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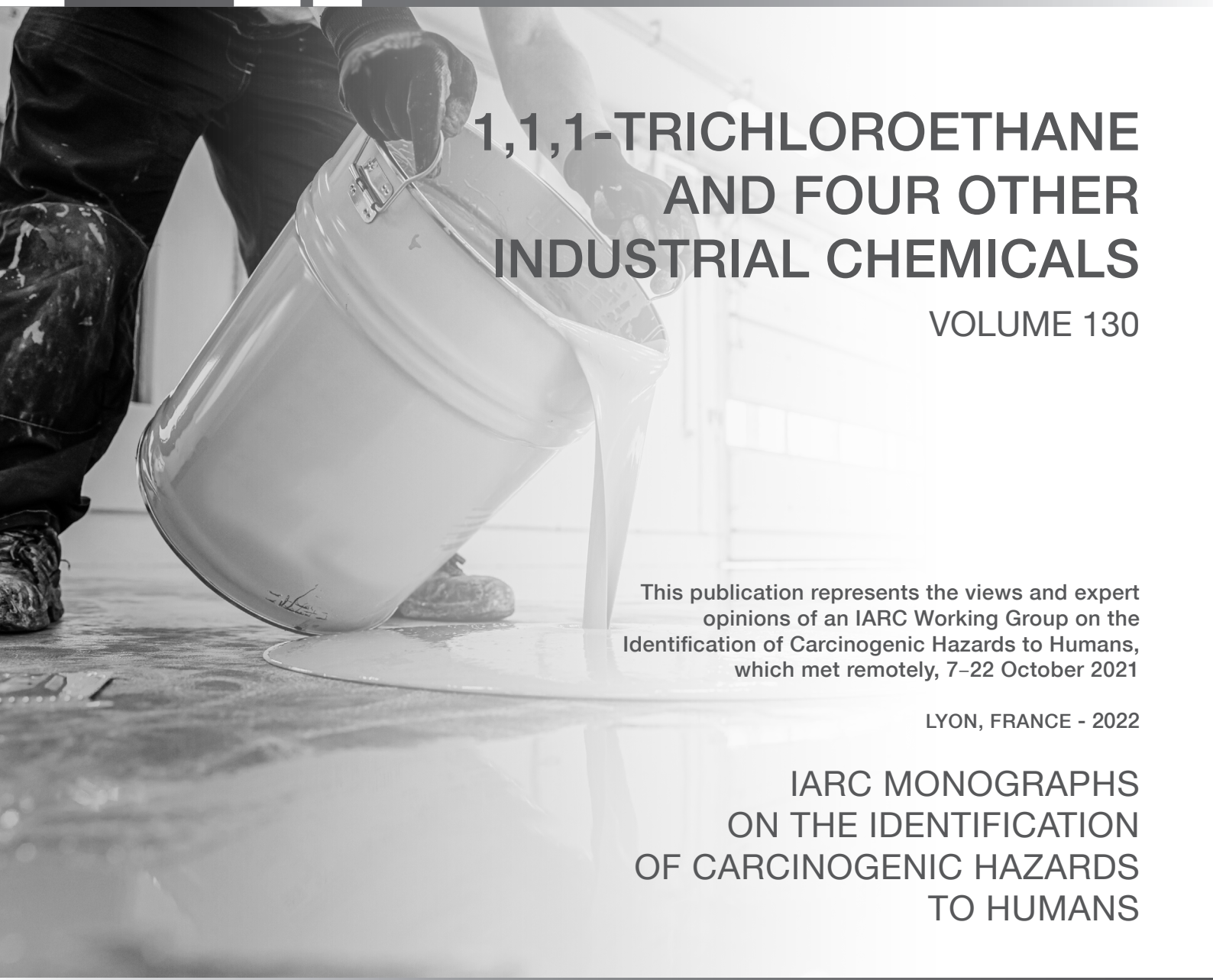

1,1,1-TRICHLOROETHANE AND FOUR OTHER INDUSTRIAL CHEMICALS

VOLUME 130

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IARC MONOGRAPHS ON THE IDENTIFICATION OF CARCINOGENIC HAZARDS TO HUMANS

International Agency for Research on Cancer

World Health Organization

Table S1.4 Exposure assessment review and critique for epidemiological studies on cancer and exposure to 1,1,1-trichloroethane

Reference and outcome	What was the study design? (n subjects)	What methods were used for the exposure assessment? (incl. data source, environmental and biological measurements etc.)	What was the exposure definition and was it well defined?	Was exposure assessment qualitative, semiquantitative or quantitative?	Were sampling and collection protocols for chemical measurements appropriate?	What routes of exposure were assessed?	How was the intensity of exposure assessed?	How was the duration of exposure assessed?	Was cumulative exposure assessed?	Was exposure assessed before outcome being ascertained?	What was the timing of exposure relative to the outcome?	Was there known exposure to any other carcinogens?	Could the 'unexposed' group have included exposed?
Anttila et al. (1995) Multiple cancers	Cohort (271 exposed subjects)	1,1,1-trichloroethane blood measurements from FIOH files	1,1,1-trichloroethane based on a positive blood result Yes, well defined	Quantitative data but assessment was qualitative, i.e. only "ever exposed"	Varied and not described	Because biologic, inhalation, dermal and (possibly) ingestion	Mean of measurements reported by year but not used	Not ssed	No	Measurements, yes. Exposure assessment, no	Cancer follow-up started before measurements	Yes, but 94% of entire cohort (n = 3974) were exposed to only one of the three chemicals (1,1,1-trichloroethane, perchloroethylene and trichloroethylene.) Other exposures not evaluated. No information on individuals having multiple exposures	Unlikely, due to low prevalence of use in general population. No information on other substances
Radican et al. (2008) Multiple cancers Exposure assessment methods described in Stewart et al. (1991) NCI study on aircraft maintenance workers	Cohort (14 455; Ever exposed: 2215 (15%))	Exposure assigned based on employer records, job descriptions, walk-through surveys, interviews of employees and air measurements. Subjects were linked to chemicals using a study-specific JEM	Exposed (ever/ never) to 1,1,1-trichloroethane and semiquantitative exposure levels for a "mixed solvents" category that included 1,1,1-trichloroethane No, not well defined, due to the difficulty of linking subjects, departments, and chemicals.	Qualitative. Exposed (yes/no) for each job-organization combination. Semiquantitative for "mixed solvents"	Not described	Not specified [presumed inhalation]	Does not appear to have been used, although used in an earlier study of this population by the same group of investigators	N/A	No	No, but used a JEM approach (although not identified as such)	Exposures occurred 1939 to 1982; outcomes (cancer death) occurred between 1982 to 2000	Yes. Evaluated trichloroethylene and several other solvents and chemicals. Other exposures not evaluated. No information on individuals having multiple exposures	Yes
Videnros et al. (2020) Breast Exposure assessment methods described in Kauppinen et al. (1998, 2009)	Nested case-control (731 cases; 1669 controls. Exposed: 10 (1%) cases; 24 (1%) controls) [the paper reports 34 exposed individuals, 10 of whom were cases.]	Study interview questionnaires for 3 latest occupations, assessed by NOCCA/FINJEM with prevalence modified by occupational hygienists for subject-specific prevalence	No, not well defined. Cited Kauppinen et al. (2009) that indicates jobs with "proportion" < 5% were considered unexposed, but Videnros et al. (2020), indicated prevalence > 0% were considered ever exposed and also as at least 5%, exposed.	Kauppinen et al. (2009) indicated original prevalence and intensity data were quantitative	Collection and analytic methods of measurements collected for FINJEM likely varied, since they were collected over many years across Finland	Not specified [presumed inhalation]	Intensity not described, but cited Kauppinen et al. (2009) who defined "levels" as the one-year average concentration during working hours in workroom air among the exposed workers. Kauppinen et al. (2009) indicated some jobs had measurement data available. Calculated a mean intensity as prevalence*intensity*duration.	Sum of years in exposed jobs	Not identified	No, but experts were blinded to case status	Exposure likely occurred before outcome, because each subject reported the 3 latest jobs and subjects held each for an average of 18 years, (which means exposures were likely to have occurred before outcome) and the outcome was ascertained in 1990–2013, most exposure was likely to have occurred before outcome	Yes. Evaluated 20 other carcinogens or groups of carcinogens. Correlations were calculated (see Supplemental Table S1.6)	Unlikely. Almost complete work histories were evaluated and low prevalence of exposure (see second column)
Callahan et al. (2018) NHL NCI-SEER study	Case-control (1189 cases; 982 controls. Probability: < 50%: 551 (46%) cases, 414 (42%)	Study interview-questionnaires for full work histories, including job-specific modules, literature,	Probability: 0, < 10, 10- < 50, 50- < 90, ≥ 90%. Yes, well defined.	Frequency was quantitative but were converted to semiquantitative. Probability and confidence were	Collection and analytic methods of measurements likely varied, since they were collected	Inhalation (potential for dermal exposure was included in 28 job	Intensity developed from modelled determinants of exposure with 947 measurements as described in Hein et al., 2010 but not used.	Sum of years with ≥ 50% probability of exposure	No. Calculated cumulative exposed hours from the mid-point of the frequency*duration for jobs > 50% probability	No, but experts were blinded to case status	Likely, because full work histories means exposures were likely to have occurred before outcome was	Yes. Evaluated other exposures, including chlorinated solvents, but no information on other carcinogens. Correlations among study control subjects were calculated.	Unlikely because exposure assessment required > 50% probability for exposure to 1,1,1-trichlorethane and low prevalence

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Assessment of intensity described by Hein et al. (2010)	controls. ≥ 50%: 14 (1%) cases, 12 (1%) controls)	published measurements		semiquantitative. Intensity was quantitative.	over many years and by many investigators	modules but there is no indication it was considered)					ascertained in 1998–2000 and age of 95% of cases and controls were > 35 years.	See Supplemental Table S1.6.	of exposure (see second column)
Gold et al. (2011) Multiple myeloma NCI-SEER study	Case-control (180 cases; 481 controls; Probability > 10%: 36 cases (20%); 65 (14% controls)	Study interview-based questionnaires for full work histories, including job-specific modules, literature, published measurements	Probability: < 1, 1 to < 10, 10 to < 50, 50 to < 90, ≥ 90%. Yes, well defined	Frequency and intensity were quantitative but were converted to semiquantitative. Probability and confidence were semiquantitative	Collection and analytic methods of measurements likely varied, since they were collected over many years and by many investigators	Inhalation. Dermal exposures were assessed indirectly by increasing the inhalation intensity score by 1	Intensity was defined as the estimated concentration in the breathing zone: < 1–10; > 10–100; > 100–200; > 200 ppm	Sum of years in exposed job(s)	Yes, defined as midpoint of the intensity*midpoint of frequency*duration	No, but experts were blinded to case status	Likely because exposures for cases started in 1941 and for controls in 1946 before outcome was ascertained in 2000–2002.	Yes. Evaluated other exposures, including chlorinated solvents, but no information on other carcinogens. See Supplemental Table S1.6.	Unlikely, due to low prevalence of exposure (see second column). In addition, results were presented where jobs assessed with low confidence were reassigned to the unexposed category to partially address this
Talibov et al. (2017) CLL NOCCA study Exposure assessment methods described in: Kauppinen et al. (2009)	Nested case–control (20 615 cases; 103 075 controls. Cumulative exposure (ppm-yrs): ≤ 5.6: 980 (5%) cases, 5178 (5%) controls; 5.6–12.9: 393 cases (2%), 2170 controls (2%); > 12.9: 186 cases (< 1%), 815 controls (< 1%))	Jobs self-reported to 10-yr census and coded to link with a region-specific JEM (NOCCA-JEM) based on the prevalence of workers in highly prevalent jobs and measurement data.	No, not well defined. Cited Kauppinen et al. (2009) that indicates jobs with "proportion" < 5% were considered unexposed.	Kauppinen et al. (2009) indicated original prevalence and intensity data were quantitative.	Collection and analytic methods of measurements collected for FINJEM likely varied, since they were collected over many years across Finland	Not specified [presumed inhalation]	Intensity not described, but cited Kauppinen et al. (2009) who defined "level" as one-year average concentration during working hours in workroom air among the exposed workers. Kauppinen et al. (2009) indicated some jobs had measurement data	Job duration in years based on census. If job code switched between censuses, it was presumed the worker left the job at the mid-point between 2 censuses	No. Authors referred to metric as cumulative exposure but defined cumulative as prevalence*intensity*duration. Prevalence is not a component of toxicity and therefore this is not cumulative exposure.	No, but used a record-linkage system and a JEM that was used in multiple studies (although subject-specific assessments replaced the JEM values where the information differed).	Likely, for most subjects because jobs held in 1960–1990 means that exposures likely occurred before outcome was ascertained in 1961–2005	Yes. Evaluated formaldehyde and ionizing radiation and other chemicals and solvents, including chlorinated solvents. No information on individuals having multiple exposures.	Unlikely, due to low prevalence of exposure (see second column). However, likely to have somewhat greater chance than in other studies for jobs in between census terms that wouldn't have been captured (censuses from every 10 years were the source of jobs).
Talibov et al. (2014) AML NOCCA study Exposure assessment methods described in: Kauppinen et al. (1998, 2009)	Nested case-control (14 982 cases; 74 505 controls. Level (ppm-yr): ≤ 5.6: 566 cases (4%); 2986 controls (4%); 5.6–12.7: 244 cases (2%), 1317 controls	Jobs self-reported to 10-yr census and coded to link with a region-specific JEM (NOCCA-JEM) based on the prevalence of workers in highly prevalent jobs and measurement data	No, not well defined. Cited Kauppinen et al. (2009) that indicated jobs with "proportion" < 5% prevalence were considered unexposed	Kauppinen et al. (2009) indicated original prevalence and intensity data were quantitative	Collection and analytic methods of measurements collected for FINJEM likely varied, since they were collected over many years across Finland	Not specified [presumed inhalation]	Intensity not described, but cited Kauppinen et al. (2009) who defined "level" as one-year average concentration during working hours in workroom air among the exposed workers. Kauppinen et al. (2009) indicated some jobs had measurement data	Job duration in years based on census. If job code switched between censuses, presumed the worker left the job at the mid-point	No. Authors referred to metric as cumulative exposure but defined cumulative as prevalence*intensity*duration. Prevalence is not a component of toxicity and therefore this is not cumulative exposure.	No, but used a record-linkage system and a JEM that was used in multiple studies (although subject-specific assessments replaced the JEM values where the	Likely for most subjects because jobs held in 1960–1990 means exposures were likely to have occurred before outcome was ascertained in 1961–2005	Yes. Evaluated formaldehyde and ionizing radiation, and other chemicals and solvents, including chlorinated solvents. No information on individuals having multiple exposures	Yes. Unlikely, due to low prevalence of exposure (see second column). However, likely to have somewhat greater chance than in other studies for jobs in between census terms that wouldn't have been captured (censuses from every 10 years

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	(2%); > 12.7: 86 cases (< 1%), 482 controls (< 1%)0.1							between 2 censuses		information differed)			were the source of jobs)
Talibov et al. (2019) Breast (male) NOCCA study Exposure assessment methods described in: Kauppinen et al. (1998, 2009)	Nested case-control (1469 cases; 7345 controls. Level (ppm-yrs): ≤ 5.6: 122 cases (8%); 623 controls (8%); 5.7–13: 41 cases (3%), 190 controls (3%); > 13: 18 cases (1%), 91 controls (1%))	Jobs self-reported to 10-yr census and coded to link with a region-specific JEM (NOCCA-JEM) based on the prevalence of workers in highly prevalent jobs and measurement data	No, not well defined. Cited Kauppinen et al. (2009) that indicated jobs with "proportion" < 5% prevalence were considered unexposed	Kauppinen et al. (2009) indicated original prevalence and intensity data were quantitative	Collection and analytic methods of measurements collected for FINJEM likely varied, since they were collected over many years across Finland	Not specified [presumed inhalation]	Intensity not described, but cited Kauppinen et al. (2009) who defined "level" as one-year average concentration during working hours in workroom air among the exposed workers. Kauppinen et al. (2009, 2014) indicated some jobs had measurement data	Job duration in years based on census. If job code switched between censuses, presumed the worker left the job at the mid-point between 2 censuses	No. Authors referred to metric as cumulative exposure but defined cumulative as prevalence*intensity*duration. Prevalence is not a component of toxicity and therefore this is not cumulative exposure	No, but used a record-linkage system and a JEM that was used in multiple studies (although subject-specific assessments replaced the JEM values where the information differed)	Likely for most subjects because jobs held in 1960–1990 means that exposures were likely to have occurred before outcome was ascertained in 1961–2005	Yes. Evaluated many other chemicals and solvents, including chlorinated solvents. No information on individuals having multiple exposures. (See Supplemental Table S1.6)	Unlikely, due to low prevalence of exposure (see second column). However, likely to have somewhat greater chance than in other studies for jobs in between census terms that wouldn't have been captured (censuses from every 10 years were the source of jobs)
Heineman et al. (1994) Brain NCI petrochemical study (Louisiana, New Jersey, & Philadelphia) Exposure assessment described in Gomez et al., 1994	Case-control (300 cases; 320 controls. Probability: low: 97 cases (32%), 93 controls (29%); medium: 11 cases (4%), 5 controls (2%); high: 4 cases (1%), 3 controls (1%))	Study interview-questionnaires for full work histories. literature, industrial hygiene reports, and personal judgement	Probability defined as low, medium and high. Assessed separately for jobs and for industries and then each metric was combined using an algorithm into a single probability or intensity estimate. No, low, medium and high are not defined	Semiquantitative	Collection and analytic methods of measurements likely varied, since they were collected over many years and by many investigators	Not specified [presumed inhalation]	Intensity defined as expected level of exposure and frequency of use. Categorical values for intensity (1, 2 and 3) were assigned separately for jobs and for industry codes, which were then combined using an algorithm into a single estimate. as described in Gomez et al. (1994)	Summed job duration for all exposed jobs (years)	Yes. Cumulative exposure was calculated as a weighted sum of years in all exposed jobs, with weights based on the square of the intensity of exposure (low = 1, medium = 2, and high = 3) assigned to each job [Gomez et al., 1994]	No, but experts were blinded to case status	Full work histories means exposure was likely to have occurred before outcome was ascertained in 1978–1981	Yes. Evaluated other chlorinated solvents, but no information on other carcinogens. No information on individuals having multiple exposures	Unlikely, due to low prevalence of exposure (see second column). However likely to have somewhat greater chance than in other studies, because jobs were reported by proxy respondents and some jobs may have been missed
Neta et al. (2012) Brain NCI hospital-based case-control in Boston, Pittsburgh, and Phoenix Assessment of intensity described in Hein et al. (2010)	Case-control (484 cases; 797 controls. Probability: possible: 140 cases (29%), 260 controls (33%); probable: 10 cases (2%), 12 controls (2%))	Study interview questionnaires for work histories, including job-specific modules, literature, published measurements used for intensity (n = 947)	Probability: 0, 1- < 10, 10- < 50, 50- < 90, ≥ 90%. Yes, well defined	Frequency and intensity were quantitative but were converted to semiquantitative. Probability and confidence were semiquantitative	Collection and analytic methods of measurements likely varied, since they were collected over many years and by many investigators	Inhalation.	Modelled identified or assumed determinants of exposure with 947 measurements to develop regression coefficients, as described in Hein et al. (2010). Assigned identified or assumed same determinants to study subjects to derive intensity	Sum of years with ≥ 50% probability of exposure	Yes. Defined as intensity*frequency*duration for jobs ≥ 50% probability	Unclear but assumed experts were blinded to case status	Likely because full work histories means exposure was likely to have occurred before outcome was ascertained in 1994–1998	Yes. Evaluated other exposures, including chlorinated solvents, but no information on other carcinogens. No information on individuals having multiple exposures	Unlikely based on the exposure assessment requiring > = 50% probability for 1,1,1-trichlorethane exposure and the low prevalence of exposure (see second column)
Ruder et al. (2013) Brain	Case-control (798 cases; 1175	Study interview-questionnaires for full work	Probability of exposure (0 = not exposed, 1 = < 0.1,	Frequency and intensity were quantitative but	Collection and analytic methods of	Not specified	Modelled identified or assumed determinants of exposure with 947	Sum of exposed days	Yes, defined as midpoint of frequency*intensity*days	No, but experts were blinded to case status	Full work histories means exposure was	Yes. Evaluated other chlorinated solvents, but no information on other	Unlikely, due to low prevalence of exposure (see

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NIOSH-NCI Upper Midwest Health Study (non-urban counties in Iowa, Michigan, Wisconsin, Minnesota) Assessment of intensity described by Hein et al. (2010)	controls. Ever exposed: 304 cases (38%); 503 controls (43%)	histories, including additional exposure modules, literature, published measurements used for intensity (n = 947)	2 = 0.1–0.49, 3 = 0.50–0.89, 4 > 0.89), Yes, well defined	converted to semiquantitative; probability was semiquantitative	measurements likely varied, since they were collected over many years and by many investigators	[presumed inhalation]	measurements to develop regression coefficients, as described in Hein et al. (2010). Assigned identified or assumed same determinants to study subjects to derive intensity				likely to have occurred before outcome was ascertained in 1995–1997	carcinogens. No information on individuals having multiple exposures	second column) especially if jobs were missed by the proxy respondents (but results were presented without proxies as well)
McLean et al. (2014) Brain INTEROCC study Some exposure assessment details described in van Tongeren et al. (2013), Kauppinen et al. (1998)	Case-control (1906 cases and 5565 controls. Ever exposed: 1 case (< 1%); ≤ 3 controls (< 1%))	Study interview questionnaire for full work history assessed by FINJEM and data from Montreal database	Somewhat described. McLean et al., 2014 defined the exposed as having a prevalence ≥ 25%, but no information as to how prevalence was determined	Kauppinen et al. (1998) indicated original prevalence and intensity data were quantitative	Collection and analytic methods of measurements collected for FINJEM likely varied, since they were collected over many years across Finland	Not specified, [presumed inhalation]	Unclear from methods (only says intensity was assessed). van Tongeren et al., (2013) indicates from FINJEM.	Duration of exposure in years	Unclear. Authors indicated cumulative exposure in ppm in tables but not defined in text. In tables indicates "Exposure in an occupation where p≥25% in job-exposure matrix for at least 1 year with a 5-year lag"	No, exposure assessment was done years after enrolment into the INTERPHONE study	Likely because full work histories and median age of 45–54, means exposure was likely to have occurred before outcome was ascertained in 2000–2004	Yes. Evaluated EMF (as this is an offshoot of the INTERPHONE study), as well as solvents, including chlorinated solvents. No information on individuals having multiple exposures	Unlikely. Exposure only assigned to those jobs with 25%+ probability of exposure, and individuals who had held any jobs with between 5 and 25% probability of exposure were also excluded from the reference group
Purdue et al. (2017) Kidney US Kidney Cancer study (Detroit & Chicago) Assessment of intensity described in Hein et al. (2010)	Case-control (1217 cases, 1235 controls. Probability: < 50%: 562 cases (47.5%), 512 controls (41.2%); 50–89: 41 cases (3.5%); 43 controls (3.9%); ≥ 90: 7 cases (< 1%), 4 controls (< 1%))	Study interview-questionnaires for full work histories, including job-specific modules, literature, published measurements	Probability: 0, < 10, 10 to < 50, 50–89, ≥ 90%) Yes, well defined	Frequency and intensity were quantitative but converted to semiquantitative; probability and confidence was semiquantitative	Collection and analytic methods of measurements likely varied, since they were collected over many years and by many investigators	Inhalation (potential for dermal exposure was included in some job-specific modules but there is no indication it was considered)	Intensity developed from modelled determinants of exposure with 947 measurements as described in Hein et al., 2010 but not used	Sum of years with ≥ 50% probability of exposure	No. Calculated cumulative exposed hours from the mid-point of the frequency*duration for jobs > 50% probability	No, but experts were blinded to case status	Likely because full work histories means exposure was likely to have occurred before outcome was ascertained in 2002–2007	Yes. Evaluated other exposures, including chlorinated solvents, assessed, but no information on other carcinogens. Correlations were developed. See Supplemental Table S1.6. A sensitivity analysis that excluded participants with 50+% probability of trichloroethylene exposure (since it's a known kidney carcinogen) was done	Unlikely because the exposure assessment required > 50% probability for exposure to 1,1,1-trichlorethane and the low prevalence of exposure (see second column)
Infante-Rivard et al. (2005) Childhood leukaemia Exposure assessment described in Gérin et al. (1985)	Case-control (790 cases, 790 controls).	Study interview questionnaire for full work history, specialized questionnaires, extensive literature review [and presumed measurement data]	Probability (referred to as "confidence"): "possible," "probable," "definite." Considered confidence = possible as unexposed No, levels are not defined	Frequency, intensity, and confidence were semiquantitative	[Presumed had measurement data: Collection and analytic methods of measurements likely varied, since they were collected over many years and by	Gérin et al. (1985) indicates both inhalation and dermal	Used codes of 0–3: 1, level slightly above background; 3, highest possible exposure level in study population; and 2, in between. Actual values not reported	Sum of years	No. Calculated cumulative metric as 0 (baseline, no exposure, confidence = none or possible), 1 (some exposure, concentration*frequency < 4) and 2 (greater exposure, concentration*frequency ≥ 4)	No. Exposure assessments done 20 years before study, but new assessments were likely done for this study	Likely because full work histories means some exposures occurred before outcome was ascertained, but others may have been essentially simultaneous, because study is of mother's	Yes. Evaluated 22 other solvents, including chlorinated solvents, but no information on other carcinogens. No information on individuals having multiple exposures	Unlikely, due to low prevalence of exposure (see second column)

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					many investigators]						exposure and childhood cancer		
Pedersen et al. (2020) Breast Exposure assessment described in Kauppinen et al. (2009)	Case-control (Age < 50: 17 332 cases; 86 660 controls. Ever exposed: 98 cases (< 1%), 470 controls (< 1%). Age > 50: 21 043 cases, 105 215 controls. Ever exposed: 158 cases (< 1%); 832 controls (< 1%))	Danish Supplementary Pension Fund Register for work history. Job codes from register were cross-walked to a region-specific JEM (NOCCA-JEM) based on prevalence of workers in highly prevalent jobs and measurement data	No, not well defined. Cited Kauppinen et al. (2009) that indicated jobs with "proportion" < 5% were considered unexposed, but Pedersen et al., 2020 indicated jobs with a "probability of exposure" ≤ 10% and women with < 1 year of employment were considered unexposed	Kauppinen et al. (2009) indicated original prevalence and intensity data were quantitative	Collection and analytic methods of measurements collected for FINJEM likely varied, since they were collected over many years across Finland	Not specified, [presumed inhalation]	Intensity not described, but cited Kauppinen et al. (2009) who defined "level" as the one-year average concentration during working hours in workroom air among the exposed workers. Kauppinen et al. (2009) indicated some jobs had measurement data	Years of employment [assumed from Danish records]	No. Authors referred to metric as cumulative exposure but defined cumulative as prevalence*intensity*duration. Prevalence is not a component of toxicity and therefore this is not cumulative exposure	No, but used a record-linkage system and a JEM that was used in multiple studies (although subject-specific assessments replaced the JEM values.) where the information differed)	Likely for most subjects because jobs were held in 1960–1990 and subjects were born > 1946	Yes. Evaluated trichloroethylene, benzene and toluene solvents, but no information on other carcinogens. No information on individuals having multiple exposures. See Supplemental Table S1.6.	Unlikely, due to low prevalence of exposure (see second column). However, likely to have somewhat greater chance than in other studies for jobs in between census terms that wouldn't have been captured (censuses from every 10 years were the source of jobs). However, considered probability < 10% and jobs with < 1 year employment as unexposed
Christensen et al. (2013) Multiple cancers Exposure assessment described in Gérin et al. (1985)	Case-control (3730 overall cases across 11 cancer sites, 533 population controls: number of cases and controls varied with disease end-point	Study interview questionnaires for full work histories including specialized questionnaires, extensive literature review [and presumed measurement data]	Probability (referred to as "confidence"): "possible," "probable," "definite." Considered confidence = possible as unexposed No, levels are not defined	Frequency, intensity, and confidence were semiquantitative	[Presumed had measurement data: Collection and analytic methods of measurements likely varied, since they were collected over many years and by many investigators]	Gerin et al., 1985 indicates both inhalation and dermal	Used codes of 0–3: 1, level slightly above background; 3, highest possible exposure level in study population; and 2, in between. Actual values not reported	Sum of years	No. Authors referred to metric as cumulative exposure but defined in tables cumulative as confidence*frequency*level*duration. Confidence is not a component of toxicity and therefore this is not cumulative exposure	No. Exposure assessments done 20 yrs before study, but new assessments were likely done for this study	Likely. Full work histories means exposures occurred in 1940–1970 before outcome was ascertained in 1979–1985	Yes. Evaluated 7 other solvents, including chlorinated solvents. solvents, but no information on other carcinogens. No information on individuals having multiple exposures	Unlikely, due to low prevalence of exposure (see second column)
Dosemeci et al. (1999) Kidney NCI population-based case–control study, Minnesota Exposure assessment described in Gomez et al. (1994)	Case-control (438 cases, 687 controls. Exposed: 15% cases; 17% controls)	Study interview questionnaires for work histories, included only the most recent and usual occupation and industry (including job tasks and duration and part-time/full-time status). Additionally, duration of employment in 13 specific occupations/	Probability defined as low, medium and high. Assessed separately for jobs and for industries and then combined using an algorithm into a single estimate. No, levels are not defined	Probability and intensity were semiquantitative	[Presumed measurements were used. If so, collection and analytic methods of measurements likely varied, since they were collected over many years and by many investigators]	Not specified, [presumed inhalation]	Intensity defined as expected level of exposure and frequency of use. Categorical values for intensity (1,2 and 3) were assigned separately for jobs and for industry codes, which were then combined using an algorithm into a single estimate as described in Gomez et al. (1994)	Duration for some jobs was collected but there is no mention of it being used	No	Interviewers were unaware of case status. No mention of experts but a JEM was developed years before the study started	Longest job was collected means that some exposures likely occurred before outcome was ascertained in 1988–1990	Yes. Evaluated other solvents, including chlorinated solvents, but no information on exposures to other carcinogens. No information on individuals having multiple exposures. See Supplemental Table S1.6	Unlikely, due to low prevalence of exposure (see second column). However, likely to have somewhat greater chance than in other studies because full work histories were not ascertained so exposed people could have been included in the unexposed category

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Reference and outcome	What was the study design? (n subjects)	What methods were used for the exposure assessment? (incl. data source, environmental and biological measurements etc.)	What was the exposure definition and was it well defined?	Was exposure assessment qualitative, semiquantitative or quantitative?	Were sampling and collection protocols for chemical measurements appropriate?	What routes of exposure were assessed?	How was the intensity of exposure assessed?	How was the duration of exposure assessed?	Was cumulative exposure assessed?	Was exposure assessed before outcome being ascertained?	What was the timing of exposure relative to the outcome?	Was there known exposure to any other carcinogens?	Could the 'unexposed' group have included exposed?
		industries and 7 jobs with specific (unidentified) exposures. In addition, the literature, exposure studies, and personal judgement											
Kernan et al. (1999) Pancreas	Case-control (63 097 cases, 252 386 controls. Intensity: low: 7600 cases (12%); medium: 1386 cases (2%), high: 1014 cases (2%))	Death certificates, assessed by a JEM	Probability defined as low, medium and high. Assessed separately for jobs and for industries and then combined using an algorithm into a single estimate. No, levels are not defined	Intensity and probability were semiquantitative	[Presumed measurements were used. If so, collection and analytic methods of measurements likely varied, since they were collected over many years and by many investigators]	Not specified, [presumed inhalation]	Not described other than none, low, medium, high	Not assessed	No	Unclear but a JEM was used	Because this is a mortality study, exposures had to have occurred before enrolment	Yes. Evaluated 12 other solvents, included chlorinated solvents, but no information on exposure to other carcinogens. No information on individuals having multiple exposures	Unlikely, due to low prevalence of exposure (see second column). However, likely to have somewhat greater chance than in other studies because full work histories were not ascertained so exposed people could have been included in the unexposed category
Miligi et al. (2006) NHL (Some of the exposure assessment described in Costantini et al. (2001)	Case-control (1428 cases, 1530 controls. Intensity: very low/low: 15 cases (1%), 23 controls (2%); medium/high: 5 cases < 1%), 9 controls (< 1%))	Study interview questionnaires for work histories, including job- and industry-specific modules	Probability defined as low, medium and high. No, levels are not defined	Intensity and probability were semiquantitative	No indication measurements were considered	Not specified, [presumed inhalation]	Intensity defined as Very Low: comparable to the upper end of normal range for general population; Low: higher than general population but controls in place; Medium: moderate to poor control measures; High: no control measures	Years	No	No, but experts assessors were blinded to case status	Likely, because full work histories means that exposures were likely to have occurred before outcome was ascertained in 1991–1993	Yes. Evaluated for other chlorinated solvents, but no information on exposure to other carcinogens. No information on individuals having multiple exposures	Unlikely, due to low prevalence of exposure (see second column). However, likely to have somewhat greater chance than in other studies because 5+ years of employment by job was required to count as exposed and lower duration jobs may have been missed
Vizcaya et al. (2013) Lung Exposure assessment described in Gérin et al. (1985), Goldberg et al. (1986)	Case-control (2016 cases, 2001 controls. Exposed: 22 cases (1%), 25 controls (1%); substantial exposure: 13 cases (< 1%), 11 controls (< 1%))	Semi-structured interviews questionnaires for complete work history, specialized questionnaires, extensive literature review [and presumed measurement data]	Probability (referred to as "confidence"): "possible," "probable," "definite." Considered confidence = possible as unexposed. No, levels are not defined	Confidence, frequency, and intensity were semiquantitative.	[Presumed had measurement data: Collection and analytic methods of measurements likely varied, since they were collected over many years and by many investigators]	Gerin et al., 1985 indicates both inhalation and dermal	Used codes of 0–3: 1, level slightly above background; 3, highest possible exposure level in study population; and 2, in between. Actual values not reported	Duration of exposed jobs	No. Authors referred to a lifetime exposure as confidence, frequency and concentration averaged, weighted by the durations of the various jobs in which exposure occurred. [It appeared that this was then divided into substantial and not substantial: the former being defined as medium or high concentration levels lasting at least 5 years, for ≥ 2 hours per	No. Exposure assessments done 20 yrs before study, but new assessments were likely done for this study	Full work histories means that exposures occurred in 1940–1970, before outcome was ascertained in 1980–1986 and 1995–2001 (note: 2 studies with differing enrolment dates were combined)	Yes, likely. Evaluated 7 other solvents, including chlorinated solvents and 8 probable or definite carcinogens as defined by IARC. No information on individuals having multiple exposures	Unlikely, due to low prevalence of exposure (see second column)

Table S1.4 Exposure assessment review and critique for epidemiological studies on cancer and exposure to 1,1,1-trichloroethane

Reference and outcome	What was the study design? (n subjects)	What methods were used for the exposure assessment? (incl. data source, environmental and biological measurements etc.)	What was the exposure definition and was it well defined?	Was exposure assessment qualitative, semiquantitative or quantitative?	Were sampling and collection protocols for chemical measurements appropriate?	What routes of exposure were assessed?	How was the intensity of exposure assessed?	How was the duration of exposure assessed?	Was cumulative exposure assessed?	Was exposure assessed before outcome being ascertained?	What was the timing of exposure relative to the outcome?	Was there known exposure to any other carcinogens?	Could the 'unexposed' group have included exposed?
									week; the latter the other exposed				
Hadkhale et al. (2017) Bladder NOCCA study Exposure assessment described in Kauppinen et al. (2009)	Case-control (113 343 cases, 566 715 controls. Cumulative: < 5.6: 6011 cases (5%); 27 807 controls (5%); 5.6–10.15: 1160 cases (1%), 5231 controls (1%); > 10.15: 703 cases (< 1%), 3234 controls (< 1%))	Jobs self-reported to 10-yr census and coded to link with a region-specific JEM (NOCCA-JEM) based on prevalence of workers in highly prevalent jobs and measurement data	No, not well defined. Cited Kauppinen et al. (2009) that indicated jobs with "proportion" < 5% prevalence were considered unexposed	Kauppinen et al. (2009) indicated original prevalence and intensity data were quantitative	Collection and analytic methods of measurements for FINJEM likely varied, since they were collected over many years and across Finland	Not specified, [presumed inhalation]	Intensity not described, but cited Kauppinen et al. (2009) who defined "level" as the one-year average concentration during working hours in workroom air among the exposed workers. Kauppinen et al. (2009) indicated some jobs had measurement data	Job duration in years based on census. If job code switched between censuses, presumed the worker left the job at the mid-point between 2 censuses	No. Authors referred to metric as cumulative exposure but defined cumulative as prevalence*intensity*duration. Prevalence is not a component of toxicity and therefore this is not cumulative exposure	No, but used a record-linkage system and a JEM that was used in multiple studies (although subject-specific assessments replaced the JEM values where the information differed)	Likely, because for most subjects, jobs were held in 1960–1990 and cases were identified as 2005	Yes. Evaluated many other solvents, including other chlorinated solvents were assessed in a model together (e.g. benzene, toluene, trichloroethane, etc) but no information on other carcinogens. No information on individuals having multiple exposures	Unlikely, due to low prevalence of exposure (see second column). However, likely to have somewhat greater chance than in other studies, for jobs in between census terms that wouldn't have been captured (censuses from every 10 years were the source of jobs)
Le Cornet et al. (2017) Testis Exposure assessment described in: Kauppinen et al. (2009, 2014)	Case-control (Mothers: 7018 cases, 23 081 controls. Low exposure: 45 cases (< 1%), 162 controls (< 1%); high exposure: 36 cases (< 1%),104 controls (< 1%). Fathers: 7855 cases, 25 496 controls. Low exposure: 380 (5%) cases, 1147 (5%) controls; high exposure: 458 (6%) cases, 1412 (6%) controls)	Finish, Norwegian and Swedish population registries. Jobs self-reported to 10-yr census and coded to link with a region-specific JEM (NOCCA-JEM) based on prevalence of workers in highly prevalent jobs and measurement data	No, not well defined. Cited Kauppinen et al. (2009) that indicated jobs with "proportion" < 5% were considered unexposed	Kauppinen et al. (2009) indicated original prevalence and intensity data were quantitative	Collection and analytic methods of measurements collected for FINJEM likely varied, since they were collected over many years across Finland	Not specified, [presumed inhalation]	Intensity not described, but cited Kauppinen et al. (2009) who "level" defined as the one-year average concentration during working hours in workroom air among the exposed workers. Kauppinen et al. (2009, 2014) indicated some jobs had measurement data	Not assessed	No.	No, but used a record-linkage system and a JEM that was used in multiple studies (although subject-specific assessments replaced the JEM values where the information differed)	Likely for most subjects because jobs were held in 1960–1990 and cases were identified in 1978 to 2012	Yes. Evaluated 8 other solvents, including chlorinated solvents, but no information on exposure to other carcinogens. (See Supplemental Table S1.6)	Unlikely, due to low prevalence of exposure (see second column). However, likely to have somewhat greater chance than in other studies for jobs in between census terms that wouldn't have been captured (censuses from every 10 years were the source of jobs). Did sensitivity analysis that excluded any of the solvents analysed, which would mean likely very small proportion of unexposed population
Sciannameo et al. (2019) Bladder Exposure assessment	Case-control (893 cases; 978 controls. Exposed: 362 cases (40%), 358 (37%)	Study interview questionnaires for full work history, assessed by FINJEM based on prevalence of	Probability: < 10%, 10–50%, > 50%. Yes, well defined. Kauppinen et al. (2009) indicates jobs	Kauppinen et al. (2009) indicated original prevalence and intensity data were quantitative	Collection and analytic methods of measurements collected for FINJEM likely	Not specified, [presumed inhalation]	Intensity not described, but cited Kauppinen et al. (2009) who defined "level" as the one-year average concentration during working hours in workroom air among	Sum of years in jobs	No. Authors referred to metric as cumulative exposure but defined cumulative as probability*intensity*durat	No, but used a record-linkage system and a JEM that was used in multiple	Likely for most subjects because jobs were held in 1960–1984 and cases were	Yes. Evaluated 5 other solvents, including 3 chlorinated solvents, and 29 IARC definite or probable carcinogens. No information on	Unlikely, due to low prevalence of exposure (see second column). However, likely to have somewhat

Table S1.4 Exposure assessment review and critique for epidemiological studies on cancer and exposure to 1,1,1-trichloroethane

Reference and outcome	What was the study design? (n subjects)	What methods were used for the exposure assessment? (incl. data source, environmental and biological measurements etc.)	What was the exposure definition and was it well defined?	Was exposure assessment qualitative, semiquantitative or quantitative?	Were sampling and collection protocols for chemical measurements appropriate?	What routes of exposure were assessed?	How was the intensity of exposure assessed?	How was the duration of exposure assessed?	Was cumulative exposure assessed?	Was exposure assessed before outcome being ascertained?	What was the timing of exposure relative to the outcome?	Was there known exposure to any other carcinogens?	Could the 'unexposed' group have included exposed?
described in: Kauppinen et al. (2009)	controls. Low: 181 cases (20%), 173 controls (18%); high: 181 cases (20%) 185 controls) (19%)	workers in highly prevalent jobs and measurement data	with < 5% prevalence were considered unexposed		varied, since they were collected over many years and across Finland		the exposed workers. Kauppinen et al. (2009, 2014) indicated some jobs had measurement data		ion and therefore this is not cumulative exposure	studies (although subject-specific assessments replaced the JEM values where the information differed)	identified in 1993 to 2012	individuals having multiple exposures	greater chance than in other studies for jobs in between census terms that wouldn't have been captured (censuses from every 10 years were the source of jobs)
Zarchy (1996) Biliary, pancreatic	Case report (2 cases)	Work history appears to be from subject. No exposure assessment	Trichloroethane (isomer not identified) Not well defined	NA	NA	Inhalation and dermal	NA	Years exposed presumably from self-report	No	No	Before	1 case also had perchloroethylene exposure and reported no other carcinogens. Both cases in machining industry and so could easily have had other exposures, such as solvents, machining oils or metals	NA
Kubo et al. (2014) Cholangiocarcinoma	Case report (4 cases)	Appears to have been from subject but possible from employer records. No exposure assessment	Reported as 1,1,1-trichloroethane. Company apparently known, so identification of 1,1,1-trichloroethane may be correct. Yes, well defined	NA	NA	Likely inhalation and possibly dermal	NA	Not reported	No	No	Before	Cases also had 1,2-dichloroethane and methylene chloride exposures	NA
Kumagai (2014) Cholangiocarcinoma	Case report (1 case)	From subject and relative. Exposure modelled	Reported as 1,1,1-trichloroethane. Detailed information on plant operations so identification may be correct Yes, well defined	NA	NA	Likely inhalation and possibly dermal	Modelled exposure [assumed at time of diagnosis]	Likely self-report	No	No	Before	Case also had 1,2-dichloropropane, methylene chloride and kerosene exposures	NA

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