

eTable 1. TCE Worker Studies: Description of Cohort and Case-Control Studies and Summary of Exposure Levels and Exposure Assessment Methods

First Author, Year, (Ref no).	Workforce Size (n)	Person-Years	Cohort Description	Quantitative or Semi-Quantitative Exposure Estimates ¹	Type of Work or Work Activity	TCE Exposure Method/Comments	Reported Relative Risks and 95% Confidence Intervals for Kidney Cancer
<i>Group I Cohort Studies</i>							
Axelson 1994 (45)	1670	23,516	Male workers ≤79 years, biomonitored for TCE from 115 facilities in Sweden 1955-1975. Cancer incidence follow-up through 1987.	Majority (81%) uTCA < 50 mg/L, which corresponds to an average air exposure ~ 20 ppm 100 mg/m ³	Facility where TCE was used. Free surveillance was offered to workers.	Urinary TCA biomonitoring: Exposure indices: 1) mean uTCA all urine samples 2) highest mean uTCA across for 3-year period	SIR = 1.16 (0.42-2.52) 6 cases among workers < 79 years old
Anttila 1995 (46)	3974 Total 3,089 (TCE)	71,800 Total 59,905 (TCE)	Finnish male (n = 2050) and female (n = 1924) solvent workers biomonitored for TCE. Over 600 different worksite or sampling laboratory codes. Follow-up (cancer incidence) 1967-1992.	<u>uTCA Before 1970 (median):</u> Men: 80-90 µ mol/L ~ 40-50 ppm Wom: 60-80 µ mol/L ~ 30-40 ppm <u>uTCA Overall: (median)</u> Men 48 µ mol/L ~ 35 ppm Women 63 µ mol/L ~ 40 ppm	TCE used primarily in degreasing or cleaning of metal surfaces. Also used in rubber work, gluing, dry cleaning, and as a component in cleaning fluid.	Urinary TCA concentrations measured 1965-1982. An average of 2.5 measurements conducted per worker.	<u>Yrs since first measurement:</u> All yrs: SIR=0.87 (0.32-1.89) 0-9 yrs SIR=0.53 (0.01-2.95) 10-19 yrs SIR=1.39 (0.45-3.24) 20+ yrs (0 cases)
Morgan 1998 (42)	20,508 Total 4,733 (TCE)	461,617 Total 105,852 (TCE)	Worked at Aerospace manufacturing site (Arizona), 1950-1985. The total cohort consisted of 13,742 men and 6,766 women. Follow-up (mortality) from 1950-1993.	“Highest levels near 50 ppm” <i>[Based on IH studies assume range of 30-50 ppm]</i>	Most TCE exposure occurred in vapor degreasing between 1952 and 1977. Potential exposure from drinking water at the plant.	Job-exposure matrix (JEM) defined TCE subcohort (high/medium/low/none). High (9): work on degreaser, medium (4): near degreaser, Low (1): occasional contact or proximity to degreaser.	<u>Standardized Mortality Analysis:</u> Any TCE: SMR=1.32 (0.6-2.6) “Low” TCE: SMR=0.47 (0.01-2.62) “High” TCE: SMR=1.78 (0.7-3.7) <u>Internal Cohort Analysis:</u> Cumulative Low: RR=0.3 (0.04-2.4) Cumulative High: RR=1.6 (0.7-3.7) Peak High: RR=1.9 (0.8-4.2)
Blair . 1998 (43)	14,457	NR	Update of Spirtas (1991). Male (n = 10,730) and female (n = 3727) workers, aircraft maintenance facility (Utah), with at least one year of work experience, 1952-1957. Follow-up (cancer mortality and incidence) through 1990.	<u>Rough estimates:</u> 600 ppm – 1934-54 400 ppm – 1955-67 200 ppm – 1968-78 15 ppm – desktop cleaning Note: “numbers should not be interpreted as ppm”	TCE used primarily in vapor degreasers to remove oils or other contaminants (large parts); cleaning small electrical parts with squeeze bottles. After 1978 “Cold state” TCE discontinued in degreasers.	Walk-through surveys, interviews, historical record review, chemical inventory, review of available industrial hygiene data.	<u>Mortality Analyses:</u> Overall RR=1.6 (0.5-5.1) <u>Males (Cumulative -TCE unit yrs)</u> No TCE RR=2.5 (0.7-8.9) < 5 U-yrs RR=2.0 (0.5-7.6) 5-25 U-yrs RR=0.4 (0.1-4.0) 25+ U-yrs RR=1.2 (0.3-4.8)

Ritz 1999 (44)	3,814	120,237	Male uranium processing workers (Ohio). Follow-up (mortality) from 1951 through 1989. Risk estimates only for bladder and kidney cancer combined.	Eighty percent of cohort had some TCE exposure, non classified as heavy. 2,792 workers: “light” TCE exp 179 workers: “moderate” TCE [Assume low exposure < 10 ppm]	Male uranium processing workers – used TCE and other chemicals, 1952-1977	IH classified TCE exposure categories: none (0), light (1), moderate (2), heavy (4).	All workers: SMR=0.65 (0.2-1.5)	
							<u>Lag 15 yrs by duration:*</u>	
							>2 yrs	RR=1.03 (0.3-3.7)
							>5 yrs	RR=1.02 (0.3-4.1)
							<u>Duration, “Light” TCE Exp*:</u>	
							2-10 yrs	RR=1.9 (0.6-6.4)
							10 yrs +	RR=0.8 (0.1-40.0)

First Author & Year	Workforce Size (n)	Person-Years	Cohort Description	Quantitative or Semi-Quantitative Exposure Estimates 1A	Type of Work or Work Activity	TCE Exposure Method/Comments	Reported Relative Risks and 95x Confidence Intervals for Kidney Cancer
Boice 1999 (41)	77,965 Total 2,267 (routine TCE exposure)	1,889,795 Total 66,183 (TCE)	Aircraft manufacturing (Burbank, California) workers (men: n = 62,477; women: n = 15,488). Cancer (mortality) follow-up between 1960-1991.	~ 3,000 workers “intermittent” exposure ~ 2,075 workers “routine” exposure No air sampling prior to 1970s. <i>[Based on IH data – assume range of 30-50- ppm for aerospace workers]</i>	Aerospace workers mainly: - Process equip oper & helpers - Electroplaters - Metal band assemblers - Sheet metal formers TCE primary organic solvent used in vapor degreasers until 1966.	Walk-through surveys, interviews, review of available industrial hygiene data, and job descriptions. Toured similar facilities. Accounted for ventilation, respiratory protection.	<u>Routine TCE Exposure:</u> All Workers: SMR=0.99 (0.4-2.0) < 1 yrs: SMR=0.97 (0.4-2.5) 1-4 yrs: SMR=0.19 (0.02-1.4) 5+ yrs: SMR=0.7 (0.2-2.1) <u>SMRs less than 1.0 for:</u> assembly, fabrication, processing, and maintenance workers
Hansen 2001 (24)	803	16,730	Danish male (n = 658) and female (n = 145) workers 275 companies. Follow-up (cancer incidence) was between 1969 - 1996.	<u>uTCA: (Mean/median)</u> µ mol/L 1947-89: 40/15 1947-64: 62/25 1965-73: 43/15 1974-79: 30/10 1980-89: 9/2	Air Monitoring (mg/m ³) 1947-89: 101 ~ 20 ppm 1974-79: 372 ~ 75 ppm 1980-89: 79~ 15 ppm Workers from 275 companies, uTCA or breathing zone air measurements, 1947-1989.	Urinary TCA or breathing zone TCE measurements. Average of 2.2 measurements per worker. The largest group: metal and iron industry.	<u>Cancer incidence risk in 803 workers:</u> Men: SIR=0.9 (0.2-2.6) Women: SIR=2.4 (0.03-14.0) Combined: SIR=1.1
Raascho u-Nielsen . 2003 (25) [IH data from Raascho u-Nielsen 2002] (59,	40,049 Total 14,360 (TCE)	706,317 Total 339,486 (TCE)	Danish blue collar workers from 347 TCE-using companies. Men contributed 588,047 p-y and women contributed 118,270 p-y. Follow-up (cancer incidence) was between 1968-1997.	<u>uTCA (means mg/L):</u> 1947-53 78 ~ 50 ppm 1960-64 58 ~ 40 ppm 1970-74 49 ~ 35 ppm 1980-85 14 ~ 10 ppm <u>TCE air measurements (total):</u> 1950s 586 mg/m ³ ~ 117 ppm 1960s 318 mg/m ³ ~ 63 ppm 1970s 198 mg/m ³ ~ 40 ppm 1980s 75 mg/m ³ ~ 15 ppm	<u>Iron & metal workers:</u> <u>Air (mean/medians) mg/m³</u> 1947-59: 693/323 ~ 138/65 ppm 1960-69: 322/261 ~ 65/52 ppm 1970-79: 302/104 ~ 60/21 ppm 1980-89: 70/27 ~ 14/1.4 ppm <u>Electronics workers:</u> <u>Air (mean/medians) mg/m³</u> 1947-59: 125/109 ~ 25/22 ppm 1960-69: 202/198 ~ 40/40 ppm 1980-89: 42/4 ~8.4/0.8 ppm	Historical IH measurement files. Predictor variables for TCE exposure: 1) size of company, 2) duration of exposure, 3) year of first exposure. Cohort restricted to workers from smaller companies (< 200) assuming increased likelihood of TCE-exposure. Most common types of workers: “metal work” (54%), electronics workers (11%).	Men: SIR=1.2 (0.97-1.48) Women: SIR=1.2 (0.56-2.11) Subcohort SIR=1.4 (1.0-1.8) <u># employees:</u> < 50 SIR=0.7 (0.3-1.4) 50-100 SIR=1.6 (1.0-2.4) 101-200 SIR=1.2 (0.8-1.6) <u>Duration of employment (men):</u> < 1 yr: SIR=0.8 (0.5–1.4) 1-4.9 yr: SIR=1.2 (0.8-1.7) 5+ yr: SIR=1.6 (1.1–2.3) <u>Yr first employment (men):</u> < 1970: SIR=1.7 (1.2-2.3) 1970-79: SIR=0.7 (0.4-1.2) 1980+: SIR=0.9 (0.4-1.7)
Zhao 2005 (40)	5,049 (incidence cohort)	80,784 (estimated by mean duration of employment)	Male workers employed before 1980 in the aerospace division of SSFL (Rockwell/Rocketdyne facility). Follow-up (incidence cohort) started in 1988 and continued through 2000.	Mean cum exp score = 10.2 Median cum exp score = 8.0 <i>[Based on IH data – assume range of 50-100 ppm]</i>	TCE exposure occurred during cleaning of rocket engines, also used as a general degreasing solvent to clean metal parts.	Industrial hygiene review, walk-through visits, interviews with managers and workers, historical facility reports. JEM constructed: high, medium, low, none.	<u>Mortality Analysis:</u> Medium TCE: RR=1.4 (0.5-4.2) High TCE: RR=2.0 (0.5-8.3) <u>Incidence Analysis:</u> Medium TCE: RR=1.9 (0.6-6.2) High TCE: RR=4.9 (1.2–19.6)
Boice 2006 (39)	41,351 all Rocketdyne workers	56,286 Test stand mechanics 254,198 Santa Suzanna Facility 1,138,610 All Rocketdyne	Rocketdyne workers (men: n = 7083; women: n = 1289) employed at the Santa Susana Field Laboratory (SSFL) (California), a rocket engine testing facility. Cancer (mortality) follow-up was between 1948-1999.	<i>[Based on IH data – assume range of 50-100 ppm]</i>	Test stand mechanics had the greatest potential for TCE exposure. Others (maintenance, machinists) had much less exposure (different from Zhao et al assessment).	Job titles extracted from work and personnel listings (phone directories). Walk-through surveys and personnel interviews.	<u>Mortality Analysis – Test Stand Mechanics:</u> Test Stand Mech: SMR=1.8 (0.8-2.5) Any TCE: SMR=2.2 (0.9-4.6) <u>Years as Test Stand Mechanic:</u> < 1 yrs RR=1.3 (0.2-9.3) 1-4 yrs RR=2.1 (0.7-6.2) 5 + yrs RR=2.1 (0.6-7.1) <u>Years Engine Flush:</u> < 4 yrs RR=2.5 (0.3-4.4) 4 + yrs RR=3.1 (0.7-13.2)

Group II Cohort Studies							
First Author & Year	Workforce Size (n)	Person-Years	Cohort Description	Quantitative or Semi-Quantitative Exposure Estimates	Type of Work or Work Activity	TCE Exposure Method/Comments	Reported Relative Risk
Garabrant 1988 (51)	14,067	222,100	Aircraft manufacturing (San Diego County, California). Male (n = 11,898) and female (n = 2169) workers. Follow-up (cancer mortality) from 1958 through 1982.	<i>[Based on IH studies assume range of 30-50 ppm]</i>	Aircraft manufacturing: Assume degreasing/solvent exposures. TCE mentioned.	Estimated that 37% of cohort had TCE exposure, based on interviews of small sample of workers.	Total Cohort: SMR = 0.93 (0.5-1.6)
Blair 1989 (50)	1,767 (Inspectors)	36,720	Male U.S. Coast Guard marine inspectors (1942-1970). Follow-up (mortality) through 1979.	<i>[Cannot be determined or estimated from IH data, highly variable given inspectors changing job sites]</i>	Male U.S. Coast Guard marine inspectors (1942-1970). Exposed to various chemicals. TCE was not evaluated as a separate exposure.	Job title analyses only	Total Cohort (n=1,767) SMR = 1.06 (0.2-3.1)
Costa 1989 (48)	8,626	132,042	7676 men and 950 women. Follow-up (mortality) between 1954-1981 (urinary system cancers).	<i>[Based on IH studies assume range of 30-50 ppm]</i>	Aircraft manufacturing workers (Italy). Assume degreasing/solvent exposure, TCE..	Solvents listed among hazardous substances used; TCE not specifically mentioned.	Total Cohort All Yrs SMR = 0.7 (0.3-1.5) Hired < 1954 SMR=0.4 (0.1-1.3) Hired > 1954 SMR=1.6 (0.4-4.0)
Selden & Ahlborg 1991 (49)	2,176	21,463	Male Swedish Armed Forces (SAF). Follow-up (cancer incidence) between 1975-1983.	<i>[Cannot be determined or estimated, very limited TCE exposure associated with degreasing activities]</i>	Jet fuel exposure during three-year period 1972-1974.	TCE used for metal degreasing to a limited extent. No data on individual exposures.	Total Cohort (n=2,176) SMR = 1.03 (0.2-3.0)
Sinks et al. 1992 (47)	2,086	36,744	Workers from a paperboard manufacturing and processing plant (Georgia). Follow-up (cancer mortality and incidence) between 1957-1998.	<i>[TCE exposure not demonstrated – may have had little opportunity for exposure]</i>	Chemicals used in finishing department, ink mixing, storage rooms	TCE listed on MSDS forms, no exposure assessment.	<u>Mortality Analyses:</u> All workers: SMR=1.4 (0.0-7.7) <u>Incidence Analyses:</u> All workers: SIR=3.7 (1.4-8.1) Finishing Dept: SIR=16.6 (1.7-453.1)
Henschler et al. 1995 (52)	169 (Exposed) 190 (Unexposed)	5,188 (Exposed) 6,100 (Unexposed)	Male cardboard manufacturers, worked at least 1 year (Germany), 1956-1975. Follow-up (incidence) through 1992.	<u>Fevotte estimates :</u> 135 ppm (range 60-270) <u>Cherrie estimated levels:</u> 10 – 225 ppm for hot degreasing peaks to 2000 ppm	TCE used in: 1) cardboard machine area (parts cleaned twice/week ~ 4-5 hours) 2) locksmith electrician shop – continuous exposures, lower concentrations, 3) cleaning floor and clothing. 1956 to 1975.	Walk-through surveys and interviews with long-term employees.	<u>Cancer Incidence by Comparison Group:</u> German Data: SIR=9.66 (3.1-22.6) Denmark Data: SIR=7.97 (2.6-8.7) <u>Distribution of cases:</u> board machining (2) locksmith (1) electricians (2)
Chang 2003 (26)	86,868	1,022,094	Workers (men: n = 16,133; women: n = 70,735). Follow-up (mortality) between 1985-1997	<i>[Levels reported in electronics facility (Singapore) ~ 30ppm – however no TCE subcohort identified]</i>	Electronics manufacturing factory (Taiwan). No job title or subgroup analyses.	TCE in wells near facility, assume worker exposures, no specific data.	<u>Cohort Mortality Analyses:</u> Males: SMR=0.0 (no cases obs) Females SMR=1.18 (0.2-3.4)

Case-control Studies							
First Author & Year	Source of Cases (n)	Source of Controls (n) ²	Confounders Evaluated	Quantitative or Semi-Quantitative Exposure Estimates	Type of Work or Work Activity	TCE Exposure Method/Comments	Reported Relative Risk
Siemiatycki 1991 (33)	Metropolitan Montreal hospitals. (177 cases)	Hospital controls: metropolitan Montreal. Population controls: electoral lists & RDD. (533 population controls; 2481 other cancers – 2 nd control group)	Age, sex, smoking.	[“Any” and ”substantial” categories - cannot be determined or estimated from IH data, Aircraft mfg and metal fabrication – can assume 30-50 ppm based on IH studies]	“Widely used in vapor degreasing since 1930s”. Solvent for adhesives and lubricants. Main Occupations: Machinist, aircraft mechanics, industrial equipment mechanics.	Self reported occupational history classified into TCE JEM - two categories “any exposure” and “substantial” exposure.	<u>TCE Exposure classification:</u> Any Exposure OR=0.8 (0.4-2.0) Substantial Exp OR=0.8 (0.2–2.6) <u>Occupations/Industries:</u> Aircraft Mfg (any) OR=1.0 (0.6-1.8) Aircraft Mfg (subt) OR=1.0 (0.4-2.7) Metal Fab & Mach (a) OR=1.0 (0.7-1.6) Metal Fab & Mach (s) OR=1.3 (0.8-2.3)
Greenland 1994 (35)	Nested case-control study transformer assembly workers (12)	Non-cancer deaths. (1202 total controls)	Age, year of death.	[Based on IH studies assume range of 30-50 ppm]	TCE was used from 1930 to 1977 as a degreaser in plant.	Work histories, TCE JEM: no exposure (0) or any exposure (1).	<u>Mortality Analysis):</u> Any TCE exp: OR=0.99 (0.3-3.32)
Vamvakas et al. 1998 (34)	Kidney cancer patients, nephrectomy in German hospital. (58 cases)	Accident wards from three hospitals < 20 km from case hospital, 1993. (84 controls)	Age, gender, obesity, high blood pressure, smoking, diuretic intake.	[Cannot be determined or estimated from IH data]		Occupational history questionnaire. Interview with patients or their colleagues/ relatives regarding work history and conditions.	Odds ratios by exposure groups: +++ OR=11.4 (2.0-66.8) ++ OR=11.9 (2.6-55.6) + OR=6.6 (0.5-87.8) All age groups: OR=9.0 (2.9-27.8)
Dosemeci et al. 1999 (36)	Minnesota Cancer Surveillance System. (438 cases)	Population based controls. (687 controls)	Age, smoking, hypertension, use of diuretics and or anti hypertension drugs, and BMI.	Overall 13% of cases exposed to TCE, 10% of control subjects exposed. [Cannot be determined or estimated from IH data]		Personal interviews with patients and next of kin, occupational history questionnaires; JEMs developed by NCI.	<u>ORs for TCE exposure by sex:</u> Males: OR=1.0 (0.6-1.7) Females: OR=1.96 (1.0-4.0) Both Sexes OR=1.3 (0.9-1.9)

Pesch et al. 2000 (7)	Kidney cancer patients from five German regions. (935 cases)	Frequency matched controls by age, sex and area from local residency registry. (4298 controls)	Age, study center, smoking.	JEM – Cannot estimate exposure levels, <i>[Degreasing activities could range from 30-100 ppm based on European IH data (Raaschou-Nielsen, 2002)]</i>	Exposure indices incorporate duration, probability and intensity of TCE exposure	Questionnaire ascertaining occupational history. Exposures defined according to British JEM, German JEM and job-task exposure matrix (JTEM).	<u>Results by job and job/task matrices: German</u> <u>Job exposure matrix:</u> Medium: OR=1.1 (0.7-1.8) High OR=1.1 (0.9-1.4) Substantial : OR=1.3 (0.9-1.8) <u>Job Task Exposure Matrix:</u> Medium OR=1.3 (1.0-1.8) High OR=1.1 (0.8-1.5) Substantial: OR=1.3 (0.8-2.1) <u>Job Titles:</u> Metal Processing OR=1.1 (0.7-1.8) Metal Cleaning OR=1.3 (0.7-2.3)
Bruning et al. 2003(27)	Kidney cancer patients from Arnsberg, Germany; urology department. (154 cases)	Hospital controls from local surgery departments without dementia or cancer, matched by age and sex. (401 controls)	Age, sex, smoking.	<i>[Self report- cannot provide exposure estimates. Degreasing activities could range from 30-100 ppm based on European IH data(Raaschou-Nielsen, 2002)]</i>		Self reported work history (occupational questionnaire) and TCE use, classified according to British JEM.	<u>Self reported TCE:</u> Self report: OR=2.5 (1.4-4.5) Self report by duration: <10 yrs OR=3.8 (1.5-9.3) 10-20 yrs OR=1.8 (0.7-4.8) 20+ yrs OR=2.7 (0.8-8.7) <u>Industry, job title or work activity:</u> Metal degreasing OR=5.6 (2.3-13.3) Degreasing (JEM) OR=1.0 (0.4-2.5) Iron/Steel Industry OR=1.2 (0.3-4.5) Contact w/ metals OR=1.5 (0.97-2.4)

First Author & Year	Source of Cases (n)	Source of Controls (n) ²	Confounders Evaluated	Quantitative or Semi-Quantitative Exposure Estimates	Type of Work or Work Activity	TCE Exposure Method/Comments	Reported Relative Risk
Charbotel et al. 2006 (28)	Kidney cancer cases from a region in France with a TCE-using screw cutting industry. (86 cases)	Controls residents in the geographic study area at the time of case diagnosis, matched on age and gender. (316 controls)	Matched on gender and year of birth. Adjusted for tobacco and BMI. [some analyses also adjusted for cutting fluids and other petroleum oils]	Arve Valley (screw cutting): 1960s air: 180-600 ppm 1960s TCA 220-505 mg/L	Mostly screw cutting industry, where degreasing and solvent use common. Also general TCE use as solvent in other industries.	Interviews, questionnaire. Task specific exposure matrix: <u>Open cold degreaser:</u> 15-18 ppm; 50 ppm above tank <u>Open hot degreasing:</u> 120 ppm; 300 ppm above tank. <u>Half – Open Hot degreasers:</u> 35ppm; 75 ppm above tank <u>Emptying and refilling degreaser:</u> average levels: 300 ppm Hand dipping: 30 ppm assigned	<u>Results by TCE Exposure Index:</u> Any TCE exp OR=1.6 (0.95-2.8) Low cuml exp OR=1.6 (0.8-3.5) Med cuml exp OR=1.2 (0.5-2..8) High cuml exp OR=2.2 (1.0-4.6) <u>High confidence in TCE exposure assign:</u> Any TCE OR=1.9 (0.9-4.0) Low cuml exp OR=0.9 (0.1-7.4) Med cuml exp OR=1.0 (0.3-3.7) High cuml exp OR=3.3 (1.3-8.7)
[in Fevotte et al., 2006] (64)				1975 air: 70-800 ppm washing areas 2- 50 ppm adjacent areas	Exposure categories in epidemiologic analysis: Very low: 1-35 ppm Low: 35-50 ppm Medium: 50-75 ppm High: 75-100 ppm Very High: > 100ppm	After	Other Exposure measures: Any metal work: OR=1.02 (0.6-1.8) Screw cutting shops OR=1.3 (0.7-2.3) Metal workers OR=1.0 (0.6-1.8)
				1984 air: up to 200 ppm within 6m of degreasing machine			
				Of screw cutters: 72% < 35ppm 13% > 50 ppm 5% > 75 ppm			

Notes:

A. Relationship between biological measurements and airborne levels (Fevotte et al):

- low UTCA + TCE < 40 mg/g ~ < 30 ppm

- med UTCA+ TCE 40-100 mg/g ~ 30-60 ppm

- high UTCA + TCE 100-170 mg/g ~ 60-80 ppm

- very high UTCA + TCE 170-300 mg/g ~ > 80 ppm

B. 1 ppm ~ 5.27 mg/m³

1. Comments in italics indicate imputation by authors based on available indicated hygiene literature (Raaschou-Nielsen, 2001, 2002; Fevotte, 2006; Bakke, 2007).

2. RDI = random digit dialing