Yueh-Ying Han, PhD, MS.

University of Pittsburgh Graduate School of Public Health,

Department of Epidemiology in collaboration with

University of Pittsburgh Cancer Institute-Center for Environmental Oncology

Age-period-cohort analysis of cancer incidence not related to screening or smoking: Estimating potentially avoidable cancer burden

Joel L. Weissfeld, MD, MPH [1,2], Gregg E. Dinse, ScD [3], David M. Umbach, PhD [3], and Devra L. Davis, PhD, MPH [1,2]

1. University of Pittsburgh, Graduate School of Public Health, Department of Epidemiology
2. University of Pittsburgh Cancer Institute, Center for Environmental Oncology
3. Environmental Diseases and Medicine Program, National Institute of Environmental Health Sciences, Research Triangle Park

Background

- Studies of cancer trends can be used to characterize current and future demands for health care and to suggest etiologic hypotheses about avoidable causes of any unexplained patterns
- Changes in medical practice, and a multiplicity of risk factors, including those related to personal behaviors and those related to carcinogens in air, water, and food.
- One simplifying approach divides primary site-specific cancer into three broad categories, tobacco-related cancer, screen-detectable cancer, and cancer unrelated to tobacco or screening.

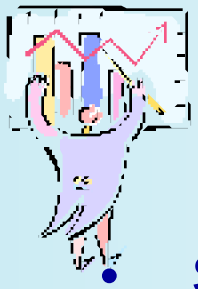
Background

- Tobacco-related cancer includes primary cancers having causal association with current and former tobacco use where 100% of the proportional attributable cancer risk tied with smoking was adapted.

- Excluding tobacco-related cancer, screen-detectable cancer includes primary cancers where shifts in incidence can be attributed, at least in part, to variation in the use of medical technologies for early cancer detection.

Background

- By definition, cancer unrelated to tobacco or screening is a residual category constituting a disease collection where variation in incidence can not easily be attributed to changes in tobacco use or in medical care.
- Compared to all-sites of cancer combined, cancer unrelated to tobacco or screening may be a more specific indicator of general environmental influences on cancer risk.



Specific Aims

- Summarize U.S. cancer incidence for three broad categories that include tobacco-related cancer, screen-detectable cancer, and cancer unrelated to tobacco or screening

- Perform age-period-cohort (APC) analysis by characterizing race- and gender-specific incidence in terms of temporal patterns associated with age, calendar year (period), and year of birth (cohort).

- Distinguish the need for research investigating controllable factors that may account for these patterns

Materials and Methods

- SEER*Stat (Surveillance Epidemiology and End Results (SEER) Program) and SEER*Stat databases were used to obtain race-, sex-, age-, year-, and cancer site-specific cancer incidence counts.
- SEER also provided race-, sex-, age-, year-, and county-specific population estimates
- SEER 9 registries were selected: Five states (Connecticut, Iowa, New Mexico, Utah, and Hawaii), three metropolitan areas (Detroit, San Francisco-Oakland, and Atlanta), and a 13-county Seattle-Puget Sound region.

Materials and Methods

- Tobacco-related cancer: oral cavity & pharynx, esophagus, pancreas, larynx, lung & bronchus, urinary bladder, kidney & renal pelvis
- Screen-detectable cancer: prostate, female breast, cervix, and colon-rectum.
- Both categories excluded lymphoma (ICD-O-3 histology code 9590-9989)
- Third Category: Cancer unrelated to tobacco or screening, (Non-Hodgkin's Lymphoma, NHL)
- Cancer site selections according to cancer primary site used the "SEER Incidence Site Recode ICD-O-3"

Materials and Methods

- Cancer incidence were restricted to blacks and whites between ages 20 and 84 years.
- For every possible combination of 3 cancer categories, sex (men and women), race (black and white), and 5-year age grouping between 20-24 and 80-84 years, we calculated age-specific cancer incidence for each of five 5-year time periods between 1975-1979 and 2000-2004
- National Cancer Institute provides race-, sex-, age-, year-, and cancer site-specific correction factors for adjusting reporting delay.

Jointpoint Regression Analysis

- Fits linear regression of cancer rates by a log scale to describe changes in rates over time
- Start with 0 joinpoint and test whether more joinpoints are statistically significant when added to the model
- Determine the number of significant joinpoints and identify if the rates have changed in a specific time period
- Simpler in describing slope changes

Age-Period-Cohort (APC) Analysis

- $\ln(R_{ijk}) = \alpha + A_i + P_j + C_k + \varepsilon_{ijk}$ ($k = N_{age} - i + j$)
- By Poisson regression, APC models estimated natural log of age-specific cancer incidence as a function of age, time period, and birth cohort
- Parameterized APC model decomposed each effect (birth cohort or time period) in two parts

  -a linear effect due to time (expressed as an ordered integer) and;

  -effects expressed as deviations added to the linear effect
- For each APC model, plotted deviations as a function of the relevant time variable. The deviations sum to zero

- Interpreted increasing deviations to represent a situation where effects from consecutive time interval (birth cohort or time period) acted to increase cancer risk. Decreasing deviations had the opposite interpretation

- Parameterized APC model can uniquely identify the sum of two parameters (D^{drift}) that represents the linear effects due to time period and birth cohort

- Average Annual Percentage Change $=100\ (e^{Ddrift/5}-1)$

  AAPC represent the age-independent relative change in cancer risk associate with a temporal change of 1 year in duration

- 25-year generational risk $(GR_{25})=(e^{Ddrift/5})^{25}$

  Generational risk of cancer rates in one generation versus the previous generation

Results (Tables and Figures)

Figure 1: Age-adjusted (U.S. 2000 standard) tobacco-related cancer incidence (corrected for reporting delay), for 20-84 year-old persons, according to gender and race. Lines show Joinpoint regression fit for white and black men and women.

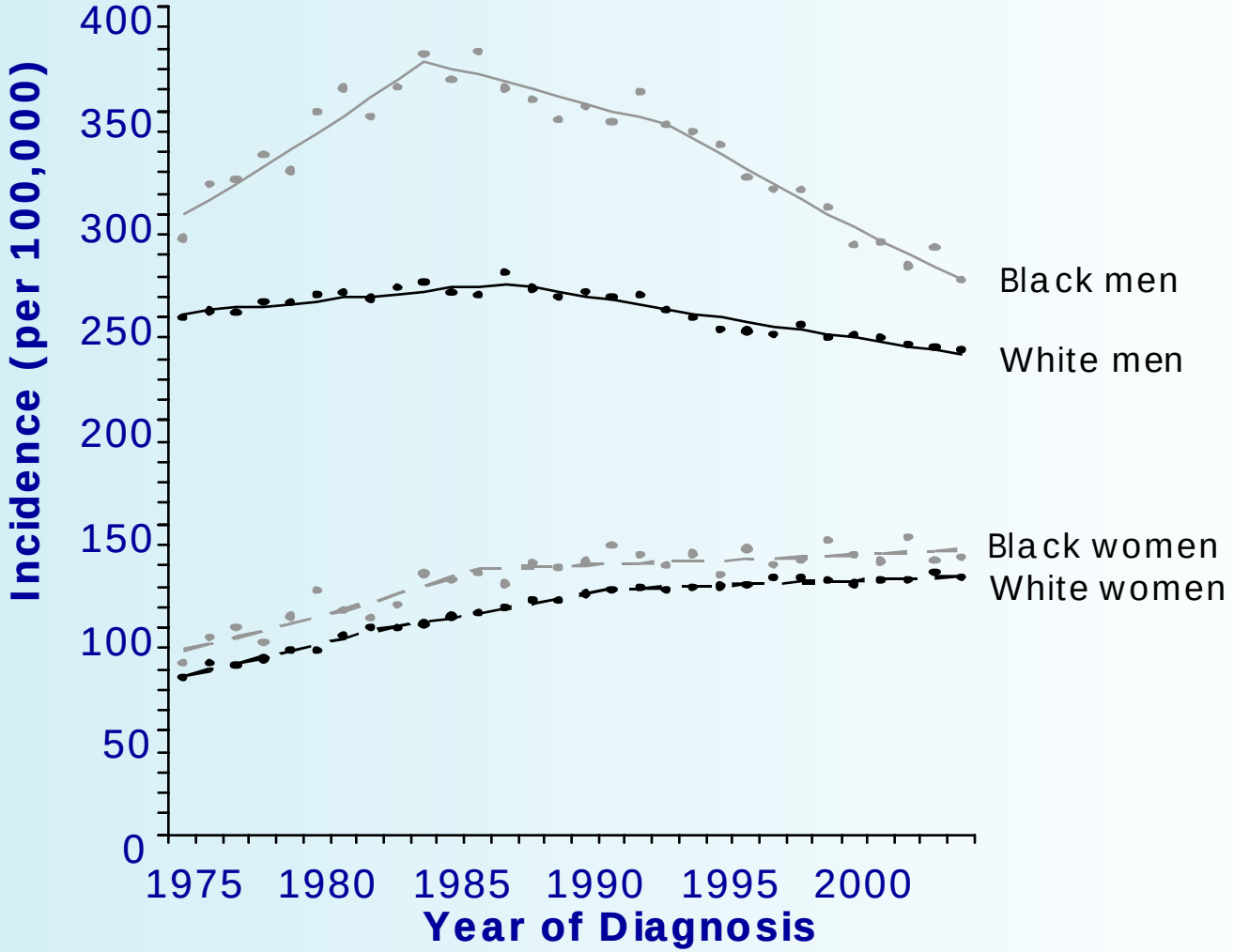


Figure 2: Age-adjusted (U.S. 2000 standard) screen-detectable cancer incidence (corrected for reporting delay), for 20-84 year-old persons, according to gender and race. Lines show Joinpoint regression fit for white and black men and women.

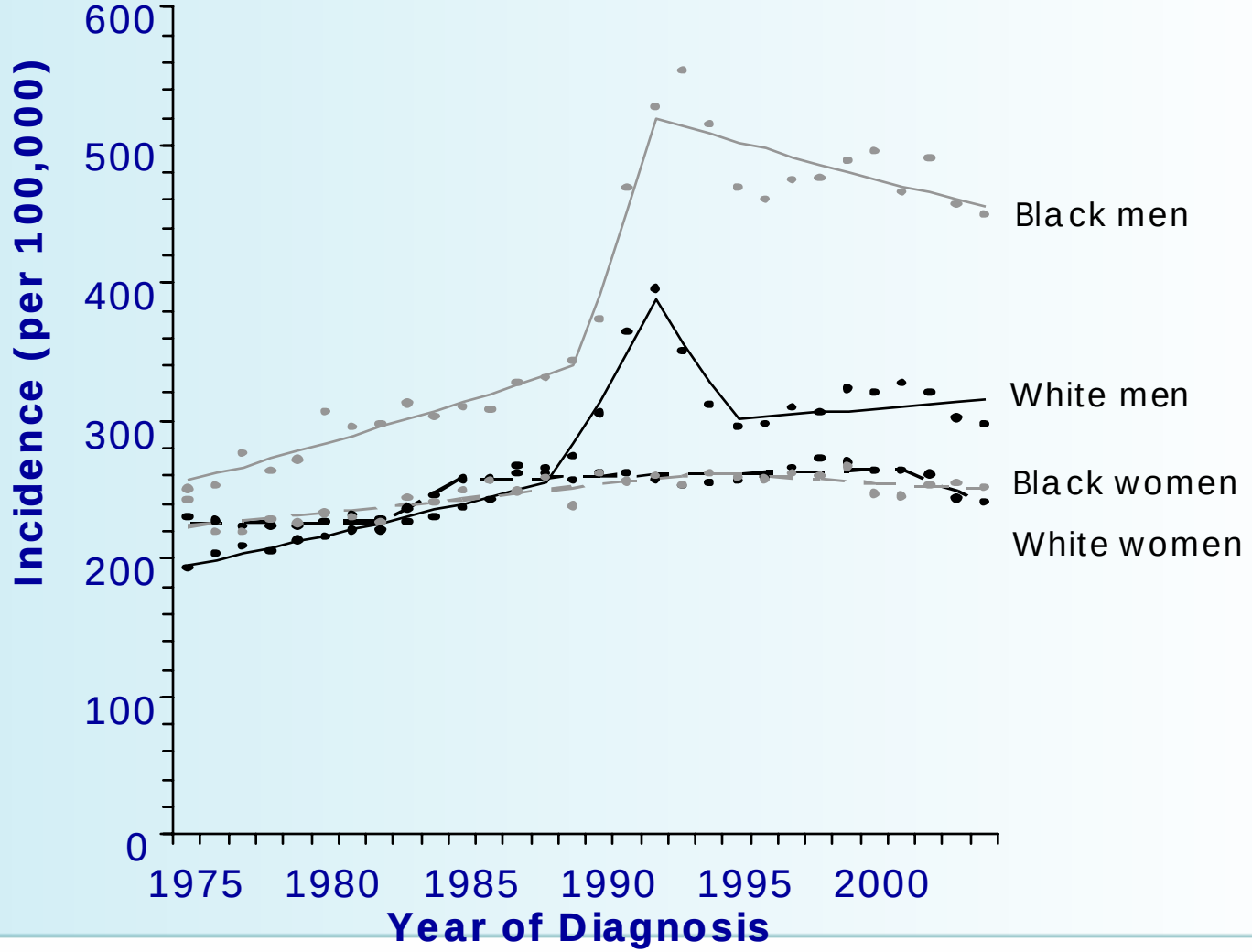


Figure 3: Age-adjusted (U.S. 2000 standard) other cancer incidence (corrected for reporting delay), for 20-84 year-old persons, according to gender and race. Lines show Joinpoint regression fit for white and black men and women.

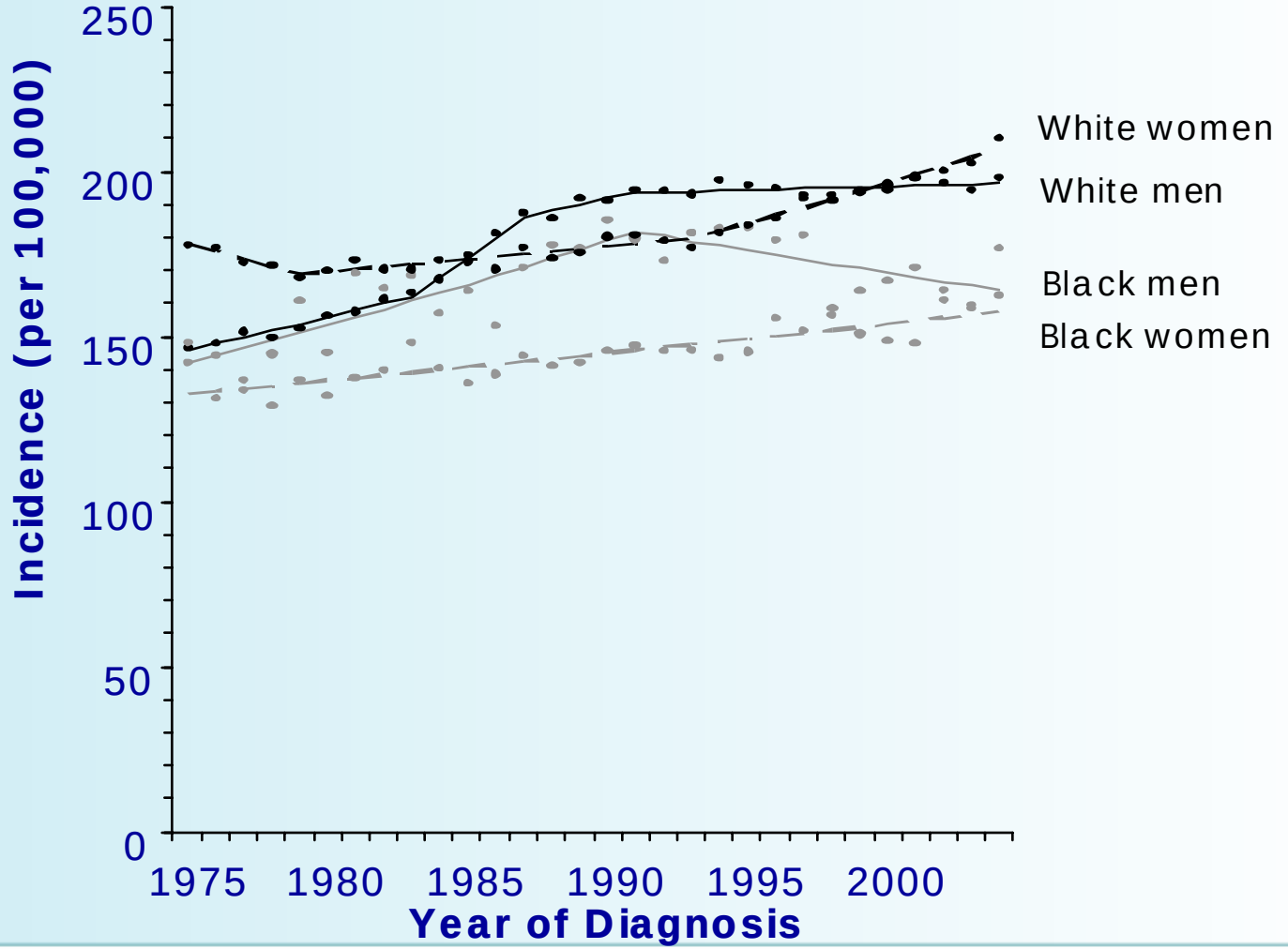


Figure 4: Age-adjusted (U.S. 2000 standard) NHL incidence (corrected for reporting delay), for 20-84 year-old persons, according to gender and race. Lines show Joinpoint regression fit for white and black men and women.

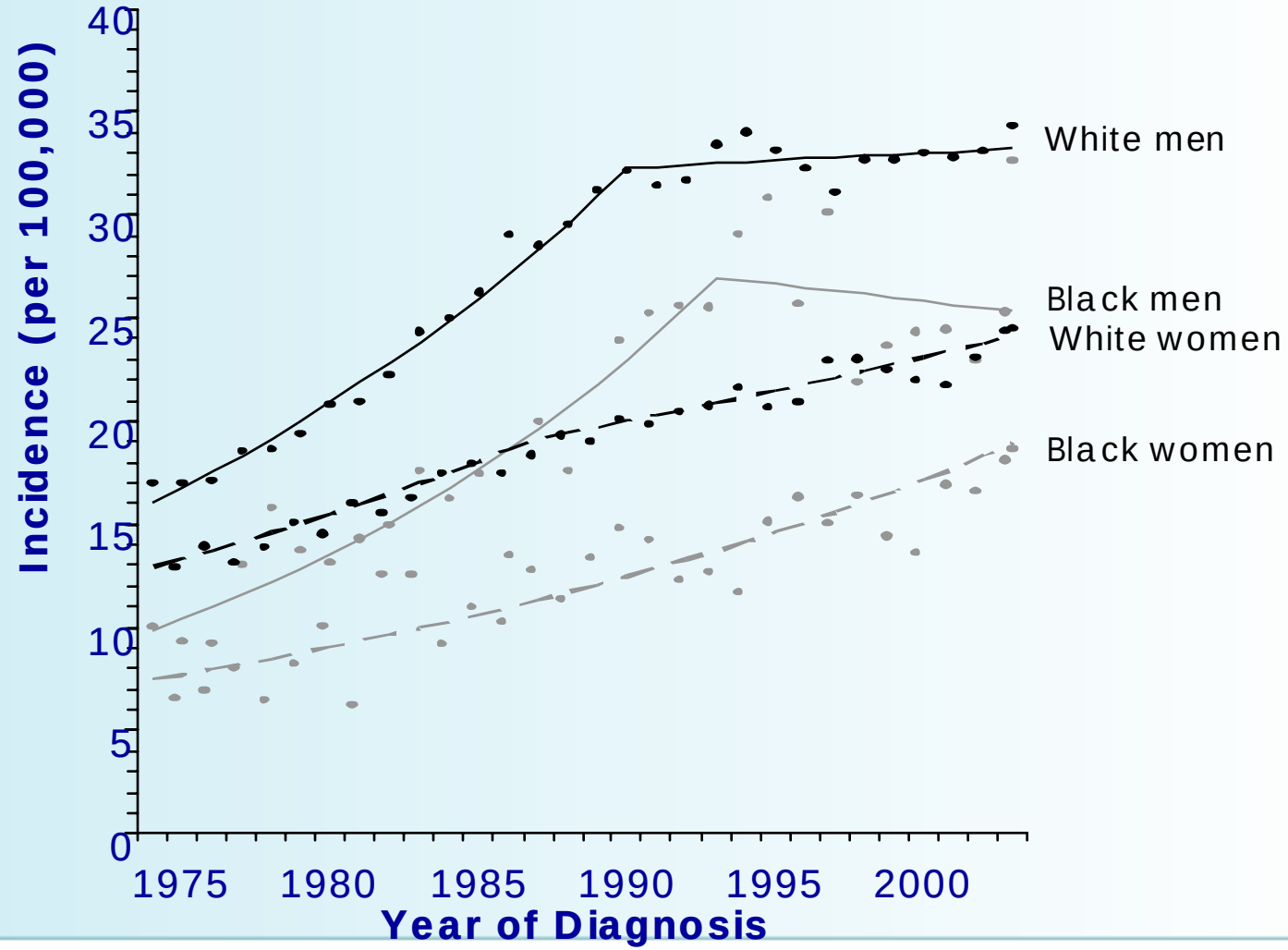


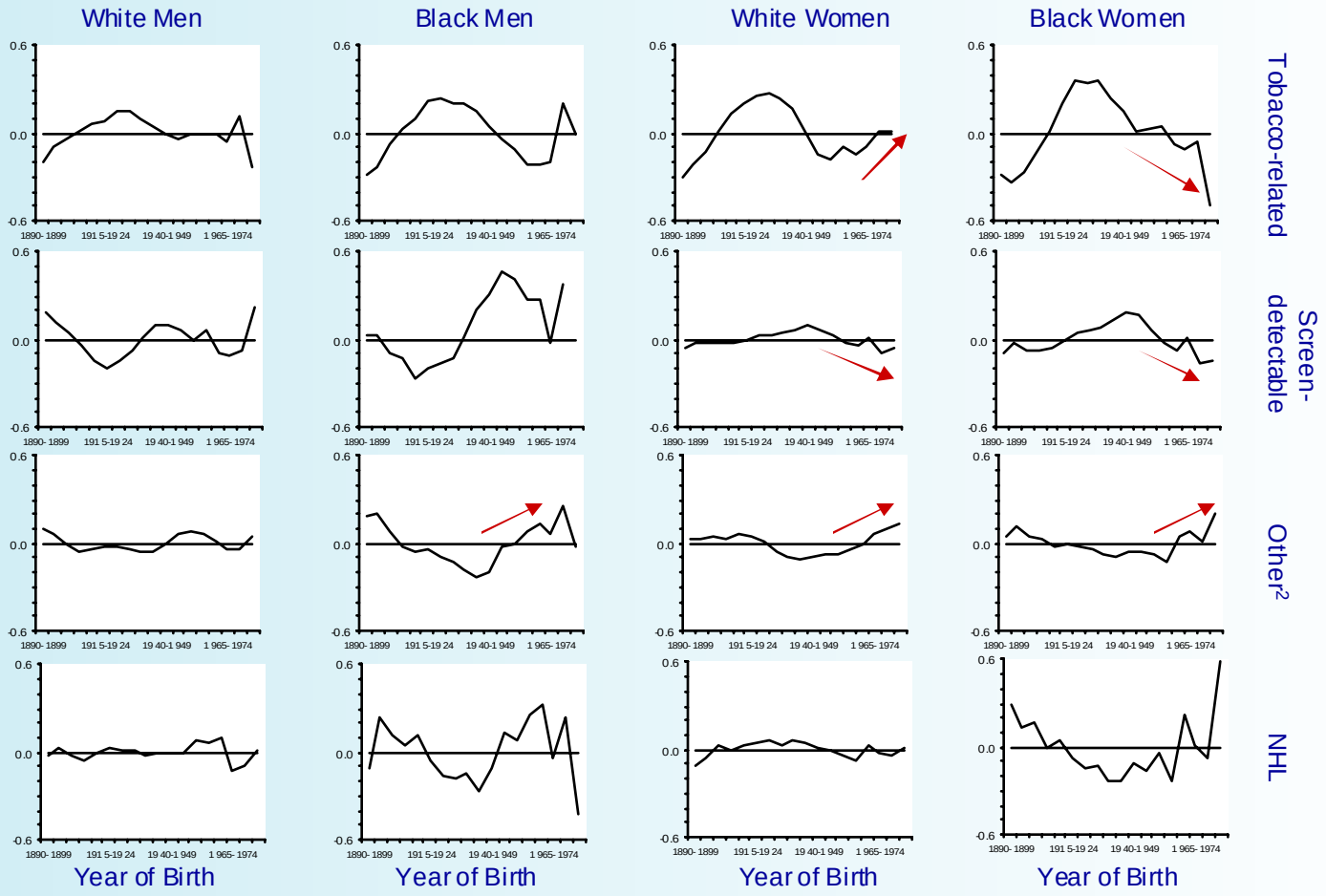
Table 1: Results from cancer category-, gender-, and race-specific APC models of SEER 1975-2004 age-specific incidence (fourteen 5-year age groups, 20-24 to 80-84), corrected for reporting delay.

							Statistical significance[1]	
Cancer category	Gender	Race	Poisson model[2]	AAPC	95% C.I.	GR_{25}	Cohort parameters	period parameters
Tobacco-related	Men	White	Extra	**-0.72**	-0.72, -0.71	0.84	****	***
		Black	Simple	**-0.98**	-1.33, -0.63	0.78	****	****
	Women	White	Extra	**0.99**	0.98, 0.99	1.28	****	**
		Black	Extra	**0.31**	-0.10, 0.73	1.08	****	***
Screen-detectable	Men	White	Extra	**2.24**	2.15, 2.33	1.74		
		Black[3]	Extra	**2.27**	2.09, 2.46	1.75	*	
	Women	White	Extra	**0.38**	0.37, 0.38	1.10	**	****
		Black	Simple	**0.12**	0.11, 0.13	1.03	****	
Unrelated to tobacco or screening	Men	White	Extra	**1.17**	1.16, 1.19	1.34		****
		Black	Extra	**0.94**	0.91, 0.98	1.26	**	****
	Women	White	Extra	**0.82**	0.82, 0.82	1.23	****	**
		Black	Simple	**0.83**	0.63, 1.02	1.23	*	
NHL	Men	White	Extra	**2.56**	2.50, 2.62	1.88		****
		Black	Extra	**3.78**	3.63, 3.92	2.53		***
	Women	White	Simple	**2.01**	1.85, 2.17	1.64		****
		Black	Simple	**3.71**	3.06, 4.73	2.49		

AAPC - Average annual percentage change, C.I. - confidence interval, GR_{25} - 25 year generational risk

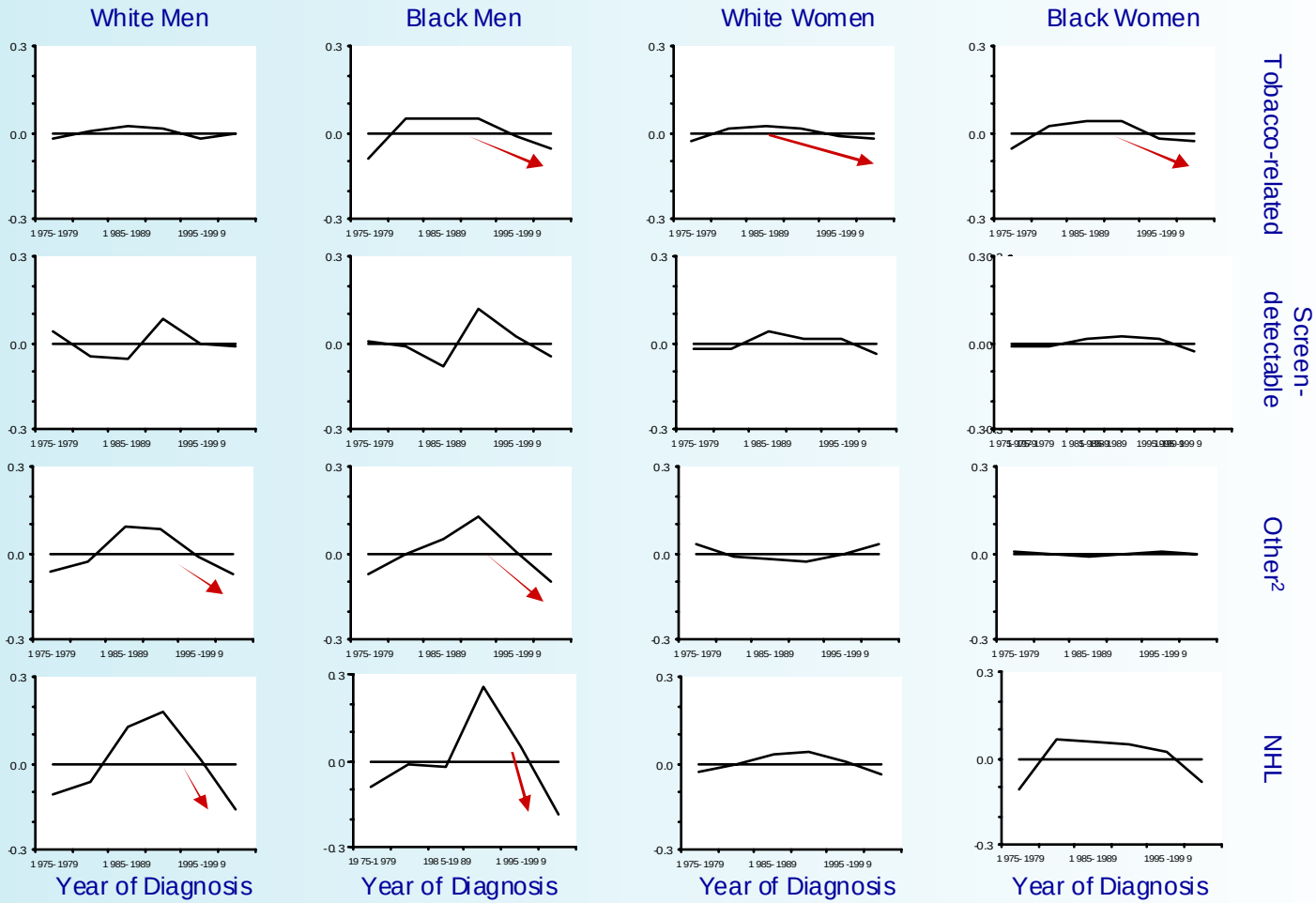
1. p-value: <0.0001****, <0.001***, <0.01**, <0.05*
2. Poisson model fitted: simple Poisson model or extra-Poisson model
3. Analysis restricted to twelve 5-year age groups between 25-29 and 80-84 years

Figure 5: Results from cancer category-, gender-, and race-specific APC models of SEER 1975-2004 age-specific incidence, corrected for reporting delay; birth cohort-specific effect added to the linear effect due to birth cohort.



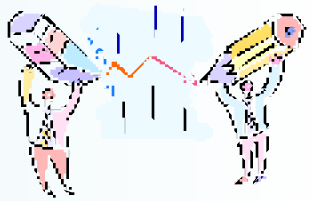
[1] The APC analysis of screen-detectable cancer incidence in black men was restricted between 25-29 and 80-84 years.
[2] Cancer unrelated to tobacco or screening.

Figure 6: Results from cancer category-, gender-, and race-specific APC models of SEER 1975-2004 age-specific incidence corrected for reporting delay; time period-specific effect added to the linear effect due to time period.



[1] The APC analysis of screen-detectable cancer incidence in black men was restricted between 25-29 and 80-84 years.
[2] Cancer unrelated to tobacco or screening.

Discussion and Conclusion



- Tobacco-related cancer incidence was decreasing in men and was increasing in women

  - Cohorts of white women born after 1950-1959 experiencing increasing pressure on incidence

  - Women in recent birth cohort adopting smoking

- Screen-detectable cancer incidence was increasing

  - Increasing incidence possibly related to widespread mammography and prostate-specific antigen testing

- Relative to the earlier birth cohorts of their parents, white women and men in recent birth cohorts may be facing more than a twofold increased risk of incidence of cancer unrelated tobacco or screening.

- NHL risk was increasing, with recent time period exerting decreasing pressure on incidence

- These trends indicate that demand for chemotherapy and related services, which are already limited by personnel and resources, will continue to increase.

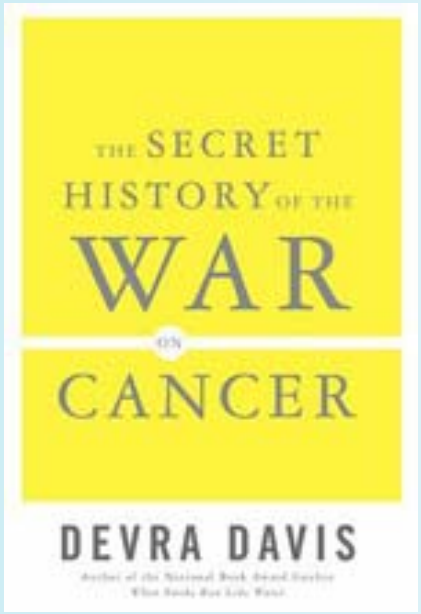
- The analysis is unable to determine the underlying reasons for the trends we have found.
- Changes in cancer not known to be tied with smoking or screening that have occurred over the past four decades are rapid and puzzling.
- Determining whether social or environmental conditions may account for these trends should lay the groundwork for preventive public health policies aimed at reducing or controlling these conditions.

- Significance of this study

  - increase awareness of available data
    (Suggestion: collect occupational information in cancer registry)
  - provide examples of modeling cancer data
  - highlight the importance of environmental cancer risk

- Contribution of this study

  - provide overview of cancer patterns in the U.S.
  - help to generate hypothesis on cancer etiologic study
  - assist public health official to plan services, and to develop and evaluate prevention program



Dr. Devra Davis, September 2007

The best wars finish fast. Nearly forty years and more than forty billion dollars since the official launch of the "War on Cancer" in 1971, that effort shows no signs of ending….. Despite spectacular progress on several fronts, many forms of the disease remain devastating…..

In recent years cancer deaths have dropped in many industrial nations chiefly because fewer are smoking, and more are getting screened and treated for survivable cancers, like those of the colon, cervix and breast. But lately, cancer is showing up in neighborhoods and at ages where it used to be quite rare……

Thank You