

**Table 2.3. Cohort studies of ethylene oxide and other cancers**

Reference, location	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustments and comments
<i>Stomach</i>							
Thiess <i>et al.</i> (1981) Germany	602 employees exposed to alkylene oxides and other substances, employed in 1928–80	Environmental monitoring	Stomach	All cohort members	4	[1.49] (NR)	
Hogstedt <i>et al.</i> (1979a, 1986); Hogstedt (1988) Sweden	89 operators with regular exposure to ethylene oxide and 78 maintenance staff with intermittent exposure, employed for ≥ 1 year at a chemical plant, followed 1962–85		Stomach	All cohort members	5	SMR 9.03 (2.9–21.1)	
Hogstedt (1988), Sweden	539 men employed for ≥ 1 year at a chemical plant followed 1960–85		Stomach	<i>Length of employment</i> 1–9 years ≥ 10 years All	4 6 10	SMR 5.97 (NR) 6.08 (NR) 6.02 (2.9–11.1)	
Kiesselbach <i>et al.</i> (1990) Germany	2658 employees from 6 chemical companies exposed to ethylene oxide for ≥ 12 months in 1928–82, followed to 31 December 1982		Stomach	All cohort members	14	SMR 1.38 (0.75–2.31)	No data on exposure levels; risk estimates may have been seriously biased since most deaths in cohort were not ascertained from death certificates.
Benson & Teta (1993) USA	278 men intermittently exposed to ethylene oxide in a chlorohydrin unit since 1949, followed to 1988		Stomach	All cohort members	1	[0.70] (0.2–3.92)	Primarily exposed to ethylene chlorohydrin, ethylene dichloride and bischloroethyl ether

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Teta <i>et al.</i> (1993) USA	1896 men potentially exposed to ethylene oxide since 1940 at 2 chemical plants but who never worked in chlorohydrin unit, followed to 1988		Stomach	All cohort members	8	SMR 1.60 (0.69–3.15)	
Hagmar <i>et al.</i> (1991, 1995) Sweden	2170 workers employed for ≥ 12 months during 1964–85 at 2 plants using medical equipment sterilized with ethylene oxide, followed for cancer incidence to 1990		Stomach	All cohort members Induction period of 10 years	0 0	SIR 0 (0–4.55) 0 (0–8.38)	
Norman <i>et al.</i> (1995) USA	1132 workers employed during 1974–80 at a sterilizing plant using ethylene oxide, followed for cancer incidence to 1957		Stomach	All cohort members	0	–	
Olsen <i>et al.</i> (1997), USA	1361 men employed for ≥ 1 year and potentially engaged for ≥ 1 month in ethylene or propylene chlorohydrin production since 1941 at 4 chemical plants, followed to 1992		Stomach	Ever in ethylene chlorohydrin production Ever in ethylene chlorohydrin production with allowance for 25-year induction period from first exposure	2 2	SMR 65 (8–234) [1.17 (0.14–4.23)]	
Coggon <i>et al.</i> (2004) United Kingdom	1471 workers in the production or use of ethylene oxide at 4 chemical companies during 1956–85, followed to 31 December 2000	Environmental and personal monitoring since 1977	Stomach	All cohort members Definite Probable Unknown	5 4 1 0	SMR [0.62 (0.20–1.46)] 0.78 (NR) 0.57 (NR) 0 (NR)	Update of Gardner <i>et al.</i> (1989) Measured TWA concentrations < 5 ppm [9 mg/m <sup>3</sup> ] in almost all jobs but with occasional peaks up to several hundred ppm; exposures probably higher in the past

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Steenland <i>et al.</i> (2004) USA	18254 workers at 14 industrial plants that used ethylene oxide for sterilization since 1943 with $\geq 3$ months exposure to ethylene oxide, followed to 1998	Exposure data over time based on a large number of measurements coupled with data of historical process changes, to quantitatively estimate cumulative exposure to ethylene oxide.	Stomach	All cohort members (Steenland <i>et al.</i> , 2004)	25	SMR 1.07 (0.74-1.49)	Update of Steenland <i>et al.</i> (1991) and Stayner <i>et al.</i> (1993)
				<i>Cumulative exposure in ppm-days</i>			
				< 1200	5	1.74 (0.57-4.07)	
				1200-8500	4	1.24 (0.29-2.60)	
				> 8500	1	0.23 (0.11-1.32)	
Total	10	0.90 (0.43-1.66)	(Stayner <i>et al.</i> , 1993) <i>p</i> trend = 0.04				
Ambroise <i>et al.</i> (2005) France	181 male workers employed as pest-control workers 1979-94, followed for mortality through to 2000		Stomach	All cohort members	1	SMR 3.18 (0.08-17.70)	No information available on individual level of exposures to pesticides, rodenticides or formaldehyde
<i>Brain</i>							
Thiess <i>et al.</i> (1981), Germany	602 employees exposed to alkylene oxides and other substances, employed in 1928-80	Environmental monitoring	Malignant tumour of the brain	<i>Duration of exposure</i>			
				0.5-4 years	0	NR	
				5-9 years	0	NR	
				10-19 years	0	NR	
				$\geq 20$ years	1	[41.7] (NR)	
Hagmar <i>et al.</i> (1991), Sweden	2170 workers employed for $\geq 12$ months in 1964-85 at 2 plants using medical equipment sterilized with ethylene oxide, followed for cancer incidence to 1990		Brain	All cohort members	4	SIR 1.69 (0.46-4.34)	
				All cohort members $\geq 0.14$ ppm-years	3	3.80 (0.78-11.1)	
				Induction period of 10 years	3	2.80 (0.58-8.19)	

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Benson & Teta (1993) USA	278 men intermittently exposed to ethylene oxide in a chlorohydrin unit since 1949, followed to 1988		Brain and other nervous system	All cohort members	1	[1.17] (0.3–6.56)	Primarily exposed to ethylene chlorohydrin, ethylene dichloride and bischloroethyl ether
Teta <i>et al.</i> (1993) USA	1896 men potentially exposed to ethylene oxide since 1940 at 2 chemical plants who never worked in chlorohydrin unit, followed to 1988		Brain and other nervous system	All cohort members		SMR 1.50 (0.55–3.27)	
Steenland <i>et al.</i> (1994) USA	18 254 workers employed at 14 industrial plants using ethylene oxide for sterilization since 1943 with ≥ 3 months exposure to ethylene oxide, followed to 1998	Exposure data over time based on a large number of measurements coupled with data of historical process changes, to quantitatively estimate cumulative exposure to ethylene oxide.	Brain	All cohort members <i>Cumulative exposure in ppm-days</i> < 1200 1200–8500 > 8500 Total	14 0 4 2 6	SMR 0.59 (0.36–0.91) 0.0 0.99 (0.27–2.53) 0.59 (0.07–2.12) 0.54 (0.20–1.18) <i>p</i> -trend = 0.43	Update of Steenland <i>et al.</i> (1991) and Stayner <i>et al.</i> (1993)
Norman <i>et al.</i> (1995) USA	1132 workers employed during 1974–80 at a sterilizing plant using ethylene oxide, followed for cancer incidence to 1957		Brain	All cohort members	0	–	
Olsen <i>et al.</i> (1997) USA	1361 men employed for ≥ 1 year and potentially engaged for ≥ 1 month in ethylene or propylene chlorohydrin production since 1941 at 4 chemical plants, followed to 1992		Brain and other nervous system (191–192)	Ever in ethylene chlorohydrin production  Ever in ethylene chlorohydrin production with allowance for 25-year induction period from first exposure	3  3	SMR 1.23 (0.25–3.58)  [2.73 (0.56–7.97)]	

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<i>Pancreas</i>							
Hagmar <i>et al.</i> (1991, 1995) Sweden	2170 workers employed for ≥ 12 months during 1964–85 at 2 plants where medical equipment was sterilized with ethylene oxide, followed for cancer incidence to 1990		Pancreas	All cohort members All cohort members ≥ 0.14 ppm-years Induction period of 10 years	2 1 1	SIR 2.47 (0.30–8.92) 2.86 (0.07–15.9) 2.22 (0.06–12.4)	
Benson & Teta (1993) USA	278 men intermittently exposed to ethylene oxide in a chlorohydrin unit since 1949, followed to 1988		Pancreas	All cohort members	8	4.92 (1.58–11.40)	Primarily exposed to ethylene chlorohydrin, ethylene dichloride and bischloroethyl ether
Teta <i>et al.</i> (1993) USA	1896 men potentially exposed to ethylene oxide since 1940 at 2 chemical plants, who never worked in chlorohydrin unit, followed to 1988		Pancreas	All cohort members	4	SMR 0.61 (0.17–1.56)	
Stayner <i>et al.</i> (1993) USA	18 254 workers employed at 14 industrial plants using ethylene oxide for sterilization since 1943 with ≥ 3 months exposure to ethylene oxide		Pancreas	<i>Cumulative exposure in ppm-days</i> < 1200 1200–8500 > 8500 Total	3 10 3 16	SMR 0.69 (0.14–2.03) 1.70 (0.81–3.12) 0.50 (0.10–1.47) 0.98 (0.57–1.61) <i>p</i> -trend = 0.38	
Norman <i>et al.</i> (1995) USA	1132 workers employed in 1974–80 at a sterilizing plant using ethylene oxide, followed for cancer incidence to 1957		Pancreas	All cohort members	2	3.92 ( <i>p</i> = 0.09)	

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Olsen <i>et al.</i> (1997) USA	1361 men employed for ≥ 1 year and potentially engaged for ≥ 1 month in ethylene or propylene chlorohydrin production since 1941 at 4 chemical plants, followed to 1992		Pancreas	Ever in ethylene chlorohydrin production	1	SMR 0.25 (0.1–1.40)	
				Ever in ethylene chlorohydrin production with allowance for 25-year induction period from first exposure	1	0.40 (0.1–2.26)	
Steenland <i>et al.</i> (2004) USA	18 254 workers employed at 14 industrial plants using ethylene oxide for sterilization since 1943 with ≥ 3 months exposure to ethylene oxide, followed to 1998		Pancreas	All cohort members	38	SMR 0.92 (0.69–1.21)	Update of Stayner <i>et al.</i> (1993)
Ambroise <i>et al.</i> (2005), France	181 male workers employed as pest-control workers 1979–94, followed for mortality through to 2000		Pancreas	All cohort members	0	SMR 0 (0–10.77)	No information available on individual level of exposures to pesticides, rodenticides or formaldehyde

ICD, International Classification of Diseases; NR, not reported; SEER, Surveillance, Epidemiology and End Results; SIR, standardized incidence ratio; SMR, standardized mortality ratio; TWA, time-weighted average