

METHODS USED TO ASSESS TCE EXPOSURE LEVELS, FREQUENCY, AND PROBABILITY IN EPIDEMIOLOGIC STUDIES

**Presentation to the National Toxicology Program
March 17, 2014**

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OUTLINE

- **Background on exposure assessment**
Frequent metrics of exposure
General approaches to assessment
- **TCE background**
- **Evaluation of studies: degreasing**
- **Summary and conclusions**

BACKGROUND ON EXPOSURE ASSESSMENT

CONCEPT OF EXPOSURE ASSESSMENT

- **Assessments are blinded**
- **Evaluate JOBS, not people**
- **Almost always airborne, with NO dermal**
- **Metrics generally evaluated:**

Probability

Intensity

Frequency

Confidence

PROBABILITY

In published studies:

- **Definition usually not provided**
- **Ever/never (ignores probability)**
- **Estimate of probability**

As a score or descriptive (uncertain, possible, probable)

As a category with identified quantitative levels

INTENSITY

- **In published studies:**

8-hour time-weighted average (full-shift)

Average level during exposure/measurement

Peak



**Sometimes
the
same**

- **BUT:**
- **duration (above) not defined and**
- **if used measurements, duration of the measurements is not usually identified**

- **May be estimated:**
 - As a score or descriptive (low, medium, high)**
 - In relation to an occupational exposure limit**
 - In measurement units (e.g., ppm)**

FREQUENCY

- **In published studies:**

As a score or descriptive (always, often, rare)

Quantitative:

Number of days/week

**Number of hours over some unit of time
(e.g., week or year)**

CONFIDENCE

In published studies:

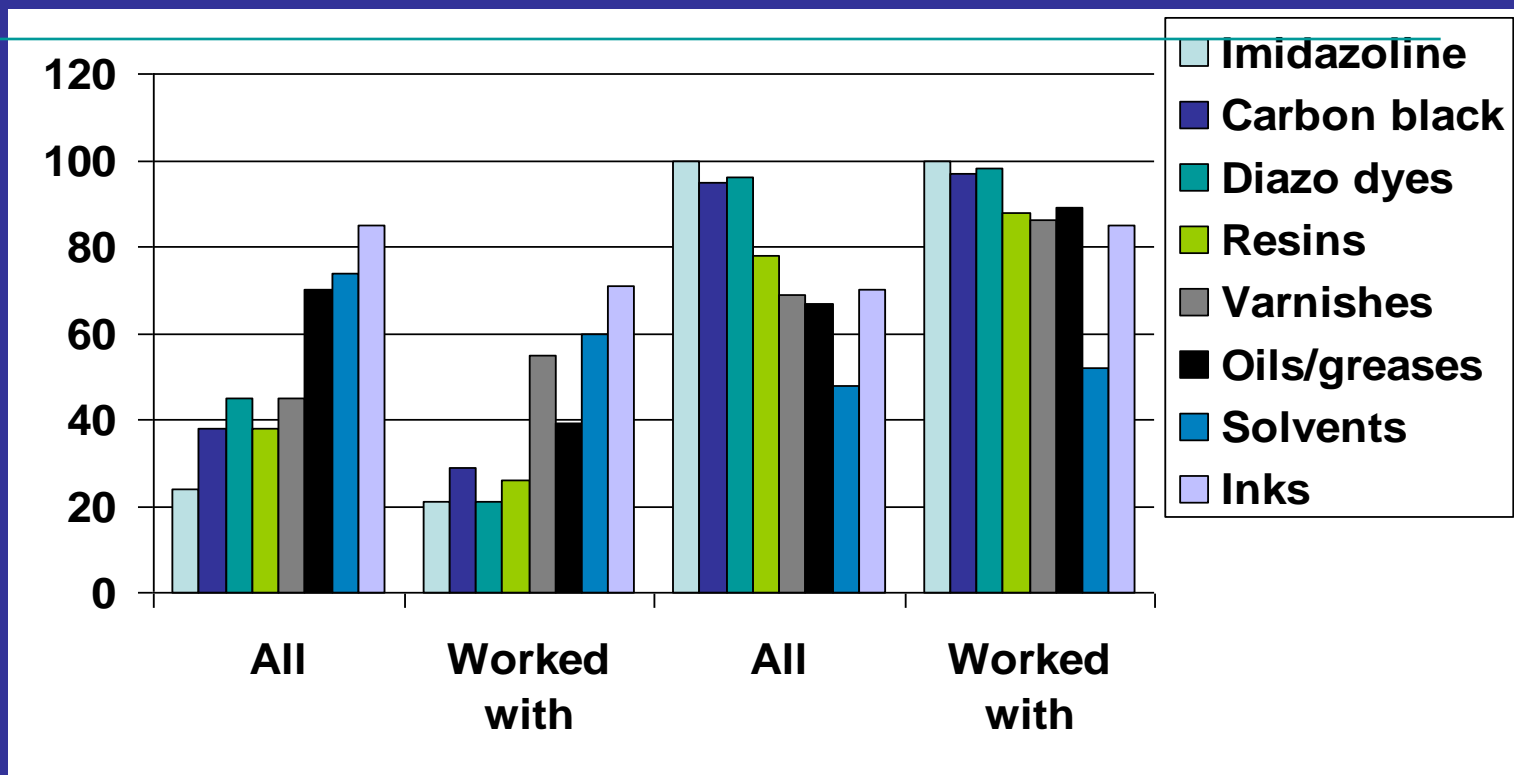
- **A score or descriptive (definite, probable, uncertain)**
- **Unclear how confidence differs from probability**
- **Based on the quality of the data (the information on jobs and the published exposure literature and measurements) and the industrial hygienist's experience**

Assessment Approaches

- **Self-reports**
- **Job exposure matrices**
- **Subject-specific expert review**

ACCURACY OF SELF-REPORTS

%
agreement



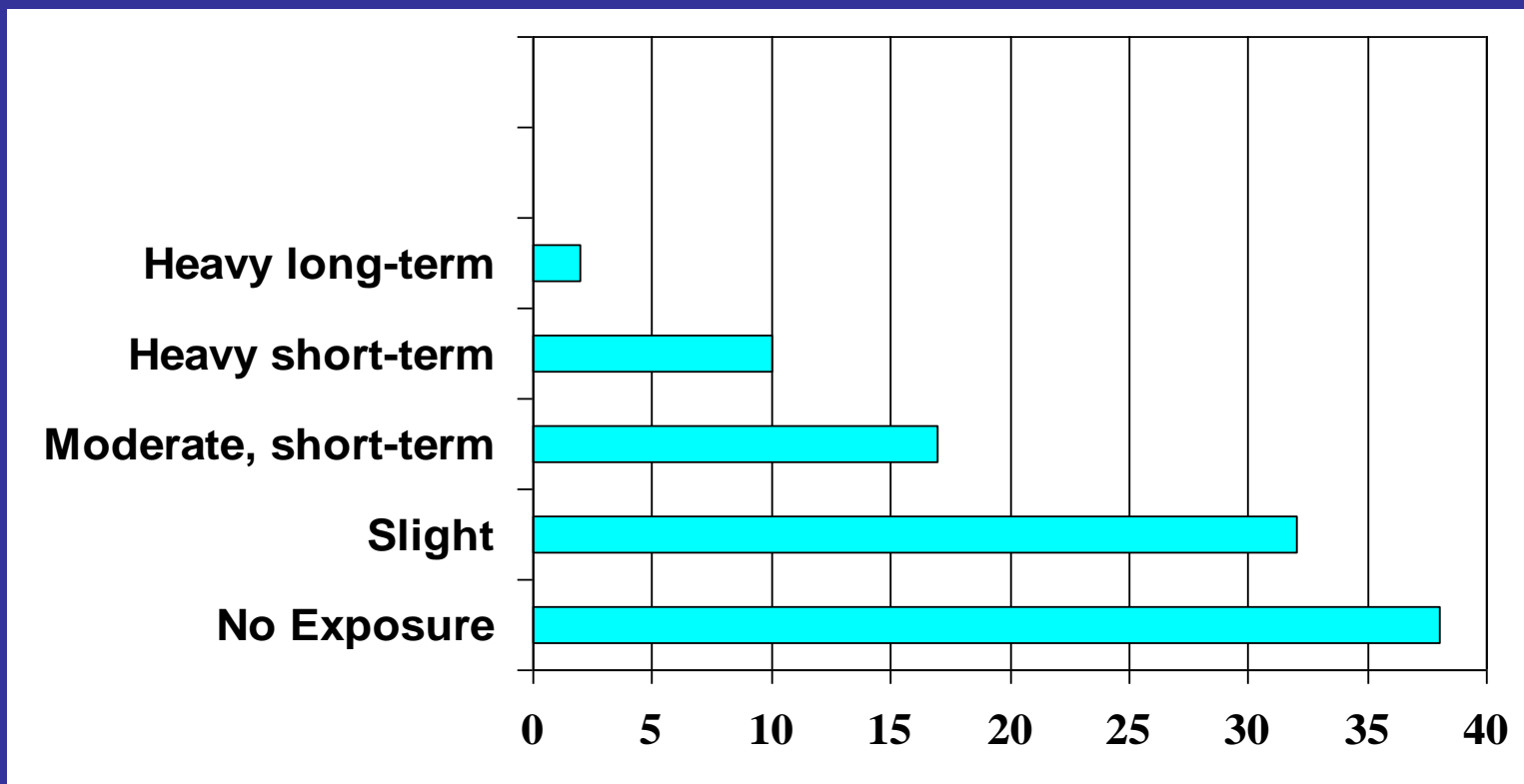
Sensitivity

Specificity

N=420, 5 worksites

Joffe, 1992

ACCURACY OF SELF-REPORTS (Are you exposed? vs IH)



% of people saying yes (N=62)

Nurminen et al., 1995

JOB EXPOSURE MATRICES

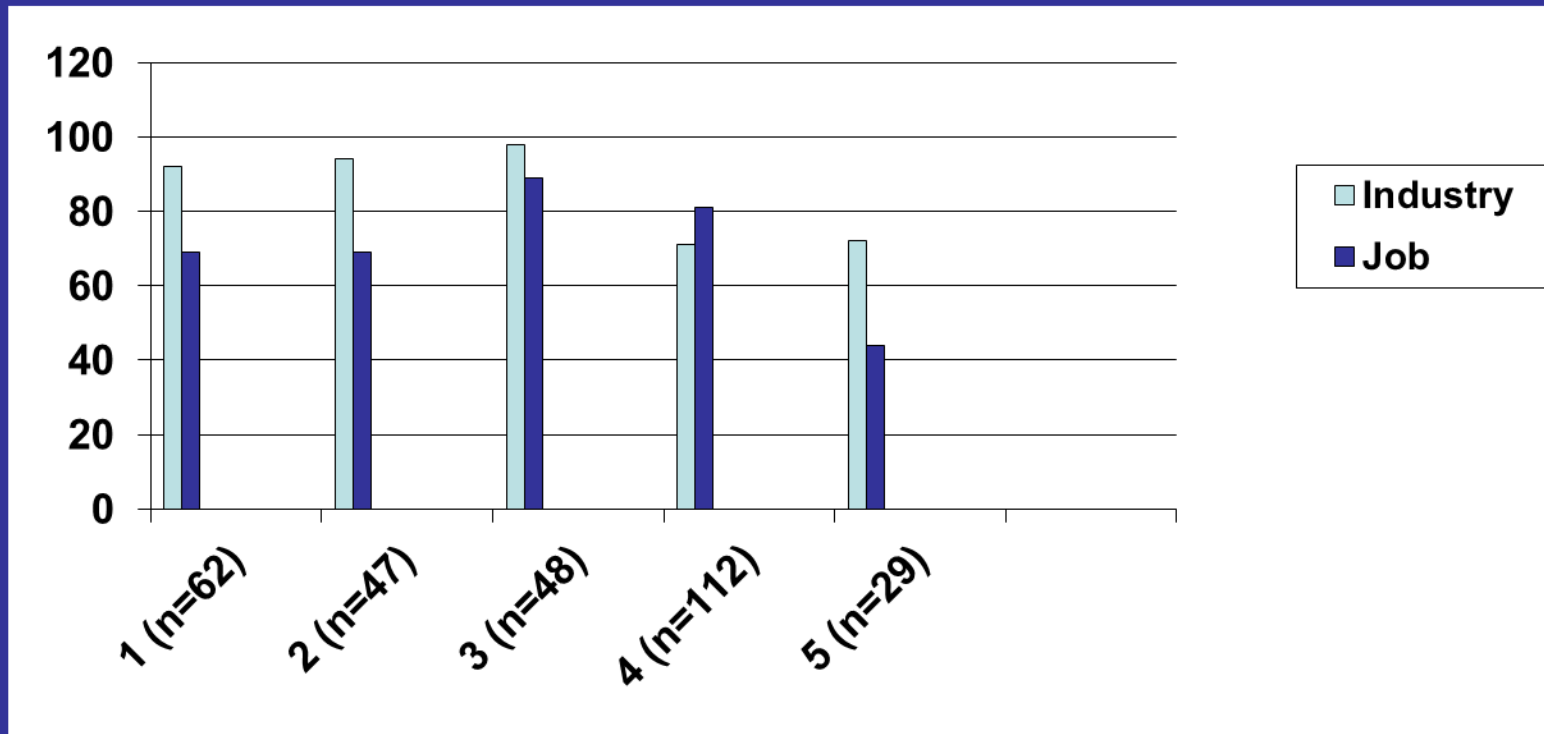
Job title and/or industry	Decade	Probability, intensity, etc.
Secretary/bank	1950s	0
Degreaser	1970s-80s	2
SOC code 7674 (folding machine op)	1970s	1

- Often uses same experts as subject-specific reviews (later slides)
- Jobs or industries often coded:
 - If cohort study, can be company –specific: may not use codes
 - If population-based : often use standard codes
 - Economic, not exposure, based , so can include very diverse jobs or industries
 - Often coding not straightforward

JOB EXPOSURE MATRICES

(Agreement in Coding by Different Coders)

%
agreement



Study (codes)

Kromhout & Vermeulen, 2001

JOB EXPOSURE MATRICES

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 - Economic, not exposure, based , so can include very diverse jobs or industries
 - Often coding not straightforward
- Do not account for variability within a job

JOB EXPOSURE MATRICES

Variability in Exposure Reported in a Single Study

JOB	SOURCE (SUBSTANCE)	FREQUENCY
Warehouseman	Driving forklift (gas/diesel exhaust)	0-40 hr/wk
Truck driver	Filling fuel tank (diesel)	0-14 times/wk
Secretary	Computer (>1970)	0-30 hr/wk
Computer programmer	Computer (EMF)	0-36 hr/wk

SUBJECT-SPECIFIC EXPERT-REVIEW

- **Usually in case-control studies**
- **Requires manual review of all information**
- **Generally uses job or industry-specific questionnaires**
- **Decision-making rarely provided**

ASSESSMENT PROCESS

Depends on type of study

- **Cohort (or nested case-control)**
- **Population-based (or community- and hospital-based) case-control or registry**

COHORT STUDY

- **Usually based on a study of a small number of industries**
- **Process**
 - Abstract work histories of employees (job, department, start/end dates)**
 - Collect historic measurement data**
 - Conduct air monitoring**

COHORT STUDIES

- **Process (cont)**

Collect historical records (organization charts, production records, job descriptions, etc.)

**Interview long-term workers to understand:
jobs and job tasks and how they relate to
sources of exposure
how sources have changed over time**

Develop job groups

COHORT STUDIES

- **Process (cont)**

Develop company-specific Job Exposure Matrix (JEM)

- 1) Estimate exposure for jobs that have current monitoring data (usually arithmetic mean)**
- 2) Estimate exposure for jobs that don't have current monitoring data**
- 3) Estimate historical exposures based on historical information**

COHORT STUDIES

- **Process (cont)**
- **Can be on a department or job or task level**
- **Can be for any metric (probability, intensity, frequency)**
- **Can be with or without regard to time**
- **Can be yes/no, score or quantitative**

COHORT STUDIES

Limitations

- **Based on available information**
- **No standard process**
- **Air measurements may not:
be representative
go back to beginning of study period
cover necessary jobs**

COHORT STUDIES

Limitations

- **Personnel records may not reflect actual tasks or may be generic titles**
- **Interviews may be biased**
- **Development of job groups may not be straightforward**

POPULATION-BASED CASE-CONTROL STUDIES

- **Based on hundreds-thousands of work places**
- **Often collect entire work histories (job title, industry, dates, activities, tools and substances used)**
- **Sometimes additional questionnaires (modules) that are job/industry specific**
- **Jobs/industries often coded using standard coding systems (SOC,SIC)**

POPULATION-BASED CASE-CONTROL STUDIES

- **Process (excludes self-reports)**
 - Review published literature**
 - Develop estimate**
 - **JEM based on coded job title/industry OR**
 - **Subject-specific estimate based on reported information**
- **Can be for one or more metric (probability, frequency, intensity)**
- **Can be with or without regard to time**
- **Generally yes/no or a score**

POPULATION-BASED CASE-CONTROL STUDIES

Limitations

- **No standard procedures; little documentation**
- **No measurements; some use published literature**
- **Published literature is sorely missing on prevalence, intensity, and frequency**
- **No technical information available so applicability is unknown**
- **Occupational codes not developed for exposure but for economic reasons**
- **Unclear what factors are considered or how they are weighted**

BACKGROUND ON TCE

TCE

Primary uses:

- **Degreasing**

Cold: typically nonchlorinated solvents

Vapor degreaser: chlorinated solvents

Typical use in cohort study, infrequent but primary source in c-c studies

- **Textile (no cohort studies, lower frequency & intensity in cc studies)**
- **Inks, glues, anesthesia (no cohort studies, lower frequency, lower intensity? in c-c studies)**

USE OF CHLORINATED SOLVENTS AS A DEGREASER OVER TIME

	Probability of Use (%) (US)						
	1930s	1940s	1950s	1960s	1970s	1980s	1990s
C Tet	2	2	2	1	1	1	0
TCE	2	2	2	2	2	2	1
Perc	1	2	1	1	1	1	1
MeCl ₂	1	1	1	1	1	1	1
TCA	1	1	1	1	1	2	1
Chlorm	1	1	1	1	1	1	1

C Tet: carbon tetrachloride; **TCE:** trichloroethylene; **perc:** perchloroethylene;
MeCl₂: methylene chloride; **TCA:** 1,1,1-trichloroethane; **chlorm:** chloroform
Scale 1:<10%; **2:**10-49%

(US) OCCUPATIONAL STANDARD

- **OSHA (1972):**

100 ppm 8-hour time-weighted average (TWA8)

200 ppm ceiling exposure limit, but can go up to 300 ppm for 5 min every 2 hours as a peak

TCE VAPOR DEGREASING (US)

Decade	Probability of TCE use (%)	Intensity? during exposure (ppm)	Frequency (hr/wk)	Confidence
1940-50s	>10-49	>100; >200 peak	2-10	Moderate
1960s	>10-49	>100; >200 peak	2-10	Moderate
1970s	>10-49	50-100; >200 peak	2-10	Moderate
1980s	<10	10-50; >100 peak	2-10	Moderate
1990s	<10	10-50; >100 peak	2-10	Moderate

Possible exposure levels estimated for presentation purposes

EVALUATION OF TCE EPIDEMIOLOGIC STUDIES: EXPOSURE ASSESSMENT

TCE STUDY EVALUATION

Evaluated exposure assessment methods in TCE studies blinded to the disease risk results

- **Detail on jobs**
- **Job groups**
- **Description of assessment**
- **Measurements**
- **Type of Assessment**
- **Estimates**
- **Metrics**
- **Dermal exposure**
- **Other possible occupational confounders**
- **Evaluated methods**

COHORT STUDIES

- **Very low (ever/never, changes over calendar period not considered)**
 - Henschler, 1995**
 - Raaschou, 2003**
- **Low (ever/never with calendar time considered or semi-quantitative without calendar period considered)**
 - Bahr, 2011**
 - Boice, 2006**
 - Greenland, 1994**
 - Lipworth, 2111**
 - Morgan, 1998**
 - Ritz, 1999**
 - Wilcosky 1984**

COHORT STUDIES

- **Moderate (semi-quantitative, calendar time considered)**
 - Hansen, 2001**
 - Radican 2008**
 - Zhao, 2005**
 - Vlaanderen, 2013**

- **Moderate to high?? (biomonitoring, but only 1-3 measurements/person)**
 - Anttila, 1995**
 - Axelsson, 1994**
 - Hansen, 2013**

COHORT STUDIES

- **Likelihood of exposure: similar across all studies except Raaschou, 2003 [lower: blue vs white collar only] Vlaanderen, 2013 [lower: country-specific JEM]**
- **Intensity of exposure: similar across all studies except Henschler, 1995 (~200 ppm)**
- **Other studies had ranges and distributions of workers could vary over time and level and frequency**

CASE-CONTROL STUDIES

- **Very low (self-reports)**
 - Bruning, 2003 (self-report)**
 - Hardell, 1994**
 - Nordstrom, 1998**
- **Low (JEM, calendar time not considered or in another country):**
 - Bruning, 2003 (JEM)**
 - Deng, 2013**
 - Dosemeci, 1999**
 - Persson Fredrickson, 1999**
 - Wang, 2009**

CASE-CONTROL STUDIES

- **Moderate (no measurements)**

Constantini, 2008

Cocco, 2010

Miligi, 2006

Moore, 2010

Pesch, 2000 (expert review)

Pesch, 2000 (JEM)

Seidler, 2007

Vamvakas, 1998

Charbotel, 2006*

***Measurements available on EPA HERO website, but unclear how used**

CASE-CONTROL STUDIES

- **High (generally subject-specific)**

Christensen, 2013

Cocco, 2013

Parent, 2000

Purdue, 2011*

Gold, 2012*

***Stewart, co-author**

CASE-CONTROL STUDIES

- **Likelihood of exposure: similar across all studies except Charbotel, 2006 and Vamvakas, 1998 [slightly higher]**
- **Intensity of exposure: similar across all studies**

SUMMARY AND CONCLUSIONS

- **Few studies document actual exposure information on TCE**
- **Cohort studies more often positively identify presence of TCE than case-control studies**
- **Probably higher confidence than case-control studies**

SUMMARY AND CONCLUSIONS

- **Degreasing is the most typical operation studied**
Likely historical levels of >100 ppm and >200 ppm (peak)