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A meta-analysis of epidemiologic studies of lung cancer in welders

by Jean Jacques Moulin, MD¹

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Objective A meta-analysis of epidemiologic studies was carried out on lung cancer risk among shipyard, mild steel, and stainless steel welders, and the role of asbestos exposure and smoking was considered.

Methods The meta-analysis consisted of calculating combined relative risks (RR) and their variances through a logarithm transformation of published RR values and a weighing using the inverted variance of each RR.

Results The literature provided 18 case-referent and 31 cohort studies. The combined RR values were 1.38 [observed 1028, 95% confidence interval (95% CI) 1.29–1.48] for “all or unspecified welding categories”, 1.30 (observed 305, 95% CI 1.14–1.48) for shipyard welders, and 1.35 (observed 173, 95% CI 1.15–1.58) for nonshipyard welders. Similar combined RR values (RR) were observed for mild steel welders (combined RR 1.50, observed 137, 95% CI 1.18–1.91) and stainless steel welders (combined RR 1.50 observed 114, 95% CI 1.10–2.05). No significant heterogeneity was discerned between studies of any welding or study design category. A marked healthy worker effect may also lead to an underestimation of the standardized mortality ratio for lung cancer among stainless steel welders. Furthermore, welders of any category are likely to be exposed to asbestos. Welders also seem to smoke more than the general male population, and therefore the hypothesis of tobacco overconsumption among welders could not be discarded.

Conclusions A 30–40% increase in the RR of lung cancer among welders cannot be explained by hexavalent chromium and nickel exposure among stainless steel welders. The combination of the carcinogenic effects of asbestos exposure and smoking may account for part of the lung cancer excess observed.

Key terms meta-analysis, stainless steel, welding.

The risk of lung cancer in welders is an important issue in occupational epidemiology since (i) there may be as many as 3 million workers engaged in welding in industrialized countries (1) and (ii) welders may have been exposed to carcinogens according to welding activities, in particular exposure to hexavalent chromium and nickel when stainless steel is welded (1, 2). In addition, asbestos exposure is likely to have occurred in shipyards (2) and in other factories where welding is done (3).

Following the multicentric European study, carried out by the International Agency for Research on Cancer (IARC), on the lung cancer risk of stainless steel welders as compared with that of mild steel welders (1), the question of whether stainless steel welders are at higher lung cancer risk than mild steel welders has been recently debated in the literature. The reviews by Langård (4, 5) and the meta-analysis of 5 epidemiologic studies by Sjögren (6) suggested a specific relationship between lung cancer and exposure to hexavalent chromium and nickel when stainless steel is welded. Other authors have, however, disagreed with this proposal (7, 8).

This paper is a meta-analysis of epidemiologic studies aimed at assessing the relationship between lung cancer and welding activities (ie, shipyard versus nonshipyard welding and stainless steel versus mild steel welding). In addition, this assessment takes into account the role of asbestos exposure and smoking as possible confounding factors.

Material and methods

Published studies providing results on lung cancer risk in welders were selected for the meta-analysis (ie, case-referent studies focused on occupational lung cancer risks and cohort studies among welders followed for mortality or cancer incidence). All the studies published between 1954 and 1994 were selected. If more than 1 paper was written reporting the same study, or if a cohort study was included in another larger study published later, only 1 paper was included in the meta-analysis. Furthermore,

¹ Institut National de Recherche et de Sécurité (INRS) (French National Institute for Research and Safety) Service d'Epidémiologie (Department of Epidemiology), Vandoeuvre Les Nancy, France.

Reprint requests to: Dr JJ Moulin, Institut National de Recherche et de Sécurité (INRS), Service d'Epidémiologie BP 27, 54501 Vandoeuvre Les Nancy, France.

some studies were excluded from the meta-analysis for other reasons: (i) cohort updates for which only the updated results were included in the meta-analysis, (ii) cohorts followed for mortality and morbidity for which only the mortality results were included in the meta-analysis, and (iii) cohorts for which the results did not provide information required by the meta-analysis.

In order to investigate risks related to specific welding processes and welding fume components, the following 5 welding categories were defined: (i) "all or unspecified welding categories", including studies providing results for "welders" as a whole, without taking into account welding processes, most of them being population-based studies and studies including subcohorts of all welding categories and providing a relative risk for all subcohorts combined; (ii) shipyard welding, including studies providing results for cohorts, or subcohorts, of shipyard welders; (iii) nonshipyard welding, including studies providing results for cohorts, or subcohorts, of welders never employed in shipyards and for which the status of mild steel or stainless steel welding was unknown; (iv) mild steel welding, including cohorts of nonshipyard welders never employed in stainless steel welding; and (v) stainless steel welding including cohorts of nonshipyard welders having been employed in stainless steel welding. Studies of the literature were included in these welding categories according to descriptions given in the study designs.

The relative risks (RR) were odds ratios (OR) for case-referent studies, standardized mortality ratios (SMR) for cohort studies, proportionate mortality ratios (PMR) for mortality studies and standardized incidence ratios (SIR) for cancer incidence studies. The observed numbers of cases, the relative risks, and their 95% confidence intervals (95% CI) obtained for welding categories were extracted from the published papers.

Due to the fact that the study reports frequently failed to give the variance of the relative risks, the estimated variance (var) of each relative risk was calculated from the 95% confidence interval on the assumption that the log-transformed relative risks followed a Gaussian distribution (9, 10):

$$var(\ln RR) = \left[\frac{\ln RR_{upper} - \ln RR_{lower}}{2 \times 1.96} \right]^2.$$

The logarithms of the combined relative risks were computed as an average of the logarithmic transformation of the RR_i values observed in each study, weighted by their inverted variance w_i ($w_i = 1/var$):

$$\ln RR = \sum w_i \ln RR_i / \sum w_i.$$

The variance of combined relative risks were taken as $var(\ln RR) = 1/\sum w_i$. The 95% confidence interval of the combined relative risks were calculated on the assumption of a log normal distribution:

$$\ln RR = \ln RR \pm 1.96 \sqrt{var(\ln RR)}.$$

The chi-squared test for the heterogeneity of the RR_i values proposed by Greenland (10) was applied:

$$\chi^2 = \sum w_i (\ln RR_i - \ln RR)^2.$$

The combined relative risks were calculated separately for the population-based studies, case-referent studies, and cohort studies and for all the studies combined since the method allows studies of different design, such as case-referent and cohort studies, to be combined (9).

Dose-response relationship was not addressed in the meta-analysis since, depending on the studies, the RR_i values for graded welding exposure were either lacking or given in terms of different surrogates.

Results

Studies included in the meta-analysis

The literature provided 49 epidemiologic, 18 case-referent (11–28), and 31 cohort (29–59) studies that reported lung cancer risks for welders. Among them, 4 case-referent studies using odds ratios (13, 15, 16, 27) and 6 cohort studies using standardized mortality ratios or proportionate mortality ratios (30, 31, 33, 37, 43, 44) were population-based studies. These population-based studies were analyzed separately. The European cohort study carried out by IARC is noteworthy because of the size of the study population (11 092 welders) and because a specific job-exposure matrix was developed (55).

The following 13 studies were excluded from the meta-analysis (the reasons for exclusion being listed in table 1): 4 cohort studies carried out in Sweden (51), Finland (52), Germany (57) and France (58), whose results are included in the European study (55); the Danish case-referent study (27), which was nested in a cohort included in the European study (55); 6 cohort studies carried out in the United States (31, 36), Italy (34), Sweden (38, 41) and Germany (46), which were updated later (39, 43, 48, 50, 51, 57); 1 Swedish cancer incidence study (50), which was conducted in the same population as a mortality study (49); the study by Decouflé (13) because of its lack of confidence intervals.

The final number of studies contributing to the meta-analysis was 36. The description of these investigations is given in table 2. Some of those which provided results for more than 1 welding category may have contributed to several welding categories. Thirty-five studies were included in the meta-analysis, leading to 49 relative risks being extracted from the published papers. Most of the relative risks [ie, 35 of them (71%)] ranged between 0.99 and 2.00. Only 2 studies (4%) provided relative risks lower than unity: odds ratios of 0.7 and 0.9 for shipyard

Table 1. Studies of the literature and studies included in the meta-analysis on lung cancer in welders.

	Included	Reason for exclusion
Case-referent studies		
Breslow et al, 1954, United States (11)	Yes	
Blot et al, 1978, United States (12)	Yes	
Decoufle et al, 1978, United States (13)	No	95% confidence intervals not provided
Blot et al, 1980, United States (14)	Yes	
Gottlieb, 1980, United States (15)	Yes	
Milne et al, 1983, United States (16)	Yes	
Gerin et al, 1984, Canada (17)	Yes	
Buiatti et al, 1985, Italy (18)	Yes	
Kjuus et al, 1986, Norway (19)	Yes	
Schoenberg et al, 1987, United States (20)	Yes	
Lerchen et al, 1987, United States (21)	Yes	
Benhamou et al, 1988, France (22)	Yes	
Rinsky et al, 1988, United States (23)	Yes	
Ronco et al, 1988, Italy (24)	Yes	
Hull et al, 1989, United States (25)	Yes	
Morabia et al, 1992, United States (26)	Yes	
Hansen & Lauritsen, 1994, Denmark (27)	No	Case-referent study nested in a cohort included in the European cohort [Simonato et al, 1991 (55)]
Jockel et al, 1994, Germany (28)	Yes	
Cohort studies		
Dunn & Weir, 1968, United States (29)	Yes	
Menck & Henderson, 1976, United States (30)	Yes	
Milham, 1976, United States (31)	No	Cohort study updated in [Milham, 1983 (43)]
Ott et al, 1976, United States (32)	Yes	
Office of Population Censuses and Surveys, 1978, United Kingdom (33)	Yes	
Puntoni et al, 1979, Italy (34)	No	Cohort study updated in [Puntoni et al, 1986 (48)]
Redmond et al, 1979, United States (35)	Yes	
Beaumont & Weiss, 1980, United States (36)	No	Cohort study updated in [Beaumont & Weiss, 1981 (39)]
Peterson & Milham, 1980, United States (37)	Yes	..
Sjögren, 1980, Sweden (38)	No	Cohort study updated in [Sjögren et al, 1987 (51)]
Beaumont & Weiss, 1981, United States (39)	Yes	
Polednak, 1981, United States (40)	Yes	
Sjögren & Malker, 1982, Sweden (41)	No	Cohort study updated in [Sjögren & Carstensen, 1986 (50)]
McMillan, 1983, United Kingdom (42)	Yes	
Milham, 1983, United States (43)	Yes	
Gallagher & Threlfall, 1983, Canada (44)	Yes	
Fletcher & Ades, 1984, United Kingdom (45)	Yes	
Becker et al, 1985, Germany (46)	No	Cohort study updated in [Becker et al, 1991 (57)]
Newhouse et al, 1985, United Kingdom (47)	Yes	
Puntoni et al, 1985, Italy (48)	Yes	
Sjögren et al, 1985, Sweden (49)	Yes	
Sjögren & Carstensen, 1985, Sweden (50)	No	Cancer incidence study in a cohort also followed up for mortality [Sjögren et al, 1986 (49)]
Sjögren et al, 1987, Sweden (51)	No	Cohort included in the European cohort [Simonato et al, 1991 (55)]
Tola et al, 1988, Finland (52)	No	Cohort included in the European cohort [Simonato et al, 1991 (55)]
Melkild et al, 1989, Norway (53)	Yes	
Merlo et al, 1989, Italy (54)	Yes	
Simonato et al, 1991, Europe (55)	Yes	
Steenland et al, 1991, United States (56)	Yes	
Becker et al, 1992, Germany (57)	No	Cohort included in the European cohort [Simonato et al, 1991 (55)]
Moulin et al, 1993, France (58)	No	Cohort included in the European cohort [Simonato et al, 1991 (55)]
Danielsen et al, 1993, Norway (59)	Yes	

welders (12, 14). Twelve relative risks (24%) were higher than 2.00, most of them (10 RR values) being observed in case-referent studies.

The meta-analysis

Table 3 shows the results of the meta-analysis for each welding category. The combined relative risks are provided for the population-based, case-referent, and cohort studies separately and combined.

For the "all or unspecified welding categories", the combined relative risks were 1.39 (observed 585, 95% CI 1.28—1.51) for the 7 population-based studies, 1.72 (observed 230, 95% CI 1.36—2.18) for the 9 case-refer-

ent studies, and 1.27 (observed 213, 95% CI 1.10—1.46) for the 3 cohort studies. When the case-referent studies and cohort studies (12 studies) were combined, the relative risk was 1.37 (observed 443, 95% CI 1.22—1.55). This value was similar to that observed for the population-based studies (RR 1.39). The combination of all studies concerning "all or unspecified welding categories" (19 studies) led to a relative risk of 1.38 (observed 1028, 95% CI 1.29—1.48).

For the shipyard welders, the combined relative risks were 1.16 (observed 144, 95% CI 0.92—1.47) for the 6 case-referent studies and 1.36 (observed 161, 95% CI 1.17—1.60) for the 8 cohort studies, the combined rela-

Table 2. Description of the studies included in the meta-analysis on lung cancer in welders. The studies have been classified by increasing relative risks in each welding or study design category. (95% CI = 95% confidence interval, OR = odds ratios, SMR = standardized mortality ratio, SIR = standardized incidence ratio, PMR = proportionate mortality ratio)

Welding categories	Observed ^a	Relative risks	95% CI
All or unspecified			
Mortality and morbidity statistics			
Peterson & Milham, 1980, United States (37)	27	PMR = 0.99	0.43—3.59
Milne et al, 1983, United States (16)	5	OR = 1.2	0.73—16.7
Milham, 1983, United States (43)	177	PMR = 1.26	0.66—1.45
Menck & Henderson, 1976, United States (30)	48	SMR = 1.37	1.08—1.47
Gallagher & Threlfall, 1983, Canada (44)	74	PMR = 1.45	1.01—1.82
Office of Population Censuses and Surveys, 1978, United Kingdom (33)	246	SMR = 1.51	1.15—1.83
Gottlieb, 1980, United States (15)	8	OR = 3.5	1.33—1.71
Case-referent studies			
Jockel et al, 1994, Germany (28)	108	OR = 1.24	0.83—1.86
Benhamou et al, 1988, France (22)	18	OR = 1.42	0.79—2.88
Morabia et al, 1992, United States (26)	18	OR = 1.5	0.8—2.7
Kjuus et al, 1986, Norway (19)	28	OR = 1.9	0.9—3.7
Gerin et al, 1984, Canada (17)	12	OR = 2.4	1.00—5.4
Buiatti et al, 1985, Italy (18)	7	OR = 2.8	0.9—8.5
Ronco et al, 1988, Italy (24)	6	OR = 2.93	0.87—9.82
Lerchen et al, 1987, United States (21)	19	OR = 3.2	1.4—7.4
Breslow et al, 1954, United States (11)	14	OR = 7.2	1.9—44.3
Cohort studies			
Dunn & Weir, 1968, United States (29)	49	SMR = 1.05	0.78—1.39
Simonato et al, 1991, Europe (55)	116	SMR = 1.34	1.10—1.60
Sjögren et al, 1986, Sweden (49)	48	SMR = 1.34	0.99—1.78
Shipyard welding			
Case-referent studies			
Blot et al, 1978, United States (12)	11	OR = 0.7	0.32—1.41
Blot et al, 1980, United States (14)	11	OR = 0.9	0.4—2.3
Rinsky et al, 1988, United States (23)	41	OR = 1.13	0.76—1.68
Schoenberg et al, 1987, United States (20)	38	OR = 1.2	0.8—1.9
Hull et al, 1989, United States (25)	37	OR = 1.7	0.9—3.1
Lerchen et al, 1987, United States (21)	6	OR = 2.2	0.5—9.1
Cohort studies			
Mc Millan, 1983, United Kingdom (42)	5	PMR = 1.04	0.34—2.43
Newhouse et al, 1986, United Kingdom (47)	26	SMR = 1.13	0.80—1.57
Simonato et al, 1991, Europe (55)	36	SMR = 1.26	0.88—1.74
Beaumont and Weiss, 1981, United States (39)	50	SMR = 1.32	0.98—1.74
Puntoni et al, 1986, Italy (48)	12	SMR = 1.57	0.82—2.76
Merlo et al, 1989, Italy (54)	16	SMR = 1.67	0.95—2.71
Melkild et al, 1989, Norway (53)	7	SIR = 2.21	0.88—4.54
Danielsen et al, 1993, Norway (59)	9	SIR = 2.5	1.14—4.75
Nonshipyard welding			
Case-referent studies			
Lerchen et al, 1987, United States (21)	13	OR = 3.8	1.4—10.7
Cohort studies			
Ott et al, 1976, United States (32)	2	SMR = 1.00	0.12—3.61
Steenland et al, 1991, United States (56)	39	SMR = 1.07	0.76—1.46
Simonato et al, 1991, Europe (55)	80	SMR = 1.37	1.09—1.71
Fletcher & Ades, 1984, United Kingdom (45)	8	SMR = 1.46	0.62—2.88
Polednak, 1981, United States (40)	17	SMR = 1.5	0.87—2.39
Redmond et al, 1979, United States (35)	14	SMR = 1.51	0.82—2.53
Mild steel welding			
Case-referent studies			
Gerin et al, 1984, Canada (17)	2	OR = 1.2	0.1—9.4
Hull et al, 1989, United States (25)	56	OR = 1.6	0.8—3.1
Cohort studies			
Steenland et al, 1991, United States (56)	39	SMR = 1.07	0.76—1.46
Simonato et al, 1991, Europe (55)	40	SMR = 1.78	1.27—2.43
Stainless steel welding			
Case-referent studies			
Hull et al, 1989, United States (25)	61	OR = 1.3	0.6—2.3
Gerin et al, 1984, Canada (17)	10	OR = 3.3	1.2—9.2
Kjuus et al, 1986, Norway (19)	16	OR = 3.3	1.2—9.3
Cohort studies			
Simonato et al, 1991, Europe (55)	20	SMR = 1.23	0.75—1.90
Polednak, 1981, United States (40)	7	SMR = 1.24	0.50—2.55

^a Observed numbers of lung cancer cases (case-referent studies), lung cancer deaths (mortality studies), lung cancer diagnoses (cancer incidence studies).

Table 3. Results of the meta-analysis on lung cancer in welders. (RR = relative risks, 95% CI = 95% confidence interval, df = degree of freedom)

Welding categories	Number	Heterogeneity	Observed ^a	Combined RR	95% CI
All or unspecified					
Population-based studies	7	$\chi^2 = 7.63$ df = 6 P < 0.30	585	1.39	1.28—1.51
Case-referent studies	9	$\chi^2 = 10.51$ df = 8 P < 0.30	230	1.72	1.36—2.18
Cohort studies	3	$\chi^2 = 2.11$ df = 2 P < 0.50	213	1.27	1.10—1.46
Case-referent and cohort studies	12	$\chi^2 = 17.51$ df = 11 P < 0.10	443	1.37	1.22—1.55
All studies	19	$\chi^2 = 25.17$ df = 18 P < 0.20	1028	1.38	1.29—1.48
Shipyards welding					
Case-referent studies	6	$\chi^2 = 4.36$ df = 5 P < 0.50	144	1.16	0.92—1.47
Cohort studies	8	$\chi^2 = 6.63$ df = 7 P < 0.50	161	1.36	1.17—1.60
All studies	14	$\chi^2 = 12.18$ df = 13 P < 0.90	305	1.30	1.14—1.48
Nonshipyards welding					
Case-referent study	1		13	3.8	1.4—10.7
Cohort studies	6	$\chi^2 = 2.32$ df = 5 P < 0.90	160	1.31	1.12—1.54
All studies	7	$\chi^2 = 6.42$ df = 6 P < 0.50	173	1.35	1.15—1.58
Mild steel welding					
Case-referent studies	2	$\chi^2 = 0.057$ df = 1 P < 0.90	58	1.56	0.82—2.99
Cohort studies	2	$\chi^2 = 3.31$ df = 1 P < 0.10	79	1.49	1.15—1.93
All studies	4	$\chi^2 = 3.38$ df = 3 P < 0.50	137	1.50	1.18—1.91
Stainless steel welding					
Case-referent studies	3	$\chi^2 = 3.43$ df = 2 P < 0.20	87	2.00	1.22—3.28
Cohort studies	2	$\chi^2 = 0.0003$ df = 1 P < 1.00	27	1.23	0.82—1.85
All studies	5	$\chi^2 = 5.67$ df = 4 P < 0.30	114	1.50	1.10—2.05

^a Observed numbers of lung cancer cases (case-referent studies), lung cancer deaths (mortality studies), lung cancer diagnoses (cancer incidence studies).

tive risk being 1.30 (observed 305, 95% CI 1.14—1.48) for all studies.

With regard to nonshipyards welders, the combined relative risk could be calculated on the basis of 6 cohort studies, 1.31 (observed 160, 95% CI 1.12—1.54), and for both the cohort and case-referent studies, 1.35 (ob-

served 173, 95% CI 1.15—1.58). The comparison of the combined relative risks obtained for the shipyard and nonshipyards welders showed similar values, 1.30 and 1.35, respectively.

Studies providing results for mild steel and stainless steel welders were less numerous. Only 2 case-referent

and 2 cohort studies were available for mild steel welders. The combined relative risks were 1.56 (observed 58, 95% CI 0.82–2.99) and 1.49 (observed 79, 95% CI 1.15–1.93), and 1.50 (observed 137, 95% CI 1.18–1.91), respectively, for all the studies combined.

Three case-referent and 2 cohort studies were focused on stainless steel welding, leading to combined relative risks of 2.00 (observed 87, 95% CI 1.22–3.28) and 1.23 (observed 27, 95% CI 0.82–1.85), respectively, and a relative risk of 1.50 (observed 114, 95% CI 1.10–2.05) for all the studies combined.

When the mild steel and stainless steel welders were compared, it appeared from table 3 that the combined relative risks observed for these welding categories were only slightly different: 1.56 versus 2.00 for the case-referent studies, 1.49 versus 1.23 for the cohort studies. Furthermore, the same combined relative risk was observed in each welding category on the basis of all the studies combined (RR 1.50).

With regard to the test for heterogeneity, it is worth noting that no significant heterogeneity was discerned for the studies of any welding or study design category.

Discussion

Cohort studies versus case-referent studies

The population-based studies used in this meta-analysis are not real cohort studies. Therefore, they were analyzed separately. However, they provided combined relative risks that were similar to those resulting from the cohort studies (RR 1.39 and 1.27, respectively) (table 3).

The combined relative risks calculated on the basis of case-referent studies seemed to differ from those of cohort studies with regard to levels of risk. The combined relative risks were higher for the case-referent studies than for the cohort studies for “all or unspecified welding categories” (RR 1.72 versus 1.27), nonshipyard welding (RR 3.8 based on 1 study versus 1.31), mild steel welding (RR 1.56 versus 1.49), and stainless steel welding (RR 2.00 versus 1.23). This finding could be the result of selection bias due to case-referent studies providing high odds ratios in the literature. The tables of some published papers may give the odds ratios of occupations showing an excess rather than occupations with low odds ratios, in particular in hypothesis-generating studies not specifically designed to address the lung cancer risk of welders (10, 60).

However, population-based cohort studies may also be affected by such a positive selection bias since the results of welders may not be given because of small numbers of exposed cases and low standardized mortality ratios. Furthermore, table 2 shows that there are more case-referent studies having relative risks of 1.00 or less

than there are cohort studies. These remarks would not seem to argue for a publication bias in case-referent studies. Nevertheless, such a selection bias would not hinder the comparison of combined relative risks between welding categories since this selection bias is likely to have affected all the welding categories.

Regarding the heterogeneity between effect estimates which appeared within the categories of studies (table 3), it may be that the lack of heterogeneity contrasts with the range of relative risks observed in the 9 case-referent studies among “all or unspecified welding categories”, from 1.24 to 7.2 with nonoverlapping 95% confidence intervals (0.83–1.86 and 1.9–44.3, respectively) (table 2). This occurrence is due to the fact that the studies having the lowest relative risks (19, 22, 26, 28), from 1.24 to 1.9, had the highest numbers of exposed cases and rather narrow 95% confidence intervals, whereas studies having the highest relative risks (11, 18, 21, 24), from 2.4 to 7.2, had smaller numbers of exposed cases and comparatively wide 95% confidence intervals, especially for the study by Breslow et al, with a relative risk of 7.2 based on 7 exposed cases and 2 exposed referents with a 95% confidence interval of 1.9 to 44.3. These studies with wide 95% confidence intervals are of little effect in calculations of combined relative risks since they have high variances.

Lung cancer risk for “all or unspecified welding categories”

Several reviews of the literature have been published previously (61–64). All the authors agreed that there is a 30% to 40% increase in the relative risk of lung cancer among welders when compared with the general population. The results of the present meta-analysis are consistent with these conclusions, since the combined relative risk of the “all or unspecified” welding category was 1.37 (95% CI 1.22–1.55) when the case-referent and cohort studies were combined and 1.38 (1.29–1.48) when the population-based studies were included (table 3).

When the possible selection bias of “positive” case-referent studies was controlled, the estimate of the lung cancer risk of all welding categories was the combined relative risk calculated from the cohort studies (RR 1.27, 95% CI 1.10–1.46).

Shipyard versus nonshipyard welders

Asbestos exposure, which is related to lung cancer occurrence (65), may be a confounding factor when the lung cancer risk of welders is assessed. Furthermore, most authors assume that asbestos exposure is more likely to have occurred in shipyards than in other workplaces (1). As a control for this possible confounding factor, shipyard welders were considered separately in the epidemiologic studies.

The present meta-analysis failed to confirm that shipyard welders were at a higher lung cancer risk than nonshipyard welders since the combined relative risks were similar, 1.30 (95% CI 1.14–1.48) and 1.35 (95% CI 1.15–1.58), respectively (table 3).

Mild steel versus stainless steel welders

Epidemiologic studies focusing on the lung cancer risk of mild steel welders as compared with that of stainless steel welders were set up in the 1980s, following the first report by Sjögren (38). The objective of these studies was to assess the lung cancer risk due to exposure to hexavalent chromium and nickel when stainless steel welding was compared with mild steel welding.

The present meta-analysis failed to confirm the hypothesis of a higher risk in association with stainless steel, since the combined relative risks were similar when the case-referent studies only (2.00 versus 1.56, respectively) or the cohort studies only (1.23 versus 1.49, respectively) or both study designs (1.50 in each category) were considered (table 3). In addition, the European study showed that the standardized mortality ratio of mild steel welders was statistically significant (SMR 1.78, 95% CI 1.27–2.43) and higher than that of stainless steel welders (SMR 1.23, 95% CI 0.75–1.90) (55). The latter did not reach statistical significance.

A meta-analysis of stainless steel welding has been published by Sjögren et al (6), including 3 case-referent studies (17, 19, 27) and 2 cohort studies (51, 58), 3 of them being included in the European study (27, 51, 58). This meta-analysis provided a combined relative risk of 1.94 (95% CI 1.28–2.93) for welders exposed to stainless steel welding fumes, a finding suggesting a relation between stainless steel welding and the occurrence of lung cancer. This conclusion has been discussed since the authors did not consider studies providing low relative risks for stainless steel welders (8). Moreover, 4 of the studies reviewed by Sjögren et al provided relative risks for mild steel welders (17, 27, 51, 58); the combination of these relative risks leads to a significantly high combined relative risk (RR 1.56, 95% CI 1.06–2.29), which does not markedly differ from that observed for stainless steel welders by Sjögren et al.

With regard to dose-response relationship, the most relevant data were provided by the European study, which used a specific job-exposure matrix to provide standardized mortality ratios by cumulative exposure to total fumes, hexavalent chromium, and nickel exposure among stainless steel welders (55, 66). No dose-response relationship was observed for lung cancer risk with these estimates for various welding fume components, even in the category of predominantly stainless steel welders. With hexavalent chromium as the variable, the standardized mortality ratios were 1.91 (observed 3, 95% CI 0.39–5.58) for a cumulative dose of <0.5 mg(year $\cdot$ m³)

versus 1.67 (observed 9, 95% CI 0.77–3.18) for a cumulative dose of ≥ 0.5 mg(year $\cdot$ m³); with nickel as the variable, the standardized mortality ratios were 2.34 (observed 8, 95% CI 1.01–1.61) for a cumulative dose of <0.5 mg(year $\cdot$ m³) versus 1.13 (observed 4, 95% CI 0.31–2.90) for a cumulative dose of ≥ 0.5 mg(year $\cdot$ m³). Although some degree of misclassification might have been introduced when the job-exposure matrix was developed, this lack of dose-response relationship with hexavalent chromium exposure is of interest because the statistical power to detect such an association was high (66).

Consequently, it appears that the lung cancer excess of welders cannot be clearly attributed to stainless steel welding.

Healthy worker effect

The European multicentric study provides results concerning subcohorts of shipyard, nonshipyard, mild steel, and stainless steel welders. The fact that these subcohorts have been included in the same study makes it easier to compare the welding category because differences in the relative risks are unlikely to be due to differences in study design.

With regard to mortality from all causes of death, the standardized mortality ratio observed for mild steel welders was close to that expected in the European study (SMR 1.01, observed 287, 95% CI 0.90–1.13), whereas a marked healthy worker effect appeared for the stainless steel welders (SMR 0.86, observed 335, 95% CI 0.77–0.96), the latter being statistically significant. In addition, a strong healthy worker effect was observed in the German cohort of stainless steel welders (SMR 0.79, observed 153, 95% CI 0.67–0.93) (57). These results suggest that the healthy worker effect might have been more marked among stainless steel welders than among mild steel welders. This possibility had been suggested in the literature because stainless steel welders are more qualified and receive higher remuneration than other welders (7, 55).

The preceding result raises the question of whether the healthy worker effect could have led to an underestimation of the lung cancer risk of stainless steel welders when compared with mild steel welders. Most studies on the healthy worker effect have demonstrated that it results in low mortality rates mainly for cardiovascular and nonmalignant respiratory diseases and that the healthy worker effect has little influence on the occurrence of cancer, in particular on lung cancer (67). The report by Sterling & Weinkam (68) disagrees, however, with this conclusion; it suggests that the healthy worker effect is observed for all causes of death, including lung cancer. Consequently, the strong healthy worker effect observed for stainless steel welders may have led to an underestimation of the lung cancer risk of stainless steel welders

when compared with mild steel welders. Moreover, the degree of underestimation is difficult to assess; therefore we were not able to evaluate the standardized mortality ratio for lung cancer among stainless steel welders in the absence of the healthy worker effect.

Asbestos exposure

When mortality from pleural mesothelioma was used as an indicator of asbestos exposure, 2 studies among shipyard welders showed high relative risks (41, 42, 69). However, such excesses were found among nonshipyard welders in 2 Swedish studies (49, 50), in the German study of stainless steel welders (57), and in the European study (SMR >5.00, observed 5) (55). It is noteworthy that, in the European study, 4 out of the 5 cases of mesothelioma leading to a significant excess occurred in the mild steel and stainless steel subcohorts (1, 55).

A French study on the retention of asbestos bodies in the lungs of welders has shown that about 40% of these workers had asbestos bodies (3). Although this study population was a biased sample of welders with lung disease suspected to be caused by asbestos, it suggests that all welding activities may also involve asbestos exposure.

In summary, it appears that asbestos is likely to be a causative factor for the lung cancer excess observed among welders.

Smoking habits

Following the reports by Axelson (70), it has been established that a lung cancer excess ranging between 1.30 and 1.50 in a cohort study may be the result of tobacco overconsumption in the study cohort when compared with the general population. The fact that the lung cancer risks of welders range between 1.30 and 1.50 raises the important question of whether these excesses are possibly partly or totally explained by smoking.

When case-referent studies only are considered, it seems unlikely that smoking accounts for the observed lung cancer excesses since most of the odds ratios were adjusted for smoking (17–22, 24, 26–28). However, this assumption may be inaccurate due to the possible selection of “positive” results which may have overestimated the lung cancer risk of welders in published reports.

The design of cohort studies does not allow such an assessment to be made since data on smoking are not available for all workers included in historical cohorts (70). The literature provides arguments suggesting that welders smoke more than the general populations used as external references. The Registrar General supplement for England and Wales showed that the “smoking ratio” of “welders, cutters and braziers”, as compared with that of the general male population was 1.22 (33). According to population surveys in the United States, the

proportions of smokers among welders as compared with that of the general male population were 52.1% versus 42.6% (71), 45.4% versus 36.8% (72), and 42.7% versus 30.1% (73). When Axelson's method is applied to these proportions, with the assumption of a relative risk of 10.00 for lung cancer among smokers as compared with nonsmokers, the lung cancer excess due to smoking among welders would be about 1.20. These estimates are lower than the risk estimates from cohort studies.

Furthermore, smoking was also more prevalent among the welders in the French study, and this prevalence was assumed to lead to a 1.06 excess of lung cancer in a comparison with the nonwelding reference group (58). This value was lower than the relative risk of 1.32 observed between welders and the internal reference group of nonwelders (58). In the American study by Steenland et al (56), smoking overconsumption was detected which would lead to an approximately 10% excess of lung cancer among welders.

Consequently, the hypothesis that smoking could be responsible for part of the lung cancer excess of welders cannot be discarded.

Concluding remarks

The results of the meta-analysis are consistent with those of previously published reviews of the literature which concluded that there is a 30% to 40% increase in the relative risk of lung cancer among welders when they are compared with the general population.

Similar combined relative risks were observed for shipyard and nonshipyard welders. The meta-analysis failed to demonstrate that stainless steel welders, although potentially exposed to nickel and hexavalent chromium, are at higher lung cancer risk than mild steel welders. This conclusion should be considered in the light of the fact that the standardized mortality ratio for lung cancer among stainless steel welders may have been underestimated by a marked healthy worker effect.

The literature shows that asbestos exposure and smoking may be confounding factors in epidemiologic studies on the lung cancer risk of welders and therefore the combination of their carcinogenic effects may account for part of the lung cancer excess observed.

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