# Can Multi-Cancer Early Detection Screening Result in Early Cancer Detection? A Modeling Study

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# BACKGROUND

- Cancer is the second leading cause of death in the United States, and the leading cause of death in 19 states in 2016.<sup>1</sup>
- Early detection is associated with a higher chance of survival, but currently around half of cancers are detected at an advanced stage.<sup>2</sup>
- Routine screening is recommended for only four cancers (breast, cervical, colorectal, and lung),<sup>3</sup> and two-thirds of incident cancers lack routine screening guidelines.<sup>4</sup>
- Emerging blood-based multi-cancer early detection (MCED) tests offer the promise of revolutionizing early cancer detection.



## **OBJECTIVES**

We evaluated the potential impact of an MCED test as a supplement to usual care for the early detection of 12 cancers, which account for nearly 80% of all cancer incidence.<sup>5</sup>



## **METHODS**

- We developed <u>Simulation Model for MCED</u> (SiMCED), a microsimulation model of 12 solid tumor cancers: breast, colorectal, endometrial, esophageal, gastric, kidney, liver, lung, ovarian, pancreatic, prostate, and urinary bladder.
- Dwell times (cancer type- and stage-specific) were synthesized from published literature and empirical estimates, and used to inform the transitions between healthy and cancer stages I-IV.
- Multiple levels of MCED test sensitivities (cancer type- and stage-specific) were derived from case-control studies with different biomarker configurations.<sup>6,7</sup>
- Unobserved cancer incidence rates were estimated for each combination of sex, age group, cancer type and stage using a backwards induction approach.<sup>8,9</sup>
- The model was calibrated to reproduce yearly incidence rates of cancer diagnosis via usual care as captured in the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database.
- We simulated the life course of 50 million US adults aged 50-84 years. Diagnosis of cancer could arise from usual care or MCED screening. The MCED test was administered annually or biennially to individuals aged <85 years.

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Table 1. Early- versus late-stage cancer diagnoses across screening scenarios							
Stages	Usual care	Usual care + MCED, annual screening			Usual care + MCED, biennial screening		
	Total diagnoses	Total diagnoses	Absolute change	Percentage change	Total diagnoses	Absolute change	Percentage change
Early-stage (I–II)	14,194	15,545 [15,223; 16,431]	1,351 -[1,028; 2,237]	10% [7; 16]%	14,957 [14,761; 15,489]	763 [567; 1,295]	5% [4; 9]%
Late-stage (III–IV)	9,229	8,067 [8,351; 7,319]	-1,162 -[878, 1,910]	-13% -[10; 21]%	8,581 [8,749; 8,132]	-649 -[480; 1,097]	-7% -[5; 12]%

Footnote: In cells corresponding to "Usual care + MCED," the first number is the value associated with the 33% sensitivity test; the numbers in square parentheses are associated with the 28% and 42% sensitivity tests.

## RESULTS

#### Cumulative Number of New Diagnoses without MCED vs. with MCED

#### Figure 1.

Cancer downstaging results by screening interval (columns) and empirical sensitivity (rows)

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#### Footnote:

*Empirical sensitivity* is the model-computed real-world sensitivity when MCED screening is performed on the general population with realistic cancer prevalences Thus, SiMCED "projects" case control sensitivities into the real world.

• **Figure 1** presents cancer downstaging results by screening interval and empirical sensitivity. • In all scenarios, there is downstaging from later stages to earlier stages due to MCED screening. • The consistent decrease in Stage IV diagnoses—ranging from 26% to 42% with annual screening and 15% to 27% with biennial screening—indicates that MCED is effective at catching cancer before it progresses to Stage IV. • MCED screening increases the total number of diagnoses by at most 1% across all scenarios. • For a given screening interval, the higher the empirical sensitivity, the greater the amount of downstaging. • For a given sensitivity level, annual screening produces more downstaging than biennial screening.



- **Table 1** compares early- and late-stage cancer diagnoses across screening scenarios.
- Using the 33% sensitivity test with an annual screening interval, the rate of early-stage diagnoses increases by 1,351 (10%) per 100,000, while the rate of late-stage diagnoses decreases by 1,162 (13%) per 100,000.
- For the same test and a biennial screening interval, the rate of early-stage diagnoses increases by 763 (5%) per 100,000, while the rate of late-stage diagnoses decreases by 649 (7%) per 100,000.

## CONCLUSIONS

- Annual MCED screening can reduce Stage IV incidence by 26-42% and late-stage incidence by 10-21% over a 50-year horizon.
- Biennial MCED screening can reduce Stage IV incidence by 15-27% and late-stage incidence by 5-12% over a 50-year horizon.

Our study suggests that MCED tests could be an effective tool for early cancer detection, which is associated with improved survival and quality of life. However, their real-world impact and costeffectiveness require further investigation.

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### DISCLOSURES

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