

Cancer mortality in German carbon black workers 1976–98

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Background: Few studies have investigated cancer risks in carbon black workers and the findings were inconclusive.

Methods: The current study explores the mortality of a cohort of 1535 male German blue-collar workers employed at a carbon black manufacturing plant for at least one year between 1960 and 1998. Vital status and causes of death were assessed for the period 1976–98. Occupational histories and information on smoking were abstracted from company records. Standardised mortality ratios (SMR) and Poisson regression models were calculated.

Results: The SMRs for all cause mortality (observed deaths (obs) 332, SMR 120, 95% CI 108 to 134), and mortality from lung cancer (obs 50, SMR 218, 95% CI 161 to 287) were increased using national rates as reference. Comparisons to regional rates from the federal state gave SMRs of 120 (95% CI 107 to 133) and 183 (95% CI 136 to 241), respectively. However, there was no apparent dose response relationship between lung cancer mortality and several indicators of occupational exposure, including years of employment and carbon black exposure.

Conclusions: The mortality from lung cancer among German carbon black workers was increased. The high lung cancer SMR can not fully be explained by selection, smoking, or other occupational risk factors, but the results also provide little evidence for an effect of carbon black exposure.

Carbon black is a powdered form of elemental carbon that is manufactured by the controlled vapour phase pyrolysis of hydrocarbons. Preferential raw materials for most carbon black production processes are oils with a high content of aromatic hydrocarbons. Over 90% of the world's carbon black production is used for the reinforcement of rubber; about two thirds are used for tires and one third for the production of technical rubber articles. Car tires contain approximately 30–35% of carbon blacks of different types. The remaining world production of carbon black is used for printing inks, colours and lacquers, stabilisers for synthetics, and in the electrical industry.¹

In 1995, a working group convened by the International Agency for Research on Cancer (IARC)¹ concluded that carbon black is possibly carcinogenic to humans (Group 2B). This evaluation was based on *sufficient evidence* for carcinogenicity in animals and *inadequate evidence* in humans. Two cohorts studies in the carbon black production industry and a few case control studies were evaluated. One American cohort was enumerated from four plants and observed no excess mortality from any type of cancer.^{2–4} This study, however, had certain methodological problems, including incomplete ascertainment of deaths.¹

A UK cohort⁵ was derived from employees of five carbon black production plants and 25 deaths from cancers of trachea, bronchus, or lung were observed up to 31 December 1980 in male manual workers who had at least one year of exposure to carbon black, yielding a standardised mortality ratio (SMR) of 154 (95% CI 100 to 228). In an update of the UK cohort,⁶ with an additional 16 years of mortality follow up, the SMR for lung cancer was 173 (61 deaths, 95% CI 132 to 222). Some limited data on work histories could be retrieved, but smoking information was unavailable. The study did not establish a link between the increased lung cancer risk and carbon black exposure nor did it provide a coherent explanation of the increased risk of lung cancer.

The objective of the current study was to investigate the mortality of blue collar workers in a large carbon black manufacturing plant in Germany, where information on work histories and on smoking habits of the employees was available.

METHODS

Study population

The cohort was recruited from one large German factory with a long history of carbon black production and was enumerated from entry and exit books from the plant and from personnel charts. A total of 2053 blue-collar workers of the carbon black plant who were continuously employed for at least one year between 1 January 1960 and 31 December 1998 were eligible. Workers who were hired before 1960, but who fulfilled the above inclusion criteria were also eligible; the cohort therefore is a census cohort. This approach was chosen to increase the power of the study. The starting point of the study period was chosen because documentation of personnel data has markedly improved in 1960.

Assessment of vital status and causes of death

Follow up for vital status started on 1 January 1961, the first date on which a subject eligible for the study could have died, and ended at 31 December 1998, age of 85 years, or loss to follow up—whichever came first. The censoring at the 85th birthday was performed because death certificates are often considered less valid for very old people.⁷ Cohort members who were employed at the plant at the end of the observation period or receiving pensions from a plant-specific pension plan were considered to be traced alive. The vital status of all

Abbreviations: HWSE, healthy worker survivor effect; IARC, International Agency for Research on Cancer; ICD, International Classification of Diseases; LDS, Landesamt für Datenverarbeitung und Statistik; NRW, North-Rhine Westphalia; SMR, standardised mortality ratio

other employees was ascertained from the local population registries of the latest place of residence. The latest residence was traced from the population registries of the last known residence as listed in the plant personnel charts and all subsequent residences. When necessary, information was also requested from the responsible register office at the person's place of birth and/or death. On average, four searches per person were necessary to determine a person's vital status; in some cases it took more than 10.

The causes of death of the deceased cohort members were determined from death certificates archived in community health departments. We asked for a copy of the death certificate for each deceased cohort member. All death certificates from community health departments were then sent to the State Institute of Statistics (Landesamt für Datenverarbeitung und Statistik, LDS) of North-Rhine Westphalia (NRW), one of the 16 federal states (Bundesländer) of Germany, where they were coded by a professional nosologist in accordance with the International Classification of Diseases (ICD), ninth revision.

Nearly all deaths occurred in North-Rhine Westphalia, where law requests that the local health departments keep the death certificates for at least 10 years. In addition, for official cause of death statistics copies of death certificates are sent to the respective State Institute of Statistics which codes the cause of death by ICD and stores for each death an anonymous, but individual data record. In North-Rhine Westphalia such individual data records have been kept since 1976. In our study, the LDS NRW supplemented the ICD code of the underlying cause of death when the cause of death could not be obtained from community health departments. A special procedure for this data transfer was arranged to guarantee adherence to data protection rules.⁸

The distribution by gender and nationality of the 2053 eligible participants and the results of the follow up are shown in table 1. Most participants are German males. Nearly half of the non-German participants, but only a few German subjects, have been lost to follow up. Ascertainment of cause of death for the period 1961–98 is not entirely satisfactory in the full study cohort (84% in the 396 deceased German males). However, in the subcohort of workers traced alive until 1976, the year when the recording of causes of death by the LDS NRW began, follow up was more successful. For the 1535 male German workers traced alive on 1 January 1976 vital status could be traced for 98.8%; in this group, cause of death was ascertained for 97.9% of those known to be deceased.

Assessment of job histories and carbon black exposure

Personnel charts were examined to reconstruct detailed job histories. We reconstructed the development of plant sections, workplaces, and job titles as they have evolved during the study period 1960–98, in close collaboration with plant personnel. Since measurements on workplace exposure to carbon black were scarce and limited to recent years, a semiquantitative scoring system to assign carbon black exposure to job histories, depending on workplaces, occupation, and calendar time was developed together with experts from the plant. The expert panel comprised current and retired staff members in leading positions familiar with historical working conditions. These experts assigned scores (intensity of exposure) to each job title. The highest score (20 units) was assigned to jobs where carbon black had to be shoveled into bags, a procedure that came to an end in the early 1960s. A score of zero was assigned to the few jobs with no contact to carbon black, like some jobs in the “logistic department”. Starting from these extreme exposure conditions, scores for the other jobs were estimated. Since the carbon black exposure was continuously reduced in the course of time, each job title was assigned a score for 1 January 1960 and a score for 31 December 1998. For the analyses it was assumed that carbon black exposure declined linearly in this time span. Exposure before 1960 was assumed to be on the same level as on 1 January 1960.

The reconstruction of complete job histories including department, work area, and job tasks was successful in 73% of male Germans still alive on 1 January 1976. For most other cohort members at least information on work area was available. When not all details for a specific job phase were available, we assigned the time specific average exposure of all employees of the same department, work area, and job tasks according to the best available information for the individual cohort member.

To investigate working areas with heavy exposure, we identified on the basis of the job histories workers who had been employed for at least one year in the carbon black manufacturing sectors “lamp or furnace black”, “gas black”, or the “preparation plant”; or in “heavily exposed jobs” comprising the three previous categories but excluding some specific job titles with less exposure.

Assessment of smoking habits

Data on individual cigarette smoking habits were collected from paper charts of the plant occupational health service. As

Table 1 Number of observed deaths and standardised mortality ratios (SMRs) with 95% confidence intervals for all-cause mortality among all eligible carbon black workers by study period, nationality, and gender

Nationality	Gender	n	Lost to follow up	deaths	Known cause of death	Exp	Person years	SMR*	95% CI
<i>Study period 1960–98</i>									
German	Men	1617	37	396	333	347.9	36071	114	103–126
	Women	106	5	17	16	18.3	2957	93	54–149
Non-German	Men	327	160	14	8	25.5	4308	55	30–92
	Women	3	3	–	–	0.01	10	–	–
<i>Traced alive on 1 January 1976†</i>									
German	Men	1535	19	332	325	275.5	25759	120	108–134
	Women	101	0	17	16	15.5	1966	110	64–176
Non-German	Men	215	49	13	8	21.3	3135	61	33–104
	Women	0	–	–	–	–	–	–	–

*Reference rates from (West) Germany.

†Due to lack of information on the underlying causes of deaths before 1976, the subsequent analyses are restricted to participants known to be alive at least until 1 January 1976; see Methods section.

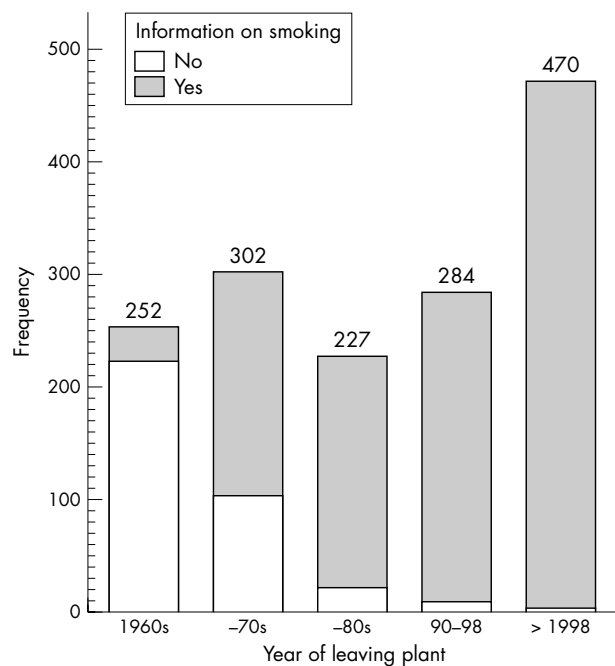


Figure 1 Number of male German carbon black workers traced alive on 1 January 1976, by year of termination of employment and availability of information on smoking.

part of regular occupational health examinations (pre-employment and roughly in three year intervals) the occupational physician requested information on smoking habits. Completeness of information on smoking status increased over time and is reasonably complete since the early 1970s. Figure 1 shows the percentage of subjects with information on smoking by year of termination of employment among the 1535 German men who were traced alive on 1 January 1976. Overall, information on smoking habits was available for 77% of the cohort. For these men there was at least one document which describes the smoking habits at the time when asked by the physician and sometimes includes information on previous smoking habits. Most often, a current smoker was asked for current cigarette consumption only, whereas previous smoking habits were most often documented in ex-smokers.

The current smokers were classified according to their average cigarette consumption, categorised at >0–12, >12–24, and >24 cigarettes per day. The average cigarette consumption was calculated from the subject's current smoking habits, as statements on past smoking habits may be less reliable. Alternative classifications of smoking habits were also employed: we calculated the average number of cigarettes smoked per day by including information on previous smoking habits. Quitting smoking was modeled as an additional variable rather than an extra category in one smoking variable or was completely ignored. In the latter case, smoking intensity was only calculated from current cigarette consumption—that is, ex-smokers and never-smokers were combined as current non-smokers.

Statistical analyses

The full study cohort (1960–98) was analysed for all-cause mortality. Analyses of cause-specific mortality were restricted to the observation period 1976–98, the period for which retrospective assessment of cause of death in NRW became feasible and follow up was reasonably complete. Such restrictions had been anticipated in the planning of the study. Indeed it turned out that there were 82 male German

workers who were censored before 1976, of whom 18 were lost to follow up and 64 had died. For these 64 deaths, the cause of death was known for only eight cases. None of them had died from lung cancer. Non-German employees were excluded from cause-specific analyses because of insufficient assessment of vital status and cause of death. Women were excluded due to small numbers. Thus, most analyses are based on 1535 male German workers, traced alive on 1 January 1976. We refer to this cohort as the main study cohort. Since it is a subset of the whole cohort, it is also a census cohort.

Since there was evidence for bias due to a selection of cohort members via a cross section of the active workers in 1960, we performed additional analyses of the cohort of male German workers who were hired in 1960 or later—that is, we defined an inception cohort within the main census cohort.

Calculation of SMRs

We calculated standardised mortality ratios (SMRs) for all-cause mortality and cause-specific mortality for the full cohort, stratified by nationality (German, non-German) and gender. The SMR compares the number of observed deaths among the study subjects with the expected numbers based on national or regional reference rates and is expressed as a percentage.^{9–10} Expected numbers are calculated by applying the age (five year age groups) and calendar year distribution of the cohort to the corresponding mortality rates of (West) Germany or North-Rhine Westphalia. The reference data for (West) Germany were obtained from the WHO Mortality Database of the WHO Statistical Information System.^{11–12} The WHO supplies German reference data for residents of the unified Germany for the years 1990 and later and for the two former German states for earlier periods. For the period up to 1990, we used the mortality data of the former Federal Republic of Germany. Reference rates for the state North-Rhine Westphalia were obtained from the Federal Statistical Office of Germany (Statistisches Bundesamt Deutschland). SMR analyses were based on an “event timetable” that was constructed by an SAS program following the ideas of Wood *et al*¹³ and allowed to consider time dependent categorical variables. Confidence intervals are exact under the assumption of a Poisson distribution for the number of events.¹⁴

Internal comparisons using Poisson regression

Relative risks for categorical explanatory variables were calculated by means of Poisson regression,¹⁰ adjusted for age (in five-year categories), and smoking. For assessment of linear trends, midpoints of the categories were used for the explanatory variables and were treated as continuous. For open ended categories, the midpoints of the previous categories were extrapolated linearly. An exception is cumulative carbon black, where the values 3.75, 7.5, 15, 30, and 60 units were used. The smoking variables described above contain a category “no information”. This approach to deal with missing values in a potential confounder variable has advantages and disadvantages.¹⁵ We therefore performed all computations also for the subset of subjects with information on smoking.

Person time for the SMR analyses and Poisson regression was accrued for the appropriate follow up periods 1960–98 and 1976–98, respectively. Individual person time does not start until the participant becomes eligible for the study—that is, after the first year of employment in the time interval 1960–98.

RESULTS

Turnover of workforce, age distribution of employees

Figure 2 shows the distribution of date of hiring in the main study cohort of German men traced alive on 1 January 1976;



Figure 2 Number of male German workers, traced alive on 1 January 1976, by decade of hiring and age at hiring.

259 workers (16.9%) were hired before 1960. About one third of the study cohort was hired in the sixties, about 20% in the seventies and eighties each, and about 7% in 1990-97. The distribution of age at hiring seems to be similar over all

decades of hiring, but with a slight tendency towards higher ages in the sixties.

SMRs for all-cause mortality

The all-cause mortality of all cohort members, in comparison with the (West) German population, is given in table 1. SMRs are stratified by nationality (German, non-German), gender, and study period (1960-98, 1976-98). All-cause mortality is slightly increased in German men, it is close to expected in German women, and decreased in non-German men. In the latter group a high percentage of cohort members was lost to follow up.

Cause specific SMRs

Table 2 lists observed numbers of cause-specific deaths and SMRs among male German blue-collar workers. Increased SMRs based on sufficiently high numbers of deaths are observed for all-cause mortality, as well as mortality from lung cancer (ICD-9 162), heart diseases (ICD-9 410-429), and (albeit not statistically significant) chronic obstructive pulmonary disease (ICD-9 490-496). These three groups of diseases account for most of the excess mortality. Based on 50 deaths lung cancer mortality was more than twice the expected rate of the (West) German population. Mortality from oesophageal or urinary bladder cancer was not increased. An increased mortality from liver cancer (based on three cases) was noted, while mortality from chronic liver

Table 2 Number of observed deaths and standardised mortality ratios (SMRs) with 95% confidence intervals among male German Carbon Black workers between 1976 and 1998 by cause of death

Cause of death	ICD-9	Deaths	Expected	SMR	95% CI
All causes*	1-999	332	275.5	120	108-134
Infectious and parasitic diseases	1-139	4	0.5	840	229-2152
Cancer					
Lip, oral cavity, or pharynx	140-149	2	3.1	65	8-233
Digestive organs or peritoneum	150-159	25	25.7	97	63-144
Oesophagus	150	3	2.5	121	25-354
Stomach	151	5	6.6	76	25-177
Colon	153	7	5.9	119	48-245
Rectum	154	2	3.3	61	7-221
Liver and intrahepatic bile ducts	155	3	1.1	271	56-791
Pancreas	157	5	3.8	130	42-304
Respiratory and intrathoracic organs	160-165	51	25.0	204	152-268
Larynx	161	0	1.3	0	0-282
Trachea or bronchus or lung	162	50	23.0	218	161-287
Pleura	163	0	0.5	0	0-714
Thymus, heart, and mediastinum	164	1	0.1	827	21-4608
Bone, connective tissue, skin	170-175	2	1.7	116	14-420
Male genitourinary organs	185-189	8	11.3	71	31-140
Prostate	185	4	5.4	74	20-189
Bladder	188	1	2.6	38	1-213
Kidney/other/unspecified urinary organs	189	3	2.9	104	22-305
Cancer of other and unspecified sites	190-199	8	6.5	122	53-241
Lymphatic and haematopoietic tissue	200-208	4	5.0	79	22-203
Lymphatic system	200-203	2	2.8	72	9-259
Leukaemia	204-208	2	2.3	88	11-320
Other neoplasms	210-239	5	2.1	239	78-558
Diabetes mellitus	250	3	4.1	73	15-213
Mental disorders	290-319	1	4.8	21	1-117
Nervous system and sense organs	320-389	2	3.8	53	6-191
Hypertensive disease	401-405	2	2.6	76	9-275
Heart diseases	410-429	103	81.7	126	103-153
Ischaemic heart disease	410-414	75	59.9	125	98-157
Other heart diseases	415-429	28	21.8	129	85-186
Cerebrovascular disease	430-438	24	20.7	116	74-173
Disease of the respiratory system	466, 480-519	18	15.8	114	68-180
Chronic obstructive pulmonary disease	490-496	17	10.8	158	92-253
Pneumoconiosis and other lung diseases	500-508	1	0.7	153	4-853
Disease of the digestive system	520-579	24	19.1	126	81-187
Chronic liver disease and cirrhosis	571	14	12.5	112	61-187
Injury and poisoning	800-999	20	20.3	99	60-152

*Includes seven additional deaths with unknown cause of death.

disease and cirrhosis was not increased. With one pulmonary tuberculosis, one septicaemia, one AIDS, and one viral hepatitis, there was no obvious cluster among the four deaths from infectious diseases. Among the five deaths from other neoplasms, four deaths were noted from neoplasms of unspecified nature (ICD-9 239) and one death from neoplasms of uncertain behavior (ICD-9 238). We observed one death (0.7 expected) from pneumoconiosis due to silica (ICD-9 502).

SMRs with reference rates from the state North-Rhine Westphalia

For male German workers traced alive on 1 January 1976 SMRs for all-cause mortality and lung cancer were also calculated based on reference rates from North-Rhine Westphalia (data not shown in tables). The results for all-cause mortality were essentially unchanged (SMR 120, 95% CI 107 to 133), and the SMR for lung cancer was about 16% lower, but still statistically significantly increased (SMR 183, 95% CI 136 to 241).

Relative risks by smoking status

Table 3 presents age adjusted relative risks for lung cancer and all-cause mortality by smoking habits. Risks for current smokers are considerably higher than for never-smokers. For lung cancer we observe a positive dose-response relationship with increasing smoking intensity. The risk for subjects with missing smoking data is between those of never-smokers and smokers. Alternatively, we eliminated subjects with missing smoking data from the analyses and obtained essentially the same results (data not shown).

SMRs for workers by date of hiring

Workers hired prior to 1960 show all-cause and lung cancer SMRs close to 100 (lung cancer SMR 109, 95% CI 52 to 201; all-cause mortality 99, 95% CI 82 to 119) (data not shown in tables). However, employees hired thereafter had increased SMRs (lung cancer SMR 289, 95% CI 206 to 394; all-cause mortality 136, 95% CI 119 to 155). Among those who started working in 1980 or later only seven deaths and no lung cancer death occurred.

Relative risks by levels of exposure surrogates

Relative risks for all-cause mortality and for lung cancer mortality during the observation period 1976 to 1998 in

Table 3 Number of subjects (n), observed deaths, and age adjusted relative risks (RR) plus 95% confidence intervals (CI) for lung cancer and all-cause mortality by categories of smoking habits among male German carbon black workers between 1976 and 1998

Smoking cigarettes/day	n	Deaths	RR	95% CI
<i>Lung cancer, ICD-9 162</i>				
Never-smoker	189	2	1.00	
>0-12	157	9	4.86	1.05-22.50
>12-24	399	17	5.89	1.35-25.60
>24	167	7	7.50	1.53-36.68
Ex-smoker	267	1	0.50	0.05-5.57
No information	349	14	2.77	0.63-12.18
<i>All-cause mortality*</i>				
Never-smoker	190	27	1.00	
>0-12	158	54	2.13	1.34-3.39
>12-24	400	92	2.27	1.47-3.49
>24	168	28	2.05	1.20-3.50
Ex-smoker	267	19	0.66	0.36-1.19
No information	352	112	1.63	1.07-2.48

*Includes seven additional deaths with unknown cause of death.

relation to different indicators of occupational exposures are shown for all male German workers and for the inception cohort of workers hired after 1 January 1960 (tables 4 and 5).

All-cause mortality in the census cohort was positively associated with age at hiring and negatively associated with years of employment and cumulative carbon black exposure. These associations, however, were not corroborated in the inception cohort. No pronounced trend in all-cause mortality with any of the other variables considered in table 4 was observed.

In the main (census) cohort, the risk of lung cancer was positively associated with the period of hiring and age at hiring and negatively associated with years of employment. These trends, however, were not observed in the inception cohort. The average and cumulative carbon black exposure tended to be inversely associated with the mortality from lung cancer, but this relation reached formal statistical significance only in the main (census) cohort. The results for the categorical carbon black variables show particularly low relative risks for the highest exposure categories.

The analyses of mortality in relation to employment in different departments or with heavy exposure showed no statistically significant increases in relative risks for all-cause or lung cancer mortality. The highest risk estimate for lung cancer was found in the main cohort for those who worked at least one year in lamp or furnace black. The smoking adjusted relative risk was 1.48. However, the confidence interval includes one and a similar increase is not seen among workers hired after 1960.

DISCUSSION

Completeness of follow up

Assessment of vital status and causes of death for the full cohort and the observation period 1960-98 is not fully satisfactory. Vital status and cause of death ascertainment of non-Germans is often lacking because substantial numbers of first generation foreign workers in Germany returned to their home country after termination of employment. Unfortunately, vital status and cause of death ascertainment in these home countries is often impossible.

Ascertainment of causes of death among deceased German cohort members is also limited, because local health authorities have to maintain death certificates for only 10 years; too often, they destroy death certificates after this minimum period. The State Institute of Statistics of North-Rhine Westphalia has computerised files on individual causes of deaths which were made available for this study for the first time, but these do not extend before 1976. For the follow up period 1976-98, however, only 1% of the cohort remained untraced and cause of death could be ascertained for 98% of the deceased.

Census cohort and healthy worker effect

Our results indicate that the main census cohort—that is, the cohort which includes employees who were active on 1 January 1960—may have resulted in an underestimation of risk. This cohort includes 259 workers who were hired before 1 January 1960. While among this group no increase in the risk for lung cancer was observed, a statistically significant, almost threefold increased SMR was noted among the inception cohort of workers who were hired during or after 1960. A similar but less pronounced pattern was seen for all cause mortality. An explanation for these findings might be a healthy worker survivor effect (HWSE), such that highly exposed cohort members may have had an increased mortality before the 1960s and only less susceptible and less exposed individuals were still active at the time when the cohort was enumerated in 1960. Furthermore, the main cohort comprises only subjects who were traced alive on 1 January 1976. Thus, a similar effect

Table 4 Relative risks (RR) and 95% confidence intervals (CI) for all-cause mortality, adjusted for age and smoking, in male German carbon black workers traced alive on 1 January 1976

Variable with levels	All workers, main (census) cohort			Workers hired 1960 or later, inception cohort		
	Deaths	RR	95% CI	Deaths	RR	95% CI
<i>Period of hiring (calendar time)</i>						
<1950	53	0.82	0.59–1.14			
1950–59	61	0.61	0.45–0.82			
1960–69	170	1.00		170	1.00	
1970–79	41	1.07	0.74–1.54	41	1.12	0.77–1.63
1980–97	7	0.76	0.34–1.69	7	0.81	0.36–1.84
Trend (10 years)		1.12	0.98–1.28		0.99	0.76–1.30
<i>Age at hiring (years)</i>						
≤25	44	1.00		26	1.00	
>25–35	101	1.15	0.80–1.66	56	0.99	0.61–1.62
>35–45	123	1.49	1.02–2.17	84	1.16	0.68–1.97
>45	64	1.41	0.91–2.19	52	0.99	0.52–1.89
Trend (10 years)		1.14	1.00–1.30		1.01	0.83–1.24
<i>Time since hiring (years), time dependent</i>						
>0–15	32	1.00		32	1.00	
>15–25	101	1.20	0.79–1.82	90	1.20	0.78–1.84
>25	199	1.02	0.66–1.58	96	1.20	0.75–1.91
Trend (10 years)		0.97	0.81–1.15		1.07	0.88–1.30
<i>Years of employment, time dependent</i>						
1–5	82	1.00		75	1.00	
>5–10	45	0.76	0.53–1.11	39	0.86	0.57–1.30
>10–20	96	0.78	0.56–1.09	72	0.85	0.58–1.24
>20	109	0.61	0.43–0.85	32	0.76	0.47–1.22
Trend (10 years)		0.85	0.76–0.95		0.91	0.77–1.08
<i>At least 1 year employment in lamp or furnace black</i>						
No	206	1.00		126	1.00	
Yes	126	1.14	0.92–1.43	92	0.99	0.75–1.30
<i>At least 1 year employment in gas black</i>						
No	256	1.00		177	1.00	
Yes	76	0.91	0.70–1.18	41	1.15	0.82–1.62
<i>At least one year employment in preparation plant</i>						
No	311	1.00		201	1.00	
Yes	21	0.79	0.51–1.23	17	0.71	0.43–1.17
<i>At least one year employment in heavily exposed jobs</i>						
No	123	1.00		80	1.00	
Yes	209	1.00	0.80–1.25	138	0.94	0.71–1.24
<i>Average carbon black exposure (carbon black scores per year), time dependent</i>						
0–1	73	1.00		54	1.00	
>1–2	75	0.92	0.67–1.27	51	0.91	0.62–1.34
>2–3	140	1.00	0.75–1.33	88	1.11	0.78–1.56
>3	44	0.98	0.67–1.42	25	0.90	0.56–1.46
Trend (1 unit)		1.00	0.91–1.11		1.00	0.89–1.13
<i>Cumulative carbon black exposure, time dependent</i>						
0–5	66	1.00		58	1.00	
>5–10	41	0.73	0.49–1.08	36	0.71	0.47–1.08
>10–20	46	0.73	0.50–1.07	35	0.71	0.46–1.08
>20–40	79	0.89	0.63–1.26	59	1.09	0.75–1.59
>40	100	0.61	0.43–0.85	30	0.63	0.39–1.00
Trend (10 units)		0.94	0.89–0.99		0.96	0.90–1.04
Total	332			218		

could have been in play in connection with this delayed start of follow up. However, comparison of all-cause mortality during the observation periods 1960–98 and 1976–98 in table 1 gives no indication of a strong HWSE induced by the delayed start of the follow up in 1976.

Another aspect of the healthy worker effect is the observation that healthy people are selectively chosen for employment in industrial occupations. As a result, mortality of occupational cohorts is usually lower than in the general population, especially in the early years after employment. However, this effect tends to decrease and mortality usually increases with length of time since hiring.^{10–16} Indeed the relative risks for all-cause mortality in the inception cohort (but not the census cohort) increase with time since hiring (table 4), although the trend is not pronounced and not statistically significant. On the other hand, the SMR for all-cause mortality is increased in the main cohort and in the inception cohort, which does not support the assumption of a strong selection of healthy workers.

Potential confounding due to smoking

Information on smoking is relatively complete, compared with other epidemiological studies on occupational hazards. We have information on smoking, obtained by occupational physicians, for 77% of the members of the cohort. This source of data, however, may have introduced an underreporting bias because workers may have had reservations about report smoking habits correctly. On the other hand, smoking habits were not permitted to be disclosed to management, so underreporting of smoking habits may not have been significant.

Our smoking data are essentially limited to the subjects' period of employment in the plant under study. Cohort members who always reported "no smoking" to the occupational health service are classified as never-smokers, a classification that would be incorrect if they started smoking after leaving the plant. This sort of misclassification, however, is unlikely to be significant since people usually do not start smoking at older ages. On the other hand,

Table 5 Relative risks (RR) and 95% confidence intervals (CI) for lung cancer mortality, adjusted for age and smoking, in male German carbon black workers traced alive on 1 January 1976

Variable with levels	All workers, main (census) cohort			Workers hired 1960 or later, inception cohort		
	Deaths	RR	95% CI		RR	95% CI
<i>Period of hiring (calendar time)</i>						
<1950	4	0.30	0.10–0.87			
1950–59	6	0.29	0.12–0.72			
1960–69	31	1.00		31	1.00	
1970–79	9	1.45	0.64–3.28	9	1.70	0.73–3.96
1980–97	0			0		
Trend (10 years)		1.61	1.14–2.28		1.06	0.54–2.09
<i>Age at hiring (years)</i>						
≤25	5	1.00		2	1.00	
>25–35	12	1.22	0.42–3.55	10	1.85	0.39–8.80
>35–45	19	2.10	0.72–6.07	17	2.03	0.40–10.39
>45	14	2.74	0.85–8.85	11	1.56	0.25–9.77
Trend (10 years)		1.46	1.03–2.05		1.03	0.64–1.67
<i>Time since hiring (years), time dependent</i>						
>0–15	7	1.00		7	1.00	
>15–25	15	0.68	0.26–1.77	15	0.63	0.24–1.65
>25	28	0.49	0.18–1.34	18	0.56	0.20–1.57
Trend (10 years)		0.73	0.47–1.12		0.79	0.50–1.25
<i>Years of employment, time dependent</i>						
1–5	12	1.00		12	1.00	
>5–10	9	0.92	0.37–2.25	8	1.05	0.40–2.74
>10–20	16	0.70	0.30–1.61	13	0.84	0.34–2.09
>20	13	0.39	0.16–0.94	7	0.96	0.33–2.81
Trend (10 years)		0.70	0.52–0.94		0.97	0.66–1.43
<i>At least 1 year employment in lamp or furnace black</i>						
No	28	1.00		22	1.00	
Yes	22	1.48	0.84–2.61	18	1.04	0.56–1.96
<i>At least 1 year employment in gas black</i>						
No	37	1.00		32	1.00	
Yes	13	1.07	0.57–2.02	8	1.21	0.55–2.64
<i>At least one year employment in preparation plant</i>						
No	46	1.00		36	1.00	
Yes	4	1.05	0.37–2.95	4	1.07	0.38–3.03
<i>At least one year employment in heavily exposed jobs</i>						
No	16	1.00		14	1.00	
Yes	34	1.29	0.71–2.34	26	0.98	0.51–1.89
<i>Average carbon black exposure (carbon black scores per year), time dependent</i>						
0–1	12	1.00		9	1.00	
>1–2	14	1.06	0.49–2.28	14	1.53	0.66–3.55
>2–3	21	0.97	0.47–1.98	15	1.13	0.49–2.60
>3	3	0.39	0.11–1.39	2	0.40	0.09–1.86
Trend (1 unit)		0.85	0.65–1.10		0.86	0.64–1.15
<i>Cumulative carbon black exposure, time dependent</i>						
0–5	10	1.00		9	1.00	
>5–10	10	1.07	0.44–2.59	8	0.97	0.37–2.54
>10–20	9	0.84	0.34–2.10	9	1.03	0.40–2.67
>20–40	12	0.70	0.29–1.70	12	1.27	0.52–3.08
>40	9	0.28	0.11–0.72	2	0.21	0.04–0.99
Trend (10 units)		0.79	0.68–0.91		0.84	0.69–1.01
Total	50			40		

“ex-smokers”—that is, cohort members who reported having quit smoking on their last visit to the occupational physician—are more likely to recommence smoking in later life.

Categorisation of smoking intensity may also be subject to misclassification due to the limited time period for which information is available. However, we observed an increasing dose-response relation between smoking and lung cancer, an observation supportive of our quantification of smoking habits. The dose-response relation is not as strong as could have been expected. We assume that this may be caused by the misclassifications discussed above and may leave some room for residual confounding when adjusting for smoking.

To assess the impact of smoking on the SMRs for lung cancer we classified cohort members, for whom information

on smoking was available, either as smokers (including ex-smokers) or non-smokers, and compared their prevalence of smoking with that of the male population in West Germany in 1998.¹⁷ The latter increases with age, from 51.6% in the age group 20–29 to 75.7% in the age group 70–79. The prevalence of smoking of their contemporaries from our study cohort was slightly higher: 55.1% for the youngest age group and between 80.8% and 89.4% in the older age groups. This excess would be expected to increase lung cancer SMRs. Following the approach of Axelson,¹⁸ we estimated that a difference in smoking prevalence could only have caused an increase of about 13% of the lung cancer SMRs when (West) Germany is used as the reference population. However, this approach requires reasonable assumptions on the lung cancer mortality of smokers and non-smokers.^{7 19}

Other potential confounders

Based on extensive discussions with the occupational hygienists from the plant only asbestos and pyrolytic oils may qualify as potential confounders in carbon black manufacturing. Pleural mesothelioma may be regarded as a sensitive indicator for exposure to asbestos and there was no observed death from mesothelioma (compared to 0.5 expected). Furthermore, it has been estimated that exposure to 25 fibre years results in an approximately twofold lung cancer risk.²⁰ Such high cumulative exposure to asbestos in carbon black manufacturing is unlikely. Therefore, our findings do not support the notion that exposure to asbestos is a major determinant of the increased mortality from lung cancer.

Exposure to pyrolytic oils was restricted to a few job titles and therefore is also not likely to be an explanation for the observed increase of SMRs. Furthermore, in a meta-analysis of studies among coke oven, coal gasification, and aluminum production workers the unit relative risk for lung cancer per cumulative exposure to 100 µg/m³ benzo[a]pyrene years has been estimated to be 1.20 (95% CI 1.11 to 1.29).²¹ Dermal exposure in the plant investigated in the current study would probably have resulted in even lower risks.

Exposure to carbon black

Based on the above results, the high lung cancer SMR cannot fully be explained by selection, smoking, or other occupational risk factors, but our results also provide little evidence for an effect of carbon black exposure. The dose-response relation of lung cancer mortality with average carbon black exposure is rather flat. Duration of employment is inversely associated in the main cohort, but this was not observed in the inception cohort of those hired 1960 or later. The estimated cumulative carbon black exposure was negatively associated with lung cancer mortality. The linear trend, however, reached statistical significance only in the census cohort and appeared to be strongly influenced by particularly low rates among those with the highest cumulative exposure. There is no significantly increased risk with one of the simple measures of employment in work areas with high carbon black exposure. However, a categorisation based on at least one year of employment in a given area may be too crude to quantify occupational exposure with reasonable precision.

Temporal patterns

Secular trends might play a role in this cohort, especially since exposure to carbon black substantially decreased over time. For example, relative risks for all cause and lung cancer mortality seem to increase with age at hiring in the main cohort. However, this pattern is not seen in the inception cohort. On the other hand, there is a (not significant) decrease in lung cancer risk with time since hiring in the census as well as in the inception cohort.

All cause mortality in the inception cohort slightly increases with time since hiring and slightly decreases with years of employment. The former may point to a healthy worker effect, as discussed before, while the latter may indicate a selection of less susceptible workers to work for longer periods in this factory. Furthermore, cause-specific analyses were restricted to workers traced alive on 1 January 1976, due to very limited availability of information on cause of death before 1976. In summary one must be aware that even in the inception cohort, which is less prone to selection processes, there are temporal patterns which are not easily interpreted and there might be some selection. Furthermore, latency may play a role. However, it is not clear how long the latency period for exposure to carbon black and development of lung cancer might be, if there is an effect of carbon black

Main messages

- The lung cancer mortality among workers of a large German carbon black manufacturing plant was markedly increased.
- Smoking habits can probably explain only a small part of this increase.
- Results stratified for categories of exposure to carbon black or various other surrogates for occupational exposure do not provide an explanation for the increased lung cancer risk.

Policy implications

- This study contributed to a recent evaluation of the International Agency for Research on Cancer on the carcinogenicity of carbon black (IARC monographs, volume 93).

on lung cancer at all. Further analyses looking at time dependent factors and occupational exposures in more detail are currently ongoing.

CONCLUSIONS

Since the last IARC evaluation of “inadequate evidence” in humans for the carcinogenicity of carbon black (IARC 1996),¹ an update of the British carbon black study⁶ observed a 73% increase in lung cancer mortality among carbon black production workers when compared with the general population (SMR 173, 95% CI 132 to 222). However, no clear association with exposure to carbon black was reported.

Our data are in line with these UK findings. We observed a more than twofold increase of lung cancer mortality in the main (census) cohort (SMR 218, 95% CI 161 to 287) and a nearly threefold increase (SMR 289, 95% CI 206 to 394) among the workers hired after 1960. The use of national (rather than regional) reference rates or residual confounding by smoking can probably account only for a small part of the increased lung cancer mortality. Confounding by other potential exposures in carbon black manufacturing, such as asbestos or pyrolytic oils, is unlikely. However, no clear link between surrogates of exposure and lung cancer risk was observed.

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REFERENCES

- 1 IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Vol 65, *Printing processes and printing inks, carbon black and some nitro compounds*. Lyon: IARC Press, 1996;65:149–262.
- 2 Robertson JM, Ingalls TH. A mortality study of carbon black workers in the United States from 1935 to 1974. *Arch Environ Health* 1980;35:181–6.
- 3 Robertson JM, Ingalls TH. A case-control study of circulatory, malignant, and respiratory morbidity in carbon black workers in the United States. *Am Ind Hyg Assoc J* 1989;50:510–15.
- 4 Robertson JM, Inman KJ. Mortality in carbon black workers in the United States. *J Occup Environ Med* 1996;38:569–70.
- 5 Hodgson JT, Jones RD. A mortality study of carbon black workers employed at five United Kingdom factories between 1947 and 1980. *Arch Environ Health* 1985;40:261–8.
- 6 Sorahan T, Hamilton L, van Tongeren M, et al. A cohort mortality study of U.K. carbon black workers, 1951–1996. *Am J Ind Med* 2001;39:158–70.
- 7 Becker N, Wahrendorf J. *Atlas of cancer mortality in the Federal Republic of Germany 1981–1990*, 3rd edn. Berlin, Heidelberg: Springer 1997.
- 8 Zeeb H, Klug S, Ahrens W, et al. Follow-up studies in Germany: further experiences and new approaches concerning the identification of causes of death [in German]. *Informatik, Biometrie und Epidemiologie in Biologie und Medizin* 2003;34:612–18.
- 9 Breslow NE, Day NE. *Statistical methods in cancer research. Volume II – The design and analysis of cohort studies*. IARC Scientific Publication No 82. Lyon: IARC Press, 1987.
- 10 Checkoway H, Pearce NE, Kriebel D. *Research methods in occupational epidemiology*. Second edition. Oxford: Oxford University Press, 2004.
- 11 World Health Organization. *World health statistics annual 1996*, Order no 0179600. Genève: WHO, 1998.
- 12 World Health Organization. WHO mortality database. Available at <http://www.who.int/healthinfo/statistics/mort/en/> (accessed January 2006).
- 13 Wood J, Richardson D, Wing S. A simple program to create exact person-time data in cohort analyses. *Int J Epidemiol* 1997;26:395–9.
- 14 Sahai H, Khurshid A. *Statistics in epidemiology. Methods, techniques, and applications*. Boca Raton: CRC Press, 1996.
- 15 Vach W. Some issues in estimating the effect of prognostic factors from incomplete covariate data. *Stat Med* 1997;16:57–72.
- 16 McMichael AJ. Standardized mortality ratios and the ‘‘healthy worker effect’’: scratching below the surface. *J Occup Med* 1976;18:165–8.
- 17 Junge B, Nagel M. Das Rauchverhalten in Deutschland. *Das Gesundheitswesen* 1999;61(Sonderheft 2):S121–S125.
- 18 Axelson O. Aspects on confounding in occupational health epidemiology. *Scand J Work Environ Health* 1978;4:85–89.
- 19 Doll R, Peto R, Wheatley K, et al. Mortality in relation to smoking: 40 years’ observation on male British doctors. *BMJ* 1994;309:901–11.
- 20 Pohlabein H, Wild P, Schill W, et al. Asbestos fibreyears and lung cancer: a two phase case-control study with expert exposure assessment. *Occup Environ Med* 2002;59:410–14.
- 21 Armstrong B, Hutchinson E, Fletcher T. Cancer risk following exposure to polycyclic aromatic hydrocarbons (PAHs): a meta-analysis. Health & Safety Executive, research report 068, 2003. Available at <http://www.hse.gov.uk/research/rrhtm/rr068.htm> (accessed March 2006).

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