The Value of Multi-Cancer Early Detection Tests and Limits to Estimating Budget Impacts of Legislation Proposed to Enable Medicare Access

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Abstract

This policy brief reviews the evidence on the health and cost impacts of multi-cancer early detection (MCED) tests, and the implications for proposed legislation to enhance their utilization in Medicare. We find that the evidence base suggests that MCED screening raises lifetime gains from improved health by an amount valued at $49,000. This implies that fully screening a cohort of 4.1 million people, the approximate Medicare-eligible population turning 65 each year, would entail a potential aggregate value of $200.9 billion in improved health. We estimated the aggregate value of MCED screening applied to the existing Medicare population of 40.9 million aged 65 years and above to be $1.1 trillion. The “Medicare Multi-Cancer Early Detection Screening Coverage Act” has been proposed to provide Medicare coverage of MCED tests. CBO scoring of the Act would be limited to these federal budget effects in the next 10 years, but offsetting benefits due to improved health are not taken into consideration for budgetary effects.
Section 1: Introduction

Multi-cancer Early Detection (MCED) tests use blood samples that can screen for more than 50 cancer types. These tests use tools including but not limited to genomics, big data analytics, and machine learning. Compared to current cancer screenings that are aimed at up to 5 individual cancers, such as mammograms for breast cancer and colonoscopies for colorectal cancer, MCED tests are expected to detect multiple cancer types and can dramatically increase the efficiency of cancer screening, reduce treatment costs by earlier detection, and alleviate inequities in cancer detection and care.

Currently, several MCED tests are in development, among which two are either approaching commercial readiness or have recently become available. CancerSEEK, an MCED test developed at Johns Hopkins University, is now under clinical investigation and has received its Food and Drug Administration (FDA) breakthrough designation (Nadauld and Goldman, 2022). A study using CancerSEEK in a combined modality approach (two sequential blood draws and a full-body diagnostic PET-CT) demonstrated sensitivity up to 30% and specificity of 98.9% which was increased to 99.6% when combined with the PET-CT (Lennon et al, 2020). GRAIL developed a multi-cancer early detection test, Galleri, which was designed as a screening test for individuals with an elevated risk of cancer, such as those 50 years of age and older. In PATHFINDER, which implemented an early version of the Galleri test, the number of cancers detected with MCED was twice the number detected by standard screening (GRAIL, 2022). GRAIL’s MCED test received a Breakthrough designation from the FDA and is actively engaged with the FDA in the pre-market approval (PMA) process. GRAIL has since launched Galleri as a Laboratory Developed Test (LDT) (GRAIL, 2021).

In anticipation of the approval of these new MCED tests, legislation known as the “Medicare Multi-Cancer Early Detection Screening Coverage Act” has been introduced in both chambers of Congress H.R. 1946 in the House and S.1873 in the Senate, which would amend title XVIII of the Social Security Act to establish a Medicare coverage pathway for FDA approved MCED tests.

In this policy brief, we assess the evidence base regarding the value of MCED tests, the limitations of Congressional Budget Office (CBO) scoring which is solely focused on budget effects of the coverage legislation, and provide a more comprehensive, holistic estimate of the impact of such technology on society.

At a valuation of a statistical life year (VSLY) of $490,000 based on a literature review conducted by Philipson and Durie (2021), we find a health outcome improvement of $49,000 per patient screened. If MCED tests were applied to the cohort of 4.1 million individuals entering Medicare, the estimated number reaching 65 years of age in a year, there would be a projected health outcome improvement of $200.9 billion. Given that the number of individuals entering Medicare is much smaller than the entire Medicare population, less than 10%, the benefit to the total Medicare population is much larger. We estimated the aggregate value to be $1.1 trillion if MCED screening is applied to the existing Medicare population of 40.9 million aged 65 years and above. The stated purpose of CBO scoring is to assess federal budget impacts as opposed to value impacts. Thus, the purpose of traditional CBO scoring – though useful for assessing federal budget impacts – is not useful for assessing overall MCED value impacts as it ignores the benefits in terms of improved health.

The policy brief is outlined as follows: Section 2 summarizes the relevant literature used to calibrate the value gains of improved health outcomes from MCED screening; Section 3 presents the overall and Medicare spending offsets from MCED leveraging literature focused
on cancer burden, including payer cost by cancer stage at diagnosis; Section 4 reviews the drawbacks of the CBO budget impact analysis on the proposed legislation; Section 5 provides the conclusion.

Section 2: Improved Health Outcomes from MCED Screening

In this section, we summarize the literature on improved health outcomes from early diagnosis through MCED screening and the implied aggregate value for Medicare beneficiaries.

Although MCED is a relatively new development there exists an emerging literature demonstrating the potential impact of a multi-cancer approach on cancer detection. One study demonstrated the efficiency of incorporating MCED testing to the current standard of care, projecting 422,105 additional cancers (across >50 cancer types) to be detected in the U.S. on an annual basis compared to 189,498 (Hackshaw, 2021). A separate analysis modeling performance of a MCED test suggests that it could substantially reduce overall cancer mortality if added to usual care, intercepting 485 cancers per year per 100,000 persons, resulting in a reduction of late-stage (III+IV) cancer incidence by 78% in those intercepted (Hubbell, 2021). Clarke et. al. (2020) estimated that detection of multiple cancer types earlier than stage IV could reduce at least 15% of cancer-related deaths within 5 years, affecting not only cancer-specific but all-cause mortality. Sasieni et al. (2023) estimated among 100,000 MCED screened individuals, 67 (17%) fewer cancer deaths per year corresponding to 2,029 fewer deaths in those screened between ages 50–79 years, reflecting the potential benefits of MCED tests to substantially reduce late-stage cancer diagnoses and mortality.

Building on the current evidence base, we estimate the total value accrued from improved health outcomes at different uptakes within the Medicare population. At 100% uptake and a VSLY of $490,000, the aggregate value accrued from improved health outcomes is $200.9 billion.

We focus on Tafazzoli et al. (2022), a cost-effectiveness analysis which quantifies the value of incorporating MCED to current standard of care screening, which includes an analysis of the Medicare-aged population. Assuming 100% uptake within a cohort aging into Medicare (i.e., 65 years of age), it is simulated that every individual can gain 0.1 life year (LY) and 0.1 quality-adjusted life year (QALY) over their lifetime with the implementation of MCED testing. Results were discounted at 3% (2021 dollars), which was consistent in the current estimates. Tafazzoli et al. (2022) also imposed the following assumptions: a five-year cancer episode (relative to cancer treatment costs), 14 MCED tests for each patient screened over 14 years, 100% uptake, and 90% testing adherence rate, where the entire cohort takes the tests but only 90% of the cohort show up for testing each year. We follow these assumptions throughout our analysis to align with Tafazzoli et al. (2022).

For estimating the aggregate value of MCED, we consider the cohort of the population turning 65 each year and thus becoming eligible for Medicare coverage. Note Tafazzoli et al. (2022) reports per patient screened results, enabling our analysis to be conducted without considering cancer incidence, as the assumption is that the cohort takes the tests rather than is entirely diagnosed with cancer. Across different sources (HHS, 2022; ACL, 2021; CDC, 2014), we observe a range of 3.7 million to 4.1 million people turning 65 each year. The CDC estimates that over 4.1 million people will become 65 years old each year for both 2022 and 2023, so we choose 4.1 million as the cohort size for slightly conservative estimates. We later
also estimate the aggregate value applied to the entire current Medicare population, assuming the values vary proportionally with age.

We first estimate the aggregate value from improved health outcomes to the cohort of 4.1 million people turning 65 in one year. Based on a large literature review by Philipson and Durie (2021), the average value of a statistical life year (VSLY) is estimated to be $490,000. Also see HHS (2021) for a range of value per QALY, including $490,000. We consider this VSLY as well as lower ones previously implemented in value assessments. At a lower bound VSLY of $150,000, a 0.1 LY improvement equates to a value of $15,000 while at the VSLY of $490,000, a 0.1 LY improved equates to $49,000.

In Table 1, we multiply these per capita values by different fractions of the 4.1 million population under different uptake scenarios to arrive at an aggregate health outcome values. If we follow the assumption of 100% uptake, at the VSLY of $490,000, the aggregate value from health outcome improvement is $200.9 billion. Under the lower VSLY, the aggregate value is equivalent to $61.5 billion. While health outcome improvements contribute substantially to the value of MCED, it is not accounted for by CBO since the duty of CBO is solely focused on budgetary effects.

To estimate the aggregate lifetime value gained from MCED screening for the entire Medicare population, we considered individuals aged 65 years and older, and a mean life expectancy of 76.1 years based on the study by Arias et al. (2021). Utilizing the Census data obtained in 2023, we derived the cohort sizes for each age till 76.1 and resulted in a total of 40.9 million individuals (Census, 2023). We assume that the entire population in this age range is enrolled in Medicare. For each age cohort, we assume the values accrued to them are proportional to the years left in comparison to the entering cohort turning 65. For example, the cohort aged 70 years has 6.1 years of expected remaining life years compared to 11.1 years for the cohort aged 65 years. Therefore, we calculated the lifetime value for people who are 70 years old by multiplying the value of $49,000 for those who are 65 years old by the ratio of 6.1 to 11.1, the respective remaining life years, yielding $26,928. After estimating the individual value, we multiply by the cohort size of 3.4 million of the age 70 years and calculate the total lifetime value gain for the cohort to be $92.7 billion. To estimate the aggregate lifetime value gain, we sum up the value gain from all of the age groups. Finally, our calculations yielded an estimated aggregate lifetime value derived from MCED screening for the entire population of 40.9 million individuals, aged 65 years until the projected life expectancy of 76.1 years, amounting to $1.1 trillion.

**Table 1: Aggregate Value at Varying uptakes in Medicare Population – Improved Health Outcomes**

<table>
<thead>
<tr>
<th>VSLY</th>
<th>Health Outcome Value Per Patient</th>
<th>Aggregate Health Outcome Value ($ billion)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>MCED Uptake Rate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50%</td>
</tr>
<tr>
<td>$150,000</td>
<td>$15,000</td>
<td>$30.8</td>
</tr>
<tr>
<td>$490,000</td>
<td>$49,000</td>
<td>$100.5</td>
</tr>
</tbody>
</table>
Section 3: Medicare Spending Impacts from Early Detection Technologies other than MCEDs

Given the recent introduction of MCED testing, we discuss cost savings for the screened population using the general literature detailing cancer cost in the first year after diagnosis by early detection.

Multiple papers record treatment cost differences when cancer is detected at different stages (Reddy et al., 2022; Kakushadze et al., 2017; Banegas et al., 2018; Homan et al., 2021), but all of them are based on patients diagnosed with cancer. Since MCED is a screening device, there can be a vast disparity between the screened population and the diagnosed population. To reconcile with the different population basis, we unify them to a per-screening basis by estimating the per-screening cost savings.

Since patients may not be at stage I when taking the MCED screening, only considering differences between stage I and stage IV would likely overestimate the cost savings. Thus, we estimated these cost savings from early diagnosis by averaging the cost differences between stages I and IV, II and IV, and III and IV. For example, if treatment costs for a given cancer are $10,000 at stage I, $15,000 at stage II, $21,000 at stage III, and $40,000 at stage IV, the differences between stages I and IV, II and IV, and III and IV are $30,000, $25,000, and $19,000 respectively. Therefore, the final estimate is the average of these values, $24,667. In this manner, the literature suggests a reduced treatment cost of $37,254 from early diagnosis in the first year after diagnosis (Table 2).

Table 2: Value of MCED Device and Early Detection – General First-Year Cost Saving

<table>
<thead>
<tr>
<th>Authors (Year)</th>
<th>Country</th>
<th>Type of Cancers</th>
<th>Method of Analysis</th>
<th>Type of Diagnosis</th>
<th>Estimate</th>
<th>Methodology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reddy et al. (2022)</td>
<td>US</td>
<td>17 cancers</td>
<td>Cost</td>
<td>Early diagnosis</td>
<td>$55,412.7 decrease in year 1 cost</td>
<td>Average across diagnosis at stage I, II, III for each cancer and then average across cancers</td>
</tr>
<tr>
<td>Kakushadze et al. (2017)</td>
<td>US</td>
<td>Breast, lung, prostate and colorectal cancers, melanoma</td>
<td>Cost</td>
<td>Early diagnosis</td>
<td>$43,967 decrease in year 1 cost</td>
<td>Average across diagnosis at stage 0, I/II, III</td>
</tr>
<tr>
<td>Banegas et al. (2018)</td>
<td>US</td>
<td>Breast, colorectal, lung, prostate cancers</td>
<td>Cost</td>
<td>Disease progression</td>
<td>$20,850 increase in year 1 cost</td>
<td>Average difference from stage IV across stage 0, I/II, III; average across cancer types and age</td>
</tr>
<tr>
<td>Homan et al. (2021)</td>
<td>US</td>
<td>Breast cancer</td>
<td>Cost</td>
<td>Disease progression</td>
<td>$28,788 increase in year 1 cost</td>
<td>Average difference from final stage across earlier stages; stages defined by in situ, localized, regional, distant</td>
</tr>
<tr>
<td>Average</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>$37,254.4</td>
<td>First-year after diagnosis per diagnosed patient</td>
</tr>
</tbody>
</table>

Section 4: CBO Scoring to Assess the Proposed Legislation

The CBO is mandated by Congress to analyze the impact of proposed legislation only on the federal budget, and it does so by performing 3 steps: identifying the influenced population, estimating the impact on healthcare spending, and concluding how these impacts affect federal budgets (CBO, 2020). Therefore, the stated goal of CBO analyses is to assess the budget impacts as opposed to value impacts, thereby focusing only on the costs and not the benefits of legislation. In addition, CBO’s ten-year horizon for budget impacts limits its
capacity to measure the longer-term health benefits of preventive health measures, which is essential for cancer screenings.

CBO’s budget impact analysis differs from two other commonly used methodologies: Cost Benefit Analysis (CBA) and Cost Effectiveness Analysis (CEA). A comparison between the methods can be seen in Table 4 below. Though the table represents CBO’s methodology for screening for opioid use disorder, it is representative of all preventive care, including cancer screening.

Table 4: Comparison between CBO Method, CBA, and CEA

<table>
<thead>
<tr>
<th>Three Analytic Approaches to Estimating the Effects of a Hypothetical Screening for Opioid Use Disorder</th>
<th>CBO’s Approach for Cost Estimates</th>
<th>Cost-Benefit Analysis</th>
<th>Cost-Effectiveness Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methodology</td>
<td>Effect on federal budget</td>
<td>Net present value</td>
<td>Cost per QALY(^a)</td>
</tr>
<tr>
<td>Factors</td>
<td>No</td>
<td>Generally, yes</td>
<td></td>
</tr>
<tr>
<td>Adjustment for Inflation</td>
<td>No</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Use of Discounting</td>
<td>Generally, 10 years</td>
<td>Period over which benefits and costs occur</td>
<td></td>
</tr>
<tr>
<td>Costs of Administering Screening and Interpreting Results by Clinician</td>
<td>Includes federal costs</td>
<td>Includes spending by all sources (for example, patients and federal, state, and local governments)</td>
<td></td>
</tr>
<tr>
<td>Changes in Spending on Treatment From Earlier Identification of the Disorder</td>
<td>Includes changes in federal costs</td>
<td>Includes changes in spending by all sources</td>
<td></td>
</tr>
<tr>
<td>Increase in Longevity</td>
<td>Includes increased federal health care spending on unrelated medical conditions and retirement and disability benefits(^b)</td>
<td>Includes QALY saved as a benefit (monetized for CBA)</td>
<td></td>
</tr>
<tr>
<td>Reduction in Disability</td>
<td>Includes avoided spending on Social Security, Medicaid, and Medicare as reduced federal spending if screening results in avoided disability; that reduction would be offset to the extent that the affected people enrolled in other forms of federally subsidized insurance(^c)</td>
<td>Includes all avoided disability costs as a benefit if screening results in avoided disability</td>
<td></td>
</tr>
<tr>
<td>Increase in Productivity</td>
<td>Typically excludes increased federal government tax revenues from higher wages or labor force participation(^d)</td>
<td>Includes increased tax revenues at all levels of government from higher wages; includes increased productivity in wage-earning activities (potentially measured by the increase in after-tax income) and increased productivity in non-wage-earning activities (for example, volunteering)</td>
<td></td>
</tr>
<tr>
<td>Improved Ability of Patients to Care for Their Children</td>
<td>Includes reductions in federal spending on foster care (including Medicaid spending for children’s health care) if the service results in an improved ability of parents to care for their children(^e)</td>
<td>Includes reductions in foster care costs if the service results in an improved ability of parents to care for their children; also counts reductions in child care burden on other family members (for example, grandparents) and positive effects on the children of improved care by their parents</td>
<td></td>
</tr>
<tr>
<td>Reduction in Criminal Justice Costs</td>
<td>Includes reductions in federal spending(^f)</td>
<td>Includes reductions in federal, state, and local spending; also counts savings to victims from crimes avoided</td>
<td></td>
</tr>
</tbody>
</table>

Source: Congressional Budget Office.

Compared to the CBO method, CBA and CEA take more factors into consideration, making them more extensive measures of product value than simply federal government cost impacts. For example, CBO focuses on a ten-year budget period because Congressional budget enforcement procedures generally apply to that period. But this period falls short when the effects of preventive healthcare policies may not be captured within ten years. The human papillomavirus vaccine is an example, as it is recommended for children between 11 to 12 years of age, while health improvements and prevention of cancer would appear later in their lives,
outside of the ten-year frame of evaluation (CBO, 2020). Similar arguments are likely valid for cancer detection as benefits from early detection can last for more than ten years from aspects like longer life expectancy. Instead, both CBA and CEA consider the full period (e.g., lifetime) over which benefits and costs occur, extending the analysis to adjust for the expected duration of the effects of new legislation.

At the same time, both methods take into consideration health outcomes as a relevant part of their cost-benefit evaluation. This is particularly important for the case of cancer screening and treatment legislations: Both CBA and CEA incorporate the calculation of QALYs (quality-adjusted life-years) and life years (LY) gained as a monetized interpretation for CBA estimates and as a cost per QALY/LY analysis for CEA (CBO, 2020). Therefore, these methods account for additional measures compared to CBO.

Additionally, for the cases of increases in longevity, productivity, and reduction in disability from cancer treatments, CBO considers the changes regarding federal costs from changes in those variables, while CBA and CEA would consider QALYs saved as additional benefits to the new legislation and would incorporate avoided disability costs as a benefit if screening results reduce disability. Thus, to fulfill its major responsibility of reporting impacts on the federal budget, CBO’s method must leave out important parts of the values of medical technologies, specifically long-term health outcome impacts.

The underestimation of the value of preventive care is not unique to cancer screening. Other preventive care measures, especially vaccines, have created significant health outcomes. According to Toumi and Ricciardi (2015), 5 million smallpox deaths, 2.7 million measles cases, 2 million neonatal tetanus cases, 1 million pertussis cases, 600,000 paralytic poliomyelitis cases, and 300,000 diphtheria cases have been estimated to be prevented by the corresponding vaccines on an annual basis. Considering the conventional valuation methods with VSLY, these would indicate billions of values annually. Ehreth (2003) also reports an annual saving of $300 million from smallpox and $13.6 billion in total savings from polio by 2040. It also reports that measles treatment costs 22 times more than the vaccination per child. Other diseases including cholera, malaria, measles, mumps, and rubella (MMR), diphtheria, tetanus, and pertussis (DTaP), and Haemophilus influenza type b (Hib) also incurred significant costs without the applications of vaccines (ibid). Wang and Wang (2021) also mention that proper preventive care can reduce illness occurrence, yielding higher productivity. However, despite the substantial values, CBO (2020) estimates only 20% of preventive care reduced costs, while 60% do not reduce costs but lead to reasonable health outcomes relative to the costs. Thus, measuring the value of preventive care solely based on cost reduction can easily lead to underestimation.

In conclusion, CBO’s estimates present a limited analysis of the overall impacts of new legislations on preventive care because of Congressional methods and the limitations of their methodology. Focusing only on the effects on the federal budget and limiting those to a ten-year period reduce the scope to which the effects of new technologies can be measured, especially for those involving treatments with effects in the long run.

**Section 5: Conclusion**

We find that the evidence base suggests that each MCED screen raises health outcomes by an amount valued at $49,000 per patient screened. For the cohort of 4.1 million people who become newly eligible for Medicare coverage each year, this would entail a potential aggregate value of $200.9 billion in improved health. For the current Medicare population of 40.9 million aged 65 years and above, the aggregate value is $1.1 trillion. CBO scoring of the Act would
only be limited to these beneficial budget effects, but the larger benefits would accrue due to the improved health of Medicare beneficiaries.
References


Arias, Elizabeth, Betzaida Tejada-Vera, Farida Ahmad, and Kenneth D. Kochanek. "Vital statistics rapid release." Age (years) 70 (2021): 75.


