



# Modeling Efforts to Inform Countries' Screening Decisions

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- **What is the need for modeling?**
  - CISNET program
  - How to assess screening effect when no RCT?
  - How to assess potential effects of interventions?
  - How to develop a microsimulation model?

## **Example:**

**Will we meet Healthy People 2010 goal?**

**One-third reduction of colorectal cancer mortality by 2010?**

# Cancer Intervention and Surveillance Modeling Network (CISNET): Purpose



- **NCI sponsored consortium of modelers with focus on**
  - **Simulation and mathematical modeling impact of cancer control interventions –, *primary prevention, screening, treatment* -**
  - **Assess current and future population trends in incidence and mortality**
  - **Optimal cancer control planning**

# Cancer Intervention and Surveillance Modeling Network (CISNET): Programs



- **Statistical Research and Applications Branch  
of Division of Cancer Control and Population  
Sciences of NCI**
- **15 grants in colorectal, prostate, breast, and  
lung**
- **3 in colorectal cancer**
  - **MSK-Erasmus (MISCAN)**
  - Harvard School of Public Health
  - Group Health Cooperative
- ***Kathy Cronin of NCI presenting on breast  
tomorrow***

# US Colonoscopy Screening Studies on Neoplastic Yield

	<i>Lieberman</i> VA Study Group 380	<i>Imperiale</i> Eli Lilly	<i>Schoenfeld</i> CONCeRN	<i>Winawer</i> National Colonoscopy Study
Study Design	Non-Randomized	Non-Randomized	Non-Randomized	Randomized Screening Colonoscopy vs Usual Care
Gender	Men (98%)	Men and Women	Women Only	Men and Women
Sample size	3121	1994	1322	1402

*Lieberman. NEJM 2000*  
*Imperiale. NEJM 2000*

*Schoenfeld. 2005*  
*Winawer, Zauber. 2002*

# Comparison of Neoplastic Findings in Colonoscopy Screening Trials

Neoplastic Findings	<i>Lieberman</i> VA Study Group 380 (N=3121)	<i>Imperiale</i> Eli Lilly (N=1994)	<i>Schoenfeld</i> CONCeRN (N=1322)	<i>Winawer</i> National Colonoscopy Study (N=1402)
Any adenoma or CR cancer	<b>38%</b>	<b>23%*</b>	<b>20%</b>	<b>18%</b>
Any <u>advanced</u> neoplasia	<b>11%</b>	<b>5%*</b>	<b>5%</b>	<b>5%</b>
Adv neoplasia in RT colon with no LF adenoma	<b>2%</b>	<b>2%</b>	<b>3%</b>	<b>2%</b>
RT adv neoplasia with no LF adenoma	<b>52%</b>	<b>46%</b>	<b>65%</b>	<b>70%</b>

\*estimated

# Modeling the Impact of Screening Colonoscopy

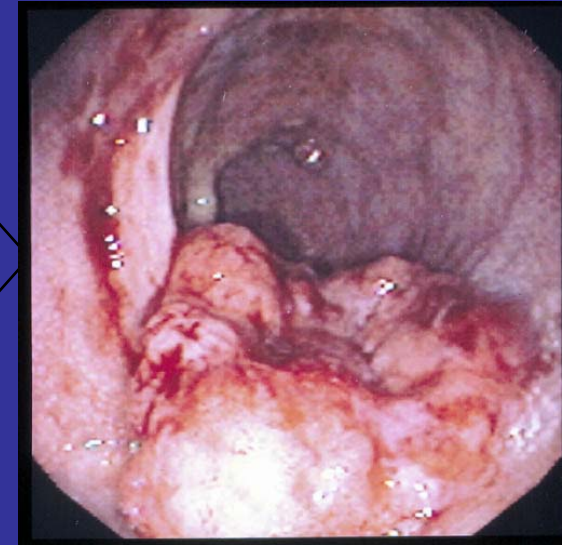
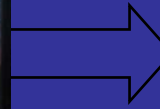
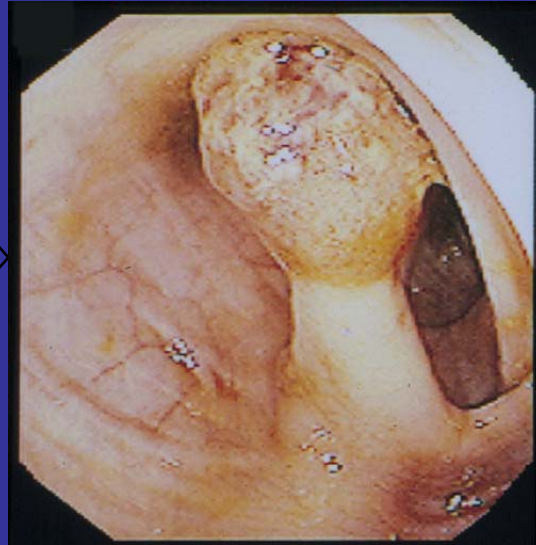
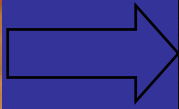
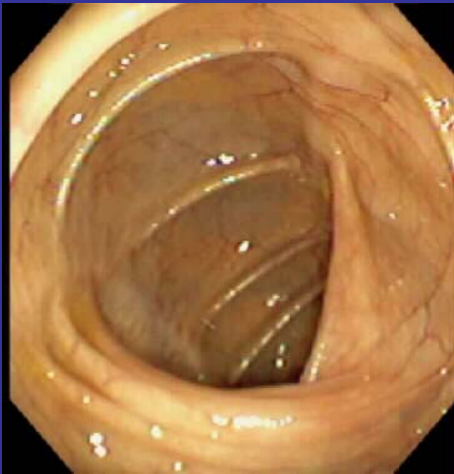


- **Colonoscopy polypectomy effect estimated from flexible sigmoidoscopy RCT's**
  - *Assume comparable effect of left sided and right sided polypectomy*
- **Effect of colonoscopic polypectomy depends on characteristics of those screened**
  - Higher risk screened or worried well?
- *Awaiting the results of the Flex Sig RCTs*

- **Microsimulation Modeling for Colorectal Cancer**



# Adenoma to Carcinoma Pathway



Normal  
Epithelium

Small  
Adenoma

Advanced  
Adenoma

Cancer

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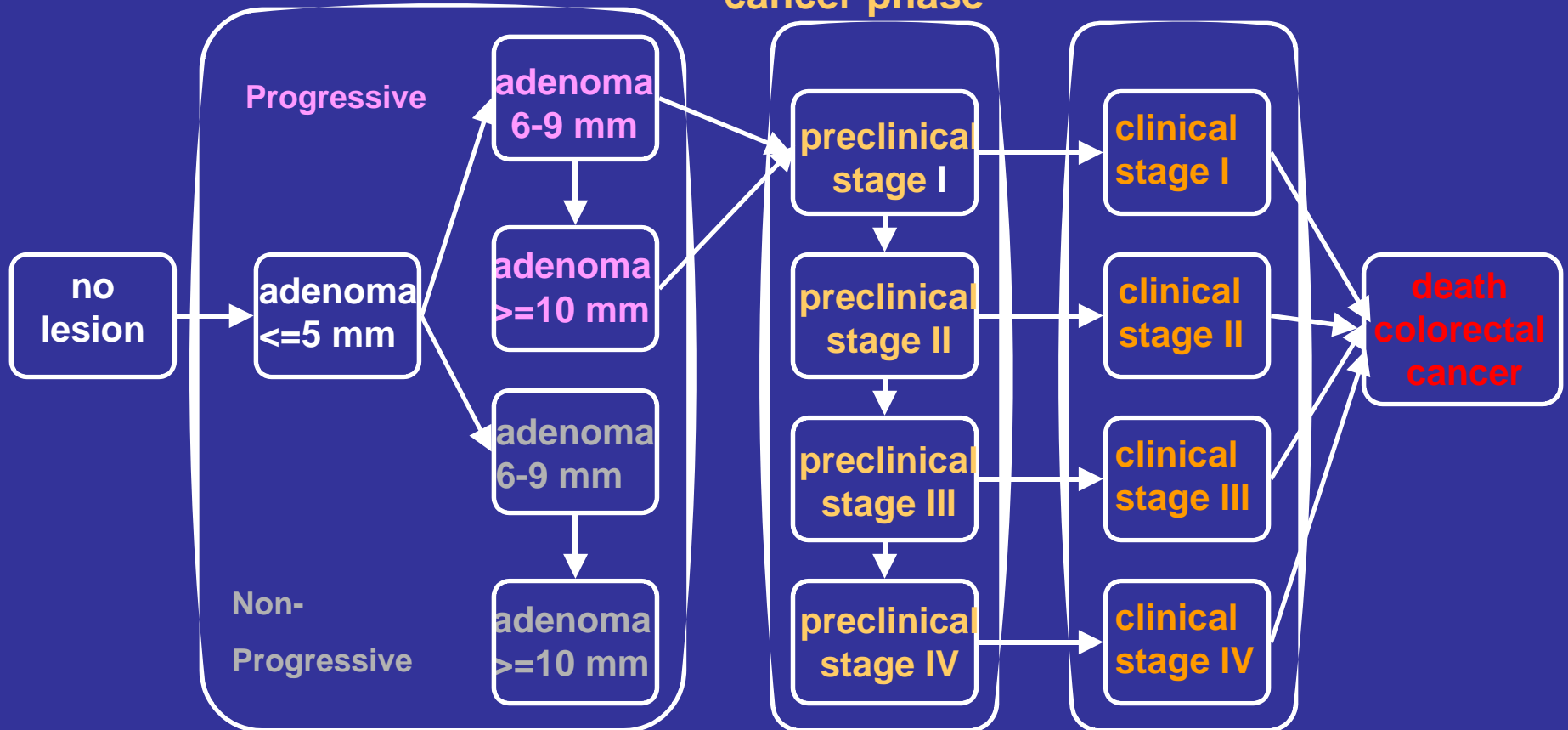
Avg. 10–15 years

# Natural History of Colorectal Cancer

ADENOMA:  
Preclinical screen-  
detectable adenoma  
phase

Preclinical  
CANCER  
screen-  
detectable  
cancer phase

Clinical  
CANCER  
phase

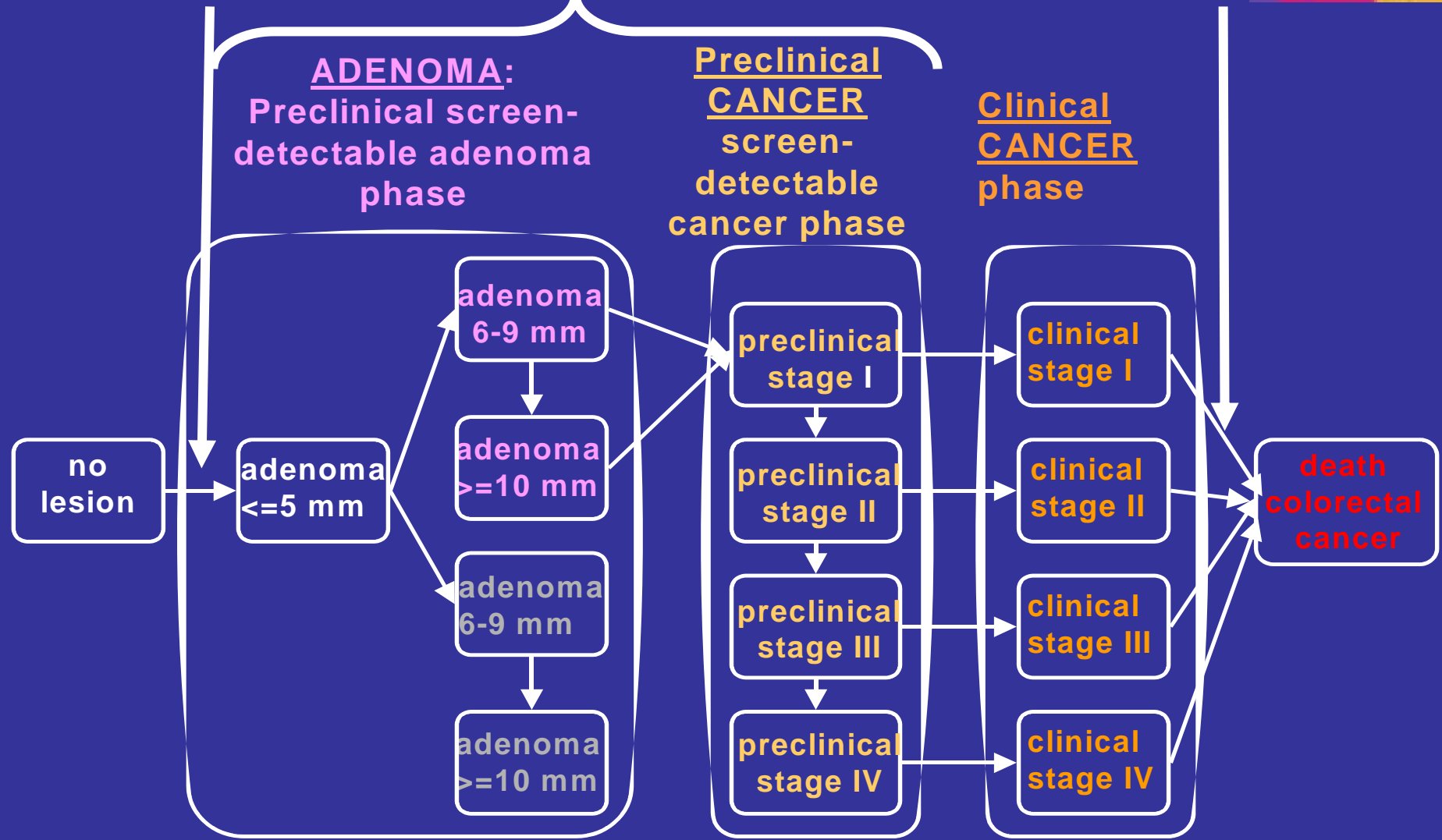


# Interventions on Colorectal Cancer

## Risk Factors

## Screening

## Treatment





# Assumptions - MISCAN-Colon

Parameter	Value	Based on:
Adenoma incidence	Age dependent: 0.9-2.6% per year	Adenoma prevalence in autopsy and colonoscopy studies
Duration progressive adenomas	16.4 years	} 20 years Expert opinion and exponential distribution
Duration pre- clinical disease	3.6 years	
Duration of non- progressive adenomas	Lifetime	Expert

# Types of Factors for Intervention

RISK FACTORS	SCREENING	TREATMENT
Smoking	FOBT	1-drug: 5-FU ( <i>pre-1996</i> )
Obesity	Flex Sig	2-drug: 5-FU and irinotecin
Red meat	Colonoscopy	( <i>post 1996</i> )
No physical activity		3-drug: 5-FU+irinotecan+oxaliplatin ( <i>post 2002</i> )
No folate (multivitamins)		3-drug + biologics (bevacuzimab/cetuximab)
No aspirin		( <i>post 2004</i> )

Relative risk of factor and prevalence of factor in population included in model

# Microsimulation of US Population

2000

- Age, sex, race of US population 2000

*from multiple birth cohorts*

- Risk factor prevalence
- Screening utilization
- Treatment dissemination



# HP2010 Objective: 33% reduction in CRC mortality by 2010

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- Use micro-simulation modeling to determine
  - if reaching Healthy People 2010 goals for **treatment, screening and prevention**
  - will enable us to
  - **fall short, meet, or exceed** 2010 mortality goals of 33% reduction in CRC mortality
  - potential interventions to reach 2010 goals

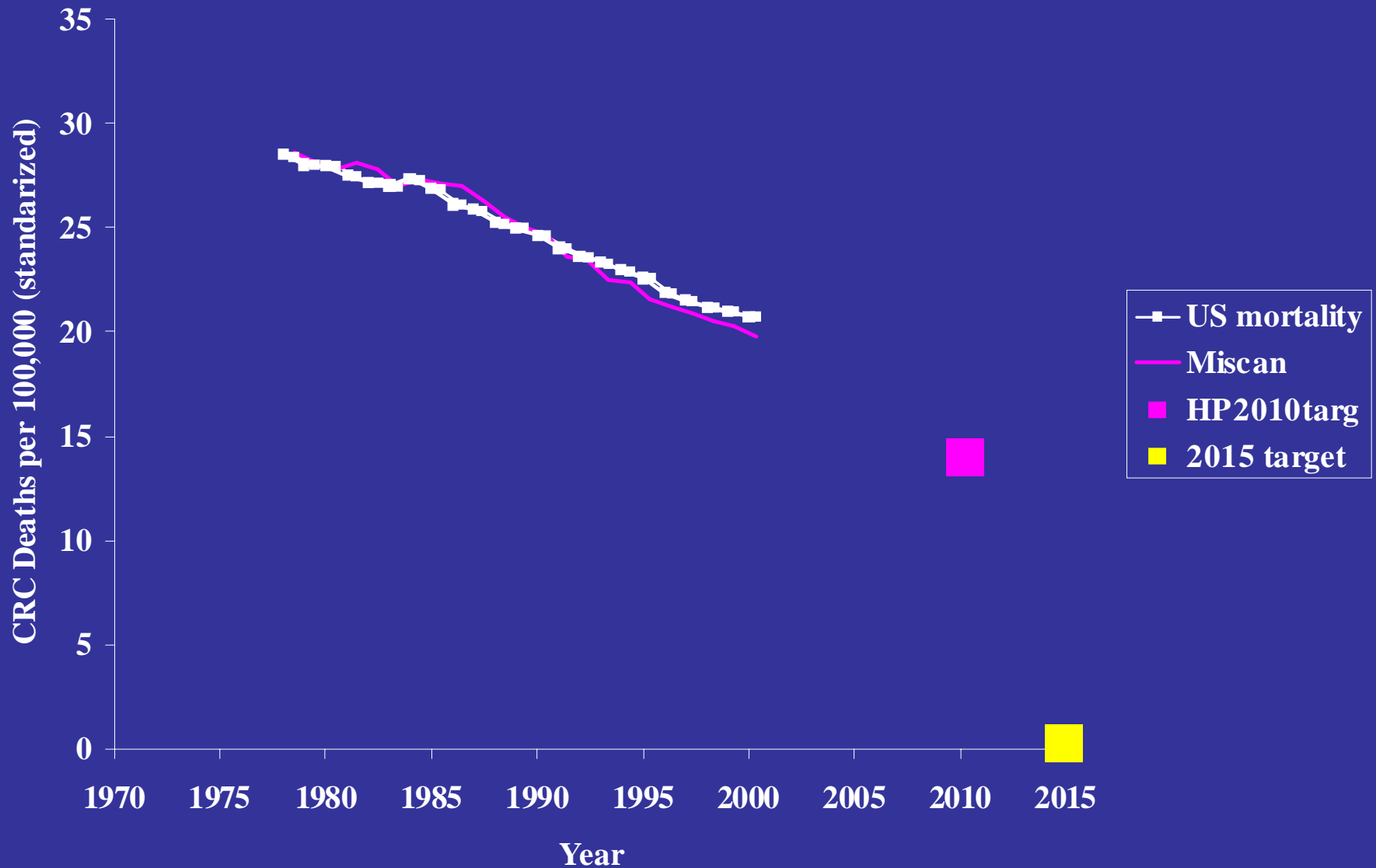
# Four Intervention Scenarios

<b>Frozen 2000</b>	All factors stay at their 2000 level.
<b>Extrapolated</b>	All trends from 1995 to 2000 continue at their current rates until 2020.
<b>Optimistic</b>	From 2005 onwards: <ul style="list-style-type: none"><li>•Risk factor prevalence improves by another 2% per year (obesity stabilizes at its 2005 level)</li><li>•CRC screening rates increase to 70% by 2010</li><li>•CRC patients get best treatment available</li></ul>
<b>Best Case</b>	From 2005 onwards: <ul style="list-style-type: none"><li>•All risk factors eliminated</li><li>•All age <math>\geq 50</math> have CRC screening</li><li>•All CRC patients receive optimal treatment</li></ul>

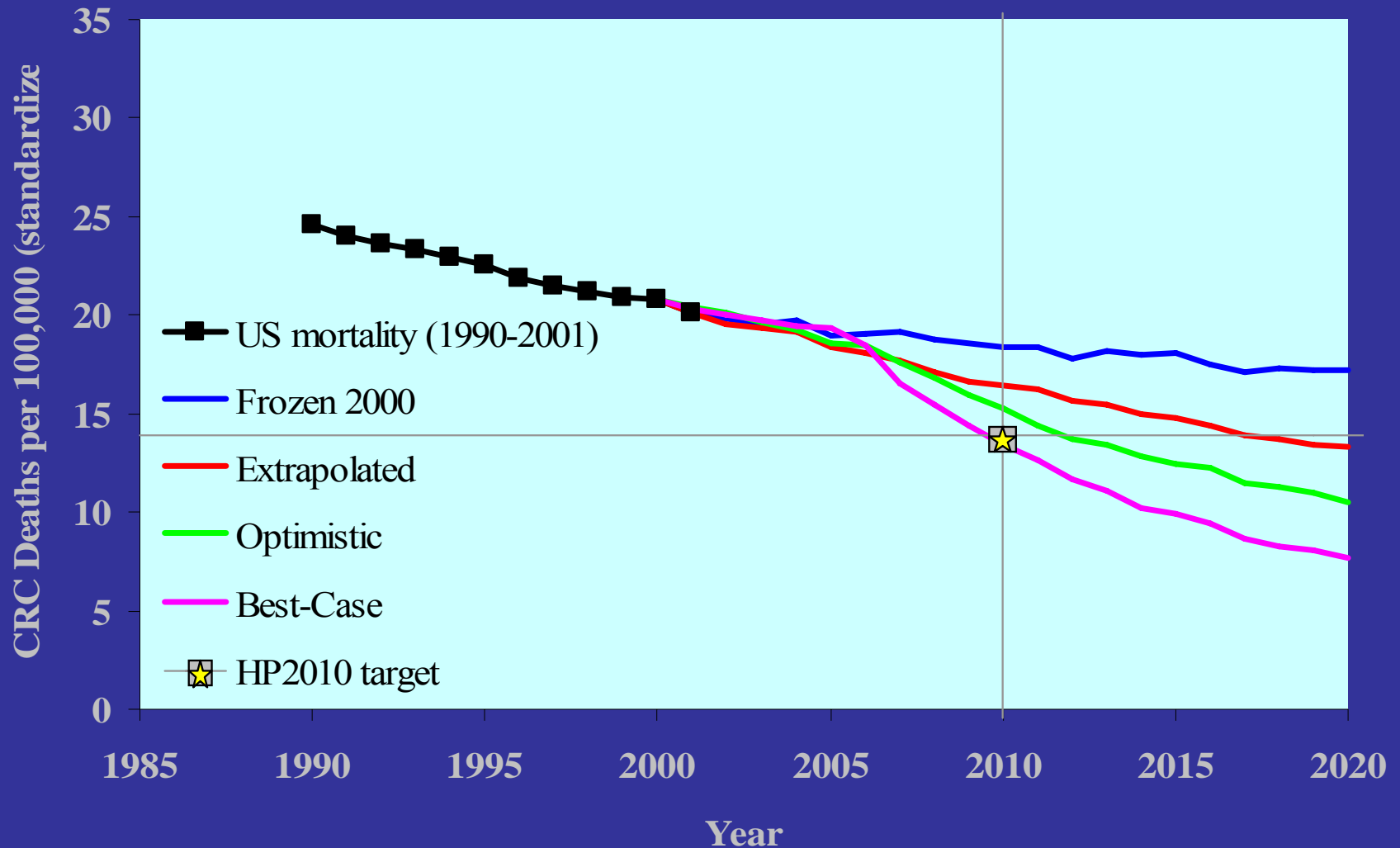


# US Colorectal Cancer Mortality Rates

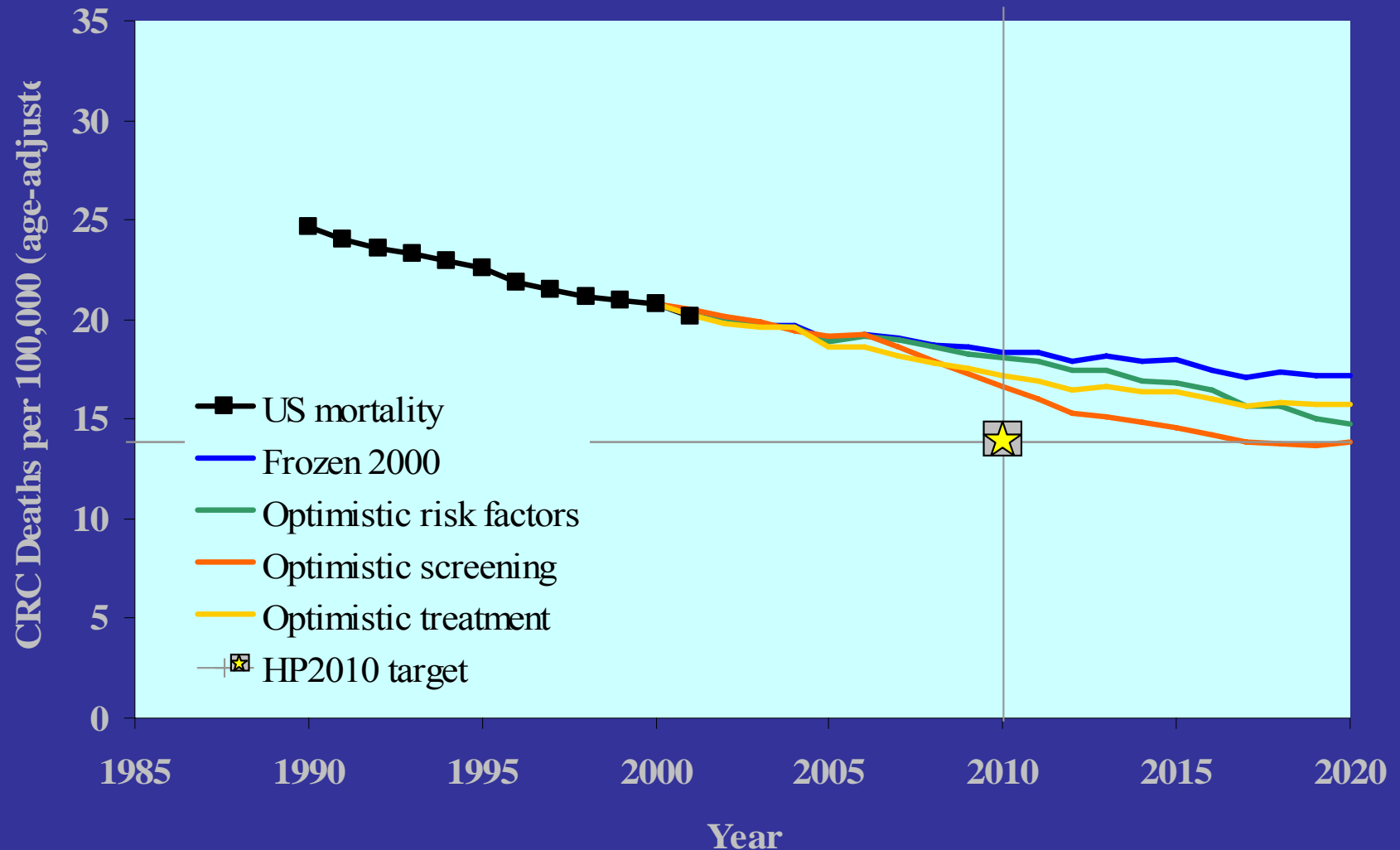
Observed and Model Predicted, with Healthy People  
2010 Goal



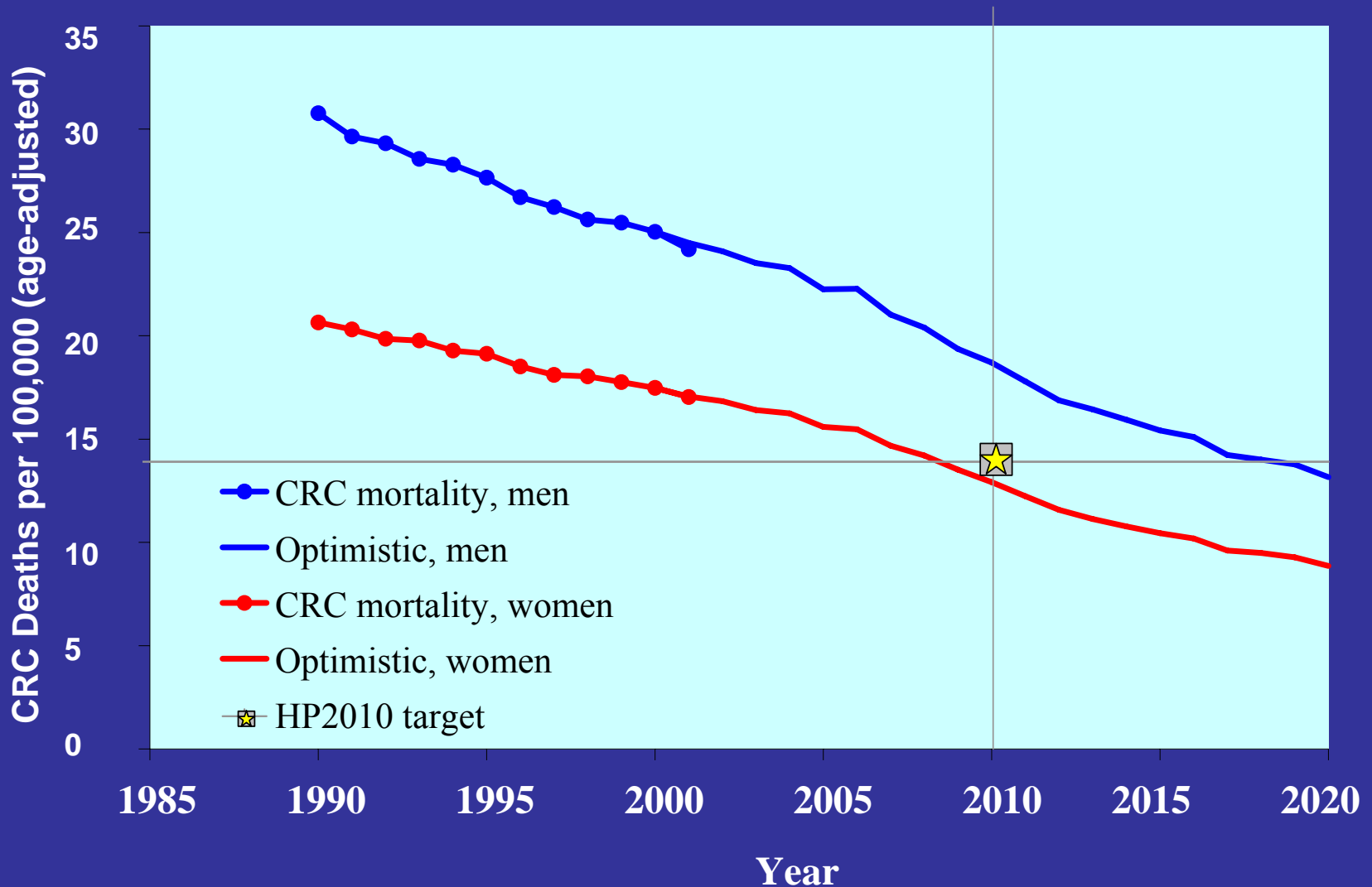
# Projected CRC Mortality for 4 Scenarios



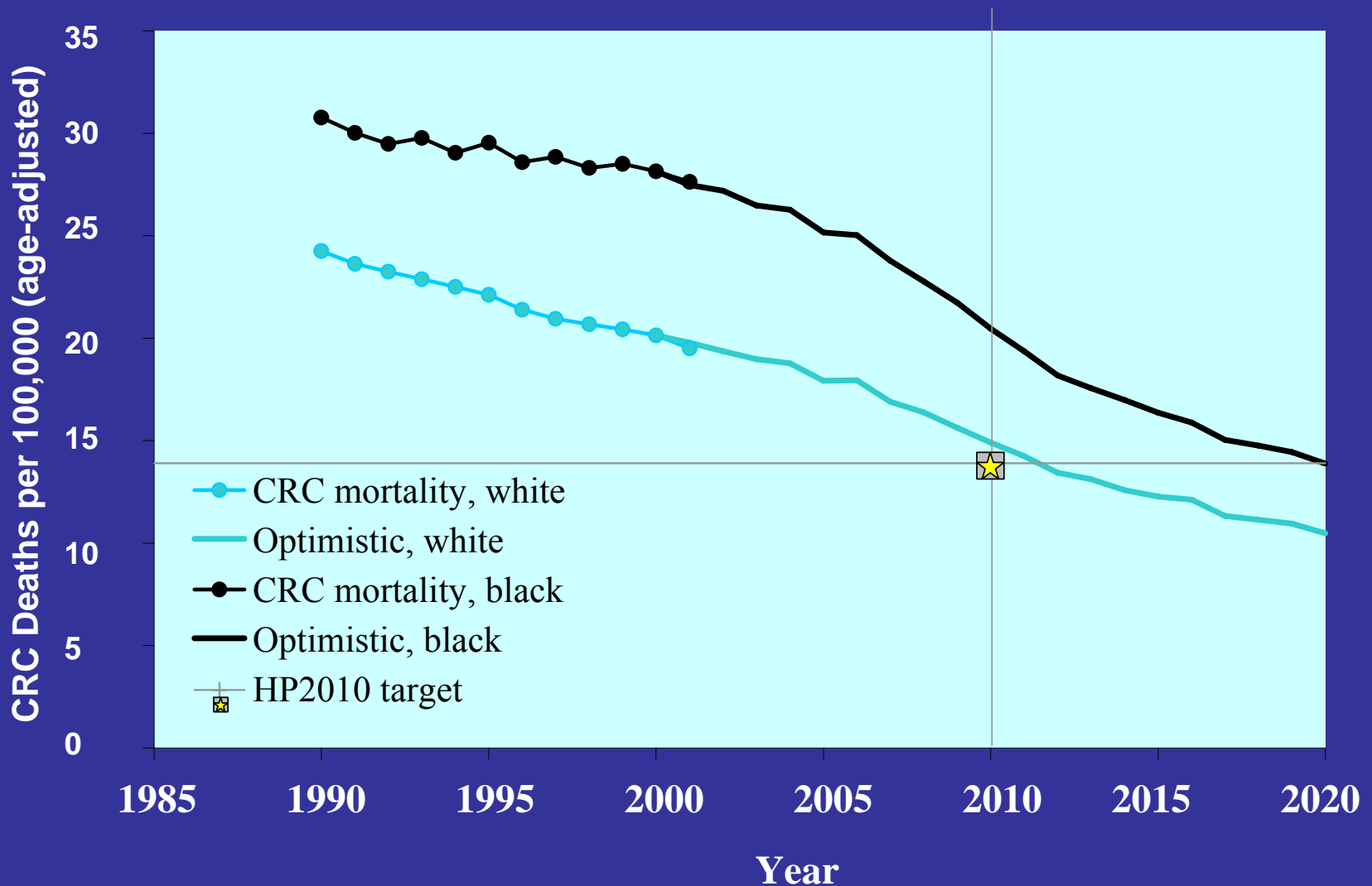
# Projected CRC Mortality for Optimistic Scenario by Risk Factor, Screening, and Treatment Interventions



# Projected CRC Mortality for Optimistic Scenario for Men and Women



# Projected CRC Mortality for Optimistic Scenario for Black and White



# **Effectiveness of Interventions**

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- **Widespread use of currently available technologies can reduce CRC mortality almost 50% from 2000 to 2020 in the US.**
- **In the short term screening provides the largest effect on CRC mortality**
- **In the long term risk factor reduction has a strong effect on CRC mortality**

# Cancer Mortality Projections Web Site Under Development



National Cancer Institute

U.S. National Institutes of Health | [www.cancer.gov](http://www.cancer.gov)

## Cancer Mortality Projections

Modeling the impact of cancer control efforts on US cancer mortality

SEARCH

Home

About CISNET

Modeling

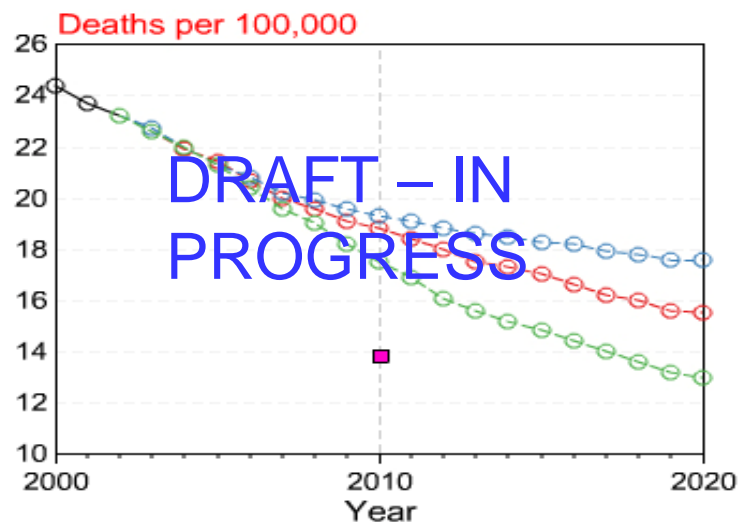
Colorectal Cancer

Breast Cancer

- Colorectal Home
- Overview
- Results
- Simulation Models
- Risk Factors
- Screening
- Treatment
- Interactive Graphs

### Colorectal Interactive Graphs - MISCAN Model

Projected colorectal cancer mortality rate, by calendar year and scenario



- HP 2010 Goal
- MISCAN : PT - ALL
- MISCAN : DFG - ALL
- US Vital Statistics
- MISCAN : PT - 2004

#### Sex

- Both
- Men
- Women

#### Race

- All
- Black
- White

#### Baseline

- Continuation of current trends (PT ALL)
- Continuation of 2004 levels (PT 2004)

#### Difficult but Feasible Goals Met

- All difficult but feasible goals met (DFG ALL)
- All Risk Factors (DFG RF)
- Screening (DFG SCR)
- Risk Factors and Screening (DFG RF-SCR)
- Treatment is best available (DFG TT-TD)
- More treated with best available (DFG TT)
- More patients are treated (DFG TD)
- Body Mass Index (BMI) (DFG ODA)
- Multivitamin (DFG MV)
- Smoking (DFG SMK)

#### Healthy People 2010 Goals Met

- All HP2010 goals met (HPG ALL)
- All Risk Factors (HPG RF)
- Screening (HPG SCR)
- Risk Factors and Screening (HPG RF-SCR)
- Body Mass Index (BMI) (HPG ODA)
- Multivitamin (HPG MV)
- Smoking (HPG SMK)

\* Age-adjusted to the 2000 standard population using age groups <1y, 1-4y, 5-14y, 15-24y, 25-34y, 35-44y, 45-54y, 55-64y, 65-74y, 75-84y, 85+y  
 † Treatment-related goals were not included in the Healthy People 2010 goals. We included treatment goals to evaluate the potential impact on colorectal cancer mortality

# Potential Impact for Other Countries?



- **How would we model the effect of screening interventions in other countries?**
  - **Assessing past impact**
  - **Projecting future impact**



# Inputs for population based microsimulation modeling for another country



- Population in 2000 by age-group
- *Life tables (all cause mortality) per 5 –year birth-cohort from births 1900-2000*
- Age-specific incidence of CRC in 2000
- Stage Distribution of CRC in 2000
- Relative Survival by Stage
- Or
- *Age-specific mortality of CRC in 2000*
  
- *Risk factor, screening, and treatment prevalence*



- **Customizing screening intervals by race and gender**
- **Customizing surveillance intervals by characteristics of adenomas detected at screening**
- **Customizing screening tests by personal characteristics**

# Acknowledgements



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