Microsimulation modeling

Decision Modeling for Public Health

November 17, 2022

What is discrete-time microsimulation?

- Micro = individual-level
- Simulation = imitation of a situation or process
- Discrete-time = fixed time intervals

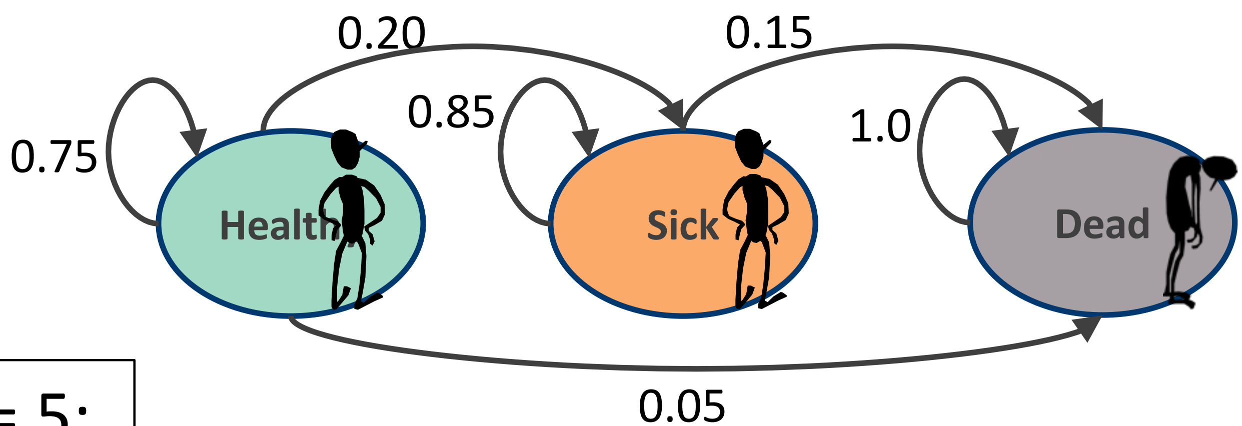
  - Reflects events experienced by an individual
  - Stochastic implementation of a dynamic process

Microsimulation terminology

- Sometimes called “Markov Monte Carlo” or “First-Order Monte Carlo” or “**Individual state-transition model**”
- Need not explicitly follow a state-transition model structure
- In our courses we refer to discrete time individual state-transition models when we talk about a microsimulation model

Simple example

- Simulates *individual* disease progression through a state-transition model
  - Track individual's health state over time (can only be in one state at any given time)



t = 5:

General Microsimulation

- Track current state of individual as well as relevant history/characteristics
  - Need not be discrete categories; continuous measures possible
- Probabilities of simulated events can depend on
  - Individual characteristics (age, gender, etc.)
  - Full clinical history, time since clinical events

Pros and Cons

Advantages

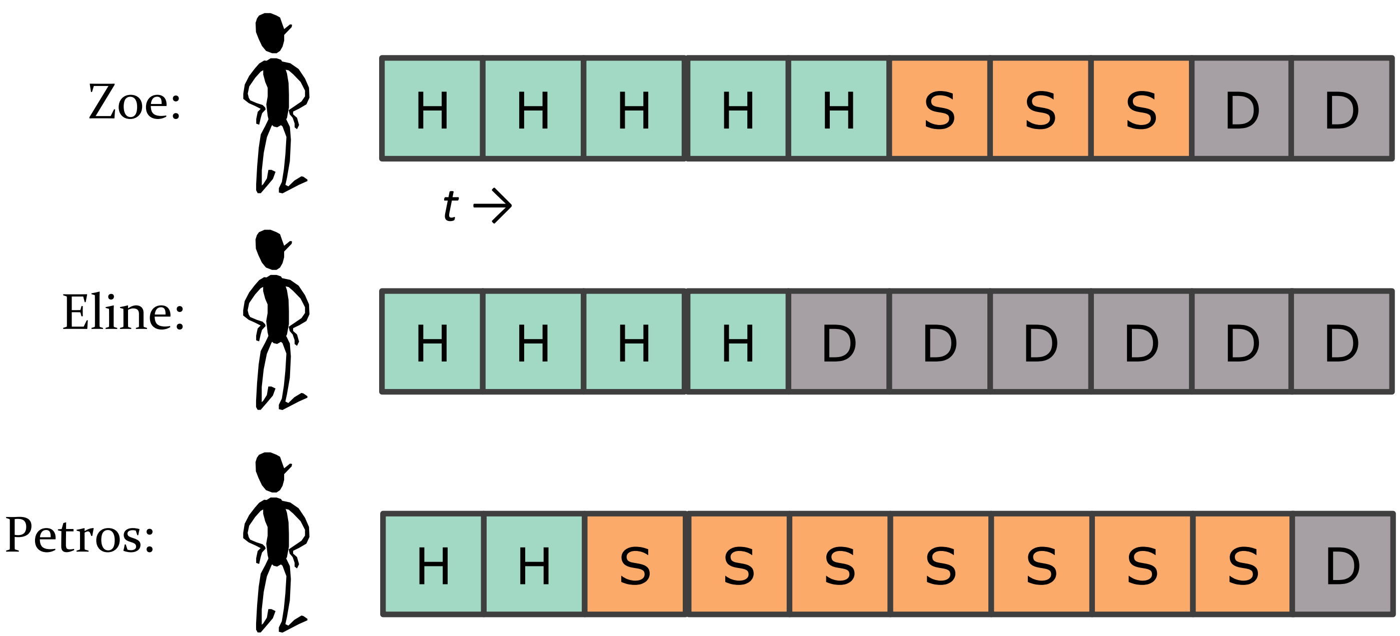
- Flexible model structure
- Easy to include:
  - Individual heterogeneity
  - Complex history-dependencies
  - Continuous health measures
  - Relation among individuals (network)

Disadvantages

- Complex to implement
- Computationally intensive
- Requires more data to inform model parameter values

Microsimulation Basics

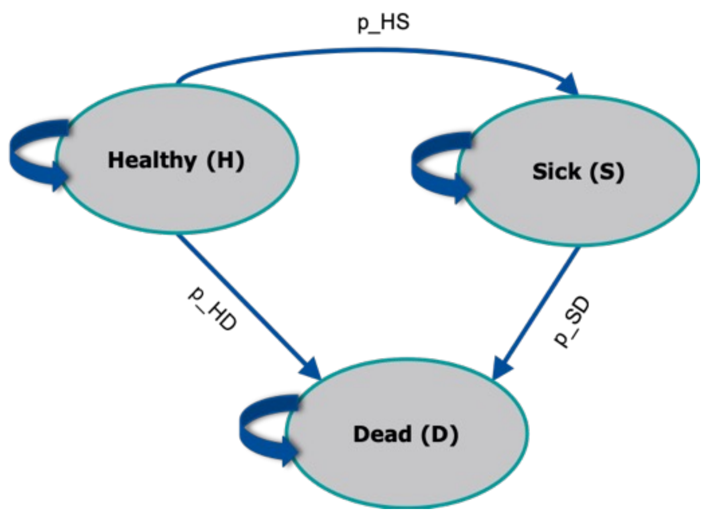
- Simulate disease progression and health outcomes in **an individual**
- Simulate **many individuals** to **estimate expected value** and standard deviation of health outcomes over a **large population**



3-state example

- Three-state model of disease: Healthy, Sick, Dead
- Time horizon: 10 annual cycles
- Probability of transitioning from healthy to dead is sex-dependent

Female	0.0382
Male	0.0463



Individual characteristics

- Sex – assume equal proportion of women and men

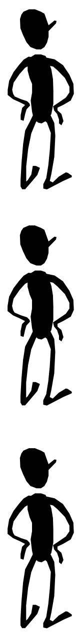
Microsimulation Mechanics

- Generate a representative, virtual population
  - Sample characteristics from demographic data
  - Male:Female ratio, age distribution, etc.

- Simulate the occurrence of events
  - Write functions that calculate individual-specific probabilities of different events
  - $p_{HD} = f(\text{sex})$
  - $p_{event1} = f(age, sex, health\ status, time\ since\ event, \ldots)$
  - Simulate events (and their consequences) over time using random numbers

- Calculate population-level outcomes by averaging individual outcomes

Structure with Individuals Characteristics



	age	sex	height	Country of birth
Zoe	35	Female	1.55	Taiwan
Eline	28	Female	1.68	NL
Petros	36	Male	1.89	Greece

Individuals Characteristics

t = 1

Zoe:	H	H	H	H	H	S	S	S	D	D
Eline:	H	H	H	H	D	D	D	D	D	D
Petros:	H	H	S	S	S	S	S	S	S	D

$t \rightarrow$

	age	sex	height	Country of birth	p_HD
Zoe	35	Female	1.55	Taiwan	0.3
Eline	28	Female	1.68	NL	0.3
Petros	36	Male	1.89	Greece	0.4

Update individuals Characteristics

t = 2

Zoe:	H	H	H	H	H	S	S	S	D	D
Eline:	H	H	H	H	D	D	D	D	D	D
Petros:	H	H	S	S	S	S	S	S	S	D

t →

	age	sex	height	Country of birth	p_HD
Zoe	36	Female	1.55	Taiwan	0.3
Eline	29	Female	1.68	NL	0.3
Petros	37	Male	1.89	Greece	0.4

Individuals Characteristics

t = 3

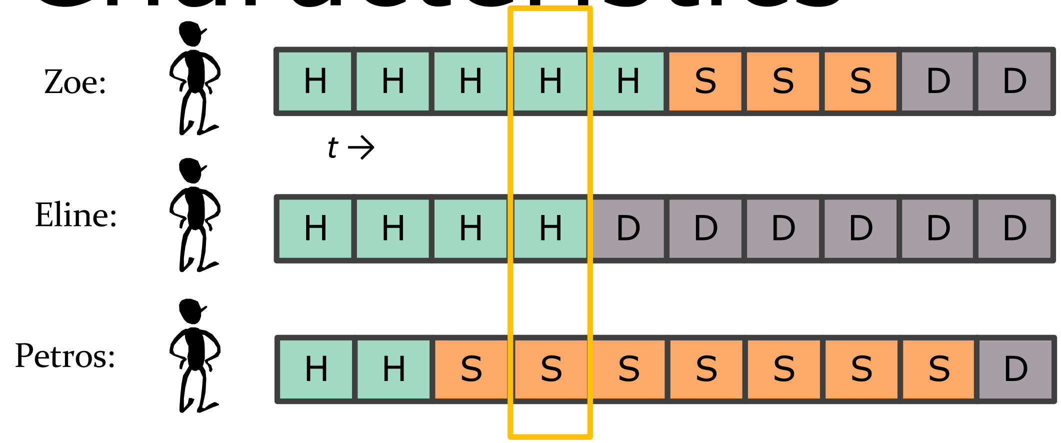
Zoe:	H	H	H	H	H	S	S	S	D	D
Eline:	H	H	H	H	D	D	D	D	D	D
Petros:	H	H	S	S	S	S	S	S	S	D

$t \rightarrow$

	age	sex	height	Country of birth	p_HD
Zoe	37	Female	1.55	Taiwan	0.3
Eline	30	Female	1.68	NL	0.3
Petros	38	Male	1.89	Greece	--

Individuals Characteristics

t = 4



	age	sex	height	Country of birth	p_HD
Zoe	38	Female	1.55	Taiwan	0.3
Eline	31	Female	1.68	NL	0.3
Petros	39	Male	1.89	Greece	--

Individuals Characteristics

t = 5

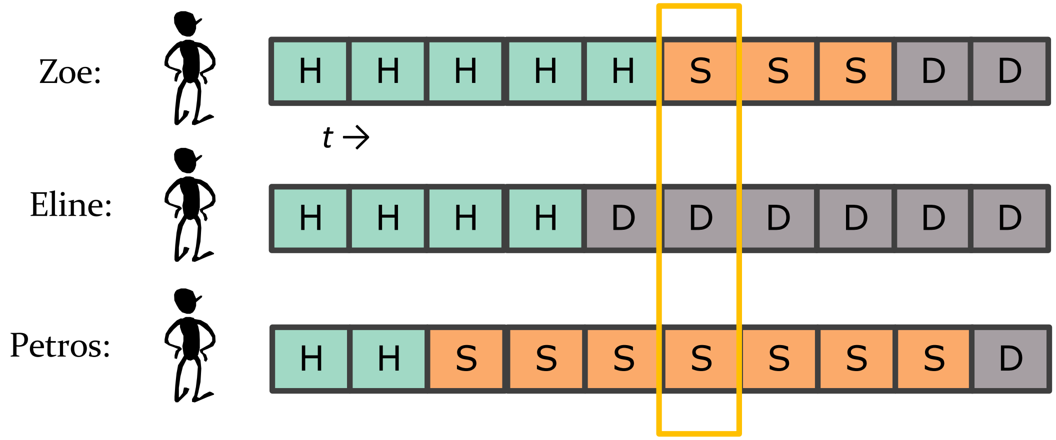
Zoe:	H	H	H	H	H	S	S	S	D	D
Eline:	H	H	H	H	D	D	D	D	D	D
Petros:	H	H	S	S	S	S	S	S	S	D

$t \rightarrow$

	age	sex	height	Country of birth	p_HD
Zoe	39	Female	1.55	Taiwan	0.3
Eline	32	Female	1.68	NL	--
Petros	40	Male	1.89	Greece	--

Individuals Characteristics

t = 6



	age	sex	height	Country of birth	p_HD
Zoe	40	Female	1.55	Taiwan	--
Eline	33	Female	1.68	NL	--
Petros	41	Male	1.89	Greece	--

Time dependency

Hey! We've seen this slide before! But now how to reflect these dependencies in a microsimulation?

Since start of the simulation

- Parameters vary by cycle
- Most often reflects probabilities that vary by age
  - Background mortality
  - Risk of disease onset

Depending on state residence time

- Some transition probabilities depend on time since an event
  - e.g., risk of developing recurrence among newly diagnosed cancer patients declines with time
- Cost or utility could vary over time spent in a health state

Time dependency

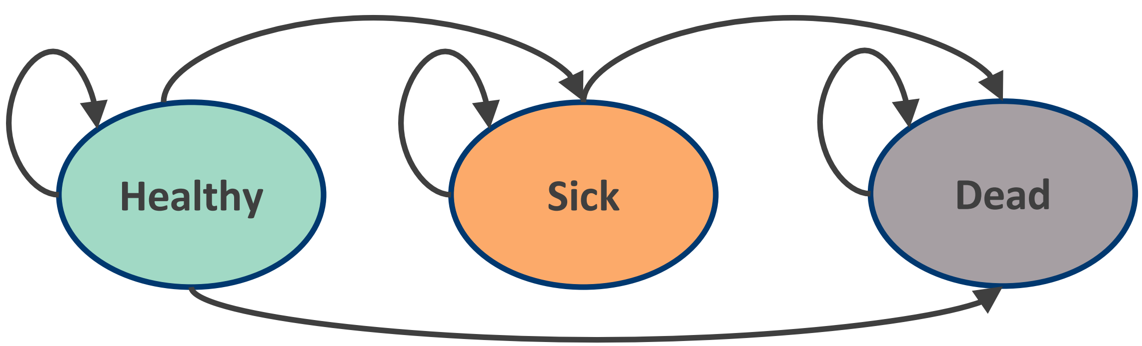
- In a microsimulation, time-dependency is implemented like any other feature-dependency
  - The relevant feature must be recorded!
- If truly dependent on time since simulation start (e.g. seasonal changes, exogenous time-trends etc.), probabilities change with the year or cycle #
- If age-dependent, each individual will experience the event probability associated with their specific age at each time step
- If state residence time dependent, need to track time spent in relevant states as a (time-varying) individual characteristics

State-residency

- **Probability** might be dependent on how long someone is in a state

Example:

- The **probability to die** depends on the duration of being sick



Duration of being sick (step)	p_SD
1	0.1
2	0.2
3	0.3
4	0.4
5	0.5
6+	0.7

State-residence

t = 1

Zoe	H	H	H	H	H	S	S	S	D	D
Eline	H	H	H	H	D	D	D	D	D	D
Petros	H	H	S	S	S	S	S	S	S	D

t →

	age	sex	height	Country of birth	time Sick	p_SD
Zoe	35	Female	1.55	Taiwan	0	--
Eline	28	Female	1.68	NL	0	--
Petros	36	Male	1.89	Greece	0	--

State-residence

t = 2

Zoe	H	H	H	H	H	S	S	S	D	D
Eline	H	H	H	H	D	D	D	D	D	D
Petros	H	H	S	S	S	S	S	S	S	D

$t \rightarrow$

	age	sex	height	Country of birth	time Sick	p_SD
Zoe	36	Female	1.55	Taiwan	0	--
Eline	29	Female	1.68	NL	0	--
Petros	37	Male	1.89	Greece	0	--

State-residence

t = 3

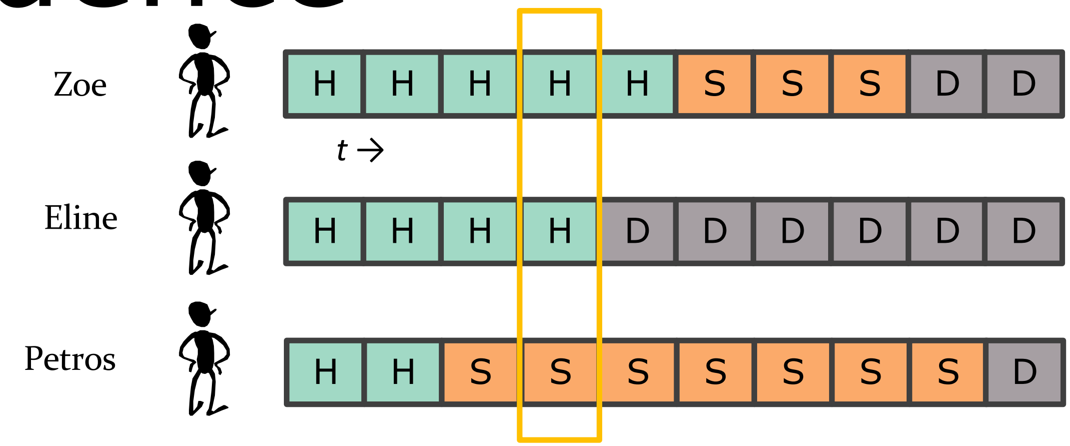
Zoe	H	H	H	H	H	S	S	S	D	D
Eline	H	H	H	H	D	D	D	D	D	D
Petros	H	H	S	S	S	S	S	S	S	D

$t \rightarrow$

	age	sex	height	Country of birth	time Sick	p_SD
Zoe	37	Female	1.55	Taiwan	0	--
Eline	30	Female	1.68	NL	0	--
Petros	38	Male	1.89	Greece	1	0.1

State-residence

t = 4



	age	sex	height	Country of birth	time Sick	p_SD
Zoe	38	Female	1.55	Taiwan	0	--
Eline	31	Female	1.68	NL	0	--
Petros	39	Male	1.89	Greece	2	0.2

State-residence

t = 5

Zoe	H	H	H	H	H	S	S	S	D	D
Eline	H	H	H	H	D	D	D	D	D	D
Petros	H	H	S	S	S	S	S	S	S	D

$t \rightarrow$

	age	sex	height	Country of birth	time Sick	p_SD
Zoe	39	Female	1.55	Taiwan	0	--
Eline	32	Female	1.68	NL	0	--
Petros	40	Male	1.89	Greece	3	0.3

State-residence

t = 6

Zoe	H	H	H	H	H	S	S	S	D	D
Eline	H	H	H	H	D	D	D	D	D	D
Petros	H	H	S	S	S	S	S	S	S	D

$t \rightarrow$

	age	sex	height	Country of birth	time Sick	p_SD
Zoe	40	Female	1.55	Taiwan	1	0.1
Eline	33	Female	1.68	NL	0	--
Petros	41	Male	1.89	Greece	4	0.4

Microsimulation Comparative Moldeing Example: Colorectal cancer screening

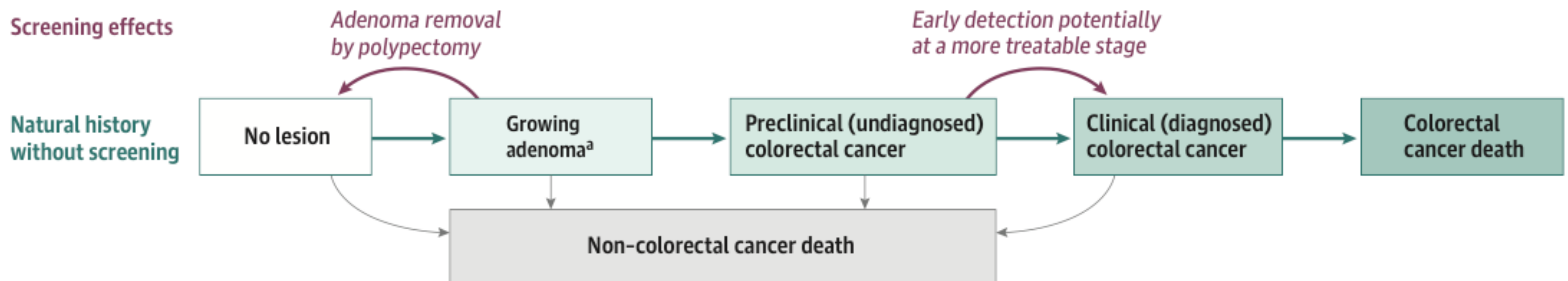
JAMA | US Preventive Services Task Force | MODELING STUDY

Colorectal Cancer Screening
An Updated Modeling Study for the US Preventive Services Task Force

Amy B. Knudsen, PhD; Carolyn M. Rutter, PhD; Elisabeth F. P. Peterse, PhD; Anna P. Lietz, BA; Claudia L. Seguin, BA; Reinier G. S. Meester, PhD; Leslie A. Perdue, MPH; Jennifer S. Lin, MD; Rebecca L. Siegel, MPH; V. Paul Doria-Rose, DVM, PhD; Eric J. Feuer, PhD; Ann G. Zauber, PhD; Karen M. Kuntz, ScD; Iris Lansdorp-Vogelaar, PhD

Natural history

Figure 1. Natural History of Colorectal Cancer and the Effects of Screening as Simulated by SimCRC, CRC-SPIN, and MISCAN



The opportunity to intervene in the natural history through screening (adenoma detection and removal and early detection) is noted in red. Screening can either remove a precancerous lesion (ie, adenoma), thus moving a person to the "no lesion" state, or diagnose a preclinical cancer, which, if detected at an earlier stage, may be more amenable to treatment. Each person's life history is simulated in the absence of screening and in the presence of screening, such that the effect of a given screening strategy on each simulated person's outcomes are known.

[a] Simulation Model of CRC (SimCRC) and Microsimulation Screening Analysis (MISCAN) simulate categorical adenoma size (1 to <6 mm; 6 to <10 mm; ≥10 mm), whereas CRC Simulated Population Model for Incidence and Natural History (CRC-SPIN) simulates continuous adenoma size. SimCRC and CRC-SPIN assume that all adenomas have the potential to progress to colorectal cancer, whereas MISCAN assumes that some adenomas are nonprogressive (ie, they do not grow or progress to cancer after reaching a certain size category) and that the likelihood that an adenoma is progressive increases with age. None of the models simulate adenoma histology.

Why a microsimulation? Example – SimCRC model profile

- Population model = people are born into the model and exit when they die with various composition of people by age, sex, race
- Extensive dependency on history

Risk Factors

Risk Factor	Categories
Body mass index	
Physical activity	0; 0.01–1.9; 2.0–9.9; 10.0+
Fruit and vegetable consumption	0–1.9; 2.0–3.9; 4.0–5.9; 6.0–7.9; 8.0+
Multivitiamin use	non–user; user
Current smoker	non–user; user
Red meat consumption	0–0.104; 0.105–0.43; >0.43
Aspirin use	non–user; user
Hormone replacement therapy	non–user; user

ND = No Disease -> LRA = low-risk adenoma

$$Pr(\mathrm{ND} \rightarrow \mathrm{LRA}) = \frac{1}{1 + exp(-\alpha - \gamma - \beta_{age} * age - \beta'_{rf} * X)}.$$

Need to track multiple factors, including time since lesion start, time to diagnosis, … etc

Can you do it as a Markov model?

https://cisnet.flexkb.net/mp/pub/cisnet_colorectal_umin_profile.pdf

Why a microsimulation? Example – SimCRC model profile

- Population model = people are born into the model and exit when they die with various composition of people by age, sex, race
- Extensive dependency on history

Risk Factors

Risk Factor	Categories
Body mass index	
Physical activity	0; 0.01–1.9; 2.0–9.9; 10.0+
Fruit and vegetable consumption	0–1.9; 2.0–3.9; 4.0–5.9; 6.0–7.9; 8.0+
Multivitiamin use	non–user; user
Current smoker	non–user; user
Red meat consumption	0–0.104; 0.105–0.43; >0.43
Aspirin use	non–user; user
Hormone replacement therapy	non–user; user

Absolutely

Side effects = “state explosion”

ND = No Disease -> LRA = low-risk adenoma

$$Pr(\mathrm{ND} \rightarrow \mathrm{LRA}) = \frac{1}{1 + exp(-\alpha - \gamma - \beta_{age} * age - \beta'_{rf} * X)}.$$

Need to track multiple factors, including time since lesion start, time to diagnosis, … etc

Can you do it as a Markov model?

https://cisnet.flexkb.net/mp/pub/cisnet_colorectal_umin_profile.pdf

Strategies evaluated

Table 2. Screening Strategies Evaluated by the Models[a]

Modality	Screening interval, y	Age to begin screening, y	Age to end screening, y[b]	No. of (unique) strategies[c]
No screening				1 (1)
COL	5, 10, 15	45, 50, 55	70, 75, 80, 85	36 (26)
CTC	5, 10	45, 50, 55	70, 75, 80, 85	24 (20)
SIG	5, 10	45, 50, 55	70, 75, 80, 85	24 (20)
FIT	1, 2, 3	45, 50, 55	70, 75, 80, 85	36 (36)
sDNA-FIT	1, 2, 3	45, 50, 55	70, 75, 80, 85	36 (36)
SIG + FIT[d]	10_1, 10_2	45, 50, 55	70, 75, 80, 85	24 (24)
Total				**181 (163)**

Abbreviations: COL, colonoscopy; CTC, computed tomography colonography; FIT, fecal immunochemical test (with positivity cutoff of 20 μg of hemoglobin per gram of feces); sDNA-FIT, multitarget stool DNA test with a fecal immunochemical assay; SIG, flexible sigmoidoscopy without biopsy.

[a] See the full report[6] for a complete list of screening strategies evaluated by the models.

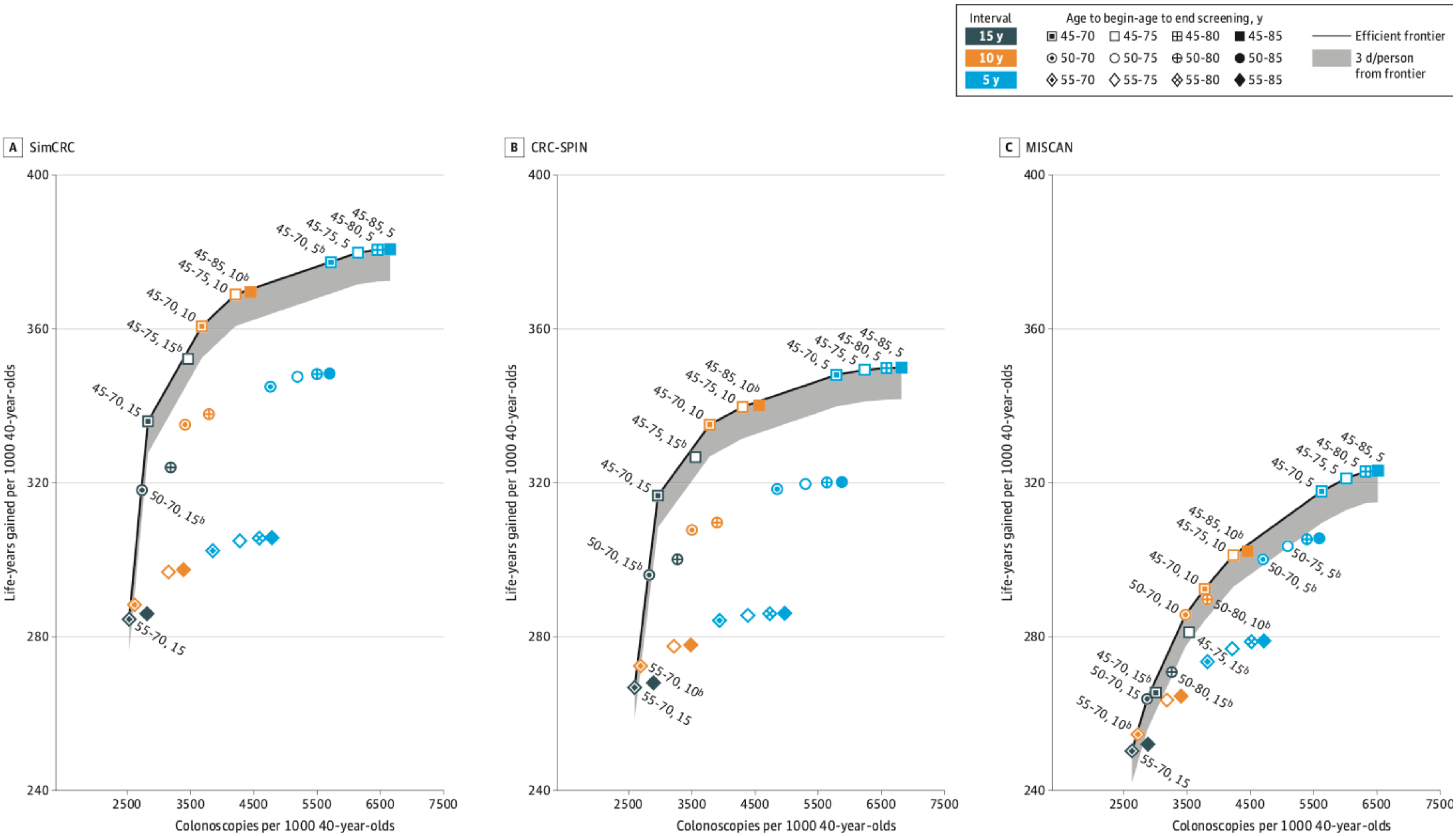
[b] Age to end screening is the last age at which screening happens; screening tests could be performed at but not after this age.

[c] The number of unique strategies excludes those with different ages to end screening that result in screens at the same ages (eg, COL every 10 years from ages 50-70 years and from ages 50-75 years both result in screening at ages 50, 60, and 70 years).

[d] The first interval is for SIG and the second interval is for FIT. If SIG and FIT were due the same year, it was assumed that the FIT was performed first. Persons with a positive FIT result did not have a SIG. Instead they had a follow-up colonoscopy. Those with a negative FIT result had a SIG, and those with SIG findings subsequently had a follow-up colonoscopy.

Strategies evaluated

Figure 2. Lifetime Number of Colonoscopies and Life-Years Gained for a Cohort of 40-Year-Olds for Colonoscopy Screening Strategies[a]



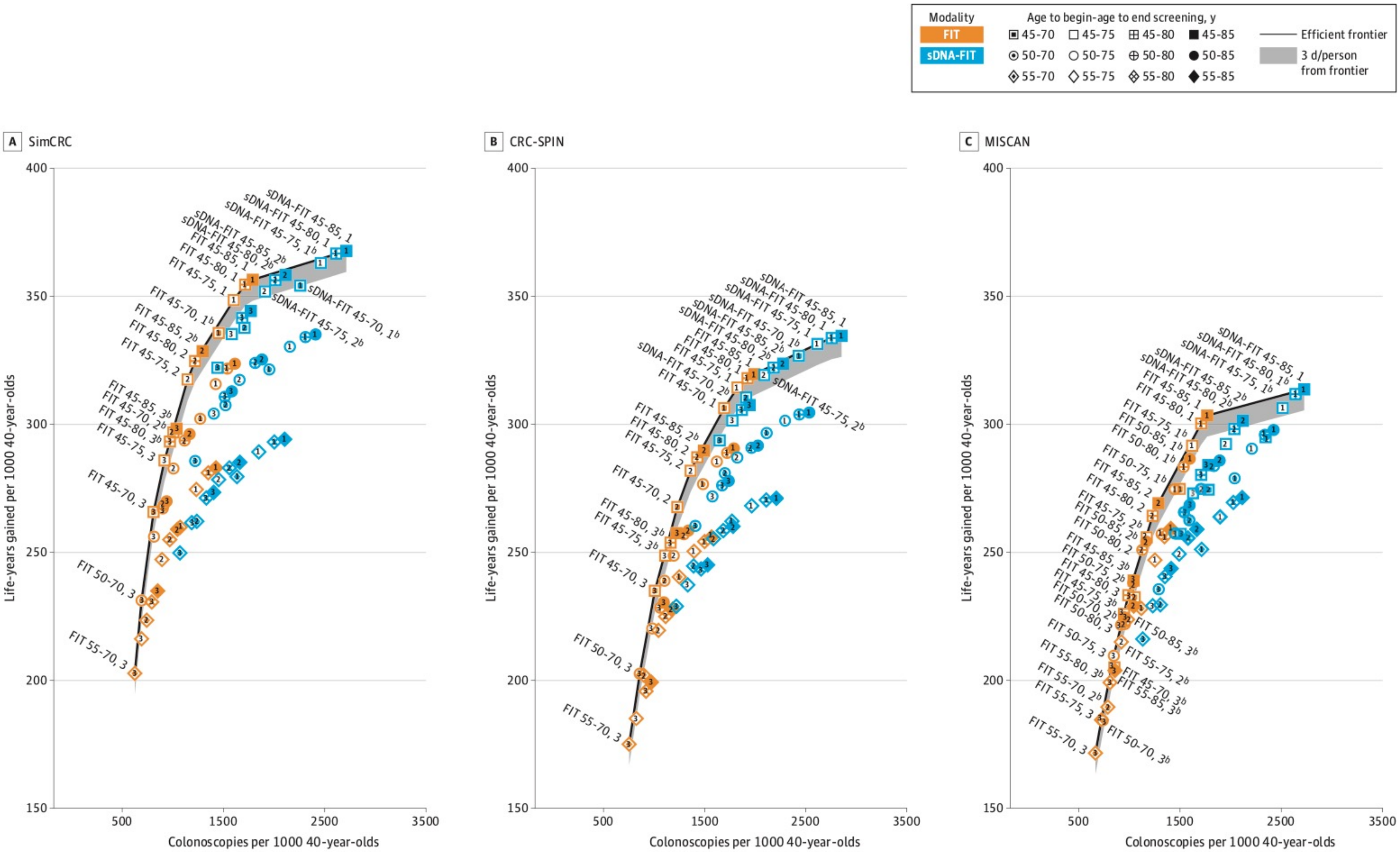
CRC-SPIN indicates CRC Simulated Population Model for Incidence and Natural History; MISCAN, Microsimulation Screening Analysis; SimCRC, Simulation Model of CRC.

[a] Analyses assume an increased population incidence of colorectal cancer based on an incidence rate ratio comparing incidence among current 20- to 44-year-olds (ie, in 2012-2016) vs 20- to 44-year-olds in the period used for initial model calibration (ie, 1975-1979) of 1.19. An interactive version of this figure is available at https://resources.cisnet.cancer.gov/projects/#crcr/uspstf2021/explorer

[b] Near-efficient strategy.

Strategies evaluated

Figure 3. Lifetime Number of Colonoscopies and Life-Years Gained for a Cohort of 40-Year-Olds for Stool-Based Screening Strategies[a]



See Figure 2 legend for expanded abbreviations.

[a] Analyses assume an increased population incidence of colorectal cancer based on an incidence rate ratio comparing incidence among current 20- to 44-year-olds (ie, in 2012-2016) vs 20- to 44-year-olds in the period used for initial model calibration (ie, 1975-1979) of 1.19. An interactive version of this figure is available at https://resources.cisnet.cancer.gov/projects/#crcr/uspstf2021/explorer

[b] Near-efficient strategy.

DARTH Workgroup

Fernando Alarid-Escudero, PhD[1]
Eva A. Enns, MS, PhD[2]
M.G. Myriam Hunink, MD, PhD[3,4]
Hawre J. Jalal, MD, PhD[5]
Eline M. Krijkamp, MSc[3]
Petros Pechlivanoglou, PhD[6]

In collaboration of:

1 Drug Policy Program, Center for Research and Teaching in Economics (CIDE) - CONACyT, Aguascalientes, Mexico
2 University of Minnesota School of Public Health, Minneapolis, MN, USA
3 Erasmus MC, Rotterdam, The Netherlands
4 Harvard T.H. Chan School of Public Health, Boston, USA
5 University of Pittsburgh Graduate School of Public Health, Pittsburgh, PA, USA
6 The Hospital for Sick Children, Toronto and University of Toronto, Toronto ON, Canada

www.darthworkgroup.com