EE126

Cost-effectiveness of Multi-cancer Early Detection (MCED) Testing using Mixture Cure Modeling (MCM)

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INTRODUCTION

- Cancer is the second-leading cause of death in the United States (US),[1] and a reduction in mortality has been observed in populations with cancer screening programs.[2,3]
- Recently, multi-cancer early detection (MCED) tests, which can simultaneously screen for multiple types of cancer, have been developed.[4-6] When used alongside standard of care (SoC) screening, an economic analysis projects these tests may improve survival outcomes and lower treatment costs.[7]
- The predicted benefits may depend on methods for projecting post-diagnosis survival. Mixture cure modeling (MCM) has been proposed for projecting survival impact with MCED tests because it includes a proportion of cured patients which is less sensitive to lead time bias.[8]

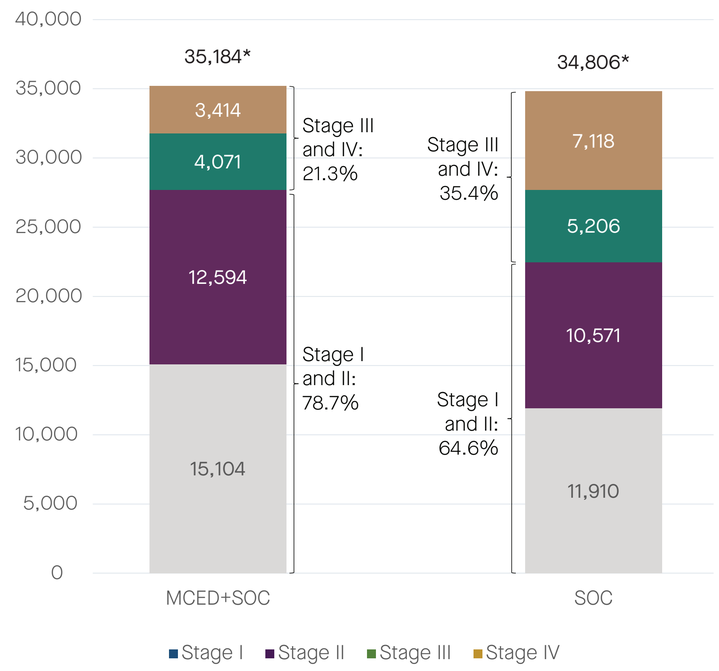
OBJECTIVE

- This study explores the impact of using MCM as compared to a standard extrapolation of survival on the cost-effectiveness of MCED testing.

RESULTS

- When adding MCED test to SoC with either method of survival projection, stage I/II cancer diagnoses increased by 23.2%, and stage III/IV cancer diagnoses reduced by 39.3% (**Figure 1**).

Figure 1: Number of Cancer Diagnoses by Stage for MCED + SoC and SoC Alone When Using Either Survival Projection



Total number of cancers was 34,806 in the SoC arm and 35,184 in the MCED + SoC arm, which included 377 additional diagnoses when using either the simple or MCM projection for survival. Stage I/II ancer diagnoses increased by a relative difference of 23.2%, and stage III/IV cancer diagnoses were reduced by a relative difference of 39.3% when using MCED + SoC.

Abbreviations: MCED = multi-cancer early detection; SoC = standard of care

- This yielded 0.15 and 0.13 incremental QALYs per person when using MCM and simple extrapolation, respectively (**Table 1**). The difference was contributed by incremental post-diagnosis survival.

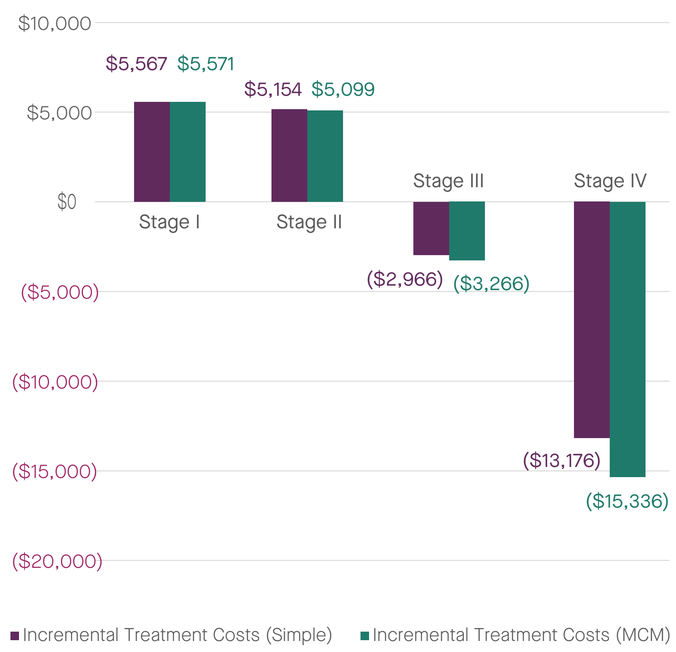
Table 1. Incremental LYs and QALYs for Simple and MCM Projections

	Simple	MCM
Total Incremental LYs	**0.14**	**0.16**
Incremental LYs for Patients with Cancer Diagnosis	0.39	0.45
Incremental Pre-Diagnosis	(0.38)	(0.38)
Incremental Post-Diagnosis	0.77	0.83
Total Incremental QALYs	**0.13**	**0.15**
Incremental QALYs for Patients with Cancer Diagnosis	0.38	0.43
Incremental Pre-Diagnosis	(0.31)	(0.31)
Incremental Post-Diagnosis	0.69	0.74

Abbreviations: LYs = life years; MCM = mixture cure modeling; QALYs = quality-adjusted life years

- Cancer-related treatment costs were reduced by $7,933 and $5,421 per person, for MCM and simple extrapolation respectively (**Figure 2**), and the value-based price (VBP) for the MCED test was $1,479/test and $1,196/test, respectively.

Figure 2: Incremental Cancer Treatment Costs by Stage at Diagnosis by Survival Projection

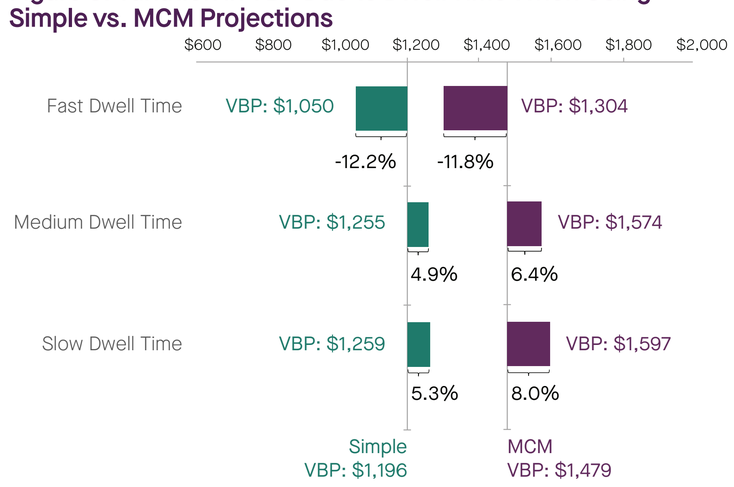


Note: Overall incremental cancer treatment costs were ($5,421) and ($7,933) when using the simple and MCM projections for survival, respectively.

Abbreviation: MCM = mixture cure modeling

- In scenario analysis, VBP was similarly sensitive to cancer dwell time assumptions with both survival methods (**Figure 3**).
  - This suggests the most important impact of dwell time in this analysis was an increase in interval cancers with more rapid dwell times, as the impact of lead time bias is explicitly accounted for in the modeling.

Figure 3: Variation in VBP Due to Dwell Time When Using Simple vs. MCM Projections



Note: The base case for each analysis uses a "medium-fast" dwell time. Percentages indicate relative percent change in VBP per scenario.

Dwell time is defined as the tumor progression rate, specifically the amount of time spent in stage I. Fast: 1-2 years; Medium-Fast: 2-4 years; Medium: 3-7 years; Slow: 4-10 years[9]

Abbreviations: MCM = mixture cure modeling; VBP = value-based price

LIMITATIONS

- The model does not account for the additional post-diagnosis risk of developing cancer later in life or consider cancer recurrence or patients who have multiple types of cancers.
- Both simple extrapolation and MCM are extrapolations of observed data and real-world outcomes may vary. Similarly, test performance is extrapolated from case-control data and may vary in real-world practice.

CONCLUSION

- Different methods for projecting post-diagnosis survival may lead to variation in estimated cost-effectiveness of MCED testing, with modeling the potential for cure supporting greater benefits.

METHODS

- A Markov model was developed to compare annual MCED testing plus SoC screening vs. SoC alone in adults aged 50 to 79 years. Patient survival, cost, and quality of life measures were calculated pre- and post-diagnosis over a lifetime time horizon. All costs and outcomes were discounted at 3% annually.[7]
- Survival by cancer, stage, and age at detection was projected from the Surveillance, Epidemiology, and End Results (SEER) program[10] using two methods (**Table 2**).
  - The first method used Kaplan-Meier survival from SEER for three years, followed by a constant hazard.
  - The second method used Kaplan-Meier survival from SEER for three years, followed by MCM projections from Hubbell et al. 2022 across all different cancer types at all stages of diagnosis,[8] including potential long-term excess mortality in survivors.
  - MCM projections by age were calculated based on an age-adjusted hazard ratio for mortality (5-year age groups starting at 50-54, 55-59, and up to 85+) vs the overall population for each cancer type and stage.
  - Both methods were capped by the age-matched general population survival.
- The VBP of MCED testing was estimated to meet a willingness-to-pay threshold of $100,000/quality-adjusted life year (QALY) for the simple and MCM projections separately.[11]
- To handle an earlier diagnosis with MCED screening than with SoC screening alone, the model stage and time shifted the cancer diagnosis to an earlier time and age based on various model inputs, including cancer dwell times, frequency of MCED screening, and sensitivity of the MCED test.[9] Further details of the model structure and methods, including the approach to stage and time shift as well as inputs, have been described previously.[7]

Table 2. Mean Survival (in years) by Cancer and Stage at Detection for Simple and MCM Projections

	Stage I		Stage II		Stage III		Stage IV	
Cancer	Simple	MCM	Simple	MCM	Simple	MCM	Simple	MCM
Anus	12.90	14.82	10.00	12.99	9.62	13.16	2.81	4.63
Bladder	7.56	9.70	4.47	6.00	4.58	6.50	2.19	3.06
Breast: HR-negative	14.90	15.20	12.15	13.99	7.50	10.08	2.46	2.60
Breast: HR-positive	15.21	15.22	13.73	14.66	9.85	12.69	3.64	4.16
Cervix	15.61	17.69	9.47	12.57	6.85	9.99	2.66	4.19
Colon and Rectum	13.69	15.21	11.43	13.82	9.61	12.62	2.43	3.19
Esophagus	4.96	6.86	3.97	6.14	2.93	4.68	1.52	1.94
Head and Neck	10.75	13.17	8.05	11.40	7.29	10.73	6.49	9.69
Kidney and Renal Pelvis	14.02	15.62	12.00	14.51	9.94	12.61	2.05	2.81
Liver and Intrahepatic Bile Duct	4.28	6.66	4.53	7.40	1.83	2.51	1.25	1.48
Lung and bronchus	6.25	8.95	4.21	6.29	2.35	3.22	1.48	1.80
Lymphoma	9.68	11.34	8.42	10.20	7.90	10.01	6.84	9.06
Other	13.25	14.04	7.80	9.77	8.54	10.97	3.44	4.92
Ovarian	15.09	16.48	9.66	12.17	4.51	6.08	2.43	2.81
Pancreas	2.91	3.76	2.21	2.95	1.50	1.84	1.18	1.33
Prostate	11.73	12.63	15.52	16.71	18.11	19.54	4.84	6.38
Stomach	5.95	7.81	4.69	6.75	3.23	4.62	1.47	1.79
Urothelial	7.69	9.73	5.40	7.14	4.81	6.67	2.21	3.07
Uterus	16.41	16.77	12.03	13.82	9.26	11.80	2.62	3.71

Note: The model assigns survival post-diagnosis by cancer, stage and age, but for illustration purposes, the table shows a weighted average of mean survival (in years) by cancer and stage, adjusted for age based on incidence.

Abbreviations: HR = hormone receptor; MCM = mixture cure modeling

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Disclosures

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