Integrating Genomic Programs into the Health System at Kaiser Permanente NW

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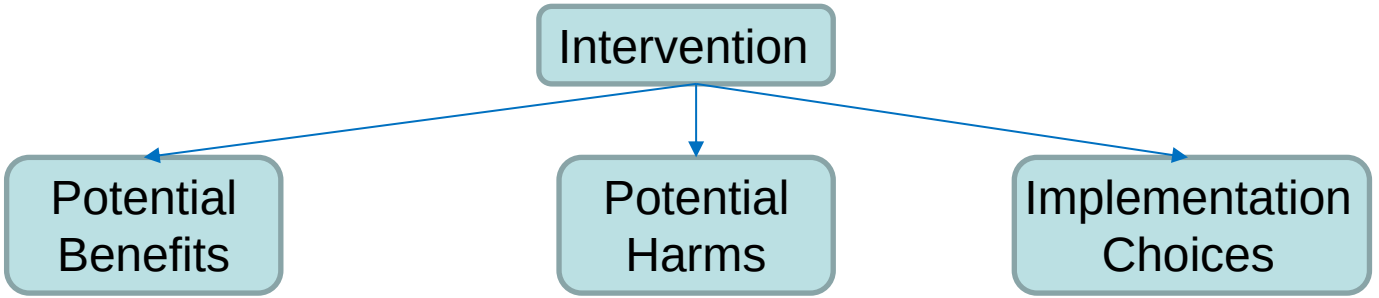
Example Studies from Kaiser Permanente NW

Study	Study Description
NCI/Lynch Syndrome Screening	Implement universal tumor screening among CRC patients. Evaluate patient management.
NHGRI/ CSER NextGen	Exploratory research on expanded preconception carrier screening using genome sequencing.
NHGRI/ ClinGen	Actionability Work Group – evidence synthesis and assessment of clinical actionability in the clinical context of adults with secondary findings.

How does the research inform the program?



Lynch Syndrome Screening: Did the intervention result in a change in care management?

Procedure	Eligible N	Recom-mended N	Observed N	Patient Adherence N (% of observed)				Average Intervals M ± SD
				0%	1-49%	50-99%	100%	
Colonoscopy	73	68	64	6 (9)	1 (2)	14 (22)	43 (67)	2.4 ± 2.0
Endoscopy	73	48	28	5 (18)	1 (4)	6 (21)	16 (57)	1.7 ± 1.0
Genet. Couns.	73	49	40	1 (5)	9 (23)	9 (23)	21 (53)	3.3 ± 3.2
Urinalysis	73	45	45	7 (16)	8 (18)	17 (38)	13 (29)	3.5 ± 2.0
Ab. Ultrasound	73	9	8	2 (25)	1 (13)	3 (38)	2 (25)	6.6 ± 3.8
TVUS	27	10	10	6 (60)	3 (30)	1 (10)	0 (0)	5.4 ± 3.3
Endom. Biopsy	25	9	8	1 (13)	4 (50)	3 (38)	0 (0)	6 ± 3.4
CA-125	27	10	10	1 (10)	4 (40)	4 (40)	1 (10)	5.1 ± 2.3

NextGen: Was there a misunderstanding of negative preconception carrier screening results?

NextGen
Understanding the impact of genome sequencing for reproductive decisions

cser
Clinical Sequencing Exploratory Research

Did women with negative carrier results use additional services following sequencing?*

Procedure	GS arm (N=100)	UC arm (N=163)	P-value
F2F Encounters			
Total	10.3 (9.3)	10.6 (10.3)	0.82
Primary Care	5.9 (6.0)	5.6 (5.8)	0.75
Mental Health	1.0 (2.9)	1.2 (3.5)	0.75
Telephone encounters	6.6 (6.0)	6.9 (7.7)	0.72
Email encounters	6.7 (7.7)	7.5 (8.8)	0.75
Mental Health Med. Use	22%	21%	0.92

GS=genome sequencing; UC=usual care
*Services are reported as the mean (standard deviation) number of encounters. We also evaluated median number of encounters (not shown).

Did women with negative carrier results decline recommended care during subsequent pregnancy?

Procedure	GS arm (N=28)	UC arm (N=45)	P-value
Ultrasound	3.4 (1.5)*	3.4 (2.7)*	0.83
Amniocentesis	0%	0%	NA
NIPT	35.7%	31.1%	0.73
Quad Screen	39.3%	44.4%	0.86
Refusals**	14.3%	6.7%	0.39
Other genetic testing	7.1%	11.1%	0.70

GS=genome sequencing; UC=usual care
*number of ultrasounds (standard deviation)
**EMR documentation of refusing a pregnancy related service that was offered to them by their provider

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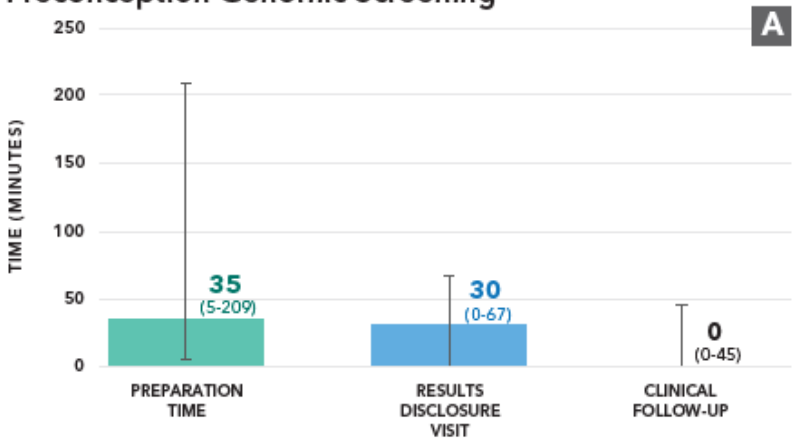
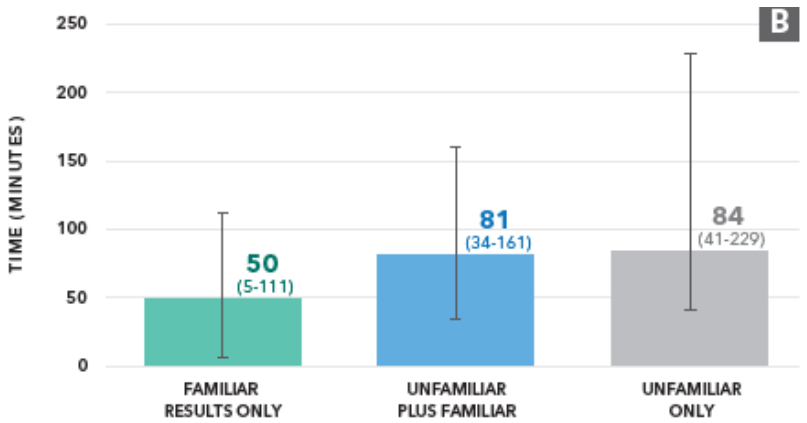
Time Costs to Disclose Genomic Information

FIGURE 1. Time for Results Disclosure Activities for Preconception Genomic Screening

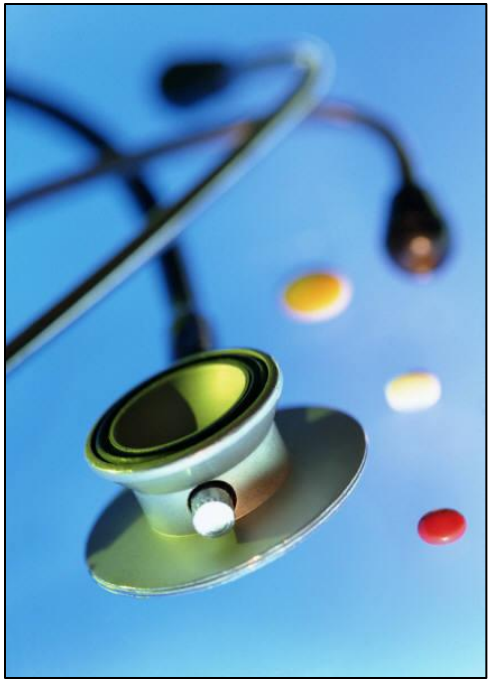


Total Time



We defined "unfamiliar" as a result that was not previously disclosed to another study participant, or not routinely encountered in clinical practice.

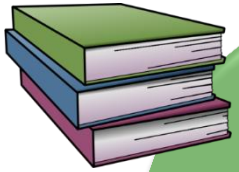
Clinical Actionability



- Well-established, clinically prescribed interventions
- Specific to the genetic disorder under consideration
- Lead to disease prevention or delayed onset, lowered clinical burden, or improved clinical outcomes

Knowledge Synthesis Team

Actionability Working Group



Qualitative Evidence Synthesis

Semi-Quantitative Metric

- Standardized search protocol
- Reproducible across curators
- Limited in scope
- Feasible for many genes

- Generate consensus score
- Quantify actionability
- Compare across genes
- Prioritize return of findings

Scoring Domains of Clinical Actionability

Gene → Disease → Outcome → Intervention

[Example: *BRCA1* → HBOC → Breast Cancer → Mammography]

DOMAIN		SCORING METRIC
OUTCOME	SEVERITY	3 = Sudden death 2 = Death or major morbidity 1 = Modest morbidity 0 = Minimal or no morbidity
OUTCOME	LIKELIHOOD*	3 = > 40% chance 2 = 5-39% chance 1 = 1-4% chance 0 = < 1% chance

DOMAIN		SCORING METRIC
INTERVENTION	EFFECTIVENESS*	3 = Highly effective 2 = Moderately effective 1 = Minimally effective 0 = Controversial/Unknown IN = Ineffective/No intervention
INTERVENTION	NATURE OF INTERVENTION	3 = Low risk and intensity, highly acceptable 2 = Moderate risk, intensity, acceptable 1 = Greater risk and intensity, less acceptable 0 = High risk and intensity, poorly acceptable

*Assess Knowledge Base

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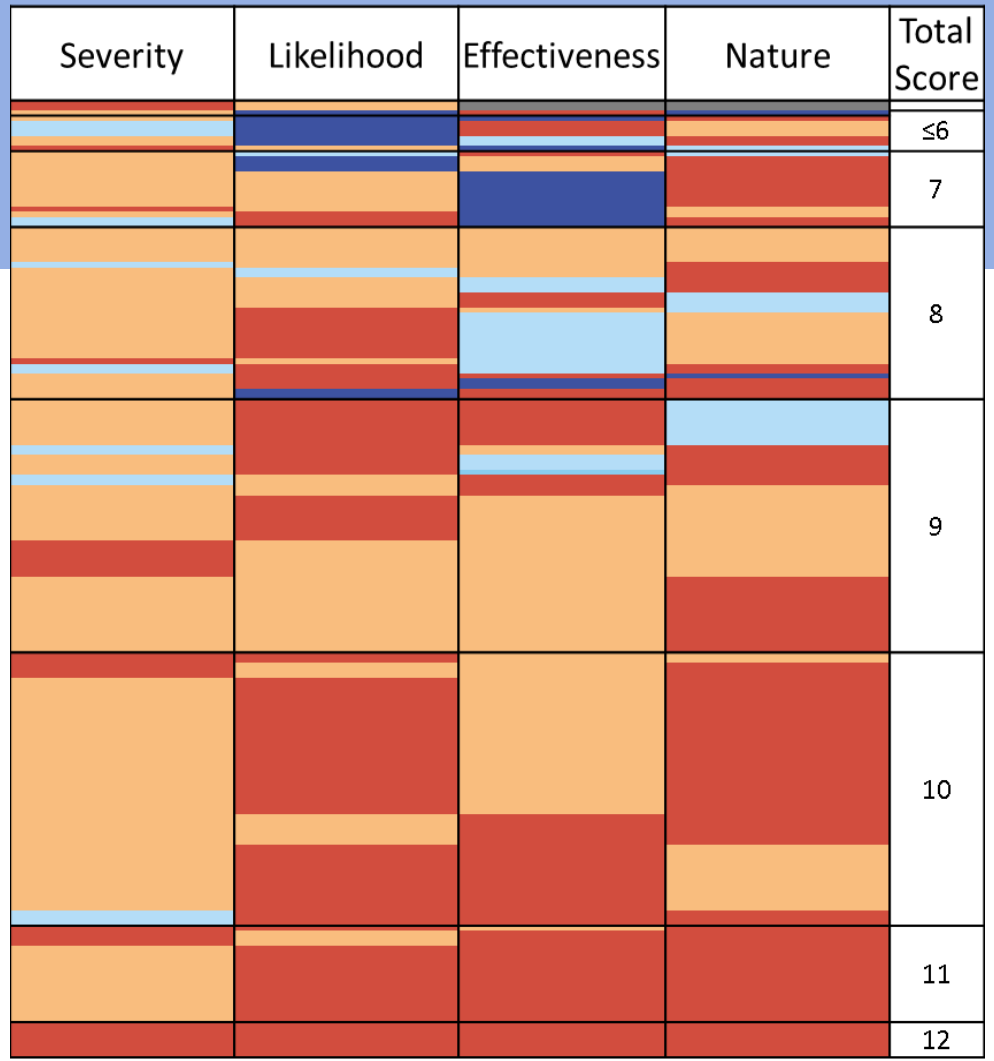

Score
0
1
2
3

ClinGen
Clinical Genome Resource

Scored to date:
74 Topics (111 genes)
186 Outcome/Intervention pairs

Question: What is the appropriate threshold?

Challenges

- ***Manual processes*** to determine testing status and test result
- Prospective studies have ***limited follow-up time*** to evaluate health outcomes so we must use surrogates
- Unclear what care can be ***attributed*** to the genetic test result
- Unclear reasons for why care is ***refused***
- Lack of a shared understanding of what is ***actionable***