

Cost-Effectiveness of Population Genomic Screening

What might screening adults for CDC Tier 1 conditions teach us about newborn screening?

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Financial Disclosures

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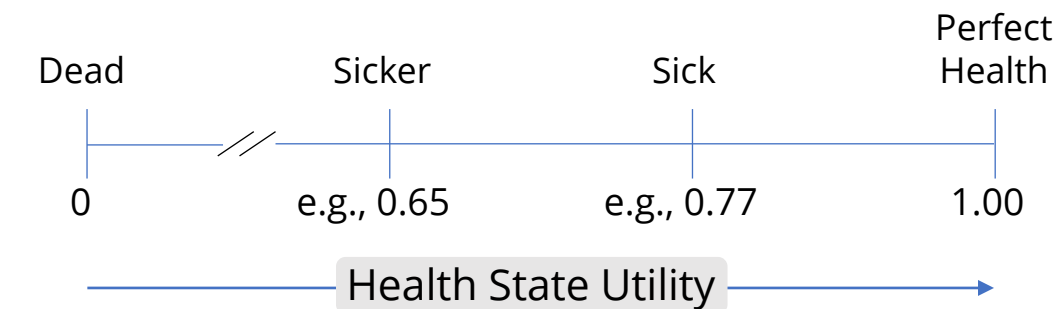
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Reimbursement for healthcare technologies

1. Increasing push for value in healthcare
2. Difficult to quantify, but established methods
3. Approaches are evolving to capture broader aspects of value
4. In the US, formal cost-effectiveness analyses do not directly influence reimbursement decisions, but provide context and inform discussions

Health Economic Modeling Primer

- Given limited health care budgets, choose the intervention that provides the most health per dollar spent.
- Modeling is used to synthesize clinical data with real world burden of disease outcomes (cost, quality of life) to estimate the lifetime costs and health impacts of a clinical decision.



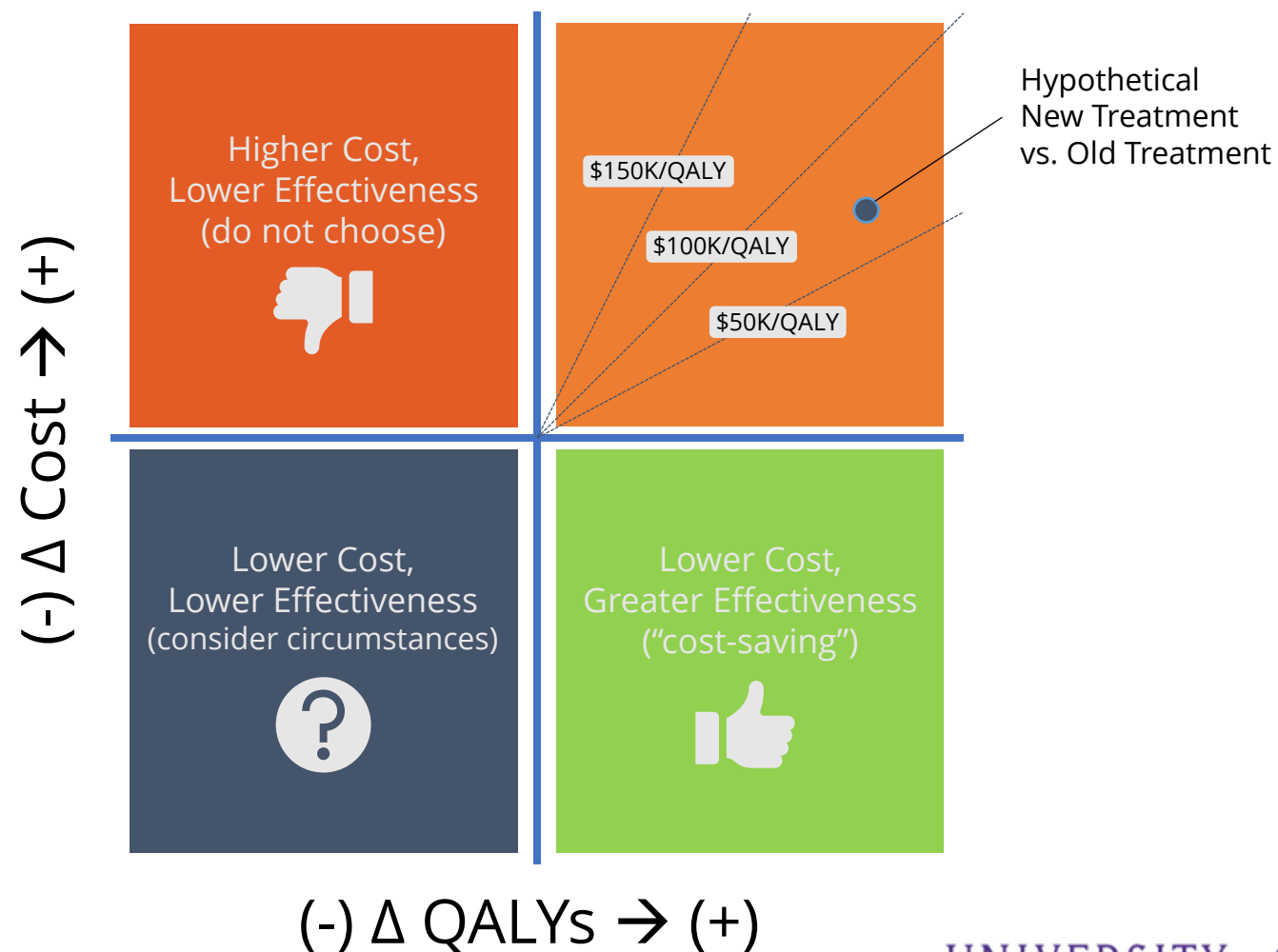
QALY=
Quality-Adjusted
Life Year

example: 3 sick years + 2 sicker years:
 $3 \times 0.77 + 2 \times 0.65 = 3.61$ QALYs

$$\text{Incremental Cost-Effectiveness Ratio (ICER)} = \frac{(\text{Cost}_{(\text{new Tx})} - \text{Cost}_{(\text{old Tx})})}{(\text{QALYs}_{(\text{new Tx})} - \text{QALYs}_{(\text{old Tx})})}$$

In the US, "acceptable" cost-effectiveness ratios $\approx$ **\$50K - \$150K**

Cost-Effectiveness



Cost-effectiveness of newborn screening

Universal Screening for Rare Newborn Genetic Conditions: Establishing Cost-Effectiveness Before Implementation

iHEA 2007 6th World Congress: Explorations in Health Economics Paper

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Cost-effectiveness of newborn **genomic** screening

LETTER TO THE EDITOR

Progress in expanding newborn screening in the United States

To the Editor: We read with interest the recent article by Kingsmore et al., who suggest that universal newborn rapid whole-genome sequencing is attractive for “comprehensive” newborn screening (NBS).¹ Existing US NBS programs are based on mandated routine testing of newborns; evidence-based decision-making processes exist for this testing.² Whether policy makers also consider routine rapid whole-genome sequencing of newborns to be warranted may depend on the resolution of a number of evidentiary, ethical, legal, social, and economic

The authors cite two sources of information for this statement: a 2020 publication by Sontag et al.⁶ that was the product of a collaboration between CDC and NewSTEPs, a program of the Association of Public Health Laboratories, and a 2008 CDC publication.⁷ Sontag et al. used state-based prevalence data from 2015 to 2017 to derive a minimum estimate of the total number of infants with RUSP core conditions expected to be detected through screening of DBS specimens in 2018, i.e., 6,646 infants. Additionally, Sontag et al. cited a model-based prevalence estimate of 6,439 infants detected with RUSP conditions through DBS testing in 2006.⁷

First, we wish to clarify that the RUSP is not restricted to conditions that are screened on the basis of DBS specimens. Currently, the RUSP includes two conditions that

Cost-effectiveness of newborn genomic screening

Universal newborn genetic screening for pediatric cancer predisposition syndromes: model-based insights

Jennifer M. Yeh ^{1,2}✉, Natasha K. Stout^{1,3}, Aeysha Chaudhry², Kurt D. Christensen^{1,3}, Michael Gooch³, Pamela M. McMahon³, Grace O'Brien², Narmeen Rehman³, Carrie L. Blout Zawatsky⁴, Robert C. Green^{1,4}, Christine Y. Lu^{1,3}, Heidi L. Rehm^{1,5}, Marc S. Williams⁶, Lisa Diller^{1,7,8} and Ann Chen Wu^{1,3,8}

PURPOSE: Genetic testing for pediatric cancer predisposition syndromes (CPS) could augment newborn screening programs, but with uncertain benefits and costs.

METHODS: We developed a simulation model to evaluate universal screening for a CPS panel. Cohorts of US newborns were simulated under universal screening versus usual care. Using data from clinical studies, ClinVar, and gnomAD, the presence of pathogenic/likely pathogenic (P/LP) variants in *RET*, *RB1*, *TP53*, *DICER1*, *SUFU*, *PTCH1*, *SMARCB1*, *WT1*, *APC*, *ALK*, and *PHOX2B* were assigned at birth. Newborns with identified variants underwent guideline surveillance. Survival benefit was modeled via reductions in advanced disease, cancer deaths, and treatment-related late mortality, assuming 100% adherence.

RESULTS: Among 3.7 million newborns, under usual care, 1,803 developed a CPS malignancy before age 20. With universal screening, 13.3% were identified at birth as at-risk due to P/LP variant detection and underwent surveillance, resulting in a 53.5% decrease in cancer deaths in P/LP heterozygotes and a 7.8% decrease among the entire cohort before age 20. Given a test cost of \$55, universal screening cost \$244,860 per life-year gained; with a \$20 test, the cost fell to \$99,430 per life-year gained.

CONCLUSION: Population-based genetic testing of newborns may reduce mortality associated with pediatric cancers and could be cost-effective as sequencing costs decline.

Genetics in Medicine (2021) 23:1366–1371; <https://doi.org/10.1038/s41436-021-01124-x>

We (should) screen adults, don't we?

CDC Tier 1 Conditions

Tier 1 Condition	Increased Risk For:	Risk-Reduction
Hereditary Breast and Ovarian Cancer	Breast cancer, Ovarian cancer, Other cancers	Mammography + <u>MRI</u> , Mastectomy, Salpingo-Oophorectomy
Lynch Syndrome	Colorectal cancer, Endometrial cancer, Other cancers	Increased colonoscopy surveillance
Familial hypercholesterolemia	Myocardial infarction, Stroke	Moderate to high-intensity statin therapy

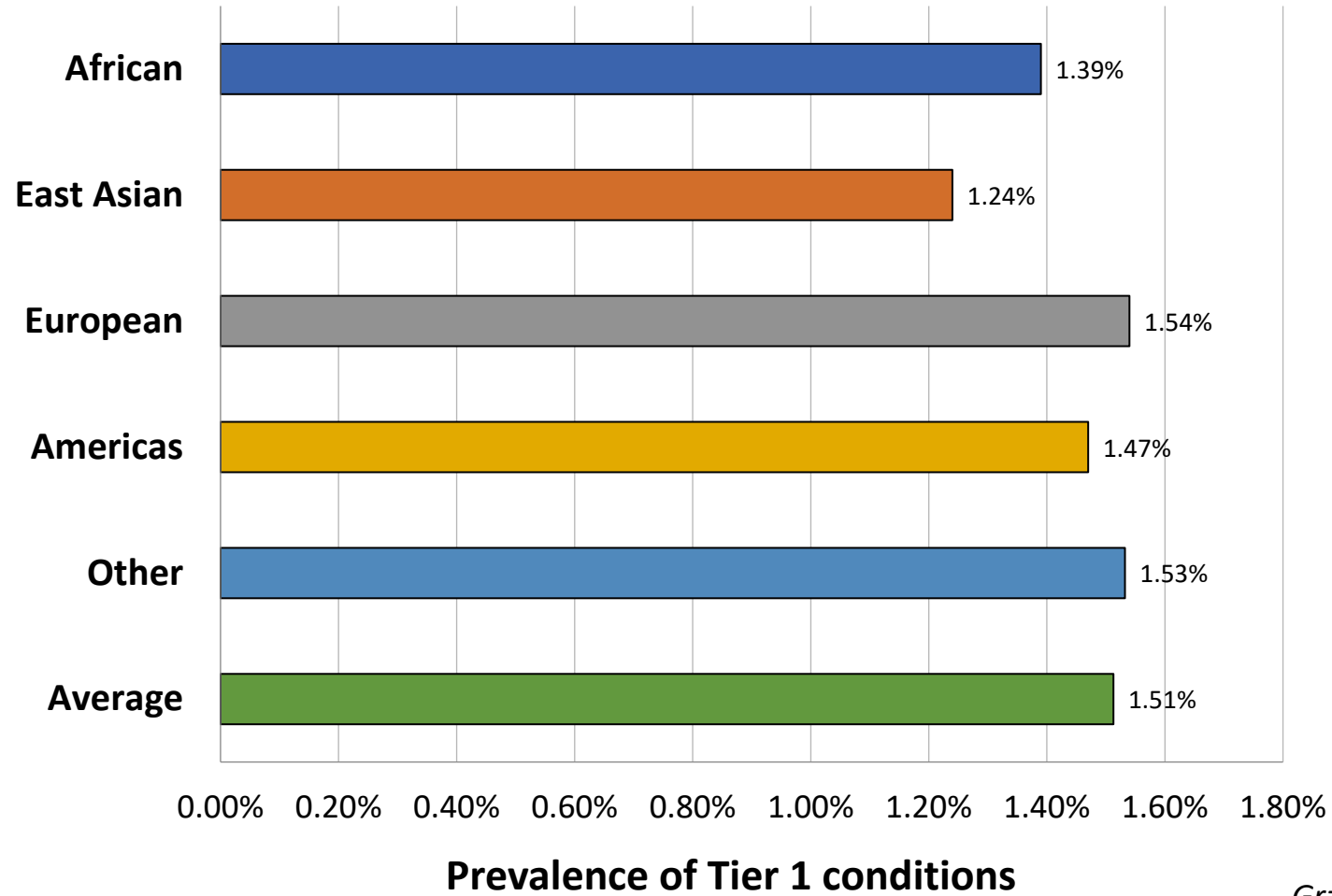


Centers for Disease Control and Prevention

CDC 24/7: Saving Lives, Protecting People™

<https://www.cdc.gov/genomics/implementation/toolkit/tier1.htm>

Prevalence across ancestries

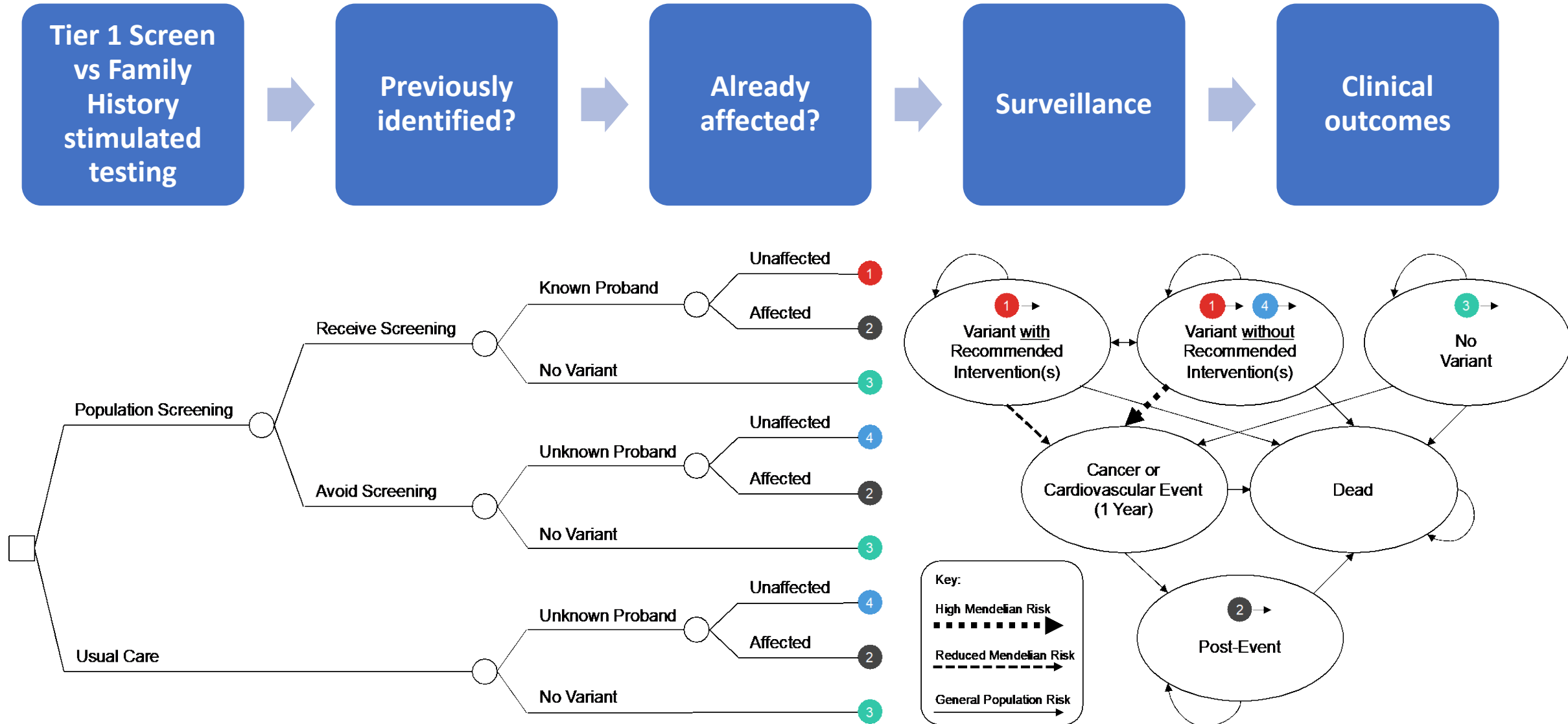


Grzymiski, unpublished data Dec 2022.

Selected Assumptions

Parameter	Value
Targeted Next Generation Sequencing (NGS)	\$250
Sanger confirmation	\$250
Genetic Counseling	
Efficacy of family history stimulated testing for HBOC	17%
Adherence to Surveillance	75%
Efficacy of cascade testing	14%

Tier 1 Model Features



Individual model results

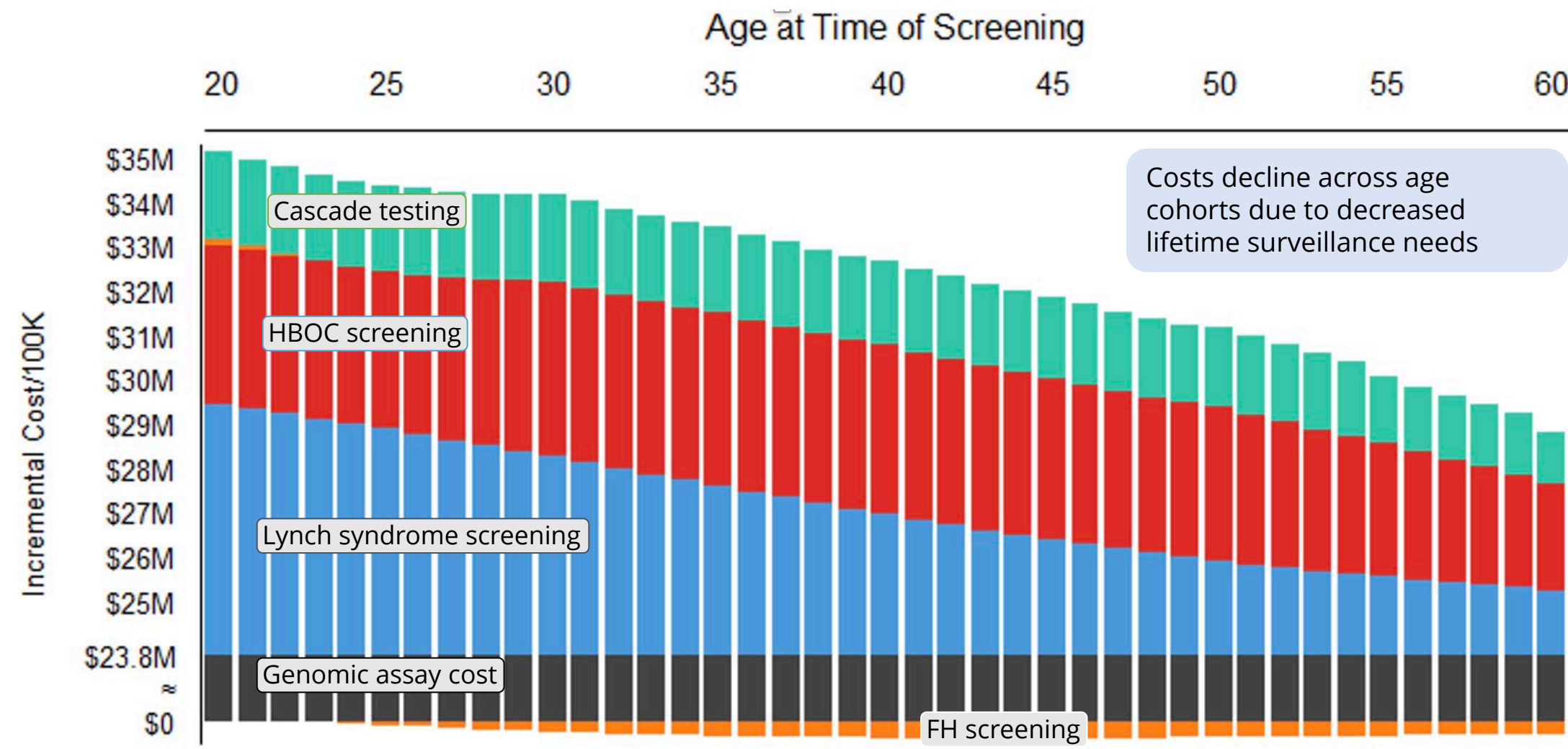
✓ cost-effective
✗ not cost-effective

Model	30 years old	50 years old
HBOC*	\$87,700/QALY ✓	\$482,100/QALY ✗
LS	\$132,200/QALY ✗	\$140,400/QALY ✗
FH	\$206,700/QALY ✗	\$463,500/QALY ✗

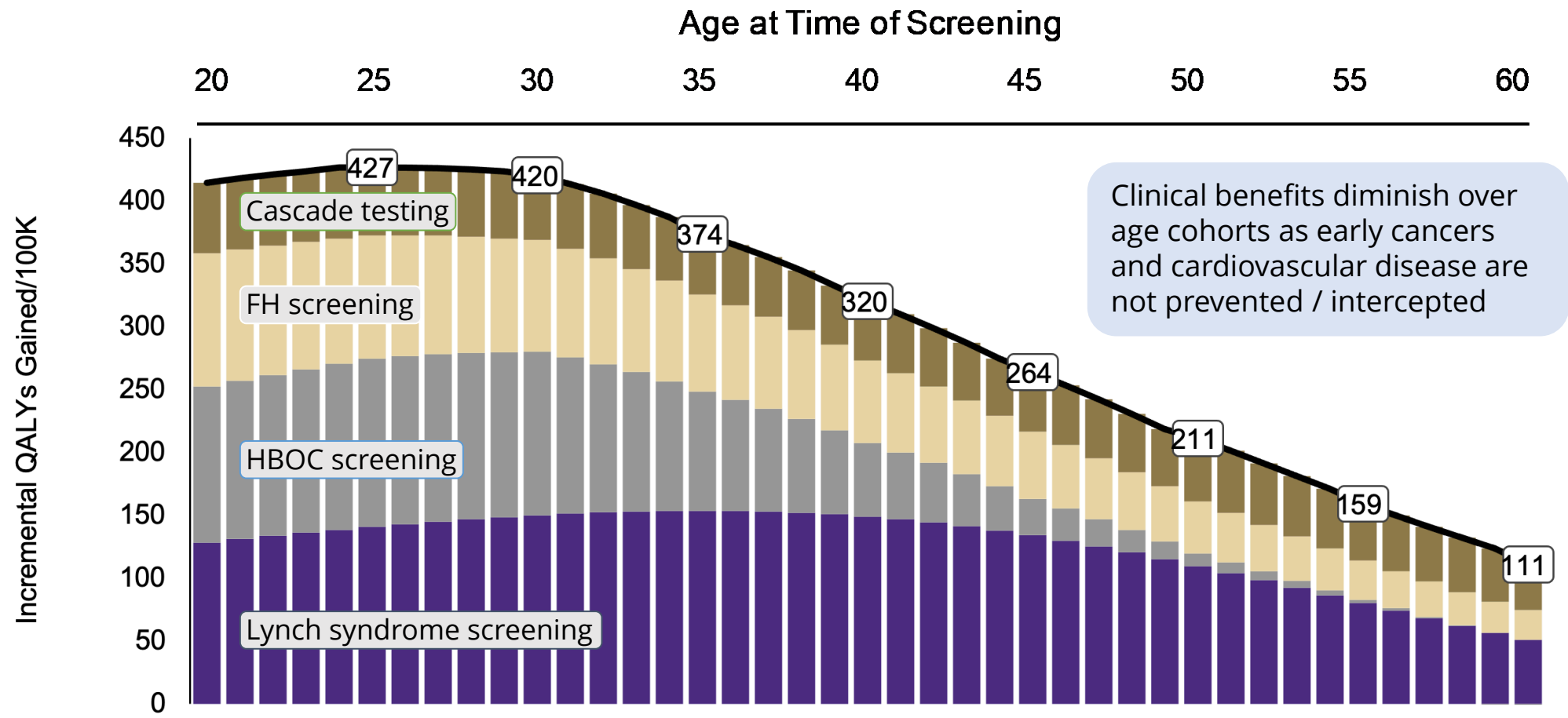
*females

Combined results:

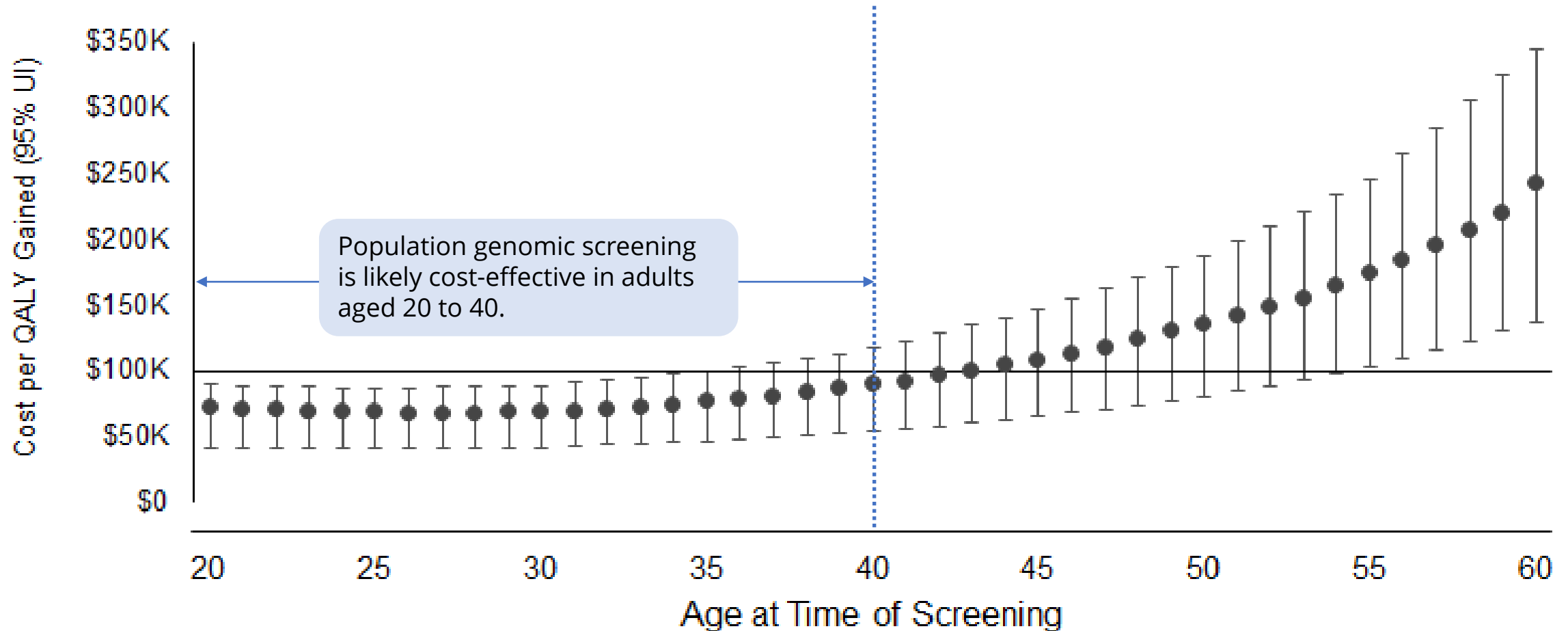
Incremental cost per 100,000 screened



Combined results: Incremental QALYs per 100,000 screened



Cost effectiveness



Implication #1

Prevalence drives economic value

- Include the most prevalent conditions
- Combine conditions

Implication #2

Clinical action is required for 'traditional' economic value

- Focus on clinical actionability for building value story and driving reimbursement

Implication #3

Screening should be efficient and relatively inexpensive

- Public or private sector reimbursement?
- Delivery and education

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