National Cancer Institute

OCCUPATIONAL FORMALDEHYDE EXPOSURE AND CANCER RISK

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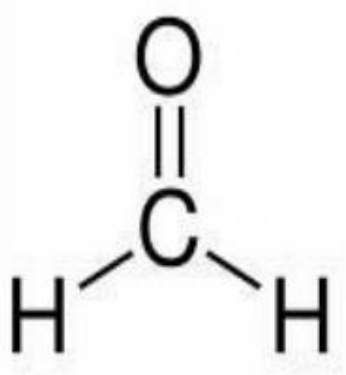
National Institutes of Health

Formaldehyde: An Important Chemical

- Ubiquitous in atmosphere and life forms
- >5% of yearly U.S. GDP
- 2.1 million U.S. workers exposed (1995)
  - Fixatives and disinfectants
  - Wood products, resins, molded plastics, crease-resistant fabrics, paper products
- Environmental exposures
  - Off-gassing from home furnishings, automobile engines, cigarette smoke, incomplete fuel combustion

Background: Evidence for Carcinogenicity



- Genotoxic
- Causes DNA-protein cross-links at site of contact
- Inhaled formaldehyde causes nasal tumors in rats

Carcinogenicity of Formaldehyde

- WHO-IARC review in 2004
  - Sufficient evidence for nasopharyngeal cancer
  - Strong, but not sufficient evidence for leukemia
- WHO-IARC review in 2009
  - Sufficient evidence for leukemia, particularly myeloid
  - Reaffirmed status for nasopharyngeal cancer
- National Toxicology Program Report on Carcinogens 2009
  - Sufficient evidence for nasopharyngeal cancer and myeloid leukemia
- EPA ongoing
  - Updating risk assessment of formaldehyde

U.S. Occupational Standard

OSHA:

0.75 ppm for 8-h time weighted average

2.0 ppm for short-term exposure limit

Formaldehyde Research: 2 Exposure Scenarios

- Study of Funeral Industry Workers
- NCI Cohort of Industrial Workers

Leukemia among Professionals

Author (year, region)	# deaths	Time period	PMR or SMR (Observed deaths) Cause of Death: Hemato-lymphopoietic malignancies	Leukemia	Myeloid leukemia
Funeral Directors and Embalmers					
Hayes (1990, USA)	4,046	1970-85	1.4* (115)	1.5* (51)	1.6* (24)
Walrath (1983, NY)	1,132	1925-80	1.2 (25)	1.4 (12)	1.5 (6)
Walrath (1984, CA)	1,007	1925.-80	1.2 (19)	1.8* (12)	1.5 (6)
Milham (1976, WA)	222	1950-71	1.9 (7)	3.0 (5)	NR
Levine (1984, Ontario)	319	1928-77	1.2 (8)	1.6 (4)	NR
Pathologists					
Harrington (1975, UK)	156	1955-73	2.0* (8)	0.6 (1)	NR
Hall (1991, UK)	194	1974-86	1.4 (10)	1.5 (4)	NR
Matanoski (1989, USA)	3,644	1912-78	1.2 (64)	1.7* (31)	NR
Anatomists					
Stroup (1986, USA)	738	1888-79	1.2 (18)	1.5 (10)	8.8* (3)

* 95% CI does not include 1.0

STUDY OF FUNERAL INDUSTRY WORKERS

Case Control Study of Funeral Industry Workers

- 6,808 deaths among 13,994 inactive/deceased funeral directors/embalmers
- Identified through professional associations and licensing boards (deaths from 1960-86)
- 168 deaths from lymphohematopoietic malignancies
  - 34 from myeloid leukemia
- 265 controls: deaths due to natural causes
  - Matched by study source, sex, dates of birth and death

Study of Funeral Industry Workers: Exposure Assessment

- 1,278 interviews with next of kin and co-workers
- Work history, including embalming characteristics
  - Per job: start/end, funeral home, embalming, # embalmings (autopsied/intact), ventilation
  - Per subject: duration of typical embalming, frequency of spills
  - Smoking history

Study of Funeral Industry Workers: Exposure Assessment

- Exposure study
  - 25 embalmings under controlled conditions
    - Ventilation
    - Solution strength
    - Type of case (intact or autopsy)
  - Continuous measurement of formaldehyde concentration in breathing zone
  - Exposure levels:
    - Average intensity while embalming: 1.7 ppm
    - 8-hr time weighted average: 0.2 ppm
    - Peak exposure while embalming: 8.6 ppm

Cancer in the Funeral Industry: Results

	Non-lymphoid LHPM OR	Myeloid Leukemia OR
Duration (y)		
<500 embalmings	REF	REF
≤20 years	0.3	0.5
>20-34 years	2.0	3.2
>34 years	2.6	3.9
	p-trend=0.046	p-trend=0.020
# of embalmings		
<500	REF	REF
≥500-1422	0.6	1.2
1423-3068	1.8	2.9
>3068	2.3	3.0
	p-trend=0.247	p-trend=0.314

Hauptmann, et al., JNCI 2009

Cancer in the Funeral Industry: Results

- Similar results for other metrics:
- Myeloid leukemia:
  - Cumulative exposure: p-trend=0.192
  - Average intensity while embalming: p=trend=0.058
  - TWA8 intensity: p-trend=0.396
  - Peak exposure: p-trend=0.036
- No associations with other LHPM

NCI COHORT OF INDUSTRIAL WORKERS

NCI Industrial Cohort Study

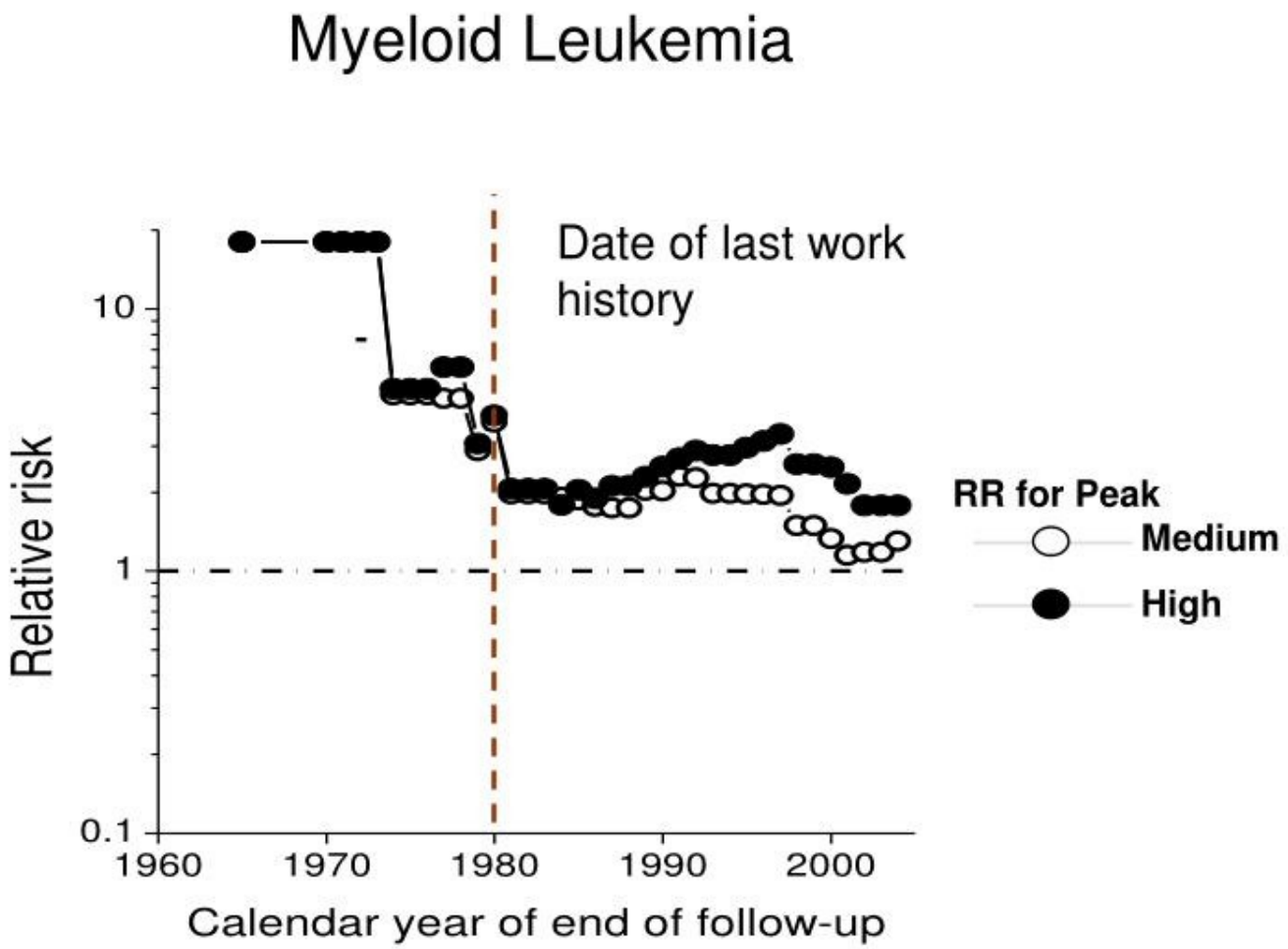
- Mortality study of 25,619 workers in 10 plants
  - Employed prior to 1966
  - Work histories through 1980
- Time-dependent exposure metrics
- 13,951 deaths as of 2004
- 42 years of median follow-up

NCI Industrial Cohort: Relative Risks by Peak Formaldehyde Exposure (ppm)

	0	>0-<2.0	2.0-<4.0	≥4.0	
	RR	RR	RR	RR	p-trend
Lymphohemato	1.07	1.0	1.17	1.37*	0.02
Leukemia	0.59	1.0	0.98	1.42	>0.50
Lymphatic leukemia	0.27	1.0	0.81	1.15	>0.50
Myeloid leukemia	0.82	1.0	1.30	1.78	0.13

Beane Freeman, et al., JNCI. 2009; 101: 751-761.

RR for Medium and High Peak Formaldehyde Exposure Categories



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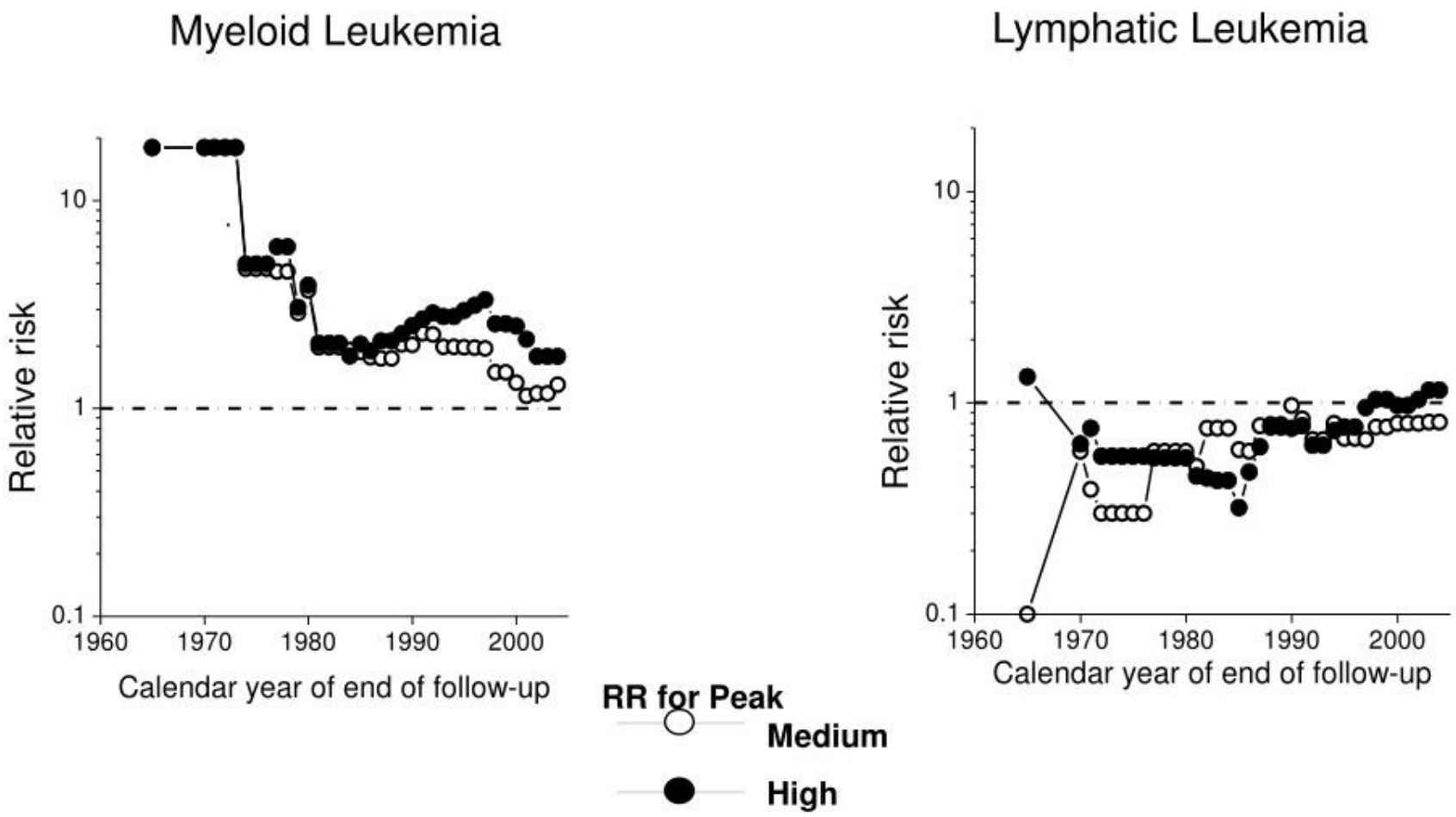
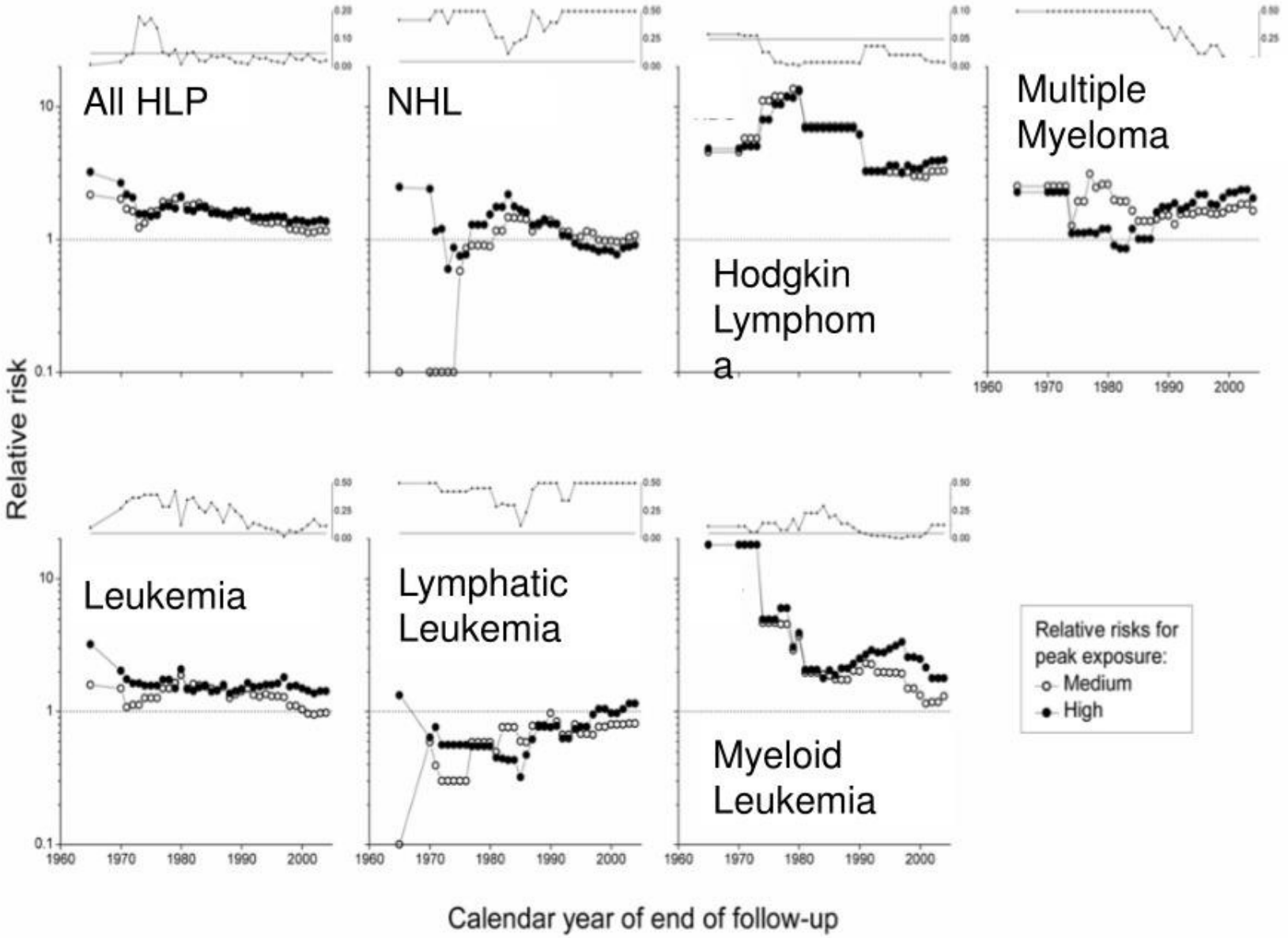
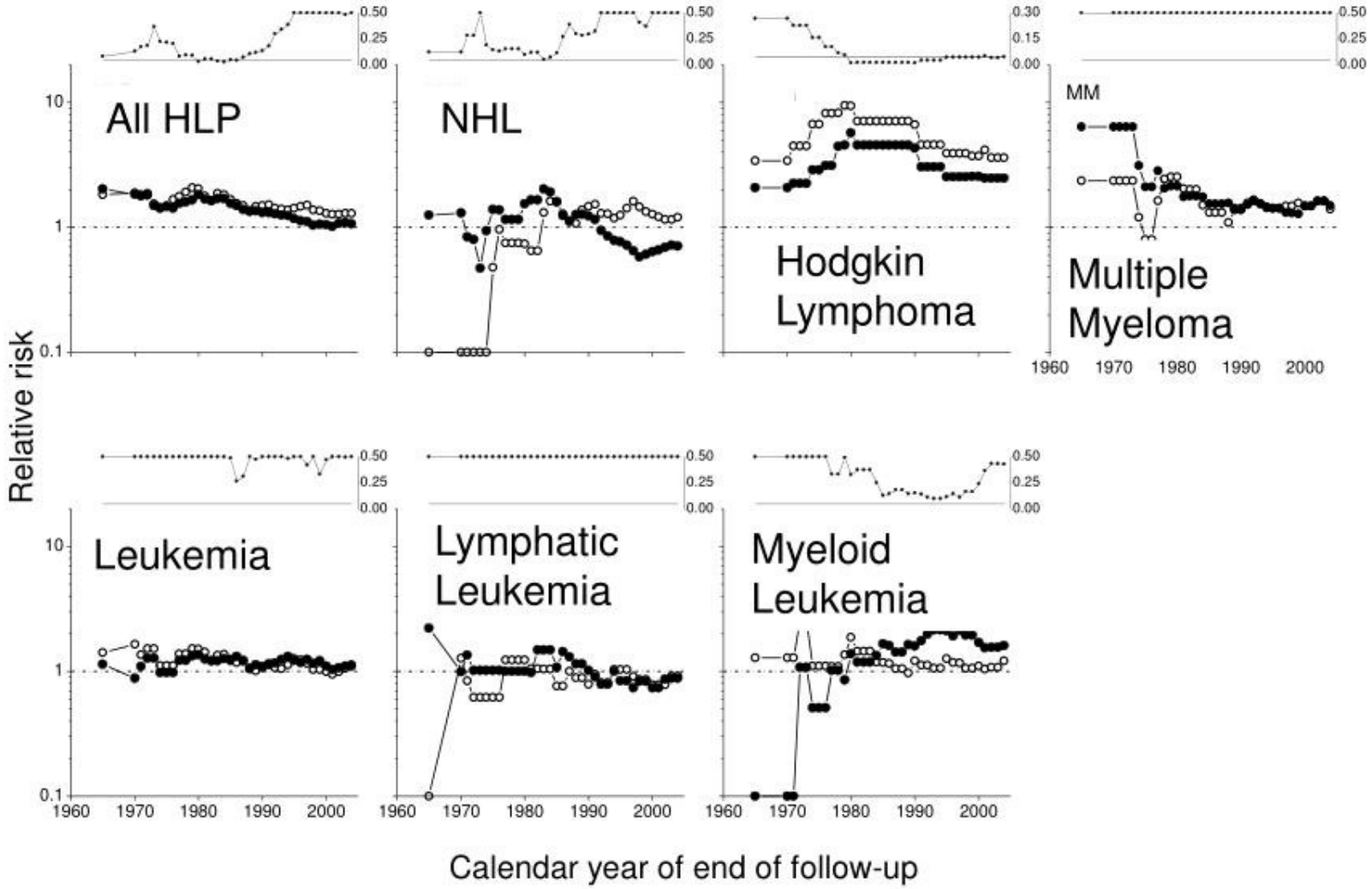


RR for Medium and High Peak Formaldehyde Exposure Categories and p-values for Trend Tests Among Exposed Person-years



RR for Medium and High Average Intensity Formaldehyde Exposure Categories and p-values for Trend Tests Among Exposed Person-years



Nasopharyngeal Cancer

- 8 exposed cases
  - All cases in highest peak exposure category:
    - RR=1.83, p-trend=0.044
- Consistent with case-control studies of nasopharyngeal cancer and animal studies

Hauptmann, et al., Amer J Epidemiol, 2004

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