

# Cancer Intervention and Surveillance Modeling Network: Scientific Update

National Cancer Advisory Board  
June 14, 2006



CANCER INTERVENTION AND  
SURVEILLANCE MODELING NETWORK

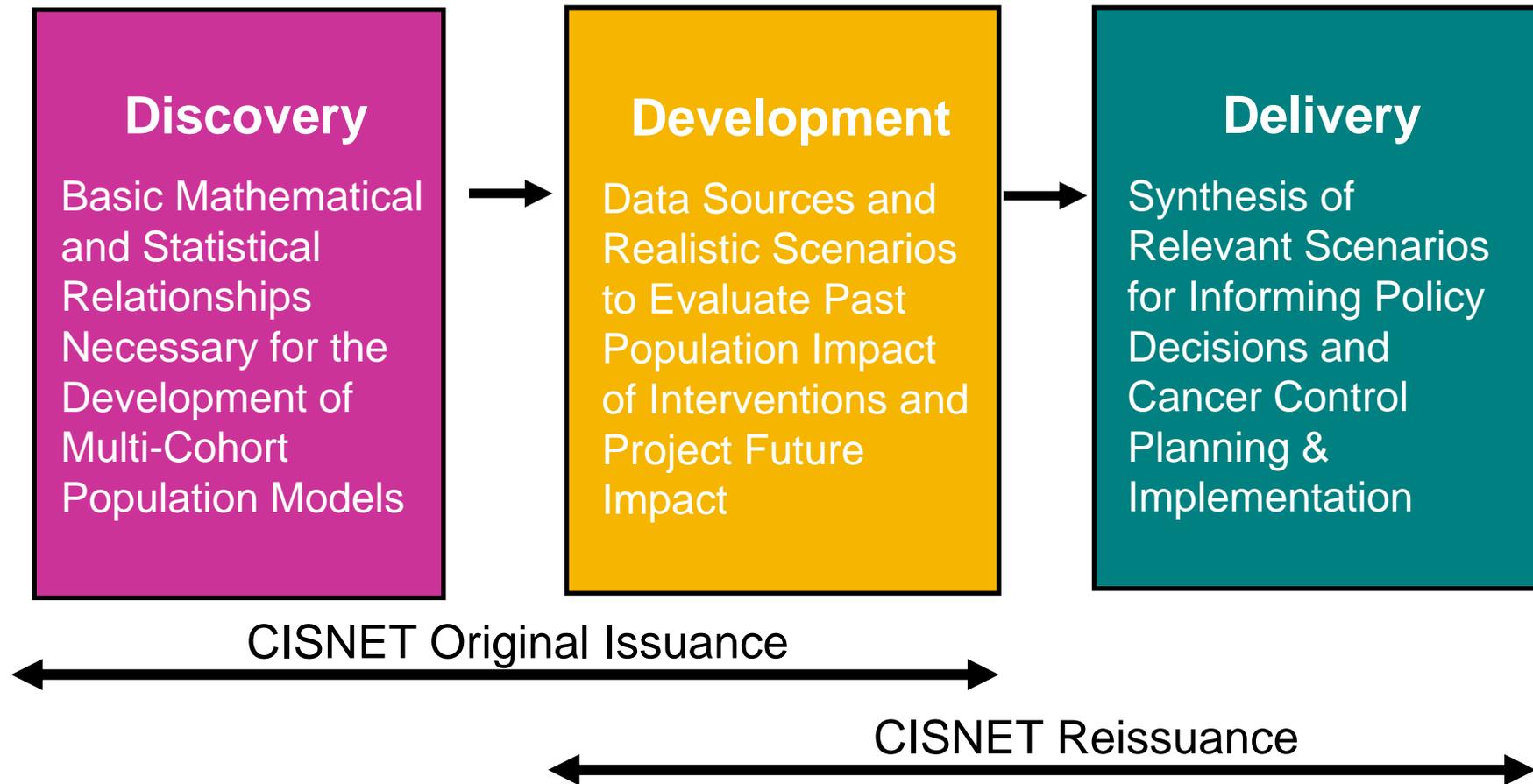
**Eric J. (Rocky) Feuer, Ph.D.**  
CISNET Program Director and Chief, Statistical  
Research and Application Branch, DCCPS

# Cancer Intervention and Surveillance Modeling Network (CISNET)

The logo for CISNET, featuring the letters 'CISNET' in a bold, black, sans-serif font. The letters are set against a background of colorful, interlocking puzzle pieces in shades of purple, yellow, and blue.

- 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
  
- Funding
  - ◆ Originally funded in two phased in rounds (FY00 and FY02)
  - ◆ Refunded in FY05 – total of 15 grants funded in breast, prostate, colorectal and lung cancer
  - ◆ 5 Affiliate Members (Funded through other mechanisms – joined CISNET collaboration)
  
- <http://cisnet.cancer.gov/>

# CISNET Provides Tools for the Evaluation of Delivery of Interventions at the Population Level

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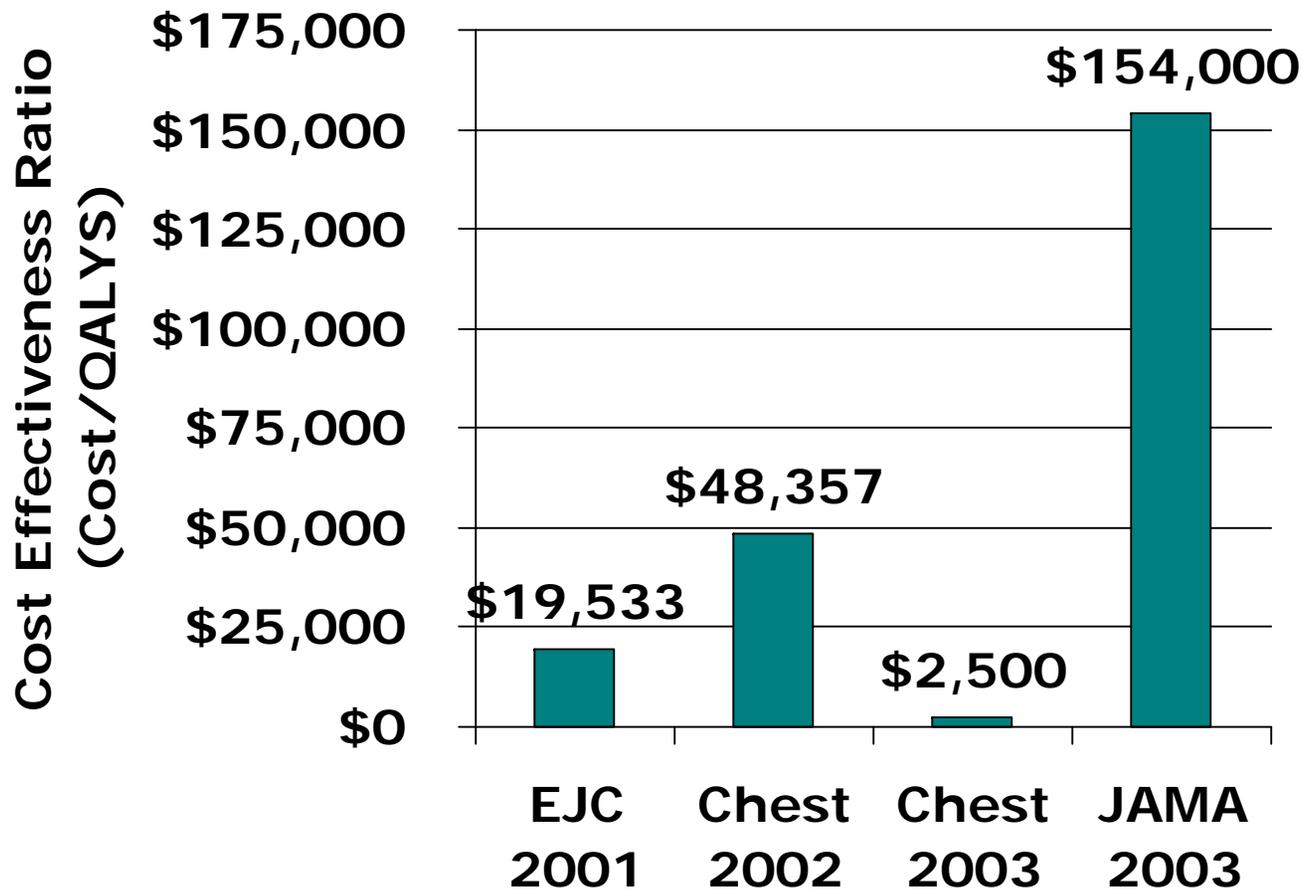
# Delivery: Translating the State-Of-Science to Assist Informed Decision Making

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- **Narrow scientifically focused questions, e.g.**
  - ◆ What is the impact of a single FOBT, flex sig., or colonoscopy at age 65 on prevented cases, adenomas detected, screen and clinically detected cases, and deaths for colorectal cancer
  
- **Broad questions to address national policy issues, e.g.**
  - ◆ What has been the impact of adjuvant therapy and mammography on the decline in breast cancer mortality in the US?

**What's Different about  
CISNET  
From  
Other Modeling Efforts?**

# Results of Four Independent Published Studies on the Cost Effectiveness of Spiral CT Screening



Differences in target population, screening frequency, stage shift, assumptions about lead time and overdiagnosis, sensitivity

# Comparative Modeling Approach



- Define Specified Questions Which are Tackled Jointly
  
- Certain Population Level Inputs are Developed Jointly and Shared, e.g.
  - ◆ Dissemination and patterns of mammography in the US
  - ◆ Dissemination and patterns of PSA testing in the US
  - ◆ Smoking patterns in the US
  
- Other model components (e.g. pre-clinical “natural” history of disease) are left up to the creativity and judgment of the investigators

# Comparative Modeling Approach



- Results are compared at frequent conference calls and biannual meetings
  
- Comparative modeling approach adds credibility
  - ◆ NCI recently applauded by international task force on good modeling practices for supporting CISNET
  
- Comparative analyses provide context for future individual modeling efforts

National Cancer Institute

# Unique Scientific Opportunities for CISNET

U.S. DEPARTMENT  
OF HEALTH AND  
HUMAN SERVICES

National Institutes  
of Health

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# Prostate Cancer: Death Rate Shows a Small Drop. But Is It Treatment or Testing?

In the late 1980's, a blood test for prostate cancer came into widespread use. The test, the P.S.A., can find cancers when they are too small to feel and before they have spread. It is only now being evaluated in clinical trials to see if it reduces the risk of dying from the disease. Gina Kolata asked two experts to assess national data on prostate cancer.

**D**R. IAN M. THOMPSON JR., a urologist and professor of surgery at the University of Texas at Health Science Center at San Antonio, looks at the data on P.S.A. screening and is encouraged.

Before the P.S.A. test came into use, the cancer's incidence was steady from year to year. That changed with increasing use of the P.S.A. for prostate specific antigen. The number of prostate cancer cases diagnosed rose from 143.3 per 100,000 in 1990 to a peak of 195.6 per 100,000 in 1992 and then fell to 155.3 per 100,000 in 1998, the most recent year for which data are available.

The pattern reflects the use of the test, which found men who had cancer and had never before had any kind of test sensitive enough to find it. The incidence fell as more and more men who had had cancer all along were tested and their cancers found.

Before the blood test was introduced, Dr. Thompson said, doctors looked for the cancer by rectal exams, which he said was "not very good." The increasing incidence shows, he said, that the P.S.A. is doing what it is supposed to do — finding cancers early.

As for the mortality rates, Dr. Thompson said they were falling steadily and dropped by 16 percent from 1990 to 1998, going from 38.6 per 100,000 to 32.3 per 100,000. Treatment improved in that time, but Dr. Thompson said that alone was not enough to explain the drop in the death rate. Prostate cancers that have spread to other organs are less common, dropping in incidence by 60 percent from 1990 to 1998.

"Metastatic disease is falling so low that we've never seen those numbers before," he said. That, he says, is a tribute to early detection with the P.S.A. test.

"Yes, there are probably some



J. Michael Short for The New York Times

Dr. Ian Thompson Jr. says P.S.A. tests find prostate cancers early.

people who are treated unnecessarily," he said. "But all of medicine is that way. Is there a chance that when you have your appendix removed it will turn out to be normal? Yes."

Dr. Thompson is 47 and has had a

P.S.A. test; it was normal. He intends to continue having the test and to be treated if cancer is found. The treatment, he said, does not worry him. It is a small price to pay for a potential cure.

**D**R. OTIS BRAWLEY, professor of medical oncology and epidemiology at the Winship Cancer Institute of Emory University, is concerned. National data, he said, make him wonder whether the P.S.A. test is saving many lives.

The test, Dr. Brawley said, has led to a huge increase in the number of prostate cancer diagnoses.

But if the P.S.A. was saving lives, the early diagnosis of prostate cancer should lead to a sharp downturn in its death rate. That has not happened, Dr. Brawley said. While the mortality rate has fallen, it did not fall precipitously and the introduction of better treatments clearly played a role.

Dr. Brawley said the data indicated that the test was finding tumors that would not be noticed and would cause no medical problems. But these tumors look exactly like dangerous ones.

"There are cancers that fulfill all the histological criteria for malignancy," Dr. Brawley said. "When a pathologist looks under the microscope, he says, 'Yes, this is cancer.'"



Marty Katz for The New York Times

Dr. Otis Brawley says screening for prostate cancer may not save lives.

But these tumors are not dangerous, and many that are dangerous may not be cured by early diagnosis and treatment.

"The concept that every cancer that can be found early can be cured

is a faulty concept," he said.

Yet, with no way of knowing which tumors are potentially lethal, doctors usually treat everyone with methods like surgery or radiation that can cause impotence and incontinence.

While the number of men with metastatic disease at the time of diagnosis has gone down, Dr. Brawley says the reason is not necessarily that the P.S.A. test is finding cancers when they can be cured.

Doctors, he said, operate and remove the prostate only when they find no evidence that cancer has spread. Those men are counted as having localized disease. But, he said, within two years, 40 percent of them have recurrences. The cancer had already metastasized, but the spread was not obvious when the original diagnosis was given. Before the test, most of those cancers would have been found after they had spread and counted as metastatic.

Dr. Brawley worries that some doctors are including P.S.A.'s in routine blood tests without discussing these issues.

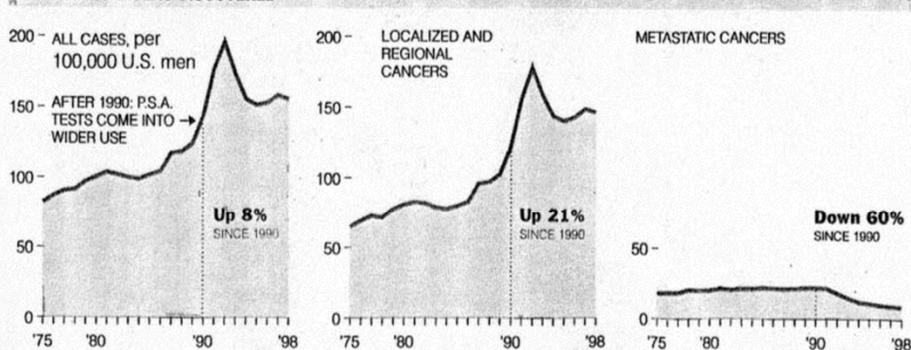
"If a man understands that the test is unproven and still wants it, he should be allowed to get it and should not be criticized," Dr. Brawley said.

At 42, Dr. Brawley has not been tested and does not want to be. Once

## Weighing the Value of Prostate Antigen Tests

How supporters and critics view the data.

### PROSTATE CANCERS DISCOVERED

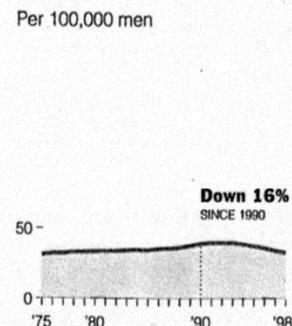


**SUPPORTERS OF THE P.S.A. TEST SAY:** Testing finds cancers. Rectal exams are ineffective at detecting all but late-stage disease, which is difficult to cure. Since the P.S.A., distant-stage cancers are declining.

**CRITICS OF THE TEST SAY:** Many tumors found by screening would not have caused medical problems. But they look like dangerous tumors, so they are treated anyway. The decline in late stage cancer may be because the P.S.A. finds cancers that seem to be early and are listed as such, but are in fact in late stages.

Sources: SEER Program, National Cancer Institute (cases); National Center for Health Statistics (deaths). All statistics are age-adjusted to a 2000 U.S. standard.

### DEATHS



**SUPPORTERS SAY:** Deaths have dropped since the early 1990's.

**CRITICS SAY:** Early detection should lead to lower death rates, but they

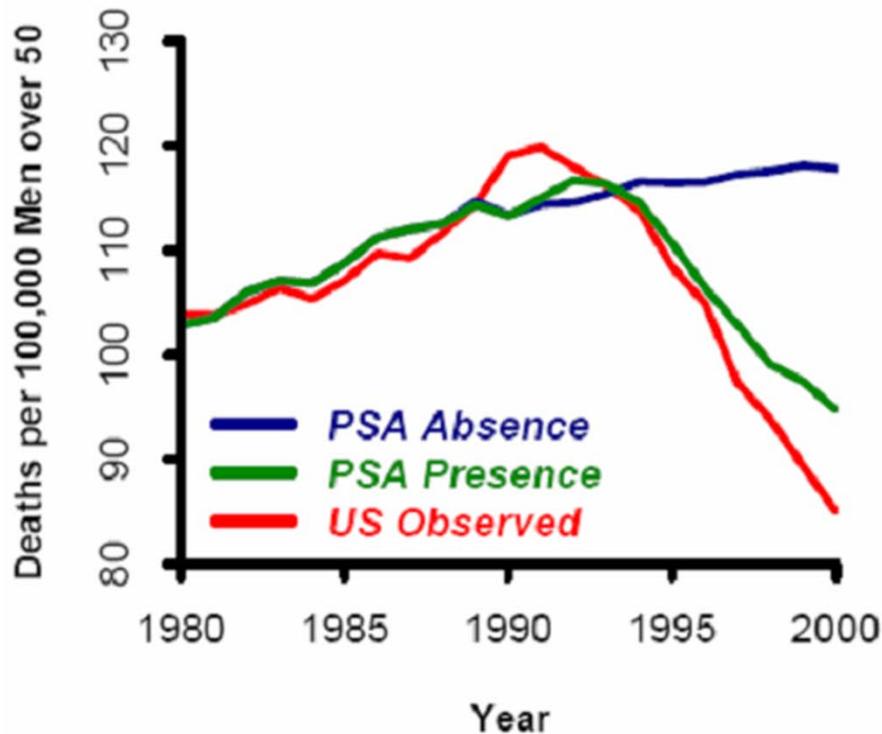
NEW YORK TIMES, April 9 2002

The New York Times asked her to scratch it off, he said.

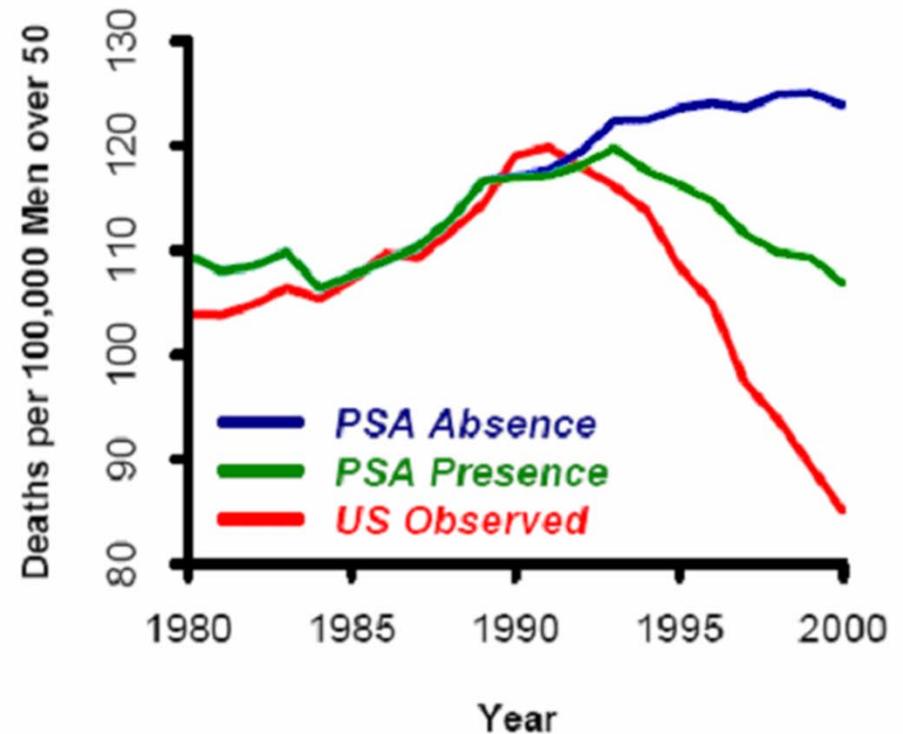
# Decline in Prostate Cancer Mortality Associated with PSA Screening: Results from Two Models

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Panel A: UCD Projected vs Observed



Panel B: FHCRC Projected vs Observed

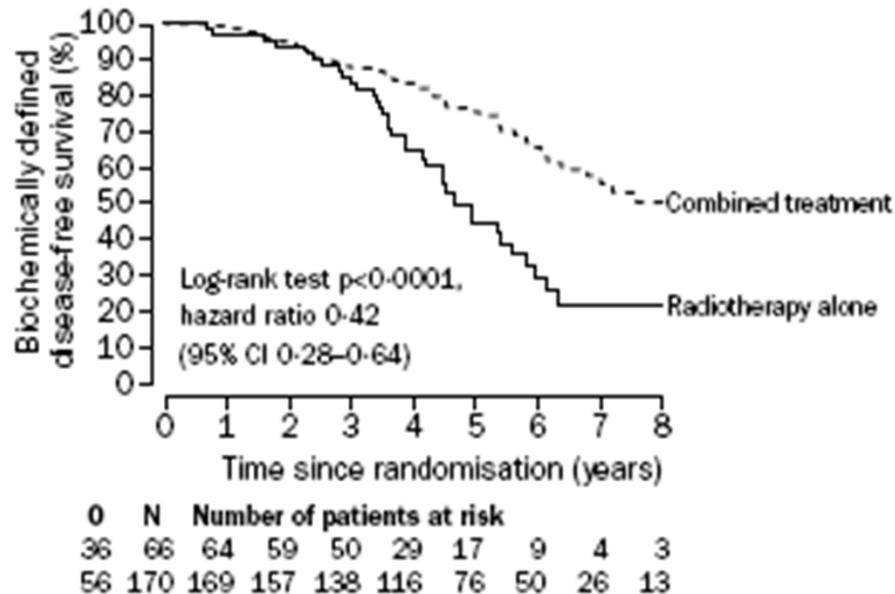


Models suggest that PSA screening can account for about 50%, but not all of the mortality decline due to screening under the stage shift assumption

# Use and Efficacy of Hormone Ablation Therapy Adjuvant to Radiotherapy



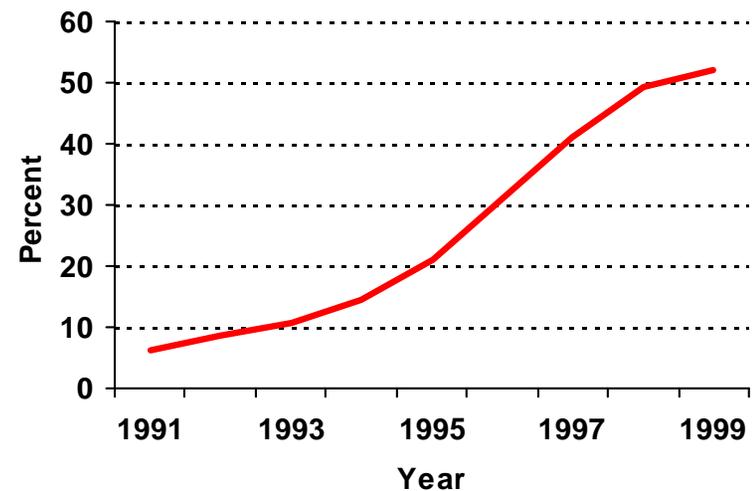
## *Efficacy*



Bolla et al, 2002  
Phase III EORTC Trial

## *Dissemination*

Proportion of Local/Regional EBRT Patients Who Also Received ADT by Calendar Year



Zeliadt et al, 2005  
Source: SEER-Medicare

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# Debates over the Natural History of Lung Cancer and Spiral CT Screening

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- Modeling allows:
  - ◆ Examination of how the growing body of evidence for spiral CT screening enhances understanding of the natural progression of lung cancer
  - ◆ Extrapolation of the conditions of a trial to different scenarios
    - Different smoking history eligibility criteria
    - Different screening schedules
    - Different amounts of non-compliance and contamination
  
- Ongoing discussions to develop collaborations with:
  - ◆ National Lung Screening Trial (NLST – LSS,ACRIN)
  - ◆ Early Lung Cancer Action Project (ELCAP)
  
- Use modeling to develop a platform for focused discussions between the two groups

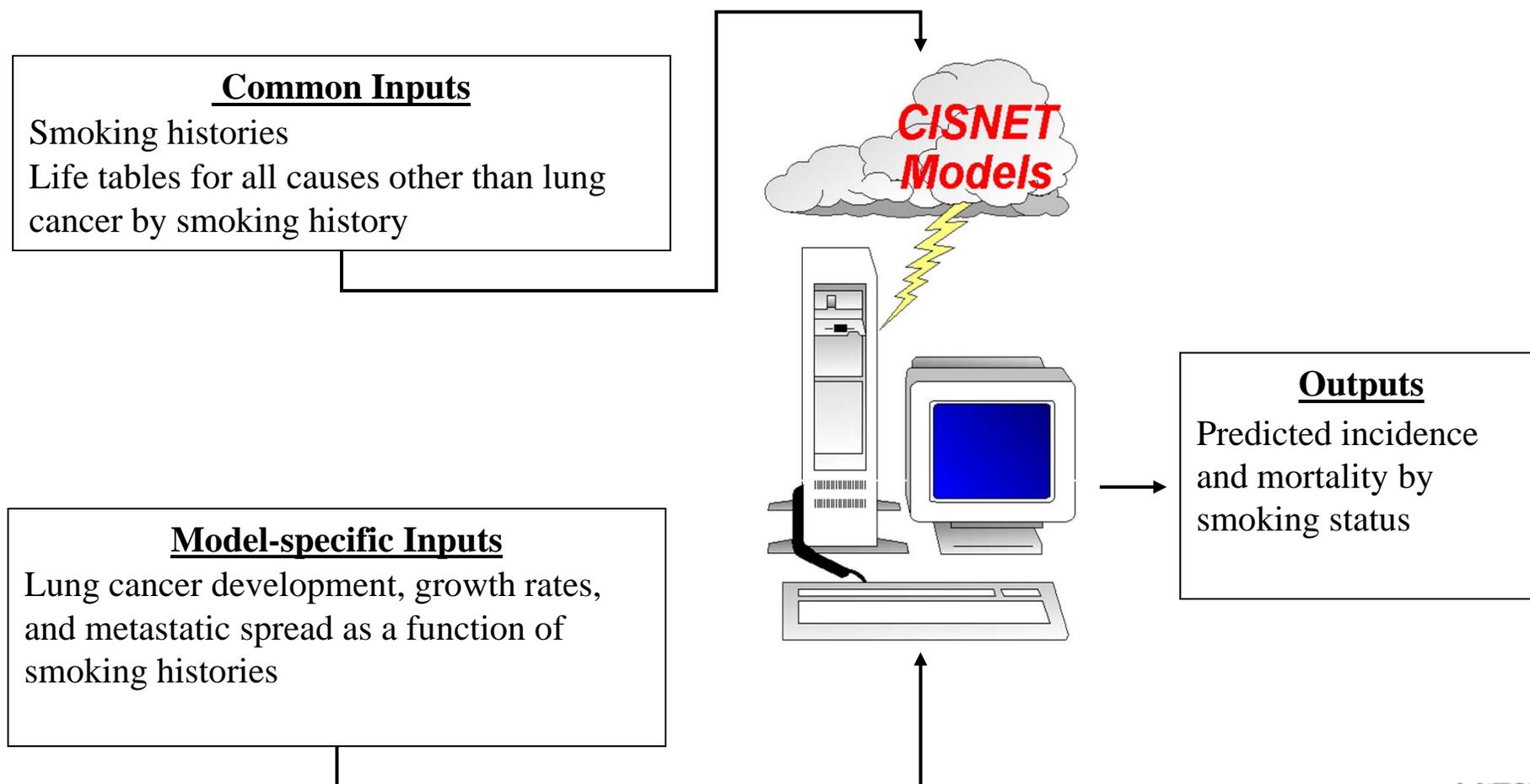
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# How Many Lung Cancer Deaths are Attributable to Never, Current, and Former Smokers given Past and Projected Smoking Histories?

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