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Outcomes associated with opportunistic screening for secondary findings

Ethical and Regulatory Aspects of Clinical Research

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National Human Genome
Research Institute

—
The **Forefront**
of **Genomics**
—

Disclaimer

I am a Federal Government employee and these are my own views; no other conflicts.

Outline

- How research participants think about and react to options for learning genomic results
- What happens after participants learn their genomic findings

Attitudes

Outcomes

Outline

- How **people** think about and react to options for learning genomic results
- What happens after individuals learn **actionable** genomic findings

Attitudes

Outcomes

Attitudes toward return of results

A C G
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A C G

- Thoughts
- Opinions
- Motivations
- Intentions
- Preferences

of

- Research participants
- Public
- Specific groups
 - Parents
 - Patients
 - Sub-studies

Overwhelming preference for return^{1,2}

- Up to 100% want “all”
- ↑ actionability = ↑ preference for return
- “Normal” findings³ and raw data are also desired⁴
- Judged of interest by researchers⁵
- Very small minority want none or primary only¹

Why?

- Empowering^{1,2}
- Disease-prevention^{3,4}
- Benefit self and/or family^{5,6}
- Curiosity^{2, 5, 7-9}
- Self-exploration/ancestry¹⁰

Why?

- Empowering^{1,2}
- Disease-prevention^{3,4}
- Benefit self and/or family^{5,6}
- Curiosity^{2, 5, 7-9}
- Self-exploration/ancestry¹⁰

Concerns

- Privacy
- Burden of knowledge
- Adverse effects on life

**Factored in but do not
override preference
for return¹**

Ownership and entitlement¹

- Control over “their” data
- Participants have highest investment
- Others may not determine “best interests”
- “Right to know” and autonomy
- Deliberation and restriction viewed as paternalistic

How?

- After broad consent^{1,2,3}
- According to plan and to foster engagement⁴
- Genetic counseling
- Face-to-face

Refusers' attitudes

- Minority¹
- Many studies report hypothetical attitudes^{2,3}
- Refusal may not be durable⁴
 - Of 8,843 enrolled, 165 (1.8%) refused secondary findings
 - 50% initial refusers contacted changed their minds
 - Most (75%) of these believed they HAD agreed

Actionable findings

Attitudes : Outcomes Ratio

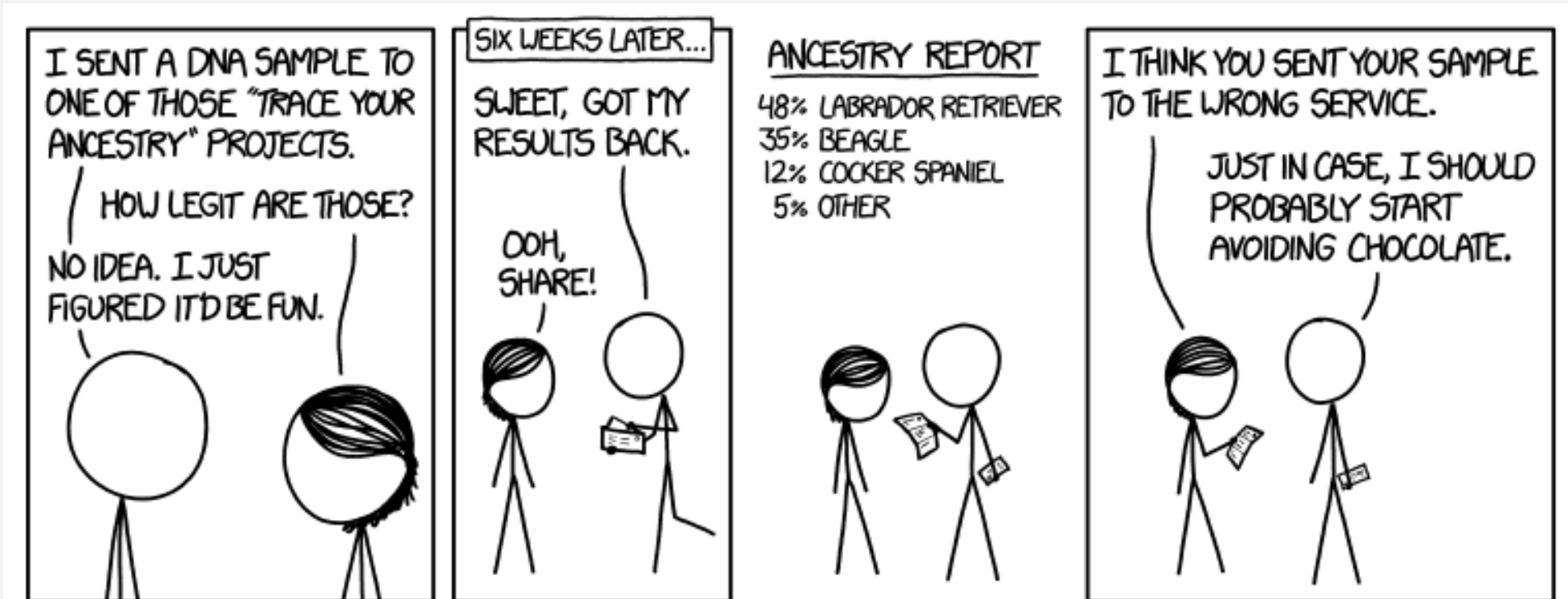
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Attitudes

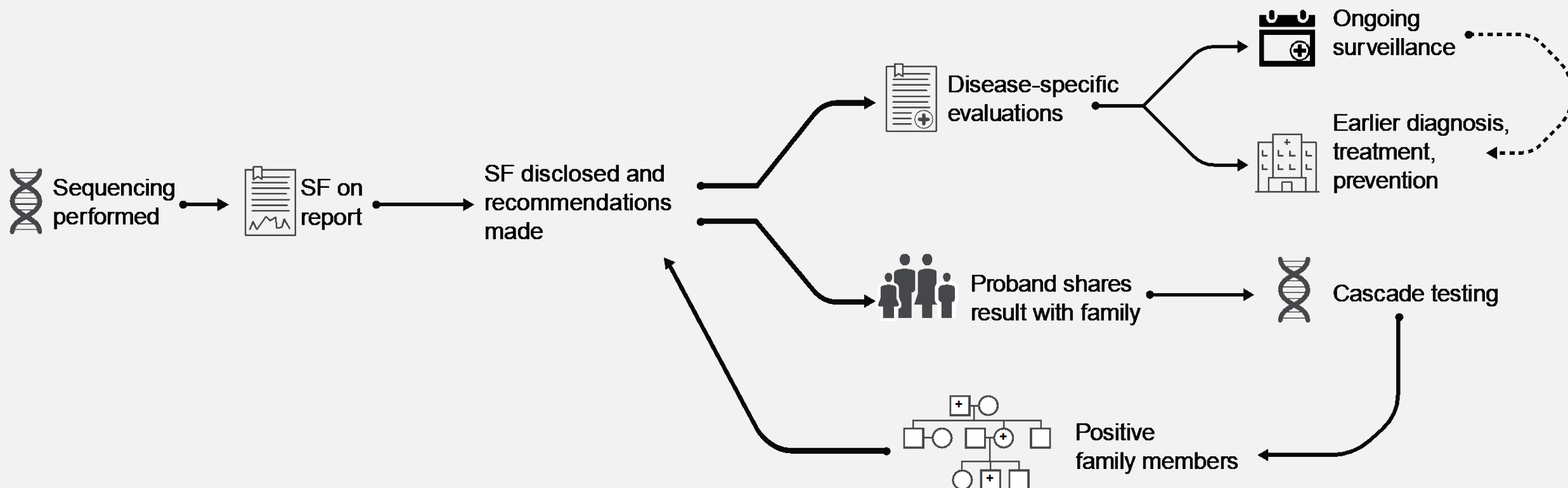
Outcomes

Defining findings

- Opportunistic screening
- Repurposing the ACMG list
- Defining what is “secondary” can be challenging
 - “Ordering clinician” and “interpreting laboratory”



Ideal secondary findings paradigm



Systematic review

- 709 reports of ACMG results return
- Disclosure process
- Outcomes following receipt
- 97% were research participants

Psychological outcomes

- Emotions include surprise, relief, and sadness¹
- Regret reported 0-5%²
- Depression/anxiety unchanged³
- Some forget⁴

Family and provider communication

- High numbers report sharing their results with family, especially close relatives^{1,2}
- Disclosure to primary care and specialists common but not universal^{1,3,4}

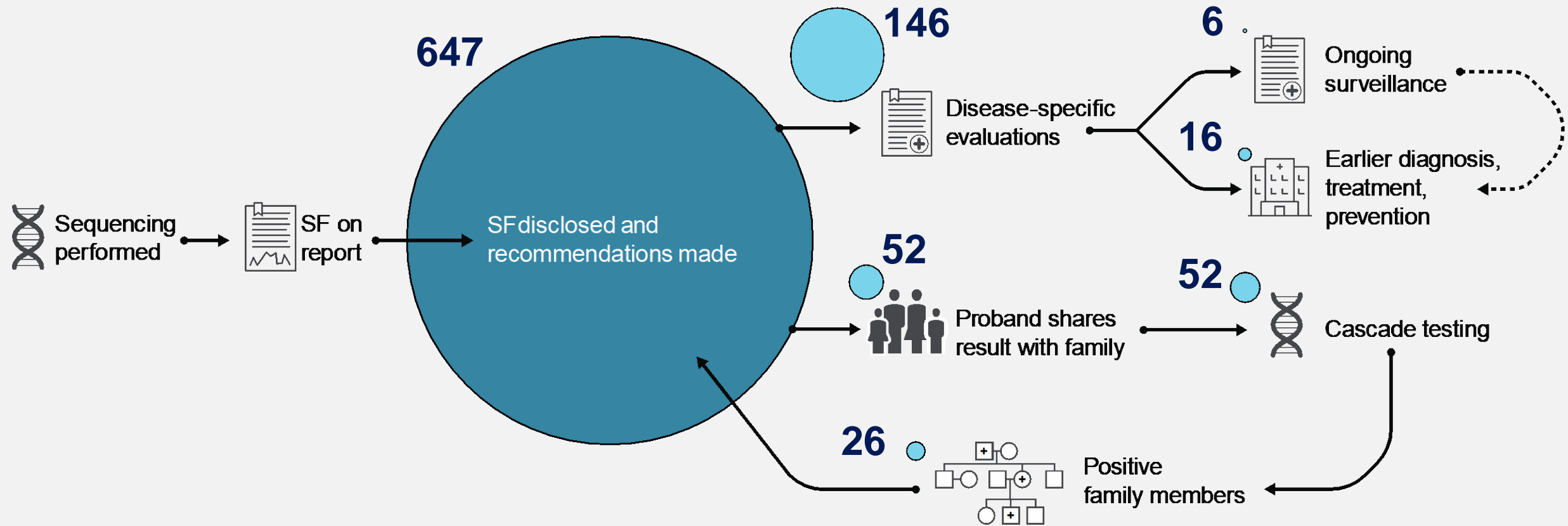
Precision medicine surveillance

- 55%-94% adherence to recommendations¹⁻³
- Genetic counseling and specialist referrals⁴
- Costs lower than expected^{1,4}

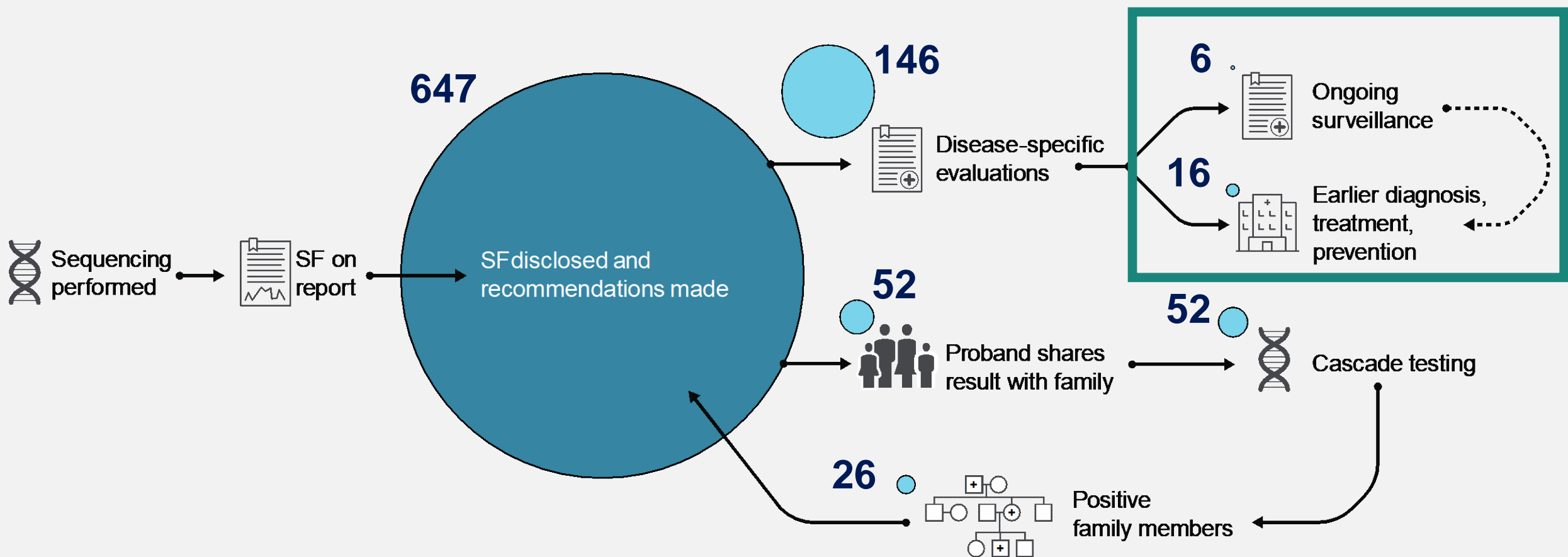
Reports of life-saving treatment

- Medication to avoid QT interval prolongation¹
- Targeted therapy for familial hypercholesterolemia²
- Early identification of lesions by imaging^{2,3}
- Prophylactic surgeries to reduce cancer risk^{1,4-7}

Actionable findings recipients understudied

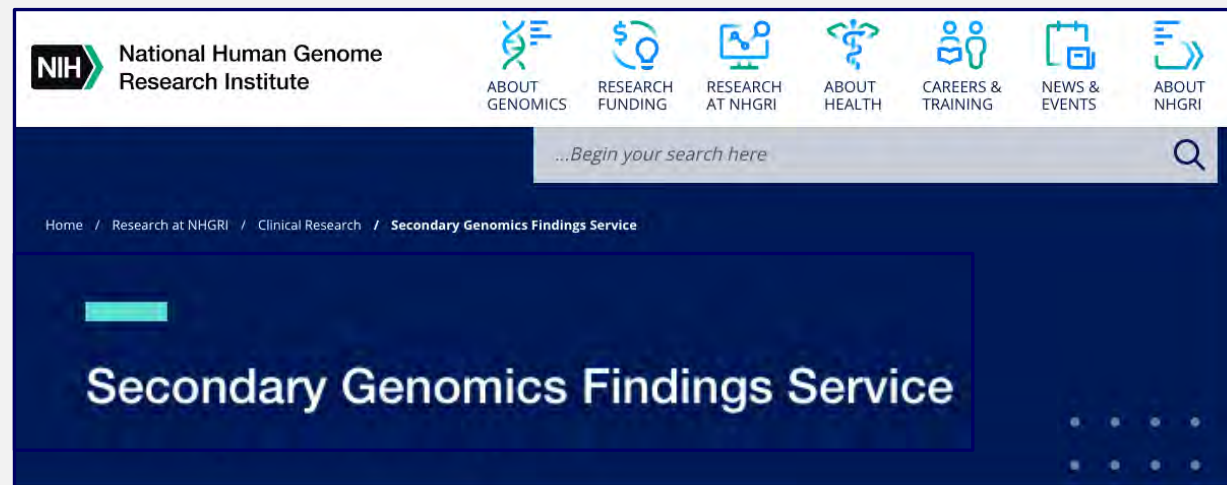
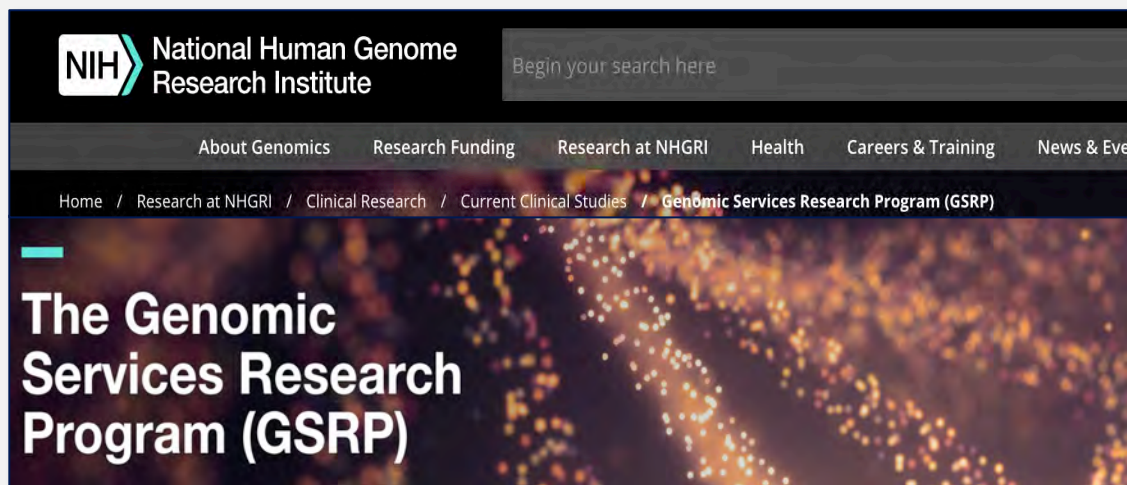


Health outcome data lacking



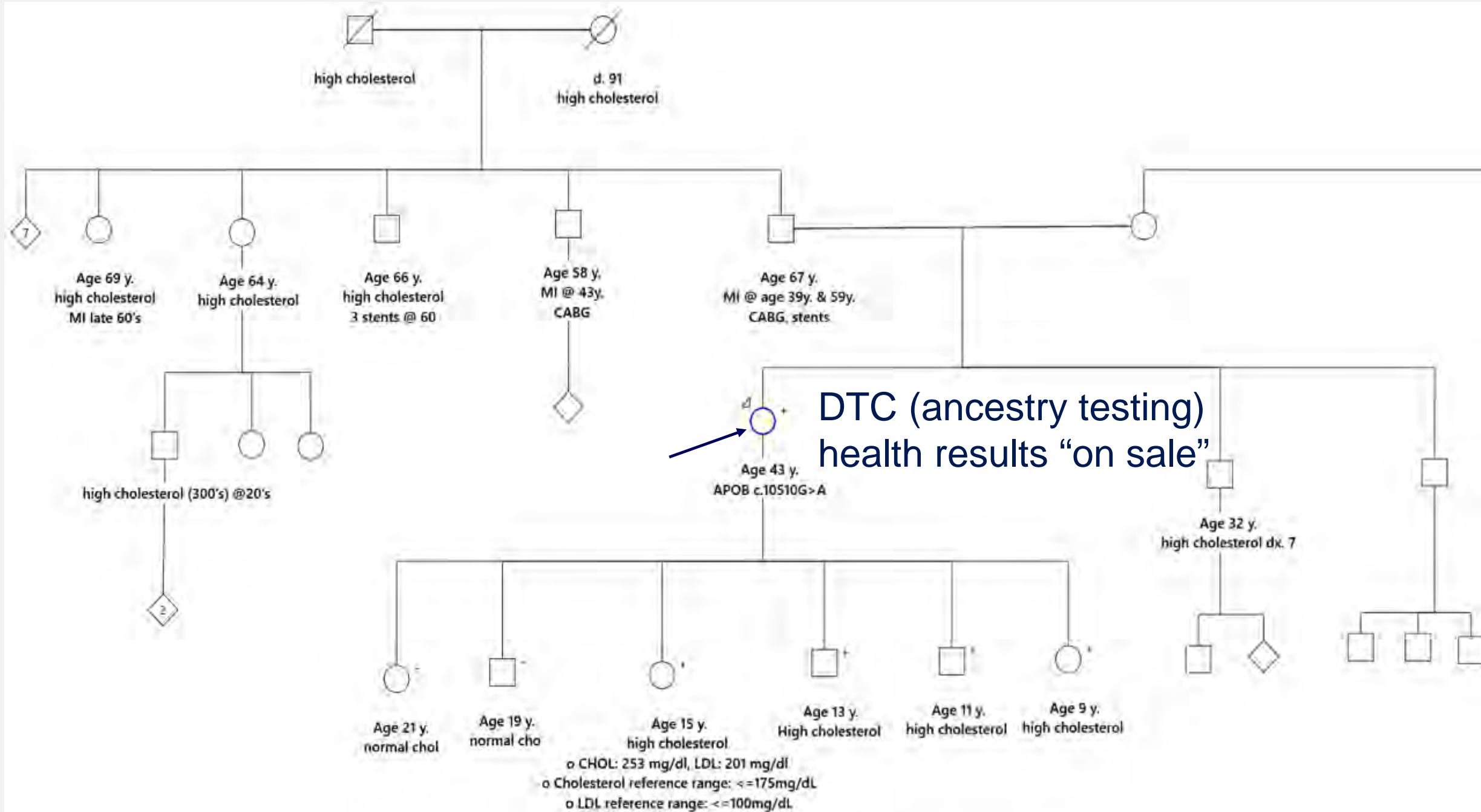
Opportunistic screening in research

- Best practices for RoR and outcomes research^{1, 2}
- Adherence and communications data emerging^{3, 4}

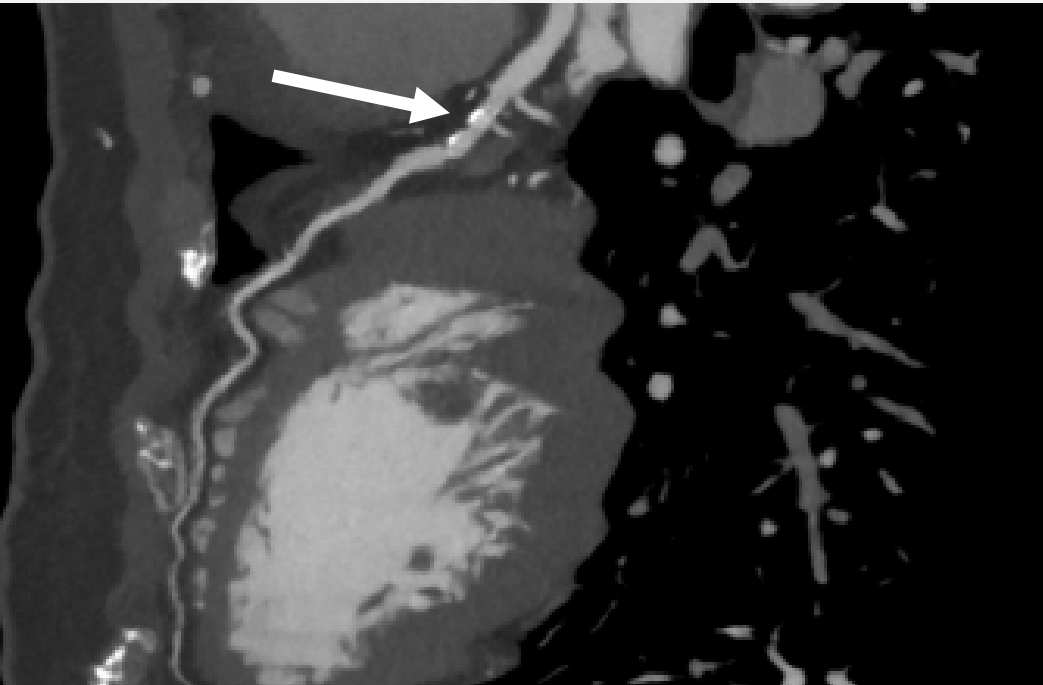


GSRP: a study for SF recipients

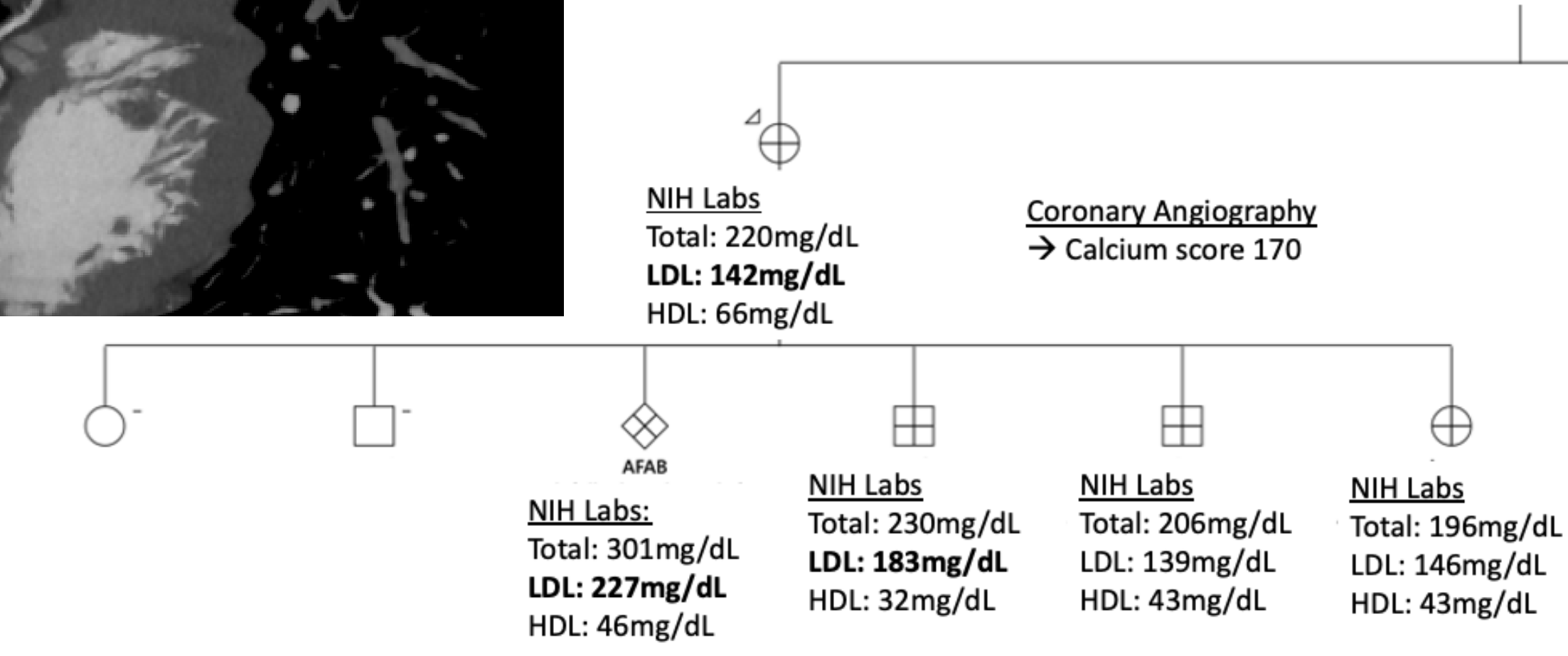
- Broad recruitment to ascertain SF recipients
- Evaluate adherence and communication outcomes
- Thoroughly genotype and phenotype family

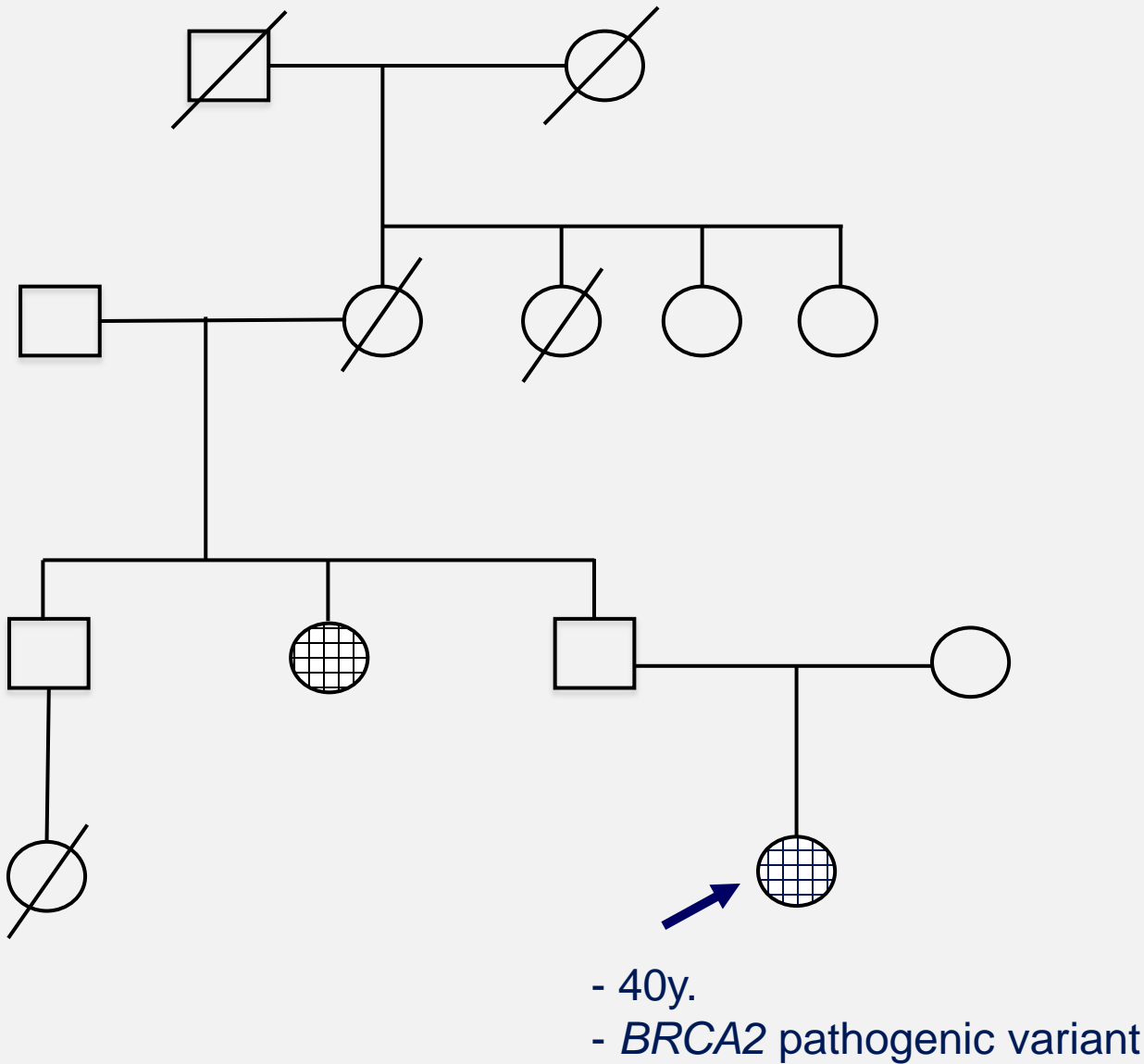


Genomic ascertainment



Overcomes barriers
in clinical care

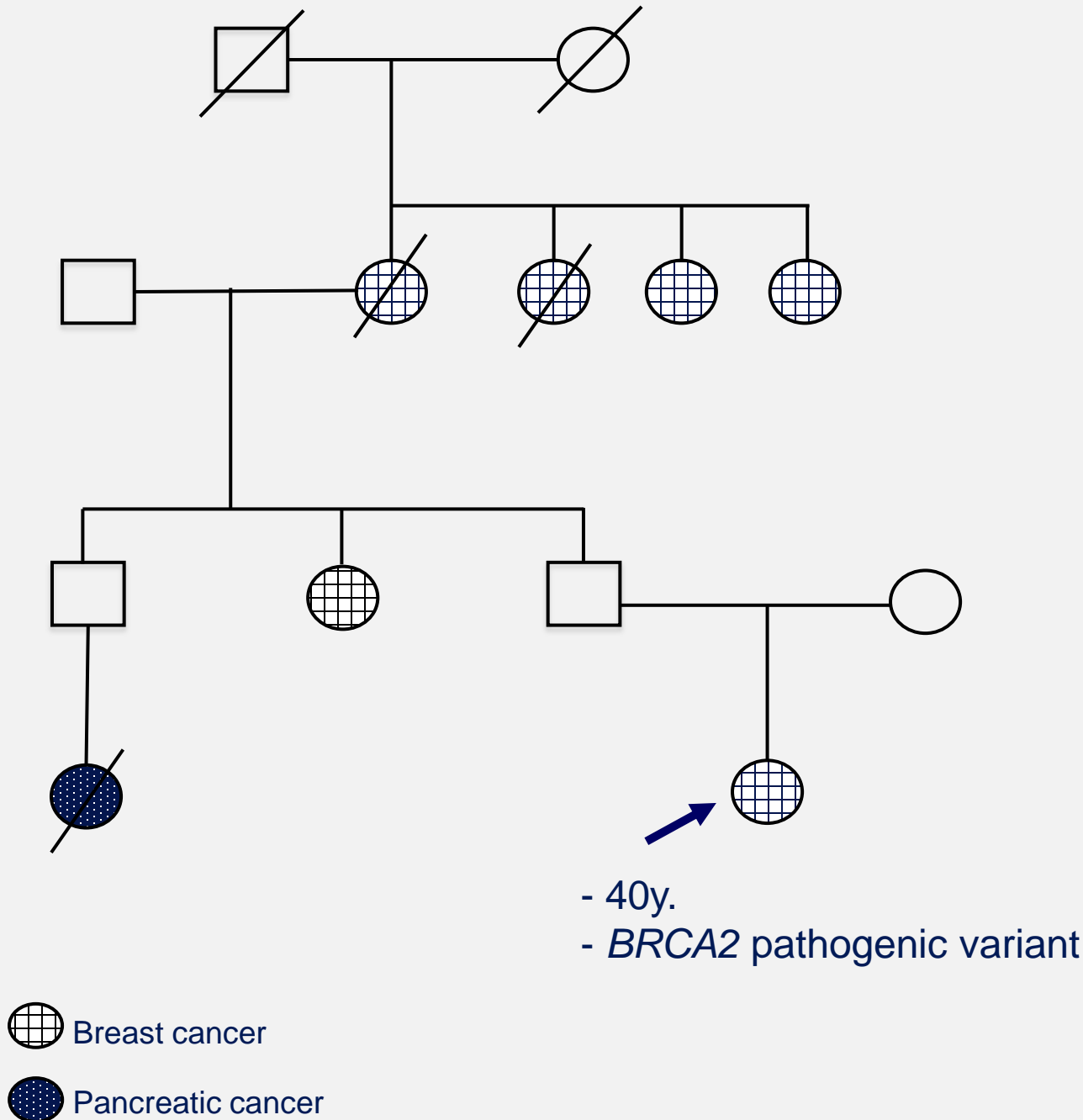




 Breast cancer

SF Recipient from a Research Study

- Joined at 36, motivated by curiosity, interest in paternal heritage, minority representation
- GC counseled screening, consideration of prophylactic surgeries
- PCP urged mammograms at 38
- Diagnosed with breast cancer at 39



SF Recipient from a Research Study

- Joined at 36, motivated by curiosity, interest in paternal heritage, minority representation
- GC counseled screening, consideration of prophylactic surgeries
- PCP urged mammograms at 38
- Diagnosed with breast cancer at 39
- Reconnected with paternal family and learned striking family history of breast and pancreatic cancer

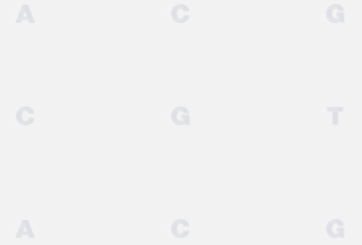
SGFS: returning results to participants

- Clinical service for Intramural protocols
- Screening and validation of ACMG findings
- Results return
 - Genetic counseling
 - Family/personal history assessment
 - Local referral

Implementation challenges

- Participant attributes
 - Age, wellness
- Local referrals
- Recontact

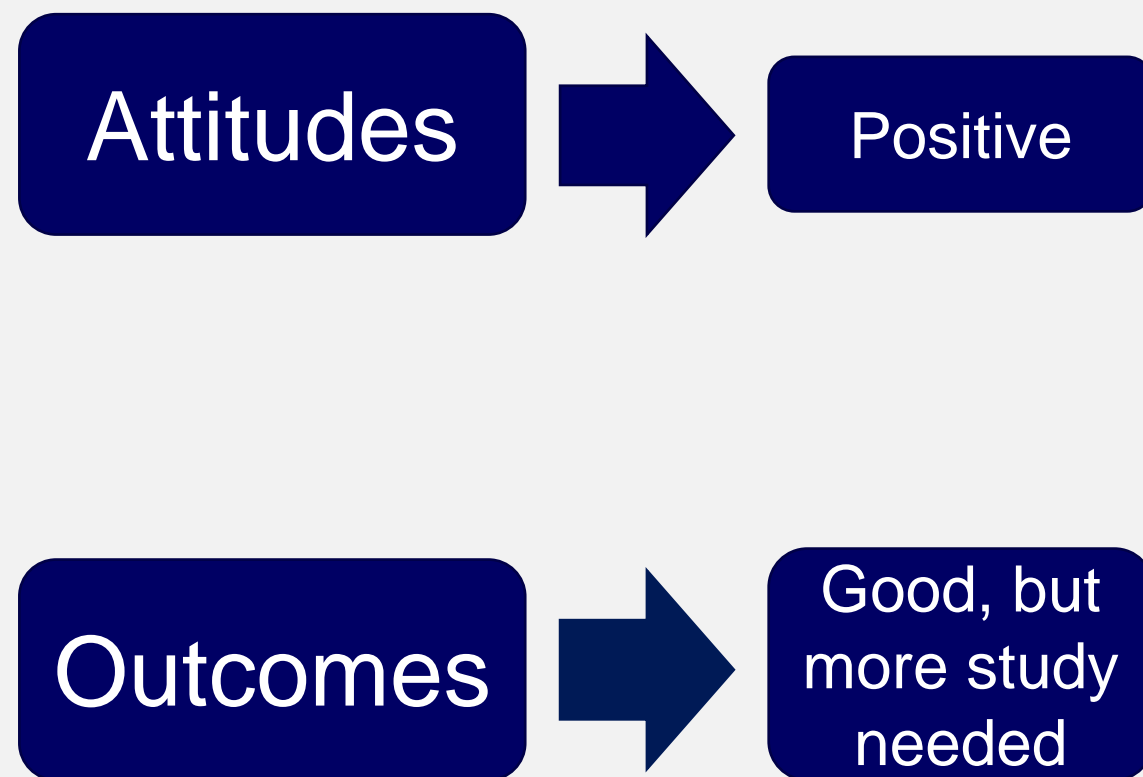
SGFS



- Clinical genetic testing uncommon
- ~25% report clinical phenotype/diagnosis but no genetic testing
- ~50% report consistent personal or family history without clinical diagnosis or genetic testing

Conclusions

- How **people** think about and react to options for learning genomic results
- What happens after individuals learn **actionable** genomic findings



Conclusions

- Potential to improve outcomes for participants
- Requires ongoing investment
 - Participants
 - Institutions/personnel
- Closes gaps in clinical care
- Highlights systemic challenges

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References

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A circular graphic with a light gray background. In the center is a white circle containing the text "The Forefront of Genomics®". The text is flanked by two short vertical bars, one on each side. Surrounding this central circle is a ring of dark blue lines. The outermost part of the graphic consists of a series of thin, dark blue lines that curve around the perimeter, resembling a DNA sequence or a stylized representation of a genome. The letters A, T, G, and C are scattered throughout the design, appearing as small, dark blue characters. The overall aesthetic is clean, modern, and scientific.

The **Forefront**
of **Genomics®**

Genomic ascertainment

- Overcomes clinical care barriers?

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C G T
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