Occupational Cancers in Taiwan: a Review

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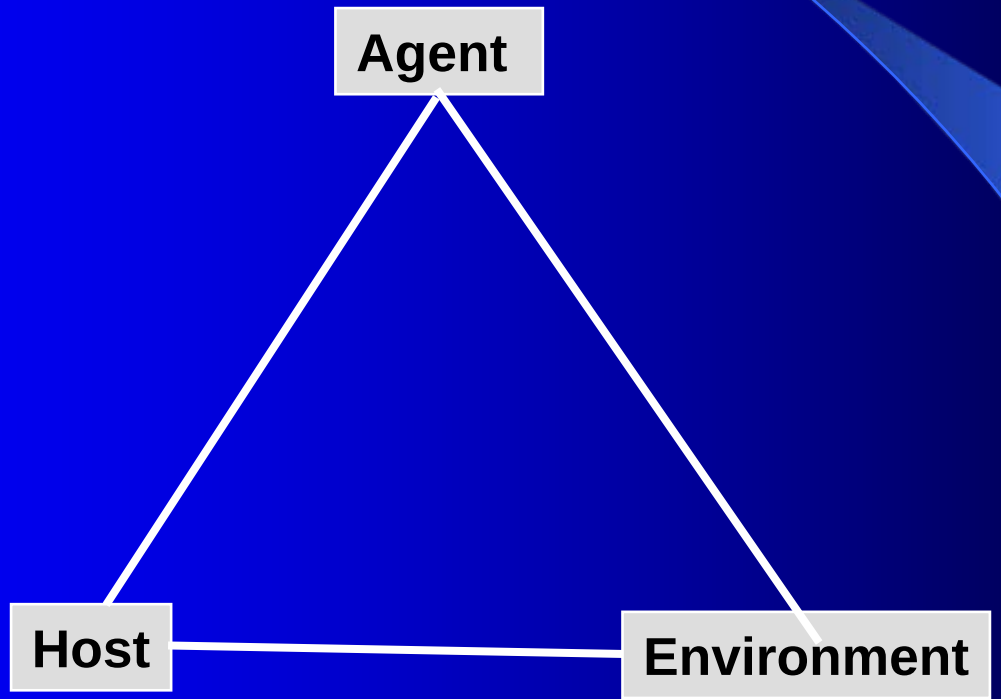
Exploration of Causes for Human Diseases: An Intellectual Journey of Health Scientists

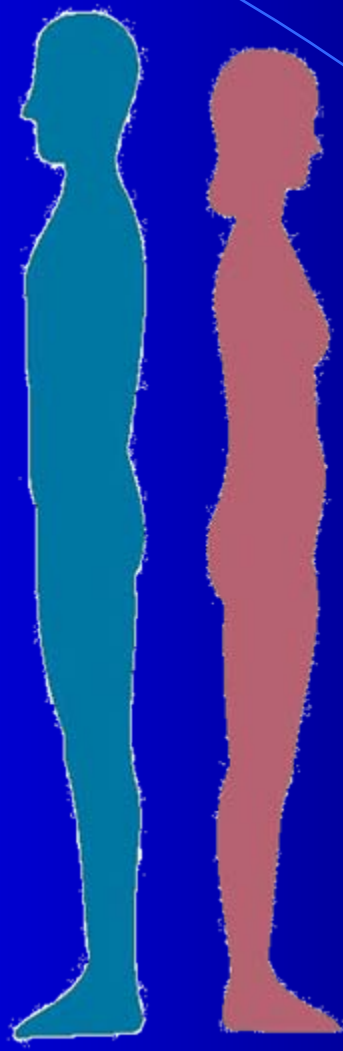
- **Hippocrates** ***Airs, Waters and Places***
- **Snow** ***On Cholera***
- **Ramazzini** ***Disease of workers***
- **Koch** ***Ueber bakteriologische Forschung***
- **Hill** ***Observation and Experiment***

Epidemiological Triangle



Ten Leading Incident Cancers in Taiwan by Sex, 2005

(case number)	incidence rate (per 100,000)	
(7,159) Liver	55.1	
(5,497) Colon and Rectum	41.8	
(5,566) Lung	41.4	
(4,310) Oral	32.4	
(2,704) Prostate	19.7	
(2,288) Stomach	16.8	
(1,403) Esophagus	10.7	
(1,363) Bladder	10.1	
(1,138) Skin	8.6	
(1,123) Nasopharynx	8.4	
(6,879) Others	-	
(39,430) All Cancer	298.6	



incidence rate (per 100,000)	(case number)
49.2	Breast (6,594)
30.9	Colon and Rectum (4,107)
21.2	Liver (2,757)
20.6	Lung (2,746)
14.7	Cervix Uteri (1,977)
9.6	Stomach (1,292)
8.9	Thyroid Gland (1,146)
7.8	Skin (1,039)
7.4	Corpus Uteri (987)
6.8	Ovary (894)
-	Others (5,938)
223.3	All Cancer (29,477)

Occupational Exposure and Lung Cancer: Case-control Study

- Cancer patients: 72 adenocarcinoma
  59 squamous/small cell carcinoma
- Matched controls: 262 hospital controls
  262 neighborhood controls
- Occupational history: Personal interview using a structured questionnaire
- Multiple conditional logistic regression analysis to estimate odds ratio with its 95% confidence interval for each risk factor

Ger *et al., Anticancer Res.*, 1993

Asbestos Exposure and Lung Cancer

Occupational exposure to asbestos	Case/Control number	Adjusted odds ratio (95% confidence interval)
Adenocarcinoma		
No	67/141	1.0 (referent)
Yes	5/3	18.7 (2.2-157.0)**
Squamous/small cell carcinomas		
No	53/116	1.0 (referent)
Yes	6/2	5.8 (0.8-41.1)*

**P<0.01, * 0.05<P<0.10 after adjustment for other risk factors

Ger *et al., Anticancer Res.*, 1993

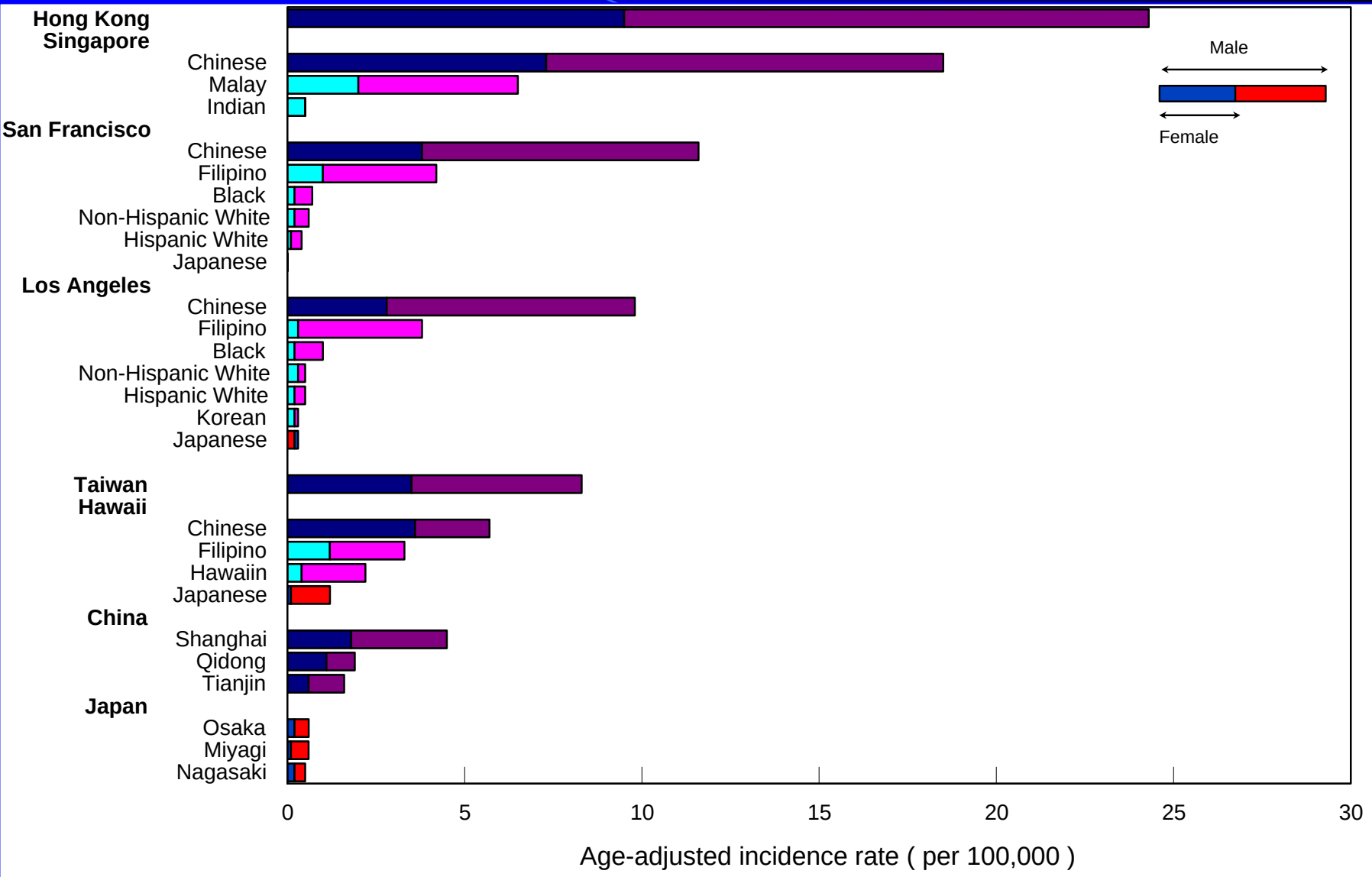
Working as a Cook and Lung Cancer

History of working as a cook	Case/Control number	Adjusted odds ratio (95% confidence interval)
Adenocarcinoma		
No	63/140	1.0 (referent)
Yes	9/4	10.4 (2.2-49.2)**
Squamous/small cell carcinomas		
No	55/111	1.0 (referent)
Yes	4/7	1.2 (0.3-4.2)

**P<0.01 after adjustment for other risk factors

Ger *et al., Anticancer Res.*, 1993

Ethnic Variation of Nasopharyngeal Carcinoma (NPC)

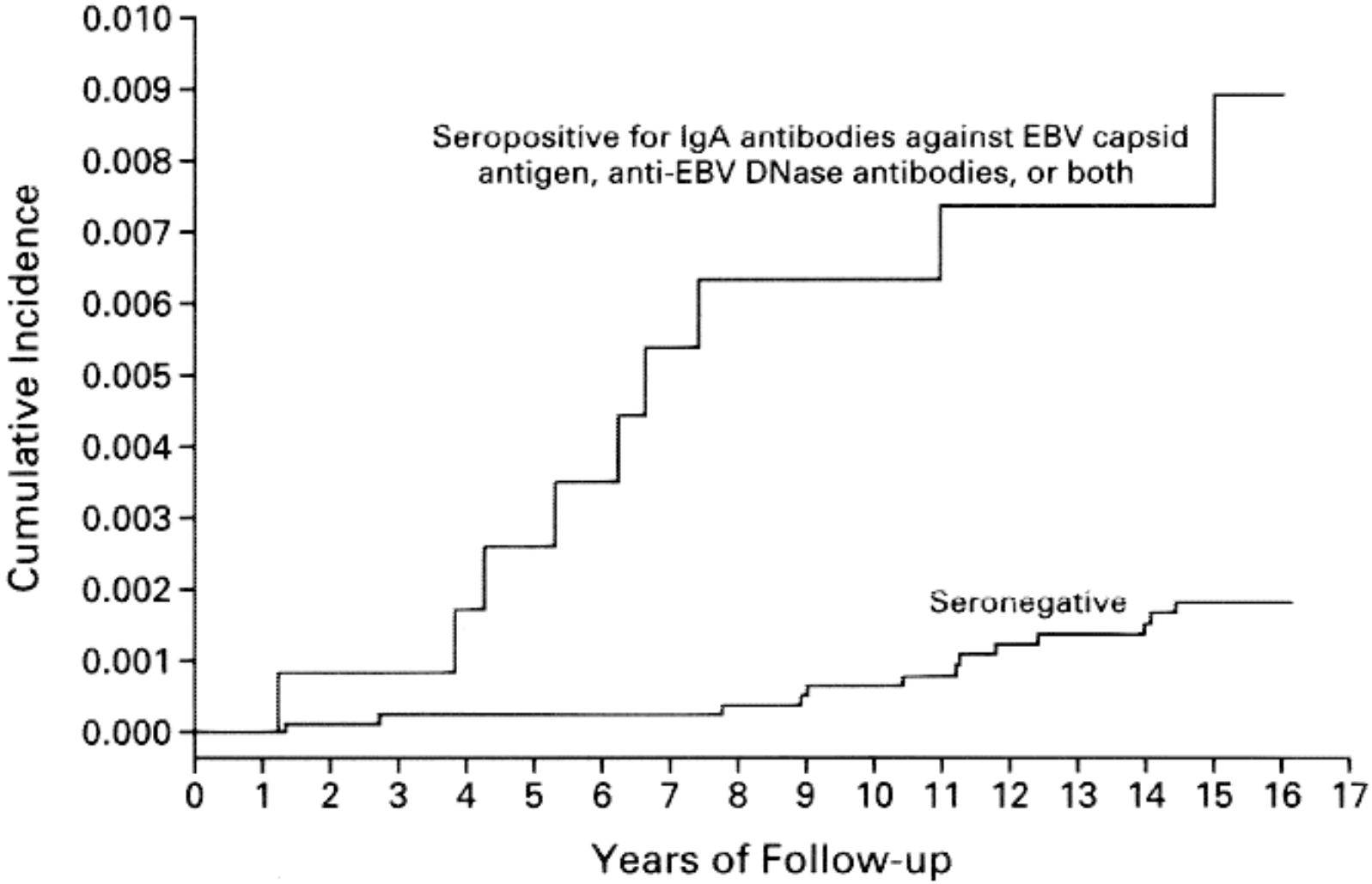


Ethnic and Migrant Variation in Age-Adjusted Incidence Rates of NPC, 1988-1992

N Engl J Med, Vol. 345, No. 26 · December 27, 2001

SEROLOGIC MARKERS OF EPSTEIN–BARR VIRUS INFECTION AND NASOPHARYNGEAL CARCINOMA IN TAIWANESE MEN

YIN-CHU CHIEN, M.SC., JEN-YANG CHEN, PH.D., MEI-YING LIU, PH.D., HWAI-I YANG, M.SC., MOW-MING HSU, M.D., CHIEN-JEN CHEN, SC.D., AND CZAU-SIUNG YANG, M.D.



Occupational Exposure and Nasopharyngeal Carcinoma: Case-control Study

- Cancer patients: 375 newly-diagnosed cases
- Community controls: 325 hospital controls
- Matching variables: age, sex and residence
- Response rate: 99% cases and 87% controls
- Occupational history: Personal interview using a structured questionnaire
- Multiple logistic regression analysis to estimate odds ratio with its 95% confidence interval for each risk factor

Hildesheim *et al., Cancer Epidemiol. Biomark. Prev.,* 2001

Assessment of Exposures to Wood Dust, Formaldehyde and Solvent

- Occupational history data were reviewed (blinded to case-control status) by a study industrial hygienist.
- Standard Industry Classification and Standard Occupational Classification codes were assigned to each occupation.
- Each Standard Industry Classification/Standard Occupational Classification code was evaluated separately for probability and intensity of exposure to formaldehyde, wood, and organic solvents.
- Occupations were classified separately on a scale of 0 (not exposed) to 9 (strong) on both the probability and intensity of each of these three exposures.

Distribution of Occupations Involving Wood Dust Exposure

SOC Codes	Title	Number (%)
6410, 6412, 6413	Brickmasons, stonemasons, & hard tile setters	26 (24.76%)
1628 & 1637	Engineers	17 (16.19%)
6313 & 6422	Carpenters & related workers	15 (14.29%)
6500 & 6560	Extractive occupations	10 (9.52%)
6310, 6311, 6479	Construction	8 (7.62%)
6444	Plasterers	5 (4.76%)
6830	Precision woodworkers	5 (4.76%)
4353	Salespersons; hardware	4 (3.81%)
8600, 7720, 1610, 5730, 6466, 6479, 6700, 6811, 6817, 6861, 7633, 7643, 7651	Other occupations (reported with frequencies 3)	15 (14.29%)

SOC: Standard occupational classification

Hildesheim *et al., Cancer Epidemiol. Biomark. Prev.*, 2001

Distribution of Occupations Involving Formaldehyde Exposure

SOC Codes	Title	Number (%)
5510, 5512, 5513, 5612	Farmers	68 (43.59%)
5252, 5253	Barbers, hairdressers, & cosmetologists	15 (9.62%)
6422	Carpenters	14 (8.97%)
2610, 2700, 2900, 3010, 3690	Health professionals	13 (8.33%)
7655	Textile sewing machine operators & tenders	5 (3.21%)
8600	Helpers	6 (3.85%)
7651	Winding & twisting machine operators & tenders	6 (3.85%)
7652	Knitting & weaving machine operators & tenders	5 (3.21%)
6440, 6442	Painters, paperhangers, & plasterers	5 (3.21%)
6830	Precision woodworkers	5 (3.21%)
5622, 7542, 6861, 7540, 7600, 3831, 5730, 6871	Other occupations (reported with frequencies 3)	14 (8.97%)

SOC: Standard occupational classification

Hildesheim *et al., Cancer Epidemiol. Biomark. Prev.*, 2001

Distribution of Occupations Involving Solvent Exposure

SOC Codes	Title	Number (%)
5510, 5512, 5513, 5612, 5622	Farmers, groundskeepers, and gardeners	71 (13.6%)
5257, 8215	Public transportation attendants and bus drivers	65 (12.5%)
6000, 6110, 6111, 6113, 6115, 6130, 6140, 8730	Mechanics, repairers, machinery maintenance, and garage/ service station-related occupations	64 (12.3%)
7720	Assemblers	32 (6.1%)
7343, 7349, 7431, 7463, 7479, 7500, 7510, 7515, 7540, 7542, 7549, 7664, 7678	Machine setup operators, operators, and tenders	25 (4.8%)
5730, 6313, 6422, 6830	Timber cutting, carpentry, precision woodworking, and related occupations	21 (4.0%)
6100, 6150, 6153, 6156, 6157, 6179, 6433	Mechanics, repairers, and installers	19 (3.6%)
1628, 1639	Engineers	17 (3.3%)
7532, 7714, 7740	Welders, cutters, and fabricators, N.E.C.	16 (3.1%)
5252, 5253	Barbers, hairdressers, and cosmetologists	15 (2.9%)
8213, 8214	Truck drivers	14 (2.7%)
6310, 6311, 6432, 6450, 6466, 6479, 6560	Construction workers, electricians, plumbers & pipefitters, and mining occupations	13 (2.5%)
3250, 6315, 6440, 6442, 6863	Painters and related occupations	12 (2.3%)
2610, 2700, 2900, 3010, 3690	Health professionals	12 (2.3%)
1440, 1845, 3831, 4300, 4342, 4348, 4353	Other occupations (reported with frequencies 10)	125 (24.0%)

SOC: Standard occupational classification

Hildesheim *et al., Cancer Epidemiol. Biomark. Prev.*, 2001

Indices of Occupational Exposures to Wood Dust, Formaldehyde and Solvent

a) Years of exposure

b) Average intensity of exposure [(intensity index for each job x duration of employment)/ years of exposure]

c) Average probability of exposure [(probability index for each job x duration of employment)/ years of exposure]

d) Cumulative exposure (intensity years of exposure, *i.e.*, duration of exposure, average intensity)

e) Age at first exposure

f) Years since first exposure

g) Duration of exposure excluding exposures occurring in the 10 years preceding diagnosis (cases) or interview (controls)

Wood Dust Exposure and Nasopharyngeal Carcinoma

Occupational exposure	Case/Control number	Adjusted odds ratio (95% confidence interval)
Ever exposed		
No	323/299	1.0 (referent)
Yes	52/26	1.7 (1.0-3.0)**
Duration		
None	323/299	1.0 (referent)
<10 years	21/15	1.2 (0.6-2.5)
>10 years	31/11	2.4 (1.1-5.0)*
		$P_{trend} = 0.02$

Hildesheim *et al., Cancer Epidemiol. Biomark. Prev.,* 2001

Wood Dust Exposure and Nasopharyngeal Carcinoma

Occupational exposure	Case/Control number	Adjusted odds ratio (95% confidence interval)
Cumulative exposure (intensity x duration)		
None	323/299	1.0 (referent)
<25	20/15	1.2 (0.6-2.5)
≥25	32/11	2.4 (1.2-5.1)*
		$P_{trend} = 0.02$
Age at first exposure		
None	323/299	1.0 (referent)
<25 years	37/15	2.3 (1.2-4.4)*
≥25 years	15/11	1.1 (0.5-2.5)

Hildesheim *et al., Cancer Epidemiol. Biomark. Prev.*, 2001

Formaldehyde Exposure and Nasopharyngeal Carcinoma

Occupational exposure	Case/Control number	Adjusted odds ratio (95% confidence interval)
Ever exposed		
No	301/284	1.0 (referent)
Yes	74/41	1.4 (0.9-2.2)
Duration		
None	301/284	1.0 (referent)
<10 years	31/21	1.3 (0.7-2.3)
>10 years	43/20	1.6 (0.9-2.9)
		$P_{trend} = 0.08$

Hildesheim *et al., Cancer Epidemiol. Biomark. Prev.*, 2001

Formaldehyde Exposure and Nasopharyngeal Carcinoma among Anti-EBV-seropositives

Occupational Exposure	Adjusted odds ratio (95% confidence interval)	
	Overall	Anti-EBV-seropositive
Ever exposed		
No	1.0 (referent)	1.0 (referent)
Yes	1.4 (0.9-2.2)	2.7 (1.2-6.2)
Duration		
None	1.0 (referent)	1.0 (referent)
<10 years	1.3 (0.7-2.3)	2.8 (0.8-9.7)
>10 years	1.6 (0.9-2.9)	2.6 (0.9-7.7)

Hildesheim *et al., Cancer Epidemiol. Biomark. Prev.*, 2001

Formaldehyde Exposure and Nasopharyngeal Carcinoma

Occupational exposure	Case/Control number	Adjusted odds ratio (95% confidence interval)
Cumulative exposure (intensity x duration)		
None	301/284	1.0 (referent)
<25	29/19	1.3 (0.7-2.4)
≥25	45/22	1.5 (0.9-2.7)
		$P_{trend} = 0.10$
Age at first exposure		
None	301/284	1.0 (referent)
<25 years	62/38	1.3 (0.8-2.0)
≥25 years	12/3	3.4 (0.9-12.0)

Hildesheim *et al., Cancer Epidemiol. Biomark. Prev.*, 2001

Formaldehyde Exposure and Nasopharyngeal Carcinoma among Anti-EBV-seropositives

Occupational Exposure	Adjusted odds ratio (95% confidence interval)	
	Overall	Anti-EBV-seropositive
Cumulative exposure (intensity x duration)		
None	1.0 (referent)	1.0 (referent)
<25	1.3 (0.7-2.4)	4.0 (0.9-17.0)
≥25	1.5 (0.9-2.7)	2.2 (0.8-5.8)
Age at first exposure		
None	1.0 (referent)	1.0 (referent)
<25 years	1.3 (0.8-2.0)	2.6 (1.1-6.5)*
≥25 years	3.4 (0.9-12.0)	3.1 (0.4-24.1)

Hildesheim *et al., Cancer Epidemiol. Biomark. Prev.*, 2001

Solvent Exposure and Nasopharyngeal Carcinoma

Occupational Exposure	Case/Control number	Adjusted odds ratio (95% confidence interval)
Ever exposed		
No	197/195	1.0 (referent)
Yes	178/130	1.2 (0.8-1.7)
Duration		
None	197/195	1.0 (referent)
<10 years	89/54	1.5 (1.0-2.3)
>10 years	89/76	0.9 (0.6-1.4)

Hildesheim *et al., Cancer Epidemiol. Biomark. Prev.,* 2001

Solvent Exposure and Nasopharyngeal Carcinoma

Occupational exposure	Case/Control number	Adjusted odds ratio (95% confidence interval)
Cumulative exposure (intensity x duration)		
None	197/195	1.0 (referent)
<25	93/68	1.3 (0.9-1.9)
≥25	85/62	1.1 (0.7-1.6)
Age at first exposure		
None	197/195	1.0 (referent)
<25 years	133/98	1.1 (0.8-1.6)
≥25 years	45/32	1.3 (0.8-2.2)

Hildesheim *et al., Cancer Epidemiol. Biomark. Prev.*, 2001

Printing Work and Nasopharyngeal Carcinoma: Follow-up Study

Study Cohort: 1564 (336 printing and 1228 non-printing) workers who had worked in the company since its establishment in 1950

Disease ascertainment: Computerized linkage with the database of the hospital records of the Labor Insurance Bureau during 1985-94

Data analysis: Multiple logistic regression analysis to estimate adjusted morbidity odds ratios (MORs) with 95% confidence intervals (CIs) for various diseases among the printing workers with cardiovascular diseases as the reference diseases.

Liu *et al., Occup. Environ. Med.*, 2002

Morbidity Odds Ratio of Nasopharyngeal Carcinoma in Printing Workes

Disease	Printing workers	Non-printing workers	Morbidity odds ratio (95% CI) CVD	All other diseases
Nasopharyngeal carcinoma (NPC)	5	0	57.0 (2.8-1155.3)	33.8 (1.9-613.8)
Cardiovascular diseases (CVD)	5	28		
All diseases other than NPC	139	435		
All workers without hospital admission	192	793		

Liu *et al., Occup. Environ. Med.*, 2002

Flame Cutting and Neoplasms of Nasopharynx and Pleura: Cohort Study

Study cohort: 2,850 flame cutters, 871 lifters, 240 odd-jobbers and 225 other workers registered in 1985 at Kaohsiung Shipbreaking Workers Union.

Mortality ascertainment: Computerized linkage with National Death Certification profiles from January 1985 to December 1997.

Statistical analysis: Standardized mortality ratio (SMR) with 95% confidence interval (CI) were derived to compare the mortality of the workers and the local reference population.

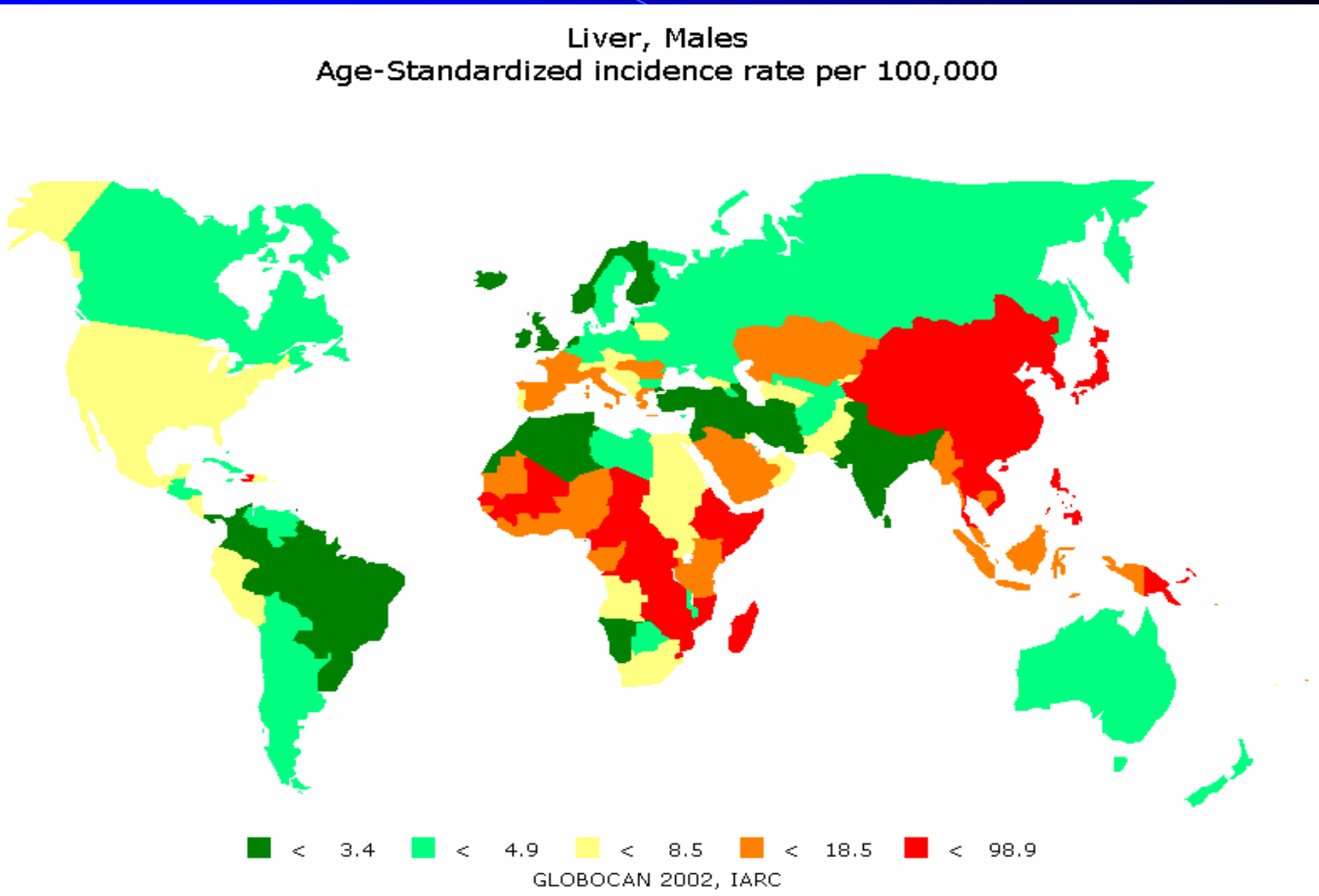
Liu *et al., J. Occup. Health*, 2003

Standardized Mortality Ratio of Nasopharyngeal and Pleural Cancer in Flame Cutting Workers

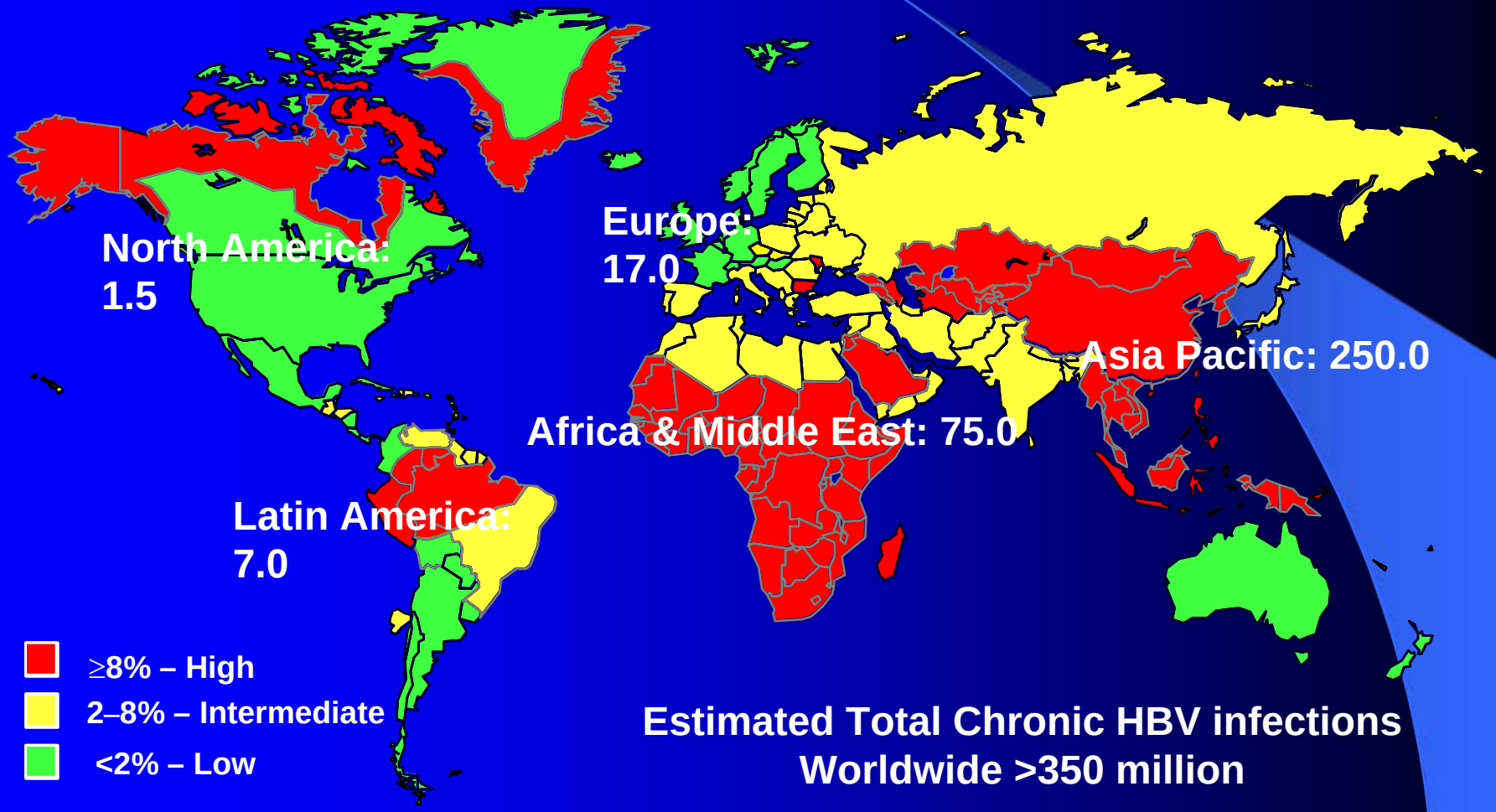
Age (year)	Person-years	Nasopharyngeal cancer No.	Nasopharyngeal cancer SMR (95% CI)	Pleura mesothelioma No.	Pleura mesothelioma SMR (95% CI)
20-39	37,857	3	5.2 (1.7-16.2)*	1	104.1 (14-739)*
40-49	9,259	2	1.1 (0.3-4.3)	0	
50-59	4,141	2	1.4 (0.4-5.7)	0	
60+	461	0		0	
Total	51,718	7	1.5 (0.7-3.2)	1	27.2 (4-193)*

Liu *et al., J. Occup. Health*, 2003

Liver Cancer Incidence in the World

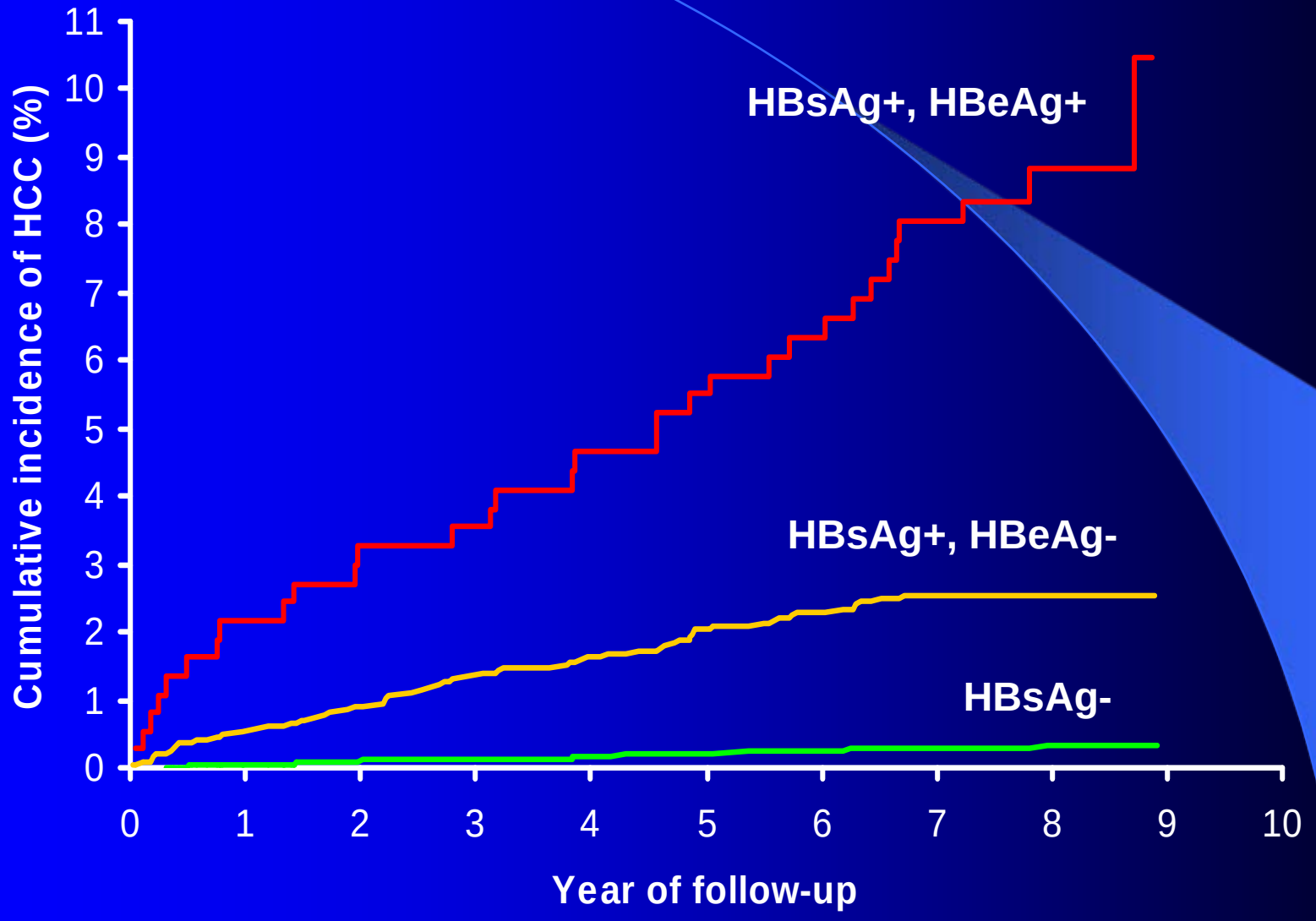


Geographic Variation of Prevalence of Chronic Hepatitis B (millions)



World Health Organisation. Geographical Prevalence of HBsAg. Data 1996

Cumulative Incidence of HCC by HBsAg and HBeAg



Yang et al., *NEJM* 2002;347:168-74

Vinyl Chloride Monomer and Hepatocellular Carcinoma: Case-control Study

Occupational cohort: 4,096 male workers from six PVC polymerization plants

Case and control selection: All 18 cases affected with hepatocellular carcinoma and 68 controls matched on age and specific plant of employment selected from the study cohort

Vinyl chloride exposure: Defined by Job titles. Tank cleaning, PVC unloading and catalyst adding considered as high exposure jobs.

Confounding variables: Alcohol consumption, cigarette use, occupation, and family history of chronic liver disease were obtained using a structured questionnaire.

Serological marker: Hepatitis B virus surface antigen (HBsAg)

Statistical analysis: Matched odds ratio with 95% confidence interval (CI)

Wong *et al., J. Occup. Environ. Med.*, 2003

Matched Odds Ratio of HCC for Vinyl Chloride Monomer Exposure and HBsAg serostatus

Vinyl chloride exposure	Multivariate-adjusted odds ratio (95% confidence interval)	
	HBsAg-seronegative	HBsAg-seropositive
Tank cleaning history		
No	1.0 (referent)	25.7 (2.9-229.4)
Yes	4.0 (0.2-69.1)	396.0 (22.6-∞)
		$P_{interaction}$<0.01
High-exposure history		
No	1.0 (referent)	26.1 (2.9-235.1)
Yes	2.9 (0.2-50.0)	184.5 (15.0-∞)
		$P_{interaction}$<0.01

Wong *et al., J. Occup. Environ. Med.*, 2003

Electronic Work and Breast Cancer: Cohort Study

Study cohort: A total of 63,982 female electronic workers identified from the database of the Bureau of Labor Insurance (BLI) in a period of 1973-1997

Cancer ascertainment: Computerized linkage with National Cancer Registry profiles up to 2001

Statistical analysis: Standardized incidence ratios (SIRs) and 95% confidence intervals (CIs) for different types of cancer derived comparing to the general population

Stratification analysis: Use of trichloroethylene as the major solvent before June 20, 1974.

Sung *et al., BMC Public Health,* 2007

Standardized Incidence Ratio of Breast Cancer for Duration of Employment in Electronic Factory

Duration of employment	Overall SIR (95% CI)	Before June 1974 SIR (95% CI)	After June 1974 SIR (95% CI)
<1 month	1.28 (0.97-1.66)	1.97 (0.98-3.52)	1.18 (0.86-1.57)
1-11 months	0.99 (0.79-1.22)	1.22 (0.73-1.90)	0.94 (0.72-1.20)
1-4 years	1.10 (0.86-1.38)	1.38 (0.81-2.22)	1.03 (0.77-1.34)
5-9 years	0.88 (0.65-1.17)	1.14 (0.70-1.76)	0.75 (0.50-1.10)
10+ years	1.68 (1.11-2.42)	1.62 (1.02-2.42)	2.03 (0.65-4.74)
Total	1.09 (0.96-1.22)	1.38 (1.11-1.70)	0.99 (0.85-1.14)

Sung *et al.*, *BMC Public Health*, 2007

Peri-conceptional Exposure to Electronic Work and Childhood Leukemia: Follow-up Study

Birth cohort: A total of 40,647 first live born singletons of female electronic workers

Cancer ascertainment: Computerized linkage with National Cancer Registry profiles up to 2001

Statistical analysis: Poisson regression analysis used to derive rate ratio with 95% confidence interval after adjustment for maternal age, maternal education, sex, and year of birth.

Peri-conceptional exposure: 3 months before and after conception (8,506 exposed and 32,141 unexposed)

Sung *et al., Reproductive Toxicology,* 2008

Adjusted Rate Ratio of Childhood Leukemia for Peri-conceptional Exposure in Electronic Factory

Malignant neoplasm	Person-years	Case no.	Rate ratio (95% CI)
All neoplasms			
Unexposed	483,930	36	1.00 (referent)
Exposed	155,121	11	2.26 (1.12-4.54)
Leukemia			
Unexposed	483,930	9	1.00 (referent)
Exposed	155,121	6	3.83 (1.17-12.55)

Sung *et al., Reproductive Toxicology*, 2008

Conclusion

- **Several occupational cancers have been documented in Taiwan.**
- **Both case-control and cohort studies may be used to assess the impact of occupational exposures on various cancers.**
- **Detail occupational history taking is essential for the success of case-control studies aimed to explore risk exposures of occupational cancers.**
- **Computerized linkage with national profiles of labor insurance, cancer registry and death certification may facilitate the complete and accurate ascertainment of cancer cases or deaths.**

Conclusion

- **Collection of history of exposures to potential confounding variables are necessary to estimate multivariate-adjusted relative risks associated with occupational exposures.**
- **Stratification analysis is used to identify time of exposure with special vulnerability.**
- **Most epidemiological studies of occupational cancers are limited by small sample size and short period of follow-up. International or regional collaboration may increase the quality and statistical power of studies on occupational cancers.**

Conclusion

- **Biomarkers of internal dose and biologically effective dose of occupational exposure as well as early health outcomes may improve the quality of studies on occupational cancers.**
- **Epidemiological study findings should be used to promote industrial hygiene and occupational health through stringent evidence-based regulation of working environments.**

Thank You!