EE509

Cost-effectiveness of Multicancer Early Detection (MCED) with Preferential Detection of Clinically Aggressive Cancers

ISPOR Europe
Conference 2023
12–15 November
(Copenhagen, Denmark)

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INTRODUCTION

- Cancer is a significant health challenge, both clinically, as the second-leading cause of death in the US, and economically, as associated with a substantial economic burden.[1-5]
- Early detection and treatment are associated with an improved treatment response, and current screening programs have been shown to reduce cancer mortality in designated populations.[6-10]
- Blood-based multi-cancer early detection (MCED) tests utilizing circulating cell-free DNA (cfDNA) methylation patterns have been developed to simultaneously screen for more than 50 types of cancer.[11,12]
- When used alongside usual care screening, MCED testing may improve survival outcomes and lower treatment costs.[13]
- Recent research suggests that DNA shedding may be a marker of tumor aggressiveness and cancers missed by MCED testing are associated with better prognosis.[14, 15]

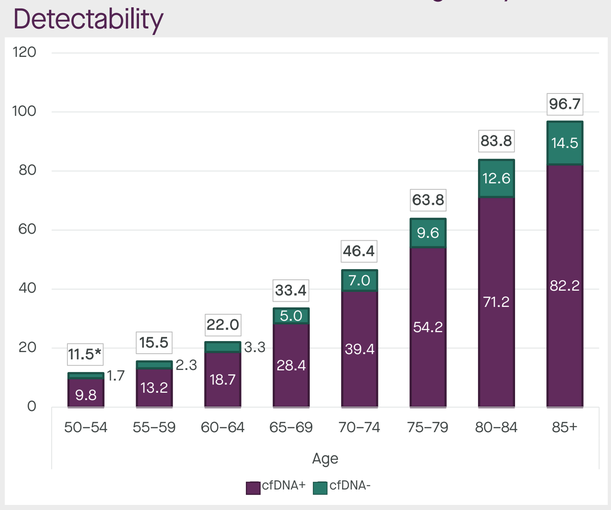
OBJECTIVE

- To evaluate the impact of the differential survival of cfDNA-detectable (cfDNA+; i.e., shedding) cancers vs. cfDNA-non-detectable (cfDNA–) cancers on the cost-effectiveness of MCED testing in addition to usual care from the US commercial perspective

METHODS

- A hybrid Markov model compared annual MCED testing plus usual care in adults aged 50 to 79 years with usual care alone in a US commercial population.
- Patient survival, cost, and quality of life measures were calculated pre- and post-diagnosis based on cancer type, age, and stage at diagnosis over a lifetime horizon. All costs and outcomes were discounted at 3% annually.[14]
- The model consisted of two cohorts accounting for differential survival depending on cfDNA detectability status.
- The incidences of detectable and undetectable cancers were assigned proportionally to each group based on published test sensitivity by cancer and stage[13] such that the total incidence and test sensitivity in the overall population were preserved (example shown in Figure 1).

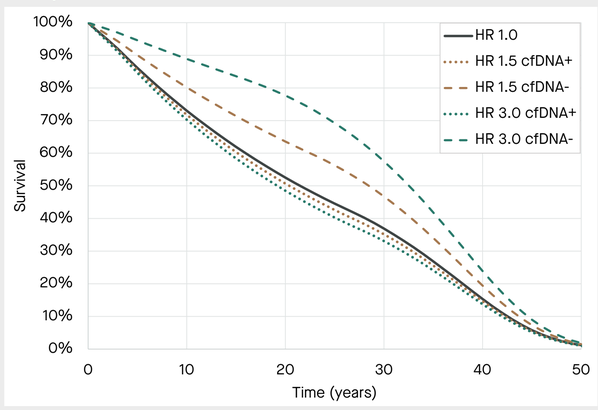
Figure 1: Example Incidence (per 100,000) of Colon and Rectum Cancer at Stage II by Detectability



*Boxed values show total incidences for each age group (numbers may not sum due to rounding). The total incidence was proportionally assigned to cfDNA+ cancers based on the sensitivity of MCED testing (e.g., 85% for stage II colon and rectum cancer).
Abbreviations: cfDNA: cell-free deoxyribonucleic acid; MCED = multi-cancer early detection

- Not all shedding cancers were detectable by the MCED test due to the presence of interval cancers. The cancer stage shift was updated to reflect actual detectability.
- The cfDNA+ cancers were modeled as having no differential survival (hazard ratio [HR] = 1), 1.5 times (HR = 1.5), or 3 times (HR = 3, i.e., extreme scenario) the stage-specific risk of cancer death compared with cfDNA– cancers of the same cancer type. An example of a Kaplan-Meier survival curve based on detectability by stage and age is shown in Figure 2.
- Mortality rates were set such the combined survival would match what was observed in the overall population with cancer of that type and stage.
- Cancer management was determined by cancer type and stage at diagnosis regardless of detectability.

Figure 2: Kaplan-Meier Survival Curves by Detectability for Differential Survival Scenarios for Colon and Rectum Cancer, Stage II, Age 50–54 years

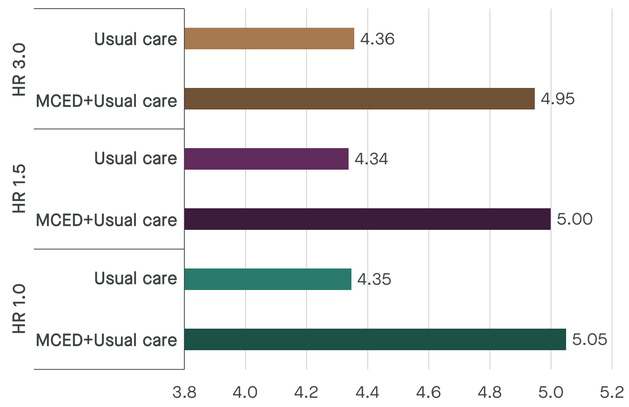


Abbreviations: cfDNA: cell-free deoxyribonucleic acid; HR = hazard ratio

RESULTS

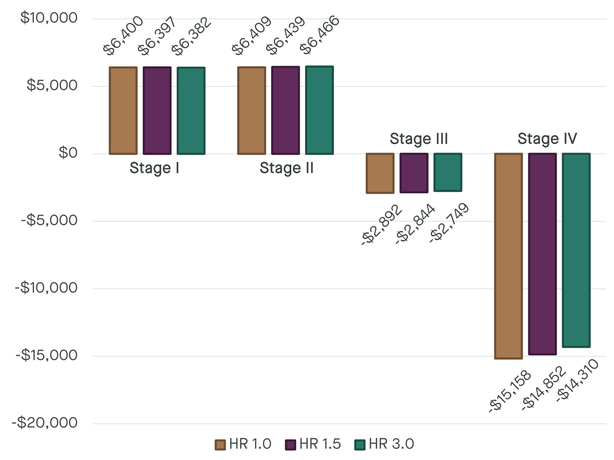
- At an MCED cost of $949, the incremental cost-effectiveness ratio (ICER) of MCED plus usual care vs. usual care alone increased from $66,044 to $77,781 and $106,962 per quality-adjusted life-year (QALY) gained when HR increased from 1 to 1.5 and 3, respectively.
- The observed increase in ICER once relative hazard of death was increased can be linked to:
  - A slightly lower impact of earlier detection on QALY gains. The QALYs per individual over lifetime for MCED plus usual care were 16.07, 16.05, and 16.03 at HR 1, 1.5, and 3, respectively vs 15.93 for usual care only. The post-diagnosis QALYs per individual with cancer is shown in Figure 3.
  - A small increase in total incremental costs ($9,162 at HR = 1, $9,545 at HR = 1.5, and $10,193 at HR = 3) mainly due to the loss of treatment cost savings in later stages. The incremental treatment costs by stage for the three differential survival scenarios is shown in Figure 4.

Figure 3: Post-diagnosis QALYs by Screening Strategy for Differential Survival Scenarios



Abbreviations: HR = hazard ratio; MCED = multi-cancer early detection; QALY = quality-adjusted life-years

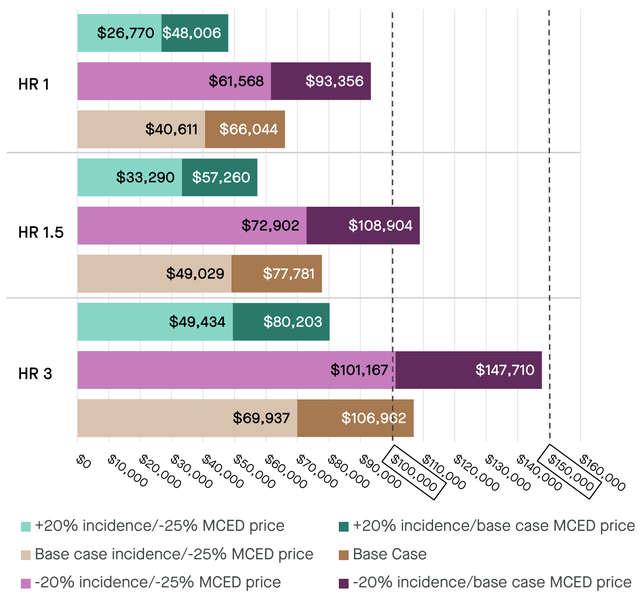
Figure 4: Incremental Treatment Costs by Stage for Differential Survival Scenarios



Abbreviations: HR = hazard ratio

- The effect of change in cancer incidence rate (by ± 20%) and reduction in MCED test price (by 25%) were further explored in the three differential survival scenarios (Figure 5).
- Elevated incidence rates and a decrease in the MCED test price led to lower ICERs, while reduced incidence rates were associated with higher ICERs. The primary factor influencing these outcomes was the alteration in the number of cancers detected and shifted by MCED.

Figure 5: Incremental Treatment Costs by Stage for Differential Survival Scenarios



Note: ICER thresholds of $100,000 and $150,000 are depicted by dashed lines.

KEY ASSUMPTIONS AND LIMITATIONS

- The model assumed that historical survival in the general population can be adjusted for MCED detectable cancers and a change in stage at diagnosis is associated with changes in survival.
- While the model was designed to capture the stage-shifting benefit from MCED testing and resulting impact on survival, MCED testing may lead to within-stage changes in cancer detection that may be prognostically relevant and confer mortality benefits[16] that were not considered in the model or captured in these analyses.

CONCLUSIONS

- When differential survival by cfDNA detectability status was adjusted with a hazard ratio of up to 3, modest shifts in population survival and treatment costs were observed in an economic model comparing MCED testing plus usual care to usual care alone.
- These analyses yielded ICERs consistently near or below commonly accepted willingness-to-pay thresholds of $100,000 to $150,000 per gained QALY,[17] indicating that MCED testing has the potential to be cost-effective across a wide range of clinical hypotheses on mortality and incidence.

References

1. CDC. https://www.cdc.gov/nchs/products/databriefs/db427.htm. Published 2021.
2. CDC. https://www.cdc.gov/cancer/dcpc/data/index.htm. Last updated: 8 June 2023
3. Mariotto AB, et a. *Cancer Epidemiol Biomarkers Prev.* 2020;29(7):1304-1312.
4. Siegel RL, et al. *CA Cancer J Clin.* 2023;73(1):17-48.
5. WHO. https://www.who.int/news-room/fact-sheets/detail/cancer. Published 2022
6. Duma N, et al. *Mayo Clin Proc.* 2019;94(8):1623-1640.
7. Tsikouras P, et al. *J BUON.* 2016;21(2):320-325.
8. Clarke CA, et al. Cancer *Epidemiol Biomarkers Prev.* 2020;29(5):895-902.
9. Etzioni R, et al. *Nat Rev Cancer.* 2003;3(4):243-252.
10. Tobore TO. *Future Sci OA.* 2019;6(2):FSO439.
11. Chen M, et al. *Hum Genomics.* 2019;13(1):34.
12. Klein EA, et al. *Ann Oncol.* 2021;32(9):1167-1177.
13. Tafazzoli A, et al. *Pharmacoeconomics.* 2022; 40(11):1107-1117.
14. Bredno J, et al. *PLoS One.* 2021;16(8):e0256436.
15. Chen X, et al. *Clin Cancer Res.* 2021;27(15):4221-4229.
16. Sasieni P, et al. *Br J Cancer.* 2023;129(1):72-80.
17. Neumann PJ, et al. *JAMA.* 2023;329(15):1312-1 314.

Disclosures

Study funded by GRAIL, LLC. SD, WY, AC, and DZ are employees of Evidera, a business unit of ThermoFisher, which has received payments from GRAIL, LLC. for services related to this poster. AK, and AT are employees of GRAIL, LLC.

Acknowledgments

The authors would like to acknowledge Evidera's Editorial & Design staff.