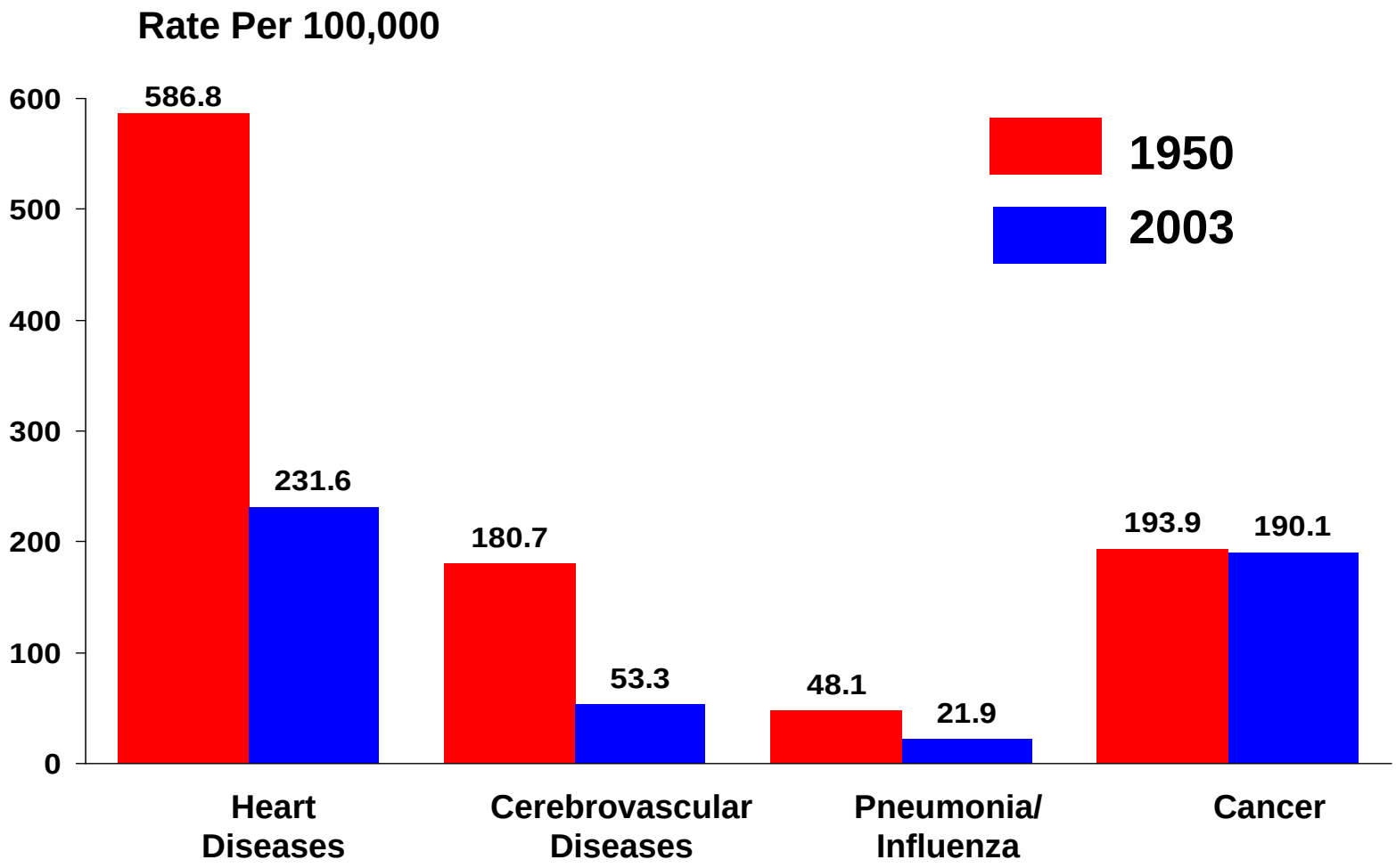
What is the current evidence for progress against cancer?

Bruce Trock, PhD

"As far as the laws of mathematics refer to reality, they are not certain; as far as they are certain, they do not refer to reality."

--Albert Einstein

Change in the US Death Rates* by Cause, 1950 & 2003



* Age-adjusted to 2000 US standard population.
Sources: 1950 Mortality Data - CDC/NCHS, NVSS, Mortality Revised.
2003 Mortality Data: US Mortality Public Use Data Tape, 2003, NCHS, Centers for Disease Control and Prevention, 2006

Lifetime Probability of Developing Cancer, by Site, 1998-2000

Site	Male Risk	Female Risk
All sites	1 in 2	1 in 3
Prostate	1 in 6	n.a.
Breast	1 in 833	1 in 7
Lung & bronchus	1 in 13	1 in 17
Colon & rectum	1 in 17	1 in 18

565,000 deaths from cancer annually

Source: DevCan: Probability of Developing or Dying of Cancer Software, Version 5.1 Statistical Research and Applications Branch, NCI, 2003. http://srab.cancer.gov/devcan

Progress Against Cancer

- NCI Goal in 1985: 50% decrease in cancer mortality by year 2000*:
  - 1985: 171 per 100,000
  - 2000: 158 per 100,000 (7.6% decrease)
  - 2004: 147 per 100,000 (14.0% decrease)
- How do you define progress against cancer?
- What has influenced progress?
- What will influence future progress?

*** age-adjusted to 1970 population**

Is overall mortality the best way to define progress?

- Advantage:
  - clinically most relevant; indicates biologic behavior
  - less subject to artifact

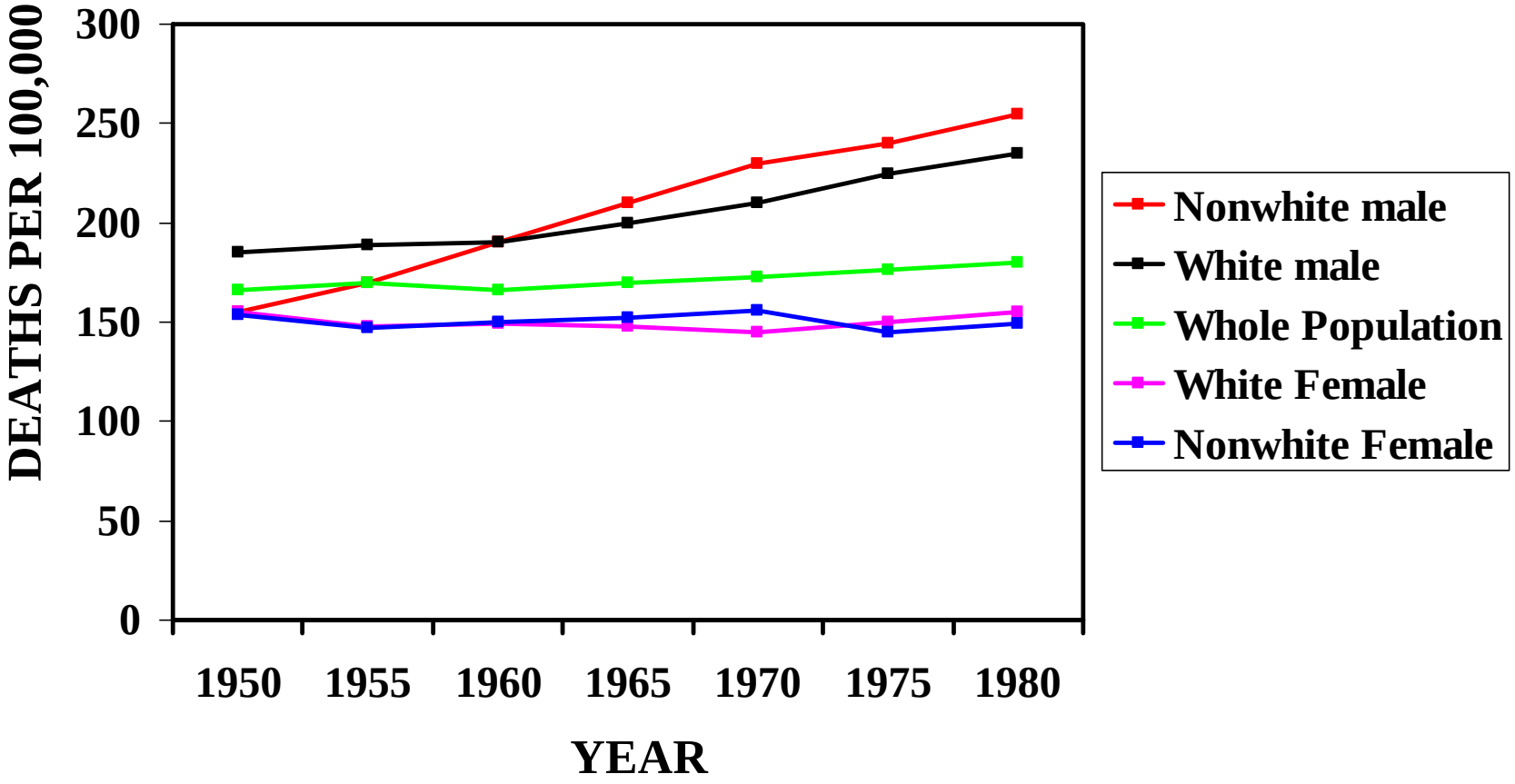
- Disadvantage:
  - obscures effects by age or tumor type
  - have to balance against true increases in incidence

- Is the most important issue whether decreases in mortality are due to improved treatment? Should the measure of progress reflect government spending?

Measures of Progress

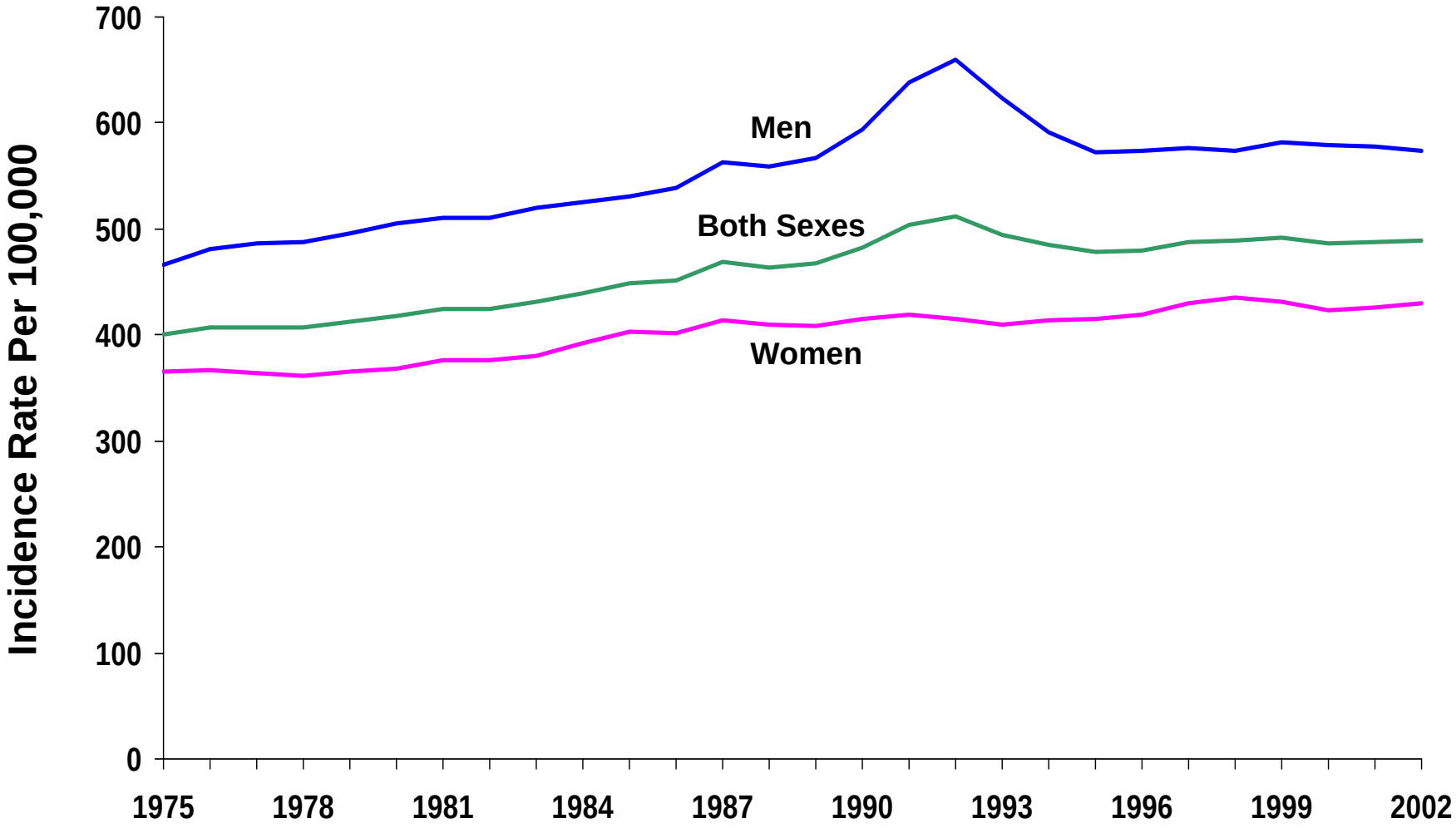
- **Incidence – affected by:**
  - changes in risk factors
  - increase in detection, treatment of premalignant lesions
  - changes in definition of cancer
- **Survival – affected by:**
  - changes in early detection
  - changes in treatment
- **Mortality – affected by:**
  - changes in incidence
  - changes in survival

Mortality from All Malignant Neoplasms 1950 - 1982, by Race and Sex*



* Bailar, NEJM 1986; 314:1226

Cancer Incidence Rates*, All Sites, All Races, 1975-2002



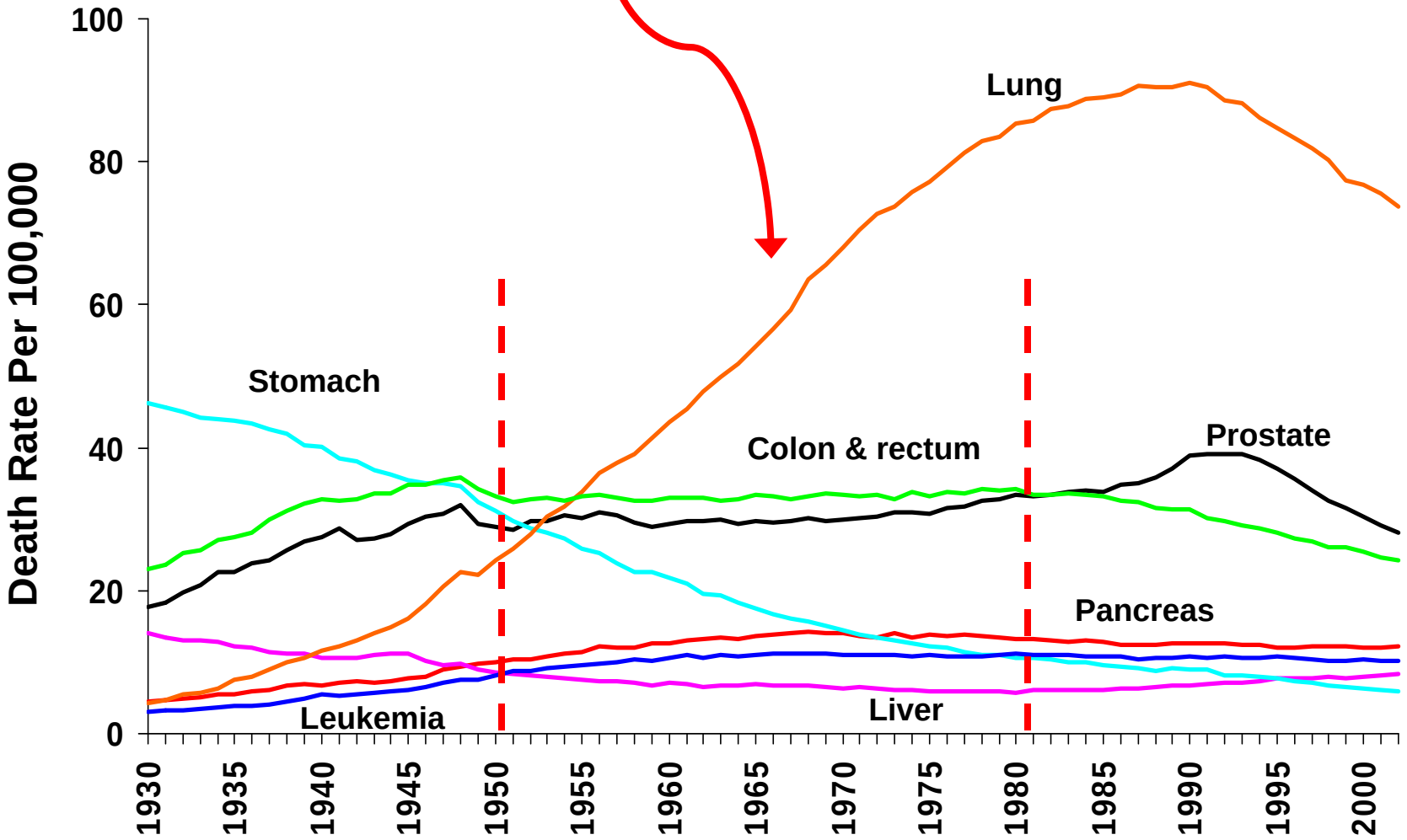
*Age-adjusted to the 2000 US standard population and adjusted for delay in reporting.
Data from American Cancer Society website, www.cancer.org: Cancer_Statistics_2006_Presentation.ppt

Bailar's Arguments (1950-1982)

Failures:

- increase in overall mortality, and in most race-sex groups.
- no decrease in breast, prostate or lung cancer mortality
- some decreases not due to treatment or to programmatic efforts at prevention (stomach, colorectum, cervix)
- should some cancers be excluded from the evaluation? Even excluding lung, stomach, cervix, < 1% decrease in overall cancer mortality (in 1986), i.e. not "progress"

Cancer Death Rates* in US Men 1930-2002
(1950-1982 period covered by Bailar)



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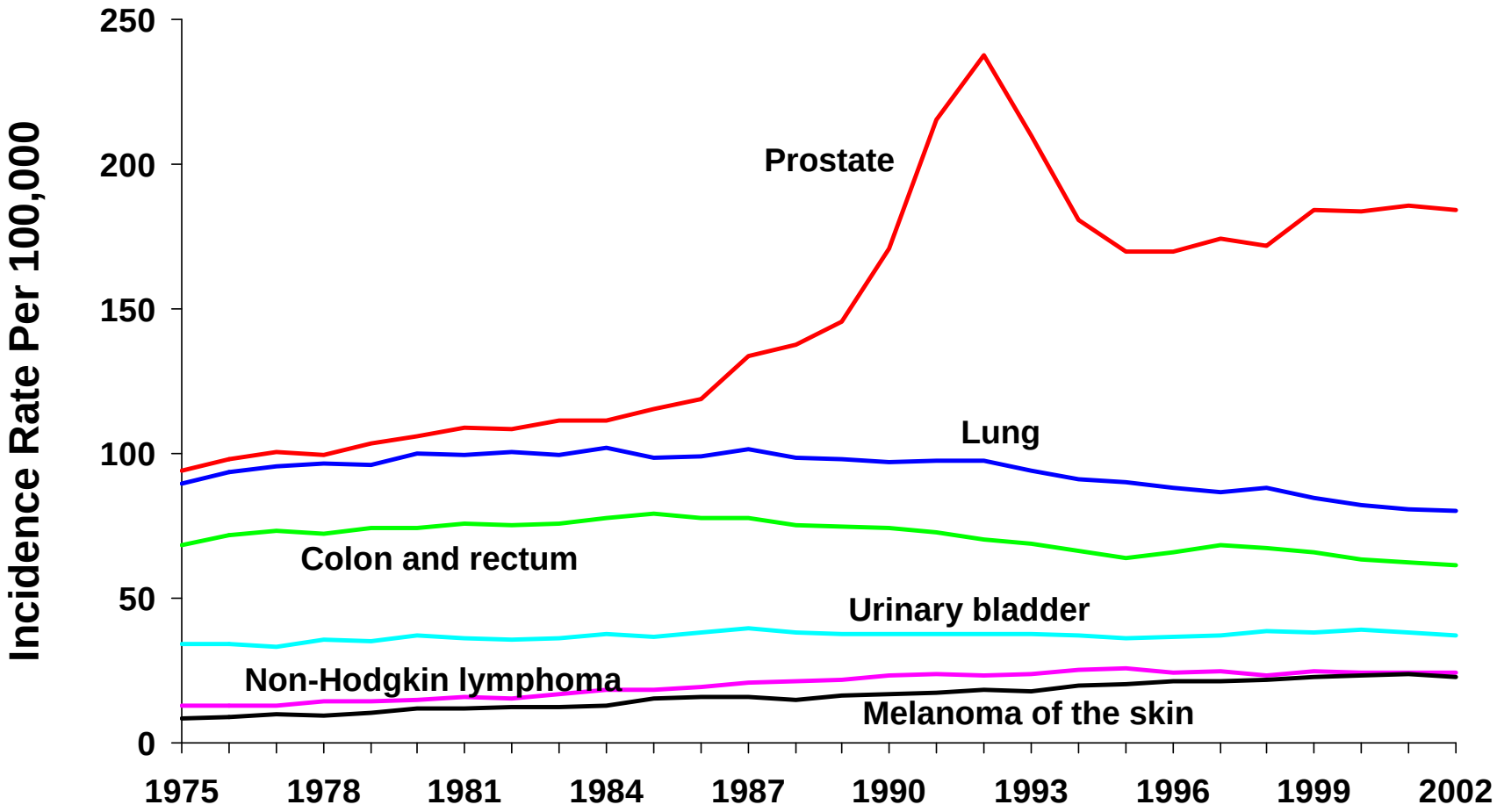
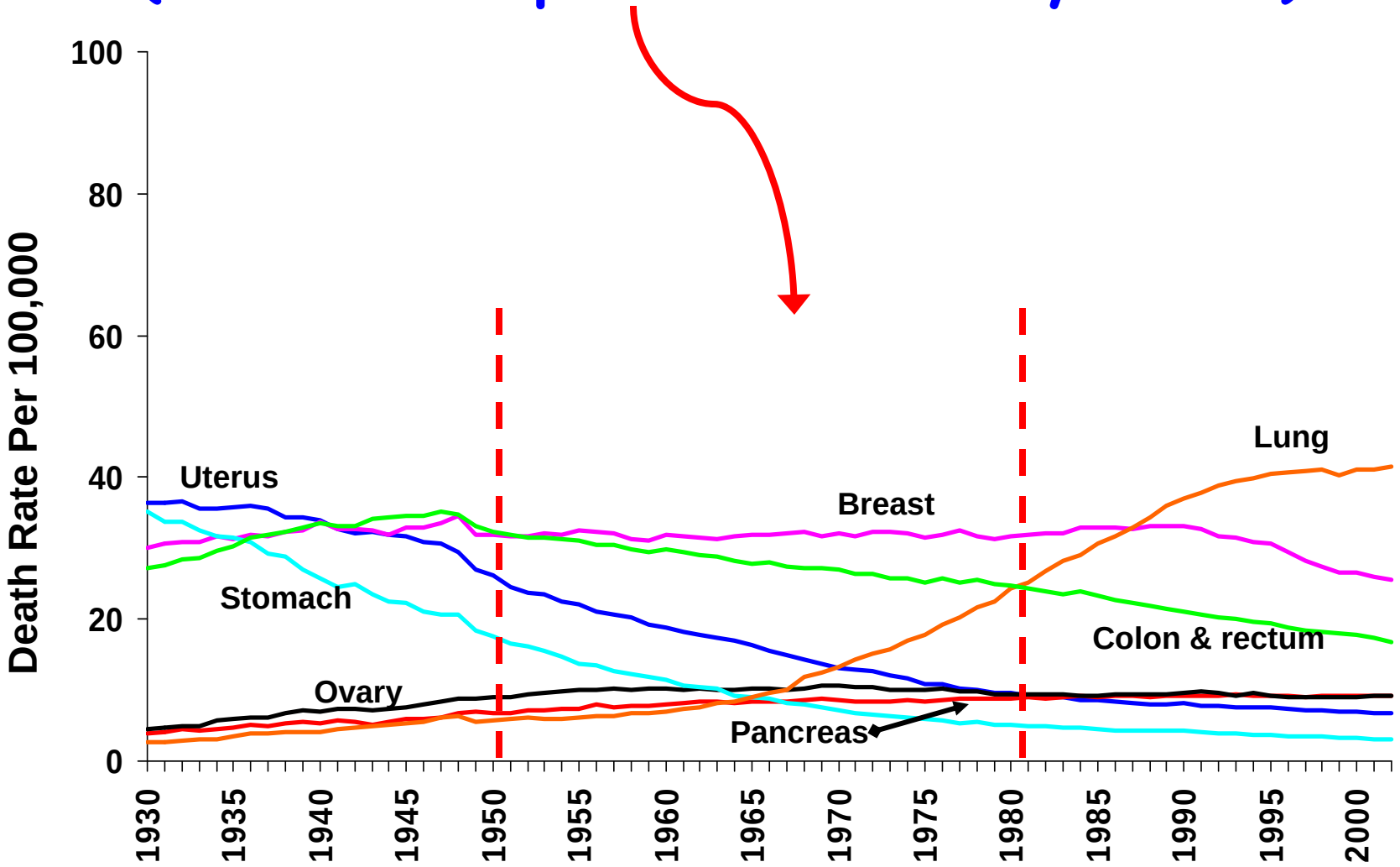
Cancer Incidence Rates* US Men, 1975-2002



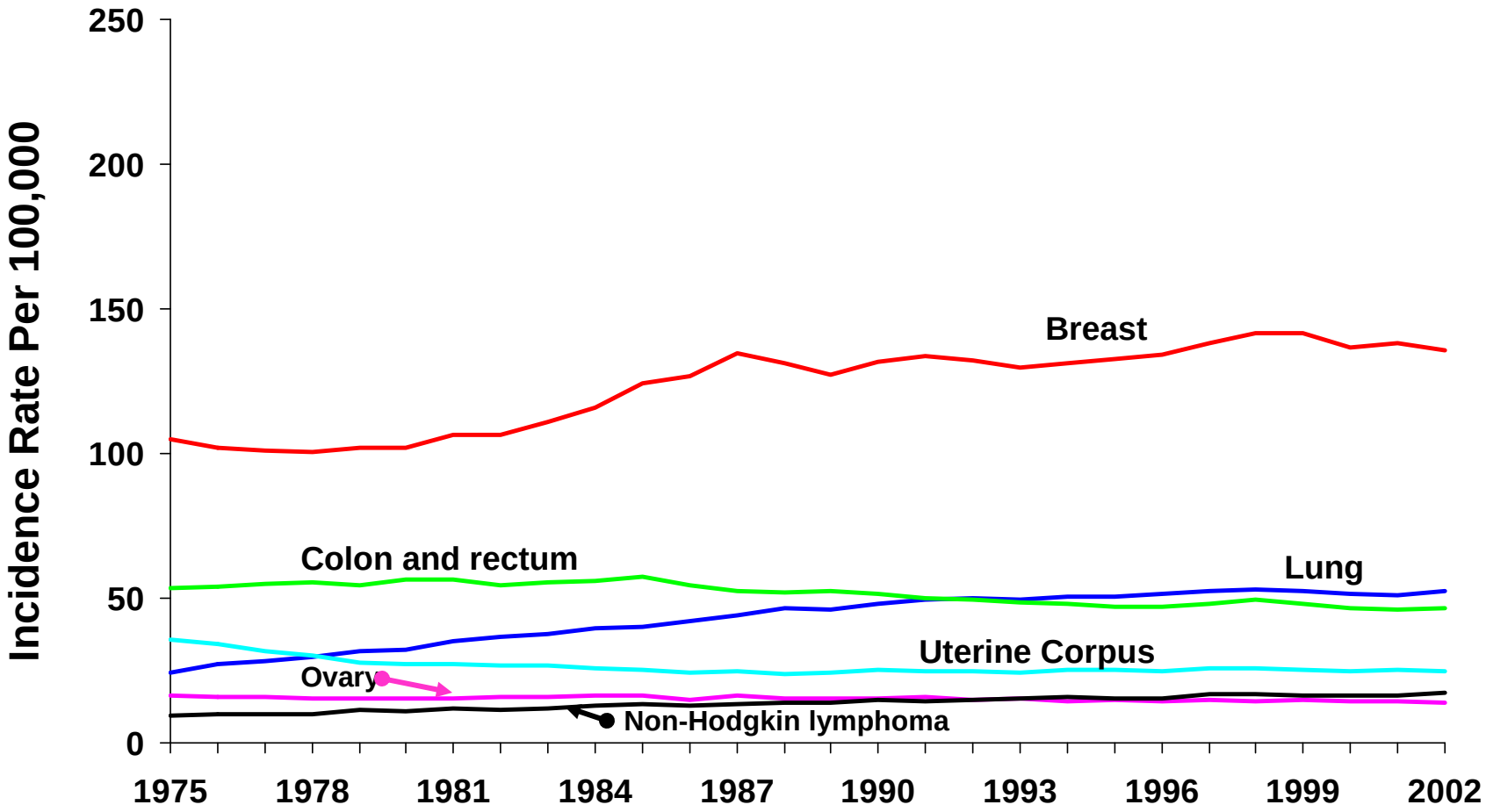
*Age-adjusted to the 2000 US standard population and adjusted for delay in reporting.
Data from American Cancer Society website, www.cancer.org: Cancer_Statistics_2006_Presentation.ppt

Cancer Death Rates* in US Women 1930-2002 (1950-1982 period covered by Bailar)



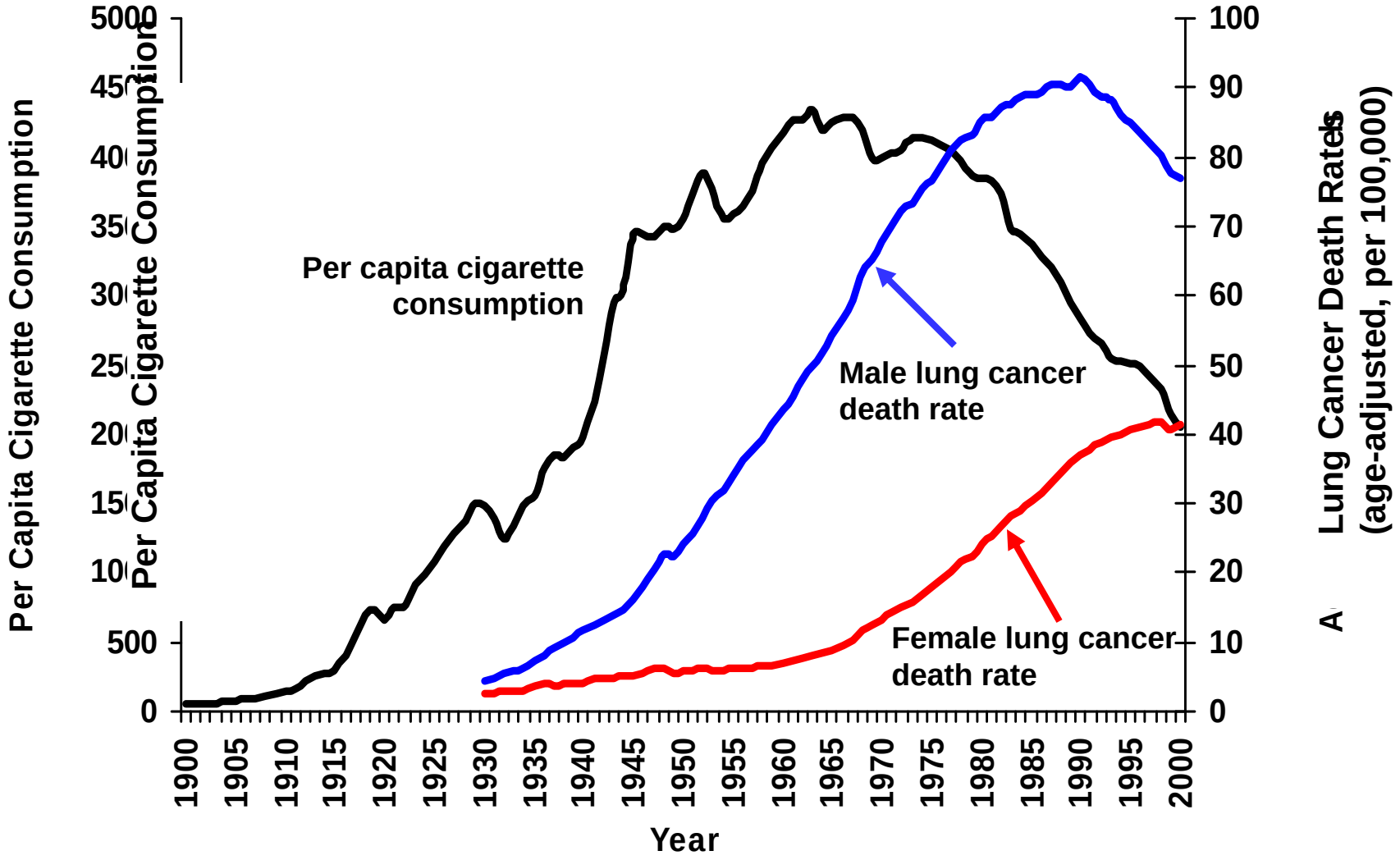
*Age-adjusted to the 2000 US standard population and adjusted for delay in reporting.
Data from American Cancer Society website, www.cancer.org: Cancer_Statistics_2006_Presentation.ppt

Cancer Incidence Rates* US Women, 1975-2002



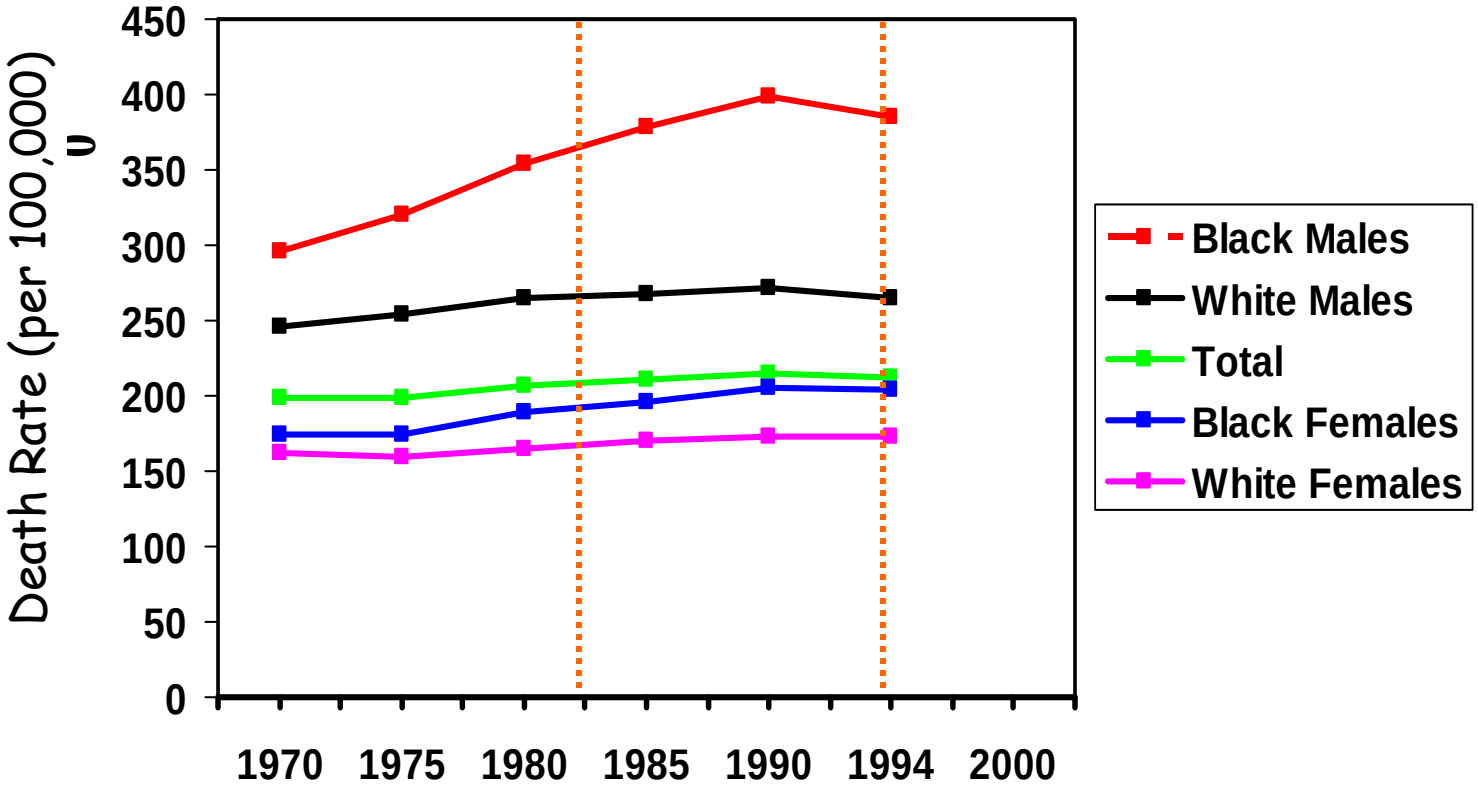
*Age-adjusted to the 2000 US standard population and adjusted for delay in reporting.
Data from American Cancer Society website, www.cancer.org: Cancer_Statistics_2006_Presentation.ppt

US Tobacco Use vs. Lung Cancer Deaths, 1900-2000



*Age-adjusted to 2000 US standard population. Source: Death rates: US Mortality Public Use Tapes, 1960-2000, US Mortality Volumes, 1930-1959, National Center for Health Statistics, Centers for Disease Control and Prevention, 2002. Cigarette consumption: US Department of Agriculture, 1900-2000.

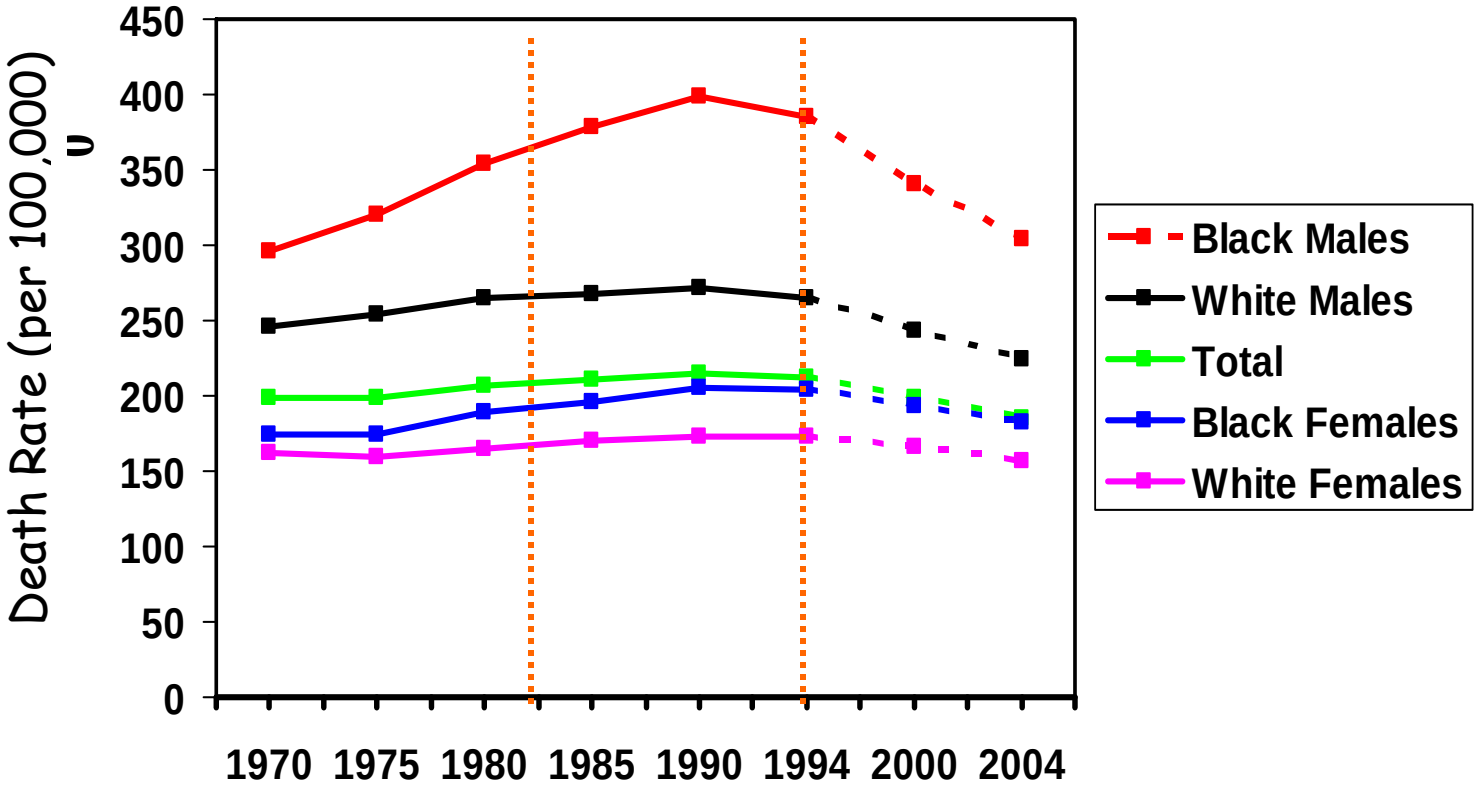
Mortality from All Malignant Neoplasms 1970 - 1994, by Race and Sex*



* vertical lines: last years of data in 1986 and 1997 Bailar papers

SEER*Stat Database: Mortality - Public-Use, Total U.S. (1969-2001)
NCI, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2004

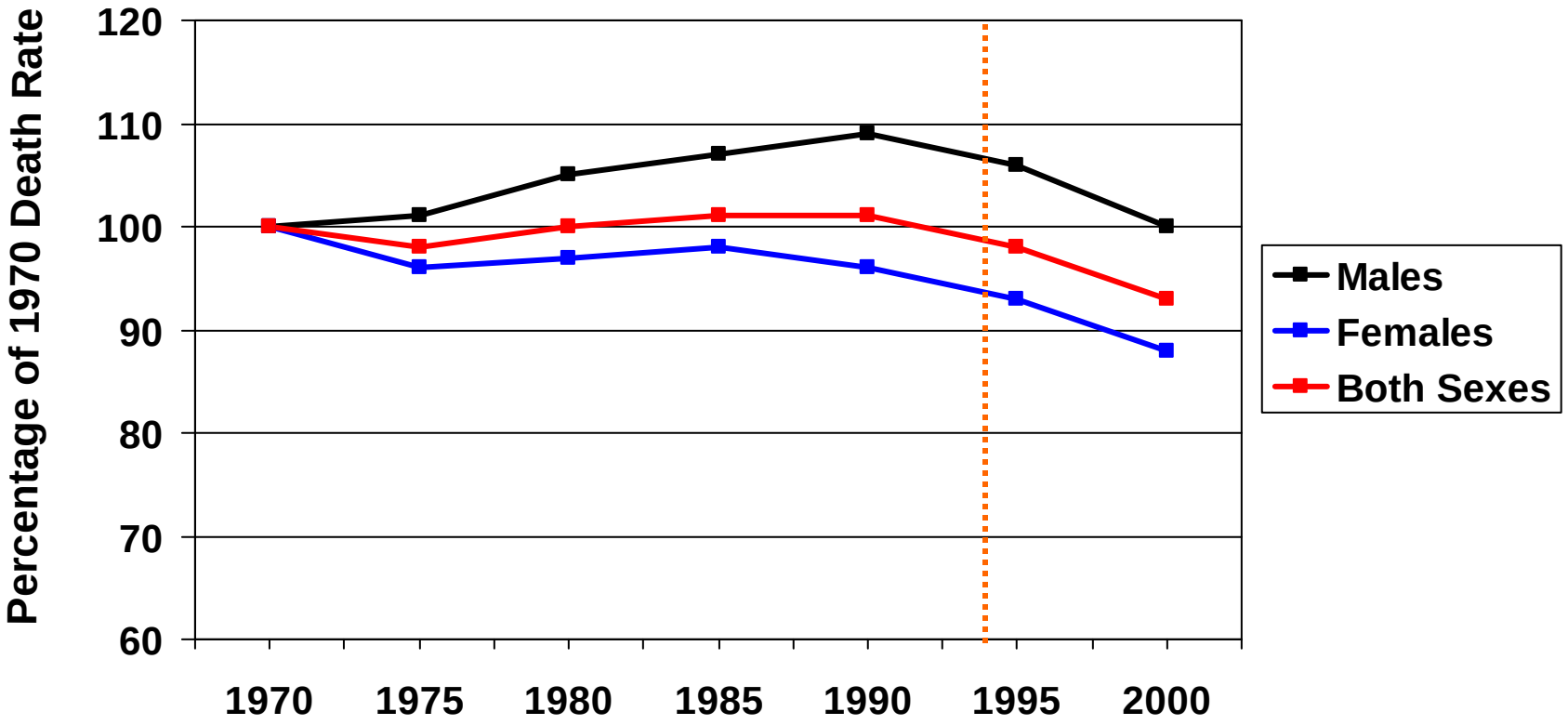
Mortality from All Malignant Neoplasms 1970 - 2004, by Race and Sex*



* dotted lines: last years of data in 1986 and 1997 Bailar papers

SEER*Stat Database: Mortality - Public-Use, Total U.S. (1969-2001)
NCI, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2004

Mortality from All Cancers except Lung, Oral/Larynx, Stomach, Cervix,1970-2000*



* SEER*Stat Database: Mortality - Public-Use, Total U.S. (1969-2001)
NCI, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2004

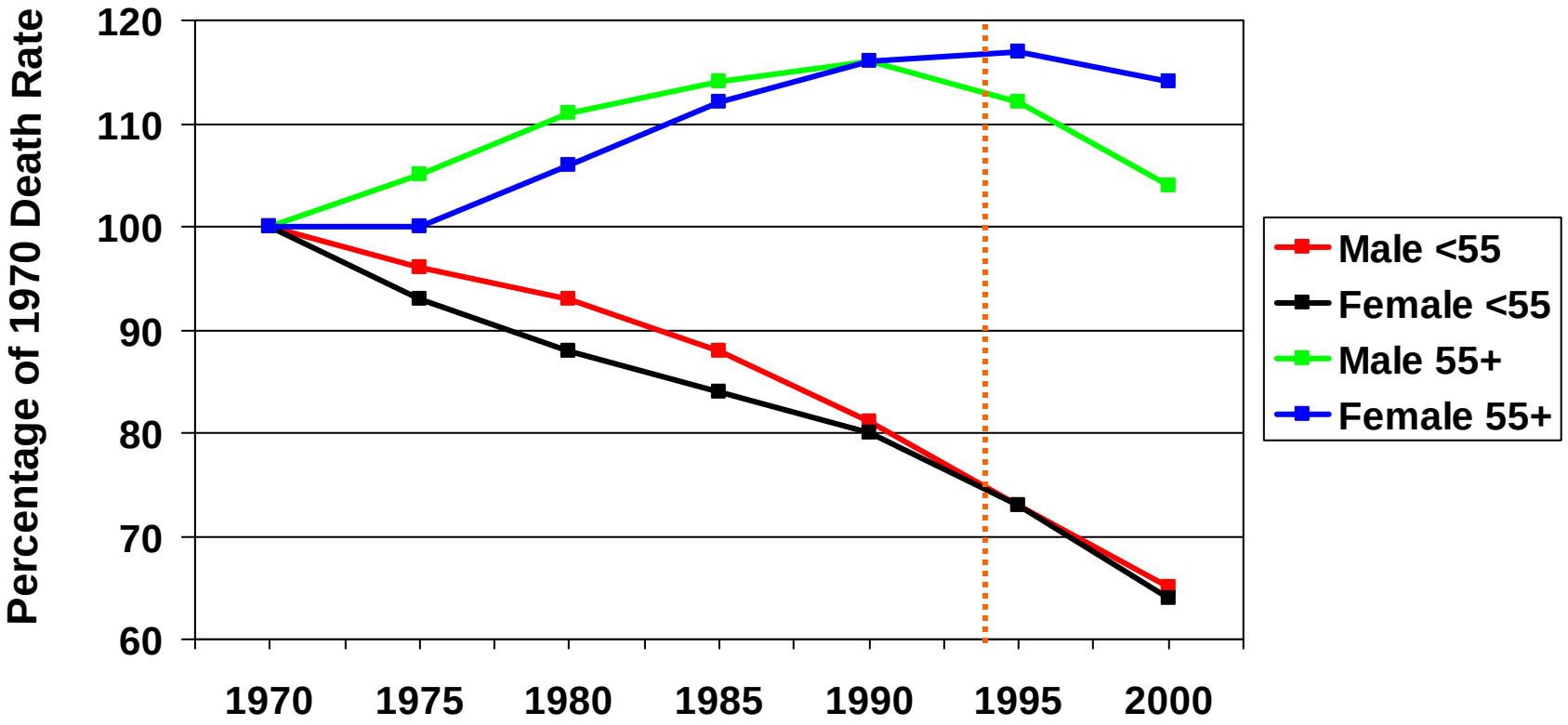
Annual percentage change in overall cancer mortality rates (1975-2004) *

	1975-1990	1990-1993	1993-2002	2002-2004
Both Sexes	0.5 %	- 0.3% **	- 1.1%	- 2.1%
Males	0.9 %	0.3%	- 1.5%	- 2.6%
Females	0.6 %	- 0.2%	- 0.8%	- 1.8%

* Espey DK, et al. Cancer 2007.

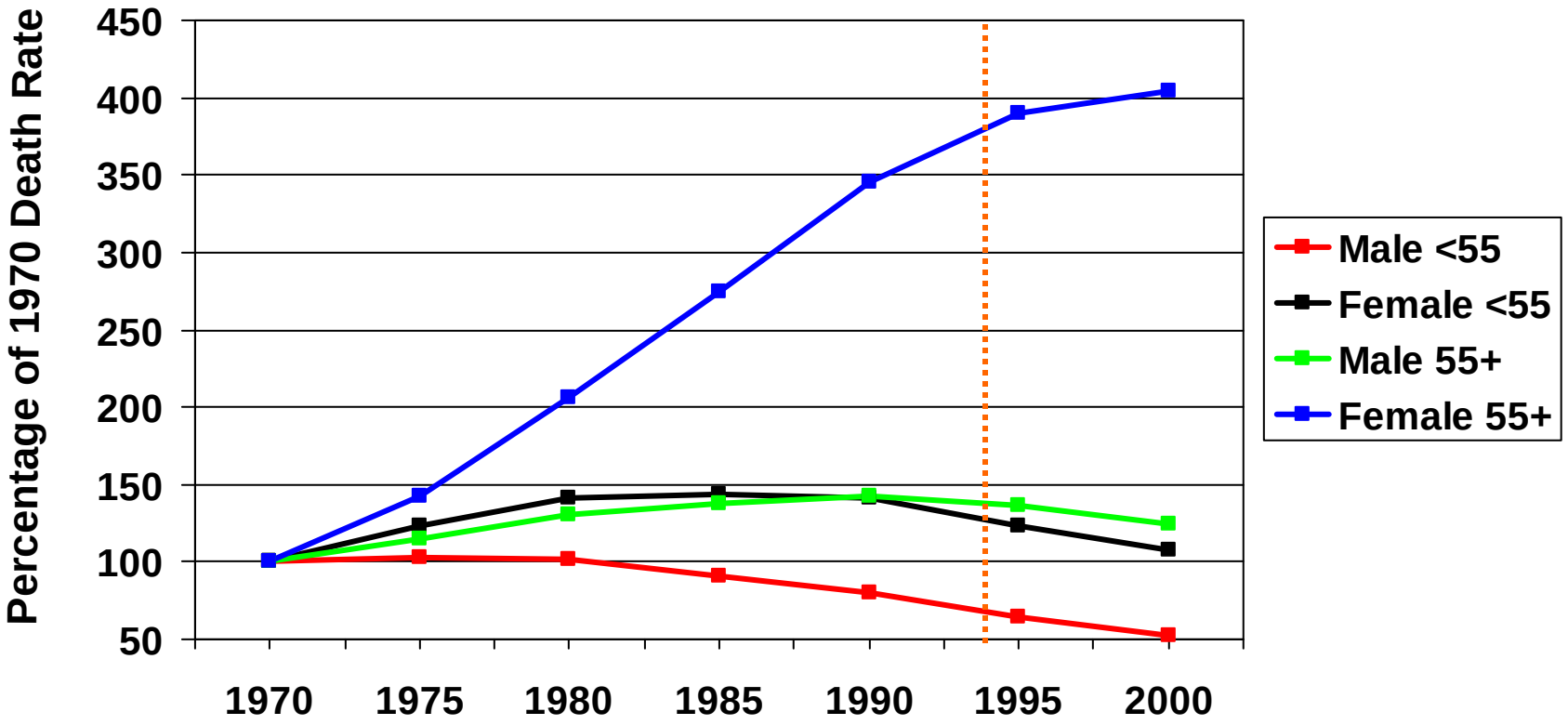
** Red font indicates change is not statistically significant

Mortality from All Cancers 1970-2000, by Age & Sex*
(extends Figure 2 from Bailar, NEJM 1997)



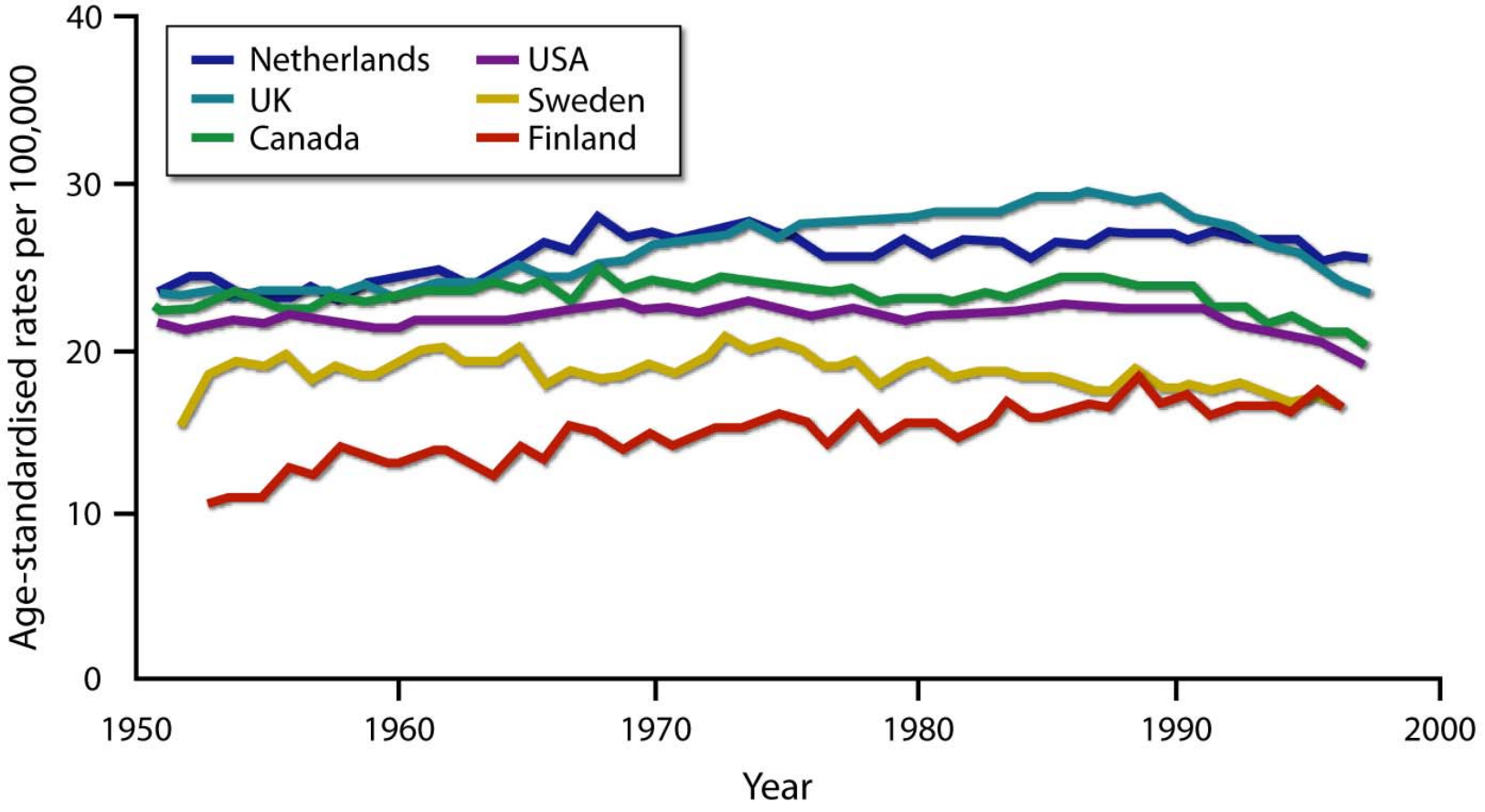
* SEER*Stat Database: Mortality - Public-Use, Total U.S. (1969-2001)
NCI, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2004

Mortality from Lung Cancer 1970-2000, by Age & Sex*
(extends Figure 4 from Bailar, NEJM 1997)



* SEER*Stat Database: Mortality - Public-Use, Total U.S. (1969-2001)
NCI, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2004

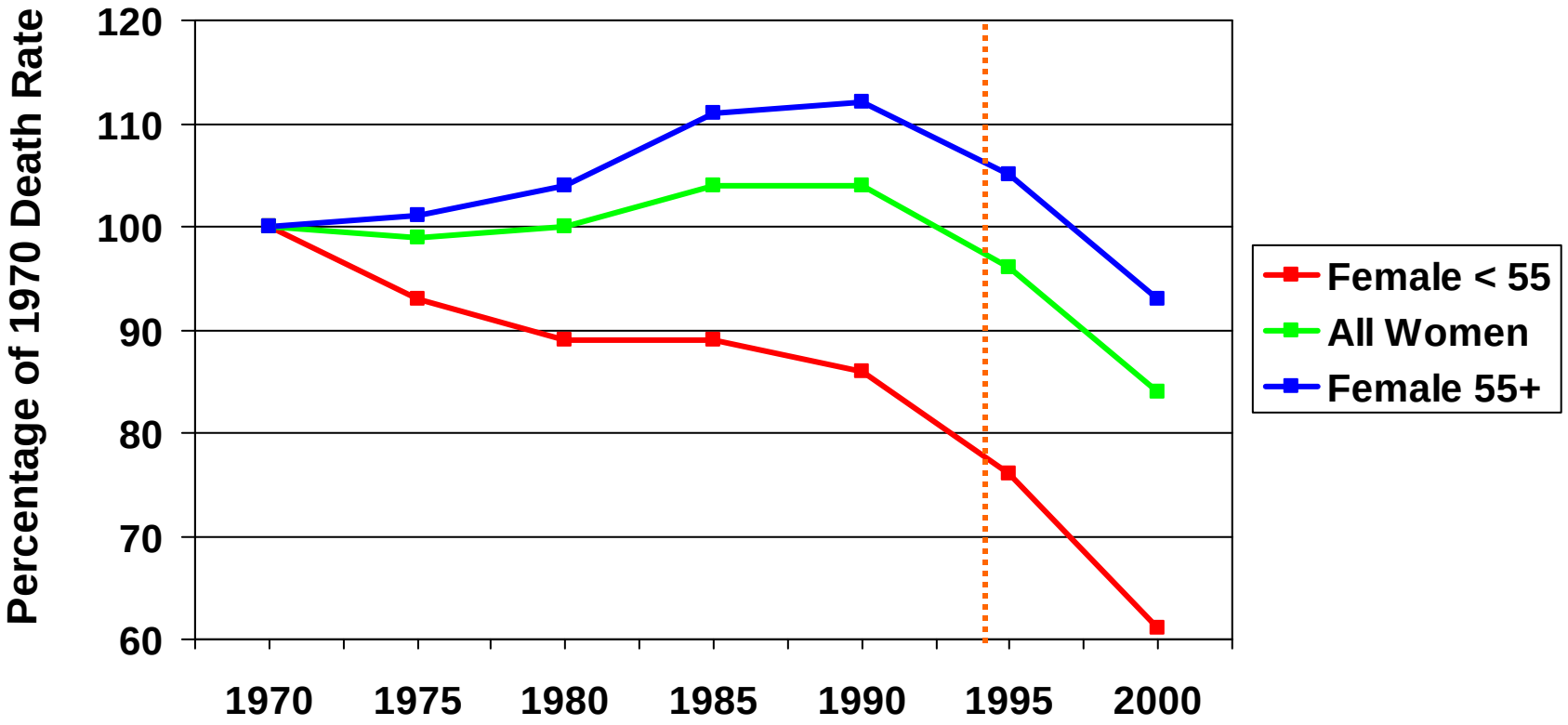
Breast cancer mortality trends in countries that have introduced screening*



Adapted by CTLT from Jatoi I, Miller AB. Lancet Oncology 2003;4:251-4.

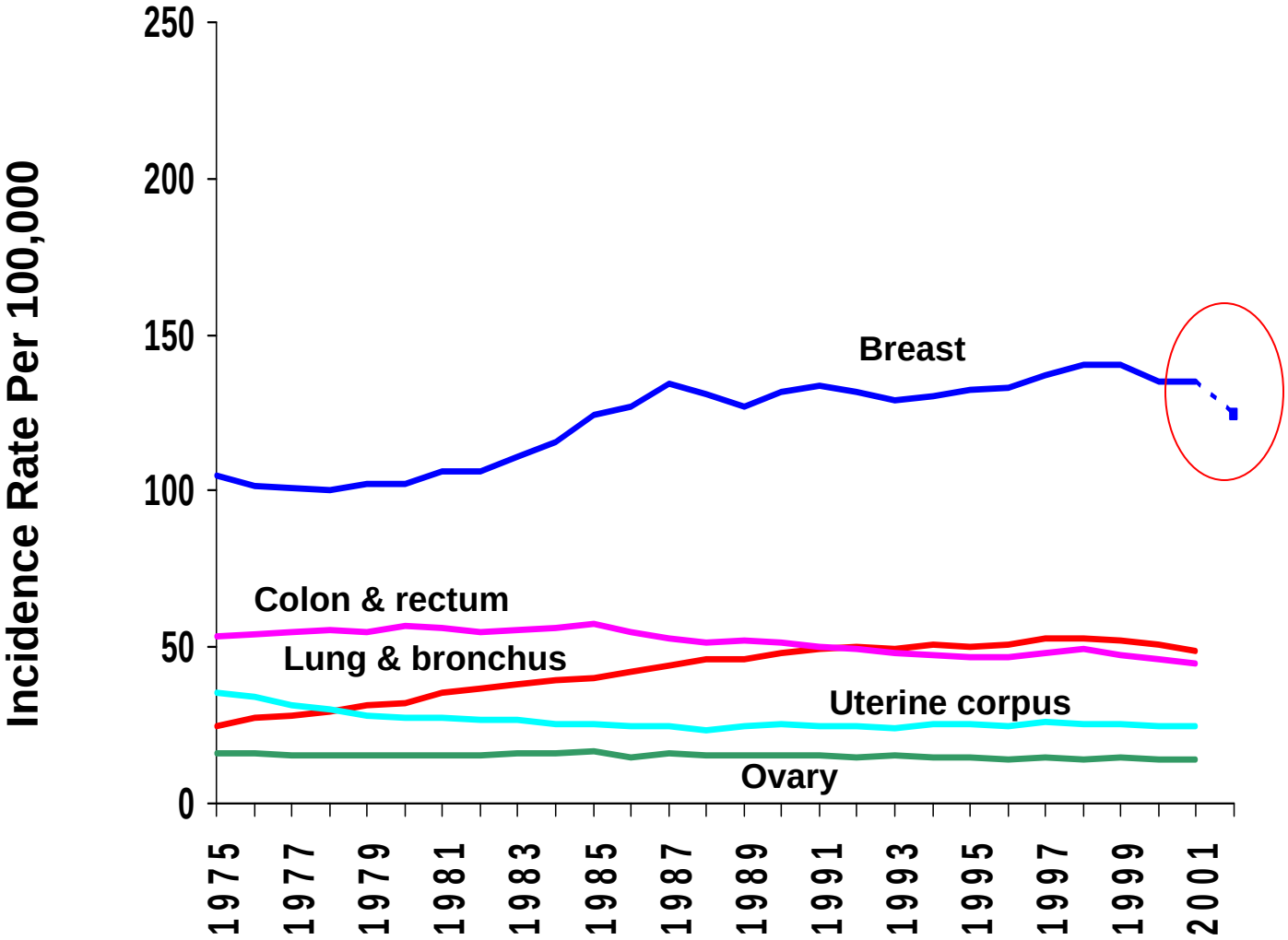
CTLT

Mortality from Breast Cancer 1970-2000, by Age & Sex*
(extends Figure 3 from Bailar, NEJM 1997)



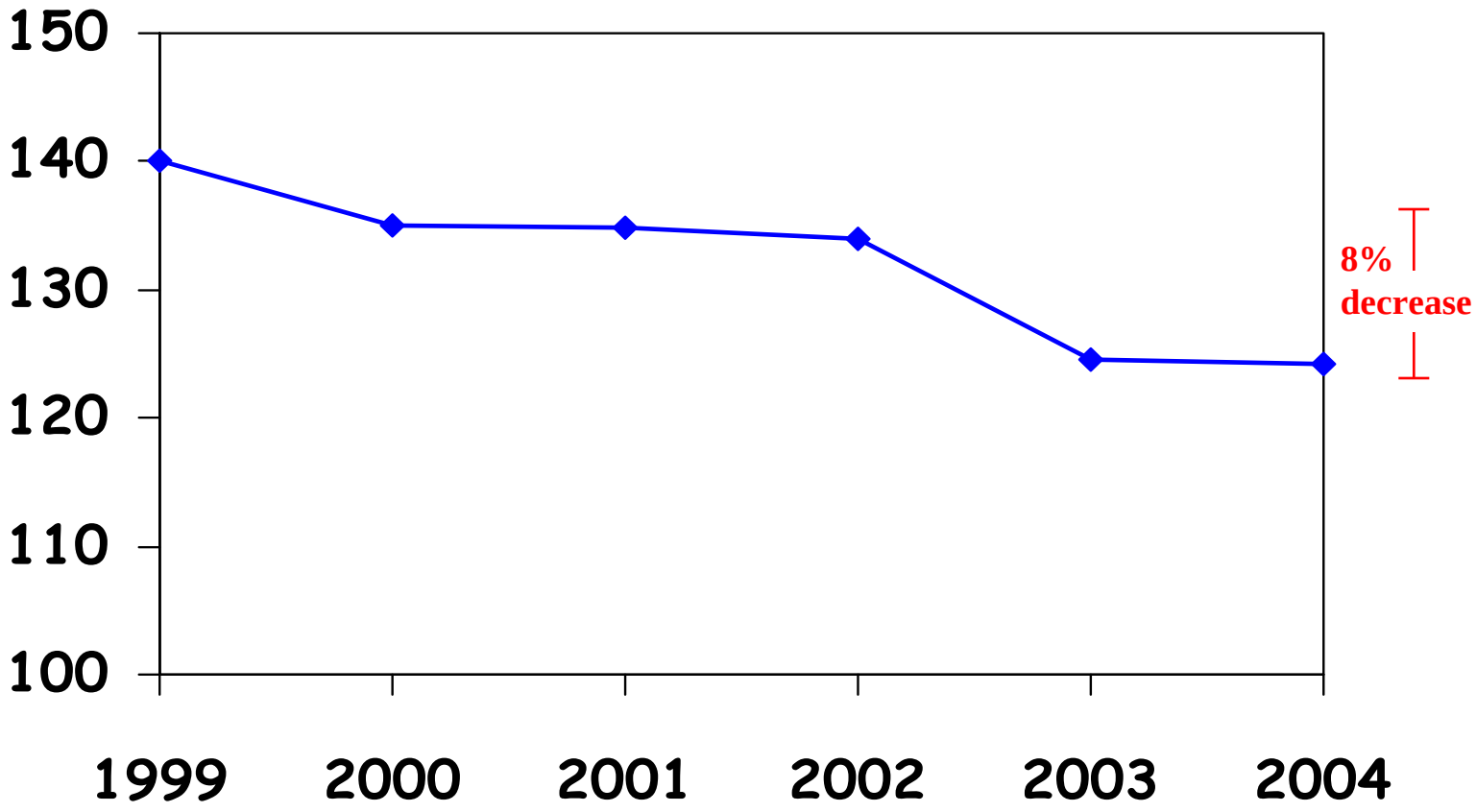
* SEER*Stat Database: Mortality - Public-Use, Total U.S. (1969-2001)
NCI, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2004

Cancer Incidence Rates* US Women, 1975-2004



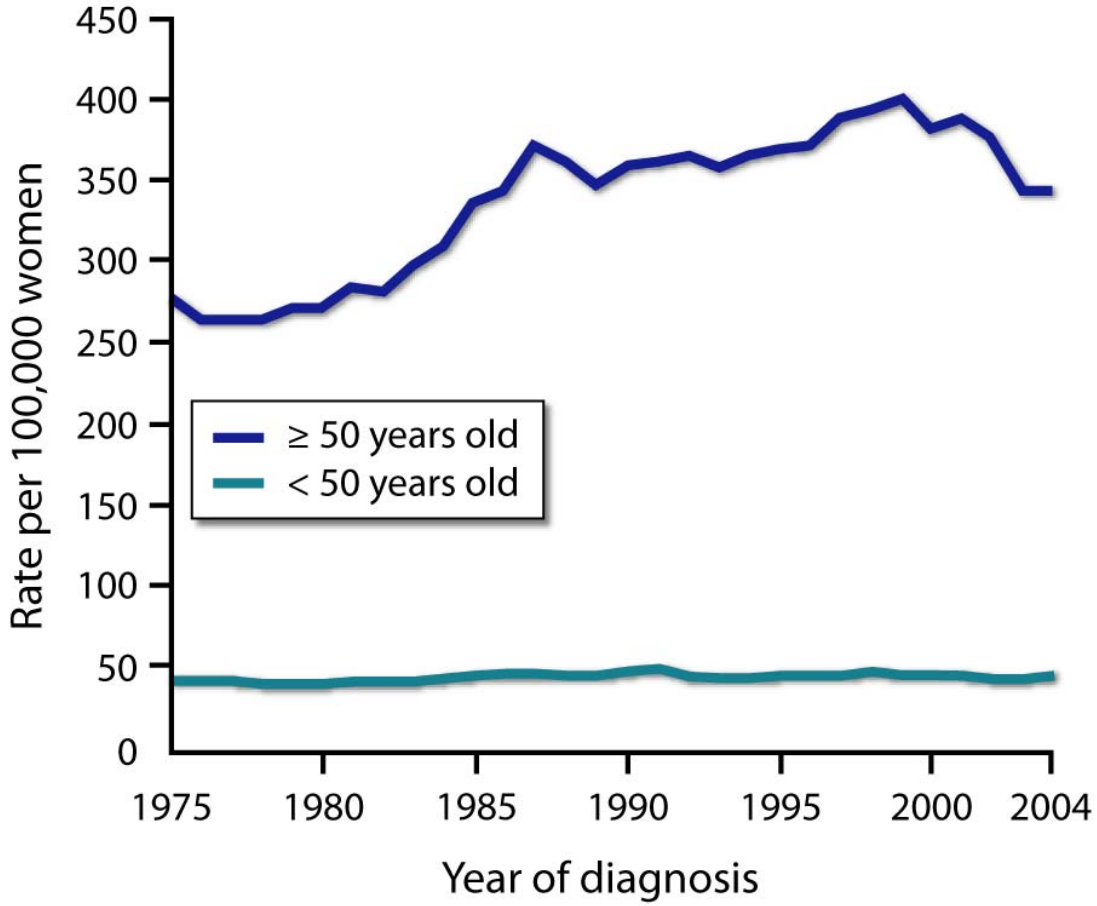
*American Cancer Society website:
Age-adjusted to 2000 US standard population (Source: SEER 2004).

Breast cancer incidence rates 1999-2004*



* SEER data

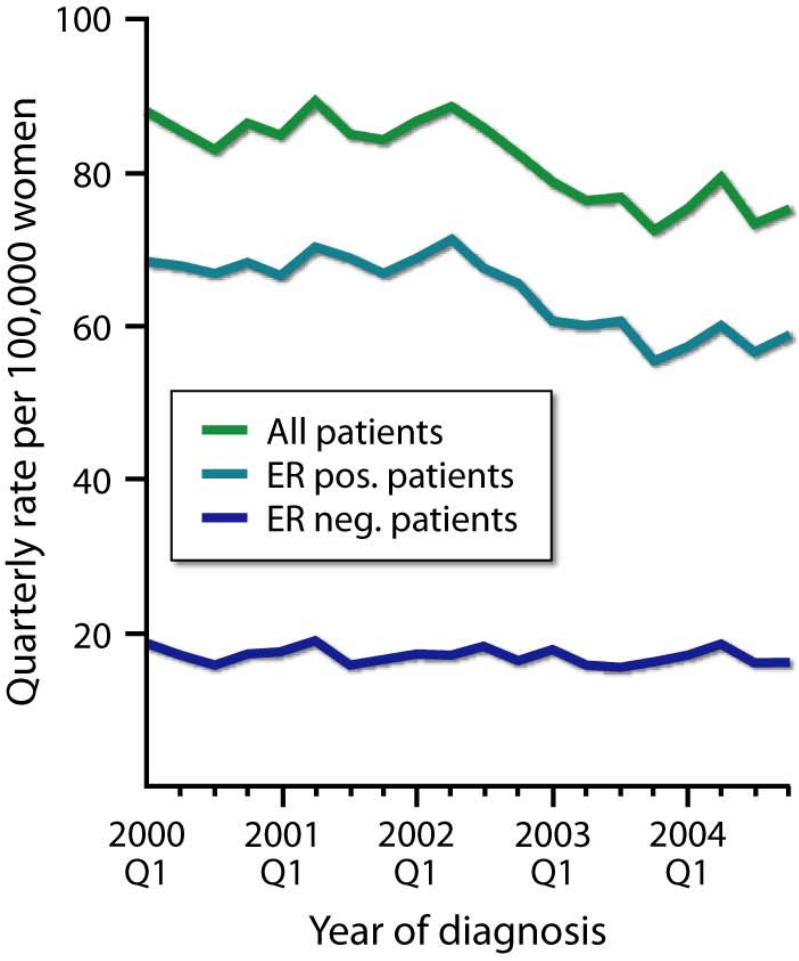
Breast cancer incidence 1975-2004, by age group

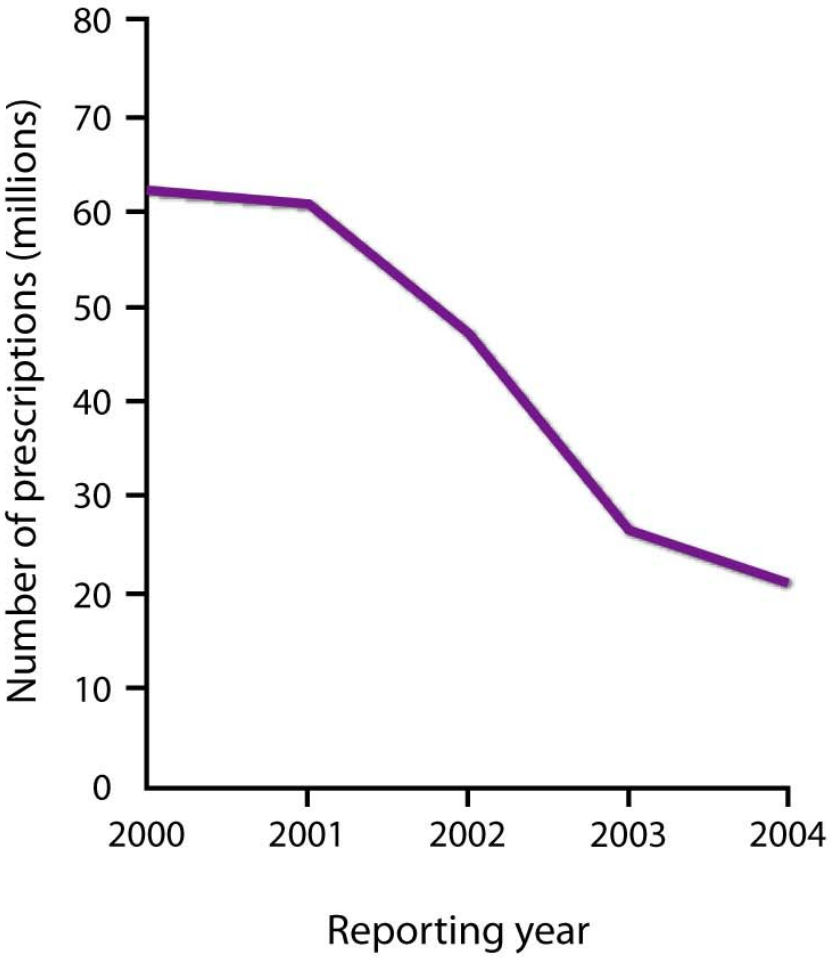


Adapted by CTLT from Ravdin, NEJM 2007.

CTLT

Breast cancer incidence vs. HRT prescriptions 2000-2004*





Adapted by CTLT from Ravdin, NEJM 2007.

CTLT

Bailar's claims of failure (1986-1994) vs. updated mortality data

- Large increases in breast and prostate 1974-1990 are overdiagnois so don't balance mortality [mortality now decreasing faster than incidence: treatment, early detection]

- 1986-1991: increase in mortality stopped in 1991, 1% decrease 1991-1994; likely to continue due to smoking change [Yes: 9% decrease from 1994-2002. But decreases since 1990 in leukemia, myeloma, brain, bladder and NHL (since 1996) – likely due to treatment]

- 1970-1994 decreases in stomach, cervical and colorectal mortality due to decreased risk factors, early detection, but not to treatment or prevention programs [mortality continues to decrease without major treatment advances]

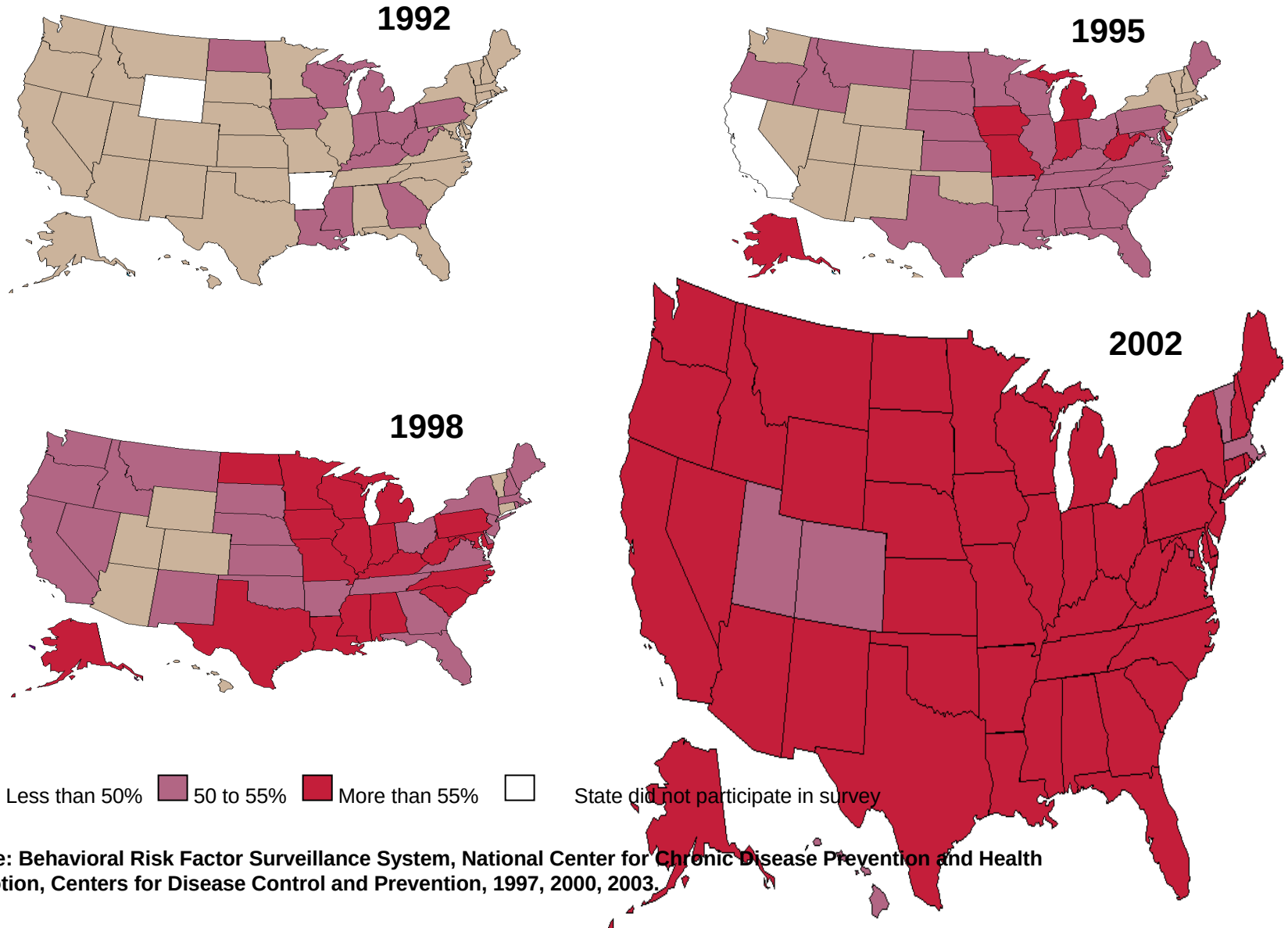
What Bailar Ignores

- Mortality decreased dramatically in ages < 55 (1973-90) or < 65 (1991-2004), not all due to early detection or cohort effects (breast).
- Different trends by age group represents a statistical interaction – in such a setting, overall age-adjusted rates are misleading
- Treatment advances (chemotherapy) slower to occur in elderly (other illnesses, less aggressive treatment, cohort effects).
- Since 1991, decreases in all of 10 biggest cancer killers

Where are we Now?

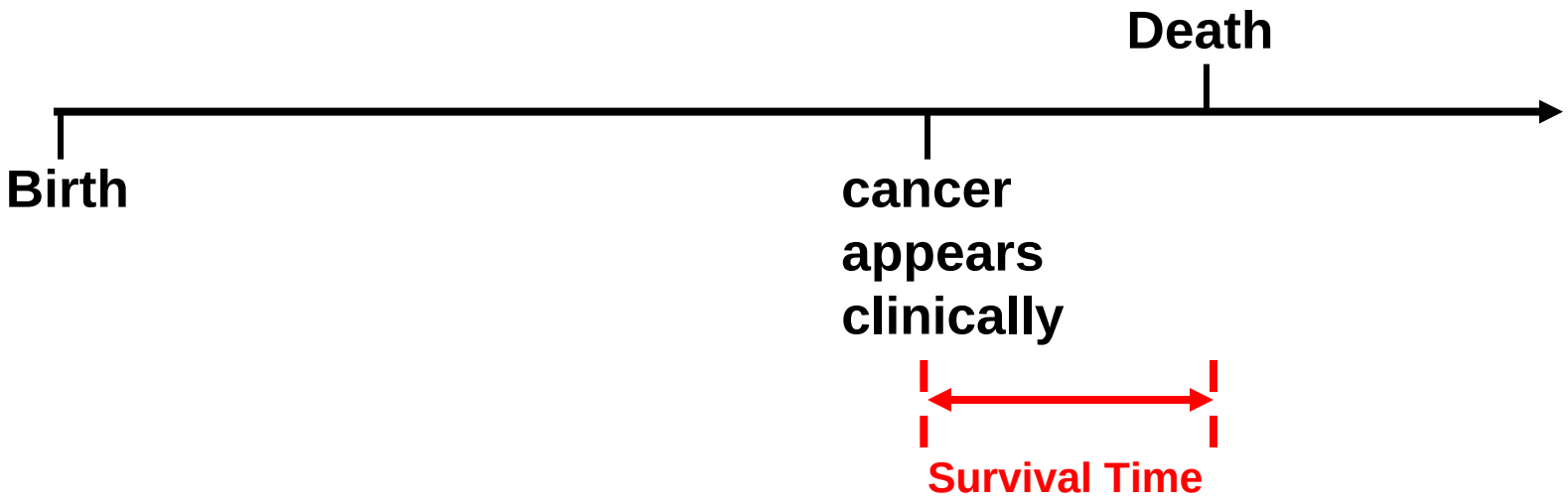
- Mortality was increasing through early 1990's, is now decreasing or flat in all major cancers except liver (males), lung (females - may be starting to decrease)
- Annual percentage changes in mortality:
  2000-2004 (2.1% decrease) vs. 1970-1990 (0.5% increase)
- Decreases in mortality have been influenced more by risk factor reduction and early detection than treatment
- Some mortality increases have clearly identifiable risk factors (melanoma, non-Hodgkin's lymphoma, liver)
- Some increases are unexplained (testis, esophageal adenocarcinoma, multiple myeloma)

Trends in Overweight (BMI>25) Prevalence (%), Adults 18 and Older, US, 1992-2002

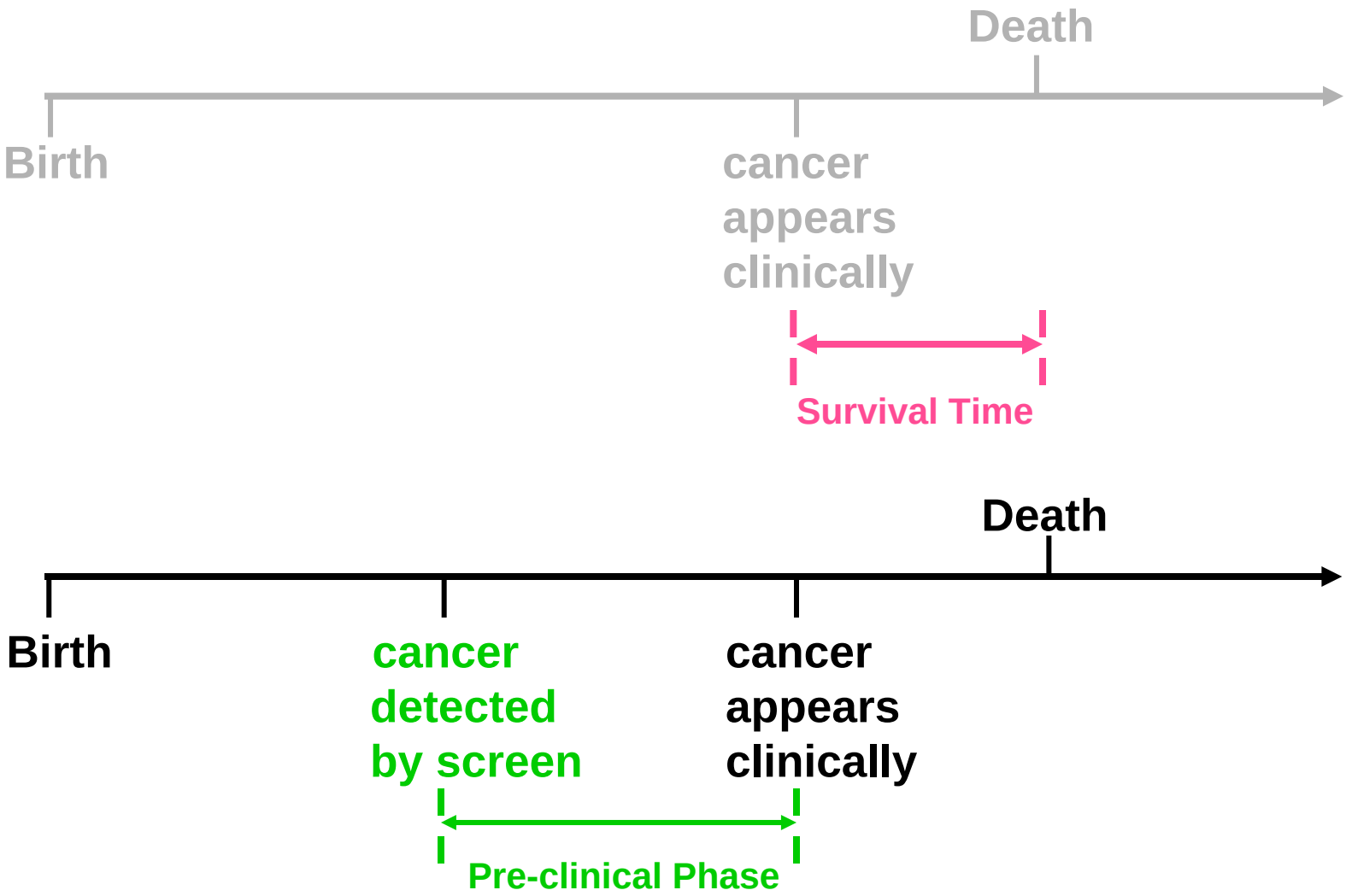


Source: Behavioral Risk Factor Surveillance System, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, 1997, 2000, 2003.

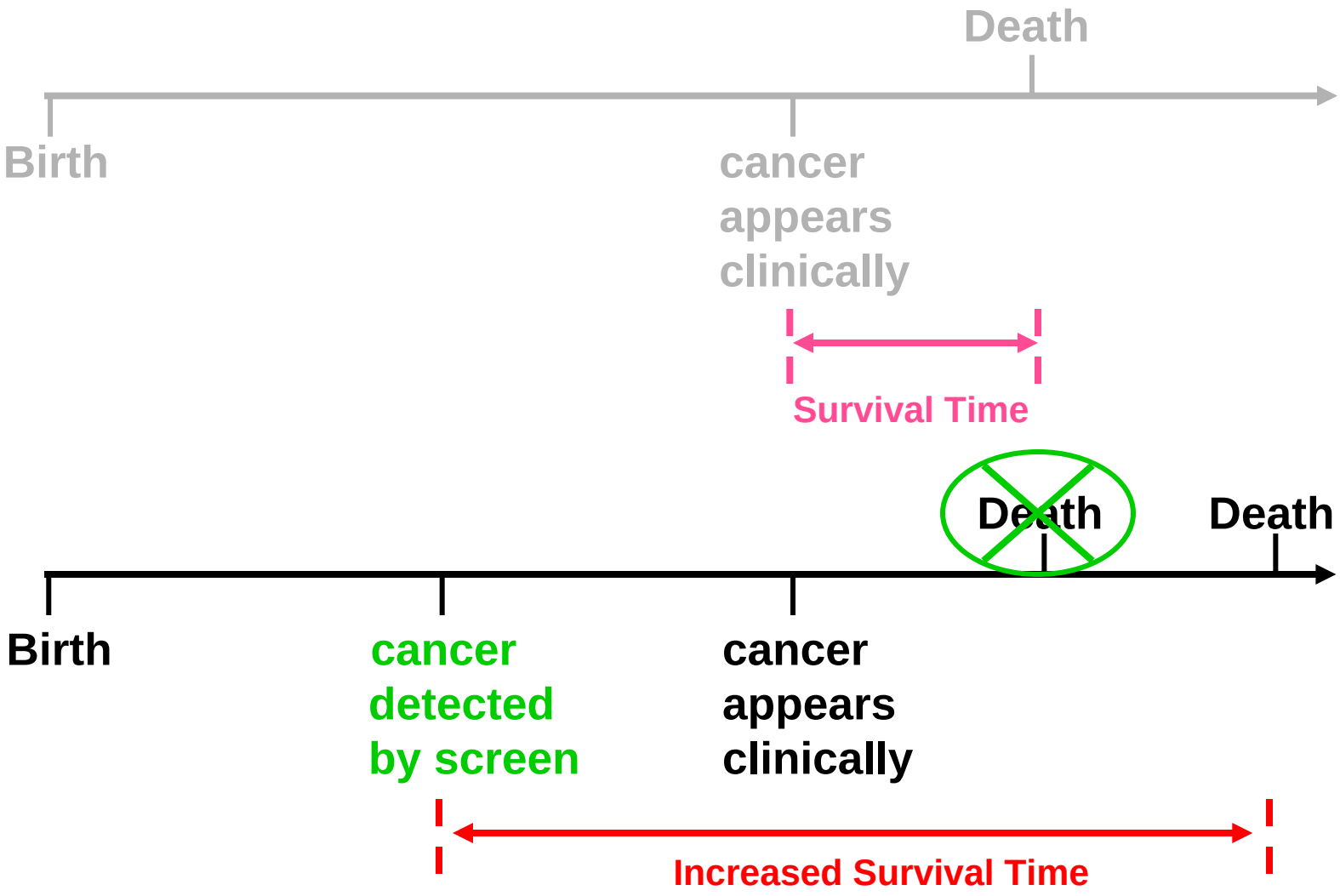
Cancer in the absence of screening



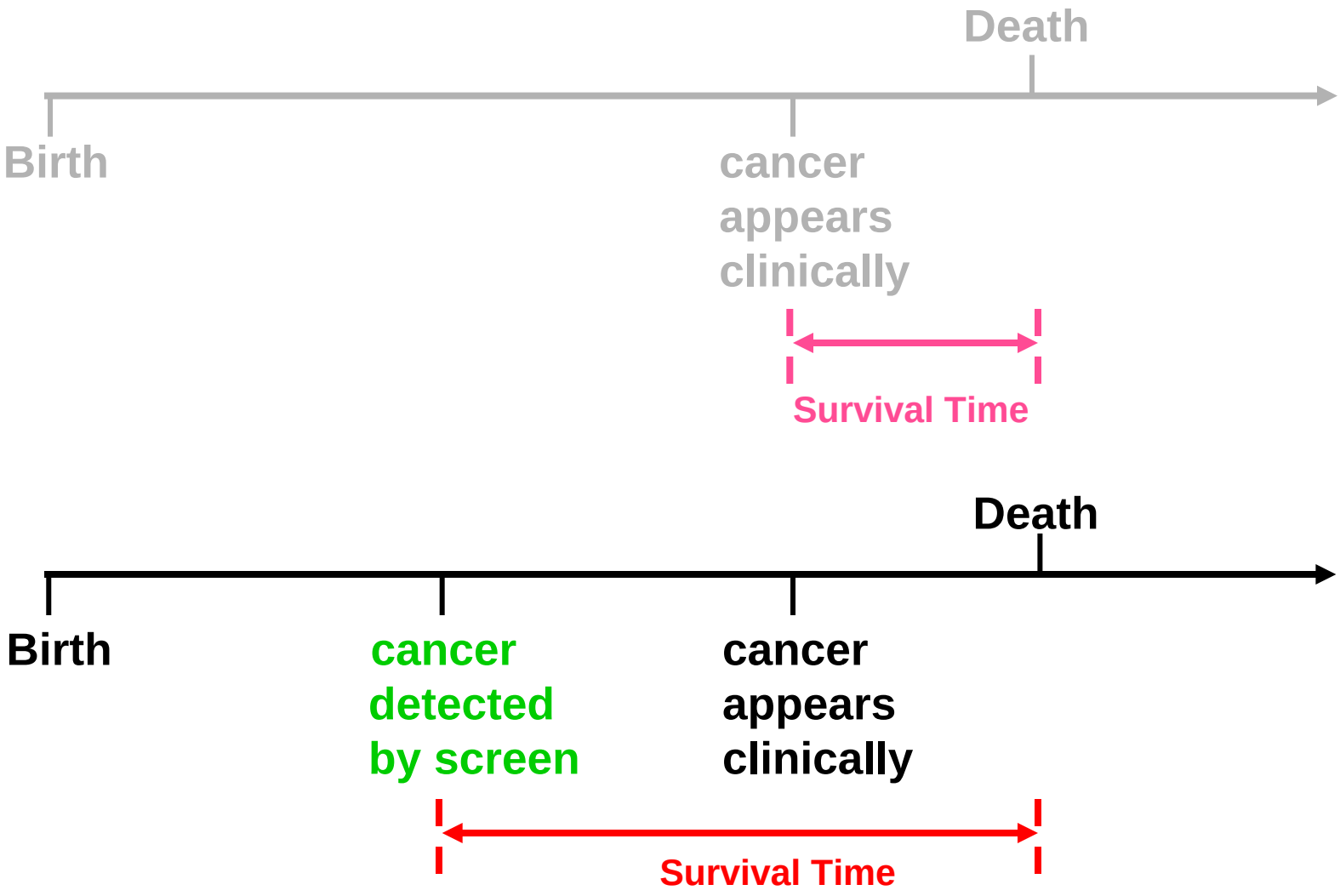
Appropriate diagnosis due to screening



Screening effective, life extended



Lead-time bias, life not extended: treatment doesn't cure screened cancers



Overdiagnosis, life not extended: screening identifies tumors of low lethality