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Costs and Benefits of a Multi-Cancer Early Detection Test in a Medicare Population

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INTRODUCTION

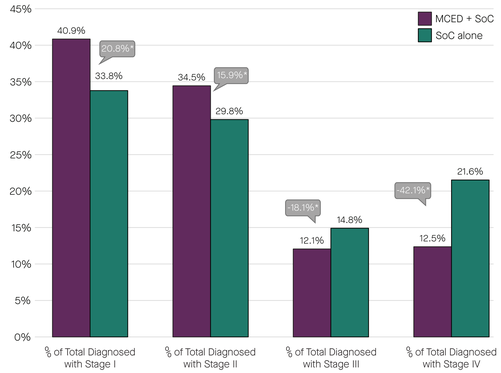
- The risk of getting cancer increases—and cancer-specific survival decreases—with age. Approximately 80% of people diagnosed in the United States (US) are older than 55 years, while 57% are older than 65.[1]
- As the US population ages, cancer-related costs are expected to increase by 34% between 2015 and 2030, based on population growth and aging alone.[1]
- The use of cancer screening programs, which can target older populations, can provide timely detection of cancer, reduce mortality, and improve treatment outcomes.[2-4] New blood-based, multi-cancer early detection (MCED) tests that can simultaneously screen for multiple types of cancer have recently been developed.[5-8]

OBJECTIVE

- This modeling study explored key drivers of the potential range of the value-based price (VBP) for MCED testing in a US Medicare population (aged 65+).

KEY RESULTS

Figure 1. Percent of Total Cancers Diagnosed by Stage



*The relative change in total diagnosed by stage between MCED + SoC and SoC alone. Total number of cancers was 29,318 in the SoC arm and 29,575 in the MCED + SoC arm (including 258 additional diagnoses due to overdiagnosis).
Abbreviations: MCED = multi-cancer early detection; SoC = standard of care

- The proportion of cancers detected at stage IV decreased from 21.6% to 12.5% (Figure 1).
- Patients diagnosed with an MCED test in addition to standard of care (SoC) screening had on average $2,006 less cancer-related treatment and diagnosis costs than SoC alone, excluding the cost of the MCED screening test or additional workup costs (**Figure 2**).

Figure 2. Treatment and Workup Costs per Patient

Note: Total cancer treatment costs were $2,006 lower in the MCED + SoC arm vs. SoC alone. Screening costs (not shown) were $9,310, $18,833, and $2,651 for the MCED + SoC arm at a $50,000 threshold, the MCED + SoC arm at the $150,000 threshold, and the SoC arm, respectively.
Abbreviations: MCED = multi-cancer early detection; SoC = standard of care

- Testing with MCED increased life years and quality-adjusted life years (QALY) by 0.10 and 0.10, respectively, for older individuals.
- Due to the consideration of overdiagnosis, 258 additional cancers were detected with MCED plus SoC vs. SoC alone, of which 87.0% were diagnosed in stages I and II.

Figure 3. Tornado Diagram Exploring Effects of Variations in Parameters on VBP

Note: Results of variations of the following parameters are not shown in the diagram due to minimal impact on VBP: disutility for false-positive workups, disutility due to cancer, and false-positive workup costs. Dwell time is cancer- and stage-specific and is defined as the time to progression between two subsequent stages of cancer.
Abbreviation: MCED = multi-cancer early detection; VBP = value-based price

- The VBP for an MCED test ranged from $730/test to $1,771/test, at willingness-to-pay (WTP) thresholds of $50,000/QALY to $150,000/QALY, respectively.
- Sensitivity analyses indicated that VBP in this population was sensitive to the number of clinically significant cancers detected, as indicated by the large impact of cancer incidence and test sensitivity at both thresholds (**Figure 3**).
- Changes in treatment cost and burden associated with false-positives had small impacts on VBP.

LIMITATIONS

- The model did not consider cancer recurrence or patients with multiple cancers; it did not account for the additional post-diagnosis risk of developing cancer later in life.

CONCLUSIONS

- As an aging population is expected to increase the overall cancer burden in the US, the addition of MCED testing to SoC in a Medicare population can improve survival and lower treatment costs as compared with SoC alone, potentially offsetting some of this burden.

References

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Disclosures

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*Tafazzoli A is currently affiliated with GRAIL, LLC, a subsidiary of Illumina, Inc.**

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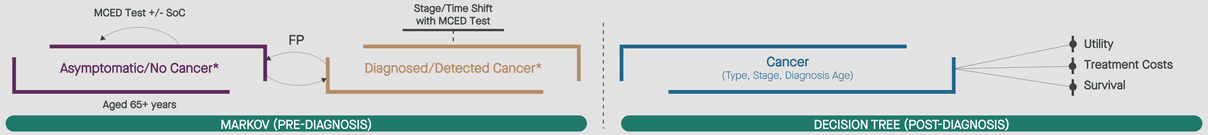
METHODS

Model Overview and Structure

- A Markov model was developed to compare annual screening with MCED plus SoC to screening with SoC alone in a cohort of asymptomatic adults ages 65 to 79, assuming 90% compliance.
- Patient survival, cost, and quality-of-life (QoL) measures were calculated pre- and post-diagnosis over a lifetime horizon, capped at 100 years. A 3% annual discount was applied to all costs and outcomes.
- The model explicitly tracked initial cancer diagnoses for 19 solid cancer groupings (**Table 1**), representing more than 40 cancer types according to the American Joint Committee on Cancer.
- VBP was estimated for WTP thresholds of $50,000/QALY and $150,000/QALY.
- A hybrid structure was created (**Figure 4**):
  - Cohort Markov: estimates the fraction of patients diagnosed with cancer during each cycle based on age- and stage-specific cancer incidence rates. Under the MCED test scenario, cancer in patients could be detected earlier in time and stage than under SoC alone.
  - Decision-tree: estimates the long-term consequences of incident cancer (survival, utility, and treatment costs).
- The model stage and time shifted the cancer diagnosis to an earlier time and age (**Figure 5**) to consider earlier diagnosis with MCED screening than with SoC alone.[9]
- The distribution of stage shift is cancer-specific and not age-dependent, and is derived using inputs on frequency of MCED screening, estimated cancer dwell times by stage, and the sensitivity of the MCED test by cancer type and stage.[9]
- The model accounted for the potential impact of overdiagnosis due to the MCED test detecting cancer in patients who would have died with undetected cancer.

Figure 4. Model Diagram

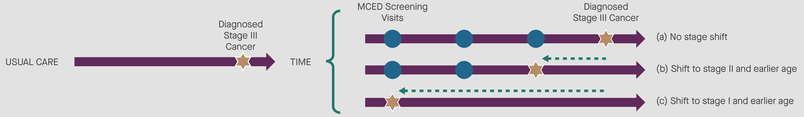


*False-positive patients (in asymptomatic/no cancer group) and those misdiagnosed due to wrong tumor of origin (in detected cancer group) accrued additional workup costs and disutilities before being accurately assigned to having cancer or not.
Abbreviations: FP = false-positive; MCED = multi-cancer early detection; SoC = standard of care

Model Inputs

- Incidence by age and stage at detection for the general population was informed by Surveillance Epidemiology and End Results (SEER) data.[10,11]
- As reported in Klein et al. 2021, MCED test sensitivity (**Table 1**) differs by cancer and stage, while specificity is 99.5% in aggregate.[8]
- Pre-diagnosis survival was based on baseline background mortality (derived from US life tables from the National Vital Statistics Report)[12] for the general population.
- Post-diagnosis mean survival was based on SEER and was assigned based on stage and age at clinical diagnosis and cancer type, considering stage shift if diagnosed with MCED.[10,11]
- The model estimated screening costs, treatment costs over five years, and costs related to additional workups for patients 65 and older. SEER Medicare-linked data informed resource use.[13,14]
- Cancer- and stage-specific utility multipliers adjusted baseline age-specific utility over five years.
- False-positives resulted in reduced QoL and additional diagnostic workups.

Figure 5. Example of Stage and Time Shifting of Diagnosed Cancers due to MCED Test



Note: The distribution of stage shift is cancer-specific and not age-dependent. Patients are shifted to an earlier age, which is based on cancer dwell time by stage.[9]
Abbreviation: MCED = multi-cancer early detection

Table 1. MCED Test Sensitivity

Cancer	Stage I	Stage II	Stage III	Stage IV
Anus	25%	75%	100%	100%
Bladder	18%	18%	75%	100%
Breast: hormone receptor-negative	3%	48%	85%	91%
Breast: hormone receptor-positive	3%	48%	85%	91%
Cervix	58%	100%	100%	100%
Colon and rectum	43%	85%	88%	95%
Esophagus	13%	65%	94%	100%
Head and neck	63%	82%	84%	96%
Kidney and renal pelvis	5%	19%	19%	55%
Liver and intrahepatic bile duct	81%	81%	100%	100%
Lung and bronchus	22%	80%	91%	95%
Lymphoma	27%	58%	66%	66%
Other	0%	0%	0%	0%
Ovarian	50%	80%	87%	95%
Pancreas	61%	61%	86%	96%
Prostate	3%	5%	14%	83%
Stomach	17%	50%	80%	100%
Urothelial	0%	0%	0%	100%
Uterus	17%	30%	74%	100%

Source: Klein et al. 2021[8]