The potential of multi-cancer early detection screening in reducing cancer incidence and mortality in high-risk groups: A modeling study

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1 BACKGROUND

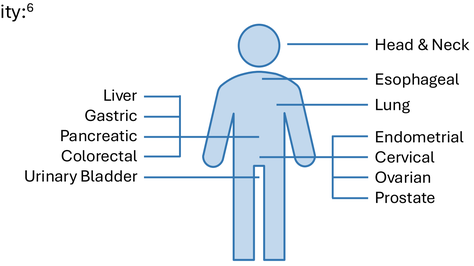
- Cancer is the second leading cause of death in the United States.[1]
- Early detection could reduce cancer-related mortality by averting progression to late-stage cancer, which is associated with lower likelihood of cure and survival.[2,3]
- Currently, around half of cancer cases in the US are detected at an advanced stage,[4] and routine screening is USPTSF-recommended for only four cancer types (breast, cervical, colorectal, lung).[5]
- Known risk factors for cancer include smoking, alcohol use, and family history of cancer. Screening may be especially beneficial in these elevated-risk groups.
- Blood-based multi-cancer early detection (MCED) tests could revolutionize cancer screening by simultaneously detecting multiple cancer types.

2 OBJECTIVE

To evaluate the potential impact of an MCED test in terms of the reduction in cancer incidence and mortality in the general population and elevated-risk groups defined by smoking status, alcohol use, and family history of cancer.

3 METHODS

- We developed **Si**mulation **M**odel for **MCED** (SiMCED), a microsimulation model of 14 solid tumor cancer types that account for nearly 80% of all cancer incidence and mortality:[6]



- 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.[7,8]
- The model was calibrated to reproduce incidence rates of usual care diagnosis as captured in the SEER database.[6]
- MCED test sensitivities were derived from a large, multi-center, prospectively-collected, retrospective case-control study (ASCEND-2).[9]
- After a cancer diagnosis, individuals follow 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 100,000 adults aged 50-84 years, representative of the US population.
- In addition, we simulated three elevated-risk groups: **smokers** (former and current), **heavy alcohol users**, and **individuals with a family history of cancer in ≥1 first-degree relatives** (FDRs).
  - The joint distribution of sex, age, race, and risk factor profile in the general population was derived from the National Health Interview Survey.[10]
  - Inflation/deflation factors for cancer incidence rates were estimated from published literature.
- We compared outcomes under two screening strategies:
  - **Usual care**: Without MCED testing, and;
  - **Usual care + MCED**: With annual MCED testing for individuals aged 50-84 years.

4 METHODS

- **Figure 1** compares 10-year stage shift across the general population and elevated-risk groups.
- **Tables 1** and **2** present cancer-specific 10-year reductions in, respectively, stage IV cancer incidence and cancer mortality.

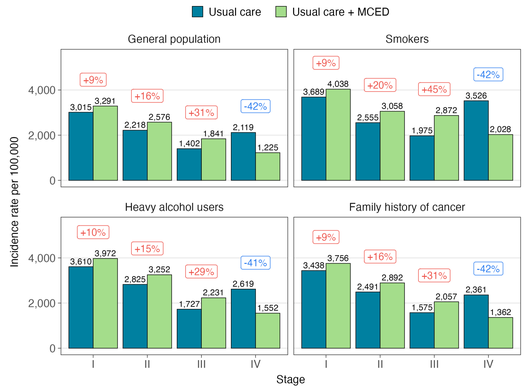


Figure 1: 10-year stage shift for the general population and elevated-risk groups.

Table 1: Reductions in 10-year stage IV cancer incidence (per 100,000) for the general population and elevated-risk groups.

Cancer	General population			Smokers			Heavy alcohol users			Family history of cancer		
	Usual care	Usual care + MCED	Change	Usual care	Usual care + MCED	Change	Usual care	Usual care + MCED	Change	Usual care	Usual care + MCED	Change
Breast	94	56	-37 (-40%)	94	56	-38 (-40%)	117	71	-46 (-40%)	108	65	-43 (-40%)
Cervical	11	3	-8 (-73%)	13	3	-9 (-75%)	16	4	-12 (-75%)	14	4	-10 (-74%)
Colorectal	238	102	-136 (-57%)	255	110	-145 (-57%)	286	124	-163 (-57%)	257	110	-147 (-57%)
Endometrial	44	26	-18 (-41%)	41	24	-17 (-41%)	44	26	-18 (-40%)	57	33	-23 (-41%)
Esophageal	50	26	-24 (-49%)	54	28	-26 (-48%)	108	57	-51 (-47%)	55	28	-26 (-48%)
Gastric	81	31	-50 (-62%)	83	32	-51 (-62%)	81	32	-50 (-61%)	98	38	-61 (-62%)
Head and Neck	173	114	-58 (-34%)	223	149	-74 (-33%)	398	266	-132 (-33%)	199	132	-67 (-34%)
Kidney	78	56	-22 (-28%)	83	60	-23 (-28%)	70	51	-20 (-28%)	83	60	-23 (-27%)
Liver	67	18	-49 (-74%)	68	17	-51 (-74%)	81	22	-59 (-73%)	79	21	-58 (-74%)
Lung	764	429	-335 (-44%)	2,028	1,145	-883 (-44%)	804	454	-350 (-44%)	820	459	-361 (-44%)
Ovarian	54	38	-15 (-29%)	57	39	-18 (-31%)	58	42	-17 (-29%)	68	48	-20 (-30%)
Pancreatic	209	89	-120 (-58%)	240	101	-139 (-58%)	223	94	-129 (-58%)	233	99	-135 (-58%)
Prostate	211	207	-5 (-2%)	234	229	-5 (-2%)	287	281	-6 (-2%)	232	227	-5 (-2%)
Urinary Bladder	47	31	-16 (-34%)	53	34	-18 (-35%)	44	30	-15 (-33%)	56	37	-19 (-34%)
Total	**2,119**	**1,225**	**-894 (-42%)**	**3,536**	**2,028**	**-1,498 (-42%)**	**2,619**	**1,552**	**-1,067 (-41%)**	**2,361**	**1,362**	**-999 (-42%)**

Table 2: Reductions in 10-year cancer mortality (per 100,000) for the general population and elevated-risk groups.

Cancer	General population			Smokers			Heavy alcohol users			Family history of cancer		
	Usual care	Usual care + MCED	Change	Usual care	Usual care + MCED	Change	Usual care	Usual care + MCED	Change	Usual care	Usual care + MCED	Change
Breast	124	93	-31 (-25%)	126	93	-32 (-26%)	154	115	-39 (-25%)	142	106	-36 (-26%)
Cervical	19	11	-8 (-43%)	21	11	-10 (-45%)	26	15	-11 (-43%)	23	13	-10 (-43%)
Colorectal	306	205	-101 (-33%)	330	221	-109 (-33%)	371	249	-122 (-33%)	328	219	-109 (-33%)
Endometrial	63	50	-14 (-22%)	60	47	-13 (-22%)	65	51	-14 (-21%)	82	65	-17 (-21%)
Esophageal	84	73	-11 (-13%)	92	80	-12 (-13%)	186	161	-25 (-13%)	92	79	-12 (-13%)
Gastric	115	86	-29 (-25%)	118	88	-30 (-26%)	115	86	-29 (-25%)	139	103	-36 (-26%)
Head and Neck	117	99	-18 (-16%)	152	128	-24 (-16%)	264	222	-43 (-16%)	133	112	-21 (-16%)
Kidney	92	78	-14 (-15%)	97	82	-15 (-15%)	83	70	-13 (-16%)	97	82	-15 (-16%)
Liver	178	141	-37 (-21%)	184	146	-38 (-21%)	220	175	-45 (-20%)	210	166	-44 (-21%)
Lung	964	831	-133 (-14%)	2,590	2,246	-344 (-13%)	1,014	876	-138 (-14%)	1,031	888	-142 (-14%)
Ovarian	72	63	-9 (-12%)	76	67	-9 (-12%)	77	68	-9 (-12%)	88	78	-11 (-12%)
Pancreatic	295	253	-42 (-14%)	338	289	-49 (-15%)	313	267	-46 (-15%)	327	279	-48 (-15%)
Prostate	82	80	-2 (-2%)	94	92	-2 (-2%)	113	111	-2 (-2%)	89	87	-2 (-2%)
Urinary Bladder	100	88	-12 (-12%)	114	101	-13 (-11%)	95	85	-10 (-11%)	117	103	-14 (-12%)
Total	**2,612**	**2,150**	**-461 (-18%)**	**4,391**	**3,692**	**-699 (-16%)**	**3,096**	**2,551**	**-545 (-18%)**	**2,897**	**2,380**	**-517 (-18%)**

5 CONCLUSION

MCED screening demonstrates the potential to reduce late-stage cancer incidence and mortality in both the general population and elevated-risk groups.

These findings highlight the value of MCED tests in advancing early detection and improving cancer outcomes.

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