# 2. CANCER IN HUMANS

### 2.1 Introduction

Welding is a broad term for the process of joining metals through coalescence (AWS, 1997). Welding processes generate fumes which contain particulate matter formed from the condensation of metal liquefied during the welding process (see Section 1.1 for further details). In the occupational literature, welding is often grouped together with flame-cutting, which is a closely related process where oxygen and a fuel gas are used to cut a metal. Welding involves concomitant exposure to ultraviolet (UV) radiation, fumes, particles, and gases.

There is extensive literature on the risks of cancer from either welding jobs or exposure to welding fumes from both cohort and casecontrol studies, and also partly from studies of routinely collected data. Since the previous IARC Monographs evaluation in 1990 (IARC, 1990), the number of published epidemiological studies has increased substantially; a few cohorts have also extended the follow-up period. For this monograph, the Working Group has focused its review on those studies that report risk estimates associated with occupation as a welder or exposure to welding fumes. Studies or risk estimates of occupations which may involve unspecific and infrequent welding (such as pipefitters, plumbers, and solderers), are excluded from this review; the frequency of welding in these occupations is not normally clear, and the groupings are too broad to meaningfully evaluate exposure as a welder. Studies that reported only broad occupational

aggregations, combining welding with related occupations, were also excluded as they lack specificity for welding.

Assessments of exposure to welding fumes were generally based on occupation as a welder or welding as a job task, rather than on quantitative estimates of individual exposures. Several cancer types have been investigated; there has been a special focus on cancer of the lung, but also a variety of other sites including cancers of the respiratory tract and urinary bladder, haematopoietic cancers, and ocular melanoma.

The cohort studies of welders typically focus on specific occupational or industrial settings; some include assessment of exposure to welding fumes at baseline, but may lack information on exposure to potential confounders such as tobacco smoking and asbestos. Some studies also lack information on exposures after baseline and have a limited number of cases other than cancer of the lung during further follow-up.

The majority of case-control studies have a simple and indirect exposure assessment, for example by job type, but some include more detailed assessments based on job-exposure matrices (JEMs), job-specific questionnaires, and/or case-by-case expert assessment. As a particular strength, case-control studies often include a lifelong assessment of welding history as well as potential confounders, both occupational and non-occupational.

Welders are exposed to a complex mixture of chemical compounds that vary by the welding method and the type of metal to be welded, for example mild steel (MS) versus stainless steel (SS); the latter involves exposure to nickel (Ni) and chromium (Cr) compounds, recognized lung carcinogens (IARC, 2012a). In evaluating the risk of cancer from welding jobs and exposure to welding fumes, it is important to distinguish between exposures which are normally part of the welding environment and those which occur as co-exposures, typically from other working processes not necessarily related to the welding or from non-welding coworkers (e.g. metal grinders in the nearby working environment). In their working environment, welders may be exposed to compounds other than those directly occurring from the welding process which may be considered as potential confounders. Examples of co-exposures that may contribute to the overall occupational exposures of welders, and therefore the potential risk of cancer, include coatings on the welded metal (e.g. paints, grease, and other compounds) as well as compounds used to prepare metal for welding (e.g. trichloroethylene (TCE) or paint strippers). Welders have also been exposed to asbestos as part of heat-protective equipment (including blankets used to cover the weld, in order to prevent abrupt cooling) and as an insulation material in the welding locality, especially in shipyards where asbestos was extensively used.

Tobacco smoking is considered a major potential confounder for certain tobacco-associated cancers observed in welders. Some studies show a higher prevalence of tobacco use in welders compared with the general population (e.g. <u>Dunn et al., 1960</u>; <u>Office of Population Censuses and Surveys, 1978</u>).

In the absence of information on specific co-exposures in studies of cancer of the lung, crude indirect indications of confounding can be considered, for example, the risk of mesothelioma as an indicator of asbestos exposure.

Overall, the Working Group considered the preceding factors in evaluating and comparing

study results; heterogeneity in results may partly reflect such differences. The Working Group noted that the studies should ideally include information on material welded, type of welding process, and co-exposure to asbestos and tobacco smoking. Studies that provided this information were considered the most informative for this evaluation. Additionally, exposure—response data were included when they were available in the published reports.

#### 2.2 Ocular melanoma

See Table 2.1 and Table 2.2

Acute overexposure of the eye to UV radiation is common among electric arc welders, and UV radiation is a confirmed cause of ocular melanoma (IARC, 2012b). Because of the rarity of this cancer and the existence of only relatively small cohorts of welders, the association between welding and ocular melanoma has mostly been investigated via case-control studies. The Working Group identified two independent cohort studies (Table 2.1) that included information on welding exposure from cancer registries in the Nordic countries (Siew et al., 2008; Pukkala et al., 2009) and Canada (MacLeod et al., 2017), and less than ten independent casecontrol studies on ocular melanoma (Table 2.2). Overall, most studies reported an increased risk of ocular melanoma based on dichotomous exposure variables. The welding exposure is self-reported and crude in most studies, and includes job titles such as welder and/or flamecutter or sheet metalworker; welding tasks are also included in some studies. Most studies did not distinguish between arc welding, which normally involves exposure to UV radiation, and gas welding without UV radiation [including gas welders may attenuate risk estimates]. Most studies specified that they excluded the rare uveal tract melanoma of the iris.

Reference, location, enrolment period/follow-up	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Kromhout et al. (1992) Zutphen, Netherlands Enrolment 1977– 1978/follow-up 1977–1985	878 men, 67 lung cancer cases; random sample of men born in 1900–1919 who lived in Zutphen for at least 5 yr. Exposure assessment method: expert judgement; two JEMs: general and population-specific (developed from self-reported exposures)	Lung	Welding fumes General JEM: Population- specific JEM	NR NR	1.54 (0.37–6.30) 1.93 (1.05–3.55)	Age, smoking	Strengths: comparison of two methods of exposure assessment for welding and soldering fumes Limitations: small numbers
van Loon et al. (1997b) Netherlands Enrolment September 1986/follow- up September 1986–1990	Case-cohort analysis: 524 lung cancer cases, 1630 men in the subcohort; general population cohort of 58 279 men aged 55-69 yr; study restricted to subjects who reported a complete job history Exposure assessment method: expert judgement from a self-administered questionnaire; assessment of probability of exposure to welding fumes, asbestos, paint dusts, and PAHs Cumulative score calculated as the sum of the duration of exposed jobs, weighted by exposure probability	Lung	Ever exposed to welding fumes Welding fumes: littertiles 0 1st tertile (low) 2nd tertile 3rd tertile (high) Trend test <i>P</i> value	457 17 26 20	0.86 (0.46–1.58)  sure index in  1 0.71 (0.31–1.60) 1.49 (0.72–3.07) 1.01 (0.49–2.06)	Age, smoking, other occupational exposures, vitamin C, β-carotene, retinol	General population levels of exposure are probably low Strengths: semi- quantitative assessment of exposure to welding fumes; adjustment for smoking, exposure to asbestos, paints, and PAHs and other potential confounders Limitations: self-administered questionnaire; short follow-up

Table 2.1 (continued)

Reference, location, enrolment period/follow-up	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Zeegers et al. (2004) Netherlands Enrolment 1986/follow-up 1986–1993 Nested case- control	Cases: 830 men with microscopically confirmed incident carcinomas of the prostate identified by cancer registries and Dutch National Database of Pathology Reports Controls: 1525 subcohort men randomly sampled from cohort Exposure assessment method: questionnaire; self-administered questionnaires recording occupational history of	Prostate	Welder: ever employed Longest-held profession:	12 12 5 5	1.41 (0.51–3.88) 1.81 (0.62–5.30) 1.07 (0.23–4.88) 1.42 (0.27–7.46)	Age Age, fruit, vegetable, dairy, meat, alcohol, smoking, education, family history of prostate cancer, physical activity Age Age, fruit,	Strengths: information on diet and lifestyle confounders; multivariate analysis Limitations: exposure misclassification; no information on occupational coexposures; multiple comparisons; few exposed cases
	each job and jobs held for > 5 yr		welder			vegetable, dairy, meat, alcohol, smoking, family history of prostate cancer, education, physical activity	

Reference, location, enrolment period/follow-up	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Zeegers et al. (2004) (cont.)		Prostate	Profession at baseline: welder	5 5	0.88 (0.21–3.75) 1.19 (0.25–5.64)	Age Age, fruit, vegetable, dairy, meat, alcohol, smoking, family history of prostate cancer, education, physical activity	
Veglia et al. (2007) Europe (multicentre study, 23 centres, 10 countries) Enrolment 1992–2000/ median follow- up for 6.1 yr	217 055 subjects; 809 lung cancer cases; men and women, mostly aged 35–70 yr at recruitment; restricted to centres with information on occupational history (Denmark, Germany, Greece, Italy, Spain, UK) Exposure assessment method: questionnaire; job titles from questionnaires	Lung	Welder Welding shop	55 72	1.67 (1.20–2.30) 1.55 (1.20–2.10)	BMI, physical activity, education, sex, age, smoking, fruits, vegetable	Strengths: large prospective cohort; detailed information on several possible confounders Limitations: job title analysis; no exposure data

Table 2.1 (continued)

Reference, location, enrolment period/follow-up	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Siew et al. (2008) Finland Enrolment 1970/follow-up	1.2 million men; 30 137 lung cancer cases; all economically active Finnish men born	Lung	Welder and flame cutter, SS > 10% Welder,	110	0.95 (0.78–1.15) 1.05 (0.69–1.55)	Age, calendar year	Overlaps with Pukkala et al. (2009) but includes quantitative analysis and further adjustment for
1971–1995	during 1906–1945 who participated in the 1970 population census Exposure assessment method: expert judgement; FINJEM linked to the longest-held job in 1970 to assess exposure to welding fumes, iron fumes, asbestos, SiO <sub>2</sub> , Cr, Ni, Pb, B[a]P, and smoking; exposure estimates based on the judgment of ~20	Lung (SCC)	shipyard Welder, building Welder, NEC Cumulative expos (mg/m³-yr) None Low (0.1–10) Medium (10.1–49.9) High (≥ 50) Cumulative expos	24 102 cure to weld 27 192 2591 287	1.31 (0.84–1.95) 1.39 (1.14–1.69) ing fumes 1 1.09 (1.05–1.14) 1.16 (1.03–1.31) 1.15 (0.90–1.46)	Smoking, asbestos, SiO <sub>2</sub> , SES, age, periods of follow-up  Smoking, asbestos, SiO <sub>2</sub> , SES, age, periods of follow-up	smoking and asbestos Strengths: very large cohort; adjustment for smoking and other occupational exposures (including asbestos) Limitations: cross- sectional information on occupation
	experts at the Finnish Institute of Occupational Health		(mg/m³-yr) None Low (0.1–10) Medium (10.1–49.9) High (≥ 50)	9275 870 110	1 1.07 (0.99–1.15) 1.26 (1.04–1.53) 1.55 (1.08–2.24)		

Table 2.1 (continued)								
Reference, location, enrolment period/follow-up	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled	Comments	
Siew et al. (2008) (cont.)		Lung (small cell/ oat cell)	Cumulative exp (mg/m³-yr)	Cumulative exposure to welding fumes (mg/m³-yr)				
			None	4570	1	asbestos,		
			Low (0.1-10)	479	1.15 (1.04-1.27)	SiO <sub>2</sub> , SES,		
			Medium (10.1–49.9)	46	1.10 (0.82–1.48)	periods of follow-up		
			High (≥ 50)	7	0.83 (0.40-1.75)			
		Lung (adenocarcinoma)	Cumulative exp (mg/m³-yr)	osure to weld	ing fumes	Smoking, asbestos,		
			None	3379	1	SiO <sub>2</sub> , SES,		
			Low (0.1-10)	342	1.08 (0.95-1.21)	age, periods		
			Medium (10.1–49.9)	46	1.42 (1.06–1.91)	of follow-up		

High (≥ 50)

1.14 (0.54-2.40)

Table 2.1 (continued)

Reference, location, enrolment period/follow-up	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Pukkala et al. (2009)	14.9 million people aged 30–64 yr participating	Lung	Welder			Age, calendar	Overlaps with <u>Siew et al.</u> (2008). Results differed
Nordic countries	in any computerized		Men	1798	1.33 (1.27–1.40)	year	by country, and risk estimates for ocular melanoma were elevated only in Finland. Results for welders excluded Denmark; 91 mesotheliomas in male welders (SIR, 1.79;
(Denmark,	population census in		Women	25	1.70 (1.10-2.51)		
Finland, Iceland,	1990 or earlier, still alive	Lung (adeno-	Men	408	1.51 (1.37–1.67)		
Norway, and	and living in the country	carcinoma)	Women	5	0.98 (0.32-2.29)		
Sweden)	on January 1 in the year following the census. The date and number of census depend on the country:	Lung (small cell/	Men	237	1.24 (1.09-1.41)		
Enrolment/		oat cell)	Women	7	2.78 (1.12-5.74)		
follow-up: Denmark 1971–		Lung (SCC)	Men	590	1.35 (1.24-1.46)		
2003; Finland	Denmark 1970; Finland		Women	4	1.73 (0.47-4.42)		95% CI, 1.44–2.20); no
1971–2005;	1970, 1980, 1990; Iceland	Kidney	Men	533	1.25 (1.14-1.36)		mesothelioma in female
Iceland 1982-	1981; Norway 1960, 1970, 1981; Sweden 1960, 1970,	·	Women	7	1.12 (0.45-2.31)		welders (0.3 expected).
2004; Norway			Both	540	1.24 (1.14–1.35)		Strengths: very large
1961–2003;	1980, 1990	Kidney (urinary	Men	56	1.39 (1.05-1.80)		cohort, long follow-up,
Sweden 1961-	Exposure assessment	pelvis/UUT)	Women	0.48	0 (0-7.63)		risk estimates for rare
2005	method: self-administered questionnaire; information	Urinary bladder	Men	822	1.06 (0.99–1.13)		cancers Limitations: information
	on occupation from the 1st	,	Women	4	0.80 (0.22-2.04)		on occupation at one
	census in which the person		Both	826	[1.05 (0.98–1.30)]		point in time; no
	participated. Original	Eye: melanoma	Men	36	1.07 (0.75–1.48)		adjustment for smoking
	national occupation	,	Women	1	1.25 (0.03-6.99)		and other lifestyle factors
	codes converted to a	Prostate	Men	2871	1.01 (0.98-1.05)		(partial data to evaluate
	common classification	Leukaemia: ICD-7	Men	294	1.09 (0.97–1.23)		confounding)
	with 53 occupational categories. Danish	(code 204)	Women	5	1.08 (0.35-2.52)		
	welders are included in	NHL (CLL): ICD-7	Men	115	0.98 (0.82–1.18)		
	the category 'mechanic	(- ),	Women	2	1.29 (0.16-4.68)		
	workers'. Results for	Leukaemia	Men	89	1.23 (0.99–1.52)		
	welders (2606 women and	(AML): ICD-7	Women	2	1.23 (0.15–4.45)		
	74 857 men) limited to	Nasal cavity and	Men	29	1.13 (0.76–1.62)		
	Finland, Iceland, Norway, and Sweden	sinuses	Women	0	0 (0–10.33)		

Table 2.1	(continue	d)
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Reference, location, enrolment period/follow-up	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Pukkala et al.		Larynx: ICD-7	Men	146	1.14 (0.97–1.34)		
(2009)		(code 161)	Women	2	4.93 (0.60-17.81)		
(cont.)		Mesothelioma	Men	91	1.79 (1.44-2.20)		
			Women	0	0 (0-12.30)		
		Brain	Men	346	0.99 (0.90-1.11)		
			Women	16	1.39 (0.80-2.26)		
		NHL: ICD-7 (code	Men	341	0.91 (0.82-1.01)		
		200, 202)	Women	9	1.12 (0.51-2.13)		
		HL: ICD-7 (code	Men	59	0.98 (0.74-1.26)		
		201)	Women	2	2.17 (0.26-7.85)		
		MM: ICD-7 (code	Men	160	0.95 (0.82-1.11)		
		203)	Women	1	0.34 (0.01-1.91)		
		Pharynx	Men	93	1.05 (0.85-1.28)		
			Women	1	1.28 (0.03-7.14)		
Neasham et al.	218 968 subjects; incident	NHL	Welder	23	0.88 (0.58-1.35)	Education,	Strengths: large
(2011)	cases of NHL $(n = 707)$		Welding shop	37	1.16 (0.72-1.88)	sex, age,	prospective cohort;
Europe, multicentre	and HL $(n = 40)$ ; EPIC	HL	Welder	1	0.55 (0.07-4.13)	smoking, alcohol,	detailed information on several possible
(23 centres,	cohort; men and women, mostly aged 35–70 yr at		Welding shop	3	1.02 (0.23-4.48)	centre	confounders
10 countries) Enrolment 1992–2000; mean follow-up 9 yr	recruitment; restricted to centres with information on occupational history (in Denmark, Germany, Greece, Italy, Spain, and the UK) Exposure assessment method: questionnaire; job titles from questionnaires		O I				Limitations: job title analysis; no exposure data

Table 2.1 (continued)

Reference, location, enrolment period/follow-up	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Pesch et al. (2013) Europe, multicentre (23 centres, 10 countries) Enrolment 1992–2000 Nested case– control	Cases: 754 incident cases of transitional cell bladder cancer, histopathologically confirmed according to WHO criteria, follow-up of 521 468 EPIC participants Controls: 833 randomly selected from all cohort members alive and free of cancer at diagnosis of the index case (incidence density sampling); matched to the cases by sex, age at time of enrolment (± 3 yr), study centre, and other factors Exposure assessment method: questionnaires	Urinary bladder: TCC	Welder Welding shop	43 63	1.39 (0.85–2.27) 1.54 (1.01–2.34)	Smoking, region, age	Strengths: large prospective cohort; detailed information on several possible confounders Limitations: job title analysis; no exposure data
Saberi Hosnijeh et al. (2013) Europe, multicentre (23 centres, 10 countries) Enrolment 1992–2000; mean follow-up 11.2 yr	241 465 subjects; 477 incident cases of myeloid and lymphoid leukaemia; men and women mostly aged 35–70 yr at recruitment; restricted to centres with information on occupational history (in Denmark, Germany, Greece, Italy, Spain, and the UK) Exposure assessment method: questionnaire; job titles from questionnaires	Leukaemia (myeloid) Leukaemia (lymphoid)	Worked in welding shop or as welder Worked in welding shop or as welder	13	1.14 (0.63–2.05) 0.99 (0.59–1.65)	Age, sex, smoking, alcohol, country	Strengths: large prospective cohort; detailed information on several possible confounders Limitations: job title analysis; no exposure data

Table 2.1 (continued)

Reference, location, enrolment period/follow-up	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled	Comments
MacLeod et al. (2017)	1 108 410 men (including 12 845 welders and 87 460	Lung	All welders by ind Non-welders	ustry NR	1	Age, region, education	The cohort of 942 905 female workers included
Canada 1991–2011	occasional welders); linkage of the 1991 Census		(ref.)	2.5	4.5 (4.00.4.01)		only 370 welders, with less than 5 cases for the cancer
1771 2011	with the CCR; restricted to		All industries	265	1.16 (1.03–1.31)		sites of interest, and was
	individuals aged 25–74 yr with a valid code for occupation on the census form		Machine equipment, appliances manufacturing	60	1.21 (0.93–1.56)		not further analysed Strengths: large numbers; internal analyses; risk
	Exposure assessment		Construction	45	1.27 (0.96-1.67)		estimates for histological types of lung cancer; subgroup analyses Limitations: exposure defined by occupation (self-reported) at one point in time; no data on smoking, asbestos, or other co-exposures; adjustment for education and analyses restricted to blue-collar workers may minimize confounding
	method: questionnaire;		Repair of	35	1.41 (1.03–1.94)		
based on occupation self-	based on occupation self- reported at census; welders		transport vehicles				
	= employed as 'welders and soldering machine operators'; occasional		Transport vehicles manufacturing	10	1.11 (0.58–2.14)		
	welders = employed in other occupations		Shipbuilding and repair	10	1.65 (0.91–2.98)		
	potentially involving		Other industries	70	0.99 (0.79-1.25)		
	welding (from a list defined a priori)		Occasional welders	1625	1.12 (1.07–1.18)		
		Lung	All workers			Age, region,	
		(adenocarcinoma)	Non-welders (ref.)	NR	1	education	
			Welders	75	1.12 (0.89-1.41)		
			Occasional welders	455	1.07 (0.97–1.18)		
		Lung (large cell	All workers			Age, region, education	
		cancer)	Non-welders (ref.)	NR	1		
			Welders	50	1.01 (0.76-1.34)		
			Occasional welders	310	1.01 (0.90-1.14)		

Table 2.1 (continued)

Reference, location, enrolment period/follow-up	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
MacLeod et al.		Lung (small cell/	All workers			Age, region,	
(2017) (cont.)		oat cell)	Non-welders (ref.)	NR	1	education	
			Welders	45	1.54 (1.15-2.07)		
			Occasional welders	220	1.16 (1.01–1.34)		
		Lung (SCC)	All workers			Age, region,	
		-	Non-welders (ref.)	NR	1	education	
			Welders	60	1.19 (0.92-1.54)		
			Occasional welders	430	1.33 (1.20–1.47)		
		Lung	Blue-collar welder	rs		Age, region	
			Non-welders (ref.)	NR	1		
			All industries	265	1.06 (0.94-1.20)		
			Machine equipment, appliance manufacturing	60	1.13 (0.87–1.46)		
			Construction	45	1.12 (0.84-1.48)		
			Repair of transport vehicles	35	1.28 (0.93–1.76)		
			Transport vehicles manufacturing	10	1.02 (0.53–1.96)		
			Shipbuilding and repair	10	1.45 (0.80-2.63)		
			Other industries	70	0.92 (0.73-1.15)		
			Occasional welders	1625	1.02 (0.96–1.07)		

**Table 2.1 (continued)** Organ site/ Risk estimate Covariates Reference, Population size, **Exposure** Exposed Comments cancer type location, description, exposure category or (95% CI) controlled cases/ enrolment level deaths assessment method period/follow-up MacLeod et al. Blue-collar welders Age, region Lung (2017)(adenocarcinoma) Non-welders NR 1 (cont.) (ref.) Welders 1.07 (0.84-1.36) 75 1.06 (0.96-1.18) Occasional 455 welders Lung (large cell Blue-collar welders Age, region cancer) Non-welders NR 1 (ref.) Welders 0.94 (0.70-1.26) 50 Occasional 310 0.92 (0.81-1.04) welders Blue-collar welders Lung (small cell/ Age, region oat cell) Non-welders NR 1 (ref.) 1.31 (0.96-1.79) Welders 45 Occasional 220 1.02 (0.88-1.18)

welders

Table 2.1 (continued)

Reference, location, enrolment period/follow-up	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
MacLeod et al.		Lung (SCC)	Blue-collar weld	lers		Age, region	
(2017) (cont.)			Non-welders (ref.)	NR	1		
			Welders	60	1.04 (0.80-1.35)		
			Occasional welders	430	1.13 (1.02–1.25)		
		Mesothelioma	All welders			Age, region,	
			Non-welders (ref.)	NR	1	education	
			Welders	15	1.78 (1.01-3.18)		
			Occasional welders	65	1.74 (1.34–2.26)		
		Mesothelioma	Blue-collar weld	lers		Age, region	
			Non-welders (ref.)	NR	1		
			Welders	15	1.54 (0.86-2.78)		
			Occasional welders	65	1.48 (1.13–1.96)		

Reference, ocation, enrolment period/follow-up	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
MacLeod et al.		Urinary bladder	All welders			Age, region,	
( <u>2017)</u> (cont.)			Non-welders (ref.)	NR	1	education	
			Welders	100	1.40 (1.15-1.70)		
			Occasional welders	515	0.99 (0.90-1.08)		
		Urinary bladder	Blue-collar weld	lers		Age, region	
			Non-welders (ref.)	NR	1		
			Welders	100	1.47 (1.21–1.79)		
			Occasional welders	515	1.03 (0.94–1.13)		
		Kidney	All welders			Age, region,	
		,	Non-welders (ref.)	NR	1	education	
			Welders	60	1.30 (1.01-1.67)		
			Occasional welders	315	0.96 (0.85-1.08)		
		Kidney	Blue-collar weld	lers		Age, region	
		·	Non-welders (ref.)	NR	1		
			Welders	60	1.34 (1.04-1.73)		
			Occasional welders	315	0.99 (0.87–1.12)		
		Nasal cavity and	All welders			Age, region,	
		sinuses	Non-welders (ref)	NR	1	education	
			Welders	NR	0 (0-0)		
			Occasional welders	25	1.25 (0.82–1.92)		
		Nasal cavity and	Blue-collar weld	lers		Age, region	
		sinuses	Non-welders (ref.)	NR	1	- 0	
			Welders	NR	0 (0-0)		
			Occasional welders	25	1.15 (0.73–1.82)		

Table 2.1 (continued)

Reference, location, enrolment period/follow-up	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
MacLeod et al.		Eye: melanoma	All welders			Age, region,	
(2017) (cont.)			Non-welders (ref.)	NR	1	education	
			Welders	5	1.55 (0.64-3.76)		
			Occasional welders	20	0.89 (0.57–1.38)		
		Eye: melanoma	Blue-collar weld	lers		Age, region	
			Non-welders (ref.)	NR	1		
			Welders	5	1.66 (0.68-4.09)		
			Occasional welders	20	0.91 (0.56–1.47)		
		Brain	All welders			Age, region,	
			Non-welders (ref.)	NR	1	education	
			Welders	35	1.16 (0.83-1.63)		
			Occasional welders	190	1.08 (0.93-1.26)		
		Brain	Blue-collar weld	lers		Age, region	
			Non-welders (ref.)	NR	1		
			Welders	35	1.17 (0.83-1.65)		
			Occasional welders	190	1.09 (0.93-1.27)		

Table 2.1 (continued)

Reference, location, enrolment period/follow-up	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Wong et al. (2017) USA Enrolment 2002– 2004/follow-up 2002–2009	53 224; 2311 ever welders; current and former heavy smokers (> 30 pack-years, quit within past 15 yr if former smoker) enrolled in the National Lung	Lung	All workers Never welded/ never foundry (ref.) Ever welder, never foundry	1824	1 1.12 (0.91–1.37)	BMI, age, sex, race, smoking, family history, study,	Cohort analysis and follow-up of subjects enrolled in a randomized control trial (findings for both arms combined) Strengths: sensitivity
	Screening Trial (NLST)	Lung: incidence (all subtypes)	Duration ever wo	rked as a we	lder (yr)	screening	statistical analyses; information on lung cancer subtypes; large number of cases; information on previous exposure to asbestos Limitations: limited exposure information on
	with occupational history information; subjects from 33 centres, randomized into two arms (CT, chest		None (ref.)	1824	1		
			$\geq 1$ to $< 3$	12	0.80 (0.50-1.25)		
			$\geq 3 \text{ to} < 10$	29	1.43 (1.04-1.96)		
	X-ray)		≥ 10 to < 25	27	1.24 (0.89-1.73)		
	Exposure assessment		≥ 25	30	1.20 (0.87–1.67)		
	method: questionnaire; job title, work duration,		Trend test P valu	e, 0.039 (ord	inal)		welding and co-exposures
	and PPE; ever worked as	Lung (SCC):	Duration ever wo	orked as a we	lder (yr)		during welding such as asbestos; short follow-up;
	welders and/or founder	incidence	None (ref)	1824	1		
	defined as held welding	(all subtypes)	$\geq 1 \text{ to } < 3$	3	1.4 (0.69-2.84)		not able to assess risk in
	job for ≥ 1 yr; information		$\geq 3 \text{ to} < 10$	13	1.74 (0.97-3.11)		nonsmokers
	on demographics, medical		$\geq 10 \text{ to} < 25$	4	1.41 (0.75–2.66)		
	history, and smoking also ascertained on		≥ 25	11	1.91 (1.13-3.22)		
	questionnaire		Trend test P valu	e, 0.003 (ord	inal)		
	1	Lung	Duration ever wo	rked as a we	lder (yr)		
		(adenocarcinoma)	None (ref)	593	1		
			≥ 1 to < 3	5	0.97 (0.46-2.05)		
			≥ 3 to < 10	5	1.07 (0.55-2.08)		
			≥ 10 to < 25	8	0.93 (0.46-1.87)		
			≥ 25	10	1.39 (0.80-2.43)		
			Trend test P valu	e, 0.418 (ord	inal)		

AML, acute myeloid leukaemia; B[a]P, benzo[a]pyrene; BMI, body mass index; CCR, Canadian Cancer Registry; CI, confidence interval; CLL, chronic lymphocytic leukaemia; Cr, chromium; CT, computerized tomography; EPIC, European Prospective Investigation into Cancer and Nutrition; FINJEM, Finnish job-exposure matrix; HL, Hodgkin lymphoma; ICD, International Classification of Diseases; JEM, job-exposure matrix; MM, multiple myeloma; NEC, not elsewhere classified; NHL, non-Hodgkin lymphoma; Ni, nickel; NR, not reported; PAH, polycyclic aromatic hydrocarbon; Pb, lead; PPE, personal protective equipment; SCC, squamous cell carcinoma; SES, socioeconomic status; SiO<sub>2</sub>, silicon dioxide; SIR, standardized incidence ratio; SS, stainless steel; TCC, transitional cell carcinoma; UUT, upper urinary tract; WHO, World Health Organization; yr, year(s)

Table 2.2 Case-control studies on ocular melanoma and welding or exposure to welding fumes

Reference, location, enrolment/follow- up period	Population size, description, exposure assessment method	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Tucker et al. (1986) USA 1974–1979	Cases: 497; participation rate, 89% Controls: 501 patients with detached retina not due to tumours matched by race, age, sex, race, date of diagnosis; participation rate, 85% Exposure assessment method: telephone interview with detailed information about medical history, family history, employment, and exposure to environmental agents and sunlight; details from ophthalmologic examination and medical history from records; interview with next-of-kin for 17% of cases and 14% of controls, half of them with spouses	Ever vs never worked as welder	4	10.9 (2.1–56.5)	Age, eye colour, history of cataract	Strengths: large number of cases and controls; high participation rate in both cases and controls Limitations: few exposed cases; no dose–response calculations; no information on other UV exposures

Reference, location, enrolment/follow- up period	Population size, description, exposure assessment method	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Seddon et al. (1990) Massachusetts, USA 1984–1987	Cases: 197 [Series 1 population-based] white patients aged 17–88 yr with clinically or histologically confirmed melanoma of the choroid, ciliary body, or both, identified at local hospital or by mailing to ophthalmologists; diagnosed within previous year Controls: 385 [Series 1 population-based] selected by random digit dialling, matched 2:1 by sex, age, city of residence Exposure assessment method: telephone interview including constitutional factors, ocular, and medical histories, and exposure to environmental factors including natural and artificial sources of UV	Arc welder vs never we Series 1 Series 2	elder 18 38	1.3 (0.5–3.1) 0.9 (0.6–1.5)	Age, sex, eye and skin colour, ancestry, use of sun lamps, eye protection, outside work, florescent lighting, southern residence, years of intense exposure, moles	Series 1: results also reported by Ajani et al. (1992), using the same numbers but with fewer covariates in the logistic regression model Series 2: not population-based, 337 cases and 800 sibling controls 140 of the cases were included in both series Strengths: high participation rates in both cases and controls; some information of exposures to UV radiation Limitations: no dose–response assessment
Siemiatycki (1991) Montreal, Canada 1984–1987	Cases: 16 histologically confirmed incident male cases of uveal melanoma, aged 35–70 yr Controls: 3058; 2525 cancer controls + 533 population controls Exposure assessment method: personal interview and collection of detailed occupational history	Exposed vs not exposed to arc welding fumes	4	8.3 (2.5–27.1)	Age, family income, cigarette index	Total number of eye melanoma cases: 16 (Siemiatycki (1991), table 1); analysis was restricted to French-Canadians and cancer controls used Limitations: no dose-respons assessment; no adjustments for UV radiation and sun exposure

Table 2.2 (continued)

Reference, location, enrolment/follow- up period	Population size, description, exposure assessment method	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Lutz et al. (2005) Denmark, France, Germany, Italy, Latvia, Portugal, Spain, Sweden, and UK 1995–1996	Cases: 292 incident cases of uveal melanoma, identified from ophthalmologic departments, hospital records, or cancer registries, aged 35–69 yr Controls: 2062 population controls selected from population registers, electoral rolls, or practitioner; frequency-matched by region, sex, and 5-yr birth cohorts; 1094 cancer controls randomly selected from colon cancer patients Exposure assessment method: questionnaire with face-to-face or telephone interview	Worked as a welder or s Men Women Men and women	15 1 16	2.18 (1.18–4.04) 0.75 (0.09–6.33) 1.95 (1.08–3.52)	Country, 5-yr age group	Data from France reported in the analysis of Guénel et al. (2001); analysis by occupation used only population controls Strengths: relatively large study size Limitations: only modest participation rate in controls; no assessment of doseresponse association; no information on UV radiation or sun exposure; use of colon cancer patients may be problematic (perhaps at higher risk of this cancer due to lack of sun exposure)
Guénel et al. (2001) France: 10 administrative areas (départements) 1995–1996	Cases: 50; 29 men, 21 women; patients with uveal melanoma Controls: 479; 321 men, 158 women selected at random from electoral polls after stratification for age, sex, and area Exposure assessment method: questionnaire; estimates of occupational exposure to solar and artificial UV light were made using a JEM	Ever vs never welder or Worked for $\geq 6$ mo $\leq 20$ yr > 20 yr Trend test $P$ value, 0.00	7 4 3	worker 7.3 (2.6–20.1) 5.7 (1.6–19.8) 11.5 (2.4–55.5)	Age	Strengths: high participation rate in cases (100%) and modest in controls (76%) Limitations: relatively small study; no adjustments for UV radiation or sun exposure
Monárrez-Espino et al. (2002) Germany 1995–1998	Cases: 118 incident cases of uveal melanoma Controls: 475 controls matched by age, sex, and region of residence Exposure assessment method: telephone interviews, exposure status classified based on job history	Welding, brazing, soldering Ever welder	13 <6	0.90 (0.43–1.76) 1.3 (0.6–2.5)	Age, region	Overlaps with <u>Lutz et al.</u> (2005)

Table 2.2 (continued)

Reference, location, enrolment/follow- up period	Population size, description, exposure assessment method	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled	Comments	
Vajdic et al. (2004) Australia 1996–1998	Cases: 246 white Australian residents, aged 18–79 yr, with histopathologically or clinically diagnosed melanoma	esidents, aged 18–79 yr, vs never birth, eye colour, with histopathologically or $Duration(yr)$ ability to tan,					
		0.1-4.0	15	0.8 (0.4-1.4)	squinting as a child,	exposure, use of personal	
	originating in the choroid, ciliary body	4.1-22	23	1.2 (0.7-2.2)	total personal sun exposure at age 10,	protective equipment, eye burns during welding; dose-	
	Controls: 893 controls matched	> 22	35	1.7 (1.0-2.7)	20, 30, and 40 yr	response assessment for welding Limitations: relatively low participation rate in controls	
	3:1 by age, sex, and residence,	Trend test P value, 0.07			20,00, 4114 10 /1		
	selected from electoral rolls Exposure assessment method: self-administered questionnaire and telephone interview regarding sun exposure, sun-protective wear, and quantitative exposure to	Lifetime exposure (h)					
		0.1-52.0	20	1.1 (0.6–1.9)			
		52.1-858.0	30	1.4 (0.8–2.3)			
		> 858	23	1.1 (0.6–1.9)			
		Trend test <i>P</i> value, 0.69		,			
		Usual exposure (h/d)					
	welding equipment and	0.05-0.50	27	1.3 (0.8-2.1)			
	sunlamps	0.51-2.00	30	1.3 (0.8–2.1)			
		> 2.00	16	1.0 (0.5–1.9)			
		Trend test <i>P</i> value, 0.74  Age at first use (yr)	10	1.0 (0.3–1.9)			
		> 20	41	1.2 (0.8-1.9)			
		≤ 20	32	1.2 (0.7–2.0)			
		Trend test <i>P</i> value, 0.59		(0.7 2.0)			
		Type of welding					
		Arc and oxy	46	1.6 (1.0-2.4)			
		Arc only	21	0.9 (0.5–1.6)			
		Oxy only	5	1.3 (0.5–3.7)			
		Electric/spot only	0	0 (0-2.1)			
		Frequency of goggle or mask use during welding	Ü	0 (0-2.1)			
		Always/almost always	67	1			
		Half of the time or less	6	1.7 (0.5–5.4)			

Table 2.2 (continued)

Reference, location, enrolment/follow- up period	Population size, description, exposure assessment method	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Vajdic et al. (2004) (cont.)		Number of eye burns during welding				
		None	44	1		
		1–2	9	0.4 (0.2-0.9)		
		3-5	6	0.6 (0.2-1.6)		
		> 5	14	1.6 (0.7-3.6)		
		Trend test P value, 0.78				
Holly et al. (1996)	Cases: 221 male white patients	Ever vs never welder	40	1.9 (1.2-3.0)	None	Strengths: high participation
USA 1978–1987	with histologically confirmed uveal melanoma, aged 20-74 yr, residing in 11 states Controls: 447 controls selected	Ever vs never welder	40	2.2 (1.3–3.5)	Age, naevi, eye colour, tanning or burning, sun exposure	rate in cases and controls Limitations: no direct assessment of UV radiation or sun exposure
	by random digit dialling	Duration (yr)			Age	
	matched 2:1 by age (5-yr age	0 (ref.)	181	1	· ·	
	group) and residential area Exposure assessment method:	≤ 1	6	2.2 (0.7-70)		
	interviewer-administered	2-10	15	1.80 (0.88-3.60)		
	questionnaire with demographic and phenotypic characteristics, occupational history, exposure to chemicals	≥ 11	19	1.9 (1.0-3.6)		

CI, confidence interval; JEM, job-exposure matrix; mo, month; NR, not reported; UV, ultraviolet; vs, versus; yr, year

In a case–control study of ocular melanoma in the USA, <u>Tucker et al. (1986)</u> reported an odds ratio of 10.9 (95% CI, 2.1–56.5) based on 4 cases who ever worked as a welder.

Seddon et al. (1990) conducted a case-control study of ocular melanoma in the USA which included two series of cases with partial overlap; either population or sibling controls were used for the analyses. The magnitude of the odds ratios reported for the association between arc welding and ocular melanoma were weaker than in other studies (described below) and, further, differed in the two series. There was overlap in the reported confidence intervals. One report from Ajani et al. (1992) includes results based on one of the two series of cases and controls already reported by <u>Seddon et al. (1990)</u>. [The Working Group noted that this study was limited by the lack of a clear description of the overlap between the two case series.]

A small case-control study of ocular melanoma based in Montreal, Canada, reported an odds ratio (OR) of 8.3 (95% CI, 2.5–27.1; 4 exposed cases), based on an expert assessment of any exposure to arc welding fumes (Siemiatycki, 1991).

Lutz et al. (2005) conducted a multicentre case-control study of rare cancers in nine European countries, which included results for ocular melanoma based on dichotomous variables for men who had worked for 6 months or more as welders/sheet metalworkers. The French and German components of this study were published separately (Guénel et al., 2001; Monárrez-Espino et al., 2002). The French component of this study (Guénel et al., 2001) further presented results by duration of employment as a welder: 20 years or more employment (OR, 5.7; 95% CI, 1.6-19.8); and less than 20 years (OR, 11.5; 95% CI, 2.4–55.5) (*P* for trend, 0.0008). They also report an elevated odds ratio for more than five eye burns not specifically due to welding, but the association disappeared when welding was excluded. There was also a

significant exposure–response relationship (*P* for trend, 0.003) for cumulative occupational exposure to artificial UV radiation, which included welding as well as other occupations. Arc welding was assigned the highest intensity level for artificial UV radiation from occupation. Another study including a subset of the German participants reported in the <u>Lutz et al. (2005)</u> paper showed an odds ratio of 1.3 (95% CI, 0.6–2.5; < 6 exposed cases) for ever welders (<u>Monárrez-Espino et al., 2002</u>).

Three studies provided information on the association between duration (years) of welding and risk of ocular melanoma (Holly et al., 1996; Guénel et al., 2001; Vajdic et al., 2004), two of which reported a tendency for increasing risk of ocular melanoma with increasing years of welding exposure (Guénel et al., 2001; Vajdic et al., 2004).

A population-based study from Australia, additionally adjusting for eye colour and sun exposure, observed odds ratios of 0.8 (95% CI, 0.4–1.4), 1.2 (95% CI, 0.7–2.2), and 1.7 (95% CI, 1.0–2.7) respectively, for 0.1–4.0, 4.1-22.0, and more than 22 years of welding performed by the worker. No tendencies for increasing risk by increasing welding hours per day or lifetime welding hours were observed. A subgroup with over five eye burns during welding had an odds ratio of 1.6 (95% CI, 0.7–3.6) compared with welders without eye burns. Compared with wearing goggles always or almost always, wearing goggles or a mask only half the time or less during welding resulted in an odds ratio of 1.7 (95% CI, 0.5-5.4) for 6 exposed cases (Vajdic et al., 2004).

A study from the USA of white men showed an overall increased risk of ocular melanoma for ever versus never welders/welding based on 40 exposed cases, but no trend concerning age-adjusted years of exposure was observed (Holly et al., 1996). [The Working Group noted that only some studies are adjusted for indicators of UV radiation from sunlight (Seddon et al.,

1990; Holly et al., 1996; Vajdic et al., 2004), which is the main risk factor for ocular melanoma and thereby a potential confounder; however, there was no evidence that confounding by sunlight explained the results.]

A meta-analysis based on several of the above-mentioned case–control studies (Tucker et al., 1985; Seddon et al., 1990; Ajani et al., 1992; Holly et al., 1996; Guénel et al., 2001; Vajdic et al., 2004), including 1137 cases in total, estimated an overall summary odds ratio of 2.05 (95% CI, 1.20–3.51) (Shah et al., 2005). [The Working Group noted that the meta-analyses included the overlapping cases (n = 197) reported by Seddon et al. (1990) and Ajani et al. (1992); this attenuates the overall association because these two studies have odds ratios of 1.3 and 1.0, respectively, which are weaker than the overall pooled result and are counted twice.]

## 2.3 Mesothelioma

Several studies reported on the association between welding and mesothelioma. These studies are an indicator of exposure to asbestos.

#### 2.3.1 Case-control studies

The association between welding and mesothelioma was investigated in a French population-based case-control study including 371 male cases and 732 male population controls (Rolland et al., 2010). A lifelong occupational history of all occupations with a duration of at least 6 months was obtained in face-to-face interviews; each job period was coded by industrial hygienists who were blinded for case-control status according to standard classifications of occupations and industries. In an ever versus never comparison, the odds ratio for the occupational group welders and flame-cutters was 4.64 (95% CI, 2.04-10.56) based on 19 exposed cases. Thirteen of these were employed in shipbuilding and repair, manufacture of structural metal products, or manufacture of fabricated metal products. [The Working Group noted that the observed risk was probably due to asbestos exposure, as all occupations that appeared to be associated with elevated odds ratios in this study are known to entail asbestos exposure (e.g. manufacture of asbestos products, pipe fitters, and sheet metal and shipyard workers). This is a particular set of welders exposed to high concentrations of asbestos, so the results should not be generalized to the exposure of all welders.]

### 2.3.2 Cohort studies

Cohort studies investigated mortality or the incidence of cancer in welders and reported risk estimates for mesothelioma or cancer of the pleura. A population-based cohort study pooling data from four Nordic countries observed a standardized incidence ratio (SIR) of 1.79 (95% CI, 1.44-2.20) for cancer of the pleura in male welders based on 91 cases (Pukkala et al., 2009). Another population-based cohort study in Canada observed 15 cases in welders, which corresponded to an adjusted hazard ratio (HR) of 1.54 (95% CI, 0.86-2.78) (MacLeod et al., 2017). In this study, the risk of mesothelioma among welders in construction was 2.5 times greater compared with non-welders. A cancer mortality study among arc welders exposed to fumes containing chromium and nickel resulted in a standardized mortality ratio (SMR) of 11.80 (95% CI, 4.73-24.31) based on 7 cases (Becker, 1999). A historical cohort study of mortality among shipyard workers in Genova, Italy, reported a statistically significant standardized mortality ratio (3.77) of cancer of the pleura in arc welders based on 3 cases, and a non-significant standardized mortality ratio (1.69) in gas welders based on a single case (Puntoni et al., 2001; see Table 2.3). [The Working Group noted that the observed risks of mesothelioma or cancer of the pleura among welders in these cohort studies is probably due to asbestos exposure.

## 2.4 Cohort studies

The increased risks of cancer associated with exposure to welding fumes have been studied in industrial (Section 2.4.1) and population-based cohorts (Section 2.4.2). Both types of study have reported cancer mortality or incidence for either exposure to welding fumes or occupation as a welder. Studies of cumulative exposure to welding fumes typically had more detailed exposure information at the individual level compared with studies of occupation as a welder, and were therefore considered to be more informative (from an exposure assessment point of view).

Almost all studies reported on mortality or incidence of cancer of the lung for welders or exposure to welding fumes. Due to the high rates of mortality/low rates of survival from cancer of the lung, mortality studies probably capture most of the cancer of the lung cases; however, it should be noted that diagnosis based on death certificate may not be as accurate as incidence data. When studying the association between welding and cancer of the lung, the major potential confounders are tobacco smoking and exposure to asbestos (especially in shipyards). In the absence of data on asbestos exposure, mesothelioma occurrence can be used as a crude indicator. SS welders are exposed to higher concentrations of the established lung carcinogens hexavalent chromium (Cr(VI)) and nickel compounds compared with MS welders.

Risk estimates for other cancer sites of interest including larynx, sinus/nasal cavity, brain, urinary bladder, kidney and lymphohaematopoietic system are reported in <u>Table 2.1</u> and <u>Table 2.3</u>.

#### 2.4.1 Industrial cohorts

See Table 2.3

Many of the industrial cohort studies of welders reported only on cancer of the lung; the reasons for not reporting on other cancers include the small population numbers or the limited power of the study groups to evaluate other common cancers. Almost all of the studies reported cancer risks for occupation as a welder, and a few studies reported risks for cumulative exposure to welding fumes. Two studies from the same population reported findings only for exposure to welding fumes (Yiin et al., 2005, 2007), and two studies (of overlapping populations) reported findings for occupation as a welder in addition to exposure to welding fumes (Simonato et al., 1991; Sørensen et al., 2007). Related studies are grouped and discussed together, and the description of cohort studies is divided into: (a) the IARC multicentre cohort and studies of contributing national subcohorts; (b) cohort studies of welders at shipyards; (c) cohort studies of welders in other industries; (d) studies considered to be less informative, due to low specificity for exposure to welding fumes or inadequate reference population; and (e) studies reporting on other cancer sites but not the lung.

## (a) The IARC multicentre cohort study

See Table 2.3 and Table 2.4

A large multicentre cohort study of welders was coordinated by the International Agency for Research on Cancer (Simonato et al., 1991). Several national subcohorts were updated after the IARC study, and these analyses (Moulin et al., 1993; Milatou-Smith et al., 1997; Becker, 1999; Sørensen et al., 2007) are also reviewed (see <u>Table 2.4</u>). An analysis of the Finnish subcohort (Tola et al., 1988) was published before the IARC study, but is not reviewed separately because the IARC study captures all the relevant findings from this population. In addition, the Working Group suspected that two studies of Italian shipyard welders may overlap with the IARC Italian subcohort, although this was not explicitly stated in the publications. These studies are discussed in the shipyard section (Section 2.4.1(b)(ii)) since there was no clear documentation about the overlap.

#### (i) IARC cohort

The IARC multicentre cohort study comprised 11 092 welders employed in 135 companies in eight European countries (Denmark, England, Finland, France, Germany, Italy, Norway, Scotland, and Sweden) (Simonato et al., 1991). The cohort included welders from different types of industries, welding different types of metals, and using different welding processes. A specific matrix for welding fumes was developed, relating 13 combinations of welding process and metals welded to average exposure levels for total welding fumes, total chromium, hexavalent chromium, and nickel (Gérin et al., 1993). Welders were assigned to three mutually exclusive groups according to type of welding: shipyards welders, only MS welders, or ever SS welders. [The Working Group noted that type of welding was based on information collected at baseline. The number of workers in each group was not reported.] The latter category included a group of predominantly SS welders that was also considered separately. National reference rates were used to compute standardized mortality and incidence ratios. Mortality analysis of the total cohort (Simonato et al., 1991) showed elevated SMRs for cancers of the lung (SMR, 1.34; 95% CI, 1.1-1.6), larynx (SMR, 1.48; 95% CI, 0.59-3.04), bladder (SMR, 1.91; 95% CI, 1.07-3.15), and kidney (SMR, 1.39; 95% CI, 0.72-2.43), and for lymphosarcoma (SMR, 1.71; 95% CI, 0.63–3.71) [lymphosarcoma is now referred to as non-Hodgkin lymphoma or NHL]. No clear increase in standardized mortality ratios with time since first employment was found for any of these cancer sites.

The standardized mortality ratios for cancer of the lung were elevated by type of welding: 1.26 (95% CI, 0.88–1.74) for shipyard welders, 1.78 (95% CI, 1.27–2.43) for MS welders, 1.28 (95% CI, 0.91–1.75) for ever SS welders, and 1.23 (95% CI, 0.75–1.90) for predominantly SS welders. Analyses of mortality from cancer of the lung

were conducted by duration of employment and time since first exposure (employment as a welder) in the four subgroups. A positive relationship was observed with time since first exposure for MS and SS welders, which was more evident for predominantly SS welders, but there was no clear positive trend with duration of employment. No association between mortality from cancer of the lung and cumulative exposure to total welding fumes was reported, but data were not shown (Simonato et al., 1991). An analysis restricted to the two groups of ever SS welders and predominantly SS welders (potentially exposed to more Cr(VI) and Ni over time), with at least 5 years of employment and 20 years since first exposure, also failed to demonstrate a dose-response relationship.

The results for incidence of cancer at several other sites (buccal cavity and pharynx, oesophagus, stomach, intestine, rectum, larynx, prostate, bladder, leukaemia, and other lymphatic neoplasms) were available for the Nordic subcohorts (68% of the total cohort); elevated standardized incidence ratios were reported for cancers of the lung (SIR, 1.37; 95% CI, 1.11–1.68), prostate (SIR,1.46; 95% CI, 1.02–2.02), bladder (SIR,1.21; 95% CI, 0.76–1.84), and buccal cavity and pharynx (SIR, 1.60; 95% CI, 0.95–2.53), and for leukaemia (SIR, 1.26; 95% CI, 0.63–2.25).

Smoking habits were available for the Finnish and Norwegian components of the cohort and were similar to that of the general population. [The Working Group noted that this suggests that smoking alone is unlikely to explain the excess cases of cancer of the lung. The finding of five deaths from mesothelioma indicates that the study population experienced exposure to asbestos. The five cases were distributed across all subgroups (one shipyard welder, two MS welders, and two SS welders) and across all categories of duration and time since first employment.]

[The Working Group noted that the strengths of the study included the large number of welders and the grouping of welders by welded material

Reference, location, enrolment period/ follow-up, study design	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments		
Simonato et al.	11 092 welders	Lung	Incidence			Age, calendar	Type of welding:		
<u>(1991)</u>	(164 077 person-yr);		Welders	92	1.37 (1.11–1.68)	period	shipyards, MS		
Europe, multicentre	workers employed as	Lung	Years since firs	t exposure			only, ever SS,		
Denmark, England, Finland,	shipyard, MS, or SS welders by 135 companies; different		0-9	14	1.65 (0.90-2.77)		predominantly SS SIR data are only		
France, Germany,	inclusion criteria for each		10-19	27	1.22 (0.81-1.78)		from cohort subjects of Denmark, Finland		
taly, Norway,	y, Norway, national cohort tland, Sweden) Exposure assessment olment and method: expert judgement; ow-up different welding process exposure		20-29	41	1.42 (1.02-1.93)				
Scotland, Sweden)			≥ 30	34	1.24 (0.86-1.73)		Norway, and Swede		
Enrolment and			Total	116	1.34 (1.10-1.60)				
ollow-up different between countries		Lung	Years since firs	t exposure: ship	yard welders				
Cohort	matrix developed to estimate exposure levels	stimate exposure levels	0-9	5	5.08 (1.65-11.85)				
	for total welding fumes,		10-19	6	1.41 (0.52-3.06)				
	total Cr, Cr(VI), and Ni		20-29	17	1.61 (0.94-2.57)				
	(described in <u>Gérin et al.</u>		≥ 30	8	0.63 (0.27-1.23)				
	<u>(1993)</u> )		Total	36	1.26 (0.88-1.74)				
		Lung	Years since first exposure: MS welders						
			0-9	4	1.35 (0.37-3.45)				
			10-19	11	1.62 (0.81-2.90)				
			20-29	11	1.86 (0.93-3.33)				
			≥ 30	14	2.07 (1.13-3.48)				
			Total	40	1.78 (1.27-2.43)				
		Lung	Years since firs	t exposure: SS e	ever welders				
			0-9	5	1.04 (0.34-2.43)				
			10-19	12	1.07 (0.55-1.86)				
			20-29	13	1.32 (0.70-2.26)				
			≥ 30	9	1.94 (0.89-3.69)				
			Total	39	1.28 (0.91-1.75)				

Table 2.3 (continued)

Reference, location, enrolment period/ follow-up, study design	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled	Comments				
Simonato et al. (1991)		Lung	Years since first welders	Years since first exposure: predominantly SS welders							
(cont.)			0-9	2	0.64 (0.08-2.32)						
			10-19	5	0.88 (0.29-2.06)						
			20-29	7	1.26 (0.51-2.60)						
			≥ 30	6	3.12 (1.15-6.79)						
			Total	20	1.23 (0.75-1.90)						
		Lung	Cumulative exp SS welders	oosure (mg/m³-	-yr): predominantly						
			Cr(VI) < 0.5	3	1.91 (0.39-5.58)						
			$Cr(VI) \ge 0.5$	9	1.67 (0.77-3.18)						
			Ni < 0.5	8	2.34 (1.01-4.61)						
			$Ni \ge 0.5$	4	1.13 (0.31-2.90)						
		Lung	Cumulative exposure (mg/m³-yr): SS ever welders								
			Cr(VI)< 0.5	7	1.23 (0.50-2.54)						
			$Cr(VI) \ge 0.5$	14	1.70 (0.93-2.86)						
			Ni < 0.5	17	1.66 (0.97-2.66)						
			$Ni \ge 0.5$	4	1.09 (0.30-2.79)						
		Urinary	Incidence								
		bladder	Welders	22	1.21 (0.76-1.84)						
		Urinary	Years since first	exposure							
		bladder	0-9	2	2.19 (0.27-7.92)						
			10-19	3	1.36 (0.28-3.97)						
			20-29	4	1.66 (0.45-4.24)						
			≥ 30	6	2.59 (0.95-5.64)						
			Total	15	1.91 (1.07–3.15)						

Reference, ocation, enrolment period/ ollow-up, study lesign	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
imonato et al. 1991)		Larynx: ICD-8 (code 161)	Welders	7	1.48 (0.59–3.04)		
cont.)		Larynx	Years since first	t exposure			
		·	0-9	0	0 (0-6.83)		
			10-19	3	2.09 (0.43-6.12)		
			20-29	4	2.41 (0.66-6.17)		
			≥ 30	0	0 (0-3.32)		
		Oral/	Total Incidence	7	1.48 (0.59–3.04)		
		pharyngeal combined	Welders	18	1.60 (0.95–2.53)		
		Nasal cavity and sinuses	Welders	0	0 (0-4.44)		
		Prostate	Incidence				
			Welders	36	1.46 (1.02-2.02)		
		Prostate	Welders	10	0.77 (0.37-1.42)		
		Kidney	Welders	12	1.39 (0.72-2.43)		
		Kidney	Years since first	t exposure			
		,	0-9	1	0.97 (0.02-5.43)		
			10-19	1	0.43 (0.01-2.41)		
			20-29	7	2.44 (0.98-5.03)		
			≥ 30	3	1.24 (0.26-3.63)		
			Total	12	1.39 (0.72-2.43)		
		NHL: ICD-8	Welders	6	1.71 (0.63-3.71)		
		(code 200)	Years since first	t exposure			
			0-9	1	1.54 (0.04-8.56)		
			10-19	1	1.06 (0.03-5.91)		
			20-29	1	0.94 (0.02-5.24)		
			≥ 30	3	3.53 (0.73-10.33)		
			Total	6	1.71 (0.63-3.71)		
		HL: ICD-8 (code 201)	Welders	2	0.60 (0.07–2.18)		

# Table 2.3 (continued)

Reference, location, enrolment period/ follow-up, study design	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Simonato et al. (1991) (cont.)		Leukaemia: ICD-8 (code 204–207)	Welders	6	0.63 (0.23–1.38)		
		Leukaemia: ICD-7 (code 204)	Incidence Welders	11	1.26 (0.63-2.25)		
		Lymphatic neoplasms ICD-8 (code 202–203)	Welders	7	1.14 (0.46–2.36)		
		Other lymphatic ICD-7 (code 200–203 205)	Welders	15	1.12 (0.63–1.85)		

Reference, location, enrolment period/ follow-up, study design	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Moulin et al. (1993) France Enrolment 1975–	2721 welders, 6683 controls; all male workers employed as welders at the beginning	Lung	Welders vs controls (internal ref.)	NR	1.29	Age	Partial overlap with the IARC study, Simonato et al. (1991)
1976/follow-up 1975–1976 to 1987–	of the follow-up in 13 factories; internal	Lung	Welders	19	1.24 (0.75–1.94)	Age, calendar time, sex	No death from pleural cancer among
1988 (depending on	comparison group:	Lung	Welders: time sin	ce first emplo	oyment (yr)		welders; 3 deaths
the factory) Cohort	6684 manual workers (excluding boilermakers,		< 10	1	[0.75 (0.03-3.70)]		from pleural cancer among controls, 1.25
Colloit	foundry workers, painters,		10-19	3	[0.90 (0.23-2.45)]		expected (SMR, 2.40 95% CI, 0.49–7.01)
	or cutters) randomly		≥ 20	15	[1.41 (0.82–2.27)]		
	selected among non-welders in the same factories; restricted to workers employed for at least 1 yr Exposure assessment	Lung	Welders: duration	of employm		Strengths: internal	
			< 10	1	[1.19 (0.06-5.86)]		comparison group; smoking habits available for 87% of the cohort
			10-19	2	[0.63 (0.10-2.08)]		
			≥ 20	16	[1.41 (0.83–2.24)]		
	method: records of welding processes, types of metal, and percentage of working time available at the individual level in eight factories and at the workshop level in five factories; smoking habits from medical records (recorded by the occupational physician	Lung	Duration of expo	Limitations: no data			
			Total welders	19	1.24 (0.75–1.94)		on asbestos exposur
			Shipyard welders	3	0.91 (0.19–2.67)		
			MS welders only	9	1.59 (0.73-3.02)		
			Ever SS welders	3	0.92 (0.19-2.69)		
			Predominantly Cr(VI) <sup>a</sup>	2	1.03 (0.12–3.71)		
		Larynx	Welders	3	0.67 (0.14-1.97)		
		Pleura	Welders	0	0 (0-8.82)		
	once a year); information	Brain	Welders	0	0 (0-2.75)		
	on asbestos available on factory level only so not relevant for the statistical analysis (it only accounted by separating shipyard from	Leukaemia: ICD-8 (code 204–208)	Welders	2	1.13 (0.14-4.10)		
		HL: ICD-8 (code 200–203)	Welders	2	1.02 (0.12–3.68)		
	non-shipyard welders)	Urinary bladder	Welders	1	0.65 (0.02–3.64)		
		Prostate	Welders	0	0 (0-2.09)		

Table 2.3 (continued)

Reference, location, enrolment period/ follow-up, study design	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Milatou-Smith et al. (1997) Sweden Enrolment 1950–1965/follow- up 1955–1992 Cohort	233 welders (high exposure cohort); 208 welders (low exposure cohort); two cohorts of welders, employed for at least 5 yr during 1950–1965: one of SS welders exposed to high levels of Cr(VI), and one of railway track welders exposed to low levels of Cr(VI) Exposure assessment method: records of information on average levels of exposure to Cr from Swedish measurements in 1975 (SS welders 110 μg/m³, railway track welders 10 μg/m³); no or minimal asbestos exposure (company statements)	Lung Lung	Exposed to high levels of Cr: SS welders Welders Exposed to low levels of Cr: MS welders Welders Exposed to high welders	6 2 vs low levels o NR	1.64 (0.60-3.58)  0.41 (0.05-1.48) f Cr 3.98 (0.84-18.80)	Age, sex, cause, calendar year	Partial overlap with the IARC study, Simonato et al. (1991) Strengths: probably very low asbestos exposure; comparison between the two groups of welders unlikely to be affected by confounding due to smoking Limitations: small cohorts; no information on individual exposure levels; no actual measurements of asbestos exposure; no data on smoking

Reference, location, enrolment period/ follow-up, study design	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Becker (1999)	1213 SS welders, 1688	Lung [includes	Mortality	,		Calendar	Partial overlap
Germany Enrolment	turners (internal reference group); arc welders exposed	bronchus and trachea]	Welders	28	1.21 (0.80–1.75)	period	with the IARC study, <u>Simonato</u>
1950–1970/follow-	to Cr and Ni and turners	Pleura	Welders	7	11.80 (4.73-24.30)		et al. (1991); strong
up 1950–1995 Cohort	employed for at least 6 mo during 1950–1970 at	Urinary bladder	Welders	5	2.08 (0.67–4.84)		excess of deaths from mesothelioma; confounding by asbestos likely to explain the lung cancer excess Strengths: internal comparison group; analyses by subgroups Limitations: no data on asbestos exposure
	25 factories of the metal- processing industry Exposure assessment	Other lymphatic and haematopoietic	Welders	0	-		
	method: exposure duration from companies records; assessment of welding exposure characteristics (welding procedure, percentage of working time) and smoking habits at the individual level by interview of the foremen and superiors; average	MM	Welders	1	1.23 (0.03-6.86)		
		Leukaemia (lymphoid): ICD-9 (code 204)	Welders	1	1.52 (0.04–8.51)		
		Leukaemia (myeloid): ICD-9 (code 205)	Welders	0	-		
			Internal analysis				
	duration of exposure of the	Lung	Welders	28	1.30 (0.80-2.12)	Age, calendar	
	welders was 18.3 yr	Lymphatic and haematopoietic	Welders	2	0.38 (0.08–1.75)	period	
		Lung	Duration of exposure (yr)			Calendar	
			0 to < 10	6	0.99 (0.36-2.15)	period	
			10 to < 20	11	1.57 (0.78-2.81)		
			20 to < 30	8	1.18 (0.51-2.34)		
			≥ 30	3	1.10 (0.22-3.23)		
		Lung	Time since first e	xposure (yr)			
			0 to < 10	0	_		
			10 to < 20	2	0.56 (0.06-2.03)		
			20 to < 30	13	1.48 (0.78-2.53)		
			≥ 30	13	1.39 (0.74–2.38)		

Table 2.3 (continued)

Reference, location, enrolment period/ follow-up, study design	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Becker (1999) (cont.)		Lung	Coated electrodes	11	1.21 (0.60-2.17)		
			Coated electrodes or MIG-MAG/WIG	14	1.40 (0.76–2.36)		
			Exclusively MIG-MAG/WIG, for malignant neoplasms	3	0.88 (0.18–2.58)		
		Urinary bladder	Coated electrodes	3	2.80 (0.57–8.19)		
			Coated electrodes or MIG-MAG/WIG	2	2.12 (0.25–7.66)		
			Exclusively MIG-MAG/WIG, for malignant neoplasms	0	-		
		Brain	Coated electrodes	4	6.18 (1.88–15.85)		
			Coated electrodes or MIG-MAG/WIG	0	-		
			Exclusively MIG-MAG/WIG, for malignant neoplasms	0	-		

Reference,	Population size,	Organ site/	Exposure	Exposed	Risk estimate	Covariates	Comments
location, enrolment period/ follow-up, study design	description, exposure assessment method	cancer type	category or level	cases/ deaths	(95% CI)	controlled	Comments
Becker (1999) (cont.)		Lymphatic and haematopoietic	Coated electrodes	1	0.46 (0.01-2.60)		
		ICD-9 (code 200–208)	Coated electrodes or MIG-MAG/WIG	1	0.39 (0.01–2.19)		
			Exclusively MIG-MAG/WIG, for malignant neoplasms	0	-		
			Effective welding	periods per d	lay (%)		
		Lung	≤ 25	15	1.24 (0.69-2.04)		
			> 25	13	1.18 (0.63-2.02)		
		Urinary bladder	≤ 25	2	1.54 (0.18-5.56)		
			> 25	3	2.71 (0.55-7.92)		
		Lymphatic and	≤ 25	0	_		
		haematopoietic	> 25	0	_		
		MM and	≤ 25	0	_		
		immuno- proliferative neoplasm	> 25	1	2.59 (0.06–14.46)		
		Leukaemia	≤ 25	1	2.86 (0.07-15.94)		
		(lymphoid): ICD-9 (code 204)	> 25	0	-		
		Leukaemia	≤ 25	0	_		
		(myeloid): ICD-9 (code 205)	> 25	0	_		
			Mortality				
		Larynx	Welders	1	0.73 (0.02-4.09)		
		Kidney and other urinary	Welders	0	-		

organs

Table 2.3 (continued)

Reference, location, enrolment period/ follow-up, study design	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Becker (1999)		Prostate	Welders	3	0.67 (0.14-1.95)		
(cont.)		Lymphatic and haematopoietic	Welders	2	0.35 (0.04–1.26)		
		HL: ICD-9 (code 201)	Welders	0	-		
		Brain and parts of nervous system	Welders	4	2.02 (0.55–5.19)		
Sørensen et al.	4539 welders; male	Lung	MS (never SS)	43	1	Age, smoking,	Partial overlap with
<u>(2007)</u>	production workers,		SS	32	0.86 (0.52-1.42)	asbestos	the IARC study, Simonato et al. (1991) and Hansen et al. (1996) Strengths: long follow-up; semi- quantitative exposure assessment;
Denmark	employed for at least 1 yr at 74 SS or MS companies	Lung	Ever welding	75	1.35 (1.06-1.70)	Age, calendar time, sex	
Enrolment 1964–1984/follow-			Ever SS	34	1.15 (0.78-1.60)		
up 1968–2003	(shipyards, apprentices, and craftsman excluded),		Ever MMA-SS	25	1.46 (0.95-2.16)		
Cohort	alive at 1 April 1968, born before 1965, who answered the questionnaire in 1986; study population restricted to ever welders who started		Never MMA-SS	9	0.72 (0.35-1.36)		
Conort			Ever MS, never	41	1.59 (1.14-2.16)		
			SS				
		Lung	All welders: duration of welding (yr)			Age, smoking,	adjustment for
		C	0-5	20	1	asbestos	smoking and asbestos
	in 1960 or later		6-15	27	1.47 (0.73-2.92)		exposure
	Exposure assessment		≥ 16	28	1.29 (0.65-2.57)		Limitations: self- reported data on
	matrix (based on > 1000 measurements) for welding	method: welding exposure matrix (based on > 1000 measurements) for welding fume particulates combined with questionnaire data on welding characteristics; questionnaire for asbestos exposure and smoking; next-of-kin questionnaire for the subgroup of					asbestos exposure

Reference, location, enrolment period/ follow-up, study design	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Sørensen et al.		Lung	MS (never SS) v	velder: duratio	n of welding (yr)		
<u>(2007)</u>			0-5	16	1		
(cont.)			6-15	19	1.19 (0.75-3.80)		
			≥ 16	8	0.83 (0.30-2.26)		
		Lung	SS welders: dur	ation of weldin	g (yr)		
			0-5	13	1		
			6-10	1	0.17 (0.02-1.28)		
			≥ 11	18	1.07 (0.50-2.28)		
		Lung	All welders: cur (mg/m³ × yr)	mulative expos	ure estimate		
			0-15	13	1		
			16-60	34	2.05 (1.02-4.09)		
			≥ 61	23	1.78 (0.84-3.66)		
		Lung	MS (never SS) v estimate (mg/m		ative exposure		
			0-10	4	1		
			11-50	26	3.29 (0.97-11.10)		
			≥ 51	8	1.79 (0.46-6.99)		
		Lung	SS welders: cun (mg/m³-yr)	nulative exposu	ire estimate		
			0-5	11	1		
			6-10	6	1.18 (0.40-3.51)		
			≥ 11	15	2.34 (1.03-5.28)		

Table 2.3 (continued)

Reference, location, enrolment period/ follow-up, study design	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Merlo et al. (1989)	527 welders:	Respiratory	Shipyard welder		•	Age, calendar	One death from
Genova, Italy Enrolment	274 oxyacetylene (MS); 253 electric arc welders	tract	All	16	1.67 (0.95–2.71)	period	asbestosis among electric arc workers:
1930–1980/follow-	(SS); all male shipyard		Oxyacetylene	12	2.34 (1.21–4.09)		no information on
up 1960–1981	workers employed for at		Electric Arc	4	0.88 (0.24–2.30)		mesothelioma
Cohort	least 6 mo as a welder;	Respiratory	Shipyard welder		•		Strengths: indirect adjustment for smoking based on survey data Limitations: small numbers of exposed cases in subcohorts; follow-up did not start until 30 yr
	electric arc slowly replaced oxyacetylene	tract	Electric arc welders (ref.)	NR	0		
	welding over time (1940s:		Welding	16	2.45 (0.77–7.83)		
	66% oxyacetylene;	,	Shipyard welder	s: external ana	alysis		
	34% electric arc; 1986:		All	0	0 (0-2.67)		
	44% oxyacetylene; 56% electric arc).		Oxyacetylene	0	0 (0-4.92)		
	Exposure assessment		Electric arc	0	0 (0-5.83)		
	method: records of job title	Bladder and	Shipyard welder	s: external ana		after first date of	
	(electric arc workers: open	kidney	All	5	2.11 (0.68-4.92)		enrolment (may have
	spaces, lower levels of gases		Oxyacetylene	5	3.70 (1.19-8.64)		missed cases)
	and fumes; oxyacetylene		Electric arc	0	0 (0-3.60)		
	workers: inside oil tankers, higher levels of gases and	Lymphatic and	Shipyard welder	s: external ana	alysis		
	fumes); air samples during	haematopoietic	All	2	0.98 (0.11-3.54)		
	cutting in oil tankers:		Oxyacetylene	1	0.93 (0.01-5.19)		
	B[a]P (3–22 μg/m³), NO <sub>x</sub> (3–8.5 ppm), dust (9–27 mg/m³); higher Ni and Cr(VI) found in SS and MIG welding; asbestos fibres not detected		Electric arc	1	1.03 (0.01–5.74)		

Reference, location, enrolment period/ follow-up, study design	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Puntoni et al. (2001) Italy Enrolment 1960–1980/follow- up 1960–1995 Cohort	3984 male shipyard workers (267 electric arc welders and 228 gas welders); male shipyard workers (whole cohort) employed at the harbour of Genoa Exposure assessment method: records of individual data on job titles from the personnel department; coding the most prevalent job for individuals with different job titles	Lung Pleura Larynx Urinary bladder Kidney	Electric arc Gas All Electric arc	19 14 3 1 1 2 5 1 5 3 2	[1.64 (1.07–2.51)] [1.57 (0.89–2.57)] [3.77 (0.96–10.26)] [1.69 (0.08–8.33)] [0.82 (0.04–4.04)] [2.00 (0.33–6.60)] [2.74 (1.00–6.07)] [0.70 (0.03–3.45)] 3.82 (1.24–8.91) 4.00 (0.82–11.69) 3.57 (0.43–12.90)		Three deaths from pleural cancer among arc welders (SMR, 3.8; NS); 1 death from pleural cancer in gas welders (SMR, 1.7; NS) Limitations: only job titles; confounding by asbestos
Newhouse et al. (1985) NE England Enrolment 1940–1968/follow- up 1940–1986 Cohort	3489 workers (welders, caulkers, electricians, and platters; identified from personnel records) at a shipyard; 1027 welders Exposure assessment method: 1960 measurements of iron oxide in mg/m³ (total general air: 6.3; personal: 13.6); confined spaces without ventilation (general air: 23.6; personal: 31.9); caulkers also exposed to fumes similar in magnitude and composition to welding fumes; asbestos used throughout shipyard but no specific information	Lung All cancers combined	Welders Caulkers Welders Caulkers	26 12 49 18	1.13 (0.80–1.57) 2.32 (1.33–3.74) 1.03 (0.79–1.27) 1.68 (1.09–2.49)	Age, calendar year	15% of workforce had died; 1 mesothelioma among welders and 1 among caulkers Strengths: exposure monitoring data available Limitations: limited exposure information; no information on smoking; incomplete employment records did not allow for assessment of employment duration; workers moved between shipyards

Table 2.3 (continued)

Reference, location, enrolment period/ follow-up, study design	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Melkild et al. (1989) Norway Enrolment: 1946–1977/follow- up: 1953–1986 Cohort	4778 male shipyard workers (783 MS workers); male workers first employed at shipyard on southwest coast of Norway for at least 3 mo during the enrolment period; MMA-MS welding predominant until 1970; SS welding did not become common until the mid-1970s; gas-shielded welding introduced in the 1960s Exposure assessment method: questionnaire and company records, classifying job titles within 10 categories; 1973 survey: total fumes 7.3 mg/m³ (3.6–23.6); Ni: 0.34 mg/m³ (0.11–1.97); Cr: 0.12 mg/m³ (0.03–0.65); personal protection equipment and ventilation provided to shops in early 1970s; asbestos used until early 1970s	Lung Lung Urinary bladder	Welders Employment dura < 1 1–5 > 5 Welders	7 ation (yr) 0 5 1 2	2.21 (0.88-4.54)  - [5.56 (2.04-12.31)] [0.59 (0.03-2.90)] [1.33 (0.22-4.41)]	Age, calendar period	Workers may have contributed to a cancer site in more than one occupational category; may have missed cases occurring during 1947–1952; 2 mesotheliomas observed among non- welders Strengths: description of the type of welding over time and some exposure monitoring data Limitations: limited exposure assessment, which was based on personnel register; no information on smoking in the cohort; exposure to asbestos possible, small numbers of exposed cases

Table 2.3	(continue	ed)
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Reference, location, enrolment period/ follow-up, study design	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Danielsen et al.	4571 male shipyard workers	Lung	Welders	9	2.50 (1.14-4.75)		Smoking differences
(1993)	(623 MS welders); identified	Lung	Duration of emp	loyment and l	ag time (yr)		were estimated to
Norway	by personnel register with		≤ 5; no lag	NR	1.7 (0.5-5.5)		explain a SIR of
Enrolment 1940–1979/follow-	information regarding name, start, and end dates;		> 5; no lag	NR	3.0 (1.3-6.9)		~1.25; Cr and Ni levels were low and
up 1953–1990	mainly MMA welding		≤ 5; 10 yr lag	NR	1.8 (0.5-5.7)		no mesotheliomas
Cohort	performed on MS		> 5; 10 yr lag	NR	3.2 (1.3-8.1)		were observed
	Exposure assessment	Lung	15-yr lag: extern	al analysis			among welders; may have missed cases occurring during
	method: records of		All	8	3.08 (1.35-6.08)		
	interviews with retired		High exposure	6	3.75 (1.38-8.19)		
	workers; high-exposure welders were defined as welders employed ≥ 3 yr and identified as a welder by veteran workers; very high exposure was defined as a subgroup employed ≥ 5 yr		Very high exposure	4	4.00 (1.10-10.20)		1940–1953 Strengths: high and very high exposure
			Shipyard excluding welders and burners	38	1.35 (0.96–1.86)		subgroups; internal reference group of shipyard production workers who were not
	as a welder and followed	Lung	Employment du	ration (yr): external analysis			welders or burners
	up from the 5th year of		$\leq 4$	3	[2.14 (0.55-5.83)]		Limitations: no
	employment		5-9	0	_		quantitative exposure (or semiquantitative exposure assessment); a small number of exposed lung cases among welders; limited information on smoking habits
	Environmental monitoring		≥ 10	6	[3.75 (1.52–7.80)]		
(0.8–9.5 mg/m <sup>3</sup> )	data: total dust 2.5 mg/m³ (0.8–9.5 mg/m³)	n³ Urinary bladder	Welders	1	0.59 (0-3.29)		

Table 2.3 (continued)

Reference, location, enrolment period/ follow-up, study design	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Danielsen et al. (2000) Norway Enrolment 1945–1980/follow- up 1953–1995 Cohort	workers; 861 welders; 908 welded some time; 24 welders in machinery production (SS); workers identified by personnel register with information regarding name, start, and end dates; mainly MS welders Exposure assessment method: records of job title and work history. Welding fumes (mg/m³): MS, 14.5 (1973) and 1.87 (1989); SS, 1.5 (1977) and 7.0–38 (1989); SS grinders, 25.5 (1977). Information on employment outside the shipyard (prior to or between jobs) available from the early 1950s; average length of employment 10.1 yr	Lung	Shipyard welders: internal analysis Non-welding shipyard workers (ref.) < 2 2-4 5-14 ≥ 15 External analysis Welders	employment 36 3 1 1 9	duration (yr):  1  2.42 (0.73–8.01) 0.66 (0.09–4.85) 0.56 (0.08–4.17) 1.90 (0.67–5.38)  1.27 (0.58–2.42)	Age, calendar year	Strengths: information on smoking habits and previous employment; internal comparison of shipyard workers excluding welders Limitations: no quantitative exposure (or semi-quantitative exposure assessment)

<b>Table 2.3</b> (	(continued)

Reference, location, enrolment period/ follow-up, study design	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments							
Danielsen et al.	428 male welders (23 with		Welders	10	1.55 (0.74-2.84)	Age, calendar	No cases of							
(1998) Nagrana	siderosis) who had welded	Kidney	Welders	2	1.13 (0.14–4.10)	period	mesothelioma or asbestosis; electric arc							
Norway Enrolment 1975/	for > 10 yr, mostly MMA welding in confined spaces	Urinary bladder	Welders	1	0.30 (0.01–1.69)		welding on MS was							
1975	examined for siderosis in	Leukaemia: ICD-7 (code 204)	Welders	1	0.69 (0.02–3.85)		predominant until 1975; gas-shielded welding introduced in the 1970s and SS after 1975 Strengths: presumed							
	method: records, assumed	Lung	Years since firs	t exposure										
	to have long-term exposure		10-19	0	0 (0-10.91)									
	to high levels 10 yr or more									20-29	3	1.49 (0.31-4.34)		high exposure cohort;
	before 1975; only limited		30-39	4	1.57 (0.43-4.01)		high exposure conort; analysis by time since first exposure Limitations: potential healthy worker effect; welders who died before 1975 or who quit welding due to adverse health effects were not included in the cohort; limited information on smoking habits or exposure to asbestos; small cohort with few							
	information about smoking		≥ 40	3	1.93 (0.40-5.64)									
	habits was available	All cancers combined: ICD-7	Welders	32	0.77 (0.53–1.09)									

Table 2.3 (continued)

Reference, location, enrolment period/ follow-up, study design	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Yiin et al. (2005) USA Enrolment 1952–1992/follow- up 1952–1996 Cohort	13 468 workers; men and women, all races, employed as civilian workers at Portsmouth Naval Shipyard for at least 1 d and monitored for radiation Exposure assessment method: expert judgement; exposure to welding fumes and asbestos (0, none; 1, possible; 2, probable) assigned to each job title/ shop combination by an expert panel; cumulative exposure score calculated as the sum of the duration of exposed jobs, weighted by exposure probability	Lung	Total exposure on intensity and Never > 0-5 <sup>b</sup> > 5		lding fumes (based  1 1.45 (1.10–1.92) 1.50 (1.09–2.06)	Radiation, age, calendar period, asbestos, SES	Strengths: large cohort; semi-quantitative exposure assessment; adjustment for radiation, asbestos, and SES as a proxy for smoking Limitations: the exposure of interest is radiation; welding fumes analysed as a potential confounder for lung cancer only (no information reported for leukaemia); possible misclassification of exposure; no actual data on smoking habits

Table 2.3	(continue	d)
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Reference, location, enrolment period/ follow-up, study design	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Yiin et al. (2007) USA	Cases: 1097 deaths from lung cancer	Lung	Shipyard weldin (mg-d/m³)	g fumes: mult	ivariate analysis	Radiation, asbestos	Radiation exposure is the focus of the
Enrolment 1952–1992/follow-	Controls: 3291 risk-set- matched controls (3 per		1000	NR	1.01 (0.98–1.04)	exposure, SES, birth cohort	paper; welding fumes as a confounder was analysed as a continuous variable;
up 1952–1996 Nested case–control	up 1952–1996 case, randomly selected by	Lung	Shipyard weldin effects (mg-d/m		vidual risk factor	None	
	Exposure assessment		1000	NR	1.03 (1.0-1.05)		unadjusted ORs
inte	method: expert judgement; intensity and frequency	Lung	Shipyard weldin individual risk f			associated with categorical exposure	
	of exposure to welding fumes (as $Fe_2O_3$ fumes) and		< 0.5	807	1		to welding fumes did not suggest a linear
	asbestos assessed by an		0.5-1	116	1.35 (1.07-1.70)		relationship
	expert panel of 3 industrial		1–2	86	1.58 (1.20-2.07)		Strengths: detailed
	hygienists for 3519 job/		2-4	40	1.20 (0.82-1.72)	adjustment asbestos, rad SES and bird (surrogates) smoking) Limitations: actual smok no monitori	exposure assessment;
	shop/period combinations. Good concordance, weak inter-rater agreement. Cr and Ni content of welding fumes were also assessed (not used in the analysis). 53% of the study subjects were ever exposed to welding fumes; 64% to asbestos, 8% to Ni and 6% to Cr		$\geq 4$	48	1.26 (0.88–1.76)		Limitations: no actual smoking data; no monitoring data to validate panel

Table 2.3 (continued)

Reference, location, enrolment period/ follow-up, study design	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Rinsky et al. (1988) Kittery, Maine, USA 1952–1977 Nested case–control	Cases: 405 white male deaths from malignant neoplasm of bronchus, trachea. or lung; diagnosis based on death certificates Controls: 1215 selected from the same cohort, matched by date of birth, year of 1st employment, and duration of employment 3:1 Exposure assessment method: personnel records indicating the specific shops to which a person had been assigned; job classification and date of each change in employment were used to code work history	Lung Lung Lung	Shipyard: asbesto Never exposed Ever exposed Min 5 yr Min 10 yr Shipyard: Weldin Never exposed Ever exposed Min 5 yr Min 10 yr Shipyard: probab Never exposed Ever exposed Min 5 yr Min 10 yr Shipyard: probab Never exposed Ever exposed Ever exposed Ever exposed Min 5 yr Min 10 yr Shipyard: probab Never exposed Ever exposed Ever exposed Min 5 yr Min 10 yr	138 267 152 96 18 shop) 364 41 28 16 le or potential 169 236 143 91	1 1.43 (1.12–1.81) 1.50 (1.11–2.04) 1.38 (0.97–1.98) 1 1.13 (0.76–1.68) 1.16 (0.73–1.86) 0.83 (0.46–1.53)		Nested case-control study of Portsmouth Naval Shipyard workers; primary research question was the assessment of lung cancer risk due to ionizing radiation emitted from nuclear reactor components Strengths: specific focus on asbestos and welding in addition to radiation exposure; classification of welding exposure by probability (potential, probable) and duration (ever, ≥ 5 yr, ≥ 10 yr) Limitations: limited confounder information; no adjustment for smoking

<b>Table 2.3 (</b>	continue	d)
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Reference, location, enrolment period/ follow-up, study design	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Stern et al. (1986) USA Enrolment 1952–1977/follow- up 1952–1980 Nested case–control	Cases: 53 deaths from leukaemia (death certificates, checked with medical records) Controls: 212; 4 matched controls by case (exclusion: deaths from haematopoietic or lymphatic malignancies) Exposure assessment method: records of job titles and duration of employment of the different jobs; radiation dose	Leukaemia Leukaemia (myeloid)	Welder Welder	NR NR	3.19 (1.09–9.37) 6.23 (1.64–23.64)	Radiation, employment as electrician, employment in jobs exposed to solvents	Strengths: ORs associated with employment as a welder adjusted for radiation exposure, employment as electrician, and jobs exposed to solvents Limitations: crude assessment of exposure
Park et al. (1994) USA Enrolment 1966–1989/follow- up 1978–1988 Cohort	16 197 hourly workers (76% assembly plant, 24% stamping plant); 3887 stamp workers; all hourly employees who worked ≥ 2 yr at 2 automotive assembly plants and a metal stamping plant before 1989 Exposure assessment method: records of six process-related categories for stamping plant; ~25 of the decedents worked in more than one exposure category; welding was performed on sheet metal	Lung  Lung  Lung  Lymphatic and haematopoietic	long latency weigexposure (mo) 0 1–50 51–100 All	7 welding lines a ghted duration  8 5 2 15 adjusted MOR	2.73 (1.20–6.30) and welder repair: a, cumulative  1 [2.00 (0.61–6.61)] [5.81 (0.92–36.8)] [1.38 (0.56–3.40)] a: weighted duration/ 1.90 (0.93–3.90) 2.73 (1.09–6.90) 3.95 (1.39–11.00) 0.99 (0.14–7.20)	Age, sex, race, chronological time	No information on mesothelioma Strengths: regression analysis and modelling to evaluate similar activities of previous employment, latency and duration Limitations: no quantitative or semi-quantitative exposure assessment only 5% of cohort had died due to young ages and short follow-up (11 yr); healthy worker effect in stamping plant; mortality odds ratio; no information on smoking and other

Table 2.3 (continued)

Reference, location, enrolment period/ follow-up, study design	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Steenland (2002) Illinois, USA Enrolment 1950s-1980s/follow- up mid-1950-1998 Cohort	4459 welders; 4286 never welders; hourly male (90% white) workers with ≥ 2 yr of experience as a production arc welder or welder helper at 3 heavy equipment manufacturing plants Exposure assessment method: records of person monitoring available from 1974 to 1987; smoking data available for subset of workers; TWA geometric mean across plants (particulate levels, 5.5–7.4 mg/m³; Fe <sub>2</sub> O <sub>3</sub> , 3–4.1 mg/m³); average duration of welder 8.5 yr	Lung	Welders vs US por 15-yr lag time Total mortality 2-5 5-10 10-15 15-20 > 20 Latency $\geq$ 20 Welders vs non-vality 2-5 5-10 10-15 15-20 > 20 Latency $\geq$ 20	97 34 23 23 12 15 66 31	1.47 (1.19–1.79) 1.39 (0.96–1.94) 1.30 (0.82–1.95) 1.94 (1.23–2.91) 1.65 (0.85–2.88) 1.02 (0.57–1.68) 1.39 (1.07–1.77) 1.66 (1.23–2.36)	Age, race, calendar time	Update of Beaumont & Weiss (1980); 26% of the population had died; potential misclassification of exposure duration since 14% of the population still worked at the end of follow-up; smoking probably cannot explain all the excess of lung cancer in welders; no deaths from asbestosis or nonspecific pneumoconiosis Strengths: exposure monitoring data; non-welder cohort; some data on smoking; exposure to asbestos unlikely
		Larynx	Welders	4	1.42 (0.39-3.62)		Limitations: no
		Kidney	Welders	10	1.84 (0.88-3.38)		quantitative or
		Urinary bladder	Welders	7	1.71 (0.69–3.53)		semiquantitative exposure assessment

Table 2.3 (continued)

al. 2957 male welders; 606 SS welders; members of the National Registry of Boiler Welders from 385 different businesses who registered before	Lung	Boiler welders: la No lag 15-yr lag SS welder: lag tin No lag	1g time (yr) 50 46	[1.33 (1.00–1.74)]	Age, calendar period	SS welders: boiler
1981 with information on DOB; foreigners without permanent addresses in Norway excluded; most registered welders welding on MS; MMA welding predominant method in early years Exposure assessment method: records of welder registration information contained the method of welding for certification and information on previous work experience	Lung  Lung  All cancers combined  Nasal cavity and sinuses  Larynx  Kidney  Urinary bladder	15-yr lag Boiler welders: ye 1940–1949 1950–1959 1960–1969 1970–1982 SS welder: year o 1940–1949 1950–1959 1960–1969 1970–1982 Boiler welders SS welders SS welders SS welders	6 2 ear of first reg 7 25 9	[1.05 (0.46–2.07)] [1.70 (1.12–2.47)] [0.75 (0.36–1.37)] [2.20 (1.07–4.03)]	peliou	welders ever welding on SS; excess risk of mesothelioma found among boiler welders (3 cases); use of gas shielded and TIG welding increased in 1970s Strengths: exposure misclassification with respect to welders unlikely Limitations: no information on exposure duration, exposure intensity, potential confounders (e.g. asbestos), or smoking; small numbers of exposed cases
	Brain	Boiler welders	10	1.02 (0.49-1.88)		

Table 2.3 (continued)

Reference, location, enrolment period/ follow-up, study design	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Danielsen et al. (1996)		HL: ICD-7 (code 201)	Boiler welders	3	1.43 (0.29–4.19)		
cont.)		NHL: ICD-7 (code 200/2)	Boiler welders	9	0.83 (0.38–1.57)		
		Leukaemia:	Boiler welders	11	1.77 (0.89-3.18)		
		ICD-7 (code 204)	SS welders	2	2.00 (0.20-7.20)		
Meguellati-Hakkas	34 305 men ever employed	Lung	Duration of arc	welding expos	ure (yr)	Age, calendar	No information on
et al. (2006)	as telephone linemen in 1978 and new hires from		0	54	1	period, engine exhaust, PAHs.	smoking but use of internal analyses decreases concerns Strengths: semi-
France Enrolment	1978 and new nires from 1978 to 1994		> 0 to 0.03	127	1.2 (0.8–1.6)		
1978–1994/follow-	Exposure assessment		> 0.03 to 0.04	64	1.3 (0.8–2.2)	asbestos	
up 1978–1996 Cohort	method: expert judgement; semiquantitative assessment based on expert assessment of job tasks for specific calendar/time periods; exposure duration was estimated for welding; highest category was 0.04 yr or more		> 0.04	63	1.4 (0.7–2.8)		quantitative exposure assessment; adjustment for exposure to asbestos Limitations: focus of the paper was exposure to asbestos; welding was assessed as a potential confounder; exposure to welding does not seem to be substantial (80% of deaths exposed to less than 0.04 yr of welding)

Reference, location, enrolment period/ follow-up, study design	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Dunn & Weir (1968) California, USA Enrolment 1954–1957/follow- up 1954–1962 Cohort	68 153 men in all occupations; 10 233 welders and burners; male workers aged 35–64 employed in 14 selected occupational groups were selected from union mailing lists and questionnaires Exposure assessment method: questionnaire; occupational title, employment duration, working conditions, type of welding, and specific exposures associated with particular occupations	Lung	Welders and burners	49	[1.05 (0.79–1.38)]	Age, smoking	Strengths: adjusted for smoking; prospective study Limitations: limited information on occupational coexposures; short follow-up (7 yr average); referent group was the total population, some owhich were exposed to asbestos

Table 2.3 (continued)

Reference, location, enrolment period/ follow-up, study design	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments	
Polednak (1981) Tennessee, USA	Cennessee, USA employed at Oak Ridge Enrolment nuclear facilities during	Lung	Total cohort of welders	17	1.50 (0.87–2.40)	Age, calendar period	16.7% of workers had died; excess risk	
Enrolment 1943–1974/follow-			Welders: 15-yr lag	16	[1.76 (1.04–2.80)]		of emphysema in total cohort and two	
up 1974 subgroups of welders:	Lung: ICD-8	K-25 plant: subg	subcohorts observed;					
Cohort	(1) 536 welders at K-25 Ni alloy pipes (MS and Ni);	Ü	Welders	7	1.24 (0.50-2.55)		smoking higher in other plants than K-25; K-25 smoking habits similar to national rates; no information on radiation exposure	
	and (2) 533 welders at Y-12 and X-10 plants conducting		Welders: 15-yr lag	6	[1.26 (0.51–2.62)]			
	various types of welding		Other welders	10	1.75 (0.84-3.22)			
	(SMA, TIG, MIG)	Respiratory	Total cohort: len	gth of employ	ment as a welder (wk)			
	Exposure assessment	tract: cancer	< 50	10	1.57 (0.75-2.89)			
	method: records of			≥ 50	7	1.21 (0.49-2.49)		Strengths:
	personal air monitoring	Respiratory	K-25 plant: lengt	monitoring data,				
	(Ni and Fe <sub>2</sub> O <sub>3</sub> ) for different welding procedures:	tract	< 50	2	[0.62 (0.10-2.05)]		including exposure to Ni, from different types of welding available; long follow-up for 50% of	
	Fe <sub>2</sub> O <sub>3</sub> , 0.18–0.47 mg/m <sup>3</sup> ;		≥ 50	5	1.75 (0.57-4.08)			
	Ni (mg/m³) was highest for MIG/Ni (0.57),	Larynx	Total cohort: welders	0	0			
intermediate for SMA/Ni (0.13) and MIG carbon steel (0.25), and lowest for TIG welding with Ni (0.04) or carbon steel (0.08). Biomonitoring data (metals) among 33 Ni welders in K-25 facility (0.053 mg/L Ni). Information on smoking available for 33% of workers	intermediate for SMA/Ni	Brain	Total cohort: welders	3	[1.94 (0.49–5.27)]		workers; some data on tobacco smoking	
	Leukaemia: ICD-8	Total cohort: welders	1	[0.64 (0.03–3.17)]		habits Limitations: small number of cases for employment duration analysis; healthy worker effect (SMR for all causes, 0.87; 95% CI, 0.75–1.01)		

Reference, location, enrolment period/ follow-up, study design	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Steenland et al. (1986) Western Washington, USA Enrolment 1950–1973/follow- up 1950–1976 Cohort	3247 welders, 5432 non-welders; male members of a metal trades union/local boilermakers, employed at least 1 d during the period 1950–1973, who had worked for at least for 3 yr Exposure assessment method: job categories from union records	Lung Lung	SMR: Welding Cox: Welding	NR NR	[1.32 (0.99–1.76)] [1.29 (0.90–1.85)]	None Age, employment	Reanalysis of the cohort reported by Beaumont & Weiss (1980, 1981) using internal reference group Strengths: internal comparison group Limitations: no exposure data
Sorahan et al. (1994) UK Enrolment 1946–1990/follow- up 1946–1978 Cohort	10 438 (total cohort); 401 welders in the fettling shop, 99 welders in pattern/ machine/maintenance/ inspection; men employed for at least 1 yr in 9 English and 1 Scottish steel foundries Exposure assessment method: records of work area and occupational category	Lung	Fettling shop: burning and welding Pattern/ machine/ maintenance/ inspection: welding	2	[1.69 (1.04–2.58)]	Age, sex, calendar year	Update of Fletcher & Ades (1984) Limitations: small number of welders; no exposure data

Table 2.3	(continued)
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Reference, location, enrolment period/ follow-up, study design	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Austin et al. (1997) Ohio, USA 1970–1987 Nested case–control	Cases: 231 deaths from lung cancer Controls: 408 selected from the same cohort matched by race, sex, and year of birth using density sampling Exposure assessment method: records of complete work history from plant personnel files; telephone interview for lifestyle characteristics	Lung Lung	Ever welding Longest welding job held	10 7	0.66 (0.29–1.50) 0.76 (0.28–2.10)	Smoking, job Smoking	Strengths: controlling for smoking Limitations: small number of welders; no exposure data; possibly inadequate control group; crude adjustment for smoking (never, former, current, unknown); no adjustment for concomitant occupational exposures in foundry
Howe et al. (1983) Canada Enrolment 1965–1977/follow- up 1965–1977 Cohort	43 826 pensioners; 4629 exposed to welding fumes; male pensioners of the Canadian National Railroad company who retired before 1965, were known to be alive in 1965, and who retired during 1965–1977 Exposure assessment method: expert classification of workers exposed to welding fumes, diesel fumes, coal dust, and other exposure based on occupation at retirement	Brain	Individuals exposed to welding fumes	10	3.18 (1.53–5.86)	Age, calendar period	Strengths: not informative Limitations: potential for exposure misclassification; exposure only based on last occupation; no information on type of welding, duration, levels, etc.; findings only reported for brain cancer; no information on smoking or other potential coexposures

Reference, location, enrolment period/ follow-up, study design	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Bonde et al. (1992) Denmark Enrolment 1964– 1984 fathers/follow- up of children (date of birth to date of death, emigration) or 1987 Cohort	27 071 fathers; 5020 children with cancer; Danish fathers who were employed at 74 MS and SS manufacturing companies (as identified by the Danish Pension Fund) for at least 1 year Exposure assessment method: metalworking cohort questionnaire sent through mail, included data on drinking and smoking habits and occupational exposures including the type of welding methods used during three calendar periods; response rate 85%	Childhood	Parental exposu SS welding MS welding	2 4	0.77 (0.13–2.54) 0.93 (0.30–2.24)	Age, sex, calendar period	Based on the Danish welding cohort study (Hansen, 1982) Limitations: limited exposure information; small number of cancers occurring in children fathered by welders

Table 2.3 (continued)

Reference, location, enrolment period/ follow-up, study design	Population size, description, exposure assessment method	Organ site/ cancer type	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Håkansson et al.	Cases: 140 incident cases of	All cancers combined: endocrine glands	Any welding: ex	xposure (h/wk)		Sex, year of	Focus of the paper is
(2005)	tumours of the endocrine		Ever	25	2.1 (1.3-3.5)	birth, solvent	exposure to ELF-EMF
Sweden	glands: adrenal glands		> 0-10	8	1.9 (0.8-4.4)	exposure, year	Strengths: individual assessment of welding type and welding frequency
1985–1994	(n = 29), parathyroid gland		> 10-30	7	1.9 (0.8-4.6)	of inclusion	
Nested case-control	(n = 67), pituitary gland $(n = 36)$ , and other subtypes $(n = 8)$		> 30-40	10	2.5 (1.2-5.5)		
			Trend test P val		Limitations: no		
	Controls: 1306 matched by sex and year of birth (3-year intervals) Exposure assessment method: questionnaire; assessment at the individual level from questionnaire and telephone interview with a contact person at the workplace; blind as to casecontrol status	All cancers	Resistance weld	ling: exposure (		assessment of	
		endocrine glands	Ever	7	1.1 (0.5-2.4)		exposure to welding
			> 0-10	3	1.2 (0.3-4.3)		fumes; small number
			> 10-30	4	1.4 (0.5-4.1)		of exposed cases in subgroups
			> 30-40	0	0 (0-0)		
			Trend test P val				
		All cancers combined: endocrine glands	Arc welding: ex				
			Ever	20	2.9 (1.6-5.3)		
			> 0-10	6	2.2 (0.8-6.0)		
			> 10-30	5	2.8 (0.9-9.1)		
			> 30-40	9	3.8 (1.6-9.3)		
			Trend test P val	Trend test <i>P</i> value, 0.00			

<sup>&</sup>lt;sup>a</sup> Included in "ever stainless steel welders"

<sup>&</sup>lt;sup>b</sup> Total exposures (based on intensity and duration) of welding fumes were arbitrarily classified into three categories (value of 0, .0–5 and .5) B[a]P, benzo[a]pyrene; CI, confidence interval; Cr, chromium; Cr(VI), hexavalent chromium; d, day(s); DOB, date of birth; ELF-EMF, extremely low frequency electromagnetic field; Fe<sub>2</sub>O<sub>3</sub>, iron oxide; h, hour(s); HL, Hodgkin lymphoma; IARC, International Agency for Research on Cancer; ICD, International Classification of Diseases; MAG, metal active gas; MIG, metal inert gas; MMA, manual metal arc; mo, month(s); MOR, mortality; odds ratio; MS, mild steel; NHL, non-Hodgkin lymphoma; Ni, nickel; NO<sub>3</sub>, nitrogen oxides; NR, not reported; NS, not significant; PAH, polycyclic aromatic hydrocarbon; SES, socioeconomic status; SIR, standardized incidence ratio; SMA, shielded metal arc; SMR, standardized mortality ratio; SS, stainless steel; TIG, tungsten inert gas; TWA, time-weighted average; vs, versus; wk, week(s); WIG, Wolfram-Inert-Gas welding; yr, year(s)

Table 2.4 Cancer and welding or exposure to welding fumes: studies included in the IARC multicentre cohort (Simonato et al., 1991)

IARC subcohorts	IARC cohort (population)	Publications of the IARC subcohorts	Comments
Denmark	4642	Hansen et al. (1996) 6180 male welders (not shipyard); 105 lung cancer cases	Follow up until 1968–1986; larger cohort
		<u>Lauritsen &amp; Hansen (1996)</u> 94 lung cancer cases from Hansen et al. (1996)	Case-control analysis; adjusted for smoking
		Sørensen et al. (2007) 4536 male welders (non-shipyard); incidence	Follow-up 1968–2003 (cohort restricted to those who started working by 1960); longer follow-up; more detailed analysis on welding types; adjusted for smoking and asbestos
England	393	No separate report published	-
Finland	1808	Tola et al. (1988) 1689 male welders (1308 shipyard, 381 machine shop); mortality	Smoking data; machine shop only SIR (minimal exposure to asbestos); complete overlap in study population with the Simonato et al. (1991) publication
France	1190	Moulin et al. (1993) 2721 male welders; mortality	Smoking data; internal referent group; expanded and longer follow-up
Germany	1199	Becker (1999) 1213 welders; mortality	Internal referent group; indirect assessment of asbestos; longer follow-up
Italy	447	Merlo et al. (1989) 527 welders; mortality Puntoni et al. (2001) 493 welders; mortality	Probable overlap between these studies and the Italian subcohort, and between these two studies; extent of overlapping unknown
Norway	737	No separate report published	-
Scotland	237	No separate report published	-
Sweden	439	Milatou-Smith et al. (1997) 233 male welders exposed to high levels of Cr; 208 railroad track male welders; incidence	Longer follow-up; separate analysis for the two different cohorts

Cr, chromium; IARC, International Agency for Research on Cancer; SIR, standardized incidence ratio

or setting (shipyards, MS, SS). A limitation was the lack of data on asbestos exposure, since confounding by asbestos may partly explain the excess of cancer of the lung, and that exposure– response analyses were not reported in the publication although they were conducted.]

## (ii) IARC subcohorts

See Table 2.4

Studies of the IARC subcohorts overlapped with the multicentre cohort, had smaller sample sizes, and were overall considered to be less informative than the pooled analyses. However, they provided additional data on smoking habits and asbestos exposure, and/or an extended follow-up. (See <u>Table 2.4</u> for information on the overlap between the IARC study and the separate reports of its subcohorts.)

The French subcohort included in the IARC study was further extended by adding new factories and by updating the follow-up from 1975 to 1988 (Moulin et al., 1993). In addition, a group of manual workers in the same factories was used as an internal reference group and smoking data were collected. The relative risk (RR) of cancer of the lung for welders compared with the reference group was 1.29 (non-significant, P value and CI not reported). [The Working Group noted that the inclusion of shipyard workers, potentially exposed to asbestos, in the reference group may have resulted in an underestimation of the relative risk.] An indirect adjustment suggested that the slight differences in smoking habits between welders and referents would result in a relative risk of 1.06. Analyses by type of welding showed a higher standardized mortality ratio in MS than in SS welders. An increase in mortality from cancer of the lung with duration and time since first employment was observed only in MS welders [the three deaths from cancer of the lung in the group of SS welders did not allow meaningful analysis]. No deaths from cancer of the pleura occurred among welders (0.41 expected), whereas three deaths from cancer of the pleura

were identified in the reference group, all shipyard workers (expected, 0.26). [The Working Group noted that these data suggest that exposure to asbestos is not likely to explain the lung cancer excess observed in non-shipyard MS welders. No actual data on asbestos exposure were available.]

Mortality from cancer of the lung was further evaluated in the two Swedish subcohorts (Sjögren, 1980; Sjögren et al., 1987; Milatou-Smith et al., 1997): a cohort of 233 SS welders, who welded mainly with coated electrodes and were exposed to high concentrations of hexavalent chromium; and a cohort of 208 railway track welders, exposed to MS fumes with low concentrations of hexavalent chromium. Exposure to asbestos was assumed to be very low in the two cohorts [the occurrence of mesothelioma was not reported]. When compared with the national population, an elevated standardized mortality ratio was observed in SS welders, whereas mortality from cancer of the lung was decreased in MS welders. The relative risk of cancer of the lung in SS welders compared with the group of MS welders was 3.98 (95% CI, 0.84-18.80). [The small numbers of deaths from cancer of the lung limited the interpretation.

The subcohort of German arc welders (Becker et al., 1985) was successively updated by Becker et al. (1991) and Becker (1999). A cohort of turners was also followed up as an internal comparison group. In the last follow-up (Becker, 1999), elevated standardized mortality ratios were found among welders for cancers of the lung (SMR, 1.21; 95% CI, 0.80-1.75), bladder (SMR, 2.08; 95% CI, 0.67-4.84), and brain (SMR, 2.02; 95% CI, 0.55-5.19). Mortality from cancer of the lung was also higher in welders than in the comparison group (RR, 1.30; 95% CI, 0.80-2.12). No clear trend with duration of employment or time since first employment was suggested. Analyses by welding technique or by average daily welding time did not reveal strong differences in mortality from cancer of the lung or from other cancer sites, with the exception of an increased standardized mortality ratio of cancer of the brain among welders only welding with coated electrodes (SMR, 6.18; 95% CI, 1.88–15.85). Seven deaths from mesothelioma occurred among welders (0.6 expected; SMR, 11.67; 95% CI, 4.69–24.04), compared with one death in the comparison group (1.0 expected). An indirect assessment of asbestos-related cancers showed that the increased mortality from cancer of the lung among welders could be entirely explained by asbestos exposure. [The Working Group agreed that exposure to asbestos is likely to explain the excess of cancer of the lung observed in this German part of the IARC cohort.]

Cancer incidence among Danish welders employed in SS or MS industrial companies has been reported (Hansen, 1982; Hansen et al., 1996; Lauritsen & Hansen, 1996; Sørensen et al. 2007). Shipyard welders were specifically excluded. Data on occupational and smoking history were collected by questionnaire at baseline. The study by Sørensen et al. (2007) is considered to be the most informative report of this population due to the longer follow-up period, better exposure assessment, reduced left truncation by excluding workers hired before 1960, and adjustment for tobacco smoking and exposure to asbestos; the analyses of incidence of cancer of the lung by Hansen et al. (1996) and the nested case-control study of mortality from cancer of the lung by <u>Lauritsen & Hansen (1996)</u> are therefore not reviewed separately. Findings for other cancer sites are reported from Hansen et al. (1996) because Sørensen et al. (2007) did not report the data (see <u>Table 2.4</u> for the overlap between these studies). In the first report (<u>Hansen et al., 1996</u>), standardized incidence ratios for other cancer sites of interest were 1.19 (95% CI, 0.78-1.74; 26 exposed cases) for the urinary tract and 0.92 (95% CI, 0.50-1.54; 14 exposed cases) for lymphatic tissues. The number of cancers of the pleura did not exceed the expected number [the numbers were not reported]. Sørensen et al. (2007)

reported data mainly for incidence of cancer of the lung, and incorporated a specific assessment of exposure to welding fumes [different from that used in the IARC multicentre study] based on a JEM using all exposure measurements specific to the calendar year in Denmark. An internal analysis was also conducted, adjusted for age, smoking, asbestos exposure from welding, and jobs prior to enrolment.

The standardized incidence ratio for cancer of the lung was increased in the whole cohort (SIR, 1.35; 95% CI, 1.06–1.70) and was higher among the group of welders who only welded MS (SIR, 1.59; 95% CI, 1.14–2.16) than among the group of ever SS welders (SIR, 1.15; 95% CI, 0.78–1.60). However, an elevated ratio was observed in ever SS welders who had ever conducted manual metal arc (MMA) welding (SIR, 1.46; 95% CI, 0.95–2.16).

In the internal comparison, the hazard ratio of cancer of the lung was not increased in ever SS welders when compared with MS welders who never welded SS (HR, 0.86; 95% CI, 0.52-1.42). The risk did not increase with increasing duration for any type of welding. The risk increased with cumulative exposure to welding fume particulates among ever SS welders, while no clear positive trend was found among MS welders who never welded SS. In the highest cumulative exposure category of SS welders, the adjusted hazard ratio was 2.34 (95% CI, 1.03-5.28). [The strengths of this study were the long follow-up, individual data on asbestos exposure and smoking, and individual semi-quantitative exposure assessment to welding fumes.]

# (b) Shipyard workers

Seven cohort studies of shipyard workers which assessed exposure by occupation as a welder, including one in England, four in Norway, and two in Italy, were identified. The two Italian shipyard studies may overlap with each other (Merlo et al., 1989; Puntoni et al., 2001) and with the Italian subcohort of the IARC study [this

is not explicitly reported in the publications]. In addition, a series of studies of workers at a naval shipyard who overhauled nuclear submarines was identified in which semi-quantitative or quantitative exposure to welding fumes was assessed. Shipyard welders in these cohorts were primarily MS welders and asbestos was widely used in the shipyards. The IARC study (see Section 2.4.1 (a)) also reported a risk estimate for cancer of the lung and shipyard welders.

Cancer mortality was evaluated in a cohort of four craftsmen groups (1027 welders, 235 caulker burners, 557 platers, and 1670 electricians) employed in a shipyard in north-east England (Newhouse et al., 1985). Standardized mortality ratios (using local rates) for cancer of the lung were 1.13 (95% CI, 0.80-1.57; 26 exposed cases) for welders and 2.32 (95% CI, 1.33-3.74) for caulker burners. Caulker burners performed burning and oxypropane cutting tasks and were exposed to fumes that were similar in magnitude and composition to welding fumes; however, these tasks were performed outside, most likely reducing exposure to the fumes. No excess risk of cancer of the lung was found for the two other groups of craftsmen. [Although there were indicators of potential confounding from asbestos (mesotheliomas) or smoking, these indicators may not explain the excess risk of cancer of the lung because they occurred in craftsmen subgroups with and without increased risk of cancer of the lung. The study was limited by incomplete records of employment, the mobility of workers in moving to other shipyards, and short follow-up time (during which only 15.7% of the workforce had died).]

# (i) Shipyards in Norway

Using a somewhat similar study design, three cohort studies reported on cancer incidence of welders employed at three different Norwegian shipyards (Melkild et al., 1989; Danielsen et al., 1993, 2000). The cohorts included all male workers employed as welders, identified from the

shipyard personnel records for the specific enrolment dates that covered several decades (from the 1940s to early 1980s). Follow-up began in 1953 with the establishment of the Norway Cancer Registry; cancer cases that occurred from the first enrolment date (1940s) to 1953 were not known. Most of the welders were MS welders, which was the predominant type of metal welding used in Norway until the mid-1970s. Asbestos was used in the shipyards until the 1970s. Little information on the smoking habits of cohort members was available. [The Working Group noted that exposure monitoring data was not used in the exposure assessment. The limitations of the studies included potential confounding from tobacco smoking and exposure to asbestos. No mesotheliomas occurred among welders in all three cohorts.]

The earliest cohort study included MS workers at a shippard in south-west Norway (Melkild et al., 1989). Compared with non-welding Norwegian men, welders had an elevated risk of cancer of the lung (SIR, 2.21; 95% CI, 0.88–4.54; 7 exposed cases) which was concentrated among workers employed as welders for 1–5 years.

The second cohort study included MS welders at a shipyard on the west coast of Norway (Danielsen et al., 1993). In external 15-year lagged analysis, the standardized incidence ratio for cancer of the lung was 3.08 (95% CI, 1.35-6.08; 8 exposed cases) for all welders and somewhat higher among welders exposed to "high" (SIR, 3.75; 95% CI, 1.38-8.19; 6 exposed cases) or "very high" levels (SIR, 4.0; 95% CI, 1.10-10.20; 4 exposed cases). Similar results were found in an internal analysis that used other shipyard workers (who were not welders, burners, or administrative workers) as the referent group and a 10-year lagged time. There was some evidence of an exposure-duration-response in the internal analysis (unlagged and 10-year lagged); risks were higher among those that had worked as welders for 5 years compared with those that had worked for fewer years.

A 1984 survey of smoking habits found that daily smoking was 10–20% higher among Norwegian shipyard production workers and welders than the general public, and these smoking differences were estimated to explain a 25% increase risk (e.g. SIR, ~1.25). [The advantages of this study were lagged analysis by exposure to "high" and "very high" levels (although based on duration), internal analyses which helped to mitigate concerns for tobacco smoking and exposure to asbestos, and information, although limited, on smoking habits. Non-welding shipyard workers were presumed to have similar smoking habits as for welders.]

The third cohort was of MS welders at a shipyard on the island Stord (<u>Danielsen et al., 2000</u>). An excess risk of cancer of the lung occurred in both external (SIR, 1.27; 95% CI, 0.58-2.42) and internal analyses, using other shipyard workers as a referent, among welders employed for less than 2 years (RR, 2.42; 95% CI, 0.73-8.01; 3 exposed cases) and for more than 15 years (RR, 1.90; 95% CI, 0.67–5.38; 4 exposed cases). [The small numbers of cases limited the ability to look at employment-duration-response relationships.] The differences in risk of cancer of the lung among different types of shipyard workers were not explained by previous work history. In 1976 and 1984 surveys of the shipyard, the proportion of shipyard welders who were daily smokers was similar to shipyard non-welders, and approximately 10% higher than Norwegian men.

Another study in Norway investigated cancer incidence among shipyard welders employed for more than 10 years at 15 shipyard companies, and examined for siderosis in 1975 (Danielsen et al., 1998). Welders who had quit welding before 1975 because of health problems were not included in the study. The predominant welding technique was electric arc on MS; SS welding was introduced after 1975. Welders had an increased risk of cancer of the lung (SIR, 1.55; 95% CI, 0.74–2.84; 10 exposed cases) compared with non-welding Norwegian males. In analyses

by time since first exposure, the highest risk was among those welders for whom 40 years had passed since their first exposure (SIR, 1.93; 95% CI, 0.40–5.64; 3 exposed cases); however, the number of exposed cases was small for each exposure period. No cases of cancer of the lung occurred among 23 welders who had siderosis. Asbestos was used in shipyards, although no cases of mesothelioma were reported among welders. [The Working Group noted the potential for a healthy worker effect, and potential confounding from exposure to asbestos and tobacco smoking.]

## (ii) Shipyards in Genoa, Italy

Cancer mortality was evaluated in a cohort of active and retired 274 oxyacetylene (mainly MS) welders and 253 electric arc (mainly SS) welders employed at a shipyard in Genova, Italy, from 1930 to 1980 (Merlo et al., 1989). Welders were presumed to be potentially exposed to low concentrations of asbestos fibres according to company records. [The Working Group questioned the validity of this statement.] An increased risk of mortality due to cancer of the lung (reported as respiratory tract) was found among oxyacetylene welders in both external (SMR, 2.34; 95% CI, 1.21-4.09; 12 exposed cases) and internal analyses (RR, 2.45; 95% CI, 0.77–7.83) using electric arc welders (mainly SS) as the referent group, since they mainly worked outdoors and were therefore presumed to have lower exposures. Oxyacetylene welders worked inside oil tankers, and were assumed to be exposed to higher levels of gases and fumes than electric arc workers who worked in open spaces. No increased risk of cancer of the lung was found among electric arc workers compared with the general population. Excess mortality from cancer of the lung due to tobacco smoking was modelled to be equivalent to an excess relative risk of 21-30% (depending on the smoking habits of the referent population); information on smoking habits was ascertained from a 1986 survey. [The Working Group noted that the use of internal analyses

reduces concerns for potential confounding from lifestyle factors such as tobacco smoking and exposure to asbestos, which were thought to be similar between the two groups of welders. Follow-up did not start until 30 years after first date of enrolment, meaning that deaths resulting from cancer of the lung during 1930–1960 may have been missed.]

The mortality in a cohort of shipyard workers employed at the harbour of Genoa, Italy, from 1960 to 1980, including 267 arc welders and 228 gas welders, was studied and subsequently updated by Puntoni et al. (1979, 2001). Mortality from cancer of the lung was increased in both arc welders (SMR, 1.64; CI not reported) and gas welders (SMR, 1.57). Electric arc welders also showed increased mortality for cancers of the bladder (SMR, 2.74) and kidney (SMR, 4.0). Elevated standardized mortality ratios were observed among gas welders for cancers of the larynx (SMR, 2.0) and kidney (SMR, 3.57). Three deaths from cancer of the pleura (SMR, 3.77) and one death from asbestosis were observed among electric arc welders; one death from cancer of the pleura (SMR, 1.69) occurred among gas welders. [The Working Group inferred from the cancer of the pleura and asbestosis deaths that this cohort may have experienced substantial asbestos exposure, which limits the interpretation of excesses of cancer of the lung in welders. The Working Group also suspected some overlap with the study by Merlo et al. (1989) described in the paragraph above.]

# (iii) Portsmouth Naval Shipyard

The risk of cancer of the lung and leukaemia was investigated in a cohort of workers monitored for radiation exposure at the Portsmouth Naval Shipyard in Maine, USA, initiated to study the effects of ionizing radiation exposure (Yiin et al., 2005). The main objective was to explore doseresponse relationships between ionizing radiation and risk of cancer, while adjusting for previously unanalysed confounders. Semi-quantitative

exposure scores were calculated for asbestos and welding fumes. After adjustment for socioeconomic status (as a proxy for smoking) and exposure to asbestos and radiation, the risk of cancer of the lung increased for workers exposed to welding fumes, although the relative risks were similar in the low (RR, 1.45; 95% CI, 1.1–1.92) and high (RR, 1.5; 95% CI, 1.09–2.06) categories of exposure.

A nested case-control study of cancer of the lung (Yiin et al., 2007) was also conducted in this cohort, extended to non-radiation workers, with an improved quantitative assessment of exposure to welding fumes, asbestos, and the chromium and nickel content of welding fumes (Seel et al., 2007). This study superseded a previous nested case-control study of cancer of the lung within the same cohort (Rinsky et al., 1988). Exposure estimates in the study population (Zaebst et al., 2009) showed that a large proportion of workers were exposed to welding fumes (53%) and to asbestos (64%). As most of the welding in this shipyard was on MS, exposure to chromium and nickel in welding fumes was much less frequent (6% and 8% of the workers, respectively), and these exposures were not considered in the epidemiological analysis. Socioeconomic status and birth cohort were used as a surrogate for smoking. When examining risk of cancer of the lung with exposure to welding fumes on a continuous scale (per 1000 mg-days/m³), the multivariate odds ratio was 1.01 (95% CI, 0.98-1.04).

Although mortality from leukaemia was also examined in this cohort, neither the cohort analysis (Yiin et al., 2005) or the nested case-control study on leukaemia (Kubale et al., 2005) examined the association with exposure to welding fumes. However, in a previous case-control study of leukaemia within the Portsmouth Naval Shipyard cohort (Stern et al., 1986), an increased risk of leukaemia (OR, 3.19; 95% CI, 1.09–9.37), particularly myeloid leukaemia (OR, 6.23; 95% CI, 1.64–23.64), was found among welders after adjustment for radiation exposure,

employment as electrician, and exposure to solvents. [The Working Group noted that the focus of the Portsmouth Naval Shipyard study was ionizing radiation exposure; despite the comprehensive exposure assessment, the effects of exposure to welding fumes were not explored in detail.]

## (c) Other welding industries

The other cohort studies evaluated cancer mortality or incidence in welders in a variety of industries including heavy equipment manufacturing plants, automobile assembly, stamp and engine plants, foundries, metal shops, telephone line workers, and nuclear plants. Some studies assembled workers from a large number of companies by using occupational registries or union records. Studies reporting on cancer of the lung are organized based on information regarding potential exposure to asbestos, and then by chronological date. Studies of welders with minimum exposure to asbestos include a cohort of automobile assembly and stamp workers (Park et al., 1994) and a cohort of heavy equipment manufacturing workers (Steenland, 2002). Exposure to asbestos may have been more substantial in the Norwegian study of boiler welders (Danielsen et al., 1996) and in a study of French telephone line workers (Meguellati-<u>Hakkas et al., 2006</u>). The remaining studies provided no or little information (such as use of asbestos or cases of mesothelioma) to evaluate potential confounding from exposure to asbestos (Dunn & Weir, 1968; Polednak, 1981; Steenland et al., 1986; Sorahan et al., 1994; Austin et al., <u>1997</u>). With the exception of the French study of telephone line workers which assessed cumulative exposure to welding fumes, all of the other studies assessed exposure by occupation as a welder.

Park et al. (1994) conducted a cohort study of hourly employees who worked at an automotive metal stamping and assembly complex. Welding in the stamp plant was performed on sheet metal.

Using controls who did not die from cancers of the lung, stomach, pancreas, and haematopoietic system, standardized mortality odds ratio (MOR) for cancer of the lung was significantly elevated for welding (MOR, 2.73; 95% CI, 1.20-6.30; 7 exposed deaths) and increased with increasing duration of employment in welding areas (although based on a small number of deaths). The highest mortality odds ratios were reported in logistic regression models that combined previous welding employment with employment in the stamping plant and models using short latency weighting. [The Working Group noted that potential exposure to asbestos was limited to a few workers in assembly operations and unlikely to be a concern for welders. No information was available on smoking habits; however, internal analyses helped to mitigate concerns from tobacco smoking. The limitations of the study included the healthy worker effect, a young cohort, and a short follow-up (5% of the cohort had died).]

Cancer mortality was evaluated in a cohort of male MS welders and non-welders employed at three heavy equipment manufacturing plants in Illinois, USA. Importantly, these workers were not exposed to asbestos, nickel, or chromium (Steenland, 2002). Workers who only worked as flame-cutters or burners, or on maintenance, were excluded. The 2002 study updated the findings of the original study (Steenland et al., 1991) with 10 years of additional follow-up. The average time since first exposure was 20 years, and 23% of the population had died. An excess risk of mortality from cancer of the lung was observed among welders compared with men in the general population (SMR, 1.47; 95% CI, 1.19–1.79; 97 deaths) or with male non-welder workers (standardized rate ratio (SRR), 1.22; 95% CI, 0.93–1.59). In internal analysis using a 10-year lagged time, standardized rate ratios increased with increasing employment duration with the exception of the longest employment duration, which showed

increased risk. Trends for years of exposure (P for trend, 0.33) or log years of exposure (P for trend, 0.17) were not statistically significant. Based on a cross-sectional survey, welders and non-welders in the cohort smoked more than the general population. The authors estimated that smoking differences would result in a risk ratio of 1.08 between welders and non-welders within the cohort, and 1.23 between cohort welders and the US population. [The strengths of the study included an internal comparison group, information on smoking habits, little or no exposure to asbestos, a relatively large number of cases, and adequate follow-up. The major limitation was the lack of semiquantitative or quantitative exposure assessment to welding fumes.]

Danielsen et al. (1996) evaluated cancer incidence among welders listed in the Norway Registry of Boiler Welders from 385 different businesses throughout Norway. Standardized incidence ratios for cancer of the lung were 1.33 (95% CI, 1.00-1.74; 50 exposed cases) for all boiler welders and 1.03 (95% CI, 0.41-2.15; 6 exposed cases) for the subset of SS welders. In analysis by date of first registration, boiler welders who first registered during the periods 1950-1959 and 1970-1982 had an increased risk of cancer of the lung. Asbestos was used until the mid-1970s and an excess of pleural mesotheliomas was observed among welders (3 cases among boiler welders and 1 case among SS welders). The standardized incidence ratio for cancer of the kidney for boiler welders was 1.78 (95% CI, 1.07–2.78; 19 exposed cases).

A cohort study of cancer mortality was conducted among 34 305 French male telephone line workers exposed to low concentrations of asbestos during the installation of telephone cables (Meguellati-Hakkas et al., 2006). The cohort included both prevalent hires (as of 1978) as well as men newly hired during 1978–1994, and the workers were followed until 1996. In multivariable models adjusting for age, calendar period, and occupational co-exposures (asbestos,

polycyclic aromatic hydrocarbons (PAHs), and engine exhausts), small, non-significant elevated risks of cancer of the lung were observed in all cumulative exposure categories of arc welding; the risk was somewhat higher in the longest exposure duration category (RR, 1.4; 95% CI, 0.7-2.8; 63 deaths). Exposure to asbestos but not engine exhaust or PAHs was associated with mortality from cancer of the lung in this study. [The advantages of this study were the use of a semiquantitative exposure assessment to arc welding and the large numbers of deaths from cancer of the lung for mortality analysis. The focus of the study was exposure to asbestos; exposure to welding fumes was included in the analyses as a potential confounder for the association with cancer of the lung. Exposure to welding fumes did not appear to be substantial in this cohort; 80% of deaths occurred in workers exposed to less than 0.04 cumulative exposure years of welding.]

Dunn & Weir (1968) conducted a prospective study of male workers employed in several different occupation groups in California, USA, chosen based on case-control studies which suggested a possible link with risk of cancer of the lung. The workers were selected from union mailing lists and questionnaires. No excess deaths from cancer of the lung occurred among the combined category of welders and burners compared with the expected deaths (adjusted for age and smoking) for the total study population (e.g. workers). [The Working Group noted that expected numbers included workers that were exposed to asbestos, and that the follow-up period was short (average 7 years).]

A cohort study was conducted of white male welders employed at three Oak Ridge nuclear plants in the USA (Polednak, 1981). The welders were divided into two groups: the first group worked at a facility (K-25 plant) that welded nickel-alloy pipes; and the second group ("other welders") worked with MS, SS, and other metals. Mortality from cancer of the lung was elevated in both type of welders, and was somewhat higher

among the "other welders" group (SMR, 1.75; 95% CI, 0.84-3.22; 10 exposed deaths) than the nickel-alloy workers ([SMR, 1.26; 95% CI, 0.51–2.62]; 7 exposed deaths); most of the risk in the latter group occurred in workers who had been employed for more than 50 weeks. [The available data on tobacco smoking suggested that a greater proportion of welders smoked compared with the general public, and tobacco smoking may be a potential confounder for cancer of the lung in this welder group. In contrast, nickel-alloy workers had smoking habits which were similar to that of the general public. The excess risk of cancer of the lung among K-25 plant workers may have been due to exposure to nickel; concentrations of nickel were above the National Institute for Occupational Safety and Health recommended standard of 0.015 mg/m<sup>3</sup>. Other study limitations were the small numbers of exposed cases and the potential for a healthy worker effect (SMR, 0.87 for all causes). No information was provided about exposure to ionizing radiation.]

Sorahan et al. (1994) updated a cohort of foundry workers previously investigated by Fletcher & Ades (1984) and Sorahan & Cooke (1989). Workers were classified into 25 occupational categories, according to the first job held. An increased standardized mortality ratio for cancer of the lung was shown for "burning and welding" in the fettling shop, but higher standardized mortality ratios were found for other occupations in the fettling shop. Welding "pattern/machine/maintenance/inspection" was not associated with elevated mortality from cancer of the lung. The numbers of deaths from cancer of the stomach were below expectations in both groups. Mortality from other cancers was not reported by occupational category. [The Working Group noted that the cohort included only a small number of welders, and no exposure data were available. However, at least some workers would have been exposed to foundry processes.]

A cohort of members of a metal trade union, including welders and non-welders, was investigated by Beaumont & Weiss (1980, 1981). Welders had an elevated mortality from cancer of the lung (SMR, 1.32), which increased with time since first employment (SMR, 1.74 for 20 years since first employment). A reanalysis of these data (Steenland et al., 1986) using Cox regression estimated the cancer of the lung rate ratio for welders versus non-welders as 1.29 (P = 0.17; CI not reported). [No exposure data were available.]

A nested case–control study of cancer of the lung (231 deaths, 408 controls) was conducted among workers at a foundry and two engine plants (Austin et al., 1997). Work histories were obtained from plant personnel files; smoking data were collected by telephone interview of next-of-kin for the cases, and of the subject (64%) or a next-of-kin for controls. After adjustment for smoking, no elevation of mortality from cancer of the lung was found in the welding group. This study did not identify any specific job or plant area with an increased risk of cancer of the lung.

#### (d) Less informative industrial cohort studies

The Working Group reviewed several additional studies of welders that were considered to be less informative because they were not specific to welding (McMillan & Pethybridge 1983; Silverstein et al., 1985; Verma et al., 1992; de Silva et al., 1999; Krstev et al., 2007; Wu et al., 2013) and/or had other limitations in the design or analysis (McMillan & Pethybridge, 1983; Verma et al., 1992; de Silva et al., 1999). Two studies were limited in their ability to detect an association between cancer of the lung and welding; one study included some welders in the reference group (McMillan & Pethybridge, 1983) and the other study was very small and had inadequate follow-up (de Silva et al., 1999). In the study by Verma et al. (1992), welders worked in a tank house in the vicinity of tar-laying operations and were exposed to high levels of PAHs (which were measured in the study).

# (e) Cohort studies that did not report on cancer of the lung

See Table 2.3

Howe et al. (1983) reported on mortality from cancer of the brain of a cohort of male pensioners exposed to welding fumes during employment with the Canadian National Railway company over the period 1965–1977. The standardized mortality ratio for cancer of the brain was 3.18 (95% CI, 1.53–5.86; 10 exposed deaths). [The Working Group noted that there was potential for exposure misclassification due to a lack of detailed information or lifetime work history. No information was available on which occupations were considered to entail exposure to welding fumes, or on smoking and potential co-exposures.]

A study of paternal exposure to welding and childhood malignancies was conducted among a cohort of men employed at 74 Danish MS or SS manufacturing companies (Bonde et al., 1992). The study was based on the Danish welding cohort study (Hansen et al., 1996). Standardized incidence ratios were close to unity for childhood cancers for offspring of SS welders (2 cases of cancer) and those of MS welders (4 cases of cancer). [The study had limited power to detect childhood cancer risks.]

To examine cancer incidence in workers exposed to high levels of extremely low frequency electromagnetic fields (ELF-EMF), a cohort with an elevated prevalence of electric resistance welders was established (Håkansson et al., 2002). The cohort comprised all subjects ever employed during 1985–1994 in industries assumed to use electric resistance welding (537 692 men and 180 29 women). A case–control study on tumours of the endocrine glands was nested in this cohort, including 140 cases and 1306 controls frequency-matched by sex and age (Håkansson et al., 2005). An increased risk of tumours of the endocrine glands was found among welders (OR, 2.1; 95% CI, 1.3–3.5), which

was limited to arc welding (OR, 2.9; 95% CI, 1.6–5.3). There was no evidence of an association with electric resistance welding (OR, 1.1; 95% CI, 0.5–2.4). Among arc welders, the risk increased with the average number of welding hours per week (*P* for trend, 0.63). Elevated odds ratios were observed for all subtypes (adrenal glands, parathyroid gland, pituitary gland). [Considering the elevated risks of arc welding and not electric resistance welding, ELF-EMF does not appear to explain these results.]

## 2.4.2 Population-based cohorts

See Table 2.1

Several studies evaluated the risk of exposure to welding fumes or occupation as a welder in population-based cohorts. In general, there was lower confidence in the exposure information than from industrial cohorts. The studies include: (1) three studies that used a JEM to assess exposure to welding fumes based on occupational questionnaire data; (2) two record-linkage studies; (3) a prospective cohort evaluating occupation and different types of cancer in Europe; and (4) a prospective cohort study evaluating the incidence of cancer of the lung among frequent smokers enrolled in a lung screening randomized trial.

A cohort of 869 men from the town of Zutphen, the Netherlands, born between 1900 and 1920, was used to compare the performance of different methods of exposure assessment in an analysis of incidence of cancer of the lung (Kromhout et al., 1992). Exposure to welding fumes and soldering fumes was assessed with a general JEM (Pannett et al., 1985) and a population-specific JEM, developed from self-reported exposures collected in a sample of the cohort. No clear associations were found between risk of cancer of the lung and exposure to fumes evaluated by the general JEM. When exposures were assessed by the population-specific JEM, elevated hazard ratios for cancer of the lung,

adjusted for smoking, were found for exposure to welding fumes (HR, 1.93; 95% CI, 1.05–3.55) and soldering fumes (HR, 2.24; 95% CI, 1.17–4.29).

A population-based cohort study was conducted in the Netherlands among 58 279 men, aged 55-69 years, who completed a self-administered questionnaire in 1986 and were followed up for incidence of cancer of the lung until 1990 (van Loon et al., 1997a). [The follow-up of this cohort was short and exposure was assessed retrospectively at baseline.] After adjustment for smoking, diet, and other occupational exposures, the relative risk for ever exposure to welding fumes was not increased (RR, 0.86; 95% CI, 0.46–1.58), and no clear trend was observed with the score of cumulative exposure. In the same cohort, the adjusted relative risk for incidence of cancer of the prostate (Zeegers et al., 2004) was 1.41 (95% CI, 0.51-3.88; 12 exposed cases) for those ever employed as a welder.

The cohort of 1.2 million economically active Finnish men who participated in the 1970 national census was followed for incidence of cancer of the lung during 1971-1995 (Siew et al., 2008). The Finnish job-exposure matrix (FINJEM) was linked to the occupation held for the longest time up to 1970 to assess cumulative exposure to welding fumes, iron fumes, asbestos, silica, chromium, nickel, lead, benzo[*a*]pyrene, and smoking. Relative risks adjusted for age, smoking, socioeconomic status, and exposure to asbestos and silica were estimated using the Poisson regression. The standardized incidence ratio of cancer of the lung was 1.31 (95% CI, 0.84-1.95) among welders in the building industry, 1.05 (95% CI, 0.69–1.55) for welders in shipyards, 1.39 (95% CI, 1.14-1.69) among welders not otherwise specified, and 0.95 (95% CI, 0.78–1.15) among SS welders. The risk for cancer of the lung increased as the cumulative exposure to welding fumes increased, and the dose-response relationship was more evident for squamous cell carcinomas than for other histological types. An increase in risk of cancer of the

lung with cumulative exposure to iron fumes was also found in this study. Exposures to iron fumes, chromium, nickel, lead, and benzo[a]pyrene were so strongly correlated with exposure to welding fumes that they could not be included in the same statistical model. To assess any potential confounding effect, additional analyses excluding workers with exposures to moderate or high levels of iron fumes, chromium, nickel, lead, and benzo[a]pyrene were performed. These exclusions did not markedly change the estimated risks associated with exposure to welding fumes. [The main strengths of this study were the large number of workers, the semi-quantitative assessment of exposure to welding fumes, and the availability of data on major potential confounders.

Pukkala et al. (2009) linked individual records of 14.9 million people aged 30-64 years in the 1960, 1970, 1980/1981, and/or 1990 censuses in Denmark, Finland, Iceland, Norway, and Sweden to the 2.8 million incident cancer cases recorded in cancer registries for these people in a follow-up study until around 2005. The original national occupation codes were converted to a common classification with 53 occupational categories. As Danish welders were included in the broader group of mechanics workers, they were excluded from the analysis of welders which concerned 74 857 men and 2606 women. Results were reported for 49 cancer sites, some of them further divided according to subsite and histological type. Among men, elevated standardized incidence ratios were found for cancer of the lung (SIR, 1.33; 95% CI, 1.27–1.40), mesothelioma (SIR, 1.79; 95% CI, 1.44–2.20), cancer of the kidney (SIR, 1.25; 95% CI, 1.14–1.36), particularly cancer of the renal pelvis (SIR, 1.39; 95% CI, 1.05–1.80), and acute myeloid leukaemia (SIR, 1.23; 95% CI, 0.99-1.52). Thirty-six cases of ocular melanoma were observed (SIR, 1.07; 95% CI, 0.75-1.48). Among women the number of cases was small for most cancer sites, but an increased risk of cancer of the lung was also reported (SIR, 1.70;

95% CI, 1.10–2.51). No case of mesothelioma was observed among female welders (vs 0.3 expected). In men, elevated standardized incidence ratios were observed for all histological types of cancer of the lung, whereas in women increased risk was limited to histological types other than adenocarcinoma. No data on smoking habits were available, but an earlier study based on a previous follow-up of the Norwegian component of this study (Haldorsen et al., 2004) showed that, in male welders, indirect adjustment for smoking increased the cancer of the lung standardized incidence ratio from 1.31 to 1.48.

The Swedish component of this study overlaps several other record-linkage studies conducted in Sweden (Englund et al., 1982; Sjögren & Carstensen, 1986; McLaughlin et al., 1987; Alguacil et al., 2003). These studies were considered to be subsumed by the Pukkala et al. (2009) study, and are not discussed further.

Cancer risks associated with welding were evaluated by linking records on current job from the 1991 Canadian census of 1.1 million male workers with the Canadian Cancer Registry, and followed up until 2010 (MacLeod et al., 2017). Welders and occasional welders were compared with non-welders. Among welders, elevated risks were found for cancer of the lung (HR, 1.16; 95% CI, 1.03-1.31), mesothelioma (HR, 1.78; 95% CI, 1.01-3.18), cancer of the bladder (HR, 1.40; 95% CI, 1.15-1.70), and cancer of the kidney (HR, 1.30; 95% CI, 1.01-1.67). Five cases of ocular melanoma were observed (HR, 1.55; 95% CI, 0.64–3.76). The risks of cancer of the lung and mesothelioma were increased among occasional welders, but no excess risks were found for other cancer sites. Analyses by industry showed higher hazard ratios for cancer of the lung among welders in vehicle repair, shipbuilding and repair, and construction. Welders in construction also had an elevated risk of mesothelioma. Less than 5 mesothelioma cases were observed in other industries, and risk estimates were not reported. The risk of cancers of the bladder and kidney was increased for welders in all industry groups. By histological type of cancer of the lung, the strongest associations were found for carcinomas of the small cell and squamous cell. In analyses restricted to blue-collar workers, risk estimates were slightly attenuated for cancer of the lung and mesothelioma, and slightly increased for cancers of the bladder and kidney, and ocular melanoma.

Associations between occupation and cancer incidence were investigated in several studies which were part of the European Prospective Investigation into Cancer and Nutrition (EPIC). These studies assessed the risk of cancer of the lung (Veglia et al., 2007), cancer of the bladder (Pesch et al., 2013), lymphoma (Neasham et al., 2011), and leukaemia (Saberi Hosnijeh et al., 2013). Data on 52 a priori hazardous job titles were collected through standardized questionnaires. After adjustment for smoking, increased risks of cancer of the lung were associated with having ever worked as a welder (RR, 1.67; 95% CI, 1.20–2.30) or in the welding shop (RR, 1.55; 95% CI, 1.20-2.10). Elevated risks of cancer of the bladder were also found for welders (RR, 1.39; 95% CI, 0.85-2.27) and for those who worked in a welding shop (RR, 1.54; 95% CI, 1.01-2.34). There was no indication of an increased risk of leukaemia or lymphoma in welding occupations.

Wong et al. (2017) analysed the association between the incidence of cancer of the lung and occupation as metalworker (foundry and welders) in a cohort of frequent smokers who were enrolled in 33 centres across the USA, included in the National Lung Screening Trial (NLST). (Workers from both arms of the randomized control trial were combined in the analysis after 5–7 years of follow-up.) The adjusted hazard ratio of incidence of cancer of the lung for ever employed as a welder (excluding foundry workers and those who previously worked in high-risk occupations, such as asbestos workers) was 1.12 (95% CI, 0.91–1.37; 101 exposed cases). In analyses by cancer subtypes, the strongest association

with welding was found for squamous cell carcinoma (adjusted HR, 1.91; 95% CI, 1.13–3.22; 11 cases) for those who had ever worked as a welder for 25 years or more, compared with workers without a history of metalwork (*P* for trend for employment duration, 0.003). [The strengths of this study included its prospective design, large number of cases, information on cancer of the lung subtypes, smoking habits, past exposure to asbestos and other carcinogens, and multivariate and sensitivity analyses. The study was limited by its short follow-up and lack of detailed exposure information for welding and occupational co-exposures.]

## 2.5 Case-control studies

## 2.5.1 Cancer of the lung

See Table 2.5 and Table 2.6

The Working Group identified more than 20 cancer of the lung case-control studies that reported on the association between welding-related occupations or exposure to welding fumes and cancer of the lung ( $\underline{\text{Table 2.5}}$ ). These include a pooled analysis of case-control studies (Kendzia et al., 2013) and a multicentre case-control study ('t Mannetje et al., 2012). The study by 't Mannetje et al. (2012) was included in the pooled analysis by Kendzia et al. (2013) for occupation as a welder; it is included in this review as it presents further analysis on exposure to welding fumes that was not presented in the analysis by Kendzia et al. (2013). We excluded studies that were superseded by subsequent publications using the same data (Jöckel et al., 1994; Richiardi et al. 2004; Brenner et al., 2010; Guida et al., 2011), but we retained studies (listed in Table 2.5) that were included in the pooling study if the original publication provided additional information. We also excluded studies whose job-exposure classification was so broad that it did not allow an assessment of the risk among welders specifically (Matos et al., 1998; Droste et al., 1999).

Two studies conducted in different US coastal regions, with a reference category restricted to shipyard workers that consisted of non-welders likely exposed to asbestos (Blot et al., 1978, 1980), were also excluded. A case-control study that only included welders as cases and controls (Hull et al., 1989) and a case-case study (Paris et al., 2010) are not reported in Table 2.5 because they do not allow estimation of the risk of cancer of the lung among welders per se.

Most case-control studies reported elevated risks for workers employed as welders who reported welding as their job task, or workers who reported exposure to welding fumes (Breslow et al., 1954; Gerin et al., 1984; Buiatti et al., 1985; Kjuus et al., 1986; Lerchen et al., 1987; Schoenberg et al., 1987; Benhamou et al., 1988; Ronco et al., 1988; Zahm et al., 1989; Morabia et al., 1992; Jöckel et al., 1998; Pezzotto & Poletto, 1999; Gustavsson et al., 2000; Soskolne et al., 2007; Brenner et al., 2010; Corbin et al., 2011; Calvert et al., 2012; 't Mannetje et al., 2012; Tse et al., 2012; Vallières et al., 2012; Kendzia et al., 2013; Luqman et al., 2014; Matrat et al., 2016), but many of the observed associations were statistically non-significant [probably due to small sample sizes]. Two studies reported risk estimates close to unity (Pezzotto & Poletto, 1999; Vallières et al., 2012), but none reported odds ratios below unity for ever welding. Most studies were able to adjust for smoking, but adjustment for occupational co-exposures, in particular adjustment for asbestos exposure, was possible in fewer studies. Most studies report risk estimates only for men due to an insufficient number of women in this occupational group.

The SYNERGY pooling study with 15 483 male cases (568 of them being welders) and 18 388 male controls (427 of them being welders) is one of the most informative case–control studies on welding occupation and cancer of the lung (Kendzia et al., 2013). This analysis based on job title included adjustment for age, study centre, smoking, and occupations known to be

associated with cancer of the lung (so-called List A jobs, many of them entailing exposure to asbestos) resulted in an adjusted odds ratio of 1.50 (95% CI, 1.20-1.88) for the longest held job as a welder. [The Working Group noted that this study was adjusted for asbestos exposure, but not specifically for welding-related asbestos exposure.] Jobs entailing occasional welding were also associated with elevated risks, but the risk estimates were smaller compared with that of regular welders. Compared with never welders, the odds ratios increased with duration of occupation as a welder from 1 to less than 3 years (OR, 1.14; 95% CI, 0.80-1.61), 3 to less than 10 years (OR, 1.46; 95% CI, 1.26-1.91), 10 to 25 years or less (OR, 1.38; 95% CI, 1.06-1.79), to more than 25 years (OR, 1.77; 95% CI, 1.31-2.39) (P for trend, < 0.0001). When stratified by histological type, odds ratios appeared to be strongest for carcinomas of the squamous cell and small cell and somewhat lower for adenocarcinomas. For never-smoker welders, the odds ratio for cancer of the lung was 2.04 (95% CI, 1.16-3.61). The overlap between this biggest pooling study (SYNERGY) (Kendzia et al., 2013), which includes 22 case-control studies conducted between 1985 and 2010, and the overlap among these other studies, is summarized in Table 2.6. Results are reported by the individual studies included in the SYNERGY pooled analysis when not reported in the pooled analysis. The study by Schoenberg et al. (1987) was not included in the pooled analysis by Kendzia et al. (2013).

Confounding by asbestos is a major concern in the assessment of the association between welding and cancer of the lung. Workers may be exposed to asbestos as a bystander in ship-yards, but also from heat-protective clothing or blankets used to cover the weld to prevent abrupt cooling. Studies that controlled for asbestos, and additionally for smoking, are described in the following.

A study in the USA (<u>Schoenberg et al. 1987</u>) not included in the analysis by <u>Kendzia et al.</u>

(2013) reported an odds ratio of 3.5 (95% CI, 1.8–6.6) in welders overall and an odds ratio of 2.5 (95% CI, 1.1–5.5) in welders not exposed to asbestos, where exposure was classified by an industrial hygienist.

In a German study, Jöckel et al. (1998) reported a detailed assessment of exposure to welding fumes and exposure to asbestos through a set of job-specific questionnaires (around 20 questions) and a supplementary questionnaire on welding. After adjustment for smoking and asbestos exposure, the odds ratio for ever being employed as a welder was 1.93 (95% CI, 1.03-3.61). In this study, ever being exposed to welding fumes and gases was associated with a slightly elevated risk (OR, 1.25; 95% CI, 0.94–1.65), but no dose-effect relationship was seen with cumulative exposure expressed in lifetime hours of welding after adjustment for smoking and asbestos. Odds ratios were reported of 1.38 (95% CI, 0.91-2.09) for less than 1000 hours, 1.14 (95% CI, 0.73–1.79) for 1000–6000 hours, and 1.10 (95% CI, 0.73-1.66) for more than 6000 hours. [There is partial overlap with the study by Kendzia et al. (2013).]

A Swedish study reported that 62% of welding entailed asbestos exposure, according to a detailed exposure assessment by an industrial hygienist (Gustavsson et al., 2000). Based on a self-completed questionnaire that gathered information on the lifetime occupational history, including company name and location, occupation, and work tasks for each job held for at least 1 year, an industrial hygienist performed a caseby-case classification of the intensity and probability (0, 20, 50, or 80%) of exposure to 7 agents. Intensity units for welding were assigned as 1, 5, and 15, where 15 units corresponded to full-time employment as a MMA welder. Cumulative exposure was calculated as the product of intensity, probability, and duration of exposure over all job periods. In analysing the dose-effect relationship with cumulative welding exposure, Gustavsson et al. (2000) did not observe

Table 2.5 Case-control studies on cancer of the lung and welding or exposure to welding fumes Reference, Population size, description, Exposure **Exposed** Risk estimate Covariates Comments location. exposure assessment method category or level cases/ (95% CI) controlled enrolment/ deaths follow-up period Cases: 518 histopathologically Non-welder or [1] Strengths: careful in-person Breslow et al. 508 None (1954)verified cases of lung cancer, 25 of flame cutter (ref.) interviews; assessment of welding as a task; non-consideration of short-California, USA them women Welder or flame 10 [10.2 (1.3–79.8)] 1949-1952 Controls: 518 patients admitted to term occupations cutter of > 5 yr the hospital around the same time Limitations: no age-adjustment; Non-welder (ref.) 479 [1] None of the same age (within 5 yr), sex, crude adjustment for smoking in Welders and sheet [7.2 (1.6-31.7)] 14 and race for a condition other than five categories; smoking status metal workers cancer or a chest disease, chosen at missing in 5% of subjects; small doing welding random as a matched control for number of welders > 5 yr each case Welders and sheet 14 [7.66 (1.36–43.23)] Smoking Exposure assessment method: metal workers questionnaire; job title doing welding > 5 yr Overlaps with the study of Vallières Gerin et al. Cases: 246 male cancer cases aged Welders Age, (1984)35–70 yr from entire Montreal smoking, et al. (2012) and therefore also Non-welders (ref.) 227 1 population at major hospitals for SES, ethnicity with the SYNERGY pooling study Montreal, All 12 2.4(1.0-5.4)Canada 12 tumour sites identified through (Kendzia et al., 2013) With Ni exposure 3.3 (1.2-9.2) 10 1979-1982 hospital pathology department Strengths: individual expert Without Ni 2 1.2(0.1-9.4)(1343 patients of whom 246 were assessment; specific and detailed exposure diagnosed with lung cancer) assessment of exposure to Ni and Cr Controls: 1241, 144 general-Limitations: no control for asbestos population healthy subjects and all or other occupational carcinogens cases of the remaining 11 tumour but stratification by Ni exposure sites Exposure assessment method: questionnaire; individual expert assessment of exposure (focusing on Ni and Cr) based on job histories and a semi-structured probing section

Table 2.5 (co	ontinued)					
Reference, location, enrolment/ follow-up period	Population size, description, exposure assessment method	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Buiatti et al. (1985) Florence, Italy 1981–1983	Cases: 376 histologically confirmed primary lung cancer cases admitted to the hospital serving as the referral centre for all lung cancers in the province of Florence (340 men and 36 women); patients not resident in the metropolitan area of Florence excluded Controls: 892 controls from the medical service of the same hospital, frequency-matched by sex, age (± 5 yr), date of admission (± 3 mo), and smoking status (7 categories) with discharge diagnoses other than lung cancer Exposure assessment method: questionnaire; personal interview including all jobs held for > 1 yr and an exposure checklist of 16 known/suspected carcinogens	Men Never welder (ref.) Welder	NR 7	1 2.8 (0.9–8.5)	Age, smoking, place of birth	Welding OR reported for men only Strengths: diligent consideration of possible selection biases possibly due to the hospital-based study design Limitations: small number; no adjustment for occupational co- exposure

Reference, location, enrolment/ follow-up period	Population size, description, exposure assessment method	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Kjuus et al.	Cases: 176 male incident lung	Exposed for > 3 yr			Smoking	Results were similar for matched
1979–1983 diagnosis of lung cancer	to the medical ward with the recent diagnosis of lung cancer Welding (ref.)  Controls: 176 age-matched controls  Welding (all types) 28 1.9 (0.9-3)	Not exposed to welding (ref.)	148	eac	and unmatched analyses (accounting for age), but it is	
		•	28	1.9 (0.9-3.7)		unclear whether this applies to
		3.3 (1.2–9.3)		unclear whether this applies to welding Strengths: case-control status blinded in 90% of interviews; detailed work history included job descriptions; additional questionnaire on 17 agents and 5 specific work processes; diligent analysis including several sensitivity analyses to assess potential biases Limitations: small numbers; multiple comparisons and collinearity of exposures; age-adjustment not specifically mentioned for the analysis of welders		

Table 2.5 (continued)

Reference, location, enrolment/ follow-up period	Population size, description, exposure assessment method	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Lerchen et al. (1987) New Mexico, USA 1980–1982	Cases: 506 Hispanic white and other white residents aged 25–84 yr with primary lung cancer identified by the New Mexico Tumor Registry; 333 men and 173 women Controls: 771; ~1.5 controls per case frequency-matched by sex, ethnicity, and 10 yr age category, randomly selected from residential telephone numbers and (for subjects aged > 65 yr) from Medicare roster; 499 men and 272 women; response proportion 83% (2% next-of-kin) Exposure assessment method: questionnaire; personal interview including lifetime occupational history and self-reported agent exposures for each job held for > 6 mo from age 12 yr; exclusion of subjects with < 20 yr of employment	Male welders Never employed as welders or in shipyard (ref.) All industries Shipyard industry Other industries	NR 19 6 13	1 3.2 (1.4–7.4) 2.2 (0.5–9.1) 3.8 (1.4–10.7)	Age, ethnicity, smoking	Welding risk estimates only reported for males Strengths: personal interview; jobs coded according to standard classifications and to an a priori list of high-risk occupations; stratification by industry (shipyard, other) Limitations: high proportion of next-of-kin in cases but not in controls

Table 2.5 (	Table 2.5 (continued)								
Reference, location, enrolment/ follow-up period	Population size, description, exposure assessment method	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments			
Schoenberg et al. (1987) New Jersey, USA 1980–1981	Cases: 763 white male residents with incident histologically confirmed cancer of the lung trachea and bronchus, identified through reporting system based on pathology departments and cancer registry; response 70.4% Controls: 900; 1415 total general-population white male controls identified through death certificates and driver's license files (randomly), frequency matched by race, age, and area of residence; additionally matched for closest date of death for cases with next-of-kin respondent; deaths from lung cancer or respiratory disease excluded Exposure assessment method: questionnaire; personal interview including the history of all jobs held for > 3 mo since age 12 yr (job title, employer, type of business, tasks, materials handled, agent exposures); supplementary questions for shipbuilding workers; review of reported asbestos exposure by an industrial hygienist	Welders or burners Combined welders Combined welders with no asbestos exposure	NR 33 17	3.8 (1.8–7.8) 3.5 (1.8–6.6) 2.5 (1.1–5.5)	Age, respondent type, smoking, study area, education, vegetable intake	Enrolment from six geographic areas, two of which had heavy concentrations of shipyard workers; reported ORs refer to welders in shipbuilding Strengths: verification of self-reported asbestos exposure by industrial hygienist blinded for case−control status; in-depth analysis of job tasks in shipbuilding; stratification by asbestos exposure (yes/no) Limitations: limited adjustment for smoking (never, cigars, or < 10 cigarettes/d, 10−29 cigarettes/d, ≥ 30 cigarettes/d, unknown) that lacked information on smoking duration			

Table 2.5 (continued)

Reference, location, enrolment/ follow-up period	Population size, description, exposure assessment method	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Benhamou et al. (1988) France 1976–1980	Cases: 1334 male cases with histologically confirmed lung cancer Controls: 2409; 1 or 2 hospital controls with nonsmoking related diseases were matched per case on sex, age at diagnosis (± 5 yr), hospital of admission, and interviewer Exposure assessment method: questionnaire; job history (jobs and duration of occupation); expert assessment of the data	Men only Never welders or flame cutters (ref.) Welders and flame cutters	1316 18	1 1.42 (0.79–2.88)	Age, sex, hospital admission, interviewer, smoking	Analysis restricted to male nonsmokers or male exclusive cigarette smokers Strengths: complete job history Limitations: crude adjustment for smoking (smoking status, age at starting (2 categories), frequency (2 categories), duration (2 categories); no adjustment for occupational carcinogens
Ronco et al. (1988) Turin, north Italy 1976–1980	Cases: 126 male residents who died from lung cancer from 1976–1980 Controls: 384, a random sample of men who died from other causes during 1976–1980, matched 3:1 by year of death and 10-yr age group (30–39 to 80–89); deaths from bladder and respiratory cancer excluded Exposure assessment method: questionnaire; next-of-kin interview at home (75–76%) or by telephone, including lifelong occupational history; job titles were coded blindly for case–control status according to ISCO and ICIT	Not welders (ref.) Welders	120 6	1 2.93 (0.87–9.82)	Age, smoking, other occupations	Strengths: detailed adjustment for smoking and List A/B jobs <sup>a</sup> Limitations: cause of death obtained from local death registers; next-of-kin interview; exposure classification only based on job title

Reference, location, enrolment/ follow-up period	Population size, description, exposure assessment method	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Zahm et al. (1989) Missouri, USA 1980–1985	Cases: 4431 histologically confirmed lung cancer cases identified through Missouri Cancer Registry; all white men Controls: 11 326 cancer controls identified through Missouri Cancer Registry from white male residents excluding cancer of the lip, oral cavity, oesophagus, lung, bladder, ill-defined/unknown sites Exposure assessment method: smoking status and occupation at the time of diagnosis obtained from medical records; codable information available from 52% of cases and 45% of controls; among subjects with known occupations, smoking status was unknown in 15% of cases and 37% of controls	Welders and solders All Adenocarcinoma SCC Small cell/oat cell Other	ers vs. all oth 29 8 15 2 4	er occupations 1.2 (0.7–2.1) 1.7 (0.7–3.8) 1.7 (0.9–3.3) 0.4 (0.1–1.8) 0.8 (0.2–2.2)	Age, smoking	Strengths: large sample size; stratification by histological type Limitations: non-standardized assessment of occupation, only current job; crude adjustment for smoking (never, ex-, current, unknown smoker); a high proportion of missing smoking status; crude age adjustment (0–59 60–69, >70 yr)
Morabia et al. (1992) Chicago, Birmingham, Detroit, Long Island, New York, Philadelphia, Pittsburgh, San Francisco (USA)	Cases: 1793 hospital-based male cases confirmed by histology Controls: 3228; 1 or 2 controls hospitalized for conditions not related to smoking, matched for age (5 yr), race (black/white), hospital, date of admission, and smoking history (never, ex-, current 1–19, current >20 cigarettes) Exposure assessment method: questionnaire	All other occupations; never worked as welder (ref.) Welders and flame cutters	1548 18	1 1.5 (0.8–2.7)	Age, race, smoking, region	Strengths: personal interview Limitations: contradictory statement regarding inclusion/ exclusion of smoking-related disorders in controls; only usual job title and the list of 44 exposure was asked; questionnaire version changed twice during the study; reference group not precisely defined

1980-1989

Table 2.5 (continued)

	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
West Germany 1988–1993  165 women from hospitals (females excluded from analysis) Controls: 1004 randomly drawn from a sample of mandatory residence registries, matched for region, sex, and age (±5 yr) Exposure assessment method: questionnaire; welding assessment for all workers reporting welding, regardless of job title, based on a welding-specific supplementary questionnaire; quantification of duration and frequency of each welding task; assessment of welding technique and type of metal; detailed quantitative assessment of asbestos exposure based on several job-specific questionnaires and a case-by-case expert assessment	Never exposed to welding fumes (ref.) Welder or burner Oxyacetylene welding Welding fumes Any type of welding Never < 1000 1000-6000 > 6000 Oxyacetylene welding Never < 1000 1000-6000 > 6000 Oxyacetylene welding Never < 1000 1000-6000 > 10 000 Gas-shielded welding Iron and steel welding Welding in air/space Never in industry/never welding Never in industry/ever welding Ever in industry/ever welding Ever in industry/ever welding Ever in industry/ever welding	608 75 65 91 ag: lifetime (h) 668 81 60 30 NR NR 218	1 1.11 (0.75-1.63) 0.95 (0.60-1.51) 1.46 (0.72-2.96) 3.28 3.6 1.17 (0.87-1.56)	Smoking, asbestos	Included in the pooled SYNERGY analysis (Kendzia et al., 2013) Strengths: detailed supplementary questionnaire on welding independent of job title; quantitative assessment of welding hours; assessment of type of welding; assessment of type of metal; detailed adjustment for smoking and asbestos

Reference, location, enrolment/ follow-up period	Population size, description, exposure assessment method	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Pezzotto and Poletto (1999) Rosario, Argentina 1992–1998	Cases: 367 men with newly diagnosed lung cancer from three hospitals of Rosario city; no refusals Controls: 576 selected from same hospitals, admitted for nonsmoking related diseases; agematched (±3 yr); no refusals Exposure assessment method: questionnaire; personal interview including lifetime occupational history (job title, tasks, employer, type of industry) for each job held for > 1 yr	Administrative staff (ref.) Welders Welders (SCC) Welders (adenocarcinoma)	98 11 7 3	1 1.1 (0.4-3.1) 2.9 (1-10.1) 0.7 (0.1-3.6)	Age, smoking	Strengths: stratification by histologic type; personal interviews Limitations: subjects with more than two different jobs were excluded; small number; diagnostic validity of case status not reported; method for job classification not standard and insufficiently described

Table 2.5 (continued)

Reference, location, enrolment/ follow-up period	Population size, description, exposure assessment method	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Gustavsson et al. (2000) Stockholm, Sweden 1985–1990	Cases: 1042 men aged 40–75 yr with diagnosis of lung cancer Controls: 2364 randomly selected from the general-population registry, frequency-matched to the cases in 5-yr groups and year of inclusion (1985–1990); additional matching for vital status to balance cases and controls with regard to being alive at data collection Exposure assessment method: expert judgement; postal questionnaire on lifetime occupational history, residential history since 1950, and smoking habits, as well as on some other potential risk factors for lung cancer; completion by telephone interview; occupational history supplemented by detailed	Welding fumes: into Unexposed to welding fumes (ref.) Low Intermediate High Welding fumes: qual 1 2 3 4  Duration of exposu 0 (ref.) > 0-9	923 41 25 33 artile of cumu 29 34 27 29	1 1.67 (1.06–2.64) 1.17 (0.66–2.06) 1.42 (0.88–2.30) lative exposure 1.41 (0.83–2.40) 1.38 (0.82–2.33) 0.79 (0.45–1.36) 0.84 (0.46–1.52)	Age, year, smoking, exposure to Rn, NO <sub>x</sub> Age, year, smoking, residential, exposure to Rn, NO <sub>x</sub> , diesel, combustion products, asbestos Age, year, smoking, exposure to	Included in the pooled SYNERGY analysis (Kendzia et al., 2013) Strengths: individual exposure assessment by industrial hygienist for intensity and probability of exposure to 7 agents for each job period, blinded for case–control status; prevalence of co-exposure to 6 agents reported (62% of welding entailed asbestos exposure, 100% metal dust, and 67% other combustion products [not engine exhaust]); detailed adjustment for smoking; additional adjustment for asbestos, combustion products, and diesel exhaust; stratification by exposure intensity, cumulative exposure, and duration Limitations: no in-person interviews, only telephone in case
	questionnaire on work tasks, frequency, and location(s) for occupations involving potential exposure to motor exhaust; next- of-kin questionnaires for deceased cases/controls	10-29 ≥ 30	NR NR	1.45 (0.96–2.20) 1.25 (0.82–1.90)	Rn, NO <sub>x</sub>	of missing items; exposure metric difficult to interpret

Reference, location, enrolment/ follow-up period	Population size, description, exposure assessment method	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments	
Soskolne et al. (2007) Campania region, Italy 1988–1990	Cases: 168 patients with respiratory tract cancers (lung $n = 111$ , larynx $n = 35$ , nasal/pharynx $n = 22$ ) Controls: 247 unmatched patients without any respiratory, bladder, or oral cavity cancers, including patients having any other reason for hospitalization; hospital-based casecontrol study Exposure assessment method: expert judgement; occupational history; exposure to 20 agents classified by the industrial hygienist	No exposure to welding fumes (ref.) Exposure to welding fumes	NR 13	1 3.91 (1.03–14.95)	Age, smoking	Strengths: exposure assessment by the industrial hygienist, blinded for case—control status Limitations: variables on which the assessment of welding fume exposure was based not described; exposure assessment method not standardized; small number; crude adjustment for smoking (based on the pack-year variable: very low, low, medium, high)	
Brenner et al. (2010) Toronto, Canada 1997–2002	Cases: 445 incident cases of cancer of the trachea, bronchus, or lung diagnosed in men and women of age anada 20–84 yr from four major tertiary	Total study populat Never worked/ exposed to welding equipment (ref.)	rer worked/ 412 1 smoki osed ethnic relding educa		Age, sex, smoking, ethnicity, education	ng, analysis ( <u>Kendzia et al., 2013</u> ) ity, Strengths: exposure category ion 'welding equipment' captures non- welding occupations with welding	
	Toronto Controls: 948 (425 population; 523 hospital); population-based controls were randomly sampled from property tax assessment files $(n = 425)$ , hospital-based controls	Exposure to welding equipment Never smokers Never worked/	33 149	1.7 (1–3)	Age, sex, education, ethnicity	fume exposure; analysis of never smokers Limitations: frequency, intensity, duration of using 'welding equipment' is not stated	

exposed

to welding equipment (ref.)

Exposure

to welding equipment

were sampled from patients seen in the Mount Sinai Hospital

Family Medicine Clinic (n = 523), frequency-matched with cases on sex and ethnicity

Exposure assessment method: detailed questionnaire administered via interview either in person or

over the telephone

ethnicity

3.4 (1.1-10.4)

Table 2.5 (continued)

Reference, location, enrolment/ follow-up period	Population size, description, exposure assessment method	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Corbin et al. (2011) New Zealand 2007–2008	Cases: 457 incident cases of lung cancer aged 20–75 yr identified through the cancer registry; 53% of those eligible participated Controls: 792 controls selected from electoral rolls and recruited in two waves; frequency-matched for age distribution for lung cancer and three other cancer sites; 48% of those eligible participated Exposure assessment method: questionnaire; complete occupational history by telephone interview except for 432 controls who were interviewed face-to-face	Never employed as welder or flame cutter (ref.) Welders and flame cutters (not SBA) Welders and flame cutters (SBA)	<ul><li>445</li><li>12</li><li>12</li></ul>	1 2.50 (0.86-7.25) 1.92 (0.90-4.10)	Age, sex, smoking, Maori ethnicity, SES	Included in the pooled SYNERGY analysis (Kendzia et al., 2013); no clear association with duration of employment (data not shown) Strengths: complete job history by interview; consideration of multiple comparisons by semi-Bayes adjustment Limitations: interviewing method not fully standardized; crude adjustment for smoking
't Mannetje et al. (2012) UK, Romania, Hungary, Poland, Russian Federation, Slovakia, and Czech Republic 1998–2001	Cases: 2197 incident lung cancer (age, < 75 yr) Controls: 2295 frequency-matched on study area, sex, age (within 3 yr) and selected from hospital patients Exposure assessment method: expert judgement; face-to-face interview, and expert assessment of 70 agent exposures	Never exposed to welding fumes (ref.) Ever worked as welder/flame cutter Ever worked as welder/flame cutter Weighted duration 1–1680 1681–7000 > 7000 Trend test <i>P</i> value, 0	173 180 229	1 1.18 (0.84–1.66) 1.36 (1.00–1.86) 1.03 (0.80–1.33) 1.05 (0.82–1.36) 1.22 (0.94–1.58)	Age, centre, education, asbestos, SiO <sub>2</sub> , Ni, Cd, As, Cr, smoking Age, centre, education, As, smoking Age, centre, education, As, SiO <sub>2</sub> , Cr, smoking	Included in the pooled SYNERGY analysis (Kendzia et al., 2013); P values for interaction between welding and co-exposures were 0.03 for asbestos and 0.54 for smoking Strengths: large multicentre study that used a common protocol; standardized exposure assessment methodology and high agreement in ratings between experts; results reported by welding activity; detailed questionnaire on welding activities Limitations: possible misclassification of assessed Cr exposure

eference, cation, nrolment/ llow-up eriod	Population size, description, exposure assessment method	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Iannetje et</u>		Cumulative exposu	ire (h)			
012)		1-2520	156	0.94 (0.73-1.21)		
.)		2521-28 900	222	1.27 (0.99-1.43)		
		> 28 900	204	1.09 (0.84-1.43)		
		Trend test <i>P</i> value,	0.19			
		Duration of arc well	lding (yr)			
		Only arc welding fumes	200	1.00 (0.78–1.29)		
		1-8	70	0.92 (0.63-1.34)		
		9-25	66	1.01 (0.68-1.49)		
		> 25	63	1.09 (0.72-1.65)		
		Duration of gas we	lding (yr)			
		Only gas welding fumes	87	1.25 (0.88–1.78)		
		1-8	42	1.12 (0.69–1.82)		
		9–25	25	1.37 (0.70-2.70)		
		> 25	20	1.46 (0.72-2.94)		
		Duration of gas and	d arc welding	•	Age, centre,	
		Gas and arc welding fumes	296	1.13 (0.90–1.43)	education, As, Cd, SiO <sub>2</sub> ,	
		1-8	65	1.08 (0.72–1.61)	Cr, smoking	
		9–25	90	0.92 (0.65-1.30)		
		> 25	141	1.38 (1.00-1.90)		
		Trend test <i>P</i> value,				
		Duration of exposu chromium (yr)	ire to welding	fumes without		
		Ever exposure	393	1.14 (0.95-1.36)		
		1-8	123	0.98 (0.74-1.30)		
		9–25	117	1.00 (0.75–1.34)		
		> 25	153	1.48 (1.11–1.97)		

Table 2.5 (continued)

Reference, location, enrolment/ follow-up period	Population size, description, exposure assessment method	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled	Comments
't Mannetje et		Duration of exposu	re to welding	fumes with		
<u>al. (2012)</u> (cont.)		chromium (yr)	100	1 24 (1 04 1 71)		
(cont.)		Ever exposed	190	1.34 (1.04–1.71)		
		1-8	54	1.47 (0.94–2.30)		
		9–25	64	1.28 (0.85–1.92)		
		> 25	71	1.27 (0.87–1.85)		
		Duration of welding			Age, centre,	
		1-8	177	1.02 (0.79–1.31)	education, As, SiO <sub>2</sub> , Cr,	
		9–25	181	1.00 (0.77–1.30)	smoking	
		> 25	224	1.29 (1.00–1.67)	Sillokilig	
		Trend test <i>P</i> value, 0	0.11			
Calvert et al. (2012) California, USA 1988–2007	Cases: 110 937 male lung cancer cases identified from cancer registries, aged 18–97 yr; year of diagnosis during 1988–2007 Controls: 322 699; up to 5 cancer controls from CCR database (prostate, colon, brain, kidney, testis, bone, joint, thyroid) were matched to each case on age (±5 yr), year of diagnosis (±5 yr), race, and ethnicity; occupational cancers excluded Exposure assessment method: demographic information as recorded in the CCR includes 'usual (i.e. longest-held) industry and occupation'; information was available in 48% of all registered cases; for job title coding the narrative was searched for 90 keywords related to construction work	Welders vs Construction workers other than welders All NSCLC Small cell/oat cell Other, including mesothelioma Adenocarcinoma SCC Large cell cancer Unspecified NSCLC	216 132 29 43 62 45 6 19	2.16 (1.81–2.58) 2.10 (1.68–2.63) 2.72 (1.64–4.51) 1.97 (1.33–2.93) 1.84 (1.33–2.53) 2.48 (1.66–3.72) 1.25 (0.47–3.36) 2.95 (1.60–5.43)	None	Morbidity ORs calculated by logistic regression Strengths: large sample size; stratification by histologic subtype Limitations: no lifestyle factors assessed; smoking status unknown; no standardized assessment of occupation or industry; women excluded

Reference, location, enrolment/ follow-up period	Population size, description, exposure assessment method	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled	Comments	
Tse et al. (2012)	Cases: 1208 male histologically	Self-reported expos	ure welding f	umes	Age,	Included in the pooled SYNERGY	
China, Hong	confirmed lung cancer cases aged	All combined	112	1.69 (1.11–2.58)	smoking,	analysis (Kendzia et al., 2013); after	
Kong SAR 2004–2006	35–79 yr Controls: 1069 male randomly	Adenocarcinoma	39	1.68 (1.00-2.81)	education,	adjustment for asbestos the result did not change significantly [data	
2004-2000	selected referents living in the same districts as the cases, identified from	Self-reported welding fumes			birth place, alcohol, Rn, lung disease	not shown] Strengths: ISCO-/ ISIC-coding	
	telephone directories, frequency- matched to cases (5-yr age groups); excluding subjects with a history of	Lung (squamous cell and small cell carcinoma)	39	2.29 (1.26–4.16)	history, cancer in family,	blinded for case–control status; self reported exposures at least 1×/wk for at least 6 mo; adjustment for	
	physician-diagnosed cancer at any site (48% participation)	Duration of exposu All combined	re to welding	fumes (yr)	consumption of meat	suspected occupational carcinogens; stratification by histologic type	
	Exposure assessment method:	1 to < 19	33	3.03 (1.30-7.07)		Limitations: self-reported agent	
	questionnaire; cases were interviewed within 3 mo of	≥ 20 Adenocarcinoma	79	1.38 (0.86–2.24)		exposure (checklist of suspected carcinogens: asbestos, Ar, Ni,	carcinogens: asbestos, Ar, Ni,
	the diagnosis of lung cancer; occupational history of jobs held at	1 to < 19	16	3.82 (1.49-9.80)		Cr, tars, asphalts, SiO <sub>2</sub> , painting, pesticides, diesel engine exhaust,	
	least 1 yr (industry, job title, specific	≥ 20	23	1.18 (0.63-2.20)		cooking fumes, welding fumes,	
	tasks performed, beginning/end dates of each job period); job titles/	Self-reported durati fumes (yr)	ion of exposu	re to welding		man-made mineral fibres); no elevated risk for asbestos observed	
	industries coded according to	Squamous cell and	small cell car	cinoma		(OR, 0.8)	
	ISCO/ISIC	1 to < 19	11	4.57 (1.34–15.54)			
		≥ 20	28	1.84 (0.93-3.64)			

Table 2.5 (continued)

Reference, location, enrolment/ follow-up period	Population size, description, exposure assessment method	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Vallières et al. (2012) Montreal, Canada Study I: 1979– 1986; Study II: 1996–2001	Cases: 857 (Study I), 736 (Study II) men, incident, histologically confirmed lung tumours, aged 35–75 yr Controls: 1066 (Study I), 894 (Study II); population controls randomly selected from electoral rolls, matched by age and area of residence Exposure assessment method: expert judgement; supplementary questionnaire for welding, including questions on the type of gases used, metal welded, and h/wk and wk/yr of exposure	Arc welding fumes: Not exposed (ref.) Any level ≤ 20 > 20 Gas welding fumes Not exposed (ref.) Any level ≤ 20 > 20 Gas welding fumes SCC Not exposed (ref.) Any level Substantial level Lung (small cell/oa Not exposed (ref.) Any level Substantial level Adenocarcinoma Not exposed (ref.) Any level Substantial level SCC Not exposed (ref.) Any level	1373 220 136 84 2 exposure dur 1369 224 136 88 exposure  528 92 31 t cell) 237 47 19 356 52 19	1 1.0 (0.8–1.2) 1.1 (0.8–1.4) 0.9 (0.6–1.3) ration (yr) 1 1.1 (0.9–1.4) 1.3 (1.0–1.7) 0.9 (0.7–1.3)  1 1.1 (0.8–1.5) 1 (0.6–1.6)  1 1.3 (0.9–1.9) 1.3 (0.7–2.3)  1 1 (0.7–1.4) 1 (0.6–1.8)  1 1.1 (0.8–1.5)	Age, ethnolinguistic group, education, asbestos, respondent, study indicator, smoking	Included in the pooled SYNERGY analysis (Kendzia et al., 2013); pooled analysis of two case-control studies; women excluded because exposure prevalence was only 1%; indication of elevated risk only in never or low-frequency smokers Strengths: sophisticated exposure assessment methodology with welding exposure assessed in individuals by experts, beyond using job title only; population-based study; comprehensive confounder adjustment including asbestos; high response proportion (79–86% among cases and 69–72% among population controls) Limitations: possible exposure misclassification due to proxy interviews in 10–20% of controls and 30–40% of cases
		Substantial level	33	1.3 (0.8–2.1)		

Reference, location, enrolment/ follow-up period	Population size, description, exposure assessment method	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Vallières et al.		Small cell/oat cell				
(2012)		Not exposed (ref.)	245	1		
(cont.)		Any level	39	0.9 (0.6-1.4)		
		Substantial level Adenocarcinoma	13	0.9 (0.5–1.6)		
		Not exposed (ref.)	353	1		
		Any level	55	1 (0.7–1.4)		
		Substantial level	22	1.2 (0.7–2.1)		
		Never smokers/low-				
		Gas welding fumes not exposed (ref.)	91	1		
		Gas welding fumes, any level of exposure	33	2.8 (1.7–4.8)		
		Gas welding fumes, substantial level	15	4.3 (1.9-9.7)		
		Arc welding fumes, not exposed (ref.)	93	1		
		Arc welding fumes, any level of exposure	31	2.2 (1.3–3.7)		
		Arc welding fumes, substantial level	13	3.5 (1.6–7.8)		

Table 2.5 (continued)

Reference, location, enrolment/ follow-up period	Population size, description, exposure assessment method	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Kendzia et al. (2013) Europe, Canada, China, and New Zealand 1985–2010	Cases: 15 483; 568 cases had worked as welders Controls: 18 388; 427 controls had ever worked as welders Exposure assessment method: questionnaire; occupational and smoking histories were assessed in face-to-face interviews (81%); subjects considered exposed if job title was (1) 'welder' for ≥ 1 yr or (2) considered as potentially and occasionally involving welding activities	All occupations Never welding- related job (ref.) Welder Longest-held occupation Ever blue-collar emp Never welding- related job (ref.) Ever welder Longest-held occupation Ever welder Never welding- related job (ref.) Shipbuilding- related job (ref.) Shipbuilding and repair Construction and related building services Manufacture of machines, equipment, appliances Manufacture of motor vehicles and motor bikes	9796 568 246 12 921 93 336 352	1 1.44 (1.25-1.67) 1.50 (1.20-1.88)  1 1.33 (1.15-1.54) 1.39 (1.11-1.73)  1 1.53 (1.06-2.21) 1.47 (1.22-1.78)  1.40 (1.17-1.68)  1.30 (0.94-1.80)	Age, centre, smoking, List A job <sup>a</sup>	SYNERGY: pooled analysis of 16 studies; overlapping studies: Jöckel et al. (1998), Gustavsson et al. (2000), Richiardi et al. (2004), Brenner et al. (2010), Corbin et al. (2011), Guida et al. (2011), 't Mannetje et al. (2012), Vallières et al. (2012), Tse et al. (2012)  Strengths: large pooled analysis that allowed stratification by duration of employment as a welder, histological type, smoking status (never smokers, pack-year), type of control, and blue-collar jobs; detailed adjustment for smoking (duration, intensity, duration of quitting, type of tobacco); adjustment for List A jobsa; restriction to blue-collar workers to indirectly and more tightly control for potential confounders Limitations: analysis based on job title with no information on welding process; no specific adjustment for asbestos exposure
		Repair of transport equipment	130	1.51 (1.12–2.03)		

Reference, location, enrolment/ follow-up period	Population size, description, exposure assessment method	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Cendzia et al. 2013) cont.)		Longest-held job Never welding- related job (ref.)	12 921	1		
		Shipbuilding and repair	33	1.53 (0.89–3.41)		
		Construction and related building services	46	1.33 (0.81–2.20)		
		Manufacture of machines, equipment, appliances	104	2.11 (1.45–3.08)		
		Manufacture of motor vehicles and motor bikes	12	0.62 (0.28–1.36)		
		Repair of transport equipment	16	1.10 (0.49–2.46)		
		All cases				
		Duration as welder	(yr)			
		Never welding- related job (ref.)	12 921	1		
		1 to < 3	82	1.14 (0.80-1.61)		
		3 to < 10	171	1.46 (1.26–1.91)		
		$10 \text{ to } \le 25$	167	1.38 (1.06-1.79)		
		> 25 Trend test <i>P</i> value, <	148	1.77 (1.31–2.39)		

Table 2.5 (continued)

Reference, location, enrolment/ follow-up period	Population size, description, exposure assessment method	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Kendzia et al.		Adenocarcinoma				
(2013)		Duration as welder	r (yr)			
(cont.)		Never welding- related job (ref.)	3313	1		
		Ever welder	132	1.23 (0.99-1.53)		
		1 to < 3	18	0.84 (0.49-1.45)		
		3 to < 10	39	1.14 (0.77-1.68)		
		10 to $\leq 25$	41	1.26 (0.85-1.87)		
		> 25	34	1.31 (0.85-2.02)		
		Trend test <i>P</i> value, <i>SCC</i>	0.1041			
		Duration as welder	r (yr)			
		Never welding- related job (ref.)	5226	1		
		Ever welder	264	1.58 (1.32-1.89)		
		1 to < 3	41	1.38 (0.90-2.11)		
		3 to < 10	77	1.62 (1.16-2.25)		
		$10 \text{ to } \le 25$	76	1.34 (0.97-1.85)		
		> 25	70	1.71 (1.19-2.46)		
		Trend test <i>P</i> value, <i>Small cell/oat cell</i>	0.0002			
		Duration as welder	r (vr)			
		Never welding- related job (ref.)	1979	1		
		Ever welder	92	1.41 (1.09–1.82)		
		1 to < 3	14	1.25 (0.67–2.35)		
		3 to < 10	32	1.49 (0.96-2.32)		
		10 to ≤ 25	28	1.30 (0.82–2.07)		
		> 25	18	1.20 (0.69–2.11)		
		Trend test <i>P</i> value,	0.1311			

deference, ocation, nrolment/ ollow-up eriod	Population size, description, exposure assessment method	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
dzia et al.		All cases				
13) nt.)		Never welding- related job (ref.)	12 921	1		
		Never-smoker welders Adenocarcinoma	15	2.34 (1.31–4.17)		
		Never welding- related job (ref.)	3313	1		
		Never-smoker welders SCC	6	1.89 (0.79–4.52)		
		Never welding- related job (ref.)	5226	1		
		Never-smoker welders	4	3.01 (1.07-8.49)		
		Small cell/oat cell				
		Never welding- related job (ref.)	1979	1		
		Never-smoker welders	2	4.45 (1.03–19.20)		
		Welding-smoking	interaction			
		Never-smoker– never welding- related job (ref.)	439	1		
		Never-smoker welders Trend test <i>P</i> value,	15	2.04 (1.16–3.61)		

Table 2.5 (continued)

Reference, location, enrolment/ follow-up period	Population size, description, exposure assessment method	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Luqman et al. (2014) Pakistan 2010–2013	Cases: 400 histologically confirmed cases of lung cancer from different hospitals Controls: 800 hospital controls with no cancer or chronic respiratory disease Exposure assessment method: questionnaire	Not exposed to welding fumes (ref.) Welding fumes	8 10	2.5 (1–6.5)	None	Strengths: the first epidemiological study on welding and lung cancer from Pakistan Limitations: a risk estimate for 'welding fumes' is presented even though there was no quantitative exposure assessment; it is unclear if there was multivariable adjustment (e.g. smoking, asbestos) in the statistical models
Matrat et al. (2016) France 2001–2007	Cases: 2276 population-based histologically confirmed, incident primary lung cancer cases in men aged 18–75 yr, identified through 10 of 11 cancer registries Controls: 2780 population controls from the same administrative department using random digit dialling, frequency-matched with cases for sex (only men) and age; additional statistical analysis on SES also performed Exposure assessment method: questionnaire; face-to-face interviews using standardized questionnaire, recording details of each occupation lasting ≥ 1 mo, with 20 job-specific questionnaires; asbestos exposure assessed by both a task-exposure matrix and a job-exposure matrix	No welding (ref.) Regular welders Frequency of welding Regular welders, ≤ 5 > 5 Trend test P value, 0 Duration (yr) Regular welders, ≤ 10 > 10 Trend test P value, 0	8 92 .19 34 58	1 1.66 (1.11–2.49) 1.17 (0.31–4.51) 1.67 (1.10–2.54) 1.53 (0.91–2.55) 1.96 (0.98–3.92)	Age, department, smoking, asbestos, number of jobs	ICARE study. Complements study by Guida et al. (2011) and presents additional analyses beyond Kendzia et al. (2013). Data on soldering and brazing also available in the study Strengths: detailed questionnaire on welding; quantification of welding exposure and assessment of the type of welding; consideration of coexposures; adjustment for asbestos exposure Limitations: each welder had worked with each type of metal, preventing isolation of groups that had welded a unique type of metal

Reference, location, enrolment/ follow-up period	Population size, description, exposure assessment method	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u> Iatrat et al.</u>		Regular ever welder	s: type of we	lding		
016)		No welding (ref.)	1629	1		
nt.)		Gas	64	1.98 (1.20-3.29)		
		Arc	65	1.99 (1.21-3.26)		
		Spot	38	1.35 (0.72-2.53)		
		Other	17	1.80 (0.72-4.51)		
		Regular welders, by surfaces to be welde		d preparation of		
		No welding (ref.)	1629	1		
		Presence of grease or paint on the pieces	53	1.98 (1.15–3.43)		
		Cleaning with mechanical preparation only	25	0.97 (0.48–1.97)		
		Cleaning with chemical or mechanical preparation	26	2.79 (1.35–5.77)		
		Regular and occasion clean the surface to		chemicals used to		
		Never used any chemical (ref.)	180	1		
		Paint stripper	33	1.46 (0.76-2.83)		
		Trichloroethylene	59	1.30 (0.77-2.20)		
		Gasoline	41	1.92 (1.01-3.65)		

<sup>&</sup>lt;sup>a</sup> List A/B jobs are defined as high-risk occupations known to be associated with lung cancer, many of which entail asbestos exposure As, arsenic; CCR, Californian Cancer Registry; Cd, cadmium; CI, confidence interval; Cr, chromium; d, day(s); h, hour(s); ICIT, Index de la Classification Type; ISCO, International Standard Classification of Occupations; ISIC, International Standard Industrial Classification; mo, month(s); NO<sub>x</sub>, nitrogen oxides; Ni, nickel; NR, not reported; NSCLC, non small cell lung carcinoma; OR, odds ratio; Rn, radon; SAR, Special Administrative Region; SBA, steel beam assembly; SCC, squamous cell carcinoma; SES, socioeconomic status; SiO<sub>2</sub>, silicon dioxide; SS, stainless steel; wk, week(s); yr, year(s)

34

26

1.69 (0.86-3.31)

2.54 (1.05-6.13)

White spirit

Acid

Table 2.6 Studies included in the SYNERGY pooling study

Study name	Country	Period	Overlapping studies
AUT	Germany	1990-1995	
HdA	Germany	1988-1993	<u>Jöckel et al. (1998)</u>
EAGLE	Italy	2002-2005	
TURIN/VENETO	Italy	1990-1994	Richiardi et al. (2004)
ROME	Italy	1993-1996	
LUCA	France	1989-1992	
PARIS	France	1988-1992	
ICARE	France	2001-2007	Guida et al. (2011); Matrat et al. (2016)
CAPUA	Spain	2000-2010	
MORGEN	Netherlands	1993-1997	
INCO	Czech Republic	1999-2002	't Mannetje et al. (2012)
INCO	Hungary	1998-2001	't Mannetje et al. (2012)
INCO	Poland	1998-2002	't Mannetje et al. (2012)
INCO	Slovakia	1998-2002	't Mannetje et al. (2012)
INCO	Romania	1998-2002	't Mannetje et al. (2012)
INCO	Russian Federation	1998-2001	't Mannetje et al. (2012)
INCO (LLP)	United Kingdom	1998-2005	't Mannetje et al. (2012)
LUCAS	Sweden	1985-1990	Gustavsson et al. (2000)
OCANZ	New Zealand	2003-2009	<u>Corbin et al. (2011)</u>
MONTREAL	Canada	1996–2002	<u>Vallières et al. (2012)</u> only study II included; <u>Gerin et al. (1984)</u> (recruitment 1979–82) not included; <u>Vallières et al. (2012)</u> includes <u>Gerin et al. (1984)</u>
TORONTO	Canada	1997-2002	Brenner et al. (2010)
HONG KONG	China	2003-2007	<u>Tse et al. 2012</u>

Compiled by the Working Group using information from Kendzia et al. (2013)

an elevated risk in the upper two quartiles of welding exposure after adjustment for asbestos and other potential confounders. Odds ratios of 1.41 (95% CI, 0.83–2.40), 1.38 (95% CI, 0.82–2.33), 0.79 (95% CI, 0.45–1.36), and 0.84 (95% CI, 0.46–1.52) were reported for quartiles 1, 2, 3, and 4, respectively. [The quality of exposure information in this study was limited due to the fact that it included mainly next-of-kin information (93% in cases, 19% in population controls, and 89% in mortality-matched controls) and was based on a mailed self-completed questionnaire. There is partial overlap with the study of Kendzia et al. (2013).]

Asbestos exposure was also assessed in detail in the multicentre study by 't Mannetje et al. (2012) conducted in eastern Europe and the UK, in which occupational histories were

collected by face-to-face interviews. A total of 70 agent exposures were assessed by experts for each job regarding the expert's confidence in the presence of the exposure (possible, probable, certain), the percentage of working time exposed (1-5%, > 5-30%, > 30%), and the intensity (low, medium, high) according to a common protocol; high agreement was observed ( $\kappa = 0.9$ ) between experts in the assessment of exposure to welding fumes. Analyses were reported adjusted for asbestos, smoking, and other occupational exposures such as chromium and nickel. In this study, the odds ratio for ever working as a welder or flame-cutter, adjusted for asbestos, silica, and metal exposure (e.g. Cr), not assessed from welding and smoking, was 1.36 (95% CI, 1.00-1.86). The similarly adjusted odds ratio for ever exposure to welding fumes was 1.18

(95% CI, 0.84–1.66). The odds ratios with lifetime exposure expressed in cumulative welding hours for 1–2520 hours, 2521–28 900 hours, and more than 28 900 hours were 0.94 (95% CI, 0.73–1.21), 1.27 (95% CI, 0.99–1.43), and 1.09 (95% CI, 0.84-1.43), respectively (P for trend, 0.19). This metric was calculated as the product of total hours exposed and intensity level (weights 1, 6, and 20). The study authors also calculated a weighted duration by multiplying the number of years (each year equivalent to 2000 hours) by the frequency (0.03, 0.175, and 0.65 for low, medium, and high, respectively) of exposure. This metric resulted in adjusted odds ratios for 1-1680 hours, 1681-7000 hours, and more than 7000 hours of 1.03 (95% CI, 0.80–1.33), 1.05 (95% CI, 0.82–1.36), and 1.22 (95% CI, 0.94–1.58), respectively (*P* for trend, 0.16). Categorized by years of exposure to both gas and arc welding fumes, adjusted odds ratios for 1-8 years, 9-25 years, and more than 25 years of 1.08 (95% CI, 0.72-1.61), 0.92 (95% CI, 0.65–1.30), and 1.38 (95% CI, 1.00–1.90), respectively, were observed (P for trend, 0.01). The Working Group noted the partial overlap with the study by Kendzia et al. (2013).]

Vallières et al. (2012) conducted a study in Montreal, Canada, using a protocol similar to that of 't Mannetje et al. (2012). Exposure to asbestos and welding fumes was assessed in great detail by industrial hygienists. No elevated risks and no duration-effect relationship were observed for arc welding (OR, 1.0; 95% CI, 0.8–1.2) or gas welding (OR, 1.1; 95% CI, 0.9–1.4) for any level of exposure after adjustment for asbestos, smoking, and other confounders. In an analysis restricted to never and low-frequency smokers, statistically significant elevated risks were observed for any level of exposure to both gas and arc welding fumes, assessed separately. No association was observed among smokers of medium and high frequency. [The Working Group noted the partial overlap with the study by Kendzia et al. (2013).]

Matrat et al. (2016) adjusted for asbestos exposure in a recent case-control study conducted in France. Exposure was based on information gathered by face-to-face interviews that included a lifelong occupational history, including job periods, and 20 job-specific questionnaires. A detailed 4-page supplementary questionnaire was used if a respondent declared that more than 5% of his working time was devoted to welding, brazing, or gas cutting. Regular welders were defined as participants who reported being employed as a welder for at least one job period. From detailed information on asbestos exposure, a cumulative exposure index was calculated as the product of the duration of the corresponding job task, the probability of exposure, and the intensity of exposure. This index was categorized into four classes and then used for adjustment. The smoking- and asbestos-adjusted odds ratio for regular welders (which corresponds to ever being employed as a welder) compared with non-welders was 1.66 (95% CI, 1.11-2.49). The adjusted odds ratios for being a regular welder for less than 10 years was 1.53 (95% CI, 0.91-2.55) and for 10 years or more was 1.96 (95% CI, 0.98–3.92) (*P* for trend, 0.02). [The Working Group noted the partial overlap with the study by <u>Kendzia et al. (2013)</u>.]

Several studies assessed the risks of cancer of the lung in relation to different welding processes (gas [oxyacetylene] welding, electric arc welding, gas-shielded welding [a type of arc welding preferably used on SS]) as well as type of metal (MS vs SS [chromium–nickel alloy]). See Section 1 for further details on welding types and processes.

Gerin et al. (1984) observed a higher odds ratio in welders with exposure to nickel (OR, 3.3; 95% CI, 1.2–9.2) than in welders without nickel exposure (OR, 1.2; 95% CI, 0.1–9.4). Kjuus et al. (1986) observed a difference in risk by material welded with an odds ratio of 3.3 (96% CI, 1.2–9.3) for 3 years or more of welding of SS and an odds ratio of 1.9 (95% CI, 0.9–3.7) for welding of any type of steel. In a case–control study

restricted to welders, Hull et al. (1989) did not consistently show higher risks due to welding of high-alloy steel/SS as compared with MS. [This study, conducted among welders only, was difficult to interpret due to a contaminated reference group.] The multicentre study by 't Mannetje et al. (2012) reported odds ratios for more than 25 years duration of exposure to welding fumes without chromium (OR, 1.48; 95% CI, 1.11–1.97) and containing chromium (OR, 1.27; 95% CI, 0.87-1.85). Although both Jöckel et al. (1998) and Matrat et al. (2016) collected information on the welding of SS in a welder-specific questionnaire, neither studies reported a corresponding risk estimate because most participants reported using different welding processes and on different metals. [These results indicate that any observed risks are not fully explained by exposure to high concentrations of nickel or chromium in the welded steel.]

Investigating the varying exposures to welding fumes between different types of welding, Jöckel et al. (1998) observed the higher odds ratio for gas welding in the highest category of cumulative exposure (6000 hours) (OR, 1.46; 95% CI, 0.72-2.96) in comparison with electric arc welding. Regular oxyacetylene welding for at least 2 hours per day, for 2 days per week for a minimum of 3 years, was associated with an odds ratio of 2.77 (95% CI, 1.20-6.38) in this study. 't Mannetje et al. (2012) also observed higher odds ratios for only gas welding for more than 25 years duration (OR, 1.46; 95% CI, 0.72-2.94) than for only arc welding for more than 25 years duration (OR, 1.09; 95% CI, 0.72-1.65). Matrat et al. (2016) also reported that gas welding exclusively was associated with a higher risk of cancer of the lung than arc welding. The study by Vallières et al. (2012) observed an association between welding and cancer of the lung mainly in nonsmokers and low-frequency smokers; odds ratios for gas as compared to arc welding (OR for substantial level of exposure to welding fumes in non-/low smokers were

4.3 (95% CI, 1.9–9.7) for gas welding and 3.5 (95% CI, 1.6–7.8), for arc welding) respectively.

Welding often takes place under particular circumstances, especially in maintenance and repair work when materials are coated or need to be cleaned before welding. When exploring the role of substances covering the metal surface to be welded and that of the cleaning procedure, Matrat et al. (2016) observed an increased risk among regular welders for the presence of grease or paint on the welded pieces (OR, 1.98; 95% CI, 1.15–3.43). They also reported an increased risk for cleaning with chemical or mechanical preparation (OR, 2.79; 95% CI, 1.35–5.77), but not for cleaning with mechanical preparation only (OR, 0.97; 95% CI, 0.48–1.97).

## 2.5.2 Cancer of the kidney

See Table 2.7

Eight case–control studies that reported on the association between cancer of the kidney and welding-related occupations or exposure to welding fumes were identified (Magnani et al., 1987; Siemiatycki, 1991; Keller & Howe, 1993; McCredie & Stewart, 1993; Mandel et al., 1995; Pesch et al., 2000; Mattioli et al., 2002; Brüning et al., 2003). [An additional report was identified (Parent et al., 2000) but not included in this review, as it covered the same study population as reported on in Siemiatycki (1991).]

Five of these studies reported odds ratios of 1.10–1.76 for welding occupations (<u>Siemiatycki</u>, 1991; <u>Keller & Howe</u>, 1993; <u>McCredie & Stewart</u>, 1993; <u>Mandel et al.</u>, 1995; <u>Brüning et al.</u>, 2003), none of which reached statistical significance.

Five of the eight case–control studies assessed exposure to welding fumes using a JEM or by expert assessment. A study from Canada (Siemiatycki, 1991), which included patients diagnosed with cancers other than kidney as controls, reported an odds ratio of 0.8 (95% CI, 0.5–1.3) for both exposure to arc welding fumes and exposure to gas welding fumes as assessed

by experts, based on 17 and 16 exposed cases, respectively. [The Working Group noted that the exposed cases and controls were likely the same for arc and gas welding fumes.] Odds ratios did not increase when analyses were restricted to "substantial" exposure to the two types of welding fumes. A study from northern Italy (Mattioli et al., 2002) reported an odds ratio of 5.67 (95% CI, 0.78–41.31) for expert-assessed exposure to welding fumes based on 8 exposed cases. Two studies used a JEM to assess exposure to welding fumes. A study from Germany (Peschetal., 2000) reported an odds ratio of 1.3 (95% CI, 1.0-1.8) for exposure to medium levels of welding fumes based on 56 exposed cases, while exposure to high levels was associated with an odds ratio of 1.1 (95% CI, 0.8–1.6). A later study from Germany (Brüning et al., 2003) using a JEM to assess exposure to welding fumes reported an odds ratio of 2.73 (95% CI, 1.06-7.06) for low levels based on 9 exposed cases and 3.10 (95% CI, 1.37-7.02) for high levels based on 13 exposed cases. [The Working Group noted that the focus of this report was TCE as a risk factor for cancer of the renal pelvis; there was no adjustment for exposure to TCE however, so it is unclear how much of the elevated odds ratio for welding fumes is due to uncontrolled confounding by exposure to TCE.]

# 2.5.3 Cancer of the haematopoietic system

See Table 2.8 (web only; available at: <a href="http://publications.iarc.fr/569">http://publications.iarc.fr/569</a>)

#### (a) Leukaemia

The Working Group identified nine case—control studies of leukaemia in adults that reported estimates of increased risk for welding-related jobs (Stern et al., 1986; Preston-Martin & Peters, 1988; Keller & Howe, 1993; Bethwaite et al., 2001; Costantini et al., 2001; Oppenheimer & Preston-Martin, 2002; Adegoke et al., 2003; Wong et al., 2010; Luckhaupt et al., 2012). Several studies reported risk estimates for a combined group

of leukaemias (Keller & Howe, 1993; Costantini et al., 2001; Adegoke et al., 2003; Luckhaupt et al., 2012), reporting odds ratios ranging from 0.90 to 2.25; these were based on relatively small numbers of exposed cases however, and none reached statistical significance. [The Working Group noted that chronic lymphocytic leukaemia (CLL) was included in the definition of leukaemia by Adegoke et al. (2003) and Luckhaupt et al. (2012), not included in the definition by Costantini et al. (2001), and it was not clear whether it was included in the definition by Keller & Howe (1993).]

## (i) Leukaemia subtypes

Several studies reported risk estimates for myeloid leukaemia or subtypes of myeloid leukaemia. An exceptionally high odds ratio was reported in 1988 for a chronic myeloid leukaemia case-control study based in Los Angeles County (Preston-Martin & Peters, 1988). A total of 22 of the 130 cases in the study had been employed as welders (compared with 4 of the 130 controls), yielding an adjusted odds ratio of 25.4 (95% CI, 2.78-232.54). A later study from California reported an odds ratio of 0.86 (95% CI, 0.29-2.53) for chronic myeloid leukaemia (Luckhaupt et al., 2012) related to welding in the construction industry. Three studies reported on acute myeloid leukaemia (AML), all with odds ratios above unity but none reaching statistical significance (Oppenheimer & Preston-Martin, 2002; Wong et al., 2010; Luckhaupt et al., 2012). A study from New Zealand on AML and acute lymphoblastic leukaemia (ALL) combined reported an odds ratio of 2.79 (95% CI, 1.2-6.8) for welders/flame-cutters; separate odds ratios for AML and ALL were not presented, however. [The Working Group assumed that the majority of the study population would be AML, but numbers were not provided.]

None of the leukaemia case-control studies reported associations with exposure to welding fumes, and none reported duration-response associations.

Table 2.7 Case-control studies on cancer of the kidney and welding or exposure to welding fumes

Reference, location, enrolment/follow- up period	Population size, description, exposure assessment method	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Magnani et al. (1987) UK (three English counties) 1959–1963/ 1965–1979	Cases: 147 deaths at age 18–54 yr, identified from death certificates Controls: 556 deaths in the same year from other causes matched for sex, county of residence, age; identified from death certificates Exposure assessment method: expert judgement; Pannett JEM, based on job title on death certificate	Welding fumes	NR	1.8 (0.7–2.2)	Sex, county, age at death	Strengths: JEM assessed exposure Limitations: small size; occupational data obtained from death certificates; occupational histories available more often for cases than for controls; no adjustment for smoking
Siemiatycki (1991) Canada, Montreal 1979–1985	Cases: 177 male residents of the Montreal metropolitan area with histologically	Arc welding fumes (any) Arc welding	17 6	0.8 (0.5–1.3) 1.0 (0.5–1.9)	Age, family income, cigarette index, ethnic	Strengths: expert assessment based on full occupational history and detailed task descriptions, and job-
	confirmed incident kidney cancer, age 35–70 yr	fumes (substantial)			origin	specific questionnaires Limitations: small size; use of cancer
	Controls: 2481 study subjects with other cancers	Gas welding fumes (any)	16	0.8 (0.5–1.3)		controls
	Exposure assessment method: expert judgement	Gas welding fumes (substantial)	5	0.7 (0.3–1.5)		
		Welding fumes	6	1.5 (0.7–3.1)		
Keller & Howe (1993) USA, Illinois 1986–1989	Cases: 1372 newly diagnosed male kidney cancer cases reported in Illinois hospitals (hospital based) Controls: 4326 random sample of approximately 10% of all other cancers Exposure assessment method: questionnaire; job title recorded at cancer registration	Male welder	NR	1.75 (0.96–3.18)	Age, history of tobacco use	This study reports on multiple cancer sites Strengths: large size Limitations: only job at cancer registration is recorded; only welders within the construction industry are selected in the exposed group; unclear how many welders (outside of the construction industry) are categorized as unexposed; cancer controls

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Reference, location, enrolment/follow- up period	Population size, description, exposure assessment method	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
McCredie & Stewart (1993) Australia, NSW 1989–1990	Cases: 636 age 20–79 yr at diagnosis (population based); 489 RCC and 147 renal pelvic cancer cases Controls: 523 electoral rolls, randomly selected (population based) Exposure assessment method: questionnaire, face-to-face interviews; employment in certain industries and occupations, exposure to chemicals with suspected associations with kidney cancer; question on employment as welder (among other)	Welder Welder (RCC and urinary pelvis)	40 8 48	1.37 (0.80–2.34) 1.66 (0.68–4.03) 1.50 (0.27–8.16)	Age, sex, method of interview	Strengths: large size, population controls, specific questions on welding Limitations: no specific assessment of exposure to welding fumes
Mandel et al. (1995) Australia, Denmark, Germany, Sweden, USA 1989–1991	Cases: 1732 cases of incident renal cell adenocarcinomas, age 20–79 yr, confirmed by histopathology or cytology Controls: 2309 population controls Exposure assessment method: questionnaire; Germany collected full occupational histories, other centres asked specific occupations and welding industry	Welder	77	1.1 (0.8–1.6)	Age, tobacco, BMI, education, study centre	Strengths: large size Limitations: no results by duration
Pesch et al. (2000) Germany 1991–1995	Cases: 935; 570 men and 365 women with no age limit (population based) Controls: 4298 population; 2650 men and 1648 women (population based) Exposure assessment method: expert judgement; British JEM	Level of exposure only Medium High Substantial	e to welding 56 46 16	fumes for men  1.3 (1–1.8)  1.1 (0.8–1.6)  1.2 (0.7–2.1)	Age, study centre, smoking, region	ORs for 'welding, soldering, milling' were also reported, but this occupational group was considered too broad Strengths: large size, welding fumes assessed through JEM Limitations: exposure assessment beyond that provided by use of a JEM not provided

Table 2.7 (continued)

Reference, location, enrolment/follow- up period	Population size, description, exposure assessment method	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Mattioli et al. (2002) North Italy 1986–1994	Cases: 249 histologically confirmed RCC cases (hospital based) Controls: 238 hospital controls with non-RCC diagnosis (hospital-based) Exposure assessment method: questionnaire; occupational history, plus expert assessment for selected exposures including welding fumes	Men only: welding fumes	8	5.67 (0.78–41.31)	Age, birthplace, residence, smoking	Strengths: expert assessment Limitations: small size, small number of exposed cases
Brüning et al. (2003) Arnsberg, Germany 1999–2000	Cases: 134 incident histologically confirmed RCC cases with nephrectomy 1992–2000 Controls: 401 hospital controls (no dementia, no cancer), 3:1 frequency-matched by sex and age (5 yr) Exposure assessment method: questionnaire; job title, plus Pannett JEM; next of kin interviews included	Welding job Level of exposure Low High	10 to welding 9 13	1.76 (0.75–4.11) 2.73 (1.06–7.06) 3.10 (1.37–7.02)	Age, sex, smoking	TCE was a risk factor in this study, but ORs for welding were not adjusted for TCE Strengths: although the study is small, the prevalence of welding is substantial Limitations: small size

BMI, body mass index; CI, confidence interval; JEM, job-exposure matrix; NR, not reported; OR, odds ratio; RCC, renal cell carcinoma; TCE, trichloroethylene; UUT, upper urinary tract; yr, year(s)

#### (b) Non-Hodgkin lymphoma

The Working Group identified 13 NHL case-control studies (Persson et al., 1989; Siemiatycki, 1991; Persson et al., 1993; Figgs et al., 1995; Costantini et al., 1998; Mao et al., 2000; Costantini et al., 2001; Fabbro-Peray et al., 2001; Zheng et al., 2002; Band et al., 2004; Dryver et al., 2004; Karunanayake et al., 2008; 't Mannetje et al., 2008) that reported on the association between NHL and welding-related occupations or exposure to welding fumes, and one large pooled case-control study ('t Mannetje et al., 2016).

Reported risk estimates for occupation as a welder were close to unity for 4 out of the 13 studies and above unity for 9 individual studies, 4 of which reported statistically significant increased risk estimates for all NHL (Persson et al., 1993; Zheng et al., 2002; Dryver et al., 2004) or specific NHL subtypes (Band et al., 2004). With the exception of the study by Dryver et al. (2004), these odds ratios were based on relatively small numbers of exposed cases. The largest NHL case-control study reporting on welding occupation was a pooled analysis of 10 case-control studies from Australia, Canada, Europe, and the USA (<u>'t Mannetje et al., 2016</u>). Ever employment in a welding-related occupation was associated with an odds ratio of 1.03 (95% CI, 0.83–1.27) based on 174 exposed cases. An odds ratio of 1.01 (95% CI, 0.69–1.48) was observed for those who had held a welding-related job for more than 10 years (53 exposed cases). Analyses were conducted for the main NHL subtypes (diffuse large B-cell lymphoma (DLBCL), follicular lymphoma, and small lymphocytic lymphoma (SLL/CLL), showing an elevated odds ratio only for DLBCL (OR, 1.31; 95% CI, 0.99–1.74). Compared with never welders, those who had worked for more than 10 years in a welding-related job had an increased risk of DLBCL (OR, 1.20; 95% CI, 0.70–2.05) and of follicular lymphoma (OR, 1.25; 95% CI, 0.63-2.49).

Three NHL case-control studies assessed exposure to welding fumes or frequency of welding tasks. A study from Canada (Siemiatycki, 1991), using patients diagnosed with cancers other than NHL as controls and expert assessment for exposure to welding fumes, reported an odds ratio of 0.8 (95% CI, 0.6-1.2) for arc welding fumes and 0.8 (95% CI, 0.5-1.2) for gas welding fumes. [The Working Group noted that the odds ratios on the same numbers of exposed cases were very similar, suggesting that most exposed cases and controls were assessed by the experts as exposed to both gas welding and arc welding fumes.] A study from Sweden (Dryver et al., 2004) reported odds ratios for both welding occupation and exposure to welding fumes (self-reported). The risk for welding was elevated (OR, 1.41; 95% CI, 1.01–1.99), while the risk for exposure to welding fumes was not (OR, 0.98; 95% CI, 0.73–1.30). [The Working Group noted that more people reported exposure to welding fumes than occupation as a welder. The group exposed to welding fumes was therefore likely to include many that only performed occasional welding or worked in areas where welding was conducted.] A study from France (<u>Fabbro-Peray</u> et al., 2001) assessed the frequency of welding-related tasks (self-reported), reporting an odds ratio of 1.7 (95% CI, 0.8–3.4) for those who welded often and one of 2.6 (95% CI, 1.4-5.1) for those who welded daily. Associations remained after adjusting for benzene exposure, which was found to be a risk factor in this study.

# (c) Multiple myeloma

The Working Group identified five case-control studies of multiple myeloma in adults that reported risk estimates for welding-related jobs (Eriksson & Karlsson, 1992; Heineman et al., 1992; Demers et al., 1993; Costantini et al., 2001; Baris et al., 2004). Most were based on 10 or less exposed cases, with the exception of a study from Canada (Demers et al., 1993) which reported an odds ratio of 1.2 (95% CI, 0.7–2.0) for

welders and cutters based on 22 exposed cases. One of the five studies (Costantini et al., 2001) reported a statistically significant increased odds ratio for welders (OR, 3.3; 95% CI, 1.3–8.5) based on 7 exposed cases.

## (d) Other haematopoietic cancers: Hodgkin lymphoma

The Working Group identified three case-control studies of Hodgkin lymphoma in adults that reported risk estimates for welding-related jobs (Persson et al., 1989; Persson et al., 1993; Costantini et al., 2001), all based on a small number of exposed cases. The oldest of these reported a statistically significant increased odds ratio (Persson et al., 1989). [The Working Group noted that information on the number of cases exposed was not available for this study but, given the size of the study and the wide confidence interval, it is expected to be small.]

## 2.5.4 Cancer of the urinary bladder

See Table 2.9 (web only; available at: <a href="http://publications.iarc.fr/569">http://publications.iarc.fr/569</a>)

The Working Group identified 18 case-control studies on cancer of the urinary bladder (Howe et al., 1980; Silverman et al., 1983, 1989a, b, 1990; Schifflers et al., 1987; Claude et al., 1988; Risch et al., 1988; Burns & Swanson, 1991; Siemiatycki, 1991; Kunze et al., 1992; Zaridze et al., 1992; Cordier et al., 1993; Teschke et al., 1997; Colt et al., 2004; Gaertner et al., 2004; Samanic et al., 2008; Colt et al., 2011) and one pooled case-control study (Kogevinas et al., 2003) that reported on the association between cancer of the bladder and welding-related occupations or exposure to welding fumes. [The Working Group excluded two studies from Islamic Republic of Iran because the occupational group was too broad (Aminian et al., 2014; Ghadimi et al., 2015). To avoid duplicate inclusion, one study from Italy (Porru et al., 1996) was not included because it

was included in the pooled analysis also listed in the table (Kogevinas et al., 2003).]

Most of the individual studies were conducted in Canada, Europe, or the USA and ranged in size from 74 to 2160 cases, most including incident cases of cancer of the bladder. Most presented risk estimates were adjusted for smoking. [The Working Group noted that the odds ratios presented in Silverman et al. (1983) were not adjusted for smoking, although the study authors reported that smoking adjustment did not change the results.] Most of the reported risk estimates for welding-related occupations from cancer of the bladder case-control studies were close to unity and did not reach statistical significance; the exception was the earliest study from Canada (Howe et al., 1980), which reported an odds ratio of 2.8 (95% CI, 1.1-8.8) based on 16 exposed cases. Several studies reported risk estimates close to unity based on a relatively large number of exposed cases (> 20) (e.g. Silverman et al., 1989b; Burns & Swanson, 1991; Cordier et al., 1993).

Three studies reported on the duration of employment as a welder. A large study from Canada reported an odds ratio of 0.93 (95% CI, 0.78–1.10) for a 10-year increment of duration of employment as a welder (Risch et al., 1988). A later study from Canada (Gaertner et al., 2004) reported an odds ratio of 1.66 (95% CI, 0.78–3.48) for the group with the longest duration of employment as a welder (> 15 years) compared with those never employed as a welder. A study from Spain (Samanic et al., 2008) reported an odds ratio of 1.32 (95% CI, 0.74–2.36) for the group with the longest duration of employment as a welder (≥ 10 years) compared with those never employed as a welder.

The largest cancer of the bladder case-control study reporting on employment as a welder, a pooled analysis of 11 cancer of the bladder case-control studies from six European countries (Kogevinas et al., 2003), reported a pooled odds ratio of 1.22 (95% CI, 0.91–1.63) after adjusting for age, smoking, and study centre,

based on 88 exposed cases (men only). [The Working Group noted there was no overlap between this pooled study and the other studies listed in Table 2.9 (web only; available at: <a href="http://publications.iarc.fr/569">http://publications.iarc.fr/569</a>). The Cordier et al. (1993) estimate for ever worked as a welder was included in the pooled estimate, but not the estimates for exposure to specific welding fumes reported on in the following paragraph and in the table.] Risk estimates by duration of employment as a welder were not reported.

Two studies used expert assessment, based on detailed work histories completed by the cases and the controls, to identify exposure to welding fumes generally and gas welding fumes versus arc welding fumes specifically. A study from Canada (Siemiatycki, 1991), using patients diagnosed with cancers other than bladder as controls, reported an odds ratio of 1.2 (95% CI, 0.9-1.5) for both arc welding fumes and gas welding fumes, based on 63 exposed cases. [The Working Group noted that the odds ratios were the same and based on the same numbers of exposed cases for both types of welding fume, suggesting that all cases were assessed by the experts as exposed to both gas welding and arc welding fumes.] Risk estimates did not increase when restricting the exposed group to those with "substantial" exposure. A study from France (Cordier et al., 1993) reported that exposure to any type of welding fumes was associated with an odds ratio of 1.40 (95% CI, 0.98–2.01) based on 86 exposed cases. An odds ratio of 1.61 (95% CI, 0.95-2.72) was reported for gas welding fumes and of 1.34 (95% CI, 0.79–2.27) for arc welding fumes, based on 40 and 37 exposed cases, respectively. [The Working Group noted that the numbers exposed to gas welding fumes and arc welding fumes would suggest that these groups were not fully, but largely, mutually exclusive.] Only 4 cases were exposed to SS welding fumes (OR, 1.10; 95%) CI, 0.24–5.05). Risk estimates by level or duration of exposure to welding fumes were not reported.

## (a) Subtypes of cancer of the bladder

With transitional cell carcinoma (TCC) being the dominant histological type of malignant tumours of the urinary bladder in industrialized countries (Fortuny et al., 1999), studies generally lacked statistical power to report on occupational risk factors for non-TCC of the bladder, including squamous cell carcinomas and adenocarcinomas. The above-mentioned pooled analysis of 11 case-control studies on cancer of the bladder from six European countries (Kogevinas et al., 2003) also reported on occupational risk factors for the 146 cases with non-TCC of the bladder (Fortuny et al., 1999), but an odds ratio specific to welding was not presented. The Working Group identified one study that reported a relative risk for welders, specifically for squamous cell carcinoma (RR, 5.9), based on 5 exposed cases; it was reported as being statistically significant, but the 95% confidence interval and P value were not provided (Kantor et al., 1988). Relative risks for all types of cancer of the bladder or adenocarcinoma of the bladder for welders were not significantly increased. [The Working Group noted that no further details were provided and that the study population overlaps that of Silverman et al. (1983); this study is therefore not included in the table.]

# (b) Meta-analysis of cancer of the bladder

A meta-analysis of cohort and case–control studies that reported on the association between occupation and cancer of the bladder (all adjusted for smoking) was published in 2008 (Reulen et al., 2008), including 14 of the reports listed in Table 2.9 (web only; available at: <a href="http://publications.iarc.fr/569">http://publications.iarc.fr/569</a>)

The meta-estimate for case-control studies was 1.04 (95% CI, 0.88–1.23). [The Working Group noted a major limitation in that the pooled analysis of 11 case-control studies on cancer of the bladder from six European countries (Kogevinas et al., 2003), which had already published by the time of the meta-analysis, was not included.]

# 2.5.5 Cancers of the head, neck, and upper aerodigestive tract

See Table 2.10 (web only; available at: <a href="http://publications.iarc.fr/569">http://publications.iarc.fr/569</a>)

Studies on specific cancers of the head and neck are reviewed in the following. Two other studies reported results for all cancers of the head and neck combined. A case-control study which was part of the ICARE (Investigation of Occupational and Environmental Causes of Respiratory Cancers) study in France reported risk estimates for occupations and duration of occupation, adjusted for tobacco and alcohol consumption, separately for women (296 cases and 775 controls) (Carton et al., 2014) and men (1833 cases and 2747 controls) (Paget-Bailly et al., 2013). Odds ratios of 2.18 (95% CI, 0.33–14.4) and 21.7 (95% CI, 1.54-304) were reported for women who had ever worked as welders and flame-cutters (4 cases) and for women who had been employed for 10 years or more in this occupational group, respectively (P for trend, 0.05) (Carton et al., 2014). For men who had ever worked as welders and flame-cutters (109 cases) or who had been employed for 10 years or more in this occupational group, odds ratios of 1.9 (95% CI, 1.3–2.8) and 2.0 (95% CI, 1.0–3.9) were reported, respectively (P for trend, 0.01) (Paget-Bailly et al., 2013). Odds ratios for type of welding were also reported for men: 3.2 (95% CI, 1.6-6.3) for gas and electric welders (44 cases) and 1.9 (95% CI, 1.0-3.6) for electric arc welders (36 cases). Paget-Bailly et al. (2013) also reported odds ratios for specific head and neck cancer sites, particularly elevated for cancers of the hypopharynx (OR, 2.1; 95% CI, 1.2–3.6), oral cavity (see Section 2.5.5(c) below), and larynx (see Section 2.5.5(d) below).

# (a) Cancer of the nasal cavity and sinuses

See Table 2.10 (web only; available at: <a href="http://publications.iarc.fr/569">http://publications.iarc.fr/569</a>)

The Working Group identified four case-control studies that reported on welding or exposure to welding fumes (Hernberg et al., 1983; Luce et al., 1993; Teschke et al., 1997; d'Errico et al., 2009). These studies were all relatively small (48–207 cases), but a pooled analysis (Leclerc et al., 1997) included 930 cases. [The Working Group noted that the Luce et al. (1993) study population was included in this pooled analysis.]

Two of these four studies (Hernberg et al., 1983; Teschke et al., 1997) and the pooled analysis (Leclerc et al., 1997) reported odds ratios for welding-related occupations. A study from Denmark, Finland, and Sweden (Hernberg et al., 1983) reported an odds ratio of 2.8 (95% CI, 1.2–6.9) based on 17 exposed cases, noting that 13 were also exposed to chromium and/or nickel (as assessed by experts). A small study from Canada (Teschke et al., 1997) reported an odds ratio of 3.5 (95% CI, 0.2–53.7) based on 2 exposed cases. The pooled analysis (Leclerc et al., 1997) reported an odds ratio of 0.92 (95% CI, 0.38–2.22) based on 6 exposed cases.

Two studies assessed exposure to welding fumes through expert assessment. A study from France (Luce et al., 1993) reported odds ratios for exposure to welding fumes of 0.5 (95% CI, 0.2-1.4) for squamous cell carcinoma and 0.8 (95% CI, 0.4-1.6) for adenocarcinoma. A study from Italy (d'Errico et al., 2009) reported an odds ratio of 2.0 (95% CI, 1.00-3.82) for ever exposure to welding fumes based on 17 exposed cases, noting that additional adjustment for exposure to wood dust further strengthened the association (OR, 2.70; 95% CI, 1.31-5.45). Odds ratios by duration of exposure to welding fumes were also presented, with one of 2.40 (95% CI, 0.92-6.38) for 1–10 years of exposure to welding fumes and 3.0 (95% CI, 1.13-8.0) for more than 10 years. Odds ratios by level of welding fumes (low/high) were also reported, with 3.30 (95% CI, 1.47-7.26) and 1.60 (95% CI, 0.34-7.75) for low and high exposure levels, respectively. The odds ratio for exposure to welding fumes was reported as 4.30 (95% CI, 1.01–18.10) for squamous cell carcinoma and 1.30 (95% CI, 0.52–3.52) for adenocarcinoma (d'Errico et al., 2009).

[The Working Group noted that results stratified by the material being welded, which could evaluate the potential effect of exposure to chromium and nickel, were not presented in the identified studies. Results adjusted for wood dust suggest that wood dust is not a strong confounder in associations between welding and cancers of the nasal cavity and sinuses.]

## (b) Cancer of the nasopharynx

One case–control study conducted in Hong Kong Special Administrative Region, China, on carcinomas of the nasopharynx was identified (Xie et al., 2017), reporting an odds ratio of 9.18 (95% CI, 1.05–80.35) for self-reported expose to welding fumes at any time in the job history, based on 7 exposed cases and 1 exposed control. [The Working Group noted that carcinomas of the nasopharynx differ from other cancers of the head and neck in terms of occurrence and identified risk factors. They are more common in certain geographical areas, including east Asia where this study is set, and found to be strongly linked to infection with the Epstein–Barr virus.]

# (c) Cancer of the oral cavity and oropharynx

The Working Group identified five case-control studies on cancer of the oral cavity and/or oropharynx (Vaughan, 1989; Merletti et al., 1991; Huebner et al., 1992; Gustavsson et al., 1998; Paget-Bailly et al., 2013). With the exception of the study from France (Paget-Bailly et al., 2013), all reported odds ratios close to unity for welding-related occupations. Paget-Bailly et al. (2013) reported an odds ratio for cancer of the oral cavity of 1.9 (95% CI, 1.1–3.3) based on 21 cases that had ever worked as a welder or flame-cutter.

#### (d) Cancer of the larynx

The Working Group identified 10 case-control studies on cancer of the larynx that reported on welding or exposure to welding fumes (Olsen et al., 1984; Brown et al., 1988; Ahrens et al., 1991; Wortley et al., 1992; Goldberg et al., 1997; De Stefani et al., 1998; Gustavsson et al., 1998; Elci et al., 2001; Shangina et al., 2006; Paget-Bailly et al., 2013).

Seven of these studies reported on welding occupations (Brown et al., 1988; Ahrens et al., 1991; Wortley et al., 1992; Goldberg et al., 1997; De Stefani et al., 1998; Elci et al., 2001; Paget-Bailly et al., 2013). Four of the studies reported odds ratios at or below unity, while three reported an odds ratio above unity (Brown et al., 1988; Goldberg et al., 1997; Paget-Bailly et al., 2013); one of these (Paget-Bailly et al., 2013) [already discussed above (at the beginning of Section 2.5.5) in relation to all cancers of the head and neck combined reported an odds ratio for cancer of the larynx of 2.4 (95% CI, 1.5-4.0) for men who had ever worked as a welder and flamecutter (33 exposed cases). An additional international case-control study on cancer of the larynx (Boffetta et al., 2003) reported that an increased risk for welders was not observed, but an odds ratio was not reported (this study was therefore not included in the table). [The Working Group identified one study that reported results by duration of welding employment (Wortley et al., 1992), but the number of exposed cases was small and a trend was not observed.

Three studies reported on the association between cancer of the larynx and exposure to welding fumes (Olsen et al., 1984; Gustavsson et al., 1998; Shangina et al., 2006). The earliest published study (Olsen et al., 1984), based in Denmark, reported an odds ratio for all cancers of the larynx combined of 1.3 (95% CI, 0.9–2.0) based on 42 cases that reported exposure to welding fumes. Results by type of cancer of the larynx were also presented, with an odds ratio

of 1.1 (95% CI, 0.7-1.8) for glottic (23 exposed cases), 1.5 (95% CI, 0.8-2.9) for supraglottic (13 exposed cases), and 6.3 (95% CI, 1.8-21.6) for subglottic (5 exposed cases). A relatively large study from Sweden (Gustavsson et al., 1998) reported an odds ratio of 1.56 (95% CI, 0.92–2.53) for cancer of the larynx associated with ever exposure to welding fumes (based on 32 exposed cases), and a positive duration-response association was reported (P for trend, 0.04). A study from central and eastern Europe (Shangina et al., 2006), including 316 cases of cancer of the larynx and 34 cases of cancer of the hypopharynx, reported an odds ratio of 0.78 (95% CI, 0.54–1.14) for exposure to arc welding fumes (56 exposed cases) and 0.89 (95% CI, 0.58-1.37) for exposure to gas welding fumes (42 exposed cases).

## (e) Cancer of the oesophagus

The Working Group identified four case-control studies on cancer of the oesophagus that reported on welding or exposure to welding fumes (Magnani et al., 1987; Siemiatycki, 1991; Gustavsson et al., 1998; Engel et al., 2002), all reporting odds ratios close to unity. Siemiatycki (1991) reported odds ratios for arc welding and gas welding separately, and for any as well as substantial exposure to welding fumes, but none were above unity.

#### 2.5.6 Cancer of the brain

See Table 2.11 (web only; available at: <a href="http://publications.iarc.fr/569">http://publications.iarc.fr/569</a>)

Six case—control studies investigating the risk of either malignant cancer of the brain or meningioma (a commonly diagnosed benign brain tumour) were identified by the Working Group.

Four studies were cancer of the brain casecontrol studies conducted in Canada, the UK, and the USA using either JEMs, job title, or exposure questionnaires, reporting on the association between malignant cancer of the brain and welding-related occupations or exposure to welding fumes (Magnani et al., 1987; Carozza et al., 2000; Pan et al., 2005; Ruder et al., 2012). Three of these studies reported odds ratios below or close to unity (Magnani et al., 1987; Carozza et al., 2000; Ruder et al., 2012), all based on a small number of exposed cases. The fourth, a large study of 1009 cases and 5039 matched controls (Pan et al., 2005), collected information on 18 employment-related chemical exposures including "welding", and reported an elevated odds ratio of 1.26 (95% CI, 0.98-1.45) based on 183 exposed cases. The same study found a 40% increase in risk of cancer of the brain in relation to duration of welding, with an odds ratio of 1.41 (95% CI, 0.98-1.84) in those exposed to welding fumes for 20 years or more (48 cases) compared with the reference group of non-exposed.

Two studies included exclusively meningiomas (Hu et al., 1999; Sadetzki et al., 2016). The first, a study from China using self-reported occupational exposures and hospital-recruited cases and controls (Hu et al., 1999), reported an odds ratio for exposure to welding rod fumes of 1.99 (95% CI, 0.40-9.89) for men based on 4 exposed cases and 3.05 (95% CI, 0.52-18.03) for women based on 5 exposed cases. The second, a large and recent international case-control study on meningioma (Sadetzki et al., 2016), reported that ever exposure to welding fumes, assessed using an updated version of FINJEM, was associated with risk of meningioma; an odds ratio of 1.19 (95% CI, 0.91-1.56) was reported, based on 94 exposed cases. Odds ratios were also reported separately for women (OR, 1.79; 95% CI, 0.78-4.10; 12 exposed cases) and men (OR, 1.15; 95% CI, 0.86–1.54; 82 exposed cases).

# 2.5.7 Parental exposure and cancer in offspring

See Table 2.12 (web only; available at: <a href="http://publications.iarc.fr/569">http://publications.iarc.fr/569</a>)

Several case-control studies on childhood cancers have reported on the association between

occupation of a parent (mostly father) as a welder and the risk of cancer in their offspring; no studies on childhood leukaemia were identified.

#### (a) All childhood cancers

One study conducted in Moscow reported on the association between the father's welding history before conception (Smulevich et al., 1999) and all childhood cancers combined. The number of fathers working as welders was significantly higher among cases than among controls, yielding an odds ratio of 1.8. [The Working Group noted that a breakdown of the specific childhood cancer sites was not provided, and no confidence interval was reported.]

# (b) Childhood cancer of the central nervous system

A neuroblastoma case-control study evaluating parental occupation from age 18 onwards as a potential risk factor (Olshan et al., 1999) reported an odds ratio for father's occupation as a welder/cutter of 0.5 (95% CI, 0.1-1.6). A childhood central nervous system tumour case-control study focusing on paternal occupations with exposure to electric and magnetic fields (Wilkins & Wellage, 1996) reported an odds ratio for preconception paternal occupation as welder of 1.75 (95% CI, 0.23-13.21) based on 3 exposed case fathers and an odds ratio of paternal occupation as welder during pregnancy of 1.00 (95%) CI, 0.09–11.03) based on 2 exposed case fathers. A broader definition of welding, also including those jobs with welding tasks (welding-related jobs), yielded an odds ratio for preconception paternal welding-related job of 3.83 (95% CI, 0.95–15.55) based on 6 exposed case fathers. [The Working Group noted that the higher odds ratio obtained when using a broader definition of welding-related jobs may suggest that exposures other than welding may have to be considered.] A large international case-control study on childhood brain tumours and parental occupations (Cordier et al., 2001) reported an

odds ratio of 0.97 (95% CI, 0.50–1.70) for paternal occupation as a welder. [The Working Group noted that the number of exposed cases on which this odds ratio was based was not reported, but estimated that it was based on 19–20 exposed cases according to the reported percentage exposed controls.]

#### (c) Wilms' tumour

The Working Group identified four case-control studies on Wilms' tumour (a childhood neoplasm of the kidney) that evaluated the association with parental welding, three of which were too small to be able to report risk estimates (Kantor et al., 1979; Wilkins & Sinks, 1984; Bunin et al., 1989). The largest study (Olshan et al., 1990) included 200 cases and 233 controls. Among different exposure periods explored (i.e. preconception, pregnancy, and postnatal), 6 of the case fathers and 1 of the control fathers worked as a welder during pregnancy, yielding the highest odds ratio of 8.22 (95% CI, 0.95–71.27).

#### (d) Other childhood cancers

A case-control study on hepatoblastoma (Buckley et al., 1989) reported an odds ratio of 1.0 related to self-reported father's exposure to welding, based on 12 exposed case fathers. A case-control study of childhood sporadic bilateral retinoblastoma (Abdolahi et al., 2013) reported an odds ratio of 1.22 (95% CI, 0.68–2.19) associated with paternal ever exposure to welding fumes, as assessed by experts using the detailed job history, based on 29 exposed case fathers. The same study reported no risk in relation to intensity of exposure to welding fumes (comparing none to low with moderate and high levels), either during the 10 years before conception or during the year before conception only, and no trends in risk were observed. A recent data linkage study from Finland, Norway, and Sweden (Togawa et al., 2016) included 8112 cases of testicular germ cell tumour (age, 14-49 years) and 26 264 controls;

the occupation of participants' parents were obtained from the census, and exposure was assessed by applying a JEM. Paternal low exposure to welding fumes based on 953 exposed cases and 2904 exposed controls lead to an odds ratio of 1.09 (95% CI, 1.01–1.18), which decreased at high exposure levels to 0.97 (95% CI, 0.79–1.19), based on 124 exposed cases. The odds ratios for maternal exposure were 1.02 (95% CI, 0.65–1.59) and 1.23 (95% CI, 0.64–2.36) for exposure to low and high levels of welding fumes, respectively.

## 2.5.8 Cancer of the pancreas

See Table 2.13 (web only; available at: <a href="http://publications.iarc.fr/569">http://publications.iarc.fr/569</a>)

A total of five case–control studies on cancer of the pancreas that reported on the association with welding or exposure to welding fumes were identified (Norell et al., 1986; Magnani et al., 1987; Siemiatycki, 1991; Ji et al., 1999; Luckett et al., 2012). [The Working Group did not include several other studies for evaluation (Ji et al., 1999; Alguacil et al., 2000; Luckett et al., 2012) as the occupational category was too broad.]

Three studies assessed exposure to welding fumes or "welding materials". A small casecontrol study from Sweden (Norell et al., 1986) reported an odds ratio of 2.0 (90% CI, 0.9-4.3) associated with exposure to "welding materials" based on 13 exposed cases. [The Working Group noted that the exact definition of "welding materials" was not reported.] A mortality study that used a JEM to assess exposure to welding fumes (Magnani et al., 1987) reported an odds ratio of 1 [the Working Group noted that the number of exposed cases was not reported]. A study using other cancer cases as controls (Siemiatycki, 1991), and expert assessment of exposure to arc welding fumes and gas welding fumes, reported odds ratios close to unity for any exposure to either type of fumes and substantial exposure to arc welding fumes; an odds ratio for substantial exposure to

gas welding fumes of 1.4 (95% CI, 0.7–2.8) was reported, based on 6 exposed cases.

None of the studies reported relative risks by duration of exposure.

#### 2.5.9 Other cancers

See Table 2.14 (web only; available at: <a href="http://publications.iarc.fr/569">http://publications.iarc.fr/569</a>)

## (a) Cancer of the stomach

The Working Group identified three casecontrol studies on cancer of the stomach that reported on associations with welding or exposure to welding fumes (Siemiatycki, 1991; Keller & Howe, 1993; Engel et al., 2002). Two studies from the USA reported risk estimates for welding occupation; one reported an odds ratio of 2.11 (95% CI, 1.09-4.09) for cancer of the stomach (Keller & Howe, 1993); and another reported an odds ratio of 2.0 (95% CI, 0.8-5.2) for adenocarcinoma of the gastric cardia and 0.8 (95% CI, 0.3-2.3) for adenocarcinoma of the gastric noncardia (Engel et al., 2002). A Canadian casecontrol study on cancer of the stomach that used expert assessment and cancer controls reported an odds ratio of 0.9 (95% CI, 0.6-1.3) for exposure to arc welding fumes and 0.9 (95% CI, 0.6-1.3) for exposure to gas welding fumes (Siemiatycki, 1991). [The Working Group noted that the estimates were likely to have been based on the same cases and controls, assessed as being exposed to both gas and arc welding fumes.]

#### (b) Cancer of the small bowel

The Working Group identified one case-control study on adenocarcinoma of the small bowel that included 79 cases from five countries (Kaerlev et al., 2000). An odds ratio of 2.6 (95% CI, 1.0–6.4; 6 exposed cases) was reported for welders and flame-cutters, with a positive duration–response relationship (*P* for trend, 0.01).

#### (c) Cancer of the colon and rectum

Three case–control studies on cancer of the colon were identified that examined the association with a welding-related occupation or exposure to welding fumes (Siemiatycki, 1991; Keller & Howe, 1993; Fang et al., 2011), reporting odds ratios ranging from 0.49 to 1.10, none reaching statistical significance. One of these studies also investigated the increased risk of cancer of the rectum in relation to exposure to welding fumes, reporting odds ratios close to unity (Siemiatycki, 1991).

#### (d) Cancer of the liver

One case–control study on cancer of the liver was identified that reported on the association between cancer of the liver and exposure to welding fumes, as assessed by expert (Kauppinen et al., 1992). Odds ratios adjusted for alcohol consumption of 1.38 (95% CI, 0.52–3.64), based on 6 exposed cases, and 13.40 (95% CI, 2.02–88.1) for exposure to high levels of welding fumes, based on 5 exposed cases, were reported.

### (e) Cancer of the prostate

The Working Group identified four casecontrol studies on cancer of the prostate that reported on the association with welding or exposure to welding fumes. A Canadian study using expert assessment and cancer controls reported odds ratios of 1.7 (95% CI, 1.0-2.6) and 1.4 (95% CI, 0.9–2.1) for exposure to substantial levels of arc welding fumes and gas welding fumes, respectively (Siemiatycki, 1991). [The Working Group noted that the estimates are likely to have been based on largely the same cases and controls, assessed as being exposed to both gas and arc welding fumes.] A case-control study from the Netherlands (van der Gulden et al., 1995) reported an odds ratio of 1.51 (95% CI, 0.48-4.78; 4 cases) for longest-held occupation as welder and an odds ratio of 1.19 (95% CI, 0.73-1.95; 22 cases) for workers "frequently exposed to

welding fumes". A study from the US reported an odds ratio of 1.0 (95% CI, 0.61–1.64) for welders (Keller & Howe, 1993). A recent cancer of the prostate case–control study from Canada (Sauvé et al., 2016) reported an odds ratio of 0.97 (95% CI, 0.62–1.50; 50 cases) for ever having worked in welding and flame-cutting occupations. Odds ratios by duration of employment in the occupational group, and separately for arc welders and gas welders, were also presented, but did not reveal a positive duration–response association or differences in risk estimates between welding types.

#### (f) Cancer of the testis

The Working Group identified one case-control study on cancer of the testis that reported a risk estimate for a welding-related occupation (Walschaerts et al., 2007), with an odds ratio of 1.49 (95% CI, 0.53–4.15) after adjusting for risk factors, based on 20 exposed cases. [The Working Group identified an additional case-control study on testicular germ cell tumours, addressing parental occupation (Togawa et al., 2016); see also Section 2.5.7.]

## (g) Melanoma of the skin

The Working Group identified two case-control studies on skin melanoma that reported on the association with exposure to welding fumes, both reporting odds ratios close to and below unity (Magnani et al., 1987; Siemiatycki, 1991).

# 2.6 Occupational studies of cancer mortality and incidence based on routinely collected data

See Table 2.15

Several studies conducted in Canada, New Zealand, the UK, and the USA evaluated the relationship between occupation and cancer using occupation reported on death certificates.

Table 2.15 Occupational studies on cancer mortality and incidence based on routinely collected data

Reference	Location	Exposure group	Cancer outcome and outcome measure	Risk estimate (95% CI)
Menck & Henderson (1976)	CA, USA	Welders	Lung; mortality and incidence: SMR	1.37 (1.01–1.81), 21 deaths, 27 cases
Decouflé et al. (1977)	NY, USA	Welders and flame cutters	Lung; incidence: RR (smoking adjusted)	0.67 (NR), 11 cases
<u>Logan (1982)</u>	UK	Welders	Lung; mortality: SMR	1951: 1.18 (NR) 1971: 1.51 (NR)
Gallagher & Threlfall (1983)	BC, Canada	Welders	Lung; mortality: PMR	1.45 (1.15-1.83), 74 deaths
Firth et al. (1993)	New Zealand	Welders	Lung; mortality: SMR	1.40 (1.20-1.61)
<u>Coggon et al. (2009)</u>	UK	Welders (men)	Mortality: PMR Lung Pleura Sinonasal	1.11 (1.05–1.17), 1263 deaths 1.40 (1.04–1.86), 49 deaths 0.61 (0.13–1.78), 3 deaths
NIOSH (2015) National Occupational Mortality Surveillance (NOMS)	USA	Welders and cutters All races/sexes combined (1999, 2003–2004, 2007–2010)	Mortality: PMR	· //
			Lung	1.22 (1.21-1.30) 1975 deaths
			Oral cavity and pharynx	1.35 (1.11-1.63), 109 deaths
			Oesophagus	1.31 (1.13-1.52), 180 deaths
			Sinonasal	1.72 (0.79–3.27), 9 deaths
			Larynx	1.78 (1.38-2.25), 69 deaths
			Mesothelioma	2.88 (2.24-3.66), 68 deaths
			Liver and gall bladder	1.17 (1.03-1.33), 241 deaths
			Urinary bladder	1.25 (1.05-1.47), 141 deaths
			Kidney	0.99 (0.82-1.17), 130 deaths
			Prostate	1.79 (1.62-1.78), 395 deaths
			Brain	0.60 (0.48-0.75), 85 deaths
			Eye	-, < 5 deaths
			Chronic myeloid leukaemia	0.86 (0.39-1.63), 9 deaths
			Acute myeloid leukaemia	0.89 (0.69-1.12), 67 deaths
			Lymphatic leukaemia	1.02 (0.77-1.34), 53 deaths
			Multiple myeloma	0.77 (0.61-0.97), 76 deaths
			Non-Hodgkin lymphoma	0.82 ((0.70-0.96), 159 deaths
Dolin & Cook-Mozaffari (1992)	UK	Welders	Urinary bladder; mortality: SMR	0.74 (0.38–1.29)
<u>Firth et al. (1993)</u>	New Zealand	Welders	Stomach; mortality: SMR	1.45 (significant)

CI, confidence interval; PMR, proportional mortality ratio; RR, relative risk; SMR, standardized mortality ratio

Less frequently, cancer incidence data from various sources (e.g. not a newly assembled cohort) have also been used. Other countries have also conducted such studies on an ad hoc basis. Most studies were described by the Working Group in 1990 (IARC, 1990), but some have been updated or extended since then. [These studies are not described in detail (see Table 2.15 for a summary) due to several limitations, including: (1) lack of detailed exposure information or the use of occupation reported on death certificates; (2) limited information on potential confounders; (3) use of different data sources for observed (death certificates) and expected (census) deaths; and (4) chance findings due to multiple comparisons in evaluating the associations between many different occupations and causes of deaths in the USA (NIOSH, 2015) and the UK (Coggon et al., 2009).] These studies have been used repeatedly for occupational mortality surveillance purposes, and only the most recent update is reported.

Among all the studies that reported on cancer of the lung in welders, an excess of cancer of the lung was found in all but one study. The two studies that reported on cancer of the pleura and/or mesothelioma also found an excess among welders (Coggon et al., 2009; NIOSH, 2015). Excesses of several other types of cancer were also reported, including cancers of the stomach (Firth et al., 1993), oral cavity and pharynx, oesophagus, larynx, liver and gall bladder, and urinary bladder (NIOSH, 2015). In contrast, no excess risk of cancer of the urinary bladder was found in a study in the UK (Dolin & Cook-Mozaffari, 1992). No clear excess of mortality from cancer of the nasal cavity and sinuses was apparent (Coggon et al., 2009; NIOSH, 2015), and no excesses of deaths from cancer of the kidney, cancer of the brain, leukaemia, multiple myeloma, or NHL were found in the only study that reported on these cancer sites (NIOSH, 2015).

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