Modeling multi cancer early detection: a tool to move between performance and outcomes

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Conflicts of interest

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What will be the population impact of MCED screening?

Test performance (e.g., Galleri test)

- High specificity (>99%)
- Sensitivity in clinically-detected patients
  - varies by cancer sites
  - highest for late stage disease.
- Per the PATHFINDER study, the positive predictive value was about 40% in a general population.

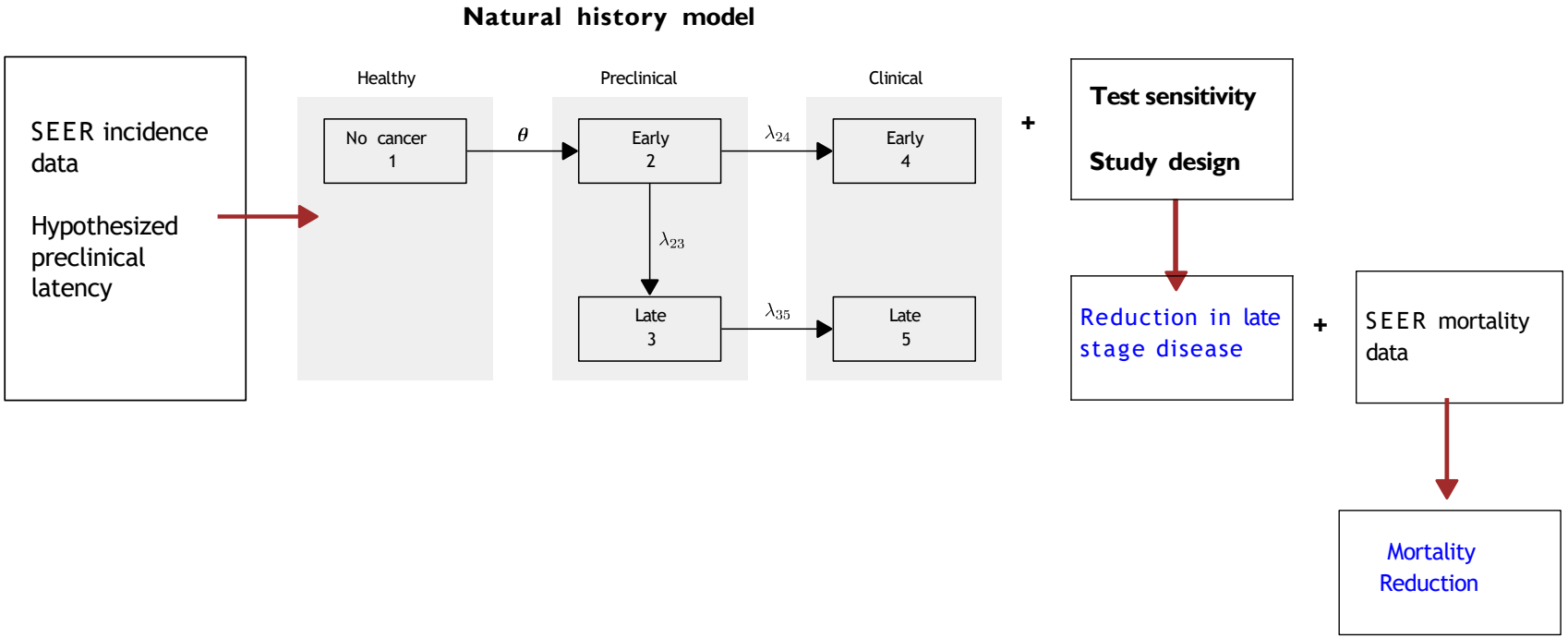
Huge gap between performance and population outcomes

Clinical trials

Modeling

- Well designed trials necessary to bridge the gap.
  - Expensive
  - Take years to yield results
- Without trials: models can get us closer.

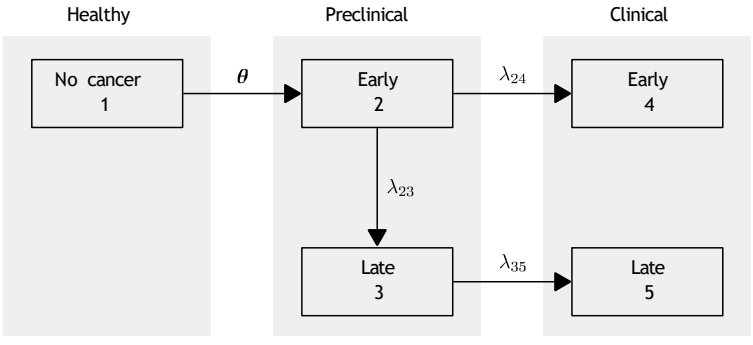
Framework for modeling the benefits of MCED screening in a clinical trial



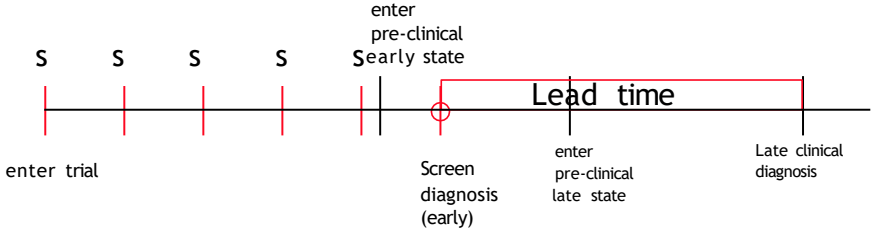
- Natural history models calibrated separately for each cancer site based on incidence data and user-provided mean overall and late pre-clinical latencies.
- Stage shift model used to project mortality outcomes.

Projecting the reduction in late stage disease

Natural history model



Superimposing screening



Individual

For on indivudal, simulate:
-Natural history of cancer
-Screen diagnosis
-Cancer specific death

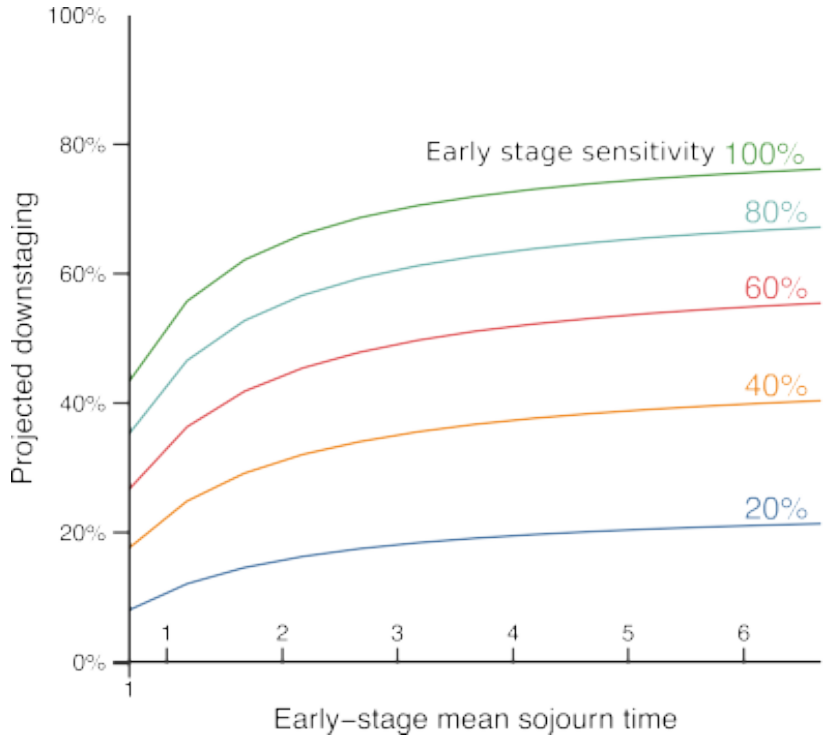
Trial

Simulate multiple individuals
based on specified distribution of
-Number in each study arm
-Ages at entry
-Number of screens

Reduction in late stage disease: single cancer

Drivers of stage shift

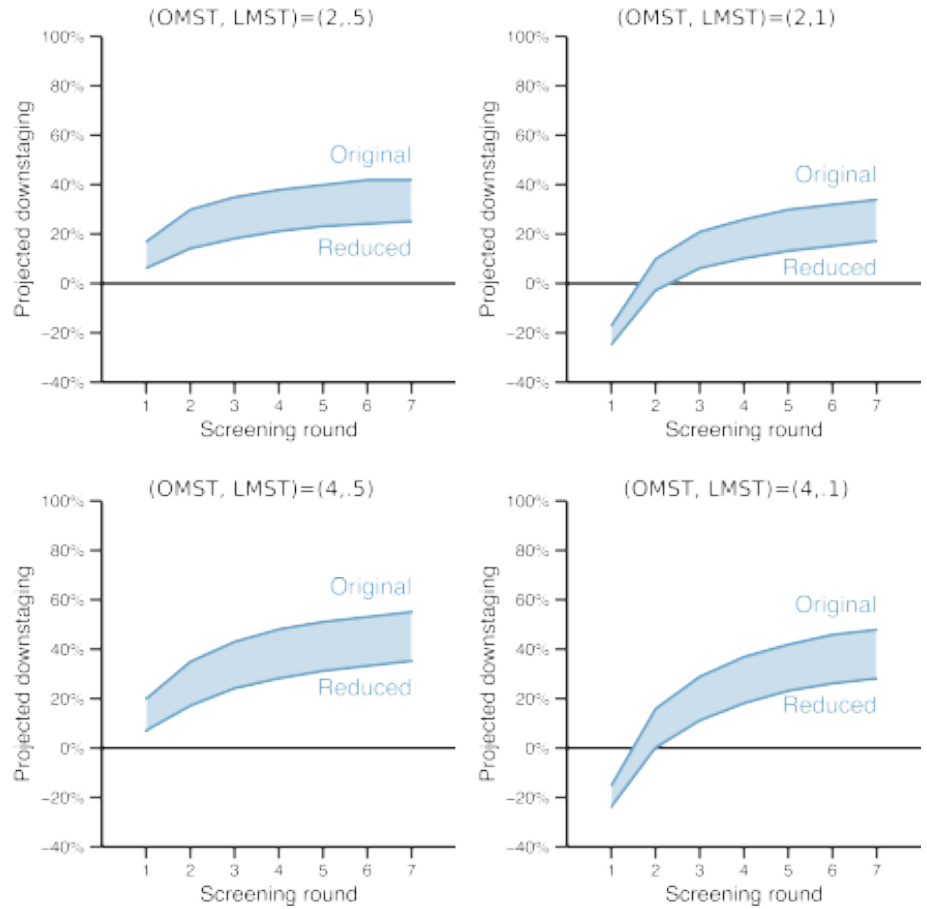
- Early stage sensitivity
- Detectable early stage pre-clinical duration (amongst progressive cancers)



Source: Lange 2024, CEBP

Expected reductions in late stage disease in a multi-cancer trial

Figure 5



Source Lange 2024, CEBP

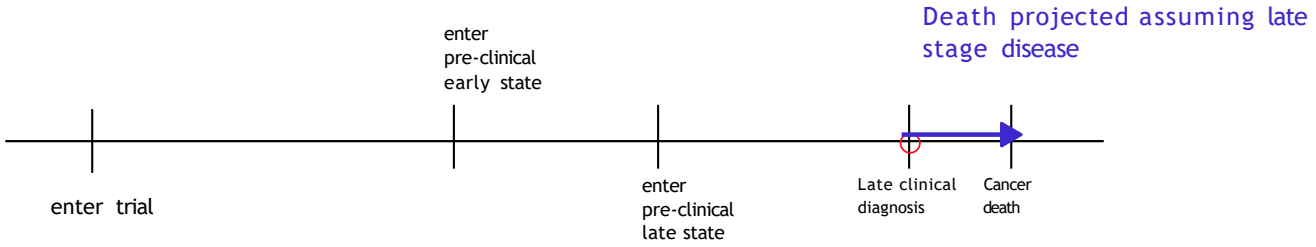
Projected reduction in distant stage disease after 3 screens:

- 21-43% (assuming sensitivity= that of clinically diagnosed patients)
- 6-24% (assuming sensitivity=50% of that of clinically diagnosed patients)

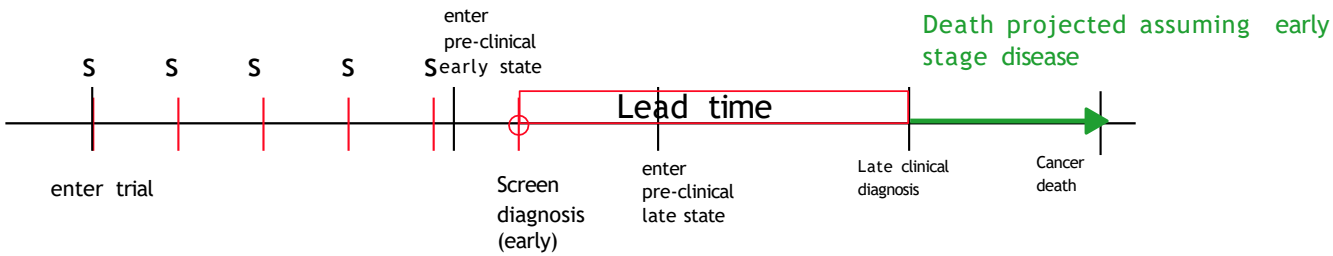
Projecting mortality

Stage shift model for projecting mortality

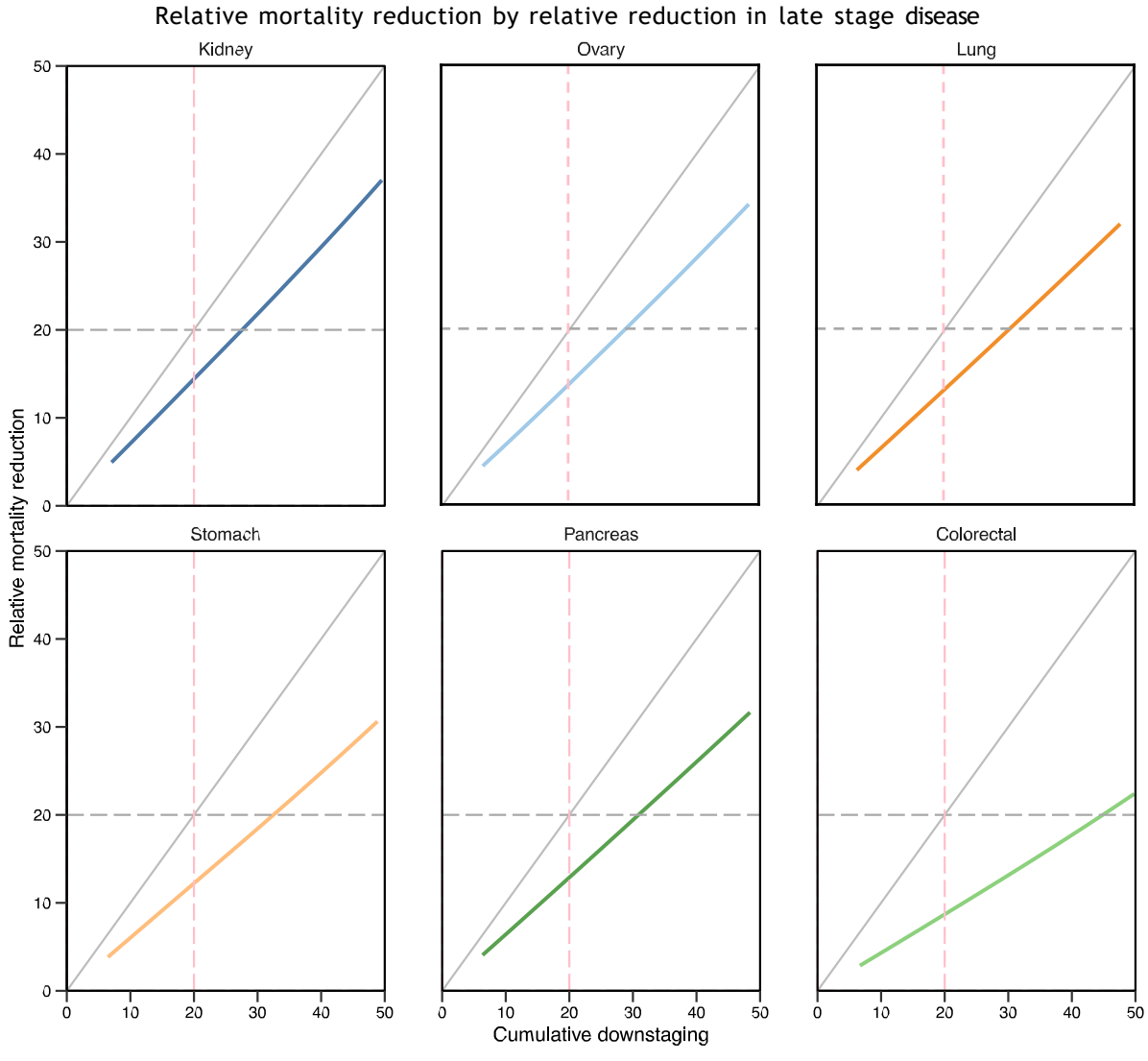
No screening



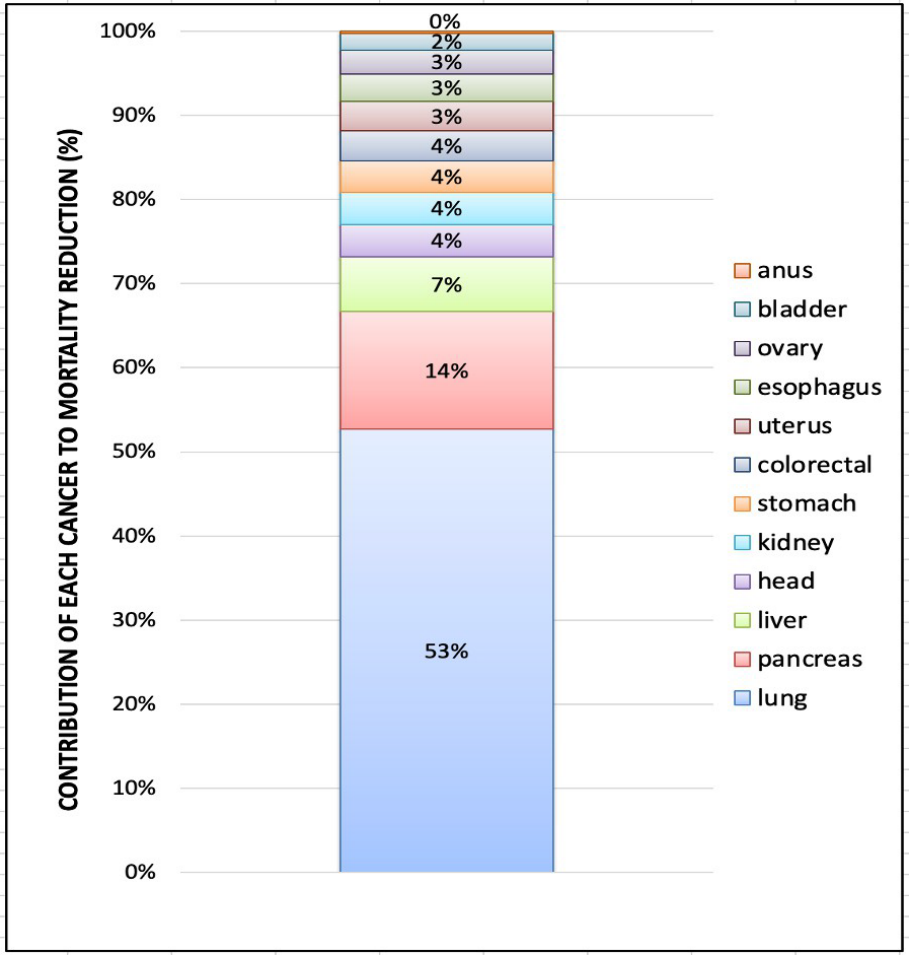
Screening



Relationship between stage shift and projected mortality reduction: single cancers



Mortality implications of late stage disease reduction in MCED trial



- We expect the relative mortality reduction to be 60% of the relative reduction in late stage disease (assuming common stage shift)
- Mortality reduction driven by cancer sites with the highest mortality in unscreened patients.

Summary and future directions

Modeling allows us to

- extract the maximal information from the limited data we have.
- learn about drivers of screening benefit and set expectations for MCED trials.
- explore the how projections relate to assumptions (inputs and structural assumptions).
- incorporate new data to inform model inputs.

Thank you!

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Key Papers

Projecting the Impact of Multi-Cancer Early Detection on Late-Stage Incidence Using Multi-State Disease Modeling

Jane M. Lange[1], Kemal Caglar Gogebakan[2], Roman Gulati[2], and Ruth Etzioni[2,3]

CEBP 2024

Stage Shift as an Endpoint in Cancer Screening Trials: Implications for Evaluating Multicancer Early Detection Tests

Lukas Owens, Roman Gulati, and Ruth Etzioni

CEBP 2022