Cost-Effectiveness of Population Genomic Screening

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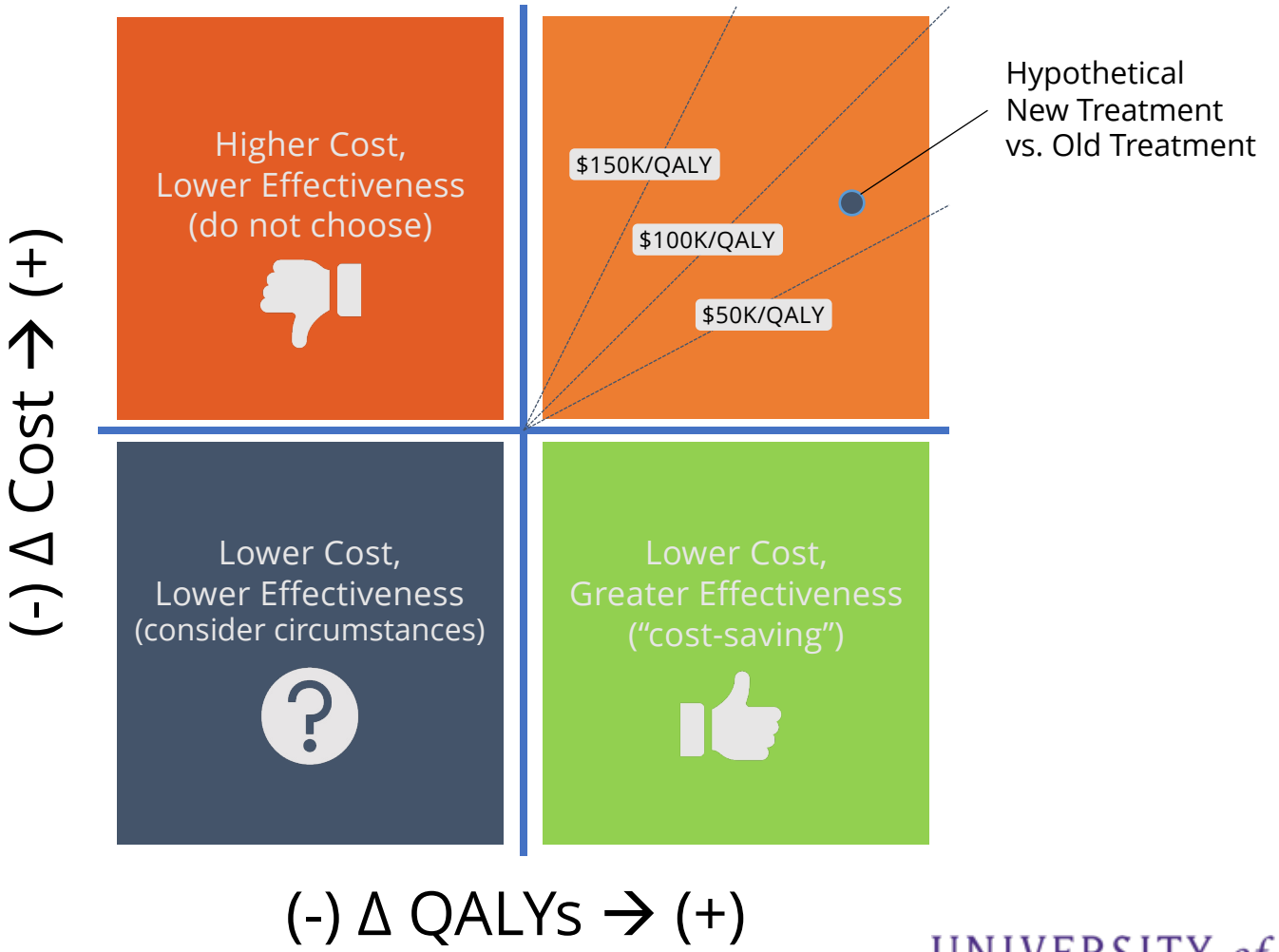
Reimbursement for healthcare technologies

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

Cost-Effectiveness



Annals of Internal Medicine

ORIGINAL RESEARCH

Population Genomic Screening for Three Common Hereditary Conditions

A Cost-Effectiveness Analysis

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CDC Tier 1 Conditions

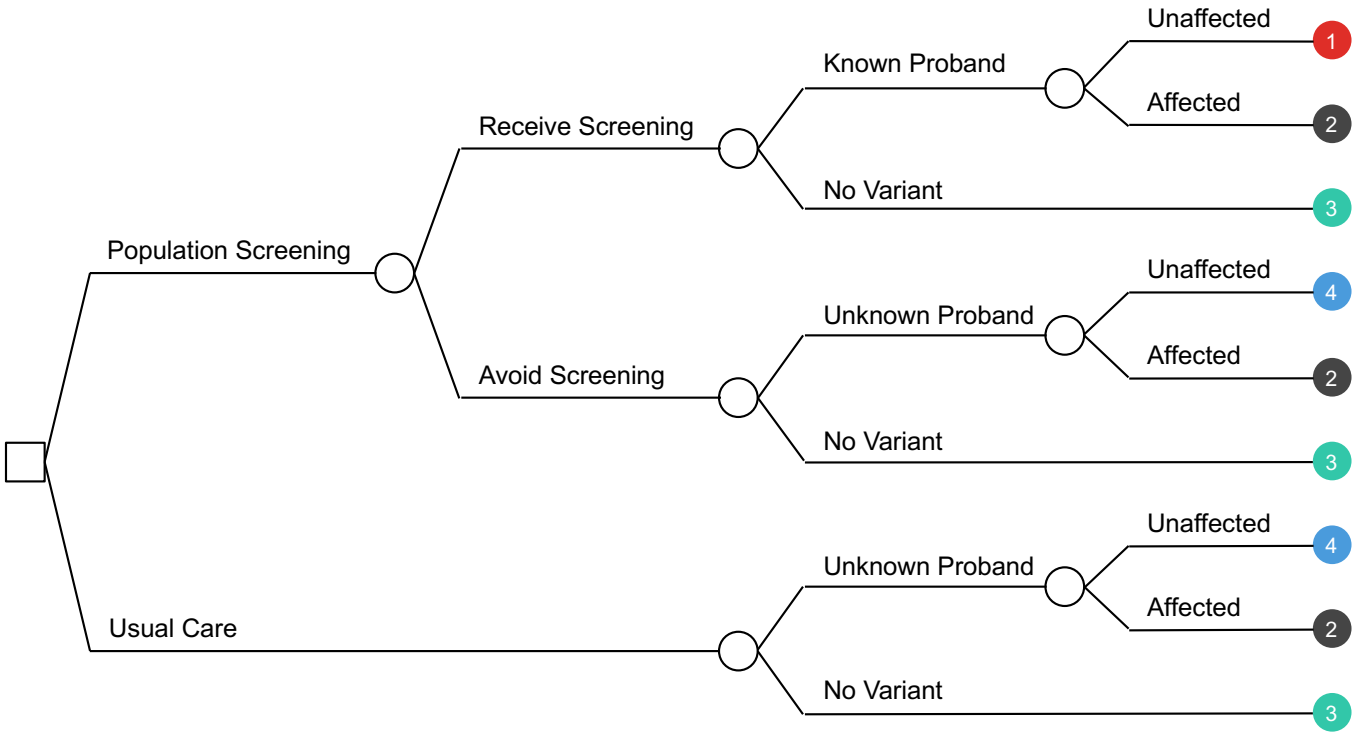
Tier 1 Condition	Increased Risk For:	Risk-Reduction
Hereditary Breast and Ovarian Cancer	**Breast cancer, Ovarian cancer,** Other cancers	Mammography + MRI, Mastectomy, Salpingo-Oophorectomy
Lynch Syndrome	**Colorectal cancer,** Endometrial cancer, Other cancers	Increased colonoscopy surveillance
Familial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

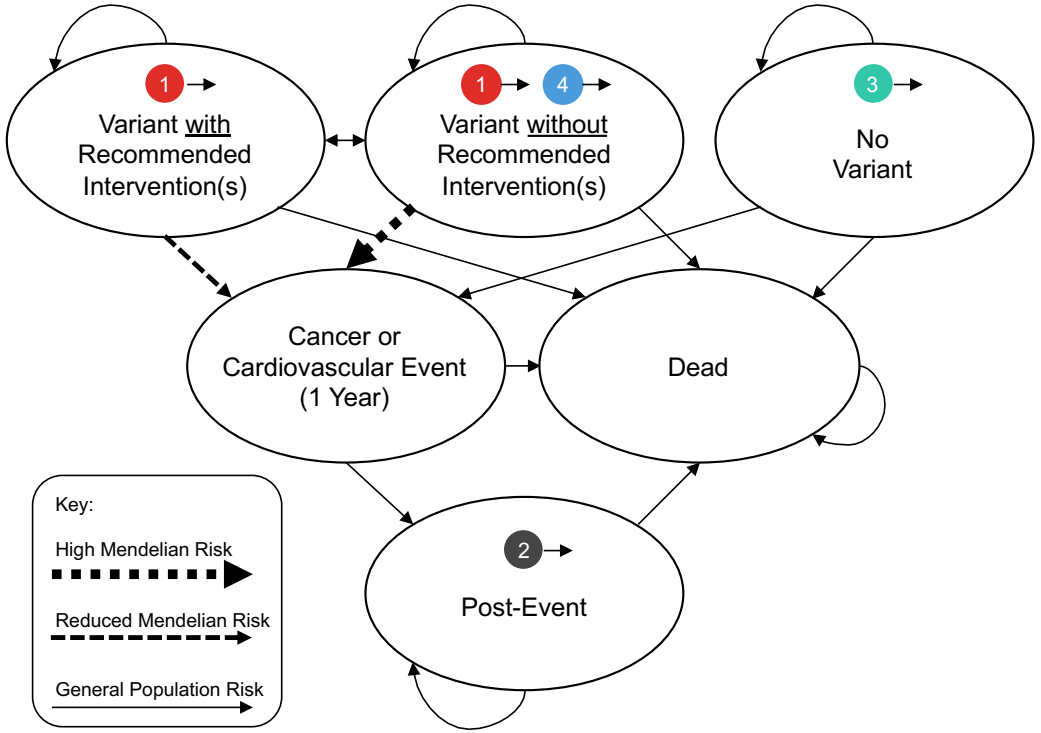
Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

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

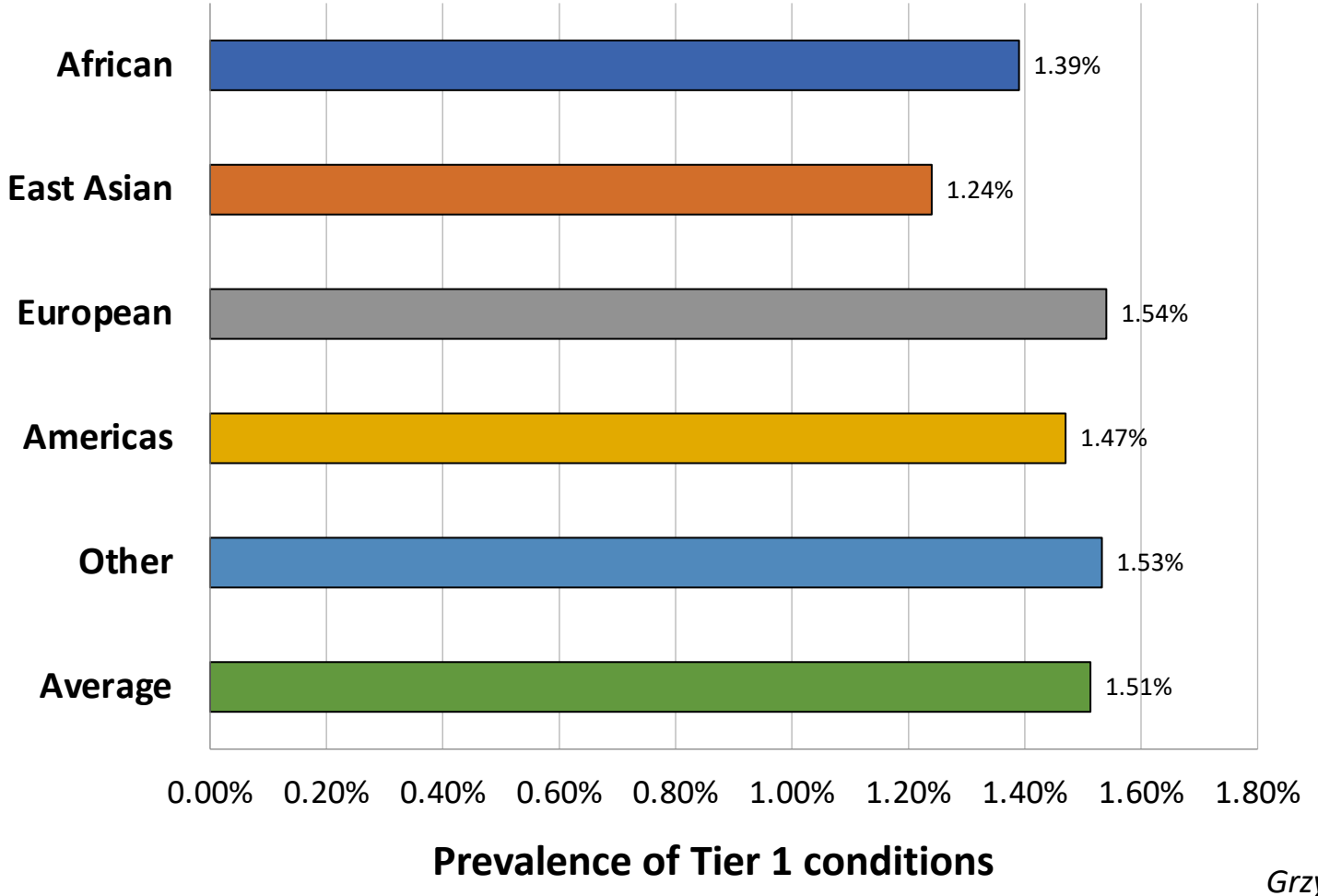
Tier 1 Model Features

Tier 1 Screen vs Family History stimulated testing → **Previously identified?** → **Already affected?** → **Surveillance** → **Clinical outcomes**





Inputs: Prevalence across ancestries



Grzymski, unpublished data Dec 2022.

Inputs: Costs

Parameter	Value
Targeted Next Generation Sequencing (NGS)	$250
Sanger confirmation	$250
Genetic Counseling	

Inputs: uptake of recommended interventions

Risk-reducing intervention uptake	
HBOC	
Relative mortality reduction: early- vs. late-stage breast cancer	0.94
Cumulative mastectomy by age 30 y, %	15
Cumulative mastectomy by age 40 y, %	30
Cumulative mastectomy by age 50 y, %	36
Cumulative mastectomy by age 60 y, %	36
Cumulative salpingo-oophorectomy by age 30 y, %	8
Cumulative salpingo-oophorectomy by age 40 y, %	48
Cumulative salpingo-oophorectomy by age 50 y, %	68
Cumulative salpingo-oophorectomy by age 60 y, %	74
LS	
Increased colonoscopy surveillance, ages 20–75 y, %	80
FH	
Proportion of tested persons who take statins, %	60

Cascade testing	
Proportion of persons who inform their family members	0.70
Proportion of family members who get tested	0.20
Proportion of family members with variants	0.50

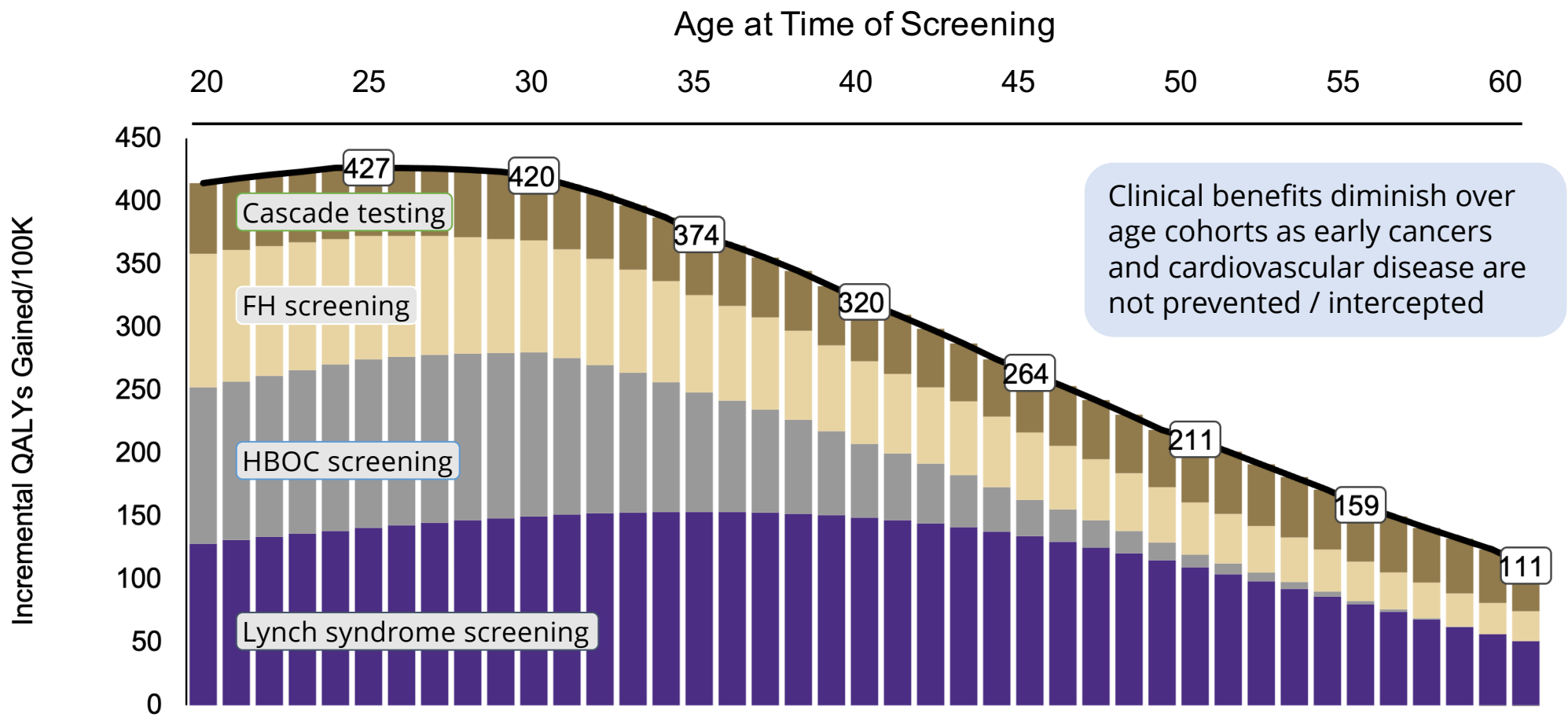
Individual model results

✓ Potentially 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 ✗

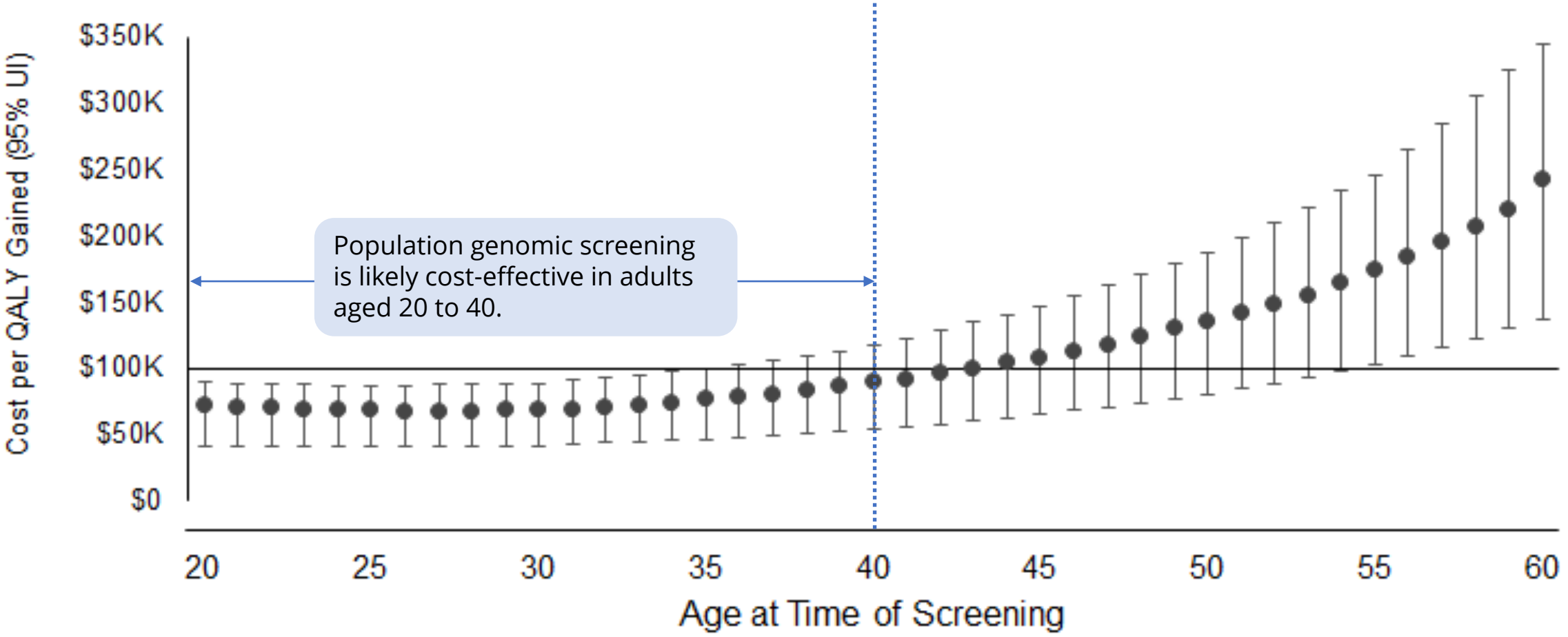
*females

Combined results:
Incremental QALYs per 100,000 screened



Guzauskas et al, Annals Int Med, May 2023

Cost effectiveness



Guzauskas et al, Annals Int Med, May 2023

But what if…

Table 3. Base-Case and Scenario Analysis Results

Scenarios for Screened 30-Year-Old Persons	Scenario Inputs					Results per 100 000 30-Year-Old Persons			
	Assay Cost, $	Follow-up Multiplier	Cascade Testing Uptake, %*	Prior Knowledge of Variant, %†	Total Variant Proportion, %‡	Incremental Cost (95% UI), $ *(millions)*	Incremental QALYs (95% UI)	ICER (95% UI), *$/QALY*	Cost-Effectiveness Probability, %§
Main (base-case) analysis	250	1	14	9	1.5	33.9 (27.0–41.1)	495 (401–757)	68 600 (41 800–88 900)	99.4
Societal perspective	250	1	14	9	1.5	25.6 (16.4–40.3)	495 (401–757)	51 700 (24 200–106 200)	99.9
Lower genetic assay cost	100	1	14	9	1.5	19.6 (15.1–24.4)	495 (401–757)	39 700 (23 500–51 800)	100
Higher genetic assay cost	500	1	14	9	1.5	57.8 (45.3–70.7)	495 (401–757)	116 800 (71 200–154 000)	44
Lower adherence to follow-up	250	0.5	14	9	1.5	31.2 (24.9–37.7)	292 (228–436)	106 800 (66 700–141 700)	57
Higher adherence to follow-up	250	1.2	14	9	1.5	35.0 (28.0–42.1)	570 (461–883)	61 400 (37 000–77 900)	100
Without cascade testing	250	1	0	9	1.5	32.0 (25.2–39.0)	436 (347–692)	73 300 (42 000–96 100)	98
Higher uptake of cascade testing	250	1	35	9	1.5	36.9 (29.3–44.7)	582 (478–865)	63 400 (41 100–79 700)	100
Low prior knowledge	250	1	14	7	1.5	34.5 (27.1–41.7)	512 (413–780)	67 400 (40 700–88 000)	99.4
High prior knowledge	250	1	14	11	1.5	33.4 (26.1–40.4)	477 (386–739)	69 900 (41 300–93 000)	98.9
Low variant prevalence	250	1	14	9	1.1	31.4 (24.6–37.9)	371 (303–576)	84 600 (50 800–108 100)	93
High variant prevalence	250	1	14	9	2.0	36.5 (29.1–44.2)	618 (501–945)	59 000 (35 900–75 400)	100

False reassurance

Potential Harm Related to False Reassurance

Under the assumption that 10% of 30-year-olds without a variant subsequently avoid routine disease screening because of receipt of a negative genomic screening result, a loss of 0.05 QALY in this population would lead to genomic screening having no incremental health benefit.

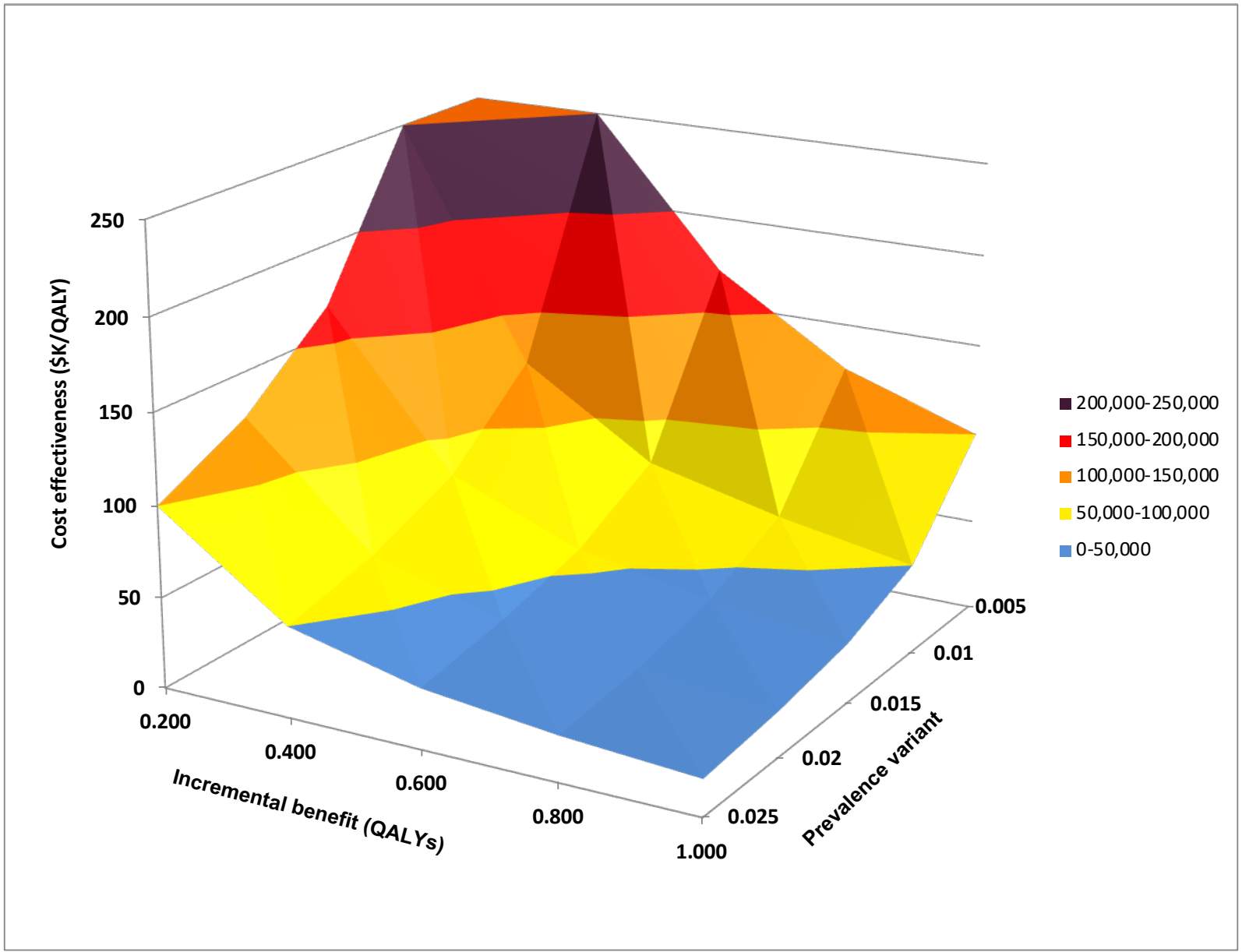
Polygenic risk scores – economic value of population screening?

- Prevalence of ‘high-risk’ is greater than monogenic conditions
- Lifetime risk lower
- Multiple conditions

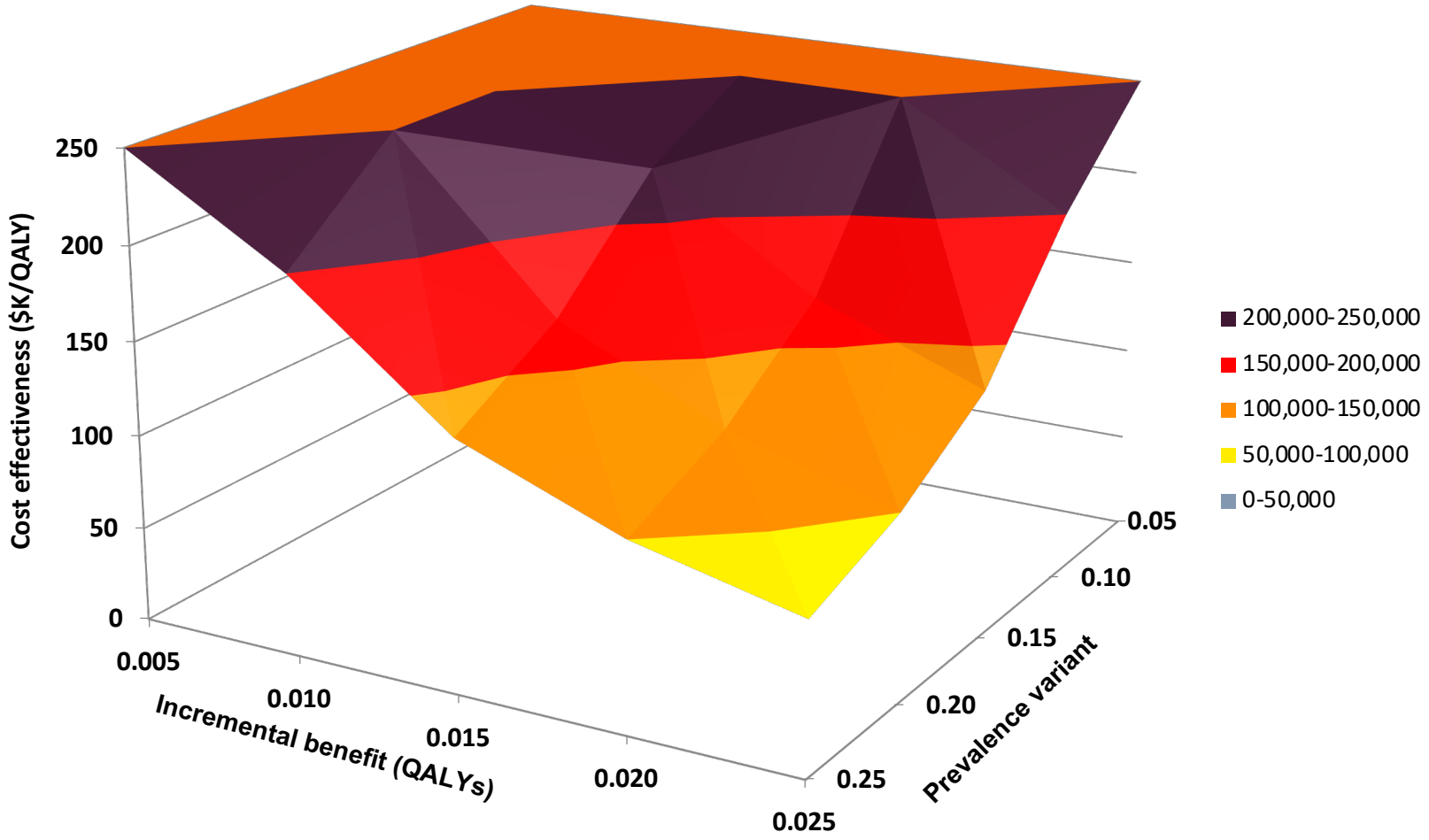
PRS vs. Tier-1

- Prevalence ~10-20x higher
- Effect size ~20-30x lower(!)
- PRS: Prevalence ~20%, Benefit ~0.03 QALYs
- Cost effectiveness likely above threshold of $100K/QALY (not cost effective)

Tier-1 cost-effectiveness ‘landscape’



PRS cost-effectiveness ‘landscape’



Newborn screening

- Large number of rare conditions
- Actionability variable
- Different policy context

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

Clinical actions – eMERGE consortium

Implication #3

Screening should be efficient and relatively inexpensive

- Public or private sector reimbursement?
- Delivery and education

Summary

- Population screening for CDC Tier-1 conditions provides an excellent model for population genomic screening
- CDC Tier-1 screening likely has beneficial risk-benefit profile and provides good economic value, but:
  - Need further clarity on behavior of those with and without a variant
  - Evidence on all aspects in underserved populations, diverse ancestries
  - Implementation outcomes
- Combining conditions is essential for economic value, but restricting to those with good clinical or patient-centered value is critical
- Genomic population screening applications will vary dramatically in their economic value and evidence requirements

Acknowledgements

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