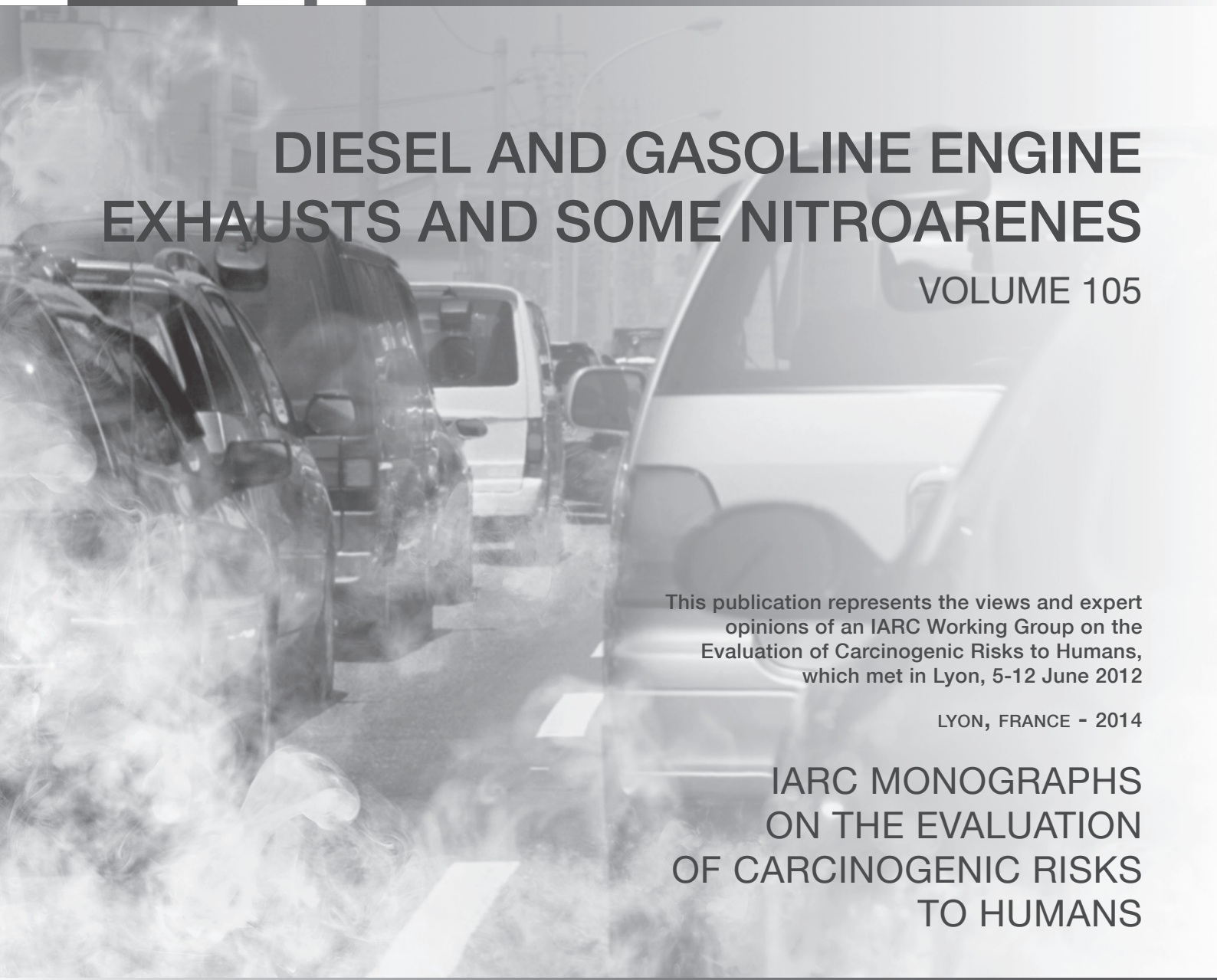
IARC MONOGRAPHS



DIESEL AND GASOLINE ENGINE EXHAUSTS AND SOME NITROARENES

VOLUME 105

This publication represents the views and expert opinions of an IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, which met in Lyon, 5-12 June 2012

LYON, FRANCE - 2014

IARC MONOGRAPHS ON THE EVALUATION OF CARCINOGENIC RISKS TO HUMANS

International Agency for Research on Cancer

World Health Organization

2. CANCER IN HUMANS

2.1 Introduction

2.1.1 General aspects

Diesel and gasoline engine exhausts have been evaluated previously in the *IARC Monographs* (IARC, 1989). Since that time, a large number of cohort and case–control studies have been published on the topic, many of which provided high-quality data on exposure and potential confounding factors. General aspects on the methodological advantages and limitations of the various study designs are discussed briefly below, including a discussion of developments in the methods of exposure assessment and problems regarding bias and confounding.

Occupational cohort studies typically provide reasonably accurate data on current exposure levels, but frequently lack information on historical exposure levels and other risk factors, such as tobacco smoking habits. Over the past few decades, the quality of cohort studies has been further improved by the inclusion of more detailed data on exposure and more advanced exposure modelling, and some now incorporate individual data on tobacco smoking. However, full lifetime occupational histories are often unavailable, which reduces the ability to adjust the findings for occupational exposures incurred during employment outside the industry under study. Comparisons are made between groups with different levels of exposure, either within or outside the study population. In general, the use of an internal unexposed group gives more valid risk estimates than that of an external group, because less bias is introduced from the incomparability of lifestyle-associated factors, such as smoking, and the general health status of the exposed and unexposed groups. Studies that investigate exposure–response associations with measures of exposure to diesel exhaust (e.g. duration, average exposure and/or cumulative exposure) have been given greater weight in the evaluation of carcinogenicity.

A specific group of cohort studies are based on record linkage, and link routinely collected population data on occupational titles to national registers of cancer incidence or mortality. These studies usually provide very crude data on exposure that typically consist of a job title in a specific year, no data on tobacco smoking and no lifetime occupational histories, and are consequently usually viewed as generating hypotheses. This type of study has been considered to give only supportive evidence for the present evaluation.

Finally, some cohort studies use proportionate mortality ratios, a methodology that is applied when data are available on deaths for those employed at a specific industry, but not for the total population at risk, and the distribution of causes of death in the study population is compared with that of an external comparison group. Proportionate mortality ratio studies may give biased results, because it is not possible to assess whether an observed excess in the proportion of deaths from a specific cause is due to a true excess of risk or a reduced risk of deaths for

other causes. For this reason, and in view of the large number of high-quality studies available, proportionate mortality ratio studies have not been considered for the present evaluation.

Case–control studies are sometimes considered to be sensitive to inaccurate recall of previous exposures, with the potential for biased findings, which is a particular concern when information on exposures is based on self-assessment. This potential bias is largely reduced when exposure assessment is based on the assignment of exposures from a lifetime occupational history by an expert assessment method or the application of a job–exposure matrix (JEM), or combinations of the two. The strength of case–control studies is that researchers can obtain detailed individual data on tobacco smoking and other potential risk factors, as well as lifetime occupational histories, from the study subjects. These studies may be based on the general population or be nested within defined occupational cohorts. A potential problem in the former is that detailed exposure data are rarely available, resulting in potential non-differential exposure misclassification, which tends to attenuate the observed risks. A design that incorporates the advantages of detailed data on exposure and individual data on risk factors is the nesting of a case–control study within a cohort. This type of study may provide very high-quality information on the association of occupational exposures with cancer. Finally, case–control studies may recruit controls directly from the general population or from individuals with diagnoses other than that under study. Controls recruited randomly from the population are considered to reflect the prevalence of exposure in the study population more accurately than hospital controls, and afford less potential for bias.

For the present evaluation, the Working Group identified three broad types of study, in order of increasing quality: (1) studies that reported risk for cancer by occupation, with no reference to whether or not the occupation indicated exposure to motor exhaust. Because the predictive value of an occupational title may differ considerably between study settings and countries, such studies have not generally been included for the evaluation of lung cancer. However, for other cancer sites, for which fewer data were available, such studies have been included; (2) studies that reported risk for cancer on the basis of occupational titles, in which the titles were used to indicate potential or definite exposure to diesel or gasoline exhaust. Frequently, duration of employment in such jobs was used as a proxy for quantitative exposure. All such pertinent studies have been reviewed; (3) studies that aimed to assess individual exposure to motor exhaust (diesel, gasoline or both) quantitatively through measurements, modelling, expert assessments, JEMs or other means. In many cases, these studies investigated the intensity and duration of exposure, in addition to cumulative exposure, and had access to full occupational and smoking histories. These studies have been given the greatest weight in the present evaluation.

2.1.2 Aspects of exposure assessment methods

Diesel exhaust is a complex mixture of variable characteristics and several markers of exposure have been used, including polycyclic aromatic hydrocarbons (PAHs), nitrogen dioxide, nitrogen oxides, particulate matter (PM) and elemental carbon (EC). Any proxy of diesel exhaust may or may not reflect accurately one of its underlying carcinogenic components. For instance, in the studies reviewed that investigated proximity to diesel emission sources, EC was a good marker for diesel exhaust. However, this does not imply that EC is, or that it accurately reflects, the causal agent. Therefore, the association between such markers and the true substances of etiological interest may differ to some extent by time and place.

The present evaluation covers both diesel and gasoline exhaust. Many occupations that entail exposure to engine exhausts, for example professional drivers and some garage workers, involve exposure to a mixture of the two exhausts. Cohort studies that more specifically addressed exposure to diesel exhaust were based on railroad workers, miners and bus garage employees. Cohorts of professional drivers often comprised individuals with combined exposure to diesel and gasoline exhausts. Several population-based case–control studies that used expert assessment or JEMs to classify exposure presented separate risk estimates for each of the two exhausts. However, in population-based studies, few occupations generally entailed exposures to specific types of engine exhaust and few individuals incurred very high exposures. Some collinearity may have also arisen between exposures to diesel and gasoline engine exhausts. The main body of available evidence was related to diesel exhaust, while the data that specifically addressed the risk of cancer from exposure to gasoline exhaust among individuals with no concurrent exposure to diesel exhaust were very limited.

2.1.3 Studies of environmental air pollution

Several studies showed associations between lung cancer and ambient air pollution. In addition, exposure to specific components of air pollution, for example $PM_{2.5}$, has been linked to lung cancer (Samet & Cohen, 2006; EPA, 2009). Ambient air pollution comprises emissions from vehicles fuelled by diesel and gasoline, but also those from a variety of other sources and processes, including industrial air pollution. At present, it is very difficult to assess the specific contributions of these sources to the observed cancer risk. These studies have not been included in the review, because they would contribute little information in addition to the studies reviewed here.

2.2 Cohort studies

See Table 2.1

2.2.1 Railroad workers

Howe *et al.* (1983) conducted a cohort study of 43 826 male pensioners of the Canadian National Railway Company who had retired before 1965 and who were alive at the start of that year, as well as those who retired between 1965 and 1977. The cause of death of 17 838 pensioners who died between 1965 and 1977 was ascertained by computerized record linkage to the Canadian national mortality database. A total of 76 different occupations were represented in the cohort. Experts classified each occupation in terms of exposure to diesel fumes (unexposed, possibly exposed and probably exposed), coal dust (unexposed, possibly exposed and probably exposed) and any other fumes or substances. The analyses compared the mortality of different groups of railroad workers with that of the Canadian population and then compared those who presumably incurred higher exposures with those who presumably incurred lower exposures, by calculating their standardized mortality ratios (SMRs). A total of 933 lung cancer deaths resulted in an overall standardized mortality ratio of 1.06. A comparison of the possibly and probably exposed with the unexposed (239 lung cancer deaths) provided a relative risk (RR) for lung cancer of 1.20 ($P = 0.013$; 407 lung cancer deaths) and 1.35 ($P < 0.001$; 279 lung cancer deaths), respectively. No data were available on tobacco smoking habits. In the same study, the authors found a standardized mortality ratio of 1.03 for urinary bladder cancer based on 175 cases, although no internal analyses were performed for this cancer. Exposures to coal dust and diesel overlapped and similar standardized mortality ratios were reported for both exposures. The deaths of those who retired before 1950, and were hence exposed primarily to coal dust, were too

Table 2.1 Selected cohort studies of cancer in railroad workers, bus garage workers, professional drivers, miners, heavy equipment operators and other workers exposed to diesel exhaust

Reference Location, follow-up period	Total No. of subjects	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Railroad workers							
Howe *et al.* (1983) Canada, 1965–77	43 826 retired railroad workers	Review of job titles by experts employed by railroad	Trachea, bronchus and lung			**SMR**	Men; Canadian mortality records; no adjustment for tobacco smoking
				All railroad workers	933	1.06 ($P > 0.05$)	
				Possibly exposed	407	1.20 ($P = 0.013$)	
				Probably exposed	279	1.35 ($P < 0.001$)	
						P for trend < 0.001	
				Possibly exposed	333	1.21	Excluded asbestos- exposed workers
				Probably exposed	256	1.33	
						P for trend < 0.001	
			Urinary bladder	All railroad workers	175	1.03 ($P > 0.05$)	
Boffetta *et al.* (1988) American Cancer Society Cohort, 1982–84	461 981	Self-reported job	Lung	Railroad workers	14	1.59 (0.94–2.69)	Men aged 40–79 yr in 1982; adjusted for age and tobacco smoking; 4–10-yr age strata and 5 strata of smoking
Garshick *et al.* (2004) US Railroad Workers cohort, 1959–96	54 973	Industrial hygiene review of yearly job title and exposure sampling	Lung	Based on job as train crew in 1959; referents: clerks and signal maintainers	4351		Update of Garshick *et al.* (1988); attained age, calendar yr, time on and off work; white men aged 40–64 yr in 1959 with 10–20 yr of employment; indirect adjustment for smoking: adjusted HR, 1.17–1.27
				Age (yr)		**HR**	
				40–44	884	1.49 (1.30–1.70)	
				45–49	732	1.37 (1.18–1.58)	
				50–54	456	1.39 (1.18–1.64)	
				55–59	286	1.34 (1.09–1,64)	
				60–64	121	0.99 (0.75–1.30)	

Table 2.1 (continued)

Reference Location, follow-up period	Total No. of subjects	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Garshick et al. (2004) US Railroad Workers cohort, 1959–96 (cont.)				**Train crew work (yr; 5-yr lag)**			
				0– < 5	391	1.41 (1.24–1.61)	
				5– < 10	484	1.39 (1.23–1.56)	
				10– < 15	618	1.51 (1.35–1.68)	
				15– < 20	707	1.33 (1.19–1.49)	
				≥ 20	204	1.31 (1.10–1.56)	
				Any exposure (5-yr lag)		1.40 (1.30–1.51)	
Garshick *et al.* (2006) US Railroad Workers cohort, 1959–96	39 388	Industrial hygiene review of job history and exposure sampling	Lung (162)	**Train crew work (yr; 5-yr lag)**	Total 4055		Subset of Garshick *et al.* (2004); attained age, calendar yr, time on and off work, tobacco smoking (pack–yr); white men aged 40–59 yr in 1959 with 10–20 yr of employment; adjusted for smoking by imputation from Garshick *et al.* (1987)
				Unexposed	895	1.0	
				0– < 5	330	1.31 (1.12–1.51)	
				5– < 10	449	1.23 (1.08–1.39)	
				10– < 15	615	1.23 (1.10–1.38)	
				15– < 20	707	1.16 (1.03–1.30)	
				≥ 20	204	1.22 (1.02–1.47)	
				Any exposure	22 305	1.22 (1.12–1.32)	
						Unadjusted for smoking	
				0– < 5	330	1.44 (1.25–1.67)	
				5– < 10	449	1.36 (1.20–1.55)	
				10– < 15	615	1.36 (1.22–1.52)	
				15– < 20	707	1.28 (1.14–1.43)	
				≥ 20	204	1.32 (1.11–1.58	
				Any exposure	22 305	1.35 (1.24–1.46)	

Table 2.1 (continued)

Reference Location, follow-up period	Total No. of subjects	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Laden *et al.* (2006) US Railroad Workers cohort, 1959–96	52 812	Industrial hygiene review of job history and exposure sampling	Lung	**Train crew work (yr; 5-yr lag)**			Subset of Garshick *et al.* (2004); attained age, calendar yr, time on and off work; white men aged 40–64 yr in 1959 with 10–20 yr of employment
				Hired 1939–44			
				Unexposed	687	1.0	
				0– < 10	211	1.19 (1.00–1.41)	
				10– < 15	330	1.28 (1.11–1.47)	
				15– < 20	454	1.37 (1.21–1.55)	
				20– < 25	577	1.37 (1.21–1.54)	
				≥ 25	355	1.16 (1.00–1.34)	
				Hired 1945–49			
				Unexposed	229	1.0	
				0– < 10	32	1.15 (0.77–1.70)	
				10– < 15	66	1.49 (1.11–1.99)	
				15– < 20	103	1.89 (1.48–2.40)	
				20– < 25	119	1.83 (1.45–2.32)	
				≥ 25	124	1.78(1.39–2.28)	
				Intensity (yr)			
				Hired 1939–44			
				Unexposed	687	1.0	
				Quintile 1	326	1.26 (1.09–1.46)	
				Quintile 2	394	1.37 (1.17–1.51)	
				Quintile 3	417	1.33 (1.17–1.50)	
				Quintile 4	427	1.28 (1.13–1.45)	
				Quintile 5	363	1.24 (1.08–1.43)	
				Hired 1945–49			
				Unexposed	229	1.0	
				Quintile 1	80	1.63 (1.24–2.14)	
				Quintile 2	98	1.54 (1.21–1.96)	
				Quintile 3	93	2.02 (1.58–2.59)	
				Quintile 4	76	1.50 (1.14–1.96)	
				Quintile 5	97	1.81 (1.39–2.35)	

Table 2.1 (continued)

Reference Location, follow-up period	Total No. of subjects	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Guo *et al.* (2004a) Finland, records from 1971–95	Finnish working population, census data in 1970; 67 121 men	Longest held job in 1970 census	Lung	Locomotive driver	85	**SIR** 0.63 (0.51–0.78)	All working Finns born after 1906; linkage to Finnish Cancer Registry; indirect adjustment for tobacco smoking
Guo *et al.* (2004b) Finland, 1971–95			Urinary bladder	Locomotive driver	22	**SIR** 0.85 (0.53–1.28)	Same census linkage study as Guo *et al.* (2004a); cases in men
Bus garage workers							
Gustavsson *et al.* (1990) Stockholm, Sweden, mortality, 1952–86; cancer incidence, 1958–84	695 bus garage workers, 1945–70	JEM for diesel exhaust exposure; intensity × duration score	Lung	Entire cohort	17	**SMR** 1.22 (0.71–1.96)	Expected numbers based on Stockholm rates; occupationally active men; no information on tobacco smoking; exposure to asbestos assessed; no effect of exposure on lung cancer
	Nested case–control study: 20 incident cases/120 controls			**Diesel exhaust score**			Controls matched on age (± 2 yr)
						OR	
				0–10	5	1.00 (referent)	
				10–20	2	1.27 (0.21–7.72)	
				20–30	3	1.56 (0.34–7.16)	
				> 30	10	2.63 (0.74–9.42)	
Professional drivers							
Bus drivers							
Balarajan & McDowall (1988) London, United Kingdom, 1950–84	3392 professional drivers	Job title in 1939 census and still alive in 1950	Lung	Bus and coach drivers	18	**SMR** [1.42] ($P > 0.05$)	Expected based on England and Wales rates; no adjustment for tobacco smoking
			Urinary bladder		1	[0.58] ($P > 0.05$)	

Table 2.1 (continued)

Reference Location, follow-up period	Total No. of subjects	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Soll-Johanning *et al.* (1998) Denmark, 1943–92	15 249 male and 958 female bus and tramway workers	Job title obtained from population register; ever employed as an urban bus driver or tramway worker, 1900–94	Lung	**Employed > 3 mo**		**SIR**	Similar to slightly greater smoking rates compared with Copenhagen * All Denmark ** Copenhagen only
				Men*	473	1.6 (1.5–1.8)	
				Men**	390	1.2 (1.1–1.3)	
				Women*	15	2.6 (1.4–4.3)	
				Men–30 yr since first employed			
				< 0.25	9	1.1	
				0.25– < 1.5	57	2 ($P < 0.0001$)	
				1.5– < 4.0	48	1.7 ($P < 0.0001$)	
				5.0–14	70	2.1 ($P < 0.0001$)	
				≥ 15	188	1.5 ($P < 0.0001$)	
			Urinary bladder	**Employed > 3 mo**			* All Denmark ** Copenhagen only
				Men*	177	1.4 (1.2–1.6)	
				Men**	165	1.1 (0.9–1.3)	
Soll-Johanning *et al.* (2003) Denmark, 1943–92	153 cases, 255 controls; all men	Job title from population register	Lung	**Duration of employment (no lag)**			Nested case–control study from the cohort of Soll-Johanning *et al.* (1998); tobacco smoking estimated from spouse, converted to pack–years in 7 categories; cases and controls aged < 85 yr; matched to 1–4 controls by yr of birth and vital status, free of urinary bladder, lung or other cancer, or non-malignant lung disease
				< 3 mo	5	0.74 (0.23–2.39)	
				3 mo– < 3 yr	29	1.0 (referent)	
				2– < 10 yr	54	1.26 (0.69–2.28)	
				10– < 20 yr	22	1.39 (0.69–2.81)	
				≥ 20 yr	43	0.63 (0.32–1.14)	
				Duration of employment (10-yr lag)			
				< 3 mo	4	0.50 (0.14–1.81)	
				3 mo– < 3 yr	27	1.0 (referent)	
				2– < 10 yr	45	1.03 (0.54–1.95)	
				10– < 20 yr	22	1.34 (0.65–2.77)	
				≥ 20 yr	43/139 (cases/controls)	0.54 (0.28–1.03)	

Table 2.1 (continued)

Reference Location, follow-up period	Total No. of subjects	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Soll-Johanning et al. (2003) Denmark, 1943–92 (cont.)	84 cases, 255 controls; all men		Urinary bladder	**Duration of employment (no lag)**			
				< 3 mo	3	2.00 (0.27–10.92)	
				3 mo– < 3 yr	13	1.0 (referent)	
				2– < 10 yr	20	1.18 (0.47–2.96)	
				10– < 20 yr	15	1.24 (0.46–3.33)	
				≥ 20 yr	33	1.13(0.47–2.68)	
				Duration of employment (10-yr lag)			
				< 3 mo	1	1.21 (0.12–12.34)	
				3 mo– < 3 yr	11	1.0 (referent)	
				2– < 10 yr	17	1.23 (0.46–3.30)	
				10– < 20 yr	15	1.61 (0.57–4.55)	
				≥ 20 yr	33	1.28 (0.52–3.13)	
Guo *et al.* (2004a) Finland, records from 1971–95	Finnish working population, census data in 1970; 667 121 men	Longest job held in 1970 census	Lung	Bus drivers	253	**SIR** 0.89 (0.78–1.00)	Indirect adjustment for tobacco smoking
Guo *et al.* (2004b) Finland, 1971–95			Urinary bladder	Bus drivers	75	**SIR** 1.29 (1.02–1.62)	Same cohort as Guo *et al.* (2004a); indirect adjustment for tobacco smoking
Petersen *et al.* (2010) Denmark, 1979–2003	2037 male Danish urban bus drivers employed in 1978	Bus company records in 3 largest cities; mailed questionnaire	Lung	Bus drivers	100	**SIR** 1.2 (1.0–1.4)	City-specific expected lung cancer rates; age, calendar time, city of employment, bus route, tobacco smoking; smoking history, details of work history from questionnaire
				≥ 15 yr employment		1.3 (1.0–1.8)	
				Per yr employment	100	**IRR** 1.00 (0.98–1.03)	
				< 15 yr	49	1.0	
				15–24 yr	24	0.89 (0.59–1.48)	
				≥ 25 yr	25	0.95 (0.55–1.63)	

Table 2.1 (continued)

Reference Location, follow-up period	Total No. of subjects	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Petersen et al. (2010) Denmark, 1979–2003 (cont.)						*P* for trend = 0.79	
				10-yr lag			
				< 15 yr		1.00	
				15–24 yr		0.9 (0.5–1.4)	
				≥ 25 yr		0.8 (0.5–1.4)	
			Urinary bladder	Bus drivers		**SIR**	
					69	1.6 (1.2–2.0)	
				≥ 15 yr employment	69	1.8 (1.2–2.5)	
						IRR	
				Per yr employment		1.02 (0.99–1.05)	
				< 15 yr	34	1.00	
				15–24 yr	17	1.11 (0.60–2.03)	
				≥ 25 yr	18	1.31 (0.70–2.48)	
						P for trend = 0.40	
				10- yr lag			
				< 15 yr		1.00	
				15–24 yr		1.6 (0.9–2.8)	
				≥ 25 yr		1.4 (0.7–2.6)	
Heavy goods vehicle (HGV) and other drivers							
Boffetta et al. (1988) American Cancer Society Cohort, 1982–84	476 648	Self-reported job	Lung	All HGV drivers	48	1.24 (0.93–1.66)	Age and tobacco smoking, including pipe/cigar only; mortality in men aged 40–79 yr in 1982; any work as HGV driver
				Reporting exposure to diesel		1.22 (0.77–1.95)	
				Not reporting exposure to diesel		1.19 (0.74–1.89)	
				1–15 yr exposure to diesel	6	0.87 (0.33–2.25)	
				≥ 16 yr exposure to diesel	12	1.33 (0.64–2.75)	

Table 2.1 (continued)

Reference Location, follow-up period	Total No. of subjects	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Balarajan & McDowall (1988) London, United Kingdom, 1950–84	3392 professional drivers	Job title in 1939 census and still alive in 1950; professional drivers identified from NHS Central Registry	Lung			**SMR**	Observed and expected based on England/Wales rates; men only; no adjustment for tobacco smoking
				Taxi drivers	30	0.86 ($P > 0.05$)	
				HGV drivers	280	1.59 ($P < 0.05$)	
			Urinary bladder	Taxi drivers	5	1.21 ($P > 0.05$)	
				HGV drivers	19	1.06 ($P > 0.05$)	
Gubéran *et al.* (1992) Geneva, Switzerland, 1949–1986 for mortality, 1970–1986 for incidence	6630 drivers holding a licence in 1949–61	Occupation on driver's licence	Lung	Professional drivers, 15 yr latency	77 deaths	**SMR** 1.50 (1.23–1.81)	Expected based on male mortality rates for Switzerland Expected based on mean incident rates for men in Geneva 1970–75, 1976–81, 1982–86
					64 incident cases	**SIR** 1.61 (1.29–1.98)	
				Mortality (time from first exposure in yr)			Men born 1900 or later; limited comparison of smoking rates with other men
				0–14	2	0.67	
				15–24	11	1.18	
				24–34	24	1.3	
				35–44	21	1.35	
				≥ 45	21	2.59	
						P for trend = 0.02	
				Non-professional drivers, 15-yr latency			
				Less exposure group	126	1.21 (1.03–1.40)	
					97 incident cases	1.15 (0.97–1.37)	
				More exposure group	24 deaths	1.32 (0.91–1.85)	
					24 incident cases	1.61 (1.11–2.27)	

Table 2.1 (continued)

Reference Location, follow-up period	Total No. of subjects	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Gubéran et al. (1992) Geneva, Switzerland, 1949–1986 for mortality, 1970–1986 for incidence (cont.)			Urinary bladder	Professional drivers, 15-yr latency	13 incident cases	**SIR** 1.25 (0.74–1.99)	
Hansen (1993) Denmark, 1970–80	14 225 HGV drivers and 43 024 unskilled labourers as reference	Job in 1970 census	Lung	HGV drivers	76	**SMR** 1.60 (1.26–2.00)	No direct control for tobacco smoking, but similar rates among HGV drivers and referents from population survey
			Urinary organs	HGV drivers	11	0.98 (0.49–1.75)	
Järvholm & Silverman (2003) Sweden, to 1995	Swedish construction workers (389 000 total), 1971–92: 6364 male HGV drivers; 110 984 carpenters and electricians as referents	Job recorded at examination	Lung	HGV drivers	57 deaths	**SMR** 1.37 (1.04–1.78)	Tobacco smoking (never, current, former, unknown), age at diagnosis or death, calendar time; national industrial health service health examination in 1971–92; smoking history from first examination; general population SIR and SMR not adjusted for smoking
					61	**SIR** 1.29 (0.99–1.65)	
					General population referents		Age- and calendar time-adjusted
					57 deaths	**SMR** 1.18 (0.89–1.53)	
					61	**SIR** 1.14 (0.87–1.46)	
Guo *et al.* (2004a) Finland, records in 1971–95	Finnish working population, census data in 1970; 667 121 men	Longest job held in 1970 census	Lung	HGV drivers	620	**SIR** 1.13 (1.04–1.22)	Indirect adjustment for tobacco smoking

Table 2.1 (continued)

Reference Location, follow-up period	Total No. of subjects	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Guo *et al.* (2004b) Finland, 1971–95			Urinary bladder	HGV drivers	144	**SIR** 1.01 (0.85–1.19)	Same cohort as Guo *et al.* (2004a); men only; indirect adjustment for tobacco smoking
Laden *et al.* (2007) USA, 1985–2000	54 319, including 36 299 union drivers	Job title and industrial hygiene survey	Lung			**SMR**	Survey of current workers in 2003 indicated similar birth cohort-specific tobacco smoking rates compared with US men; results by job title presented only in figures
				All workers	769	1.04 (0.97–1.12)	
				Drivers	NR	1.10 (1.02–1.19)	
				Loading dock workers	NR	1.10 (0.94–1.30)	
			Urinary bladder	All workers	29	0.80 (0.56–1.15)	
Garshick *et al.* (2008) USA, 1985–2000	31 135 union drivers	Job title and industrial hygiene survey	Lung (underlying or secondary cause)			**Change in HR (%) per yr increase**	Age, calendar yr, time period of hire, attained age in 1985, time on and off work, race, census region; men only; indirect adjustment for tobacco smoking using smoking rates from 2003 worker survey
				Long-haul drivers	323	2.5 (0.2–4.9)	
				Pick-up and delivery drivers	233	3.6 (1.2–6.1)	
				Dock workers	205	3.4 (0.8–6.0)	
				Combination workers (local drivers/dock workers)	150	4.0 (1.5–6.6)	
						HR for > 1 yr work	
				Mechanics	38	0.95 (0.66–1.38)	
				Hostlers	29	0.99 (0.68–1.45)	
				Clerks	15	0.55 (0.32–0.95)	
						HR for 20 yr work	
				Long-haul drivers	323	1.65 (1.04–2.62)	
						1.40 (0.88–2.24)	Smoking-adjusted

Table 2.1 (continued)

Reference Location, follow-up period	Total No. of subjects	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Garshick et al. (2008) USA, 1985–2000 (cont.)				Pick-up and delivery drivers	23	2.04 (1.28–3.25)	
						2.21 (1.38–3.52)	Smoking-adjusted
				Dock workers	205	1.94 (1.18–3.18)	
						2.02 (1.23–3.33)	Smoking-adjusted
				Combination workers (local drivers/dock workers)	150	2.20 (1.35–3.61)	Smoking-adjusted
						2.34 (1.42–3.83)	
Birdsey *et al.* (2010) USA, 1989–2004	156 241 members of US HGV owners/ operators trade association	None	Lung	Trade association membership	557	**SMR** 1.00 (0.92–1.09)	Expected deaths from US population; 94% men; only 32% had more than 9 yr of follow-up; overall SMR, 0.76, suggesting healthy-worker effect; no adjustment for tobacco smoking
			Bladder and other urinary	Trade association membership		0.93 (0.62–1.34)	
Garshick *et al.* (2012) USA, 1985–2000	31 135 union drivers	Job title and industrial hygiene survey, workers employed ≥ 1 yr in 1985	Lung	**Cumulative exposure (µg/m3–mo)**			Age, calendar year, time period of hire, attained age at study entry, race, census region; men only; mechanics excluded
				No lag			
				< 530	153	Reference	
				530– < 1061	193	1.13 (0.90–1.42)	
				1061– < 2076	202	1.13 (0.87–1.46)	
				≥ 2076	193	1.02 (0.76–1.36)	
				Adjusted for duration			
				< 530		Reference	
				530– < 1061		1.25 (0.99–1.71)	
				1061– < 2076		1.30 (0.99–1.72)	
				≥ 2076		1.24 (0.89–1.71)	
				5-yr lag			
				< 371	122	Reference	
				371– < 860	191	1.18 (0.92–1.52)	
				860– < 1803	202	1.17 (0.88–1.55)	
				≥ 1803	226	1.19 (0.86–1.63)	

Table 2.1 (continued)

Reference Location, follow-up period	Total No. of subjects	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
				Adjusted for duration			
Garshick et al. (2012) USA, 1985–2000 (cont.)				< 371		Reference	
				371– < 860		1.31 (1.01–1.71)	
				860–1803		1.38 (1.02–1.87)	
				≥ 1803		1.48 (1.05–2.10)	
				10-yr lag			
				< 167	112	Reference	
				167– < 596	179	1.06 (0.80–1.40)	
				596– < 1436	202	1.05 (0.77–1.45)	
				≥ 1436	248	1.12 (0.78–1.61)	
				Adjusted for duration			
				< 167		Reference	
				167– < 596		1.17 (0.88–1.57)	
				596– < 1436		1.26 (0.90–1.78)	
				≥ 1436		1.41 (0.78–1.61)	
				Average exposure, 5-yr lag (µg/m3)			
				< 3.6	146	Reference	
				3.6– < 5.4	211	1.15 (0.93–1.43)	
				5.4– < 7.9	221	1.11 (0.89–1.39)	
				≥ 7.9	163	1.11 (0.87–1.43)	
				Adjusted for duration			
				< 3.6		Reference	
				3.6– < 5.4		1.15 (0.93–1.43)	
				5.4– < 7.9		1.12 (0.89–1.40)	
				≥ 7.9		1.13 (0.88–1.44)	

Table 2.1 (continued)

Reference Location, follow-up period	Total No. of subjects	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Miners							
Boffetta *et al.* (1988) American Cancer Society Cohort, 1982–84	476 648	Self-reported job	Lung	Miners	15	2.67 (1.63–4.37)	Age and tobacco smoking, including pipe/cigar only; mortality in men aged 40–79 yr in 1982; any work as a miner
Guo *et al.* (2004a) Finland, records in 1971–95	Finnish working population in 1970 census; 667 121 men	Longest job held in 1970 census	Lung			**SIR**	Indirect adjustment for tobacco smoking
				Metal ore miners	36	3.26 (2.28–4.51)	
				Non-metal ore miners	181	1.85 (1.59–2.14)	
				Other miners	70	1.73 (1.35–2.19)	
Guo *et al.* (2004b) Finland, 1971–95			Urinary bladder			**SIR**	Same cohort as Guo *et al.* (2004a); men only; indirect adjustment for tobacco smoking
				Non-metal ore miners	22	1.16 (0.73–1.76)	
Neumeyer-Gromen *et al.* (2009) Former East Germany, 1970–2001	5862 former East German potash miners employed after 1969	Industrial hygiene job review and total carbon measurements	Lung (mortality)			**SMR**	Follow-up of Säverin *et al.* (1999); expected based on male population of former East Germany; median duration of exposure, 14.9 yr; mean follow-up, 26 yr since hire
				All workers	61	0.73 (0.57–0.93)	
			Urinary bladder (mortality)	All workers	8	0.80 (0.40–1.60)	
			Lung (mortality)	> 4.9 [mg/m^3]–yr	61	1.28 (0.61–2.71)	Age, tobacco smoking (nonsmoker, smoker, missing); men; data on smoking available from medical examinations
				Exposure quintiles [mg/m3]–yr			Age, smoking, duration of follow-up
				< 1.29	9	1.0	
				1.29– < 2.04	11	1.13 (0.46–2.75)	
				2.04– < 2.73	17	2.47 (1.02–6.02)	
				2.73– < 3.90	9	1.50 (0.56–4.04)	

Table 2.1 (continued)

Reference Location, follow-up period	Total No. of subjects	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Neumeyer-Gromen et al. (2009) Former East Germany, 1970–2001 (cont.)	3335			> 3.90	15	2.28 (0.87–5.97) *P* for trend = 0.09	
				Subcohort with more accurate exposure data			
				> 4.9 [mg/m³]–yr	37	1.50 (0.66–3.43)	Age, smoking (nonsmoker, smoker, missing)
Attfield *et al.* (2012) USA, depending on mine, through 1997	12 315 non-metal miners in 8 mines 1947–67	Modelled estimate of respirable EC underground; no historical measurements for surface miners				**SMR**	SMRs calculated using state-specific rates Exposures to radon, asbestos and silica low; no effect on results of exposure to EC
			Lung (mortality)	Ever underground	122	1.21 (1.01–1.45)	
				Surface only	81	1.33 (1.06–.66)	
			Urinary bladder (mortality)	Ever underground		0.69 (0.23–1.62)	
				Surface-only		1.68 (0.72–3.30)	
		Cumulative EC, 15-yr lag	Lung (mortality)	**Ever underground (µg/m3–yr)**		**HR**	Unadjusted for tobacco smoking; similarly elevated risks with average EC exposure in underground workers
				< 108	30	1.0	
				108– < 445	31	1.50 (0.86–2.62)	
				445– < 946	30	2.17 (1.21–3.88)	
				≥ 946	31	2.21 (1.19–4.09)	
				Excluding persons with < 5 yr work, limiting exposure to < 1280 µg/m³–yr	79	4.06 (2.11–7.83) per 1 000 µg/m³–yr ($P < 0.001$)	
				Surface only (µg/m3–yr)		**HR**	Unadjusted for tobacco smoking
				0– < 0.70	19	1.00	
				0.70– < 4.6	20	1.28 (0.64–2.58)	
				4.6– < 14	19	0.73 (0.35–1.53)	
				≥ 14	20	1.00 (0.44–2.28)	

Table 2.1 (continued)

Reference Location, follow-up period	Total No. of subjects	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Attfield et al. (2012) USA, depending on mine, through 1997 (cont.)				Excluding persons with < 5 yr work	57	1.02 (1.00–1.03) per μg/m^3–yr (P = 0.026)	
		Average EC intensity, 15-yr lag		0– < 0.57	19	1.00	
				0.57– < 0.91	18	1.71 (0.82–3.58)	
				0.92– < 1.4	21	2.22 (1.01–4.90)	
				≥ 1.4	20	2.56 (1.09–6.03)	
		Cumulative EC, 15-yr lag		**Entire cohort (μg/m3–yr)**		**HR**	Unadjusted for tobacco smoking; adjusted for work location: above or underground
				0– < 02.5	50	1.00	
				2.5– < 56	50	0.55 (0.35–0.85)	
				56– < 583	50	1.03 (0.60–1.77)	
				> 583	50	1.39 (0.78–2.48)	
		Average EC intensity, 15-yr lag		**Entire cohort (μg/m3)**			
				0– < 0.86	50	1.00	
				0.86– < 5.2	50	1.13 (0.72–1.76)	
				5.2– < 60	50	1.98 (1.12–3.52)	
				≥ 60	50	1.57 (0.86–2.86)	
Silverman *et al.* (2012) USA, depending on mine, through 1997	Non-metal miners in 8 mines, nested case-control study, 1947–67; 198 cases and 562 controls	See Attfield *et al.* (2012) Cumulative EC, no lag	Lung	**Ever underground (μg/m3–yr)**		**OR**	Tobacco smoking status; history of respiratory disease; previous history of a high-risk job
				< 298	29	1.00	
				298– < 675	29	1.45 (0.68–3.11)	
				675– < 1465	29	1.81(0.84–3.89)	
				≥ 1465	29	1.93 (0.90–4.15)	P for trend = 0.123
				< 81	29	1.00	
				81– < 325	29	2.46 (1.01–6.01)	
				325– < 878	29	2.41(1.00–5.82)	
				≥ 878	29	5.10 (1.88–13.87)	P for trend = 0.004

Table 2.1 (continued)

Reference Location, follow-up period	Total No. of subjects	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Silverman et al. (2012) USA, depending on mine, through 1997 (cont.)				**Surface only (µg/m3–yr)**		**OR**	
				0– < 0.6	13	1.00	
				0.60– < 0.9	13	3.98 (0.69–23.02)	
				0.9– < 1.4	13	0.76 (0.12–4.98)	
				≥ 1.4	14	0.42(0.05–3.59)	*P* for trend = 0.117
				All workers		**OR**	
				< 3	49	1.00	
				3– < 72	50	0.74 (0.40–1.38)	
				72– < 536	49	1.54 (0.74–3.20)	
				≥ 536	50	2.83 (1.28–6.26)	*P* for trend = 0.001
		Cumulative EC, 15-yr lag, ≥ 2 pack/day smoker		< 8 µg/m³–yr	19	26.79 (6.15–116.63)	Adjusted for location, history of respiratory disease; previous history of a high-risk job
				< 8–304 µg/m³–yr	15	22.17 (4.84–101.65)	
				≥ 304 µg/m³–yr	10	17.38 (3.48–86.73)	
		Cumulative EC, 15-yr lag, < 1 pack/day smoker		< 8 µg/m³–yr	10	6.25 (1.42–27.60)	
				< 8–304 µg/m³–yr	10	7.42 (1.62–34.00)	
				≥ 304 µg/m³–yr	15	16.35 (3.45–77.63)	

Table 2.1 (continued)

Reference Location, follow-up period	Total No. of subjects	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Other exposed workers							
Heavy equipment operators							
Wong *et al.* (1985) USA, 1964–1978	34 156 members of a construc-tion union for at least 1 yr	Job category review	Lung	All members	309	**SMR** 0.99 (0.88–1.10)	Expected deaths from USA age-, sex-, cause-specific rates; men only; no direct information on tobacco smoking; survey of only 107 members with similar rates to USA
				Membership			
				< 5 yr	10	0.45	
				5–9 yr	25	0.75	
				10–14 yr	53	1.08	
				15–19 yr	58	1.02	
				≥ 20 yr	163	1.07	
				Retired at/after age 65 yr and early retirees	86	1.30 (1.04–1.61)	
		Categorization of job title provided by union based on proximity		High		0.94	Not clear if longest job held was used to categorize exposure to diesel exhaust
				Low		0.86	
				Unknown		0.67	
				No history		1.19 ($P < 0.05$)	
			Urinary bladder	All members	27	1.18 (0.78–1.72)	
Boffetta *et al.* (1988) American Cancer Society Cohort, 1982–84	476 648	Self-reported job	Lung	Heavy equipment operators	5	2.60 (1.12–6.06)	Age and tobacco smoking; mortality in men aged 40–79 yr in 1982; any work as a heavy equipment operator

Table 2.1 (continued)

Reference Location, follow-up period	Total No. of subjects	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Järvholm & Silverman (2003) Sweden, to 1995	Swedish construction workers (389 000 total), 1971–92: 14 364 operators of heavy construction vehicles; 110 984 carpenters and electricians as referents	Job recorded at examination	Lung (162)	Heavy construction vehicle operators	49 deaths	**SMR** 0.83 (0.61–1.09)	Lung cancer rates from Swedish cancer and death registries; tobacco smoking (never, current, former, unknown), age at diagnosis or death, calendar time; national industrial health service examination 1971–92; tobacco smoking history from first examination
					61	**SIR** 0.87 (0.66–1.11)	
				Use of a cabin on construction vehicle		**SIR**	
				Never	10	0.86 (0.4–1.6)	
				Sometimes	37	0.71 (0.5–1.0)	
				Always	7	0.50 (0.2–1.0)	
						P for trend < 0.001	
Guo *et al.* (2004a) Finland, records in 1971–95	Finnish working population in 1970 census; 667 121 men	Longest job held on 1970 census	Lung	Forklift drivers	80	**SIR** 0.91 (0.72–1.13)	Indirect adjustment for tobacco smoking
				Excavation machine operators	76	1.12 (0.88–1.40)	
				Road building machine operators	121	1.07 (0.89–1.28)	
				Construction machine operators	104	1.13 (0.92–1.37	
Guo *et al.* (2004b) Finland, 1971–95			Urinary bladder	Forklift drivers	19	**SIR** 1.07 (0.65–1.67)	Same cohort as Guo *et al.* (2004a); indirect adjustment for tobacco smoking
				Excavation machine operators	18	1.10 (0.65–1.74)	
				Road building machine operators	23	1.04 (0.66–1.57)	
				Construction machine operators	19	0.93 (0.56–1.46)	

Table 2.1 (continued)

Reference Location, follow-up period	Total No. of subjects	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Dock workers							
Gustafsson *et al.* (1986) Sweden, 1961–80	6071 Swedish dock workers	None	Lung	Cohort membership	70 deaths; 86 incident cases	**SMR** 1.32 (1.05–1.66) **SIR** 1.68 (1.36–2.07)	Lung cancer deaths and cases linked to national cancer and mortality register; expected rates from county/metro area of workers; diesel HGVs first in ports in the late 1950s, increased use in the 1960s; no information on tobacco smoking
Emmelin *et al.* (1993) Sweden, 1950–74	Nested case–control study in update of Swedish dock worker cohort: 50 cases/154 controls	Duration of use of diesel equipment and indices related to fuel consumption, 2-yr lag	Lung	**Yr of work since diesel introduced**			Lung cancer deaths and cases linked to national cancer and mortality register; adjusted for tobacco smoking and exposure variables; controls matched on port and date of birth; results presented with 90% CI
				Low/nonsmoker	9	1.00	
				Medium	27	1.8 (0.5–6.6)	
				High	14	2.9 (0.6–14.4)	
				Fuel use index			
				Low	10	1.00	
				Medium	25	1.5 (0.5–4.8)	
				High	15	2.9 (0.7–11.5)	
				Exposure time			
				Low/non-smoker	12	1.00	
				Medium	19	2.7 (0.6–11.3)	
				High	19	6.8 (1.3–34.9)	
Guo *et al.* (2004a) Finland, records in 1971–95	Finnish working population in 1970 census; 667 121 men	Longest job held on 1970 census	Lung	Stevedores	236	**SIR** 1.32 (1.16–1.50)	Indirect adjustment for tobacco smoking
Guo *et al.* (2004b) Finland, 1971–95			Urinary bladder	Stevedores	31	**SIR** 0.95 (0.65–1.35)	Same cohort as Guo *et al.* (2004a); men only; indirect adjustment for tobacco smoking

Table 2.1 (continued)

Reference Location, follow-up period	Total No. of subjects	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Occupations entailing exposure to diesel exhaust							
Boffetta *et al.* (1988) American Cancer Society Cohort, 1982–84	476 648	Self-reported exposure to diesel exhaust at work in 1982	Lung	Any exposure 1–15 yr ≥ 16 yr	174	1.18 (0.97–1.44) 1.05 (0.80–1.39) 1.21 (0.94–1.56)	Age strata, tobacco smoking, other occupational exposures; mortality in men aged 40–79 yr in 1982
Van Den Eeden & Friedman (1993) California, USA, 1964–88	160 230	Questionnaire; self-reported exposure in past and previous to past yr	Lung	Exposure in past yr Exposure in past yr and before	1 662	1.13 (0.93–1.36) 1.02 (0.81–1.29)	Age, gender, education, race and tobacco smoking; health plan participants, aged 18–79 yr, free of cancer at time of examination
			Urinary bladder	Exposure in past yr Exposure in past yr and before	650	1.17 (0.86–1.59) 1.16 (0.81–1.67)	
Boffetta *et al.* (2001) Sweden, 1971–89	Men, 28 million PY; women, 15 million PY	Linkage to Swedish Cancer Environment Register for job and industry title from 1960 census; JEM	Lung	Any diesel exposure Unexposed Low probability Medium probability High probability	6 266 17 979 2 222 1 881 1 841	**SIR** 1.09 (1.06–1.12) 1.0 (reference) 1.1 (1.04–1.13) 0.90 (0.86–0.94) 1.2 (1.10–1.21)	Expected based on Swedish rates; age, calendar period, region and urban/rural residence; rates for men shown; few cases in women; no information on tobacco smoking
			Urinary bladder	Unexposed Low probability Medium probability High probability	12 287 1 380 1 220 1 069	1.0 (reference) 0.99 (0.94–1.05) 0.84 (0.79–0.89) 0.98 (0.92–1.04)	
Zeegers *et al.* (2001) Netherlands, 1986–92	58 279 from 204 municipal population registries	JEM from job history	Urinary bladder	No exposure Low Medium High	428 35 31 32	1.0 1.00 (0.65–1.54) 0.96 (0.60–1.53) 1.17 (0.74–1.84)	Age, other occupational exposures, intensity and duration of cigarette smoking

Table 2.1 (continued)

Reference Location, follow-up period	Total No. of subjects	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Guo *et al.* (2004a) Finland, records in 1971–95	Finnish working population in 1970 census; 667 121 men	JEM using longest held job in 1970 census, 20-yr lag	Lung	None Lowest Middle Highest	26 723 2 436 758 120	1.0 (reference) 0.98 (0.94–1.03) 1.04 (0.97–1.12) 0.95 (0.83–1.10)	Asbestos, quartz dust, SES, age, time period; indirect adjustment for tobacco smoking
Guo *et al.* (2004b) Finland, 1971–95		JEM using longest held job in 1970 census, 20-yr lag	Urinary bladder	None None Lowest Middle Highest	6 026 5 872 493 200 78	1.0 (reference) 1.0 (reference) 1.00 (0.91–1.11) 0.95 (0.83–1.10) 0.97 (0.77–1.21)	Same cohort as Guo *et al.* (2004a); adjusted for tobacco smoking, SES, age and time period; men only

CI, confidence interval; EC, elemental carbon; HR, hazard ratio; ICD, International Classification of Diseases; IRR, incidence rate ratio; JEM, job–exposure matrix; mo, months; NHS, national health service; NR, not reported; OR, odds ratio; PY, person–years; SES, socioeconomic status; SIR, standardized incidence ratio; SMR, standardized mortality ratio; yr, year

few for a meaningful analysis. [Although exposure to coal dust has not been proven to be associated with the risk for lung cancer, it is probable that workers who incurred this exposure also had concurrent exposure to coal combustion before conversion to diesel-powered locomotives. Therefore, although these results are consistent with an increased risk of lung cancer attributable to exposure to diesel exhaust, it is possible that coal combustion products contributed to this risk.]

Boffetta *et al.* (1988) examined the relationship between lung cancer and occupational exposure to diesel exhaust using data from a prospective mortality study including more than 1.2 million American men and women that was begun in 1982 by the American Cancer Society. Volunteers from across the USA were enrolled by completing a questionnaire that included information on tobacco smoking, current and last jobs, and the job held for the longest period, other exposures and self-reported exposure to diesel exhaust. An assessment of mortality up to September 1984 was conducted in men aged 40–79 years at enrolment. Of these, 2973 men reported working in the railroad industry during any period of their life. Their relative risk for lung cancer was 1.59 (95% confidence interval [CI], 0.94–2.69; based on 14 deaths), compared with men who did not report working in the railroad industry and who reported no exposure to diesel exhaust, after adjusting for age and smoking. Similar results were obtained for those who reported railroad work as their principal occupation. The risk for lung cancer among railroad workers who reported exposure to diesel exhaust was not stated (approximately 50% of persons who had railroad work as their principal occupation reported exposure to diesel exhaust). [The Working Group found some indication of an increased risk of lung cancer, although this was weakened by the use of self-reporting to assess exposure.]

Nokso-Koivisto & Pukkala (1994) studied 8391 members of the Finnish Locomotive Drivers' Association and determined their cancer incidence between 1953 and 1991 by linkage to the Finnish Cancer Registry. The standardized incidence ratio (SIR) was 0.86 (95% CI, 0.75–0.97; 236 cases) for lung cancer, 1.08 (95% CI, 0.80–1.43; 48 cases) for urinary bladder cancer, 1.25 (95% CI, 0.88–1.17) for kidney cancer and 1.12 (95% CI, 0.92–1.32) for prostate cancer. [These locomotive drivers had also been exposed to asbestos while in training, to coal combustion products (in the 1950s) and to diesel exhaust thereafter. However, in the Finnish railroad industry, much overlap occurred between the periods of steam, diesel and electric locomotive use. Because of the lack of specific information that linked job titles and duties to periods of diesel exhaust use, and in the absence of an internal comparison group, this study was regarded as uninformative in relation to associations between cancer and exposure to diesel exhaust.]

Garshick *et al.* (2004) studied mortality from lung cancer in 54 973 railroad workers in the USA between 1959 and 1996 (38 years). This study was an update of an earlier study of the same cohort (Garshick *et al.*, 1988), and a pilot study by Schenker *et al.* (1984). The cohort comprised a sample of men aged 40–64 years and with 10–20 years of railroad service in 1959. Work histories and death follow-up were extended to 1996. The sample comprised approximately 75% of subjects in diesel exhaust-exposed jobs (engineers, conductors, brakemen, hostlers and shop workers) and 25% in jobs with low or no exposure (ticket agents, clerks and signal maintainers), determined from job categories in 1959. Exposure assignment was validated by an industrial hygiene review of current and historical jobs and work practices and measurement of exposure in current workers (Woskie *et al.*, 1988a, b). By 1959, the railroad industry in the USA had largely converted from coal-fired to diesel-powered locomotives and, in this

study, exposure to diesel exhaust was considered to have begun in 1959. Work histories were obtained from the US Railroad Retirement Board, and mortality was ascertained using Railroad Retirement Board, Social Security and Health Care Financing Administration records. Cause of death was obtained from the National Death Index and death certificates. A total of 43 593 deaths occurred, including 4351 from lung cancer. Analyses consisted of internal comparisons (using workers with low or no exposure as the referents). Efforts were made to adjust for a healthy-worker survivor effect by including a variable in the models for total years worked and also terms for time off work.

Compared with workers with low and no exposure, exposed workers had a relative risk for mortality from lung cancer of 1.40 (95% CI, 1.30–1.51), using a 5-year lag, which did not increase with increasing number of years worked in these jobs. The increased risk was associated with all groups stratified by age in 1959, with the exception of the oldest group (aged 60–64 years). Indirect adjustment for tobacco smoking using the methods of Schlesselman and Axelson (Schlesselman, 1978; Axelson & Steenland, 1988), based on job-specific smoking information from a survey among 547 railroad workers in 1982 and an accompanying case–control study (Garshick *et al.*, 1987; Larkin *et al.*, 2000), suggested some positive confounding which would account for a decrease of about 10–20% in exposed versus unexposed railroad workers. Adjustment using these estimated effects of smoking resulted in rate ratios of 1.17–1.27 for exposed versus unexposed railroad workers. [The Working Group noted that mechanics did not have an elevated risk of lung cancer, probably due to exposure misclassification, because this job title included workers with and without repair shop-related exposures to diesel exhaust.]

An additional approach to adjust for cigarette smoking (Garshick *et al.*, 2006) used information on age- and job-specific cigarette smoking histories available from a previous case–control study of railroad workers based on US Railroad Retirement Board records (Garshick *et al.*, 1987). Data on cause of death, birth cohort, and age- and job-specific smoking habits were used to simulate the smoking behaviour of 39 388 deceased railroad workers. Unadjusted for smoking, the risk of lung cancer among exposed workers with a 5-year lag was 1.35 (95% CI, 1.24–1.46), and an excess risk remained after adjustment (1.22; 95% CI, 1.12–1.32).

To improve the estimation of historical exposures during the transition from steam to diesel locomotives (starting in 1945 and during the decade of the 1950s), yearly locomotive rosters from builders' records and company-specific information were obtained starting in 1945 (Laden *et al.*, 2006). Although only information on the last railroad worked was available in the computerized database, a review of a sample of work history records of railroad employers that were available on paper indicated that the majority of workers (95%) did not change railroads during their careers. The rosters were used to determine the make, model and horse power (hp) of each locomotive in service for 93% of the eligible cohort (52 812 subjects). From this information, the number and type of locomotives that were diesel-fuelled were calculated annually for each railroad. An estimate of the relative amount of PM produced by diesel locomotives (in grams of particulate per hour) for a given railroad in a given year was estimated using Environmental Protection Agency emission factors and information on engine horse power. The probability of diesel exposure per year per railroad (diesel fraction) was then calculated using the year-specific ratios of grams of particulate until this value became constant or the railroad was known to be 100% diesel-powered. Years of exposure to diesel exhaust were calculated by weighting yearly months worked with a specific railroad and the yearly diesel fraction, which allowed the estimation of years of exposure for each worker

before 1959 in contrast to the previous analysis (Garshick *et al.*, 2004), in which exposure was considered to start in 1959. Among workers hired in 1945–49, who started work when diesel locomotives were introduced into the industry, the relative risk of lung cancer with a 5-year lag for any exposure was 1.77 (95% CI, 1.50–2.09) and, for workers hired in 1939–44, was 1.30 (95% CI, 1.19–1.43; *P* for interaction = 0.003). There was evidence of an exposure–response relationship with years of exposure duration that plateaued at 15 years and was not present for workers hired before 1945. Compared with no exposure, the relative risks for exposure for 0– < 10 years, 10– < 15 years, 15– < 20 years, 20– < 25 years and ≥ 25 years were 1.15 (95% CI, 0.77–1.70), 1.49 (95% CI, 1.11–1.99), 1.89 (95% CI, 1.48–2.40), 1.83 (95% CI, 1.45–2.32) and 1.78 (95% CI, 1.39–2.28), respectively, for workers hired in 1945–49. For workers hired before 1945, these were 1.19 (95% CI, 1.00–1.41), 1.28 (95% CI, 1.11–1.47), 1.37 (95% CI, 1.21–1.55), 1.37 (95% CI, 1.21–1.54) and 1.16 (95% CI, 1.00–1.34), respectively. Another more complex metric was calculated as a measure of exposure intensity. Railroad-specific emission estimates based on emission factors and engine horse power were converted to intensity categories using the overall distribution to group values below the median, at the median and above the median level (score 1, 2 or 3). For each cohort member, the year-specific intensity score was multiplied by months of work in each year and by diesel fraction to obtain an index of cumulative exposure to diesel exhaust, or 'intensity–years'. Using this exposure metric, the risk of lung cancer was significantly elevated in all exposure quintiles compared with unexposed workers, but with no evidence of a greater risk with greater exposure.

In a case–control study of railroad workers in the USA that used the same source of work records and directly adjusted for smoking behaviour (Garshick *et al.*, 1988), the magnitude of the lung cancer risk estimate was similar to that reported in the cohort studies described by Garshick *et al.* (2004) and Laden *et al.* (2006).

[This series of studies of railroad workers includes some of the stronger epidemiological studies, due to the well defined linkage between job titles and exposure to train and diesel exhaust, the availability of yearly job titles for a large number of workers, sufficient latency for the development of lung cancer, and consideration of smoking behaviour. In the report of Laden *et al.* (2006), there was indication of an exposure–response relationship with duration based on estimates of years of work with diesel locomotives after 1945 but not with a cumulative exposure metric. The Working Group noted that the calculation of the metric for intensity score of exposure involved much uncertainty, which limited its interpretation with regard to trends in risk based on exposure intensity.]

Guo *et al.* (2004a) linked the occupation held for the longest period in the 1970 census to data in the Finnish Cancer Registry from 1971 up to 1995. A JEM was used to estimate exposures to gasoline and diesel exhaust and non-occupational risk factors, including tobacco smoking, based on job descriptions (see Section 2.2.5). Expected cancer cases were calculated using national rates and adjusted for smoking, where relevant. The standardized incidence ratio for lung cancer in locomotive engineers was not elevated (SIR, 0.63; 95% CI, 0.51–0.78; 85 cases). Guo *et al.* (2004b) used the same data (Guo *et al.*, 2004a) to study incident cancers other than of the lung in locomotive engineers. The standardized incidence ratio for urinary bladder cancer in locomotive engineers was 0.85 (95% CI, 0.53–1.28; 22 cases), and ratios for oesophageal cancer (SIR, 0.93; 95% CI, 0.30–2.17; five cases), kidney cancer (SIR, 1.11; 95% CI, 0.71–1.66; 24 cases) and leukaemia (SIR, 0.84; 95% CI, 0.38–1.59; nine cases) were not elevated. [The Working Group noted that these studies were limited due to the lack of detailed information on work history.]

2.2.2 Bus garage workers

Gustavsson *et al.* (1990) studied mortality from, and incident cases of, lung cancer in a cohort of 695 Stockholm (Sweden) bus mechanics, servicemen and hostlers who had worked for at least 6 months from 1945 to 1970. Mortality was assessed from 1952 to 1986 and incidence from 1958 to 1984. Diesel-powered buses were first introduced in the 1930s in Stockholm and all buses were diesel-fuelled after 1945. A JEM was designed by industrial hygienists to categorize the intensity of exposure to diesel exhaust and asbestos by work period and specific workplace. Specific exposure measurements were limited, and relative exposures were therefore estimated on the basis of work practice, number and characteristics of buses, and garage ventilation. Intensity was estimated over six levels, starting at zero, and cumulative exposure was calculated (intensity × years) for each period and summed. A nested case–control study was performed to match each incident lung cancer case (n = 20) to six controls by age. Relative to the lowest category of cumulative exposure to diesel exhaust, an increased risk was observed with increasing categories of the exposure index: 10–20–relative risk, 1.27 (95% CI, 0.21–7.72; two cases); 20–30–relative risk, 1.56 (95% CI, 0.34–7.16; three cases); and > 30–relative risk, 2.63 (95% CI, 0.74–9.42; 10 cases). The relative risk per unit of a continuous diesel exhaust 'score' was 1.37 (95% CI, 0.91–2.07). No evidence of an exposure–response relationship with asbestos score was observed. Compared with mortality rates of other occupationally active men, the standardized mortality ratio was 1.22 (95% CI, 0.71–1.96; 17 deaths) for lung cancer and 1.23 (95% CI, 0.45–2.68; six deaths) for haematopoietic cancer. Compared with the Stockholm general population, the standardized mortality ratio was 1.93 (95% CI, 0.53–4.94; four deaths) for oesophageal cancer, 0.97 (95% CI, 0.32–2.27; five deaths) for stomach cancer and 0.52 (95% CI, 0.01–2.88; one death) for urinary bladder cancer. [The Working Group noted that no information on tobacco smoking was available. However, confounding by smoking based on diesel exposure category was improbable. The major limitation of this study was the small number of cases, which limited statistical inferences.]

2.2.3 Professional drivers

(a) Bus drivers

Balarajan & McDowall (1988) used the National Health Service Central Register to identify 3392 men, who were employed as professional drivers, and were required to hold a professional licence, in London (United Kingdom) according to the 1939 census, and were alive in January 1950. Mortality compared with the general population was subsequently assessed from 1 January 1950 until the end of 1984. Among bus drivers, the risk for lung cancer (SMR, 1.42 [95% CI, 0.84–2.24]; 18 deaths) was not significantly elevated. [The Working Group calculated the exact 95% confidence intervals that were not provided by the authors.] No significant increase in risk of mortality was observed for cancer of the stomach (SMR, 1.68; 95% CI, 0.72–3.31; eight deaths) or for urinary bladder cancer (SMR, 0.58; 95% CI, 0.015–3.23; one death). No deaths from leukaemia or other lymphatic neoplasms occurred. A significantly elevated standardized mortality ratio was found for bronchitis, emphysema and asthma (SMR, 1.66; 95% CI, 1.06–2.47; 24 deaths). [The Working Group noted that no information was available regarding tobacco smoking, and the relationship between occupational title and the specific periods of work with exposure to diesel exhaust was not described. These drivers were unlikely to have been exposed to appreciable levels of diesel exhaust before the 1950s, when diesel engines were introduced.]

Soll-Johanning *et al.* (1998) conducted a retrospective cohort study of 18 174 bus drivers and tramway employees in Copenhagen (Denmark)

who were employed 1900–94. In Copenhagen, the first diesel-powered buses were introduced in 1936, but, during the Second World War, all buses were fuelled with gasoline. Diesel-powered buses gradually replaced gasoline-powered models after that time, and, in the 1960s, they also replaced the trams. Cancer rates were compared with those of the general population of Denmark by linkage to the Danish Cancer Registry and National Death Index to identify cancers that occurred after 1943. Among male workers employed for 3 months or longer, the standardized incidence ratio was 1.6 (95% CI, 1.5–1.8; 473 cases) for lung cancer, 1.0 (95% CI, 0.8–1.3; 82 cases) for stomach cancer, 1.2 (95% CI, 1.0–1.5; 105 cases) for rectal cancer, 1.4 (95% CI, 1.0–1.9; 39 cases) for laryngeal cancer, 1.6 (95% CI, 1.3–1.6; 83 cases) for kidney cancer, 1.4 (95% CI, 1.2–1.6; 177 cases) for urinary bladder cancer, 1.9 (95% CI, 1.2–2.8; 22 cases) for pharyngeal cancer and 1.1 (95% CI, 0.8–1.5; 46 cases) for leukaemia. In women, the standardized incidence ratio for lung cancer was 2.6 (95% CI, 1.5–4.3; 15 cases). In both men and women, a greater risk of lung cancer was observed with longer time since first employment. No trend in lung cancer risk was found based on periods of predominantly gasoline or diesel vehicle use, and the risks were similarly elevated for workers who started before, at the onset, or during the use of diesel buses. [The Working Group noted that no information on specific exposures or tobacco smoking was available and the periods of diesel and gasoline emissions overlapped. Compared with other men in Copenhagen, the smoking rates among the bus drivers were slightly higher during some time periods, suggesting the possibility of some confounding by smoking.]

A nested case–control study (Soll-Johanning *et al.*, 2003) was conducted with 153 cases of lung cancer and 84 cases of urinary bladder cancer included in the cohort of Copenhagen bus drivers and tramway employees. The cases and controls or next of kin were interviewed regarding tobacco smoking history. Deaths from cancer or non-neoplastic respiratory disease were excluded from the control group and cases and controls were matched on date of birth. Both 10-year lag and no lag models, based on duration of employment, were assessed, adjusting for smoking history in seven categories based on pack–years. No consistent increase in lung cancer risk was observed based on categories of duration of employment in either lag model. The risk, although not statistically significant, increased with greater number of years of employment, but then decreased after > 20 years. With a 10-year exposure lag, there was a suggestion of an increased risk for urinary bladder cancer in persons with 10– < 20 years of work (relative risk, 1.61; 95% CI, 0.57–4.55).

In the cohort study described in Section 2.2.1, Guo *et al.* (2004a) reported on lung cancer risk in male bus drivers who had exposure to both gasoline and diesel exhausts; the standardized incidence ratio was not significantly elevated (SIR, 0.89; 95% CI, 0.78–1.00; 253 cases). [The Working Group noted that this study was limited due to the lack of detailed work histories relating to exposures to exhaust and information on tobacco smoking.]

In a separate report, Guo *et al.* (2004b) presented data for other cancers in bus drivers. The risk was elevated for urinary bladder cancer (SIR, 1.29; 95% CI, 1.02–1.62; 75 cases), oesophageal cancer (SIR, 1.10; 95% CI, 0.60–1.85; 14 cases), kidney cancer (SIR, 1.29; 95% CI, 1.00–1.64; 67 cases) and leukaemia (SIR, 1.04; 95% CI, 0.68–1.51; 27 cases). [The Working Group noted that this study was limited due to the lack of detailed work histories relating to exposures to exhaust and information on tobacco smoking.]

Petersen *et al.* (2010) studied the cancer incidence in a cohort, established in 1978, of 2037 male Danish urban bus drivers over a 25-year period of follow-up (1979–2003). In 1978, public bus drivers in the three largest cities of Denmark received a mailed questionnaire on occupational

history, information regarding bus routes and tobacco smoking habits. Information on incident cases of cancer up to 2003 was obtained by linkage to the Danish Cancer Registry. In analyses comparing external rates for men in the three cities, the standardized incidence ratios were 1.2 (95% CI, 1.0–1.4; 100 cases) for lung cancer and 1.6 (95% CI, 1.2–2.0; 69 cases) for urinary bladder cancer; no cancer at other sites had an elevated risk. The risk for urinary bladder cancer was increased for drivers employed for 15 years or longer (SIR, 1.81; 95% CI, 1.2–2.5) and for drivers with less than 15 years of employment (SIR, 1.5; 95% CI, 1.0–2.1). The standardized incidence ratio for lung cancer was also marginally increased for bus drivers with 15 years or more of employment (SIR, 1.3; 95% CI, 1.0–1.8). A Cox regression model was used to assess the relationship between risk and duration of employment. After adjustment for smoking, city of employment and usual type of bus route operated (urban versus rural), in addition to age and calendar time, each additional year of employment as a bus driver was associated with slightly, non-significantly increased risks for bladder cancer (RR, 1.02; 95% CI, 0.99–1.05). No overall increased risk was observed for lung cancer (RR, 1.00; 95% CI, 0.98–1.03). In a comparison of drivers employed for 15–24 and 25 years or longer with those with those employed for less than 15 years, the relative risks were 1.1 and 1.3, respectively, for bladder cancer and 0.9 and 1.0, respectively, for lung cancer. No change in the estimates was found in a 10-year lag model. [The Working Group noted that these data indicated that, when adjusted for smoking and other risk factors and using an internal comparison group, there was little to no increased risk for urinary bladder or lung cancer in bus drivers with increasing duration of employment. This finding contrasted with the elevated risks for bus drivers suggested by the standardized incidence ratio results reported. Adjustment for the type of bus route (urban versus rural) may have limited the ability to demonstrate an effect of occupational exposure to diesel exhaust.]

(b) Heavy goods vehicle and other drivers

In the USA, Menck & Henderson (1976) reviewed 2161 death certificates that reported lung cancer (trachea, bronchus and lung) in white men, aged 20–64 years, in 1968–70 and all 1777 incident cases of lung cancer in white men of the same age reported to the Los Angeles County Cancer Surveillance Program in 1972–73. These mortality and morbidity data were pooled because of the high accuracy of lung cancer death ascertainment and high mortality. Information on either occupation or industry was not available for 1911 subjects. The population at risk by age group, occupation and industry was estimated from a '1-in-50' sample of Los Angeles County white men, aged 20–64 years, obtained from the 1970 census for Los Angeles. Expected deaths and expected incident cases were calculated for each specific occupation, assuming that the age-specific rates of cancer in each occupation were the same as those for all occupations. The standardized mortality ratio was 3.44 ([95% CI, 2.18–5.16]; 16 deaths, seven incident cases) among taxi drivers and 1.65 ([95% CI, 1.35–1.99]; 58 deaths, 51 incident cases) among heavy goods vehicle (HGV) drivers. [The Working Group calculated the exact 95% confidence intervals, which were not provided by the authors. This study was limited by the absence of data and the use of the occupation recorded on the death certificate as a proxy for exposure.]

In the study by Boffetta *et al.* (1988) described in Section 2.2.1, 9738 men stated their main occupation as an HGV driver, of whom 47% reported exposure to diesel exhaust, 33% reported no such exposure and 20% did not respond. Among the 16 208 HGV drivers, based on any past employment in this occupation, the relative risk for lung cancer was 1.24 (95% CI, 0.93–1.66; 48 deaths) compared with other men who were not HGV drivers and who reported no employment in a

job that entailed exposure to diesel exhaust, after controlling for age and tobacco smoking. No difference in relative risks for lung cancer was observed between HGV drivers who reported exposure to diesel (RR, 1.22; 95% CI, 0.77–1.95; 18 deaths) and those who reported no exposure to diesel (RR, 1.19; 95% CI, 0.74–1.89; 18 deaths). However, in a direct comparison between drivers exposed and those not exposed to diesel exhaust, a suggestion of a positive trend with duration was found for the diesel-exposed HGV drivers (duration 1–15 years–RR, 0.87; 95% CI, 0.33–2.25; six exposed deaths; duration > 16 years–RR, 1.33; 95% CI, 0.64–2.75; 12 exposed deaths). [The Working Group noted that this study was limited by the small number of HGV drivers who reported exposure, and categorization of exposure by self-reporting.]

In the study by Balarajan & McDowall (1988) described in Section 2.2.2, a significant excess of lung cancer was observed among HGV drivers (SMR, 1.59 [95% CI, 1.41–1.79]; 280 deaths), but not among taxi drivers (SMR, 0.86 [95% CI, 0.58–1.23]; 30 deaths). [The Working Group calculated the exact 95% confidence intervals which were not provided by the authors.] Among HGV drivers, the standardized mortality ratio for cancer of the stomach was 1.41 ([95% CI, 1.11–1.77]; 73 deaths), but was not significantly elevated for urinary bladder cancer (SMR, 1.06; 19 deaths), leukaemia (SMR, 1.02; nine deaths) or other lymphatic neoplasms (SMR, 0.92; 12 deaths). Among taxi drivers, no significant increase in risk of mortality was found for cancer of the stomach (SMR, 0.68; eight deaths), urinary bladder cancer (SMR, 1.21; five deaths), leukaemia (SMR, 1.64; three deaths) or other lymphatic neoplasms (SMR, 1.61; four deaths). [The Working Group noted that the interpretation of this study was limited by the lack of information on tobacco smoking.]

Rafnsson & Gunnarsdóttir (1991) identified 868 HGV drivers and 726 taxi drivers in Reykjavik (Iceland) in 1951 from union records and assessed mortality up to 1988. The standardized mortality ratio was 2.14 (95% CI, 1.37–3.18; 24 deaths) for HGV drivers and 1.39 (95% CI, 0.72–2.43; 12 deaths) for taxi drivers. The risk for HGV drivers was also evaluated on the basis of duration of employment and no variation was found.

Gubéran *et al.* (1992) conducted a cohort mortality and cancer morbidity study of 6630 drivers from the Canton of Geneva (Switzerland) who were licensed from 1949 to 1961. The exposed group was compared with the general population of Geneva. The drivers were distributed into three groups: (1) professional drivers (n = 1726), (2) non-professional drivers 'more exposed' to exhaust gas and fumes (this group included occupations such as vehicle mechanic, policeman and road sweeper; n = 712), and (3) non-professional drivers 'less exposed' (comprising all other occupations; n = 4192). The cohort was followed up from 1949 to 1986 for mortality and from 1970 to 1986 for cancer morbidity. With a 15-year latency, significant excesses for lung cancer mortality (SMR, 1.50; 90% CI, 1.23–1.81; 77 deaths) and morbidity (SIR, 1.61; 90% CI, 1.29–1.98; 64 cases) were observed among professional drivers, and the risk of lung cancer increased significantly with time from first exposure. Among non-professional drivers, no significant excess risk was found except for lung cancer mortality among the 'less exposed' group (SMR, 1.21; 90% CI, 1.03–1.40), and for the incidence of lung cancer among the 'more exposed' group (SIR 1.61; 90% CI, 1.11–2.27). For 15 years of latency, the authors reported a standardized mortality ratio of 1.43 (95% CI, 0.80–2.36; 11 deaths) and a standardized incidence ratio of 1.25 (95% CI, 0.74–1.99; 13 cases) for urinary bladder cancer. An excess of mortality and morbidity from rectal cancer (SMR, 2.58; 95% CI, 1.62–3.92, 16 deaths; SIR, 2.00; 95% CI, 1.27–3.00; 17 cases) and stomach cancer (SMR, 1.79; 95% CI, 1.17–2.63; 19 deaths; SIR 2.33; 95% CI, 1.56–3.36; 21 cases) was also observed. No significantly increased risk was

found for leukaemia or lymphatic cancers, prostate cancer or cancer at other sites. [The Working Group noted that this study was limited by a lack of specific information on tobacco smoking, and uncertainty on the extent to which these broad occupational titles indicated exposure to diesel exhaust.]

Hansen (1993) identified a cohort of 14 225 HGV drivers and 43 024 other workers based on occupations reported in the 1970 Danish census. The group of non-HGV drivers included unskilled labourers from other industries with no exposure to combustion products. Up to 1980, 627 drivers and 3811 non-drivers died. The risk for mortality from lung cancer was significantly elevated (SMR, 1.60; 95% CI, 1.26–2.00; 76 cases), whereas mortality from urinary bladder cancer (SMR, 0.87; 95% CI, 0.32–1.89) and cancer of the blood and lymph-forming tissues (ICD-8 200–209; SMR, 1.26; 95% CI, 0.78–1.92; 21 deaths) was not increased. [The Working Group noted that the interpretation of these results was limited by the lack of information on specific exposures and tobacco smoking. However, the use of a blue-collar, non-HGV driver comparison group was liable to reduce possible confounding by smoking.]

Järvholm & Silverman (2003) analysed a computerized register of Swedish construction workers (389 000 workers) who participated in health examinations to assemble a cohort of male HGV drivers (n = 6364) and drivers of heavy construction vehicles (see Section 2.2.5). Carpenters/electricians constituted the reference group (n = 119 984). Workers were identified from health examinations in 1971–92 and were linked to the Swedish National Cancer Registry and National Death Registry, from which cases of lung cancer were ascertained up to 1995. For the analysis, data were stratified into never, former and current smokers, on the basis of tobacco smoking habits recorded at the baseline or when available. HGV drivers had an increased risk of lung cancer after adjusting for smoking (SIR, 1.29; 95% CI, 0.99–1.65; 61 cases); it was not possible to conduct an analysis based on duration and latency. In the same cohort, a significant excess of prostate cancer was also found among HGV drivers (SIR, 1.24; [95% CI, 1.04–1.48]; 124 cases). No significant excess of cases of cancer at other sites was observed, including laryngeal cancer (SIR, 1.25; seven cases), urinary tract cancer [probably bladder] (SIR, 0.72; 26 cases), nasopharyngeal cancer (SIR, 0.82; 12 cases), stomach cancer (SIR, 1.23; 27 cases), rectal cancer (SIR, 1.46; 35 cases), kidney cancer (SIR, 1.12; 23 cases), and lymphoma and leukaemia (SIR, 1.21; 53 cases). [The Working Group noted that the interpretation was limited by the lack of specific information on exposure to diesel exhaust. The strengths of the study were the adjustment for smoking and the use of another blue-collar comparison group, which was liable to reduce possible confounding.]

In the study by Guo *et al.* (2004a) described in Section 2.2.1, among male HGV drivers who were exposed to both gasoline and diesel exhaust, the risk of lung cancer was elevated (SIR, 1.13; 95% CI, 1.04–1.22; 620 cases); the standardized incidence ratio for taxi drivers was 1.10 (95% CI, 0.96–1.26; 209 cases). In a separate report, Guo *et al.* (2004b) presented data for other cancers among male HGV drivers. The risk of leukaemia (SIR, 1.29; 95% CI, 1.02–1.60; 82 cases) was significantly elevated, but not that of kidney cancer (SIR, 1.00; 95% CI, 0.84–1.19; 131 cases), oesophageal cancer (SIR, 1.10; 95% CI, 0.76–1.54; 34 cases) or urinary bladder cancer (SIR, 1.01; 95% CI, 0.85–1.19; 144 cases). In male taxi drivers, the risk of kidney cancer was significantly elevated (SIR, 1.39; 95% CI, 1.06–1.79; 61 cases), but not that of oesophageal cancer (SIR, 1.28; 95% CI, 0.70–2.15; 14 cases), urinary bladder cancer (SIR, 1.06; 95% CI, 0.80–1.38; 55 cases) or leukaemia (SIR, 1.09; 95% CI, 0.70–1.62; 24 cases). [The Working Group noted that these studies were limited by the lack of detailed work histories.]

A cohort was assembled from the records of four transport companies in the USA, from which 54 319 male workers employed in 1985 were identified (Laden *et al.*, 2007). Cause-specific mortality was assessed up to 2000 using the National Death Index; 769 deaths from lung cancer were ascertained. Standardized mortality ratios and 95% confidence intervals were calculated for the entire cohort and by job title, using US mortality rates as the referent. Rates of lung cancer were elevated among all drivers (SMR, 1.10; 95% CI, 1.02–1.19) and loading dock workers (SMR, 1.10; 95% CI, 0.94–1.30). The standardized mortality ratio for urinary bladder cancer was 0.80 (95% CI, 0.56–1.15; 29 deaths) for the entire cohort, with similar estimates for drivers and non-drivers.

Garshick *et al.* (2008) conducted an internal analysis in the same cohort, based on employment records for 31 135 male workers, aged 40 years and over, with at least 1 year of employment as of 1985. Exposure to engine exhaust was estimated for eight job categories (long haul driver, pick-up and delivery driver, loading dock worker, combined driver and dock worker, mechanic, hostler in the vehicle yard, clerk and other) through an industrial hygiene review of previous exposures and current measurements of work-shift exposures to EC. Time-varying cumulative years of work in each of the categories were calculated. Group level adjustment for cigarette smoking was carried out using the methods of Schlesselman and Axelson (Schlesselman, 1978; Axelson & Steenland, 1988). Job-specific information on the distribution of smoking habits was obtained from a survey of 11 986 workers that included all clerks and a random sample of active and retired workers from three of transport companies who contributed to the cohort. In the assessment of mortality from lung cancer, all eight job-specific exposure variables were included in Cox regression models to adjust the risk for lung cancer for different jobs held throughout a worker's career. The healthy-worker survivor effect was controlled for using variables for duration of employment and time since leaving work. Hazard ratios (HRs) for lung cancer were elevated in workers who held jobs associated with regular exposure to vehicle exhaust, including long-haul drivers (HR, 1.15, 95% CI, 0.92–1.43; 323 deaths), pick-up and delivery drivers (HR, 1.19; 95% CI, 0.99–1.42; 233 deaths), dock workers (HR, 1.30; 95% CI, 1.07–1.58; 205 deaths) and combination dock workers/drivers (HR, 1.40; 95% CI, 1.12–1.73; 150 deaths). No excess risk was seen in the other job groups. The risk of mortality increased linearly with years of employment in long-haul drivers, pick-up and delivery, dock workers and combination dock workers/drivers. Estimates of risk for 20 years of employment in a job versus no employment in the job, adjusted for smoking, were 1.40 (95% CI, 0.88–2.24) for long-haul drivers, 2.21 (95% CI, 1.38–3.52) for pick-up and delivery drivers, 2.20 (95% CI, 1.23–3.33), for dock workers and 2.34 (95% CI, 1.42–3.83) for combination drivers/dock workers. Risks not adjusted for smoking were slightly greater than the adjusted estimates for long-haul drivers and slightly lower for pick-up and delivery drivers and for dock workers. [The Working Group noted that this study had particular strengths because detailed historical work records were available, exposures in each job were supported by an industrial hygiene review and exposure measurements, and variation in smoking behaviour by job was considered. Compared with the standardized mortality ratio analysis of the same cohort by Laden *et al.* (2007), greater risks were observed in this study that used an exposure assessment and an internal comparison of risks based on job titles. Although the risks for lung cancer in mechanics, who had greater current and historical exposures, was not elevated, it was noted that the number of mechanics was relatively small (6% of the cohort) and contributed relatively few cases of lung cancer (n = 38). The Working Group also noted that there was no consensus on the optimal method to adjust for

the healthy-worker survivor bias, and that the applied adjustment probably did not negate the positive findings.]

Birdsey *et al.* (2010) conducted a cohort mortality study of independent HGV owners/operators using files from a trade association. The 156 241 subjects were members of the trade association between 1989 and 2004, and mortality was assessed using the National Death Index up to 2004. Indirect adjustment was made for tobacco smoking. Most of the cohort (86%) was aged 25–54 years at entry into the study. No excess mortality from lung cancer (SMR, 1.00; 95% CI, 0.92–1.09; 557 deaths), urinary bladder cancer (SMR, 0.93; 95% CI, 0.62–1.34; 29 deaths) or any other type of cancer was observed. [The Working Group noted that the interpretation of this study was limited by the lack of individual information on smoking and information on how association membership served as a surrogate for exposures to exhaust.]

Garshick *et al.* (2012) investigated the risk for lung cancer in the cohort of Laden *et al.* (2007) in relation to a reconstruction of occupational exposure to EC. An exposure assessment was conducted in 2001–06 by collecting more than 4000 cross-shift samples of EC measured in PM ≤ 1.0 μm diameter at representative transport terminals. Separate exposure models were constructed for drivers and terminal workers. Historical trends in the ambient levels of EC in terminals were modelled on the basis of historical trends available for 1971–2000 in the coefficient of haze, a measurement of PM based on optical density that is highly predictive of ambient EC. A 1988–89 assessment of EC in the same industry that used the same methodology as the current assessment was used to calibrate model estimates. Historical data on jobs and terminal-specific monthly EC concentrations determined by the exposure model were summed by year for 1971–2000 to estimate cumulative exposure (μg/m^3–months) for individuals. Job-specific EC values before 1971 (8% of total exposure time) were assigned values for 1971 exposures because data on coefficient of haze were not available to estimate background. Combination workers were assumed to spend 50% of their time as a pick-up and delivery driver and 50% as a dock worker. When adjusted for race, calendar year and census region, with a 5-year lag, mortality from lung cancer was elevated for the upper three cumulative EC quartiles compared with the lowest quartile, but the differences were not statistically significant (HR, 1.17–1.19 for 5-year lagged exposures excluding mechanics). However, the risk for lung cancer was inversely associated with the total duration of employment. The association of lung cancer with cumulative exposure to EC was stronger after adjustment for duration of employment, and when mechanics were excluded. The job duties of mechanics changed over time and their exposures were intermittent. The risks for 5- and 10-year lagged exposures increased with each cumulative exposure quartile when mechanics were excluded, resulting in estimated hazard ratios of 1.48 (95% CI, 1.05–2.10) and 1.41 (95% CI, 0.95–2.11) for the highest versus lowest quartiles of 5- and 10-year lagged exposures, respectively, when adjusted for duration of employment. Associations were weaker for average exposure to EC. In addition, adjusting for duration of employment, a linear exposure–response relationship was suggested when cumulative EC was used as a continuous covariate and splines were incorporated into the models. For each 1000 μg/m^3–months of cumulative EC, based on a 5-year exposure lag, the hazard ratio was 1.07 (95% CI, 0.99–1.15) with a similar association for a 10-year exposure lag (HR, 1.09; 95% CI, 0.99–1.20). [The Working Group noted that this analysis provided similar results to those of Garshick *et al.* (2008), who did not use quantitative exposure measurements. An additional strength was a comprehensive exposure assessment and the development of exposure models that were linked to accurate historical job title records and incorporated

historical trends in background exposures. Although uncertainty is inherent when estimating historical exposures, systemic bias was improbable. It was not possible to adjust directly for tobacco smoking, but previous adjustment in the same cohort revealed little difference in the risk for lung cancer with or without adjustment. A possible interaction between average exposure and duration of employment on mortality from lung cancer may explain some of the apparent paradoxes of the results, such as the observation that cumulative exposure, adjusted for duration of employment, had a greater effect while average exposure, adjusted for duration of employment, did not. The study provided evidence for an association between sources of EC (predominantly diesel) and the risk for lung cancer.]

2.2.4 Miners

In the cohort described in Section 2.2.1, Boffetta *et al.* (1988) studied 2034 men who reported working as a miner on the basis of any past employment in this occupation. The age- and tobacco smoking-adjusted relative risk for lung cancer was 2.67 (95% CI, 1.63–4.37; 15 deaths) compared with other men who did not report working as a miner and who reported no exposure to diesel exhaust. [The Working Group noted that this study was limited by the small number of miners and the lack of information regarding specific exposures to exhaust. Only 14% of miners reported exposure to diesel exhaust; these miners may also have been exposed to other lung carcinogens, such as silica or radon.]

In the cohort described in Section 2.2.1, Guo *et al.* (2004a) reported that male miners in three different occupational categories had an elevated risk of lung cancer. These included mine and quarry work involving metal ore (SIR, 3.26; 95% CI, 2.28–4.51; 36 cases), mine and quarry work involving non-metal ore (SIR, 1.85; 95% CI, 1.59–2.14; 181 cases) and other unspecified mine and quarry work (SIR, 1.73; 95% CI, 1.35–2.19; 70 cases). All three groups were classified by an expert review as having been exposed to diesel exhaust but not gasoline exhaust. In a separate report, Guo *et al.* (2004b) presented data for other cancers in male miners. In non-metal ore miners and quarry workers, the risks were elevated for leukaemia (SIR, 2.31; 95% CI, 1.39–3.61; 19 cases), oesophageal cancer (SIR, 1.74; 95% CI, 0.70–3.58; seven cases), kidney cancer (SIR, 0.88; 95% CI, 0.47–1.50; 13 cases) and urinary bladder cancer (SIR, 1.16; 95% CI, 0.73–1.76; 22 cases). Too few cases occurred in other mining groups to carry out a meaningful assessment. [The Working Group noted that these studies were limited due to the lack of detailed work histories and information on tobacco smoking. In particular, for lung cancer, these miners may have had confounding exposures to other substances, such as silica and radon.]

Neumeyer-Gromen *et al.* (2009) updated the mortality from lung cancer in a cohort of 5862 German underground potash miners, first described by Säverin *et al.* (1999), from 1970 up to 2001. Diesel equipment was introduced into potash mines in 1969 and, in 1991, the mines were closed. Tobacco smoking histories were available from medical and personnel records for 80% of the cohort. Estimates of diesel exposure were obtained in 1992, and expressed as total carbon in respirable dust. Because technology had not changed, these levels were assumed to be representative of previous exposure and were used for its categorization. The overall standardized mortality ratio was not elevated for lung cancer (SMR, 0.73; 95% CI, 0.57–0.93; 61 deaths) or urinary bladder cancer (SMR, 0.80; 95% CI, 0.40–1.60; 8 deaths). Using Cox regression modelling, the smoking-adjusted relative risk in the highest category of exposure dichotomized at 4.90 mg/m^3–years was 1.28 (95% CI, 0.61–2.71; 61 cases). In a subgroup of 3335 workers who had worked underground for at least 10 years, the age- and smoking-adjusted relative risk was 1.50 (95% CI, 0.66–3.43; 37 cases). Adjusting for smoking

resulted in higher risk estimates. In a model that further adjusted for time since hire and calendar year, the relative risk in the entire cohort was 2.53 (95% CI, 1.13–5.69) and that in the subcohort of workers who had worked for more than 10 years after 1969 was 3.30 (95% CI, 1.30–8.37). Using time since first hire as the time variable in a Cox regression analysis to account for duration of employment, and adjusting for age and smoking, a non-significant trend (P = 0.19) in risk for mortality from lung cancer was observed with greater exposure in the entire cohort (RR, 1.81; 95% CI, 0.92–3.58; and 1.59; 95% CI, 0.75–3.40; for the second and third tertiles, respectively). A non-significant increased trend (P = 0.17) in risk of was also found within the subcohort, for which more accurate information on exposure was available. [The Working Group noted that, although the power of the study was limited by the sample size, one of its strengths was that the effects of smoking were considered together with quantitative estimates of exposure based on measurements. The study also used an internal comparison group. Another strength in the design was the control of confounding for other mining-related occupational risk factors for lung cancer, because exposure to radon, silica dust, asbestos and heavy metals were not significant in potash mining. This study was supportive of an effect of exposure to diesel exhaust on the risk of lung cancer.]

Attfield *et al.* (2012) studied the mortality of a cohort of 12 315 blue-collar workers who were employed in one of eight non-metal mines in the USA for at least 1 year after diesel equipment had been introduced. The mines were selected to minimize exposures to silica, radon and asbestos. Detailed work histories were abstracted from company records and mortality was assessed up to 1997. The dates of the introduction of diesel equipment ranged from 1947 to 1967. Historical estimates of exposure to respirable EC were constructed on the basis of personal measurements taken in the mines in 1998–2001, which were extrapolated retroactively based on a model using diesel exhaust-related determinants, including diesel engine horse power and ventilation rates, and historical measurements of carbon monoxide. The modelled trends in concentrations of CO for previous years were then used to adjust the 1998–2001 levels of exposure to respirable EC to estimate historical annual concentrations of respirable EC for each job. Estimates of exposure to silica, asbestos, respirable dust, radon and other PAHs were also made. Estimates of exposure to diesel exhaust in surface workers were based on measurements made in 1998–2001 and no reconstruction of historical exposure was carried out. The mean exposure of surface workers only was 1.7 μg/m^3 and that of the ever-underground miners was 128.2 μg/m^3. Standardized mortality ratios using external referents were determined from state-specific mortality rates, and their calculation was limited to persons employed since 1960 (12 270 subjects), because state-specific rates were not available for earlier years. The standardized mortality ratio for lung cancer was 1.26 (95% CI, 1.09–1.44) for the complete cohort, 1.21 (95% CI, 1.01–1.45) for workers involved in any underground work and 1.33 (95% CI, 1.06–1.66) for workers involved exclusively in surface work. In the complete cohort, standardized mortality ratios were 1.09 (95% CI, 0.58–1.86) for urinary bladder cancer, 1.18 (95% CI, 0.76–1.74) for leukaemia, 0.98 (95% CI, 0.54–1.64) for kidney cancer, 1.12 (95% CI, 0.76–1.60) for pancreatic cancer and 0.85 (95% CI, 0.60–1.16) for prostate cancer. Mortality from oesophageal cancer was significantly elevated in all workers (SMR, 1.83; 95% CI, 1.16–2.75). In an internal analysis of the entire cohort, adjustment for the location of work (ever surface or underground) and a 15-year lag for cumulative exposure resulted in relative risks by quartile of 1.0, 0.55 (95% CI, 0.35–0.85), 1.03 (95% CI, 0.60–1.77) and 1.39 (95% CI, 0.78–2.48). In an analysis of surface workers only, the corresponding relative risks by quartiles of cumulative exposure

were 1.0, 1.28 (95% CI, 0.64–2.58), 0.73 (95% CI, 0.35–1.53) and 1.00 (95% CI, 0.44–2.28). The relative risks for average exposure among surface workers were 1.0, 1.71 (95% CI, 0.82–3.58), 2.22 (95% CI, 1.01–4.90) and 2.56 (95% CI, 1.09–6.03). In an analysis of ever underground miners only, the relative risks by quartile of cumulative exposure were 1.0, 1.50 (95% CI, 0.86–2.62), 2.17 (95% CI, 1.21–3.88) and 2.21 (95% CI, 1.19–4.09), and those by quartile of average exposure were 1.0, 1.73 (95% CI, 0.99–3.05), 2.11 (95% CI, 1.14–3.90) and 1.86 (95% CI, 0.98–3.52). Further analysis of underground miners with ≥ 5 years of exposure showed similar patterns (test for trend using log cumulative exposure as a continuous variable, $P = 0.015$). [The Working Group noted that the log cumulative exposure best fit the exposure–response curve over the entire range. In addition, all the internal analyses of surface workers involved groups with very small ranges of exposure. Moreover, no historical exposure assessments were available for surface workers, which further limited the interpretation of the analyses of surface workers alone.]

In a nested case–control study of the above cohort of miners, Silverman *et al.* (2012) obtained histories of tobacco smoking, occupation and previous respiratory disease by interview for 198 lung cancer cases and 562 control subjects. Controls were assigned by random sampling from all members of the cohort who were alive before the day the case subject died and were matched on birth year, gender, ethnicity and mine. Analyses of trend in risk by level of respirable EC were adjusted for smoking, previous respiratory disease and a history of jobs that entailed a high risk of lung cancer. Smoking adjustments included separate terms for levels of smoking of surface and underground miners, to take into account that the differences in the odds ratios (ORs) for levels of smoking between these two groups. In analyses of surface and underground miners combined, the odds ratios by quartile of cumulative exposure (15-year lag) were 1.0, 0.74 (95% CI, 0.40–1.38), 1.54 (95% CI, 0.74–3.20) and 2.83 (95% CI, 1.28–6.26; P for trend = 0.001). Corresponding odds ratios for average exposure (15-year lag) were 1.0, 1.11 (95% CI, 0.59–2.07), 1.90 (95% CI, 0.90–3.99) and 2.28 (95% CI, 1.07–4.87; P for trend = 0.062). Analyses restricted to surface miners gave odds ratios by quartile of cumulative exposure (15-year lag) of 1.0, 3.98 (95% CI, 0.69–23.02), 0.76 (95% CI, 0.12–4.98) and 0.42 (95% CI, 0.05–3.59; P for trend = 0.12), and corresponding odds ratios for average exposure (15-year lag) of 1.0, 4.38 (95% CI, 0.56–34.24), 5.67 (95% CI, 0.77–42.06) and 1.31(95% CI, 0.14–12.01; P for trend = 0.66). For underground miners, odds ratios by quartile of cumulative exposure (15-year lag) were 2.46 (95% CI, 1.01–6.01), 2.41 (95% CI, 1.00–5.82) and 5.10 (95% CI, 1.88–13.87; P for trend = 0.004), and the corresponding odds ratios for average exposure (15-year lag) were 1.0, 1.04 (95% CI, 0.45–2.43), 2.19 (95% CI, 0.87–5.53) and 5.43 (95% CI, 1.92–15.31; P for trend = 0.001). Analysis of the interaction between cumulative exposure to respirable EC and smoking showed an increased risk with increased cumulative exposure (15-year lag) for both never smokers and ever smokers (P for interaction = 0.09). Among never smokers, the odds ratio increased with increasing cumulative exposure to respirable EC from 1.47 (95% CI, 0.29–7.50; four exposed cases) for tertile 2 up to 7.30 (95% CI, 1.46–36.57; seven exposed cases). The trend of increasing risk with increased cumulative diesel exposure was attenuated in heavy smokers. [The Working Group noted that the exposure assessment methodology applied in the National Institute of Occupational Safety and Health/National Cancer Institute (NIOSH/NCI) studies was of high quality and used an established approach for occupational cohort studies. Because surface workers formed a group that had very low exposures, no significant trends were observed with increasing exposure. Consequently, the Working Group focused primarily on the combined analyses of surface

and underground miners, in which the surface workers formed part of the low-exposure group. The Working Group gave the results of the case–control greater weight than those of the cohort because the former included an adjustment for tobacco smoking. The research team appeared to have used the available data most effectively. However, in any such study, uncertainties exist that may result in measurement error, and, although historical exposures might have been over- or underestimated, this could have affected the risk per unit exposure but not the pattern of the exposure–response relationship.]

2.2.5 Other groups exposed to vehicle exhausts

(a) Heavy equipment operators

Wong *et al.* (1985) conducted a cohort mortality study of 34 156 men who had been members of a heavy construction equipment operators union for at least 1 year between 1964 and 1978. The mortality experience of the cohort was compared with that of white men in the USA. Historical environmental measurements were not available, and only partial work histories were accessible for some cohort members. Mortality from respiratory cancer for the whole cohort was similar to that expected (SMR, 0.99; 95% CI, 0.88–1.10), with no trend by duration of union membership. A significant excess of mortality from lung cancer was found among the 4075 retirees, after excluding early retirees who were thought potentially to have retired due to illness (SMR, 1.30; 95% CI, 1.04–1.61). The standardized mortality ratio for urinary bladder cancer was 1.18 (95% CI, 0.78–1.72), with no trends by duration or latency. Data on cigarette smoking were available for a small sample of 107 workers, and did not indicate any difference in smoking habits between the cohort and the general population. [The Working Group noted that the main limitation of this study with regard to diesel exhaust was the lack of any information documenting such an exposure; in general, it is not known to what degree heavy equipment operators have appreciable exposure to diesel exhaust.]

In the study described in Section 2.2.1, Boffetta *et al.* (1988) studied 855 men who reported working as heavy equipment operators. The age- and tobacco smoking-adjusted relative risk for lung cancer was 2.60 (95% CI, 1.12–6.06) compared with men who reported no such employment and no exposure to diesel exhaust. [The Working Group noted that this study was limited by the small number of heavy equipment operators included and the categorization of exposure from self-reporting. Less than half (46%) of the heavy equipment operators reported exposure.]

In the study described in Section 2.2.3, Järvholm & Silverman (2003) found that 14 364 heavy equipment operators had a lower incidence of lung cancer than a reference group of electricians/carpenters after adjusting for tobacco smoking (SIR, 0.87; 95% CI, 0.66–1.11; 61 cases; smoking-adjusted SMR, 0.83; 95% CI, 0.61–1.09; 49 cases) compared with the referents. The cohort of heavy equipment operators also showed no significant excess of cancer at other sites, including the prostate (SIR, 0.93; 116 cases), larynx (SIR, 1.03; nine cases), urinary tract [probably bladder] (SIR, 1.15; 61 cases), nasopharynx (SIR, 0.75; 18 cases), stomach (SIR, 1.05; 32 cases), rectum (SIR, 0.82; 29 cases), kidney (SIR, 0.74; 24 cases), and lymphoma and leukaemia (SIR, 1.08; 78 cases). [The Working Group noted that the interpretation was limited by the lack of specific information on exposure to diesel exhaust.]

In the cohort study described in Section 2.2.1, Guo *et al.* (2004a) carried out a separate analysis in other male exhaust-exposed workers, including forklift drivers and three categories of heavy equipment operators, none of whom had a significantly elevated risk of lung cancer. The standardized incidence ratios ranged from 0.89 to 1.13 with 36–121 cases in each occupational

group. Guo *et al.* (2004b) presented data for cancers at other sites in these workers. Neither forklift drivers nor the three categories of heavy equipment operators had a significantly increased risk of urinary bladder cancer, oesophageal cancer or leukaemia: the standardized incidence ratios ranged from 0 to 1.32 with 0–23 cases in each occupational group. However, the risk for kidney cancer in this group was significantly elevated (SIR, 1.65; 95% CI, 1.11–2.36). [The Working Group noted that these studies were limited by the lack of detailed information on exposures and tobacco smoking.]

(b) Dock workers

Gustafsson *et al.* (1986) compared the incidence of cancer among male Swedish dock workers with that of the Swedish male population. Diesel trucks were introduced into Swedish ports in the late 1950s and became prevalent during the 1960s. The cohort comprised 6071 men first employed at the beginning of 1961, and mortality and lung cancer incidence were assessed from 1961 to 1981. In the cohort, 70 deaths from and 86 cases of lung cancer occurred. The risk for lung cancer was significantly increased (SMR 1.32; 95% CI, 1.05–1.66; SIR, 1.68; 95% CI, 1.36–2.07). The standardized mortality and standardized incidence ratios, respectively, were 0.98 (95% CI, 0.83–1.15) and 1.06 (95% CI, 0.89–1.27) for digestive cancer, 1.10 (95% CI, 0.85–1.42) and 0.97 (95% CI, 0.80–1.17) for urogenital cancer, 0.71 (95% CI, 0.46–1.10) and 0.86 (95% CI, 0.60–1.23) for all leukaemias, and 1.23 (95% CI, 0.91–1.66) and 1.22 (95% CI, 0.91–1.64) for stomach cancer. [The Working Group noted that the interpretation of the elevated standardized mortality ratios was limited by the lack of information on tobacco smoking and on the extent of occupational exposures to exhaust.]

Emmelin *et al.* (1993) conducted a nested case–control study on and assessed the exposure of subjects in the above Swedish cohort study (Gustafsson *et al.*, 1986), and included 6573 men employed as dock workers for at least 6 months in 1950–74 in 15 Swedish ports where data for exposure assessment were available. Up to four referents were matched by port and date of birth to each of 50 eligible cases that had occurred between 1960 and 1982. Information on tobacco smoking was obtained from living referents, next of kin and from interviews with retired workers. No measurements of exposure to exhaust were available, and exposure was therefore estimated on the basis of annual fuel consumption divided by the number of employees in the same port in that year. 'Exposed time' was an indicator variable that indicated exposure in a year when the annual fuel consumption per person exceeded the lower quartile of the overall distribution of all years and ports. Exposure was categorized as time worked with diesel equipment ('machine time'), cumulative fuel consumption (in person–L) and exposed time (three classes per category), with a 2-year exposure lag, and 90% confidence intervals were calculated. The three exposure metrics gave largely similar results, and the greatest odds ratios were found for persons with the highest exposure after adjusting for smoking. The inclusion of smoking in the regression models increased the effects of exposure: for machine time, the odds ratio for medium exposure was 1.8 (90% CI, 0.5–6.6) and that for high exposure was 2.9 (90% CI, 0.6–14.4). Similar odds ratios were obtained for fuel consumption. For exposed time, the odds ratio for medium exposure was 2.7 (90% CI, 0.6–11.3) and that for high exposure was 6.8 (90% CI, 1.3–34.9) compared with low exposure/nonsmokers. Further analyses for exposed time with smoking reclassified as ever/never resulted in an odds ratio of 1.7 for medium exposure and 4.6 for high exposure. [The Working Group noted that confidence intervals were not provided, nor were odd ratios provided for the other exposure metrics. The interpretation was limited by the classification of smoking into two categories, the imprecise results attributable to small sample size, and the

imprecise categorization of exposure, but the results were nevertheless suggestive of an association between exposure and the risk for lung cancer. The Working Group also noted that there may have been some exposure to asbestos during work in ports but this would probably not fully explain the observed associations.]

In the cohort study described in Section 2.2.1, Guo *et al.* (2004a) reported that stevedores, who were classified as having exposure to both diesel and gasoline exhausts, had an elevated risk of lung cancer (SIR, 1.32; 95% CI, 1.16–1.50). Guo *et al.* (2004b) presented data for cancers at other sites and reported that stevedores had an elevated risk for oesophageal cancer (SIR, 2.03; 95% CI, 1.11–3.40) but no increased risk for urinary bladder cancer (SIR, 0.95; 95% CI, 0.65–1.35), kidney cancer or leukaemia. [The Working Group noted that this study was limited by the lack of detailed work histories, and information on exposures and smoking.]

(c) Occupations entailing exposure to diesel exhaust based on expert reviews or self-reporting

In the American Cancer Society cohort, Boffetta *et al.* (1988) also reported results based on self-reporting of exposure to diesel exhaust. Among the 378 622 subjects who provided information regarding self-reported exposure to diesel exhaust, 174 cases of lung cancer occurred among those who stated that they had been exposed. In this group, the relative risk for lung cancer, adjusted for tobacco smoking and other occupational exposures (asbestos, coal, coal tar and gasoline exhaust), was 1.18 (95% CI, 0.97–1.44,) for all men with self-reported exposure to diesel exhaust. Based on duration of exposure, the adjusted relative risk for lung cancer was 1.05 (95% CI, 0.80–1.39) for men with 1–15 years of exposure, with a suggestion of a positive trend for men with 16 or more years of exposure (RR, 1.21; 95% CI, 0.94–1.56). The relative risks for other cancers based on self-reported exposure to diesel exhaust, adjusted for smoking and other occupational exposure, were not significantly elevated: 1.21 for multiple myeloma (14 deaths), 1.29 for all leukaemias (17 deaths), 1.39 for pancreatic cancer (27 deaths) and 1.04 for urinary bladder cancer (13 deaths). Analysis of urinary bladder cancer by duration of exposure showed no trend (1–15 years exposure: RR, 1.43; 95% CI, 0.61–2.33; > 15 years of exposure: RR, 0.94; 95% CI, 0.35–2.51). [The Working Group noted that the reliance on self-reported exposure to diesel exhaust may have led to misclassification and reduced the ability to detect an effect of exposure.]

Van Den Eeden & Friedman (1993) studied 160 230 members of a health maintenance organization who self-reported whether they had been exposed to engine exhausts in the past year or more than 1 year previously during the years 1964–72; 3% reported exposure in both periods. Follow-up for cancer incidence was up to 1988, during which time 1662 lung cancers and 650 urinary bladder cancers were observed. After adjusting for tobacco smoking and other covariates, the rate ratios for those exposed in the past year and more than 1 year previously were 1.02 (95% CI, 0.81–1.29) for lung cancer and 1.16 (95% CI, 0.81–1.67) for urinary bladder cancer. [The Working Group noted that this study did not specify whether the exhaust was from diesel engines; reliance on self-reported exposure to engine exhausts was a limitation.]

Boffetta *et al.* (2001) investigated the risk of cancer among workers exposed to diesel exhaust by linking the occupations and industries reported in the 1960 census with the Swedish Environment Register III that contains nationwide data on cancer incidence and mortality for 1971–89. Using a JEM, exposures were graded on the basis of intensity and probability of exposure to diesel exhaust. A total of 28 million person-years of observation were accrued, 28% of which was related to persons classified as exposed. In men, increasing risks for lung cancer were observed with increasing exposure intensity: the

relative risks were 0.95 (95% CI, 0.92–0.98), 1.1 (95% CI, 1.08–1.21) and 1.3 (95% CI, 1.26–1.42) for low, medium and high intensity of exposure, respectively. Corresponding results for probability of exposure were 1.1 (95% CI, 1.04–1.13), 0.90 (95% CI, 0.86–0.94) and 1.2 (95% CI, 1.10–1.24). Fewer cases (n = 57) and less exposure occurred in women, and the risk for lung cancer was not increased. Among men exposed to diesel exhaust, the standardized incidence ratio for urinary bladder cancer was 1.00 (95% CI, 0.97–1.03), with no trends by intensity or probability. For men with a high probability of exposure, the standardized incidence ratios were 1.1 (95% CI, 0.96–1.28) for laryngeal cancer, 0.98 (95% CI, 0.92–1.04) for urinary bladder cancer, 1.0 (95% CI, 0.96–1.14) for kidney cancer, 1.1 (95% CI, 0.99–1.21) for oral and pharyngeal cancer, 1.1 (95% CI, 1.05–1.20) for stomach cancer and 1.1 (95% CI, 0.99–1.19) for pancreatic cancer. A significantly increased risk of oral/pharyngeal (SIR, 1.64) and cervical (SIR, 1.48) cancers was observed among women, with a suggestion of a dose–response relationship. [The Working Group noted that the lack of work histories, which prohibited analyses by duration and latency, and the lack of smoking data were factors that weakened this study.]

In a population-based study in the Netherlands, Zeegers *et al.* (2001) studied 58 279 men who answered a questionnaire on occupation in 1986 and were followed up for the incidence of urinary bladder cancer until 1992. Experts using a JEM assigned the levels of exposure to diesel exhaust as none, low, medium and high to each subject. Using a case–cohort approach (532 cases, 1630 non-cases), the relative risks for urinary bladder cancer, after adjustment for smoking, demographics and other occupational exposures, were 1.00 (95% CI, 0.65–1.54), 0.96 (95% CI, 0.60–1.53) and 1.17 (95% CI, 0.74–1.84) for low, medium and high exposure, respectively, relative to no exposure (P for trend = 0.76).

Lee *et al.* (2003) analysed the risk for multiple myeloma in relation to diesel exposures in a large Swedish cohort of construction workers who were followed up from 1971 to 1999. By linkage with the Swedish National Cancer Registry, 446 cases of primary multiple myeloma were identified. A JEM was developed to classify exposure to occupational agents, including diesel exhaust, using a 1971–76 survey of occupational exposures in the construction industry and nitric oxide as a marker of exposure to diesel exhaust. However, few occupations were considered to entail exposure to diesel exhaust in the original survey: drivers, earthmoving, mountain and asphalt workers, as well as some repair and concrete workers, were classified as occupationally exposed to diesel exhaust. Tobacco smoking status, body mass index and age, as well as socioeconomic status and other occupational exposures, were considered as potential confounders. Among diesel-exposed workers, the adjusted relative risk for multiple myeloma was 1.3 (95% CI, 1.00–1.77). No evidence of a dose–response was found. [The Working Group noted that the lack of information on duration of exposure, as well as the overall low levels of exposure to diesel exhaust in exposed cohort members, were limitations of the study.]

In a study described in Section 2.2.1, Guo *et al.* (2004a) also used a Finnish JEM (FINJEM) to estimate exposures to gasoline and diesel exhaust based on job reviews, and to assign exposure to diesel exhaust to different jobs reported in the census. In FINJEM jobs were classified as diesel-exposed when nitrogen dioxide had been found in surveys, and as gasoline-exposed when carbon monoxide had been found. The overall relative risk for lung cancer was 0.99 (95% CI, 0.96–1.03) among men and 1.22 (95% CI, 0.85–1.73) among women estimated to have been exposed to diesel exhaust, and 1.05 (95% CI, 1.01–1.09) among men and 1.61 (95% CI, 1.23–2.1) among women estimated to have been exposed to gasoline exhaust. The Finnish occupational exposure database included occupation, gender, age and period-specific tobacco smoking

rates that were used to adjust for smoking in the analysis of lung cancer risk. [The Working Group noted that the authors also developed estimates of cumulative exposures to diesel and gasoline exhausts, but these were of doubtful validity due to the lack of work histories.] Guo *et al.* (2004b) presented risks for other cancers, based on JEM-estimated exposure to diesel and gasoline exhausts. No overall risk for exposure to either diesel or gasoline exhaust was presented. No consistent increased risk for leukaemia, kidney cancer, urinary bladder cancer or oesophageal cancer was observed based on estimated cumulative exposure to either diesel or gasoline exhaust. Vasama-Neuvonen *et al.* (1999) reported similar findings for ovarian cancer in the same registry. [The Working Group noted that these studies were limited due to the lack of detailed work histories and information on tobacco smoking.]

Tarvainen *et al.* (2008) studied cancers of the mouth and pharynx using the same Finnish Cancer Registry data and assessed the risk of cancer based on categories of exposure to diesel and gasoline engine exhausts. For exposure to diesel exhaust, the risks for the lowest, mid-and highest levels of exposure were 1.26 (95% CI, 1.04–1.53), 1.15 (95% CI, 0.83–1.55) and 1.62 (95% CI, 0.99–2.50), respectively. For exposure to gasoline exhaust, the corresponding risks were 1.28 (95% CI, 1.07–1.52), 1.37 (95% CI, 1.02–1.80) and 1.43 (95% CI, 0.62–2.82), respectively, suggesting an association with exposure. [The Working Group noted that this study was of limited value due to the lack of lifetime work histories and information on smoking.]

Boers *et al.* (2005) studied 1386 cases of prostate cancer and 2335 subcohort members from a prospective cohort of 58 279 subjects in the Netherlands. Cancer incidence was determined by linkage to nine regional cancer centres and assessed up to 1995. Information on diet and job history was retrieved from self-administered questionnaires completed at baseline in a previous cohort study. Occupational histories were assessed by experts to categorize exposure to pesticides, PAHs, diesel exhaust, metal dust and metal fumes. No association was found between exposure to diesel exhaust and prostate cancer (RR, 0.81; 95% CI, 0.62–1.06) in the highest tertile compared with unexposed subjects.

Bender *et al.* (1989) studied 4849 men with 1 or more years of experience as a highway maintenance worker for the Minnesota Department of Transportation (USA) and who had worked at least 1 day after 1 January 1945. Mortality was assessed up to 31 December 1984. The standardized mortality ratio was 0.69 (95% CI, 0.52–0.90) for lung cancer and 1.09 (95% CI, 0.56–1.90; 12 deaths) for urinary bladder cancer. [The Working Group noted that this study was limited by the lack of details regarding job history.]

2.3 Case–control studies

2.3.1 Cancer of the lung

See Table 2.2

Coggon *et al.* (1984) carried out a case–control study based on information from death certificates for England and Wales. Cases were 598 men, aged less than 40 years, who died from bronchial carcinoma during 1975–79, and controls were 1180 men who died from causes other than lung cancer, matched to the cases on age, year of death and area of residence. The most recent full-time occupation was mentioned on the death certificate. A JEM was developed for nine occupational exposures, including diesel exhaust, and jobs were classified as entailing any or high exposure. Any exposure to diesel exhaust was associated with an increased risk of lung cancer (RR, 1.3; 95% CI, 1.0–1.6), whereas the risk for high exposure to diesel exhaust was lower (RR, 1.1; 95% CI, 0.7–1.8). [The Working Group noted that the study demonstrated an increased risk of lung cancer associated with exposure to diesel exhaust, although no dose–response was indicated. The lack of full-time occupational

Table 2.2 Case–control studies of lung cancer and exposure to engine exhausts

Reference Location, period	Total No. of cases/ controls	Source of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Coggon *et al.* (1984) England and Wales, 1975–79	598 men aged < 40 yr/1180 men matched for age, yr of death, area of residence; based on death certificates	Deaths from causes other than lung cancer	JEM developed and applied to the occupation on death certificates	**Diesel fumes**			Bronchial carcinoma; age, yr of death, sex and area of residence; no data on tobacco smoking available
				Any exposure	172	1.3 (1.0–1.6)	
				High exposure	32	1.1 (0.7–1.8)	
Garshick *et al.* (1987) USA, 1981–82	1256/2385 individually matched (age, time of death) excluding deaths from cancer, accidents and suicide; nested within a cohort of male railway workers	Railway worker cohort identified from Railway Retirement Board	Industrial hygiene sampling survey used to classify job tasks as exposed or unexposed to DME; diesel–yr calculated for job tasks after 1959	**Age ≤ 65 yr**			Age, asbestos and tobacco smoking
				0–4 diesel–yr	NR	1.00	
				5–19 diesel–yr	NR	1.02 (0.72–1.45)	
				> 20 diesel–yr	117	1.64 (1.18–2.29)	
				Age > 65 yr			
				0–4 diesel–yr	NR	1.00	
				5–19 diesel–yr	NR	0.95 (0.79–1.13)	
				> 20 diesel–yr	26	0.94 (0.56–1.59)	
Hayes *et al.* (1989) USA, 1976–83	2291 men/2570; pooled analysis of 3 NCI-organized studies	Hospital and population	Full occupational histories used to classify duration of jobs in motor exhaust-exposed occupations	No exposure	1567	1.00	Birth cohort, cigarette use and study area; underlying 3 studies not summarized individually here, hence no overlap
				< 10 yr	362	1.0 (0.9–1.2)	
				> 10 yr	348	1.3 (1.1–1.5)	
Boffetta *et al.* (1990) (includes previous study reported by Hall & Wynder, 1984) USA, six cities, 1977–87	2584 men (primary lung cancer)/5099 men	Hospital, selected among patients with non-tobacco-related diseases	Occupations classified as low probability of (reference group), possible (19 occupations) and probable exposure (13 occupations); interviews	Possible exposure	240	0.92 (0.76–1.10)	Age, hospital, yr of interview, tobacco smoking habits, race, education and exposure to asbestos; only usual occupation available for cases in 1977–85; men only
				Probable exposure	210	0.95 (0.78–1.16)	
				Duration of probable exposure (1985–87 only)			
				1–15 yr	4	0.52 (0.15–1.86)	
				16–30 yr	15	0.70 (0.34–1.44)	
				≥ 31 yr	17	1.49 (0.72–3.11)	
						P for trend = 0.18	

Table 2.2 (continued)

Reference Location, period	Total No. of cases/ controls	Source of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Steenland *et al.* (1990) USA, 1982–83	994 deceased teamsters' union members with ≥ 20 yr of membership/1085	Union members deceased in the same period, excluding deaths from lung cancer, urinary bladder cancer and motor vehicle accidents	Mail and telephone interviews with next of kin; additional job information obtained from union records	**Long-haul (yr after 1959)**			Age, tobacco smoking, asbestos and other jobs with potential exposure to diesel exhaust
				1–11	162	1.08 (0.68–1.70)	
				12–17	228	1.41 (0.90–2.21)	
				≥ 18	213	1.55 (0.97–2.47)	
						P for trend = 0.04	
				Short-haul (yr after 1959)			
				1–11	36	1.11 (0.61–2.03)	
				12–17	37	1.15 (0.63–2.43)	
				≥ 18	40	1.79 (0.94–3.42)	
Steenland *et al.* (1998) (re-analysis of Steenland *et al.*, 1990)	994/1085	See Steenland *et al.* (1990)	Estimates of exposure to EC (marker of DME) obtained from exposure measurements in 1990 and modelling of historical levels	**Quartiles of cumulative exposure (EC–years; no lag)**			Age, race, tobacco smoking and asbestos
				0–174		1.20 (0.79–1.81)	
				174–268		1.16 (0.77–1.75)	
				268–360		1.39 (0.91–2.11)	
				≥ 360		1.72 (1.11–2.64)	
						P for trend = 0.023	
Swanson *et al.* (1993) Detroit metropolitan area, USA, 1984–87	3792 male incident/1996 colon cancer	Registry	Duration of employment based on lifetime occupational histories	**HGV drivers**		**OR**	White men only; age and tobacco smoking; separate ORs estimated for black men; potential confounding from socioeconomic factors possible due to use of carcinogen-free occupations as unexposed, but would not affect dose–response
				0 yr	88	1.00	
				1–9 yr	78	1.4 (0.8–2.4)	
				10–19 yr	38	1.6 (0.8–3.5)	
				≥ 20 yr	121	2.5 (1.4–4.4)	
				LGV drivers			
				0 yr	88	1.00	
				1–9 yr	46	1.7 (0.9–3.3)	
				≥ 10 yr	36	2.1 (0.9–4.6)	
				Garage and service station workers			
				0 yr	88	1.00	
				1–9 yr	47	2.2 (1.1–4.4)	
				≥ 10 yr	7	2.3 (0.5–10.8)	

Table 2.2 (continued)

Reference Location, period	Total No. of cases/ controls	Source of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Brüske-Hohlfeld *et al.* (1999) (same study base as Jahn *et al.*, 1999) Germany	3498 male incident/3541	Population	Personal interview on occupational history and tobacco smoking habits; exposure to DME from expert assessment	Ever exposed	716	1.43 (1.23–1.67)	Age, area, tobacco smoking and exposure to asbestos
				Duration of DME exposure (yr)			
				> 0–3	132	1.28 (0.95–1.73)	
				3–0	155	1.21 (0.91–1.61)	
				10–20	165	1.84 (1.34–2.52)	
				20–30	148	1.62 (1.16–2.24)	
				≥ 30	116	1.35 (0.95–1.93)	
Gustavsson *et al.* (2000) Stockholm County, Sweden, 1985–90	1042 male incident/2365	Population	Mailed questionnaire and supplementary telephone interview with study subjects or next of kin; quantitative DME exposure from expert assessment of lifetime occupa-tional history	**DME (mg–yr/m3 of NO2)**			Age, year of diagnosis, tobacco smoking, residential radon, residential air pollution and other occupational exposure to lung carcinogens
				Unexposed	842	1.00	
				> 0–0.53	29	0.65 (0.40–1.04)	
				0.54–1.41	54	1.13 (0.77–1.66)	
				1.42–2.37	45	1.05 (0.70–1.60)	
				≥ 2.38	72	1.63 (1.14–2.33)	
				Mixed exhaust (gasoline/diesel) (mg–yr/m3 of CO)			
				Unexposed	833	1.00	
				> 0–13.5	19	0.43 (0.25–0.74)	
				13.6– 8.8	47	1.10 (0.74–1.65)	
				38.9–113.6	78	1.32 (0.92–1.90)	
				≥ 113.7	65	1.09 (0.74–1.61)	
Richiardi *et al.* (2006) Turin, Italy, 1991–92	595 incident > 76 yr of age/845	Population	Interviewed on life time occupational history; supplementary questionnaires evaluated for DME exposure by industrial hygienist	**Cumulative exposure (intensity yr, h/wk)**			Age, cigarette consumption, exposure to list A occupations and educational level; environmental exposure to motor exhaust not included
				No exposure	436	1.00	
				I tertile (< 440)	53	1.01 (0.66–1.56)	
				II tertile (440–519)	51	0.99 (0.64–1.53)	
				III tertile (≥ 2520)	55	0.86 (0.56–1.31)	

Table 2.2 (continued)

Reference Location, period	Total No. of cases/ controls	Source of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Tse *et al.* (2011) Hong Kong Special Administrative Region SAR, China, 2004–06	132 nonsmoking men/536 nonsmokers	Population	Lifetime occupational history (job title, job task) obtained from personal interview; exposure to 16 occupational agents, including diesel exhaust	Diesel exhaust, any exposure (self-assessed)	6	4.17 (1.3–13.5)	Age, place of birth, education level, residential radon, history of lung diseases, cancer in relatives and intake of meat; reference group never exposed to confirmed or suspected human carcinogens
				Gasoline exhaust	7	1.52 (0.51–4.53)	
Villeneuve *et al.* (2011) Eight Canadian provinces, 1994–97	1681 male incident aged > 40 yr/2053	Population	Self-administered questionnaires inquiring about lifetime occupational and residential history	**Diesel exhaust (cumulative)**			Age, province, cigarette pack–yr, secondhand smoke, silica (yes/no) and asbestos
				Lowest tertile	267	0.93 (0.75–1.17)	
				Middle tertile	307	1.03 (0.83–1.29)	
				Highest tertile	326	1.12 (0.89–1.40)	
						P for trend = 0.07	
				Gasoline exhaust (cumulative)			
				Lowest tertile	261	0.92 (0.74–1.14)	
				Middle tertile	351	1.08 (0.88–1.33)	
				Highest tertile	314	1.11 (0.88–1.39)	
						P for trend = 0.68	
Olsson *et al.* (2011) Europe and Canada	13 304 men and women/16 282; pooled from 11 studies	Mixed	Lifetime occupational histories; population JEM developed to assign no, low or high exposure to DEM	**Cumulative exposure to DME (unit–yr)**			Age, sex, study, ever employed in other occupation noted to be at high risk for lung cancer, pack–yr and time since quitting smoking; partial overlap with Brüske-Hohlfeld *et al.* (1999), Gustavsson *et al.* (2000), Richiardi *et al.* (2006) and Pintos *et al.* (2012)
				Never	7676	1.00	
				< 6	1269	0.98 (0.89–1.08)	
				6–17.33	1325	1.04 (0.95–1.14)	
				17.34–34.5	1440	1.06 (0.97–1.16)	
				> 34.5	1594	1.31 (1.19–1.43)	
						P for trend < 0.0	
				Low levels of DME (yr of exposure)			
				0	7676	1.0	
				1–10	1576	1.00 (0.92–1.09)	
				11–20	785	0.98 (0.88–1.10)	
				1–30	660	1.03 (0.91–1.17)	
				> 30	1246	1.17 (1.07–1.29)	
						P for trend < 0.01	

Table 2.2 (continued)

Reference Location, period	Total No. of cases/ controls	Source of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
				High levels of DME (yr of exposure)			
Olsson et al. (2011) Europe and Canada (cont.)				0	7676	1.0	
				1–10	858	1.28 (1.14–1.45)	
				11–20	228	1.21 (0.98–1.51)	
				21–30	149	1.52 (1.15–2.02)	
				> 30	126	1.45 (1.07–1.96)	
						P for trend < 0.01	
Pintos *et al.* (2012) Montreal, Canada, Study I 1979–86, Study II 1996–2001 (expansion and re-analysis of Parent *et al.*, 2007)	1593/1427	Population	Interview with subjects or proxies on lifetime occupational history; exposure intensity to diesel exhaust and 293 other factors were coded by expert assessment	**Study I**			Adjusted for age, ethnicity, level of education, SES, tobacco smoking, respondent status and occupational carcinogens; men only
				Ever exposed	165	1.48 (1.0–2.1)	
				Non-substantial	97	1.25 (0.8–1.9)	
				Substantial	68	2.00 (1.1–3.6)	
				Study II			
				Ever exposed	298	1.30 (1.0–1.7)	
				Non-substantial	224	1.21 (0.9–1.6)	
				Substantial	74	1.74 (1.1–2.8)	
				Pooled			
				Ever exposed	463	1.34 (1.1–1.7)	
				Non-substantial	309	1.21 (1.0–1.5)	
				Substantial	75	1.80 (1.3–2.6)	
Parent *et al.* (2007) Montreal, Canada, 1979–85 (expansion of Siemiatycki *et al.*, 1988)	857 men aged 35–70 yr/1349 cancer and 533 population	Population and cancer patients	Interview with subjects or proxies on lifetime occupational history; exposure intensity to diesel exhaust, gasoline exhaust and other factors coded by expert assessment	**Diesel exhaust (population controls)**			Age, SES, ethnicity, self/ proxy respondent, tobacco smoking, asbestos and crystalline silica; men only
				Any exposure	166	1.2 (0.8–1.8)	
				Non-substantial	92	1.1 (0.7–1.7)	
				Substantial	74	1.6 (0.9–2.8)	
				Gasoline exhaust (population controls)			
				Any exposure	380	0.8 (0.6–1.1)	
				Non-substantial	110	0.9 (0.6–1.3)	
				Substantial	270	0.8 (0.6–1.1)	

CI, confidence interval; CO, carbon monoxide; DME, diesel motor exhaust; EC, elemental carbon; HGV, heavy goods vehicle; JEM, job–exposure matrix; LGV, light goods vehicle; NCI, National Cancer institute; NO_2, nitrogen dioxide; NR, not reported; OR, odds ratio; SES, socioeconomic status; wk, week; yr, year

histories may have reduced the precision of the exposure classification, and the absence of data on tobacco smoking could have resulted in confounding.]

Garshick *et al.* (1987) conducted a nested case–control study of lung cancer among a cohort of male railroad workers in the USA. Study subjects were identified from approximately 650 000 members of the US Railroad Retirement Board, which kept a register of virtually all railroad workers with 10 years of service or more. All deaths from lung cancer between March 1981 and February 1982 were identified; two controls per case were selected from deaths from causes other than cancer, accidents or suicide and were matched to cases on age and date of death. Tobacco smoking habits were obtained from questionnaires completed by the next of kin. Exposure to diesel exhaust was assessed on the basis of yearly job title after 1959, and validated through an industrial hygiene sampling survey and a review of job titles. During the 1950s, the railroad industry in the USA converted from coal-fired to diesel-powered locomotives; starting in 1959, workers were classified as exposed or unexposed and years of work in a job associated with exposure to diesel exhaust were summarized. Odds ratios were estimated after adjustment for age, tobacco smoking and exposure to asbestos. The risk for lung cancer was significantly increased in cases aged < 65 years at the time of death with ≥ 20 diesel–years of exposure (OR, 1.64; 95% CI, 1.18–2.29). No increased odds ratio was noted for those aged ≥ 65 years at the time of death, when the prevalence of exposure to diesel exhaust was believed to have been lower because fewer had worked for ≥ 20 years after 1959. A sensitivity analysis gave no indication that residual confounding from exposure to asbestos could explain the positive findings. [The Working Group noted that this study, based on a large data set, used yearly job records to classify exposure and was nested within the retrospective cohort mortality study that was conducted by the same authors using US Railroad Retirement Board records (Garshick *et al.*, 2004). The positive findings were probably not caused by bias or confounding (see Table 2.2).]

Hayes *et al.* (1989) reported the findings of a pooled analysis of three US NCI-organized case–control studies that used both population-based and hospital-based designs and were conducted in Florida in 1976–79 (Blot *et al.*, 1982), Louisiana in 1979–83 (Correa *et al.*, 1984) and New Jersey in 1980–81 (Schoenberg *et al.*, 1987). The original studies were not reviewed by the Working Group, and hence there was no overlap. A total of 2291 male cases of lung cancer and 2570 controls were identified. Full occupational histories and tobacco smoking habits were obtained by interview with study subjects or next of kin. Occupations were coded from the work histories and classified in relation to exposure to motor exhaust. Jobs coded as exposed to motor exhaust were HGV drivers, heavy equipment operators, bus drivers, taxi drivers, other groups of drivers and HGV mechanics. [The Working Group noted that the coding did not specifically address exposure to diesel or gasoline exhaust.] Odds ratios were estimated according to the duration of exposure to motor exhaust. The odds ratio, adjusted for birth cohort, study area and smoking, was 1.0 (95% CI, 0.9–1.2) for < 10 years of exposure versus no exposure and 1.3 (95% CI, 1.1–1.5) for > 10 years of exposure. Findings were consistent among the three study populations. An analysis limited to study subjects who were interviewed directly showed an odds ratio of 1.5 (95% CI, 1.2–1.9) in the group with a duration of > 10 years of exposure. Restriction of the analysis to those who had never smoked gave an odds ratio in the group with > 10 years of exposure of 1.7 (95% CI, 0.6–4.5; eight cases). [The Working Group noted that this study was based on full occupational histories; the positive findings could not be explained by uncontrolled confounding or bias. The study assessed exposure to mixed motor exhaust, but diesel motor

exhaust was probably the predominant source of exposure in most of the jobs coded as exposed.]

A hospital-based case–control study carried out in 18 hospitals in six cities in the USA aimed primarily at investigating the health effects of tobacco smoking (Boffetta *et al.*, 1990) included cases and controls reported in an earlier study (Hall & Wynder, 1984). Cases were 2584 men diagnosed with primary lung cancer, interviewed in 1977–87, and matched to 5099 controls selected from male patients without tobacco-related diseases on age, year of interview and hospital. Occupations were classified according to the probability of exposure to diesel exhaust (low, possible and probable). Self-assessed exposures were also recorded. After adjustment for tobacco smoking, the odds ratio for lung cancer was not related to the probability of exposure to diesel exhaust or the duration of probable exposure. However, duration of exposure was only available for a subset of study subjects, giving wide confidence intervals (*P* for trend with duration not significant). [The Working Group noted that this study provided limited data on occupations, which may have led to a misclassification of exposure.]

Steenland *et al.* (1990) reported a case–control study of men who had been members of the US Teamsters' union for more than 20 years and who had died in 1982–83. Among these, 994 had died from lung cancer and 1085 controls were selected from Teamsters' union members who had died during the same period from causes excluding lung cancer, urinary bladder cancer and motor vehicle accidents. Data on tobacco smoking and jobs driving diesel or gasoline HGVs were obtained from the next of kin, and additional data on long-haul/short-haul driving was obtained from the Teamsters' union. Odds ratios were adjusted for age, tobacco smoking, exposure to asbestos and other jobs with potential exposure to diesel exhaust. Based on the information from union records, a positive trend in the risk for lung cancer was observed with duration of long-haul HGV driving. The duration of short-haul driving after 1959 gave increasing odds ratios with increasing duration of exposure, but the trend was not statistically significant. Driving diesel-powered vehicles for > 35 years was associated with a significantly increased risk for lung cancer (OR, 1.89; 95% CI, 1.04–3.42) and driving gasoline-powered vehicles for > 35 years was also associated with an increase (OR, 1.34; 95% CI, 0.81–2.22). Shorter durations gave lower odds ratios for both diesel and gasoline vehicles. [The Working Group noted that this study, which was based on detailed work histories and adjusted for tobacco smoking habits, showed positive evidence of an increased risk for lung cancer after a long duration of employment in jobs that entailed exposure to diesel exhaust. No data were available on the intensity of exposure.]

A re-analysis of the study by Steenland *et al.* (1990) was carried out (Steenland *et al.*, 1998). Quantitative group-based exposure estimates were applied to the study subjects, using EC as a marker of exposure, and were based on an industrial hygiene survey of the HGV transport industry performed in 1990 (Zaebst *et al.*, 1991). Earlier exposure levels were modelled on the basis of available exposure measurements and changes in fuels, motors and traffic intensity. The robustness of historical exposure assessments were tested in a sensitivity analysis. Odds ratios were adjusted for age, race, tobacco smoking and exposure to asbestos. The risk for lung cancer increased (although not monotonically) with cumulative exposure to EC, showing a statistically significant trend ($P = 0.023$). The odds ratio in the highest quartile of cumulative exposure versus no exposure was 1.72 (95% CI, 1.11–2.64). The use of alternative assumptions for time trends in past exposure levels did not change the conclusions. [The Working Group noted that this study was based on a large data set, and demonstrated a positive and significant association between cumulative dose of diesel motor exhaust and the risk for lung cancer. The general

pattern of trends of exposure to EC, particularly a consistent decrease after the 1970s, was similar in the studies of Steenland *et al.* (1998) and Garshick *et al.* (2012) of the HGV industry. The Working Group also noted that Garshick *et al.* (2012) calibrated their exposure estimates to those of Zaebst *et al.* (1991), which, to a large extent, were the basis of the exposure estimation in Steenland *et al.* (1998).]

Swanson *et al.* (1993) conducted a population-based case–control study in the Detroit metropolitan area (USA). Incident cases of histologically confirmed cancer, aged 40–84 years in 1984–87, were identified from a cancer surveillance programme, including 3792 cases of lung cancer and 1966 colon cancer controls. Lifetime occupational and tobacco smoking histories were obtained by telephone interview with the subjects or surrogates. Odds ratios were estimated by occupational group, which defined a set of occupations with little or no exposure to carcinogens as unexposed, and were adjusted for age, pack–years of smoking and race. Results were presented separately for black and white men. Among white men, the odds ratio was significantly increased among long-term (> 20 years) HGV drivers and was raised among long-term (> 10 years) lighter vehicle drivers. The number of cases among black men was smaller and the odds ratios were not significant, but were elevated for those employed long-term. Short- and long-term white male garage and service station workers had non-significantly increased odds ratios; again, the numbers of similarly employed black men were very low. [The Working Group noted that the study was based on occupational titles only and no estimates of exposure to motor exhaust were used. The classification of nearly carcinogen-free occupations as unexposed may have introduced a systematic difference between the exposed and unexposed, resulting in biased risk estimates.]

Brüske-Hohlfeld *et al.* (1999) reported the risk for lung cancer among men in relation to exposure to diesel motor exhaust from two pooled case–control studies in Germany. One study identified cases of lung cancer in the Bremen and Frankfurt/Main areas in 1988–93 and the other study covered parts of Nordrhein-Westfalen, Rheinland-Pfalz and Bayern, the Saarland, Thüringen and Sachsen in 1990–96. A total of 3498 male incident cases of lung cancer and 3541 population controls were interviewed in person regarding occupational history and tobacco smoking habits. Special questionnaires were used to assemble information on specific job tasks. Exposure to diesel motor exhaust was investigated by expert assessment. The findings were adjusted for age, region, smoking and exposure to asbestos. The risk for lung cancer among those ever exposed to diesel motor exhaust was significantly elevated (1.43; 95% CI, 1.23–1.67), and increased, although not monotonically, with duration of exposure. The odds ratio was higher among those most recently exposed. An analysis by job titles showed a significantly increased odds ratio for professional drivers, those in other traffic-related jobs and heavy equipment operators. For professional drivers, the increased risk was found only in West Germany (OR, 1.44; 95% CI, 1.18–1.76) and not in East Germany (OR, 0.83; 95% CI, 0.60–1.14). [The Working Group noted that this study was based on detailed occupational data including information on job tasks, as well as detailed data on smoking. A low response rate among controls in one part of the study may have contributed to the discrepant results found for drivers in former West and East Germany.]

Gustavsson *et al.* (2000) conducted a population-based case–control study in Stockholm County, Sweden, of 1042 male cases of lung cancer diagnosed in 1985–90, who were identified from the regional cancer registry, and 2364 frequency-matched controls from the general population. Lifetime occupational and residential histories and information on tobacco smoking were obtained from a postal questionnaire supplemented by a telephone interview

with study subjects or next of kin. Occupational exposures were assessed by an occupational hygienist, who coded the intensity and probability of exposure to diesel motor exhaust and seven other occupational exposures. The odds ratio for cumulative exposure to diesel exhaust, adjusted for age, year of diagnosis, tobacco smoking, residential radon, residential exposure to traffic-generated air pollution and exposure to asbestos, was significantly increased in the highest quartile of cumulative exposure (OR, 1.63; 95% CI, 1.14–2.33). No increased risk for lung cancer was noted for exposure to vehicle exhaust in general (mixed diesel and gasoline exhaust). [The Working Group noted that this study was based on full occupational histories and lifetime data on smoking. It is improbable that the positive finding for diesel exhaust was caused by bias or confounding.]

A population-based case–control study of lung cancer conducted in the Turin area, Italy, was reported by Richiardi *et al.* (2006). Incident cases of primary lung cancer among men and women aged < 76 years (n = 595) were identified from hospitals in the city. Controls (n = 845) were randomly selected from population registers, and were frequency-matched for sex and 5-year age group. Subjects were interviewed regarding tobacco smoking habits, lifetime occupational history and exposure to secondhand smoke. Interviewers administered supplementary questionnaire modules for subjects in occupations with potential exposure to diesel exhaust. Questionnaires were evaluated for exposure to diesel exhaust by an industrial hygienist, who assessed the probability, intensity and daily frequency of exposure. Odds ratios were adjusted for age, gender, cigarette smoking, exposure to other occupational lung carcinogens and level of education, and were estimated for any exposure, for duration, intensity and probability of and for cumulative exposure to diesel exhaust; no indications of increasing risk for any of these parameters were observed. Analyses by job group and histological types of lung cancer showed no evidence of increased risk in association with exposure to diesel exhaust. [The Working Group noted that data on environmental exposure to motor exhaust, which may be substantial in the study area, were not available. The lack of such data may possibly have reduced the ability of the study to detect an association with occupational exposure. This study was later expanded and re-analysed using a JEM in a pooled, multicentre study (Olsson *et al.*, 2011).]

Tse *et al.* (2011) carried out a study on occupational exposures and the risk for lung cancer among nonsmoking men in Hong Kong Special Administrative Region (China). Histologically confirmed cases of primary lung cancer among Chinese men, aged 35–79 years, were identified from the largest oncology centre in Hong Kong Special Administrative Region during 2004–06 (response rate, 96%). Community controls were randomly selected from same districts as the cases (response rate, 48%) and frequency-matched by age. The analysis among lifelong nonsmokers included 132 cases and 536 controls with lifetime occupational histories (jobs and job tasks) obtained by personal interview. Regular exposure (at least once a week for at least 6 months) to specific agents or groups of agents at each workplace was determined based on a list of confirmed or suspected human carcinogens, including diesel exhaust and 13 other occupational agents. Odds ratios were adjusted for age, place of birth, level of education, residential radon, history of lung diseases, cancer in first-degree relatives and intake of meat. Only six cases were exposed to diesel exhaust which gave an odds ratio of 3.47 (95% CI, 1.08–11.14) when those not exposed to diesel exhaust were defined as unexposed, and 4.17 (95% CI, 1.28–13.53) when those not exposed to any of the agents were defined as unexposed. No increased risk was noted for exposure to gasoline exhaust, based on seven cases. A positive association was noted for exposure to silica and work as a painter but not for exposure to

asbestos. [The Working Group noted that one strength of this study was the analysis of lifelong nonsmokers, which considerably reduced the risk of residual confounding from smoking. Although the odds ratio for exposure to diesel exhaust was significantly increased, the confidence interval was wide because of the small numbers. The low response rate among controls may have biased the risk estimates. Self-assessed exposures may have resulted in misclassification, although a positive bias appeared to be improbable because no increased risks were noted for most of the other agents studied.]

A population-based case–control study of lung cancer among men aged > 40 years in eight Canadian provinces (excluding Montreal) was reported by Villeneuve *et al.* (2011). Living incident cases of lung cancer were identified from cancer registries in British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, Nova Scotia, Newfoundland and Prince Edward Island from 1994 to 1997, and age- and sex-matched controls were identified from the population. Self-administered postal questionnaires provided information on lifetime occupational and residential histories. Response rates were 64% for cases and 61% for controls. Occupation and industry codes were assigned by two hygienists, who also coded exposure (concentration, frequency and reliability; four levels for each) to diesel and gasoline emissions, asbestos and crystalline silica. Odds ratios were estimated adjusting for age, province, cigarette pack–years, secondhand smoke, silica and asbestos. For cumulative exposure to diesel emissions, the odds ratios across the increasing tertiles of cumulative exposure were 0.93, 1.03 and 1.12 (P = 0.07). A stronger trend with cumulative exposure was observed for squamous cell (P = 0.04) and large cell carcinoma (P = 0.02) of the lung. The odds ratio for exposure to diesel exhaust was significantly increased for large cell carcinoma in the upper tertile of cumulative exposure to diesel exhaust (OR, 1.68). (A positive association was noted for exposure to silica and work as a painter but not for exposure to asbestos; OR, 1.03–2.74; 36 cases). No consistent indications of increased risk were observed with exposure to gasoline exhaust. [The Working Group noted that the findings suggest that exposure to diesel engine emissions increased the risk of lung cancer, particularly for squamous and large cell carcinoma subtypes. This study used detailed data on occupational exposures and tobacco smoking and a weak positive association with cumulative exposure to diesel exhaust was noted.]

Olsson *et al.* (2011) reported a pooled re-analysis of 11 case–control studies from 41 study centres in 12 European countries and Canada. The study base partially overlapped with other studies reported by Brüske-Hohlfeld *et al.* (1999), Gustavsson *et al.* (2000), Richiardi *et al.* (2006) and Pintos *et al.* (2012), and included 13 304 cases (10 812 men and 2492 women) and 16 282 controls (13 031 men and 3251 women). For most centres, controls were recruited from the population, but some used hospital controls. Lifetime occupational and smoking histories were taken from the original studies. Work histories were recoded to a common classification (ISCO-68), and smoking histories were harmonized to enable a pooled analysis. A population JEM was developed (independently from earlier exposure assessments in the participating studies) to assign no, low or high exposure to diesel motor exhaust (representing relative intensities of 0, 1 and 4) for every work period for all study subjects. Cumulative lifetime exposure to diesel motor exhaust was expressed as unit–years. Odds ratios were adjusted for age, sex, study, occupational exposure to known carcinogens (based on A-list jobs; Mirabelli *et al.*, 2001), and pack–years of and time since quitting smoking. The odds ratio for lung cancer was significantly increased in the highest quartile of cumulative exposure to diesel exhaust, with evidence of a dose–response trend (P < 0.01). Subgroup analyses of workers never employed in jobs involving exposure to known

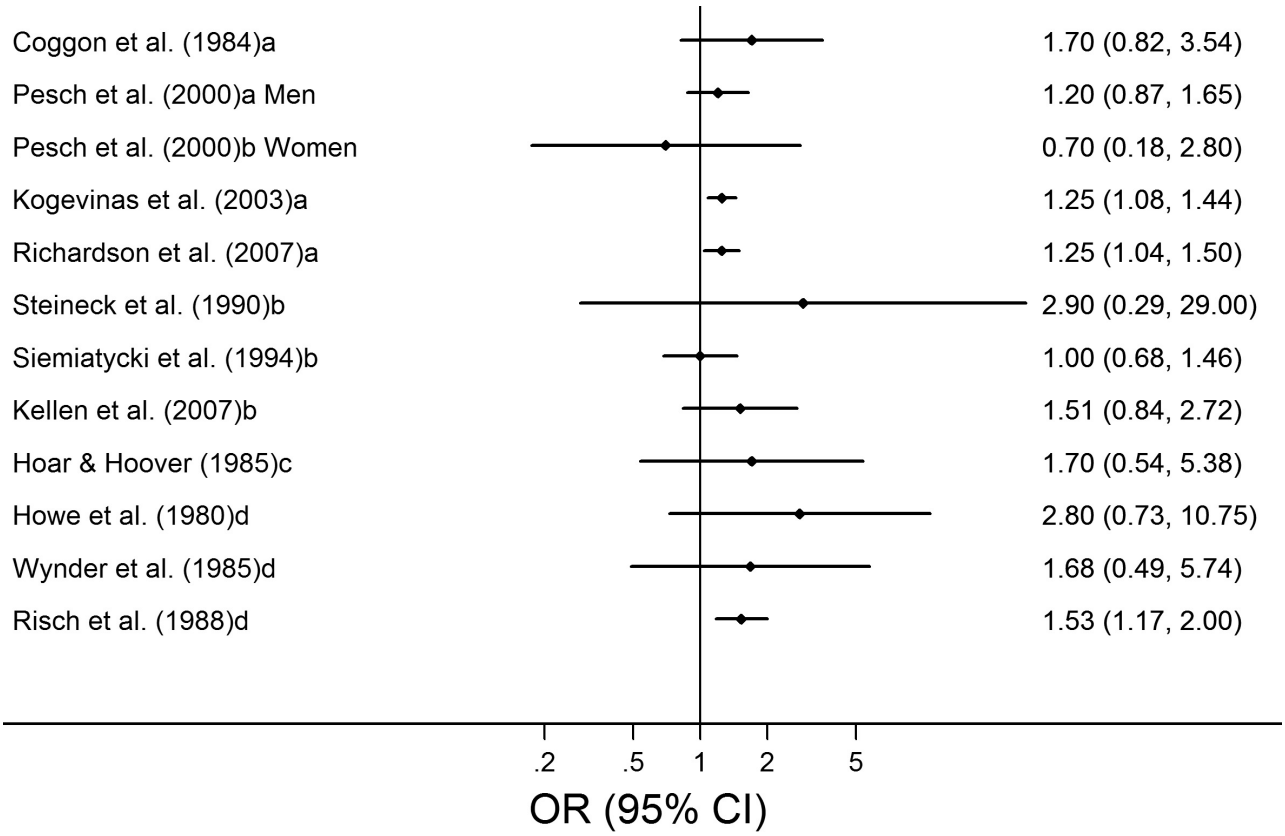
carcinogens showed similar results. Analysis of risk among never-smokers also showed an increased odds ratio in the highest quartile of cumulative exposure to diesel exhaust (OR, 1.26; 95% CI, 0.90–1.78). A positive and significant trend with duration of exposure was observed among those exposed to low ($P < 0.01$) and high levels ($P < 0.01$) of diesel motor exhaust. The risk estimates were similar for population-based and hospital-based case–control studies, and no significant heterogeneity for the effect of diesel motor exhaust in the highest quartile of cumulative exposure was found across studies ($P = 0.29$). [The Working Group noted that this study was based on a very large data set with detailed information on job histories and smoking habits. Exposure was coded in a standardized manner by the application of a JEM, although temporal changes in exposure were not taken into account. Although this study base partially overlapped with some earlier publications, these present findings were considered to be independent in so far as a new exposure assessment was used. The association between exposure to diesel motor exhaust and the risk for lung cancer reported here probably could not be explained by bias or confounding.]

Pintos *et al.* (2012) reported an expansion (Montreal II) of an earlier case–control study from the Montreal area, Canada (Siemiatycki *et al.*, 1987; Parent *et al.*, 2007; Montreal I), and covered the findings from Montreal I and Montreal II, as well as those from the pooled data set. Cancer cases were identified from area hospitals and population controls were recruited from electoral lists. Subjects or proxies were interviewed regarding lifetime occupational history, including data on work site and work tasks, and several other risk factors, including tobacco smoking. Exposure to diesel exhaust and several other occupational exposures were coded by expert assessment which was improved in relation to the method employed in the original study (Siemiatycki *et al.*, 1987). Odds ratios were adjusted for age, ethnicity, level of education, socioeconomic status, smoking, respondent status and occupational carcinogens. Study I (sampled in 1979–86) comprised 857 cases and 533 population controls; study II (sampled in 1996–2001) comprised 736 cases and 894 population controls, all of whom were men. An increased odds ratio of 1.34 (95% CI, 1.1–1.7) was found for subjects ever-exposed versus those never-exposed to diesel motor exhaust; for substantial cumulative exposure, the odds ratio was 1.80 (95% CI, 1.3–2.6). The findings were essentially similar for study I and study II when analysed separately. An analysis of risk in relation to histological type of lung cancer showed that the risks were more pronounced for squamous cell carcinomas (OR, 2.09; 95% CI, 1.3–3.2) for ever exposure to substantial levels of diesel exhaust but were lower for adenocarcinomas (OR, 1.17; 95% CI, 0.7–1.9). An intermediate risk was reported for small cell carcinomas (OR, 1.52; 95% CI, 0.8–2.7). A previous analysis based on the subjects in study I (Parent *et al.*, 2007) investigated the risk of lung cancer in relation to diesel exhaust and gasoline exhaust. No excess risk was found with exposure to gasoline exhaust. [The Working Group noted that this large study showed an increased risk of lung cancer after occupational exposure to diesel motor exhaust. A detailed exposure assessment and adjustment for potential confounders was applied, and the findings were internally consistent between the two sampling periods. The study showed a stronger effect for squamous cell carcinoma than for other histological types.]

2.3.2 Cancer of the urinary bladder

Numerous case–control studies that evaluated the risk for urinary bladder cancer and potential occupational exposure to diesel or motor exhaust were identified. The major limitation of the studies reviewed was the small number with well characterized exposure to

Fig. 2.1 Case–control studies of urinary bladder cancer with odds ratios for the highest exposure to diesel exhaust



a Job–exposure matrix
b Expert assessment
c Proxy
d Combined jobs
CI, confidence interval; OR, odds ratio

diesel or gasoline exhaust. A few studies used JEMs or experts to assess exposure, while others provided risk estimates for exposure to diesel exhaust for combined occupations based only on job titles or proxy exposure, and a large number of studies reported risk estimates for occupations that had potential for exposure to diesel exhaust. These studies are discussed in Section 2.3.2(a–c), and are summarized in Table 2.3. Odds ratios are plotted in Fig. 2.1. The use of expert or JEM assessment of exposure to diesel exhaust increased the probability of distinguishing exposed workers from unexposed workers, and these studies were most influential in the evaluation of risks for urinary bladder cancer. Studies that used job titles alone as a surrogate for exposure to diesel exhaust were less informative with regard to specific exposure to diesel or gasoline exhaust; however, some studies that provided a more focused analysis of HGV drivers were given more weight. Studies that reported risk estimates for specific occupations are described by occupation in Table 2.4, and the findings across studies are briefly discussed in Section 2.3.2(d). The odds ratios for urinary bladder cancer by occupational title are plotted in Fig. 2.2–2.7.

Table 2.3 Case–control studies of urinary bladder cancer and exposure to engine exhausts

Reference Location, period	Total No. of cases/ controls	Source of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Job–exposure matrix							
Coggon *et al.* (1984) England and Wales, 1975–79	291/638	Death certificates, including deaths from other cancers	JEM from occupational codes on death certificates	**Diesel fumes**			Men under 40 yr, controls matched by date of birth; no information on tobacco smoking, only most recent full-time job on death certificate
				All occupations (versus no exposure)	69	1.0 (0.7–1.3)	
				Occupations with high exposure	19	1.7 (0.9–3.9)	
Dolin & Cook-Mozaffari (1992) United Kingdom, 1965–80	2457	External controls	Death certificates, JEM to identify jobs with exposure to diesel exhaust	Occupations with low exposure	125	**SMR** 1.06 (0.88–1.26)	Age and degree of urbanization; men aged 25–64 yr; no information on tobacco smoking
Pesch *et al.* (2000) Germany, 1991–95	1035/4298	Population	In-person interview using structured questionnaire (JEM, JTEM)	**Exhaust JEM**		**OR**	Urothelial cancer (urinary bladder: 90% men, 84% women); tobacco smoking, study centre and age; controls matched by region, sex and age
				Men			
				Medium	157	1.0 (0.8–1.3)	
				High	173	1.3 (1.0–1.6)	
				Substantial	57	1.2 (0.9–1.7)	
				Women			
				Medium	21	1.3 (0.7–2.2)	
				High	18	1.0 (0.6–1.8)	
				Substantial	2	0.7 (0.2–3.2)	
				Self-assessed			ORs for women < 1.0, small number of exposed cases
				Men			
				Medium	38	0.6 (0.4–0.9)	
				High	74	1.0 (0.8–1.3)	
				Substantial	19	0.8 (0.5–1.4)	
Kogevinas *et al.* (2003) Europe, 1976–96	3346/6840 matched on age and geographical area	Population and hospital	JEM	Highest tertile of exposure to diesel exhaust (compared with unexposed)	NR	~1.25 (~1.05–1.4) estimated from graph	Age, tobacco smoking and study centre; pooled analysis of 13 studies; men aged 30–79 yr

Table 2.3 (continued)

Reference Location, period	Total No. of cases/ controls	Source of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Richardson *et al.* (2007) British Columbia, Canada, 1983–90	1062/8057	Other cancers except lung from cancer registry	NOES–JEM	**Diesel exhaust**			
				No cumulative exposure		1.0 (reference)	Tobacco smoking, alcohol consumption and questionnaire respondent; same cancer registry database as Band *et al.* (2005)
				Ever exposure	605	1.18 (0.95–1.37)	
				Cumulative exposure			
				Low	NR	1.14 (0.95–1.37)	
				Medium	NR	1.17 (0.97–1.40)	
				High	NR	1.25 (1.04–1.49)	
						P for trend = 0.01	
Expert assessment							
Steineck *et al.* (1990) Stockholm, Sweden, 1985–87	256/287	Population	Postal questionnaire and interview, expert classification of exposure to diesel or petrol exhaust	**Diesel exhausts**			
				Exposed	25	1.7 (0.9–3.3)	Urothelial cancer and/or squamous cell carcinoma of lower urinary tract; yr of birth and tobacco smoking; men born 1911–45; participation rate: 80% cases, 79% controls
				Annual dose			
				Low	NR	1.3 (0.6–3.1)	
				Moderate	NR	2.2 (0.7–6.6)	
				High	NR	2.9 (0.3–30.0)	
				Petrol exhausts			
				Ever exposed	24	1.0 (0.5–1.9)	
				Annual dose			
				Low	NR	0.6 (0.3–1.3)	
				Moderate	NR	1.4 (0.5–3.7)	
				High	NR	3.9 (0.4–35.5)	
				Diesel and petrol exhausts			Moderate/high annual dose
				None	247	1.0 (reference)	
				Diesel only	4	1.1 (0.3–4.3)	
				Petrol only	6	1.0 (0.3–3.4)	
				Both	7	7.1 (0.9–58.8)	Yr of birth and tobacco smoking
				Both	7	5.1 (0.6–43.6)	Yr of birth, tobacco smoking and benzene

Table 2.3 (continued)

Reference Location, period	Total No. of cases/ controls	Source of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Siemiatycki *et al.* (1994) Montreal area, Canada, 1979–86	484/1879 cancer and 533 population	Other cancers and population	In-person (some proxy) interview with detailed job history, semiquantitative exposure assessment by experts	**Diesel engine exhaust**			Age, ethnicity, smoking, SES, regular coffee consumption and respondent status (self or proxy)
				Non-substantial	46	1.3 (0.9–1.8)	
				Substantial	32	1.0 (0.7–1.5)	
				Confidence			
				Probable	28	1.0 (0.7–1.6)	
				Definite	50	1.2 (0.9–1.7)	
				Concentration			
				Low	27	1.2 (0.8–1.9)	
				Medium/high	51	1.1 (0.8–1.50	
				Frequency			
				Low	48	1.1 (0.8–1.5)	
				Medium/high	30	1.3 (0.8–1.9)	
				Duration (yr)			
				≥ 11	56	1.3 (0.8–1.5)	
Kellen *et al.* (2007) Belgium, 1999–2004	200/385	Population	Structured interview, expert assessment	**Diesel**	144	1.0 (reference)	Transitional cell carcinoma; age, sex and tobacco smoking; same population as Reulen *et al.* (2007)
				No exposure			
				Low	20	0.8 (0.4–1.57)	
				High	56	1.51 (0.85–2.75)	
						P for trend = 0.25	
				Ever exposure			Sex and age
				Never smoked	2	1.24 (0.30–5.03)	
				Ever smoked	54	1.34(0.83–2.16)	
Self-reported assessment							
Howe *et al.* (1980) Canada, 1974–76	480 men, 152 women/480 men, 152 women	Population	In-person interviews; occupational history coded according to the 1971 Canadian census, more details collected on a-priori suspect industries, exposure to fumes, dust or chemicals	Diesel and traffic fumes	11	2.8 (0.8–11.8)	Work in a-priori suspect industries considered; control matched by sex, province and age
				Railroad workers	9	9.0 (1.2–394.5)	

Table 2.3 (continued)

Reference Location, period	Total No. of cases/ controls	Source of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Hoar & Hoover (1985) New England, USA, 1975–79	325/673	Population	In-person interviews with next of kin; lifetime occupation	**Exposure to diesel, any occupation**		**OR**	Coffee drinking, tobacco smoking and education considered but did not change crude OR in duration analysis; controls matched on state, sex, age, race, yr of death, county or residence and age at death
				Never	197	1.0 (reference)	
				Ever	26	1.5 (0.8–2.8)	
				1–19 yr	5	0.9 (0.3–2.8)	
				20–29 yr	5	2.1 (0.5–8.6)	
				30–39 yr	6	3.2 (0.8–13.7)	
				> 40 yr	7	1.7 (0.5–5.0)	
						P for trend = 0.024	
Risch *et al.* (1988) Canada, 1979–82	826/792	Population	In-person interview using structured questionnaire; occupational history	**Occupation/industry: job entailing contact with diesel or traffic fumes**			Control for lifetime tobacco smoking; other factors considered include SES, marital status, educational group, urban versus rural residence and birth place; controls matched by birth yr, age and area of residence; response rate: 67% cases, 53% controls
				Men	309		
				Ever employed		1.53 (1.17–2·00)	
				Employed 8–28 yr before diagnosis		1.69 (1.24–2.31)	
				Trend with duration		1.23 (1.08–1.41)	
				Women	19		
				Ever employed	NR	0.62 (0.23–1.57)	
				Employed 8–28 yr in past	NR	0.49 (0.10–2.11)	
				Trend with duration		0.83 (0.27–2·50)	
Wynder *et al.* (1985) USA (American Health Foundation Study), 1981–83	194/582	Hospital; men with non-tobacco-related diseases	Interview with structural questionnaire, exposure to diesel exhaust classified by: (1) jobs with probable exposure, (2) high, moderate or minimal occupations by % of workers exposed to diesel exhaust	No exposure to diesel exhaust	178	1.0 (reference)	Age, smoking habit and SES; controls matched by age, race, yr of interview and hospital (% of workers exposed to diesel exhaust)
				Probable exposure			
				Minimal (< 10%)	189	1.0 (reference)	
				Moderate (10–19%)	1	0.16	
				High (≥ 20%)	4	1.68 (0.49–5.73)	

Table 2.3 (continued)

Reference Location, period	Total No. of cases/ controls	Source of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Iyer *et al.* (1990) USA (American Health Foundation Study), NR	136/272	Hospital; non-tobacco-related diseases	Lifetime and self-reported occupational history	No exposure to diesel	95	1.0 (reference)	Primary cancer; educational status and tobacco smoking; controls matched by age, race, sex, yr of interview and hospital
				Any exposure to diesel (possible, probable or self-reported)	41	1.24 (0.77–2.00)	
				Main occupation with exposure to diesel			
				Possible	19	1.11 (0.6–2.08)	
				Probable	13	0.86 (0.41–1.81)	

CI, confidence interval; JEM, job–exposure matrix; JTEM, job-task–exposure matrix; NOES, National Occupational Exposure Survey; NR, not reported; OR, odds ratio; SES, socioeconomic status; SMR, standardized mortality ratio; yr, year

Table 2.4 Case–control studies of urinary bladder cancer and exposure to engine exhaust estimated from job title

Reference Location, period	Total No. of cases/ controls	Source of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Steenland *et al.* (1987) Ohio, USA, 1960–82	731/1275	Death certificates	Occupation and industry from death certificates and city directories	**Occupation as HGV driver**			Mortality study
				< 20 years	49	1.06 (0.89–1.26)	
				> 20 years	1	12.00 (2.29–62.9)	
				Railroad industry			
				< 20 years	10	0.42 (0.23–0.78)	
				> 20 years	19	2.21 (1.21–4.03)	
Siemiatycki *et al.* (1994) Montreal area, Canada, 1979–86	484/1879 cancer and 533 population	Other cancers except lung and kidney and population	Interview with detailed job history, semiquantitative exposure assessment by experts	**Occupation as HGV driver**			Age, ethnicity, tobacco smoking, SES, regular coffee consumption and respondent (self or proxy)
				Exposure duration			
				< 10 yr	25	1.1 (0.7–1.8)	
				≥ 10 yr	26	1.2 (0.8–1.9)	
Colt *et al.* (2004) New Hampshire, USA, 1994–98	424/645	Population	In-person interview, occupational history, SOC codes	Male tractor-trailer drivers	47	2.4 (1.4–4.1)	Primary cancers, aged 25–74 yr, identified from cancer registry; age and tobacco smoking
				< 5 yr	19	1.5 (0.8–3.1)	
				≥ 5 yr	28	4.0 (1.8–8.7)	
						P for trend, 0.0003	
				HGV drivers	3	0.8 (0.2–3.5)	
				LGV drivers	27	1.3 (0.7–2.3)	
				Bus drivers	5	0.5 (0.2–1.6)	
				Taxicab drivers/ chauffeurs	8	0.8 (0.3–2.3)	
				Female auto mechanics	17	Reported as < 1.3 (NS)	
				Garage or gas station workers	19	1.7 (0.8–3.4)	
				< 5 yr	14	1.4 (0.6–2.9)	
				≥ 5 yr	5	6.3 (0.7–54.8)	
						P for trend, 0.07	

Table 2.4 (continued)

Reference Location, period	Total No. of cases/ controls	Source of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Colt *et al.* (2011) New England, USA, 2001–04	1158/1402	Population	In-person interview, occupational history, SOC codes	**Men only** Tractor-trailer drivers	54	0.9 (0.6–1.3)	Cases identified from hospital and state registries and records, including carcinoma *in situ*; age, race, ethnicity, tobacco smoking and employment in other high-risk occupations; participation rate, 65%
				HGV drivers	57	1.3 (0.9–2.0)	
				LGV drivers	43	0.8 (0.5–1.2)	
				Taxicab drivers/ chauffeurs	23	1.1 (0.6–2.0)	
				Vehicle/mobile equipment mechanics/repairers	119	1.5 (1.1–2.0)	
				Automobile mechanics	59	1.6 (1.05–2.4)	
				< 5 yr	25	1.4 (0.7–2.5)	
				5– < 15 yr	17	1.6 (0.7 –3.4)	
				≥ 15 yr	17	2.1 (0.98–4.6)	
						P for trend, 0.03	
Dolin & Cook-Mozaffari (1992) United Kingdom, 1965–80	2457	External	Death certificates; JEM to identify jobs with exposure to diesel exhaust			**SMR**	Death certificate study; no information on tobacco smoking
				HGV driver	92	1.08 (0.88–1.32)	
				HGV driver's mate	1	0.95 (0.03–5.31)	
				Railroad industry	74	2.22 (1.77–2.79)	
				Railway engine driver	13	1.61 (0.85–2.75)	
				Railway shunter	4	1.49 (0.40–3.82)	
				Railway signallman	5	1.46 (0.47–3.39)	
				Railway guard	4	2.58 (0.70–6.61)	
				Railway lengthman	11	1.47 (0.73–2.63)	
				Bus driver	14	0.81 (0.44–1.36)	
				Taxi driver	18	1.24 (0.73–1.36)	
Coggon *et al.* (1986) United Kingdom, 1975–80	179/NR	Hospital pathology and cancer registry files; other cancers	Postal questionnaire	HGV drivers (ever versus never employed)	NR	1.6 (1.0–2.4)	Urinary bladder and renal pelvis; age, tobacco smoking, county and source of interview; men aged 18–54 yr

Table 2.4 (continued)

Reference Location, period	Total No. of cases/ controls	Source of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Silverman *et al.* (1986) USA, 1977–78 (National Bladder Cancer Study)	1909/3569 (white men)	Population	Interviewer-administered questionnaire	**Truck driver or delivery man**			Age and tobacco smoking; controls matched for age and geographic location; response rate: 75% cases, 83–84% controls
				Usual	99	1.5 (1.1–2.0)	
				Ever	488	1.3 (1.1–1.4)	
				Duration of employment (yr)			
				< 5	208	1.1 (NR)	
				5–9	102	1.3 (NR)	
				10–14	58	1.7 (NR)	
				15–24	59	2.2 (NR)	
				≥ 25	54	1.1 (NR)	
						P for trend, < 0.001	
				Duration of employment (yr) among drivers first employed > 50 yr before diagnosis			
				5–9	74	1.2 (NR)	
				10–14	32	1.4 (NR)	
				15–24	33	2.1 (NR)	
				≥ 25	22	2.2 (NR)	
						P for trend, < 0.0001	
				Bus driver			
				Usual	9	1.5 (0.6–3.9)	
				Ever	49	1.3 (0.9–1.9)	
				Duration of employment (yr)			
				< 5	21	1.3	
				5–9	11	1.2	
				≥ 10	16	1.3	
						P for trend, 0.2	
				Taxicab driver/chauffeur			
				Usual	10	6.3 (1.6–29.3)	
				Ever	77	1.6 (1.2–2.2)	
				Duration of employment (yr)			
				< 5	44	1.9	
				5–9	14	1.0	
				≥ 10	16	2.0	

Table 2.4 (continued)

Reference Location, period	Total No. of cases/ controls	Source of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Iyer *et al.* (1990) USA (American Health Foundation Study), NR	136/272	Hospital; non-tobacco-related diseases	Lifetime and self-reported occupational history	HGV driver	4	0.48 (0.15–1.56)	Primary cancer; educational status and tobacco smoking; controls matched by age, race, sex, yr of interview and hospital
Hoar & Hoover (1985) New England, USA, 1975–79	325/673	Population	In-person interviews with next of kin; lifetime occupation	**HGV driver**		**OR**	Coffee drinking, tobacco smoking and education considered but did not change crude OR in duration analysis; controls matched on state, sex, age, race, yr of death, county of residence and age at death
				Ever	35	1.5 (0.9–2.6),	
				1–4 yr	9	1.4 (0.6,3.3)	
				5–9 yr	12	2.9 (1.2–6.7)	
				> 10 yr	11	1.8 (0.8–4.1)	
						P for trend, 0.006	
				Reported exposure to diesel fuel	NR	1.8 (0.5–7.0)	
				Not reported exposure to diesel fuel	NR	1.5 (0.8–2.7)	
				Calendar year first employed			
				< 1929	10	1.2 (0.5–2.6)	
				1930–49	18	2.6 (1.3–5.1)	
				> 1950	6	1.4 (0.5–4.1	

Table 2.4 (continued)

Reference Location, period	Total No. of cases/ controls	Source of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Silverman *et al.* (1983) Detroit, USA, 1977–78 (National Bladder Cancer Study)	303/296	Population	Interviewer-administered questionnaire; details on HGV driving	HGV driver	42	2.1 (NR)	Lower urinary tract (95% bladder); age and tobacco smoking; white men; age-matched controls
				Duration of employment (yr)			
				< 10	23	1.4 (NR)	
				≥ 10	16	5.5 (NR)	
						P for trend, 0.004	
				Yr employment started			
				1910–29	8	1.6 (NR)	
				1930–39	12	2.0 (NR)	
				1940–49	10	1.5 (NR)	
				1950–69	7	6.5 (NR)	
						P for trend, 0.03	
				Ever operated a vehicle with diesel engine			
				No	21	1.4 (0.7–2.9)	
				Yes	13	11.9 (2.3–61.1)	One exposed control
						P for trend, 0.014	
Brownson *et al.* (1987) Missouri, USA, 1984–86	823 white men/2469	Cancer registry; other patients without smoking-related diseases	Registry records, occupation coded using 1980 US census code	**Occupation**	18	**OR**	Age, tobacco smoking and alcohol use; age-matched controls
				HGV drivers		1.2 (0.7–2.1)	
				Industry	17	1.2 (0.7–2.2)	
				Transport service			
				Railroads	18	1.3 (0.7–2.3)	
Kogevinas *et al.* (2003) Europe, 1976–96	3346/6840	Population and hospital	Occupational history, job codes	**Occupations**			Age, tobacco smoking and study centre; controls never employed in a-priori suspect occupation
				Railway engine drivers/ firemen	34	1.41(0.87–2.28)	
				Railway brakemen, signallmen and shunters	18	1.43(0.77–2.63)	
				Motor vehicle mechanics	108	1.16(0.90–1.50)	
				Automobile mechanics	78	1.38(1.02–1.87)	

Table 2.4 (continued)

Reference Location, period	Total No. of cases/ controls	Source of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Band *et al.* (2005) British Columbia, Canada, 1983–90	1129/14 334	Cancer registry; other cancers except lung	Self-administered questionnaire, SOC and SIC codes	**Usual occupation**			Smoking (yr), alcohol consumption and proxy response; controls matched on age and yr of diagnosis; 65% response rate
				HGV driver			
				Usual	44	1.21 (0.92–1.60)	
				Ever	145	1.20 (1.02–1.41)	
				Railroad transport			
				Usual	11	1.01 (0.59–1.75)	
				Ever	26	1.11 (0.77–1.59)	
				Locomotive operations			
				Usual	8	1.84 (0.92–3.68)	
				Ever	13	1.26 (0.75–2.12)	
				Taxi drivers/chauffeurs			
				Usual	6	1.82 (0.85–3.90)	
				Ever	27	1.17 (0.82–1.66)	
				Motor vehicle mechanics (8581)			
				Usual	29	1.37 (0.97–1.94)	
				Ever	75	1.49 (1.20–1.86)	
				Usual industry			
				HGV transport			
				Usual	33	1.38 (0.99–1.99)	
				Ever	92	1.28 (1.05–1.56)	
				Rail transport			
				Usual	28	0.83 (0.59–1.17)	
				Ever	71	0.93 (0.74–1.15)	
				Taxicab service			
				Usual	6	1.94 (0.90–4.20)	
				Ever	22	1.02 (0.70–1.51)	
				Gasoline service			
				Usual	6	1.69 (0.79–3.61)	
				Ever	38	1.75 (1.28–2.38)	

Table 2.4 (continued)

Reference Location, period	Total No. of cases/ controls	Source of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Zheng *et al.* (2002) Iowa, USA, 1986–89	1452/2434	Population	Postal questionnaire (some telephone interviews)	**Occupation**			*In situ* and invasive cancers; age, tobacco smoking (lifetime) and first-degree relative with bladder cancer; cases identified from state registry; controls matched by gender and age
				Automobile mechanic			
				All	44	1.6 (1.0–2.6)	
				Duration of employment			
				< 10 yr	8	1.4 (0.5–3.7	
				≥ 10 yr	36	1.7 (1.0–2.8)	
				Garage/service station–related			
				All	27	1.7 (0.9–3.1)	
				Duration of employment			
				< 10 yr	10	1.8 (0.7–4.8)	
				≥ 10 yr	17	1.6 (0.8–3.5)	
				Supervisors: transport and material moving			
				All	11	6.5 (1.4–29.9)	
				Duration of employment			
				< 10 yr	1	NR	
				≥ 10 yr	10	6.0 (1.3–28.2)	
				Material-moving equipment operators			
				All	26	1.9 (1.0–3.6)	
				Duration of employment			
				< 10 yr	6	1.9 (0.5–7.3)	
				≥ 10 yr	20	1.9 (0.9–3.9)	
				Industries			
				Automotive dealer/service station			
				All	54	1.6 (1.0–2.4)	
				Duration of employment			
				< 10 yr	15	1.4 (0.7–3.0)	
				≥ 10 yr	39	1.7 (1.0–2.7)	
				Railroad transport (40)			
				All	33	1.4 (0.8–2.3)	
				Duration of employment			
				< 10 yr	4	0.6 (0.2–2.0)	
				≥ 10 yr	29	1.7 (1.0–3.1)	

Table 2.4 (continued)

Reference Location, period	Total No. of cases/ controls	Source of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Samanic *et al.* (2008) Spain, 1988–2000	1159/1231	Hospital	In-person interview, SOC and SIC codes	**Occupation** *HGV driver*			White cases of carcinoma or carcinoma *in situ*; age, hospital region, tobacco smoking and ever employed in high-risk occupation; controls matched by age at diagnosis/interview, sex, race/ethnicity and hospital
						0.97 (0.66–1.43)	
				Railroad transport			
				Overall	11	1.04 (0.40–2.69)	
				0– < 10 yr	4	0.62 (0.15–2.55)	
				≥ 10 yr	7	1.56 (0.43–5.70)	
				≥ 10 yr	3	0.31 (0.08–1.24)	
				Taxi driver			
				Overall	37	1.14 (0.69–1.90)	
				0– < 10 yr	16		
				Industry *Local urban transport*			
				0– < 10 yr	15	0.72 (0.35–1.48)	
				≥ 10 yr	18	0.64 (0.34–1.22)	
				Auto repair services/garages			
				Overall	55	1.21 (0.81–1.81)	
Risch *et al.* (1988) Canada, 1979–82	826/792	Population	In-person interview using structured questionnaire; occupational history	**Railway occupations**			Lifetime tobacco smoking; other factors considered included SES, marital status, educational group, urban versus rural residence and birth place; controls matched by age and area of residence; response rate: 67% cases, 53% controls
				Ever employed	113	1.07 (0·71–1.61)	
				Employed 8–28 yr in past	NR	1.17 (0.65–2·12)	
				Trend with 10 years duration	NR	1·09 (0.87–1.36)	

Table 2.4 (continued)

Reference Location, period	Total No. of cases/ controls	Source of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Burns & Swanson (1991) Detroit, USA, 1973–91	2160/3979	Cancer registry; colon cancers	Telephone interview with subject or surrogate; occupations coded by duties rather than job title	**Usual occupation** Railroad worker **Usual industry** Railroads Automobile repair	 12 12	 0.7 (0.2–2.4) 0.7 (0.3–1.4) 0.5 (0.2–1.1)	Cigarette smoking, gender, race and age at diagnosis; white and black men and women; response: 94% cases, 95% controls
Decouflé *et al.* (1977) USA, 1956–65	6434 men/ NR	Hospital non-cancer	Structured questionnaire	Ever employed as HGV driver Locomotive engineers/ firemen Bus driver Taxicab drivers and chauffeurs	26 8 4 5	1.66 ($P > 0.05$) 1.65 ($P > 0.05$) 2.78 (NR) 1.70 ($P > 0.05$)	Age; clerical workers were the unexposed referent group
Dryson *et al.* (2008) New Zealand, 2003–04	213/471	Population	In-person interview	HGV or tanker drivers Bus drivers Car, taxi and light van operators Road freight transport industry	16 7 12 12	1.36 (0.60–5.09) 1.69 (0.55–5.26) 0.73 (0.33–1.60) 1.65 (0.61–4.47)	Cases (aged 25–70 yr) identified from cancer registry; age, gender, Maori ethnicity and tobacco smoking; SES semi-Bayes methods adjusted for multiple comparisons; response rate: 64% cases, 48% controls
Silverman *et al.* (1989a) USA, 1977–78 (National Bladder Cancer Study)	2100/3874 (white men)	Population	Interviewer-administered questionnaire	Railroad worker Auto mechanic (HGV transport industry)	57 11	1.3 (0.9–2.0) 10.2 (2.1–68.6)	Same population as Silverman *et al.* (1986); tobacco smoking; controls matched by age
Silverman *et al.* (1989b) USA 1977–78 (National Bladder Cancer Study)	126/383 (non-white men)	Population	Interviewer-administered questionnaire	Taxicab driver/ chauffeur Auto mechanic Garage worker/gas pump attendant	10 6 6	1.3 (0.5–3.2) 1.4 (0.4–4.4) 1.6 (0.5–4.5)	Population included in Smith *et al.* (1985); tobacco smoking and high-risk occupations

Table 2.4 (continued)

Reference Location, period	Total No. of cases/ controls	Source of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Schifflers *et al.* (1987) Belgium, 1984–85	74/203	Population	In-person interviews using standard form, analysis on jobs considered a-priori as hazardous	HGV/engine drivers	10	2.15 (0.88–5.29)	Tobacco use; controls matched for yr of birth and sex
Brooks *et al.* (1992) Missouri, USA, 1984–88	1415/NR	Cancer registry; case/case analysis	Registry records			**OR**	Age and tobacco smoking; same population as Brownson *et al.* (1987); ORs for high-grade tumours
				Truck driver	14	2.7	
				Vehicle mechanic	5	1.2	
Gaertner *et al.* (2004) Canada, 1994–97	887/2847	Population	Mailed questionnaires	**Men only**			Cases identified from cancer registry; age, race, tobacco smoking, province, several dietary factors and employment in suspect industries
				HGV driver	68	1.23 (0.88–1.75)	
				> 1–5 yr	19	1.14 (0.63–2.04)	
				> 5–15 yr	16	1.50 (0.73–3.10)	
				> 15 yr	33	1.19 (0.74–1.91)	
						P for trend, 0.25	
				Auto mechanic	36	1.69 (1.02–2.82)	
				> 1–5 yr	15	1.37 (0.66–2.83)	
				> 5–15	9	1.93 (0.76–4.88)	
				> 15	12	2.48 (0.97–6.34)	
						P for trend, 0.01	
				Gas station attendant	13	0.65 (0.33–1.32)	
Reulen *et al.* (2007) Belgium, 1996–2004	202/390	Population	In-person interviews	Male motor vehicle mechanics	5	0.6 (0.2–1.9)	Men and women (aged 40–96 yr) with transitional cell carcinoma identified by cancer registry (same population as Kellen *et al.*, 2007); age, sex, tobacco smoking and educational status; very low response rate: 26% controls, 9% cases

Table 2.4 (continued)

Reference Location, period	Total No. of cases/ controls	Source of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Smith *et al.* (1985) USA, 1977–78 (National Bladder Cancer Study)	2108/4046 (black and white men)	Population	Interview with structured questionnaire	**Auto and HGV mechanics**			Age, education and coffee consumption; controls: unexposed, never worked in occupations with similar exposures as mechanics or with suspected chemical exposures
				Smokers	NR	1.21 (0.90–1.63)	
				Duration (yr)			
				1–5	NR	1.53 (1.07- 2.20)	
				6–10	NR	0.74 (0.43–1.28)	
				11–20	NR	1.13 (0.67–1.92)	
				21–29	NR	2.77 (1.34- 5.71)	
				≥ 30	NR	1.19 (0.66–2.13)	
				Nonsmokers	NR	1.33 (0.77–2.31)	
				Duration (yr)			
				1–5	NR	1.48 (0.73–2.75)	
				6–10	NR	1.29 (0.54–3.11)	
				11–20	NR	0.73 (0.21–2.53)	
				21–29	NR	0.51 (0.06–4.11)	
				≥ 30	NR	2.13 (0.78–5.80)	
Schoenberg *et al.* (1984) New Jersey, USA, 1978–79	658/1258	Population	In-person interviews using structured questionnaires	Taxicab drivers	25	1.36 (0.79–2.34)	White men (aged 21–84 yr) with carcinoma; age and duration of smoking; part of the in the National Bladder Cancer Study
				Motor vehicle mechanics	55	1.26 (0.87–1.84)	
				Duration (yr)			
				< 2	NR	2.96 ($P < 0.05$)	
				2–4.9	NR	0.82	
				5–9.9	NR	1.34	
				10–19.9	NR	0.77	

Table 2.4 (continued)

Reference Location, period	Total No. of cases/ controls	Source of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Schoenberg et al. (1984) New Jersey, USA, 1978–79 (cont.)				≥ 20	NR	2.31	
						P for trend, 0.63	
				Garage and/or gas station workers	43	2.35 (1.47–3.78)	
				Age at first exposure (yr)			
				≤ 25	NR	2.15 ($P < 0.05$)	
				26–40	< 5	5.44	
				≥ 41	< 5	4.75	
						P for trend, 0.25	
				Latency (yr)			
				< 20	NR	3.06 ($P < 0.05$)	
				20–39	NR	3.16 ($P < 0.05$)	
				≥ 40	NR	1.66	
						P for trend = 0.29	
				Duration (yr)			
				< 2	NR	1.58	
				2–4.9	NR	5.02 ($P < 0.05$)	
				5–9.9	NR	4.08	
				≥ 20	NR	0.63	
						P for trend, 0.45	
Cassidy *et al.* (2009) Texas, USA, 1999–NR	604/604	Hospital; non-cancer	Interviews with structured questionnaire; OCC and SIC codes	**Occupations**	37	1.43 (0.81–2.53)	Age, sex and tobacco smoking; controls matched to cases by age, gender and ethnicity; participation rate: 92% cases, 75% controls
				Motor freight			
				< 10 yr	22	1.49 (0.72–3.11)	
				≥ 10 yr	15	1.30 (0.57–3.01)	
				Automobile mechanic	23	1.05 (0.54–2.04)	
				< 10 yr	13	1.26 (0.50–3.14)	
				≥ 10 yr	10	0.87 (0.34–2.23)	

Table 2.4 (continued)

Reference Location, period	Total No. of cases/ controls	Source of controls	Exposure assessment	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Cassidy et al. (2009) Texas, USA, 1999–NR (cont.)				**Industry**	36	1.17 (0.66–2.07)	
				Motor freight transportation/ warehousing			
				< 10 yr	18	1.18 (0.54–2.60)	
				≥ 10 yr	18	1.16 (0.52–2.58)	
				Railroad transport	13	1.46 (0.56–3.75)	
				< 10 yr	7	1.39 (0.40–4.87)	
				≥ 10 yr	6	1.54 (0.37–6.42)	
				Automotive repair, services/ parking	19	0.80 (0.40–1.61)	
				< 10 yr	8	0.65 (0.24–1.73)	
				≥ 10 yr	11	0.99 (0.37–2.67)	
				Automotive dealers/ gasoline service station	37	0.98 (0.58–1.64)	
				< 10 yr	22	0.81 (0.43–1.53)	
				≥ 10 yr	15	1.47 (0.59–3.63)	
Steineck *et al.* (1990) Stockholm, Sweden, 1985–87	256/287 (men)	Population	Postal questionnaire and interview, expert classification exposure to diesel or petrol exhaust	**Occupation**			Urothelial cancer and/or squamous cell carcinoma in the lower urinary tract; yr of birth and tobacco smoking; born 1911–45; participation rate: 80% cases, 79% controls
				Petrol station/auto repair	17	1.2 (0.6–2.8)	
				Railroad	8	0.4 (0.2–1.0)	
Wynder *et al.* (1985) USA, six cities, 1981–83	194/582	Hospital; non-tobacco-related diseases	Interview with structured questionnaire; a-priori high-exposure jobs and percentage of workers exposed	Railroad worker	2	2.0 (0.34–11.61)	Men only; age, tobacco smoking and SES; controls matched by age, race, yr of interview and hospital
				Bus/HGV driver	10	0.9 (0.44 –1.87)	
				Heavy equipment mechanic	2	0.75 (0.16–3.53)	
				Warehouse materials handler	2	0.85 (0.18–4.14)	

CI, confidence interval; HGV, heavy goods vehicle; JEM, job–exposure matrix; LGV, light goods vehicle; NR, not reported; NS, not significant; OCC, occupational codes; OR, odds ratio; SES, socioeconomic status; SIC, standard industrial classification; SMR, standardized mortality ratio; SOC, standard occupational classification; yr, year

(a) Studies that used job–exposure matrices to assess exposure to diesel exhaust

Two death certificate studies, a case–control study (Coggon *et al.*, 1984) and a record linkage study (Dolin & Cook-Mozaffari, 1992) were identified that used a crude JEM to identify certain occupations and industries that entailed exposure to diesel exhaust. The study by Coggon *et al.* (1984), described previously in Section 2.3.1, included 291 men who died from urinary bladder cancer (underlying cause of death) and 638 aged-matched controls identified from death certificates collected in England and Wales between 1975 and 1979 for all men aged 40 years or younger. The odds ratios for exposure to diesel exhaust were 1.0 (95% CI, 0.7–1.3; 68 exposed cases) for all occupations and 1.7 (95% CI, 0.9–3.3; 19 exposed cases) for occupations with high exposure. Dolin & Cook-Mozaffari (1992) reported findings for 2457 men, aged 25–64 years, who died from urinary bladder cancer during 1965–80 in selected regions in England and Wales. The standardized mortality ratio for exposure to 'diesel fuel/fumes' in occupations in which most workers had low exposure was 1.06 (95% CI, 0.88–1.26; 125 deaths). No occupations were considered to have high exposure to diesel fuel or fumes. [The Working Group noted that, although Dolin & Cook-Mozaffari (1992) used the term 'diesel fuel/fumes', the occupations identified by the JEM (HGV, bus and taxi drivers and HGV drivers' mates) were those associated with exposure to diesel exhaust. The preceding two studies were not very informative for an evaluation of cancer risk because of inaccuracies and incompleteness of occupational history on the death certificates (on which only the most recent full-time occupation was listed) and the lack of information on tobacco smoking or other potential confounders. In the study of Coggon *et al.* (1984), the subjects were young and thus the latency period was inadequate to evaluate cancer risk.]

A multicentre population-based case–control study was conducted between 1991 and 1995 in Germany to evaluate risks from specific occupational exposures (Pesch *et al.*, 2000). The study population consisted of 1035 incident cases of urothelial cancer (predominantly of the urinary bladder) and 4298 controls randomly selected from resident registries and matched to cases by region, sex and age. Information on exposures and other risk factors was obtained by in-person interviews using structured questionnaires with lists of specific agents. Exposure to specific substances was assessed using a JEM and a job-task–exposure matrix, which assigned probability and intensity of exposure to each job title or task. Among men, the odds ratio (adjusted for age, tobacco smoking and study centre) for the association of bladder cancer with exposure to 'exhaust' (as classified by the JEM) was 1.3 (95% CI, 1.0–1.6) for high exposure and 1.2 (95% CI, 0.9–1.7) for substantial exposure. No excess risk of urinary bladder cancer was found for self-assessed exposure to 'traffic exhaust' among men or women or for JEM-assessed exposure to exhaust in women. [The Working Group noted that this study did not distinguish between exposure to gasoline or other types of exhaust and exposure to diesel exhaust. Documentation on the source of identification of the cases was incomplete, and it was unclear whether case ascertainment was complete for the five geographical areas.]

Kogevinas *et al.* (2003) combined data from 11 case–control studies of urinary bladder cancer conducted between 1976 and 1999 in six European Countries, including three studies from Germany (Claude *et al.*, 1988; Pohlabeln *et al.*, 1999; Pesch *et al.*, 2000), two studies each from France (Cordier *et al.*, 1993; Hours *et al.*, 1994), Italy (Vineis & Magnani, 1985; Porru *et al.*, 1996) and Spain (González *et al.*, 1989; Serra *et al.*, 2000), and one study each from Greece (Rebelakos *et al.*, 1985) and Denmark (Jensen *et al.*, 1987). With the exceptions of Jensen *et al.*, (1987), which provided additional information on

duration of employment as an HGV driver, and Pesch *et al.* (2000), which used a different JEM to assess exposure to exhaust, these studies were not reviewed independently because their findings were captured in the pooled analyses. The analysis included 3346 male incident cases and 6840 male controls, aged 30–79 years. Controls from populations and hospitals were matched to the cases on age and geographical area. Information on every job held for more than 6 months was available from 10 studies and for the longest-held job from one study. The FINJEM was applied to evaluate exposure to diesel exhaust. Risk estimates were calculated by job duration, calendar year of first employment and age at diagnosis for all occupations with at least 10 subjects; individuals never employed in the occupation or any of the a-priori defined high-risk occupations were used as the unexposed population. Odds ratios were adjusted for age, tobacco smoking and study centre. Associations with diesel exhaust were presented in graphical form (Fig. 2.1), which showed an odds ratio of approximately 1.25 (95% CI, ~1.05–1.4) for urinary bladder cancer among subjects with the highest tertile of exposure to diesel exhaust compared with the unexposed; odds ratios were less than 1.0 for medium and low exposure to diesel exhaust. [The Working Group noted that this was one of the more informative case–control studies for evaluating the potential risk for urinary bladder cancer from exposure to diesel exhaust because it was large and used high-quality exposure assessment. The number of exposed subjects in each diesel exhaust exposure category was not reported. The study provided some evidence for an association between exposure to diesel exhaust and the risk of urinary bladder cancer.]

Richardson *et al.* (2007) investigated the risks of exposure to specific chemicals using the same cancer registry database as an earlier study in British Columbia, Canada, which found an association between several occupations with potential exposure to diesel engine emissions and an excess incidence of urinary bladder cancer (Band *et al.*, 2005). Self-administered questionnaires were completed by 15 463 men (response rate, 60.1%), aged 20 years or older, diagnosed with cancer from 1983 to 1990. Complete occupational histories were available for 1062 cases of urinary bladder cancer (94% transitional cell carcinoma) and 8057 cancer controls, matched to cases by year of birth and year of diagnosis. Exposure to specific chemical agents, classified by IARC as definite or probable urinary bladder carcinogens, was assessed using the National Occupational Exposure Survey JEM, which predicts the probability of exposure to a specific substance in a specific job, based on walk-through assessments in a stratified sample of workplaces within the USA during 1981–83. Odds ratios were estimated after matching for age and year of diagnosis and adjusting for ethnicity, years of smoking, alcohol consumption and questionnaire responder. The odds ratios for urinary bladder cancer for ever and high cumulative exposure to diesel exhaust were 1.18 (95% CI, 1.04–1.35; 604 exposed cases) and 1.25 (95% CI, 1.04–1.49), respectively; a significant exposure–response trend was observed for cumulative exposure (P for trend = 0.01). [The Working Group noted that the advantages of this study were the use of a JEM to assess exposure specific for diesel exhaust and adequate power to evaluate an exposure–response relationship; however, the exposure assessment was not calendar year-specific and was based on occupational data collected over a 3-year period in a different country. Despite its limitations, the study added some support for an association between urinary bladder cancer and exposure to diesel exhaust.]

(b) Studies that used expert assessments or self-reporting to estimate exposure to diesel exhaust

(i) Expert assessments

A population-based case–control study of 256 male incident cases of urothelial cancer and/or squamous cell carcinoma of the lower urinary tract and 287 controls, selected randomly from registers, was conducted in Stockholm, Sweden, during 1985–87 (Steineck *et al.*, 1990). Information on all occupations and industries for all jobs held was obtained by postal questionnaires and in person. Men were classified as being exposed or unexposed to 38 agents or groups of substances and were assigned to categories of annual dose (low, moderate or high) by an industrial hygienist who was blinded to case–control status. Exposure after 1981 was ignored in the analyses. An elevated risk was found for ever exposure to diesel exhaust (RR [adjusted for year of birth and smoking], 1.7; 95% CI, 0.9–3.3; 25 exposed cases); the risks increased with increasing annual dose, but the estimates were imprecise and not statistically significant, and no trend test was performed. A similar pattern of increasing risk with increasing annual dose was found for exposure to petrol exhausts. The joint effects from exposure to diesel and petrol exhausts were calculated (RR, 7.1; 95% CI, 0.9–58.8; seven exposed cases); the magnitude of the relative risk decreased to 5.1 (95% CI, 0.6–43.6) after further adjustment for exposure to benzene. [The Working Group noted that the advantages of this study were the use of experts to assess exposure to diesel and petrol (i.e. gasoline) exhausts using lifetime occupational data, including the exposure period; however, the assignment of annual dose of exposure to exhaust appeared to be mainly based on job title. The ability to evaluate exposure–response relationships was limited because of the relatively small numbers of exposed cases and the inability to distinguish reliably between exposure to diesel exhaust and exposure to gasoline exhaust.]

Siemiatycki *et al.* (1994) investigated occupational risk factors in a population-based case–control study in Montreal, Canada, comprising 484 men with histologically confirmed urinary bladder cancer, 1879 cancer controls (excluding lung cancer) and 533 population controls. The cases and cancer controls were identified from major hospitals between 1976 and 1986. Occupational histories, including a detailed description of lifetime jobs held by the subject, and information on potential confounders were obtained from in-person (82%) or proxy interviews. A team of experts and hygienists translated this information into exposure to specific substances and characterized suspected exposures for each job. Using a-priori criteria related to the certainty of exposure, exposure duration and frequency × concentration scores, individuals were classified into three exposure groups: no exposure, non-substantial exposure and substantial exposure; lifetime prevalence of exposure to diesel exhaust was estimated to be 15%. Odds ratios for urinary bladder cancer in relation to exposure to diesel exhaust, adjusted for age, family income, ethnicity, cumulative tobacco smoking index, coffee consumption and respondent status (self or proxy), were 1.3 (95% CI, 0.9–1.8) for non-substantial exposure and 1.0 (95% CI, 0.7–1.5) for substantial exposure to diesel engine emissions. Risk estimates, adjusted for non-occupational factors, ranged from 1.1 to 1.3 (statistically non-significant) among individuals in the highest categories of certainty, duration and frequency of exposure to diesel exhaust. An earlier report of this study population, which analysed 486 cases of urinary bladder cancer and 2196 cancer controls, did not find an association between the risk for urinary bladder cancer and any exposure to diesel exhaust (OR adjusted for age, socioeconomic status, ethnic group, cigarette smoking and blue-/white-collar job history, 1.0; 95% CI, 0.8–1.2; 82 exposed cases) or any

exposure to gasoline exhaust (adjusted OR, 1.0; 95% CI, 0.9–1.1; 208 exposed cases) (Siemiatycki *et al.*, 1988). [The Working Group noted that the 1994 study was more informative for the current evaluation because of the attempts made to evaluate exposure specific to diesel exhaust.]

A Belgian case–control study included 200 cases selected from the Limburg Cancer Registry, diagnosed between 1991 and 2004 with histologically confirmed transitional cell carcinoma of the urinary bladder, and 385 population controls (Kellen *et al.*, 2007). Lifetime occupational history was obtained from in-person interviews using a structured questionnaire. Two occupational hygienists, blinded to case–control status, assigned individuals into three categories (no, low and high) of probability of cumulative exposure to diesel exhaust. Compared with individuals with no exposure to diesel exhaust, the odds ratios, adjusted for tobacco smoking, age and sex, were 0.80 (95% CI, 0.40–1.57) for low and 1.51 (95% CI, 0.85–2.75) for high cumulative probability of exposure to diesel exhaust (*P* for trend = 0.25). Odds ratios were similar for smokers and nonsmokers and no effect modification was observed for several cytochrome P450 polymorphisms. [The Working Group noted that an advantage of this study was the use of detailed lifetime occupational information to calculate the probability of cumulative exposure. However, it was not clear whether the statistical power was adequate to evaluate exposure–response relationships; the Working Group also noted that only two cases of urinary bladder cancer who had never smoked were ever exposed to diesel exhaust.]

(ii) Self-reporting

Howe *et al.* (1980) conducted a population-based case–control study of urinary bladder cancer among 480 pairs of men and 180 pairs of women between 1974 and 1976, and age- and sex-matched controls from three regions in Canada. Subjects were interviewed in person to obtain information on lifestyle habits and occupational history, including duration of employment in every job, details on a-priori suspected occupations and ever exposure to fumes, dusts or specific substances. The odds ratio was 2.8 (95% CI, 0.8–11.8; 11 exposed cases) for ever exposure to diesel and traffic fumes in non-a-priori suspected industries. [The Working Group noted that this study was not considered to be very informative because the exposure assessment was purely based on self-reported job titles, and the small number of exposed cases affected the precision of the odds ratios.]

Hoar & Hoover (1985) evaluated mortality from urinary bladder cancer in a case–control study comprising 325 cases and 673 controls who died in New Hampshire and Vermont (USA) during 1975–79. In-person interviews were conducted with the next of kin and provided information on lifetime occupations, demographics, and medical and lifestyle factors. Cigarette smoking, coffee consumption, education and age at death were considered in all analyses. The odds ratio for exposure to diesel exhaust in any occupation (as reported by the next of kin) was 1.5 (95% CI, 0.8–2.8). A significant duration–response (*P* for trend = 0.024) was observed reaching a threefold excess risk for 30–39 years of employment in these jobs; the odds ratio decreased among men employed for 40 years or longer. [The Working Group noted that this study was limited because exposures were reported only by the next of kin, the specificity of the assessment for exposure to diesel exhaust was unclear and the study was based on mortality rather than incidence.]

Risch *et al.* (1988) conducted a population-based case–control study in Edmonton, Calgary, Toronto and Kingston, Canada, from 1979 to 1982. Cases of histologically confirmed urinary bladder cancer, aged 35–79 years, were identified from hospital, medical and cancer institute records, and a tumour registry. Controls were randomly selected from population lists

and matched to cases by sex, age and area of residence. Analyses were performed on 826 cases and 792 controls who completed interviews, during which structured questionnaires were used to obtain information on 26 occupations and exposures to 18 substances. Among men, elevated risks of urinary bladder cancer, adjusted for year of birth and lifetime tobacco smoking, were observed for ever employment (OR, 1.53; 95% CI, 1.17–2.00), employment for 8–18 years before diagnosis (OR, 1.69; 95% CI, 1.24–2.31) and for every 10 years of duration of employment (OR, 1.23; 95% CI, 1.08–1.41) in jobs that entailed contact with 'diesel or traffic fumes'. [The Working Group noted that no information was provided on which occupations were considered to entail exposure to diesel exhaust; this study has limited utility for the evaluation of the risk for cancer.]

Data from the American Health Foundation hospital-based, case–control study of tobacco-related neoplasms were used in two analyses of the relationship between exposure to diesel and traffic fumes and the risk for urinary bladder cancer (Wynder *et al.*, 1985; Iyer *et al.*, 1990). Both analyses included cases of histologically confirmed urinary bladder cancer diagnosed from 1981 to 1983 and controls with non-tobacco-related diseases (both malignant and non-malignant) at 18 hospitals located in six cities in the USA. [The Working Group was unsure whether the study populations overlapped.] The first analysis by Wynder *et al.* (1985) included 194 male cases and 582 controls matched by age, race, hospital and year of interview, and the second analysis by Iyer *et al.* (1990) included 136 cases and 272 controls matched for sex, age, race, hospital and year of interview. Occupational histories were obtained by in-person interviews using a structured questionnaire. In the first analysis, occupational exposure to diesel exhaust fumes was assessed for specific occupations (titles for usual employment) defined as entailing probable high exposure and for occupations with high, moderate and minimal probable exposure to diesel exhaust, based on the percentage of employees in a given occupation entailing exposure to diesel exhaust. The odds ratios were 1.0 or less for all specific occupations related to diesel exhaust, except for railroad workers (OR, 2.0; 95% CI, 0.34–11.61; two exposed cases) (Wynder *et al.*, 1985). The odds ratio for combined occupations with high probable exposure was 1.68 (95% CI, 0.49–5.73; four exposed cases). In the second analysis, occupations were grouped into low (referent), possible and probable categories of exposure to diesel exhaust according to an a-priori list of job titles. Self-reported exposure to diesel exhaust was also considered. The odds ratio was 1.24 (95% CI, 0.77–2.00; 41 exposed cases) for any exposure to diesel exhaust (including possible or probable exposure classified by job title and self-reported exposure). The odds ratios for possible and probably exposure considered separately were equivalent to unity or below. [The Working Group noted that both studies were limited by small numbers of cases and controls in the categories or occupations with a higher probability of exposure. Although these studies reported risk estimates for different categories of probable exposure to diesel exhaust, the categories appeared to be based on job titles only.]

Dolin & Cook-Mozaffari (1992) did not report an odds ratio because the only available estimate was for low exposure to diesel exhaust, and Pesch *et al.* (2000) reported no odds ratio because the authors reported results for 'exhaust' in general and not diesel exhaust.

(c) Studies that reported risk estimates from job titles

Numerous studies of occupation and the risk for urinary bladder cancer have found that reported risk estimates from job titles – either specific occupations or industries with potential exposure to diesel and/or engine exhaust – and comprised the following:

Population-based studies: these included a series of reports that analysed data from the US National Bladder Cancer Study in New Hampshire (Colt *et al.*, 2004), New England (Colt *et al.*, 2011) and Iowa (Zheng *et al.*, 2002), studies from Canada (Gaertner *et al.*, 2004), Limburg, Belgium (Kellen *et al.*, 2005; Reulen *et al.*, 2007) and New Zealand (Dryson *et al.*, 2008) with a similar study design, in which regional or local cancer registries were used to identify cases and matched controls were selected from the same geographical regions, a matched population-based case–control study in two industrial regions in Belgium (Schifflers *et al.*, 1987) and a case–control study in Copenhagen and surrounding areas (Jensen *et al.*,1987).

The US National Bladder Cancer Study was a population-based case–control study comprising all histologically confirmed cases of carcinoma of the urinary bladder diagnosed from 1978 to 1979 identified from 10 cancer registries that participated in the US NCI Surveillance, Epidemiology, and End Results Program. Findings that focused on occupations involving motor vehicles were reported separately for white men (Silverman *et al.*, 1989a), non-white men (Silverman *et al.*, 1989b) and white women (Silverman *et al.*, 1990). Silverman *et al.* (1986) reported findings that focused on motor-related occupations in white men (1909 cases and 3565 controls), and Smith *et al.* (1985) reported findings specific for automobile and HGV mechanics for all men (2108 controls and 4046 cases). Two studies reported findings separately by individual regions: Silverman *et al.* (1983) for men in Detroit and Schoenberg *et al.* (1984) for white men in New Jersey. [Although the latter four populations were included in the larger studies, they are included in the tables because they provided more detailed analyses.]

Studies with hospital or other cancer controls: these included three studies that identified cases of urinary bladder cancer and controls with other cancers from cancer registries in Missouri, USA (Brownson *et al.*, 1987; Brooks *et al.*, 1992), Detroit, USA (Burns & Swanson, 1991), British Columbia, Canada (Band *et al.*, 2005), and the United Kingdom (limited to men aged 18–54 years) (Coggon *et al.*, 1986), a study that used cancer and non-cancer controls (oral cancer or diseases) in Bombay, India (Notani *et al.*, 1993), and four studies that used non-cancer controls in La Plata, Argentina (Iscovich *et al.*, 1987), Spain (Spanish Bladder Study) (Samanic *et al.*, 2008), the USA (Decouflé *et al.*, 1977) and Texas, USA (Cassidy *et al.*, 2009). Brooks *et al.* (1992) reported risks for invasive urinary bladder cancer using the Detroit population.

Mortality studies: two studies that measured mortality were identified, including a study that used city directories and death certificates as a source for occupational information in Ohio, USA (Steenland *et al.*, 1998), and one that provided detailed analyses of HGV drivers in New Hampshire and Vermont, USA (Hoar & Hoover, 1985). For cancers that have higher survival rates, such as urinary bladder cancer, studies that report mortality are less informative than those that report incidence, because mortality studies overlook cases of cancer that do not result in death.

Several other studies of occupations with potential exposure to motor exhaust were identified, but were not reviewed because either the numbers of exposed cases were small (Bonassi *et al.*, 1989; Ahmad & Pervaiz, 2011) or no formal analyses of risk estimates were performed (Tola *et al.*, 1980; Yaris *et al.*, 2006).

The studies on occupational titles were the least informative to evaluate risks specific for exposure to gasoline or diesel exhaust, because job titles alone are a crude surrogate of exposure. Diesel engines were introduced into the workplace at various rates and at different times, and thus the confidence that the individual workers in the study were actually exposed to diesel exhaust was low. Other limitations included potential confounding from co-exposures to

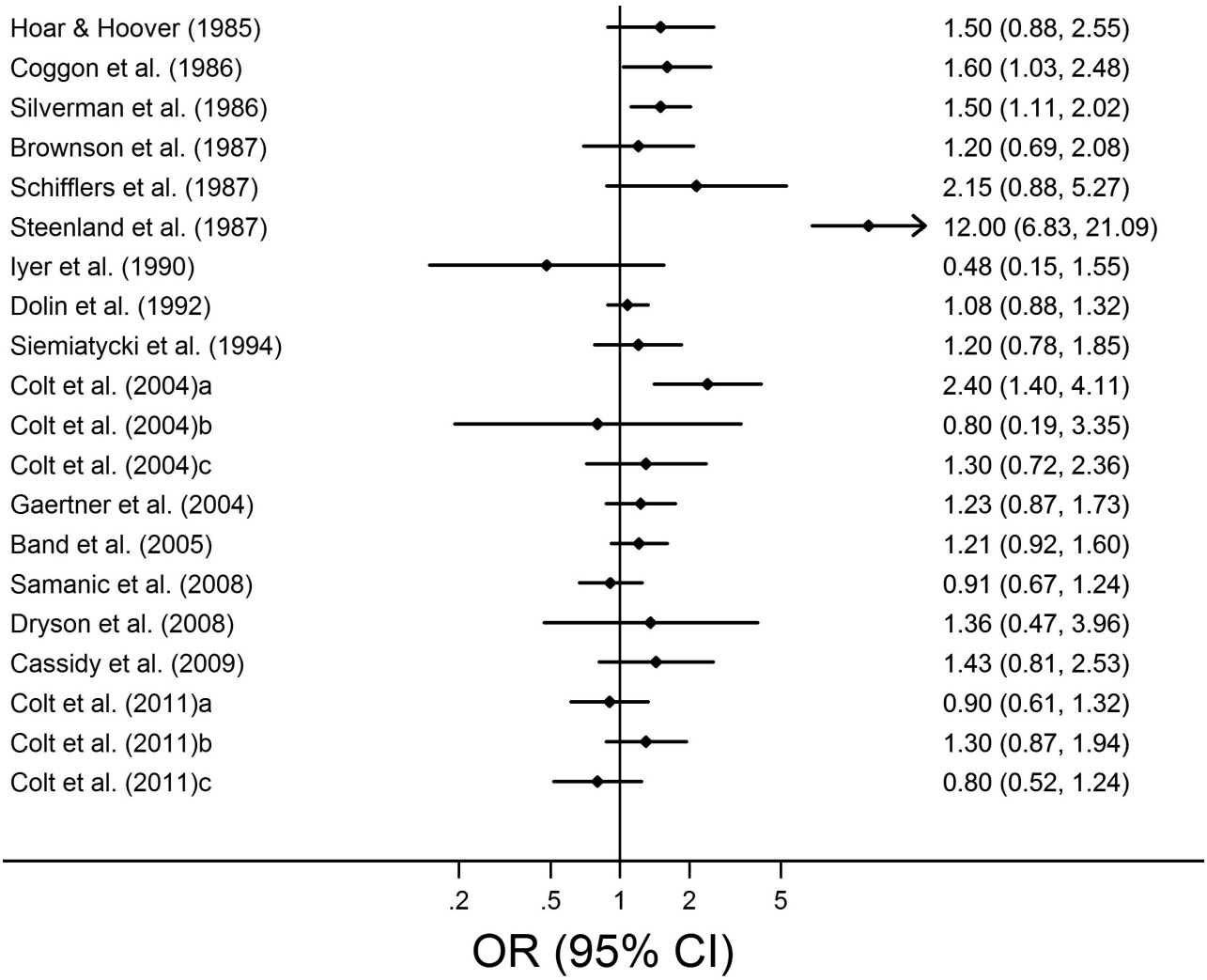
other occupational substances, multiple comparisons and insufficient statistical power because of small numbers of exposed cases and controls. In general, most analyses were restricted to men, because few women were employed in occupations with potential exposure to diesel or gasoline engine exhausts. Because of these limitations, the methods and findings are presented in Table 2.4 and are not reviewed individually in the text; the odds ratios for ever or usual employment are plotted in Fig. 2.2–2.7 and the findings are briefly summarized across studies for each specific occupation with potential for exposure to diesel exhaust. The studies in the figures are organized chronologically by study period. Occupations or industries that were thought to entail potential contact with diesel or gasoline exhaust included railroad workers, HGV drivers, bus drivers, taxicab drivers, automobile mechanics, gasoline station attendants and garage workers. Of these, HGV drivers, railroad workers and bus drivers were considered to have the highest probable exposure to diesel exhaust.

(i) HGV drivers

Case–control studies reporting risk estimates for urinary bladder cancer and employment as an HGV driver are described in Table 2.4 and a summary of the odds ratios for ever or usual exposure are depicted in Fig. 2.2. Steenland *et al.* (1987) and Siemiatycki *et al.* (1994) did not present findings for ever employment, and those for the longest duration of employment are indicated in the graph. Multiple odds ratios are plotted from two studies (Colt *et al.*, 2004, 2011) because they reported odds ratios for different types of HGV driver, such as tractor-trailer, light and heavy. Of the 21 odds ratios reported for employment as an HGV driver (Fig. 2.2), 15 were greater than 1.10 (ranging from 1.2 to 2.4 for ever or usual employment), one was between 1.01 and 1.1 (Dolin & Cook-Mozaffari, 1992) and five were below 1.0. The 12-fold elevated odds ratio plotted in the graph was for employment of more than 20 years and was based on six exposed cases (Steenland *et al.*, 1987). Four of the elevated odds ratios were statistically significant (Coggon *et al.*, 1986; Silverman *et al.*, 1986; Steenland *et al.*, 1987; Colt *et al.*, 2004; tractor-trailer HGV drivers). Two of the odds ratios that were below 1.0 were based on estimates that used fewer than five exposed cases (Iyer *et al.*, 1990; Colt *et al.*, 2004; HGV drivers). Four of the seven independent studies that evaluated duration of employment found higher risks with longer duration of employment as an HGV driver (Hoar & Hoover, 1985; Silverman *et al.*, 1986; Steenland *et al.*, 1987; Colt *et al.*, 2004).

Two studies provided more detailed analysis of HGV drivers in an attempt to evaluate risks from potential exposure to diesel or motor exhaust and thus were somewhat more informative for an evaluation of cancer risks: (1) an analysis of 300 cases and 296 controls from Detroit, one of the 10 geographical areas in the US National Bladder Cancer Study (Silverman *et al.*, 1983), and a case–control study of mortality from urinary bladder cancer comprising deceased cases and controls from New Hampshire and Vermont, USA (Hoar & Hoover, 1985). Silverman *et al.* (1983) was not plotted in Fig. 2.2 because the same population was included in Silverman *et al.* (1986). In the Detroit study (Silverman *et al.*, 1983), a significant trend in risk was found with duration of employment (P for trend < 0.004) and year of starting employment (P for trend = 0.03). Diesel fuel became more prevalent in the USA after 1950, and the risk for urinary bladder cancer was highest among men who started employment between 1950 and 1969 (RR [adjusted for age and smoking], 6.5; CI not reported; seven exposed cases). In an analysis of duration of employment as an HGV driver that was restricted to the period 1950–78 and controlled for duration before 1950, relative risks increased with increasing duration of employment, and reached 2.6 for a duration of 5 or more years compared with never having worked as an HGV driver from 1950 to 1978. No association between the risk for urinary bladder

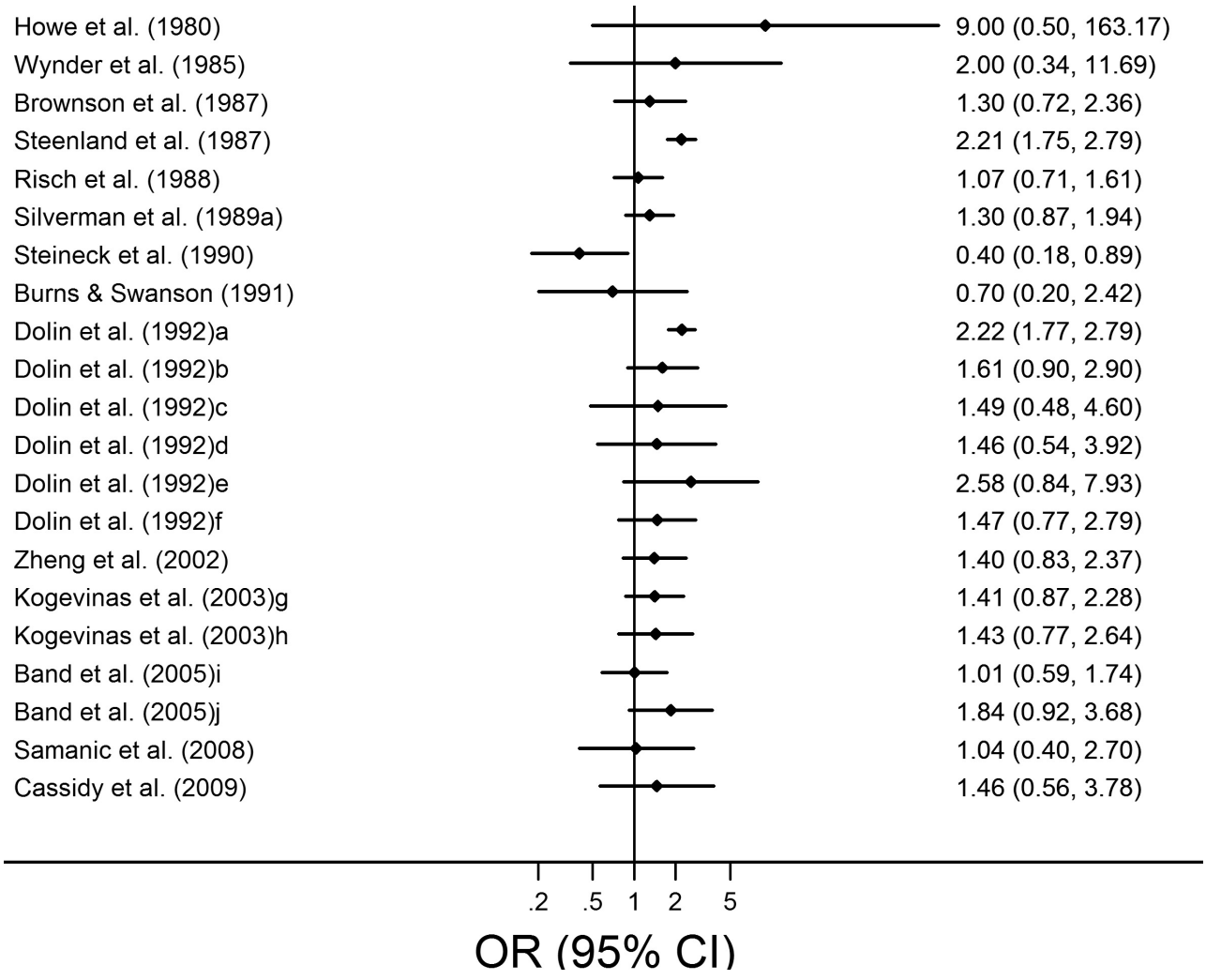
Fig. 2.2 Case–control studies of urinary bladder cancer that reported risk estimates for ever or usual exposure as a heavy goods vehicle driver



a Tractor trailer
b Heavy goods vehicle
c Light goods vehicle
CI, confidence interval; OR, odds ratio

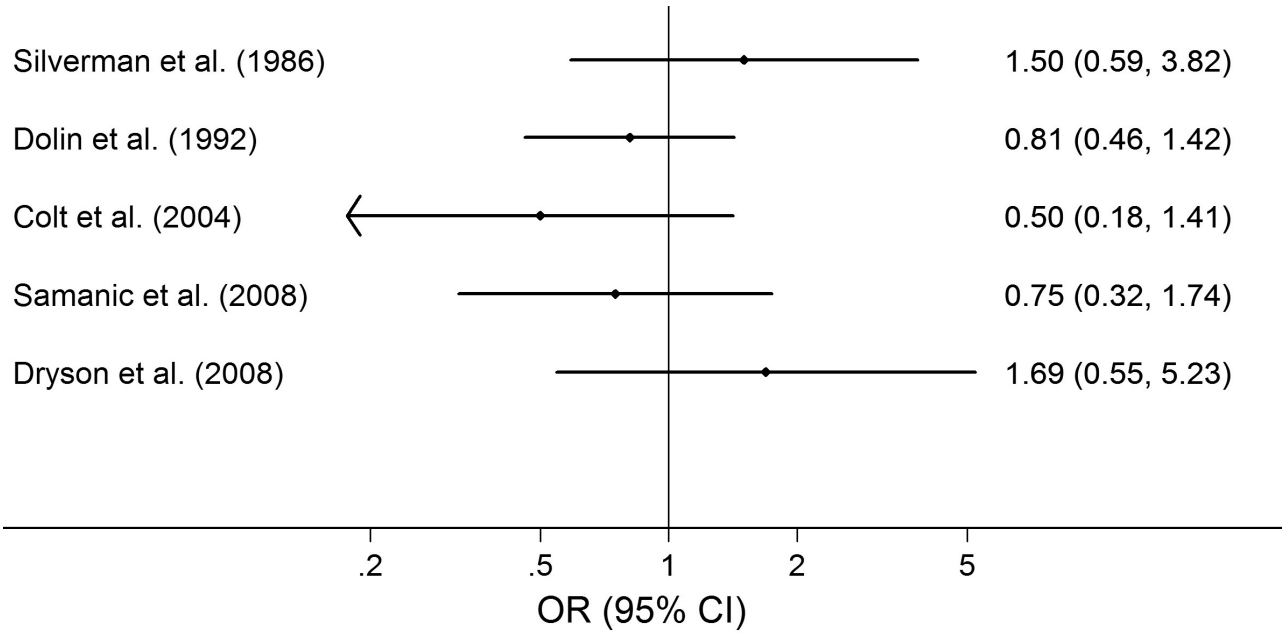
cancer and duration of employment as an HGV driver before 1950 was observed in an analysis that adjusted for duration between 1950 and 1978 (CI not reported; 14 exposed cases). Among HGV drivers, the risk for those who reported operating a vehicle with a diesel engine was 11.9 (95% CI, 2.3–61.1; 13 exposed cases) compared with 1.4 (95% CI, 0.7–2.9; 21 exposed cases) for never having operated a vehicle with a diesel engine. In addition, an interaction between employment as an HGV driver and cigarette smoking was observed ($P = 0.04$). [The Working Group noted that this study provided some evidence that the elevated odds ratio observed for HGV drivers may be due (or at least in part) to exposure to diesel exhaust.]

Fig. 2.3 Case–control studies of urinary bladder cancer that reported risk estimates for ever or usual exposure as a railroad worker



a Railroad industry
b Engine driver
c Shunter
d Signalman
e Guard
f Lengthman
g Driver
h Brakeman
i Railroad transport industry
j Locomotive operation
CI, confidence interval; OR, odds ratio

Fig. 2.4 Case–control studies of urinary bladder cancer that reported risk estimates for ever or usual exposure as a bus driver



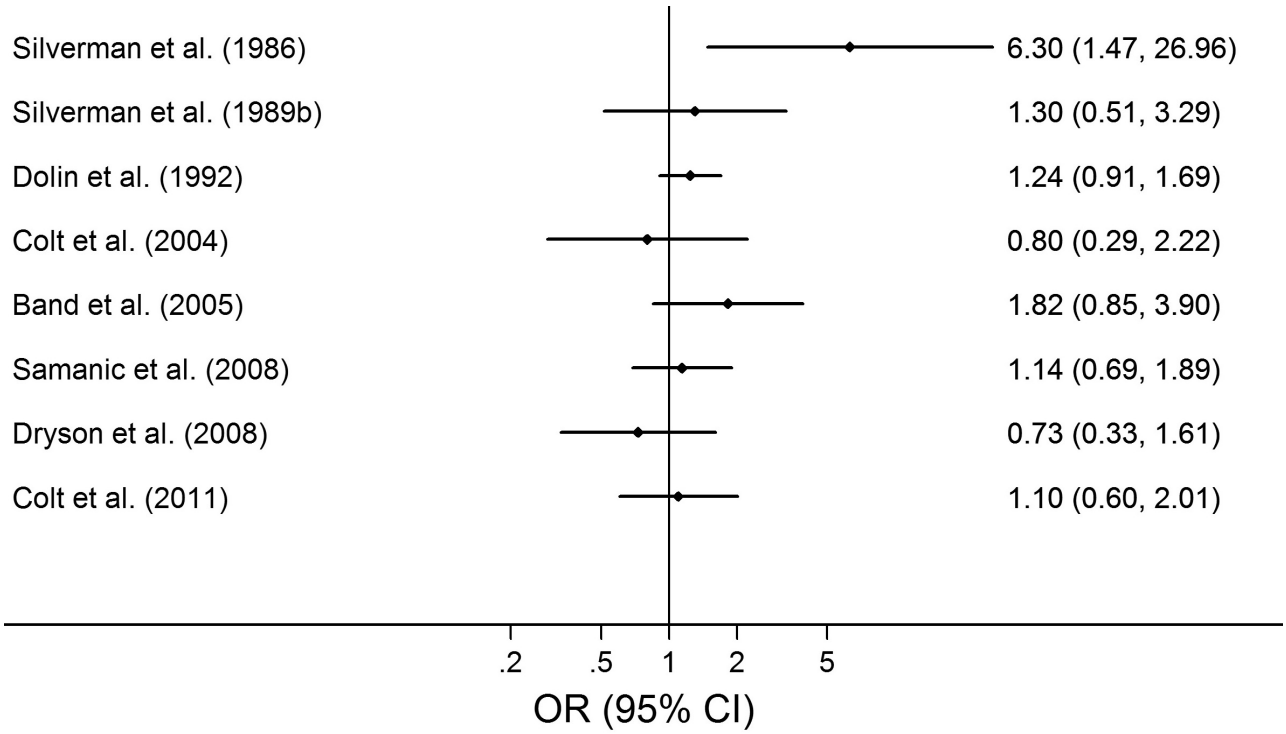
CI, confidence interval; OR, odds ratio

In the mortality study of Hoar & Hoover (1985), the odds ratio for any employment as an HGV driver was 1.5 (95% CI, 0.9–2.6) and the number of years of driving an HGV was associated with mortality from urinary bladder cancer (*P* for trend = 0.006). The highest risk was observed for driving HGVs for 5–9 years (OR, 2.9; 95% CI, 1.2–6.7), but decreased for driving for more than 10 years (OR, 1.8; 95% CI, 0.8–4.1). Among HGV drivers, the odds ratio [adjusted for age and county of residence] when next of kin reported exposure to diesel exhaust was 1.8 (95% CI, 0.5–7.0) compared with 1.5 (95% CI, 0.8–2.7) for those with no report of exposure to diesel exhaust. In an analysis by year of first employment, the highest odds ratio was observed among HGV drivers who were first employed from 1930 to 1949 (OR, 2.6; 95% CI, 1.3–5.1), but was lower for first employment after 1950 (OR, 1.4; 95% CI, 0.5–4.1). Among all occupations that reported exposure to diesel exhaust, a significant duration–response trend (*P* for trend = 0.024) was seen, reaching a threefold excess risk for 30–39 years of employment and a decrease in risk among men employed for 40 years or more. Cigarette smoking, coffee consumption, education and age at death were consid ered in all analyses. [The Working Group noted that a limitation of this study was that mortality from rather than incidence of urinary bladder cancer was assessed. Some analyses were also limited by small numbers of exposed cases.]

(ii) Railroad workers

Case–control studies that reported risk estimates for urinary bladder cancer and employment as a railroad worker are described in Table 2.4 and a summary of the odds ratios for ever or usual exposure is depicted in Fig. 2.3. Multiple odds ratios are plotted from the studies by Dolin & Cook-Mozaffari (1992), Kogevinas *et al.* (2003) and Band *et al.* (2005) because they reported risks for different types of railroad worker; the risk estimate for Steenland *et al.* (1987) was for

Fig. 2.5 Case–control studies of urinary bladder cancer that reported risk estimates for ever or usual exposure as a taxi driver



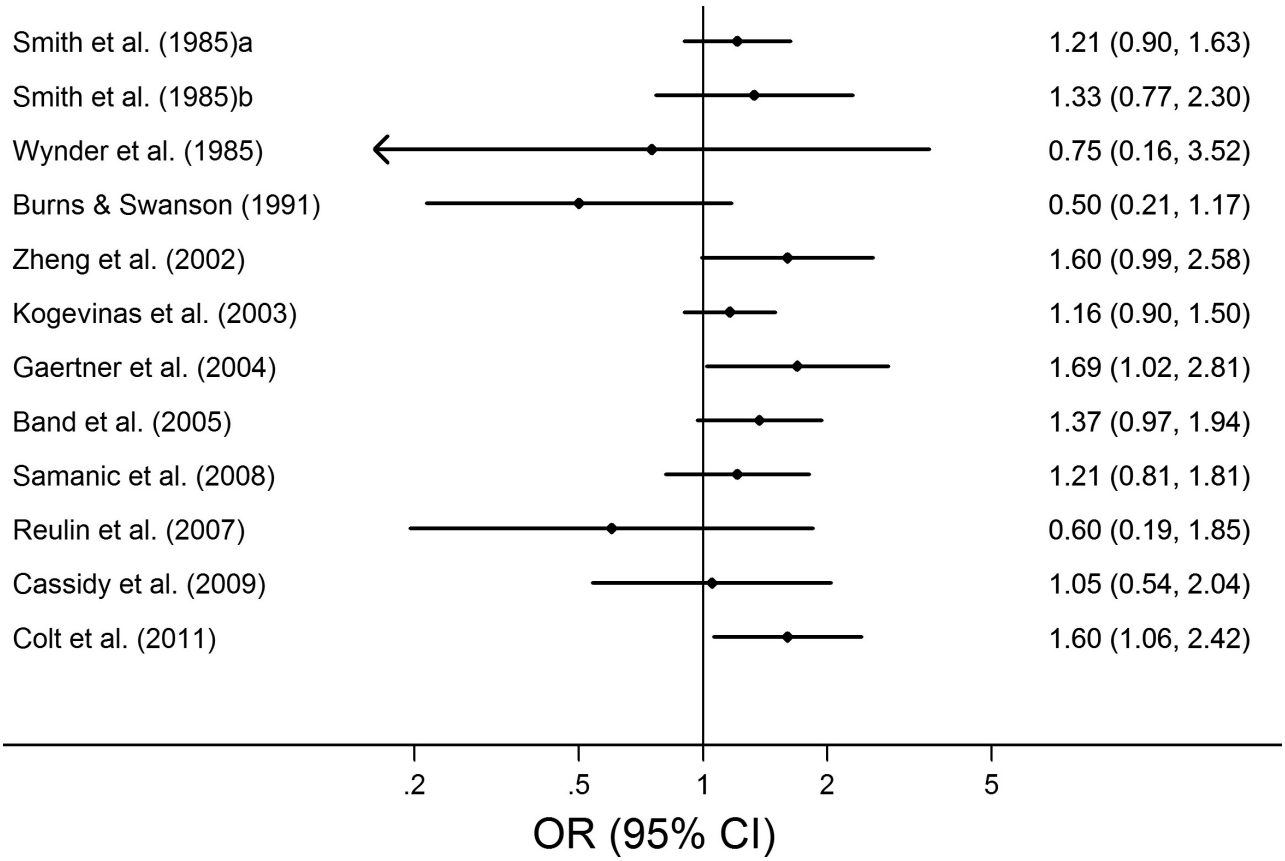
CI, confidence interval; OR, odds ratio

20 years of employment. Of the 22 odds ratios reported for employment as a railroad worker (Fig. 2.3), 17 were greater than 1.10 (ranging approximately from 1.3 to 9), three were between about 1.01 and 1.10 and two were below 1.0. No information on tobacco smoking was available in the study by Dolin & Cook-Mozaffari (1992). Only three of the odds ratios were statistically significant. Two of the three studies that stratified by duration of employment found higher risks with longer employment as a railroad worker (Steenland *et al.*, 1987; Zheng *et al.*, 2002; Samanic *et al.*, 2008); a fourth study reported an odds ratio of 1.09 (95% CI, 0.87–1.36) for every 10 years of employment (Risch *et al.*, 1988).

(iii) Bus and taxi drivers

Case–control studies that reported risk estimates for urinary bladder cancer and employment as bus or taxi driver are summarized in Table 2.4, Fig. 2.4, and Fig. 2.5. Of the six odds ratios reported for employment as a bus driver (Fig. 2.4), three were greater than 1.0, and none was statistically significant (Decouflé *et al.*, 1977; Silverman *et al.*, 1986; Dryson *et al.*, 2008). No association with duration of employment was found in the two studies in which it was evaluated. For taxicab drivers (including chauffeurs), risk estimates were reported separately for white and non-white males in the US National Bladder Cancer Study (Silverman *et al.*, 1986, 1989a, b). The majority of the odds ratios (from seven of the nine studies) were greater than 1.0 (ranging from 1.1 to 6.3), one of which was statistically significant (white men; Silverman *et al.*, 1986). Both of the studies that evaluated duration of employment found indications of a higher risk among workers with the longest employment as a taxicab driver (Silverman *et al.*, 1986; Samanic *et al.*, 2008).

Fig. 2.6 Case–control studies of urinary bladder cancer that reported risk estimates for ever or usual exposure as a motor vehicle mechanic



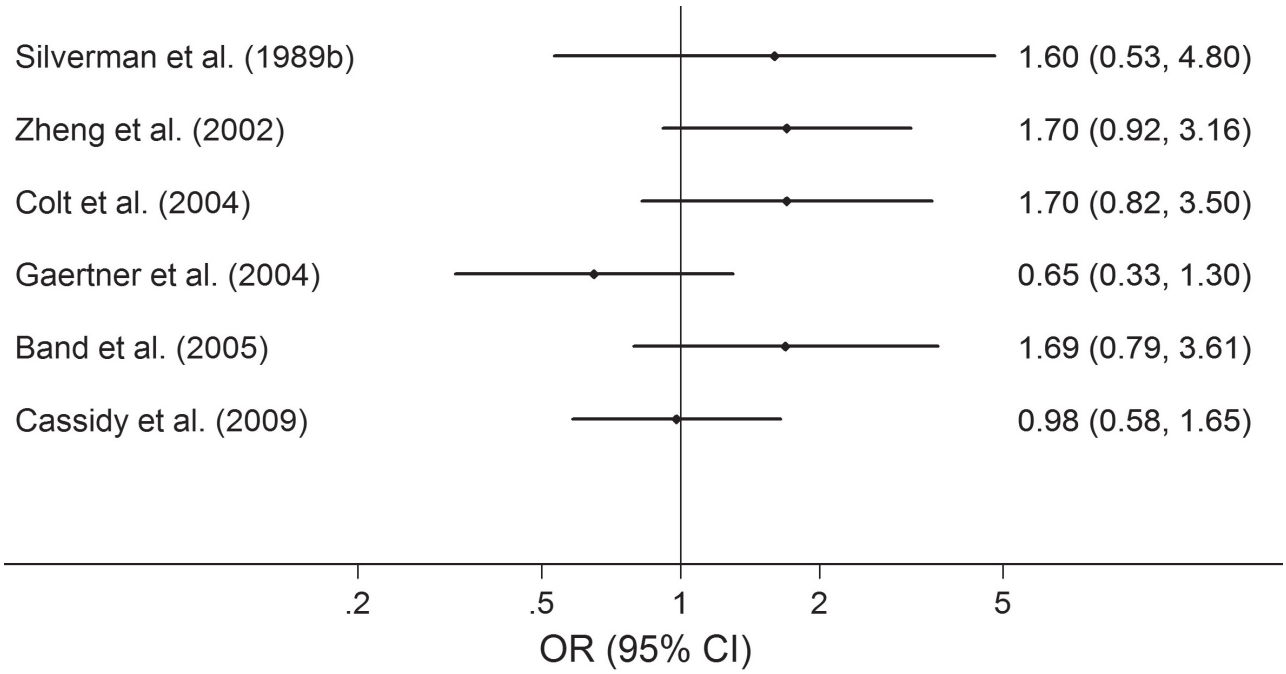
a Smokers
b Nonsmokers
CI, confidence interval; OR, odds ratio

(iv) Motor vehicle mechanics, gasoline station and garage workers, and other occupations

For employment as a motor vehicle mechanic, eight studies reported odds ratios greater than 1.1, three of which were statistically significant (Zheng *et al.*, 2002; Kogevinas *et al.*, 2003; Gaertner *et al.*, 2004); three studies reported odds ratios below 1.0, and one reported an odds ratio of 1.05 (see Table 2.4 and Fig. 2.6). Findings were reported separately for vehicle mechanics in the US National Bladder Study (Smith *et al.*, 1985); risks were higher among workers with a longer duration of employment in three of six studies in which it was evaluated (Smith *et al.*, 1985 (both smokers and nonsmokers); Gaertner *et al.*, 2004; Colt *et al.*, 2011).

Of the six studies that reported risk estimates for garage workers and/or gasoline station attendants, four reported odds ratios greater than 1.1; none was statistically significant (see Table 2.4 and Fig. 2.7). Two of the four studies that evaluated duration of employment found higher risks among workers with a longer duration (Colt *et al.*, 2004; Cassidy *et al.*, 2009). A study of one of the geographical regions in one of the 10 areas that contributed to the US National Bladder Cancer study did not find an employment duration–response relationship (Schoenberg *et al.*, 1987).

Fig. 2.7 Case–control studies of urinary bladder cancer that reported risk estimates for ever or usual exposure as a garage worker



CI, confidence interval; OR, odds ratio

Zheng *et al.* (2002) found elevated risks for employment as a transport or material-moving supervisor (OR, 6.5; 95% CI, 1.4–29.9), which they stated were occupations associated with exposure to diesel exhaust (see Table 2.4). No elevated risk for urinary bladder cancer was found for ever employment as a warehouse materials handler in the American Health Foundation study, which was also an occupation that the authors stated was associated with exposure to diesel exhaust (Wynder *et al.*, 1985).

2.3.3 Cancer at other and multiple sites

See Table 2.5

A study by Decouflé *et al.* (1977) of cancer and occupation included cancer cases and hospital controls admitted to a large hospital in Buffalo, NY, USA, from 1956 to 1965. Ever employment in an occupation and duration of employment of at least 5 years were analysed on the basis of personal interviews. A large number of different occupations and cancer sites were evaluated, using clerical occupations as an unexposed comparison group. For employment as an HGV or tractor driver, relative risks [CI not provided] of 1.53 (29 exposed cases; $P > 0.05$) for laryngeal cancer, 0.60 (24 exposed cases; $P = 0.04$) for colon/rectal cancer and 0.63 (23 exposed cases; $P > 0.05$) for lymphoma were reported. For cancers at other sites, numbers were generally low and the risks were close to unity. [The Working Group noted that the report included many comparisons, lacked detailed descriptions of occupations and information on confounders, and was of limited value for the evaluation of exposure to exhaust.]

In a large population-based case–control study in Canada (Siemiatycki *et al.*, 1988), the associations between 10 types of engine exhaust and combustion products and cancers at 12 sites

Table 2.5 Case–control studies of other and multiple sites of cancer and exposure to engine exhaust

Reference, Location, period	Total No. of cases/ controls	Source of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Decouflé *et al.*, (1977), Buffalo, USA, 1956–65	13 949/NR	Hospital	Personal interviews; ever employment, duration	Larynx Lymphoma Colon/ rectum	HGV and tractor drivers (ever employment)	29 23 24	1.53 ($P > 0.05$) 0.63 ($P > 0.05$) 0.60 ($P = 0.04$)	Clerical occupations as comparison group, response rate not specified
Siemiatycki *et al.* (1988) Montreal, Canada, 1979–85	3276/3276	Hospital; other cancers	Interviewer-administered standardized questionnaire; detailed lifetime job history; expert assessment	12 sites Colon Rectum Kidney	 Any exposure to diesel exhaust Long-term high exposure to diesel exhaust Long-term high exposure to gasoline exhaust Occupation as driver (bus, HGV, taxi)	 68 30 36 34 24	**90% CI** 1.3 (1.1–1.6) 1.7 (1.2–2.5) 1.6 (1.1–2.3) 1.4 (1.0–2.0) 1.5 (1.0–2.2)	Men only; age, SES, tobacco smoking, ethnic group and blue-/white-collar job history; response rate: 82%; cases in one analysis served as controls for other comparisons
Goldberg *et al.* (2001) Montreal, Canada, 1979–85	497/1514 and 553	Hospital (cancers at other sites) and population	Interviewer-administered standardized questionnaire; detailed lifetime job history; expert assessment	Colorectum	**Diesel engine exhaust (frequency, level, duration, confidence in assessment)** Non-substantial Substantial	 45 35	 1.2 (0.8–1.8) 1.6 (1.0–2.5) (all controls) 2.1 (1.1–3.7) (population controls)	Same population as Siemiatycki *et al.* (1988); age, SES, tobacco smoking, ethnic group and other non-occupational factors
Fang *et al.* (2011) British Columbia, Canada, 1983–90	1155/registry (other cancer cases)	Hospital	Self-administered questionnaire, lifelong occupational history	Colon	**Occupation and industry titles (ever versus never)** Taxi driver/ chauffeur HGV driver Bus driver Locomotive operator	 30 124 20 8	 1.54 (1.01–2.25) 1.08 (0.88–1.33) 0.84 (0.52–1.36) 0.71 (0.33–1.54)	Marital status, education, tobacco smoking, alcohol consumption and respondent (self/ proxy); response rate: 65.4% cases, 60% controls; controls (excluding lung and rectum) matched on age and yr of diagnosis

Table 2.5 (continued)

Reference, Location, period	Total No. of cases/ controls	Source of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Seidler *et al.* (1998) Frankfurt and Hamburg, Germany, NR	192/210	Hospital	Self-administered questionnaire, lifelong occupational history, JEM	Prostate	**Diesel engine exhaust (intensity, probability and duration)**			Age, tobacco smoking and region; response rate: 71% cases, 55% controls
					0 dose–yr	118	1.0 (reference)	
					> 0–25 dose–yr	53	1.1 (0.7–1.8)	
					> 25 dose–yr	17	3.7 (1.4–9.8)	
Fritschi *et al.* (2007) Western Australia, 2001–02	606/471	Population	Self-administered questionnaire, telephone interview, lifelong occupational history, expert assessment	Prostate	**Diesel engine exhaust (substantial, non-substantial and unexposed)**			Age; response rate: 57% cases, 37% controls
					Substantial	36	1.07 (0.67–1.72)	
					Non-substantial	213	0.92 (0.71–1.19)	
Santibañez *et al.* (2010) Eastern Spain, 1995–99	161/455	Hospital	Interviewer-administered standardized questionnaire; JEM	Pancreas	Employment as HGV/LGV driver	5	3.46 (1.01–11.83)	Sex, age, province, level of education, alcohol consumption and tobacco smoking; response rate: 81% cases, 99.6% controls; 60% of cases histologically confirmed
					Low exposure to diesel exhaust	14	1.49 (0.72–3.08)	
					High exposure to diesel exhaust	8	1.88 (0.72–4.90)	
					Low exposure to gasoline exhaust	11	1.38 (0.62–3.07)	
					High exposure to gasoline exhaust	8	1.85 (0.71–4.80)	
Brown *et al.* (1988) Texas, USA, 1975–80	183/250	Population	Interviewer-administered standardized questionnaire; occupational history; expert assessment	Larynx	Exposure to diesel/gasoline fumes	79	1.5 (1.0–2.26)	Men only; tobacco smoking and alcohol consumption; response rate: 70% cases, 61–86% various controls; deceased cases and respective controls included

Table 2.5 (continued)

Reference, Location, period	Total No. of cases/ controls	Source of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Muscat & Wynder (1995) New York, USA, 1985–92	235/205	Hospital	Interviewer-administered standardized questionnaire; detailed history for six main jobs	Larynx	Employment in job with substantial exposure to diesel exhaust	36	0.96 (0.5–1.8)	Men only; tobacco smoking and alcohol consumption (alcohol not used for adjustment); response rate: 90% cases and controls; tobacco smoking and alcohol consumption high in case patients, lower in controls
					Automobile mechanic	13	1.30 (0.4–4.1)	
					Self-reported exposure to diesel exhaust	13	1.47 (0.5–4.1)	
					Self-reported exposure to diesel fumes	17	6.4 (1.8–22.6)	
Elci *et al.* (2003) Istanbul, Turkey, 1979–84	940/1519	Hospital	Interviewer-administered standardized questionnaire; detailed lifetime occupational history; expert assessment	Larynx	**Diesel exhaust** Ever	297	1.5 (1.3–1.9)	Age, tobacco smoking and alcohol consumption; response rate unclear; crude adjustment for major risk factors
					Intensity			
					Low	161	1.5 (1.1–1.8)	
					Medium	91	1.7 (1.2–2.3)	
					High	45	1.6 (1.0–2.4)	
					Diesel exhaust probability			
					Low	92	1.6 (1.2–2.2)	
					Medium	148	1.5 (1.1.-1.9)	
					High	57	1.6 (1.1.-2.4)	
					Gasoline exhaust Ever	220	1.6 (1.3–2.0)	
					Intensity			
					Low	141	1.5 (1.2–2.0)	
					Medium	78	1.8 (1.3–2.5)	
					High	NR	NR	
					Probability			
					Low	86	1.6 (1.1–2.2)	
					Medium	131	1.7 (1.3–2.2)	
					High	3	0.7 (0.2–2.9)	

Table 2.5 (continued)

Reference, Location, period	Total No. of cases/ controls	Source of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Karunanayake *et al.* (2008) Canada, six provinces, 1991–94	513/1506	Population	Standardized written questionnaire, lifetime occupational history	NHL (200–202)	Exposure to diesel engine exhaust fumes (ever/never)	183	1.33 (1.03–1.67)	Age and province; self-reported exposure, no detailed exposure assessment
					Longest held occupation			
					Driver	27	1.45 (0.88.2.37)	
Flodin *et al.* (1987) Sweden, 1973–83	131/431	Population	Postal questionnaire, lifetime occupational history	Multiple myeloma (203)	Occupational exposure to engine exhaust	35	**OR** 2.3 (1.3–4.7)	Crude OR, no major change after adjustment for tobacco smoking and X-ray treatment; population not well described; unclear adjustment; exposure self-reported
Boffetta *et al.* (1989) USA, 1982–86 (American Cancer Society (ACS) Study)	282/1128	Nested in ACS study	Self-administered questionnaire at base-line, self-assessment	Multiple myeloma	Diesel exhaust	14	1.40 (0.70–2.70)	Age, sex, ACS division, race, education, diabetes, X-ray treatment, farming, and exposure to pesticides and herbicides; incident cases only used for risk analysis
					Gasoline exhaust	14	0.9 (0.5–1.6)	
					HGV driver	3	4.0 (0.9–17.6)	
					Railroad worker	3	6.0 (1.3–28.9)	
					Auto mechanic	3	0.9 (0.2–3.5)	
Eriksson & Karlsson (1992) Sweden, 1982–86	275/275	Population	Self-administered questionnaire, self-assessment	Multiple myeloma	Engine exhausts	61	1.11 (0.60–2.05)	Age, sex, county and vital status; participation rate: 97%
Heineman *et al.* (1992) Denmark, 1970–84	1098/4169	Population	Employment data from registries; expert assessment	Multiple myeloma	**Engine exhausts**			Men only; age and 'other agents'
					Possible exposure	125	1.3 (1.0–1.6)	
					< 5 yr, no lag	52	1.5 (1.0–2.3)	
					< 5 yr, 10-yr lag	56	1.5 (1.0–2.3)	
					≥ 5 yr, no lag	76	1.3 (1.0–1.9)	
					≥ 5 yr, 10-yr lag	73	1.5 (0.9–2.7)	
					Probable exposure	89	1.2 (0.9–1.6)	
					< 5 yr, no lag	25	1.2 (0.7–2.1)	
					< 5 yr, 10-yr lag	94	1.0 (0.6–1.7)	
					≥ 5 yr, no lag	52	1.2 (0.8–1.9)	
					≥ 5 yr, 10-yr lag	19	1.0 (0.5–2.0)	

Table 2.5 (continued)

Reference, Location, period	Total No. of cases/ controls	Source of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Pottern *et al.* (1992) Denmark, 1970–84	1010/4040	Population	Employment data from registries, and expert assessment	Multiple myeloma	**Exhaust gases** Possible exposure Probable exposure	 8 4	 1.4 (0.6–3.2) 1.6 (0.4–5.5)	Women only; same study as Heineman *et al.* (1992); age
Demers *et al.* (1993) USA, 1977–81	692/1683	Population	Interviews	Multiple myeloma	Motor vehicle operators Rail and water transport workers	76 4	1.2 (0.8–1.6) 0.3 (0.1–1.1)	Age, sex, race and study area; response rate: 89% cases, 83% controls; 32% of case interviews with proxy
Flodin *et al.* (1988) Sweden, 1973–83	111/431	Population	Postal questionnaire, life-time occupational history	Chronic lymphocytic leukaemia (204)	Occupational exposure to engine exhaust	31	**OR** 2.5 (1.5–4.0)	Crude OR, see Flodin *et al.* (1987)
Lindquist *et al.* (1991) Sweden, 1980–83	125/125	Population	Interviewer-administered questionnaire, detailed life-time occupational history	Acute leukaemia	Occupation as professional driver Rally driver (hobby)	18 3	3.0 (1.1–9.2) 3.0 (NR)	Solvents, radiation treatment, tobacco smoking, sex and age; response rate: > 90% cases and controls; exposure of drivers to petroleum products [not further specified]
Clavel *et al.* (1995) France, 1980–90	291/541	Hospital	Postal questionnaire, life-time occupational history	Hairy cell leukaemia	Self-reported occupational exposure to engine exhaust	43	1.6 (1.0–2.6)	Men only; response rate: 61% cases, 58% controls; only live cases included; retrospective case ascertainment; control for confounders not reported
Blair *et al.* (2001) USA, 1980–83	513/1087	Population	Interviews; JEM for selected exposures	Leukaemia (ICD-9: 204–208)	LGV drivers **Motor vapour and exhausts** Low High	13 187 60	3.4 (1.4–8.4) 1.0 (0.8–1.2) 1.3 (0.9–1.9)	Age, residence state, proxy interview, education, pesticides, hair dyes, tobacco smoking and first- degree relative with lymphatic or haematopoietic tumour; response rate: 86% cases, 77–79% controls

Table 2.5 (continued)

Reference, Location, period	Total No. of cases/ controls	Source of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Seniori Costantini *et al.* (2001) Italy, 1991–93	2737/1779	Population	Interviewer-administered questionnaire; expert assessment	Hematolymphopoietic neoplasms (200–208)				Age, sex and area; all newly diagnosed cases among residents aged 20–74 yr; response rate: 81% cases, 74% controls; job-specific results reported for men only
				NHL (ICD-9: 200, 202, 204.1)	Material-handling and related equipment operators	43	1.2 (0.8–2.0)	
					Transport operators	74	0.9 (0.7–1.3)	
				Hodgkin lymphoma (ICD-9: 201)	Material-handling and related equipment operators	5	1.0 (0.4–2.7)	
					Transport operators	10	0.8 (0.4–1.7)	
				Leukaemia (ICD-9: 204–208)	Material-handling and related equipment operators	25	2.5 (1.4–4.5)	
					Transport operators	34	1.1 (0.7–1.7)	
				Multiple myeloma (ICD-9: 203)	Material-handling and related equipment operators	3	0.6 (0.2–1.9)	
					Transport operators	7	0.5 (0.2–1.1)	
Adegoke *et al.* (2003) Shanghai, China, 1987–89	486/502	Population	Interview; self-reported; JEM	Leukaemia (ICD-9: 204–208)	Water and rail transport	11	0.5 (0.2–1.1)	Age, sex and income
					Auto and truck drivers	8	0.8 (0.3–2.0)	

Table 2.5 (continued)

Reference, Location, period	Total No. of cases/ controls	Source of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Covariates Comments
Wong *et al.* (2010) Shanghai, China, 2003–07	722/1444	Hospital	Interviewer-administered questionnaire; detailed lifetime occupational history; expert assessment	Acute myeloid leukaemia (205)	Occupational exposure to diesel or gasoline engine exhaust	2	0.57 (0.12–2.57)	Sex, age, education, alcohol, rural residence and other occupational factors (not used in analysis presented in this table); response rate: 97% cases; exposure assessment not detailed for exhausts and other exposures
					Exposure to diesel fuel (all acute myeloid leukaemia)	36	1.23 (0.89–1.81)	
West *et al.* (1995) United Kingdom, NR	400/400	Hospital	Interviewer-standardized questionnaire; self- and expert assessment	Myelodys-plasia	**Exhaust gases**			Age, sex, area of residence, hospital and yr of diagnosis; response rate: 63% cases
					10 h low exposure	79	1.26 (0.86–1.86)	
					> 50 h, > medium intensity	31	1.72 (0.93–3.20)	
					> 2500 h, > medium intensity	22	1.57 (0.77–3.23)	

ACS, American Cancer Society; CI, confidence interval; h, hour; HGV, heavy goods vehicle; ICD, International Classification of Diseases; JEM, job–exposure matrix; LGV, light goods vehicle; NHL, non-Hodgkin lymphoma; NR, not reported; OR, odds ratio; SES, socioeconomic status; yr, year

(oesophagus, stomach, colon, 'rectosigmoid', rectum, pancreas, lung, prostate, bladder, kidney, skin melanoma and non-Hodgkin lymphoma) were evaluated for 3726 male cancer patients, aged 35–70 years, diagnosed in any of the 19 participating hospitals in Montreal and interviewed (response rate, 82%). For each cancer site, patients with cancers at other sites comprised the control group. The interview elicited a detailed job history, and a team of chemists and industrial hygienists translated each job into a list of potential exposures (Gérin *et al.*, 1985). The probability of exposure ('possible', 'probable' and 'definite'), the frequency of exposure (< 5, 5–30 and > 30% working time) and the level of exposure (low, medium and high) were estimated. After stratifying for age, socioeconomic status, ethnic group, cigarette smoking and blue-/white-collar job history, elevated odds ratios were seen for exposure to diesel engine exhaust and colon cancer (OR, 1.3; 90% CI, 1.1–1.6 for any exposure; OR, 1.7; 90% CI, 1.2–2.5 for long-term, high-level exposure), for long-term high-level exposure to gasoline engine exhaust and cancer of the rectum (OR, 1.6; 90% CI, 1.1–2.3) and kidney cancer (OR, 1.4; 90% CI, 1.0–2.0) and for bus, HGV and taxi drivers and rectal cancer (90% CI, 1.5; 1.0–2.2). [The Working Group noted that the study included numerous comparisons and used 90% confidence intervals; at the 95% level, most of the intervals would have included unity. Thus, this study was considered to give weak evidence of an association between cancers of the colon, rectum and kidney with exposure to engine exhaust.]

In the framework of the previous Canadian multisite population-based case–control study of occupational exposures and risks for various cancers (Siemiatycki *et al.*, 1988), Goldberg *et al.* (2001) assessed the associations of colon cancer with diesel engine emissions, and many other occupational exposures, in 497 male case patients compared with 1514 other cancer patients (excluding lung and peritoneal cancer, and cancers possibly associated with known risk factors for colon cancer and other cancers of the digestive tract) and 533 population controls. Exposures were assessed as described above (Siemiatycki *et al.*, 1988). The results differed according to the control group: when the pooled group of cancer and population controls was used, the odds ratio for substantial exposure to diesel engine exhaust was 1.6 (95% CI, 1.0–2.5), whereas the risk increased to 2.1 (95% CI, 1.1–3.7) when only the population-based controls were used. [The Working Group noted that the reasons for these differences were not discussed, but the use of cancer controls was a potential source of bias. Multivariate models were adjusted for an extended list of risk factors including socioeconomic status, tobacco smoking and body mass index, but no detailed dietary factors or physical activity.]

Another Canadian study obtained information on lifetime occupational history through a questionnaire from male cancer patients, aged 20 years and over, registered by the British Columbia Cancer Registry between 1983 and 1990. A case–control study was conducted on 1155 cases of colon cancer and 7752 cases of other cancers matched on age and year of diagnosis as controls (Fang *et al.*, 2011). Occupations and industries were coded according to Canadian and international standard classifications. Having ever/never been employed in a specific occupation or industry, as well as the usual occupation or industry of employment, were analysed for all of the 597 occupational titles and 1104 industry titles used in Canada, but results were only reported for those that concerned at least five cases. The analyses showed elevated risks for colon cancer (OR, 1.54; 95% CI, 1.01–2.25) for ever employment as a taxi driver/chauffeur, while other occupational titles, including bus drivers, HGV drivers and locomotive operators, showed no association. [The Working Group noted that no specific assessment of exposure to diesel or gasoline exhaust was carried out. The large number of

statistical comparisons and the crude exposure assessment were among other limitations of this study, which contributed minimally to an assessment of engine exhausts.]

The association between prostate cancer and occupational exposure to diesel fuels and fumes was studied in a case–control study in Germany of 192 histologically confirmed cases and 210 controls with negative biopsies assembled in one university hospital (Frankfurt) and two urology practices (Frankfurt, Hamburg) (Seidler *et al.*, 1998). Lifelong job titles and frequency of exposure to occupational agents were assessed through a self-administered questionnaire, which also included questions on alcohol and coffee consumption, education and other issues. The Pannett JEM, which lists exposures to approximately 50 agents according to probability and intensity of exposure, was used for exposure estimation. A further JEM was used in a second analysis that focused only on those exposures that were significantly associated with prostate cancer in the first evaluation. In a multivariate logistic regression analysis, exposure to diesel fuels and fumes for more than 25 dose–years was significantly associated with the risk for prostate cancer (OR, 3.7; 95% CI, 1.4–9.8; 17 cases, six controls). The odds ratio for up to 25 years of exposure was close to unity. When only subjects with a high probability of exposure were considered as exposed, no cases were observed in the ≥ 25 dose–years category and an odds ratio of close to unity was found for prostate cancer and exposure to diesel fuels and fumes in the lower dose–years category. [The Working Group noted that the study, in particular the subgroup analyses, had low statistical power to detect elevated risks. While exposure to diesel fuel and fuel vapours appeared to be assessed, the occupations considered to entail exposure to these agents included drivers of road transport vehicles, motor mechanics and automobile engineers, deck and engine-room ratings, barge- and boatmen, drivers of other motor vehicles, firemen and railway engineers. Although these occupations mostly entailed exposure to exhausts to a varying extent, the exposure assessment was relatively weak, being based on job titles and external JEMs.]

In an Australian case–control study, 606 patients with prostate cancer identified through the Western Australian Cancer Registry and 471 population controls were studied with regard to occupational exposures, including diesel fumes (Fritschi *et al.*, 2007). The response rate was 57% for cancer cases and 37% for controls. Information on lifetime occupation was obtained through written questionnaires and telephone interviews on job-specific modules for a set of 14 pre-specified jobs. Using information on probability, level and duration, exposure was classified by an occupational hygienist as substantial, non-substantial or unexposed. The odds ratio for the risk of prostate cancer in association with exposure to diesel fumes was 1.07 (95% CI, 0.67–1.72) for those with substantial exposure compared with the unexposed. [The Working Group noted that this study reported data for exposure to 'diesel fumes' rather than diesel exhaust and the extent to which these categories overlap was not clear. The low response rates among both eligible cases and controls were a further limitation of this study.]

The association between pancreatic cancer and exposure to diesel and gasoline exhaust fumes was investigated in a hospital-based case–control study of occupational exposures and gastrointestinal cancers in Spain (Santibañez *et al.*, 2010). Occupational exposures among 161 cases (96 men and 65 women) and 455 frequency-matched controls with non-cancer diseases were assessed on the basis of information from interviews about the two main jobs held and through the application of the FINJEM for 21 specific chemical substances and other exposures. Only ~60% of cases were histologically confirmed. Male patients with ductal adenocarcinoma of the pancreas were more frequently employed as

HGV and light goods vehicle drivers (OR, 3.46; 95% CI, 1.01–11.83). For male cases in the highest tertile of exposure to diesel engine exhaust, the odds ratio was 1.88 (95% CI, 0.72–4.90), calculated from a multivariate model with adjustment for confounding by age, sex, hospital province, alcohol consumption, tobacco smoking and educational status. The corresponding odds ratio for exposure to gasoline engine exhaust was 1.85 (95% CI, 0.71–4.80). [The Working Group noted that the study had a high proportion of direct interviews with case patients. Some known risk factors for pancreatic cancer, such as diabetes and obesity, were not controlled for in the analyses. The sample size and number of exposed cases were small, and multiple comparisons were made, which hampered the interpretation of the positive findings.]

A case–control study of laryngeal cancer included 183 male patients from 56 hospitals on the Texas Gulf Coast (USA), diagnosed between 1975 and 1980, and 250 controls frequency-matched for age group, vital status, ethnicity (all white) and area of residence, recruited through various population sources and records (Brown *et al.*, 1988). Information on employers, job titles and duties was collected by interview. Exposure data were categorized into industrial and occupational categories and potential exposure to specific agents was coded by an industrial hygienist. In the agent-specific analyses, results were given for potential exposure to diesel/gasoline fumes. The risks for laryngeal cancer were non-significantly elevated for the occupational category of drivers. [The Working Group noted that it was unclear whether the target exposure was fumes of diesel fuel or diesel exhaust, and the study was therefore regarded as uninformative with regard to engine exhausts.]

The risk from occupational exposure to diesel fumes and exhaust was investigated in a hospital-based case–control study of 235 male cases of laryngeal cancer and 205 control patients frequency-matched for age, hospital and year of interview (Muscat & Wynder, 1995). Control patients had malignancies such as prostate cancer and lymphoma or various non-malignant diseases. The response rate was 90% for the eligible study subjects who were approached. Detailed data were collected on tobacco smoking, alcohol consumption, lifetime occupational history and self-reported exposure to occupational agents, including diesel exhaust and fumes. Jobs with known substantial exposure to diesel exhaust (HGV drivers, mine workers, fire-fighters and railroad workers) were analysed jointly and yielded a smoking-adjusted odds ratio of 0.96 (95% CI, 0.5–1.8). Self-reported exposure to diesel exhaust had no significant association with laryngeal cancer (OR, 1.47; 95% CI, 0.5–4.1), with an exposure prevalence of 5.5% for cases and 4.4% for controls. Work as an automobile mechanic yielded an odds ratio of 1.3 (95% 0.4–4.1) for laryngeal cancer. [The Working Group noted that the exposure assessment in this study was crude and, overall, the level of detail was limited; the interpretation of the results was hampered by low numbers, and residual confounding from tobacco smoking and alcohol consumption was possible.]

A larger hospital-based case–control study included 940 male cases of laryngeal cancer and 1519 controls from a referral hospital in Istanbul, Turkey (Elci *et al.*, 2003). Controls were patients with other cancers, including Hodgkin lymphoma, soft tissue sarcoma and non-melanoma skin cancer, and several non-cancer diseases. Based on a standardized personal interview, occupations and industries were coded using standard classification schemes, and exposure intensity and probabilities for diesel exhaust, gasoline exhaust and other agents were assigned by an industrial hygienist. Analyses were adjusted for age and ever consumption of alcohol and tobacco. For ever exposure to diesel exhaust, the odds ratio was 1.5 (95% CI, 1.3–1.9). Analyses that used exposure intensity and those that used exposure probability both

showed elevated odds ratios for laryngeal cancer associated with exposure to diesel exhaust; the highest risks, by a small margin, were found for the subgroup of supraglottic laryngeal cancers. When the odds ratios were adjusted for smoking pack–years, positive dose–response trends were observed for all laryngeal cancers and supraglottic cancers. For gasoline exhaust, the results were similar to those for diesel exhaust, with an odds ratio of 1.6 (95% CI, 1.3–2.0) for all laryngeal cancers. However, no cases occurred in the high-exposure intensity group exposed to gasoline exhaust. Adjustment for alcohol and tobacco consumption did not alter the results. [The Working Group noted that the strengths of this study included the comparatively large number of cases and expert assessment of exposure to diesel and gasoline exhausts. The use of hospital controls and the rather superficial assessment of potential confounders, as well as the absence of information on duration of exposure, were limitations of the study.]

A Canadian case–control study investigated the risk of non-Hodgkin lymphoma associated with various occupational exposures (Karunanayake *et al.*, 2008) in 513 male patients, diagnosed between 1991 and 1994, in six provinces and 1506 population controls frequency-matched by age. A postal questionnaire providing information on all jobs held for more than 1 year was the basis for the occupational exposure assessment. Exposure to diesel exhaust fumes showed a statistically significant odds ratio of 1.33 (95% CI, 1.03–1.67). Exposure to diesel fuel or exhaust was evaluated as a confounder in a previous analysis based on the same cases and controls, with similar results (McDuffie *et al.*, 2002). [The Working Group noted that the large number of exposures studied and the multiple tests performed, as well as the limitations of an approach that measured exposures by self-reporting, led to cautious interpretation of these results.]

In a hypothesis-generating case–control study in Sweden, Flodin *et al.* (1987) analysed the association between occupation and the risk for multiple myeloma. Cases were diagnosed between 1973 and 1983 and still alive in 1981–83, and controls were drawn randomly from population registers; 131 cases and 431 controls were available for analysis. Information on occupational history, X-ray treatment and tobacco smoking habits were obtained by a mailed questionnaire. The crude odds ratio for occupational exposure to engine exhaust was 2.3 (95% CI, 1.4–3.7); this association remained significant after adjusting for confounding variables. [The Working Group noted that a limitation of this study was the unclear descriptions of the population and the control for confounding. Exposure to engine exhausts was self-reported and not further defined by the authors, which limited the informativeness of the study.]

Boffetta *et al.* (1989) studied multiple myeloma in a case–control study nested in the American Cancer Society Prevention Study II. Study participants who had died of multiple myeloma (282 cases) were each matched to four randomly selected controls. Occupational information on current job, last occupation if retired, and any other job held for the longest period of time were assessed from a written questionnaire completed at enrolment into the cohort. Specific exposures in the workplace to any of 12 groups of substances, including diesel and gasoline exhausts, were also assessed by questionnaire. The odds ratio for exposure to diesel engine exhaust was 1.4 (95% CI, 0.7–2.7; 14 exposed incident cases, 43 controls) and that for gasoline exhaust was 0.9 (95% CI, 0.5–1.6; 14 cases). An elevated odds ratio of 6.0 (95% CI, 1.3–28.9; three cases, two controls) was found for main occupation as a railroad worker. [The Working Group noted that incident cases were enrolled and the exposure was assessed prospectively, thus eliminating recall bias; however, self-reporting of workplace exposures was a limitation. The result

for railroad workers was based on a very small number of cases, and may be a chance finding.]

Eriksson & Karlsson (1992) investigated occupational risk factors, including engine exhaust, in 275 cases of multiple myeloma (43% deceased) and an equal number of matched population controls in Sweden. Jobs held and tasks associated with exposure to specific chemicals were assessed from mailed questionnaires, together with information on tobacco smoking habits and various other exposures. No increases in risk were found for occupation as a railroad worker or motor vehicle driver. Exposure to engine exhaust was assessed based on work with tractors, power saws or as a driver. The odds ratio for exposure to engine exhaust was 1.11 (95% CI, 0.60–2.05) in a multivariate analysis. [The Working Group noted that the exposure assessment was limited with regard to engine exhausts, being based on occupational titles, and did not differentiate between diesel and gasoline exhausts.]

Two reports from Denmark described the results of a large population-based case–control study on occupational exposures and multiple myeloma. Heineman *et al.* (1992) reported 1098 male cases diagnosed between 1970 and 1984 and 4169 age-matched male controls. Pottern *et al.* (1992) performed an analysis of 1010 women with multiple myeloma and 4040 age-matched female controls. Cases were identified from the Danish Cancer Registry, and controls were drawn from the population registry. Information on employment was retrieved from the pension fund and occupational titles were taken from tax forms held at the population registry. This information was used to assess exposure to 20 broad categories of substances and 27 specific substances by industrial hygienists. Pottern *et al.* (1992) reported odds ratios of 1.4 (95% CI, 0.6–3.2; eight cases) for possible exposure to exhaust and 1.6 (95% CI, 0.4–5.5; four cases) for probable exposure to exhaust among women. Among men, the odds ratios were 1.3 (95% CI, 1.0–1.6; 125 cases) for possible and 1.2 (95% CI, 0.9–1.6; 89 cases) for probable exposure to engine exhaust. Lagging of exposure and stratification by duration of exposure (< 5 years versus ≥ 5 years) showed some evidence of a dose–response for duration of exposure, but the risks were lower for those probably exposed compared with those possibly exposed. When men with at least 5 years of employment were considered separately, exposure to engine exhaust with a 10-year lag was associated with elevated risks for possible exposure, but no elevation for probable exposure in either category of exposure duration, showing no evidence of a dose–response in this analysis. [The Working Group noted that the overall number of cases was relatively large in these studies, but few cases were available for specific comparisons. Occupational information was not reported for 10% of male cases (15% of controls) and 40% of female cases (36% of controls). It was not clear which occupations among women entailed exposure to engine exhaust. No information on confounders beyond the matching factors and other jobs was available, and exposure misclassification may have been a problem in these studies due to the sources of information used.]

Demers *et al.* (1993) conducted a case–control study of 692 cases of multiple myeloma and 1683 population controls recruited between 1977 and 1981 in Washington, Atlanta, Utah and Detroit, USA. Lifetime work histories were collected during personal interviews. Results were reported by occupation and industry group. Rail and water transport workers had an odds ratio of 0.3 (95% CI, 0.1–1.1) and motor vehicle operators had an odds ratio of 1.2 (95% CI, 0.8–1.6). No elevations in risk were found for other occupational groups with some potential for exposure to engine exhaust. [The Working Group noted that the study was limited by the use of occupational/industry titles, and the large number of risk estimates presented. No specific results pertaining to engine exhaust were provided.]

In a Swedish study that used the same source of cases, the same set of 431 controls and the

same methods as those described in Flodin *et al.* (1987), Flodin *et al.* (1988) investigated the association between risk and occupational exposures in 111 cases of chronic 'lymphatic' (lymphocytic) leukaemia. The crude odds ratio for occupational exposure to engine exhausts was 2.5 (95% CI, 1.5–4.0); the association remained significant after adjustment for confounding variables.

In another study in Sweden, 125 patients with acute leukaemia and the same number of population controls were included in a study of the association between exposure to petroleum products and leukaemia (Lindquist *et al.*, 1991). Cases were diagnosed between 1980 and 1983 in five participating Swedish hospitals. Personal interviews to obtain information on environmental and professional exposures to petroleum products, including gasoline and diesel fuels and exhausts, and a checklist of occupations were conducted by one investigator. For the occupational group of professional drivers and rally drivers combined, an odds ratio of 3.0 (95% CI, 1.2–8.4; 21 cases) was estimated. Adjustment for exposure to solvents, radiation treatment and tobacco smoking did not change the results. [The Working Group noted that the study used a very short minimum duration of exposure (1 month) and relied on a crude exposure assessment based on occupational titles. Types of exhaust could not be evaluated separately, and the study therefore contributed little to an assessment of the risks of exposure to exhaust.]

Cases of hairy cell leukaemia were recruited from 18 hospitals in France in a hospital-based case–control study to investigate the risks associated with occupational exposures and tobacco smoking (Clavel *et al.*, 1995). Living cases first diagnosed between 1980 and 1990 were included, and controls were retrospectively selected from admission records mostly from orthopaedic and rheumatology departments in the same hospitals. Two controls per case were matched by date of birth, gender, area of residence and date of admission. The analysis set included 229 live male patients (425 controls) and 62 live female patients (116 controls). The response rate was 61% for cases and 58% for controls. Exposure to engine exhaust was associated with a risk for leukaemia (OR, 1.6; 95% CI, 1.0–2.6) among men. Results for exposure to exhaust for women were not reported. [The Working Group noted that exposure to gasoline and diesel exhaust could not be separated further in the study. The exclusion of deceased cases could have led to survivor bias. In addition, the choice of hospital controls was a limitation of this study.]

Blair *et al.* (2001) carried out a study of 513 cases of leukaemia and 1087 frequency-matched population controls in Iowa and Minnesota, USA, in 1980–83. The main focus was to evaluate the risks associated with agriculture. Personal interviews were conducted to obtain lifetime occupational histories, and selected exposures were evaluated using a JEM. Next of kin were interviewed as surrogates for ~40% of cases who were deceased or too ill to be interviewed (similar for controls). Increases in the risk for leukaemia were associated with driving light goods vehicles (OR, 3.4; 95% CI, 1.4–8.4; 13 exposed cases). Exposure to motor vapours and exhausts was associated with odds ratios of 1.3 (95% CI, 0.9–1.9) in the group considered to be highly exposed and 1.0 (95% CI, 0.8–1.2) in the 'low' exposure group. Analyses by different histological types also showed no significant increase in risk associated with these exposures. [The Working Group noted that the study used a detailed exposure assessment; however, information on exposure to engine exhausts was limited. Potential confounders, such as age, type of interview and education, were adjusted for. The number of cases of different histological types of leukaemia for specific exposures was small.]

Seniori Costantini *et al.* (2001) studied occupational risk factors for haematolymphopoietic malignancies in Italy among 2737 cases diagnosed between 1991 and 1993 (652 cases of leukaemia) and 1779 population controls from 12 areas,

who were interviewed to obtain information on occupational history and specific exposures. The results were reported by occupation. Groups with potential exposure to exhaust included transport operators (OR for leukaemia, 1.1; 95% CI, 0.7–1.7) and material handling and related equipment operators, dockers and freight handlers (OR for leukaemia, 2.5; 95% CI, 1.4–4.5). No significant risks were noted for these occupations in relation to non-Hodgkin lymphoma, multiple myeloma or Hodgkin lymphoma. [The Working Group noted that no specific information regarding exposures to exhaust was presented, and that the occupational groupings were rather broad.]

A population-based case–control study from Shanghai, China, included 486 cases of leukaemia and 502 controls (Adegoke *et al.*, 2003). Information was collected on jobs held and exposure to certain agents, but not specifically to engine exhausts. No increases in risk were seen for occupations that potentially involved some exposure to exhaust (water and rail transport, and drivers). The odds ratio for automobile and HGV drivers was 0.8 (95% CI, 0.3–2.0; eight exposed cases). [The Working Group noted that the exposure assessment in this study was crude.]

Acute myeloid leukaemia subtypes and their association with specific occupational and environmental exposures were investigated in a hospital-based case–control study of 722 case patients and 1444 age- and gender-matched controls from 29 hospitals in Shanghai, China (Wong *et al.*, 2010). Cases and controls were diagnosed in the period 2003–07; controls with malignant or non-malignant diseases of the lymphatic or haematopoietic system were not eligible. The participation rate was ~97% for cases but was not reported for the control group. Personal interviews were conducted to obtain data on occupational exposures and employment history. These data were categorized according to the Chinese standard classification system, and exposure assessment was performed by experts familiar with workplace exposures in Shanghai. Among the large number of risk estimates reported, exposure to diesel or gasoline engine exhaust was very rare and the odds ratio for acute myeloid leukaemia was 0.57 (95% CI, 0.12–2.75; two exposed cases). [The Working Group noted that there was concern about the large number of associations investigated, as well as the choice of hospital controls. Only two cases had been exposed to engine exhaust, which limited the interpretation of the results.]

West *et al.* (1995) studied 400 cases of myelodysplasia and an equal number of hospital or outpatient controls in Wales, Wessex and Yorkshire, United Kingdom [exact period of recruitment not specified]. A lifetime occupational history and exposure to specific chemicals or potential hazards were elicited by questionnaires and interviews. Occupational histories and self-reported exposures were reviewed by hygiene and chemical experts. For exposure to exhaust gases, an odds ratio of 1.26 (95% CI, 0.86–1.86; 63 exposed cases) was estimated. For reported exposures of > 2500 hours and greater than medium intensity, the odds ratio was 1.57 (95% CI, 0.77–3.23), and was slightly lower than that for the group with less intense exposure. [The Working Group noted that the study used an exposure assessment that relied mainly on self-reporting with some further review by experts. Some details, including the statistical analysis, were not adequately described, and potential confounders related to occupation and lifestyle were not assessed. No evidence of a dose–response relationship and no significant increases in risk were found seen for myelodysplasia.]

2.4 Meta-analyses

2.4.1 Cancer of the lung

Bhatia *et al.* (1998) conducted a meta-analysis of occupational exposure to diesel exhaust and the risk for lung cancer using data from 23 case–control and cohort studies that met the

inclusion criteria of adequate latency – at least 10 years from first exposure to diesel exhaust to the end of follow-up (for at least some of the subjects) – and for which work with diesel engine equipment could be confirmed or inferred. Studies of miners were excluded because of potential confounding by exposure to carcinogens such as radon and silica for certain types of miner. Tobacco smoking-adjusted risk estimates were used whenever available and, when risks were reported by duration of exposure, the longest duration category was used in the analysis. Standardized mortality ratios for lung cancer in cohort studies with external referent groups were adjusted by the all-cause standardized mortality ratio to account for the healthy-worker effect. Combined estimates were calculated using a fixed-effects model for all studies and for subsets of studies grouped by (1) study design, (2) type of comparison group for cohort studies, (3) adjustment for tobacco smoking and (4) occupation, including railroad workers, equipment operators, HGV drivers and bus drivers. Confidence intervals were adjusted for heterogeneity. A random-effects model was not used because the underlying assumption that interstudy variance was constant was unlikely to be met. The relative risk for all studies was 1.33 (95% CI, 1.24–1.44); and similar results were obtained when studies were stratified by study design (case–control and cohort) or adjustment for smoking (e.g. a significant 30% excess risk was found for studies that adjusted for smoking and for studies that did not adjust for smoking; see Table 2.6). Summary estimates were higher for cohort studies that used an internal comparison group (RR, 1.43; 95% CI, 1.29–1.58) than for those that used an external comparison group (RR, 1.22; 95% CI, 1.04–1.44). Estimates also varied among occupational groups. Evidence for heterogeneity was found for all studies combined, all cohort studies and all case–control studies, but was reduced after stratification by occupation. Greater heterogeneity was observed for cohort studies that used external comparisons compared with those that used internal comparisons. Six of seven studies (all using internal referent groups) that evaluated duration of exposure found a positive exposure–response relationship. Funnel chart analysis showed little evidence of publication bias (Bhatia *et al.*, 1998).

Another meta-analysis of lung cancer and occupational exposure to diesel exhaust (Lipsett & Campleman, 1999) included studies that reported risk estimates and confidence intervals or adequate data to obtain them, had an adequate latency for the development of lung cancer after the onset of exposure (≥ 10 years) and adequate case ascertainment, and were independent. Studies of miners were excluded because of potential confounding by exposure to carcinogens such as radon, arsenic and silica. Risk estimates for the highest level or duration of exposure for occupations with the most specific exposure to diesel and adjustment for tobacco smoking were used when available. A random-effects model was designed for the meta-analyses, which were based on 39 effect estimates from 30 studies. Subset analyses were performed for studies that could be grouped in relation to several characteristics, including study design, adjustment for tobacco smoking, occupational category, referent group, latency, duration of exposure, selection methods, year of publication, covariates controlled for in the analysis and the presence of a healthy-worker effect. Sensitivity and influence analyses were also conducted. Similar to that reported by Bhatia *et al.* (1998), the overall summary risk estimate was 1.33 (95% CI, 1.21–1.46), which showed significant heterogeneity. Increased risk estimates and lower heterogeneity were observed for studies that adjusted for smoking (RR, 1.43 versus 1.25 for studies that did not adjust for smoking), had a lower risk of selection bias (i.e. did not show evidence of a healthy-worker effect; RR, 1.52 versus 1.06 for cohort studies with clear evidence of a healthy-worker effect) and used internal controls (RR, 1.48 versus 1.14

Table 2.6 Meta-analyses of cohort and case–control studies of cancer and exposure to engine exhaust

Reference	Organ site	Exposure	No. of estimates	Relative risk (adjusted 95% CI)	Heterogeneity *P*-value	Covariates Comments
Bhatia *et al.* (1998)	Lung	All studies	29	1.33 (1.24–1.44)	58	Fixed-effects model; χ^2 for heterogeneity
		All exposed occupations	24	1.37 (1.27–1.49)	48.4	
		Railroad workers	6	1.44 (1.30–1.60)	5.6	
		Equipment operators	3	1.11 (0.89–1.38)	4.3	
		HGV drivers	10	1.49 (1.36–1.65)	9.8	
		Bus workers	5	1.24 (0.93–1.64)	14.8	
		Tobacco smoking-adjusted	16	1.35 (1.20–1.52)	23.4	
		Not adjusted for tobacco smoking	13	1.33 (1.20–1.47	34.5	
Lipsett & Campleman (1999)	Lung	All studies	39	1.33 (1.21–1.46)	0.001	Random-effects model
		Railroad workers	6	1.45 (1.08–1.93/)	< 0.001	
		Heavy equipment operators /dock workers	4	1.28 (0.99–1.66)	0.046	
		HGV drivers	9	1.47 (1.33–1.63)	0.398	
		Mechanics/garage workers	6	1.35 (1.03–1.78)	0.010	
		Professional drivers/ transportation operatives	6	1.45 (1.31–1.60)	0.716	
		Diesel exhaust	5/5	0.97 (0.95–1.00)	0.585	
Boffetta & Silverman (2001)	Urinary bladder	Heavy equipment operators	5	1.37 (1.05–1.81)	0.6	Only studies with ≥ 5 yr latency; fixed-effects model; evidence of publication bias for all studies and HGV and bus drivers
		HGV drivers	15	1.17 (1.06–1.29)	0.3	
		Bus drivers	10	1.33 (1.22–1.45)	0.4	
		JEM for diesel	10	1.13 (1.00–1.27)	0.3	
		Any exposure to diesel exhaust	12	1.23 (1.12–1.36)	0.5	
		High exposure to diesel exhaust	12	1.44 (1.18–1.76)	0.1	
Manju *et al.* (2009)	Urinary bladder	**HGV drivers**				Case–control studies with no adjustment for tobacco smoking excluded; fixed-effects model
		Overall	17	1.18 (1.09–1.28)	0.25	
		Yr of publication				
		1977–87		1.30 (1.16–1.46)		
		1998–2008		1.20 (1.00–1.40)		
		Bus drivers				
		Overall	9	1.23 (1.06–1.44)	0.25	

Table 2.6 (continued)

Reference	Organ site	Exposure	No. of estimates	Relative risk (adjusted 95% CI)	Heterogeneity *P*-value	Covariates Comments
		Yr of publication				
Manju et al. (2009) (cont.)		1977–87		1.30 (1.10–1.53)		
		1998–2008		1.21 (0.72–2.01)		
		Railroad worker				
		Overall	14	1.20 (1.02–1.41)	0.31	
		Yr of publication				
		1977–87		1.33 (0.98–1.54)		
		1998–2008		1.25 (0.96–1.61)		
		Other motor vehicle drivers	10	1.11 (0.99–1.23)	0.11	
Reulen *et al.* (2008)	Urinary bladder	**All studies**				Random-effects model
		Car, taxi and van drivers	9	1.20 (1.03–1.39)	NR	
		Bus drivers	8	1.29 (1.08–1.53)	NR	
		HGV drivers	15	1.18 (1.06–1.33)	NR	
		Motor vehicle drivers	32	1.11 (1.06–1.17)	NR	
		Adjusted for tobacco smoking				
		Car, taxi and van drivers	NR	1.20 (0.99-1.46)	NR	
		Bus drivers	NR	0.96 (0.65-1.42)	NR	
		HGV drivers	NR	1.18 (1.06-1.31)	NR	
		Motor vehicle drivers	NR	1.11 (1.04-1.18)	NR	
		Not adjusted for tobacco smoking				
		Car, taxi and van drivers	NR	1.27 (0.83-1.93)		
		Bus drivers	NR	1.39 (1.22-1.58)		
		HGV drivers	NR	1.45 (0.83-2.53)		
		Motor vehicle drivers	NR	1.14 (1.02-1.27)		

CI, confidence interval; HGV, heavy goods vehicle; JEM, job–exposure matrix; NR, not reported; yr, year

for studies that used national rates). Among the studies that adjusted for smoking, some evidence of an exposure–response relationship with duration of exposure was found; a higher summary estimate was observed for ≥ 10 years of duration (RR, 1.64 versus 1.39 for < 10 years of duration). Sensitivity or influence analyses did not substantially alter the results. In meta-regression analyses of the case–control studies, higher risks were reported in studies that were published after 1989 compared with those published before 1989. No systematic relationship was observed between study size and the magnitude of risk in funnel plot analyses.

Mahjub & Sadri (2006) conducted a meta-analysis of case–control studies of lung cancer that evaluated occupational or environmental pollutants, including exposure to motor and diesel exhaust. Case–control studies included in the analysis were published in English during 1990–2006 and focused on environmental or occupational exposures. Risk estimates from 12 studies were summarized using a random-effects model. Summary risk estimates were 1.42 (95% CI, 1.26–1.59) for exposure to 'motor and diesel exhaust'. [The Working Group noted that the restricted focus of this meta-analysis limited its usefulness to address cancer hazard identification for exposure to diesel exhaust.]

Tsoi & Tse (2012) conducted a systematic review of studies of professional drivers potentially exposed to diesel exhaust that were published in English from 1996 to 2011 and reported data on risks for lung cancer. The review included 19 cohort and case–control studies (seven historical cohorts, one prospective cohort and 11 case–control studies) of workers who were bus, taxi, HGV and mixed or unspecified drivers. The combined relative risk was 1.21 (95% CI, 1.10–1.32; *P* for heterogeneity < 0.01) for all studies and 1.22 (95% CI, 1.09–1.36; *P* for heterogeneity = 0.02) for higher-quality studies. Funnel plot analysis revealed no evidence of publication bias. [The Working Group noted that this meta-analysis provided little new information regarding exposure to diesel exhaust and the risk for lung cancer because it focused on professional drivers and did not consider exposure assessment in the quality evaluation.]

2.4.2 Cancer of the urinary bladder

Boffetta & Silverman (2001) conducted a meta-analysis of exposure to diesel exhaust and the risk for urinary bladder cancer. The analysis included studies of exposure to diesel exhaust based on JEMs or expert assessments of individual occupational histories for five occupational groups: railroad workers, bus garage maintenance workers, HGV drivers, bus drivers and operators of heavy construction machines. Only studies with at least 5 years between the first exposure to diesel engines or equipment and the development of urinary bladder cancer were included in the final analysis, which included seven cohort studies, 16 case–control studies and six studies of routinely collected data. Most of the case–control studies adjusted for tobacco smoking. Risk estimates were not calculated for all studies combined or for studies of railroad workers because of heterogeneity (*P* for heterogeneity = 0.002 and 0.02, respectively), or for garage workers because the number of studies was too small. An indication of an excess risk of urinary bladder cancer was found for the other occupational groups (OR, 1.13–1.37). Evidence of publication bias was found for studies of bus and HGV drivers, and for the entire set of studies. Although studies that did not adjust for smoking were included in the analysis, in general, those that adjusted for smoking did not have lower risk estimates, and smoking did not explain the heterogeneity of the results. The authors also combined eight relative risks for high exposure to diesel exhaust, most of which were for the longest duration of employment in a specific occupation with potential exposure to diesel exhaust. The summary relative risks were 1.23 (95% CI,

1.12–1.36) for any exposure and 1.44 (95% CI, 1.18–1.76) for high exposure to diesel exhaust.

The risk of urinary bladder cancer among motor vehicle drivers was evaluated in a meta-analysis of data reported in 30 studies, including 27 case–control studies and three cohort studies, published from 1977 to 2008 (Manju *et al.*, 2009). Studies excluded from the analysis were case–control studies that did not adjust for tobacco smoking and cohort studies that did not provide numbers of observed and expected cases. For cohort studies, a pooled observed/expected ratio for urinary bladder cancer was calculated by summarizing the observed and expected numbers of events across studies. No overall summary estimate was calculated for case–control studies because of significant heterogeneity in the results. However, summary odds ratios and corresponding 95% confidence intervals were calculated as a weighted average of odds ratios for occupational groups and subsets of studies stratified by publication date. The pooled observed/expected ratio for all cohort studies of motor vehicle drivers and railroad workers was 1.08 (95% CI, 1.00–1.17). Increased risks were observed for each of the occupational groups, and there was some evidence that risks were lower for HGV, bus drivers, and railroad workers in more recent publications (1998–2008) than in earlier publications (1977–87). Funnel chart analysis suggested some evidence of publication bias; however, some studies were excluded from the analysis because of the unavailability of case numbers.

Reulen *et al.* (2008) combined data from 130 studies (66 cohort and 64 case–control studies) that evaluated occupation and the risk for urinary bladder cancer. Occupations were coded and grouped together using the International Classification of Occupations. For each occupation, a random-effects model was used to calculate summary relative risks and 95% confidence intervals. Statistically significant summary relative risks were observed for several occupations, which have been associated with potential exposure to diesel or motor exhaust (see Table 2.6). Stratified analyses were performed for study design (cohort versus case–control), tobacco smoking status and publication date. Summary relative risks (for diesel-related occupations) did not significantly differ when stratified by study design (cohort versus case–control) or smoking status; however, the summary relative risks for HGV and bus drivers were somewhat higher in studies that did not control for smoking compared with those that did. The authors also stratified by the time period during which the study was conducted (before 1980, 1980–90 and after 1999); no significant linear trends were observed, although risk estimates were generally lower for studies of all occupations, except motor vehicle drivers, conducted after 1990. [The Working Group noted that this study calculated risk estimates for many different types of occupation, of which only a few were associated with potential exposure to diesel fuel; thus the specificity of exposure was limited and multiple comparisons may have been a concern.]

2.4.3 Cancer of the pancreas

A meta-risk ratio of pancreatic cancer with exposure to diesel exhaust was calculated as part of a larger meta-analysis of pancreatic cancer and exposure to 23 chemicals present in the workplace (Ojajärvi *et al.*, 2000). Relative risks for exposure to diesel exhaust or job titles with verified exposure to diesel exhaust from seven studies were combined using a simple random-effects model. When available, relative risks that were adjusted for confounders and social class, and had a latency period closest to 20 years were used in the analysis. No excess risk for pancreatic cancer was found for exposure to diesel exhaust (meta-risk ratio, 1.0; 95% CI, 0.9–1.20).

2.4.4 Summary of meta-analyses

The meta-analyses found consistent elevated risk estimates for occupations associated with exposure to diesel exhaust and lung cancer and urinary bladder cancer, but not for pancreatic cancer, although fewer data were available for the latter. The analyses for lung cancer by Bhatia *et al.* (1998), Lipsett & Campleman (1999) and Tsoi & Tse (2012), and those for urinary bladder cancer by Boffetta & Silverman (2001) found significant heterogeneity for the overall results, which was explained in part by the type of occupation. (Boffetta & Silverman, 2001) did not calculate an overall risk estimate because of the significant heterogeneity.) The major limitation of the meta-analyses was the paucity of data relating job titles to exposure to diesel exhaust, and the inclusion of studies with varying quality of exposure information. Moreover, most of the individual studies included in the analyses evaluated risks for occupations and not for exposure to diesel exhaust, and the most recent meta-analyses (Reulen *et al.*, 2008; Manju *et al.*, 2009) included only studies that evaluated risk according to occupation.

A further limitation of the earlier studies was their inclusion of subjects who worked before or at the beginning of the diesel era or workers with a latency period that was inadequate to attribute any increases in lung cancer to exposure to diesel exhaust.

Most of the meta-analyses included studies that did not adjust for tobacco smoking, but the analyses were stratified by this factor. In general, meta-risk estimates for studies that did not adjust for smoking were similar to those that did and meta-risk estimates for lung cancer from cohort studies that used internal comparison groups, which should have reduced the potential for confounding from smoking, were higher than the those from studies that used an external comparison group (Bhatia *et al.*, 1998; Lipsett & Campleman, 1999).

2.5 Studies of childhood cancer

See Table 2.7

Studies have been carried out to examine hypotheses that the risk of childhood cancer is associated with exposure to engine exhausts, including parental exposure that results in germ cell mutations, direct intrauterine exposure of the fetus or early postnatal exposure. A common limitation of these studies was the non-specific assessment of exposure, which was often based on records of parental job titles without a more specific assessment of exposure to engine exhaust. Studies have also been conducted on traffic-related air pollution and childhood cancer, but these were not considered to be informative and are not reviewed here.

In a case–control study in Québec, Canada (Fabia & Thuy, 1974), occupation of the father at the time of birth was ascertained from the birth certificates of 386 children who had died from malignant disease before the age of 5 years in 1965–70. The study included 772 control children whose birth registration immediately preceded or followed that of the case in the official records. The occupation of the father was not known for 30 cases or 56 controls. Paternal occupation was recorded as motor vehicle mechanic or service station attendant for 29 (7.5%) cases and 29 (3.8%) controls and as driver for 19 (4.9%) cases and 49 (6.4%) controls. [Odds ratios were not reported, but crude odds ratios calculated by the Working Group were 2.1 (95% CI, 1.2–3.4) for mechanics/service station attendants and 0.76 (95% CI, 0.4–1.3) for drivers. The Working Group noted that no cancer-specific analyses were conducted and the study was limited in terms of details of exposure.]

In a case–control study in Finland (Hakulinen *et al.*, 1976), all 1409 incident cases of cancer in children under 15 years of age reported to the Finnish Cancer Registry in 1959–68 were ascertained. Paternal occupation was obtained from antenatal clinic records for the first trimester of

Table 2.7 Studies of childhood cancer and exposure to engine exhaust

Reference Location, period	Total No. of cases/controls	Source of controls	Exposure assessment	Organ site	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates Comments
Fabia & Thuy (1974) Quebec, Canada, 1965–70	386/772	Population	Occupation of father on birth certificate	All childhood cancers	**Registered occupation**		**Crude OR**	Controls matched by birth date, no exposure details; specific sites/cancer types not assessed; ORs NR: crude ORs calculated by the Working Group
					Motor vehicle mechanic/service station attendant	29	[2.1 (1.2–3.4)]	
					Driver	19	[0.76 (0.4–1.3)]	
Hakulinen *et al.* (1976) Finland, 1959–68	852/852	Population	Occupation of father on antenatal records		**Registered occupation**			Only 60% of cases with suitable information; controls matched by birth date and district; no details of exposure
				Leukaemia (age < 5 yr)	Driver	14	0.74 (0.34–1.6)	
				Leukaemia and lymphoma	Driver	35	1.06 (0.63–1.8)	
				Brain tumour (age < 5 yr)	Driver	4	0.17 (0.0–1.4)	
				Brain tumour	Driver	16	0.67 (0.29–1.5)	
Kantor *et al.* (1979) Connecticut, USA, 1935–73	149/149	Population	Occupation of father on birth certificate	Wilms tumour	**Registered occupation**		**Crude OR**	Controls matched by sex, race, birth yr; no details of exposure; ORs NR; crude ORs calculated by the Working Group
					Driver	8	[2.1 (0.6–6.7)]	
					Motor vehicle mechanic	6	[6.2 (0.8–49.8)]	
					Service station attendant	3	NR (no exposed controls)	
Kwa & Fine (1980) Massachusetts, USA, 1947–57 and 1963–67	692/1384	Population	Occupation of father on birth certificate		**Registered occupation**		**Crude OR**	Controls matched by birth date; ORs NR: crude ORs calculated by the Working Group; no details of exposure
				Leukaemia/ lymphoma	Mechanic/service station attendant	21 deaths	[1.1 (0.7–1.5)]	
				Neurological	Mechanic/service station attendant	6 deaths	[1.02 (0.4–2.4)]	
				Urinary tract	Mechanic/service station attendant	4 deaths	[2.9 (1.0–8.9)]	

Table 2.7 (continued)

Reference Location, period	Total No. of cases/controls	Source of controls	Exposure assessment	Organ site	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates Comments
Zack *et al.* (1980), Houston, TX, USA, 1976–77	296/566/838/465	Hospital/ parents/ siblings and neighbourhood	Personal interview with parents on job history in yr before birth	All childhood cancers	**Paternal occupation as mechanic/service station attendant/driver**			No exposure details, choice of controls not clear; OR calculated by the Working Group from Table 1 in the publication; details of maternal occupation NR
					Control uncles	12	[0.79 (0.38–1.63)]	
					Neighbourhood controls	12	[0.92 (0.40–2.17)]	
					Hospital controls	12	[0.59 (0.28–1.23)]	
Hemminki *et al.* (1981), Finland, 59–1975	948/1892	Population	Occupation of parents from on welfare centre records		**Registered occupation as driver**			Extension of Hakulinen *et al.* (1976)
				Leukaemia		96	1.50 ($P < 0.10$)	
				Brain		84	0.92 ($P > 0.10$)	
				All cancers		303	1.25 ($P < 0.10$)	
Gold *et al.* (1982), Maryland, USA, 1965–74	43 leukaemia, 70 brain tumour/43 and 70 population, 43 and 70 hospital	Population and hospital	Personal interview with mother		**Paternal occupation as mechanic/service station attendant/driver before birth of index child**			Information for occupation before birth missing for 16–40% of cases; controls matched on sex, race, age and date of diagnosis (cancer controls only); ORs and 95% CIs NR.
				Leukaemia		3	$P < 0.05$ for cancer or population controls	
				Brain tumour		3	$P > 0.05$ for cancer and population controls	
Vianna *et al.* (1984), New York, USA, 1949–78	60 leukaemia, 103 brain tumour/60 and 103	Population	Personal interview with mother	Leukaemia	**Paternal job group with presumed exposure to exhaust (≥ 1 yr before birth)**			Controls matched on birth yr, sex, race and county; jobs grouped according to presumed exposure level
					High exposure		2.4 [1.1–3.7]	
					Low exposure		1.3 [0.8–2.1]	
Wilkins & Sinks (1984), Columbus,Ohio, USA, 1950–1981	62/124	Population	Occupation of father on birth certificate	Wilms tumour	Paternal occupation as mechanic/service station attendant/ driver/metal worker	5	1.37 (0.59–3.11) compared with 2 controls	Controls matched on sex, race birth yr and county; incomplete records of paternal occupation; only 62 pairs for analysis

Table 2.7 (continued)

Reference Location, period	Total No. of cases/controls	Source of controls	Exposure assessment	Organ site	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates Comments
van Steensel-Moll *et al.* (1985), Netherlands, 1973–80	519/507	Population	Postal questionnaire on occupations before and during pregnancy	Acute lymphatic leukaemia	**Hydrocarbon-related occupations OR**			Matching on age, gender place of residence, social class and birth order; response rate: 88% cases, 66–67% controls; hydrocarbon-related group included broad range of occupations
					Mother	7	2.5 (0.7–9.4)	
					Father	37	1.0 (0.6–1.7)	
					Exposure to exhaust during pregnancy			
					Mother	4	NR	
					Father	89	1.3 (0.8–1.9)	
Cordier *et al.* (2001), Australia, Canada, France, Israel, Italy, Spain, USA, 76–1994 (differed by centre)	1218/2223	Population	Personal interview with parents on occupational history 5 yr before diagnosis; JEM	Brain	Paternal occupation as driver	127	1.3 (1.0–1.7)	Centre, age of child, yr of birth and gender; response rate: 75% cases and controls
					Paternal occupation as mechanic	45	1.5 (1.0–2.3)	
McKinney *et al.* (2003), United Kingdom, 1991–96	3838/7629	Population	Personal interview with parents including full occupational history; JEM	Leukaemia	**Periconceptual exposure to exhaust**			Age of child, gender and region of residence; response rate: 87% cases, 64% controls
					Mother	9	1.58 (0.74–3.40)	
					Father	147	1.33 (1.09–1.61)	
					Periconceptual occupation as driver			
					Mother	5	1.48 (0.53–4.13)	
					Father	121	1.36 (1.10–1.68)	
				Central nervous system	**Periconceptual exposure to exhaust**			
					Mother	3	1.33 (0.40–4.42)	
					Father	47	1.08 (0.79–1.47)	
					Periconceptual occupation as driver			
					Mother	1	0.85 (0.11–6.50)	
					Father	36	1.04 (0.73–1.48)	

Table 2.7 (continued)

Reference Location, period	Total No. of cases/controls	Source of controls	Exposure assessment	Organ site	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates Comments
Reid *et al.* (2011) Australia, 2003–06	511/2071	Population	Parental occupation, job-specific modules; expert assessment	Acute lympho-blastic leukaemia	**Prenatal and postnatal paternal/maternal exposure**			Sex (child), age at diagnosis, socioeconomic status, smoking, alcohol consumption, age (mother) and state
					Moderate/substantial pre-birth exhaust exposure combined			
					Mother	17	1.97 (0.99–3.90)	
					Diesel only	14	2.06 (0.97–4.39)	
					Petrol only	7	1.59 (0.58–4.41)	
					Father	127	1.37 (1.01–1.86)	
					Diesel only	101	1.24 (0.91–1.69)	
					Petrol only	48	1.20 (0.82–1.77)	

CI, confidence interval; JEM, job–exposure matrix; NR, not reported; OR, odds ratio; yr, year

pregnancy. After excluding twins and cases for which the paternal occupation was unobtainable, 852 cases were available for analysis. For each case, a child whose date of birth was immediately before that of the case and who had been born in the same maternity welfare district was chosen as a control. Leukaemias and lymphomas (339 pairs; 158 under 5 years of age), brain tumours (219 pairs; 77 under 5 years of age) and other tumours (294 pairs; 160 under 5 years of age) were analysed separately; analyses were carried out for the whole group and for children under 5 years of age at the time of diagnosis. Paternal occupation as a motor vehicle driver was not more frequent in any group of cases than in controls: the odds ratio for paternal occupation as a driver was 0.74 (95% CI, 0.34–1.6) for leukaemia in children under 5 years, 1.1 (95% CI, 0.63–1.8) for leukaemia and lymphoma in the whole group, 0.17 (95% CI, 0.00–1.4; four cases) for brain tumours in children under 5 years and 0.67 (95% CI, 0.29–1.5) for brain tumours in the whole group. [The Working Group noted that the study had several limitations: only 60% of cases were available for analysis due to the lack of records or information on paternal occupation, the exposure assessment was crude and the odds ratios were not adjusted for other risk factors.]

In a case–control study in Connecticut, USA (Kantor *et al.*, 1979), paternal occupation was ascertained from birth certificates for all 149 cases of Wilms tumour (aged 0–19 years) reported to the Connecticut Tumor Registry in 1935–73 and for 149 controls selected from State Health Department files and matched for sex, race and year of birth. The paternal occupation was recorded as driver for eight cases and four controls [OR, 2.1; 95% CI, 0.6–6.7], as motor vehicle mechanic for six cases and one control [OR, 6.2; 95% CI, 0.8–49.8] and as service station attendant for three cases and no control. [Odds ratios were not reported; crude odds ratios were calculated by the Working Group. The Working Group noted that the number of exposed cases in this study was small, the exposure assessment was crude and other risk factors were not taken into account. The study was therefore judged to be not very informative.]

In a case–control study of the association between paternal occupation and childhood cancer (Kwa & Fine, 1980), 692 children born in 1947–57 or 1963–67 and who had died of cancer before the age of 15 years in Massachusetts, USA, were identified from the National Center for Health Statistics. Two controls were selected from the registry of births for each case – one born immediately before the case and the other immediately after. Paternal occupation was taken from birth certificates and classified into one of nine categories on the basis of the type of chemical exposures involved. Mechanic/service station attendant was recorded as the paternal occupation for 21 cases of leukaemia/lymphoma [OR, 1.1; 95% CI, 0.7–1.5], six cases of neurological cancer [OR, 1.02; 95% CI, 0.4–2.4], four cases of urinary tract cancer [OR, 2.9; 95% CI, 1.0–8.1], four cases of all other cancers [OR, 0.93; 95% CI, 0.34–2.6] and 61 controls. In the children of fathers who were motor vehicle drivers, no excess of leukaemia/lymphoma, neurological cancer, urinary tract cancer or all other cancers was observed. [The Working Group noted that, as in the other studies with a similar approach, the nature of the exposure assessment allowed only limited inference of an association of parental exposures to engine exhaust with subsequent childhood cancer. In addition, no risk factors other than date of birth were taken into account in the analysis.]

In a case–control study of associations between childhood cancer and parental occupation (Zack *et al.*, 1980), the parents of 296 children with cancer followed at a haematology clinic in Houston, Texas, USA, from March 1976 to December 1977 and three sets of controls were interviewed to obtain demographic information and job history from the year preceding the birth of the child until the diagnosis of cancer. The

first set of controls comprised 283 fathers and stepfathers and 283 mothers and stepmothers of children without cancer in the same clinic; the second set comprised siblings of the parents of the case (413 uncles and 425 aunts), matched by age and number of children; and the third set was selected from among residents in the neighbourhood of the cases (228 fathers and 237 mothers). The proportion of cases with paternal occupation as a motor vehicle mechanic, service station attendant or driver did not differ substantially from that in any control group (crude OR, 0.59; 95% CI, 0.28–1.23 in comparison with fathers' siblings; 0.79; 95% CI, 0.38–1.63 in comparison with the fathers of cancer cases; and 0.92; 95% CI, 0.40–2.17 in comparison with neighbourhood fathers). [The Working Group noted that the limitations of the study included unclear selection criteria for cases and controls and a lack of control for confounders. The completeness of the data on the occupations of mothers was also unclear.]

Hemminki *et al.* (1981) obtained data from the Finnish Cancer Registry for children under 15 years of age with a cancer that was diagnosed in 1959–75 and on parental occupation (see the study of Hakulinen *et al.*, 1976), and included approximately twice the number of cases as the earlier study. Data were analysed separately for the periods 1959–1968 and 1969–1975. The odds ratio for the father of a child with leukaemia in 1969–1975 being a professional driver was 1.25 ($P < 0.10$) for all childhood cancers, 1.5 ($P < 0.10$) for leukaemia and 0.92 ($P > 0.10$) for brain tumours. Odds ratios for leukaemia and all cancers were somewhat higher when only occupations in the later period were considered. Detailed data were not reported for maternal occupations. [The Working Group noted that the exposure information was limited to occupational titles and that a large number of occupations were assessed; thus, multiple comparisons were a limitation. The interpretation of this study was further limited by the lack of information on potential confounders.]

Associations between paternal occupation and childhood leukaemia (43 cases) and brain tumour (70 cases) were investigated in a case–control study in Maryland, USA (Gold *et al.*, 1982). Children and adolescents under the age of 20 years with leukaemia (diagnosed in 1969–74) or brain tumours (diagnosed in 1965–74) were ascertained in the Baltimore area from hospital records, death certificates, hospital tumour registries and from the pathology, radiotherapy and clinical oncology records of 21 Baltimore hospitals. Two control groups were included: one comprised children with no malignant disease, selected from birth certificates at the Maryland State Health Department and matched for sex, date of birth and race; the other group comprised children with malignancies other than leukaemia or brain cancer, matched for sex, race, date of diagnosis and age at diagnosis. Information on occupational exposures of both parents before the birth of the child and between the birth and diagnosis was collected from interviews with the mothers. Odds ratios and 95% confidence intervals were not reported. The paternal occupational category that included driver, motor vehicle mechanic, service station attendant or railroad worker was not more frequent for children with leukaemia or brain tumours compared with the population control children, but was for leukaemia cases in comparison with the cancer controls (six exposed cases, no exposed controls; $P < 0.05$). [The Working Group noted that the small numbers involved, the choice of cancer controls and the lack of control for potential confounders were limitations of the study. In addition, the occupations included in the motor vehicle-related group represented a somewhat diverse group of occupations with different potential exposure to exhaust.]

In a case–control study of childhood leukaemia in the USA (Vianna *et al.*, 1984), children born in 1949–78 who were diagnosed with

acute leukaemia during the first year of life and reported to the Tumor Registry of the New York State Health Department or with neuroblastoma up to 12 years of age at diagnosis were identified. Using information from birth certificates, two sets of controls were selected: the primary control group was matched by year of birth, sex, race and county of residence; the second group was additionally matched for age of the mother and birth order of the child. Information on parental age, race, education and occupation, and medical, obstetrical and therapeutic histories were obtained by telephone interviews with the mothers. A similarly designed case–control study of 103 children diagnosed with neuroblastoma before the age of 13 years was conducted simultaneously to assess data quality, but few details were reported. Of the 65 eligible cases of leukaemia, 60 were finally included in the analysis, each with two controls. The odds ratio for acute leukaemia for children with 'high' presumed paternal exposure to motor exhaust fumes (service station attendants, automobile or HGV repairmen and aircraft maintenance personnel) was 2.4 [95% CI, 1.1–3.7] in comparison with the main control group and 2.5 [95% CI, 1.2–5.3] in comparison with the second control group. For 'lower' presumed exposure (taxi drivers, travelling salesmen, HGV or bus drivers, railroad workers, toll-booth attendants, highway workers and police officers), the odds ratio was 1.3 [95% CI, 0.8–2.1] in comparison with the first control group and 3.4 [95% CI, 1.4–10.2] in comparison with the second. Data were not tabulated for the study of neuroblastoma, but no significant difference was found in the number of fathers who had had 'high' or 'moderate' exposure. [The Working Group noted that, as a limitation, the categorization of exposures as 'high' and 'lower' on the basis of the jobs listed appeared questionable, because jobs classified as having low exposure to one type of exhaust may have high exposure to another type. No potential confounders beyond the matching factors were controlled for in the analysis.]

In a case–control study of paternal occupation and Wilms tumour (Wilkins & Sinks, 1984), 105 patients were identified through the Columbus (OH, USA) Children's Hospital Tumor Registry during the period 1950–81. For each case, two controls were selected from Ohio birth certificate files: the first control series was individually matched for sex, race and year of birth, and the second series was additionally matched for mother's county of residence when the child was born. Due to changes in birth certification, the study included only the 62 cases and their matched controls for which paternal occupation was recorded. The crude odds ratio for Wilms tumour in children with paternal occupation as motor vehicle mechanic, service station attendant or driver/heavy equipment operator was 1.37 (95% CI, 0.59–3.11) compared with both groups of controls combined. [The Working Group noted that the study was limited with regard to the small number of exposed cases, crude exposure assessment and the lack of control for confounders other than demographic characteristics.]

Using a nationwide registry of childhood leukaemia, a case–control study including 519 cases of childhood acute lymphatic leukaemia (period of diagnosis, 1973–80) and 507 population-based controls matched for year of birth, gender and place of residence was conducted in the Netherlands (van Steensel-Moll *et al.*, 1985). A postal questionnaire provided information on parental occupations and selected exposures before and during pregnancy. The response rate was 88% for parents of cases and 66% for those of controls. Four mothers of cases compared with no control mother indicated exposures to exhausts during pregnancy, while 89 case fathers and 70 control fathers reported such exposure (OR, 1.3; 95% CI, 0.8–1.9). [The Working Group noted that this study relied on job titles and self-reporting for exposure assessment, with the

potential for misclassification and low specificity. Exposures to diesel and gasoline exhausts were not separated.]

In a joint analysis of case–control studies of childhood brain cancer that formed part of an international study coordinated by the IARC, 1218 cases and 2223 controls were analysed with regard to parental occupation (Cordier *et al.*, 2001). All studies were population-based, but the upper age of inclusion varied from up to 15 years in European and Australian centres to up to 19 years in Israel and centres in the USA. The overall response rate among cases was 75%. Population-based controls were either individually or frequency-matched to cases, depending on the centre, with a 75% response rate. Exposure assessment was based on parental interviews and coding occupations and industries according to international standard classifications. For paternal occupation during the 5-year period before birth, the odds ratio was 1.3 (95% CI, 1.0–1.7) for occupation as a driver and 1.5 (95% CI, 1.0–2.3) for all childhood brain tumours combined. Maternal occupations related to motor vehicles were not associated with an increased risk, but some indication of a positive association was observed with employment in a motor vehicle-related industry during pregnancy. [The Working Group noted that this study was notable for its large size and improved methods relative to most of the earlier studies. However, no specific information was available on exposure to engine exhausts and the numbers of mothers in exposed occupations was small.]

Different diagnostic groups of childhood cancer and their association with 31 categories of parental occupation were investigated in the framework of the United Kingdom Childhood Cancer Study (McKinney *et al.*, 2003). In total, 3838 cases, including 1737 cases of leukaemia (1461 acute lymphoblastic leukaemia) and 687 cases of central nervous system cancer, and 7629 randomly selected controls (1:2 matched by sex, age and area) participated. The response rate was 87% for case and 64% for control parents. Personal interviews including a complete occupational history were conducted with each parent; surrogate information was collected mainly from spouses if one parent could not be contacted. Occupations were classified according to standard schemes, and further categorized into 31 occupational exposure groups using a JEM. Paternal exposures to exhaust fumes and inhaled particulate hydrocarbons, as well as occupation as a driver showed small but statistically significant associations with childhood leukaemia and the subgroup of acute lymphoblastic leukaemia. The odds ratio for exhaust fumes was 1.33 (95% CI, 1.09–1.61) for leukaemia and slightly lower for acute lymphoblastic leukaemia. The odds ratio for occupation as driver and leukaemia was 1.36 (95% CI, 1.10–1.68). The risks for maternal exposures and leukaemia were non-significantly elevated. The number of cases of central nervous system cancer with exposed mothers was very small and the odds ratios were not notably elevated for fathers employed as drivers or with exposure to exhaust. [The Working Group noted a substantial overlap between the three different indicators of exposure (exhaust, inhaled particulate hydrocarbons and occupation as a driver). Specific exposure to diesel or gasoline exhaust was not assessed in the study.]

A case–control study of children with acute lymphoblastic leukaemia was conducted in Australia (Reid *et al.*, 2011). Parents of 511 cases (response rate, 80%; diagnosis in 2003–06) and of 2071 population controls (response rate, 70%) completed a written questionnaire and were interviewed in greater detail if they had worked in one of 14 occupations. Information on parental exposure to specific chemicals, including exhausts, during different time periods around the birth of the children was assessed through the use of job-specific modules; probability, frequency and intensity of exposure was estimated by an expert industrial hygienist, and grouped exposure variables were created. The odds ratio was 2.06 (95%

CI, 0.97–4.39) for maternal exposure to moderate/high levels of diesel exhaust any time before the child's birth and 1.59 (95% CI, 0.58–4.41) for maternal exposure to petrol exhaust before birth. Paternal pre-birth exposure to diesel exhaust was associated with an increased odds ratio of 1.24 (95% CI, 0.91–1.69); for paternal pre-birth exposure to moderate/substantial petrol exhaust, the odds ratio was 1.20 (95% CI, 0.82–1.77). [The Working Group noted that this study provided improved exposure assessments in relation to most of the earlier studies and showed some evidence of an increased risk for acute lymphoblastic leukaemia associated with prenatal parental exposure to exhausts. However, the numbers of exposed cases were small in some of the exposure categories.]

References

Adegoke OJ, Blair A, Shu XO *et al.* (2003). Occupational history and exposure and the risk of adult leukemia in Shanghai. *Ann Epidemiol*, 13: 485–494. doi:10.1016/S1047-2797(03)00037-1 PMID:12932623

Ahmad MR & Pervaiz MK (2011). Occupational risk factors of urinary bladder cancer among men in Punjub, Pakistan. *Med Channel*, 17: 9–12.

Attfield MD, Schleiff PL, Lubin JH *et al.* (2012). The Diesel Exhaust in Miners Study: A Cohort Mortality Study With Emphasis on Lung Cancer. *J Natl Cancer Inst*, 104: 869–883 PMID:22393207

Axelson O & Steenland K (1988). Indirect methods of assessing the effects of tobacco use in occupational studies. *Am J Ind Med*, 13: 105–118. doi:10.1002/ajim.4700130107 PMID:3344750

Balarajan R & McDowall ME (1988). Professional drivers in London: a mortality study. *Br J Ind Med*, 45: 483–486. PMID:3395584

Band PR, Le ND, MacArthur AC *et al.* (2005). Identification of occupational cancer risks in British Columbia: a population-based case-control study of 1129 cases of bladder cancer. *J Occup Environ Med*, 47: 854–858. PMID:16093936

Bender AP, Parker DL, Johnson RA *et al.* (1989). Minnesota Highway Maintenance Worker Study: cancer mortality. *Am J Ind Med*, 15: 545–556. doi:10.1002/ajim.4700150507 PMID:2741960

Bhatia R, Lopipero P, Smith AH (1998). Diesel exhaust exposure and lung cancer. *Epidemiology*, 9: 84–91. doi:10.1097/00001648-199801000-00017 PMID:9430274

Birdsey J, Alterman T, Li J *et al.* (2010). Mortality among members of a truck driver trade association. *AAOHN J*, 58: 473–480. doi:10.3928/08910162-20101018-01 PMID:20964270

Blair A, Zheng T, Linos A *et al.* (2001). Occupation and leukemia: a population-based case-control study in Iowa and Minnesota. *Am J Ind Med*, 40: 3–14. doi:10.1002/ajim.1066 PMID:11439392

Blot WJ, Davies JE, Brown LM *et al.* (1982). Occupation and the high risk of lung cancer in Northeast Florida. *Cancer*, 50: 364–371. doi:10.1002/1097-0142(19820715)50:2<364::AID-CNCR2820500234>3.0.CO;2-Q PMID:7083144

Boers D, Zeegers MP, Swaen GM *et al.* (2005). The influence of occupational exposure to pesticides, polycyclic aromatic hydrocarbons, diesel exhaust, metal dust, metal fumes, and mineral oil on prostate cancer: a prospective cohort study. *Occup Environ Med*, 62: 531–537. doi:10.1136/oem.2004.018622 PMID:16046605

Boffetta P, Dosemeci M, Gridley G *et al.* (2001). Occupational exposure to diesel engine emissions and risk of cancer in Swedish men and women. *Cancer Causes Control*, 12: 365–374. doi:10.1023/A:1011262105972 PMID:11456233

Boffetta P, Harris RE, Wynder EL (1990). Case-control study on occupational exposure to diesel exhaust and lung cancer risk. *Am J Ind Med*, 17: 577–591. doi:10.1002/ajim.4700170504 PMID:1692445

Boffetta P & Silverman DT (2001). A meta-analysis of bladder cancer and diesel exhaust exposure. *Epidemiology*, 12: 125–130. doi:10.1097/00001648-200101000-00021 PMID:11138807

Boffetta P, Stellman SD, Garfinkel L (1988). Diesel exhaust exposure and mortality among males in the American Cancer Society prospective study. *Am J Ind Med*, 14: 403–415. doi:10.1002/ajim.4700140405 PMID:3189356

Boffetta P, Stellman SD, Garfinkel L (1989). A case-control study of multiple myeloma nested in the American Cancer Society prospective study. *Int J Cancer*, 43: 554–559. doi:10.1002/ijc.2910430404 PMID:2703267

Bonassi S, Merlo F, Pearce N, Puntoni R (1989). Bladder cancer and occupational exposure to polycyclic aromatic hydrocarbons. *Int J Cancer*, 44: 648–651. doi:10.1002/ijc.2910440415 PMID:2793238

Brooks DR, Geller AC, Chang J, Miller DR (1992). Occupation, smoking, and the risk of high-grade invasive bladder cancer in Missouri. *Am J Ind Med*, 21: 699–713. doi:10.1002/ajim.4700210510 PMID:1609816

Brown LM, Mason TJ, Pickle LW *et al.* (1988). Occupational risk factors for laryngeal cancer on the Texas Gulf Coast. *Cancer Res*, 48: 1960–1964. PMID:3349470

Brownson RC, Chang JC, Davis JR (1987). Occupation, smoking, and alcohol in the epidemiology of bladder cancer. *Am J Public Health*, 77: 1298–1300. doi:10.2105/AJPH.77.10.1298 PMID:3631363

Brüske-Hohlfeld I, Möhner M, Ahrens W *et al.* (1999). Lung cancer risk in male workers occupationally exposed to diesel motor emissions in Germany. *Am J Ind Med*, 36: 405–414. doi:10.1002/(SICI)1097-0274(199910)36:4<405::AID-AJIM1>3.0.CO;2-W PMID:10470005

Burns PB & Swanson GM (1991). Risk of urinary bladder cancer among blacks and whites: the role of cigarette use and occupation. *Cancer Causes Control*, 2: 371–379. doi:10.1007/BF00054297 PMID:1764561

Cassidy A, Wang W, Wu X, Lin J (2009). Risk of urinary bladder cancer: a case-control analysis of industry and occupation. *BMC Cancer*, 9: 443 doi:10.1186/1471-2407-9-443 PMID:20003537

Claude JC, Frentzel-Beyme RR, Kunze E (1988). Occupation and risk of cancer of the lower urinary tract among men. A case-control study. *Int J Cancer*, 41: 371–379. doi:10.1002/ijc.2910410309 PMID:3346100

Clavel J, Mandereau L, Cordier S *et al.* (1995). Hairy cell leukaemia, occupation, and smoking. *Br J Haematol*, 91: 154–161. doi:10.1111/j.1365-2141.1995.tb05261.x PMID:7577624

Coggon D, Pannett B, Acheson ED (1984). Use of job-exposure matrix in an occupational analysis of lung and bladder cancers on the basis of death certificates. *J Natl Cancer Inst*, 72: 61–65. PMID:6363790

Coggon D, Pannett B, Osmond C, Acheson ED (1986). A survey of cancer and occupation in young and middle aged men. II. Non-respiratory cancers. *Br J Ind Med*, 43: 381–386. PMID:3718882

Colt JS, Baris D, Stewart P *et al.* (2004). Occupation and bladder cancer risk in a population-based case-control study in New Hampshire. *Cancer Causes Control*, 15: 759–769. doi:10.1023/B:CACO.0000043426.28741.a2 PMID:15456989

Colt JS, Karagas MR, Schwenn M *et al.* (2011). Occupation and bladder cancer in a population-based case-control study in Northern New England. *Occup Environ Med*, 68: 239–249. doi:10.1136/oem.2009.052571 PMID:20864470

Cordier S, Clavel J, Limasset JC *et al.* (1993). Occupational risks of bladder cancer in France: a multicentre case-control study. *Int J Epidemiol*, 22: 403–411. doi:10.1093/ije/22.3.403 PMID:8359955

Cordier S, Mandereau L, Preston-Martin S *et al.* (2001). Parental occupations and childhood brain tumors: results of an international case-control study. *Cancer Causes Control*, 12: 865–874. doi:10.1023/A:1012277703631 PMID:11714115

Correa P, Pickle L, Fontham E *et al.* (1984). *The Causes of Lung Cancer in Louisiana*. In: *Lung cancer Causes and Prevention*. Mizell M, Correa P, editors. Berlin, Germany: Verlag Chemie International Inc., pp. 83–89.

Decouflé P, Stanislawczyk K, Houten L *et al.* (1977). *A Retrospective Survey of Cancer in Relation to Occupation*. Cincinnati, OH, USA: National Institute for Occupational Safety and Health.

Demers PA, Vaughan TL, Koepsell TD *et al.* (1993). A case-control study of multiple myeloma and occupation. *Am J Ind Med*, 23: 629–639. doi:10.1002/ajim.4700230410 PMID:8338527

Dolin PJ & Cook-Mozaffari P (1992). Occupation and bladder cancer: a death-certificate study. *Br J Cancer*, 66: 568–578. doi:10.1038/bjc.1992.316 PMID:1520596

Dryson E, 't Mannetje A, Walls C *et al.* (2008). Case-control study of high risk occupations for bladder cancer in New Zealand. *Int J Cancer*, 122: 1340–1346. doi:10.1002/ijc.23194 PMID:18027852

Elci OC, Akpinar-Elci M, Blair A, Dosemeci M (2003). Risk of laryngeal cancer by occupational chemical exposure in Turkey. *J Occup Environ Med*, 45: 1100–1106. doi:10.1097/01.jom.0000085890.50021.6f PMID:14534452

Emmelin A, Nyström L, Wall S (1993). Diesel exhaust exposure and smoking: a case-referent study of lung cancer among Swedish dock workers. *Epidemiology*, 4: 237–244. doi:10.1097/00001648-199305000-00007 PMID:7685637

EPA (2009). *Integrated Science Assessment for Particulate Matter (Final Report).* Washington, DC: US Environmental Protection Agency, EPA/600/R-08/139F.

Eriksson M & Karlsson M (1992). Occupational and other environmental factors and multiple myeloma: a population based case-control study. *Br J Ind Med*, 49: 95–103. PMID:1536825

Fabia J & Thuy TD (1974). Occupation of father at time of birth of children dying of malignant diseases. *Br J Prev Soc Med*, 28: 98–100. PMID:4853418

Fang R, Le N, Band P (2011). Identification of occupational cancer risks in British Columbia, Canada: a population-based case-control study of 1,155 cases of colon cancer. *Int J Environ Res Public Health*, 8: 3821–3843. doi:10.3390/ijerph8103821 PMID:22073015

Flodin U, Fredriksson M, Persson B (1987). Multiple myeloma and engine exhausts, fresh wood, and creosote: a case-referent study. *Am J Ind Med*, 12: 519–529. doi:10.1002/ajim.4700120506 PMID:2446496

Flodin U, Fredriksson M, Persson B, Axelson O (1988). Chronic lymphatic leukaemia and engine exhausts, fresh wood, and DDT: a case-referent study. *Br J Ind Med*, 45: 33–38. PMID:2449239

Fritschi L, Glass DC, Tabrizi JS *et al.* (2007). Occupational risk factors for prostate cancer and benign prostatic hyperplasia: a case-control study in Western Australia. *Occup Environ Med*, 64: 60–65. doi:10.1136/oem.2006.027706 PMID:17018583

Gaertner RR, Trpeski L, Johnson KC; Canadian Cancer Registries Epidemiology Research Group (2004). A case-control study of occupational risk factors for bladder cancer in Canada. *Cancer Causes Control*,

15: 1007–1019. doi:10.1007/s10552-004-1448-7 PMID:15801485

Garshick E, Laden F, Hart JE *et al.* (2004). Lung cancer in railroad workers exposed to diesel exhaust. *Environ Health Perspect*, 112: 1539–1543. doi:10.1289/ehp.7195 PMID:15531439

Garshick E, Laden F, Hart JE *et al.* (2006). Smoking imputation and lung cancer in railroad workers exposed to diesel exhaust. *Am J Ind Med*, 49: 709–718. doi:10.1002/ajim.20344 PMID:16767725

Garshick E, Laden F, Hart JE *et al.* (2008). Lung cancer and vehicle exhaust in trucking industry workers. *Environ Health Perspect*, 116: 1327–1332. doi:10.1289/ehp.11293 PMID:18941573

Garshick E, Laden F, Hart JE *et al.* (2012). Lung cancer and elemental carbon exposure in trucking industry workers. *Environ Health Perspect*, 120: 1301–1306. doi:10.1289/ehp.1204989 PMID:22739103

Garshick E, Schenker MB, Muñoz A *et al.* (1987). A case-control study of lung cancer and diesel exhaust exposure in railroad workers. *Am Rev Respir Dis*, 135: 1242–1248. PMID:3592400

Garshick E, Schenker MB, Munoz A *et al.* (1988). A retrospective cohort study of diesel exhaust exposure and lung cancer in railroad workers. *Am Rev Respir Dis*, 137: 820–825. PMID:3354987

Gérin M, Siemiatycki J, Kemper H, Bégin D (1985). Obtaining occupational exposure histories in epidemiologic case-control studies. *J Occup Med*, 27: 420–426. PMID:4020500

Gold EB, Diener MD, Szklo M (1982). Parental occupations and cancer in children–a case-control study and review of the methodologic issues. *J Occup Med*, 24: 578–584. doi:10.1097/00043764-198208000-00011 PMID:6750059

Goldberg MS, Parent ME, Siemiatycki J *et al.* (2001). A case-control study of the relationship between the risk of colon cancer in men and exposures to occupational agents. *Am J Ind Med*, 39: 531–546. doi:10.1002/ajim.1052 PMID:11385637

González CA, López-Abente G, Errezola M *et al.* (1989). Occupation and bladder cancer in Spain: a multicentre case-control study. *Int J Epidemiol*, 18: 569–577. doi:10.1093/ije/18.3.569 PMID:2681016

Gubéran E, Usel M, Raymond L *et al.* (1992). Increased risk for lung cancer and for cancer of the gastrointestinal tract among Geneva professional drivers. *Br J Ind Med*, 49: 337–344. PMID:1376139

Guo J, Kauppinen T, Kyyrönen P *et al.* (2004a). Occupational exposure to diesel and gasoline engine exhausts and risk of lung cancer among Finnish workers. *Am J Ind Med*, 45: 483–490. doi:10.1002/ajim.20013 PMID:15164392

Guo J, Kauppinen T, Kyyrönen P *et al.* (2004b). Risk of esophageal, ovarian, testicular, kidney and bladder cancers and leukemia among Finnish workers exposed to diesel or gasoline engine exhaust. *Int J Cancer*, 111: 286–292. doi:10.1002/ijc.20263 PMID:15197784

Gustafsson L, Wall S, Larsson LG, Skog B (1986). Mortality and cancer incidence among Swedish dock workers–a retrospective cohort study. *Scand J Work Environ Health*, 12: 22–26. doi:10.5271/sjweh.2178 PMID:3961438

Gustavsson P, Jakobsson R, Nyberg F *et al.* (2000). Occupational exposure and lung cancer risk: a population-based case-referent study in Sweden. *Am J Epidemiol*, 152: 32–40. doi:10.1093/aje/152.1.32 PMID:10901327

Gustavsson P, Plato N, Lidström EB, Hogstedt C (1990). Lung cancer and exposure to diesel exhaust among bus garage workers. *Scand J Work Environ Health*, 16: 348–354. doi:10.5271/sjweh.1780 PMID:1701566

Hakulinen T, Salonen T, Teppo L (1976). Cancer in the offspring of fathers in hydrocarbon-related occupations. *Br J Prev Soc Med*, 30: 138–140. PMID:953378

Hall NE & Wynder EL (1984). Diesel exhaust exposure and lung cancer: a case–control study. *Environ Res*, 34: 77–86. doi:10.1016/0013-9351(84)90077-X PMID:6202502

Hansen ES (1993). A follow-up study on the mortality of truck drivers. *Am J Ind Med*, 23: 811–821. doi:10.1002/ajim.4700230514 PMID:7685146

Hayes RB, Thomas T, Silverman DT *et al.* (1989). Lung cancer in motor exhaust-related occupations. *Am J Ind Med*, 16: 685–695. PMID:2480711

Heineman EF, Olsen JH, Pottern LM *et al.* (1992). Occupational risk factors for multiple myeloma among Danish men. *Cancer Causes Control*, 3: 555–568. doi:10.1007/BF00052753 PMID:1420859

Hemminki K, Saloniemi I, Salonen T *et al.* (1981). Childhood cancer and parental occupation in Finland. *J Epidemiol Community Health*, 35: 11–15. doi:10.1136/jech.35.1.11 PMID:7264527

Hoar SK & Hoover R (1985). Truck driving and bladder cancer mortality in rural New England. *J Natl Cancer Inst*, 74: 771–774. PMID:3857373

Hours M, Dananche B, Fevotte J *et al.* (1994). Bladder cancer and occupational exposures. *Scand J Work Environ Health*, 20: 322–330. doi:10.5271/sjweh.1390 PMID:7863295

Howe GR, Burch JD, Miller AB *et al.* (1980). Tobacco use, occupation, coffee, various nutrients, and bladder cancer. *J Natl Cancer Inst*, 64: 701–713. PMID:6928984

Howe GR, Fraser D, Lindsay J *et al.* (1983). Cancer mortality (1965–77) in relation to diesel fume and coal exposure in a cohort of retired railway workers. *J Natl Cancer Inst*, 70: 1015–1019. PMID:6574269

IARC (1989). Diesel and gasoline engine exhausts and some nitroarenes. *IARC Monogr Eval Carcinog Risks Hum*, 46: 1–458. PMID:2483415

Iscovich J, Castelletto R, Estève J *et al.* (1987). Tobacco smoking, occupational exposure and bladder cancer

in Argentina. *Int J Cancer*, 40: 734–740. doi:10.1002/ijc.2910400604 PMID:3692621

Iyer V, Harris RE, Wynder EL (1990). Diesel exhaust exposure and bladder cancer risk. *Eur J Epidemiol*, 6: 49–54. doi:10.1007/BF00155549 PMID:1693120

Jahn I, Ahrens W, Brüske-Hohlfeld I *et al.* (1999). Occupational risk factors for lung cancer in women: results of a case-control study in Germany. *Am J Ind Med*, 36: 90–100. doi:10.1002/(SICI)1097-0274(199907)36:1<90::AID-AJIM13>3.0.CO;2-V PMID:10361592

Järvholm B & Silverman D (2003). Lung cancer in heavy equipment operators and truck drivers with diesel exhaust exposure in the construction industry. *Occup Environ Med*, 60: 516–520. doi:10.1136/oem.60.7.516 PMID:12819286

Jensen OM, Wahrendorf J, Knudsen JB, Sørensen BL (1987). The Copenhagen case-referent study on bladder cancer. Risks among drivers, painters and certain other occupations. *Scand J Work Environ Health*, 13: 129–134. doi:10.5271/sjweh.2070 PMID:3602967

Kantor AF, Curnen MG, Meigs JW, Flannery JT (1979). Occupations of fathers of patients with Wilms's tumour. *J Epidemiol Community Health*, 33: 253–256. doi:10.1136/jech.33.4.253 PMID:231629

Karunanayake CP, McDuffie HH, Dosman JA *et al.* (2008). Occupational exposures and non-Hodgkin's lymphoma: Canadian case-control study. *Environ Health*, 7: 44 doi:10.1186/1476-069X-7-44 PMID:18687133

Kellen E, Zeegers M, Lousbergh D *et al.* (2005). A Belgian case control study on bladder cancer: Rationale and design. *Arch Public Health*, 63: 17–34.

Kellen E, Zeegers M, Paulussen A *et al.* (2007). Does occupational exposure to PAHs, diesel and aromatic amines interact with smoking and metabolic genetic polymorphisms to increase the risk on bladder cancer? The Belgian case control study on bladder cancer risk. *Cancer Lett*, 245: 51–60. doi:10.1016/j.canlet.2005.12.025 PMID:16504378

Kogevinas M, 't Mannetje A, Cordier S *et al.* (2003). Occupation and bladder cancer among men in Western Europe. *Cancer Causes Control*, 14: 907–914. doi:10.1023/B:CACO.0000007962.19066.9c PMID:14750529

Kwa SL & Fine LJ (1980). The association between parental occupation and childhood malignancy. *J Occup Med*, 22: 792–794. doi:10.1097/00043764-198012000-00012 PMID:7218055

Laden F, Hart JE, Eschenroeder A *et al.* (2006). Historical estimation of diesel exhaust exposure in a cohort study of U.S. railroad workers and lung cancer. *Cancer Causes Control*, 17: 911–919. doi:10.1007/s10552-006-0027-5 PMID:16841258

Laden F, Hart JE, Smith TJ *et al.* (2007). Cause-specific mortality in the unionized U.S. trucking industry. *Environ Health Perspect*, 115: 1192–1196. doi:10.1289/ehp.10027 PMID:17687446

Larkin EK, Smith TJ, Stayner L *et al.* (2000). Diesel exhaust exposure and lung cancer: adjustment for the effect of smoking in a retrospective cohort study. *Am J Ind Med*, 38: 399–409. doi:10.1002/1097-0274(200010)38:4<399::AID-AJIM5>3.0.CO;2-D PMID:10982980

Lee WJ, Baris D, Järvholm B *et al.* (2003). Multiple myeloma and diesel and other occupational exposures in Swedish construction workers. *Int J Cancer*, 107: 134–138. doi:10.1002/ijc.11351 PMID:12925968

Lindquist R, Nilsson B, Eklund G, Gahrton G (1991). Acute leukemia in professional drivers exposed to gasoline and diesel. *Eur J Haematol*, 47: 98–103. doi:10.1111/j.1600-0609.1991.tb00129.x PMID:1889488

Lipsett M & Campleman S (1999). Occupational exposure to diesel exhaust and lung cancer: a meta-analysis. *Am J Public Health*, 89: 1009–1017. doi:10.2105/AJPH.89.7.1009 PMID:10394308

Mahjub H & Sadri GH (2006). Meta-analysis of case-referent studies of specific environmental or occupational pollutants on lung cancer. *Indian J Cancer*, 43: 169–173. doi:10.4103/0019-509X.29422 PMID:17192688

Manju L, George PS, Mathew A (2009). Urinary bladder cancer risk among motor vehicle drivers: a meta-analysis of the evidence, 1977–2008. *Asian Pac J Cancer Prev*, 10: 287–294. PMID:19537898

McDuffie HH, Pahwa P, Spinelli JJ *et al.* (2002). Canadian male farm residents, pesticide safety handling practices, exposure to animals and non-Hodgkin's lymphoma (NHL). *Am J Ind Med*, Suppl 2: 54–61. doi:10.1002/ajim.10041 PMID:12210683

McKinney PA, Fear NT, Stockton D; UK Childhood Cancer Study Investigators (2003). Parental occupation at periconception: findings from the United Kingdom Childhood Cancer Study. *Occup Environ Med*, 60: 901–909. doi:10.1136/oem.60.12.901 PMID:14634180

Menck HR & Henderson BE (1976). Occupational differences in rates of lung cancer. *J Occup Med*, 18: 797–801. doi:10.1097/00043764-197612000-00005 PMID:993873

Mirabelli D, Chiusolo M, Calisti R *et al.* (2001). [Database of occupations and industrial activities that involve the risk of pulmonary tumors] *Epidemiol Prev*, 25: 215–221. PMID:11789462

Muscat JE & Wynder EL (1995). Diesel exhaust, diesel fumes, and laryngeal cancer. *Otolaryngol Head Neck Surg*, 112: 437–440. doi:10.1016/S0194-5998(95)70280-6 PMID:7870446

Neumeyer-Gromen A, Razum O, Kersten N *et al.* (2009). Diesel motor emissions and lung cancer mortality–results of the second follow-up of a cohort study in potash miners. *Int J Cancer*, 124: 1900–1906. doi:10.1002/ijc.24127 PMID:19123464

Nokso-Koivisto P & Pukkala E (1994). Past exposure to asbestos and combustion products and incidence

of cancer among Finnish locomotive drivers. *Occup Environ Med*, 51: 330–334. doi:10.1136/oem.51.5.330 PMID:8199683

Notani PN, Shah P, Jayant K, Balakrishnan V (1993). Occupation and cancers of the lung and bladder: a case-control study in Bombay. *Int J Epidemiol*, 22: 185–191. doi:10.1093/ije/22.2.185 PMID:8505172

Ojajärvi IA, Partanen TJ, Ahlbom A *et al.* (2000). Occupational exposures and pancreatic cancer: a meta-analysis. *Occup Environ Med*, 57: 316–324. doi:10.1136/oem.57.5.316 PMID:10769297

Olsson AC, Gustavsson P, Kromhout H *et al.* (2011). Exposure to diesel motor exhaust and lung cancer risk in a pooled analysis from case-control studies in Europe and Canada. *Am J Respir Crit Care Med*, 183: 941–948. doi:10.1164/rccm.201006-0940OC PMID:21037020

Parent ME, Rousseau MC, Boffetta P *et al.* (2007). Exposure to diesel and gasoline engine emissions and the risk of lung cancer. *Am J Epidemiol*, 165: 53–62. doi:10.1093/aje/kwj343 PMID:17062632

Pesch B, Haerting J, Ranft U *et al.* (2000). Occupational risk factors for urothelial carcinoma: agent-specific results from a case-control study in Germany. MURC Study Group. Multicenter Urothelial and Renal Cancer. *Int J Epidemiol*, 29: 238–247. doi:10.1093/ije/29.2.238 PMID:10817119

Petersen A, Hansen J, Olsen JH, Netterstrøm B (2010). Cancer morbidity among Danish male urban bus drivers: A historical cohort study. *Am J Ind Med*, 53: 757–761. PMID:20583138

Pintos J, Parent M-E, Richardson L, Siemiatycki J (2012). Occupational exposure to diesel engine emissions, and risk of lung cancer: evidence from two case-control studies in Montreal, Canada. *J Occup Med*, 69: 787–792. doi:10.1136/oemed-2012-100964 PMID:22843434

Pohlabeln H, Jöckel KH, Bolm-Audorff U (1999). Non-occupational risk factors for cancer of the lower urinary tract in Germany. *Eur J Epidemiol*, 15: 411–419. doi:10.1023/A:1007595809278 PMID:10442466

Porru S, Aulenti V, Donato F *et al.* (1996). Bladder cancer and occupation: a case-control study in northern Italy. *Occup Environ Med*, 53: 6–10. doi:10.1136/oem.53.1.6 PMID:8563860

Pottern LM, Heineman EF, Olsen JH *et al.* (1992). Multiple myeloma among Danish women: employment history and workplace exposures. *Cancer Causes Control*, 3: 427–432. doi:10.1007/BF00051355 PMID:1525323

Rafnsson V & Gunnarsdóttir H (1991). Mortality among professional drivers. *Scand J Work Environ Health*, 17: 312–317. doi:10.5271/sjweh.1697 PMID:1947916

Rebelakos A, Trichopoulos D, Tzonou A *et al.* (1985). Tobacco smoking, coffee drinking, and occupation as risk factors for bladder cancer in Greece. *J Natl Cancer Inst*, 75: 455–461. PMID:3861898

Reid A, Glass DC, Bailey HD *et al.* (2011). Parental occupational exposure to exhausts, solvents, glues and paints, and risk of childhood leukemia. *Cancer Causes Control*, 22: 1575–1585. doi:10.1007/s10552-011-9834-4 PMID:21866372

Reulen RC, Kellen E, Buntinx F *et al.* (2008). A meta-analysis on the association between bladder cancer and occupation. *Scand J Urol Nephrol Suppl*, 42: 64–78. doi:10.1080/03008880802325192 PMID:18815919

Reulen RC, Reulin E, Buntinx F, Zeegers MP (2007). Bladder cancer and occupation: a report from the Belgian case-control study on bladder cancer risk. *Am J Ind Med*, 50: 449–454. doi:10.1002/ajim.20469 PMID:17450546

Richardson K, Band PR, Astrakianakis G, Le ND (2007). Male bladder cancer risk and occupational exposure according to a job-exposure matrix-a case-control study in British Columbia, Canada. *Scand J Work Environ Health*, 33: 454–464. doi:10.5271/sjweh.1169 PMID:18327514

Richiardi L, Mirabelli D, Calisti R *et al.* (2006). Occupational exposure to diesel exhausts and risk for lung cancer in a population-based case-control study in Italy. *Ann Oncol*, 17: 1842–1847. doi:10.1093/annonc/mdl307 PMID:16971668

Risch HA, Burch JD, Miller AB *et al.* (1988). Occupational factors and the incidence of cancer of the bladder in Canada. *Br J Ind Med*, 45: 361–367. PMID:3395572

Samanic CM, Kogevinas M, Silverman DT *et al.* (2008). Occupation and bladder cancer in a hospital-based case-control study in Spain. *Occup Environ Med*, 65: 347–353. doi:10.1136/oem.2007.035816 PMID:17951336

Samet JM, Cohen AJ (2006). *Air pollution and cancer*. In *Cancer epidemiology and prevention*. Schottenfeld D, Fraumeni JF, editors. New York: Oxford University Press.

Santibañez M, Vioque J, Alguacil J *et al.* (2010). Occupational exposures and risk of pancreatic cancer. *Eur J Epidemiol*, 25: 721–730. doi:10.1007/s10654-010-9490-0 PMID:20640489

Säverin R, Bräunlich A, Dahmann D *et al.* (1999). Diesel exhaust and lung cancer mortality in potash mining. *Am J Ind Med*, 36: 415–422. doi:10.1002/(SICI)1097-0274(199910)36:4<415::AID-AJIM2>3.0.CO;2-Q PMID:10470006

Schenker MB, Smith T, Muñoz A *et al.* (1984). Diesel exposure and mortality among railway workers: results of a pilot study. *Br J Ind Med*, 41: 320–327. PMID:6743578

Schifflers E, Jamart J, Renard V (1987). Tobacco and occupation as risk factors in bladder cancer: a case-control study in southern Belgium. *Int J Cancer*, 39: 287–292. doi:10.1002/ijc.2910390304 PMID:3818120

Schlesselman JJ (1978). Assessing effects of confounding variables. *Am J Epidemiol*, 108: 3–8. PMID:685974

Schoenberg JB, Stemhagen A, Mason TJ *et al.* (1987). Occupation and lung cancer risk among New Jersey white males. *J Natl Cancer Inst*, 79: 13–21. PMID:3474440

Schoenberg JB, Stemhagen A, Mogielnicki AP *et al.* (1984). Case-control study of bladder cancer in New Jersey. I. Occupational exposures in white males. *J Natl Cancer Inst*, 72: 973–981. PMID:6585596

Seidler A, Heiskel H, Bickeböller R, Elsner G (1998). Association between diesel exposure at work and prostate cancer. *Scand J Work Environ Health*, 24: 486–494. doi:10.5271/sjweh.373 PMID:9988091

Seniori Costantini AS, Miligi L, Kriebel D *et al.* (2001). A multicenter case-control study in Italy on hematolymphopoietic neoplasms and occupation. *Epidemiology*, 12: 78–87. doi:10.1097/00001648-200101000-00014 PMID:11138825

Serra C, Bonfill X, Sunyer J *et al.*; Working Group on the Study of Bladder Cancer in the County of Vallès Occidental (2000). Bladder cancer in the textile industry. *Scand J Work Environ Health*, 26: 476–481. doi:10.5271/sjweh.571 PMID:11201394

Siemiatycki J, Dewar R, Nadon L, Gérin M (1994). Occupational risk factors for bladder cancer: results from a case-control study in Montreal, Quebec, Canada. *Am J Epidemiol*, 140: 1061–1080. PMID:7998589

Siemiatycki J, Gérin M, Stewart P *et al.* (1988). Associations between several sites of cancer and ten types of exhaust and combustion products. Results from a case-referent study in Montreal. *Scand J Work Environ Health*, 14: 79–90. doi:10.5271/sjweh.1949 PMID:2455336

Siemiatycki J, Wacholder S, Richardson L *et al.* (1987). Discovering carcinogens in the occupational environment. Methods of data collection and analysis of a large case-referent monitoring system. *Scand J Work Environ Health*, 13: 486–492. doi:10.5271/sjweh.2009 PMID:3433050

Silverman DT, Hoover RN, Albert S, Graff KM (1983). Occupation and cancer of the lower urinary tract in Detroit. *J Natl Cancer Inst*, 70: 237–245. PMID:6571931

Silverman DT, Hoover RN, Mason TJ, Swanson GM (1986). Motor exhaust-related occupations and bladder cancer. *Cancer Res*, 46: 2113–2116. PMID:2418962

Silverman DT, Levin LI, Hoover RN (1989b). Occupational risks of bladder cancer in the United States: II Nonwhite men. *J Natl Cancer Inst*, 81: 1480–1483. doi:10.1093/jnci/81.19.1480 PMID:2778835

Silverman DT, Levin LI, Hoover RN (1990). Occupational risks of bladder cancer among white women in the United States. *Am J Epidemiol*, 132: 453–461. PMID:2389750

Silverman DT, Levin LI, Hoover RN, Hartge P (1989a). Occupational risks of bladder cancer in the United States: I. White men. *J Natl Cancer Inst*, 81: 1472–1480. doi:10.1093/jnci/81.19.1472 PMID:2778834

Silverman DT, Samanic CM, Lubin JH *et al.* (2012). The Diesel Exhaust in Miners Study: A Nested Case-Control Study of Lung Cancer and Diesel Exhaust. *J Natl Cancer Inst*, 104: 855–868. PMID:22393209

Smith EM, Miller ER, Woolson RF, Brown CK (1985). Bladder cancer risk among auto and truck mechanics and chemically related occupations. *Am J Public Health*, 75: 881–883. doi:10.2105/AJPH.75.8.881 PMID:2411155

Soll-Johanning H, Bach E, Jensen SS (2003). Lung and bladder cancer among Danish urban bus drivers and tramway employees: a nested case-control study. *Occup Med (Lond)*, 53: 25–33. doi:10.1093/occmed/kqg004 PMID:12576562

Soll-Johanning H, Bach E, Olsen JH, Tüchsen F (1998). Cancer incidence in urban bus drivers and tramway employees: a retrospective cohort study. *Occup Environ Med*, 55: 594–598. doi:10.1136/oem.55.9.594 PMID:9861180

Steenland K, Burnett C, Osorio AM (1987). A case-control study of bladder cancer using city directories as a source of occupational data. *Am J Epidemiol*, 126: 247–257. doi:10.1093/aje/126.2.247 PMID:3605053

Steenland K, Deddens J, Stayner L (1998). Diesel exhaust and lung cancer in the trucking industry: exposure-response analyses and risk assessment. *Am J Ind Med*, 34: 220–228. doi:10.1002/(SICI)1097-0274(199809)34:3<220::AID-AJIM3>3.0.CO;2-Z PMID:9698990

Steenland NK, Silverman DT, Hornung RW (1990). Case-control study of lung cancer and truck driving in the Teamsters Union. *Am J Public Health*, 80: 670–674. doi:10.2105/AJPH.80.6.670 PMID:1693040

Steineck G, Plato N, Gerhardsson M *et al.* (1990). Increased risk of urothelial cancer in Stockholm during 1985–87 after exposure to benzene and exhausts. *Int J Cancer*, 45: 1012–1017. doi:10.1002/ijc.2910450605 PMID:1693598

Swanson GM, Lin CS, Burns PB (1993). Diversity in the association between occupation and lung cancer among black and white men. *Cancer Epidemiol Biomarkers Prev*, 2: 313–320. PMID:8348054

Tarvainen L, Kyyrönen P, Kauppinen T, Pukkala E (2008). Cancer of the mouth and pharynx, occupation and exposure to chemical agents in Finland [in 1971–95]. [in 1971–95]*Int J Cancer*, 123: 653–659. doi:10.1002/ijc.23286 PMID:18470913

Tola S, Tenho M, Korkala ML, Järvinen E (1980). Cancer of the urinary bladder in Finland: association with occupation. *Int Arch Occup Environ Health*, 46: 43–51. doi:10.1007/BF00377458 PMID:7380572

Tse LA, Yu IS, Au JS *et al.* (2011). Silica dust, diesel exhaust, and painting work are the significant occupational risk factors for lung cancer in nonsmoking Chinese men. *Br J Cancer*, 104: 208–213. doi:10.1038/sj.bjc.6606006 PMID:21102581

Tsoi CT & Tse LA (2012). Professional drivers and lung cancer: a systematic review and meta-analysis. *Occup Environ Med*, 69: 831–836. doi:10.1136/oemed-2012-100666 PMID:22767869

Van Den Eeden SK & Friedman GD (1993). Exposure to engine exhaust and risk of subsequent cancer. *J Occup Med*, 35: 307–311. PMID:7681109

van Steensel-Moll HA, Valkenburg HA, van Zanen GE (1985). Childhood leukemia and parental occupation. A register-based case-control study. *Am J Epidemiol*, 121: 216–224. PMID:3860001

Vasama-Neuvonen K, Pukkala E, Paakkulainen H *et al.* (1999). Ovarian cancer and occupational exposures in Finland. *Am J Ind Med*, 36: 83–89. doi:10.1002/(SICI)1097-0274(199907)36:1<83::AID-AJIM12>3.0.CO;2-Q PMID:10361591

Vianna NJ, Kovasznay B, Polan A, Ju C (1984). Infant leukemia and paternal exposure to motor vehicle exhaust fumes. *J Occup Med*, 26: 679–682. PMID:6207280

Villeneuve PJ, Parent MÉ, Sahni V, Johnson KC; Canadian Cancer Registries Epidemiology Research Group (2011). Occupational exposure to diesel and gasoline emissions and lung cancer in Canadian men. *Environ Res*, 111: 727–735. doi:10.1016/j.envres.2011.04.003 PMID:21536265

Vineis P & Magnani C (1985). Occupation and bladder cancer in males: a case-control study. *Int J Cancer*, 35: 599–606. doi:10.1002/ijc.2910350506 PMID:3997281

West RR, Stafford DA, Farrow A, Jacobs A (1995). Occupational and environmental exposures and myelodysplasia: a case-control study. *Leuk Res*, 19: 127–139. doi:10.1016/0145-2126(94)00141-V PMID:7869741

Wilkins JR 3rd & Sinks TH Jr (1984). Paternal occupation and Wilms' tumour in offspring. *J Epidemiol Community Health*, 38: 7–11. doi:10.1136/jech.38.1.7 PMID:6323612

Wong O, Harris F, Armstrong TW, Hua F (2010). A hospital-based case-control study of acute myeloid leukemia in Shanghai: analysis of environmental and occupational risk factors by subtypes of the WHO classification. *Chem Biol Interact*, 184: 112–128. doi:10.1016/j.cbi.2009.10.017 PMID:19900423

Wong O, Morgan RW, Kheifets L *et al.* (1985). Mortality among members of a heavy construction equipment operators union with potential exposure to diesel exhaust emissions. *Br J Ind Med*, 42: 435–448. PMID:2410010

Woskie SR, Smith TJ, Hammond SK *et al.* (1988a). Estimation of the diesel exhaust exposures of railroad workers: I. Current exposures. *Am J Ind Med*, 13: 381–394. doi:10.1002/ajim.4700130307 PMID:3354586

Woskie SR, Smith TJ, Hammond SK *et al.* (1988b). Estimation of the diesel exhaust exposures of railroad workers: II. National and historical exposures. *Am J Ind Med*, 13: 395–404. doi:10.1002/ajim.4700130308 PMID:3281456

Wynder EL, Dieck GS, Hall NE, Lahti H (1985). A case-control study of diesel exhaust exposure and bladder cancer. *Environ Res*, 37: 475–489. doi:10.1016/0013-9351(85)90129-X PMID:2410250

Yaris F, Dikici MF, Sabuncu HH, Yaris E (2006). A case-control study on the etiology of urinary bladder cancer in Istanbul, Turkey. *Asian Pac J Cancer Prev*, 7: 591–594. PMID:17250433

Zack M, Cannon S, Loyd D *et al.* (1980). Cancer in children of parents exposed to hydrocarbon-related industries and occupations. *Am J Epidemiol*, 111: 329–336. PMID:7361757

Zaebst DD, Clapp DE, Blade LM *et al.* (1991). Quantitative determination of trucking industry workers' exposures to diesel exhaust particles. *Am Ind Hyg Assoc J*, 52: 529–541. doi:10.1080/15298669191365162 PMID:1723577

Zeegers MP, Swaen GM, Kant I *et al.* (2001). Occupational risk factors for male bladder cancer: results from a population based case cohort study in the Netherlands. *Occup Environ Med*, 58: 590–596. doi:10.1136/oem.58.9.590 PMID:11511746

Zheng T, Blair A, Zhang Y *et al.* (2002). Occupation and risk of non-Hodgkin's lymphoma and chronic lymphocytic leukemia. *J Occup Environ Med*, 44: 469–474. doi:10.1097/00043764-200205000-00015 PMID:12024692