Understanding Cancer Trends Through Modeling

National Cancer Advisory Board

September 9, 2002

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Outline

- **Breast Cancer**
  - **Using Modeling to Understand the Impact of Mammography and Adjuvant Therapy on Breast Cancer Mortality**
- **Prostate Cancer**
  - **Overdiagnosis in PSA Screening: Lessons From US Prostate Cancer Incidence Trends**

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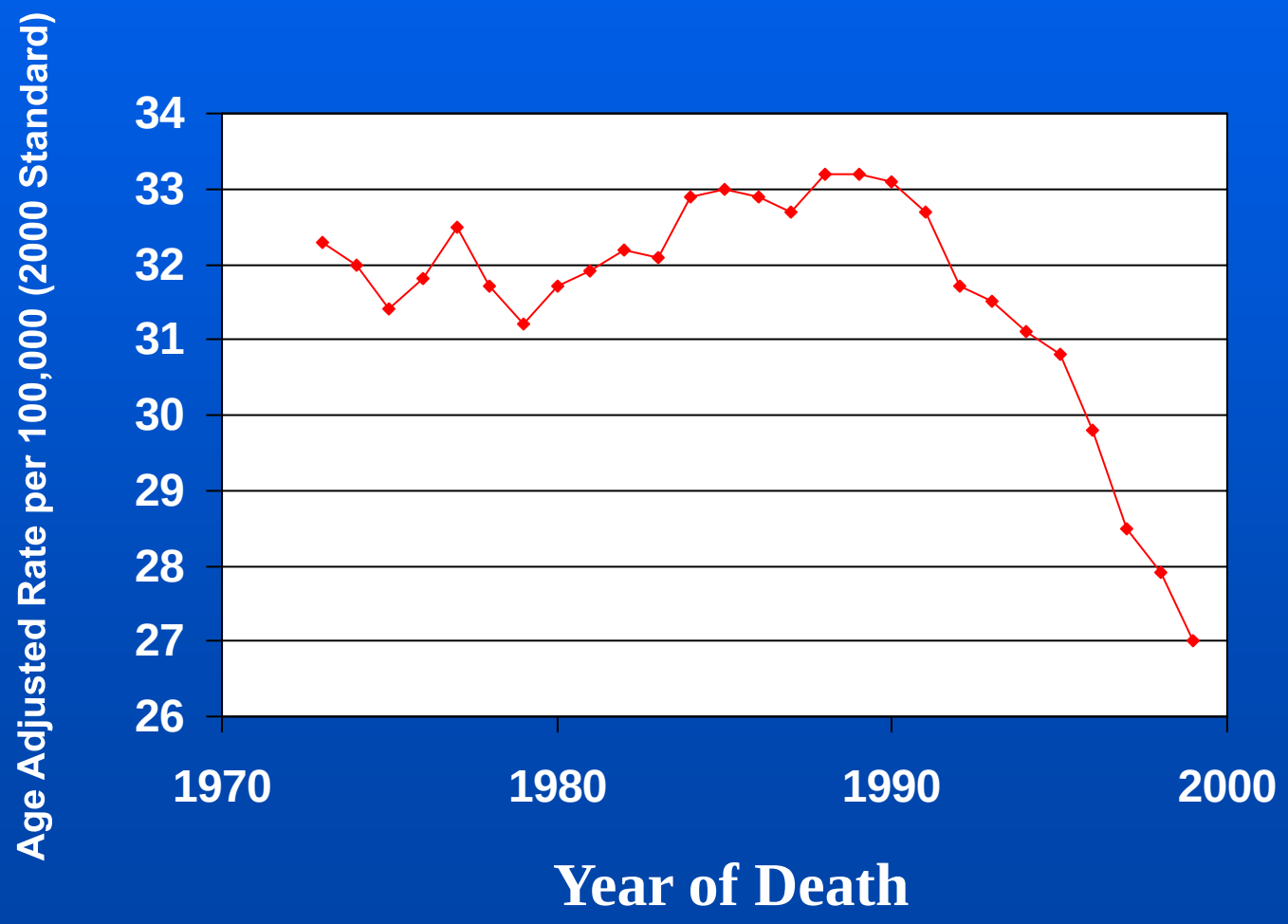
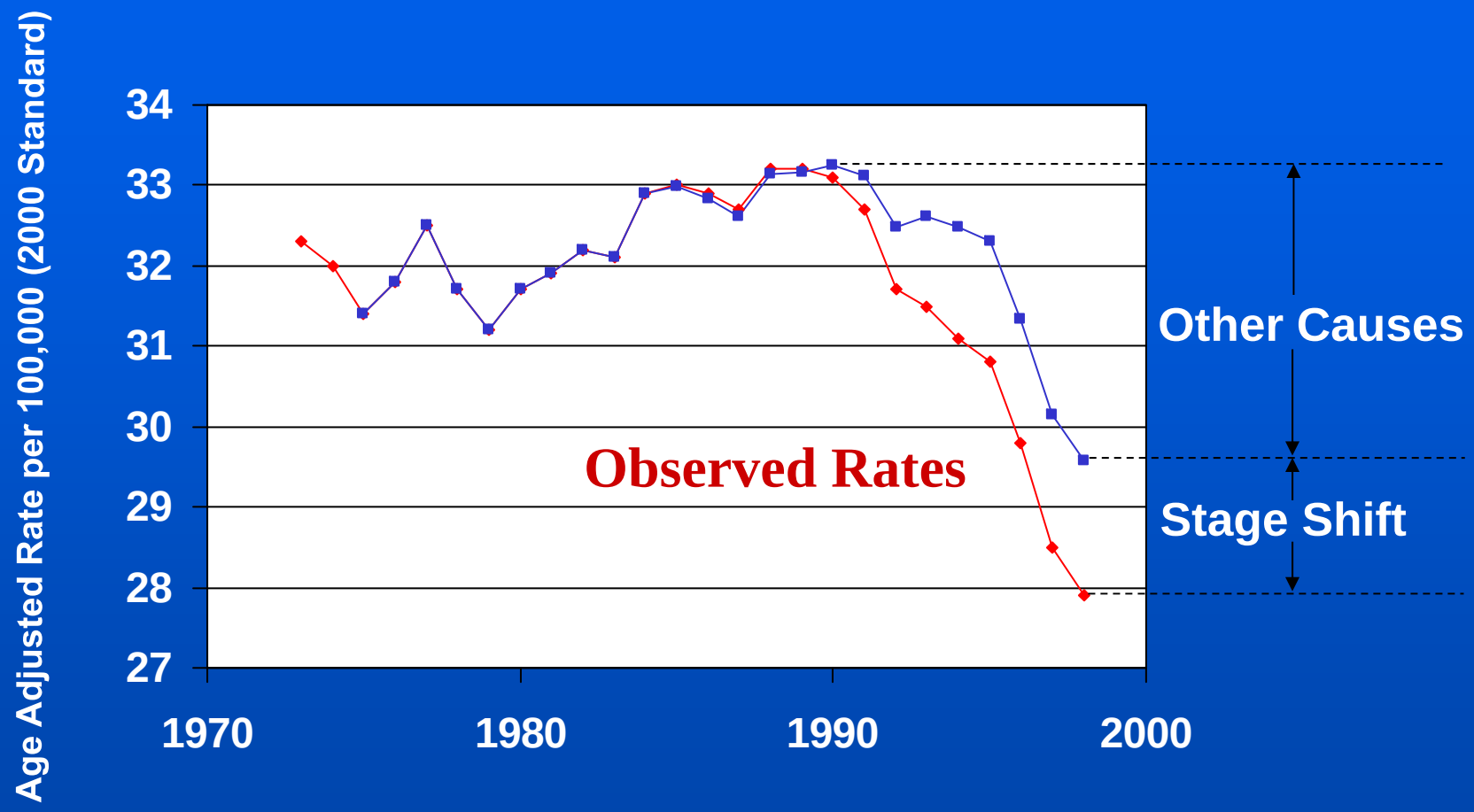
US Breast Cancer Mortality All Ages



Projected Impact of the Observed Stage Shift on US Breast Cancer Mortality



Observed stage shift shows a net beneficial impact on mortality

(exact magnitude of the impact should not be derived from this model)

Cancer Intervention and Surveillance Modeling Network (CISNET)

- **NCI Sponsored Consortium of Modelers Focused on**
  - **Modeling the Impact of Cancer Control Interventions (Screening, Treatment, Primary Prevention) on Current and Future Trends**
  - **Optimal Cancer Control Planning**
- **Sept. 2000: 9 Grantees Funded in Breast, Prostate and Colorectal Cancer**
- **Aug. 2002: 8 Additional Grantees in Prostate, Colorectal, and Lung Cancer**

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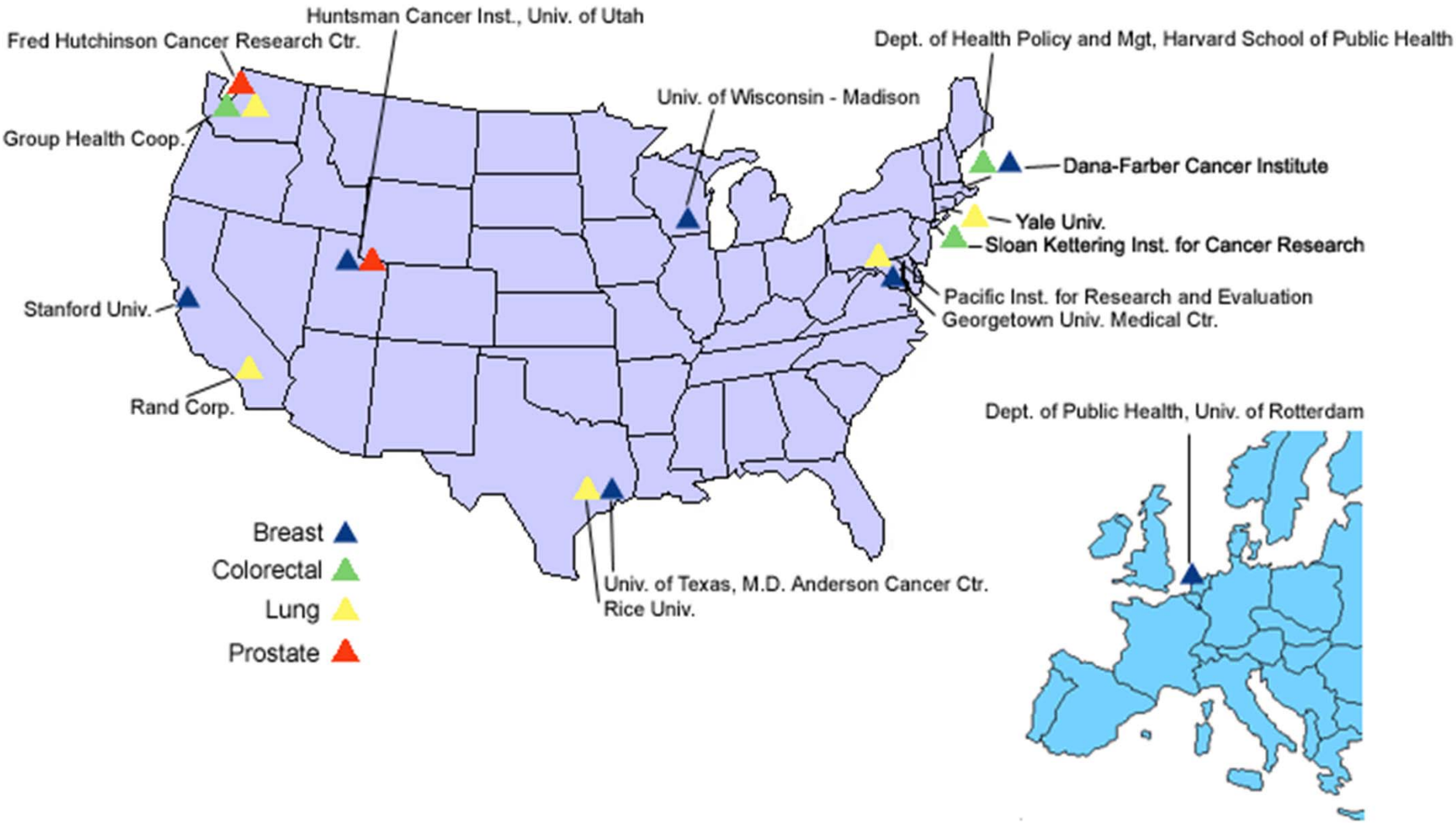
Funded CISNET Grantees



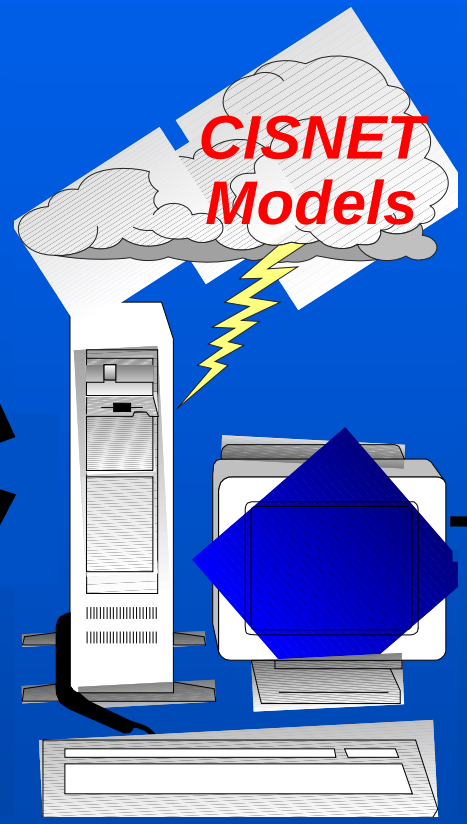
CISNET Breast Cancer Base Question:
What is the Impact of Mammography, Adjuvant Therapy, and the Combination on U.S. Breast Cancer Mortality: 1975-2000?

Population Inputs
(Common to all models)

- Dissemination of Adjuvant Therapy
- Dissemination of Mammography
- Change in Background Risk
- Mortality from Other Causes

Model Specific Inputs and Assumptions

- Efficacy of Treatment
- Tumor Growth Rates and Metastatic Spread
- Operating Characteristics of Screening (e.g., Sensitivity, Lead Time, Overdiagnosis)
- Post Diagnosis Survival by Tumor Characteristics



Predicted Incidence

Predicted Mortality
For

- Treatment Alone
- Screening Alone
- Treatment and Screening

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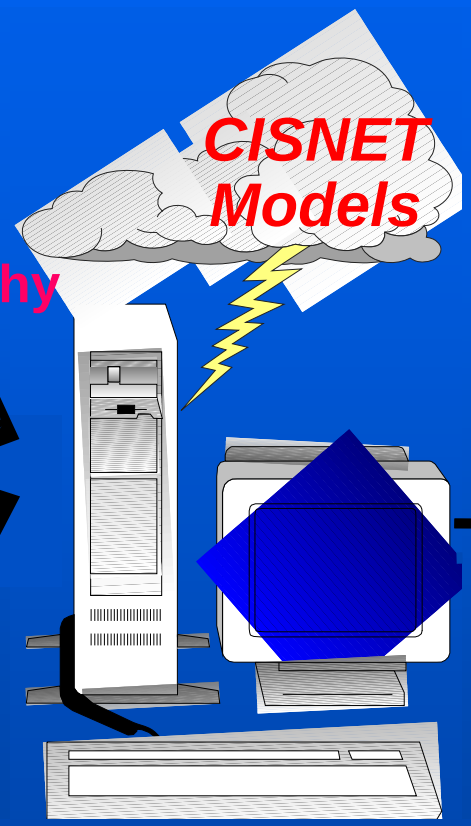

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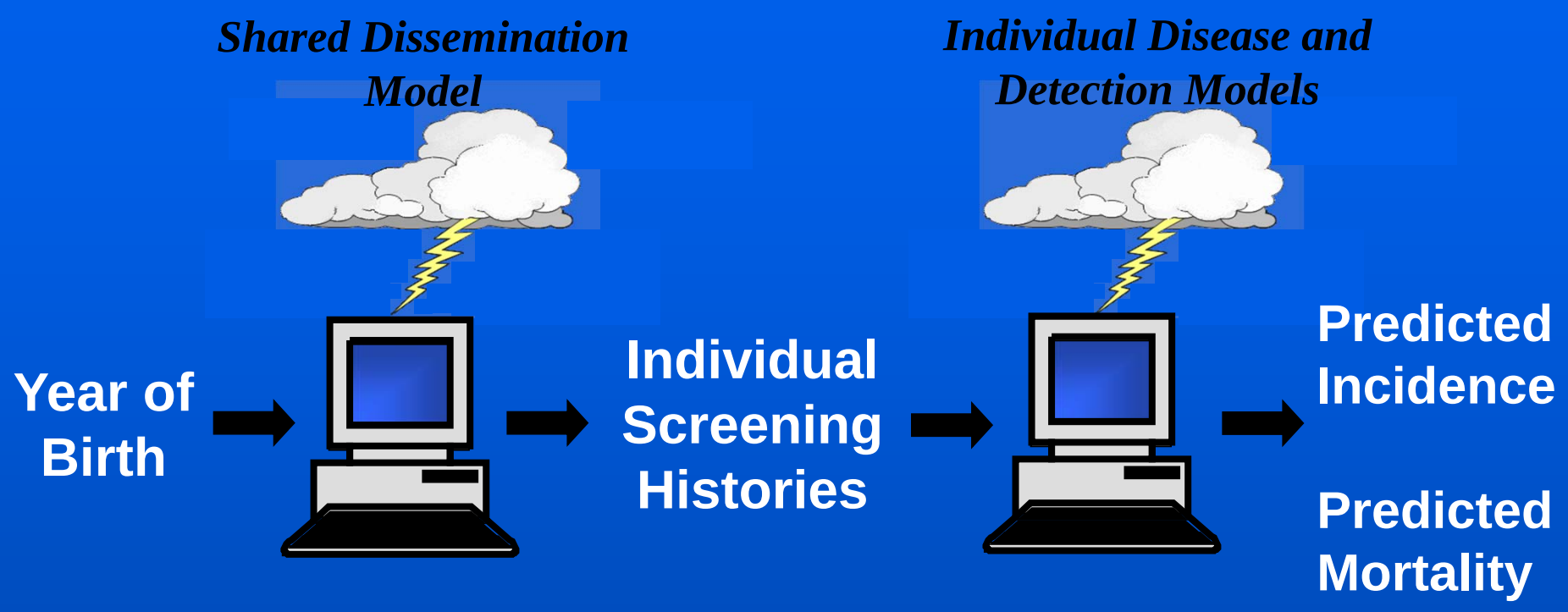
Modeling Dissemination of Mammography



Step 1. Age of first screening exam

Source: Cross-Sectional National Surveys

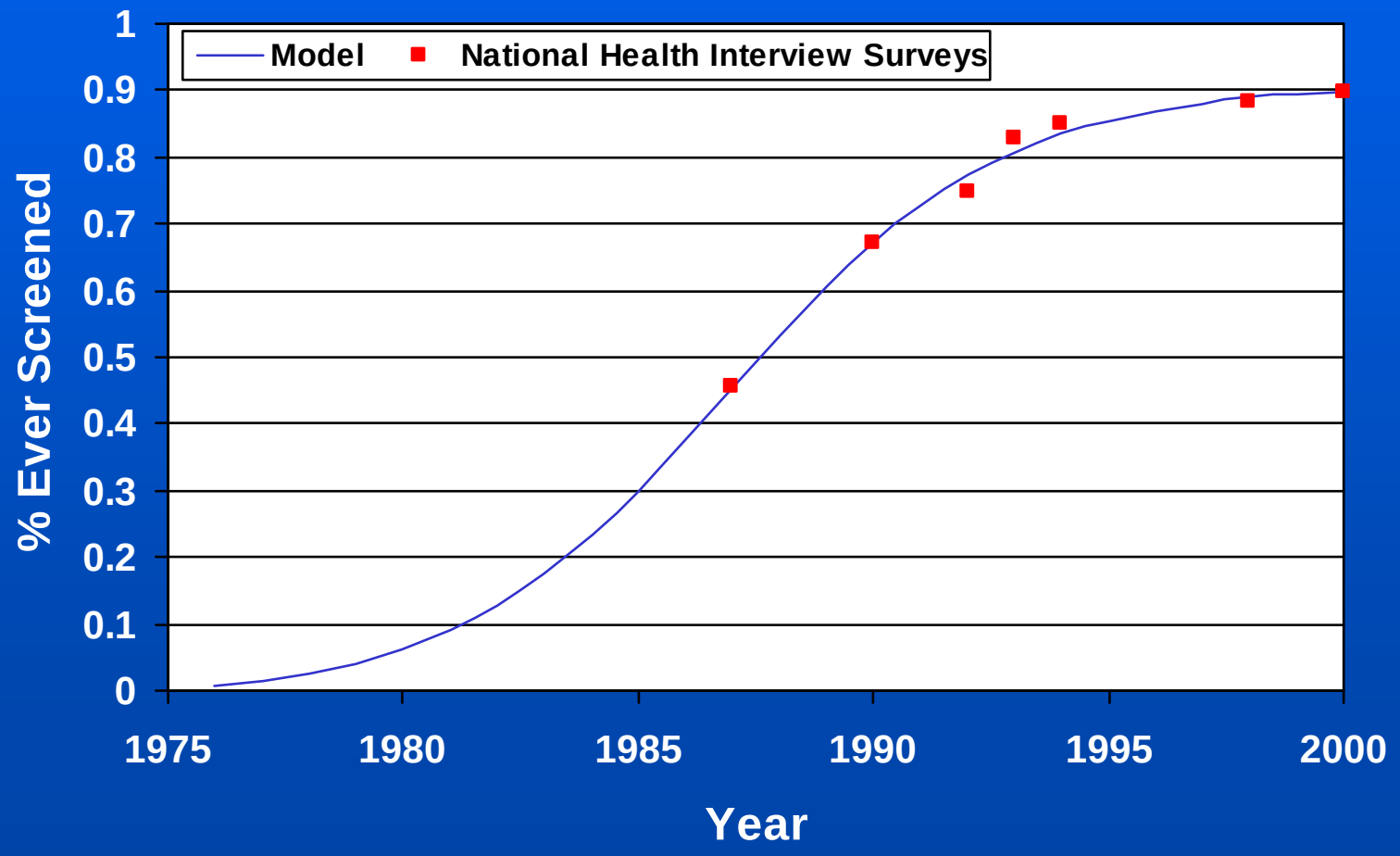
National Health Interview Survey

Step 2. Interval between consecutive screening exams

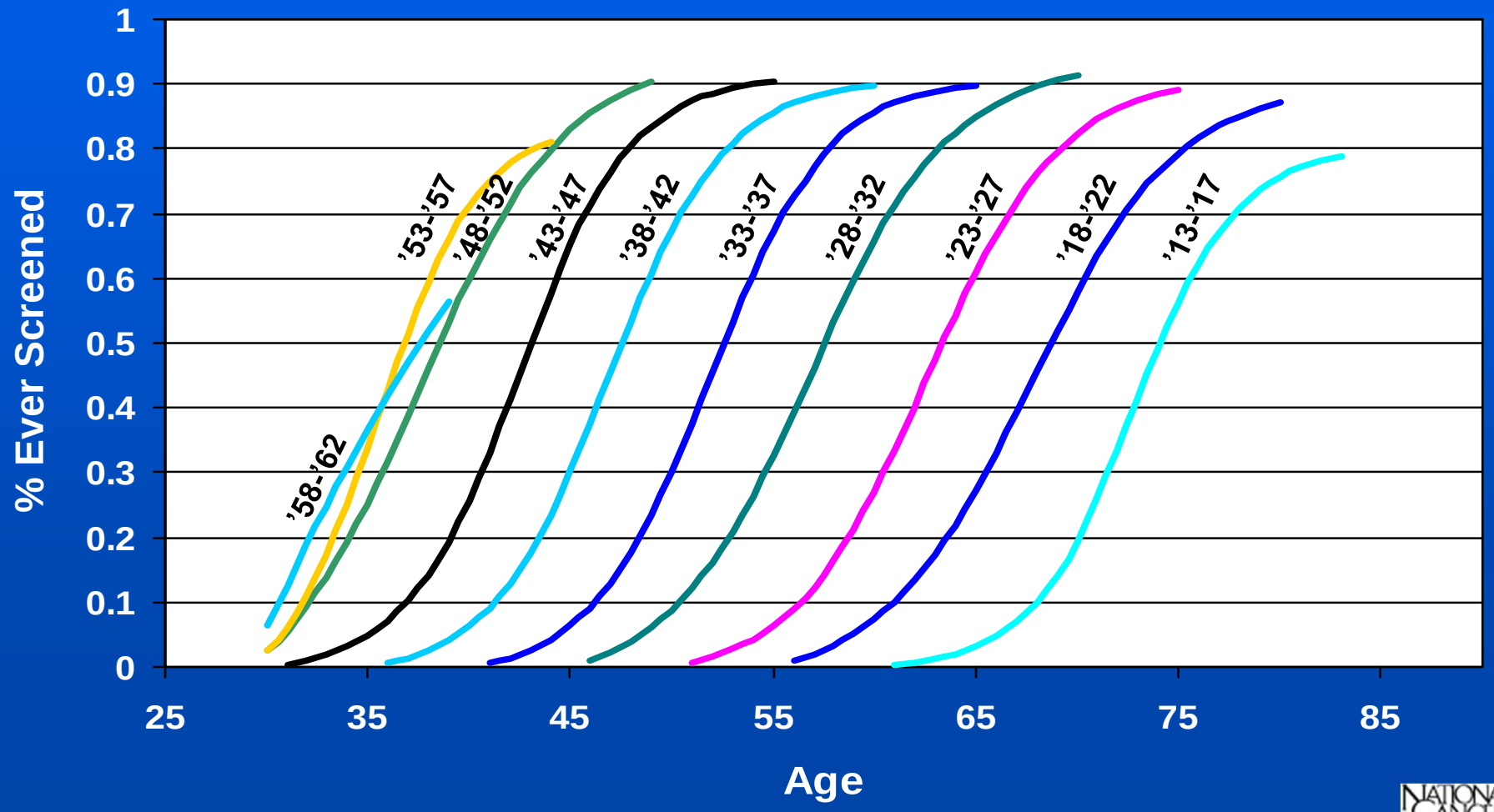
Source: Linked Mammography Registries

Breast Cancer Surveillance Consortium

Step 1. Time distribution to first screening exam – Sample Birth Cohort Born Between 1933-1937



Time Distribution To First Screening Exam By 5 Year Birth Cohort



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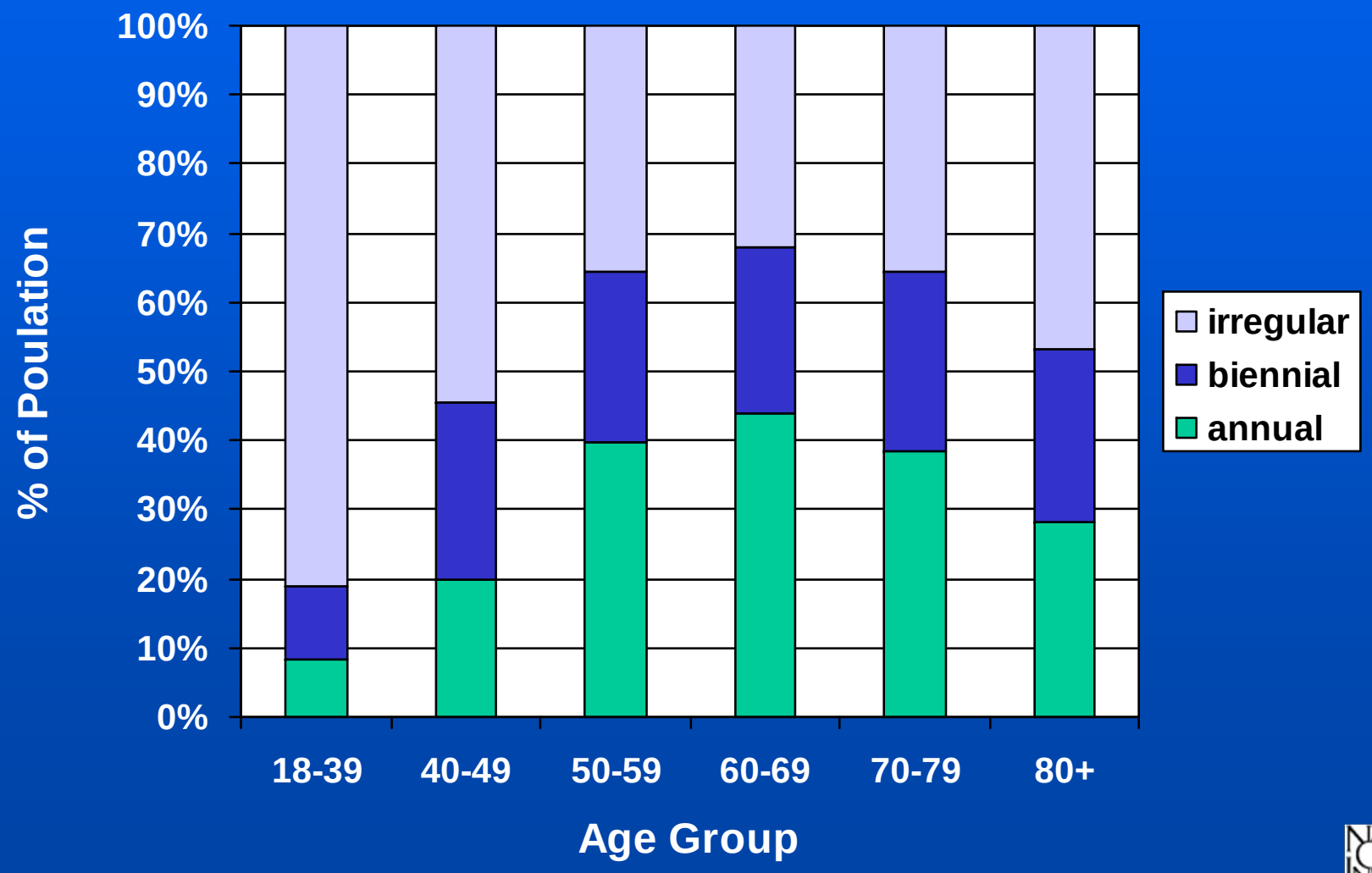
Step 2. Modeling The Interval Between Consecutive Screening Exams – Classification Of Screening Type



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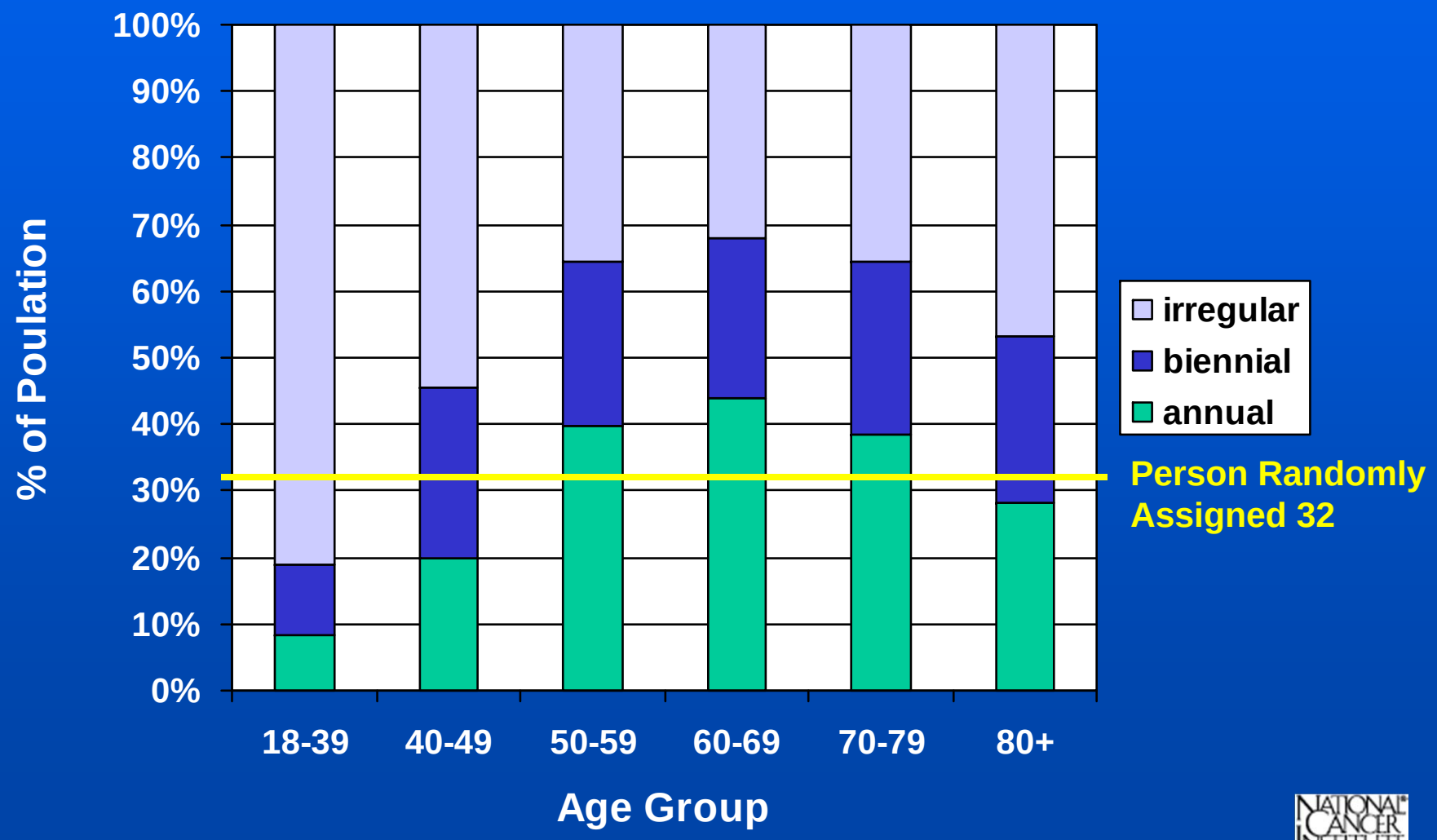

Simulated Screening History

Birthday is 01/01/1940

Group Selection Parameter = 32%

Age: 43.0	Date: 01/14/1983		
Age: 44.9	Date: 12/11/1984	Gap Time: 1.9	Group: Biennial
Age: 48.1	Date: 01/31/1988	Gap Time: 3.1	Group: Biennial
Age: 49.6	Date: 08/20/1989	Gap Time: 1.6	Group: Biennial
Age: 54.2	Date: 03/27/1994	Gap Time: 4.6	Group: Biennial
Age: 56.1	Date: 02/12/1996	Gap Time: 1.9	Group: Annual
Age: 57.1	Date: 02/09/1997	Gap Time: 1.0	Group: Annual
Age: 58.0	Date: 01/16/1998	Gap Time: 0.9	Group: Annual
:	:	:	:
Age: 80.891	Date: 11/22/2020	Gap Time: 1.184	Model: Annual
Age: 82.066	Date: 01/25/2022	Gap Time: 1.175	Model: Biennial

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Summary

- Modeling of this type puts the populations dynamics in our control.
  - Evaluate the impact of the observed mammography trends on US mortality
  - Can vary the model parameters to study the impact of various cancer control strategies on US mortality and differences between subpopulations
    - More women get first mammograms
    - More women get regular mammograms
    - Optimal schedules
    - Estimate mammography histories for those without health insurance/racial/ethnic/SES groups

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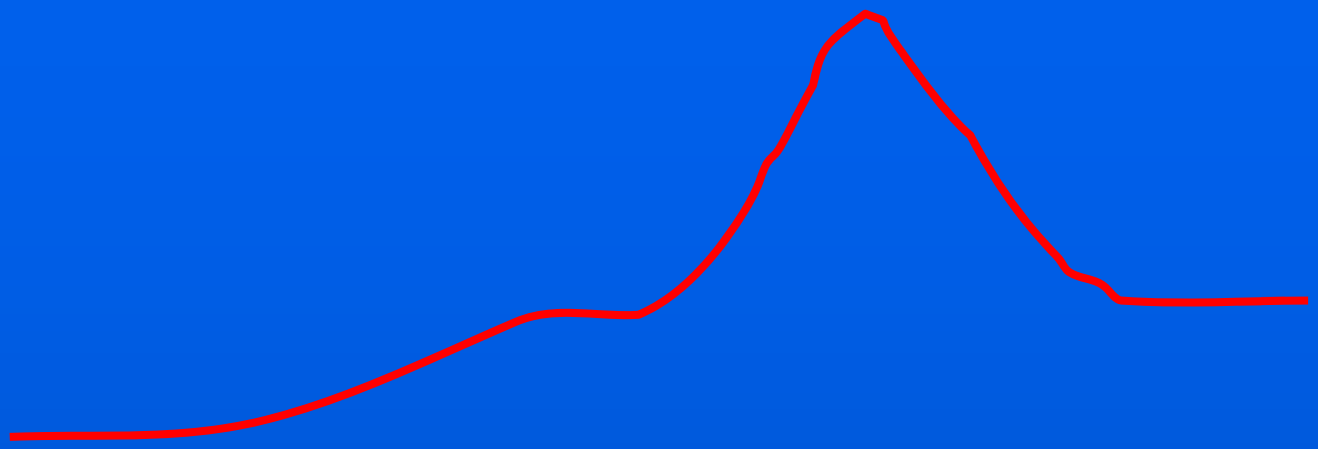


Overdiagnosis in PSA screening:

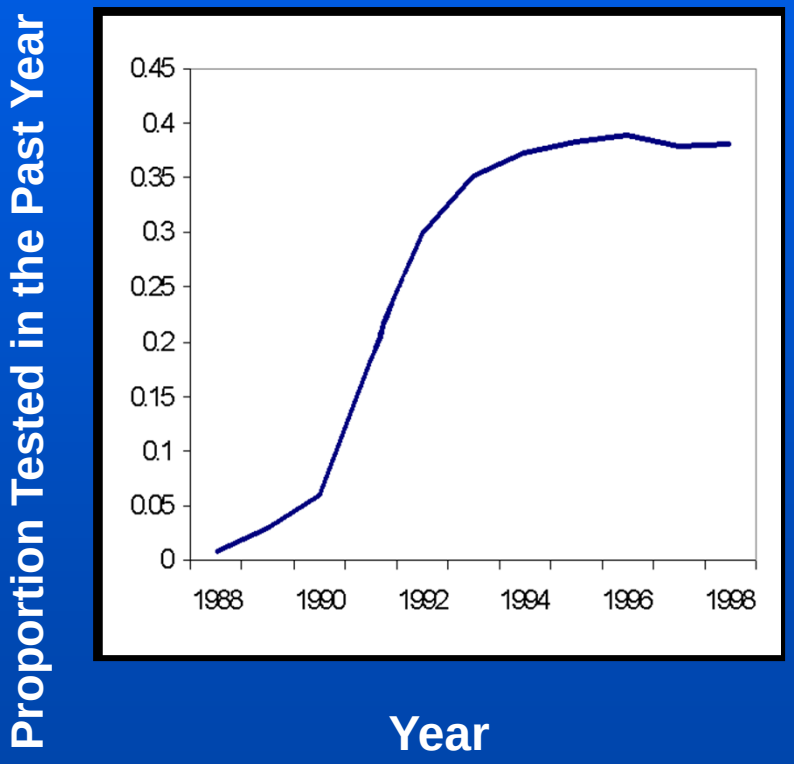
Lessons from US Prostate Cancer Incidence Trends

Work supported by Prostate CISNET Grant
Fred Hutchinson Cancer Research Center
Ruth Etzioni

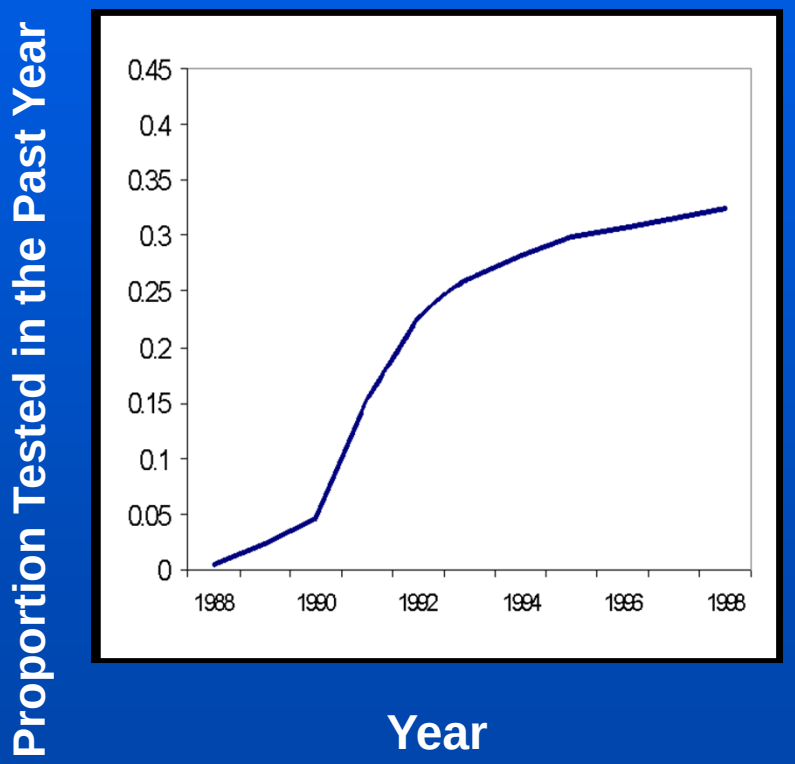
Rx UNITED DRUGS
KATTERMAN'S SAND POINT PHARMACY
PSA TESTS HERE!!!
CHOLESTEROL TESTS HERE!!!
Harry Potter

Proportion of Men Getting a PSA Test in the Past Year: 1988-1998

Whites 65+



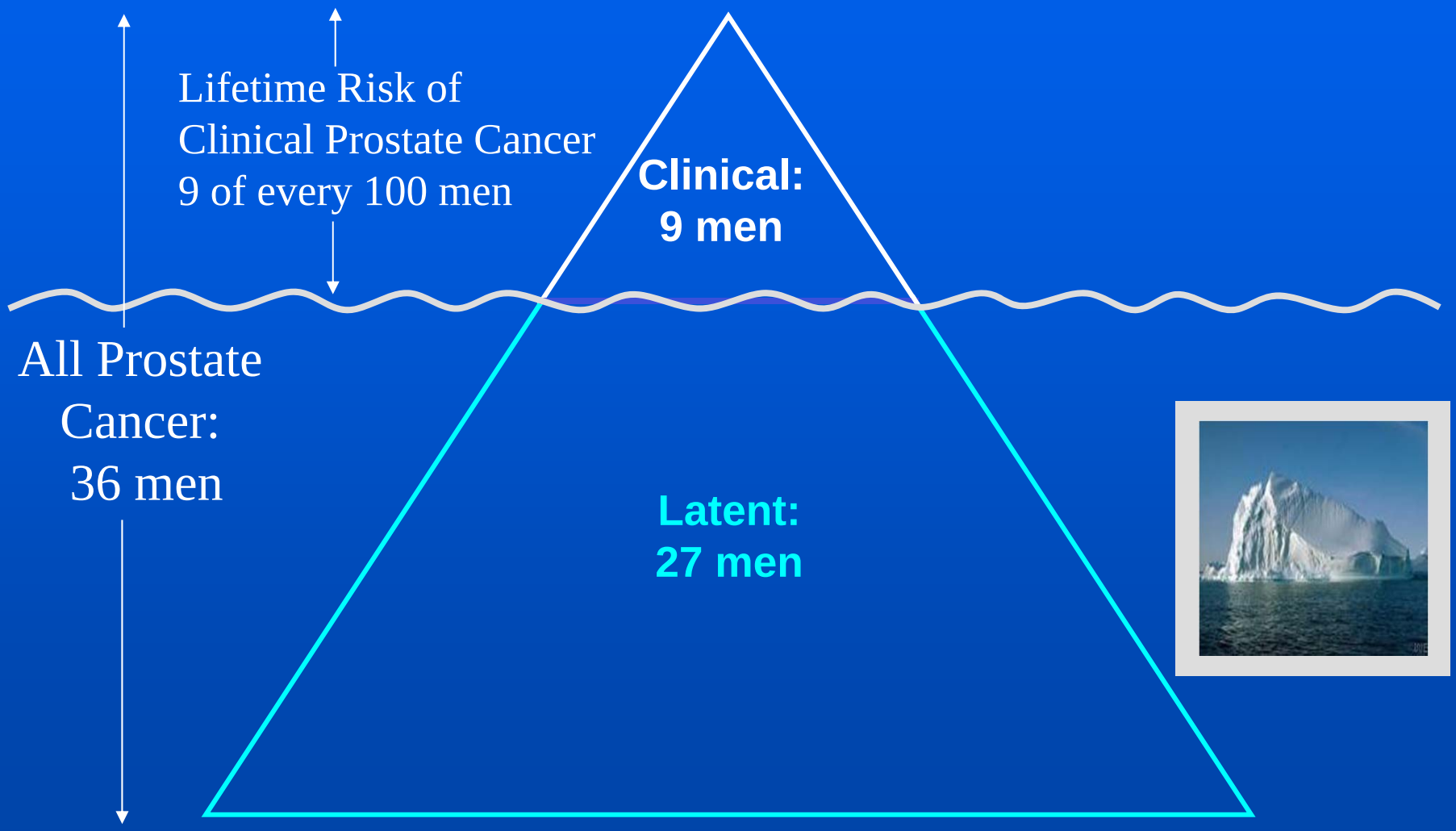
Blacks 65+



Source: SEER-Medicare (Legler et al 1998; Etzioni et al, ROCKY!!!)

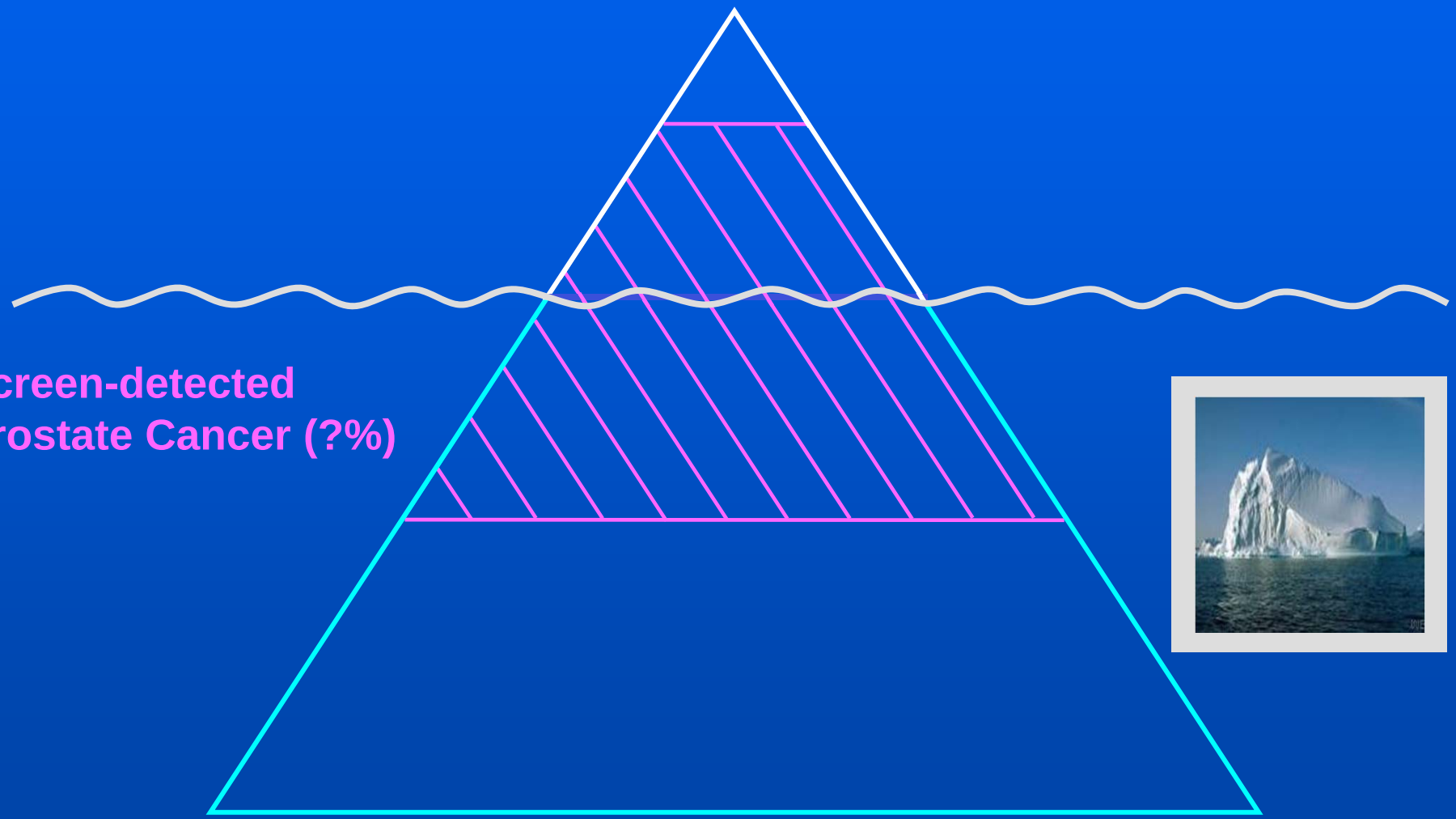
Prostate Cancer in the Pre-PSA Era

Lifetime Risk of Autopsy Detectable Cancer: 36 of every 100 men



[Whites; Etzioni et al, AJE 1998]

How Far Into the Latent Pool Does PSA Testing Reach?



[Whites; Etzioni et al, AJE 1998]

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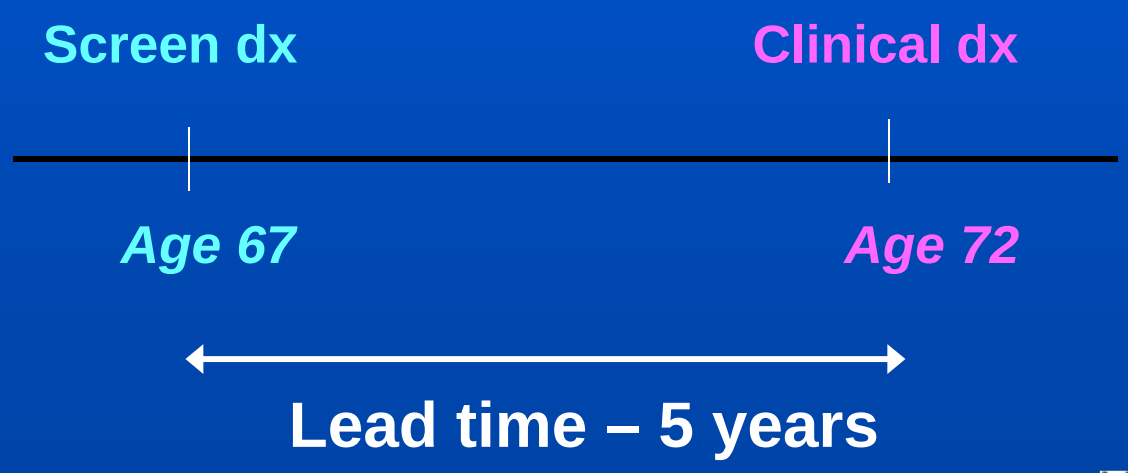
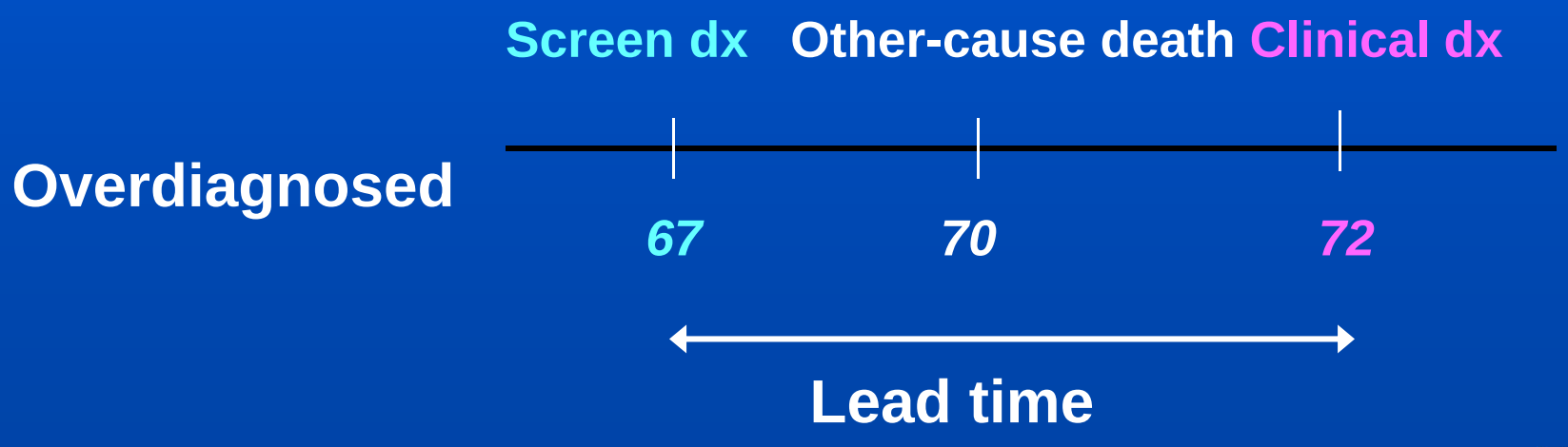
Definition of Lead Time

The time that a diagnosis of cancer is advanced due to early detection through screening



Definition of Overdiagnosis

Cases detected by screening that, in the absence of screening, would never have been diagnosed

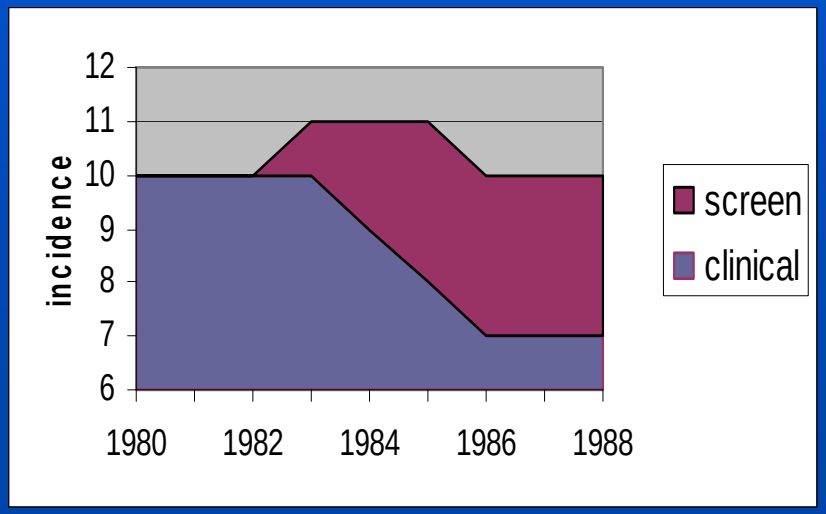


Impact of the Introduction of Screening on Population Trends in Incidence

- Introduction of a screening test in a population causes:
  - Initial "bulge" in incidence (cases found earlier)
  - Followed by declines (depletion of future clinical cases)
  - Incidence stabilizes after screening use stabilizes

One Year Lead Time

No Overdiagnosis



Screen-detected incidence: 0 0 0 1 2 3 3 3 3

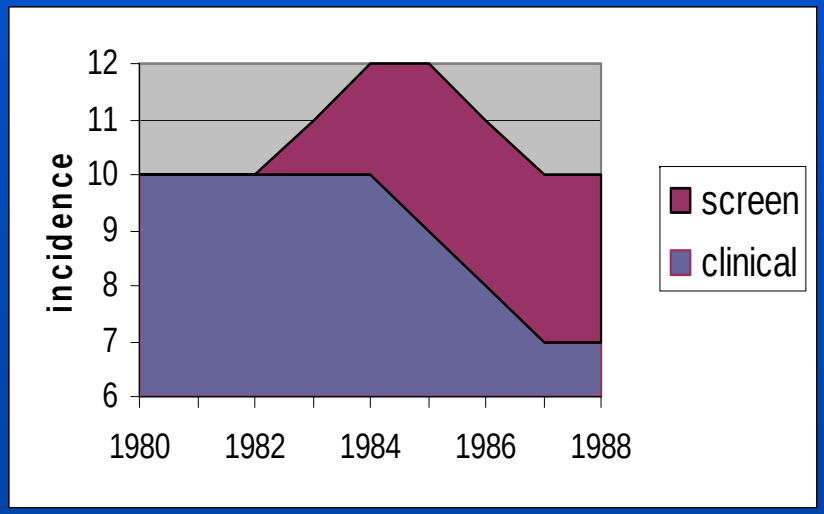
Feuer & Wun, AJE (1992)

Impact of Longer Lead Time on Incidence Patterns

- **Larger lead times ➔ More pronounced and extended incidence peak**

Two Year Lead Time

No Overdiagnosis



Screen-detected incidence: 0 0 0 1 2 3 3 3 3

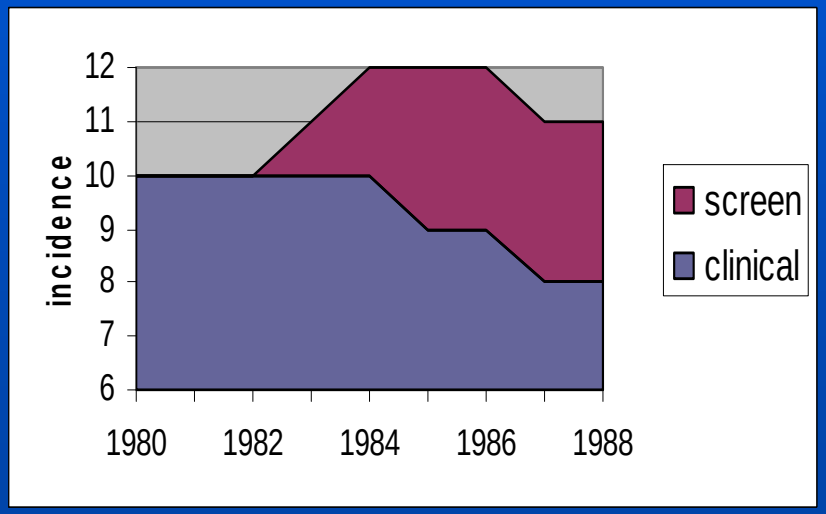
Impact of Overdiagnosis on Incidence Patterns

- **More overdiagnosis ➔ More extended incidence peak**

  No return to original levels

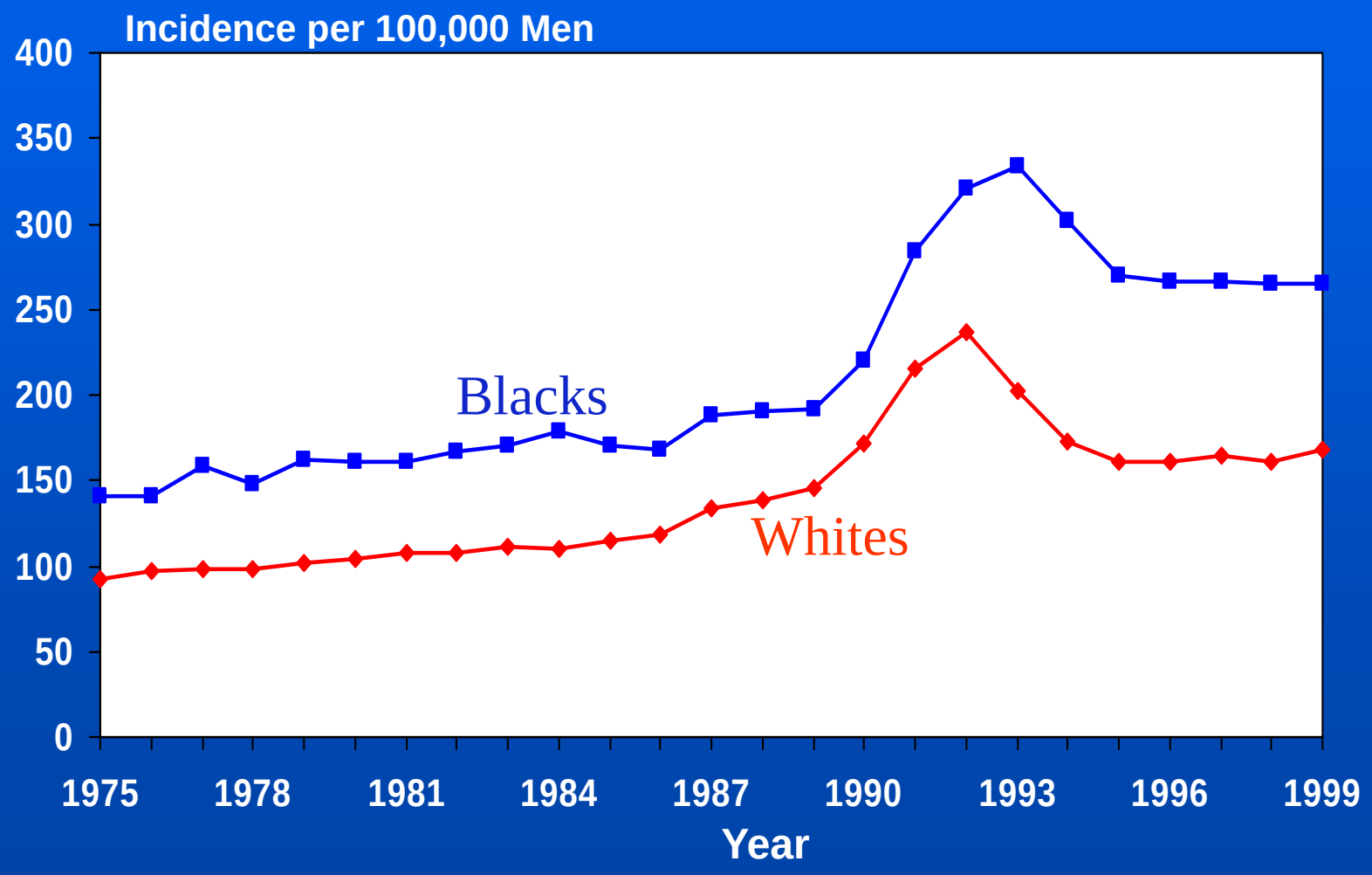
Two Year Lead Time

33% overdiagnosis



Screen-detected incidence: 0 0 0 1 2 3 3 3 3

Prostate Cancer Incidence, All Ages by Race



9 SEER Registries, Age Adjusted to US 2000 Standard

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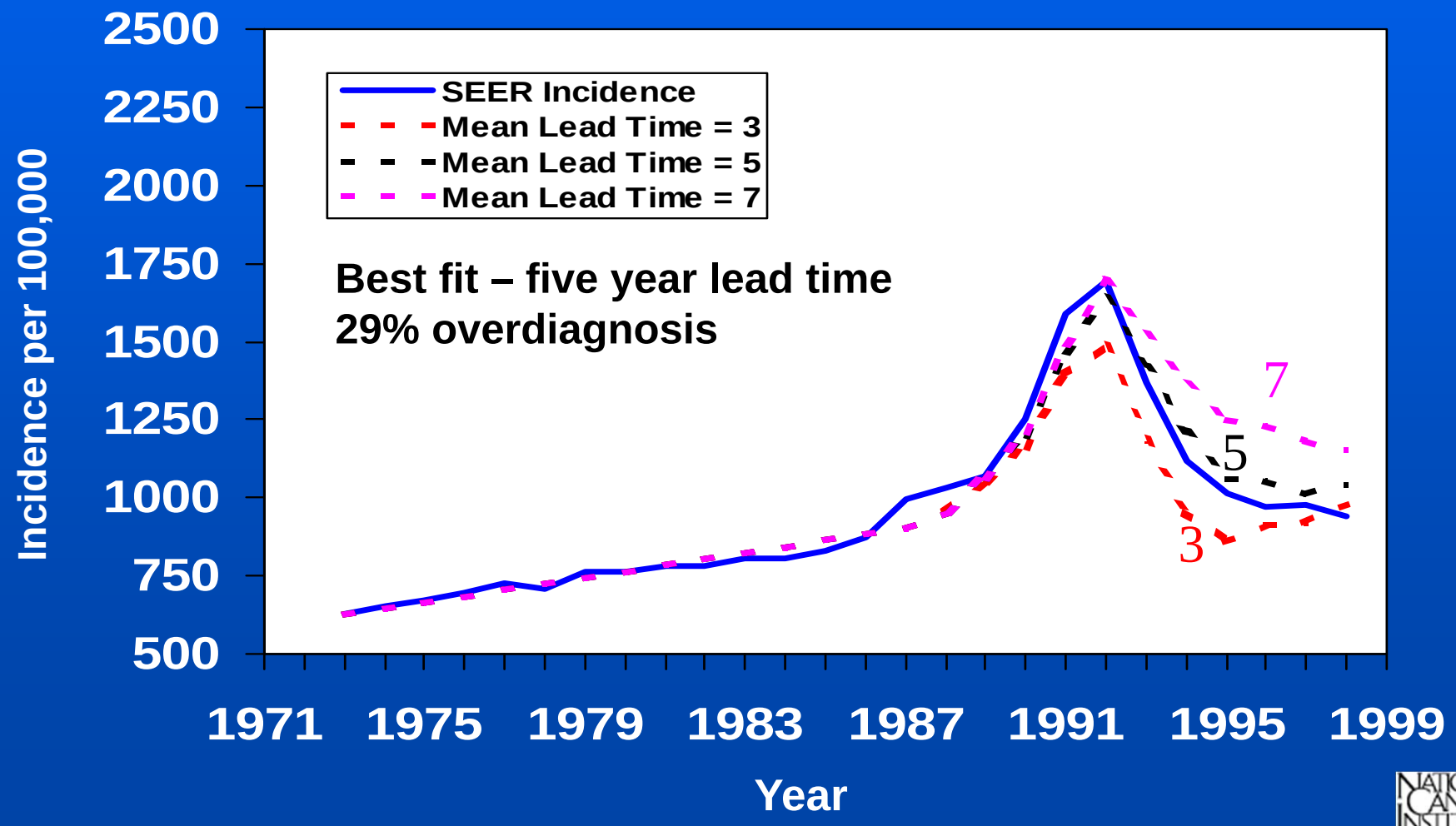
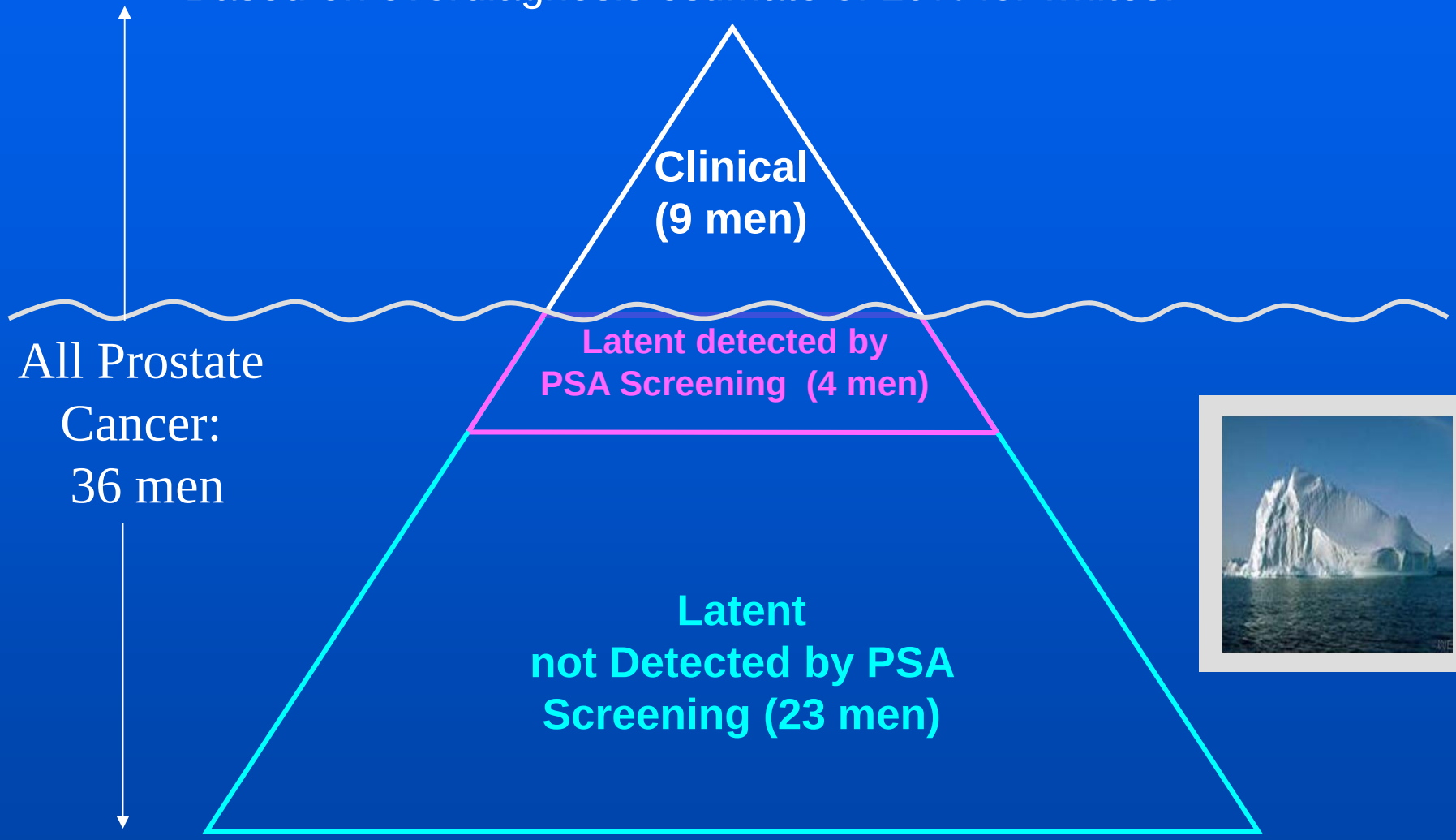
Observed and model-projected incidence for white men aged 70 to 84 under constant secular trend assumption



Overdiagnosis in PSA Testing

Based on overdiagnosis estimate of 29% for whites:



Extent to which PSA reaches into latent reservoir: 4/(4+23) = 15%

[Whites; Etzioni et al, JNCI 2002]

Summary

- Estimates of overdiagnosis are important as we weigh the potential mortality gains of screening against the morbidity burden
- This is a “ballpark” estimate of overdiagnosis
- Interpretation of this estimate is subject to the half empty/half full philosophies of life
  - ***Half empty*** – 29% of PSA detected cases being overdiagnosed represents a lot of unnecessary treatment
  - ***Half full*** – Fears that we were reaching deep into the latent pool appear unwarranted. The tradeoff for some men getting unnecessary treatment is the potential to save other men's lives.
- The challenge of screening is to determine (through various prognostic factors) which screen-detected men are destined to have progressive disease.

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