

Methods Themes

Instructor: Rebecca E. Graff, ScD

Friday, January 25, 2019, 8:45am – 10:15am

Mission Hall 1105

Discussion:

**WHAT METHODOLOGICAL ISSUES
OR CONSIDERATIONS DID YOU
DISCOVER IN THE READINGS FOR
TODAY?**

Discussion:

**WHAT ARE THE POSSIBLE
EXPLANATIONS FOR AN INVERSE
ASSOCIATION BETWEEN CANCER
AND ALZHEIMER'S DISEASE?**

Outline

- Basic considerations for studying older adults
- Study design in older adults
- Missing data
- Selection bias
- Age, cohort, and period effects

BASIC CONSIDERATIONS FOR STUDYING OLDER ADULTS

Discussion:

**HOW IS STUDYING OLDER ADULTS
DIFFERENT FROM STUDYING
YOUNGER POPULATIONS?**

Key Differences

- Multimorbidity
- Signs and symptoms are common
- Clinical manifestations may be different
- Difficulty of information acquisition
- Differences of physiology
- Vulnerability to environmental challenges
- Shorter potential follow-up times

Key Differences, Cont.

- Bodily system dysfunction
- Altered usual medical care practices
- Fewer prevention interventions
- Different clinical outcomes
- Range of “Oldness”
- Residences
- Burden of study protocols

Discussion:

WHY STUDY OLDER ADULTS?

A Note About Consent Issues

- Cognitive impairment
 - Sometimes after study start
- Reasoning deficits
- Excess information
- Sufficient information

STUDY DESIGN IN OLDER ADULTS

Finding the Elderly

- Sources:
 - Medicare files
 - Census data
 - Commercial mailing lists
 - Patient registries / clinical records
- Impediments:
 - Protected environments
 - Diminished willingness
 - Social or economic deterrents

Principles of Recruitment and Retention

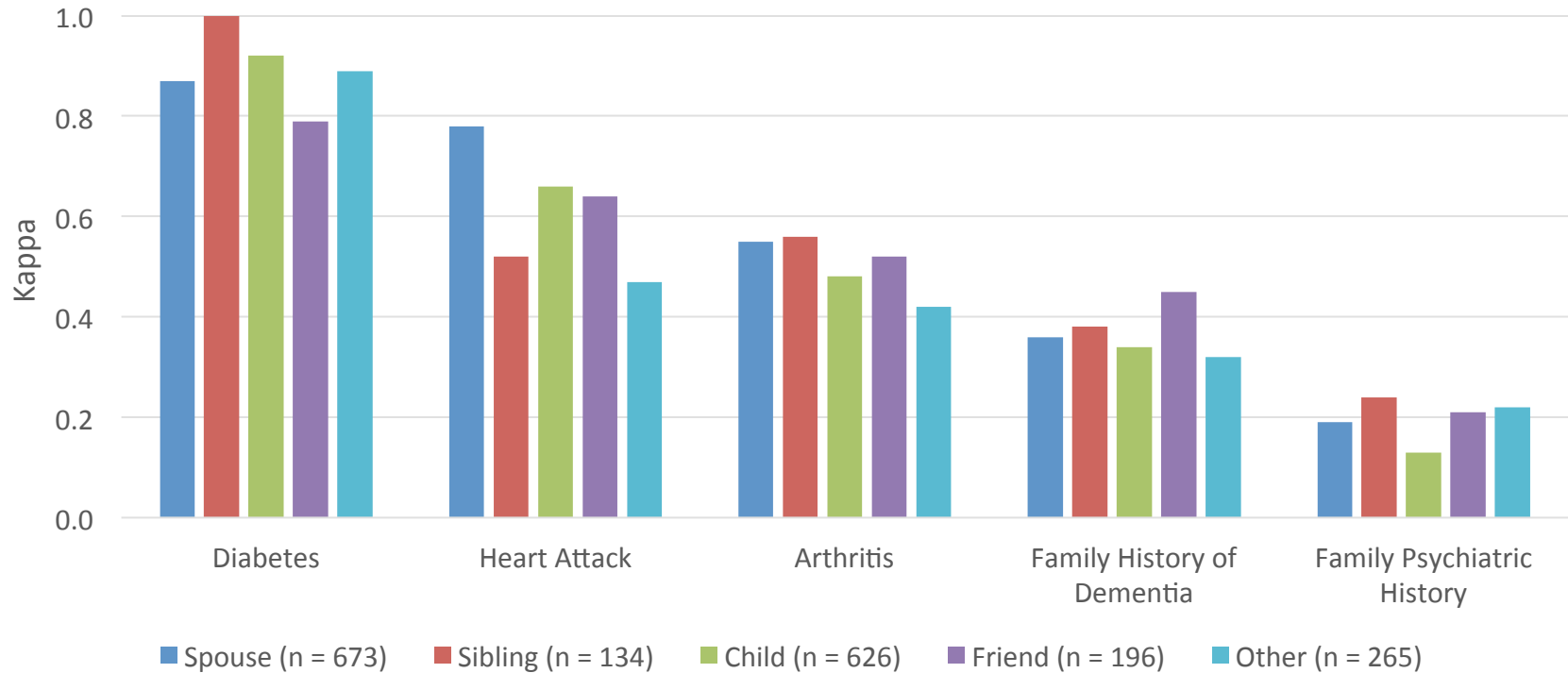
1. Achieving a representative sample
2. Promoting participation
3. Considering feasibility
4. Retaining participants

Data Collection

- Primary Issues:
 - Declining cognitive abilities / limited recall
 - Lack of available proxies
- Possible Solutions:
 - Use of memory aides
 - Use of biomarkers

On the Use of Proxies

Proband-Informant Agreement



Notes on Specific Designs

- Case-control studies:
 - Numerous variables on which to match
 - Necessity for careful consideration of hypothesized causal pathways
- Randomized controlled trials:
 - Older adults often excluded
 - Adherence
 - Risk of adverse events

MISSING DATA

Attrition

- Loss in sample study related to death, refusal to continue, loss to follow up, non-response
- Possible bias:
 - Refusal may be associated with health status
 - Death is associated with health status but may or may not be associated with exposures of interest
- Affects any study with a longitudinal component

E.g., Cognitive Function Study

Table 2: Potential bias in the non-responders from the original sample and wave 2 interviews

	Cambridge	Gwynedd	Newcastle	Nottingham	Oxford	Total
Refused wave 1	641	807	484	521	813	3266
Traced	641	806	482	518	808	3255
Died	123 (19)	155 (19)	115 (24)	93 (18)	177 (22)	663 (20)
Moved before wave 1	33	78	6	98	40	255
Traced	29	70	6	86	39	230
Died	10 (34)	13 (19)	1 (17)	27 (31)	11 (28)	62 (27)
Wave 1 interview complete	2601	2625	2524	2514	2740	13004
Traced	2600	2622	2520	2510	2736	12988
Died	437 (17)	384 (15)	482 (19)	409 (16)	525 (19)	2237 (17)
Wave 2 status of those in wave 1						
Wave 2 interview complete	1720 (66)	1703 (65)	1707 (68)	1733 (69)	1963 (72)	8826 (68)
Died ⁺	253 (10)	238 (9)	244 (10)	277 (11)	268 (10)	1280 (10)
Died and Refused	41 (2)	56 (2)	54 (2)	31 (1)	32 (1)	214 (2)
Died and Moved	0 (0)	2 (<1)	3 (<1)	2 (<1)	1 (<1)	8 (<1)
Refused	560 (22)	590 (22)	471 (19)	431 (17)	438 (16)	2490 (19)
Moved	27 (1)	36 (1)	45 (2)	37 (1)	36 (1)	181 (1)

⁺ Five individuals are excluded as they were reported to have died, but death has not been confirmed by ONS

Strategies for Missing Data

- Account for it in the design phase
- Minimize during follow-up
- Statistical handling

SELECTION BIAS

Consider the Claim:

Although the medical system may not work ideally for younger African-Americans, these problems are ameliorated among the elderly

Black / White Crossover – Mortality

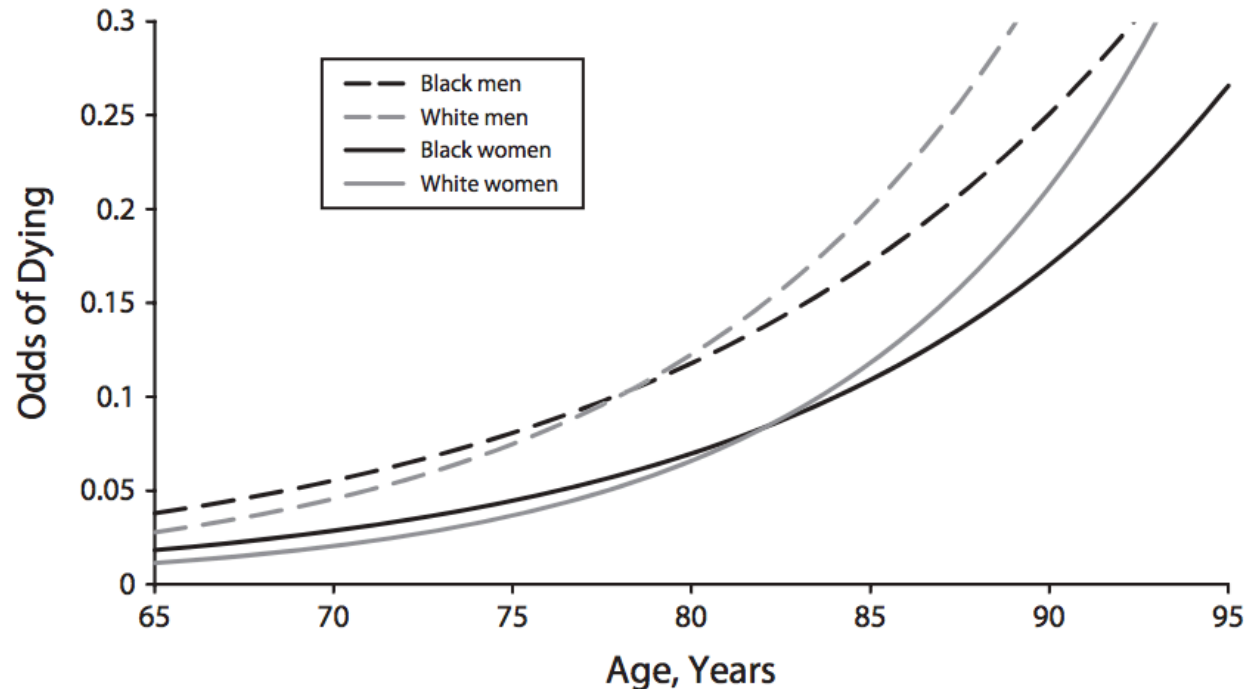
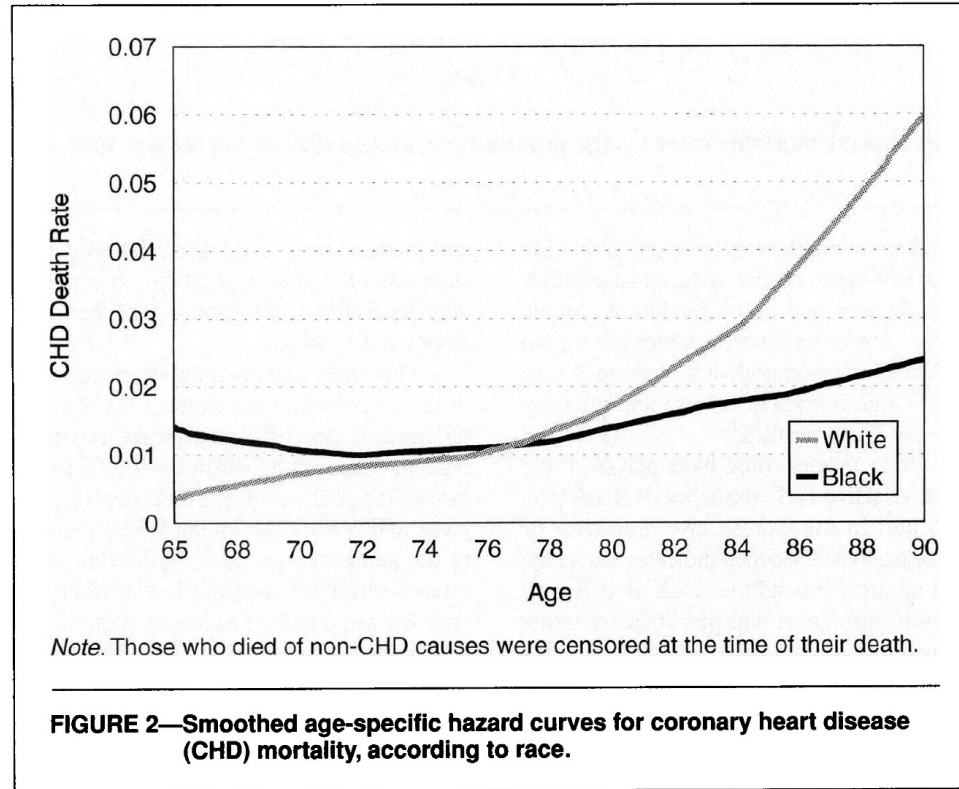


FIGURE 1—Predicted age-specific mortality by race for men and women: North Carolina Established Populations for Epidemiologic Studies of the Elderly, 1986–1996.

Black / White Crossover – CHD Death



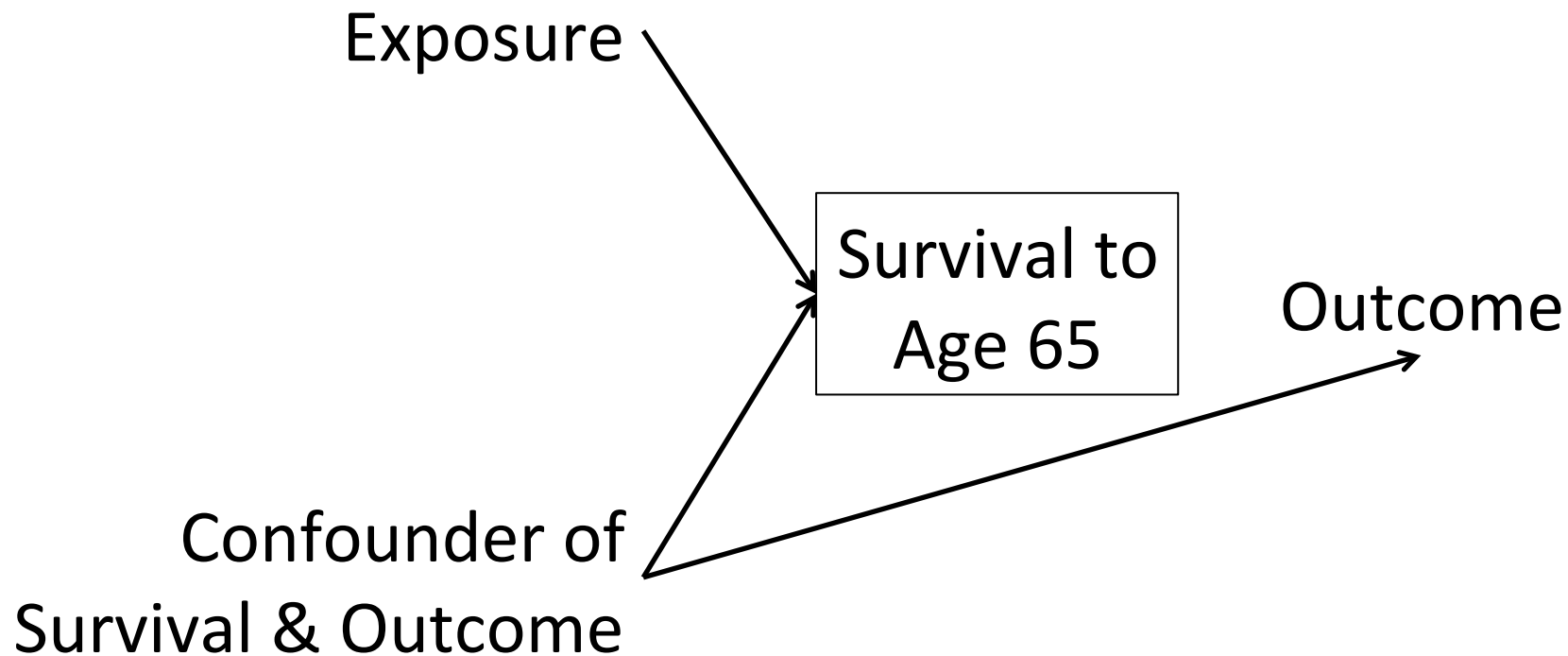
Discussion:

**IS THERE AN ALTERNATIVE
EXPLANATION?**

Explanations

- Age misreporting
- Selective survival
 - The exposed (African-Americans) are more likely to die before reaching old age
 - Attenuated associations among survivors at old ages (even though effects are undiminished)

The DAG



In General

- Risk factors often show smaller relative effect sizes in the elderly
 - Selective survival
 - Competing risks
 - High disease prevalence
 - Greater measurement error

AGE, COHORT, AND PERIOD EFFECTS

Definitions

EXHIBIT 1-1 Definitions of age, cohort, and period effects.

Age effect:	Change in the rate of a condition according to age, irrespective of birth cohort and calendar time
Cohort effect:	Change in the rate of a condition according to year of birth, irrespective of age and calendar time
Period effect:	Change in the rate of a condition affecting an entire population at some point in time, irrespective of age and birth cohort

$$\text{Age (years since birth)} = \text{Period (year)} - \text{Cohort (year of birth)}$$

Example – Prevalence of Disease Y

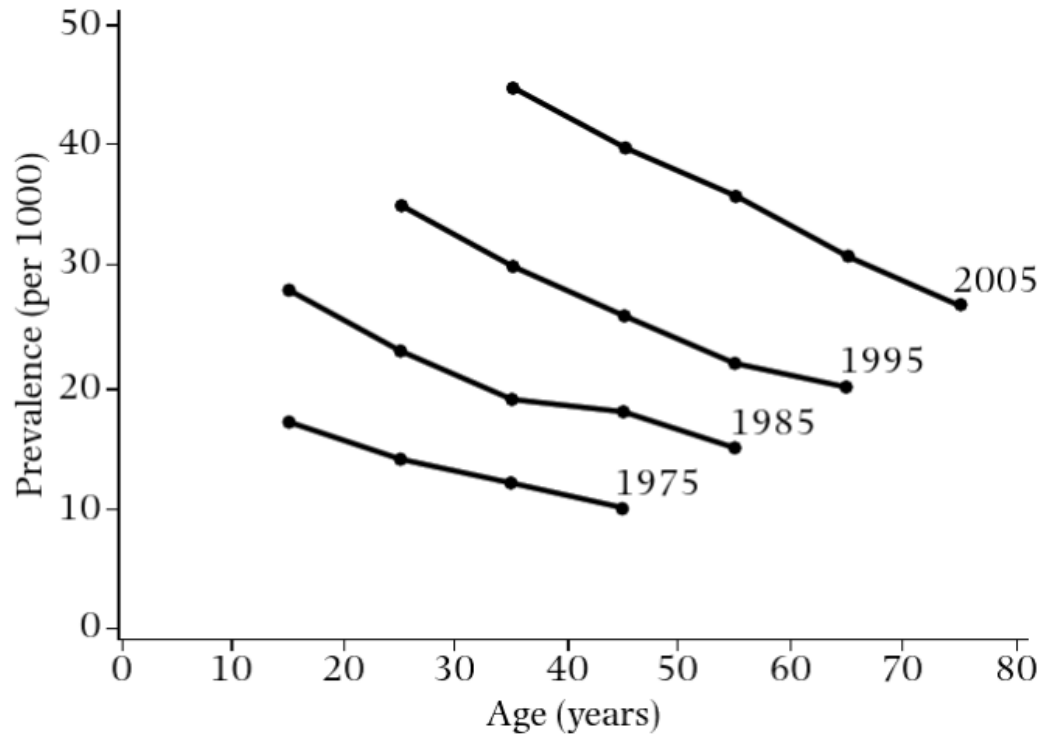
Age Group	Prevalence in 2005 (per 1000)
30-39	45
40-49	40
50-59	36
60-69	31
70-79	27

Does the prevalence of Disease Y decrease with age?

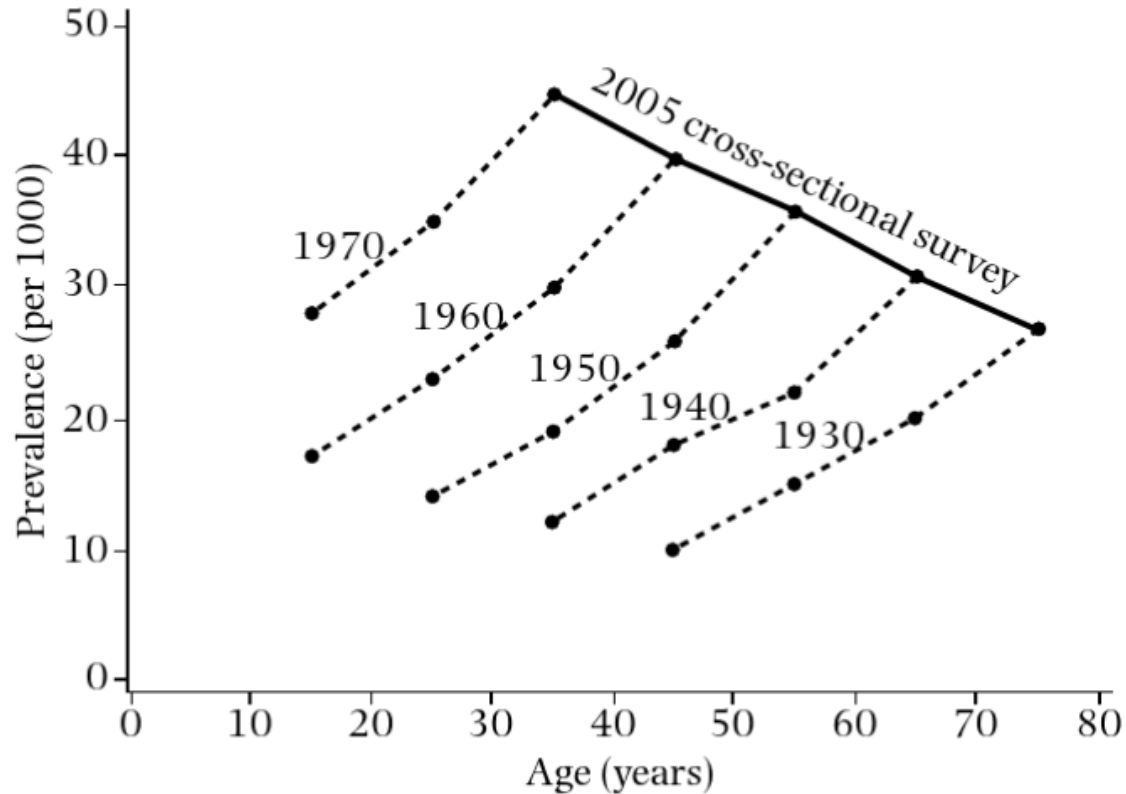
Prevalence of Disease Y Over Time

Age Group	1975	1985	1995	2005
10-19	17	28		
20-29	14	23	35	
30-39	12	19	30	45
40-49	10	18	26	40
50-59		15	22	36
60-69			20	31
70-79				27

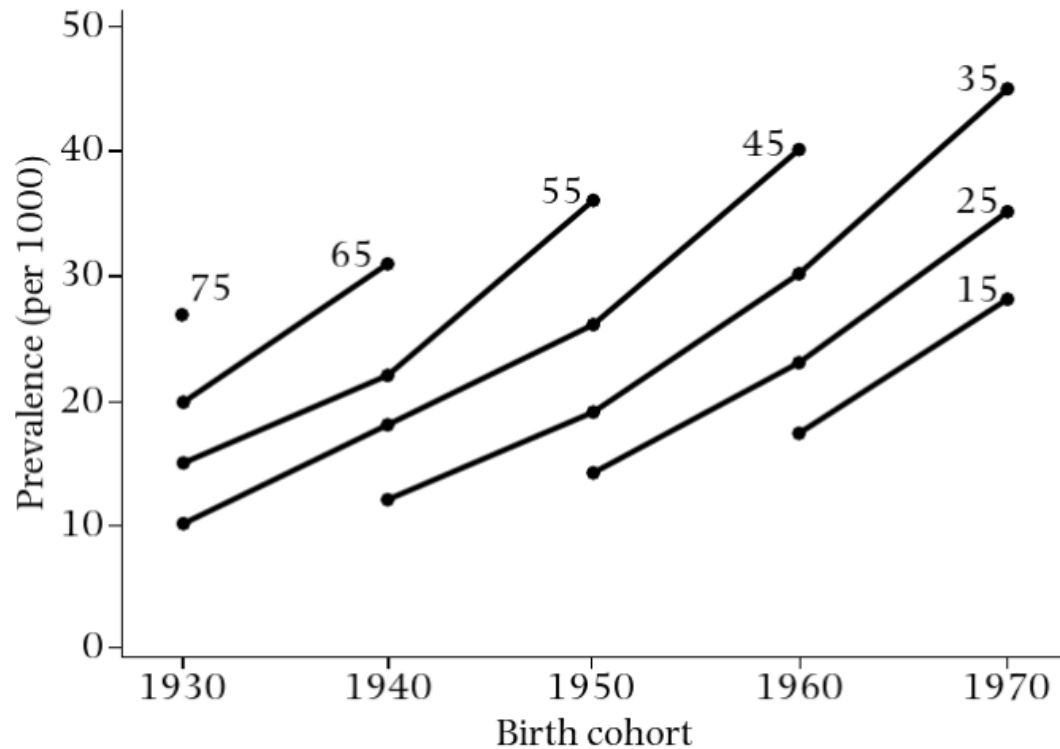
Shown Another Way



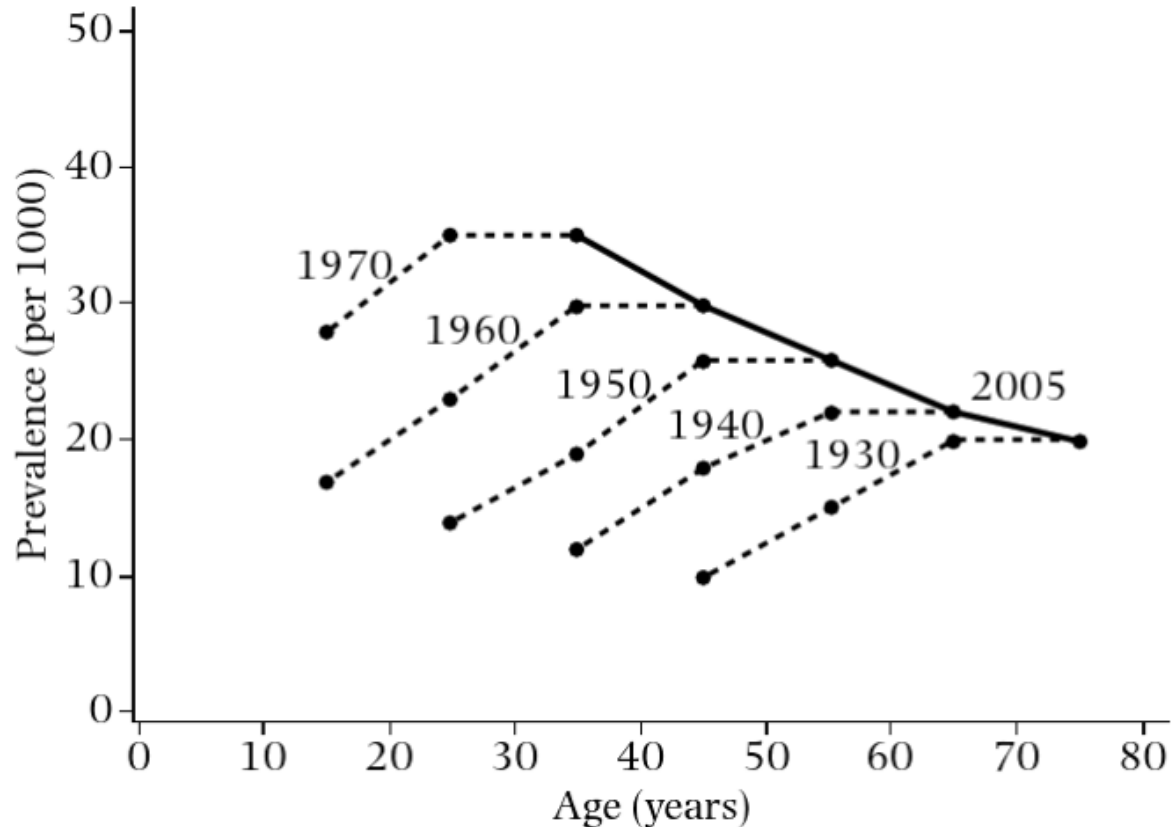
Yet Another Way



And One Final Way



Example – Period Effect



British Doctors Study

- $n \sim 35,000$
- Prospective cohort study 1951-2001
- Male British doctors born 1851-1930
- Provided convincing statistical proof of that tobacco smoking increases the risk of lung cancer

Original Results

TABLE IV.—*Standardized Death Rate Per Annum Per 1,000 Men Aged 35 Years and Above in Relation to the Most Recent Amount of Tobacco Smoked*

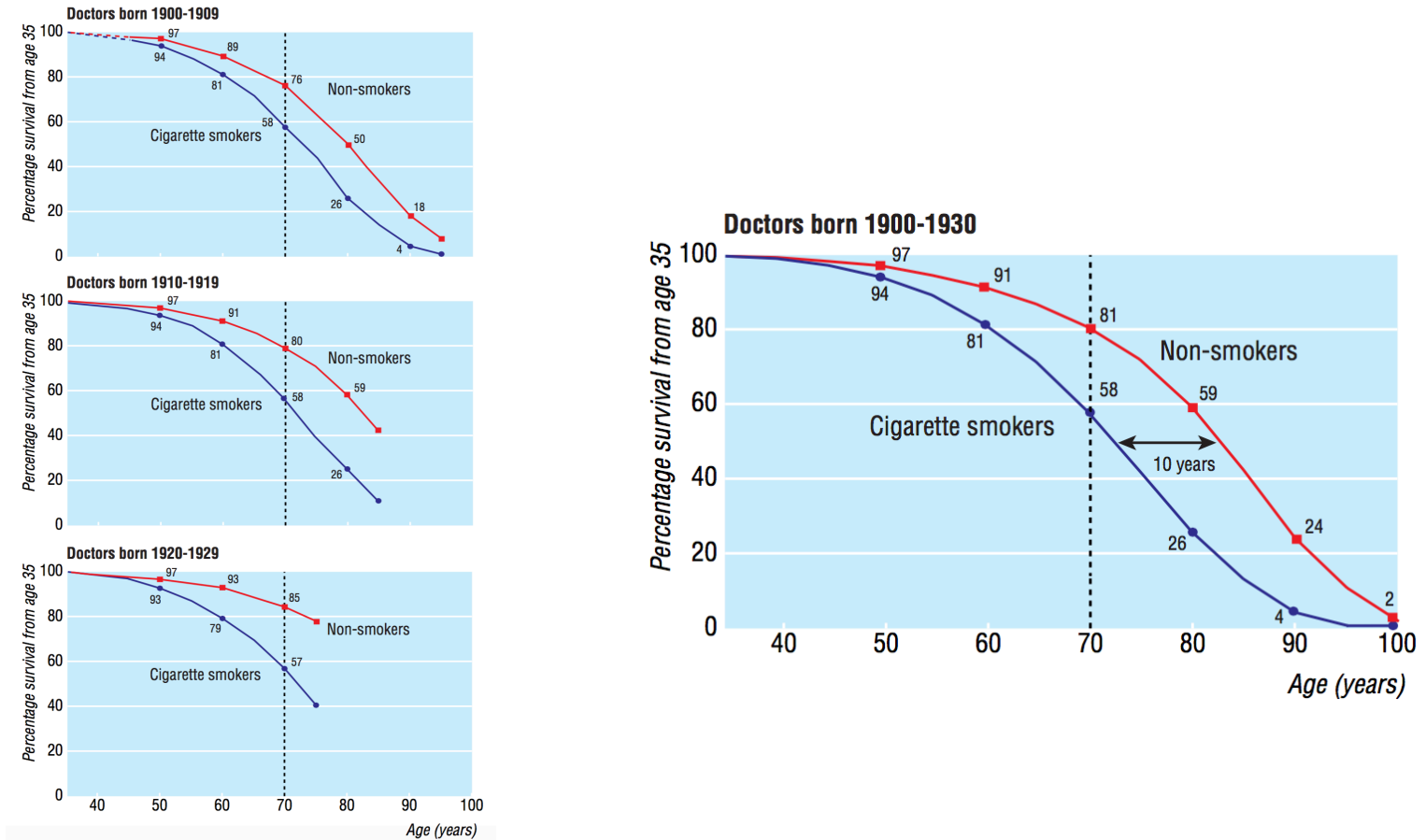
Cause of Death	No. of Deaths Recorded	Death Rates of Non-smokers	Death Rates of Men Smoking a Daily Average of			Death Rate of All Men
			1 g.—	15 g.—	25 g. +	
Lung cancer	36*	0.00	0.48	0.67	1.14	0.66
Other cancers	92	2.32	1.41	1.50	1.91	1.65
Respiratory disease (other than cancer)	54	0.86	0.88	1.01	0.77	0.94
Coronary thrombosis ..	235	3.89	3.91	4.71	5.15	4.27
Other cardiovascular diseases	126*	2.23	2.07	1.58	2.78	2.14
Other diseases	247	4.27	4.67	3.91	4.52	4.36
All causes	789	13.61	13.42	13.38	16.30	14.00

* 1 case in which lung cancer was recorded as a contributory but not a direct cause of death has been entered in both groups.

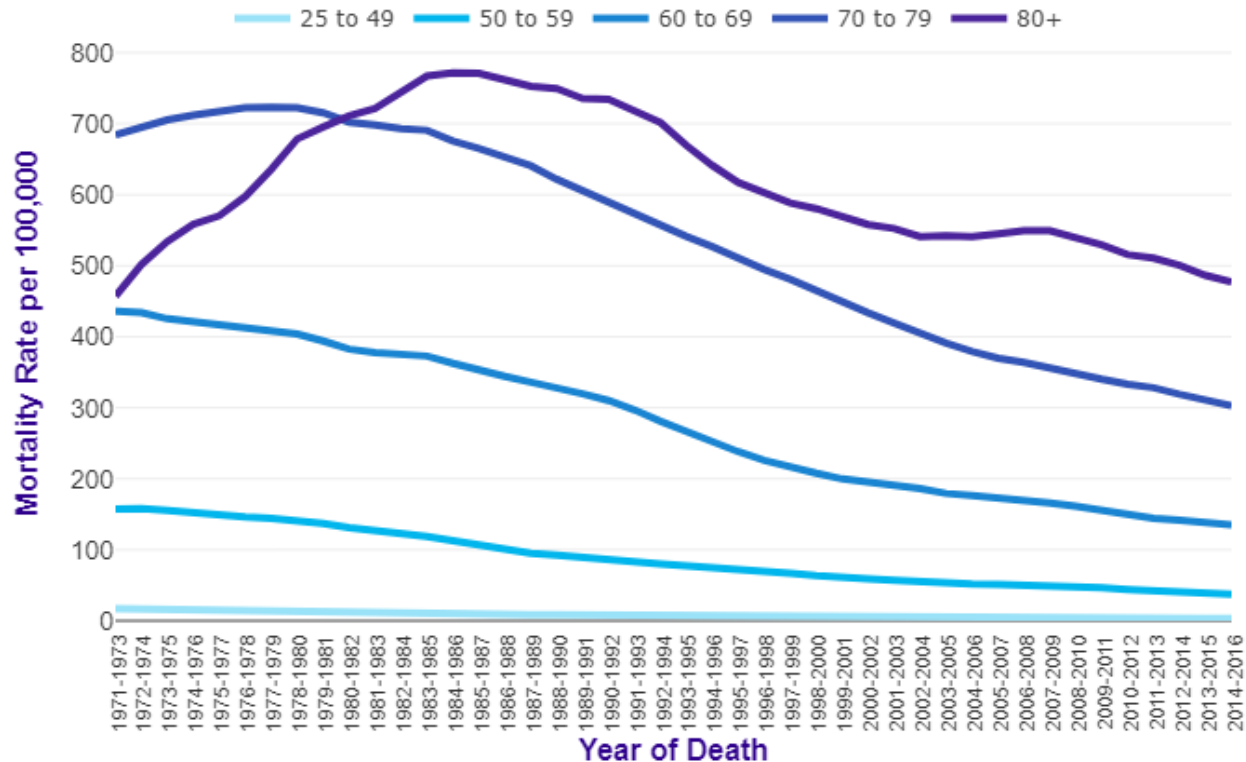
Discussion:

**WHAT IS THE ROLE OF AGE,
COHORT, AND PERIOD IN THE
ASSOCIATION BETWEEN SMOKING
AND SURVIVAL?**

Example – Cohort Effects



What Does This Plot Tell You?



How Does Aging Come Into Play?

- Stay tuned for the longitudinal methods lecture...

Next Week:

LECTURE: MEASUREMENT

HOMEWORK: MEASUREMENT

ASSIGNMENT, READINGS