

The Pratt & Whitney Epidemiology Study

Presentation of Final Results

East Hartford, Connecticut
May 23, 2013



Graduate School of Public Health
Department of Biostatistics
Center for Occupational Biostatistics & Epidemiology

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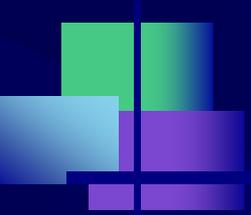
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3-Part Presentation

- Part 1: Background / methods of study
- Part 2: Methods / results of exposure assessment
- Part 3: Results / conclusions of study





Part 1a

Background of Study



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Background

- May 2000 - August 2001
 - CT Dept. of Public Health (CTDPH) investigated perceived increase of brain cancer at North Haven (NH) facility
 - Identified several cases of primary malignant brain cancer (most were common type, glioblastoma (GB))
 - Results deemed inconclusive
 - CTDPH recommended comprehensive, rigorous study by independent research group



Background II

■ August 2001- February 2002

- U. Pittsburgh and U. Illinois at Chicago evaluated feasibility of conducting formal study
- Concluded sufficient data available to study NH and 7 other CT P&W sites

■ July 2002

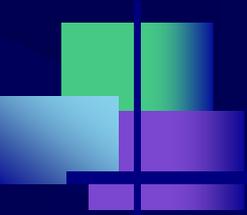
- Work began on large, multi-part, *exploratory* epidemiological investigation



Primary Study Objectives

- To determine definitively whether mortality or incidence rates from central nervous system (CNS) neoplasms, including GB, were elevated at NH or 7 other sites:
 - E. Hartford, Middletown, Rocky Hill, Southington-Aircraft Rd., Southington-Newell St., Cheshire, Manchester Foundry
- To determine definitively whether these rates are associated with specific workplace exposures or experiences





Part 1b

Methods of Study



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3-Phase Study

- Historical cohort study of workers employed between 1952-2001 at NH or 7 other sites
 - Phase 1: Mortality study, 222,123 workers, 1952-2004, 68,701 total deaths, 462 CNS cancer deaths (2008)
 - Phase 2: CNS cancer incidence study, 210,784 workers, 1976-2004, 723 total cases, 277 GBs from 21 state cancer registries (2010)
 - Phase 3: Are CNS cancer and other causes of death associated with P&W work experiences or exposures? (new results to be published May 23, 2013)



Phase 3 Study Components

- Updated CNS cancer incidence in relation to exposures and work experiences
- Nested case-control study
 - 723 CNS cancer cases age-time-gender matched to 723 controls (non-cases) from cohort
 - Collect data on lifestyle, behavior, medical and occupational history via interview with worker or surviving family member
 - Despite extensive promotion, low participation rates for cases (40%) and controls (18%) precluded analysis of data
 - Provided foundation for more refined exposure assessment not possible at total cohort level



How does updated Phase 3 data compare to Phases 1-2 data?

- Slightly different numbers of observed CNS cancer cases (and deaths) due to changes in cohort member eligibility and additional cases from other state registries
- Possible to identify work in 5 plant groups: NH, E. Hartford, Southington, Middletown, “All Other”
- Discontinued use of study factor “payroll type” due to availability of detailed work history and exposure information



Other Phase 3 Study Components

- Exposure assessment (UIC)
- Updated mortality analysis (non-CNS cancer) in relation to exposures (UPitt)



Data Analysis Strategy

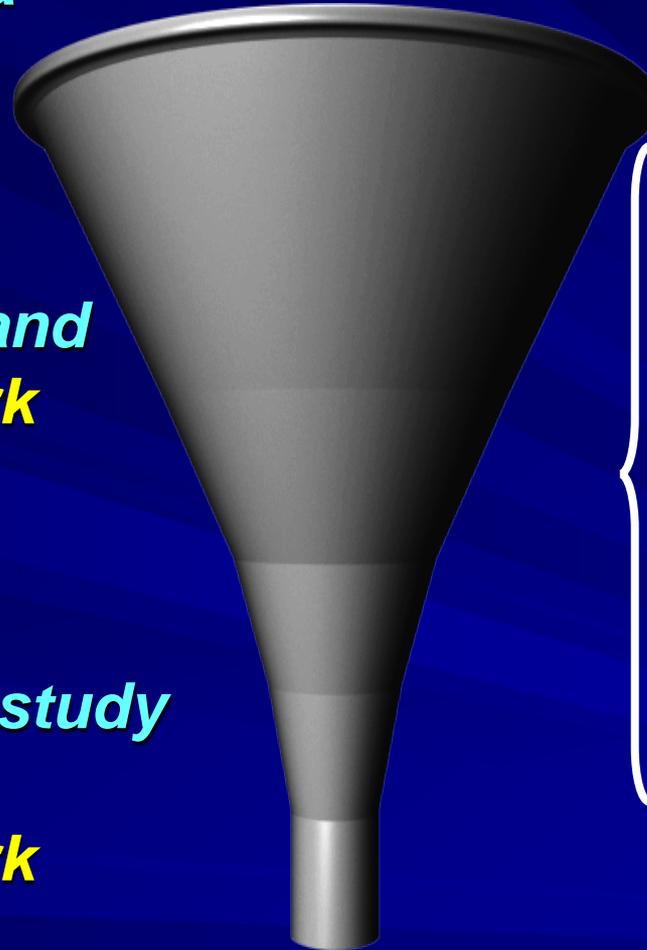
Combined Data



Study factors and exposures/work practices



Subgroups by study factors and exposures/work practices



*All workers at risk
1952 (76) - 2001*



Work-related factors

Plant group, year of hire, age at hire, duration of work, time since first work, exposures/work practices

Non work-related factors

Race, sex, age group, time period



North Haven workers by study factors and exposures/work practices



P&W Study Highlights

- Remains one of the largest and most comprehensive occupational cohort studies ever done
 - 222,123 workers, 7.6 million person-years of observation
- First large-scale study of jet engine manufacturing workers
- Participation by several groups
 - Scientific Advisory Committee, CTDPH, P&W Union Representatives, Communications Facilitation Workgroup (CFW)
- Results reported in 10 peer-reviewed journal articles



Part 2

Exposure Reconstruction for the Epidemiological Study

May 2013

UIC Environmental and Occupational
UNIVERSITY OF ILLINOIS
AT CHICAGO Health Sciences Division
SCHOOL OF PUBLIC HEALTH



Exposure Reconstruction

- Defines common exposure subgroups
- Assigns exposures for subgroups
- If there is an excess adverse health effect, then exposure reconstruction seeks an association between exposure and health effect
- If there is no excess health effect, exposure reconstruction, however refined, will not associate an agent with an effect or explain an observation

Exposure Reconstruction Protocol

- The study examined:
 - All employment categories as defined by the job dictionary
 - 11 classes of chemical and physical agents
 - 20 part categories
 - 16 process categories

Exposure Subgroups: Job Dictionary

- Data came from P&W work history records
 - UPitt provided anonymized combinations of job title, job code, department title, department code, and occupational group from several million lines of data
 - Because many tasks were performed across plants, plant was not considered a critical field for combinations at the cohort level
- 312,646 unique combinations categorized into 42 classes

Exposure Subgroups: Job Dictionary

Group	Number of job classes	Working years (%)
Background	1	28.0
Intermittent	7	40.7
Exposed	31	30.5
CANEL	1	0.05
Null	1	0.75
No data	1	0.02

- No data class: no data in any of the critical fields; not included in analysis
- Null class: less than 1 year total employment and no job title present in record; assigned exposures of “0”
- CANEL: All CANEL-related jobs included for workers with P&W employment after 1966

Exposure Subgroups: Job Dictionary

TABLE 1. Job Dictionary Classes With Descriptions and Job Title Examples and the Number of People and Working-Years Within Each Cohort-Level Job Class*

Job Class	Description	Job Title Example	Number of Workers	Working-Years (All Workers)
IA	Intermittent exposed A; research and development	Materials engineer, chemist	15,607	87,317
IB	Intermittent exposed B; manufacturing supervisors	Foreman, group supervisor	6,867	76,966
IC	Intermittent exposed C; managers	Industrial hygienist, maintenance engineer	17,498	93,006
ID	Intermittent exposed D; support and trades	Crib attendant, pipefitter, machine tool mechanic	46,936	295,160
IE	Intermittent exposed E; engine mechanics and assembly	Engine mechanic, engine assembler	13,410	71,153
IF	Intermittent exposed F; assembly (other than engine)	Subassembler	11,858	48,703
IG	Intermittent exposed G; part preparation	Cleaner masker, marker	2,165	8,207
	<i>Total I</i>		<i>114,341</i>	<i>680,513</i>

Individually Examined Agents

- Selected based upon:
 - Status as a known or suspected carcinogen (through inhalation, at any organ)
 - Availability of information on usage (how and how much)
 - Availability of industrial hygiene exposure measurements



Individually Examined Agents

Cohort & case-control

- 1) Chromium
- 2) Cobalt
- 3) Solvents
- 4) Ionizing radiation*
- 5) Lead-cadmium*
- 6) Electromagnetic fields*
- 7) Mineral oil metalworking fluids
- 8) Soluble metalworking fluids
- 9) Nickel

Case-control only

- 1) Polychlorinated biphenyls (PCBs)*
- 2) Metalworking combustion products specific to North Haven (“blue haze”)

*Qualitative (Yes/No) exposure estimates

Individually Examined Agents

- Generated and validated mathematical models for quantitatively evaluated agents
- Data used:
 - IH sampling measurements
 - P&W engineering time studies

COBALT

Background-level job classes:

B, CA, IE, IF, IG, VEECM, VEEDM, VEEM,
IE, EO, VEDG, VESM, VECOMP, EIMI, EIXI,
EIPT, EIM, EIQADX

Exposed job classes:

Characteristic exposure groups (CEGs) Characteristic exposure levels (CELs)

$$\text{CEG}_1 = \text{GAF, GB, GV, GBV, GAF} \quad \text{CEL}_1 = \begin{cases} 1.0 & X \in X_1 \\ 0 & \text{Else} \end{cases}$$

$\text{CEG}_2 = \text{EB, ED, EL, EM, ES, GBP, VEAR}$

$$\text{CEL}_2 = \begin{cases} 0.8 & X \in X_2 \\ 0 & \text{Else} \end{cases}$$

$\text{CEG}_3 = \text{IA, IB, IC, ID, IE, GIDOD, GO, VEPT, VEGW, VESB, VEST}$

$$\text{CEL}_3 = \begin{cases} 0.08 & X \in X_3 \\ 0 & \text{Else} \end{cases}$$

$\text{CEG}_4 = \text{GBP, VEF, VELD, VEPT, GIDOD, GO}$

$$\text{CEL}_4 = \begin{cases} 0.15 & X \in X_4 \\ 0 & \text{Else} \end{cases}$$

$$\delta = \begin{cases} 1 & \text{Exposed} \\ 0 & \text{Background} \end{cases}$$

Time adjustment factors:

$$\beta_0 = 1$$

$$\beta_1 = \begin{cases} e^{1-0.2(T-1967)} & 1967 \leq T < 1995 \\ 1 & \text{Else} \end{cases}$$

$$\beta_2 = \begin{cases} 0.0037 & T \geq 1995 \\ 1 & \text{Else} \end{cases}$$

$$\text{For GO only } \beta_3 = \begin{cases} 1.75 & T < 1975 \\ 1.25 & T \geq 1975 \end{cases}$$

$$\text{For VEF only } \beta_4 = \begin{cases} 1.75 & T \leq 1981 \\ 1.25 & T > 1981 \end{cases}$$

$$\text{Exposure level } (L) = \text{CEL}_1 + \text{CEL}_2 + \text{CEL}_3 + \text{CEL}_4$$

$$\text{Point estimate} = \delta L \beta_0 \beta_1 \beta_2 \beta_3 \beta_4$$

Specific Agent Results

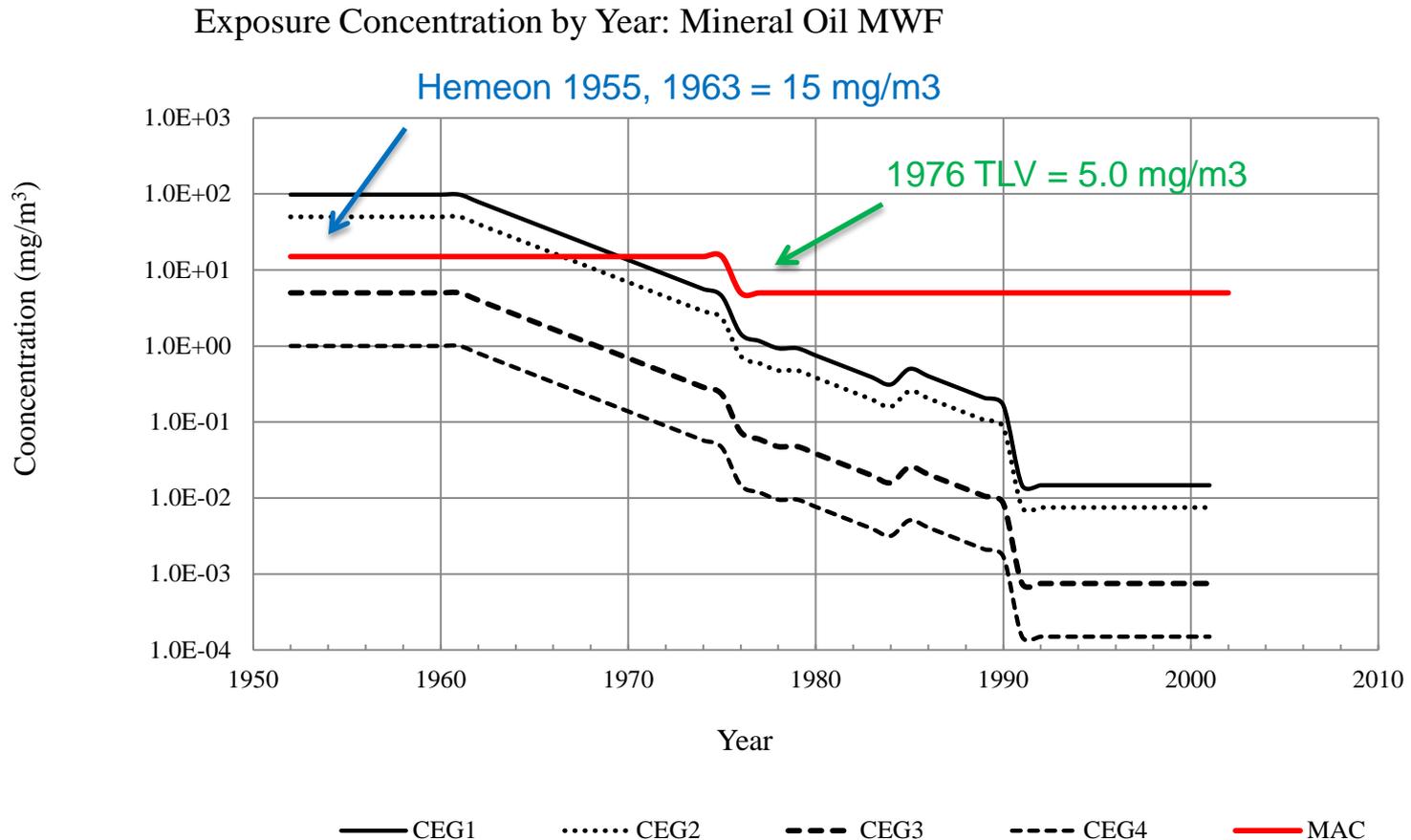
TABLE 2. Mineral Oil MWF Exposure Intervals by Exposed Job Class and Time Period

Mineral Oil MWF Exposure Interval, mg/m ³	Exposed Job Class			
	GBV, GB, GV, and GAF	EL, EM, ED, EB, ES, GIDOD, and VEAR	IC, ID, IE, EO, GBP, and GO	IB
50–100	1952–1964			
10–50	1965–1971	1952–1968		
5–10	1972	1969–1971		
1–5	1973–1980	1972–1977	1952–1968	
0.5–1.0	1981–1984	1978–1980	1969–1971	1952–1964
0.1–0.5	1985–1990	1981–1989	1972–1977	1965–1971
0.05–0.1		1990–1991	1978–1980	1972–1974
0.01–0.05	1991–2001		1981–1988	1975–1979
0.005–0.01		1992–2001	1989–1990	1980–1982
0.001–0.005			1991–1994	1983–1991

EB, exposed broaching; ED, exposed drilling; EL, exposed lathe; EM, exposed milling; EO, exposed other slow-moving operations; ES, exposed shaping; GAF, grinding airfoils; GB, grinding blades; GBP, grinding buff and polish; GBV, grinding blades and vanes; GO, grinding other; GIDOD, grinding internal diameter, outer diameter, and centerless; GV, grinding vanes; IB, intermittent exposed B; IC, intermittent exposed C; ID, intermittent exposed D; IE, intermittent exposed E; MWF, metalworking fluid; VEAR, various exposed all-around machining.

Specific Agent Results

Study levels similar to or less than professional practice recommendations.



Specific Agent Results

Study levels similar to or less than those published for other industries.

Agent	Year	Task	Published Value	Highest study interval
Nickel	1978	Buff, polish, grind, weld (aircraft parts)	0.01 – 252 $\mu\text{g}/\text{m}^3$	0.5 – 1.0 $\mu\text{g}/\text{m}^3$
Chromium	1996	Saw blade grinding	1 – 12 $\mu\text{g}/\text{m}^3$	0.005 – 0.01 $\mu\text{g}/\text{m}^3$
Blue Haze	N/A	N/A	None reported	1000 – 5000 million particles/ m^3

Part/Process Methods

- Part and process analyzed to ensure any unsuspected agent that may be associated with a possible effect would not be missed
 - Estimated >3,000 agents over study period 1952-2001
- Used a screening method developed by Pierce & Esmen designed for complex exposure scenarios
 - Yields a reduced set for further in-depth investigation when an association between a set and health effect is detected

Pierce JS and Esmen NA. A novel method for reducing the number of agents to be studied in an occupational epidemiologic study. *Journal of Occupational and Environmental Hygiene* 2011;8:236-248.



Part/Process Methods

- 20 part families determined with aid of P&W engineers
 - > 90 meeting hours with 95 engineers/experts
 - Selected “representative parts” for each family
- Processes abstracted from SOPs for representative parts and classified into 16 categories based upon:
 - Energy used in contaminant dispersion (thermal, mechanical, electrical, chemical)
 - Relative magnitude of air currents generated from energy form impacting contaminant dispersion
 - Type of contaminant evolved (particulate, fume, mist, vapor)

Part/Process Methods

Qualitative exposures (Yes/No) assigned to part/process job class and year

- Part Families

1. Baffles
2. Blades
3. Combustion chamber
4. Composites
5. Diffuser cases
6. Disks
7. Gearboxes
8. Gears
9. Hollow fan blades
10. Hubs
11. Integrally bladed rotors
12. Inlet cases/fans
13. Intermediate cases
14. Nozzle assembly
15. Seals
16. Shafts
17. Sheet metal fabrication
18. Stators
19. Tubes
20. Vanes

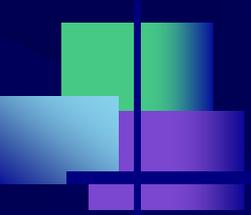
- Process Categories

1. Hot gas cutting
2. Hot machining
3. Hot joining
4. Hot curing
5. High airflow operations
6. Medium airflow operations
7. Low airflow operations
8. Very low airflow operations
9. Inspection and EDM
10. Hot dipping operations
11. Cleaning operations
12. Chemical surface treatment
13. Composite processes
14. Sheet metal processes
15. Facilities and Services
16. Limited manufacturing exposure



Exposure & Health Outcome

- An exposure in and of itself is not particularly meaningful or informative
 - It is relevant if there is a health effect demonstrated
- Agent-specific exposure estimates and part/process assignments provided to UPitt for use in their statistical analyses of exposures and health outcomes



Part 3a

Phase 3 Results



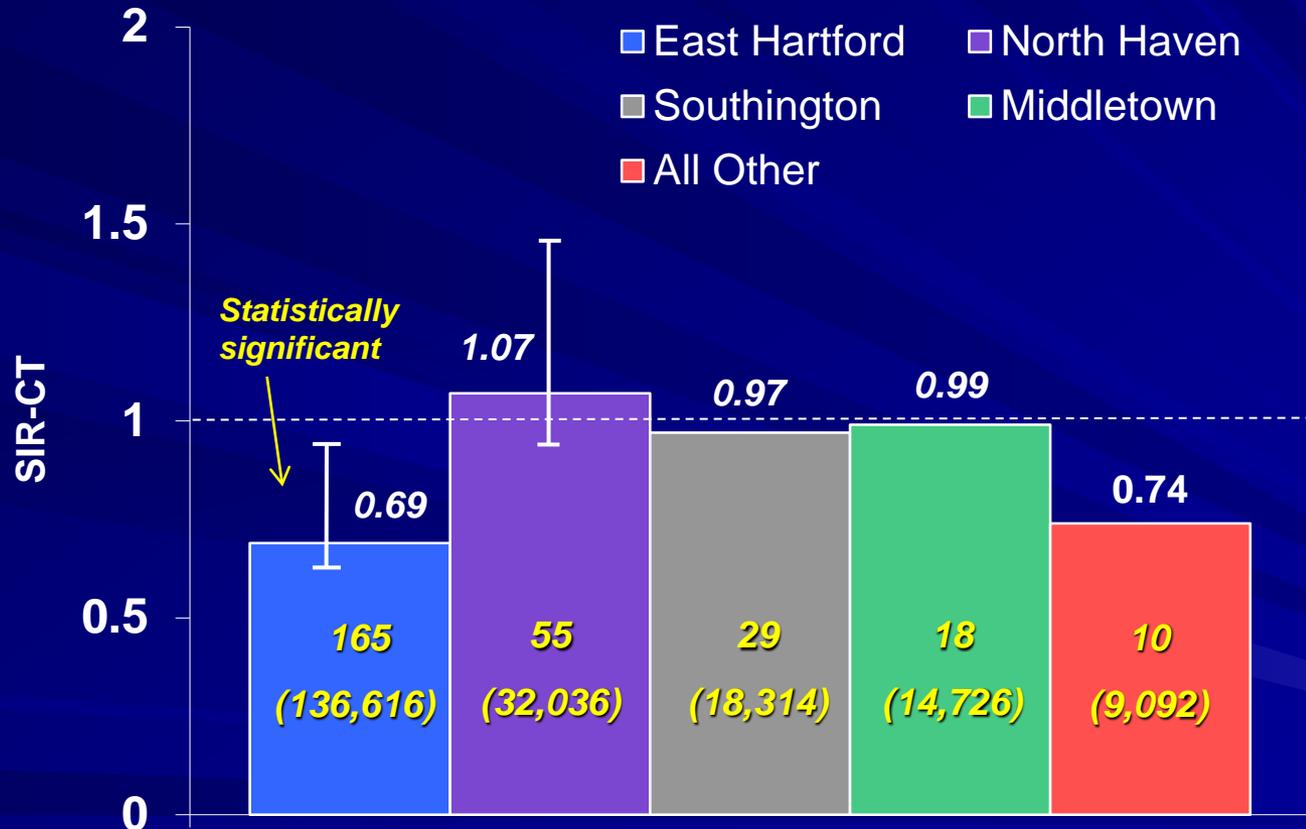
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Study Results Published in 10 Peer-Reviewed Journal Articles

Paper (Yr)	Study Component	Health Outcomes-Factors
I -2008	Original Cohort Mortality Study (Phase 1)	CNS Neoplasms Deaths- Demographic
II – 2008	Original Cohort Mortality Study (Phase 1)	Non-CNS Deaths- Demographic
III – 2010	Original Cohort Incidence Study (Phase 2)	CNS Neoplasms Cases- Demographic
IV- 2010	Methodological	--
V- 2011	Methodological	--
VI- 2013	Updated Cohort Incidence Study (Phase 3)	CNS Neoplasms Cases- Exposure Classes
VII – 2013	Exposure Assessment– Methods & Results	--
VIII - 2013	Updated Cohort Incidence Study (Phase 3)	Glioblastoma Incidence – Parts & Processes
IX – 2013	Updated Cohort Mortality Study (Phase 3)	Non-CNS Deaths - Exposure, Parts & Processes
Editorial-2013	Summary of Entire Study	All



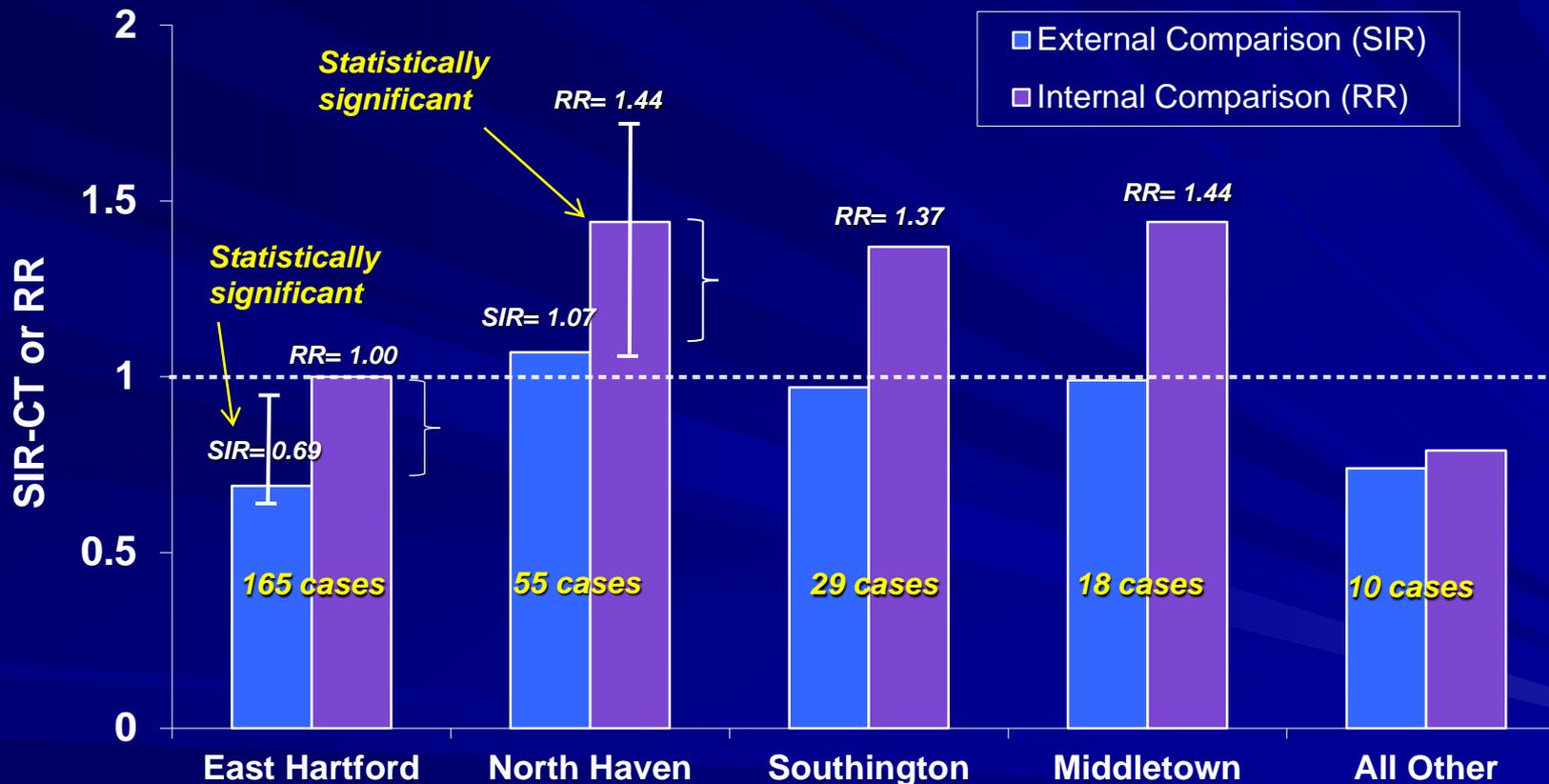
Plant Group Comparisons: Glioblastoma Incidence Based on CT External Comparisons Slightly Elevated but Not Statistically Significant in North Haven



= observed cases
() = number of workers



Plant Group Comparisons: Glioblastoma Risk Based on Internal Comparisons Higher in North Haven, Southington and Middletown Compared with East Hartford



Exposure Analysis: Strategy

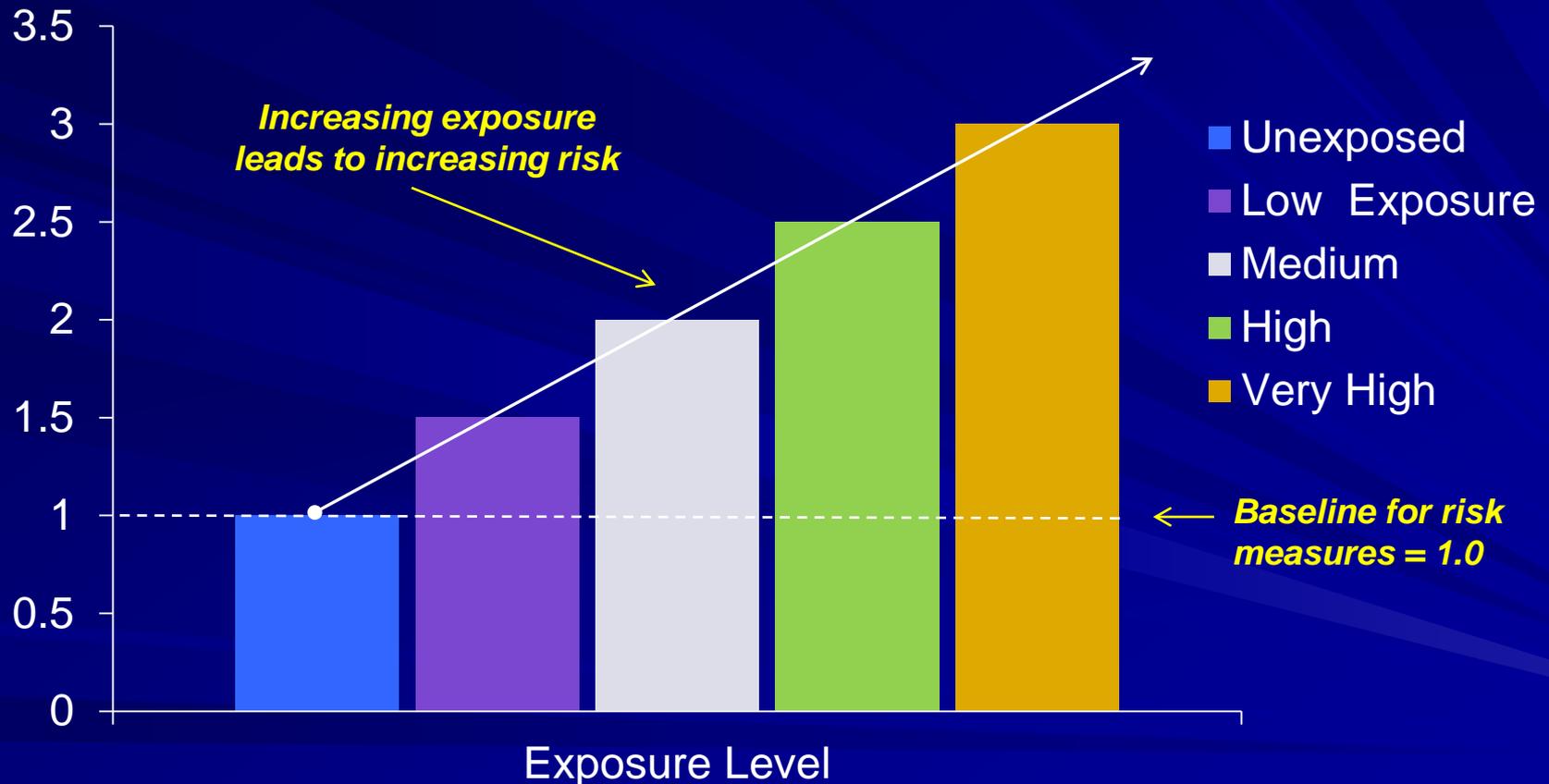
- Evaluated at case-control and cohort level (external and internal comparisons) and across all plants (exception: NH-blue haze)
- 11 exposure classes: MWF-Min, MWF-Sol, nickel, cobalt, chromium, ionizing radiation, EMF, lead-cadmium, solvents, PCBs, blue haze (NH only)
- 4 metrics of exposure: exposed/unexposed, duration of exposure, average intensity of exposure*, cumulative exposure*
- Results of 104 agent_exposure-response evaluations shown in published articles

* computed only for quantitative measures



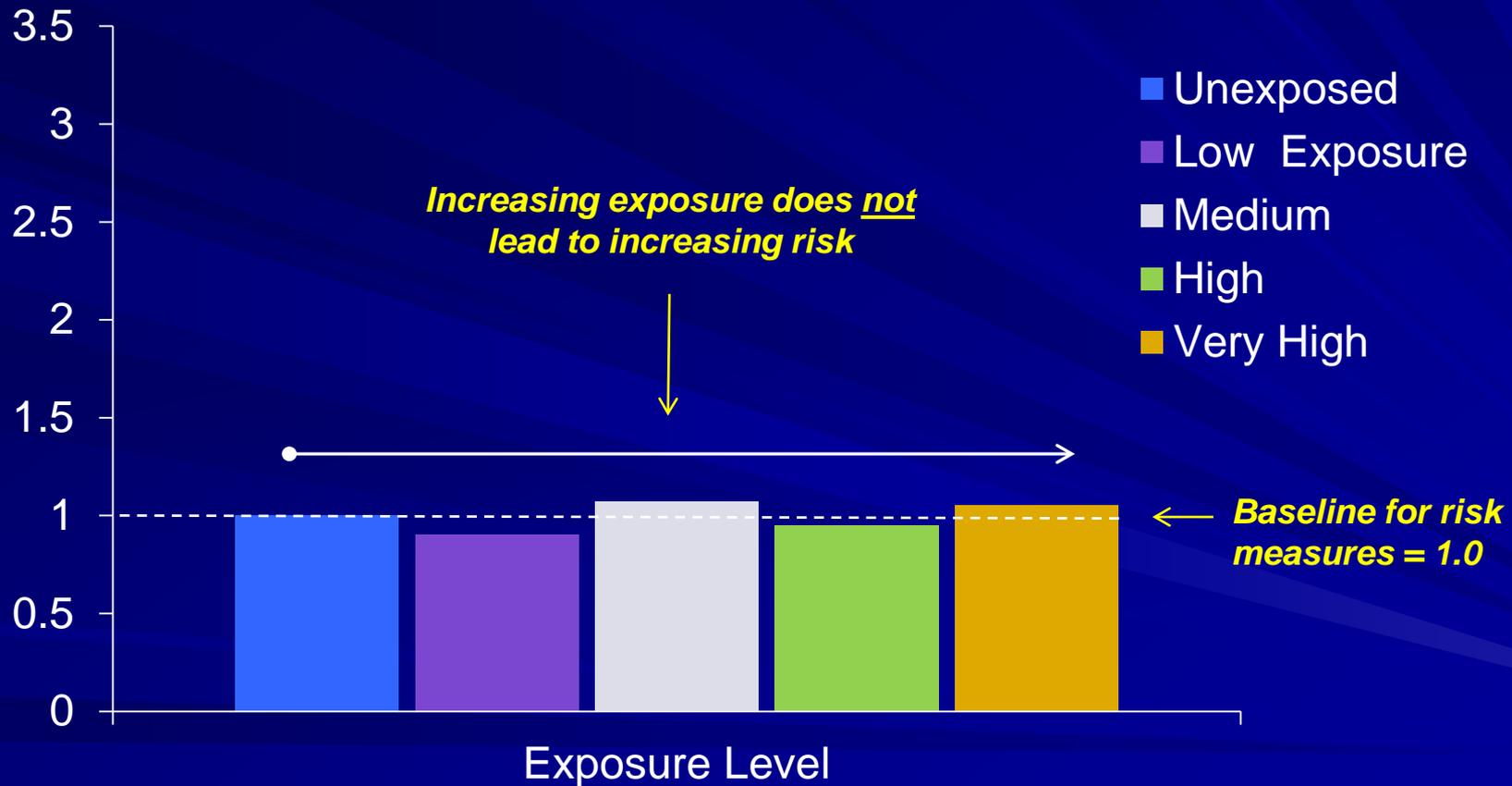
Hypothetical Example of Positive Exposure-Response Relationship

Risk Measure (OR, RR, SIR)

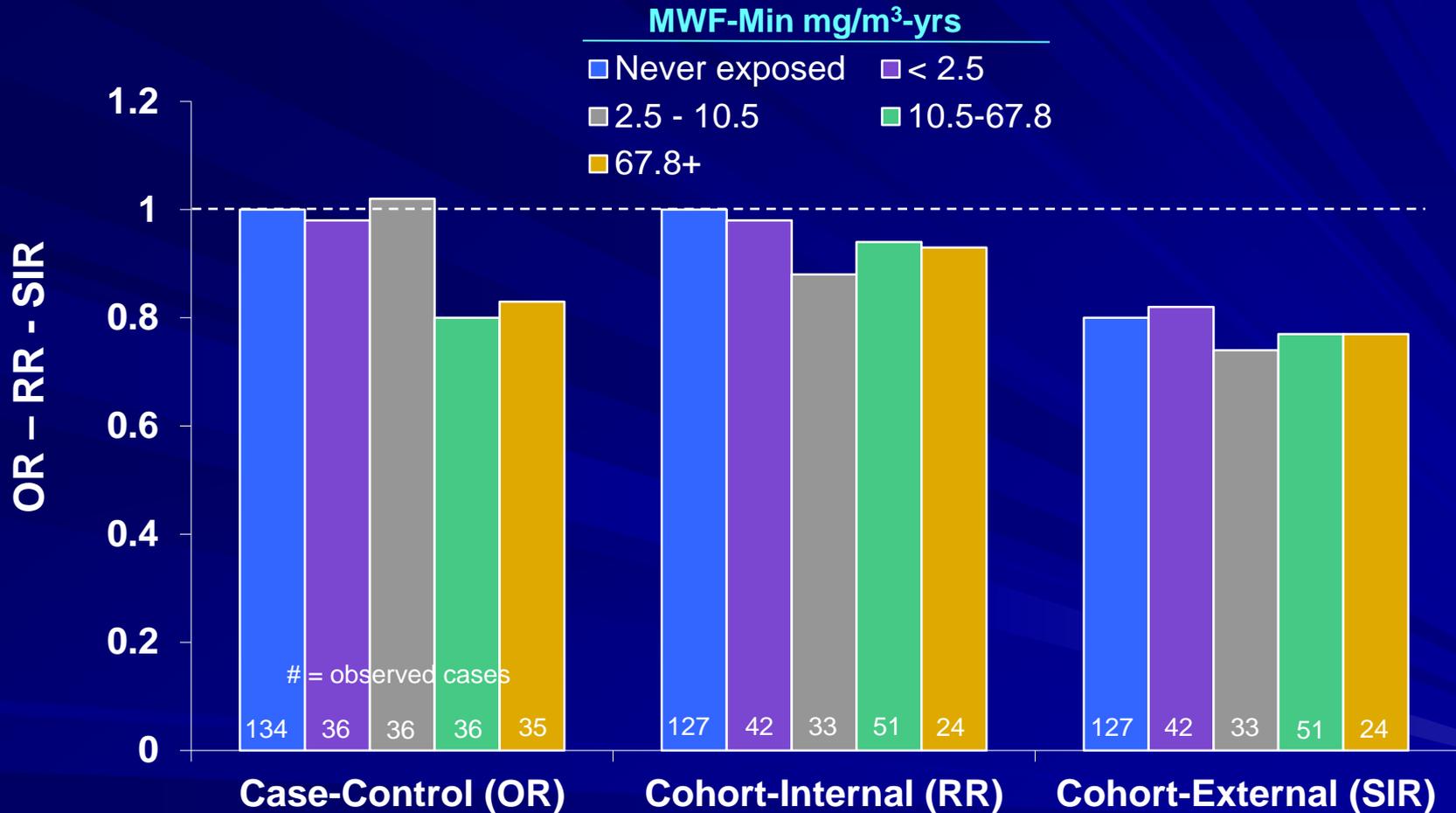


Hypothetical Example of Null Exposure-Response Relationship

Risk Measure (OR, RR, SIR)

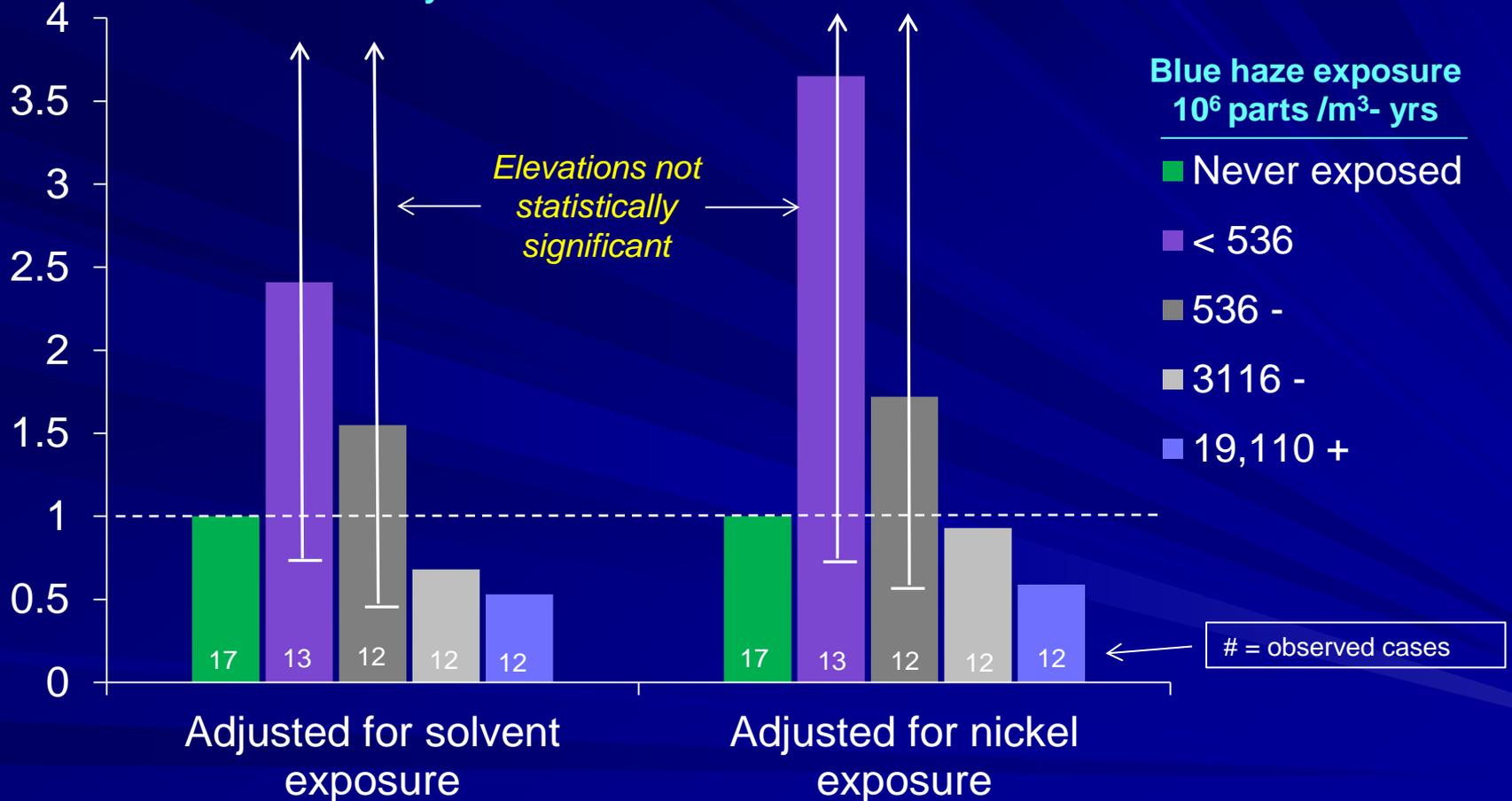


Example: For All Workers, Glioblastoma Incidence Not Related to Cumulative Exposure to Metalworking Fluids



Glioblastoma Incidence in North Haven Not Related to Blue Haze Exposure

Odds Ratio: case-control study



Exposure Analysis: Summary

- In both the total incidence cohort and case-control studies, none of the chemical class metrics considered were associated with increased GB risk
- GB incidence rates in NH were not related to workplace exposures, including the “blue haze” exposure unique to NH



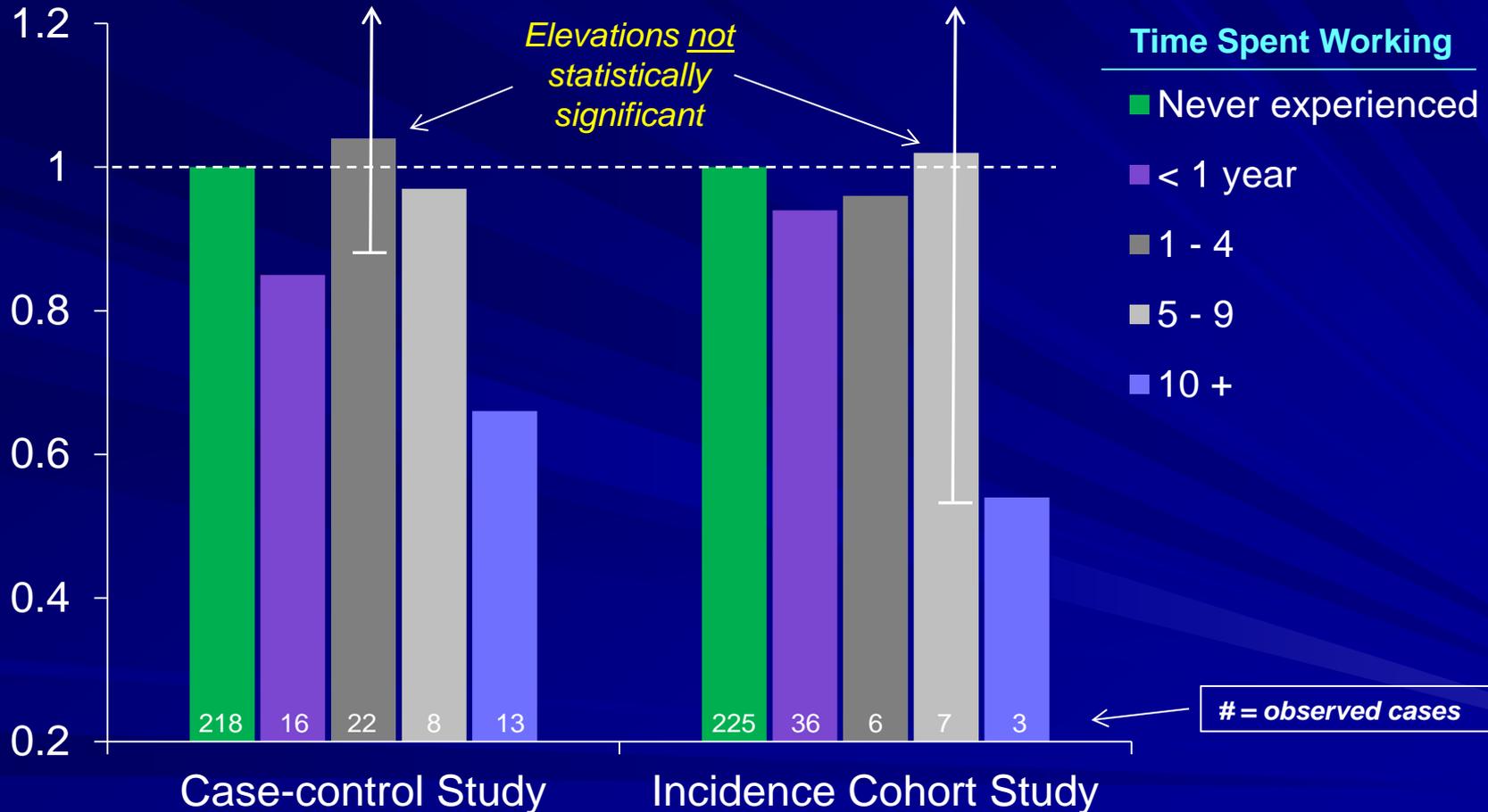
Work Experience Analysis: Strategy

- Used as a screening tool to identify possible workplace associations not otherwise feasible to examine (3,000+ chemical agents present in P&W work environment)
- Evaluated at case-control and cohort level (external and internal comparisons) and across all plants
- 20 part families and 16 process categories and 4 part x process combined groups
- Metric of exposure: Time spent in given category
- Results of 88 part, process and part x process evaluations shown in published article



Example: For All Workers, Glioblastoma Incidence Not Related to Time Spent Working with Blades

Odd Ratio or Relative Risk



Work Experience Analysis: Summary

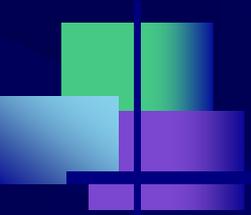
- In both the incidence cohort and case-control studies, none of the part families and/or process categories considered were associated with increased GB risk



Updated Cohort Mortality Analysis: Summary

- In Phase 1 mortality study, screening criteria (1.25-fold+ elevation in risk *and* statistically significant) applied (met criteria → evaluated further)
- Phase 1 screen identified kidney cancer and non-malignant respiratory disease but these were not related to factors examined
- Phase 3 screen based on updated data identified 2 COPD-related cause of death categories (*original causes did not meet criteria*)
 - Bronchitis, emphysema, asthma in Southington plant group
 - Emphysema in Middletown plant group
- COPD findings not related to relevant exposures (MWF - Min/Sol)
- Smoking or occupational exposure outside P&W cannot be ruled out as reasons for the COPD results; full evaluation limited by lack of smoking data for workers in study





Part 3b

Conclusions of Overall Study



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Study Conclusions I

- In the P&W plants studied, occupational exposures to chemical or physical agents decreased over the time frame of the study and quantitatively estimated levels were similar to or less than published data from other industries.
- With the exception of elevated COPD-related mortality in two of five study plant groups, our evaluation of total and cause-specific mortality rates (excluding CNS neoplasms) found no evidence of elevated rates.
- Smoking or occupational exposure outside P&W cannot be ruled out as reasons for the COPD results.



Overall Study Conclusions II

- For CNS neoplasms, including GB, the results of our incidence study revealed no statistically significant elevations in overall rates among the P&W workforce compared with rates in the general populations of the U.S. and CT.
- If not due to chance alone, the small to moderately elevated GB rates in NH may reflect unmeasured external occupational factors or non-occupational factors unique to NH or the baseline E. Hartford plant used in the internal comparisons.



What do the results mean?

- Based on the results of our 12-year comprehensive investigation, we conclude that:
 - The P&W workforce and their family members should be reassured that employment before 2002 at the P&W plants studied, including the NH plant, does not increase your risk of developing brain cancer and does not increase your risk of dying from any cause of death.



Acknowledgments

- We gratefully acknowledge the support, cooperation and assistance of the following groups without whose help this study would not have been possible:
 - The CT Department of Public Health
 - The Scientific Advisory Committee
 - P&W operators and HR, EH&S, engineering and management personnel
 - The International Association of Machinists and Aerospace Workers (IAMAW)
 - The Communications Facilitation Workgroup



Questions?



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