Quartz in Swedish iron foundries
– exposure and cancer risk

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Abstract

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The aims of the studies underlying this thesis were to assess the exposure to quartz in Swedish iron foundries and to determine the cancer morbidity for Swedish foundry workers. A cohort of 3,045 foundry workers and a final measurement database of 2,333 number of samples was established.

The exposure measurements showed high levels of respirable quartz, in particular for fettlers and furnace and ladle repair workers with individual 8 hr TWA (GM=0.041 and 0.052 mg/m^3; range 0.004-2.1 and 0.0098-0.83 mg/m^3). In our database, the quartz concentrations as 8hr TWAs of current and historical data varied between 0.0018 and 4.9 mg/m^3, averaging 0.083 mg/m^3, with the highest exposures for fettlers (0.087 mg/m^3) and furnace and ladle repair workers (0.42 mg/m^3). The exposure for workers using respirators assuming full effect when used were assessed quantitatively, revealing workers with actual exposure exceeding the occupational exposure limits.

Overall cancer morbidity was not increased, but the incidence of lung cancer was significantly elevated (SIR 1.61; 95 % CI 1.20-2.12). In the cohort study, significant associations between lung cancer and cumulative quartz exposure were detected for quartz doses of 1-2 mg/m^3* year (SIR 2.88; 95 % CI 1.44-5.16) and >2 mg/m^3* year (SIR 1.68; 95 % CI 1.07-2.52). These findings were not confirmed in the case-control analysis.

The agreement between the estimated exposure in our early historical model and the development model showed a regression coefficient of 2.42, implying an underestimation of the historical exposure when using the development model data. The corresponding comparison between the development and the validation model based on our survey data showed a B of 0.31, implying an overestimation of present exposures when using data from the validation model.

The main conclusions of the thesis are that certain foundry workers are still exposed to high levels of quartz, and the overall excess lung cancer could not be confirmed in the exposure-response analysis.

Keywords: Case-control study, crystalline silica, exposure assessment, iron foundry, lung cancer, morbidity, occupational hygiene, respirable quartz.

Publications

This thesis is based in the following papers, which are referred to in the text by their roman numerals:

I. Andersson L, Bryngelsson IL, Ohlson CG, Naystrom P, Lilja BG, Westberg H. (2009) Quartz and dust exposure in Swedish iron foundries. *J Occup Environ Hyg*; 6: 9-18.

II. Westberg H, Andersson L, Bryngelsson IL, Ngo Y, Ohlson CG. (2011) Cancer morbidity and quartz exposure in Swedish iron foundries. *Int Arch Occup Environ Health*, submitted.

III. Andersson L, Bryngelsson IL, Ngo Y, Ohlson CG, Westberg H. (2011) Exposure assessment and modeling of quartz in Swedish iron foundries for a nested case-control study on lung cancer. *J Occup Environ Hyg*, accepted for publication.

IV. Andersson L, Burdorf A, Bryngelsson IL, Westberg H. (2011) Estimating trends in quartz exposure in Swedish iron foundries – predicting past and present exposure. *Ann Occup Hyg*, pp.1-11, doi: 10.1093/annhyg/mer106

Abbreviations

ACGIH	American Conference of Governmental Industrial Hygienists
AIC	Akaike Information Criterion
AM	Arithmetic Mean
ANOVA	Analysis Of Variance
CI	Confidence Interval
DataRAM	Data-logging Real-time Aerosol Monitor
DL	Detection Limit
GM	Geometric Mean
GSD	Geometric Standard Deviation
IARC	International Agency for Research on Cancer
LOQ	Limit Of Quantification
NBOSH	National Board of Occupational Safety and Health
NIOSH	National Institute of Occupational Safety and Health
OEL	Occupational Exposure Limit
OR	Odds Ratio
OSHA	Occupational Safety and Health Administration
PAH	Polycyclic Aromatic Hydrocarbons
PEL	Permissible Exposure Limit
PF	Protection Factor
RPE	Respiratory Protective Equipment
XRD	X-ray diffraction
SCOEL	Scientific Committee on Occupational Exposure Limits
SD	Standard Deviation
SIR	Standard Incidence Ratio
SMR	Standard Mortality Ratio
SWEA	Swedish Work Environment Authority
TLV	Threshold Limit Value
TWA	Time-Weighted Average

Content

1 Introduction

The Swedish foundry industry produced in 2010 270,000 tonnes of castings, of which some 200,000 tonnes were from the iron foundries, employing 6,300 foundry workers (Nayström, 2011).

Quartz is a major part in the sand used for cores and moulds and is also used in the heat protecting layers in furnaces and ladles. Crystalline quartz is known to cause silicosis but is also classified as group 1 carcinogenic to humans by the International Agency for Research of Cancer (IARC) (IARC, 1997). Historically, IARC have considered employment in iron and steel foundries as associated with an increased incidence of cancer (IARC, 1987). In addition to quartz the foundry environment entails exposures to a large number of carcinogens, including polycyclic aromatic hydrocarbons (PAHs), formaldehyde, aromatic amines, benzene and asbestos.

Occupational exposure related to quartz is internationally still an issue, and with many Swedish foundry workers exposed to air levels of respirable quartz exceeding 0.1 mg/m^3, which has been the Occupational Exposure Limit (OEL) in Sweden since 1979. A proposal from EU:s Scientific Committee on Occupational Exposure Limits (SCOEL) to reduce the OEL by half for respirable quartz to 0.05 mg/m^3. No comprehensive survey regarding quartz exposure in Swedish iron foundries has been carried out since the late 1970s.

Workers in Swedish iron foundries are at certain jobs exposed to levels of quartz where personal protective equipment is required. The exposure for workers using respirators assuming full effect when used should be assessed quantitatively, revealing workers with actual exposure exceeding the OELs.

No epidemiological studies of cancer disease in Swedish iron and steel foundries have been carried out. At many work operations in iron foundries quartz exposure still occurs at high concentrations and there is a need to describe the exposure. International studies on quartz exposures and cancer in iron foundries are also sparse.

In epidemiological studies regarding cancer retrospective exposure assessment plays an important role, requiring measurement data for time periods in the past. The Swedish foundry industry has a long tradition of enforced workplace surveys with measurements of quartz from the 1960s and onwards. The availability of historical and present exposure information over almost 40 years presents a unique opportunity to study trends over time and to evaluate the validity of exposure models based on shorter periods over time.

This thesis aims to explore the quartz exposure in Swedish iron foundries today, and investigate the cancer risks in the iron foundry industry. Exposure modeling aspects and implications for our study based on our measurement database will be investigated.

2 Background

2.1 Quartz exposure in Swedish iron foundries

Occupational exposure related to quartz is internationally still an issue, in Europe more than 3 million workers are exposed to quartz at work (Kauppinen et al., 2000). In the US 100,000 workers are exposed to air levels of respirable quartz exceeding 0.1 mg/m^3 respirable dust, which has been the OEL in Sweden since 1979. Exposure at the levels of the Swedish OEL will lead to 13 new cases of silicosis per 1,000 exposed workers after 45 years of work. A reduction of the OEL to 0.05 mg/m^3 would still lead to 6 cases of silicosis per 1,000 exposed workers.

EU:s SCOEL presented a proposal in June 2002 to reduce the OEL by half for respirable quartz to 0.05 mg/m^3. Every year exposure measurements of respirable quartz are reported to the Swedish Work Environment Authority (SWEA) and a survey of their reports showed some 8 % of the measurements exceeding the Swedish OEL, 0.1 mg/m^3. A reduction of the OEL by half would imply some 22-23 % of the exposure measurements exceeding the OEL.

Exposure data from iron founding are described in a number of studies. In a Finnish study dust measurements were performed in 51 iron, 9 steel and 8 nonferrous foundries at which 4,316 foundry men were working (Siltanen, Koponen, Kokko, Engstrom, & Reponen, 1976). In this study a total of 3,188 samples were collected and the highest concentrations of respirable quartz were measured during fettling, sand mixing and shake out operations. In a national wide Swedish survey quartz exposure measurements were preformed in different industrial sectors such as mining, tunnelling, steel mills, ceramic industry, iron and steel foundries, representing 1,700 Swedish work places (Gerhardsson, 1976). The measurements of dust and respirable quartz revealed very high concentrations in most industrial sectors. In the iron foundries dust and respirable quartz concentrations as an average were exceeding the OELs for all job titles.

In a US study 1,743 samples were collected from 205 foundries, of which 111 were iron foundries, representing 1,149 samples. More than 40 % of the 8-hour daily time-weighted average (TWA) measurement data exceeded the Occupational Safety and Health Administration (OSHA) Permissible Exposure Limit (PEL) (Oudiz, Brown, Ayer, & Samuels, 1983). Surprisingly few surveys have been published in recent years, furthermore stressing the need of obtaining measurement data in the Swedish foundry industry.

2.2 Swedish foundry industry

There are three main types of foundries in Sweden: iron foundries, steel foundries and foundries using non-ferrous metals, here named metal foundries. Within the groups different alloys are moulded. The industry consists of a few big and a large number of small companies.

In 2010 6,300 persons were employed in the Swedish foundry industry and the foundries produced about 270,000 tonnes of foundry products, with the iron foundries as the largest producers of more than 200,000 tonnes of foundry products (table 1).

Table 1. Overview of the Swedish foundry industry in 2010 (Nayström, 2011)

Type of foundry	Number of foundries	Employees	Production 1,000 tonnes
Iron foundries	32	2,600	201.2
Steel foundries	13	950	18.1
Metal foundries	73	2,750	47.3
Total	**118**	**6,300**	**266.6**

The foundry industry's products are ferrous, steel or non-ferrous metal castings produced by pouring molten metal into moulds typically which are in total or in parts made of bounded quartz sand. The foundry industry is an important supplier to the automotive industry, mechanical workshops, and other industries.

There has been a reduction of quartz exposure and a reduction of silicosis cases in the past 20 years. This has been achieved by general improvement in the physical work environment, built-in of dusty transports and administration of material, improvement of the hygiene in the work premises, technical improvement resulting in elimination of high exposed work operations and improvement in the use of respirators (Nayström, 2011).

2.2.1 Work operations in the iron foundry industry

General work operations in the foundry industry are melting, sand mixing, core making, moulding, casting, shake out and fettling (figure 1). Maintenance, transportation and cleaning are other work operations generally occurring. Maintenance and repair of furnaces and ladles are performed less frequently in most of the foundries.

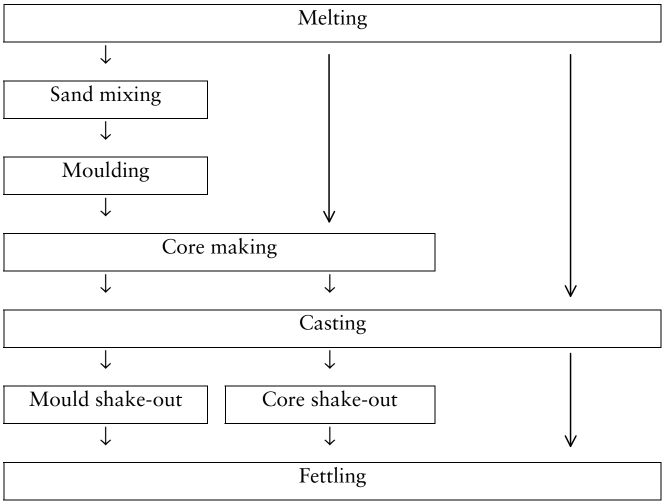


Figure 1. Work operations in iron foundries

2.3 Exposure assessment

2.3.1 Sampling strategy and sampling techniques

When monitoring the personal air exposure, the concentration of the agent of interest is quantified in the persons breathing zone, representing the inhaled air. Dermal exposure as well as ingestion can also occur and contribute to the total personal dose but the airborne exposure dominates in most work environments

(Mulhausen & Damiano, 1998). For dust and respirable quartz inhalation is the most important route of exposure.

Various sampling methods exist for determining aerosol air concentrations. Personal, breathing zone and general air samples can be used. Personal samples are devices attached to the workers clothing as close as possible to the mouth. Aerosols are collected on a filter placed in a monitor connected to a pump carried by the worker (Swedish Standard, 1997). This sampling is normally performed for a longer time period, between 1-8 hours (Swedish Standard, 1994, 1995). For real time monitoring of aerosols a data logger can be used for different substances such as dust providing continuous air concentration levels (Lynch, 1994).

In designing a sampling strategy, environmental variability, purpose of the measurement, selection of workers, sampling period, sampling time and sampling techniques are considered (Liedel & Busch, 1994). The result from exposure assessments can be used for comparison with occupational exposure limits, evaluation of work environment improvements, surveillance and general monitoring programmes as well as various comparisons of sampling sand analytical methods (Swedish Standard, 1994, 1995). They are also used in epidemiological studies where a relationship between exposure and health are studied.

2.3.2 Variability in exposure measurement data

In general the sampling and analytical errors play a minor role compared to the overall exposure variability (Kromhout, Symanski, & Rappaport, 1993). Geometric mean and geometric standard deviation are often used when describing the exposure since air concentrations of different substances are often approximately log normal distributed. Systematical and analytical sampling errors can be avoided by using calibrated sampling equipment and a laboratory participating in quality control programs, random errors are described by using statistical techniques. (Swedish Standard, 1994, 1995)

The within- and between-worker variability as well as the overall variability of air concentrations are important to analyse (Kromhout et al., 1993; Rappaport, 1991). Many factors can influence the variation such as work operation, task performed, type of production and production rate. Ventilation, temperature and humidity are environment characteristics to consider (Swedish Standard, 1994).

2.3.3 Occupational exposure limits

OEL is a generic term used to represent allowable concentration or intensity of the agent in the work environment. The OEL used in this study is defined as the TWA concentration for an 8-hour workday to which almost all workers may be exposed repeatedly, day after day, without adverse health effect. Air concentration data are compared to OEL according to the Swedish standard by SWEA (table 2) (SWEA, 2005). EU:s SCOEL presented a proposal in June 2002 to reduce the OEL by half for quartz to 0.05 mg/m^3, and furthermore the American Conference of Governmental Industrial Hygienists-Threshold Limit Values (ACGIH-TLV) committee has adapted an even lower concentration level 0.025 mg/m^3 (ACGIH, 2006).

Table 2. Swedish and European SCOEL occupational exposure limits (OEL) and the American recommended ACGIH-TLV for respirable dust, quartz, cristobalite and tridymite (ACGIH, 2006)

Substance	**Swedish OEL (mg/m^3)**	**EU:s SCOEL OEL (mg/m^3)**	**ACGIH-TLV (mg/m^3)**
Respirable dust	5		3
Respirable quartz	0.1	0.05	0.025
Cristobalite	0.05		
Tridymite	0.05		

2.4 Epidemiological evaluation

2.4.1 Cohort study

In occupational epidemiology, cohort studies are commonly used when studying association between exposure and disease. In a cohort study a group (i.e. cohort) of subjects is followed over time to assess whether they develop the disease of interest or not (Nieuwenhuijsen, 2007). A risk estimate (e.g. relative risk or incidence rate ratio) is obtained by comparing the disease rate in subpopulations with different levels of exposure or external control. A cohort study can be prospective or retrospective. The retrospective cohort study design offers valuable alternative to the prospective cohort design for studying relatively rare health outcomes, including those with long induction and latency intervals (Harvey. Checkoway, Pearce, & Kriebel, 2004).

2.4.2 Nested case-control study

In a case-control study the exposure of diseased subjects (cases) is compared to exposure of randomly selected controls from the underlying sampling population. A risk estimate (e.g. odds ratio) is obtained by dividing the odds of exposure for the cases with the odds of exposure for the controls. A case-control study nested within the cohort reduces the effort required for exposure assessment but also results in a smaller number of subjects (Nieuwenhuijsen, 2007). In addition, the nested case-control study has the adventage of greater efficiency of obtaining data on potential confounding factors due to the smaller size of the study (Harvey. Checkoway et al., 2004).

2.5 Particles

2.5.1 Properties

Dust particles appears everywhere in the environment; airborne as well as deposited on surfaces. It is a heterogen substance of many organic and inorganic compounds with different physical and chemical qualities. Inorganic dust and quartz is among the substances found in dust at iron and steel foundries.

Dust particles are classified into different fractions depending on the size of the particle. The different size fractions represent deposition in different parts of the airways. A standard for characterization of aerosols defines dust particles as inhalable, thoracic and respirable fraction (table 3) (Swedish Standard, 1993).

Table 3. The definition and particle size for inhalable fraction, thoracic fraction and respirable fraction (Swedish Standard, 1993)

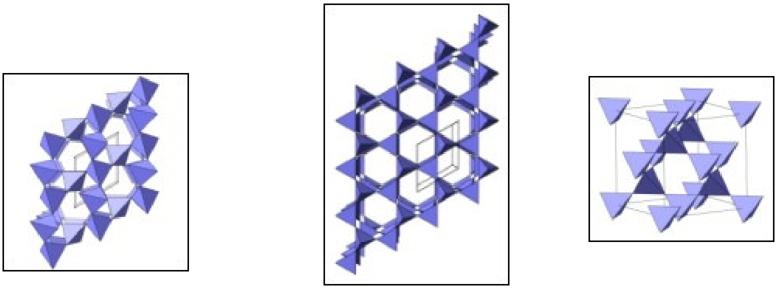
Fraction	Definition	Particle size
Inhalable fraction	particles that can be inhaled by the mouth and nose	< 50-100 µm
Thoracic fraction	particles that pass the larynx	< 10 µm
Respirable fraction	particles that penetrate to the parts of the respiratory passage that lack cilia	< 4 µm

2.6 Crystalline silica: quartz, cristobalite and tridymite

2.6.1 Properties

A group of minerals composed of silicon and oxygen, the two most abundant elements in the earth's crust, have been named silica. Silica exists in many different forms in spite of its simple chemical formula, SiO_2. It is found commonly in the crystalline state but occurs also in the amorphous (non-crystalline) state. Crystalline silica is hard, chemically inert and has a high melting point, which are prized qualities in various industrial uses (Hägg, 1984).

The minerals quartz, cristobalite and tridymite (figure 2) are three different forms of crystalline silica and quartz is by far the most common form. Quartz is one of the most common minerals on the earth's surface and it is found in almost every type of rock i.e. igneous, metamorphic and sedimentary. Since it is so abundant, it is present in nearly all mining operations. Quartz is found in many different materials, with sandstone being almost pure quartz. Respirable quartz is present in the environment independent of industrial activities (Gerhardsson et al., 1974).



Quartz Tridymite Cristobalite

Figure 2. Crystal structures of quartz, tridymite and cristobalite (pictures from Crystal-maker™)

Cristobalite and tridymite are found in some igneous rocks although they are not abundant in nature. Cristobalite and tridymite are obtained when quartz is heated at high temperature (figure 3), for example during the production of refractory materials (SWEA, 1992). At the foundry, these high temperatures can be obtained when melting the iron.

$$\text{quartz} \xrightarrow{870^{\circ}C} \text{tridymite} \xrightarrow{1470^{\circ}C} \text{cristobalite}$$

Figure 3. Steps of transformation from quartz to tridymite and cristobalite (SWEA, 1992)

Occupational exposure to respirable quartz occurs in many industries for example quarrying, mining, stone crushing, foundry work, brick and tile making, some refractory processes, construction work and ceramic industries. Exposure in the foundry industry is due to quartz sand used in the binders for cores and moulds (green sand moulding) and in the heath protective layer in furnaces and ladles.

Respirable dust particles are very small (<5 µm) and they take a very long time to settle once they are airborne. Minor emissions of dust into the workplace air can therefore lead to significant occupational exposure and it may remain airborne in the workplace for days in situations where the air is constantly stirred-up and where no fresh air is being introduced.

2.6.2 Health effects

At the workplace, people are rarely exposed to pure quartz. The airborne dust is usually composed of a mixture of quartz and other materials and the individual response is likely to depend on many factors as the nature (particle size and surface chemistry), the quartz content of the dust, and the area of deposition. The properties of the dust also depends on the geological source and can change during the industrial process (CICAD, 2000). These property variations can cause changes in the biological activity and toxicity of the inhaled dust. The dust fraction, the extent and nature of personal exposure (duration, frequency and intensity, which may be influenced by the working methods) as well as personal psychological characteristics and smoking habits may also be depending factors for the individual response.

Inhalation and deposition of dust containing quartz produces the fibrotic disease silicosis. The severity of silicosis can vary greatly, from "simple silicosis" to "progressive massive fibrosis". A risk assessment of quartz, silicosis and lung cancer shows that the exposure-response relation is not linear and reduction of dust exposure would have a greater than linear benefit in terms of risk reduction. The available data suggests that 30 years exposure at 0.1 mg/m^3 might lead to a lifetime silicosis risk of 25 %, whereas reduction of the exposure to 0.05 mg/m^3 might reduce the risk to less than 5 % (Finkelstein, 2000). Implementing appropriate measures, such as improved work practices, engineering controls, respiratory protective equipment and training programmes, to reduce exposure to quartz-containing dusts can reduce future cases of silicosis.

In Poland a mortality cohort study was carried out on 11,224 men with pneumoconiosis diagnosed during the period 1970-1985 (Starzynski, Marek, Kujawska, & Szymczak, 1996). Mortality from lung cancer was significantly elevated in the group of metallurgical industry and iron and nonferrous foundry workers. A British cohort study of 2,670 employees of the North American sand industry, followed through 1994, provided strong evidence of a causal relationship between quartz exposure and death from both silicosis and lung cancer, after allowance for cigarette smoking and in the absence of known occupational carcinogens (McDonald, McDonald, Rando, Hughes, & Weill, 2001).

The work environment in iron and steel foundries is a known risk factor of causing cancer diseases, mainly lung cancer (IARC, 1987). It is not clear what individual exposure causes the increasing risk, but possible causes can be exposure to products due to decomposition of different binding agents, polycyclic aromatic hydrocarbons (PAHs), quartz and metals. Respirable quartz is classified at present as carcinogenic both by the ACGIH and the IARC (ACGIH, 2006; IARC, 1997).

IARC concluded on the basis of literature review that inhaled respirable quartz from occupational sources is carcinogenic to humans. They also noted that carcinogenicity was not detected in all industrial circumstances studied and may be dependent on inherent characteristics of the quartz or on external factors affecting its biological activity (IARC, 1997). In the IARC-review only three studies are evaluated. The first is a Danish cohort study where 6,144 foundry workers were followed up through 1985 (Sherson, Svane, & Lynge, 1991). The relative risk for silicotics to develop lung cancer was 1.71, the corresponding for non silicotics was 1.25. The second is a US cohort study where 8,774 workers were followed up to 1985 and the relative risk of developing lung cancer for white males was 1.23 (NS) for non-white males 1.32 (S) (Andjelkovich, Mathew, Richardson, & Levine, 1990). The third evaluated study is a Chinese case-control study where 903 cases and 959 controls were analysed by cumulative quartz dust as exposure measures (Xu, Brown et al., 1996). A trend was seen between quartz dust exposure and lung cancer.

A German study provided further evidence of an increased risk of lung cancer and possibly other cancers of the upper aero digestive tract among foundry workers

(Adzersen, Becker, Steindorf, & Frentzel-Beyme, 2003). No studies of cancer related sickness and other health problems in Swedish iron and steel foundries have been done earlier. Although double risk for lung cancer have been observed among workers in aluminium foundries using the same technique with sand moulding as iron and steel foundries use (Selden, Westberg, & Axelson, 1997).

2.7 Objectives

The objectives of the studies underlying this thesis were:

- What are the exposure levels of respirable quartz in different types of iron foundries? Are they in compliance with the OELs?
- What special high exposure jobs could be determined?
- Does the use of respiratory protective equipment reduce the personal exposure?
- Are Swedish iron foundry workers at risk regarding cancer, in particular lung cancer?
- Could a dose–response relationship be established between cancer morbidity and quartz exposure?
- Can present measurement data be used to predict past exposures?
- What measures need to be taken to reduce the personal exposure levels as well as emission to the environment?

3 Study design and analysis

3.1 Study objects - foundries

To represent the Swedish iron foundry industry we included in our study iron foundries of different sizes using different types of sand, binders for moulds and cores as well as different production methods, representing a blend of old and new casting techniques. Using these criteria we selected 11 Swedish iron foundries for further investigation, all foundries invited to participate accepted. One of the foundries was excluded from parts of the research due to incomplete personnel records (Paper II and III).

The number of employees in the foundries ranged from 8 to 388, and the production was between 400 and 120,000 tonnes per year (Table 4). The different types of iron used were grey iron (3.0-3.5 % C, 1.3-2.5 % Si, 0.4-0.8 % Mn, 0.15-0.2 % P, 0.06-0.15 % S), nodular iron (3.3-3.9 % C, 2.1-2.7 % Si, 0.1-0.5 % Mn, max 0.06 % P, max 0.02 % S, 0.03-0.06 % Mg) and compacted graphite iron (3.3-3.9 % C, 2.1-2.7 % Si, 0.1-0.5 % Mn, max 0.06 % P, max 0.02 % S) (Svensson, 2004). The sand used for moulding was mostly green sand (75 % SiO_2, 6 % carbon black, 5-6 % bentonite and water) but chemical binders such as furan (furfuryl alcohol, urea, phenol, formaldehyde, p-toluenesulphonic acid or phosphoric acid) and silicate ester (sodium metasilicate and organic ester) as well as shell sand (phenol formaldehyde and hexamethylenetetramine) were added to the quartz sand. Mechanized and manual moulding and casting occurred at the foundries. The most common binder for the cores was coldbox (isocyanate-MDI, polyol, phenol formaldehyde resin and an amine as the catalytic agent) but hot-box, epoxy-SO_2 and sodium silicate were also used as core binders at some of the foundries (Table 4).

Table 4. Annual production, number of employees, type and amount of iron cast, production techniques and binders for moulds and cores at the participating iron foundries

Company	Production (tonnes/year)	Employees	Type of iron cast	Production techniques	Binders for moulds	Binders for cores
1	600	10	grey iron 50 %, nodular iron 50 %	manual moulding	ester cured alkaline phenolic (no bake) resin	ester cured alkaline phenolic (no bake) resin
2	9,500	135	grey iron 95 %, white iron 5 %	mechanical moulding	green sand (carbon black, bentonite)	coldbox (phenol formaldehyde resin+isocyanate, amine), ester sand
3	1,700	26	grey iron 100 %	manual moulding	green sand (carbon black, bentonite), ester cured phenolic resin	core-oil (linseed oil + water)
4	13,000	100	nodular iron 60 %, compact graphite iron 30 %, grey iron 10 %	manual moulding	furan resin	furan resin
5	120,000	388	grey iron 100 %	moulding in lines and manually	green sand (carbon black, bentonite)	coldbox (phenol formaldehyde resin+isocyanate, amine), hotbox (phenol formaldehyde resin + ammonium nitrate, urea) epoxy-SO_2 (epoxy resin, organic hydroperoxide, SO_2)
6	2,300	17	grey iron 80 %, compact graphite iron 19 %, nodular iron 1 %	manual moulding	sodium silicate	sodium silicate
7	28,000	279	nodular iron 75 %, grey iron 25 %	mechanical moulding	green sand (carbon black, bentonite), phenol resin and shellsand	coldbox (phenol formaldehyde resin+isocyanate, amine), phenol formaldehyde resin
8	14,000	161	grey iron 100 %	mechanical moulding	sodium silicate, green sand (carbon black, bentonite)	coldbox (phenol formaldehyde resin+isocyanate)
9	400	8	grey iron 100 %	manual moulding	sodium silicate, furan/phenol resin	sodium silicate
10	12,000	116	grey iron 60 %, nodular iron 40 %	mechanical moulding	green sand (carbon black, bentonite), phenol formaldehyde resin	resole-CO_2
11	1,500	30	grey iron 70 %, nodular iron 30 %	manual moulding	phenol formaldehyde resin with furfuryl alcohol + acid	phenol formaldehyde resin with furfuryl alcohol + acid

3.2 Subjects

Data from ten iron foundries where complete lists of employees were available were analyzed in Paper II and III. Company personnel records of the foundries were used to identify workers, whose employment began before 2005, providing an initial cohort of 3,996 employees. Of these, 951 subjects were excluded, including those who died before 1 January 1958 (n=4), were employed for less than one year (n=676), whose identities were uncertain (n=4), or for whom employment information was inadequate (n=33). Data for female subjects (n=234) were also excluded, giving a final set of 3,045 quartz-exposed male workers employed for more than 1 year. The mean and median durations of employment of this cohort were 13 and 9 years, respectively, and their total employment comprised 70,388 person-years, with a distribution of person-years of 33 % for individuals born before 1930, 54 % for subjects born between 1930 and 1959 and 13 % for individuals born after 1960.

The cohort was matched against Swedish Social Services mortality and morbidity registers. The methodology used in this study was approved by the Ethical Committee of Örebro County Council (D-no. 2004:M-374).

3.3 Exposure assessment

3.3.1 Recent exposure measurements

To explore the quartz exposure by today a measurement study between April 2005 and May 2006, performed at the 11 selected iron foundries on as many subjects as possible at all work operations at the foundries, resulting in 415 quartz measurements. The exposure study is described in detail under 3.4.

3.3.2 Historical measurements

Historical measurement data were collected only from the 11 companies; area measurements were not included. Exposure measurement data, historically (up to 1980) sampled as total dust and analyzed as fine quartz were adjusted to respirable quartz data. For the measurements before 1980, total dust samples were collected and a sedimentation method was used to separate the fine fraction. The quartz concentrations sampled using this method are usually double those sampled with the present cyclone separation method, and the historical quartz concentrations were corrected accordingly (NBOSH, 1979; Orenstein, 1965). Current exposure measurements were performed according to Swedish and international standards. To facilitate comparisons with historical measurements in the epidemiological study, we performed sampling using a cyclone system with the characteristics specified in the Johannesburg convention (NBOSH, 1979), and a flow rate of 1.9 l/min. The definition of the respirable dust fraction, based on a flow rate of 2.3 l/min, normally results in lower concentrations of dust and of respirable quartz than the lower flow rate that we used (Swedish Standard, 1995).

Historical measurement data were also available in the form of compulsory measurements collected by the participating foundries and from national exposure surveys from 1968 to 1974; the latter were provided by the Swedish Work Environment Authority (SWEA). The resulting measurement database compiled from these 2 sources (n=1,918) and from the recent exposure measurements (n=415) contained 2,333 values for the air concentration of respirable quartz, with measurement times in the range 240-600 minutes. The measurement database served as a base for our exposure modeling. When one foundry was excluded from the measurements the historical measurements contributed with 1,327 measurements together with the recent 340 measurements resulting in a measurement database of 1,667 measurements.

The job titles used in the recent and historical measurements were caster, core maker, fettler, furnace and ladle repair, maintenance, melter, moulder, sand mixer, shake out, transportation and other specified. The job title 'other specified' included cleaners, painters and model carpenters. There were also three further job categories in the foundry cohort: many jobs, foundry workers and other unspecified. The 'many jobs' category included workers who performed more than one well-defined job, whereas 'foundry workers' included subjects for whom there was no specific working task information. Exposures for the job category foundry worker were assumed to correspond to the mean exposure of employees with all the other job titles. However, 'other unspecified workers' had wholly unknown job titles, and their exposure was estimated to be equivalent to that of other specified employees. Office workers within the production area were also included in the job title-specific analysis, and their quartz exposure was estimated to be identical to that of other specified workers.

3.4 Exposure study (Paper I)

3.4.1 Exposure measurements

Measurements were performed during two following workdays. Exposure assessment of respirable dust and respirable quartz as well as measurements of dust with a personal data logger, DataRAM were performed. Temperature and relative humidity were also measured. The sampling sites were chosen in consultation between the management and representatives for the project to include as many people exposed to respirable quartz as possible.

At specific working tasks, where conditions for high exposure to dust existed and known risk for quartz exposure monitoring was done by using a personal data logging, real time aerosol monitor (DataRAM; MIE, Bedford USA). A data logger in the instrument made registrations of the dust concentration every 20 s. After the measurement the data was transferred to a computer. The workers were asked to keep a work diary and to register time as well as duration of different working tasks during the DataRAM measurements and careful studies of the dust exposure could be made afterwards.

3.4.2 Actual exposure

For fettlers, furnace and ladle repairmen, and shakeout operators using respirators during periods of high exposure, the actual exposure was determined by assuming zero exposure when respirators were used. To achieve this, the worker wore two sampling filters, each connected to an air pump: one filter was employed when respirators were used and the other during the rest of the workday.

3.4.3 Respirable dust

Personal sampling of respirable dust was performed for all the workers included in the study. The respirable fraction was determined using a SKC Aluminum cyclone (SKC 225-01-01, Eighty Four PA, USA) with a 25 mm cellulose acetate filter (Millipore 0.8µm pore size). The cyclones were connected to an air pump (SKC AirCheck 2000, Eighty Four PA, USA, MSA Escort, Pittsburgh PA, USA, or GSA SG4000, Gut Vellbrüggen, Neuss, Germany) operated at an airflow rate of 1.9 l/min with separation characteristics according to the Johannesburg convention (NBOSH, 1979; Orenstein, 1965). The filters were analyzed gravimetrically according a modified NIOSH method (NIOSH, 1994a), with conditioning at 20 ± 1°C and 50 ± 3 % relative humidity for 48 hours before analysis. The sampling time ranged from 2.2 to 9.9 hours, the shorter sampling times (< 4hrs) concerning predominantly furnace and ladle repair. The detection limit for respirable dust was 0.10 mg/sample resulting in detection concentrations for an 8-hour TWA sample of approximately 0.10.

3.4.4 Crystalline silica: quartz, cristobalite and tridymite

The sampling of respirable crystalline silica was performed as sampling of respirable dust. After gravimetric analyses of respirable dust respirable crystalline silica, as quartz and cristobalite, was determined according to NIOSH 7500 (NIOSH, 1994b)(modified). The samples were ashed in an oxygen-plasma and then the sample particulate was deposited on a silver membrane filter and analysed by X-ray diffraction (XRD). In crystalline materials, XRD measures distances in the crystal lattice. The diffraction pattern is specific for the crystalline phase of the substance. To minimize the risk of interference, both area and height were analyzed for the diffraction angles $2\theta = 20, 26$ and 50°. Selected samples, in particular from the melting and casting department, where conditions were assumed to involve high temperatures (>1000 °C) were also analyzed for tridymite; the melters and casters work in these areas. The detection limit for respirable quartz and cristobalite was 0.005 mg/sample, resulting in detection concentrations for an 8-hour TWA sample of approximately 0.005 mg/m^3 for quartz and cristobalite.

3.4.5 Real-time monitoring of dust

The DataRAM (MIE, Bedford USA) is a photometric monitor and measures particles with a diameter between 0.1 and 10 µm in the range 0.001-400 mg/m^3. According to the manufacturer the optimal sensitivity is, for the respirable fraction of dust (<5 µm). The DataRAM relies on the diffusion of ambient air into a sensing chamber. It has been calibrated by the manufacturer against a test dust, SAE Fine (ISO Fine; Powder Technology, USA). The DataRAM was placed on the upper body of the worker for intake of ambient air. A data logger in the instrument made registrations of the dust concentration and after the measurement the data was transferred to a computer. The workers were asked to keep a work diary and to register time as well as duration of different working tasks during the DataRAM measurements and careful studies of the dust exposure could be made afterwards (figure 4).

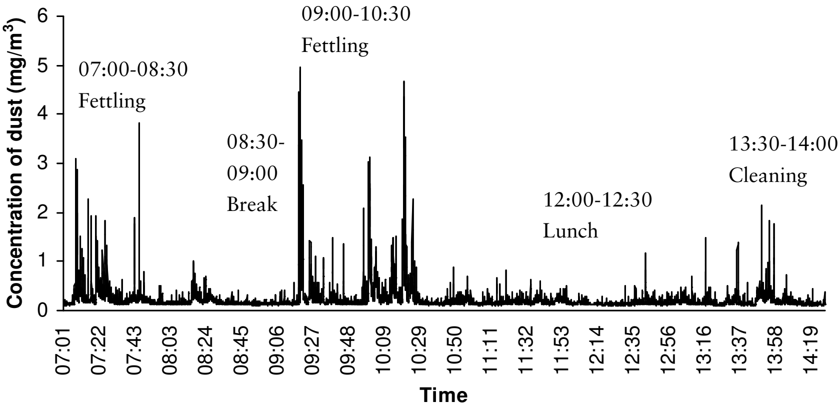


Figure 4. Result of Data-RAM measurements for a fettler at an iron foundry

3.5 Cancer morbidity study (Paper II)

The cancer morbidity analyses covered the period from 1958 through to 2004. The vital status for all cohort members (n=3,045) was determined by matching personal identification numbers of individuals in the cohort with the Swedish Cancer Registry. The cancer incidence was coded according to the International

Classification of Disease (ICD-7). Mixed model analysis was used to calculate quartz exposure and individual cumulative quartz doses (see 3.8.2-3).

3.5.1 Smoking habits

The smoking habits of the iron foundry workers were estimated from data gathered in national surveys performed by Statistics Sweden that cover the period from 1963 to 2002 and include data on smoking habits classified according to occupational groups (Lundberg, Rosen, & Rosen, 1991; Nordlund, 1998; Rosen, Wall, Hanning, Lindberg, & Nystrom, 1987). The smoking frequencies of blue-collar workers were used as proxies for the foundry workers, and by comparison with the corresponding frequencies in the general Swedish male population, were summed into crude, unweighted rates for five periods between 1963 and 2002. In addition, responses of a sample of individuals from the cohort to a questionnaire were used to validate our estimates of smoking habits of blue-collar workers in the Swedish national statistics database as proxy data for iron foundry workers. From the cohort about 500 subjects were randomly collected to explore smoking habits, answers were received from 61 % of the subjects.

Using the rates obtained from the survey, smoking-adjusted estimates of the observed numbers of lung cancers were calculated, assuming a ten-fold increase in risk of lung cancer for smokers (Rosen et al., 1987). The adjustment was made by multiplying the observed number of lung cancers by a factor of 0.85, representing the unweighted mean of adjustment factors calculated from the estimated smoking rates for the five periods between 1963 and 2002. Both unadjusted and smoking-corrected data are presented and discussed in Paper II to illustrate the effect of smoking habits on differences in lung cancer incidence between foundry workers and the general population.

3.6 Nested case-control study (Paper III)

In our cohort (n=3,045) 52 cases of lung cancer were observed and only 1 of the cases was diagnosed with silicosis. For each case 5 controls were selected, resulting in 52 cases and 260 controls. The controls selected were the 5 individuals closest to the case with respect to age. Individuals who were diagnosed with lung cancer, or who had died or emigrated before the case was diagnosed with lung cancer were excluded from being controls. Mixed model analysis was used to calculate quartz exposure and individual cumulative quartz doses (see 3.8.2-3). To investigate the relationship between quartz exposure and lung cancer conditional logistic regression described in 3.8.4 was used.

3.7 Predicting exposures (Paper IV)

The 11 iron foundries were divided into 3 groups; small, medium, and large, due to the size of the companies regarding the number of employees (less than 20, 25-120 and more than 120, respectively). Mixed model analysis described in 3.8.5 was used to study trends over time and the possibility to predict past and present exposures.

3.8 Statistics

3.8.1 General statistics

The air concentrations of respirable dust, quartz, cristobalite and tridymite were determined for various job titles and periods with the sampling time ranging from 2.2 to 9.9 hours. Exposure was calculated as an 8-hour time weighted average concentration (8-hour TWA) for the full workday. Assuming zero exposure during non-sampling times, the actual exposure was calculated as a TWA exposure based on the assumption that exposure was zero when a respirator was used. Differences in average air concentrations of quartz and respirable dust for different binder types and production levels were analysed using the nonparametric Mann-Whitney U test: This nonparametric technique is preferred for handling values falling below the detection limits (Helsel, 2006). For the real time air measurements collected using the Data-RAM, the number of 15-minute sampling periods, the arithmetic mean (AM), and standard deviation (SD) as well as the geometric mean (GM) and geometric standard deviation (GSD) were determined. In addition, the peak exposure, determined by the integration of 20-second intervals, is shown. Standard parameters (AM, SD, GM, GSD, range) were calculated for the log normal distribution of the measurements. The analytical detection limit (DL) was defined as 3 standard deviations at a concentration with a signal-to-noise ratio of 3 (EURACHEM, 1993). Concentrations below the DL were estimated by multiplying the DL by $1/\sqrt{2}$ since there is a low variability in the data and less than 10 % of the data is below the DL (Hornung & Reed, 1990; Mulhausen & Damiano, 1998). In Paper III the relationships between different exposure measures were assessed by calculating Spearman's rank correlation coefficients (r_s). The Statistical Package for Social Sciences (SPSS) for Windows 14.0 was used for all calculations in Paper I-III and in Paper IV the Proc Mixed code in SAS version 6.12 software (SAS Institute, Cary, NC, USA) was used.

3.8.2 Mixed model (Paper II-III)

To model the quartz exposure concentrations for different time periods, foundries and job titles, we used a mixed model incorporating time divided in 4 different periods (1968-1979, 1980 -1989, 1990-1999, 2000-2006), type of foundries (10 foundries) and job titles (11 categories as described in methods section) as independent variables. Since the data on exposure measurements were skewed, a transformation using the natural logarithm was performed. The estimates from the model allowed us to identify factors affecting quartz concentration levels and use these to calculate the surrogate quartz dose for each individual. The mixed model applied has the following equation (Brown & Prescott, 1999):

$$Y_{ijk} = \ln(X_{ijk}) = \mu + \beta_1\chi_{1j} + \beta_2\chi_{2j} + \beta_3\chi_{3j} + \ldots + \beta_m\chi_{mj} + \varphi_{j(i)} + \varepsilon_{k(ij)} \qquad (1)$$

where μ is the overall average quartz concentration on log-scale and $\beta_1, \ldots, \beta_m$ are coefficients of the fixed effects of time periods, type of foundries and job titles. The model also includes the random effects of workers nested within job titles, $\varphi_{j(i)}$, to account for variation between workers with the same job title. X_{ijk} and Y_{ijk} are, respectively, quartz concentration and log-transformed quartz concentration in the i^{th} group for the j^{th} worker on the k^{th} day. The results of the mixed model are presented as antilogarithmic β-values with specified reference categories, and enabled determination of quartz concentrations for different time periods, job and companies.

3.8.3 Cumulative exposure (Paper II-III)

For the cohort as well as for the cases and controls, the concentration of respirable quartz derived from the mixed model based initially on employment duration, job title, time period, specific foundry and exposure time was expressed as a cumulative exposure measure in mg/m^3*years (i.e. exposure level multiplied by exposure time). The cumulative doses for respirable quartz for each individual were calculated according to:

$$CE(j) = \Sigma E_k(jk)\ T(jk) \qquad (2)$$

where CE(j) is the individual cumulative exposure expressed as mg/m^3*year, $E_k(jk)$ is the estimated level of quartz exposure for the j^{th} individual during the k^{th} time period and T(jk) is the number of years at the exposure level prevailing for the k^{th} time period. Exposures before 1968 were allocated the same concentration levels calculated for the period 1968-1979.

The calculated values were then categorized as low, medium or high; defined as 12.5 %-<25 %, 25 %-50 % and >50 %, respectively, of the 4 mg maximum permitted lifetime exposure, based on the current Swedish OEL of 0.1 mg/m^3 per year over 40 years. The high cumulative exposure group represent 40 years of exposure to a quartz concentration of >0.05 mg/m^3; this is twice as high as the present ACGIH-TLV of 0.025 mg/m^3 (ACGIH, 2006). In addition, several other exposure measures such as years of exposure (duration), maximum and median concentration intensity were calculated and the correlations evaluated. However, when considering lung cancer outcomes in relation to occupational exposure, it is usual to use cumulative exposure measure (H. Checkoway, 1986; H. Checkoway et al., 1987), which also were used in our epidemiologic analysis.

3.8.4 Conditional logistic regression (Paper III)

To investigate the relationship between quartz exposure and lung cancer in the matched case–control study, conditional logistic regression was applied (Kleinbaum & Klein, 2002), using

$$\text{logit}(p_i) = \eta_1 Z_{1i} + \eta_2 Z_{2i} + \ldots + \eta_k Z_{ki} + \alpha_{\text{stratum(i)}} \qquad (3)$$

where p_i is the probability of subject *i* being a lung cancer case given the predictors ($Z_{1i}, \ldots, Z_{ki}$), $\eta_1, \ldots, \eta_k$ are regression coefficients and the α-values ($\alpha_1, \ldots, \alpha_s$) are stratum effects (matched sets). For the conditional logistic regression the exposure reference used was <0.5 mg/m^3* years.

3.8.5 Mixed model (Paper IV)

The quartz concentrations were lognormally transformed before devising a linear mixed-effect model for repeated measurements. The measurements taken in the period from 1968 to 2004 by both the SWEA and the surveyed companies were used to build two of the three different mixed models described in this paper. The first model (the historical model) was based on measurements taken between 1968 and 1989 (22 years), reflecting the period where there were substantial improvements in working conditions. The second model (the development model) was based on the measurements conducted between 1990 and 2004 (15 years), a period of relatively minor changes in the production process. This model was used to predict historical exposure patterns. This may reflect a commonly occurring situation, where exposure information is available for more recent times, but is not available for older periods. The third model (the validation model) was derived from the measurements taken by the research group between 2005 and 2006. This validation model allowed us to evaluate the validity of the development model.

In Paper IV the mixed model used the following equation:

$$Y_{ghkij} = \ln(X_{ghkij}) = \mu + \alpha_g + \beta_h + \varphi_k + \delta_i + \varepsilon_{ghkij} \qquad (4)$$

where

X_{ghkij} = the quartz concentration measured for the i^{th} worker on the j^{th} day at the g^{th} time period in the h^{th} foundry with k^{th} job title

$Y_{ghkij} = \ln(X_{ghkij})$

μ = the overall average quartz concentration on a log-scale

α_g = the fixed effect of the g^{th} time period g=1…4

β_h = the fixed effect of the h^{th} foundry h=1…11

φ_k = the fixed effect of the k^{th} job title k=1…11

δ_i = the random effect of the i^{th} worker

ε_{ghkij} = the random within-worker variation

The model assumed that δ_i and ε_{ghkij} are normally distributed with means equal to zero and variances of σ^2_{BW} and σ^2_{WW} respectively, representing the between-worker and within-worker variance components. Furthermore, δ_i and ε_{ghkij} were assumed to be statistically independent of each other.

A linear mixed-effect model for repeated measurements was used to describe trends over time. In all mixed-effect models, the time period, company size, and job title were included as fixed (categorical) determinants of exposure. Approximately 56 % of the 2,333 quartz measurements were repeated measurements within workers. These variance components were pooled across all workers and approximated as equal across all time periods, job titles, and company sizes. This approximation, though eliminating information such as the dependence of variances on time period, was chosen because of the relatively few measurements available for some determinants, which limited the number of parameters that could be estimated in the model (Burdorf, 2005). The Akaike information criterion (AIC) was used as a measure of the overall fit of the mixed model. The contribution of the determinants of exposure was evaluated by their influence on the estimated mean exposure as well as their influence on the reduction of the between-worker variance. It has to be noted that the fixed effects were collected at the individual worker level and, thus, could not have any impact on the within-worker variance.

A linear regression analysis was performed to investigate agreement between the historical model and the development model and also between the development model and the validation model. For each combination of job title and company size, the average exposure was estimated in each model, resulting in 33 comparisons. For example, using a linear regression model, the intercept reflects the systematic difference in quartz exposure estimates; the regression coefficient represents the change in predicted concentration between 2005 and 2006 due to a one unit change of the estimated concentration in the development model based on measurements from 1990 to 2004.

4 Results

4.1 Quartz exposure data

In our survey (Paper I), a total of 436 personal samples of respirable dust were collected; of these, 435 were analyzed for quartz, 408 for cristobalite and 26 selected samples for tridymite. For all samples of respirable dust the TWAs varied between 0.076 and 31 mg/m^3 and the GM was 0.58 mg/m^3. Only 2 % of the samples exceeded the Swedish OEL (5 mg/m^3); these were all samples from fettlers and furnace and ladle repair operatives. The TWA concentrations of respirable quartz varied between 0.003 and 2.1 mg/m^3 for all samples, with a GM of 0.028 mg/m^3. The overall air concentration variability was expressed as the GSD. The mean GSD for all respirable dust measurements was 2.5 and varied for different jobs between 1.5 and 3.1. For respirable quartz samples, the mean GSD was 2.8 and varied between 1.7 and 3.7 for the different job titles (Table 6).

Selected samples from melters, who where assumed to be exposed to high temperature operations, were analysed for tridymite. For all the tridymite (n=26) and cristobalite (n=408) samples, the air concentration levels were lower than the Swedish OEL (0.05 mg/m^3) and 100 % of tridymite and 92 % of cristobalite analyses found concentrations lower than the DL (0.01 mg/m^3). The samples of cristobalite (n=32) with detectable concentrations (range 0.01-0.04 mg/m^3) were associated with furnace and ladle repair, fettling and moulding.

Averages of the 8-hour TWA for quartz were made for different foundries. We compared those using green sand moulding, which was expected to produce higher dust exposures, with foundries using chemical binders for moulds. In fact, the average respirable quartz concentration associated with green sand moulding was lower (0.046 mg/m^3) than that associated with chemical binder moulding (0.079 mg/m^3), although the difference was not statistically significant (p=0.070). However, higher quartz concentrations were recorded for shake out operators, maintenance workers, furnace and ladle repairmen, moulders and casters at the green sand foundries. Smaller foundries (<10,000 tonnes produced) had higher concentrations than larger ones (>10,000 tonnes produced), 0.061 and 0.045 mg/m^3 respectively, although the difference was not statistically significant (p=0.889). We think that the difference in quartz levels however may reflect that the large foundries in our study are more mechanized and automatized, the processes more closed and properly ventilated than in the smaller foundries. This is valid for most of the work operations, i.e. moulding, casting, shake out operations and fettling.

The overall individual TWA quartz exposure concentrations in our database from the 11 foundries with 2,333 measurements from 1968 to 2006 varied between 0.0018 and 4.9 mg/m^3, average 0.083 mg/m^3. Less than 10 % of the quartz concentrations were below the DL of 0.005 mg/m^3. Some 15 % of the TWAs exceeded the Swedish OEL (0.1 mg/m^3), 32 % exceeded the EU SCOEL recommended OEL (0.05 mg/m^3), and 57 % of all the quartz exposure measurements exceeded the ACGIH-TLV of 0.025 mg/m^3 (ACGIH, 2006; SCOEL, 2002). The job titles that had means for the whole period exceeding 0.05 mg/m^3 were fettlers (0.087 mg/m^3), furnace and ladle repair (0.42 mg/m^3) and maintenance (0.054 mg/m^3), and as many as 10 out of the 11 job titles exceeded 0.025 mg/m^3 over the whole study period. Comparing the quartz exposure measurements collected during 2005-2006 (mean/job title and time period 0.023-0.13 mg/m^3) with measurements from the period 1968-2004 (mean/job title and time period 0.024-0.47 mg/m^3), we found that furnace and ladle repair operators were exposed to the highest levels by far. This was the case in the present and the past and no reduction in exposure was seen during the study (Table 5). The lowest exposures at present and in total were recorded among core makers, while old measurements indicated that casters had the lowest exposures.

Table 5. Quartz exposure (arithmetic mean, median, minimum and maximum) of individual time-weighted averages from 1968 to 2006 by job title and time period at 10 Swedish iron foundries

Job title	Time periods	Number of measurements	Number of persons	Quartz exposure (mg/m^3) mean	median	min	max
Caster	1968-1979	15	10	0.078	0.061	0.015	0.17
	1980-1989	15	13	0.019	0.015	0.0088	0.036
	1990-1999	19	18	0.025	0.016	0.0054	0.14
	2000+	19	12	0.015	0.011	0.009	0.04
	total	68	53	0.033	0.018	0.0054	0.17
Core maker	1968-1979	19	15	0.038	0.038	0.003	0.1
	1980-1989	43	36	0.019	0.018	0.0036	0.082
	1990-1999	46	38	0.022	0.016	0.0052	0.088
	2000+	63	39	0.025	0.016	0.0033	0.19
	total	171	128	0.024	0.017	0.003	0.19
Fettler	1968-1979	119	64	0.13	0.078	0.005	0.71
	1980-1989	125	109	0.06	0.031	0.004	0.31
	1990-1999	151	108	0.062	0.027	0.0025	0.77
	2000+	178	122	0.1	0.036	0.0035	2.1
	total	573	403	0.087	0.039	0.0025	2.1
Furnace and ladle repair	1968-1979	12	9	0.28	0.14	0.014	1.8
	1980-1989	16	12	0.57	0.14	0.0086	4.9
	1990-1999	20	10	0.42	0.092	0.0028	1.9
	2000+	23	14	0.39	0.099	0.0098	2.1
	total	71	45	0.42	0.12	0.0028	4.9
Maintenance	1968-1979	6	6	0.086	0.042	0.016	0.31
	1980-1989	17	16	0.084	0.029	0.0055	0.67
	1990-1999	11	10	0.051	0.058	0.0052	0.088
	2000+	33	17	0.034	0.027	0.0065	0.19
	total	67	49	0.054	0.029	0.0052	0.67
Melter	1968-1979	3	2	0.19	0.28	0.024	0.28
	1980-1989	13	11	0.084	0.05	0.0038	0.27
	1990-1999	42	27	0.062	0.035	0.0047	0.52
	2000+	53	32	0.028	0.02	0.0042	0.22
	total	111	72	0.052	0.022	0.0038	0.52
Moulder	1968-1979	46	27	0.11	0.081	0.027	0.41
	1980-1989	51	34	0.044	0.027	0.004	0.22
	1990-1999	69	46	0.043	0.028	0.004	0.21
	2000+	91	50	0.051	0.035	0.0034	0.98
	total	257	157	0.058	0.039	0.0034	0.98
Sand mixer	1968-1979	28	16	0.22	0.099	0.017	1.1
	1980-1989	19	16	0.036	0.027	0.0086	0.11
	1990-1999	26	14	0.031	0.027	0.0052	0.083
	2000+	18	14	0.025	0.016	0.0036	0.11
	total	91	60	0.088	0.034	0.0036	1.1
Shake out	1968-1979	44	19	0.18	0.062	0.0067	3.3
	1980-1989	23	18	0.027	0.017	0.0048	0.099
	1990-1999	46	29	0.029	0.024	0.0047	0.12
	2000+	35	15	0.051	0.04	0.01	0.2
	total	148	81	0.079	0.037	0.0047	3.3
Transportation	1968-1979	0	0				
	1980-1989	2	2	0.037	0.037	0.03	0.044
	1990-1999	19	9	0.035	0.028	0.0018	0.11
	2000+	8	6	0.021	0.017	0.0051	0.056
	total	29	17	0.031	0.023	0.0018	0.11
Other	1968-1979	11	10	0.1	0.051	0.006	0.41
	1980-1989	23	21	0.17	0.037	0.0054	2.1
	1990-1999	23	17	0.054	0.022	0.005	0.46
	2000+	24	15	0.036	0.028	0.0074	0.2
	total	81	63	0.088	0.03	0.005	2.1

Figure 5 depicts the long-term trend in exposure among three typical jobs, illustrating the sharp decreasing during 1968-1984 and the slow decrease after 1985. The job of furnace and ladle repair consistently had a high exposure, with a 3.9 to 8.0 fold higher average exposure than the core maker.

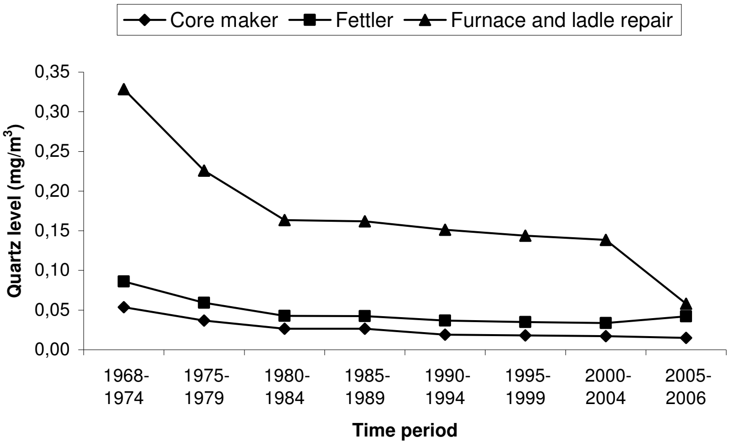


Figure 5. Long-term trend over time in exposure to quartz among three typical job titles in medium sized Swedish foundries between 1968 and 2006

4.2 Exposure study (Paper I)

In our study, a comparison to the adopted ACGIH value (0.025 mg/m^3), 56 % of all the TWA exposures exceeded the TLV with all work categories represented. Comparing our data with the European proposed OEL (0.05 mg/m^3), 23 % of all the measurements exceeded the OEL for all work categories except for caster. The Swedish OEL (0.1 mg/m^3) was exceeded in 9 % of the samples, representing the work categories fettling, furnace and ladle repair, maintenance, melting, moulding, sand mixing, shake out and transportation (Table 6). The quartz contents in the respirable dust fraction varied between 5 and 7 % for all job titles, except for furnace and ladle repair, for which the concentration was 11 %.

Table 6. Exposure to respirable quartz, 8-hour TWA. Arithmetic and geometric means, standard deviation, range and number of measurements (TWA, percent) exceeding ACGIH-TLV, SCOEL-OEL and the Swedish OEL by job title

Job title	Respirable quartz (mg/m^3) n	AM	SD	GM	GSD	Range	No (%) of TWA >ACGIH-TLV	>SCOEL-OEL	>Swedish OEL
Caster	22	0.024	0.014	0.020	1.8	0.009 – 0.047	41	0	0
Core maker	55	0.023	0.020	0.016	2.3	0.003 – 0.091	33	11	0
Fettler	115	0.092	0.23	0.041	2.9	0.004 – 2.1	71	35	16
Furnace and ladle repair	33	0.13	0.20	0.052	3.7	0.0098 – 0.83	70	39	30
Maintenance	26	0.034	0.041	0.021	2.6	0.007 – 0.19	46	19	8
Melter	49	0.028	0.031	0.022	2.0	0.005 – 0.22	43	6	2
Moulder	64	0.043	0.044	0.029	2.6	0.003 – 0.27	61	28	6
Sand mixer	14	0.029	0.028	0.020	2.3	0.007 – 0.11	36	14	7
Shake out	16	0.070	0.042	0.060	1.7	0.022 – 0.20	94	63	13
Transportation	13	0.026	0.028	0.017	2.6	0.0048 – 0.11	31	15	8
Other	28	0.024	0.014	0.020	2.0	0.0048 – 0.051	46	7	0
Total	435	0.056	0.14	0.028	2.8	0.003 – 2.1	56	23	9

n: number of samples AM: arithmetic mean SD: standard deviation
GM: geometric mean GSD: geometric standard deviation, dimensionless
ACGIH-TLV: American Conference of Governmental Industrial Hygienists - Threshold Limit Value
SCOEL-OEL: European Scientific Committee on Occupational Exposure Limits - Occupational Exposure Limit
Swedish OEL: Swedish Occupational Exposure Limit

4.2.1 Actual exposure

The actual exposure is an estimated 8-hour TWA based on the assumption of zero exposure during respirator use. Depending on working task the use of respirators varied from 2 % to 95 % of the workday. The assessment of actual exposure was possible due to our sampling strategy, based on separate sampling of periods with and without use of respirators. The actual respirable quartz concentrations for fettlers exceeded the Swedish OEL in 7 % (n=42) of the measurements. This implies that respirators were not used for a sufficiently long time period during jobs associated with high dust levels. All measurements for furnace and ladle repair operatives recorded actual exposures below the Swedish OEL. However, we assumed zero exposure when using respirators; this will not be the case if respirator filters do not provide full protection or if respirators do not fit properly. The protection factor (PF) is defined as the ratio between the concentration outside and inside the mask. The actual quartz concentrations, based on different PFs (PF 2 to PF 200), are shown for fettlers, furnace and ladle repairmen and shake out operators in Table 7. To reduce the actual quartz exposures for fettlers, furnace and ladle repairmen and shake out operators to 25 % of the

Swedish OEL, a respirator protection factor of at least 200 is necessary, thus disqualifying the use of filtering face pieces and half masks and only allowing the use of powered air-purifying respirators or more efficient filters, minimum filter quality P3 (European standard, US standard P100*)*. Notably, these figures are only valid for a perfect fit between the mask and the face.

Table 7. Exposure to respirable quartz using respirators with different protection factors. Arithmetic mean and range for fettlers, furnace and ladle repairmen and shake out operators

		Arithmetic mean and range of respirable quartz corrected for protection factors (mg/m^3)				
Job title	**n**	**PF 1**	**PF 200**	**PF 20**	**PF 5**	**PF 2**
Fettler	42	0.17 (0.009-2.1)	0.02 (0.003-0.21)	0.03 (0.01-0.21)	0.05 (0.01-0.44)	0.10 (0.01-1.1)
Furnace and ladle repair	13	0.20 (0.01-0.83)	0.03 (0.003-0.08)	0.04 (0.003-0.09)	0.07 (0.004-0.20)	0.11 (0.01-0.44)
Shake out	3	0.067 (0.04-0.09)	0.01 (0.004-0.02)	0.01 (0.01-0.02)	0.02 (0.02-0.02)	0.04 (0.03-0.05)
Total	58	0.17 (0.01-2.1)	0.02 (0.003-0.21)	0.03 (0.003-0.21)	0.05 (0.004-0.44)	0.10 (0.01-1.1)

n: number of samples
PF: protection factor, ratio of air concentrations outside and inside the mask

4.2.2 DataRAM

Measurements with the DataRAM (n=51) were collected at the 11 foundries for different job titles, supposedly those exposed to high dust concentrations (Table 8). In total, 51 sets of measurements were collected, with sampling times ranging from 5 minutes to 8 hours, representing specific activities. To describe short-term exposures, the results are presented as 15-minute average concentrations and as peak exposures (sampling integration time 20 sec.). The AM of individual 15-minute samples for different jobs varied between 0.15 and 87 mg/m^3, the highest concentrations were recorded for fettlers and furnace and ladle repair operatives. The overall individual peak air concentrations varied between 9.6 and 388 mg/m^3. Considering individual jobs, high peak concentrations were recorded for fettlers undertaking fettling within a moulded product (252 mg/m^3) and for furnace and ladle repairmen when standing in the furnace and using a pneumatic drill on old wall material (388 mg/m^3). The peak exposure of 388 mg/m^3 may possibly be substantially higher than reported, since the DataRAM has an operation dust load limit of 400 mg/m^3 with an error estimate of +or- 5 %. Notably, almost all jobs had short-term peaks above 100 mg/m^3. Other jobs with high peak exposures included maintenance (sand preparation), melting (introducing iron into the furnace, covering the mould with sand), moulding (filling the mould with sand, removal of sand from the transportation system), shakeout (sand shuffling and work at a mechanical and ventilated shake out unit), transportation (surveillance of vacuum sand transportation) and other jobs, such as driving a cleaning machine. Time-exposure profiles are shown for a fettler (Figure 4).

Table 8. Data-RAM measurement results presented as averages of 15-minute samples and peak exposures (20 sec.). Number of 15-minute measurements, arithmetic and geometric means, standard deviation and range by job title

	Concentration of dust (mg/m^3)						
	15-minute samples						Peak exposure
Job title	**n**	**AM**	**SD**	**GM**	**GSD**	**Range**	
Fettler	166	2.5	4.9	1.1	3.1	0.15 – 37	252
Furnace and ladle repair	229	3.6	6.7	2.2	2.5	0.20 – 87	388
Maintenance	2	10	14	3.0	15	0.45 – 20	159
Melter	22	2.4	2.6	1.7	2.3	0.55 – 12	112
Moulder	73	2.5	3.4	1.5	2.6	0.25 – 17	102
Shake out	56	1.9	2.6	1.2	2.5	0.23 – 14	97
Transportation	22	1.4	2.2	0.8	2.4	0.36 – 10	228
Other	2	7.7	2.4	7.5	1.4	6.0 – 9.4	9.6
Total	572	2.9	5.3	1.5	2.8	0.15 - 87	388

n: number of 15-minute samples AM: arithmetic mean SD: standard deviation
GM: geometric mean GSD: geometric standard deviation, dimensionless
Peak exposure: highest 20 sec-measurement per job title

4.3 Cancer morbidity study (Paper II)

The overall cancer morbidity (Table 9) for the sample cohort based on 347 observed cases was close to the expected value derived from the general population, with an SIR of 1.00 (95 % CI 0.90-1.11). Significantly increased risks were noted only for cancer of the lung and pleura (SIR 1.58, 95 % CI 1.18-2.06) and bronchus and lung cancers (SIR 1.61, 95 % CI 1.20-2.12). For cancers at sites with at least five observed cases and an increased incidence of ≥25 % (SIR>1.25), non-significant enhanced risks were found for cancer of the liver, larynx, testis, urinary organs, connective tissue muscle and lymphatic leukaemia.

For all cancers analysed by standard measures of exposure, a weak but non-significant trend was observed for the duration of employment, with the SIR increasing from 0.85 (95 % CI 0.56-1.22) to 1.04 (95 % CI 0.88-1.22). No increased risk was observed for short-term employees (<2 years) (SIR 0.85, 95 % CI 0.56-1.22).

Table 9. Cancer incidence ratios in male workers at iron foundries, Sweden 1958-2004

ICD 7[a]	Cancer site	Obs[b]	Exp[c]	SIR[d]	95% CI[e]
140-209	All	347	347.22	1.00	0.90 – 1.11
140-148	Mouth and throat	9	9.56	0.94	0.43 – 1.79
150	Oesophagus	0	4.31		
151	Stomach	14	17.14	0.82	0.45 – 1.37
152	Small intestine	1	1.85	0.54	0.01 – 3.02
153	Colon	27	24.13	1.12	0.74 – 1.63
154	Rectum and anus	13	16.60	0.78	0.42 – 1.34
155	Liver	12	7.53	1.59	0.82 – 2.78
157	Pancreas	5	9.87	0.51	0.16 – 1.18
150-158	Digestive organs and peritoneum	73	82.68	0.88	0.69 – 1.11
160	Nose and nasal sinuses	0	0.77		
161	Larynx	6	3.39	1.77	0.65 – 3.85
162	Lung and pleura	53	33.64	1.58	1.18 – 2.06
162.1	Bronchus and lung, primary	52	32.24	1.61	1.20 – 2.12
160-164	Respiratory organs	59	39.06	1.51	1.15 – 1.95
177	Prostate	85	83.83	1.01	0.81 – 1.25
178	Testis	6	3.90	1.54	0.56 – 3.35
180	Kidney	9	12.61	0.71	0.33 – 1.36
181	Urinary organs	31	23.70	1.31	0.89 – 1.86
181.0	Bladder	29	22.76	1.27	0.85-1.83
177-181	Urinary tract and sexual organs	131	125.33	1.05	0.87 – 1.24
190	Skin (melanoma)	8	12.06	0.66	0.29 – 1.31
191	Skin (other)	11	16.43	0.67	0.33 – 1.20
193	Nervous system	7	11.02	0.64	0.26 – 1.31
194	Thyroid gland	1	1.80	0.56	0.01 – 3.09
195	Endocrine glands	3	4.15	0.72	0.15 – 2.11
197	Connective tissue, muscle	5	2.58	1.94	0.63 – 4.52
199	Other and unspecified sites	5	10.30	0.49	0.16 – 1.13
200. 202.205	Malignant lymphoma	16	15.29	1.05	0.60 – 1.70
201	Hodgkin's disease	2	2.34	0.85	0.10 – 3.08
203	Multiple myeloma plasmocytma	8	5.06	1.58	0.68 – 3.11
200-203.205	Lymphatic tissue	26	22.70	1.15	0.75 – 1.68
204	Lymphatic leukaemia	7	4.63	1.51	0.61 – 3.11

a: Coded according to the 7th revision of the International Classification of Diseases
b: Observed number of cases c: Expected number of cases
d: Standardised incidence ratio e: 95 % confidence interval for the SIR

For lung cancer incidence, as analyzed by duration of exposure, the SIRs of the different exposure groups were non-significant ranging from 2.05 (95 % CI 0.75-4.47) for the short-term workers to 1.58 (95 % CI 0.99-2.40) for the long-term exposure group exposed for >20 years. For liver and bladder cancers non-significant values were observed for SIRs for duration of exposure with dose-response trends. The SIRs for the long-term exposed groups were 2.11 (95 % CI 0.85-4.36) and 1.45 (95 % CI 0.77-2.48), respectively.

Analysis of lung cancer incidence by duration of employment and latency time (years) showed no significantly enhanced risk for lung cancer among the 0-19 and >20 year exposure groups for latency times of less than 20 years. However, for the group with >20 year latencies, the SIRs reached 2.18 (95 % CI 0.71-5.08), 1.55 (95 % CI 0.67-3.06), 2.35 (95 % CI 1.12-4.31) and 1.72 (95 % CI 1.08-2.61) for workers employed in the foundries for <2, 2-9, 10-19 and ≥20 years, respectively, with significantly increased risks for workers employed for 10-19 and >20 years (Table 10). As expected, the same result was found when the analysis was performed using duration of exposure instead of duration of employment.

Table 10. Lung cancer incidence among iron foundry workers by latency time, duration of exposure (years) and cumulative quartz exposure ($mg/m^3 * years$), Sweden 1958-2004

Latency	**Duration of exposure** (years)	**Cumulative quartz exposure** ($mg/m^3 * years$)	**Obs**[a]	**Exp**[b]	**SIR**[c]	**95% CI**[d]
0-19	<2		1	0.62	1.61	0.04 - 8.98
	2-9		6	3.11	1.93	0.71 - 4.20
	10-19		0	2.89		
	20+		0	1.13		
20+	<2		5	2.30	2.18	0.71 - 5.08
	2-9		8	5.16	1.55	0.67 - 3.06
	10-19		10	4.27	2.35	1.12 - 4.31
	20+		22	12.76	1.72	1.08 - 2.61
0-19		<1	6	3.73	1.61	0.59 - 3.50
		1-2	1	1.87	0.53	0.01 - 2.97
		2+	0	2.15		
20+		<1	11	6.99	1.57	0.79 - 2.81
		1-2	11	3.82	2.88	1.44 - 5.16
		2+	23	13.68	1.68	1.07 - 2.52

a: Observed number of cases b: Expected number of cases
c: Standardised incidence ratio d: 95 % confidence interval for the SIR

Using specific measures of exposure, and cumulative exposure to quartz, no significantly increased risk was observed for any of the quartz exposure groups when the latency time was less than 20 years (Table 10). However, when the latency time was >20 years, significant SIRs were noted for both the 1-2 mg/m^3* years exposure group (SIR 2.88, 95 % CI 1.44-5.15) and the ≥2 mg/m^3* years group (SIR 1.68, 95 % CI 1.07-2.52). Nevertheless, no clear dose-response relationship was noted. Significantly increased risks were found at dose levels corresponding to air concentrations of respirable quartz of 0.025-0.05 mg/m^3 and >0.05 mg/m^3.

Our calculated adjustment factor of 0.85 for smoking-related cancer incidence was used to adjust for the effects of smoking in the study population. This resulted in a non-significant excess overall risk for lung cancer (SIR 1.31, 95 % CI 0.95-1.76) in contrast to the unadjusted, significant SIR of 1.61. The results of the analysis of lung cancer incidence in relation to duration of exposure showed the same trend. However, significant excess risks of lung cancer for workers with exposure durations of 10-19 and >20 years and a latency time of >20 years became non-significant, with SIRs reduced from 2.35 and 1.72 to 2.11 and 1.49, respectively. Identical patterns were seen when the duration of employment was analyzed in the same manner. Analysis of effects of cumulative quartz exposure detected significant, unadjusted excess lung cancer risks for the exposed groups with quartz doses of 1-2 and >2 mg/m^3 * years, with SIRs of 2.88 and 1.68, respectively, declining to 2.36 and 1.68 following adjustment.

4.4 Nested case-control study (Paper III)

45 out of the 52 cases (87 %) had well defined job titles in our measurement database; in many cases, involving a variety of well-defined jobs held during each individual's working life. The corresponding figures for the controls were 161/260 (62 %), thus with a larger proportion of well-defined jobs among the cases. Of the controls, 32 were used to 2 or 3 cases. For the 52 cases the average duration of employment was 17 years, ranging from 1 to 42 years; the 260 controls had the same average duration of employment as the cases, but a wider range from 1 to 55 years.

The correlation between the different measures of exposure was high, for both cases and controls, for exposure duration and cumulative exposure (r_s=0.95 and 0.97, respectively) as was the correlation between maximum intensity and cumulative exposure (r_s=0.94 and 0.96, respectively). The weakest correlations, for both cases and controls, were between exposure duration and median intensity (r_s=0.53 and 0.68, respectively).

The mixed model allowed us to identify factors affecting quartz concentration levels where the β-estimate represent the size of the analyzed factor compared to the reference category. The only job that was associated with significantly elevated levels was furnace and ladle repair (β=4.06; 95 % CI 2.78-5.93) when compared to the reference job title others. In contrast, caster and core maker were associated with lower exposure levels (β=0.54; 95 % CI 0.38-0.79 and β=0.59; 95 % CI 0.43-0.80, respectively). There were almost no differences in exposure levels when the time periods between 1980 and 2006 were considered; however, the first time period, 1968-1979, was associated with significantly higher quartz concentration levels (β=2.08; 95 % CI 1.75-2.47) when compared to the reference time period 2000-2006. 2 small iron foundries had significantly higher quartz concentration levels: one that uses green sand (company 3) and a second that uses synthetic binders (company 8) (β=1.31; 95 % CI 1.00-1.71 and β=1.63; 95 % CI 1.00-2.65 respectively) when compared to the reference company 10. Relatively low quartz levels were recorded at two large grey iron foundries (β=0.65; 95 % CI 0.50-0.83 and β=0.76; 95 % CI 0.57-1.0, respectively).

In the case–control analysis, the cumulative quartz exposure, categorized as low, medium and high exposure (0.5-<1, 1-1.9 and ≥2 mg/m^3* years, respectively), showed the highest OR for lung cancer (OR 1.17; 95 % CI 0.53-2.55) for the medium exposure group. There was no significant positive relationship between OR and cumulative exposure (Table 11). Analysis by duration of exposure showed the same pattern. For the 52 cases examined, the average cumulative exposure was 1.2 mg/m^3* years, ranging from 0.09 to 10 and for the 260 controls, the corresponding figure was 1.1 mg/m^3* years, varying from 0.06 to 5.7.

Table 11. Cumulative quartz exposure (mg/m³*years) and conditional logistic regression expressed as odds ratio (OR) and 95% confidence interval (CI) for lung cancer cases and controls in low, medium and high exposure groups at 10 Swedish iron foundries

Group	Cumulative quartz exposure (mg/m³*years)	Cases	Controls	Total	OR	95% CI
Reference	<0.5	20	103	123	1.00	
Low	0.5-<1	12	61	73	1.02	0.46 – 2.29
Medium	1-1.9	17	76	93	1.17	0.53 – 2.55
High	≥2	3	20	23	0.79	0.20 – 3.02

4.5 Predicting exposures (Paper IV)

The distribution of measurements across time periods, company size, and job titles were studied. The total numbers of measurements by 5 year time periods are 208-398, generating a large database divided in a historic model of 1,109 measurements, a development model of 809 measurements, and a validation model of 415 measurements. The number of measurements conducted in the four largest companies was considerably higher than available measurements in the four medium and three small companies. Some job titles had relatively few measurements, most notably transportation jobs, melter, and caster.

Trends in quartz exposure are presented as regression coefficients for the different mixed models (Table 12). The exposure levels in the periods 1968 to 1974 and 1975 to 1979 were 51 % and 28 % higher respectively than the exposure levels between 1985 and 1989. In later periods, quartz exposure was reduced by 8 % per 5 years at best. In the first period, smaller companies had approximately 50 % higher exposure levels than large companies, but these differences became much smaller in later years. The data used for the model fit are presented in Table 12 as the percent reduction of the between-worker variability, being 27 %, 48 % and 19 % for the historical, development and validation models respectively.

The comparison of the three mixed models for different time periods showed the same relative ranking of exposure levels across jobs in the three models with lowest exposures for core maker and highest exposures for furnace and ladle repair. However, profound differences were observed in actual exposure levels, both in absolute and relative terms.

The agreement between the estimated exposure in the first time period by the historical model and the last time period by the development model, showed a regression coefficient (B)=2.42, 95 % CI 1.99-2.84, an intercept value of 0.018 and an R-square value of 0.81 (Figure 6), showing that the development model underestimates the historical exposure levels between 1968 and 1974 by a factor of 2.4. Comparison with other time periods in the historical model showed that the agreement tends to improve with the later periods, as can be seen from the decreasing B values (2.42, 1.66, 1.20, and 1.19) and intercept values. The corresponding data for the agreement between estimated exposure in the last time period of the development model and the validation model (Figure 6), produced regression values of B=0.31, 95 % CI 0.15-0.47, an intercept value of 0.019, and an R-square value of 0.33, indicating that the development model overestimates current exposure levels.

Table 12. Results of mixed model analyses presented as regression coefficients (± standard error) by the historical, the development and the validation model

Determinant	n	Historical model	n	Regression coefficient Development model	n	Validation model
Intercept		-4.104 ± 0.102		-4.247 ± 0.145		-4.140 ± 0.167
Time period						
1968-1974	208	0.708 ± 0.116 *		n/a		n/a
1975-1979	237	0.334 ± 0.086 *		n/a		n/a
1980-1984	266	0.009 ± 0.083		n/a		n/a
1985-1989	398	0		n/a		n/a
1990-1994		n/a	341	0.089 ± 0.098		n/a
1995-1999		n/a	251	0.038 ± 0.103		n/a
2000-2004		n/a	217	0		n/a
2005-2006		n/a		n/a	415	0
Company level						
Small (n=3)	88	0.716 ± 0.134 *	91	0.051 ± 0.135	49	-0.077 ± 0.204
Medium (n=4)	270	0.471 ± 0.093 *	346	0.189 ± 0.092 *	144	-0.068 ± 0.136
Large (n=4)	751	0	372	0	222	0
Job title						
Caster	35	0.038 ± 0.208	25	-0.101± 0.249	22	0.252 ± 0.315
Core maker	118	0	76	0	55	0
Fettler	425	0.474 ± 0.109 *	279	0.663 ± 0.143 *	114	1.042 ± 0.200 *
Furnace and ladle repair	56	1.812 ± 0.178 *	50	2.080 ± 0.210 *	26	1.359 ± 0.267 *
Maintenance	50	0.699 ± 0.168 *	21	0.821 ± 0.278 *	26	0.239 ± 0.284
Melter	29	0.163 ± 0.215	63	0.511 ± 0.187 *	48	0.343 ± 0.245
Moulder	136	0.438 ± 0.137 *	114	0.587 ± 0.166 *	62	0.625 ± 0.234 *
Sand mixer	56	0.528 ± 0.181 *	35	0.409 ± 0.224	14	0.134 ± 0.361
Shake out	72	0.222 ± 0.182	66	0.318 ± 0.195	16	1.365 ± 0.350 *
Transportation	24	0.651 ± 0.222 *	27	0.534 ± 0.252 *	9	0.202 ± 0.414
Others	108	0.724 ± 0.136 *	53	0.715 ± 0.193 *	23	0.326 ± 0.301
Variances (full model)						
σ^2_{WW}		0.267		0.857		0.287
σ^2_{BW}		0.699		0.245		0.653
Reduction in σ^2_{BW}		27 %		48 %		19 %

*: $p < 0.05$
n: number of measurements
n/a: not available
ref: reference category
σ^2_{WW}: within-worker variance
σ^2_{BW}: between-worker variance
Reduction in σ^2_{BW} (%) = $((\sigma^2_{BW,\text{ intercept model}} - \sigma^2_{BW,\text{ full model}}) / \sigma^2_{BW,\text{ intercept model}}) \times 100$

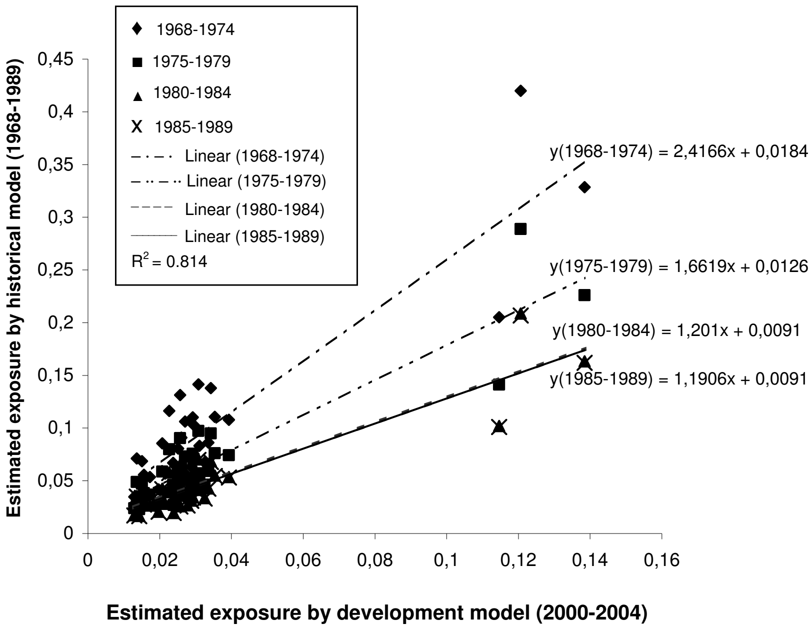


Figure 6. Agreement between estimated quartz exposure for the last time period in the development model and the four time periods in the historical model by job titles in small, medium and large companies. The line representing the time period 1980–1984 is covered by the line representing the time period 1985–1989

5 Discussion

5.1 Exposure measurements (Paper I)

Exposure measurements were performed according to Swedish and international measurement standards, providing valid exposure data for further exposure assessment (Swedish Standard, 1995). To provide comparable quartz concentration data for different time periods, i.e., to make comparisons with historic measurements in our retrospective cohort study, we used a sampling cyclone with characteristics specified in the Johannesburg convention (NBOSH, 1979), resulting in slightly higher quartz concentrations compared to sampling with the present standard (Swedish Standard, 1993).

The Swedish Board of Accreditation and Confirmity Assessment (SWEDAC) has accredited our analysis of respirable dust, quartz and cristobalite, ensuring valid analysis results.

The foundries in our survey represented different sizes and production rates as well as different binders for the cores and moulds, based on green sand or chemicals. All jobs were represented, a large number of measurement data was included and manual and automated techniques were represented. Therefore, the selection of Swedish iron foundries in our study should adequately reflect the variety of techniques and types of casting used in the Swedish iron foundry industry.

Data from our survey, showed average respirable quartz concentrations between 0.024 and 0.17 mg/m^3. A Swedish and comparable Finnish study from the late 1960s and the early 1970s (Gerhardsson et al., 1974; Siltanen et al., 1976), showed much higher concentrations compared to our survey data, illustrating the development of foundry technology as well as improved elimination techniques during a number of decades of foundry development.

The quartz content in the respirable dust fraction in our study varied between 5 and 7 % for all job titles, except for furnace and ladle repairmen for whom a concentration of 11 % was recorded. This could be compared to higher quartz content in the respirable fraction as determined in Swedish and US studies from the late 1960s and the early 1970s (Gerhardsson et al., 1974; Oudiz et al., 1983), implying that improvements to exposure conditions have been particularly successful with respect to quartz.

Within- and between-worker variability was examined using the statistic GSD. In total, the mean GSD for respirable quartz was 2.8 and ranged between 1.7 and 3.6. In other industrial environments the same degree of variability has been recorded (Rappaport, 1991). The GSDs are in the same order of magnitude as estimates of exposure variability used by the SWEA to adopt 0.2 OEL as an action limit for quartz exposure (NBOSH, 1979).

The effectiveness of a respirator depends on proper use during periods of high dust levels, filter penetration and filter pressure drop, as well as how well the respirator fits the face. Therefore, the PF (the ratio between the air concentration of a pollutant outside and inside the respirator) varies considerably depending on the type of mask. Filtering face pieces, half masks and blower assisted particle filters have PFs from 4 to 200 depending on the filter quality and a perfect facial fit (which require a clean shaven face) (Wilhelmsson, 2007). The jobs with the highest exposure in our study would comply with the ACGIH-TLV of 0.025 mg/m^3 only if operatives used respiratory equipment with a PF equal to or greater than 200, i.e. the use of blower assisted filtering masks or respirators with an air supply. Most of the work performed by furnace and ladle repair operatives in our study was undertaken by workers wearing filtering face pieces or half masks. Quantitative fit tests on negative pressure respirators, i.e. half masks or full face masks, indicate that 3-day stubble reduces the PF by approximately 10 and a short, trimmed beard by a factor of 100 (Wilhelmsson, 2007). As a consequence, workers using filtering face pieces or half masks are “actually exposed“ to concentrations exceeding the ACGIH-TLV for quartz and should be using, at least, blower assisted filtering protection equipment with an appropriate quality of filter.

Short-term exposure to dust is not considered by the work-environment agencies and consequently no short-term exposure limit exists. However, the development of personal real-time data loggers to record aerosols has made it possible to conduct studies that simultaneously determine the short-term exposures along with respiratory symptoms and effects, as well as irritation of the mucous membranes (Hu, Wegman, Eisen, Woskie, & Smith, 1992; Wegman et al., 1994). In addition, very high momentary concentration peaks of total aerosol, ranging from 9.6 to 388 mg/m^3, were recorded, strongly indicating the risk of acute respiratory effects.

5.2 Epidemiological data (Paper II and III)

5.2.1 Cohort study

In our cohort, the total employment of the cohort comprised 70,388 person years, with a mean duration of employment of 13 years. The majority of the cohort members were born before 1960, thus providing sufficient exposure and latency time of the cohort to enable robust statistical evaluation of their lung cancer risks. For our study we were able to make use of the comprehensive records in the Swedish mortality and cancer morbidity registers, run by the Swedish National Board of Health and Welfare. In addition, a foundry-specific measurement database of respirable dust and quartz air concentrations, based on data from our survey and our historical measurement database was available. We were thus able to calculate quantitative exposure measures of respirable quartz doses for each individual and, in addition to standard measures of exposure, we also applied cumulative quartz measures.

Data for our iron foundry cohort were extracted from registers of a number of Swedish iron foundries, reflecting wide ranges in the scale of production, production techniques, the chemical binders used for cores and moulds and (hence) possible chemical exposures. In addition to respirable dust and quartz, phenol, formaldehyde, furfuryl alcohols, polycyclic aromatic hydrocarbons (PAHs), carbon black, isocyanates and asbestos are used or generated by foundry production techniques and exposure to any of these substances could have potentially carcinogenic effects.

5.2.2 Nested case-control study

We also performed a nested case-control study within the cohort. This design is applied when confounders and effect modifiers are particularly important for the outcome, and by retrieving the cases and controls from the same study group the differences in these background aspects could be adjusted for. The cases and controls were originally retrieved from the personnel files from 11 iron foundries. However, 1 foundry appeared to have incomplete records when we compared the observed and expected number of deaths, 5 and 57 respectively, so this was excluded from the study, leaving 10 iron foundries, 52 lung cancer cases and 260 controls to be used in the case-control study and to contribute to the measurement database.

5.2.3 Lung cancer

Our cohort analysis results indicated an overall increased risk for lung cancer (SIR 1.61), but no dose-response trends were detected when the data were analysed by either duration of employment or duration of exposure. The highest SIR was observed for foundry workers with short-term (<2 years) employment. However, when 20 years of latency was applied, the duration of employment, exposure and cumulative quartz exposure showed significant risks for the long term or high exposure groups, representing quartz doses of 1-2 mg/m^3* year and >2 mg/m^3* year. In the nested case-control analysis, we found the highest odds ratios of lung cancer (OR 1.17) for the medium exposure group. No dose–response trend or significantly increased risk was determined for our high exposed group (≥2 mg/m^3), representing 40 years of exposure at 0.05 mg/m^3 of quartz. The contradiction between our findings in the cohort and nested case-control studies, where we assign the case-control study higher validity in terms of adjusting for confounders since the cases and controls derive from the same study population.

Other international cohort or case-control studies have found varying dose-response patterns when using standard exposure measures. The cohort study of United States foundry workers (Andjelkovich et al., 1990) found an overall increase but no dose-response relationship, similar results when cumulative quartz exposure measures were used in a nested case-control study within the cohort (Andjelkovich et al., 1994). For Chinese iron and steel foundry workers, a significant excess risk (Xu, Pan et al., 1996) was determined, and similar results were determined in a cohort of Danish foundry workers (Sherson et al., 1991). In addition, for German male iron foundry workers an increased risk was also noted (Adzersen et al., 2003).

Comparisons of our data with previous cohort or case-control studies with quantitative quartz exposures are vital. In a US study of grey iron foundry workers (Andjelkovich et al., 1994), the nested case-control study used dose measures of high, medium and low exposure (1.5; 0.55 and 0.05 mg/m^3, respectively), no dose-response was detected. A case control study of Chinese iron foundry workers with cumulative respirable quartz exposures ranging from <3.7 up to >27.7 mg/m^3* year established a significant excess risk for all exposure groups (Xu, Brown et al., 1996). Exposure of the low exposed group would correspond to approximately 0.1 mg/m^3 of respirable quartz exposure for a working life of 40 years. In a nested case-control study (Westberg & Bellander, 2003) of quartz exposure and lung cancer, Swedish aluminium foundry workers were found to have an excess risk of SIR 1.6 for cumulative quartz exposures up to 1.0 mg/m^3* year and SIR 2.6 for exposures exceeding 1.0 mg/m^3* year (median 1.4 mg/m^3* year), however these excess risks were not statistically significant. These exposures roughly correspond to respirable quartz concentrations up to 0.025 mg/m^3 for an SIR of 1.86 and >0.025 mg/m^3 for an SIR of 2.5 over a working life of 40 years. A recent meta-analysis of associations between quartz exposure and lung cancer (Lacasse, Martin, Gagne, & Lakhal, 2009), 10 studies including two foundry studies showed statistically significant relative risks >1 were determined for cumulative quartz doses >1.84 mg/m^3* years. The results from our cohort study are in line with these previous findings; we determined significant SIRs of 2.88 and 1.68 with a latency of >20 years at life time quartz doses of 1-2 and >2 mg/m^3*

year, however our case-control study showed no slightly different results and no significances.

5.2.4 Confounders, effect modifiers

5.2.4.1 PAH

A review of published cohort studies on lung cancer in various occupational settings and exposures to PAHs included several iron and steel foundries (Bosetti, Boffetta, & La Vecchia, 2007), but the excess lung cancer found in the review was not attributed to this exposure. Furthermore, in an earlier review (Boffetta, Jourenkova, & Gustavsson, 1997), the excess lung cancer among workers in iron foundries potentially due to PAH exposure was considered to be too complex to assess independently because of competing exposures to quartz and asbestos. However, a nested case-control study of Chinese foundry workers has addressed this issue, dose-response patterns were and excess risks of lung cancer at BaP levels >2 µg/m^3 (Xu, Brown et al., 1996). In European iron and steel foundries, PAH concentrations in the range of 0.1 to 1 µg/m^3 have been found (Verma et al., 1982), and measurements of PAHs in aluminium foundries have also been reported, with concentrations ranging from <0.002 to 0.32 µg/m^3 (Westberg, Selden, & Bellander, 2001). Considering the relatively low exposure levels generally reported in foundries and the conclusions in the meta-analysis PAHs could not be a major cause of lung cancer in iron foundries.

5.2.4.2 Asbestos

Asbestos has been used in iron foundries for insulation purposes, but published measurement data and epidemiological studies focusing on asbestos exposure in iron foundries are rare. In the IARC monograph on cancer risk factors in iron and steel foundries, those posed by asbestos were not specifically addressed (IARC, 1977), but reported exposure levels in iron foundries were low, ranging from 0.0001 to 0.0033 fibres cm^{-3} (Gullickson & Doninger, 1980), implying that levels of asbestos exposure were low. On the other hand, asbestos-related changes have been observed in x-rays of foundry workers' lungs (Rosenman & Reilly, 1998) and a study of respiratory patients in Lithuania has indicated that a fraction of the lung cancer cases might be attributed to heavy occupational exposure to asbestos (Everatt, Smolianskiene, Tossavainen, Cicenas, & Jankauskas, 2007). Even though the fibre levels would appear to be low, the contribution to cancer incidence of asbestos exposure in iron foundries should not be completely ignored. However, in our study only one case of mesothelioma was detected amongst the cohort of foundry workers, supporting the idea of low exposure levels of asbestos in the foundry environment.

5.2.4.3 Smoking

Adjustment for differences in smoking habits between the foundry worker and the general population is necessary to assess risks attributed to other environmental factors than smoking. Data from the register of individuals in the cohort provided no information on individual smoking habits, so we adjusted the calculated incidence ratios for smoking, based on unweighted calculations of smoking habits from national registers over the same time period. The calculations (Rosen et al., 1987) resulted in an adjustment factor of 0.85. Such an estimate may not be completely reliable, as both the estimates of smoking frequencies of the foundry workers and the general population, and the assumed 10-fold difference in lung cancer incidence between smokers and non-smokers, are crude. However, the adjustment factor may be quite insensitive to differences in smoking frequencies; a 5-, 10- or 20-fold difference in smoking frequencies resulted in weighted adjustment factors ranging from 0.85 to 0.89. Although adjustment for smoking habits in our study caused some change in the SIR for lung cancer (SIR 1.61 vs an adjusted value of 1.31; 95 % CI 1.20-2.12 vs an adjusted value of 0.95-1.76) and in the significance of excess cancer risks for some exposure groups, the overall dose-response and latency findings remained unchanged. We consider the figures achieved performing adjustment for different smoking habits indicative rather than absolute.

The relative incidences of other tobacco smoke-related cancers (IARC, 1986), such as cancers of the bladder, larynx and oesophagus were also evaluated. The overall SIR for bladder and larynx cancers was elevated among our cohort (SIR 1.22, 95 % CI 0.85-1.83 vs 1.77 95 % CI 0.65-3.85), supporting our assumptions regarding possible differences in smoking habits between the foundry workers and the general population, or some other occupational exposure.

5.3 Measurement database (Paper IV)

5.3.1 Database quality

Establishing relationships between risks and individual exposures determined as respirable quartz concentrations for different time periods, companies, and job titles require high quality data. Retrospective exposure data rarely exist for each individual over the whole time period of interest. Relying on information present in personnel and company registers calls for models based on accessible data. In addition, an analysis of determinants or fixed effects can also facilitate interpretation of their relevance to outcomes and influences on the model, i.e. the extent to which they explain the variation within the data or the association with random effects. For our data, the use of a mixed model offered substantial advantages (in particular the within- and between-worker variation) compared to various forms of multiple linear regressions. No formal evaluation was done (comparing our set of data with a subset) however our database contains many measurements evenly distributed over jobs and time periods implying a robust model.

Model validation is seldom undertaken; at best, a subset of data is saved for validation purposes or a cross-validation is carried out to investigate the model performance where real data is compared to model data. However, for validating the modelling in Paper IV we also investigated whether the later period used in the development model (2000 to 2004) agreed with the validation model, based on the comprehensive survey carried out for the research. The analysis of the intercept, 0.019 (95 % CI 0.011 - 0.026), produced by the linear regression validation is of special interest. It implies that there is a constantly elevated exposure level calculated by the validation model for very low actual quartz exposures, and lower levels determined by the validation model for higher actual quartz concentrations. However, the B value of 0.31 suggests decreased quartz levels over time, clearly shown in the measurement database.

Trends in quartz exposure over time show a strong reduction of 6 to 7 % per year between 1968 and 1974 and between 1975 and 1979. In the later periods, quartz exposure was reduced by 8 % per 5 years at best. Through the earliest period, smaller companies had approximately 50 % higher exposure levels than the large companies, but these differences were much reduced in later years. Evaluating trends in exposure using a mixed model analysis applied to data from the nickel production industry (Symanski, Chan, & Chang, 2001) using a database of measurements made from 1973 to 1995 revealed significant negative trends for smelting (-5.9 % per year), refining (-7.7 % per year) and almost significantly for milling (-13 % per year). Analysis of another international database, containing 700 datasets on exposure to chemical agents in various industries published over a 30-year period (1967 - 1996), showed a median annual trend of –8 % (Symanski, Kupper, & Rappaport, 1998), while most exposure levels declined at rates ranging from –4 % to –14 % per year. Other studies of long-term trends in occupational exposure in industries such as paving, carbon-black manufacture, rubber manufacturing and wood dust all described annual reductions of 6 to 14 %, which also corroborate the results of this research (Burstyn, Kromhout, Kauppinen, Heikkila, & Boffetta, 2000; Teschke, Marion, Vaughan, Morgan, & Camp, 1999; van Tongeren, Kromhout, & Gardiner, 2000; Vermeulen, de Hartog, Swuste, & Kromhout, 2000). Whilst evaluating control measures, the exposure to inhalable dust in the Dutch rubber industry was measured over a ten year period: the average (annual) decrease in the levels of inhalable dust ranged from 0.7–7 % for different job categories (Burstyn et al., 2000; Teschke et al., 1999; van Tongeren et al., 2000; Vermeulen et al., 2000). The trends in exposure to bitumen and PAHs seen in the period 1970 to 1998 revealed a reduction of exposures to bitumen fume by 6 %, to bitumen vapour by 14 % and to PAHs by 11 % (Burstyn et al., 2000).

Although the general trends of annual decline seem to produce comparable percentage reductions in exposures when different branches and industrial sectors are compared, the limitations are obvious. First, it would be necessary for the industrial sectors that were compared to be part of the same technological development. Secondly, these declines could only be used for overall evaluations and not for predicting time trends for individual workers. These types of data are often required when exposure data is to be used in epidemiological studies i.e. resolution of exposure measurements for individual workers in specific jobs.

5.3.2 Prediction of exposures

The development model, using data from the more recent set of measurements, was compared with a corresponding model based on historical measurements. This is a common situation when analysing retrospective exposures in epidemiological studies, in particular when trying to predict what long-term adverse health effects may result from past exposures.

It is clear from the historical exposure data that a significant change in foundry production techniques occurred in the 1970s. This change in exposure levels was the result of the introduction of new mechanical working methods, which replaced manual operations and used new chemical binders, as well as improving the overall exhaust ventilation systems. The large decrease in exposure levels needs to be considered when developing exposure models for estimating historical exposure patterns. In this research, the agreement between the last period of the development model (2000 - 2004) and the first time period of the historical model (1968 - 1974) has a surprisingly high correlation coefficient ($R^2 = 0.81$). However, comparing other historical periods (1975 - 1979, 1980 - 1984 and 1985 - 1989) produces the same R^2 for all correlations, due to the mixed model where an additive approach was used when calculating the exposures. Notably, the regression coefficient, B, ranges from values of 2.42 down to 1.2, all strongly suggesting a positive linear relationship with the modelled data from the development model that was used to estimate data from historical periods. The models fit less well for the older time periods, which is partly explained by the fact that extreme exposures were more frequent in the past. These extreme exposures have a large influence on the models.

The historical exposures were underestimated when using the development model, with the underestimation reduced in more recent years. As a consequence, those workers from the older time periods will have experienced a true cumulative exposure that is much higher than the estimated cumulative exposure based on the development model. Since the exposure is underestimated, the risk due to exposure will be overestimated in cohorts that rely primarily on workers for whom more historical measurements were taken. The underestimation is the consequence of the observed trend in exposure levels over time not being accounted for by the models. This demonstrates the importance of knowing general information on changes in production processes and the consequent changes in exposure patterns. In some epidemiological studies, authors have adopted multipliers to compensate for the expected elevated exposure levels in the more distant past (H. Checkoway, Heyer, Demers, & Breslow, 1993). The prediction of historical exposure patterns may indeed be improved by the use of these multipliers, provided that they accurately reflect the true changes in average exposure levels across the industry.

5.4 Suggestions for future research

Further research on this material is to investigate the causes of mortality for foundry workers, and especially cardiovascular disease and particle exposure.

Another study to be done is international evaluation of the existing studies, conducted by an international body such as IARC. Focus should be directed on studies with good exposure data. In addition, due to high aerosol and quartz exposure, more studies on other adverse health effects in the foundry environment should be conducted.

In Swedish iron foundries I would wish for a large measurement program together with a cohort study in the iron foundries with measurements of all carcinogens in the foundry environment to be able to investigate suspected substance by type of cancer. This large measurement study would preferably be combined with health measurements such as respiratory function of the participating workers. Another unexplored area in Swedish iron foundries is biological monitoring. For example can serum levels of TNF-alpha (tumor necrosis factor alpha) be used as a sign of quartz exposure, a biomarker of exposure.

6 Conclusions

- Measurements in Swedish iron foundries revealed high exposures to respirable quartz, regardless of the type of foundry. Air concentrations of respirable quartz exceeding the Swedish OEL were found most commonly for fettlers and furnace and ladle repairmen, but melters, moulders, sand mixers and shake out operators were also exposed to levels over the threshold. In all, 15 % of the 8-hour TWA measurements exceeded the Swedish OEL, 32 % exceeded the suggested EU-OEL and 57 % of the measurements exceeded the ACGIH-TLV.
- The high exposure jobs that could be determined were in particular fettlers and furnace and ladle repair workers. High peak-exposures (>100 mg/m^3) to respirable dust were also found for almost all work categories.
- The use of respiratory protective equipment can reduce the personal exposure if proper protection factor is used according to the exposure and the respirators are used during all the moments of high exposure. The workers are still in need of continuous education/information to make sure that the protective equipment is used properly. The use of respirators was evaluated and, for some jobs, the actual exposure levels exceeded the OELs in spite of using the masks during dusty jobs and even assuming a perfect fit and appropriate protection factors.
- The results of the cancer morbidity study indicate an increased lung cancer risk for Swedish foundry workers exposed to quartz particles. The overall risk for lung cancer was significant, 1.61, but with adjustment for smoking habits the relative risk decreased to 1.31, a non-significant increase. In the nested case–control study on lung cancer and quartz exposure, no statistically significant increasing rate of lung cancer was identified.
- No dose-response trends were detected between lung cancer morbidity and quartz exposure amongst the male iron foundry workers we considered when the data was analysed by either duration of employment or duration of exposure. However, when 20 years of latency was applied, the duration of employment, exposure and cumulative quartz exposure showed significant risks for the long term or high exposure groups. These findings were not clearly

replicated in our case-control study, introducing uncertainty in our dose-response findings or implying safe levels <0.05 mg/m^3.

- The ability to predict the past may be done if jobs and time period are taken into account since the actual exposure levels differ substantially which is due to the observed rapid changes in the years 1968-1974, whereas in more recent years there have been less dramatic changes in production process. Additional information needs to be taken into account when carrying out back-extrapolation of current exposure levels. In particular, long-term trends are not sufficiently reliable to describe exposure by company, job and time period for the purposes of retrospective exposure assessment i.e. creating individual dose measures based on historical exposure patterns.
- To reduce the personal exposure levels as well as emission to the environment there is a need of further research and for preventive measures to be introduced with respect to production, ventilation and the use of personal protective equipment.

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