# The potential of multi-cancer early detection screening for reducing cancer mortality

Poster

Jagpreet Chhatwal[1,2,3*], Jade Xiao[3], Andrew ElHabr[3], Christopher Tyson[4], Xiting Cao[4], Sana Raoof[5], A. Mark Fendrick[6], A. Burak Ozbay[4], Paul Limburg[4], Tomasz M. Beer[4], Ashish Deshmuk[7], Andrew Briggs[8]

[1] Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA, [2] Center for Health Decision Science, Harvard University, Boston, MA, USA, [3] Value Analytics Labs, Boston, MA, USA, [4] Exact Sciences Corporation, Madison, WI, USA, [5] Memorial Sloan Kettering Cancer Center, New York, NY, USA, [6] School of Public Health, University of Michigan, Ann Arbor, MI, USA, [7] Medical University of South Carolina, Charleston, SC, USA, [8] London School of Hygiene & Tropical Medicine, London, UK

* **Corresponding author:** JagChhatwal@mgh.harvard.edu

## 1 BACKGROUND

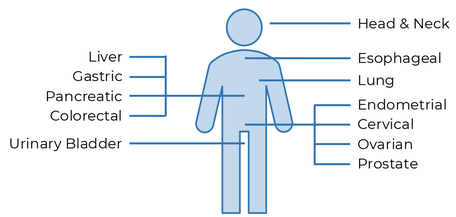
- Cancer is the second-leading cause of death in the United States, and the leading cause among people aged <85 years.[1]
- Early detection is associated with a higher chance of survival, but currently around half of all cancer cases are detected at an advanced stage.[2]
- Routine screening is USPSTF-recommended for only four cancer types: breast, cervical, colorectal, and lung.[3]
- Emerging blood-based multi-cancer early detection (MCED) tests have the potential to revolutionize early cancer detection. Their impact on cancer mortality remains uncertain. Computer models are needed to forecast long-term outcomes.

## 2 OBJECTIVES

We evaluated the potential impact of screening with an MCED test on stage IV cancer incidence and cancer mortality in the general US population.

## 3 METHODS

- We developed **Si**mulation Model for **MCED** (SiMCED), a continuous-time, discrete-event microsimulation model of 14 solid tumor cancer types that account for nearly 80% of all cancer incidence and mortality:[4]




- **Figure 1** is a high-level model schematic.
- An individual can develop only one cancer type in their lifetime.
- In the absence of a diagnosis, cancer progresses according to cancer type- and stage-specific dwell times.
- Unobserved cancer prevalence and incidence were estimated using a backwards induction approach.[5,6]
- The model was calibrated to reproduce annual incidence rates of usual care diagnosis as captured in the SEER database.[4]
- The MCED test was modeled as a supplemental screening approach with test sensitivities derived from a large, multi-center, prospective, case-control study (ASCEND-2).[7]
- After a cancer diagnosis, individuals followed SEER survival curves to determine the time and cause of death, i.e., cancer- or non-cancer-related.
- Using a 10-year horizon, we simulated the life course of 5 million adults aged 50-84 years, representative of the US population.
- The model was run twice, once without MCED testing (**Usual care**) and once with annual MCED testing for individuals aged <85 years (**Usual care + MCED**).

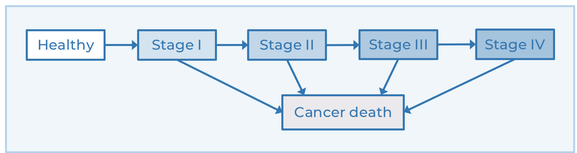



**Figure 1:** High-level model schematic of SiMCED

## 4 RESULTS

| Cancer | Stage IV cancer incidence | | | | Cancer mortality | | | |
|---|---|---|---|---|---|---|---|---|
| | Usual care | Usual care + MCED | Absolute change | Relative change | Usual care | Usual care + MCED | Absolute change | Relative change |
| Breast | 113 | 62 | -51 | -45% | 133 | 95 | -38 | -29% |
| Cervical | 18 | 2 | -16 | -89% | 22 | 12 | -10 | -44% |
| Colorectal | 230 | 97 | -133 | -58% | 290 | 192 | -99 | -34% |
| Endometrial | 41 | 22 | -19 | -46% | 60 | 47 | -13 | -22% |
| Esophageal | 47 | 26 | -21 | -45% | 84 | 74 | -10 | -12% |
| Gastric | 77 | 32 | -45 | -58% | 109 | 84 | -25 | -23% |
| Head and Neck | 174 | 114 | -60 | -34% | 113 | 94 | -19 | -17% |
| Kidney | 80 | 63 | -17 | -21% | 93 | 81 | -12 | -13% |
| Liver | 67 | 20 | -47 | -70% | 184 | 148 | -36 | -19% |
| Lung | 783 | 457 | -326 | -42% | 974 | 845 | -129 | -13% |
| Ovarian | 58 | 40 | -18 | -31% | 74 | 66 | -8 | -11% |
| Pancreatic | 219 | 85 | -134 | -61% | 302 | 259 | -44 | -14% |
| Prostate | 217 | 215 | -2 | -1% | 86 | 84 | -2 | -2% |
| Urinary Bladder | 42 | 26 | -16 | -38% | 93 | 81 | -12 | -13% |
| **Total** | **2,166** | **1,261** | **-905** | **-42%** | **2,618** | **2,162** | **-456** | **-17%** |

**Table 1:** Cancer-specific reductions in stage IV cancer incidence and cancer mortality

- **Table 1** shows cancer-specific reductions in stage IV cancer incidence and cancer mortality. Absolute numbers are rates per 100k people in the initial closed cohort.
- The reduction in 10-year stage IV incidence was 905 (42%).
- The reduction in 10-year cancer mortality was 456 (17%).
- Lung cancer had the highest absolute mortality reduction at 129 (13%).
- Among the four screening cancers, the mortality reduction was 275 (19%).
- Among the ten non-screening cancers, the mortality reduction was 180 (15%).

- **Figure 2** shows individual-level downstaging flows as rates per 100k.
- Of the 185 additional diagnoses, 62 were made in individuals who died from non-cancer-related causes under **Usual care** after their counterfactual time of MCED diagnosis, and 123 were made in individuals who were eventually diagnosed by usual care after the first 10 years.
- **Figure 3** shows, for each downstaging flow, the relative frequency (top) and expected population-level 10-year life-year gain (LYG) among US adults aged 50-84 years (bottom).

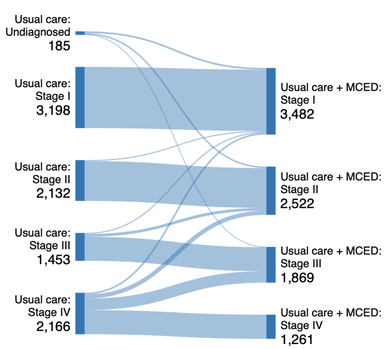



**Figure 2:** Individual-level downstaging flows

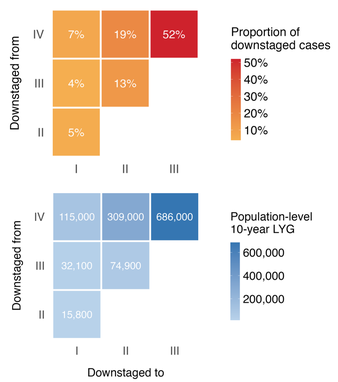



**Figure 3:** Population-level 10-year LYG

- Downstaging from stage IV accounted for 78% of all downstaging.
- Stage IV to III was the most common downstaging flow, accounting for 52% of all downstaging and generating a population-level 10-year LYG of 686,000 life-years.
- Over the 10-year horizon, the total cohort-level LYG was 1,070 per 100k, which translates to a population-level LYG of 1.23 million life-years.

## 5 LIMITATIONS

- There is uncertainty around epidemiological parameters, such as dwell times. We conducted sensitivity analysis on dwell times (not included in this poster) to demonstrate model robustness.
- Uptake/adherence to annual MCED testing was assumed to be 100%, therefore these outcomes may be optimistic.
- The LYG calculations do not account for the potential LYG due to within-stage earlier diagnosis, which may increase the mortality benefit of MCED testing.

## 6 CONCLUSIONS

- Our study suggests that supplemental screening with an MCED test could be effective for preventing stage IV cancer and cancer mortality.
- The real-world impact and cost-effectiveness of MCED tests warrant further investigation.

**Supplemental screening with an MCED test could be effective for preventing stage IV cancer and cancer mortality.**

**Reference**

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This study was funded by Exact Sciences Corp., Madison, WI.