Quantitative Approaches to Summarizing the Benefits and Risks of Screening

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National Cancer Policy Forum Workshop

Advancing Progress in the Development and Implementation of Effective, High-Quality Cancer Screening

Which risks and benefits?

Risks of screening

- Deaths & complications
- False-positive results
- Patient burden:
  - total tests,
  - total invasive test/biopsies
- Costs

Timescale:

- Mostly short-term

Which risks and benefits?

Risks of screening

- Deaths & complications
- False-positive results
- Patient burden:
  - total tests,
  - total invasive test/biopsies
- Costs

Benefits of screening

- Cancers prevented,
  Late-stage cancers prevented,
  Cancer deaths prevented
- Life years gained
- Quality adjusted life years gained

Timescale:

- Can be short-term
- Long term or lifetime
- The end-user matters

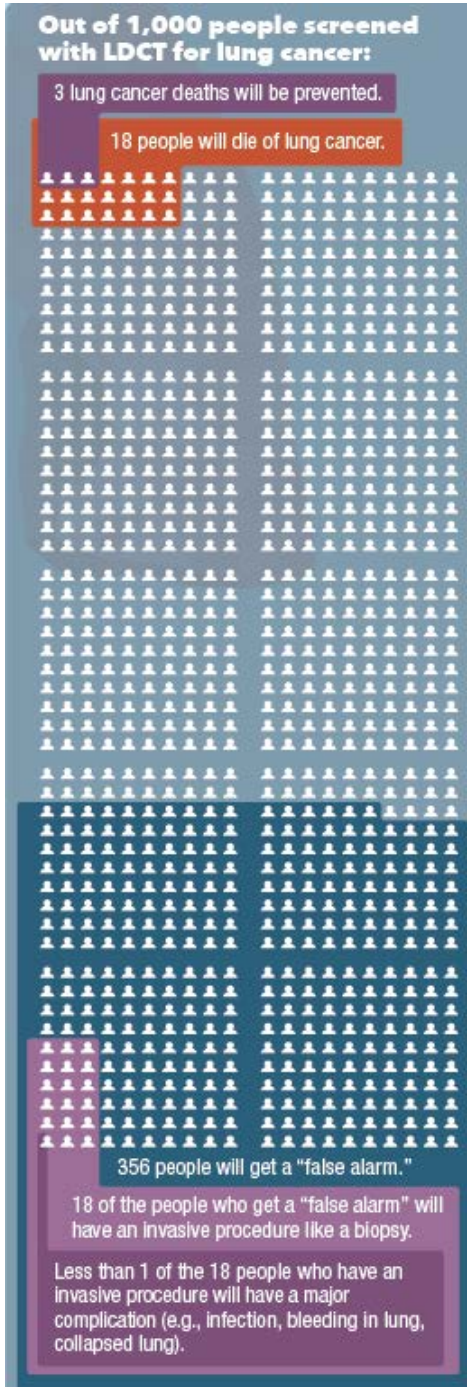
Patient decision-aids

This decision aid from the Agency for Healthcare Research and Quality will help prepare you to talk with your doctor about whether lung cancer screening is right for you.

CDC Centers for Disease Control and Prevention

AHRQ Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

https://www.cdc.gov/cancer/dcpc/prevention/screening.htm



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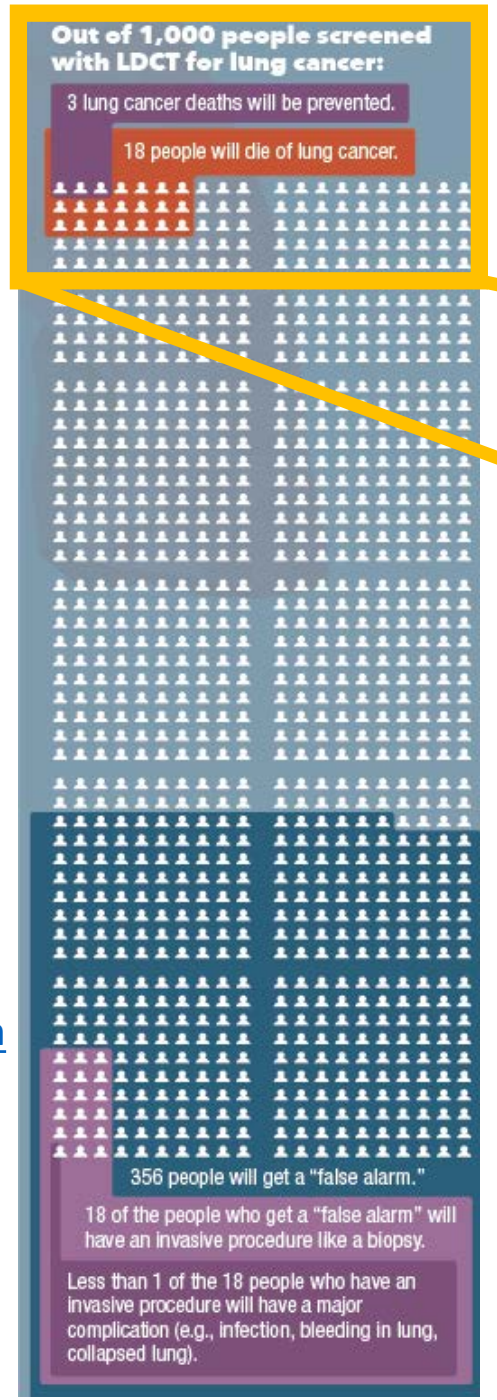
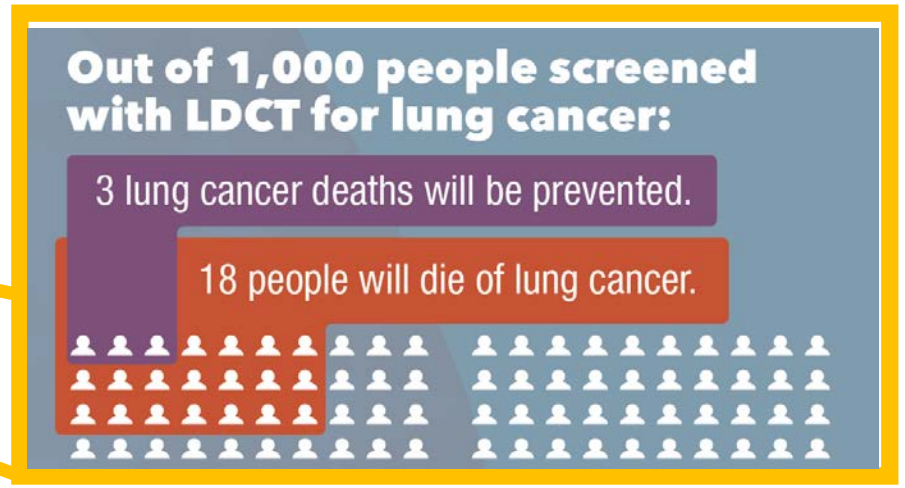
https://effectivehealthcare.ahrq.gov/decision-aids/lung-cancer-screening/patient.html





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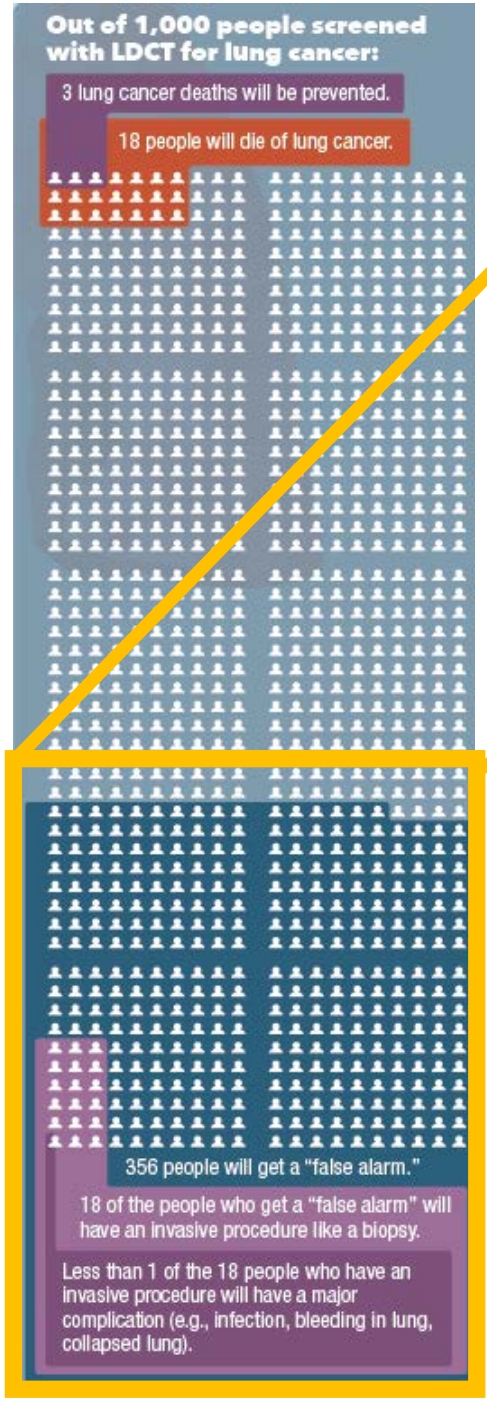
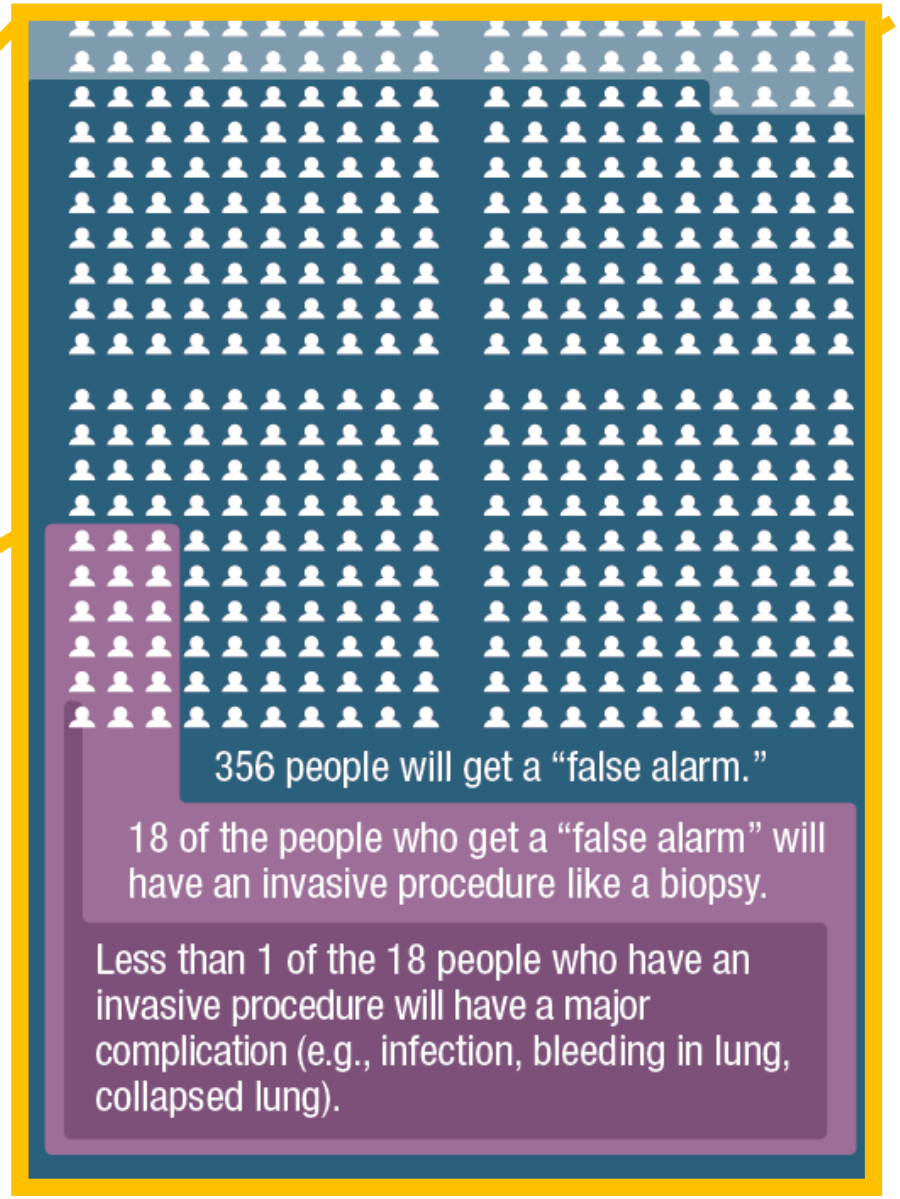
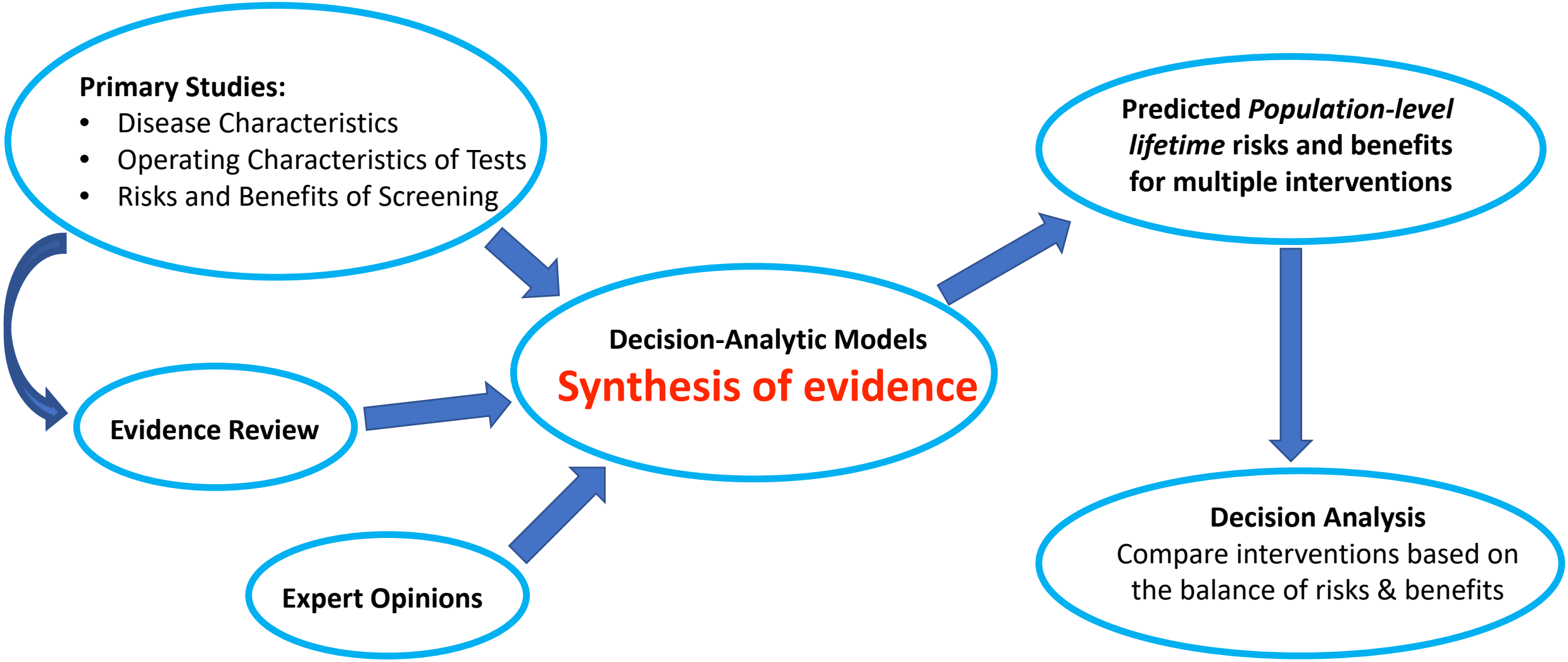
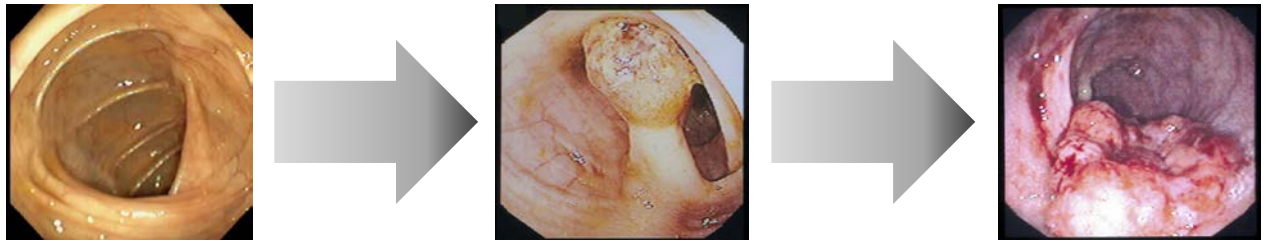


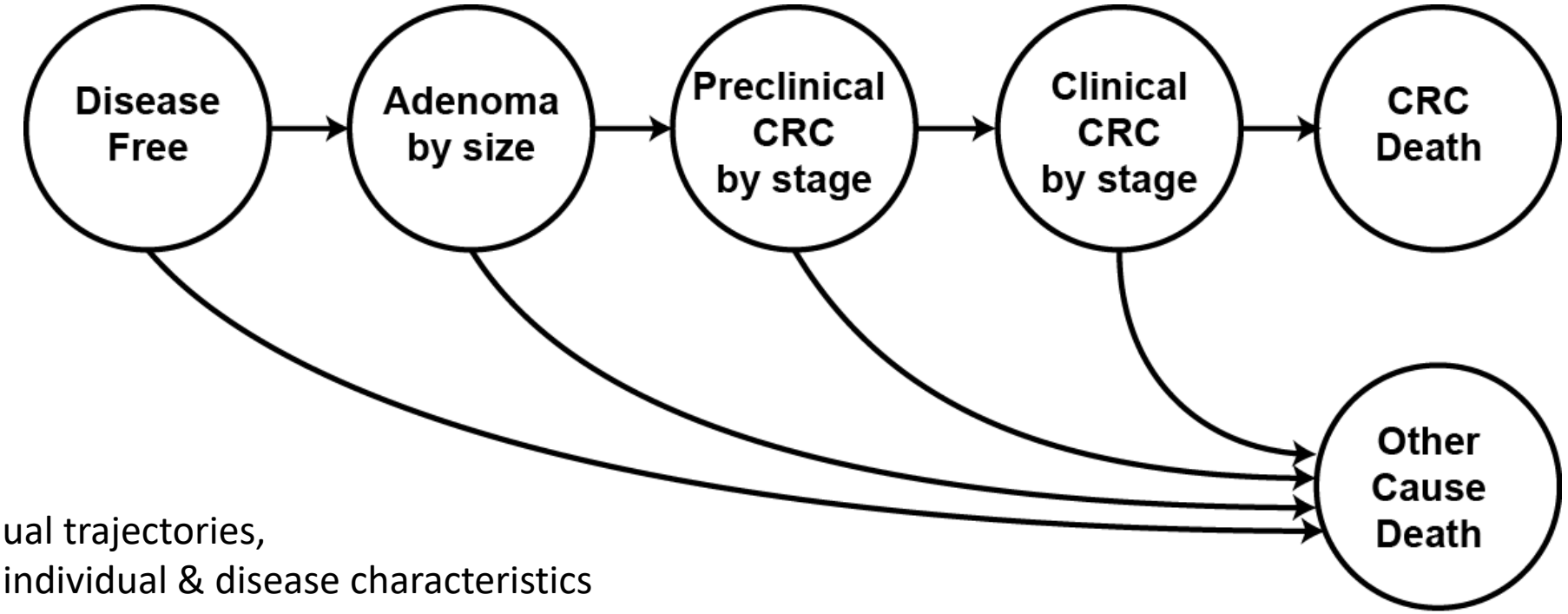


Modeling to Estimate Risks & Benefits



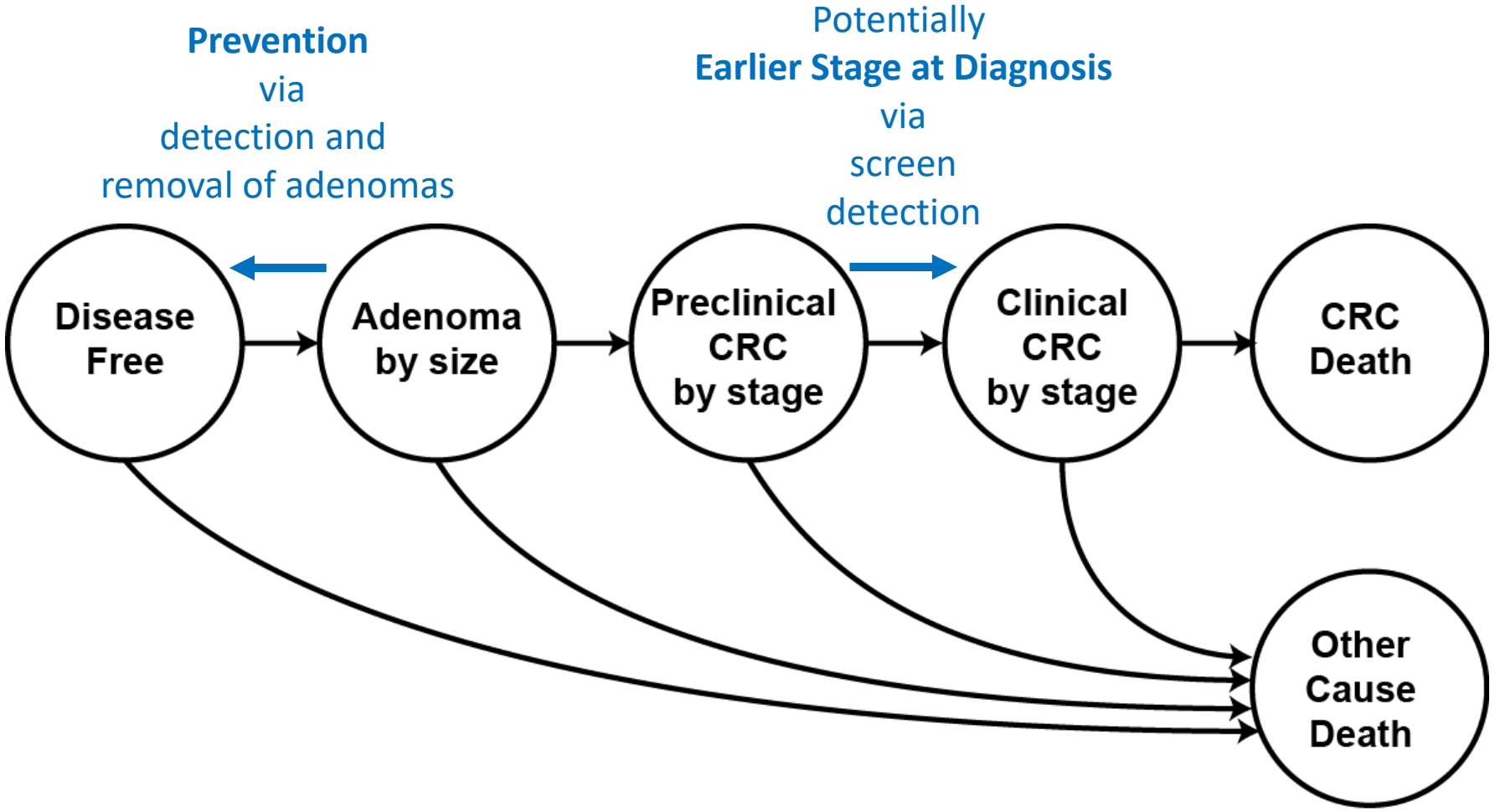
Natural History Model for Colorectal Cancer





Microsimulation:
Simulation of individual trajectories,
to describe multiple individual & disease characteristics

Natural History Model + Screening Model



Screening Model

Optimal screening

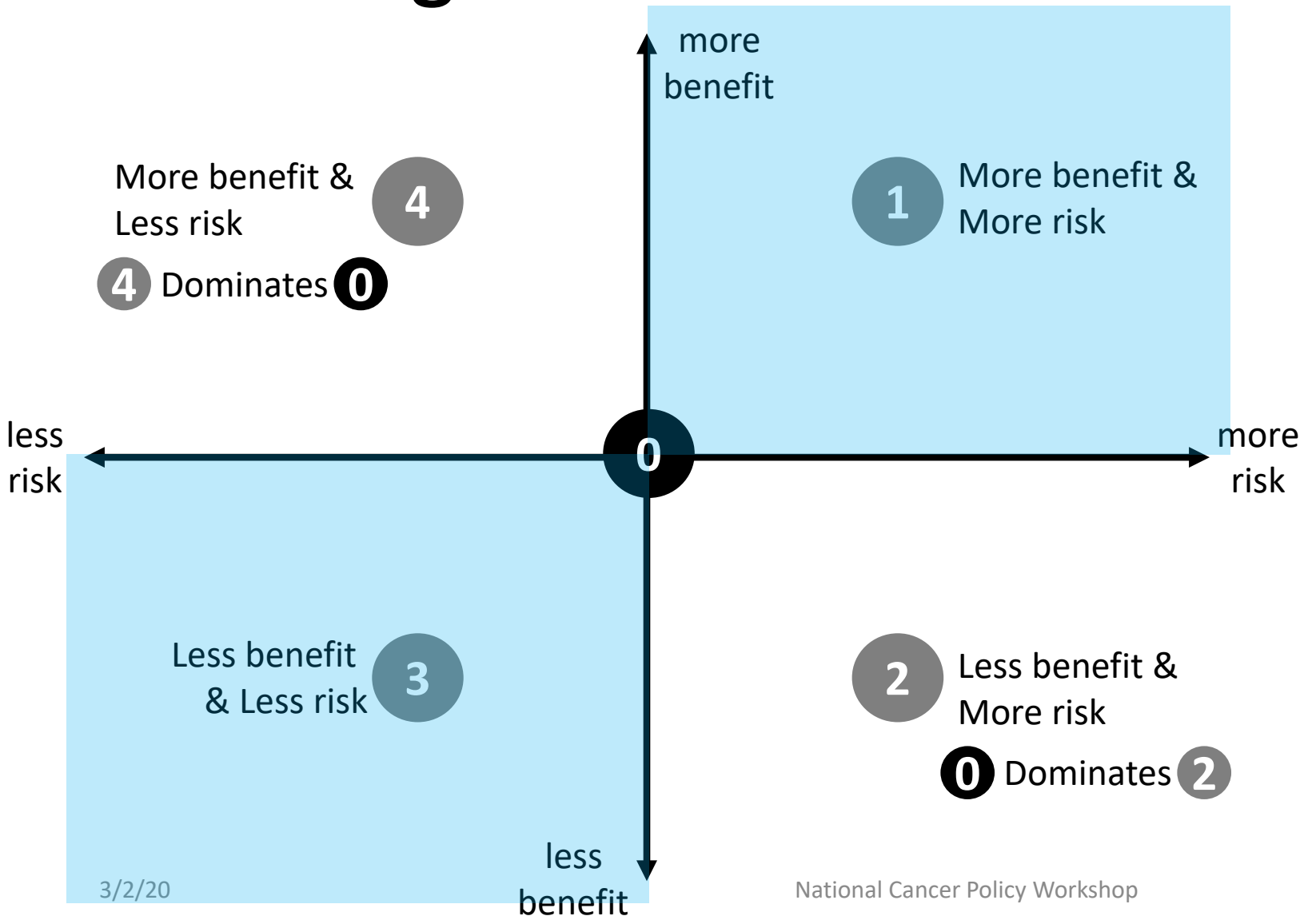
- What is the best you can expect?

Realistic screening

- What do we really expect?
- What do we make realistic?
  - Test operating characteristics
  - Screening behaviors

Modeling human behavior is hard

Balancing benefits and risk

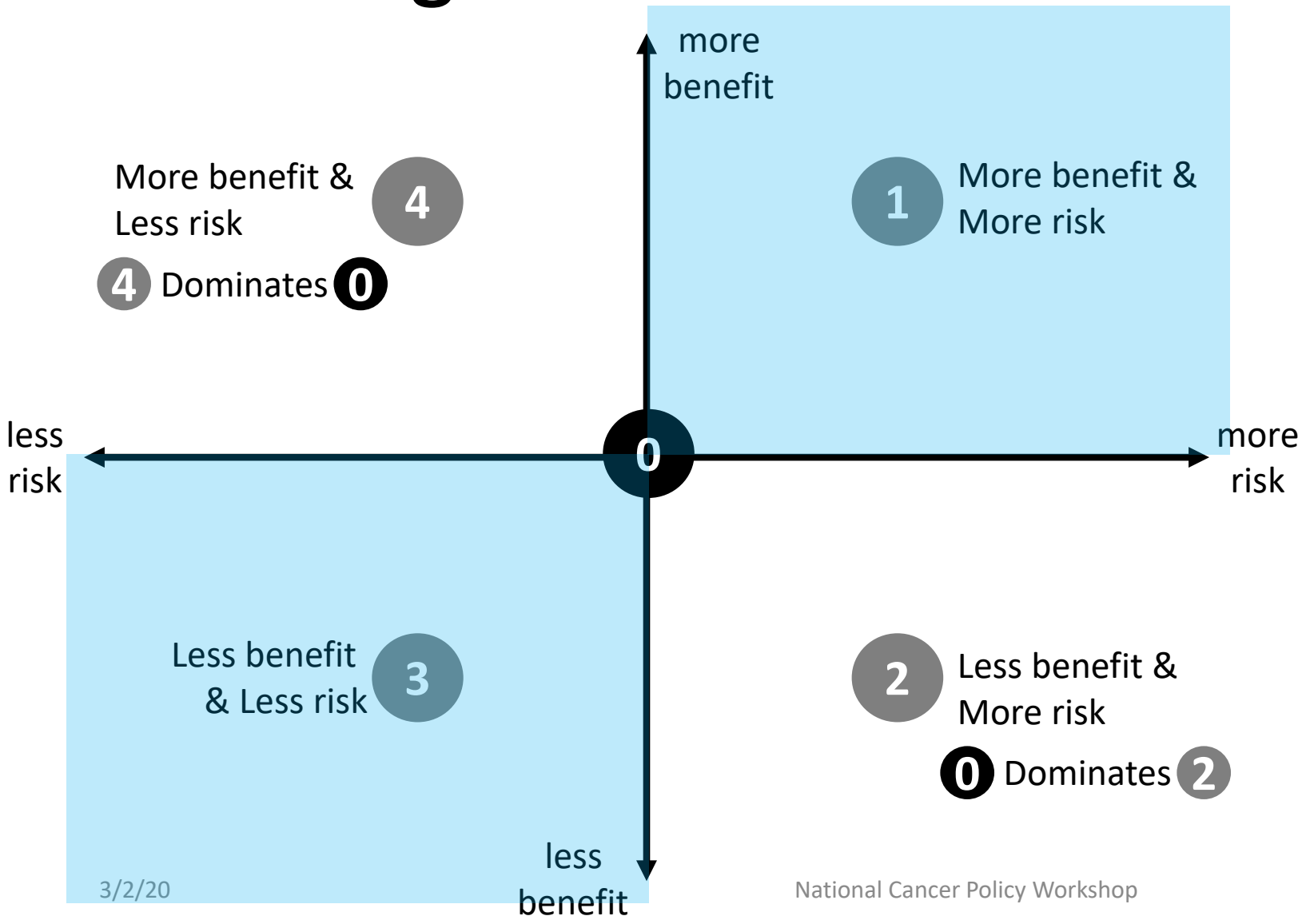


Incremental cost effectiveness (or risk benefit) ratio

$$ICER = \frac{\Delta\, risk}{\Delta\, benefit}$$

ICER may be large because of large differences in risk
or
small differences in benefit

Balancing benefits and risk



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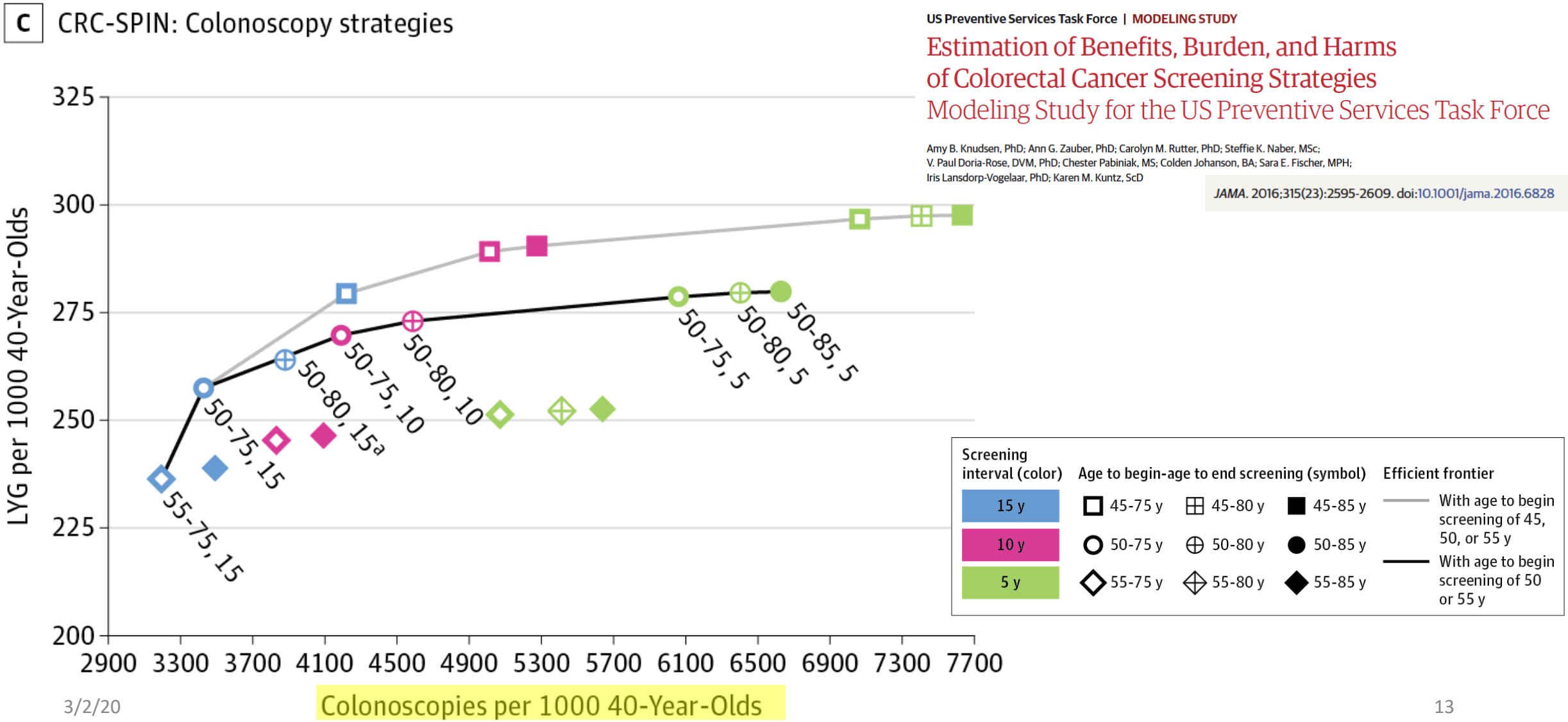
$$ICER = \frac{\Delta\, risk}{\Delta\, benefit}$$

Balancing risk and benefit: Frontier Curve



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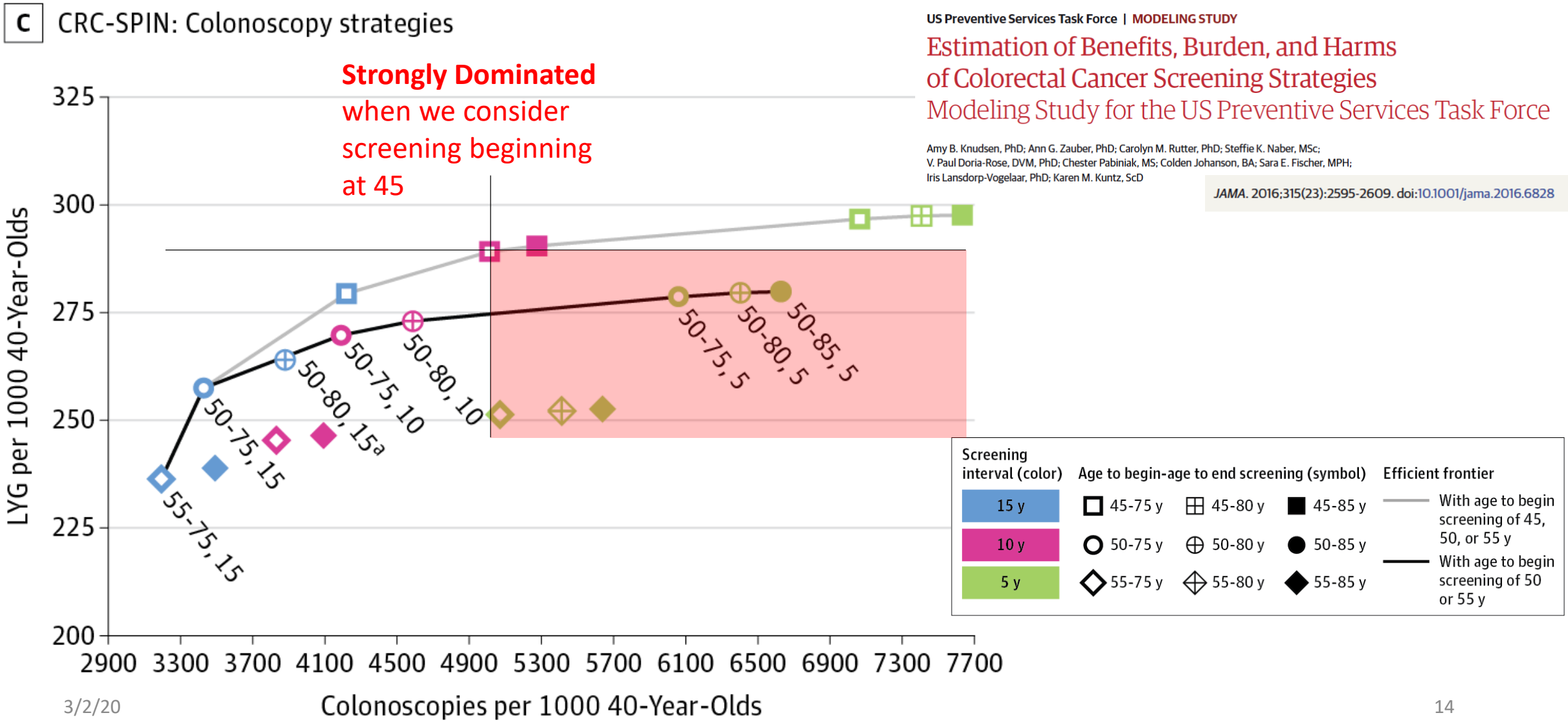

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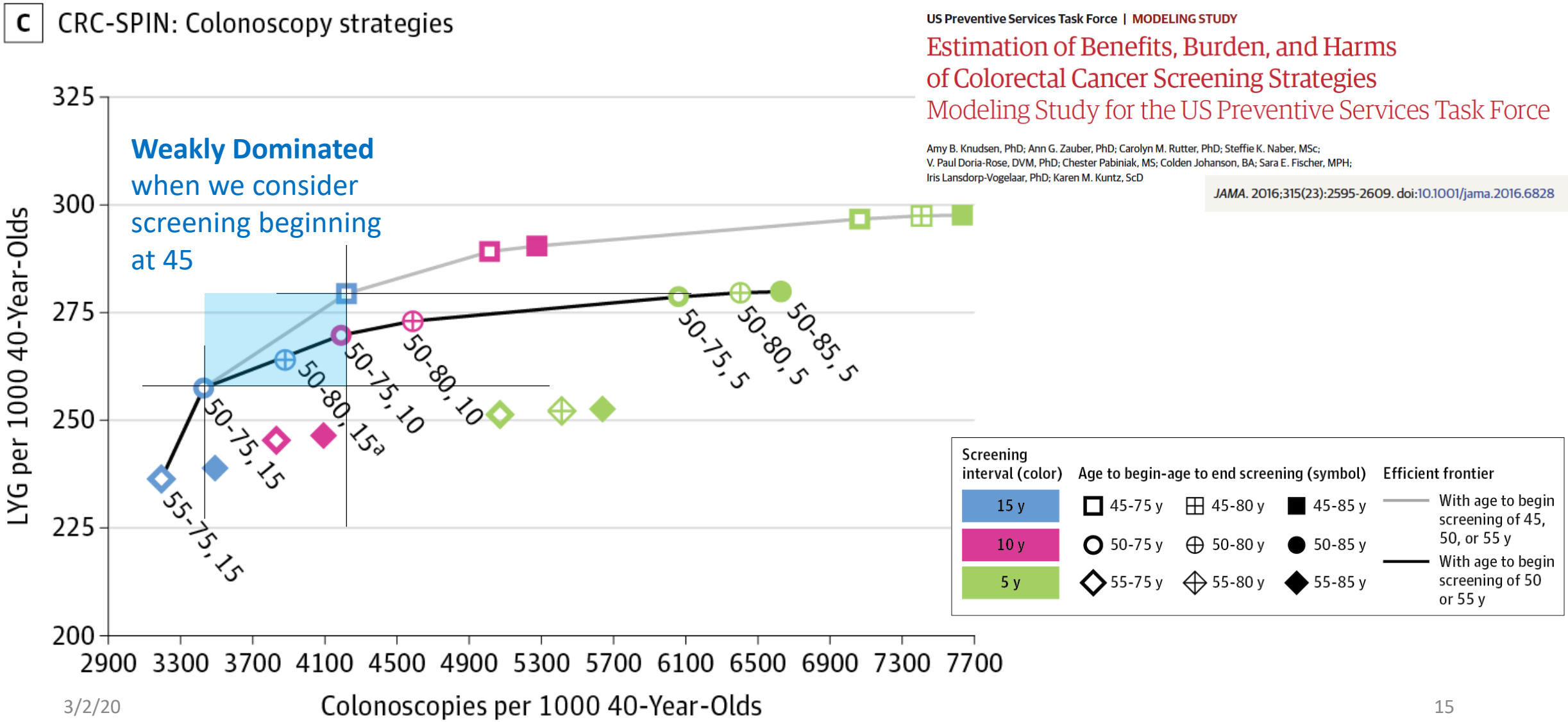
Estimation of Benefits, Burden, and Harms of Colorectal Cancer Screening Strategies
Modeling Study for the US Preventive Services Task Force

Amy B. Knudsen, PhD; Ann G. Zauber, PhD; Carolyn M. Rutter, PhD; Steffie K. Naber, MSc; V. Paul Doria-Rose, DVM, PhD; Chester Pabiniak, MS; Colden Johanson, BA; Sara E. Fischer, MPH; Iris Lansdorp-Vogelaar, PhD; Karen M. Kuntz, ScD

JAMA. 2016;315(23):2595-2609. doi:10.1001/jama.2016.6828

Balancing risk and benefit: Frontier Curve



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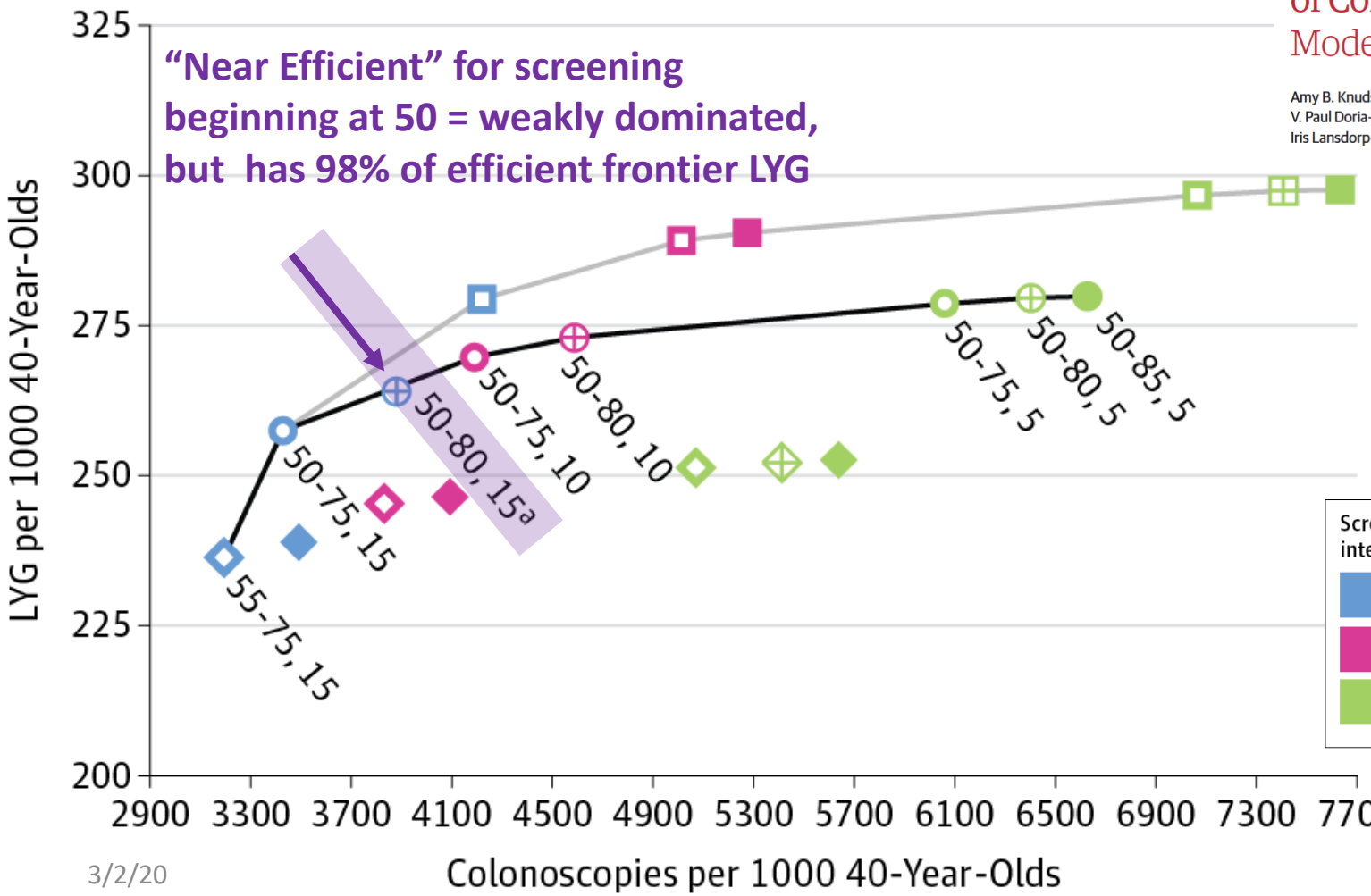
Balancing risk and benefit: Frontier Curve

C CRC-SPIN: Colonoscopy strategies



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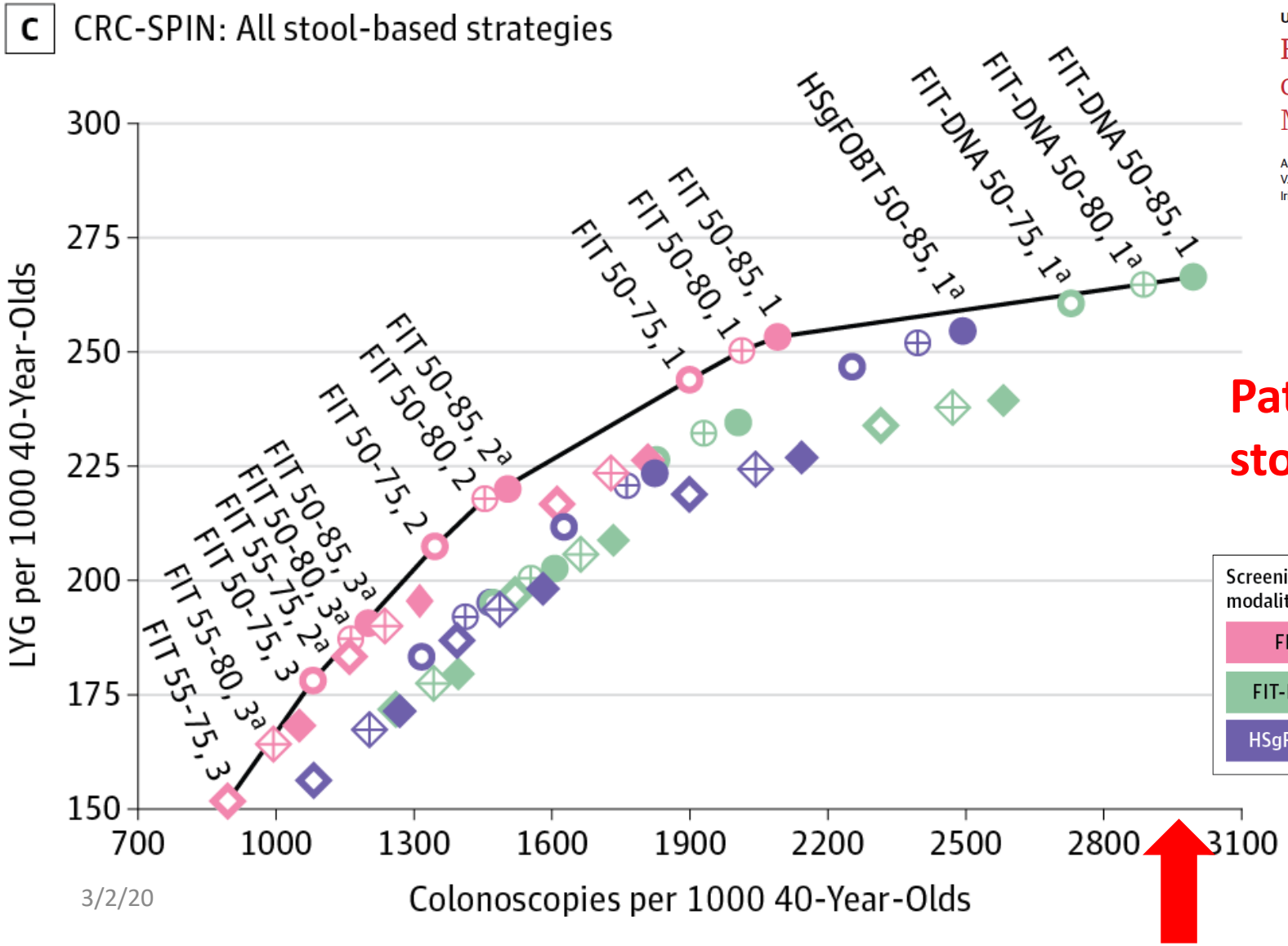
Screening interval (color)	Age to begin-age to end screening (symbol)			Efficient frontier
15 y	45-75 y	45-80 y	45-85 y	With age to begin screening of 45, 50, or 55 y
10 y	50-75 y	50-80 y	50-85 y	With age to begin screening of 50 or 55 y
5 y	55-75 y	55-80 y	55-85 y	

Balancing risk and benefit: Frontier Curve



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Patient burden is different for stool-based tests & colonoscopy

Screening modality (color)
- FIT
- FIT-DNA
- HSgFOBT

Age to begin-age to end screening (symbol)
- 50-75 y
- 50-80 y
- 50-85 y
- 55-75 y
- 55-80 y
- 55-85 y

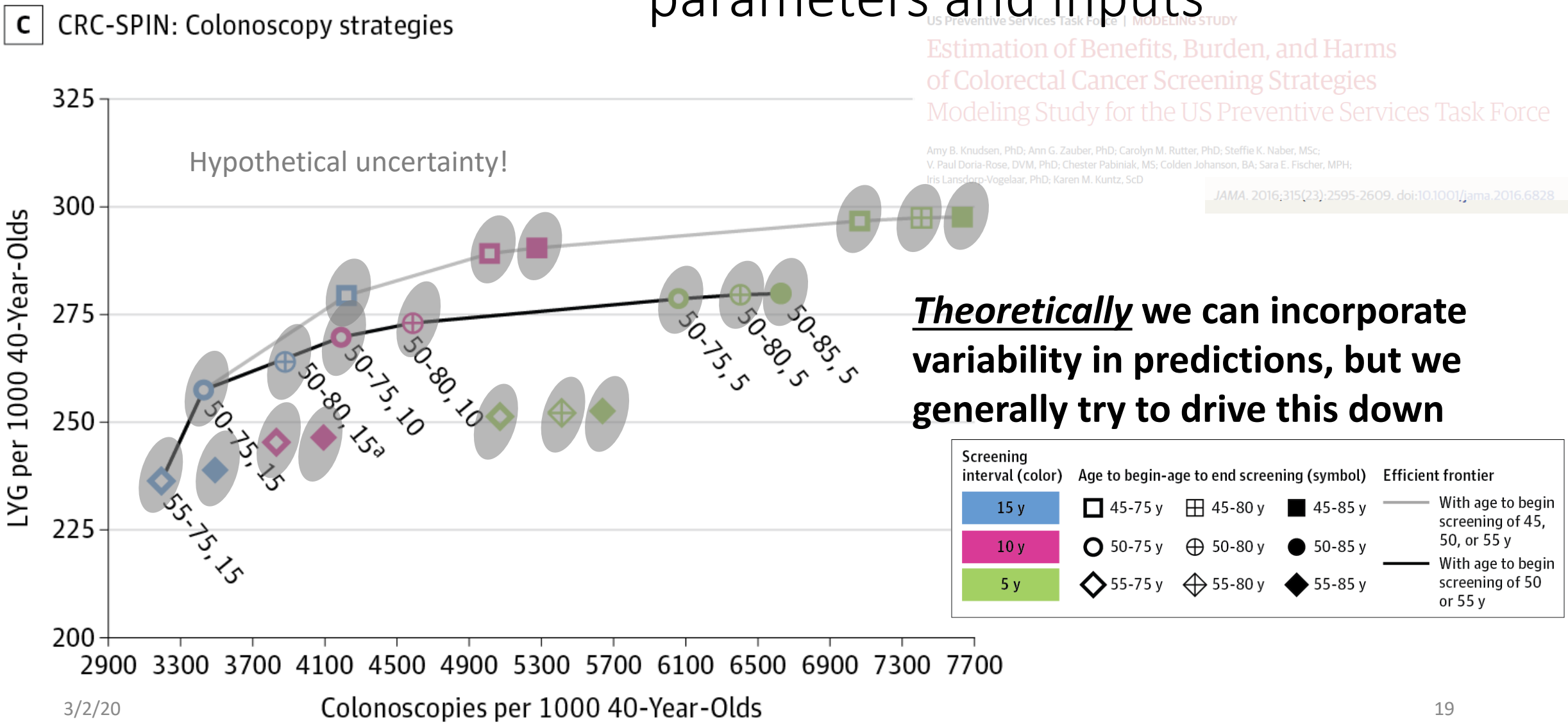
Efficient frontier
- With age to begin screening of 50 or 55 y

Types of Uncertainty

Sculpher, Mark J., Anirban Basu, Karen M. Kuntz, & David O. Meltzer. Chapter 11: Reflecting uncertainty in cost-effectiveness analysis. In *Cost-Effectiveness in Health and Medicine* (2016).

1. Uncertainty in model **predictions**
2. Uncertainty in model **structure**
3. Uncertainty about unknown model **parameters**
4. Uncertainty about model **inputs** (often treated as fixed), e.g., test characteristics & screening behaviors

Prediction Uncertainty: variability given the model, parameters and inputs



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Theoretically **we can incorporate variability in predictions, but we generally try to drive this down**

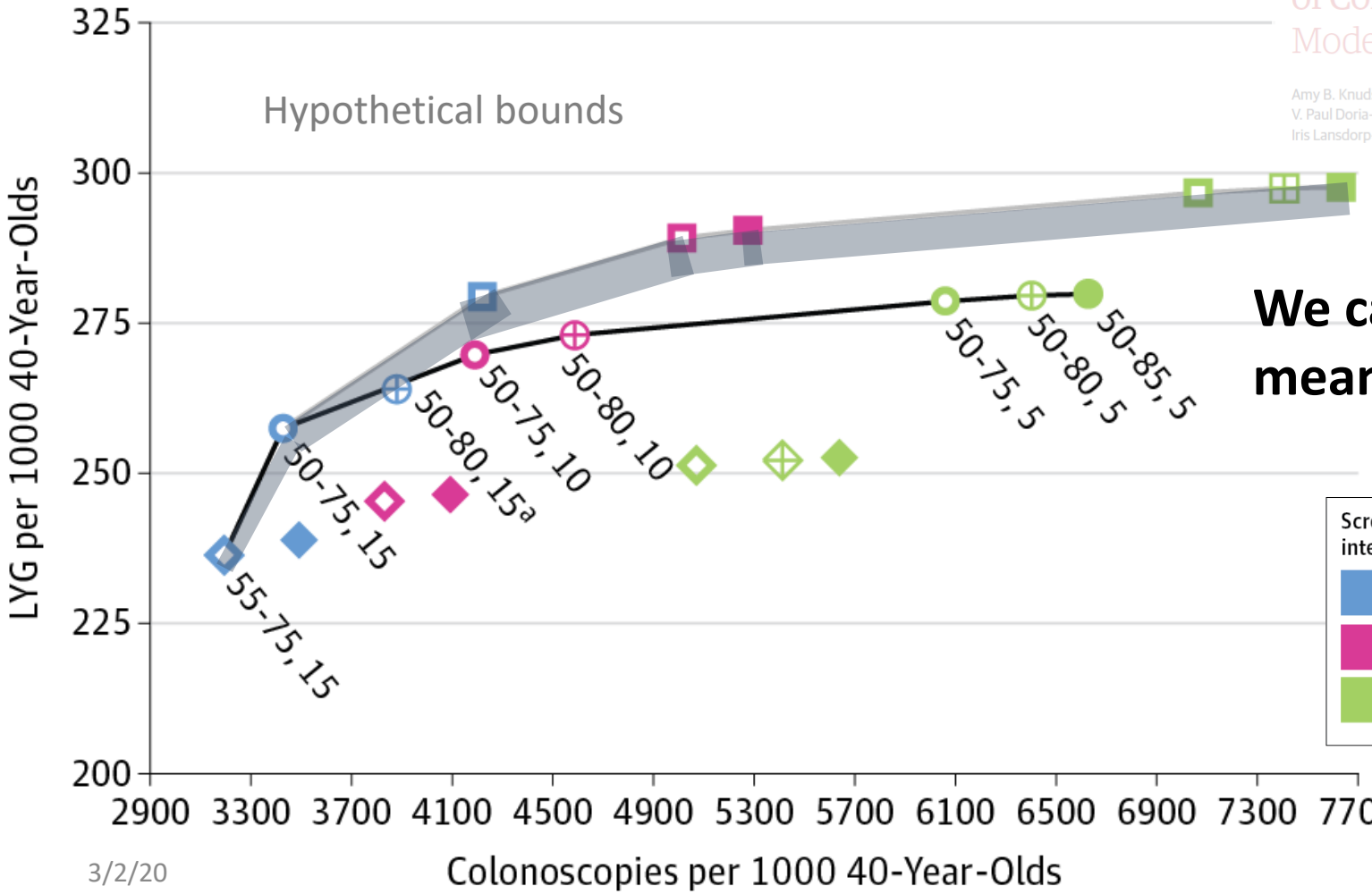
Prediction Uncertainty

- When using simulation models, the population size can be increased until the risks and benefits are estimated precisely
  - However, the ICER could remain uncertain when there are small differences in benefit for two interventions.
  - Is there a logical limit to the simulated population size?

$$ICER = \frac{\Delta\, risk}{\Delta\, benefit}$$

Prediction Uncertainty

C CRC-SPIN: Colonoscopy strategies



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We can define similarity based on a meaningful risk & benefit differences

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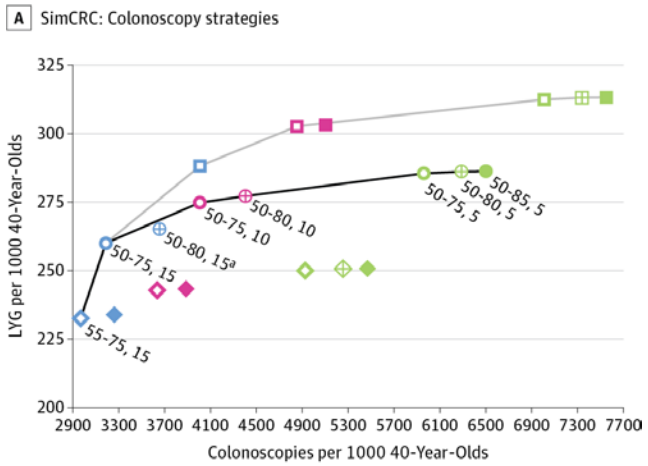

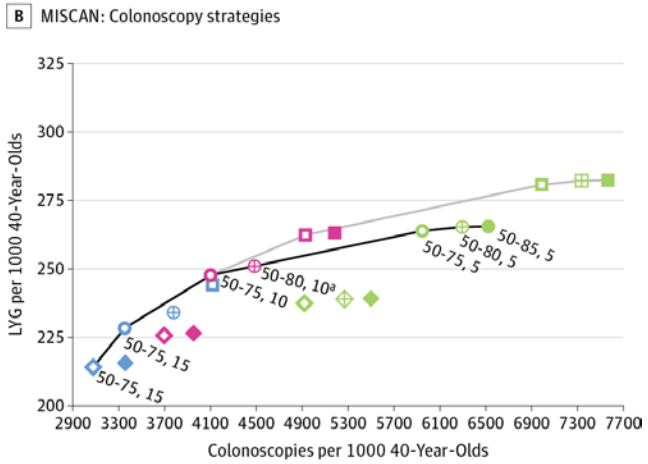

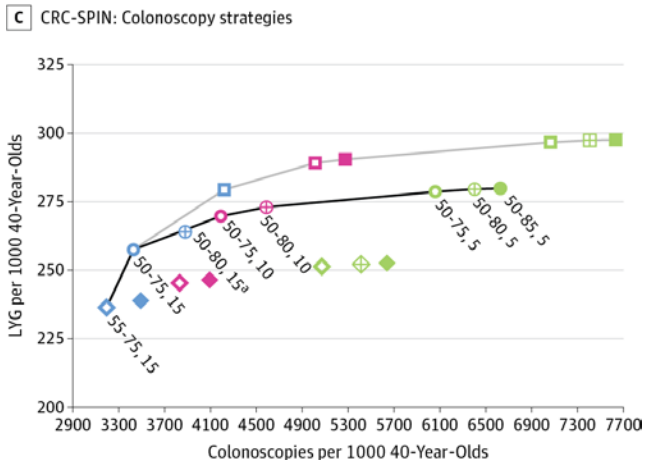

Structural Uncertainty

Uncertainty about model assumptions & structure

Can be addressed using collaborative modeling. Look for consistency in results – a *qualitative* rather than quantitative comparison.

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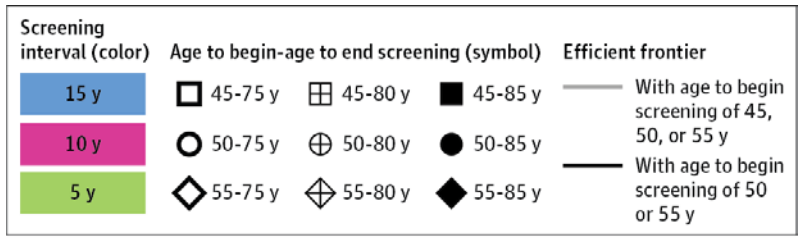
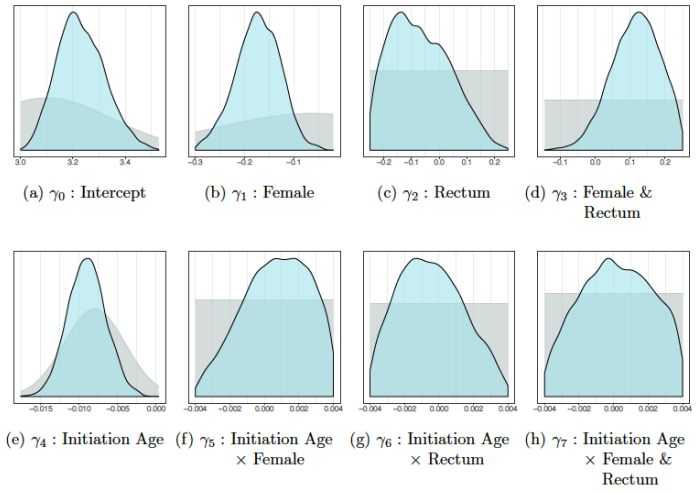


Parameter Uncertainty: variability of calibrated model parameters

Address with probabilistic sensitivity analysis (PSA)

- Estimate (or specify) a distribution for unknown model parameters
- Sample from these distributions and predict risks and benefits

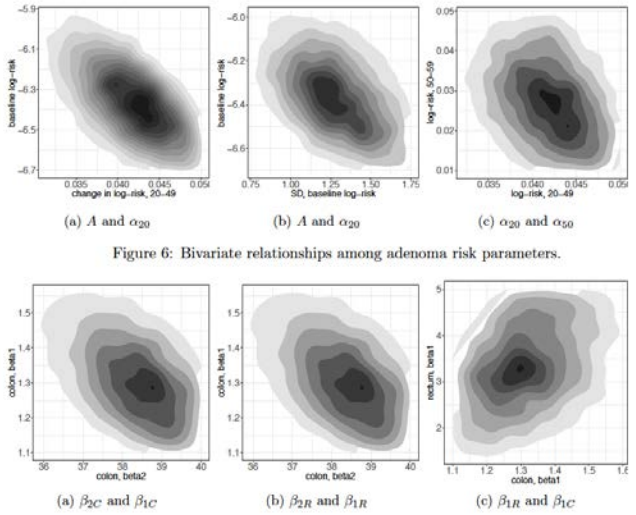
Estimated distributions of model parameters



(a) γ_0 : Intercept (b) γ_1 : Female (c) γ_2 : Rectum (d) γ_3 : Female & Rectum

(e) γ_4 : Initiation Age (f) γ_5 : Initiation Age × Female (g) γ_6 : Initiation Age × Rectum (h) γ_7 : Initiation Age × Female & Rectum

Parameters are not independent



(a) A and α_{20} (b) A and α_{20} (c) α_{20} and α_{50}

Figure 6: Bivariate relationships among adenoma risk parameters.

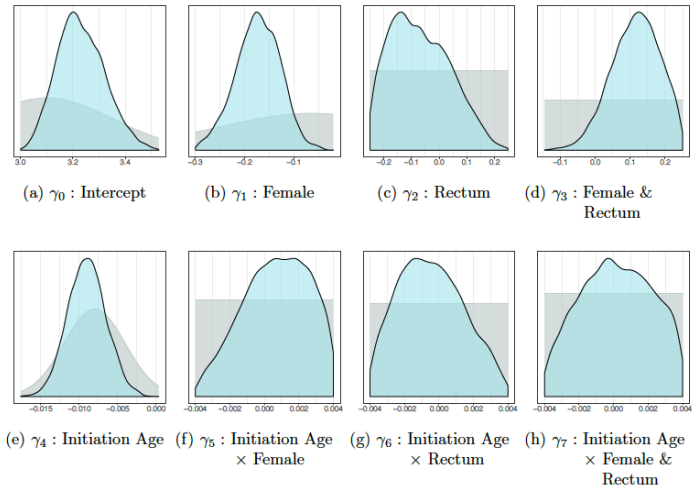
(a) β_{2C} and β_{1C} (b) β_{2R} and β_{1R} (c) β_{1R} and β_{1C}

For each parameter vector sampled, we get different predicted risks & benefits

Parameter Uncertainty

Use PSA to get a distribution of risks, benefits & risk: benefit ratios.

Estimated distributions of model parameters



Summarize results:

- Average benefit, risk, risk:benefit
- Percentage of the time each screening scenario is on the efficient frontier

Probabilistic Sensitivity Analysis

- Limited by computational burden
  - Estimation of distribution of model parameters
  - Prediction of risk and benefit for multiple parameter sets
- Computation – and research – is catching up (stay tuned)

Parameter & Input Uncertainty

Many layers of uncertainty

Parameters × test operating characteristics × screening behaviors

Acknowledgement

We've had many discussions within the CISNET-CRC team that have touched on topics in this presentation. Thanks to:

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MISCAN-CRC Team: Iris Lansdorp-Vogelaar, Elleke Peterse

Coordinating Center: Ann Zauber

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Thank You