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Cost-Effectiveness of a Multi-Cancer Early Detection (MCED) Test in Populations with Varying Cancer Risk

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Background and Objective

Main Objective:
To evaluate cost-effectiveness of MCED in elevated cancer risk subpopulations

- Blood-based multi-cancer early detection (MCED) tests can simultaneously screen for multiple types of cancers
- 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
  - An ICER of $66,043/QALY was estimated in the general population[1] (at $949 per MCED test)
- Prognostic factors can define a range of subpopulations with varying cancer incidence, which each cover a subset of cancer burden

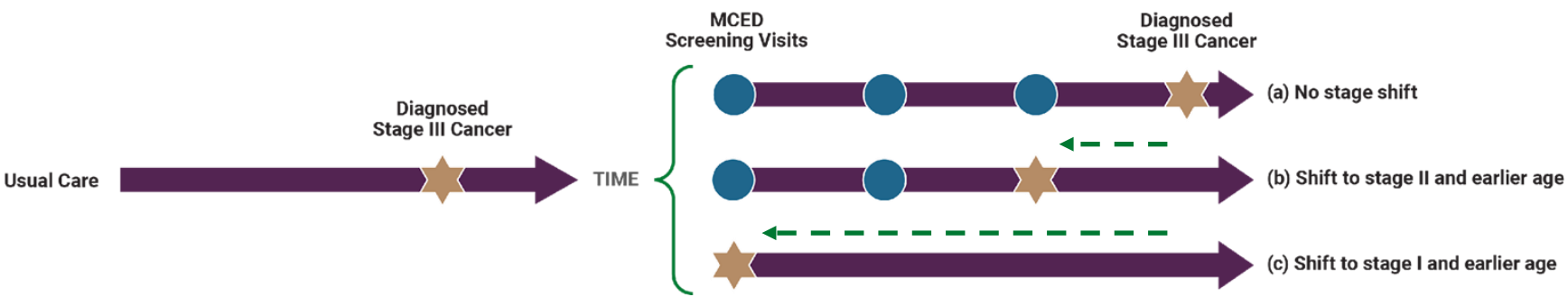
ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

[1] Kansal et al. Cost-effectiveness of a Multi-cancer Early Detection Test in the USA. *American Journal of Managed Care*, In Press.

Methods

- A hybrid model structure compared the outcomes of annual MCED testing plus SoC versus SoC alone in US adults aged 50 to 79 years, tailored for various high-risk groups
  - Cohort Markov: estimates the fraction of high-risk patients diagnosed with cancer
  - Decision-tree: estimates the long-term consequences of incident cancer
- The model tracked initial cancer diagnoses for 19 solid cancer groupings, representing >80% of cancer incidence

Overview of Stage and Time Shifting of Diagnosed Cancers due to MCED Testing



MCED, multi-cancer early detection; QoL, quality of life; SoC, standard of care.
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.[1]
[1] Hubbell E, et al. Cancer Epidemiol Biomarkers Prev. 2021;30(3):460-468.

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Key Model Inputs

- The cancer-specific incidence for each subgroup was identified from the literature by cancer type using a relative risk versus the general population
  - Surveillance Epidemiology and End Results (SEER) data informed incidence by age and stage at detection for the general population
- Competing mortality computed using a hazard ratio by subgroup as derived by data from the literature vs the general population
  - Age-specific competing mortality derived from US life tables for the general population
- MCED test performance was informed based on a case-control study[1] and test cost based on public price of Galleri® (Grail, Inc.)
  - Sensitivity varies by cancer and stage, while specificity is 99.5% for the test

MCED, multi-cancer early detection.

[1] Klein EA, et al. *Ann Oncol.* 2021;32(9):1167-1177.

Example High-Risk Subpopulation: Current smokers

- Subpopulations were defined by their **elevated cancer incidence** and **excess competing mortality rates** relative to the general population
  - Incidence rate ratio (IRR) by cancer type for current smokers[1]
  - Hazard ratio of competing mortality = 1.95[2]

Cancer Type	IRR
Lung and Bronchus	3.75
Colon and Rectum	1.33
Pancreas	1.52
Liver and Bile Duct	1.64
Breast: HR-negative	1
Esophagus	2.20
Head and Neck	2.81
Stomach	1.49
Ovarian	1
Kidney and Renal Pelvis	1.30
Prostate	1
Breast: HR-positive	1
Lymphoma	1
Anus	1
Uterus	1
Bladder	2.12
Cervix	1.48
Urothelial*	2.12
Other	1

*Assumed equal to bladder cancer.

[1] Islami F, et al. *CA Cancer J Clin*. 2018;68(1):31-54. [2] Carter BD, et al. *N Engl J Med*. 2015;372(7):631-40.

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Summary of Studied High-Risk Subpopulations

Subpopulation	Overall IRR*	Prevalence	Mortality Hazard Ratio
Immunocompromised SOT	2.90	0.06%	4.50
Cancer Survivor	1.69	10.7%	-
Current Smoker	1.57	11.6%	1.95
First-Degree Family History	1.38	55%	1.00
Ever Smoker	1.27	42.7%	1.41
Heavy Alcohol Use	1.26	9.4%	1.16
Obesity	1.14	38.7%	1.06
Diabetes	1.12	24.1%	1.42
Hereditary Cancer Syndromes	1.86	2.18%	1.00
HCS BRCA-like	1.86	1.54%	-
HCS ATM	1.34	0.40%	-
HCS Lynch	2.65	0.24%	-
HCS MUTYH	3.92	0.01%	-
HCS Other	3.76	0.002%	-

HCS, hereditary cancer syndrome; IRR, incidence rate ratio; SOT, single organ transplant.
*Versus the general population.
HCS patients assumed not received risk reducing surgery and without a prior history of cancer. ***BRCA-like***: *BARD1, BRCA1, BRCA2, BRIP1, RAD51C, RAD51D, CHEK2, PALB2 (double stranded DNA damage repair via homologous recombination);* ***ATM:*** *ATM (dsDNA damage sensor in homologous recombination);* ***Lynch:*** *EPCAM, MLH1, MSH2, MSH6, PMS2 (mismatch repair - Lynch Syndrome);* ***MUTYH:*** *MUTYH (base excision repair);* ***Other:*** *PTEN, STK11 (other tumor suppressors).*

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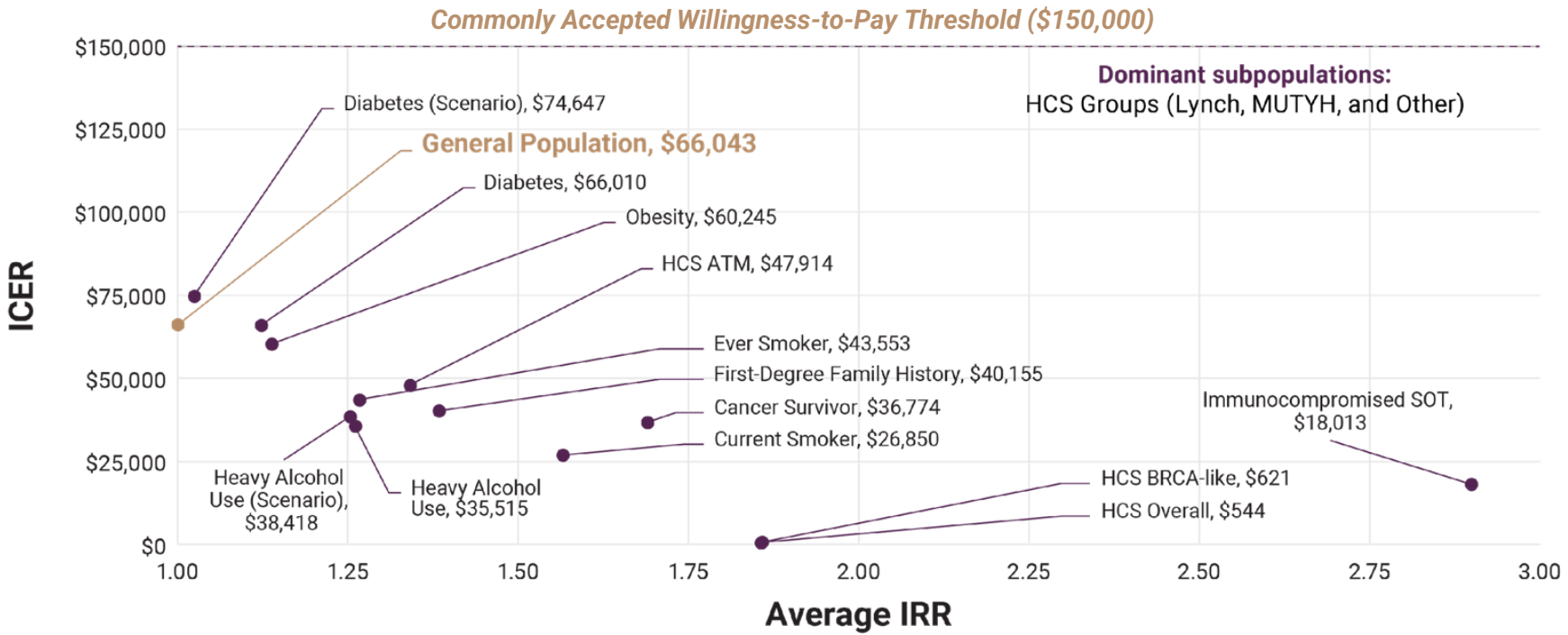
Estimated ICER vs. Incidence Rate Ratio



HCS, hereditary cancer syndrome; ICER, incremental cost-effectiveness ratio; IRR, incidence rate ratio; SOT, single organ transplant.

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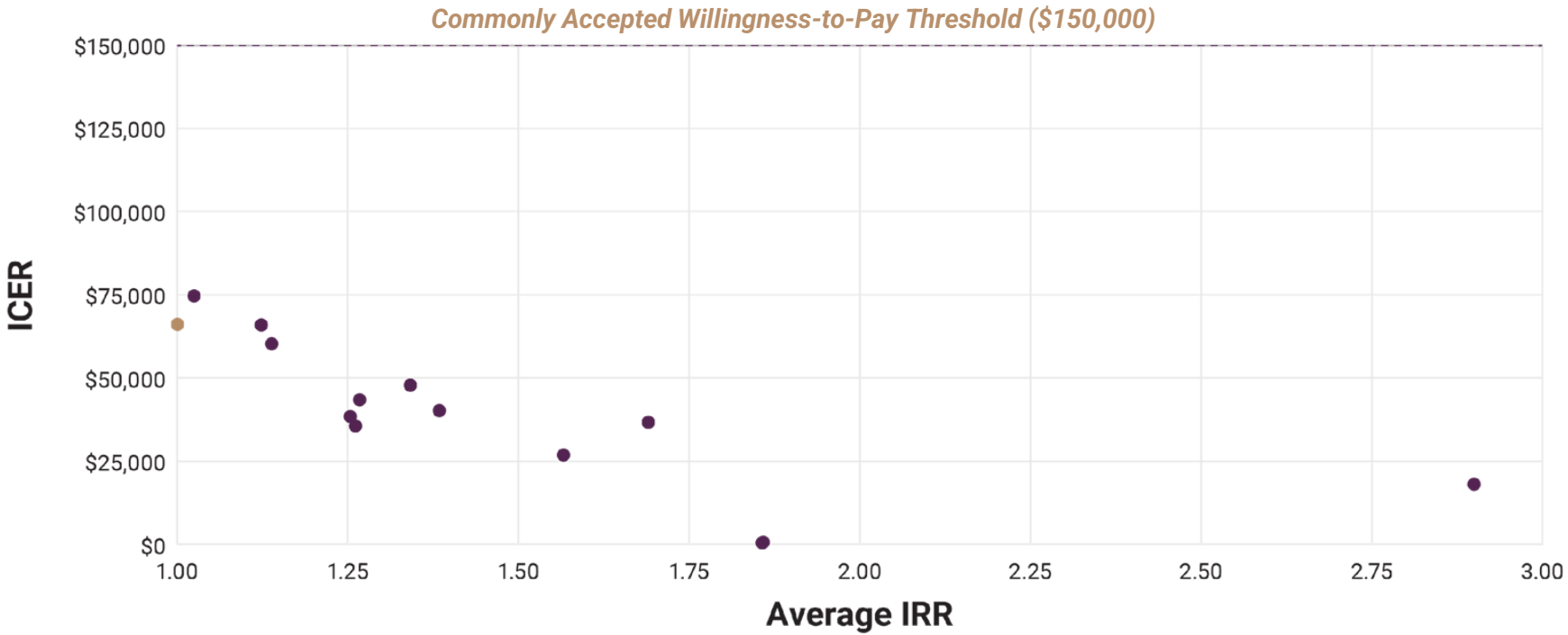

ICER, incremental cost-effectiveness ratio; IRR, incidence rate ratio.

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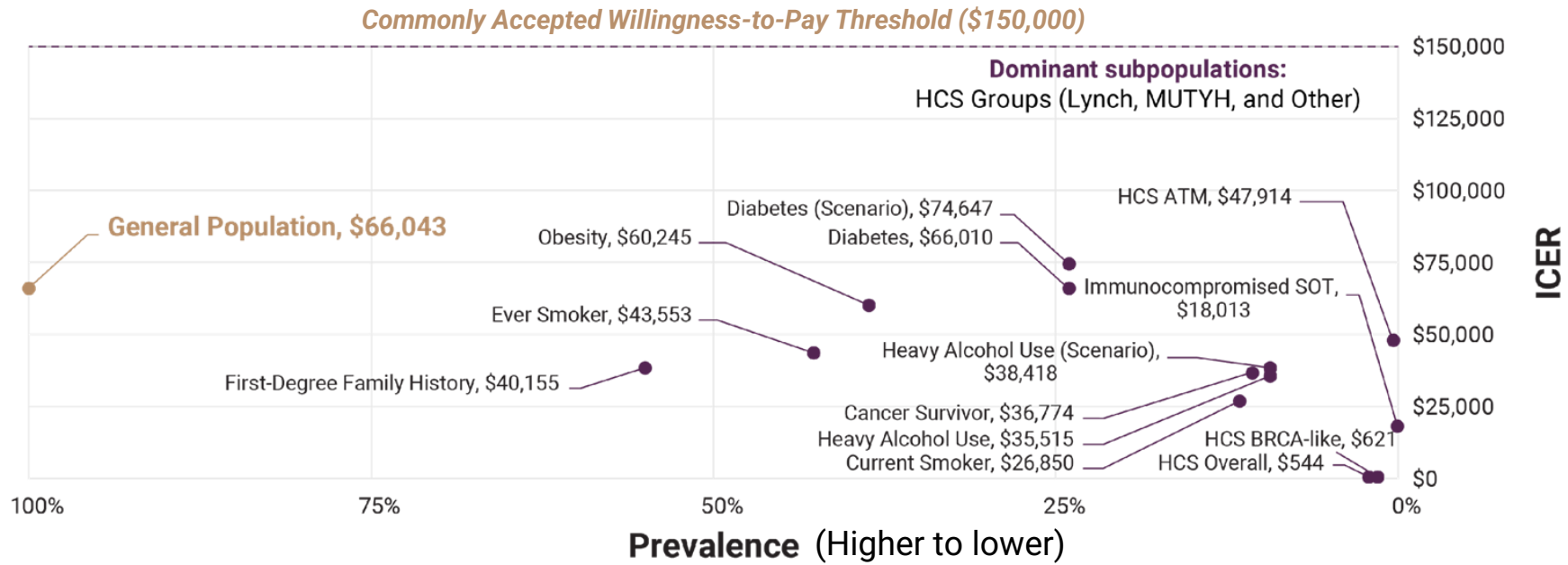
Estimated ICER vs. Subpopulation Prevalence

- Several high-prevalence subpopulations had ICERs <$50,000/QALY, while the lowest ICERs were predicted in smaller subpopulations



HCS, hereditary cancer syndrome; ICER, incremental cost-effectiveness ratio; MCED, multi-cancer early detection; QALY, quality-adjusted life year; SOT, single organ transplant.

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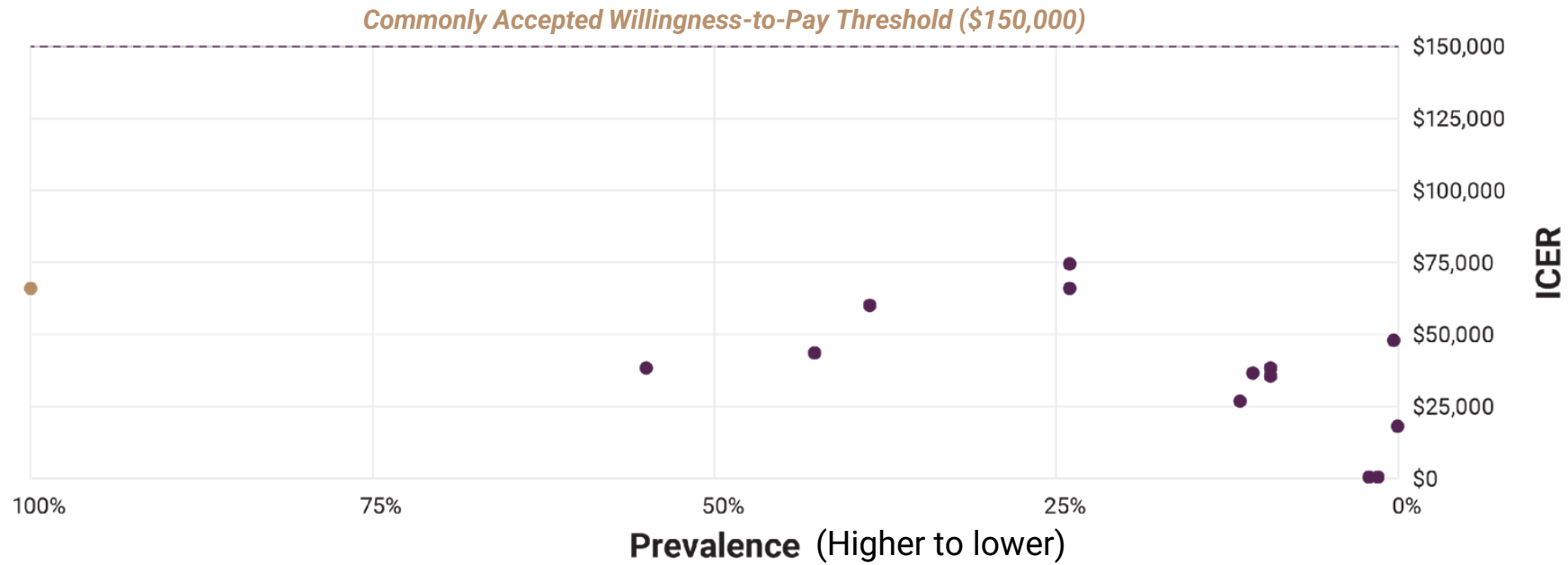

ICER, incremental cost-effectiveness ratio; MCED, multi-cancer early detection; QALY, quality-adjusted life year.

Discussion Points

While MCED testing has been projected to be cost-effective for the general population aged ≥50 years, higher cancer incidence is associated with even better cost-effectiveness

Prioritizing higher cancer risk groups allows targeting more favorable ICERs but at the cost of addressing a smaller fraction of the total population burden

ICER, incremental cost-effectiveness ratio; MCED, multi-cancer early detection.

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