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

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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

  } **Some-times 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**
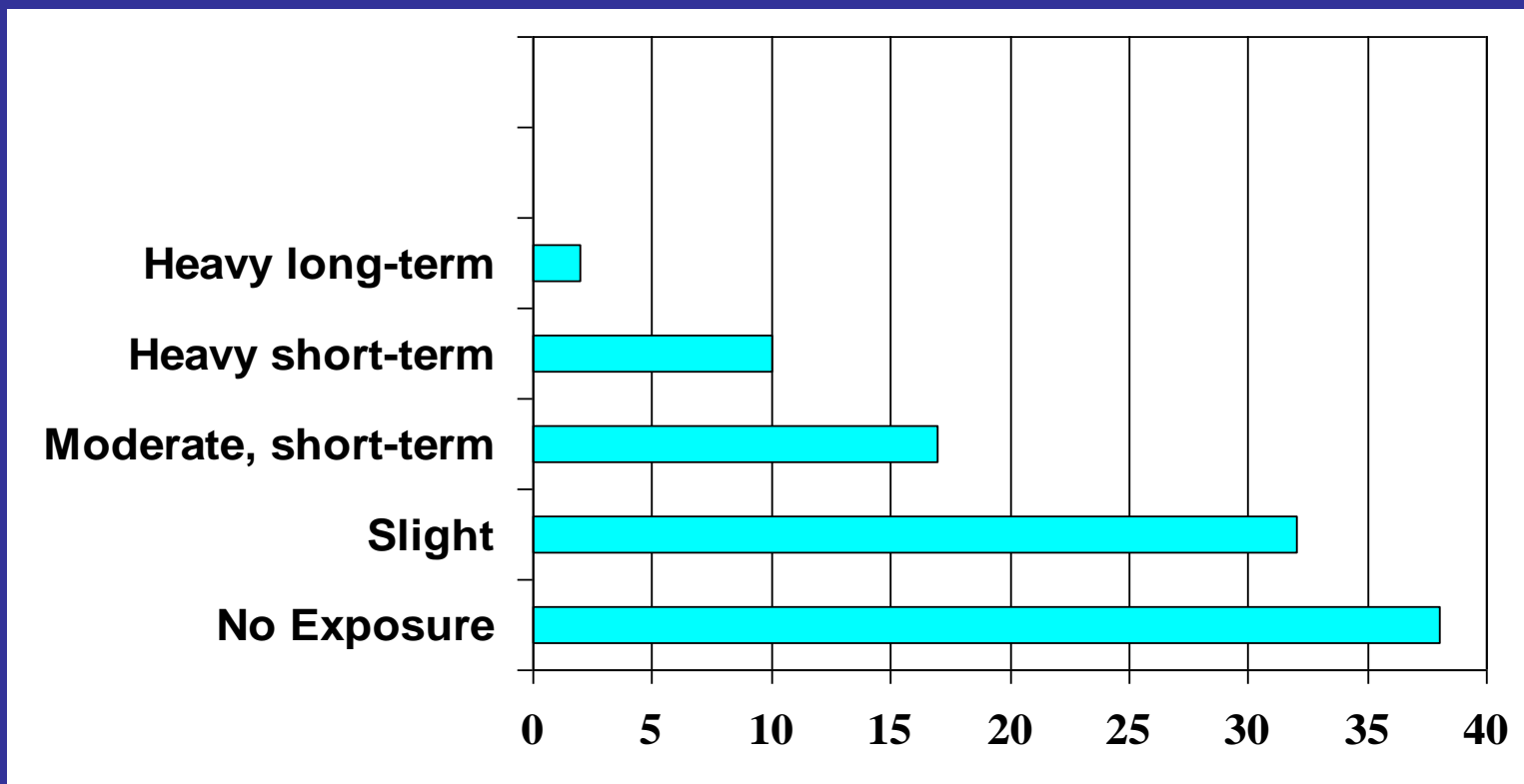
ACCURACY OF SELF-REPORTS

% agreement
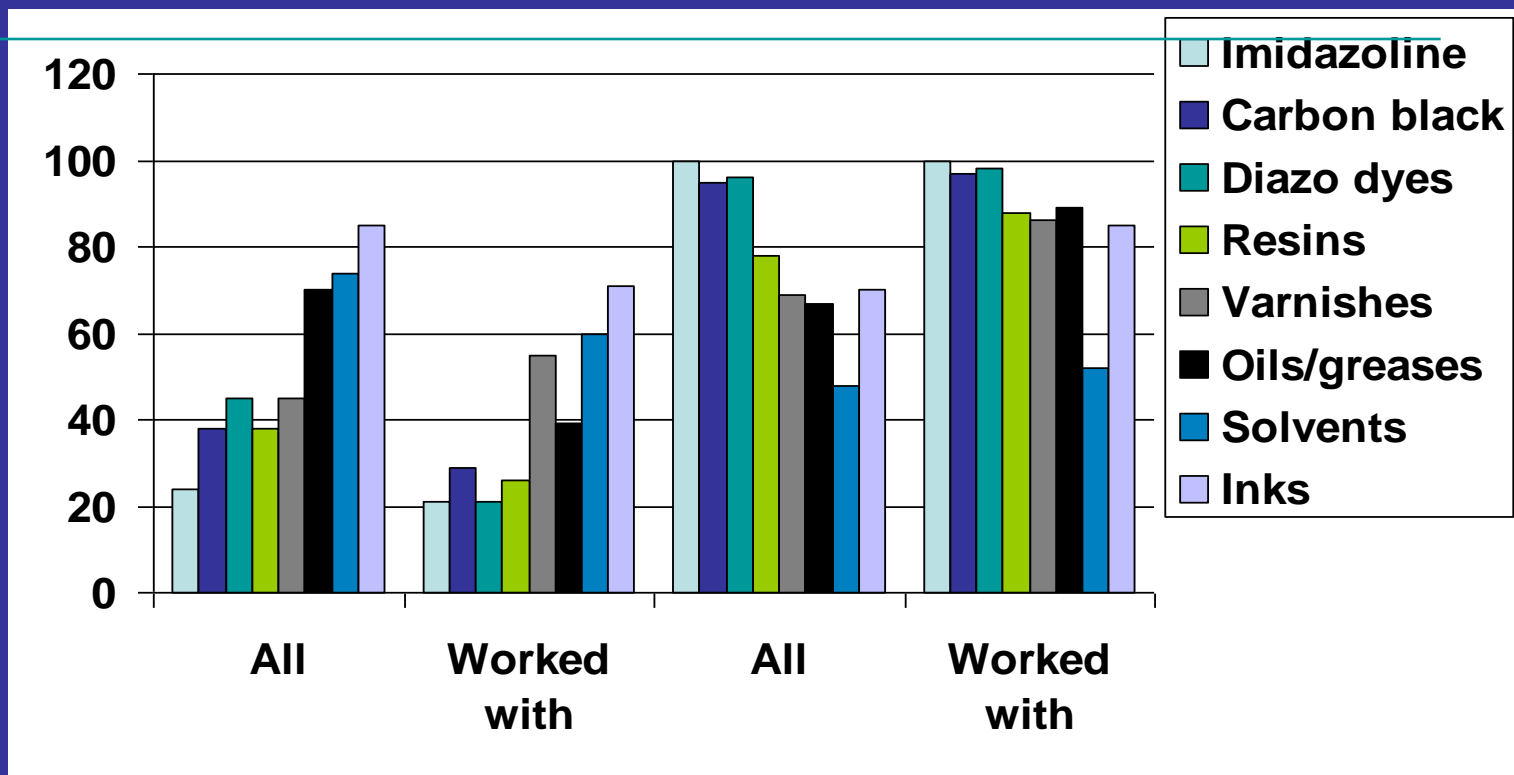
Sensitivity   **Specificity**

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 expert s 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 (y-axis)
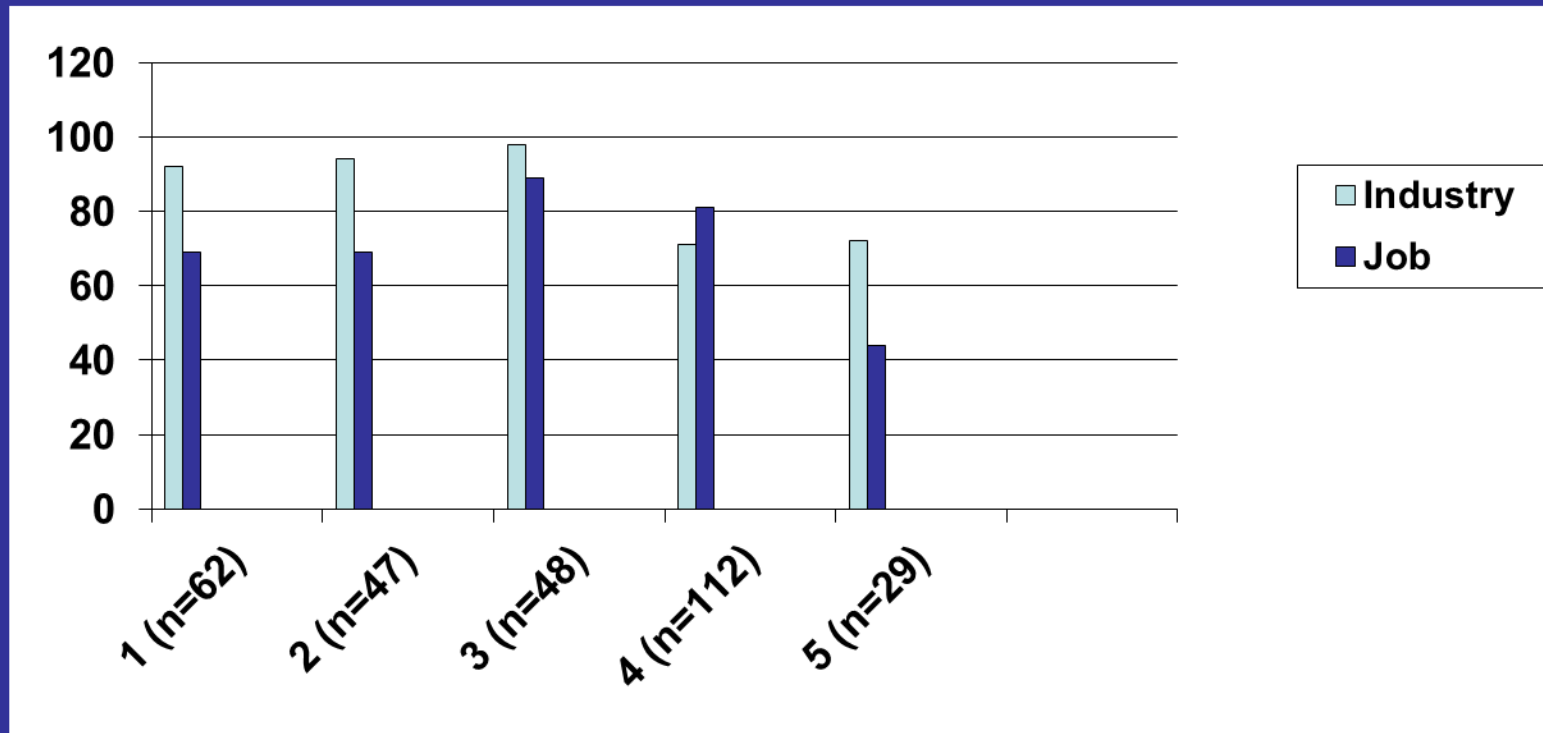
Study (codes) (x-axis)

Kromhout & Vermeulen, 2001

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- 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; MeCl$_2$: 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

Stewart P, Stewart Exposure Assessments, LLC: Occupational Exposure Assessment to TCE. Presentation to the NTP, March 17, 2014

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**
  - **Axelson, 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)