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Modeled Economic and Clinical Impact of a Multi-Cancer Early Detection (MCED) Test in a Population with Hereditary Cancer Syndromes (HCS)

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INTRODUCTION

- Individuals with hereditary cancer syndromes (HCS) face a significantly elevated risk of developing cancer and usually develop cancer at younger ages than average-risk individuals[1-3]
- Multi-cancer early detection (MCED) tests have the potential to reduce the occurrence of late-stage cancer by enabling detection at early asymptomatic stages[4-9]
- Early detection is associated with better survival outcomes and reduced treatment costs[10-13]
- MCED has been projected to be a cost-effective approach in adults aged 50 years or older who are at average-risk for developing cancer;[14] however, the economic and clinical impact of MCED testing in high-risk individuals with HCS remains unclear

OBJECTIVES

- Primary: Investigate the key economic and health outcomes of MCED testing in adults with HCS in the US
- Secondary: Assess the outcomes based on different gene mutation groupings

ADDING ANNUAL MCED TESTING TO SOC IS HIGHLY COST-EFFECTIVE FOR HIGH-RISK INDIVIDUALS WITH HCS

RESULTS:

- MCED plus standard of care (SoC) screening was estimated to improve outcomes across all HCS populations modeled here, with incremental life years (LYs) ranging from 0.24 to 1.30 and incremental quality-adjusted life years (QALYs) from 0.18 to 1.08 (**Table 1**)
- In the overall HCS population, MCED was projected to reduce initial incidence of cancers diagnosed in stage III or IV by 42%, leading to lower cancer treatment costs (**Table 1**)
- This reduction resulted in a projected 17% decrease in modeled cancer mortality, largely driven by a 56% decrease in stage IV mortality resulting from stage shift of cancers to earlier stages
  - This reduction was estimated using general population survival data based on SEER and didn't account for the potentially more aggressive nature of MCED-detected cancers
- At a price of $949 per test, MCED resulted in an incremental cost-effectiveness ratio (ICER) of $545/QALY in the overall population (**Table 1**), with sensitivity analysis indicating the ICER could range from $12,699 to being dominant (more effective and less costly)

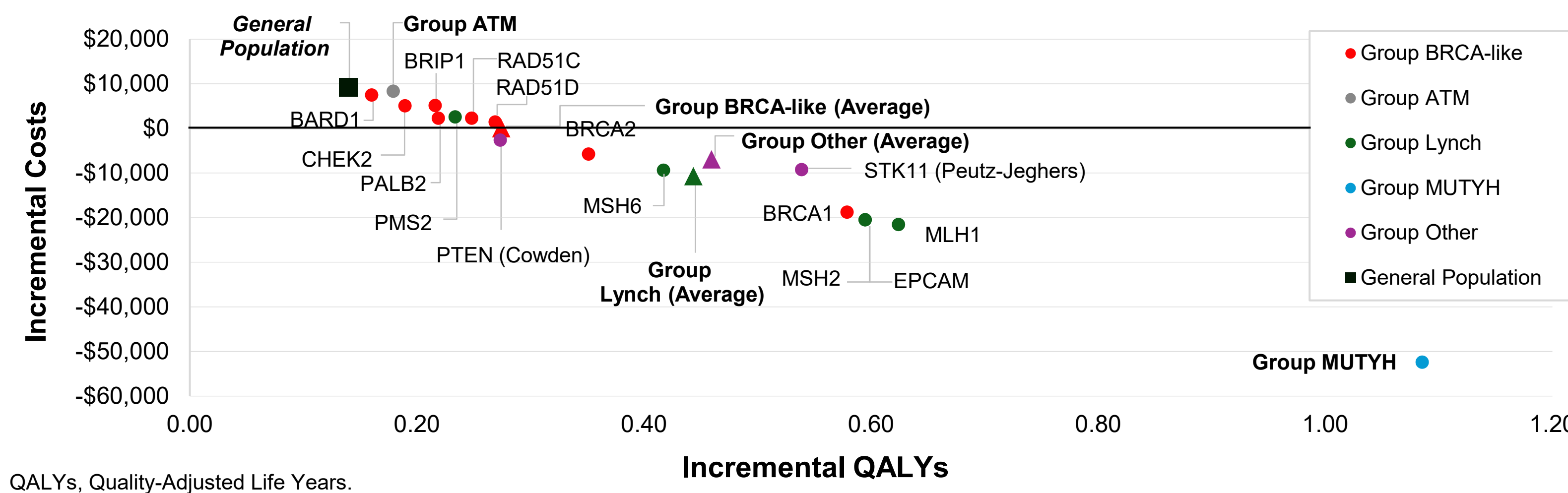
Table 1. Cost-Effectiveness Results for the Overall HCS Population and Gene Mutation Groupings (Mean and CI)

Group	Incremental LYs	Incremental QALYs	Incremental Cost	ICER per QALY
Overall	0.34 (0.29, 0.39)	0.27 (0.23, 0.32)	$149 ($2,921, -$2,715)	$545 ($12,699, Dominant)
Group BRCA-like	0.32 (0.28, 0.37)	0.27 (0.23, 0.30)	$165 ($2,750, -$2,443)	$621 ($12,088, Dominant)
Group ATM	0.24 (0.21, 0.37)	0.18 (0.16, 0.30)	$8,490 ($8,779, -$2,443)	$47,914 ($54,365, $42,249)
Group Lynch	0.53 (0.40, 0.65)	0.44 (0.32, 0.55)	-$10,426 (-$3,081, -$17,691)	Dominant
Group MUTYH	1.30	1.08	-$52,428	Dominant
Group Other	0.58 (0.54, 0.63)	0.45 (0.42, 0.49)	-$6,888 (-$6,657, -$7,235)	Dominant

HCS, Hereditary Cancer Syndromes; CI, Confidence Interval; LY, Life Year; QALY: Quality Adjusted Life Year; ICER, Incremental Cost-Effectiveness Ratio

- The cost-effectiveness plane for individual gene mutations and groupings shows considerable variation in QALY gain and incremental costs, with larger QALY gain associated with lower net costs (**Figure 1**)

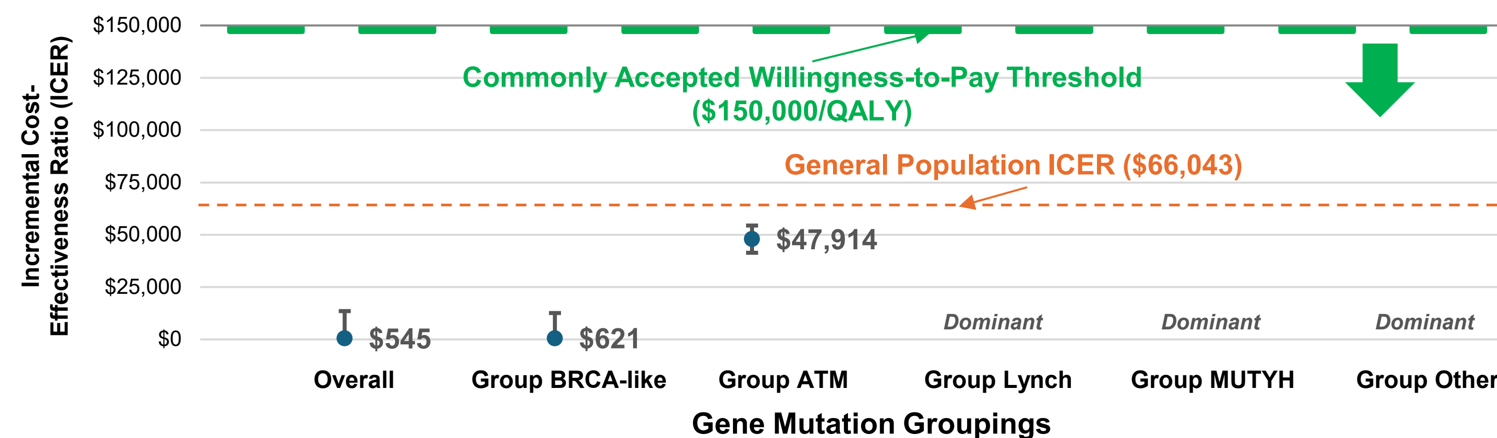
Figure 1. Cost-Effectiveness Plane for Individual Gene Mutations and Groupings



QALYs, Quality-Adjusted Life Years.

- **Figure 2** illustrates that the ICER for nearly all mutation groupings was either dominant or significantly lower than the $66,043 estimated for the general population and the $150,000/QALY commonly accepted willingness-to-pay threshold[14]
- Mutation grouping B demonstrated the smallest benefit among those with HCS, mainly due to a lower incidence of cancer compared to other groupings and the nature of impacted cancers

Figure 2. ICER for the Overall HCS Population and Gene Mutation Groupings (Mean and CI)



ICER, Incremental Cost-Effectiveness Ratio; HCS, Hereditary Cancer Syndromes; QALY, Quality-Adjusted Life Year.

CONCLUSIONS

- Many people with HCS, who are at a higher risk of developing cancer, are unaware of their condition, and there is an unmet need for both identifying those individuals and detecting their cancers early
- Adding MCED testing to standard care was predicted to be highly cost-effective and nearly cost-neutral for high-risk individuals with HCS
- Among patients with HCS, higher cancer incidence is associated with better cost-effectiveness of MCED testing

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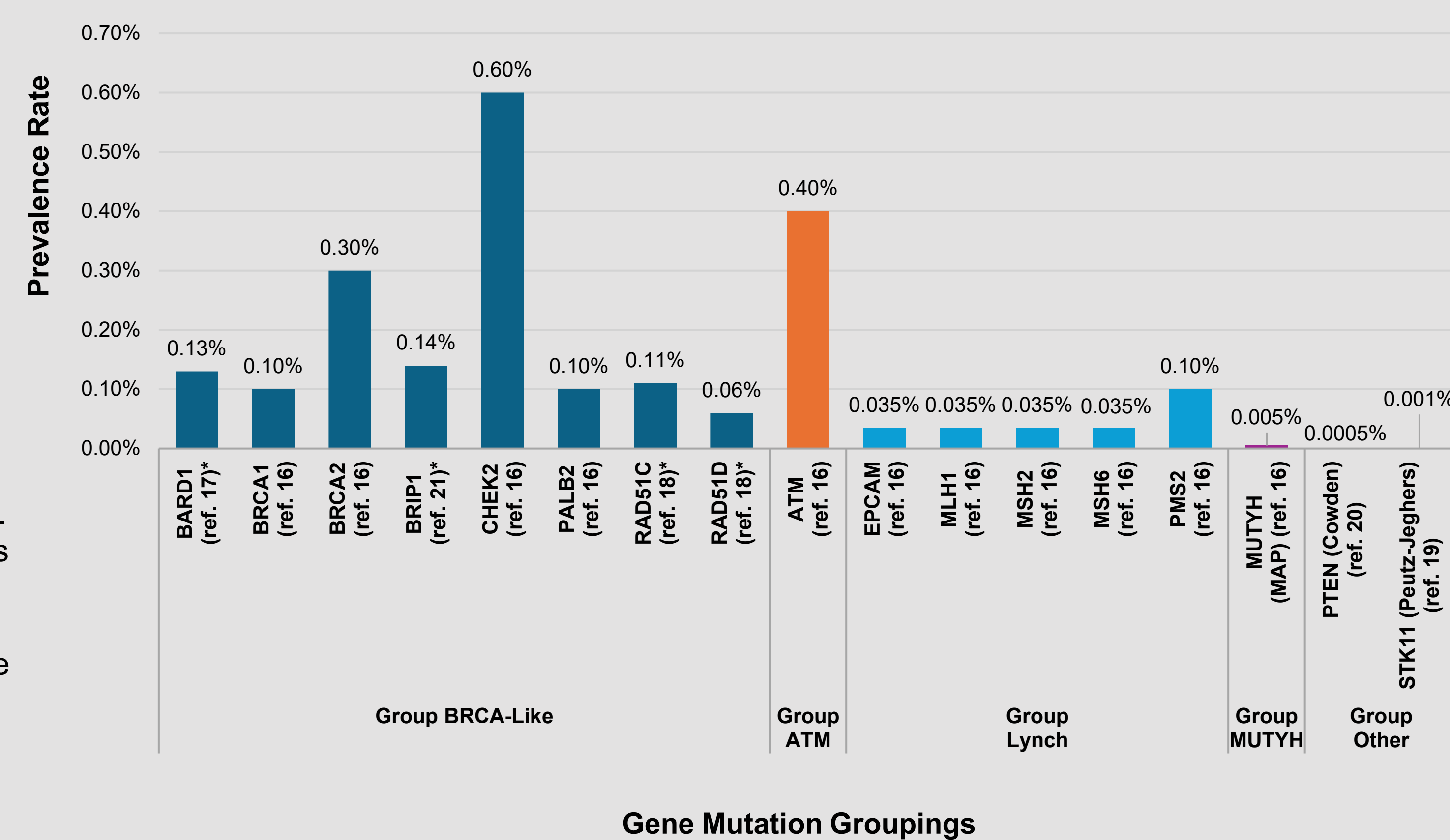
SUPPORTING INFORMATION

METHODS

- A state transition model was developed to compare the outcomes of annual MCED plus SoC screening versus SoC screening alone
- Nineteen solid cancer types, collectively representing over 80% of all cancers in the US, were modeled
- The simulation considered high-risk individuals with HCS aged 50 to 79 who have not received risk reducing surgery and without a prior history of cancer
  - Seventeen gene mutations were considered (see the list in **Figure 3**), associated with eight common cancer types: breast, ovarian, pancreatic, prostate, colorectal, stomach, endometrial, bladder
- The global prevalence of each mutation was derived from mostly US-based studies in adults[16-21] (**Figure 3**).
- Five gene mutation groupings based on their pathways were also studied:
  - **Group BRCA-like:** BARD1, BRCA1, BRCA2, BRIP1, RAD51C, RAD51D, CHEK2, PALB2 (double stranded DNA damage repair via homologous recombination)
  - **Group ATM:** ATM (dsDNA damage sensor in homologous recombination)
  - **Group Lynch:** EPCAM, MLH1, MSH2, MSH6, PMS2 (mismatch repair - Lynch Syndrome)
  - **Group MUTYH:** MUTYH (base excision repair)
  - **Group Other:** PTEN, STK11 (other tumor suppressors)

Figure 3. Gene Mutation Groupings and the Prevalence Rate for Each Mutation

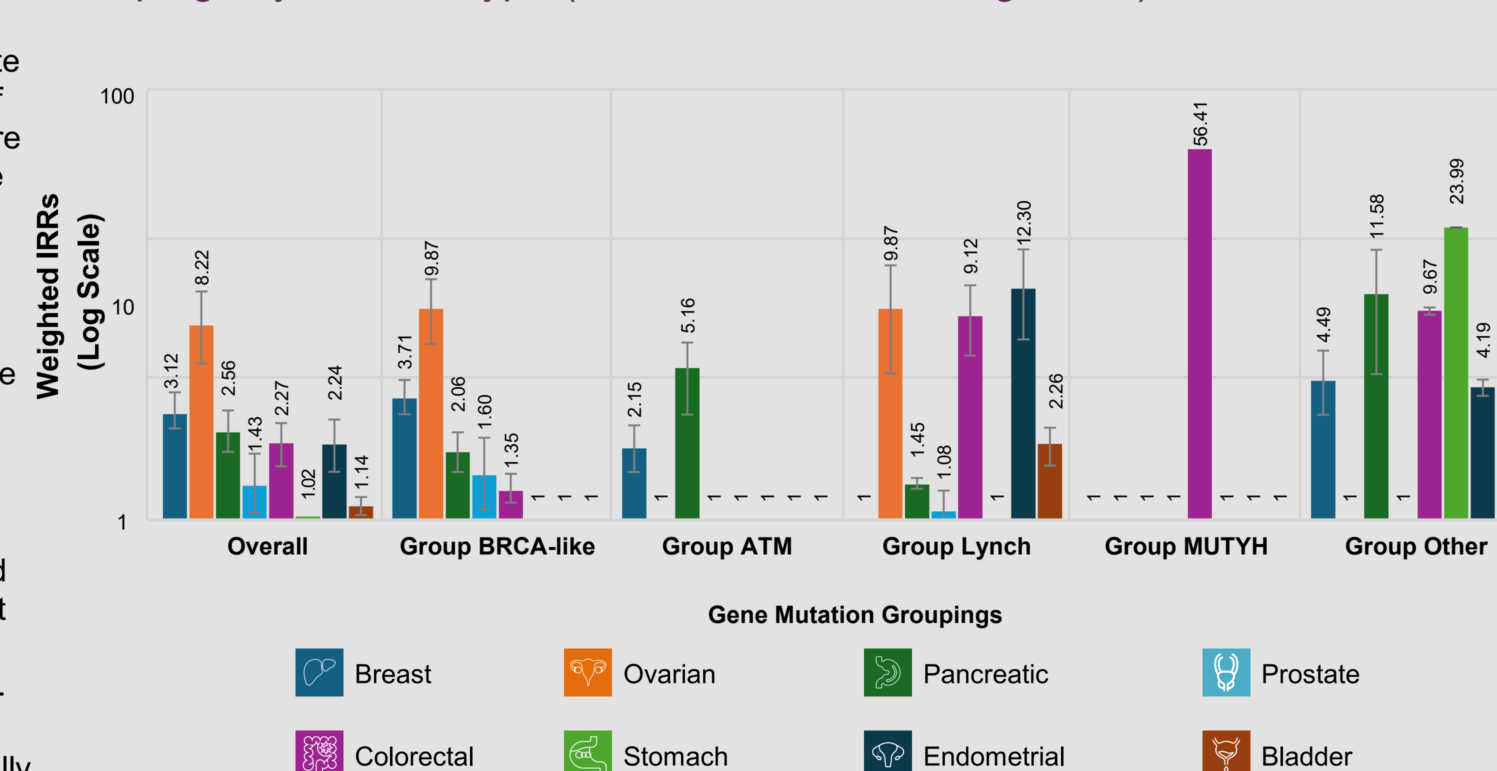


*Estimated by comparing gene prevalence in cancer-specific populations with control populations within the same studies.
Note: APC, CDH1, CDKN2A, and TP53 (Li-Fraumeni) mutations were excluded due to their association with earlier cancer risk occurring before age 50, while HOXB13, CDK4, and NBN were excluded due to insufficient evidence of increased risk for the cancers included in this study.[15]

SUPPORTING DATA

- For each gene mutation, the incidence rate ratios (IRRs) for cancer and their range of uncertainty vs. the general population were estimated using the published data on the lifetime risk of affected cancer types,[15] assuming a constant rate
- These IRRs were then weighted by the global prevalence of each mutation, to determine an average IRR per cancer type for an overall HCS population and each mutation grouping (**Figure 4**)
- SEER-Medicare linked data informed resource use and costs,[22] while the performance of the MCED test was based on Klein et al (2021)[4]; cost per MCED test was assumed to be $949
- Costs, life-years, and quality adjusted life-years (QALYs) were estimated over an individual's lifetime and discounted annually at a rate of 3%
- The robustness of the base results was tested using the upper and lower bounds of the estimated IRRs for each cancer type

Figure 4. Weighted IRRs for Overall HCS Population and Gene Mutation Groupings by Cancer Type (Mean and Bounds; Log Scale)



IRRs, Incidence Rate Ratios; HCS, Hereditary Cancer Syndromes.