Optimizing Multicancer Early Detection (MCED) Testing Based on Patient Stratification: A Comprehensive Analysis of Economic and Clinical Impact from a US Payer Perspective

EE429

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INTRODUCTION

- The incidence of early-onset cancers (occurring at age <50 years) increased at a 0.3% annual rate between 2010–2019, and obesity is a risk factor for many of these cancers[1]
- Cancer types that lack recommended screening protocols account for 50% of cancer diagnoses each year[2]
- Multicancer early detection (MCED) testing via liquid biopsy is an emerging technology intended to improve outcomes and costs of cancer care through earlier diagnoses
  - However, concerns regarding population-wide utilization exist, including MCED testing costs, MCED false positives, and MCED overdiagnoses

OBJECTIVE

- Dynamic modeling of MCED test utilization in specific populations that can identify the age ranges, risk factors, cancer types, and test performance requirements for the most effective testing strategy to improve clinical and economic outcomes from a US commercial payer perspective

RESULTS

Scenario 1: Obesity-related Cancers

- Testing the population aged 40–54 years with severe obesity for 10 obesity-related cancers (Figure 3) resulted in testing 9.0% of the age cohort, intercepting 21.8% of evaluated cancers, and shifting the mean cancer stage at diagnosis from 1.9 to 1.6 (Table 1)
- Cost savings (not including test cost) from standard of care (SoC) to the Future state with MCED testing were $67 per MCED-tested patient (Table 1)
  - Savings per MCED-tested patient for treatment and end-of-life (EOL) care were $393 (Figure 1)
  - These savings were offset by costs of $326 for MCED false positives and MCED overdiagnoses

Scenario 2: 3 Risk Factors and All Cancers Evaluated

- Testing the population aged 40–54 years with any of 3 risk factors (severe obesity, smoking, or HPV infection) for 14 cancers (Figure 3) resulted in testing 13.5% of the age cohort selected, intercepting 37.0% of evaluated cancers, and shifting mean stage at diagnosis from 2.2 to 1.7 (Table 1)
- Cost savings were $477 per MCED-tested patient (Table 1)
  - Treatment and EOL savings were $960, while costs of $483 were incurred for MCED false positives and overdiagnoses (Figure 1)

Result	Scenario 1	Scenario 2
	Savings Future vs SoC	
Savings per MCED-tested patient	$67	$477
Per-member per-month savings	$0.09	$1.00
Cost savings (relative reduction)	0.7%	6.2%
	MCED Test Characteristics	
MCED-tested patients[a]	9.0%	13.5%
Cancers intercepted by MCED test[a]	21.8%	37.0%
Mean stage at detection (SoC/Future)[b]	1.9/1.6	2.2/1.7
	Scenario Parameters	
Cancers tested	10	14
Risk factors included	Severe obesity	Severe obesity, smoking, or HPV infection
Ages tested (years)	40–54	40–54

[a] Of members in the selected age ranges of the evaluated cancers. [b] Based on MCED-intercepted cancers in the Future and equivalent cancers in SoC.

Table 1. Key results for 2 MCED testing scenarios

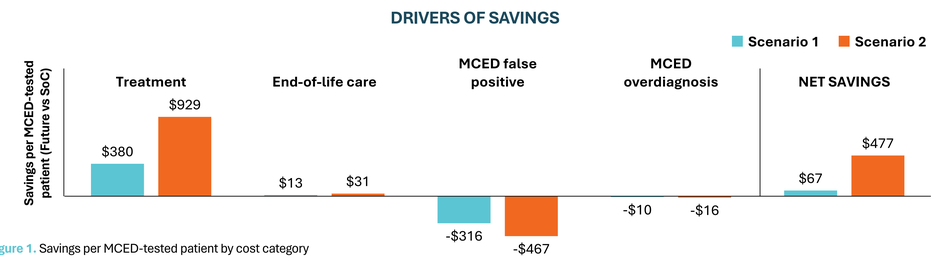

Figure 1. Savings per MCED-tested patient by cost category

CONCLUSIONS

- Stratifying the population for MCED testing reduces the number of tested patients and enriches the testing protocol for the detection of cancer
- MCED screening strategies may be viable in the context of increasing incidence of early-onset cancer and for cancers without current screening paradigms
- The scenario examples demonstrate that dynamic modeling of MCED test utilization can identify combinations of ages, risk factors, and cancer types to create effective testing strategies to improve clinical and economic outcomes
- Modeling also identifies areas for further research and real-world evidence production for MCED test development and adoption

METHODS

Model

- Using a hypothetical 1-million–payer population, the SoC for a 1-year patient cohort across 14 solid-tumor cancers was modeled for 1-year incidence, stage at detection, mortality, and costs over 5 years of both treatment and EOL care
- The Future state modeled the effects of MCED test use on cancers intercepted, stage at detection, and mortality and accounted for costs of treatment, EOL care, MCED false positives, and MCED overdiagnoses
  - An MCED overdiagnosis occurs when a cancer that would have remained undetected and not caused harm is instead detected and treated
- The modeled population can be stratified by age range, risk factors, and cancer types evaluated, producing multiple scenarios for analysis (Figure 2)

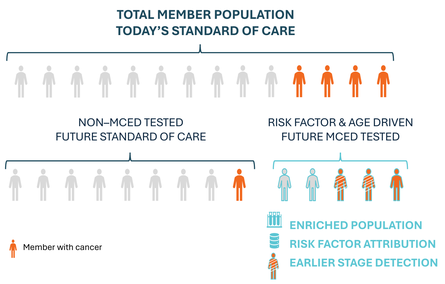

Figure 2. Population for MCED testing in the Future state

- The model estimates potential net savings from SoC to the Future state for MCED-tested patients
- MCED testing is utilized once and occurs at the beginning of the 5-year model
- In the model, MCED testing shifts the stage at detection to an earlier cancer stage and pulls forward detected cancer cases to younger age cohorts[3]

Cancer Incidence and Mortality

- Incidence and mortality rates for each cancer type were derived from the 2020 Surveillance, Epidemiology, and End Results (SEER) database by 5-year age cohorts over ages 30–74 years, published literature, and the population for each age cohort from US Census data[3-5]

Risk Factors

- The proportion of each cancer type attributable to common risk factors was derived from published literature[6-9]
- The percentage of the population with each risk factor by age cohort was derived from published sources (Table 2)[7,10,11]
- A 10% overlap of patients with multiple risk factors was assumed
- Attribution risk factors were derived for the model, enriching the population for testing (Figure 2)

MCED Impact

- Cancer stage at detection in SoC was derived from SEER data by cancer type and age[3,4] and was weighted by the incidence of the selected cancer types
- The cancer stage at detection by cancer type (which is shifted earlier in the Future state) was based on published literature[3]

Model input	Value
Payer member population	1,000,000
End-of-life costs	$80,000
MCED false positive cost (Scenario 1/Scenario 2)	$4,972/$5,256
MCED test specificity	90%
MCED false positive rate (Scenario 1/Scenario 2)	6.4%/8.9%
MCED overdiagnoses, incremental rate (age <50/≥50 years)	1.0%/5.0%
MCED pulled-forward cancers (Stage I/II/III/IV)	20%/40%/60%/70%
Years of treatment costs	5
Risk factors (proportion of patients)	
Severe obesity	9%
Smoking	5%
Heavy alcohol use	5%
Family/genetic risk	14%
HPV infection	1%
Overlap of risk factors	10%

Table 2. Key inputs to the MCED testing model

- The rates of cancer cases pulled forward to younger age cohorts because of earlier detection are greater with higher cancer stages (Table 2)
- The MCED false positive rate is determined by MCED test specificity and varies depending on the number and types of cancers selected (Table 2)
- The MCED overdiagnosis rate is dependent on cancer type and age at detection and is assumed to be lower for younger adults (Table 2)

Costs

- Commercial payer costs are calculated based on 5 years of treatment and are expressed in 2023 US dollars (Table 2)
- For both the SoC and Future states, treatment costs by cancer type and stage at diagnosis were derived from published literature[3]
- Twelve-month EOL costs are estimated to be $80,000 if a mortality event occurs (Table 2)
- A false positive MCED test leads to additional evaluation costs (Table 2)
- The cost of the MCED test was not modeled

Scenarios

- Two scenario examples of model functionality and outputs were developed
  - Scenario 1 tested the population aged 40–54 years with severe obesity, with 10 obesity-related cancers evaluated (Figure 3)
  - Scenario 2 tested the population aged 40–54 years and with any of 3 risk factors (severe obesity, smoking, or HPV infection), with 14 cancers evaluated (Figure 3)

MCED-Qualifying Risk Factors	Scenario 1	Scenario 2
Severe obesity	X	X
Smoking		X
Heavy alcohol		
Family/genetic		
HPV infection		X

Age Ranges Included (Years)		
30–34		
35–39		
40–44	X	X
45–49	X	X
50–54	X	X
55–59		
60–64		
65–69		
70–74		
>74		

MCED-Detected Cancers Evaluated	Scenario 1	Scenario 2
Breast	X	X
NSCLC		X
Colorectal	X	X
Melanoma		X
Kidney	X	X
Endocrine/uterine	X	X
Pancreatic	X	X
Esophageal	X	X
Thyroid		X
Liver	X	X
Ovarian	X	X
Cervical		X
Gallbladder	X	X
Stomach/gastric	X	X

Figure 3. Model inputs for 2 MCED testing scenarios

REFERENCES

1. Koh B, et al. *JAMA Netw Open*. 2023;6(8):e2328171. 2. American Cancer Society. Cancer Facts & Figures 2024. 3. Tafazzoli A, et al. *PharmacoEconomics*. 2022;40(11):1107–1117. 4. US Census Bureau. Accessed August 21, 2023. https://www.census.gov/data/tables/time-series/demo/popest/2020s-national-detail.html 5. SEER Cancer Statistics Explorer Network. Accessed August 21, 2023. https://seer.cancer.gov/statistics-network/ 6. Islami F, et al. *CA: A Cancer Journal for Clinicians*. 2018:68(1);31–54.6. 7. American Cancer Society. Accessed August 21, 2023. https://www.cancer.org/cancer/types/breast-cancer/risk-and-prevention/breast-cancer-risk-factors-you-cannot-change.html 8. Underferth D. 2021. Accessed August 21, 2023. https://www.mdanderson.org/cancerwise/why-are-more-young-adults-getting-colorectal-cancer-what-to-know.h00-159385890.htm 9. AIM at Melanoma Foundation. Accessed August 21, 2023. www.aimatmelanoma.org/melanoma-101/understanding-melanoma/melanoma-risk-factors/personal-and-family-history/ 10. Okano M et al. *J Hum Genet*. 2021 Mar;66(3):307-314. 11. Centers for Disease Control and Prevention. 2020. Accessed August 21, 2023. https://www.cdc.gov/nchs/products/databriefs/db360.htm

DISCLOSURES

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Please download the poster handout from the ISPOR congress app for additional details of the MCED testing model methodology and findings.