

Maria E. Mayorga, PhD
Professor of Personalized Medicine



**EDWARD P. FITTS DEPARTMENT OF
INDUSTRIAL AND SYSTEMS ENGINEERING**

Center for Healthcare Engineering & Patient Safety
University of Michigan
September 24, 2018

Precision Medicine Cluster

- The goal of precision medicine is to make optimal treatment decisions for an individual patient based on all information available thus allowing the tailoring of treatment to the patient.
- A partnership of faculty from the Statistics, Mathematics and ISE departments
- What we can bring: the development and implementation of quantitative methods toward this goal

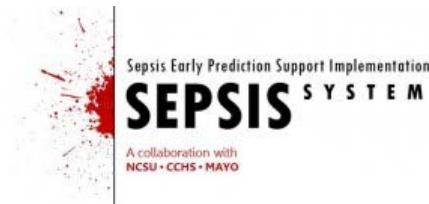
“the right treatment for the right person, at the right time”

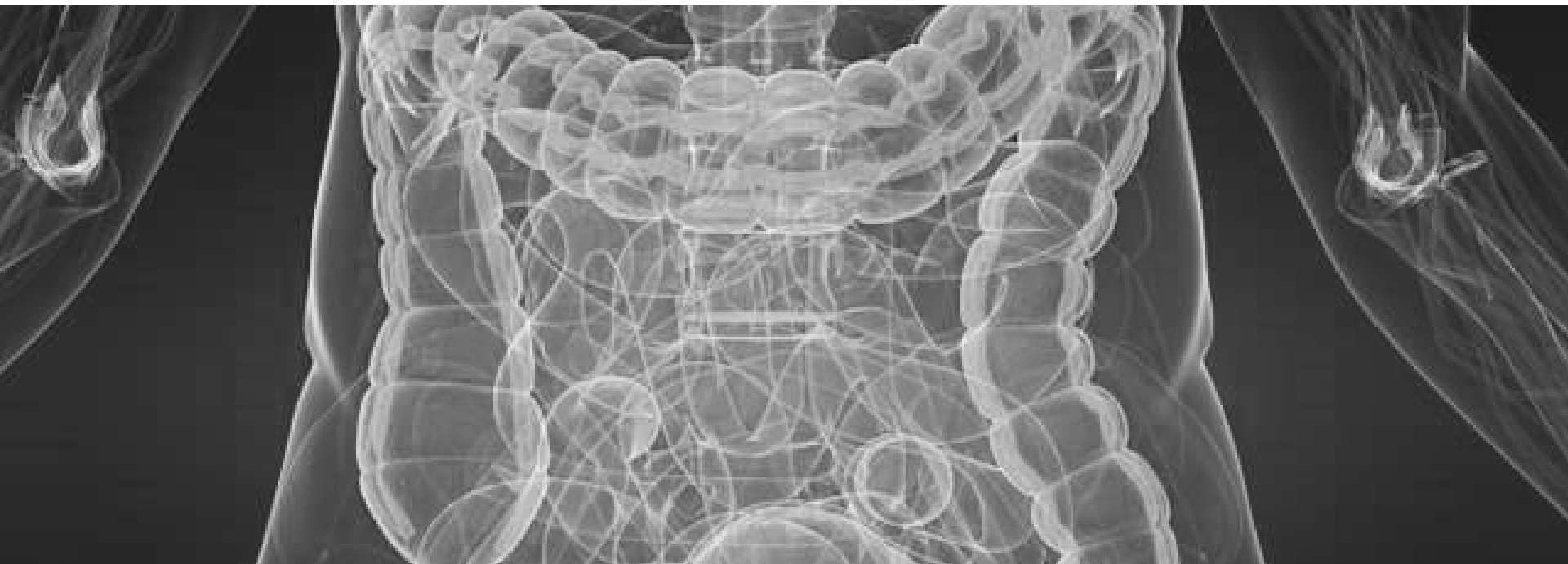
My Research Interests

- Modeling, analyzing and optimizing service systems under uncertainty and with heterogeneous consumers
- Goal is to use Operations Research to make recommendations that have a broad impact, **inform policy level decisions and reduce inequality**
- Focus on the human condition can be divided into two main streams:
 - Predictive models of health and economic outcomes
 - Resource allocation in emergency and disaster situations

Predictive Models of Health Outcomes

- Use multiple sources of secondary and observational data and a mixed methods approach to enable predictions of health outcomes at levels for which it is difficult to conduct studies in practice





THE IMPACT OF INSURANCE EXPANSION ON COLORECTAL CANCER SCREENING



Stephanie Wheeler,



Melinda Davis,



Rachel Townsley



Kristen Hassmiller



Stephanie Renfro
Bonnie Lind
Yifan Gu



Sid Nambiar

Meghan O'Leary
Leah Frerichs

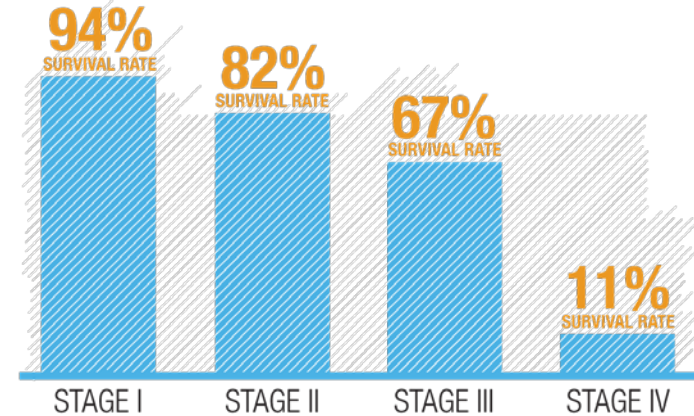
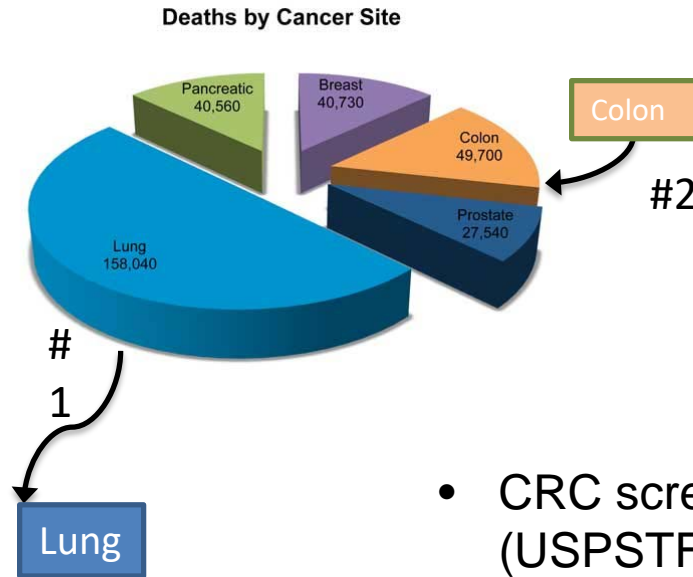


THE UNIVERSITY
of NORTH CAROLINA
at CHAPEL HILL



CPCRN
Cancer Prevention and
Control Research Network

Background on Colorectal Cancer



- CRC screening is recommended for adults ages 50-75 (USPSTF)
- Effectively reduces CRC incidence and mortality
- Is cost-effective

CRC screening

- Is underutilized, 62% up to date (in 2015)
- 27% had never screened (in 2012)
- Lower screening rates
 - 58% for younger adults (50-64)
 - 52% for Latinos
 - 48% for those living in poverty
 - 45% for those without HS graduation
 - 27-47% for those living in rural areas

* Sources: Behavioral Risk Factor Surveillance System (BRFSS), ACS

Setting the Stage

- High differential in screening rates associated with Insurance
 - proportion that had never been screened was greater among those without insurance (55.0% vs. 24%) and without a regular care provider (61.0% vs. 23.5%)
 - Up-to-date among younger adults, 25% for uninsured, 57% for publically insured (vs. 62% for privately insured)
- Patient Protection Affordable Care Act (ACA)
 - Signed into law March 23 2010
 - Health insurance exchange rolled out Oct 1 2013
 - Bulk of provisions rolled out 2013 and 2014
 - “No cost sharing on essential preventative care”
 - [Medicaid Expansion](#)

Research Questions

What is the impact of Medicaid expansion and ACA on colorectal cancer screening?

What is the potential impact of changes in screening on long term outcomes?

NC-CRC Simulation Model

- Developed a geo-spatially explicit, population-based, individual-level, discrete event simulation model of the natural history of CRC progression and of screening behavior
- Accounts for heterogeneous compliance with screening and choice of modality
- Used synthetic population and cancer registries in North Carolina
- Analyzed cost-effectiveness of interventions being considered by CDC and North Carolina
- Partnered with Oregon to expand model beyond NC

Demography

Census data
2005-2010 American
Community Survey/Public
Use Microdata Sample

Project from
sample to
population

Synthetic population
Realistic population of all
individuals who will be eligible
for CRC screening over the
10-year policy window

Population
input file

Natural History

RTI Model
Natural history of adenomas
and cancer

Cancer Registry
Population-based data on
incident CRC cases (counts,
patient demographics, stage
at diagnosis)

Calibration of CRC
natural history
parameters

Parameter
estimates

Screening and Testing

Claims data
Medicare, Medicaid, Blue
Cross Blue Shield and linked
community data such as the
Area Resource File

Statistical model
development and testing

Statistical models
Logistic regression models
predicting individuals'
preferred screening modality
and likelihood of compliance

Predicted
probabilities

Literature Review
Evidence on interventions
to increase CRC screening,
existing CRC simulation
models, and cost studies

Interventions to consider;
intervention effects and costs

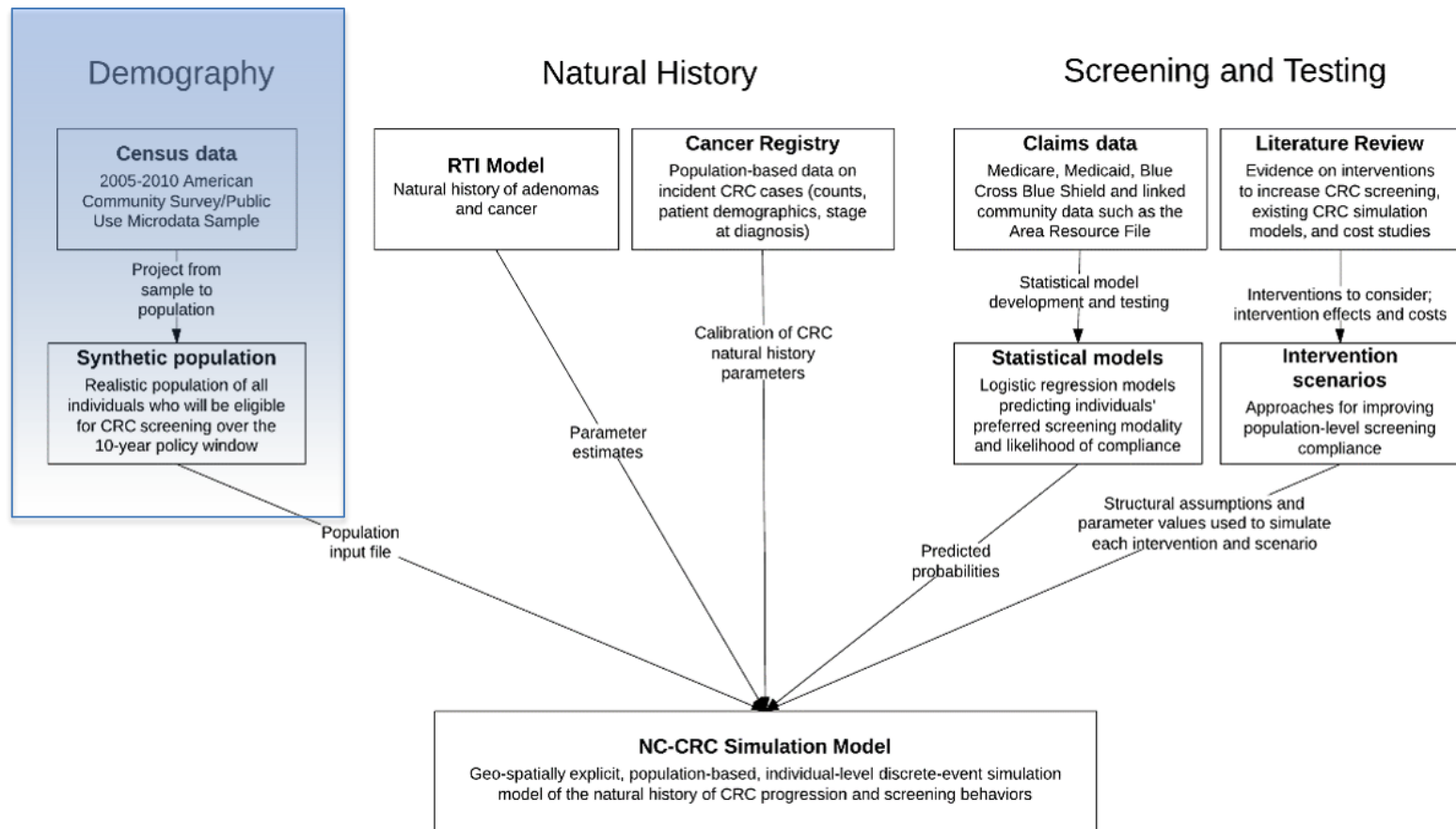
**Intervention
scenarios**
Approaches for improving
population-level screening
compliance

Structural assumptions and
parameter values used to simulate
each intervention and scenario

NC-CRC Simulation Model

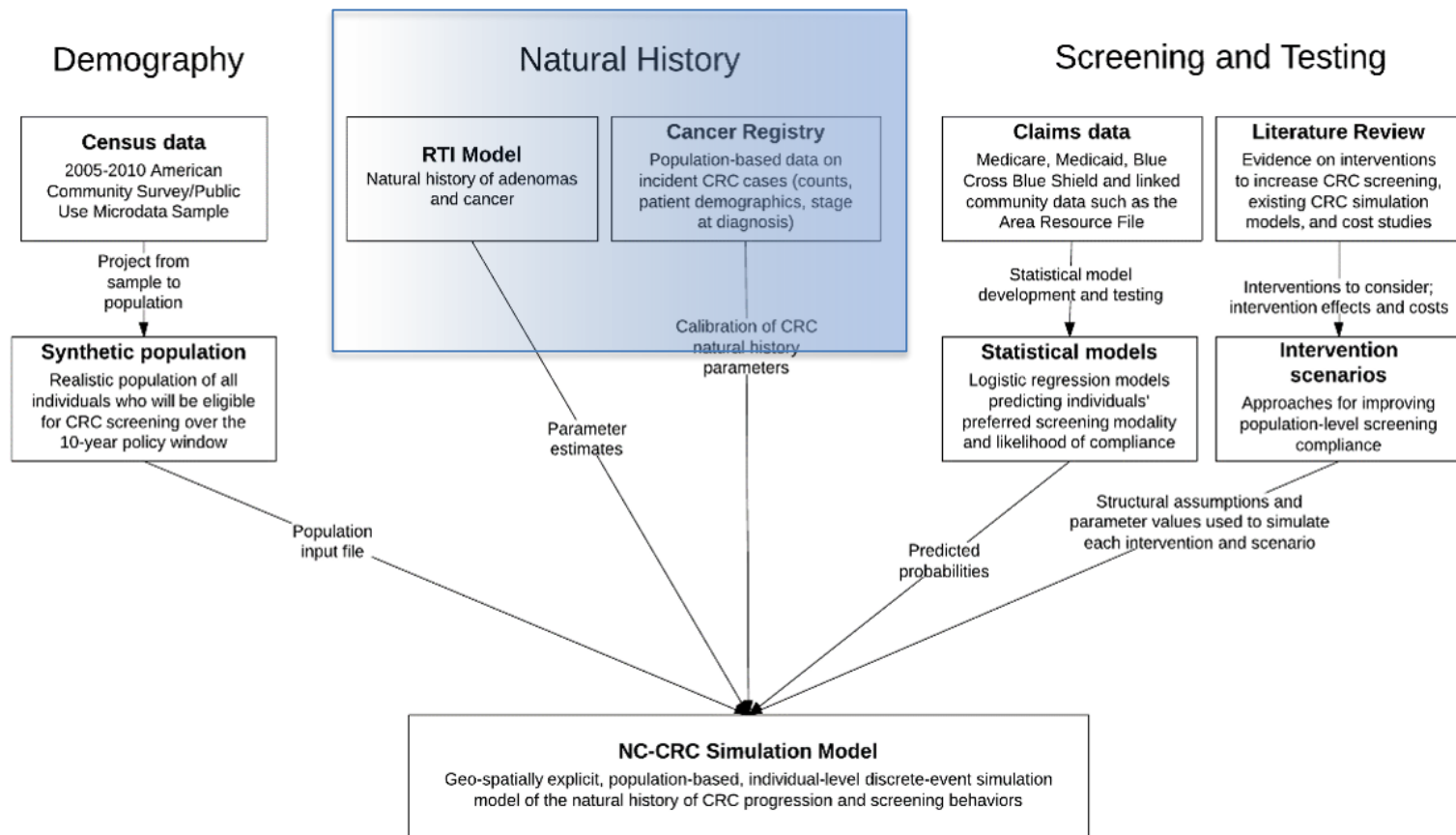
Geo-spatially explicit, population-based, individual-level discrete-event simulation
model of the natural history of CRC progression and screening behaviors





Demography and Synthetic Population

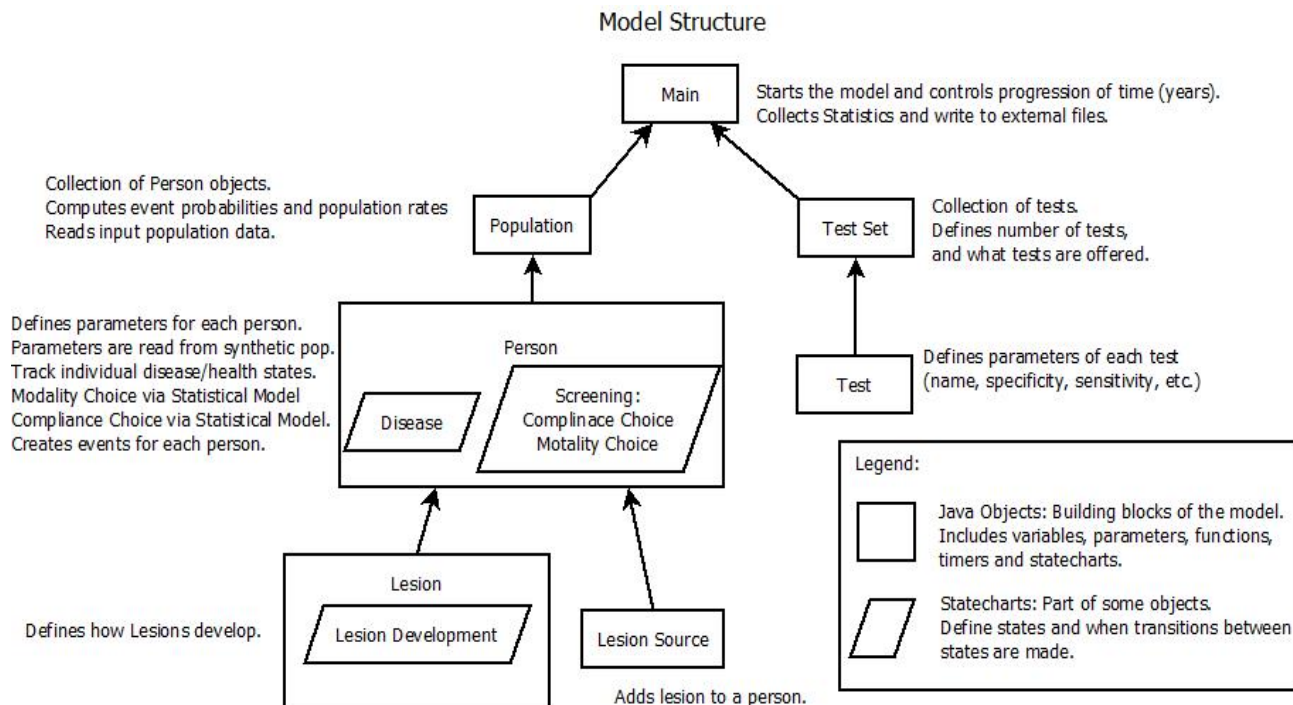
- We use a synthetic population that is designed to be realistic (useful!) but not real (a pain!)
- The population was created using the American Community Survey (ACS) of the U.S. Census Bureau from 2005-2009
 - Four variables were used to de-identify households by intelligently “shuffling”: age, race, income and household size
 - There is no health insurance indicator in the ACS, so we used the four ACS variables to estimate predicted probabilities of each insurance type for each individual based on 2010 ACS sample data using multinomial logit model



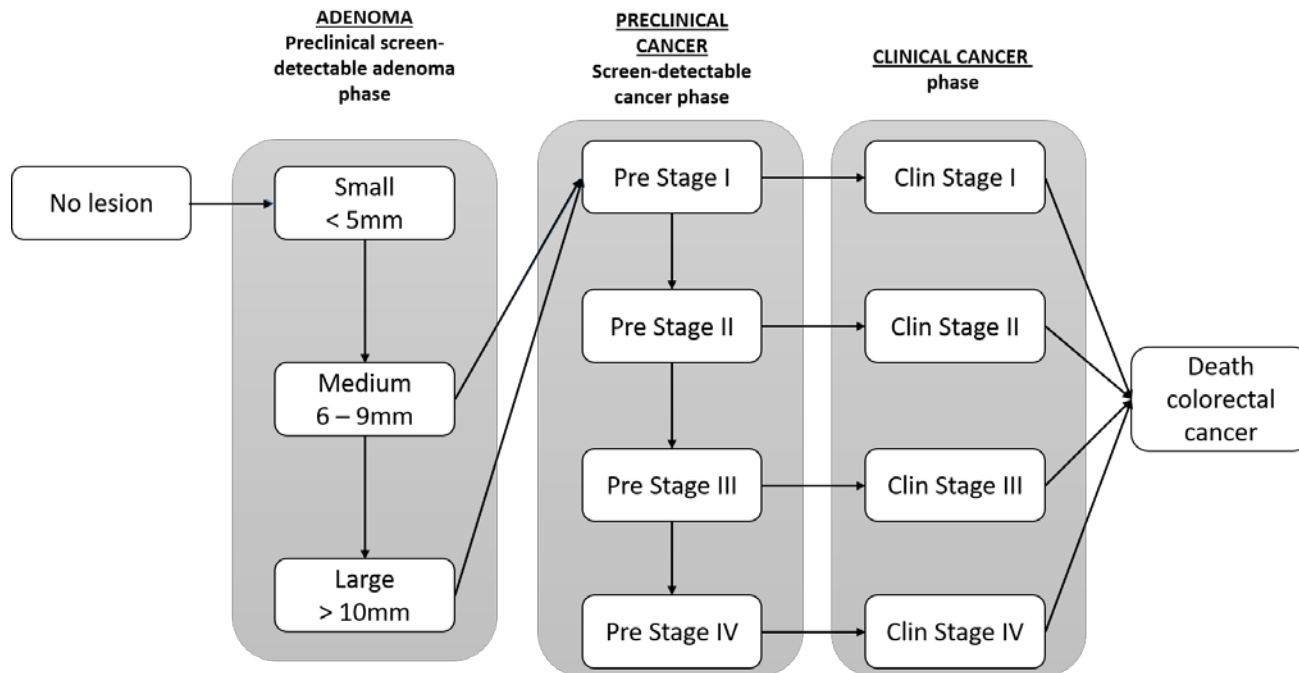
Natural History Model

- Polyp-adenoma process modeled
- Multiple polyps possible that appear and progress independently
- Generation and progression of polyps differentiated by age, race, and gender.
- Polyps detectable through screening tests
- Disease stage and detection time affect survival rates.
- When cancer causes death, compared to predicted cancer free life to determine lost life.

Model Structure



Natural History Model



Calibration – Cancer Incidence Counts

NC CRC Cancer Counts					
Year	Localized CRC Cases	Total CRC Cases	CRC cases for age group 32-44	CRC cases for age group 45-64	CRC cases for age group 65-92
2008	1608	3968	207	1507	2254
2009	1546	3890	230	1497	2163
2010	1433	3810	216	1454	2140
2011	1409	3822	205	1469	2148
2012	1371	3755	211	1487	2057
2013	1384	3870	231	1526	2113
2014	1364	3930	218	1555	2157

Source: Cancer Incidence and Mortality in North Carolina. N.C. Central Cancer Registry.
State Center for Health Statistics. N.C. Division of Public Health.

Calibration – Cancer Incidence Rates

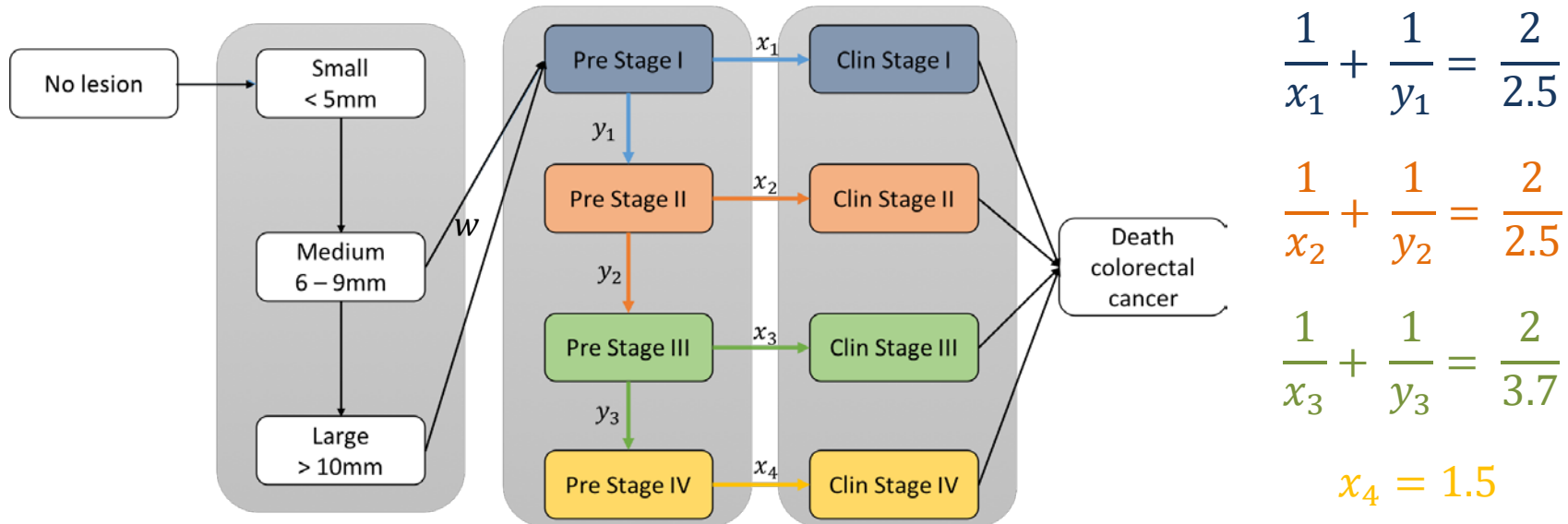
NC CRC Cancer Counts (per 100,000)					
Year	Localized CRC Cases	Total CRC Cases	CRC cases for age group 32-44	CRC cases for age group 45-64	CRC cases for age group 65-92
2008	30.67	75.69	12.16	62.88	197.14
2009	28.94	72.81	13.54	60.82	182.83
2010	26.55	70.60	13.06	57.69	175.03
2011	25.56	69.34	12.09	57.54	170.03
2012	24.64	67.48	12.56	58.00	155.78
2013	24.44	68.33	13.52	59.19	153.51
2014	23.75	68.43	12.73	59.77	151.00

Source: Cancer Incidence and Mortality in North Carolina. N.C. Central Cancer Registry.
State Center for Health Statistics. N.C. Division of Public Health.

Calibration – Cancer Incidence

- Calibrate to cancer incidence rates per year, distribution by type and age
- Calibration error is computed as RMS error between the simulated and actual values for localized cases (loc_{rms}), total cases (tot_{rms}), and cases by age group (age_{rms}).
- An iterative algorithm is performed in four successive stages by varying each of four parameters one at a time.
 - w : Polyp to preclinical cancer,
 - x_1 : Preclinical 1 to preclinical 2,
 - x_2 : Preclinical 2 to preclinical 3,
 - x_3 : Preclinical 3 to preclinical 4.
- In each stage, the parameter value chosen for the next stage is one that corresponds to the smallest value of $((loc_{rms} + tot_{rms} + age_{rms})/3)$
- Achieve average RMS of about **9 cases per 100,000**

Calibration – Cancer Incidence

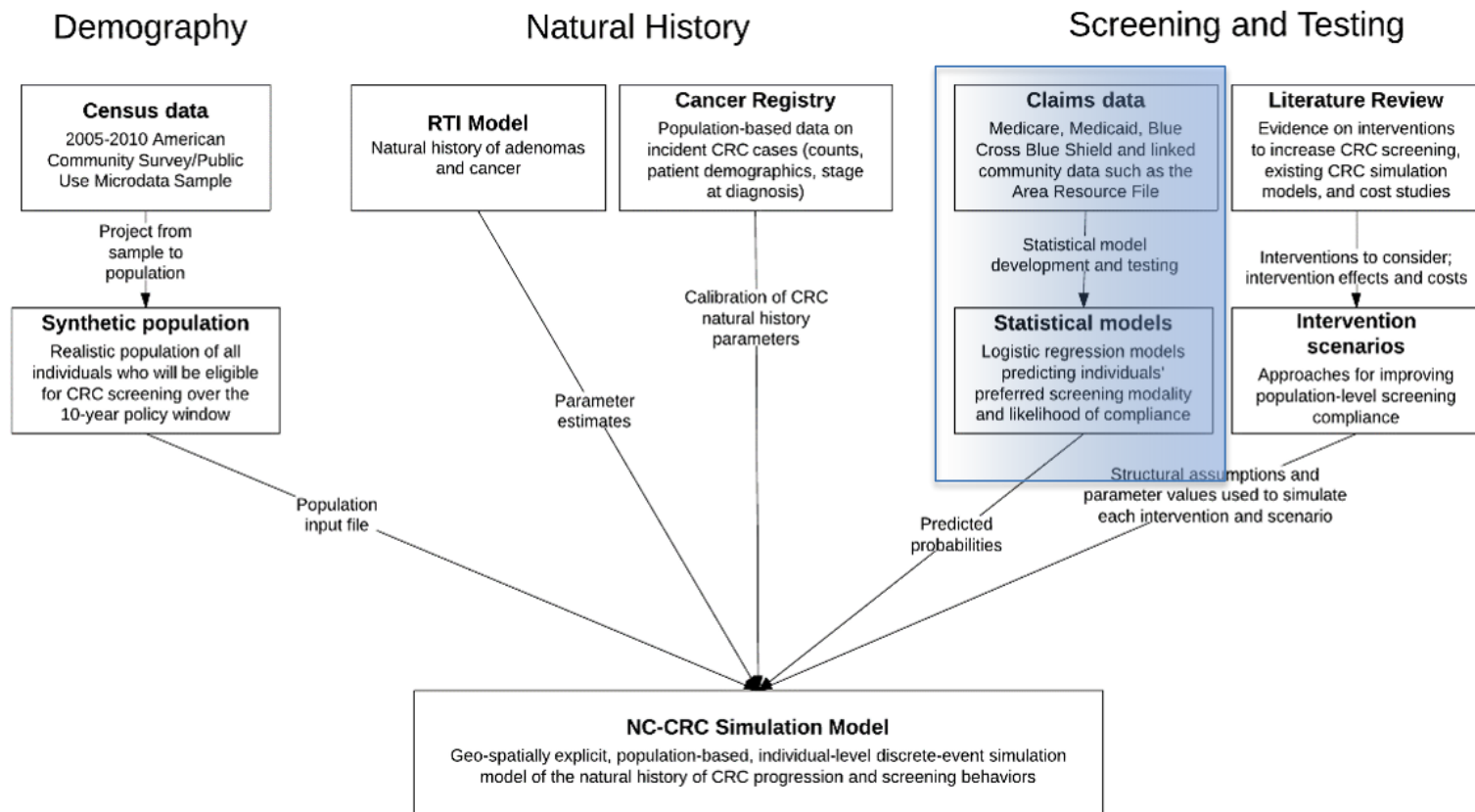


$$\frac{1}{x_1} + \frac{1}{y_1} = \frac{2}{2.5}$$

$$\frac{1}{x_2} + \frac{1}{y_2} = \frac{2}{2.5}$$

$$\frac{1}{x_3} + \frac{1}{y_3} = \frac{2}{3.7}$$

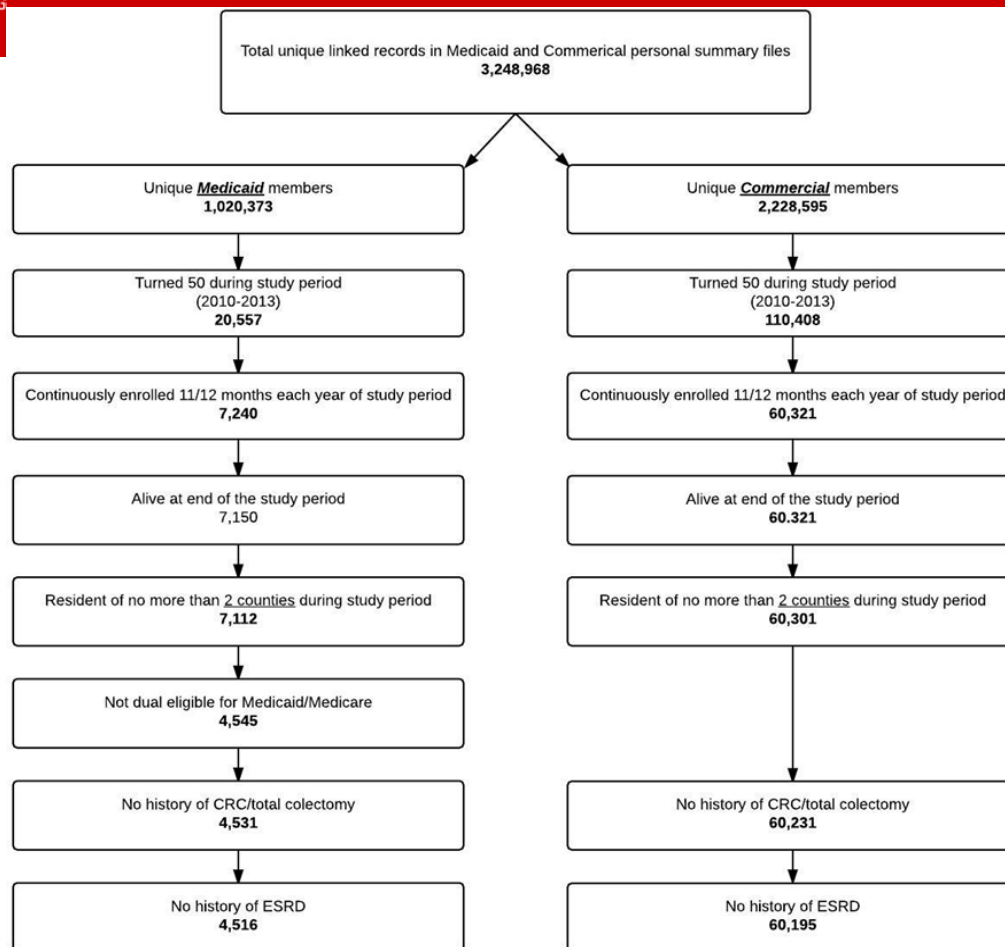
$$x_4 = 1.5$$



Screening and Testing

- Screening compliance, as well as an individual's choice of test modality are based on a probabilistic distribution of choices.
- The compliance and modality choice models are comprised of a statistical analysis based on observational **claims data** of individuals enrolled in either a state-sponsored health plan or private insurance.
- The multi- level, random effects logistic regression allows for individual attributes (e.g. sex, income) to have varying impacts between county level attributes (e.g. percent below poverty line).

Claims Data



Statistical Analysis

- Primary Outcome- whether the beneficiary received any type of CRC screening test procedure, consistent with USPSTF guidelines, during the study period
- Services identified using ICD-9, CPT, and HCPCS codes
- Independent variables
 - Individual level: gender, race/ethnicity, insurance type, observed years, geographic location, use of PC, distance to nearest facility
 - County level characteristics from AHRF data
- Multilevel multivariable logistic regression models by insurance type
- included a county-level random effect to account for additional unmeasurable, county specific regional differences across the state

Screening and Testing

- The specifications of the multi-level model are provided below
- i indexes over individuals, j indexes over counties (100 counties in NC), k is the number of person level characteristics in the model, l is the number of county level characteristics.
- The linear formulation of the logistic regression value function is converted into a probability as follows.

$$\text{logit}(\pi_{ij}) = Y_{ij} = \beta_{0j} + \sum_k \beta_k X_{ik} + \sum_l \beta_l X_{jl} + \varepsilon_{ij} \quad \pi_{ij} = \frac{e^{Y_{ij}}}{1 + e^{Y_{ij}}}$$

- Where π_{ij} is the probability for the binary outcome (CRC Screening vs. No Screen or Colonoscopy Choice vs. FOBT) for person i at county j .
- β_{0j} is the county level intercept X_{ik} and X_{jl} represent the person level (e.g. race, gender) and county level (e.g. distance to endoscopy facility).

Screening and Testing

- A summary of the independent variables is defined in the table below

Gender	Female vs. Male	Regional % Non-White	Low-Medium vs Low
Race	Black vs. white		Medium-High vs Low
	Other vs. white		High vs Low
Year turned 50	2003 vs 2008	Regional Unemployment Rate	Low-Medium vs Low
Distance	5-10 vs < 5 miles		Medium-High vs Low
	10-15 vs < 5 miles		High vs Low
	15-20 vs < 5 miles	Facility Test Volume (per 10,000)	1-200 vs 0
	20-25 vs < 5 miles		200-400 vs 0
	25+ vs < 5 miles		400-600 vs 0
Regional Uninsurance (40-64)	Low-Medium vs Low	Generalist Count	600-800 vs 0
	Medium-High vs Low		800+ vs 0
	High vs Low		Above median vs below median

Screening and Testing

- The outcomes of the regression are compliance and modality within a 6 year window.
- Since FIT is recommended every year and colonoscopy every 5 years we convert these from 6 year probabilities (π) to the appropriate time interval.
 - $P_{FIT} = 1 - (1 - \pi)^{1/6}$
 - $P_{col} = 1 - (1 - \pi)^{5/6}$
- This is done assuming that the probability of screening in a single year is distributed as a Bernoulli random variable, thus the number of screens in a given time period are binomially distributed.

Screening and Testing

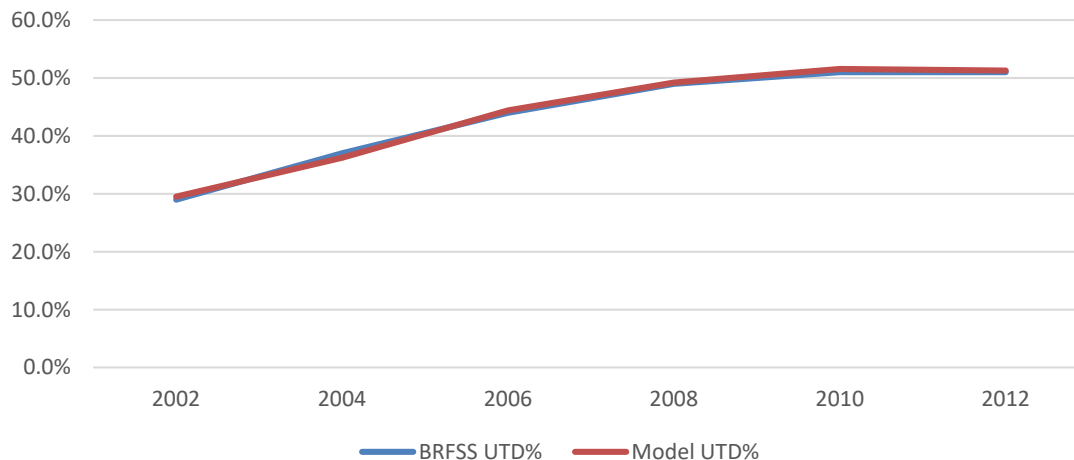
Increase in compliance for first time screeners

- First time screeners have an increased probability of being screened over a five-year-period.
- For colonoscopy screeners,
 - $\widehat{P}_{col} = \min(P_{col} + p', 1)$.
- For FIT screeners,
 - $\widehat{P}_{FIT} = P_{FIT} + x = 1 - \sqrt[5]{(1 - P_{FIT})^5 - p'}$.

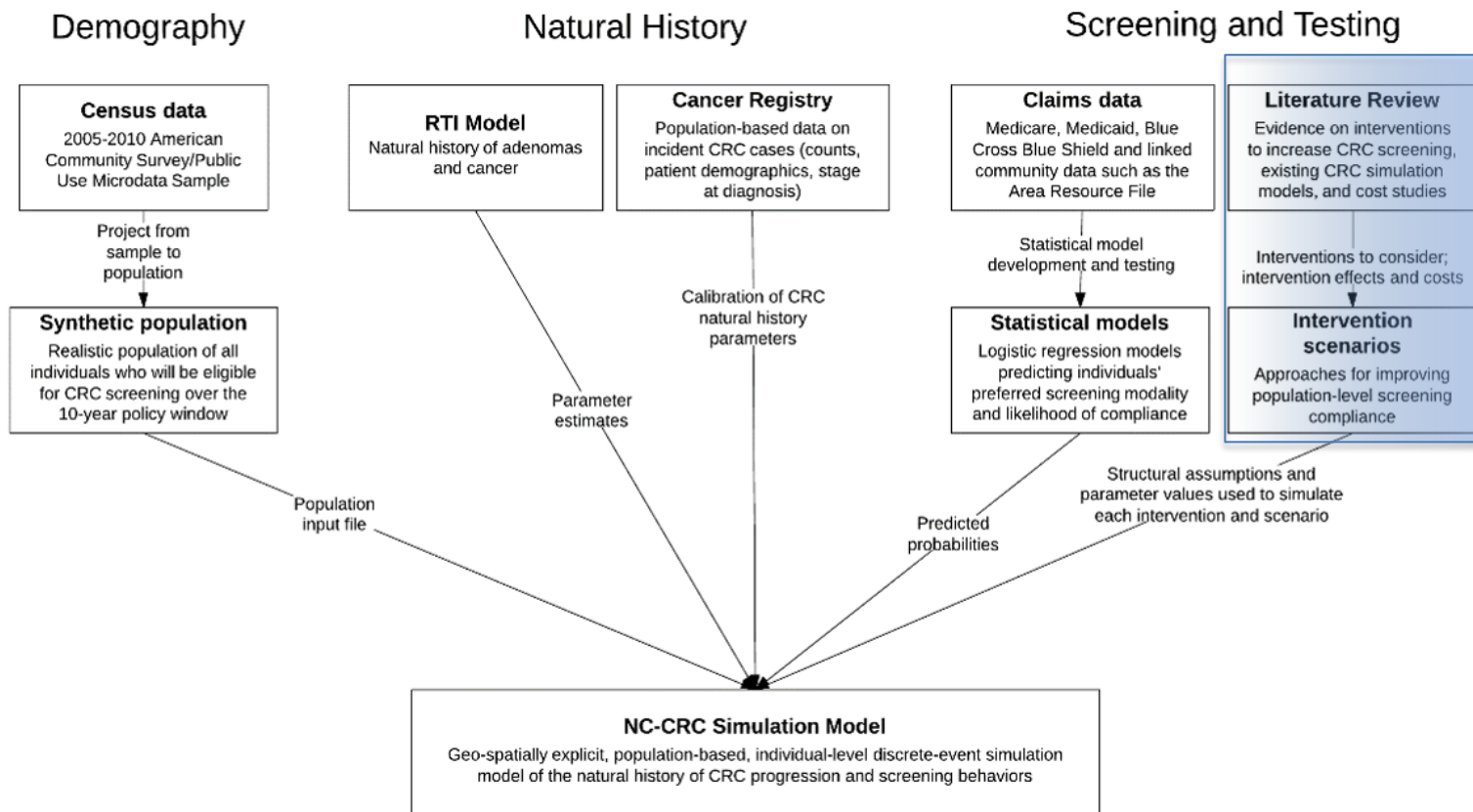
Calibration – Secular Trend

- We used data from BRFSS between 2002 and 2012 (conducted every 2 years) to estimate the proportion of NC residents aged 50-75 years who reported being up-to-date with CRC screening.
- The estimated proportions likely were overestimates of the true proportions of North Carolinians up-to-date with screening.
- We determined values by which the compliance probabilities of an individual are to be increased such that the % UTD obtained from the model matched the BRFSS data after adjustment for self-report.
- Calibration was performed in an iterative fashion by year.

Calibration – Secular Trend



Secular trend values					
2002	2004	2006	2008	2010	2012
-0.15	0.02	0.13	0.11	0.11	0.09



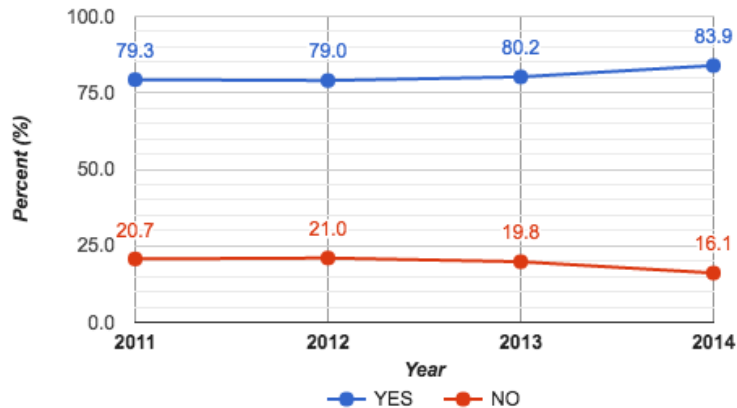
Policy Scenarios

- **Scenario 1 (Status Quo):** The development and use of the health insurance exchange under the ACA as implemented in North Carolina (i.e., without Medicaid expansion).
- **Scenario 2:** The expansion of the state's Medicaid program, increasing the threshold for Medicaid eligibility for all residents to 138% of the federal poverty level (FPL).
- **Scenario 3:** If insurance expansion did not happen under the ACA, i.e., insurance reduction or removal of ACA

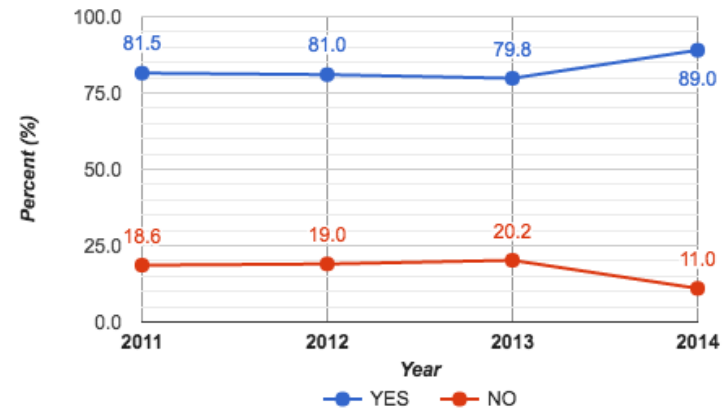
How has ACA/Medicaid expansion changed insurance uptake in North Carolina and Oregon?

Trends in BRFSS, % Insured among all individuals 2011-2014

NC: Do you have any kind of health care coverage?



OR: Do you have any kind of health care coverage?



Insurance uptake between 2013 and 2014

- State specific data was extracted from BRFSS, combined 2013 and 2014 datasets
- Modeled health insurance (yes=1, no=0) using multivariable logistic regression with interactions
- Independent variables include:
 - Sex
 - Age category (18-24, 25-34, 35-44, 45-54, 55-64, 65+)
 - Race, 6 collapsed into 4 (Non-Hispanic White, Non-Hispanic Black, Hispanic, Other)
 - Income category*, (<15, 15-25, 25-35, 35-50, 50+)
 - Marital Status, collapsed 6 into 2 (Married and Not-Married)
 - Year
- Significant two-way interactions included
 - Race and Age, Sex and Married, Race and Income, Income and Year

*imputed using monotone logistic regression in the PROC MI procedure in SAS

Modeling Insurance Uptake between 2013 and 2014

- For all subgroups, we estimate the predicted probabilities of having insurance in both 2013 and 2014
- For each group we calculate the **conditional probability that a person will become newly insured in 2014 given that they were not insured in 2013**
- We then apply this increase to each individual (probabilistically)
- Those who become newly insured will either get private insurance (e.g., through the exchange) or Medicaid (if they qualify)

**How has/would CRC screening
and outcomes changed
following ACA/Medicaid
expansion?**

Hardware Specifications

- The simulation model run via AnyLogic software
- Runs performed on a
 - Dedicated 64-core machine,
 - 64-bit Windows Server 2008 r2 Datacenter,
 - 1TB of ram,
 - 2 GHz Intel Xeon X7550 processors,
 - 2 TB of disk storage.
- We run five replications with a total run time of approximately 150 minutes.

Simulation Runs

- Simulate the full life course of every NC resident between the ages of 50 and 75 intervention window (January 1, 2014 through December 31, 2023)
- This includes 3,918,469 people, as of January 1, 2009 when the synthetic population was created

Characteristic	N	%
Total	2,852,111	100.0
Sex		
Male	1,363,984	47.8
Female	1,488,127	52.2
Race		
White	2,187,959	76.7
Black	534,103	18.7
Other	130,049	4.6
Ethnicity		
Hispanic	84,217	3.0
Non-Hispanic	2,767,894	97.0
Age		
50-64	1,898,525	66.5
65-75	953,586	33.5

CRC incidence by stage and CRC mortality of full cohort projected for lifetime.

	No ACA	ACA	ACA + Medicaid Expansion
CRC Cases	140,837	139,432	137,918
Stage 1	47,911	47,544	47,164
Stage 2	42,665	42,170	41,752
Stage 3	28,507	28,194	27,834
Stage 4	21,754	21,524	21,168
CRC Deaths	56,561	55,967	55,244

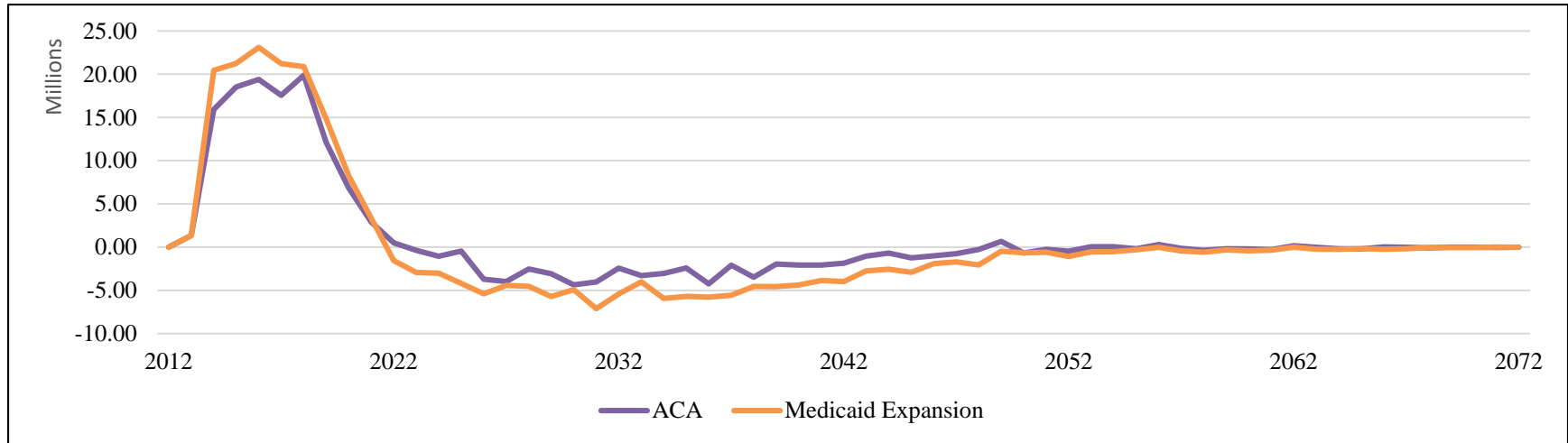
**Simulated age-eligible NC
population up to date with
CRC screening on
January 1, 2023**

Variable	No ACA	Percentage-point change in percent up to date on CRC screening compared with the No ACA	
		ACA	ACA + Medicaid Expansion
Overall	48.65%	+1.03%	+1.74%
By sex			
Male	46.13%	+0.94%	+1.55%
Female	51.00%	+1.11%	+1.92%
By race			
White	49.92%	+0.73%	+1.29%
Black	45.92%	+2.01%	+2.88%
Hispanic	42.22%	+0.05%	+2.90%
Other	42.36%	+1.40%	+3.40%
By insurance			
Private	53.87%	+0.01%	+0.03%
Dual	58.02%	+0.02%	+0.99%
Medicare	59.85%	+0.09%	+0.15%
Medicaid	42.63%	+0.07%	+0.02%
Uninsured	17.84%	-0.04%	-0.04%

Results

- Reduce cancers, deaths
- Increase % up-to-date
- Model total cost of treating CRC from the state's perspective
- Costs include routine and diagnostic screenings, treating complications arising from a colonoscopy and the lifetime treatment costs

Difference in all CRC costs by year, compared to the No ACA scenario, 2013+



Discussion

- Both ACA and ACA + Medicaid scenarios provided **lower total CRC treatment costs** when compared to the removal of ACA scenario.
- ACA scenario resulted in increasing the percentage of the NC population screened, resulting in **fewer CRC cases, decreased severity of CRC cases, and reduced mortality**
- Increased health care coverage was also found to **reduce racial disparities** in screening.
- Although the changes in outcomes are somewhat modest they are commensurate with other state-wide interventions

CRC Model Conclusions

- NC-CRC model is intended to be used as a “virtual world” in which to simulate the effects of alternate scenarios about population demographics, disease determinants, clinical interventions, or policies on CRC screening, incidence, treatment, and mortality.
- The object oriented structure of the model allows us to easily compartmentalize the components that make up the core of the model.
- The model can simulate realistic cohorts (e.g., for comparative effectiveness research) or the entire population of NC.
- The real power of the model becomes more evident when estimating the impact of future policies.

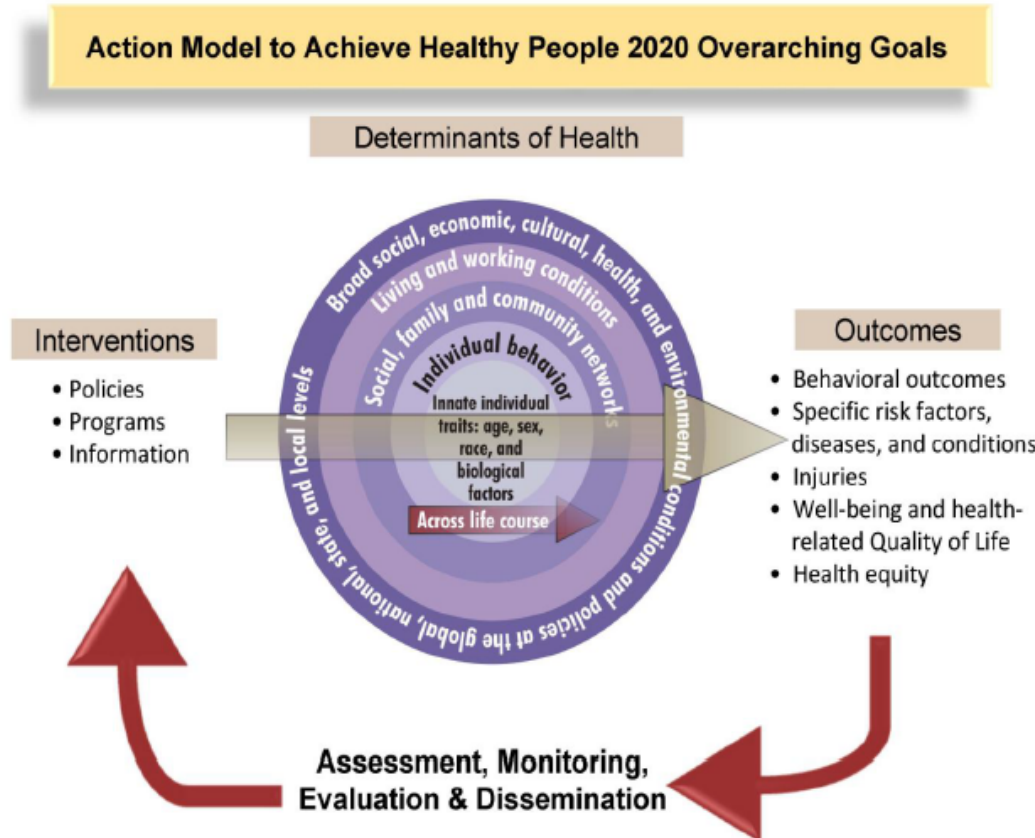
***“TO ACHIEVE 80% BY
2018, YOU HAVE TO DO
IT ALL.”***

Richard Wender, MD – American Cancer Society
Oregon CRC Roundtable – April 22, 2016

Future work

- The simulation need not be restricted to North Carolina's populations and policies.
- We simulate Oregon, in addition to insurance expansion, testing Evidence Based Interventions (e.g. Direct Mail, patient navigators, etc.)
- Other models of patient choice to take into account past behavior

The problem is complex



Conclusions

- Operations research & systems engineering provides a powerful tool
- I hope to use OR to make recommendations that inform public and health policy
- Focus on implementable results that consider issues of fairness- thereby improving the human condition.



Thank you!

Questions?