



Having an impact on public health: Lessons learned from Environmental Epidemiology

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Presentation at the HA Tyroler Award Ceremony

University of North Carolina at Chapel Hill

School of Public Health

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had an Impact
If I have ~~seen further~~ ^ it is
by standing on the shoulders of giants.

UNC Dissertation Committee:

Dr. Herman (Al) Tyroler

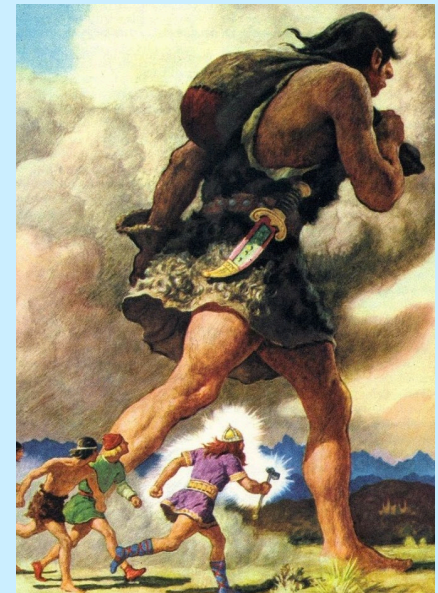
Dr. Carl Shy

Dr. Larry Kupper

Dr. Tim Wilcosky

Special thanks: Dr. Harvey Checkoway

Be in the right place at the right time





Outline

- Examples from environmental epidemiology
 - Cholesterol and CVD: Al Tyroler
 - Air Pollution and Respiratory Diseases: Carl Shy
 - State of the Art Methods: Larry Kupper and David Kleinbaum
 - Tobacco and Lung Cancer: Richard Doll
 - Asbestos and Mesothelioma: Irving Selikoff
 - Water Contamination: John Snow
- Lessons learned from examples



Cardiovascular Disease



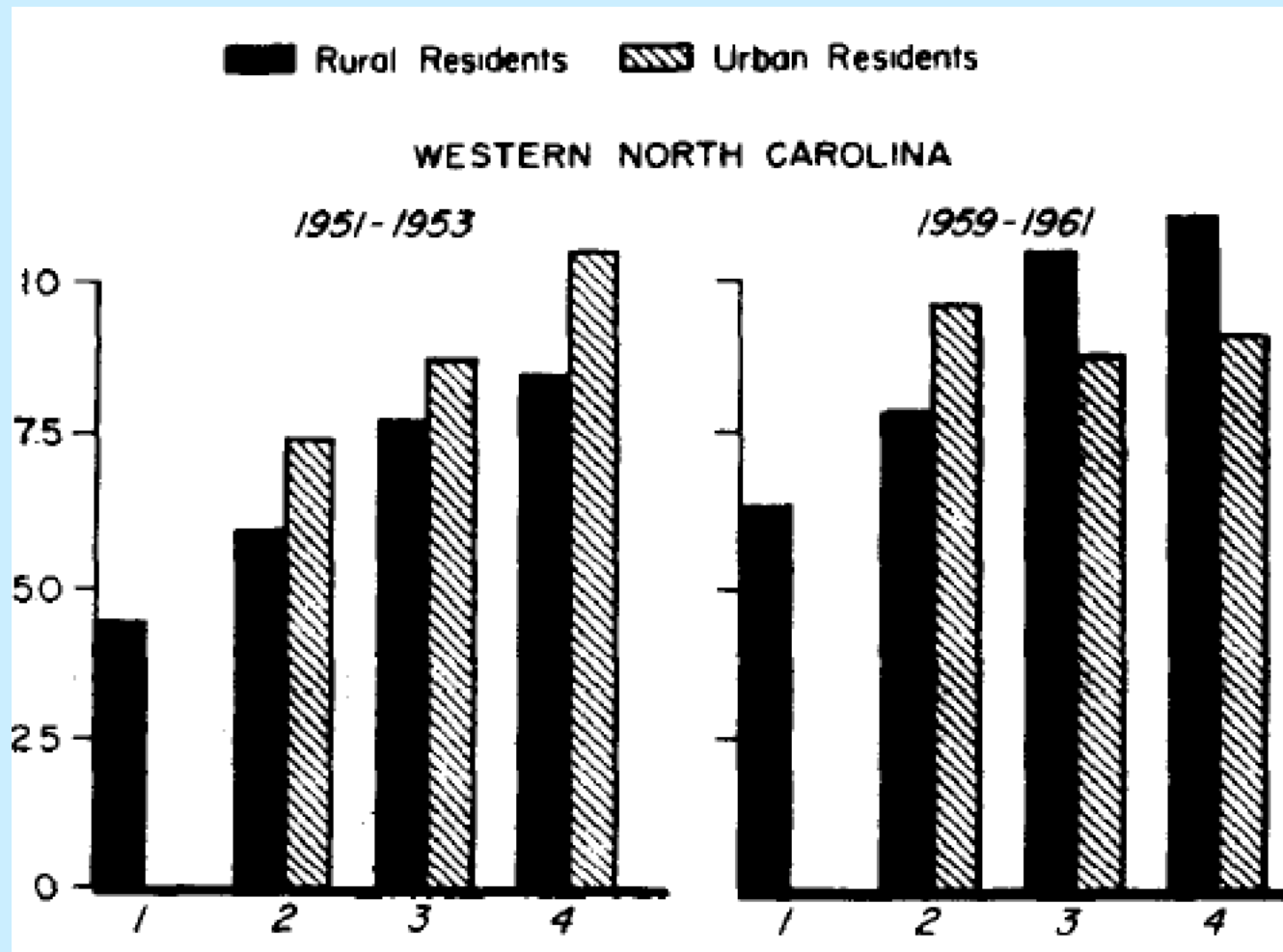
Herman (Al) Tyroler

Ask the right questions



Tyroler HA and Cassel J. 1964. The effect of urbanization on CHD mortality in rural residents

Coronary Heart Disease mortality
Rates per 1000 in White Males

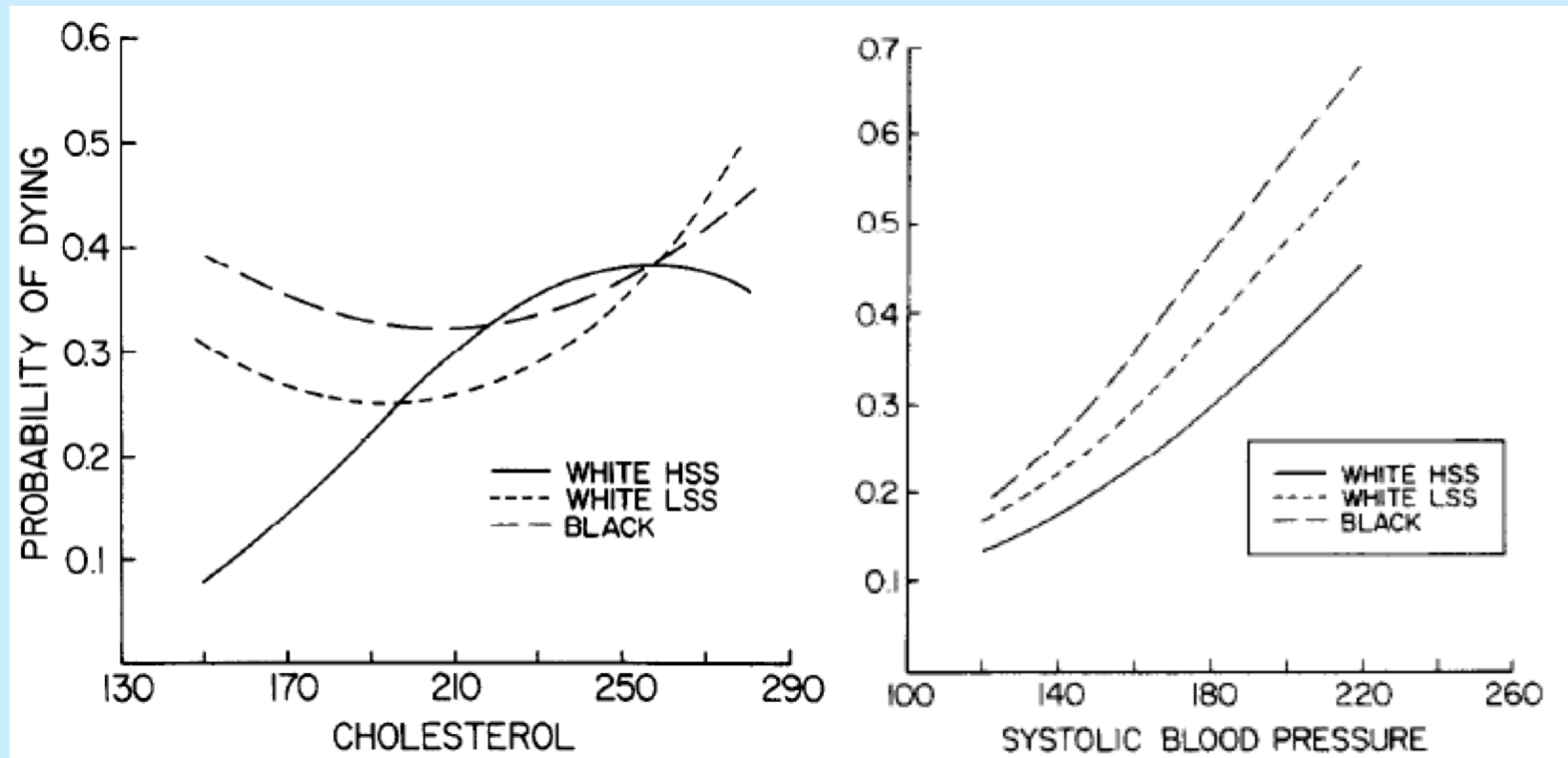


Index of Urbanization

J. chron. Dis. 1964, Vol. 17, pp. 167477.

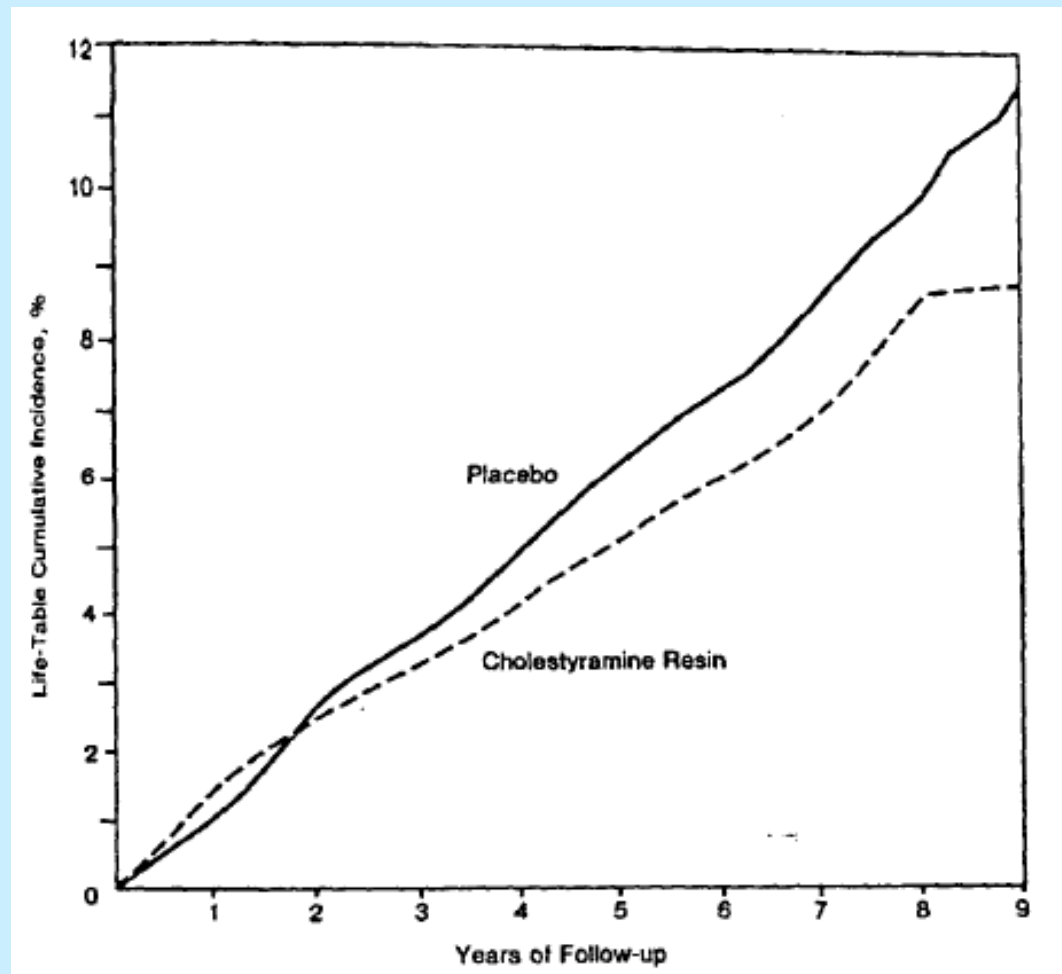


Tyroler et al. 1984. Ischemic heart disease risk factors and mortality in Evans County black males.



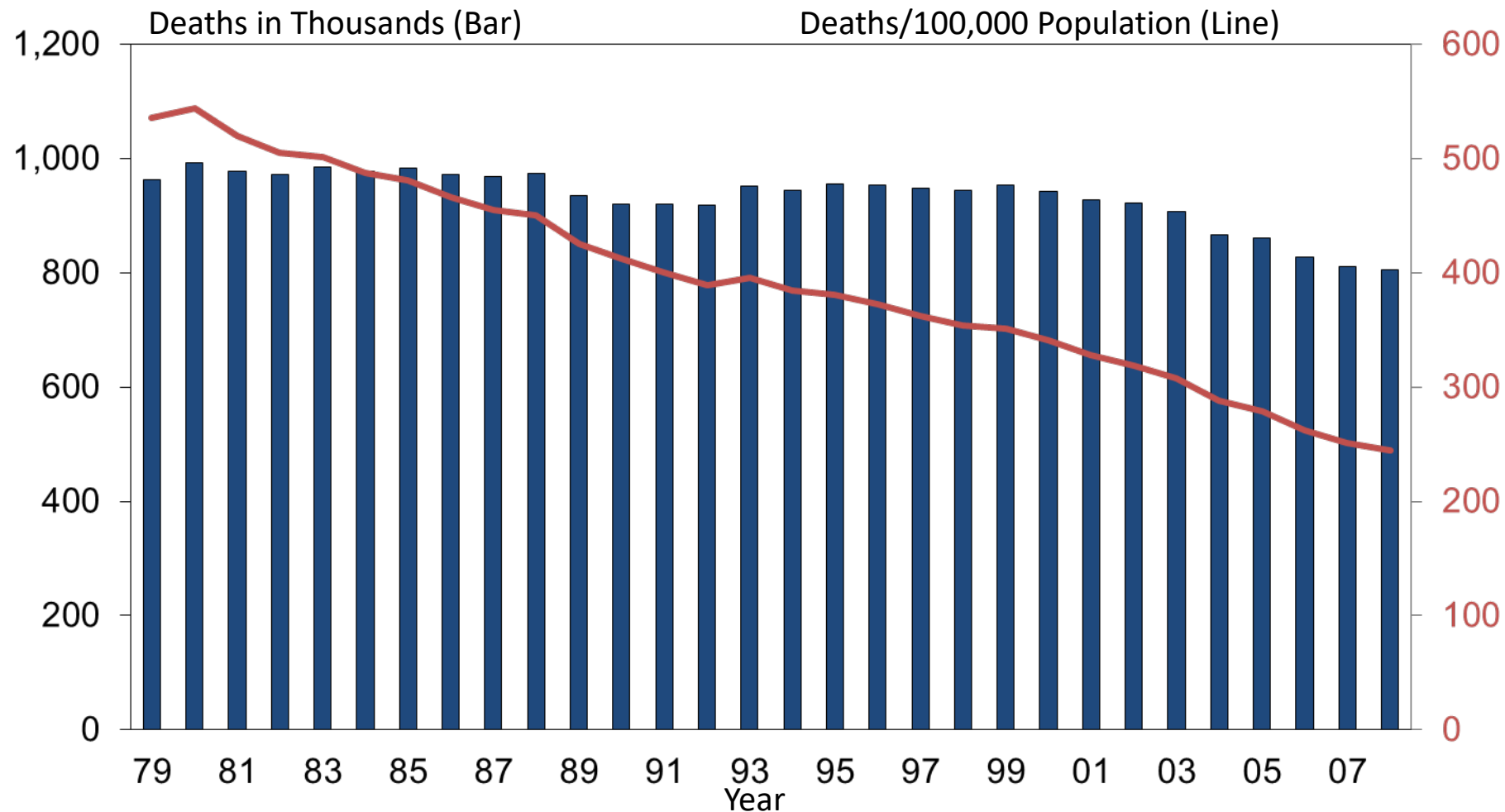
Am Heart J. 108(3); 738-46.

The Lipid Research Clinics Coronary Prevention Trial Results



Lipid Research Clinics Program. 1984 JAMA 3:351-64

Deaths and Age-Adjusted Death Rates for Cardiovascular Diseases, U.S., 1979–2008

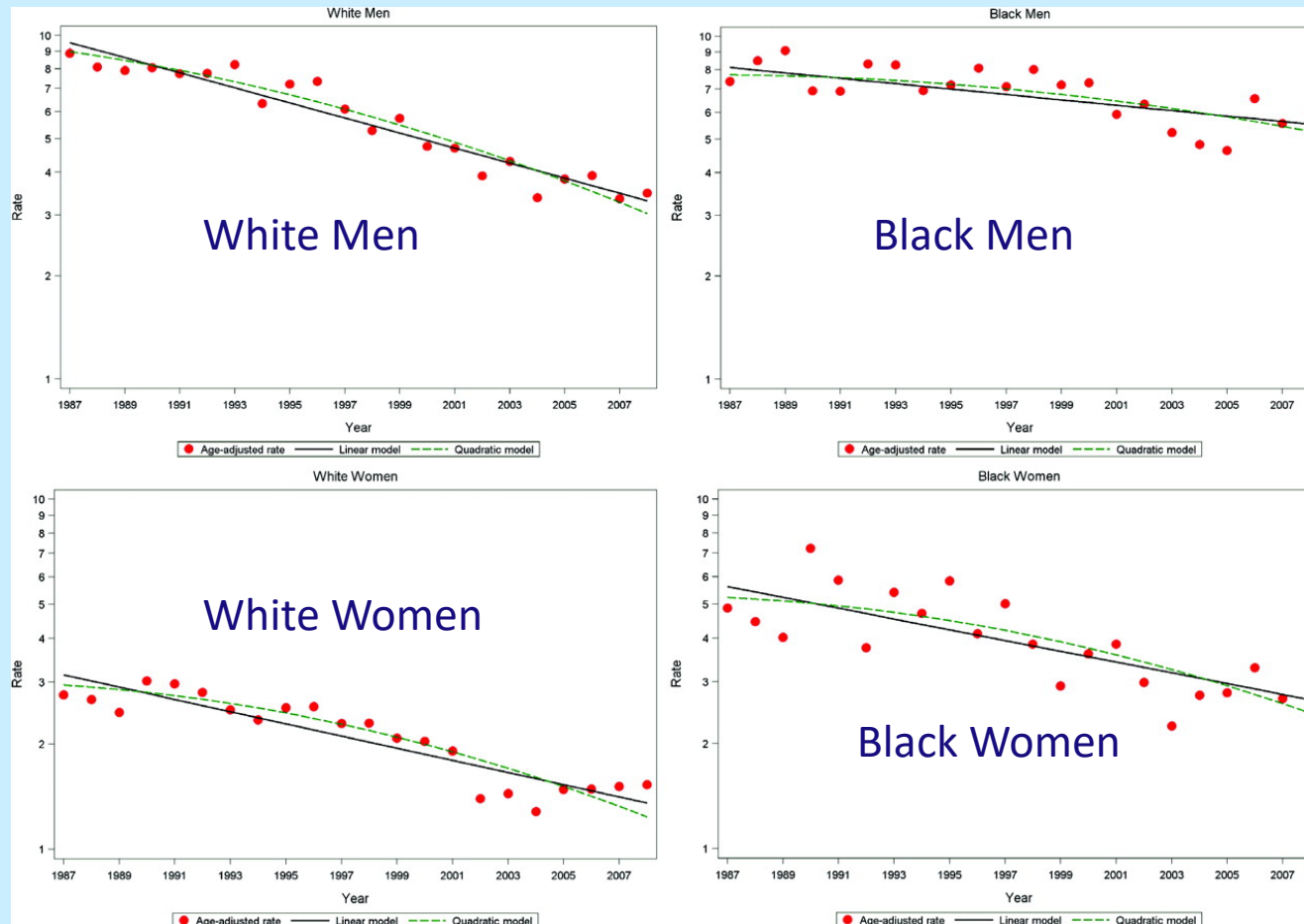


2012 NHLBI Morbidity and Mortality Chart Book

<http://www.nhlbi.nih.gov/resources/docs/cht-book.htm>

ARIC Study

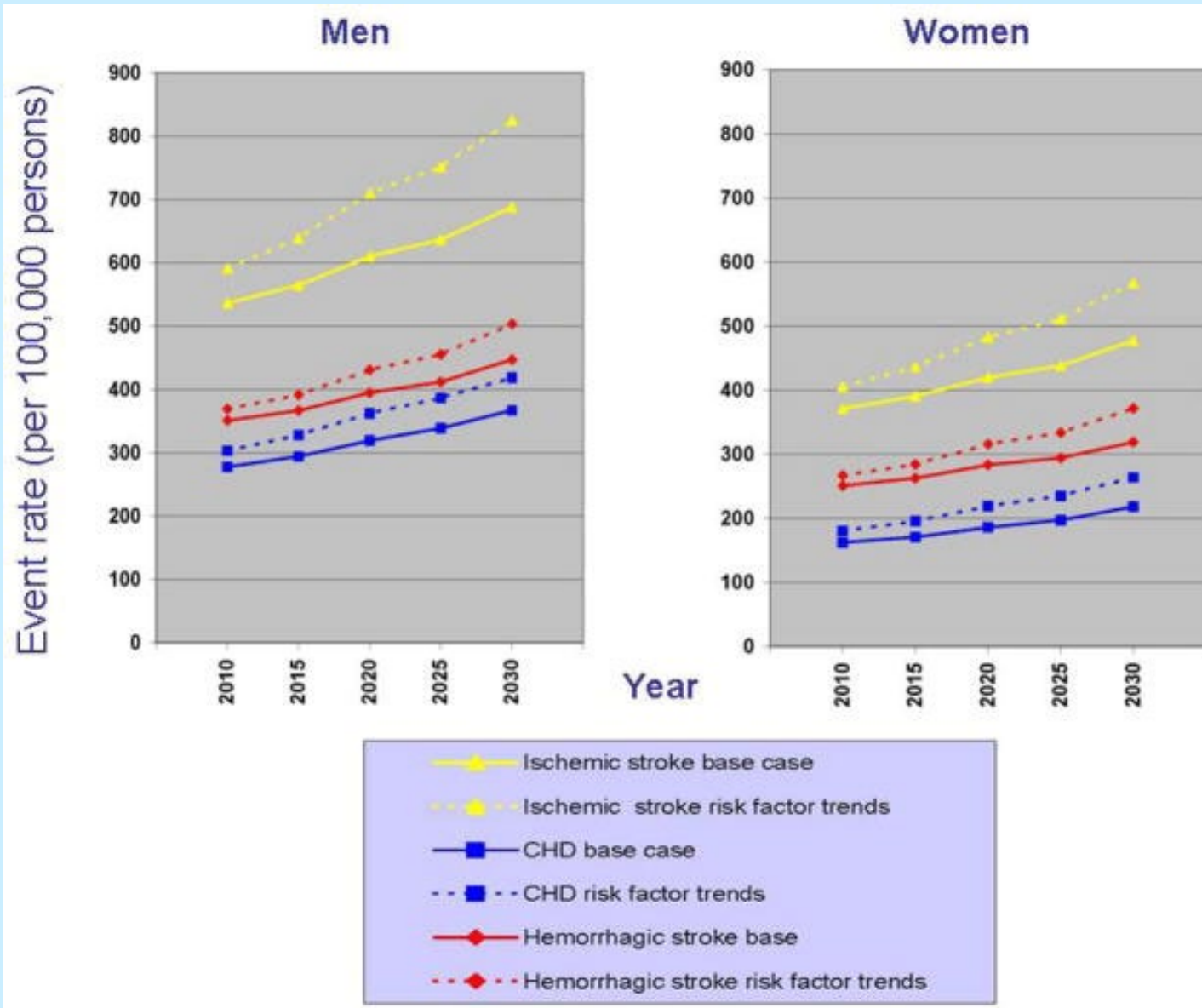
Twenty-Two-Year Trends in Incidence of Myocardial Infarction, Coronary Heart Disease Mortality, and Case Fatality in 4 US Communities, 1987–2008



Rosamond W D et al. *Circulation* 2012;125:1848-1857



Future cardiovascular disease in China



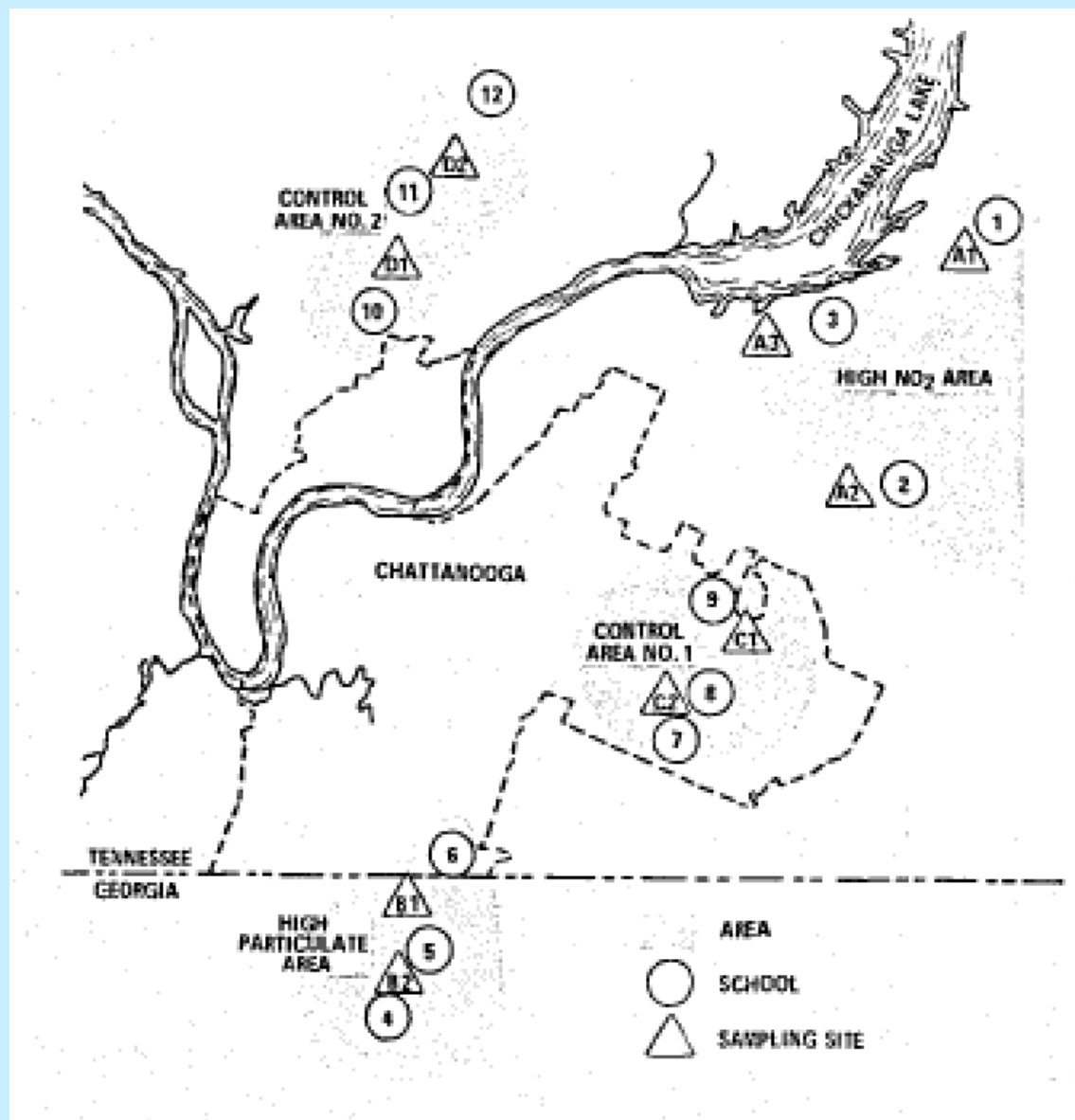


Air Pollution



Carl Shy circa 1971

The Chattanooga School Children Study.

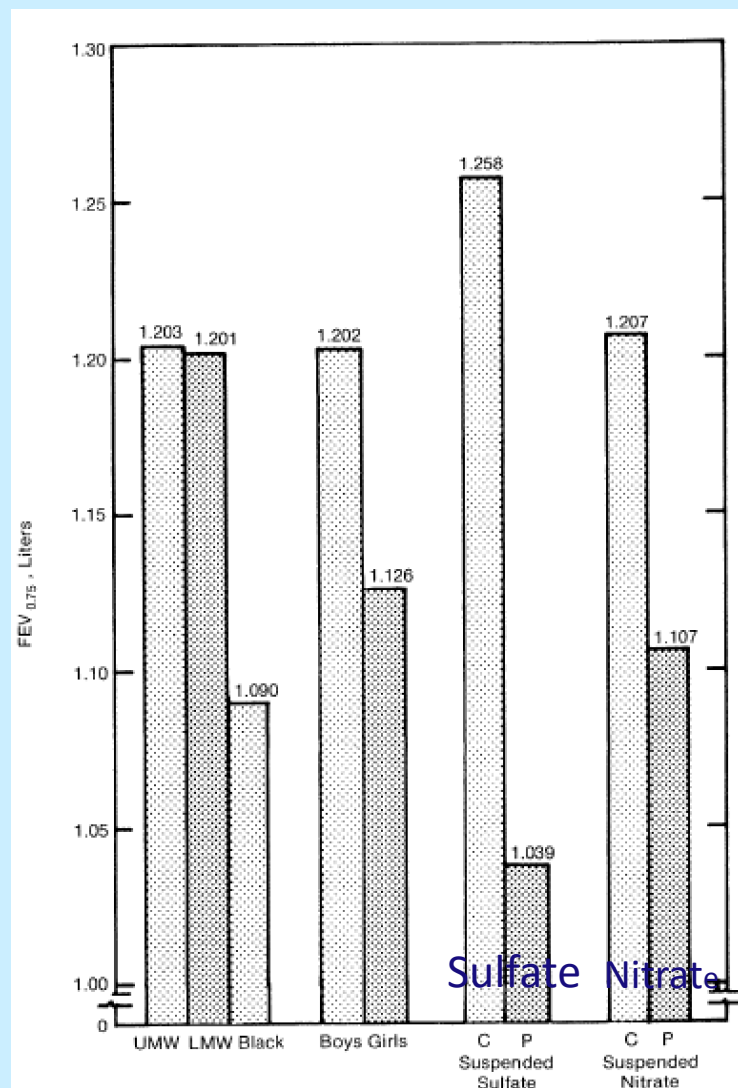


Shy et al. 1970 J Air Pol. Control Assoc. 20(8);539-45.

Analysis of Variance of height adjusted FEV_{0.75}

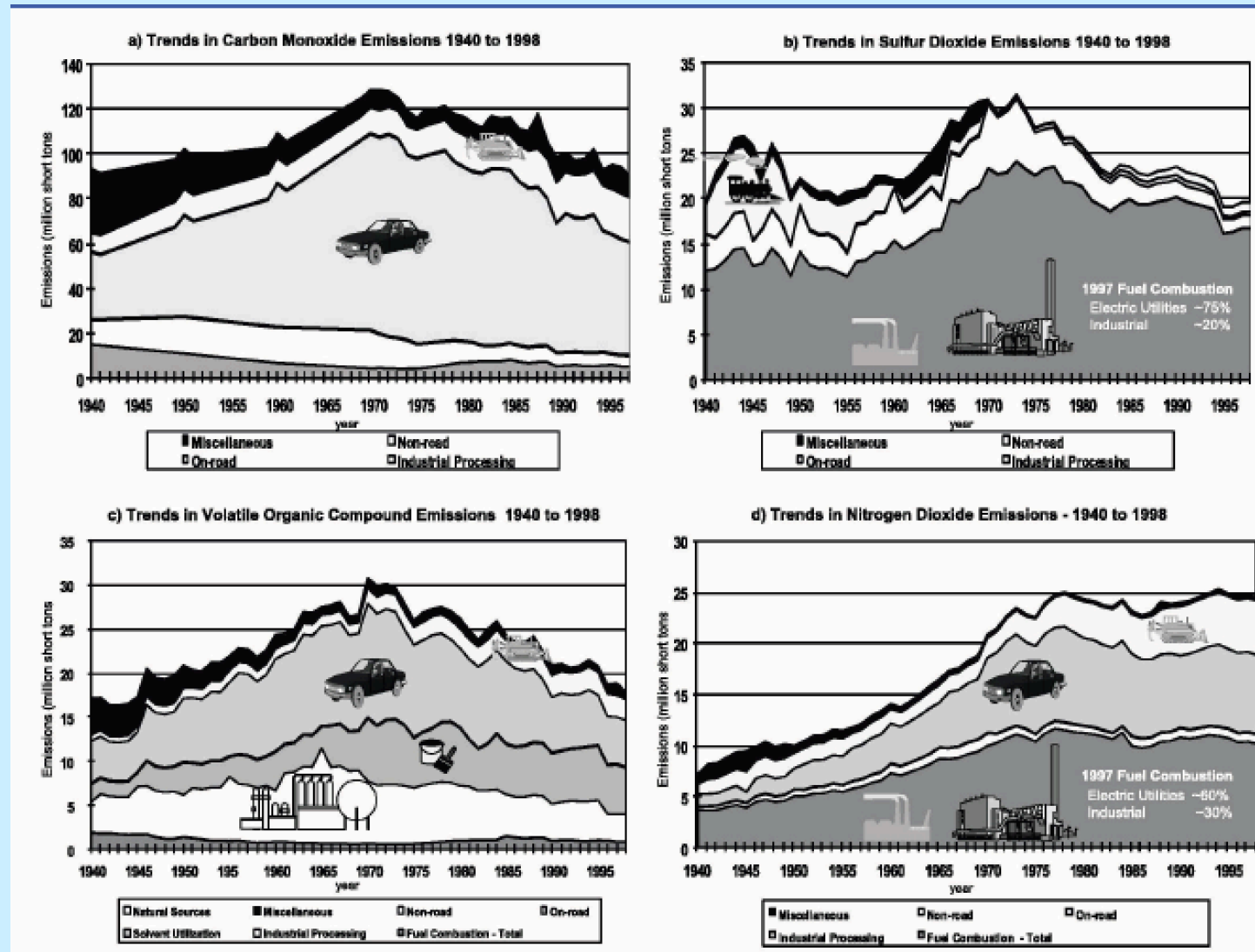
Factor	Mean square	F value	Probability of significant difference
Sex of child	0.3852	189.3	$p < 0.01$
Month of test	0.0318	15.6	$p < 0.01$
Study area			
High NO ₂ vs. Controls 1 & 2	0.0098	4.8	$p < 0.05$
High TSP ^a vs. Controls 1 & 2	0.0011	0.6	Not significant
Control 1 vs. Control 2	0.0004	0.2	Not significant

Pulmonary function in Cincinnati Children



Shy CM. Archives of Env Health. 1973;27(3):124-8.

TRENDS IN CRITERIA AIR POLLUTANTS



Bachman 2007. J Air & Waste Man. 57:652-697

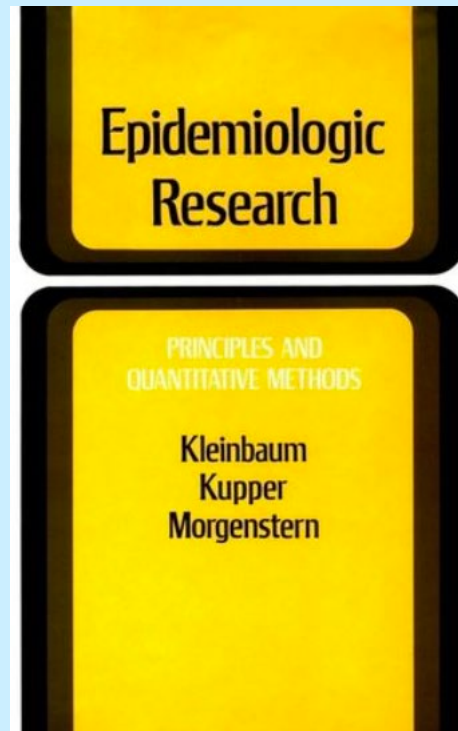
Global Burden of Disease – Estimated over 3.5 million deaths in 2010 from air pollution.

Table 3. Deaths attributable to risk factors and risk factor clusters, worldwide

	Men		Women		Both sexes	
	1990	2010	1990	2010	1990	2010
Air pollution	..	..	..	..	..	..
Ambient particulate matter pollution	1 549 448 (1 345 894– 1 752 880)	1 850 428 (1 614 010– 2 082 474)	1 360 712 (1 166 992– 1 559 747)	1 373 113 (1 187 639– 1 563 793)	2 910 161 (2 546 184– 3 286 508)	3 223 540 (2 828 854–3 619 148)
Household air pollution from solid fuels	2 251 932 (1 677 785– 2 743 681)	1 867 043 (1 359 090– 2 452 588)	2 221 558 (1 862 975– 2 581 337)	1 611 730 (1 243 516– 2 027 067)	4 473 490 (3 651 253– 5 206 632)	3 478 773 (2 638 548–4 386 590)
Ambient ozone pollution	77 087 (25 256–134 021)	86 335 (30 551–153 776)	66 274 (22 424–116 663)	66 100 (21 362–115 225)	143 362 (47 539– 251 885)	152 434 (52 272–267 431)

Lim et al. Global Burden of Disease Study. Lancet 2012; 380: 2224–60

Use of State of the Art Methods



Dr. David Kleinbaum

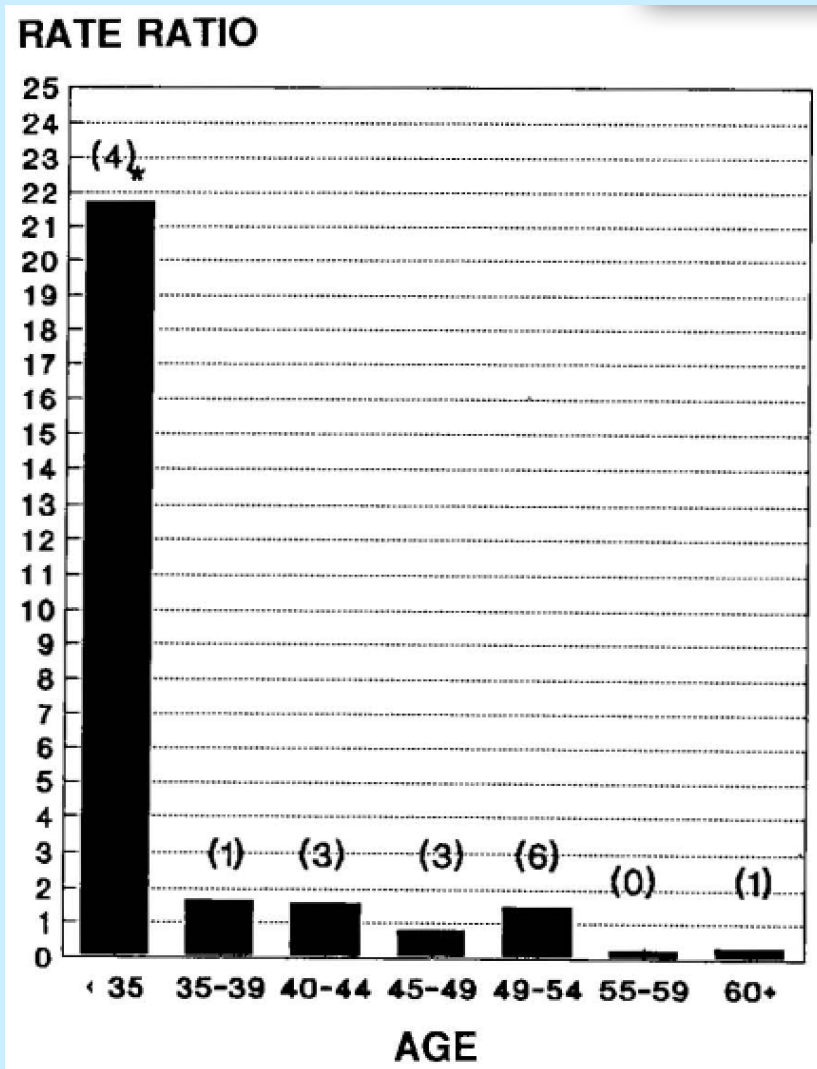
Dr. Larry Kupper

Cardiovascular mortality among munitions workers exposed to nitroglycerin

Death category	Nitroglycerin-exposed		
	Observed deaths (N)	SMR	SRR
Cerebrovascular disease	41	0.90	0.87
Ischemic heart disease	344	1.07	1.07
Rheumatic heart disease	2	0.23	.
Chronic disease of the endocardium	2	0.74	.
Other myocardial degeneration	2	0.58	.
Hypertension with heart disease	3	0.52	.
Hypertension without heart disease	1	0.47	.
Disease of the arteries and veins	22	1.02	.
Other diseases of the heart	17	0.87	.

Stayner et al 1992. Scan J Work Env Health. 18(1):34-43

Mortality rate ratios for IHD Poisson regression for active nitroglycerin exposure by age in years



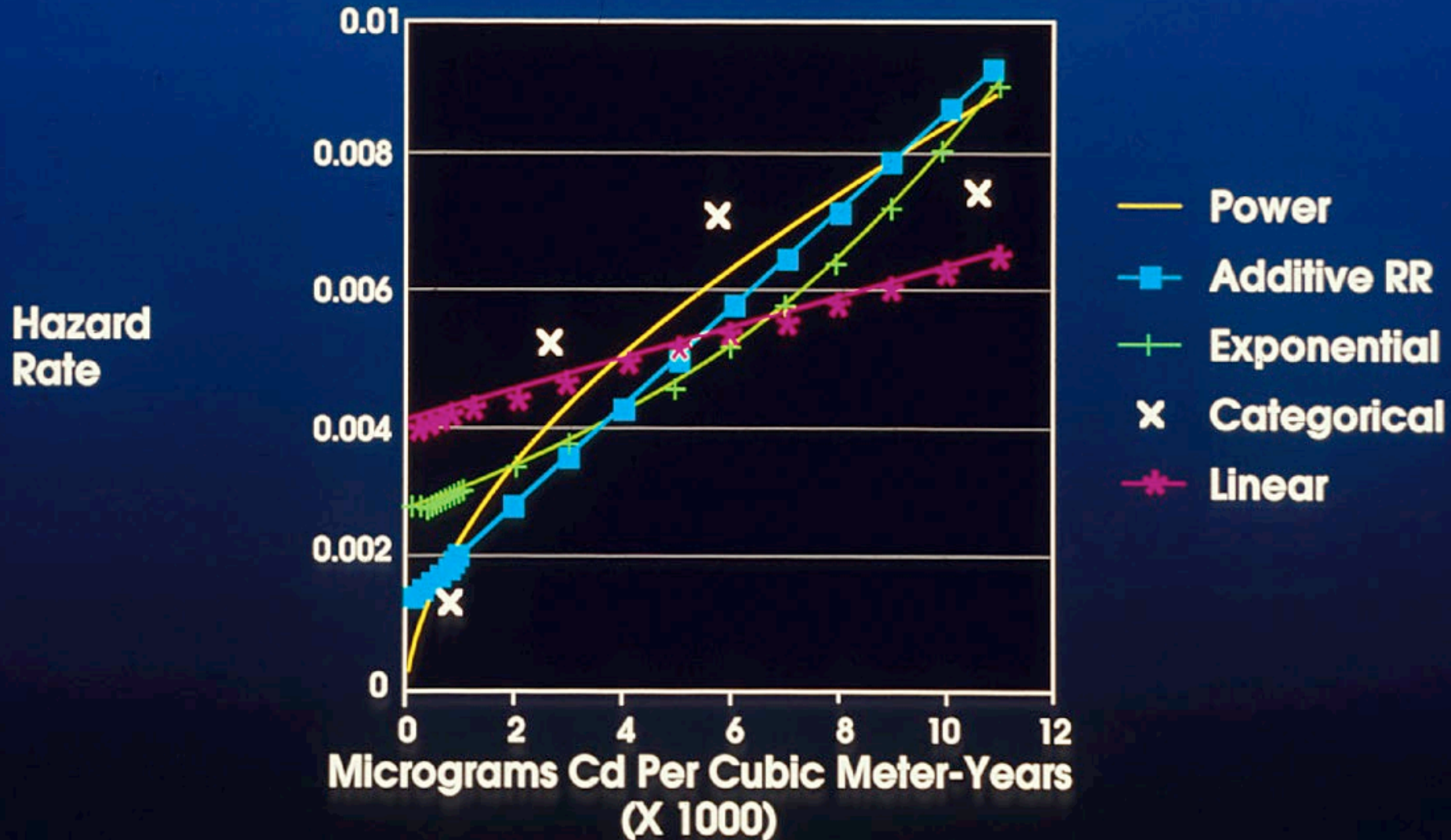
Stayner et al 1992. Scan J Work Env Health. 18(1):34-43

Lung cancer and cadmium exposure.



Stayner et al. 1992. Ann Epi 2(3):177-194

MODEL DERIVED HAZARD RATES AS A FUNCTION OF CUMULATIVE EXPOSURE



Stayner et al. 1992. Ann Epi 2(3):177-194



Estimates of excess risk per 1000 workers for 45 years of exposure based on Poisson and Cox Additive Relative Rate Models

Exposure ($\mu\text{g}/\text{m}^3$)	Excess Risk per 1000 workers	
	Poisson Model	Cox Model
5	6	0.5
50	58	24
100	111	50
200	205	96

Stayner et al. 1992. Ann Epi 2(3):177-194

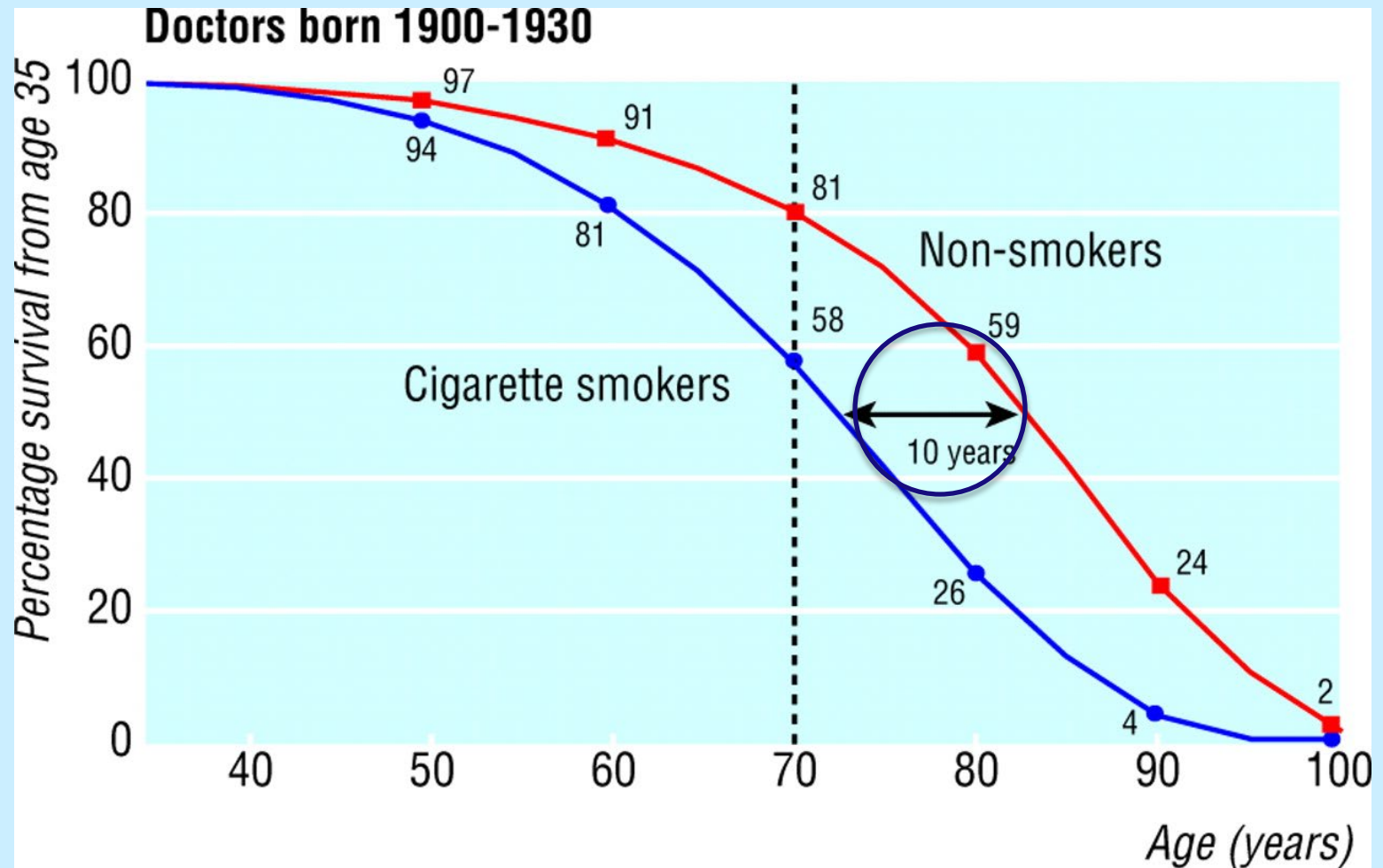
TOBACCO SMOKE



Sir Richard Doll (1912-2005)

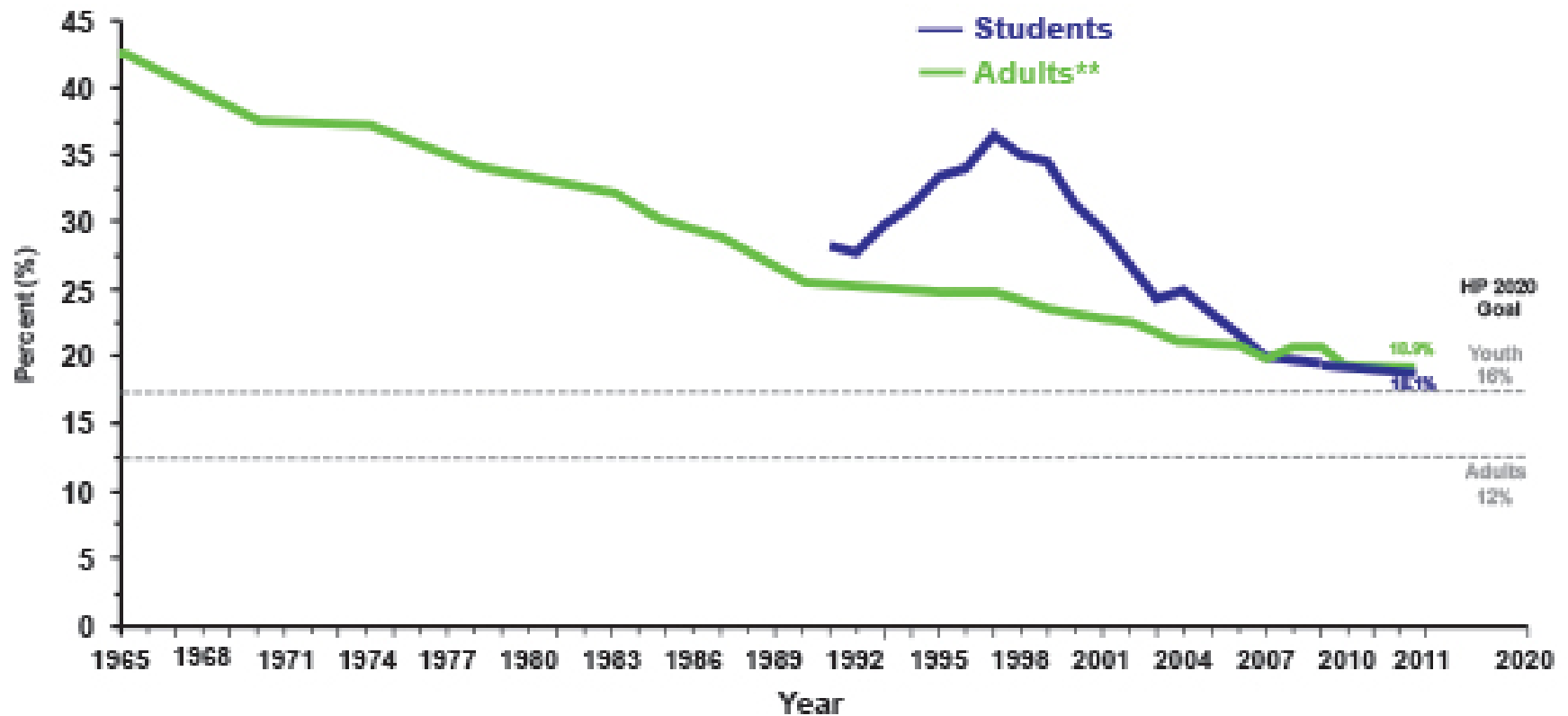


Survival from age 35 for continuing cigarette smokers and lifelong non-smokers among UK male doctors



Doll, R. et al. BMJ 2004;328:1519

Trends in Current Cigarette Smoking by High School Students* and Adults** — United States, 1965-2011

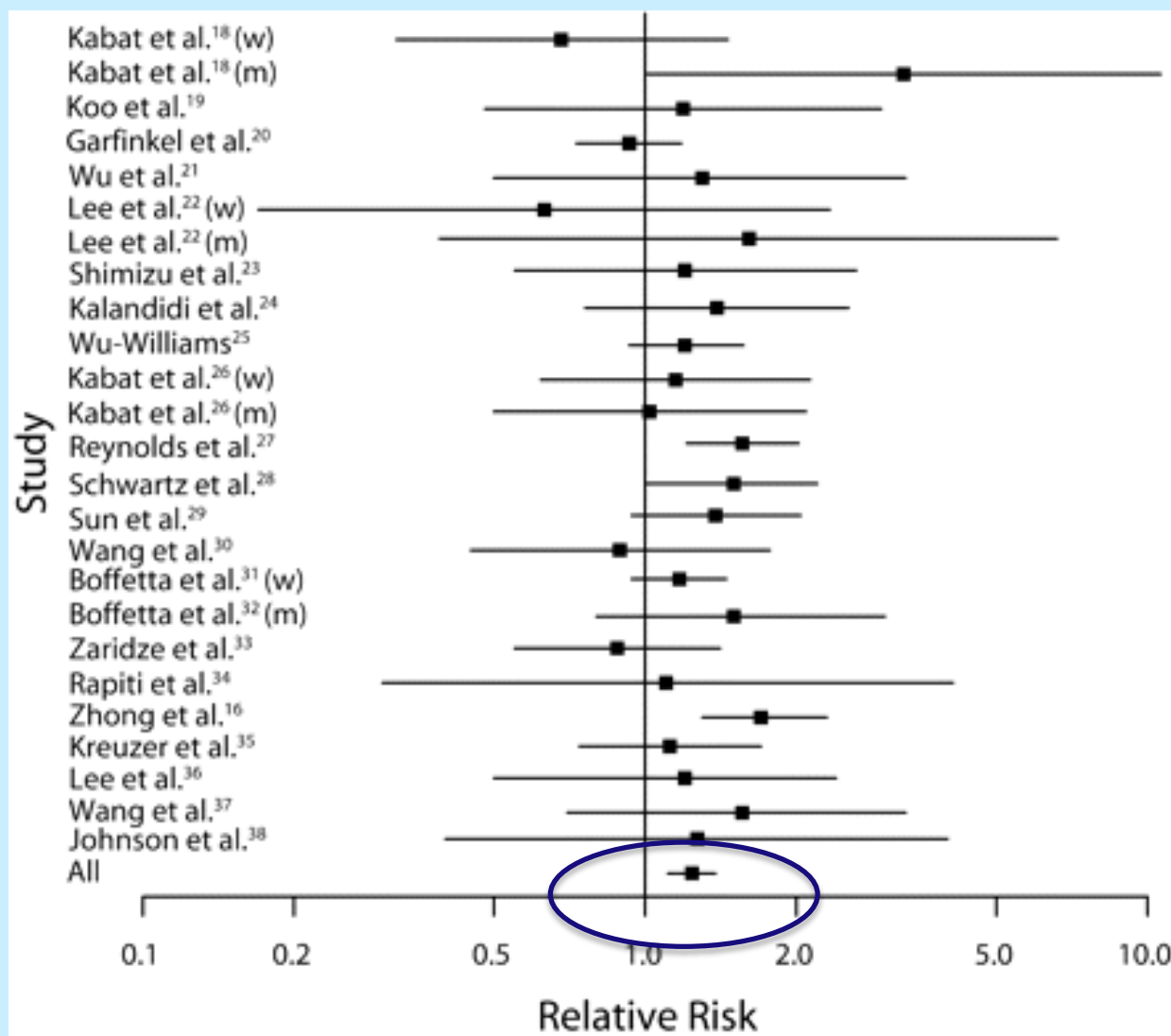


*Percentage of high school students who smoked cigarettes on 1 or more of the 30 days preceding the survey (Youth Risk Behavior Survey, 1991-2011).

**Percentage of adults who are current cigarette smokers (National Health Interview Survey, 1965-2011).

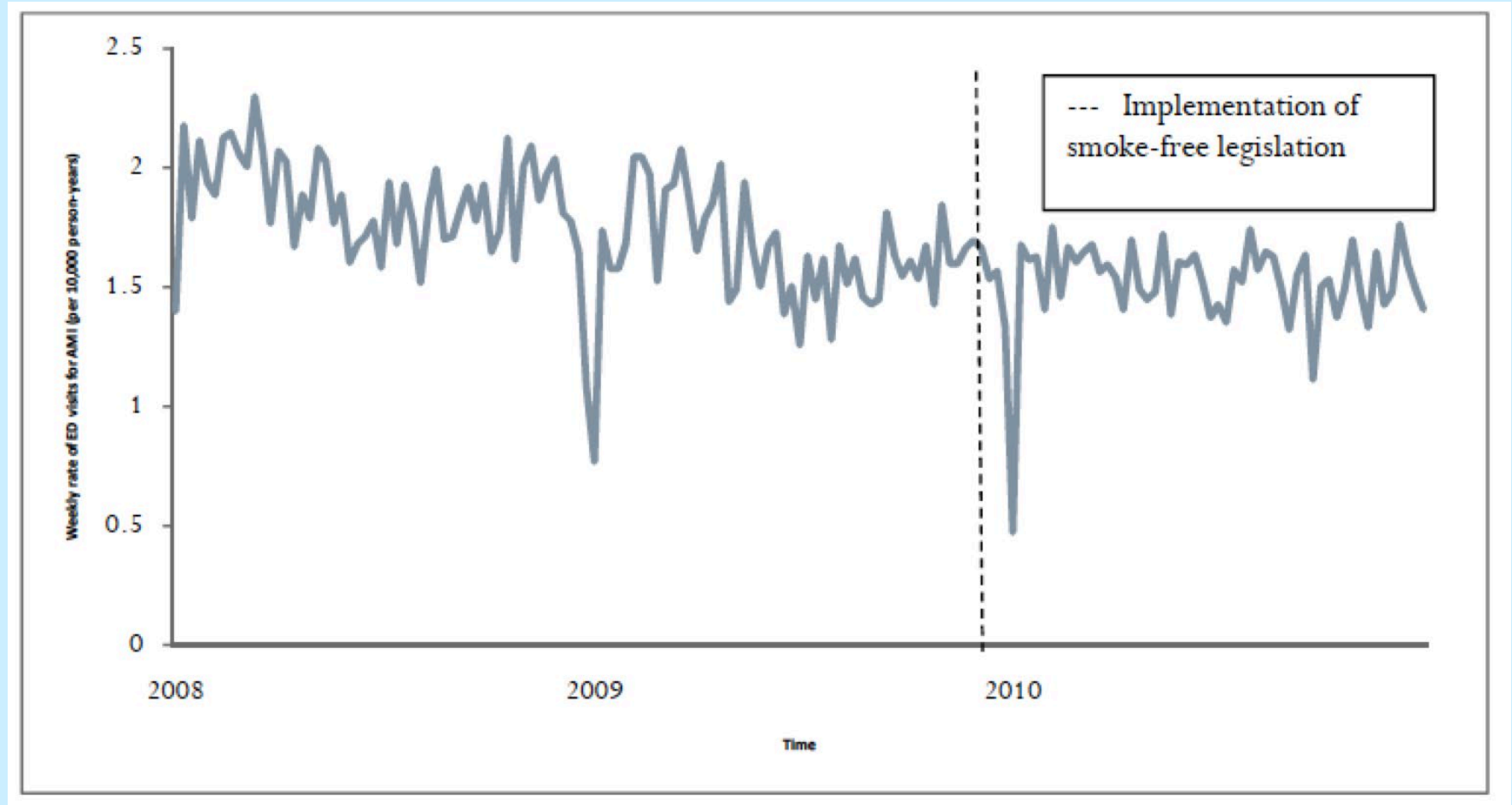
http://www.cdc.gov/tobacco/data_statistics/tables/trends/cig_smoking/index.htm

Lung cancer risk and workplace exposure to environmental tobacco smoke.



Stayner et al. 2007 Am J Public Health Mar;97(3):545-51.

Declines in Hospital Admissions for Acute MI in North Carolina After Banning Smoking in Bars and Restaurants



<http://tobaccopreventionandcontrol.ncdhhs.gov/smokefreenc/docs/TPCB-2011SFNCReport-SHD.pdf>.

Global Cigarette Production

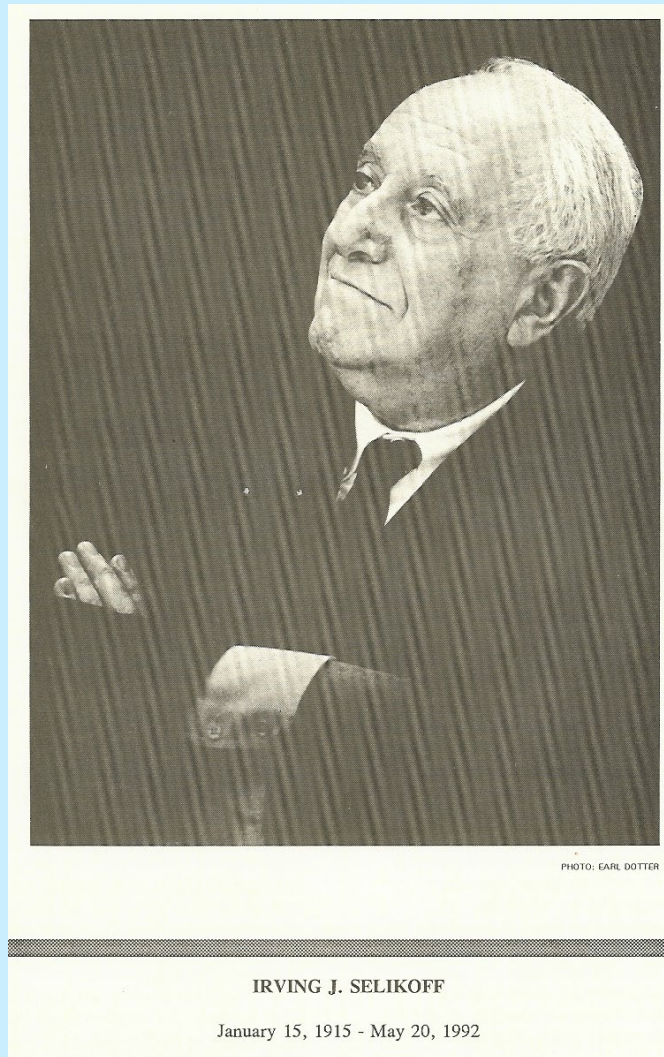
*In millions of cigarettes,
2000 and 2010*

Between 2000 and 2010,
cigarette production noticeably
shifted from the western
to the eastern part of Europe.





Asbestos



Irving J. Selikoff 1915-1992



The Amphibole Hypothesis

"There are two types of asbestos:
One is potentially lethal
and one is as harmless as a Cheez Doodle....
The Cheez Doodle variety of asbestos
is known as chrysotile. It accounts for
95 percent of the asbestos used
in the United States.
And it is utterly, totally harmless."

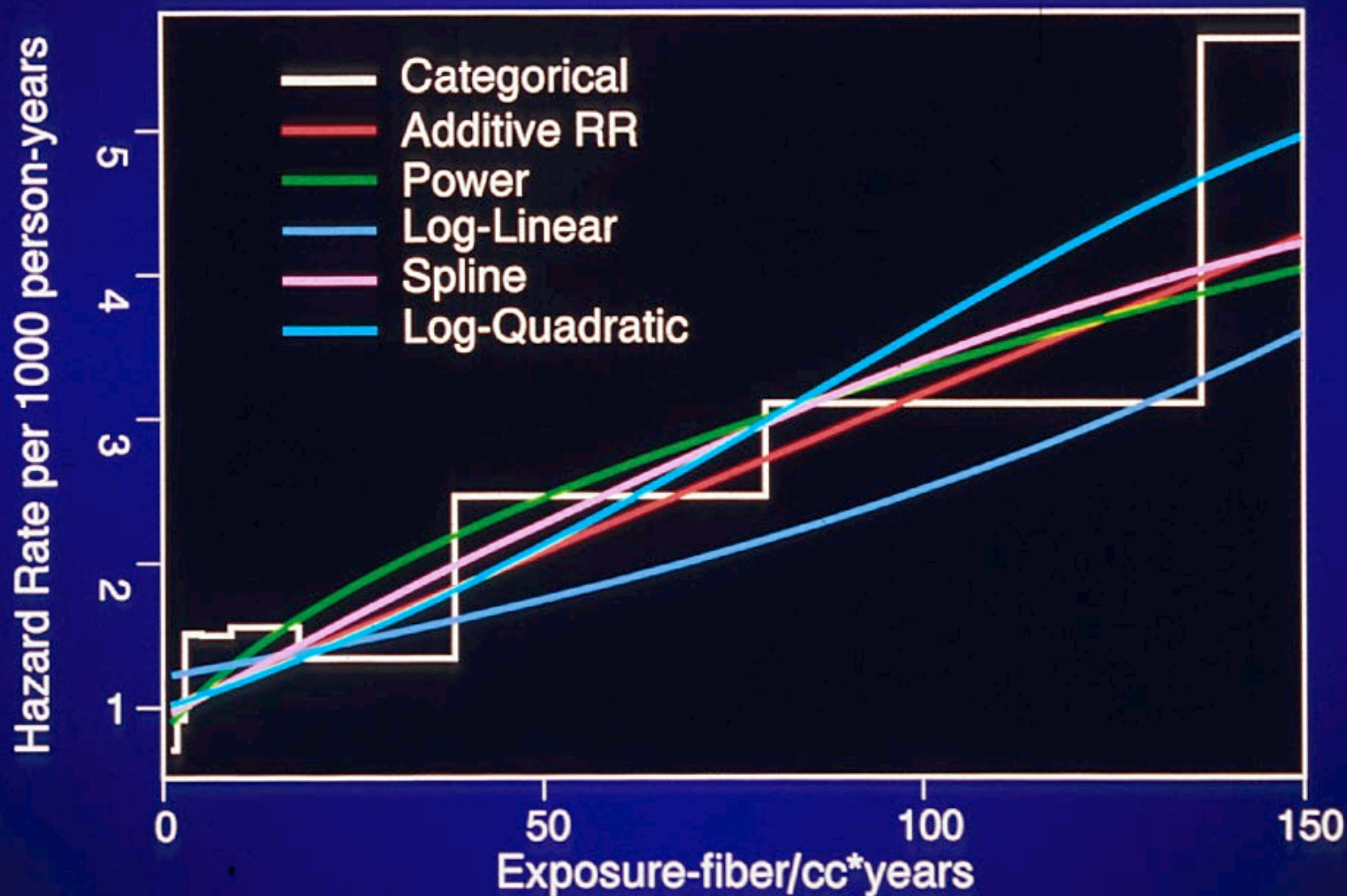
Rush Limbaugh, TV, 9/20/93

From: The Way Things Aren't: Rush Limbaugh's Reign of Error.
by Steve Rendall, Jim Naureckas, and Jeff Cohen



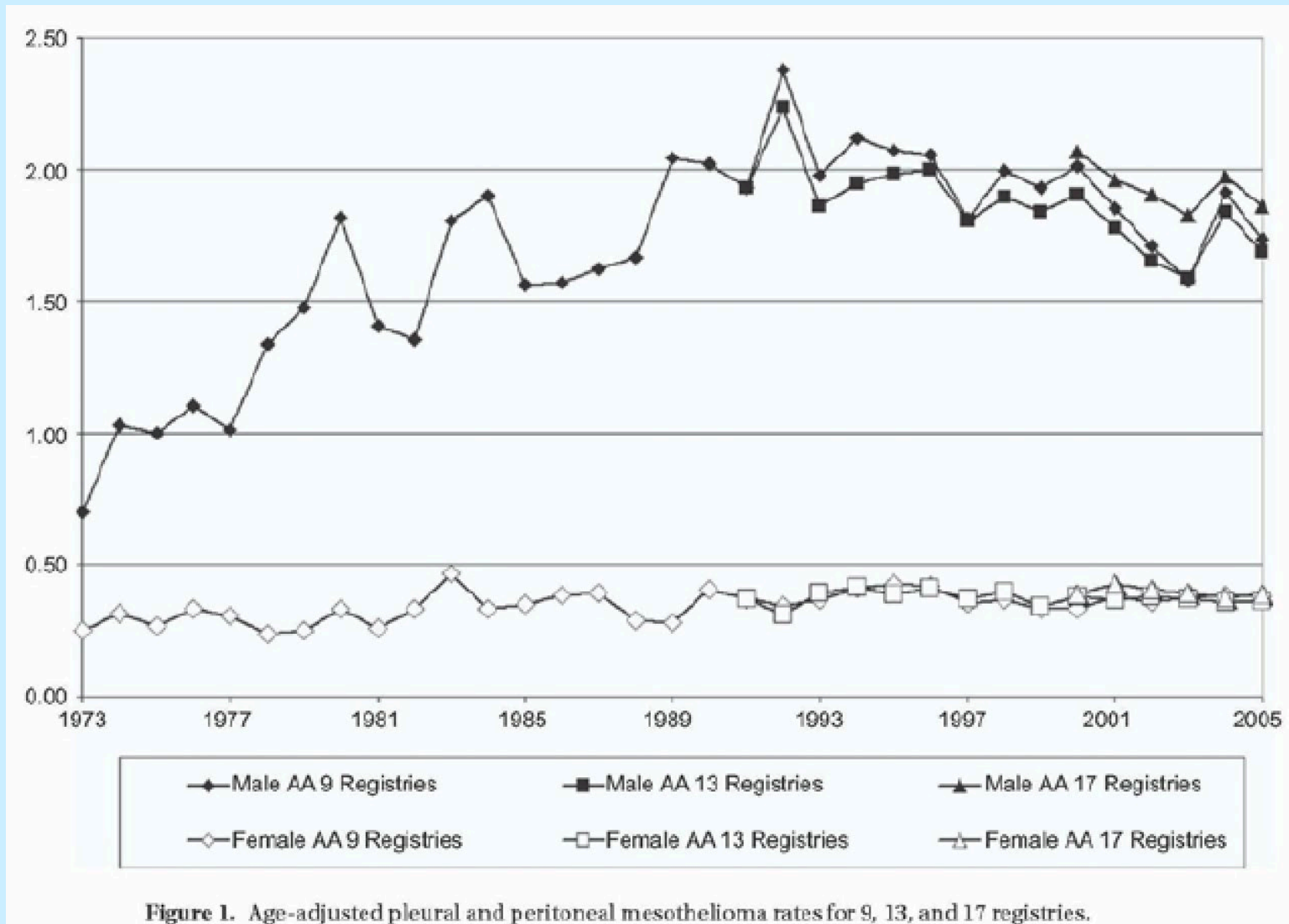
- Stayner, Dankovic and Lemen. AJP. 1996 Feb;86(2):179-86. - Toxicologic and epidemiologic studies provide strong evidence that chrysotile is associated with an increased risk of lung cancer and mesothelioma.
- IARC 2011. There is sufficient evidence in human for the carcinogenicity of all forms of asbestos (chrysotile, crocidolite, amosite, tremolite, actinolite and anthophyllite). Asbestos causes mesothelioma and cancer of the lung, larynx and ovary

***Lung Cancer Mortality Rates as a Function of
Cumulative Asbestos Exposure Predicted by Alternative Models
for White Males, Age 50 in 1940-1969***



Stayner et al. *Occ Env Med* 1997; 54:646-652.

Mesothelioma is also leveling off in the U.S.
where use was greatly reduced in the 1970s





Joint Policy Committee of the Societies of Epidemiology – June 4, 2012

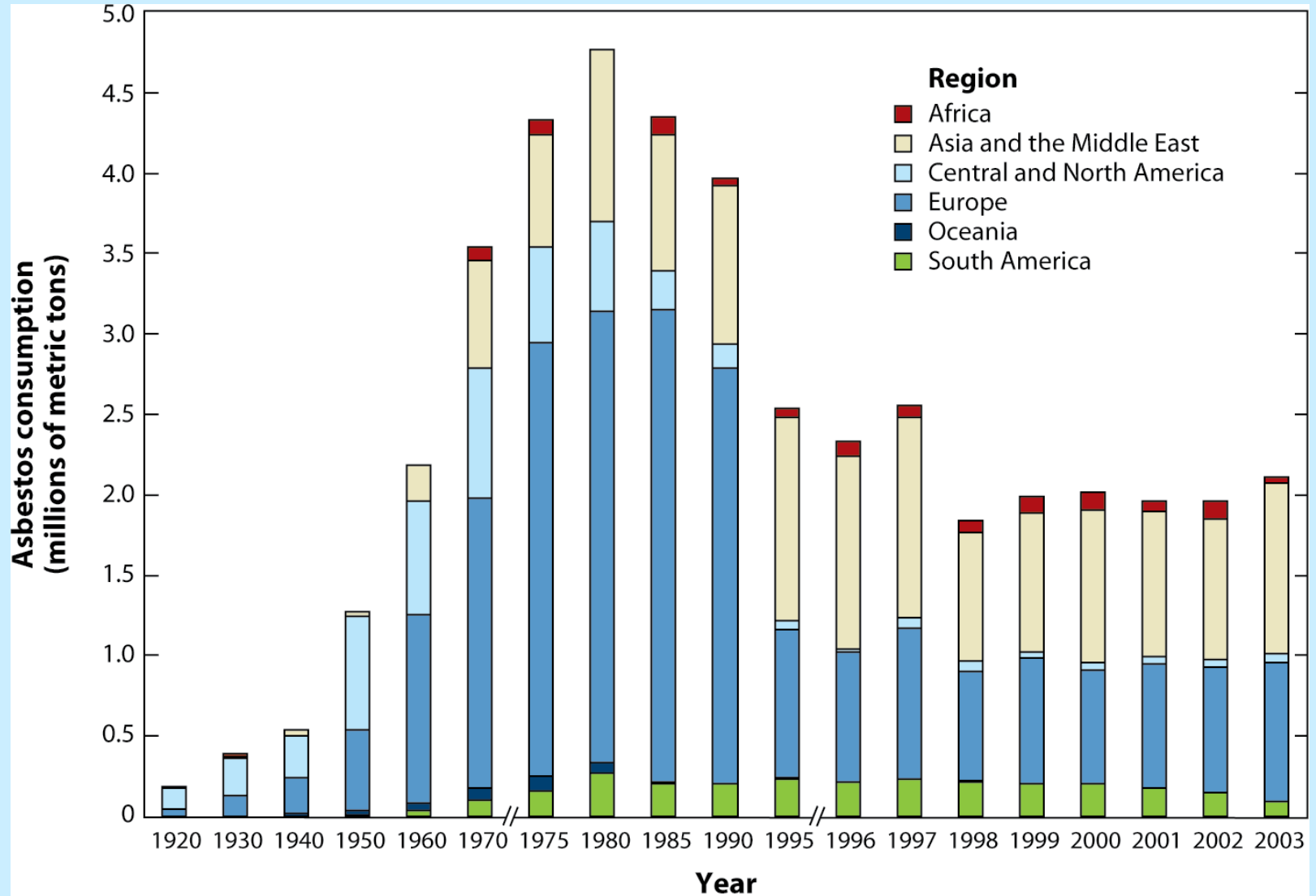
Called for a global ban on the
mining, use and export of all
forms of asbestos

Asbestos has been banned in 54 countries



http://ibasecretariat.org/alpha_ban_list.php

Trends in worldwide consumption of asbestos



Stayner L, et al. 2013.

Annu. Rev. Public Health. 34:205–16

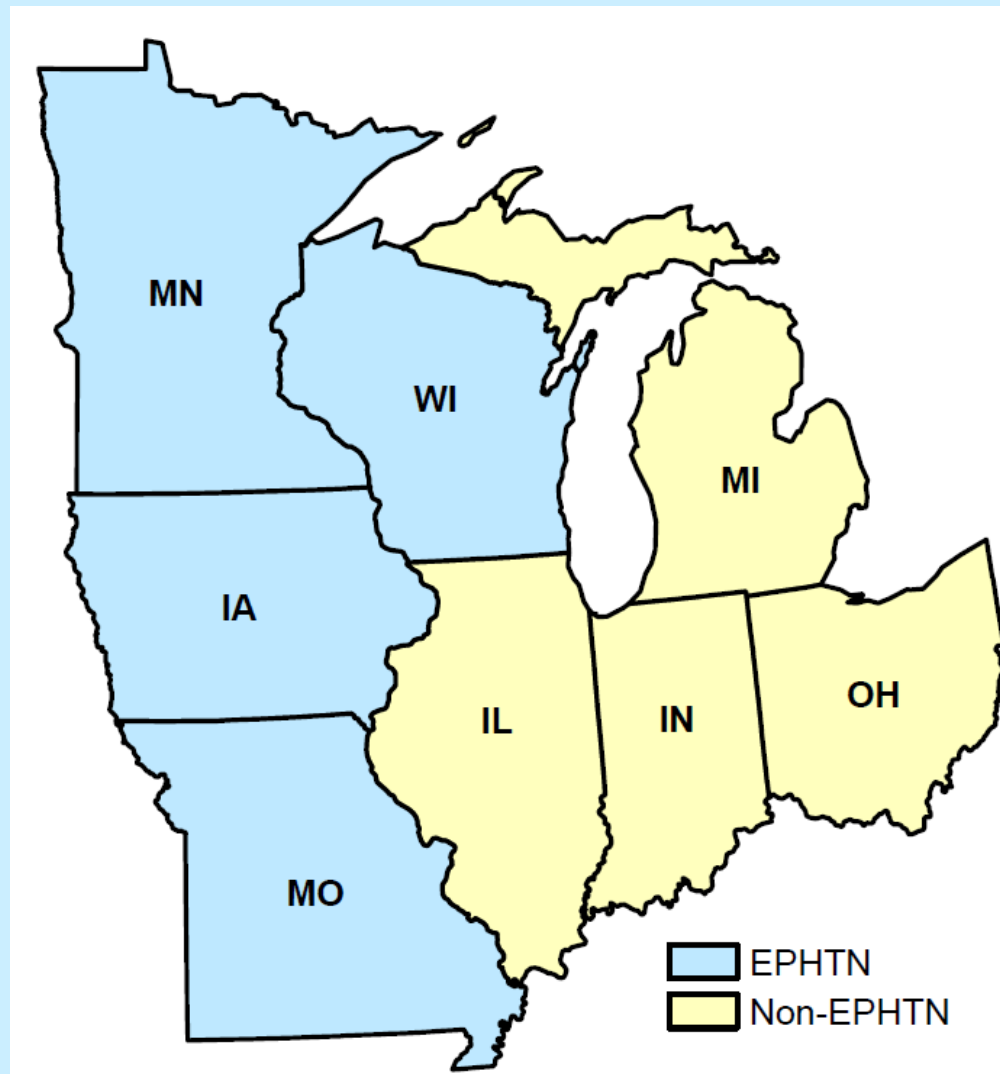


Water Contamination and Cholera

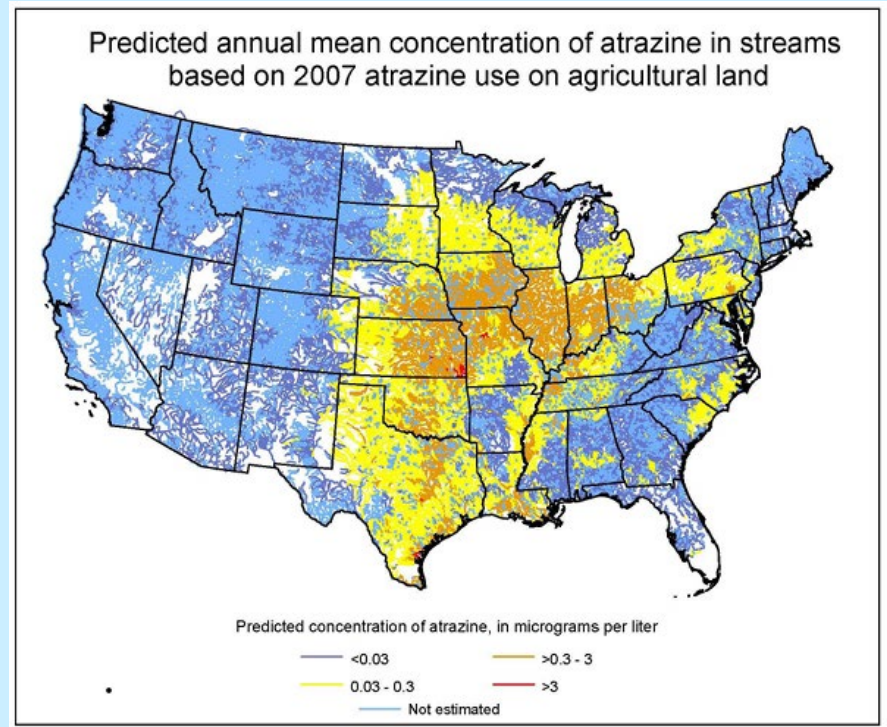
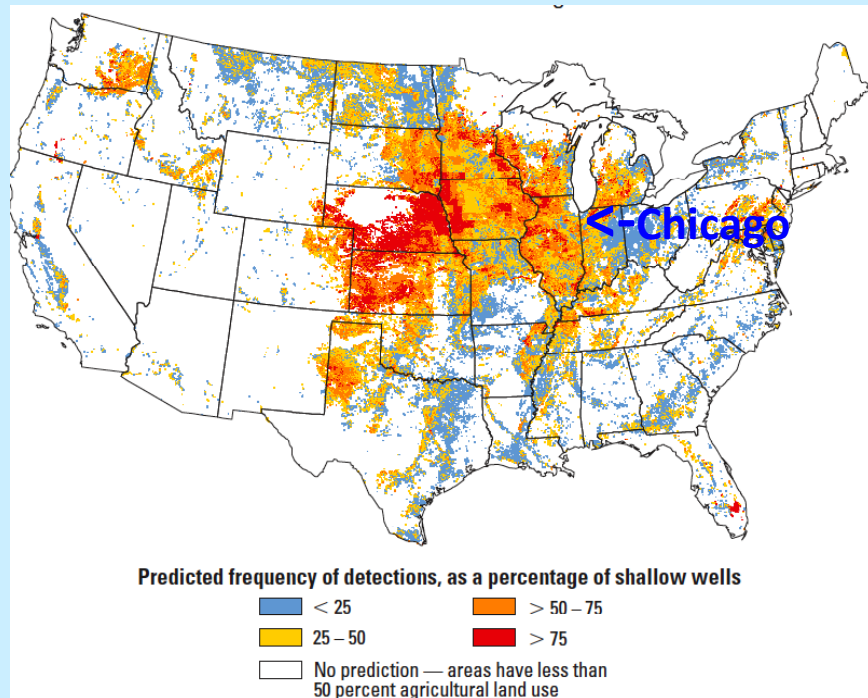


John Snow (1813-1858)

Adverse Birth Outcomes and Water Contamination by Atrazine & Other Agrichemicals in the Midwest



Atrazine concentrations in ground and surface water in the U.S.



http://water.usgs.gov/nawqa/home_maps
<http://infotrek.er.usgs.gov/warp/>

BOTANIC LESSON 1
***Genetically modified corn is
not dangerous for human beings***





Atrazine induces complete feminization in male African clawed frogs (*Xenopus laevis*)



Hayes TB et al. Atrazine induces complete feminization and chemical castration in male African clawed frogs (*Xenopus laevis*). *Proc Natl AcadSci U S A*. 2010 Mar 9;107(10):4612-7.

Epidemiologic Evidence for Atrazine

Limited evidence suggests atrazine may be associated with:

- Low Birth Weight - Sathyanarayana et al. 2010
- Small for gestational age - Bukowski 2001, Munger et al. 2007, Ochoa et al. 2009, Chevrier et al. 2011
- Birth defects - Winchester et al. 2009
- Childhood Cancer - Thorpe et al. 2005, Carozza et al. 2008



UIC Environmental Public Health Tracking Study

Phase 1: Ecologic Study

- Study Population - Singleton Births 2004-2008
- 4 million births
- County level data from SDWS and AMP program

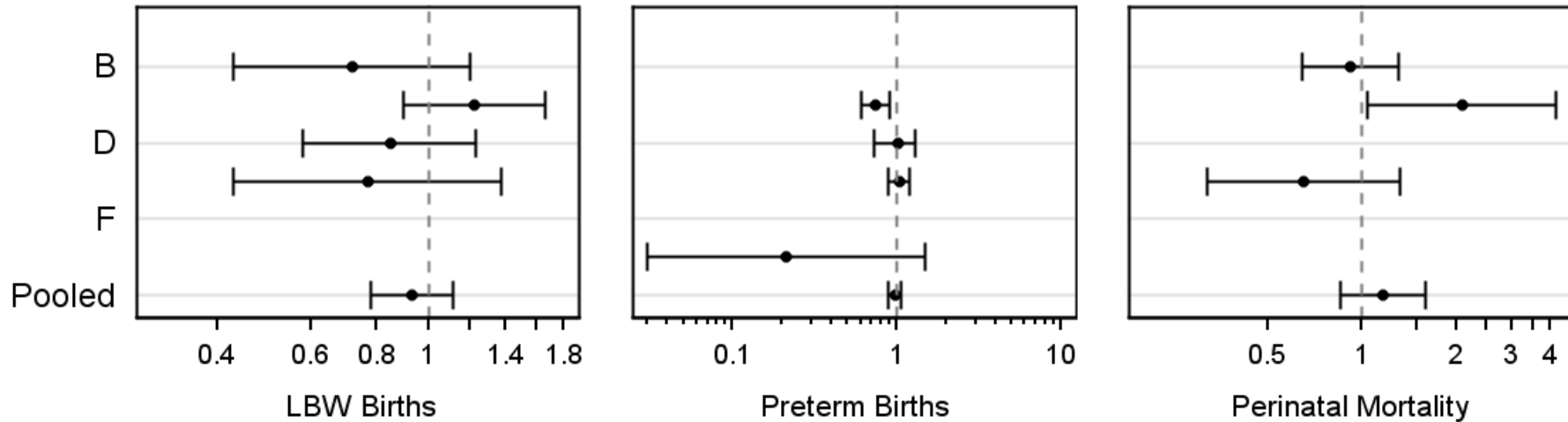
Phase 2: Individual Births Study

Ohio & Missouri Individual birth outcomes
& risk factors, county level exposures.



Atrazine Concentration and Adverse Birth Outcomes in 7 Midwestern States, 2004-2006

Relative Risks and 95% Confidence Intervals



Models adjusted for race/ethnicity, gender, season and year of birth, county median household income, county-level rates of maternal age groups, population and population density. Analysis restricted to counties of < 300,000 with >75% on public water.



Missouri - Crop Production and Birth Outcomes

Outcome	Exposure Variable	Method 1	Method 2	Method 3
		RR (95% CI)	RR (95% CI)	RR (95% CI)
Low birth weight	Corn	1.03 (0.86 - 1.24)	1.03 (0.86 - 1.24)	1.05 (0.77 - 1.42)
	Soybean	1.10 (0.97 - 1.24)	1.10 (0.98 - 1.24)	1.11 (0.91 - 1.34)
	Wheat	1.14 (0.78 - 1.68)	1.14 (0.85 - 1.54)	0.97 (0.51 - 1.84)
	Rice	1.85 (1.18 - 2.90)	1.85 (1.22 - 2.82)	1.74 (0.96 - 3.15)
	Cotton	1.50 (1.25 - 1.80)	1.50 (1.31 - 1.71)	1.76 (1.32 - 2.33)
Preterm births	Corn	0.84 (0.78 - 0.91)	0.84 (0.75 - 0.94)	0.91 (0.76 - 1.08)
	Soybean	0.95 (0.90 - 1.00)	0.95 (0.88 - 1.03)	1.00 (0.89 - 1.13)
	Wheat	0.91 (0.77 - 1.08)	0.91 (0.73 - 1.13)	0.94 (0.66 - 1.33)
	Rice	1.77 (1.46 - 2.14)	1.77 (1.49 - 2.09)	1.66 (1.15 - 2.40)
	Cotton	1.19 (1.09 - 1.29)	1.19 (1.09 - 1.29)	1.19 (0.98 - 1.44)

Method 1=Poisson Regression, 2=GEE, 3=GAMEPHT



Top Ten Lessons Learned on How to Impact Public Health

1. Be in the right place & time (UNC), also need to work hard and be persistent (Doll)
2. Ask the right questions (Tyroler)
3. Study sensitive subpopulations (Shy- Air)
4. Do the best studies (e.g. Tyroler, Shy, Doll)
5. Use the best statistical methods (e.g. Kupper & Kleinbaum)

6. Study modifiable factors (e.g. cholesterol, workplace, air and water exposures)
7. Need to work more with policy makers
8. May need to work with advocates (e.g. Joint Commission Statement)
9. We need to have a global perspective
10. We need to understand the fundamental societal factors underlying exposure and disease



Shy Carl. The Failure of Academic Epidemiology:
Witness for the Prosecution AJE 1997;145:479-84.

“To understand how to deal with important public health problems, such as sexually transmitted diseases violence in society, teenage pregnancies, and disparities in mortality rates between economic classes, the public health community needs research on the population determinants of these problems and on the effectiveness of interventions at the community level.”



“Nobody any longer who looks at any of the data doubts the importance of the social environment on the distribution of disease in populations. ...But when you get around to asking “What do you do about it”? That’s when you get into the real problem. ...Do you go to your Congressman? Do you go to your revolutionary?”

From Interview with Herman A. Tyroler,
September 5, 2001

<http://www.epi.umn.edu/cvdepi/pdfs/Tyroler.pdf>

Thank You

