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Occupational exposures estimated by a population specific job exposure matrix and 25 year incidence rate of chronic nonspecific lung disease (CNSLD): the Zutphen Study

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Occupational exposures estimated by a population specific job exposure matrix and 25 year incidence rate of chronic nonspecific lung disease (CNSLD): the Zutphen Study. W.K. Post, D. Heederik, H. Kromhout, D. Kromhout. ©ERS Journals Ltd 1994.

ABSTRACT: The influence of occupational exposures on total mortality and respiratory mortality and morbidity was examined, employing a population specific Job Exposure Matrix (JEM). Moreover, the relationship between time-related variables of exposure to dust and chronic nonspecific lung disease (CNSLD) incidence was analysed, using time since first exposure and duration of exposure.

Occupational exposures in the Zutphen cohort were assessed by application of a JEM, arbitrarily considering jobs as exposed when at least 10% of men who had held the job of interest reported an exposure to one or more from a list of 27 chemical agents.

None of the exposures was related to mortality due to CNSLD, although results were influenced by the healthy-worker effect and low mortality rates. Exposure to wood dust and a high probability of exposure to dust were associated with total mortality. Exposures to dust and solvents were statistically significantly related to CNSLD incidence. An exposure-response relationship was found for the probability of exposure to dust with CNSLD incidence. Time-related estimates of exposure to dust based on work history were negatively related to CNSLD incidence.

The results suggest the presence of a healthy-worker effect, in a general population study, resulting in an underestimation of the relationship between occupational exposures and respiratory diseases based on the evidence published so far. The use of the full work history to determine exposure to dust leads to stronger relationships with CNSLD incidence, compared to conventional analyses using exposure at the start of follow-up.

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In community-based and occupational group studies, the relationship between occupational exposures and total mortality and nonmalignant respiratory mortality and morbidity have been studied since the 1950s. Following the debate in the early 1960s on the aetiology of respiratory disorders, they were often considered as different expressions of one disease entity, in The Netherlands. Therefore, it has been customary to gather all obstructive respiratory diseases under an umbrella term "chronic nonspecific lung diseases" (CNSLD). Recently, the use of this term has again been advocated [1]. In other European countries and in the United States of America, a distinction is usually made between asthma and chronic obstructive pulmonary diseases (COPD).

Results concerning occupational risks for mortality have been conflicting. Some authors have stated that occupational exposures form a minor risk, as compared to the effect of smoking [2, 3]. Others believe that an occupational exposure does augment the mortality risk [4–8].

Morbidity due to CNSLD forms a major problem in populations occupationally exposed to dust, gases and fumes. It has been speculated that of all adult asthma cases 2–15% might be caused by occupational exposures, although the information underlying these figures has not been published explicitly [9, 10]. Similar figures for COPD are lacking, but ample evidence for a causal relationship between occupational exposures and COPD exists [11–13]. Recently, the aetiological fraction of CNSLD attributable to occupational exposures has been estimated as 11–19% for males [13, 14]. Several general population studies have shown a positive relationship between occupational exposures and symptom prevalence or incidence rate of CNSLD; in cross-sectional studies, odds ratios varied between 1.3–2.0 for exposed *versus* unexposed workers, and in longitudinal studies risks ratios were about 1.4 [15–25].

Information on occupational exposure to dust, gases and fumes was gathered mainly by use of questionnaires or by interviews. More recently, so-called Job Exposure Matrices (JEMs) have been introduced, to generate occupational exposures based on job titles [14–17, 25]. The JEM provides the possibility of converting occupational titles into potential exposures in epidemiological

studies [26]. In absence of detailed questionnaires or assessment by experts, exposure assessment using JEMs may provide useful information in large population studies [25].

Information on the validity of exposure estimates generated by external JEMs has been reported on a limited scale only [26–28]. KROMHOUT *et al*. [28] compared exposure estimates generated with the Medical Research Council (MRC) JEM [29], and with a population specific JEM based on self-reported data. Their analysis suggests that the JEM based on self-reported data is superior in comparison with the MRC JEM. This could imply that the latter gives an underestimation of the true relationship between occupational exposures and CNSLD. Assuming more valid results when assessing exposure by a population specific JEM, we re-examined the influence of occupational exposures on total mortality and respiratory mortality and morbidity.

Most general population studies performed so far were cross-sectional. The longitudinal studies used information on occupational exposures at one point in time in relation to subsequent lung function changes, symptoms of CNSLD, or data on CNSLD incidence. In this study, information about time since first exposure and duration of exposure was used to facilitate an analysis between time-related exposure variables and CNSLD incidence.

Subjects and methods

Subjects

From 1960 until 1985, risk factors for chronic diseases were investigated longitudinally in the Zutphen Study, the Dutch contribution to the Seven Countries Study [30, 31]. Zutphen is an old industrial town in the eastern part of The Netherlands. In 1960, it had a population of 25,000 inhabitants. A random sample of the male population, born between 1900 and 1919 and living in Zutphen for at least 5 yrs, was taken. Information on risk factors, such as smoking, was collected according to the Seven Countries Study protocol [30]. Information on cigarette smoking was used to compute the number of pack-years of cigarettes smoked. Pack-years were calculated as the product of the number of years smoked before 1960, and the number of packs of cigarettes smoked per day.

Medical examination

During the 25 yrs of follow-up, the morbidity of the 878 men was verified regularly. The vital status was checked at the end of the study. Each person underwent complete follow-up. One physician coded all information about morbidity and mortality during the follow-up, using strict criteria. The causes of death were coded according to the 8th revision of the International Classification of Diseases (ICD) [32]. The mortality was considered to be due to CNSLD if ICD codes 490–496 were mentioned on the death certificate as primary, secondary or tertiary cause of death. For the diagnosis of CNSLD morbidity, the following criteria had to be met: 1) episodes of respiratory symptoms (regular cough and phlegm for longer than three months, or episodes of wheezing) reported to the survey physician; or 2) a diagnosis of CNSLD by a clinical specialist. Incidence of CNSLD was defined as the first year in which CNSLD was diagnosed. More details about the medical examinations and coding of morbidity and mortality data have been reported elsewhere [8, 16].

Exposure assessment

In 1960, 1965, 1977/1978 and 1985, information about occupation was collected. The information about jobs was coded in 1989 according to the British Registrar General's classification of occupations [33]. Coding procedures have been described in detail elsewhere [15]. In 1977 and 1978, a complete work history of the surviving members of the 1960 cohort was obtained using a self-administered questionnaire [28]. The cohort members could also indicate to which of 27 (groups of) chemical agents they had been exposed in the jobs they had carried out during their working life.

A population specific JEM was generated for 10 specific exposures relevant for respiratory epidemiological purposes. To allow use of the total follow-up data, jobs held in 1960 were arbitrarily considered exposed when at least 10% of the men performing a job reported an exposure during the 1977/1978 interview, as described previously [28]. The JEM generated the following (groups of) exposures: welding materials and welding fumes; soldering fumes; pesticides; asbestos; oils (drilling oil, cooling oil and lubricants); wood dust (finishing and conservation products); solvents; paints (paint, varnish, lacquers and pigments); coal tar (asphalt, tar, pitch and bitumen). Also exposure to dust was generated, comprising an exposure to asbestos, wood dust, cement, chalk or quartz. The cohort members with exposure to dust were subsequently divided into two groups with high and intermittent probability of exposure to dust, respectively. Jobs in which 10–50% of the men reported exposure to dust were considered to have an intermittent probability of exposure to dust. When over 50% of the men in a job reported exposure to dust, the job was considered to have a high probability of exposure to dust.

Based on the information from 1960, 1965, 1977–1978 and 1985, the occupational history of the cohort members was reconstructed. When available, self-reported information on exposure to dust and the period of exposure obtained during the 1977/1978 interview was used.

For men exposed to dust, the duration of, and the time since the first exposure was computed. The exposure period ended in the year CNSLD was diagnosed, the year of death, or the end of study. To calculate duration of exposure, information on the year of the first exposure and the year of cessation of exposure was used. This information was obtained by using self-reported data

concerning the period on which exposure to dust had occurred.

For members for whom this information was lacking (*i.e.* because they died before the 1977/1978 survey), the job held in 1960 was used to generate exposure to dust, using the population specific JEM. Average duration and time since first exposure were assigned, distinguishing two birth cohorts (born between 1900–1910; or between 1911–1920) broken down to 11 job categories, according to the British Registrar General's 1966 classification of occupations (farmers; furnace workers; engineering and metal workers; wood and paper workers; textile workers and tailors; food processing workers; other production workers; construction workers and painters; transport workers; warehouse workers; and white collar workers).

Statistical analysis

Relationships between occupational exposures and total mortality, CNSLD mortality and CNSLD incidence were analysed using proportional hazard analysis, allowing for smoking habits (number of years smoked, or pack-years until 1960) and age [34]. The survival-analyses were performed using the PHREG procedure of SAS on a VAX computer [35]. The discrete algorithm was used, since the time-scale (person-years) was discrete. All exposures were first analysed separately, allowing for age and smoking habits. Two-sided p-values <0.05 were considered as statistically significant. The relationship between occupational exposures and CNSLD incidence was also analysed simultaneously. Using the stepwise option of PHREG, and allowing for age and smoking habits, specific exposures were included and excluded until the following conditions were met: the significance of the residual Chi-squared was less than 0.25, and the significance of the relative risks was less than 0.10.

Relative risks were estimated from regression coefficients by taking the antilogarithm of the regression coefficients. Using the standard error of the regression coefficient, the 95% confidence intervals were estimated. For further details, reference is made to a previous paper [8].

Results

Of the group of 1,088 men invited, 878 took part in the medical examination in 1960. For 11 men, information about occupation was incomplete. For 11 men, the number of cigarettes smoked and numbers of years smoked before 1960 was lacking; and for three men the duration was known, but no information about the quantity of tobacco consumption was available.

From the men at risk for CNSLD mortality and total mortality, a complete set of data from the baseline survey was available for 856 and 853 men, respectively. Fifty seven subjects had experienced CNSLD before 1960 and were excluded from the analyses with CNSLD incidence, leaving a group of 796 men. A summary of confounding factors and outcome measures is given in table 1.

Table 1. – Age, smoking habit, total mortality, CNSLD mortality and CNSLD incidence of 867 men aged 40–59 yrs in 1960 in Zutphen

Confounding factors (mean±SD)		
Age yrs	50±6	
Number of years smoked yrs*	28.7±11.2	
Pack-years cigarettes pack/day·yrs**	13.9±11.2	
Outcome measures n (%)		
Total mortality	425	(49)
CNSLD mortality (all subjects)	53	(6)
CNSLD mortality (without CNSLD cases)†	33	(4)
CNSLD incidence†	233	(29)

Mean±SD for age and smoking habit; mortality results are number (% population). *: n=856, for 11 subjects unknown; **: n=853, for 14 subjects unknown; †: n=796, 57 incident CNSLD cases before 1960 excluded. CNSLD: chronic nonspecific lung disease.

Approximately 50% of the 1960 cohort died during the follow-up period. However, only 53 deaths were due to CNSLD. When incident cases of CNSLD before 1960 were excluded, 33 of the 799 men at risk died of CNSLD. Given these numbers, a relative risk of 1.5 (α=0.05; β=0.80) can be detected, with $p<0.05$. Almost 30% of the 796 subjects at risk developed CNSLD between 1960–1985. For every hundred person years of observation, 1.5 incident cases were observed, during 25 yrs of follow-up.

Population-specific JEM based on 1960 job

Approximately 40% (327/853) of the cohort members had at least one specific exposure. Less then 10% of the cohort had been exposed to pesticides, asbestos, soldering fumes, wood dust, solvents or coal tar. About 10% had been exposed to paints or welding fumes. Almost a quarter of the cohort had been exposed to dust. Sixteen percent had carried out jobs with an intermittent probability of exposure to dust, while 8% was classified as having a high probability of exposure to dust. For the exact numbers of exposed men and the number of deaths or subjects who developed CNSLD reference is made to tables 2 and 3, respectively. Specific exposures rarely occurred alone; soldering fumes, welding fumes, asbestos, wood dust and tar coal always occurred in combination with another exposure. Nineteen percent of 114 men had only been exposed to dust. Unique exposures to pesticides, oils, solvents, and paints occurred on a very limited scale (less then 5%), not allowing separate analyses.

In all analyses, age and past smoking habits were included as confounders. An earlier analysis revealed that pack-years of cigarettes smoked was a better predictor of total mortality and CNSLD incidence than the number of years smoked [16]. The number of years smoked, however, was a better predictor of CNSLD mortality [16]. The relative risks per 25 pack-years smoked for total mortality and CNSLD incidence were 1.6 and 1.1,

Table 2. – Relationships between different occupational exposures and 25 yr total mortality, adjusted for age and smoking, in 853 men aged 40–59 yrs, at risk in 1960 in Zutphen

Exposure	Exposed men n	Exposed cases n	RR	95% CI
Welding fumes	84	42	0.88	0.63–1.22
Soldering fumes	62	32	0.93	0.64–1.34
Pesticides	19	10	0.91	0.48–1.73
Asbestos	32	20	1.40	0.88–2.22
Oils	133	63	0.90	0.69–1.19
Wood dust	69	38	1.37	0.97–2.93
Solvents	80	41	0.95	0.69–1.32
Paints	84	42	1.02	0.74–1.41
Coal tar	49	22	0.71	0.46–1.10
Dust	198	101	1.03	0.82–1.29
Intermittent dust exposure*	136	63	0.87	0.66–1.14
High dust exposure*	62	38	1.47	1.04–2.08
At least one exposure	327	160	0.94	0.77–1.15

RR: relative risk; 95% CI: 95% confidence interval. *: simultaneously in one model.

Table 3. – Relationship between different occupational exposures with 25 yr CNSLD incidence, adjusted for age and smoking, in 796 men aged 40–59 yrs, at risk in 1960 in Zutphen

Exposure	Exposed men n	Exposed cases n	RR	95% CI
Welding fumes	77	26	1.12	0.74–1.69
Soldering fumes	56	18	1.02	0.63–1.65
Pesticides	18	7	1.38	0.64–2.95
Asbestos	31	12	1.63	0.90–2.93
Oils	124	41	1.13	0.80–1.58
Wood dust	66	23	1.31	0.85–2.02
Solvents	75	33	1.66	1.14–2.41
Paints	87	26	1.05	0.68–1.62
Coal tar	43	17	1.32	0.80–2.17
Dust	187	68	1.42	1.07–1.90
Intermittent dust exposure*	126	43	1.26	0.89–1.76
High dust exposure*	61	25	1.85	1.21–2.83
At least one exposure	321	112	1.46	1.12–1.89

RR: relative risk; 95% CI: 95% confidence interval; CNSLD: chronic nonspecific lung disease. *: simultaneously in one model.

respectively, allowing for age. The relative risk per 10 years smoked for CNSLD mortality was 2.1. Age in 1960 was related to total mortality, CNSLD mortality and CNSLD incidence, with relative risks of 2.7, 2.0 and 1.4, respectively, per 10 years increase of age, adjusted for smoking habits.

Results of the proportional hazard analysis applied to total mortality are given in table 2. Being occupationally exposed was not significantly related to total mortality. Only a high probability of exposure to dust was significantly related to total mortality. The relative risk of exposure to wood dust was borderline significantly elevated. Exposure to asbestos and to dust had not statistically significantly elevated relative risks for total mortality. Exposures to welding or soldering fumes, pesticides, oils, organic solvents, and coal tar were inversely related to total mortality, but statistically nonsignificant.

None of the specific exposures was significantly related to mortality due to CNSLD, even after exclusion of the prevalent CNSLD cases in 1960. Occupational exposure to at least one agent showed a statistically significant lower relative risk (RR) on mortality due to CNSLD for exposed men as compared to unexposed men (RR 0.49; confidence interval (CI) 0.26–0.92), but this association was no longer statistically significant after exclusion of the prevalent CNSLD cases (RR 0.73; CI 0.35–1.51).

The proportional hazard ratios for specific occupational exposures on CNSLD incidence are presented in table 3.

Table 4. – Relationship between occupational exposure to dust and solvents in one model and 25 yr CNSLD incidence adjusted for age and smoking in 796 men aged 40–59 yrs, at risk in 1960 in Zutphen

Exposure	RR	95% CI
Model 1		
Solvents	1.48	1.00–2.20
Dust	1.31	0.96–1.77
Model 2		
Solvents	1.73	1.14–2.62
Intermittent dust exposure	1.04	0.72–1.52
High dust exposure	1.91	1.24–2.93

RR: relative risk; 95% CI: confidence interval; CNSLD: chronic nonspecific lung disease.

Being exposed to at least one agent resulted in an elevated relative risk of 1.5, compared to people without exposure. All survival analyses revealed positive relationships between CNSLD incidence and specific exposures. Exposure to asbestos showed a statistically nonsignificantly, elevated relative risk (RR 1.6; CI 0.90–2.93). The large confidence interval is in part due to the limited number of subjects occupationally exposed to asbestos (less than 5% of the cohort). Relationships with CNSLD incidence were statistically significant for exposure to dust and exposure to solvents (RR 1.4 and 1.7, respectively). Comparing 114 men with an exposure to dust only with 475 unexposed men resulted in a statistically significant elevated relative risk of 1.6 (CI 1.13–1.60). For other unique exposures, re-analysis in a similar fashion led to higher relative risks, but confidence intervals increased as well, because of the smaller numbers involved in analyses.

The results of the simultaneous analysis of exposure to dust and solvents are presented in table 4. The relationship between exposure and CNSLD incidence becomes slightly weaker than those compared to the risk ratios presented in table 3, but the findings are still consistent with the previous analyses. Although the criteria of significance were not met when exposure to solvents was analysed in combination with intermittent probability and high probability of exposure to dust, results of this model are also given in table 4. For an intermittent probability of exposure to dust, no relationship was found. For an exposure to solvents and high probability of exposure to dust, the results of the previous analysis were confirmed as well.

Time-related exposure to dust

In 1977/1978, information about work history of 633 men was obtained, comprising a total of 1,610 observations. The number of men ever exposed to dust is smaller than obtained with the population specific JEM (151 (19%) *versus* 187 (23%)). This difference is found because for 603 men the self-reported exposure to dust was used, which did not always correspond to the exposure data generated by the JEM, using the arbitrarily chosen 10% criterion for exposure.

Duration

The duration of exposure to dust varied between 5–54 yrs, with an average duration of 32.6 yrs (standard deviation 10.9 yrs). Figure 1 shows the relative risks and the 95% confidence interval for three subgroups by duration of exposure to dust, compared to a reference group without exposure to dust. The group exposed 1–20 yrs to dust had a statistically significant elevated risk for developing CNSLD, after allowing for smoking habits and age. Men exposed to dust for a longer duration, showed a smaller risk for developing CNSLD than those with a shorter exposure time.

Time since first exposure

The time since initial exposure ranged between 9–72 yrs. The average time since first exposure was 44.6 yrs (standard deviation 13.1 yrs). Figure 2 presents the relative risks of three subgroups of time since first exposure, as compared to the groups of subjects without exposure. The results of analysing the relationship between the time since first exposure and CNSLD incidence suggest that the risk of developing CNSLD is larger when exposure occurred more recently. For men who had been first exposed longest ago the relative risk was (statistically not significant) lower compared to men who had never been exposed to dust.

The survival analysis for 7 yrs of follow-up, using the self-reported exposure data for 397 men obtained during the 1977/1978 survey, yielded similar results, though no longer statistically significant due to smaller numbers.

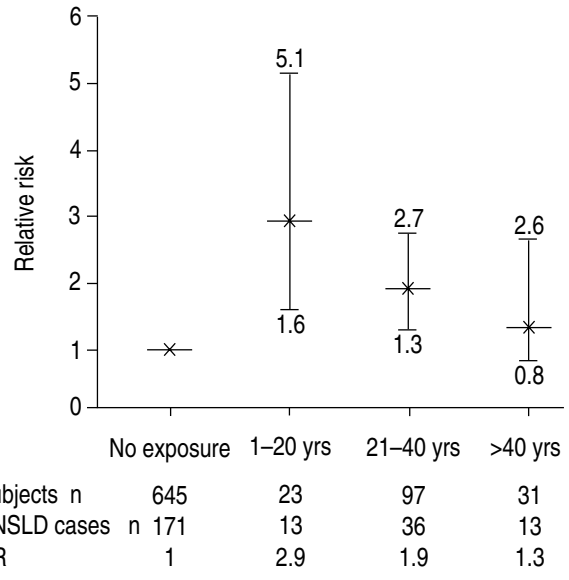

Fig. 1. – Relative Risk (RR) and 95% confidence interval (95% CI) for the relationship between duration of exposure to dust and 25 yr CNSLD incidence corrected for age and smoking habits. Vertical bars indicate 95% CI. CNSLD: chronic nonspecific lung disease.

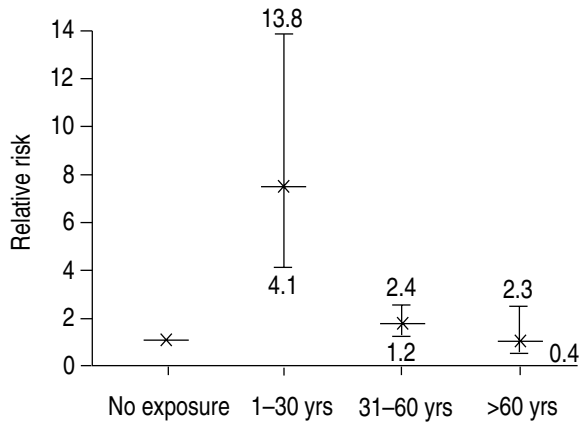

Fig. 2. – Relative Risk (RR) and 95% confidence interval (95% CI) for the relationship between time since first exposure to dust and 25 yr CNSLD incidence corrected for age and smoking habits. Vertical bars indicate 95% CI. CNSLD: chronic nonspecific lung disease.

Discussion

This study focused on occupational exposures, assessed with an internal JEM or self-reported exposure information, in relation to total mortality, cause specific mortality of CNSLD, and the development of CNSLD. A broad definition of CNSLD was used, comprising asthma, chronic bronchitis and emphysema. Considering the age of the population in 1960, the results of the study are probably biased towards more strongly age-related forms of CNSLD, such as chronic bronchitis and emphysema. COPD is expected to be predominant among most cases diagnosed as having CNSLD [16].

The cumulative CNSLD incidence is high compared to prevalence figures, what might be explained by the definition of CNSLD used [15, 16]. Although the diagnostic criteria used by clinical specialists could not be made explicit, the diagnosis of CNSLD did correlate well with symptoms of CNSLD (1960 questionnaire). This questionnaire comprised questions about cough, phlegm and shortness of breath. Analyses of the relationship between lung function in 1965 and 20 yr CNSLD incidence also suggest that incidence data are valid. Lung function in 1965 was found to be a very strong predictor of subsequent CNSLD incidence [8].

It is unlikely that the relationship between occupational exposures and health outcome is obscured by recall bias (overreporting of occupational exposures among the subjects with respiratory symptoms), because the study was not aimed at establishing the relationship between occupational exposures and respiratory symptoms or CNSLD. Selection bias towards higher occupationally-exposed jobs was improbable because a random sample out of the general population was taken. The results may still be influenced by a "healthy-worker effect" though, because those with better health may be selected into the workforce [36]. This aspect will be discussed further on.

In all analyses, exposed men were compared to men not exposed to the exposure of interest. However, members of the reference category could be exposed to exposures other than the specific exposure. On the other hand, exposed men could also be exposed to other exposures next to the specific exposure of interest. Consequently, true relative risks of a specific exposure can be obscured by interferences with other exposures. Since most exposures appeared in combination with others, separate analyses with unique exposures were hindered by a restricted population size.

Mortality

An earlier study among members of the Zutphen Study cohort still alive in 1965 showed a relationship between occupational groups and 20 yrs survival, after controlling for lung function, smoking habits and age [8]. In the present analyses, occupational exposure to at least one agent was not related to total mortality, and only exposure to wood dust and high probability of exposure to dust were significantly related to total mortality.

Men exposed to at least one agent according to the population specific JEM were found at lower risk for CNSLD mortality; though this relationship was no longer statistically significant after exclusion of the incident cases who developed CNSLD before 1960. The results are influenced by low mortality rates from CNSLD and the limited number of persons exposed to specific exposures, leading to a considerable instability of the risk estimates, a reduced statistical power and large confidence intervals. Given the numbers in this study, a relative risk of 1.5 or larger (α=0.05; β=0.80) could be detected, with $p<0.05$. Furthermore, the healthy-worker effect has influenced the results, since subjects suffering from CNSLD are likely to exchange exposed jobs for less exposed jobs. A previous analysis showed a higher CNSLD mortality among blue collar workers than among white collar workers [8]. Since exposures generated with the population specific JEM were not related to CNSLD mortality, this could imply that the elevated relative risks found in the previous analyses were not related to occupational exposures, but to other factors related to socioeconomic status, such as housing, as suggested as an alternative explanation of the findings in the same paper. Since the mortality rate is very low, the results of the present analysis should not be generalized.

CNSLD incidence

The results of the analyses of the relationship between occupational exposures and CNSLD incidence confirm results from other community-based studies. In cross-sectional studies, relationships between occupational exposures and respiratory symptoms, decreased lung function and/or respiratory disease were found, with odds ratios varying between 1.3–2.0 [14, 15, 19, 21, 24]. In the few longitudinal community-based studies

published, exposed workers had higher risks of respiratory dysfunction than unexposed workers, with risk ratios of about 1.4 [16, 20].

The assumption that the internal JEM based on self-reported data gives more valid results could not be confirmed in this study. A comparison of the performance of both JEMs was made indirectly, by studying relationships with end-points. A direct and more straight forward comparison of the performance of the population specific JEM and the MRC JEM is hindered by the differences in exposure attribution. Subjects with specific exposures to heavy metals, mineral dusts and adhesives, according to the MRC JEM, were previously found to be at significantly higher risk [16]. These exposures were not generated by the population specific JEM. Using the population specific JEM, a strong relationship between exposure to solvents and CNSLD incidence was found. A cross-sectional analysis of the Zutphen Study [15], also detected a statistically significant relative risk for exposure to solvents. This correlation was not present in the longitudinal analyses when the MRC JEM was used. Neither has any other general population study shown the existence of this relationship. The importance of the finding remains to be established, preferably by occupational population-based studies. It is possible that the 10% criterion in generating exposure is too lenient, leading to misclassification, especially false-positive. Such a bias can have a strong influence on the estimated relative risks [28]. However, the consistency in the relationship between occupational exposure to at least one agent and to dust with CNSLD incidence for the cohort specific JEM and the external JEMs leads to the conclusion that the use of self-reported data gives at least similar information as the use of an external JEM.

Almost 30% of the Zutphen population was occupationally exposed to dust, gas or fumes, according to the MRC JEM, and had a relative risk of CNSLD of 1.40 (CI 1.07–1.85) [16]. In the present study, exposure to dust comprises wood dust, asbestos, cement dust, talc and quartz. Almost 40% of the men were occupationally exposed and had a risk ratio of 1.46 (CI 1.12–1.89) compared to unexposed men. The influence of exposure to dust on CNSLD incidence was of equal magnitude in previous and present analyses, with risk ratios of about 1.4. Analysing the subgroup of subjects only exposed to dust against subjects without any exposure revealed an even stronger relationship between exposure to dust and CNSLD incidence. The most striking difference between the internal JEM and the MRC JEM was the exposure-response gradient for the probability of exposure to dust on CNSLD incidence. This association suggests the existence of an exposure response relationship and was not found with the external JEM.

An advantage of using self-reported data on exposure is the possibility to analyse time-related exposure estimates. In this particular study, the relationship between time-related exposure to dust and CNSLD incidence was analysed. A negative relationship between duration of exposure and CNSLD incidence was found. Subjects exposed for 1–20 yrs to dust had a clearly statistically significant elevated risk for developing CNSLD (RR 2.9). Subjects exposed to dust for a longer duration, showed a lower risk for developing CNSLD (RRs 1.9 and 1.3). Subjects whose first exposure to dust occurred more recently were at higher risk for developing CNSLD, as compared to subjects with the longest time since the first exposure (RR 7.5 *vs* 0.9). It should be noted that subjects who had an exposure which began relatively recently, also have a limited duration of exposure. Because of the coherence between results with time since first exposure and duration of exposure, it is probable that these estimates do, to a certain degree, display the same effect. A further breakdown by both time since first exposure and duration of exposure was not feasible, because of the limited population size, resulting in unstable risk estimates, potential colinearity and missing observations.

Earlier analyses suggested that a selection effect influences relative risks found between occupational exposure and CNSLD incidence to a minor degree [16]. The more elaborate analyses with time-related estimates of exposure to dust did, however, suggest the existence of strong selecting processes, influencing the relationship between occupational exposures and CNSLD mortality. This finding is probably explained by subjects with initial exposures further back in the past, who transferred to other jobs or developed CNSLD before 1960 and were, therefore, excluded from analyses.

Conclusion

The consistency of the relationship between occupational exposure to at least one agent and to dust and CNSLD incidence in the Zutphen cohort for the cohort specific JEM and external JEMs leads to the conclusion that the use of self-reported data gives at least similar information to the use of an external JEM. This supports the use of self-reported time-related exposure data in general population studies.

The gradient of response in relation to exposure to dust and the relationship found between time-related estimates of exposure to dust are important indications for a causal relationship between occupational exposure and CNSLD [12]. Using the work history to determine exposure to dust led to a stronger relationship with CNSLD incidence for specific subgroups compared to a conventional analysis using exposure at the start of follow-up. The existence of a healthy-worker effect might have led to an underestimation of the risk estimates of occupation and occupational exposures on CNSLD in earlier studies. A similar approach, using time-related exposure variables as used in the present study, should be applied in other general population studies to confirm these findings.

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