Cost-effectiveness of Multi-cancer Early Detection (MCED) Test in Subgroups with Smoking History or Obesity

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INTRODUCTION

- In 2020, cancer accounted for more than 10 million deaths, making it a leading cause of global mortality.[1,2]
- Cancer incidence and survival can be influenced by external risk factors such as history of smoking and obesity.[3-5]
- In 2014, smoking accounted for 19% of cancer cases and 28.8% of cancer-related deaths, while excess body weight accounted for 7.8% of cases and 6.5% of cancer-related deaths in the United States (US).[4,6,7]
- Cancer screening is associated with a reduction in mortality in populations with screening programs,[8,9] and recently, new blood-based multi-cancer early detection (MCED) tests that can simultaneously screen for multiple types of cancers have been developed.[10-12]
- Benefits of MCED testing in high-risk groups such as those with a smoking history or obesity could include increasing early-stage cancer detection, improving cancer-related survival, and lowering cancer-related treatment costs. Although, these benefits can be masked by the competing risks of reduced survival for such high-risk populations.

OBJECTIVE

- This modeling study explores key economic and health outcomes of multi-cancer testing in patients aged 50–79 years with additional risk factors of smoking or obesity versus the general population in the US.

KEY RESULTS

- Initial cancer diagnoses were 13%, 7%, and 5% higher, respectively, in populations currently smoking, with a smoking history, and with obesity compared to the general population.
- For currently smoking and smoking history populations, the proportion of cancers detected at stage IV due to MCED testing decreased by 16.7% and 13.1%, respectively, compared to the SoC arm (Figure 1). MCED testing decreases stage IV diagnoses by 9% in the general population when compared to the SoC arm.
- Based on analyses using general population VBPs ($769 and $1,615 at WTP of $50,000/QALY and $150,000/QALY, respectively), use of MCED testing in the subpopulations was more cost-effective than use in the general population.
- MCED screening was most cost-effective in the currently smoking population, accruing the most life years and QALYs, as well as having the lowest incremental cost-effectiveness ratios (ICERs) compared to the general population using VBPs for the two thresholds ($11,112/QALY and $65,829/QALY, respectively[Figure 2]). Results for all risk groups are shown in Table 1.
- Adjusted incidence and survival were explored in sensitivity analysis (Figure 3). Incidence RRs and survival HRs were varied by ± 20%, and an additional scenario was run with alternative sources[29,30] for survival adjustments.
- The most impact was seen when increasing/decreasing the RR applied to incidence rates by 20%, which decreased/increased the ICER by $4,519/$5,562 for current smoker, $3,646/$4,120 for ever smoker and $1,200/$1,237 for obesity as compared with the base case at the $50,000 threshold.

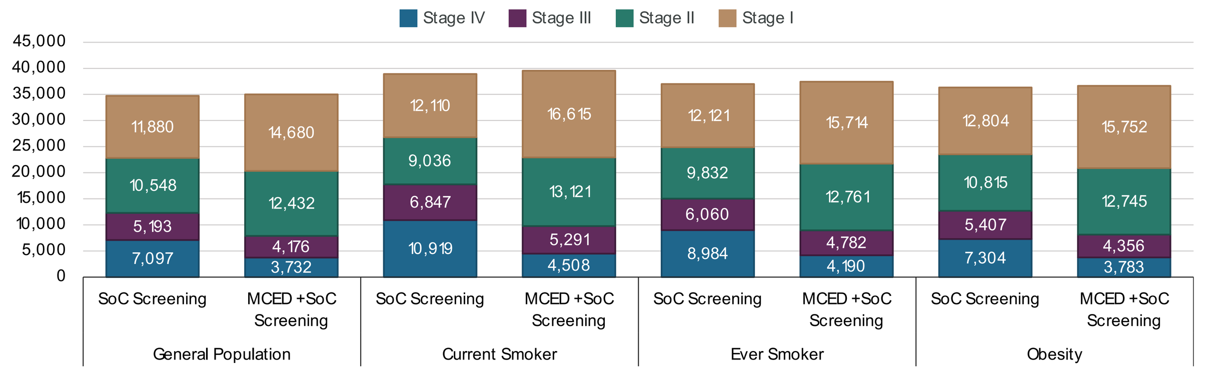
Table 1. Summary of Results

Cancer	Incremental LYs	Incremental QALYs	Incremental Percent Diagnosed in Early Stage between MCED and SoC	ICER (VBP $769)	ICER (VBP $1,615)
Base case	0.14	0.13	77%	$50,000	$150,000
Current Smoker	0.21	0.21	75%	$11,112	$65,829
Ever Smoker	0.17	0.16	76%	$27,534	$101,209
Obesity	0.14	0.13	78%	$44,650	$138,983

ICER = incremental cost-effectiveness ratio; LY = life year; MCED = multi-cancer early detection; QALY = quality-adjusted life year; SoC = standard of care; VBP = value-based price

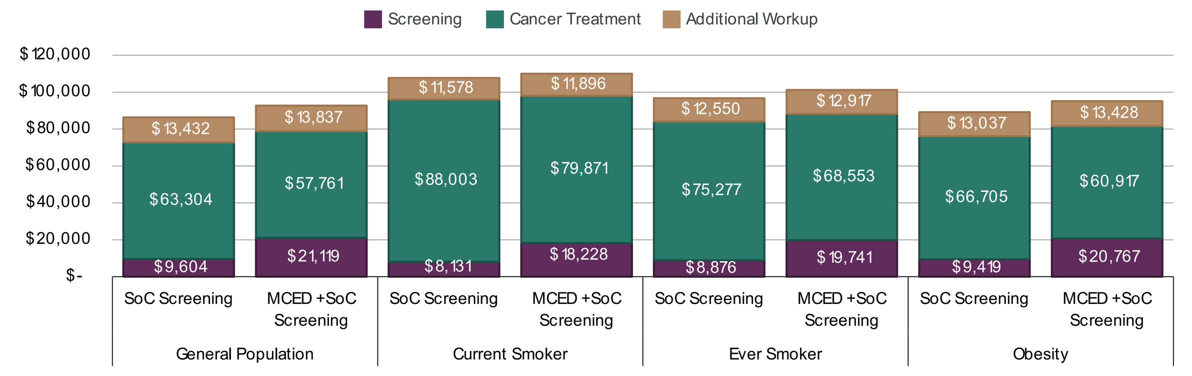
- The overall impact of adjusting the HR for survival was minimal, except when using the alternative source for current smoker and ever smoker, which decreased the ICER by $2,499 and $1,994 respectively as compared with the base case at the $50,000 threshold.

Figure 1. Number of Initial Cancers Diagnosed by Stage and Population



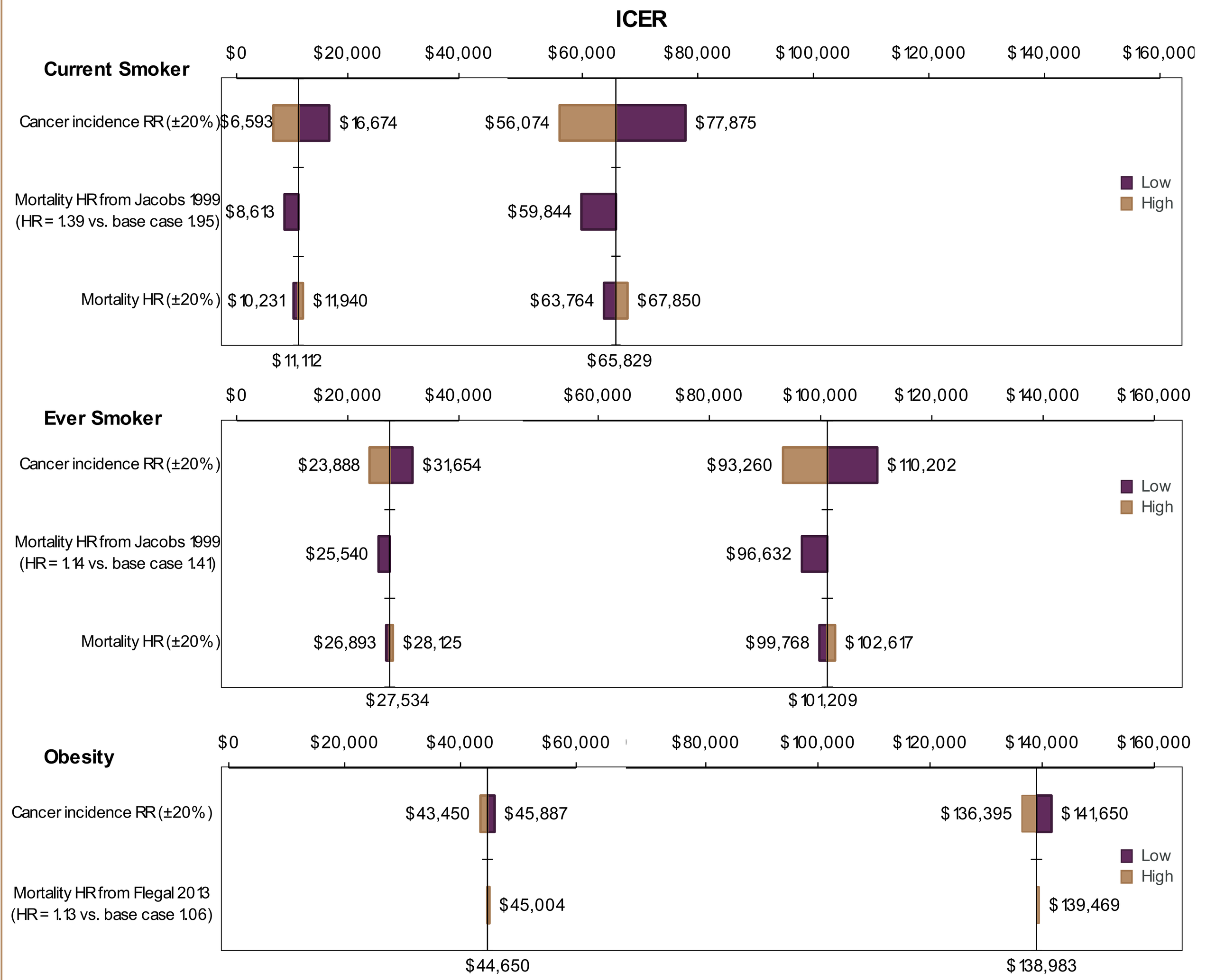
MCED = multi-cancer early detection; SoC = standard of care
Under MCED scenarios, the number of cancers diagnosed due to overdiagnosis by stage is as following:
General population: stage I = 136, stage II = 127, stage III = 39; Current smoker: stage I = 257, stage II = 286, stage III = 81; Ever smoker: stage I = 191, stage II = 200, stage III = 59; Obesity: stage I = 139, stage II = 127, stage III = 40

Figure 2. Costs Accrued by Population



MCED = multi-cancer early detection; SoC = standard of care
Note: MCED +SOC screening costs at $150,000 threshold: General population: $33,872; Current Smoker: $29,468; Ever Smoker: $31,800; Obesity: $33,339; SOC screening costs are unchanged.
Results presented in Figure 2 are based on VBP $769 for $50,000 threshold

Figure 3. Sensitivity Analysis Results



HR = hazard ratio; ICER = incremental cost-effectiveness ratio; RR = relative risk
Note: Two scenarios based on VBP of $769 and $1,615. Mortality HR scenario was not included for the obesity subgroup as the mortality HR was low and therefore the impact was minimal.

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.

CONCLUSIONS

A cost-effective MCED test in the general population is increasingly cost-effective in populations with smoking or obesity, as the effect of competing mortality risks is outweighed by the increased number of cancers found.

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Disclosures

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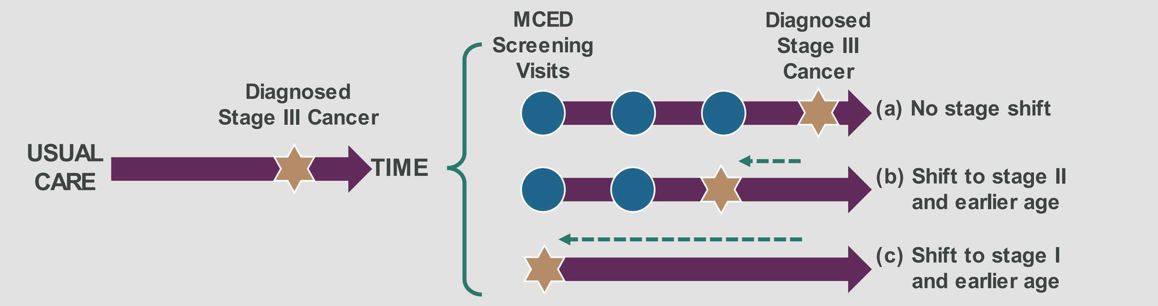
METHODS

Model Overview and Structure

- A Markov model was implemented to compare annual MCED plus standard of care (SoC) screening with SoC alone in adults starting at age 50 until age 79, without cancer history, who are currently smoking, have ever smoked, or have obesity (body mass index [BMI] ≥ 30kg/m2).
- Patient survival, cost, and quality of life measures were calculated pre- and post-diagnosis over a lifetime time horizon, capped at age 100 years.
- SoC is defined as current screening practices as recommended by National Comprehensive Cancer Network (NCCN) and US Preventive Services Task Force (USPSTF) for lung, colon, breast, cervical, and prostate cancers.[13-18]
- Initial cancer diagnoses for 19 solid cancer groupings (Table 2), representing >80% of cancer incidence, were explicitly tracked in the model.
- Value-based price (VBP) was estimated for willingness-to-pay (WTP) thresholds of $50,000/quality-adjusted life years (QALY) and $150,000/QALY.[19] All costs and outcomes were discounted at 3% annually.
- A hybrid structure was created:
  - Cohort Markov: estimates the fraction of high-risk patients diagnosed with cancer during each cycle based on age- and stage-specific cancer incidence rates that were adjusted by exposure (i.e., current smoker, ever smoker, obesity). 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 adjusted by exposure, utility, treatment costs) in higher risk populations.
- 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 (example shown in Figure 4).[20]

Figure 4. Example of Stage and Time Shifting of Diagnosed Cancers due to MCED Test



MCED = multi-cancer early detection
Note: The distribution of stage shift is cancer-specific and not age-dependent. Patients are shifted back in time to an earlier age, which is based on cancer dwell time by stage.[20]

Model Inputs

- Surveillance Epidemiology and End Results (SEER) data informed incidence by age and stage at detection for the general population.[21]
- The cancer-specific incidence was adjusted using a relative risk (RR) by subgroup as derived from the literature to reflect the higher incidence associated with smoking status or obesity (Table 2).[4] The RRs were adjusted based on the prevalence of each exposure in the general population.
- MCED test sensitivity differs by cancer and stage, while specificity is 99.5% across cancers.[22] SoC screening included breast, lung, colon and rectum, prostate, and cervical cancer with an associated specificity of 89%, 87%, 87%, 91%, and 85%, respectively.[23-25]
- Baseline background mortality (derived from US life tables from the National Vital Statistics Report)[26] for the general population was assigned pre-cancer diagnosis.
- The model adjusted this baseline mortality using a hazard ratio (HR) by subgroup (1.95 for current smoker, 1.41 for ever smoker, 1.06 for obesity) as derived by data from the literature to reduce life expectancy in high-risk patients.[3,4,27] The HRs were adjusted based on the prevalence of each exposure in the general population.

Table 2. Adjustments to Cancer Incidence by Subgroup as Compared to General Population[4]

HR = hormone-receptor

Cancer	Current Smoker	Ever Smoker	Obesity
Anus	1	1	1
Bladder	2.12	1.61	1
Breast: HR-negative	1	1	1.12
Breast: HR-positive	1	1	1.12
Cervix	1.48	1.29	1
Colon and rectum	1.33	1.16	1.05
Esophagus	2.2	1.65	1.53
Head and neck	2.81	1.68	1
Kidney and renal pelvis	1.3	1.22	1.34
Liver and intrahepatic bile duct	1.64	1.3	1.35
Lung and bronchus	3.75	2.13	1
Lymphoma	1	1	1
Ovarian	1	1	1.04
Pancreas	1.52	1.17	1.17
Prostate	1	1	1
Stomach	1.49	1.24	1.36
Urothelial	2.12	1.61	1
Uterus	1	1	1.53
Other	1	1	1

- Post-diagnosis mean survival based on SEER was assigned based on stage and age at clinical diagnosis and cancer type, considering stage shift if diagnosed with MCED.[21,22] Three years of observed survival data were incorporated, and exponential parametric functions were fitted to the subsequent seven-year survival data to generate long-term projections, which were capped by the mean age-specific survival based on the adjusted background mortality rate.[3,4,27]
- SEER Medicare-linked data informed resource use with a 2.34x multiplier for commercial costs.[29] The model estimated screening costs, treatment costs over five years, and costs related to additional workups.
- Cancer- and stage-specific utility multipliers adjusted baseline age-specific utility over five years.
- False positives resulted in reduced quality of life and additional diagnostic workups.
- The model accounted for potential impact of overdiagnosis due to the MCED test detecting cancer in patients who would have died with undetected cancer.