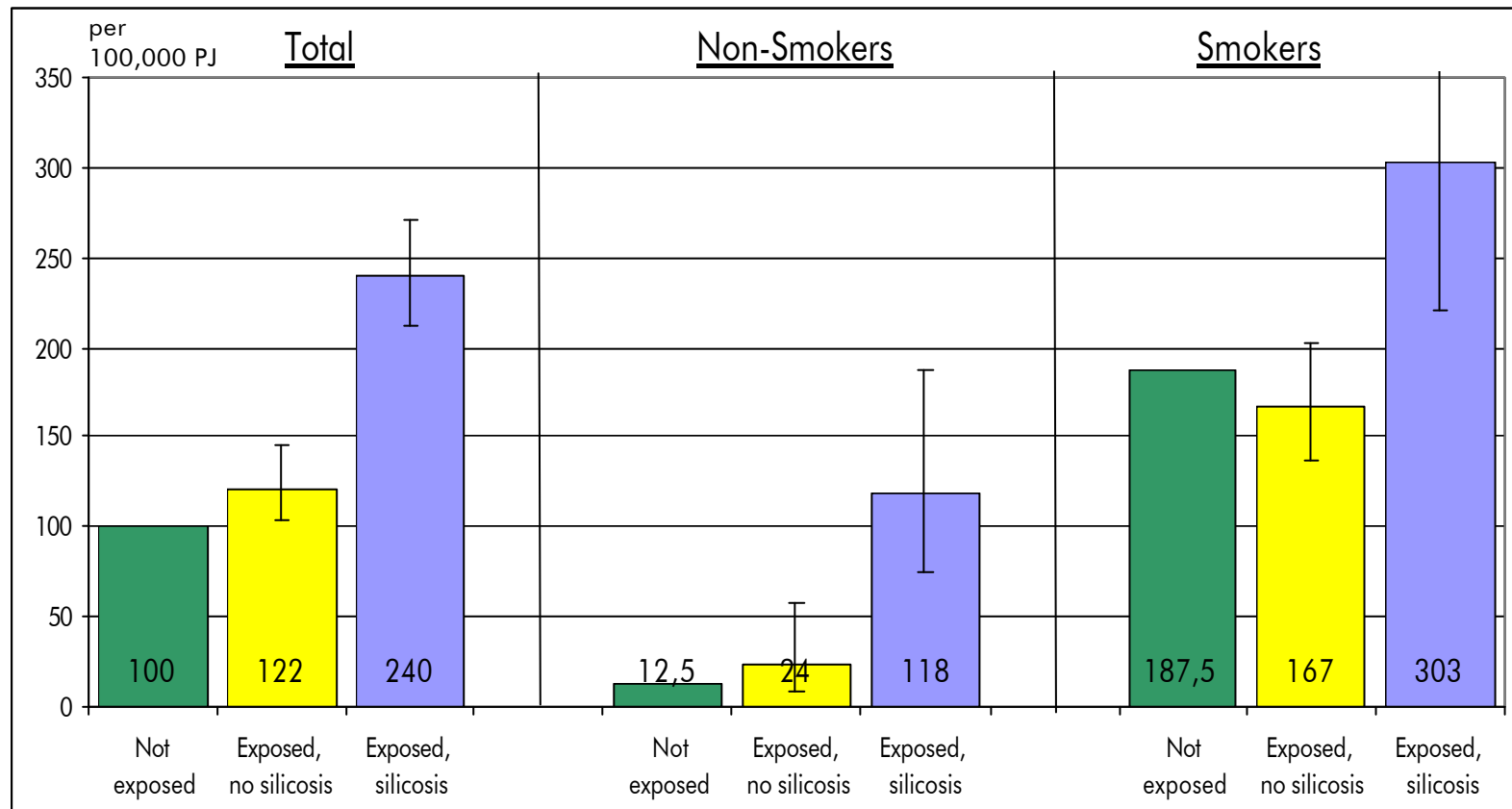
■ Results of indirect adjustment (SMR cohort studies)

Assumption: 50% smokers, $RR_{smk} = 15$

Author	Smokers		Non-smokers	
	SMR	Adj. RR	SMR	Adj. RR
- With silicosis				
Zambon, 1987	2.1 (1.6-2.7)	1.1 (0.9-1.4)	0.8 (0.2-2.0)	6.4 (1.6-16.0)
Infante-R., 1989	4.8 (4.2-5.7)	2.6 (2.2-3.0)	0.0 (0.0-2.5)	0.0 (0.0-20.0)
Rubino, 1990	1.7 (1.3-2.2)	0.9 (0.7-1.2)	1.6 (0.9-2.9)	12.8 (7.2-23.2)
Amandus, 1991	2.2 (1.0-4.1)	1.2 (0.5-2.2)	0.5 (0.01-3.0)	4.0 (0.1-24.0)
Carta, 1991	4.1 (2.1-8.1)	2.2 (1.1-4.3)	0.7 (0.3-1.8)	5.6 (2.4-14.4)
Chia, 1991	2.2 (0.9-4.3)	1.2 (0.5-2.3)	1.3 (0.0-7.2)	10.4 (0.0-57.6)
Partanen, 1994	6.7 (4.3-9.9)	3.6 (2.3-5.3)	0.4 (0.0-2.4)	3.2 (0.0-19.2)
Amandus, 1995	3.4 (2.0-5.3)	1.8 (1.1-2.8)	1.7 (0.5-3.9)	13.6 (4.0-31.2)
Rosenman, 1995	1.8 (1.2-2.8)	1.0 (0.6-1.5)	1.5 (0.4-2.9)	12.0 (3.2-23.2)
Wang, 1996	2.6 (2.0-3.3)	1.4 (1.1-1.8)	2.1 (1.4-3.0)	16.8 (11.2-24.0)
Oksa, 1997	6.1 (2.8-11.0)	3.3 (1.5-5.9)	1.1 (0-3.5)	8.8 (0.0-28.0)
Pooled	3.0 (2.2-4.2)	1.6 (1.2-2.2)	1.2 (0.8-1.8)	9.6 (6.4-14.4)
- No silicosis				
Amandus, 1991	1.7 (1.4-2.0)	0.9 (0.7-1.1)	0.2 (0.1-0.6)	1.8 (0.8-4.8)

Quartz, Silicosis, Smoking and Lung Cancer

■ Lung cancer frequency / smoker and silicosis status



■ Preventive approaches

Prevention	Reduction in lung cancer cases per year
of silicosis	118 / 100,000 persons exposed to quartz dust + silicosis
of smoking	164 / 100,000 smokers exposed to quartz dust

and

percentage of persons exposed to quartz dust (Information from publications)

- **Silicotics:** approx. 16 %
- **Smokers:** approx. 50 %

For every 100,000 persons exposed to quartz dust:

Prevention	Reduction in lung cancer cases per year
of silicosis	Approx. 19
of smoking	Approx. 82

Quartz, Silicosis, Smoking and Lung Cancer

- **Quartz, silicosis, smoking and lung cancer**

Results will be published in a BIA Report

