**Table 2.1. Cohort studies of vinyl chloride monomer and polyvinyl chloride production workers and liver cancer**

| Reference, location, name of study | Cohort description | Exposure assessment | Organ site (ICD code) | Exposure categories | No. of cases/ deaths | Relative risk (95% CI)* | Adjustment for potential confounders | Comments |
|---|---|---|---|---|---|---|---|---|
| Mundt *et al*. (2000) USA | 10109 male workers employed ≥ 1 year in jobs that entailed exposure to VCM in 1942–72; mortality follow-up, 1942–95; vital status, 96.8%; cause of death, 99%; 37 plants | JEM | Liver and biliary tract (ICD-9 155–156) | | 80 | **SMR** (state rates)<br>3.59 (2.84–4.46) (state rates) | | Reference rates: state and USA population |
| | | | | Job exposed to VCM<br>*Duration of exposure (years)* | | | | In Cox model, duration of exposure strongest and significant versus age at and year of first exposure |
| | | | | 1–4 | 7 | 0.83 (0.33–1.71) | | |
| | | | | 5–9 | 10 | 2.15 (1.03–3.96) | | |
| | | | | 10–19 | 39 | 6.79 (4.83–9.29) | | |
| | | | | ≥ 20 | 24 | 6.88 (4.40–10.23) | | |
| | | | | *Latency (years)* | | | | |
| | | | | 10–19 | 9 | 2.87 (1.31–5.44) | | |
| | | | | 20–29 | 21 | 3.23 (2.00–4.93) | | |
| | | | | ≥ 30 | 50 | 4.34 (3.22–5.72) | | |
| | | | | *First exposure (year)* | | | | |
| | | | | ≤ 1950 | 48 | 4.99 (3.68–6.62) | | |
| | | | | 1950–59 | 23 | 3.11 (1.97–4.67) | | |
| | | | 48 ASL (33 death certificate, 15 World Angiosarcoma Registry) | *Duration of exposure (years)* | | **Hazard ratio** | Age at first exposure, duration of exposure and year of first exposure | |
| | | | | 1–4 | 3 | Reference | | |
| | | | | 5–9 | 6 | 3.7 (0.9–14.7) | | |
| | | | | 10–19 | 26 | 15.9 (4.6–54.8) | | |
| | | | | ≥ 20 | 13 | 9.7 (2.6–36.4) | | |

**Table 2.1. Cohort studies of vinyl chloride monomer and polyvinyl chloride production workers and liver cancer**

| Reference, location, name of study | Cohort description | Exposure assessment | Organ site (ICD code) | Exposure categories | No. of cases/ deaths | Relative risk (95% CI)* | Adjustment for potential confounders | Comments |
|---|---|---|---|---|---|---|---|---|
| Lewis *et al*. (2003) USA | 2200 male workers employed ≥ 1 year in jobs that entailed exposure to VCM in 1942–72; mortality follow-up, 1942–95; vital status, 98.5% | JEM | Liver and biliary tract (ICD-9 155-156) | | | **SMR** | Age, calendar period | Reference rates: states of Kentucky; part of study by Mundt *et al*. 2000. |
| | | | | Job exposed to VCM | 24 | 4.00 (p< 0.05; 6 exp.) | | |
| | | | | *Duration of exposure (years)* | | | | |
| | | | | 1–4 | 2 | 0.91 (2.19 exp.) | | |
| | | | | 5–9 | 2 | 2.20 (0.91 exp.) | | |
| | | | | 10–19 | 14 | 10.85 (p< 0.05; 1.29 exp.) | | |
| | | | | ≥ 20 | 6 | 3.64 (p< 0.05; 1.65 exp.) | | |
| | | | | *Latency (years)* | | | | |
| | | | | 1–9 | 0 | 0 (0.27 exp.) | | |
| | | | | 10–19 | 5 | 6.49 (p< 0.05; 0.77 exp.) | | |
| | | | | 20–29 | 10 | 6.94 (p< 0.05; 1.44 exp.) | | |
| | | | | ≥ 30 | 9 | 2.55 (p< 0.05; 3.53 exp.) | | |
| | | | | *First exposure (year)* | | | | |
| | | | | < 1950 | 12 | 3.57 (p< 0.05; 3.36 exp.) | | |
| | | | | 950–59 | 10 | 4.76 (p< 0.05; 2.10 exp.) | | |
| | | | | 1960–72 | 2 | 3.51 (0.57 exp.) | | |

**Table 2.1. Cohort studies of vinyl chloride monomer and polyvinyl chloride production workers and liver cancer**

| Reference, location, name of study | Cohort description | Exposure assessment | Organ site (ICD code) | Exposure categories | No. of cases/ deaths | Relative risk (95% CI)* | Adjustment for potential confounders | Comments |
|---|---|---|---|---|---|---|---|---|
| Ward *et al*. (2001) Italy, Norway, Sweden, UK | 12700 male workers employed in 19 VCM/PVC plants for ≥ 1 year in 1950–85; mortality follow-up, 1955–97; incidence follow-up, 1955–96 | Calendar period JEM for 13/19 factories grouped in 22 broad categories; factory-specific JEM with validated exposure estimates (ppm) | Liver cancer (ICD-9 155) | | | **SMR** | | Reference rates: national |
| | | | | | 53 | 2.40 (1.80–3.14) | | |
| | | | | | | **SIR** | | Reference rates: national |
| | | | | | 29 | 3.98 (2.67–5.72) | | |
| | | | | | | **SMR** | | |
| | | | | PVC production | 10 | 2.28 (1.09–4.18) | | |
| | | | | VCM and PVC production | 41 | 2.85 (2.05–3.87 | | |
| | | | | *Duration (years)* | | | | |
| | | | | 1–9 | 15 | 1.00 | | |
| | | | | 10–16 | 17 | 2.58 (1.28–5.24) | | |
| | | | | 17–20 | 9 | 3.48 (1.49–8.15) | | |
| | | | | 21–25 | 18 | 8.21 (3.98–16.9 | | |
| | | | | ≥ 26 | 12 | 9.39 (4.17–21.1) | | |
| | | | | | | Test for linear trend, $p < 0.001$ | | |
| | | | | *Latency (years)* | | | Age, calendar period | Internal comparisons, poisson regression analysis |
| | | | | 0–20 | 17 | 1.00 | | |
| | | | | 21–25 | 13 | 2.44 (1.09–5.45) | | |
| | | | | 26–30 | 12 | 2.99 (1.26–7.09) | | |
| | | | | 31–36 | 17 | 5.58 (2.34–13.3) | | |
| | | | | ≥ 37 | 12 | 6.20 (2.30–16.7) | | |
| | | | | | | Test for linear trend, $p < 0.001$ | | |

**Table 2.1. Cohort studies of vinyl chloride monomer and polyvinyl chloride production workers and liver cancer**

| Reference, location, name of study | Cohort description | Exposure assessment | Organ site (ICD code) | Exposure categories | No. of cases/ deaths | Relative risk (95% CI)* | Adjustment for potential confounders | Comments |
|---|---|---|---|---|---|---|---|---|
| Ward *et al*. (2001) Contd. | | | | *Cumulative exposure (ppm–years)* | | | | |
| | | | | 0–734 | 13 | 1.00 | | |
| | | | | 735–2379 | 12 | 3.97 (1.81–8.71) | | |
| | | | | 2380–5188 | 15 | 7.55 (3.57–15.9) | | |
| | | | | 5189–7531 | 13 | 14.0 (6.43–30.7) | | |
| | | | | ≥ 7532 | 15 | 28.27 (12.84–62.25) | | |
| | | | | | | Test for linear trend, $p < 0.001$ | | |
| | | | | *Autoclave workers* | | | | |
| | | | | Never | 22 | 1.00 | | |
| | | | | Ever | 38 | 6.61 (3.90–11.2) | | |
| | | | | Unknown | 11 | 5.43 (2.63–11.2) | | |
| | | | ASL | *Duration (years)* | | | | |
| | | | | 1–9 | 7 | 1.00 | | |
| | | | | 10–16 | 8 | 3.01 (1.06–8.54) | | |
| | | | | 17–20 | 2 | 2.04 (0.41–10.3) | | |
| | | | | 21–25 | 12 | 15.7 (5.60–44.0) | | |
| | | | | ≥ 26 | 8 | 19.67 (6.28–61.59) | | |
| | | | | | | Trend test, $p < 0.001$ | Age, calendar period | |
| | | | | *Latency (years)* | | | | |
| | | | | 0–20 | 10 | 1.00 | | |
| | | | | 21–25 | 6 | 2.77 (0.89–8.69) | | |
| | | | | 26–30 | 7 | 4.80 (1.47–15.7) | | |
| | | | | 31–36 | 10 | 10.38 (3.09–34.9) | | |
| | | | | ≥ 37 | 4 | 7.99 (1.71–37.3) | | |
| | | | | | | Trend test, $p < 0.001$ | | |

**Table 2.1. Cohort studies of vinyl chloride monomer and polyvinyl chloride production workers and liver cancer**

| Reference, location, name of study | Cohort description | Exposure assessment | Organ site (ICD code) | Exposure categories | No. of cases/ deaths | Relative risk (95% CI)* | Adjustment for potential confounders | Comments |
|---|---|---|---|---|---|---|---|---|
| Ward *et al*. (2001) (contd) | | | | *Cumulative exposure (ppm–years)* | | | | |
| | | | | 0–734 | 4 | 1.00 | | |
| | | | | 735–2379 | 6 | 6.56 (1.85–23.3) | | |
| | | | | 2380–5188 | 8 | 13.6 (4.05–45.5) | | |
| | | | | 5189–7531 | 7 | 28.0 (8.00–98.2) | | |
| | | | | ≥ 7532 | 12 | 88.2 (26.4–295) | | |
| | | | | | | Trend test, $p < 0.001$ | | |
| | | | | *Autoclave workers* | | | | |
| | | | | Never | 4 | 1.0 | | |
| | | | | Ever | 26 | 25.5 (8.86–73.2) | | |
| | | | | Unknown | 7 | 19.3 (5.66–66.2) | | |
| | | | HCC | *Duration (years)* | | | | |
| | | | | 1–9 | 1 | 1.0 | | |
| | | | | 10–16 | 3 | 6.94 (0.71–67.5) | | |
| | | | | 17–20 | 2 | 12.6 (1.11–143) | | |
| | | | | 21–25 | 1 | 7.34 (0.44–122) | | |
| | | | | ≥ 26 | 3 | 35.5 (3.34–377) | | |
| | | | | | | Trend test, $p = 0.002$ | | |
| | | | | *Latency (years)* | | | Age calendar period | |
| | | | | < 26 | 2 | 1.00 | | |
| | | | | 26–30 | 1 | 3.72 (0.29–48.3) | | |
| | | | | 31–36 | 3 | 15.9 (1.86–135) | | |
| | | | | ≥ 37 | 4 | 35.7 (3.56–359) | | |
| | | | | | | Trend test, $p = 0.001$ | | |

**Table 2.1. Cohort studies of vinyl chloride monomer and polyvinyl chloride production workers and liver cancer**

| Reference, location, name of study | Cohort description | Exposure assessment | Organ site (ICD code) | Exposure categories | No. of cases/ deaths | Relative risk (95% CI)* | Adjustment for potential confounders | Comments |
|---|---|---|---|---|---|---|---|---|
| Ward *et al*. (2001) Contd. | | | | *Cumulative exposure (ppm–years)* | | | | |
| | | | | 0–734 | 3 | 1.0 | | |
| | | | | 735–2379 | 2 | 3.02 (0.50–18.1) | | |
| | | | | 2380–5188 | 1 | 2.47 (0.26–23.9) | | |
| | | | | 5189–7531 | 1 | 5.33 (0.54–52.5) | | |
| | | | | ≥ 7532 | 2 | 20.27 (2.98–138) | | |
| | | | | | | Trend test, $p = 0.004$ | | |
| | | | | *Autoclave workers* | | | | |
| | | | | Never | 5 | 1.0 | | |
| | | | | Ever | 4 | 2.97 (0.80–11.1) | | |
| | | | | Unknown | 1 | 2.04 (0.24–17.4) | | |
| Gennaro et al. (2008), Porto Marghera, Italy | 1658 male workers employed in 1950–85; mortality follow- up, 1972–99 | JEM | Liver cancer (ICD-9 155) | Autoclave workers | 7 | 9.57 (**3.71–24.68**) | Age, calendar time, employment duration, latency | Part of the study by Ward et al. (2001) and an update of Gennaro et al. (2003). Internal comparisons; 'job title Groups' versus Other workers |
| | | | | PVC baggers | 1 | 0.82 (0.23–2.93) | | |
| | | | | PVC Compound workers | 5 | 2.46 (0.94–6.42) | | |

**Table 2.1. Cohort studies of vinyl chloride monomer and polyvinyl chloride production workers and liver cancer**

| Reference, location, name of study | Cohort description | Exposure assessment | Organ site (ICD code) | Exposure categories | No. of cases/ deaths | Relative risk (95% CI)* | Adjustment for potential confounders | Comments |
|---|---|---|---|---|---|---|---|---|
| Pirastu *et al*. (2003) Italy | 1658 male workers employed in 1956–99; mortality follow-up, 1973–99; vital status, 100%; cause of death, 99% | JEMs: job-and time-specific VCM estimates (ppm); ever/never autoclave worker | Primary liver cancer (ICD-9 155.0) | *Autoclave workers* ever/never | 17 | **SMR** 2.78 (1.86–4.14)[a] **Relative risk** 4.4 (1.9–10.0) [a] | Age, calendar time, latency | Part of the study by Ward *et al*. 2001. Reference rates: regional Internal comparison of rates |
| | | | ASL | Autoclave worker: ever/never | 6 | 21.1 (3.5–128.7)[a] | Age, calendar time, latency | Best available clinical and pathological data; internal comparison of rates |
| | | | HCC | Autoclave worker: ever/never | 12 | 3.5 (1.4–9.2) [a] | | |
| | | | HCC and ASL | *Cumulative exposure (ppm–years)* | | **Rate (x 100 000)** | | |
| | | | | 0–735 | 3 | 10.0 | | |
| | | | | 735–2379 | 1 | 18.6 | | |
| | | | | 2379–5188 | 7 | 191.7 | | |
| | | | | 5188–7531 | 1 | 62.8 | | |
| | | | | 7531-9400 | 0 | - | | |
| | | | | | | $\chi^2$ 14.52 Trend test, $p < 0.001$ | | |

**Table 2.1. Cohort studies of vinyl chloride monomer and polyvinyl chloride production workers and liver cancer**

| Reference, location, name of study | Cohort description | Exposure assessment | Organ site (ICD code) | Exposure categories | No. of cases/ deaths | Relative risk (95% CI)* | Adjustment for potential confounders | Comments |
|---|---|---|---|---|---|---|---|---|
| Thériault & Allard (1981) Canada | 451 male workers exposed to VCM for ≥ 5 years in a polymerization plant, employed in 1948–72; mortality follow- up, 1948–77 | JEM | Digestive tract Cancer (ICD-7 150-159) | | 14 (6 deaths from liver cancer) | 6.25 (2.69–14.52) | | Reference rates: Canadian population in 1971; comparison population: 870 workers not exposed to VCM for ≥ 5 months |
| Weber *et al*. (1981) Germany | 7021 male VCM/PVC production workers from beginning of operation to 1974; mortality follow-up, from beginning of operation to 1974; vital status, > 90%; cause of death unknown, 7–13% | JEM | Malignant tumour of the liver (ICD-8 155) | | **12** | **SMR** 15.23 | | Reference rates: national |
| | | | | *Duration of exposure (months)* | | | | |
| | | | | < 12 | 0 | - | | |
| | | | | 13-60 | 2 | 8.74 | | |
| | | | | 61-120 | 3 | 15.25 | | |
| | | | | ≥ 121 | 7 | 25.28 | | |

**Table 2.1. Cohort studies of vinyl chloride monomer and polyvinyl chloride production workers and liver cancer**

| Reference, location, name of study | Cohort description | Exposure assessment | Organ site (ICD code) | Exposure categories | No. of cases/ deaths | Relative risk (95% CI)* | Adjustment for potential confounders | Comments |
|---|---|---|---|---|---|---|---|---|
| Smulevich *et al*. (1988) Soviet Union | 3232 (2195 men, 1037 women) VCM/PVC production workers employed for ≥ 1 month in VCM-exposed jobs; mortality follow-up, 1939– 77 | Exposure data in 1953-66 from JEM | Malignant liver neoplasm (ICD-8 155) | Estimated area Exposure: low, medium and high | 0 | | | City (Gorki) mean death rates in 1959, 1696 and 1975 |
| Laplanche *et al*. (1992) France | 1100 VCM-exposed and 1100 unexposed subjects; matched on age, plant, physician, aged 40–55 years, identified in 1980; mortality and morbidity follow-up, 1980–88 | JEM | Liver cancer (ICD-9 155) | | 3 exposed 0 unexposed | NR | | |
| Du & Wang (1998) Taiwan, China | 2224 workers with occupational exposure to VCM; controls were optical or motor cycle equipment workers. | | Liver cancer (ICD-9 155) | VCM versus optical workers<br>VCM versus motor cycle workers | | 4.5 (1.5–13.3)<br>6.5 (2.3–18.4) | | Proportionate morbidity analysis |

**Table 2.1. Cohort studies of vinyl chloride monomer and polyvinyl chloride production workers and liver cancer**

| Reference, location, name of study | Cohort description | Exposure assessment | Organ site (ICD code) | Exposure categories | No. of cases/ deaths | Relative risk (95% CI)* | Adjustment for potential confounders | Comments |
|---|---|---|---|---|---|---|---|---|
| Wong *et al*. (2002) Taiwan, China | 3293 male workers in 6 PVC polymerization plants exposed to VCM ≥ 1 year in 1950–92; mortality follow- up, 1985–97; vital status, 99% | | Malignant neoplasm of the liver (ICD- 9 155) | | 25 | **SMR** 1.78 (1.15–2.62) | | Reference rates, national; cohort assembled from records of Labour Insurance Bureau |
| | | | | *Duration of exposure (years)* | | | | |
| | | | | < 10 | 13 | 2.45 (1.30–4.19) | | |
| | | | | 10–19 | 10 | 1.76 (0.84–3.24) | | |
| | | | | 20 | 2 | – (3.2 exp.) | | |
| | | | | *Latency (years)* | | | | |
| | | | | < 15 | 8 | 1.29 (0.56–2.54) | | |
| | | | | 15–24 | 7 | 1.46 (0.58–3.61) | | |
| | | | | ≥ 25 | 10 | 3.13 (1.50–5.75) | | |
| | | | | *First exposure (year)* | | | | |
| | | | | ≤1970 | 11 | 4.82 (2.41–8.63) | | |
| | | | | 1970–79 | 8 | 1.92 (0.83–3.79) | | |
| | | | | After 1980 | 6 | 0.78 (0.28–1.69) | | |
| | | | | *Age at first exposure (years)* | | | | |
| | | | | < 30 | 10 | 2.24 (1.07–4.12) | | |
| | | | | 30–39 | 6 | 1.78 (0.65–3.88) | | |
| | | | | ≥ 40 | 9 | 1.43 (0.65–2.71) | | |

**Table 2.1. Cohort studies of vinyl chloride monomer and polyvinyl chloride production workers and liver cancer**

| Reference, location, name of study | Cohort description | Exposure assessment | Organ site (ICD code) | Exposure categories | No. of cases/ deaths | Relative risk (95% CI)* | Adjustment for potential confounders | Comments |
|---|---|---|---|---|---|---|---|---|
| Lewis & Rempala (2003), Louisville, KY, USA | Cases, 23 men, histologically confirmed. Nested case control study; 1817 white men hired before 1967 who had worked at least 1 year; Controls matched by year of birth and duration of employment | Semi-quantitative expert assessment | ASL | Ranked, six categories | 23 | Beta = 0.0039 (SE= 0.0014) *p*-value 0.0038; logistic regression | Other production chemicals | In Lewis *et al*. (2003), 28 ASL reported |

**Table 2.1. Cohort studies of vinyl chloride monomer and polyvinyl chloride production workers and liver cancer**

| Reference, location, name of study | Cohort description | Exposure assessment | Organ site (ICD code) | Exposure categories | No. of cases/ deaths | Relative risk (95% CI)* | Adjustment for potential confounders | Comments |
|---|---|---|---|---|---|---|---|---|
| Wong *et al*. (2003) Taiwan, China | 18 men; 5 histologically confirmed; 5 AFP > 1000 mg/L + at least one positive image from angiography, sonography, liver scan and/or CT; 8 from clinical manifestation and imaging studies 68 randomly selected from a pool of eligible workers; matched on age and specific plant employment | Job titles; high VCM-exposure jobs: tank cleaning, unloading PVC, adding catalyst; HBsAg status from medical surveillance records | Liver cancer; HCC | | 18 | | | For deceased individuals, validation of exposure by next of kin versus co-workers and industrial hygienist Reference: HBsAg-negative status and no history of tank cleaning |
| | | | | History of high-exposure job | | 2.9 (1.1–7.3) | | |
| | | | | HBsAg-positive versus HBsAg-negative status | | 15.7 (3.6–68.4) | | |
| | | | | History of tank cleaning versus no history | | 3.6 (1.4–9.2) | | |
| | | | | HBsAg-negative status and history of tank cleaning | | 4.0 (0.2–69. | | |
| | | | | HBsAg-positive status and history of tank cleaning | | 396 (22.6–8) | Family history of chronic liver disease | |
| | | | | HBsAg-positive status and no history of tank cleaning | | 25.7 (2.9–229.4) | | |
| | | | | HBsAg-negative status and history of high exposure job | | 2.9 (0.2–50.0) | | |
| | | | | HBsAg-positive status and history of high exposure job | | 184.5 (15.0–8) | | |
| | | | | HBsAg–positive status and no history of high exposure job | | 26.1 (2.9–235.1) | | |

**Table 2.1. Cohort studies of vinyl chloride monomer and polyvinyl chloride production workers and liver cancer**

| Reference, location, name of study | Cohort description | Exposure assessment | Organ site (ICD code) | Exposure categories | No. of cases/ deaths | Relative risk (95% CI)* | Adjustment for potential confounders | Comments |
|---|---|---|---|---|---|---|---|---|
| Mastrangelo *et al*. (2004) Italy | Nested case-control study; 13 men; 8 histologically confirmed; 5 focal hepatic lesions at sonography + AFP > 400 µg/L 139 workers with no clinical or biochemical evidence of chronic liver disease or cancer at any site from medical surveillance in 1999 - 2002 | JEMs, job-and time-specific VCM estimates (ppm); information for cases from company file from medical surveillance data for controls; alcoholic beverage consumption from hospital/clinical records and surveillance data; serological markers for HBsAg and anti-HCV antibodies | HCC | *Cumulative VCM exposure (ppm–years)*<br>< 500<br>500–2500<br>>2500<br>< 2500/alcohol < 60 g/day<br>> 2500/alcohol < 60 g/day<br>< 2500/alcohol > 60 g/day<br>> 2500/alcohol > 60 g/day<br><2500/HBsAg/HCV negative<br>> 2500/HBsAg/HCV negative<br><2500/HBsAg/HCV positive<br>>2500/HBsAg/HCV positive | | Reference<br>6.32 (0.48–336)<br>29.3 (3.61–1298)<br>Reference<br>18.8 (1.62–218.0)<br>42.9 (3.41–540.0)<br>409 (19.6–8553.0)<br>Reference<br>25.0 (2.77–226.0)<br>106.9 (4.43- 2578.0)<br>210.3 (7.13-6203.0) | Adjusted for age, hepatitis infection<br>Age, alcoholic beverage consumption | |

ASL, angiosarcoma of the liver; HCC, hepatocellular carcinoma; JEM, job exposure matrix; vinyl chloride monomer (VCM); polyvinyl chloride (PVC)