Genetic Counseling at NWGAAP

DATE: OCTOBER 3, 2025

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Learning Objectives

- Review the role of genetic counseling in a multi-disciplinary clinic (NWGAAP)

- Review current testing strategies and possible outcomes

NWGAAP Multidisciplinary Clinic

- Genetic Aortopathy and Arteriopathy Program
  - Team based approach to care:
    - Sherene Shalhub, MD, MPH (vascular surgery)
    - Lidija McGrath, MD (adult cardiology)
    - Kathryn Holmes, MD (pediatric cardiology)
    - Castigliano Bhamidipati, DO, PhD (cardiothoracic surgery)
    - Wojciech Wiszniewski, MD (medical genetics)
    - Rodrigo Starosta, MD (medical genetics)
    - Erika Jackson, MS, CGC (genetic counseling)

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Role of Genetic Testing in NWGAAP

- Syndromic vs Nonsyndromic Aortopathy/Arteriopathy
  - Marfan syndrome, Loeys-Dietz syndrome, vascular Ehlers-Danlos syndrome
  - Familial Thoracic Aortic Aneruysms and Dissections (fTAAD)
- Medical Management
- Family Screening

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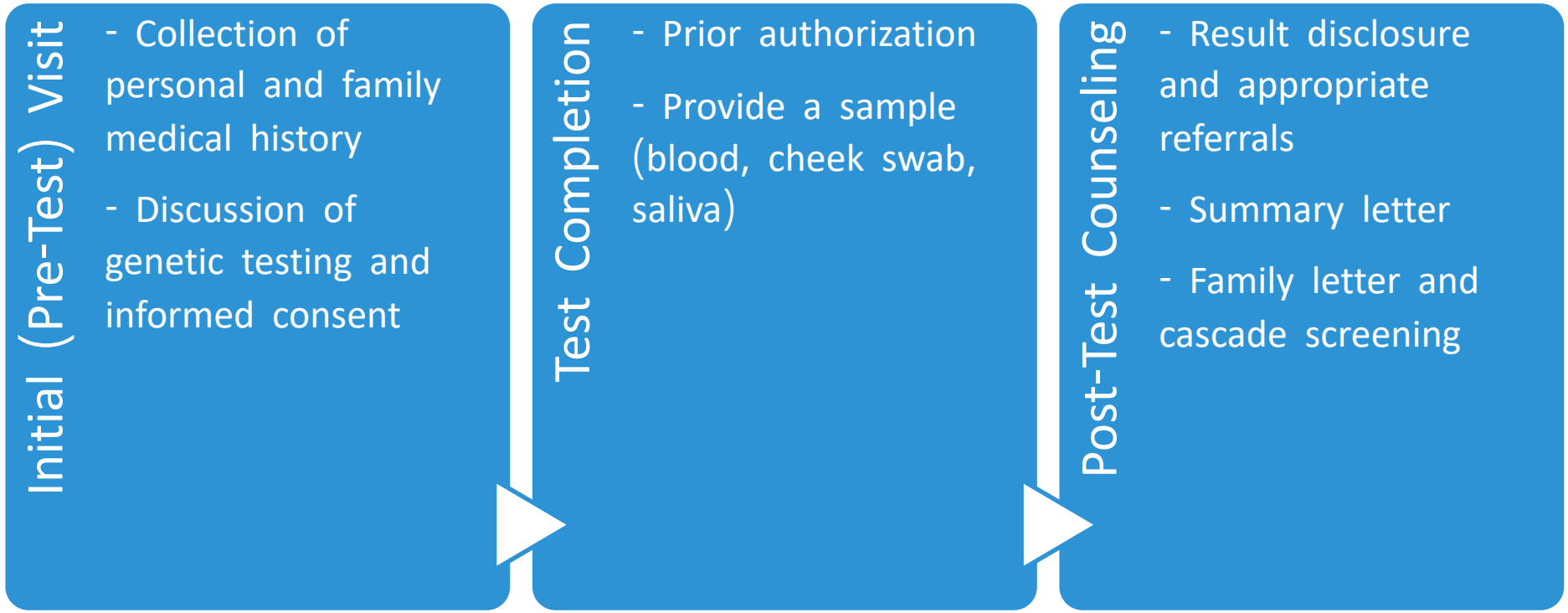
The Genetic Counseling Process



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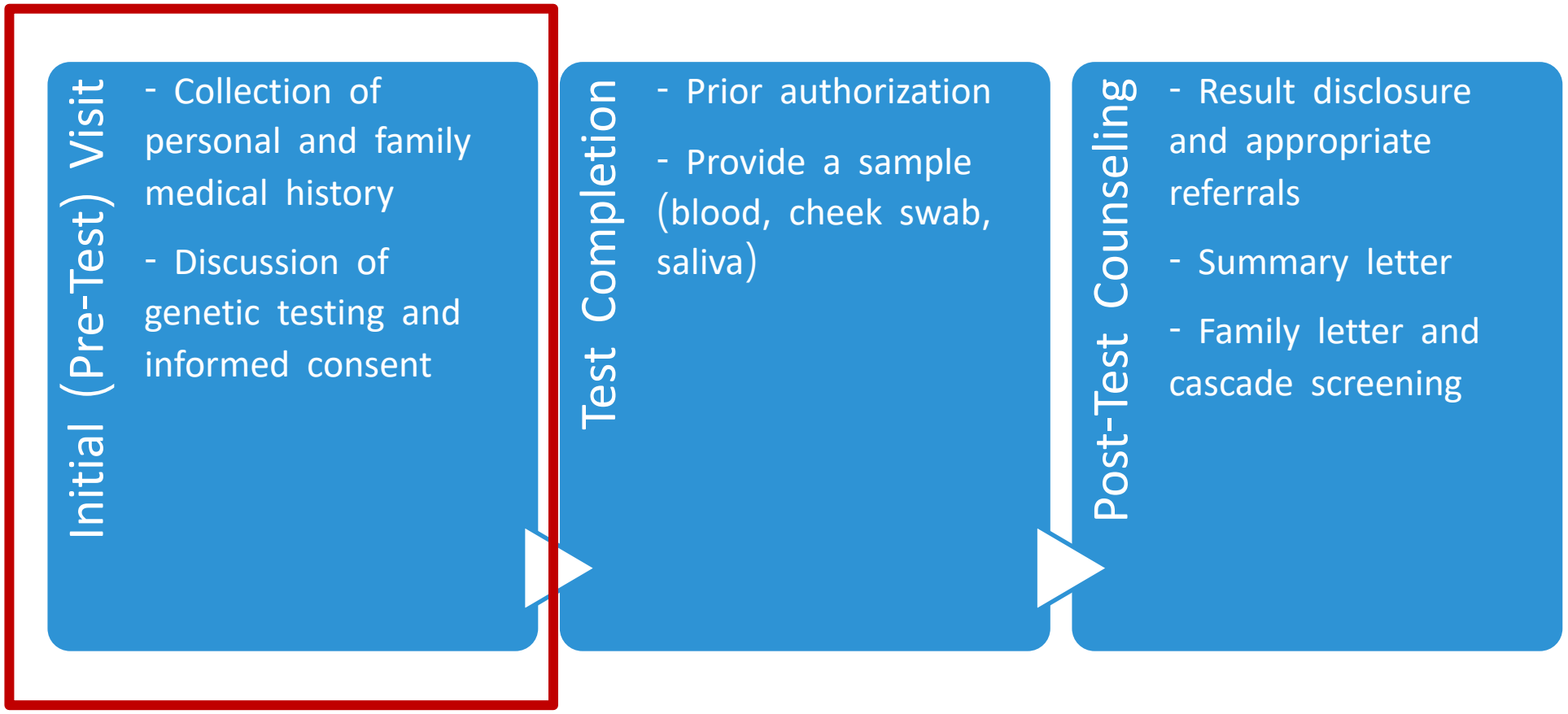
The Genetic Counseling Process



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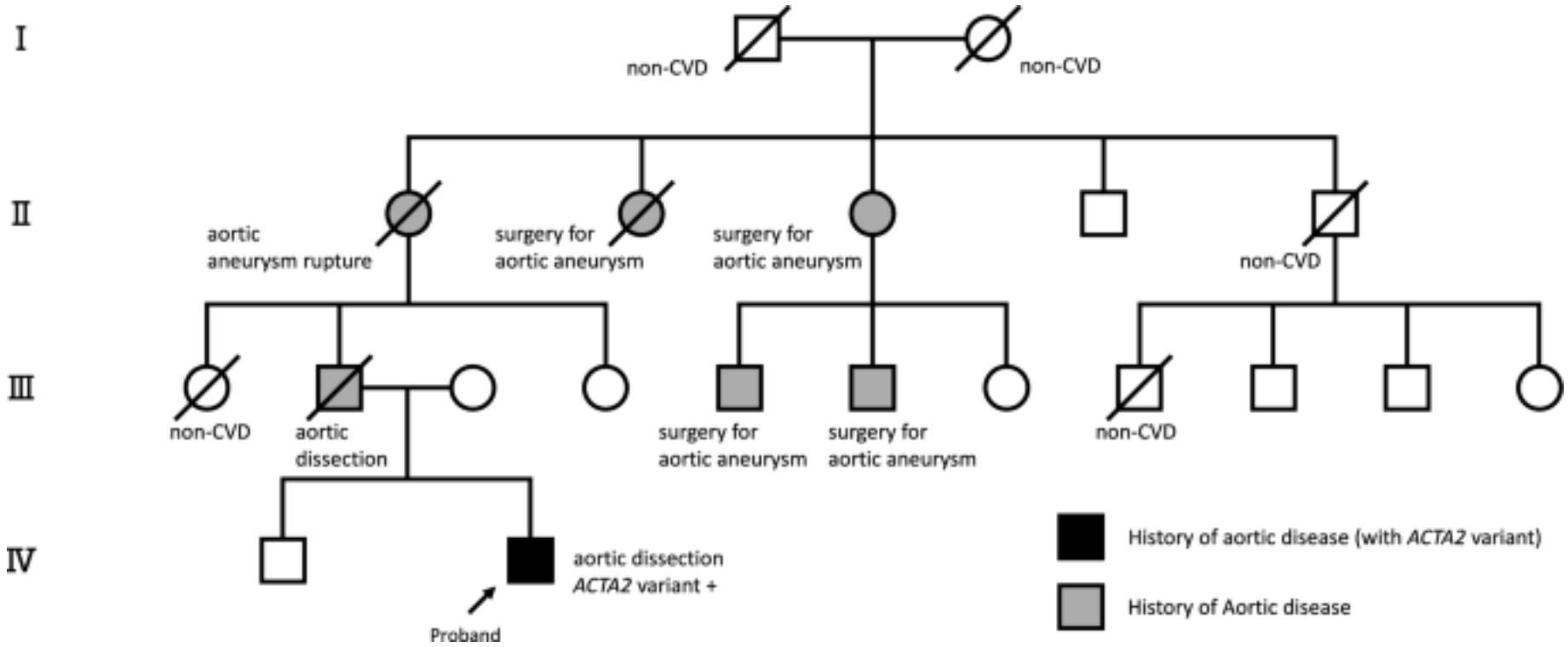
The Genetic Aortopathy Family History (Pedigree)



https://doi.org/10.1007/s12928-023-00977-0

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Genetic Testing - strategies

- Panel Testing
  - Targeted (e.g. *FBN1* for Marfan syndrome, Loeys-Dietz Panel)
  - Comprehensive (e.g. Genetic Arteriopathy/Aortopathy Panel)
- Whole Exome/Whole Genome Sequencing?
- Sample collection: blood, saliva, cheek swab

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Genetic Testing - outcomes

Table 2. Variant Classification Categories and Clinical Implications

Implication	Classification				
	Benign or No Variant[a]	Likely Benign[a]	Variant of Uncertain Significance[b]	Likely Pathogenic[c]	Pathogenic[c]
Meaning	No important variants detected; genetic disease cannot be excluded	Variant detected is likely to be harmless; genetic disease cannot be excluded	Ambiguous result; may be reclassified if additional information becomes available	Likely responsible for causing phenotype; family segregation studies may provide additional evidence for causality	Responsible for causing phenotype
Utility for proband	None	None	Unknown	Likely suggests diagnosis; may inform management or lead to additional diagnostic studies	Establishes diagnosis; may inform management
Utility for family	No option for predictive genetic testing; rely on longitudinal phenotypic evaluation	No option for predictive genetic testing; rely on longitudinal phenotypic evaluation	Should not be used for predictive genetic testing; testing affected relatives for segregation may provide evidence of causality	Predictive genetic testing of unaffected relatives should be approached carefully; may be combined with phenotypic evaluation and surveillance	Can be used for predictive genetic testing

[a] Result considered to be negative.
[b] Result considered to be uncertain.
[c] Result considered to be positive.

Cirino AL, Harris S, Lakdawala NK, et al. Role of Genetic Testing in Inherited Cardiovascular Disease: A Review. JAMA Cardiol. 2017;2(10):1153–1160. doi:10.1001/jamacardio.2017.2352

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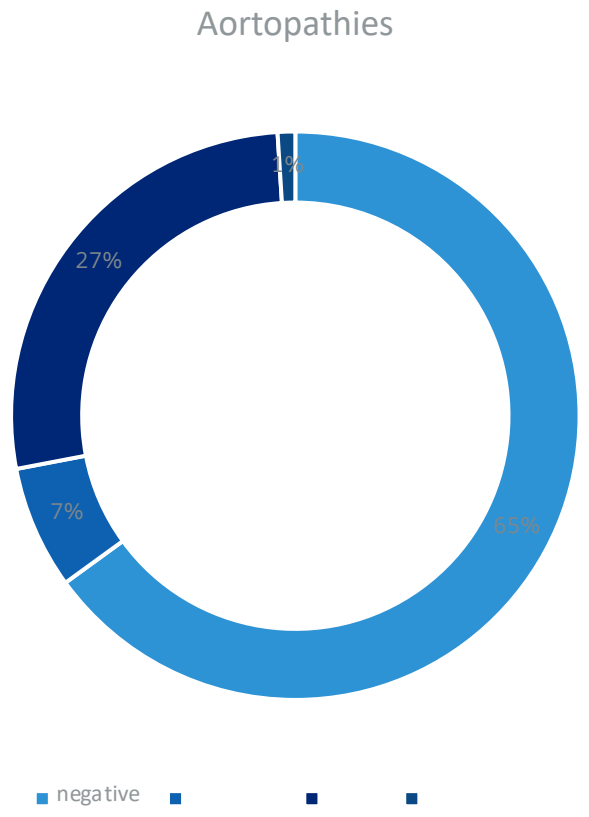
Genetic Testing - outcomes

- OHSU Cardiogenetics/NWGAAP Clinic - Aortopathies
  - Diagnostic yield 10-15%
  - VUS rate 25%
- VUS Reclassification (Cardiology)
  - Invitae 78% downgraded
  - Ambry 95% downgraded



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https://www.ocwr.gov/

- Genetic Information Nondiscrimination Act of 2008
  - Protects individuals from discrimination based on genetic information
    - Genetic testing results, family history

Protects	Does NOT Protect
- Health insurance - Employment*	- **Life, disability, long-term care insurance**

*military, small companies excluded

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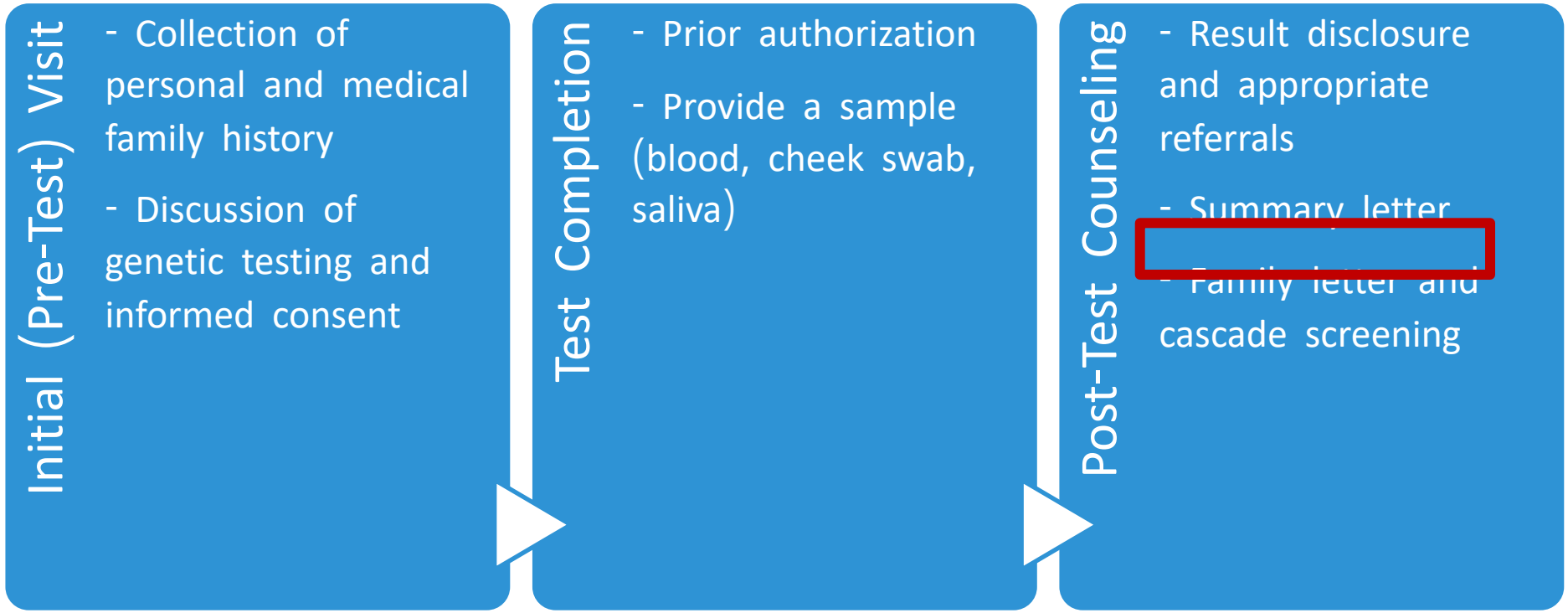
Typical Genetic Counseling Process



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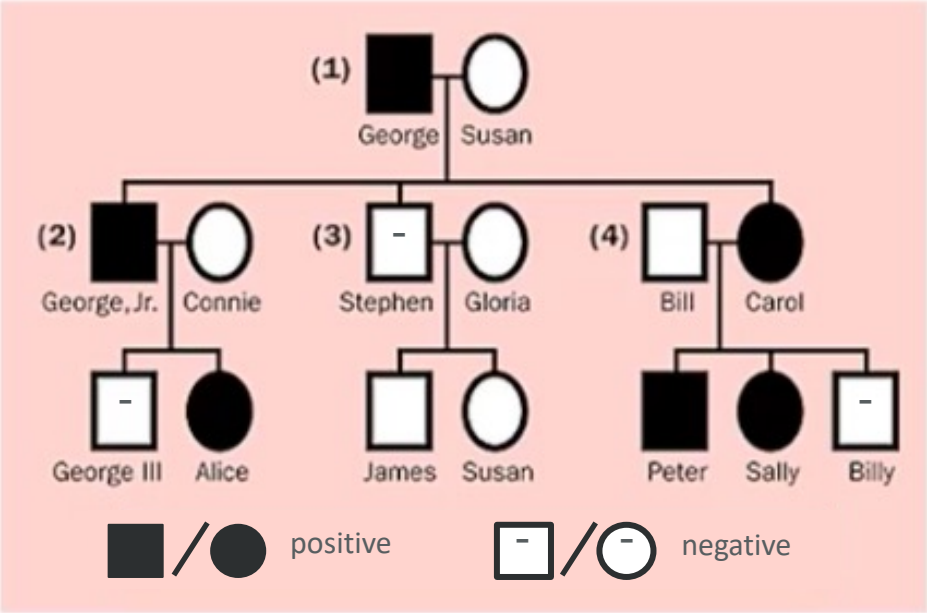
Cascade Genetic Screening



- Most efficient way to screen at-risk family members **when there is a known gene mutation**
- Positive genetic testing ≠ guaranteed disease
- Negative imaging ≠ negative genetic testing

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Family Result Letter

To the family of [redacted]:

I am writing to inform you that I recently underwent genetic testing which identified a genetic cause for my aortic dissection. The purpose of this letter is to give you information about this test result in case you decide you would also like to pursue genetic testing of your own. My specific test result is:

Lab: Invitae
Gene: *ACTA2*

Accession#: [redacted]
Mutation: c.808G>A (p.Gly270Arg)

Overview:
I recently had genetic testing, which showed that my aortic disease is due to a mutation in the *ACTA2* gene. When the *ACTA2* gene is working properly, it is responsible for creating α-actin, a protein that helps make your vascular smooth muscle cells work. Vascular smooth muscle cells are found throughout the body, including, for example, the aorta and blood vessels. Defects of the *ACTA2* gene make it so the α-actin protein and smooth muscle cells don't work properly, which in turn causes increased risk for things like aortic aneurysm and dissection.

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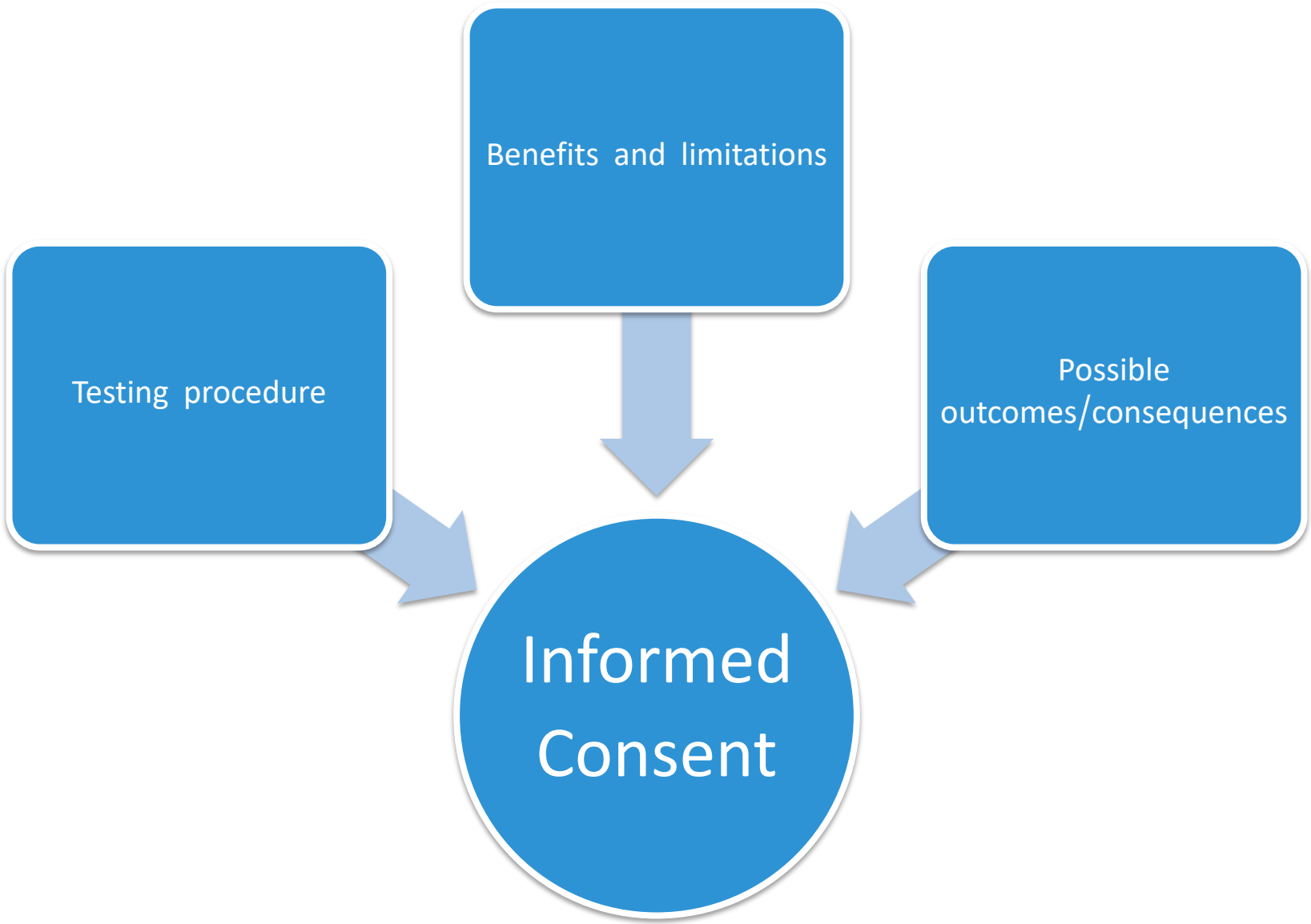
Benefits and limitations
Testing procedure
Possible outcomes/consequences
Informed Consent

Thank You!