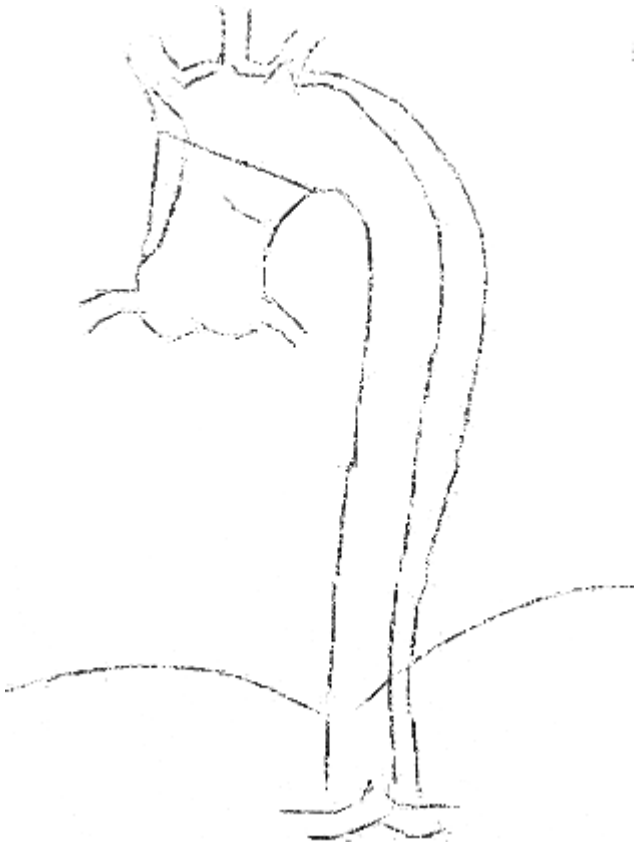
Discussing Genetic Risk as Often as Hypertension in Your Patients with Aortic & Vascular Disease



Houston Aortic Symposium
March 6, 2019

Alana Cecchi, MS, CGC
Assistant Professor, McGovern Medical School
University of Texas Health Science Center at Houston

UTHealth
The University of Texas Health Science Center at Houston

McGovern Medical School

"This is difficult to talk about, but I know that it will **prevent my kids** from having to go what I went through. **I almost died**"

- 38 year old thoracic aortic dissection survivor discussing genetic testing for his children

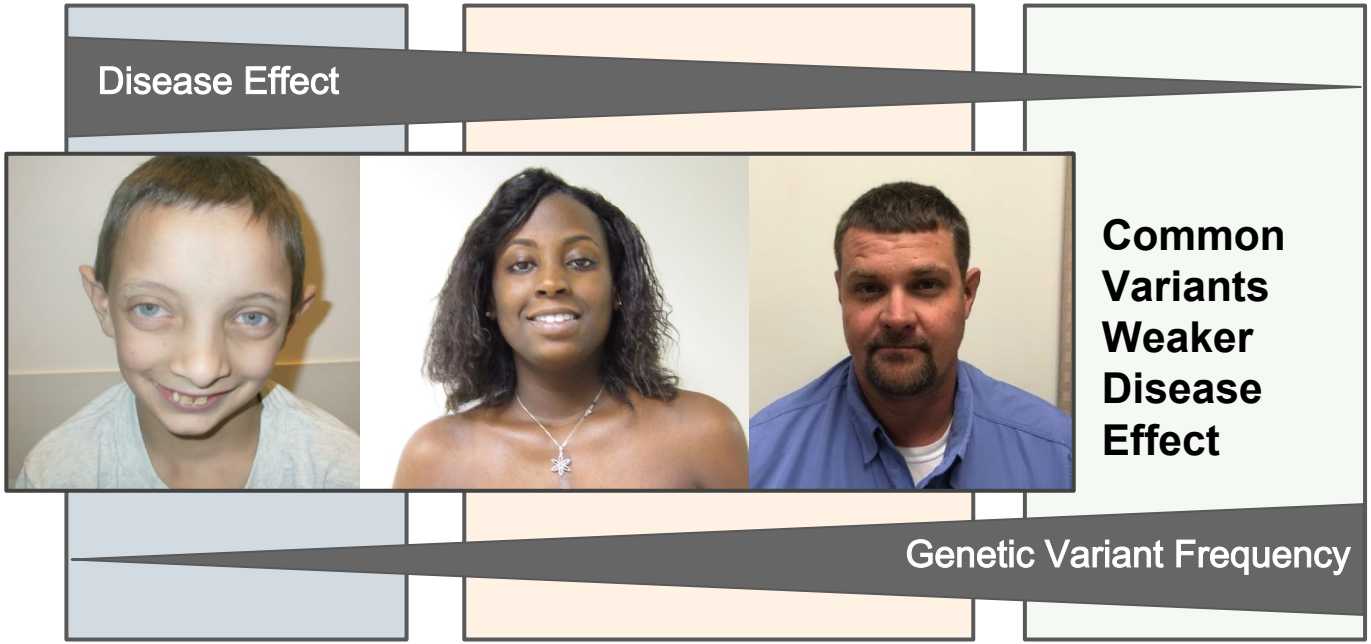
Objectives

- Define the utility of genetic testing for patients and families

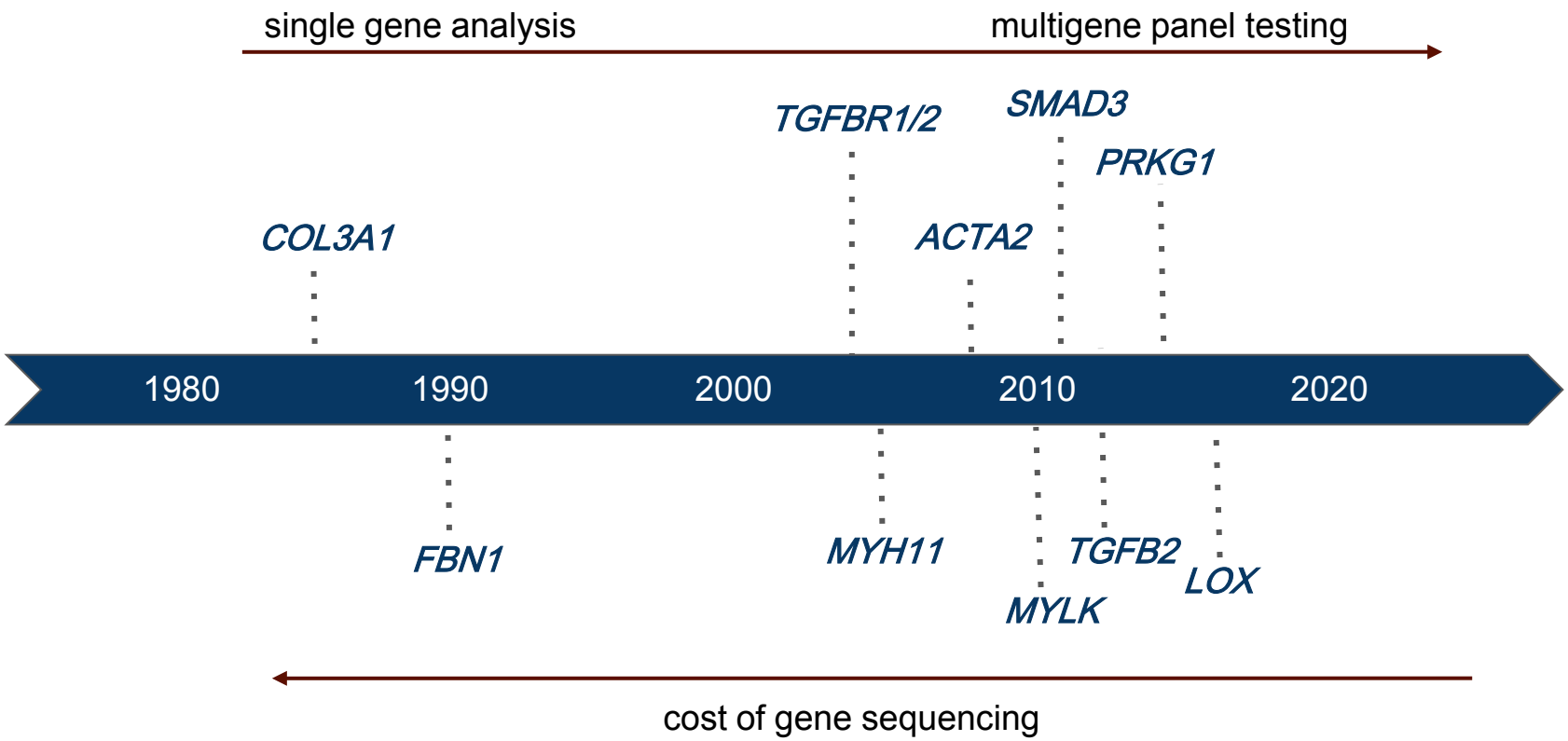
- Identify patients who can benefit from genetic testing/counseling

- Implement into your practice

Variable Heritable Arteriopathy Disease Spectrum

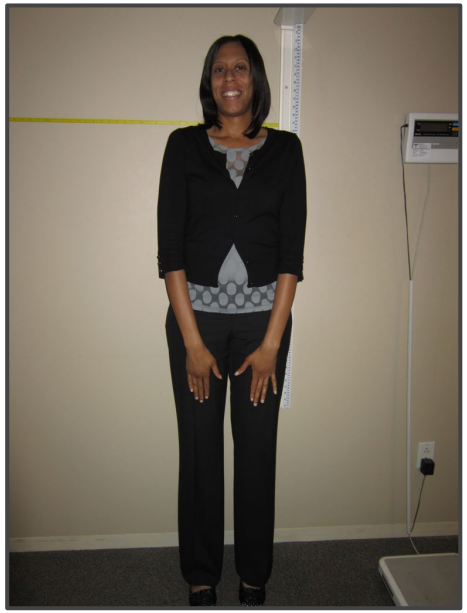


The Landscape of Genetic Testing Has Evolved



Marfan Syndrome is Not the Only Genetic Arteriopathy

SMAD3



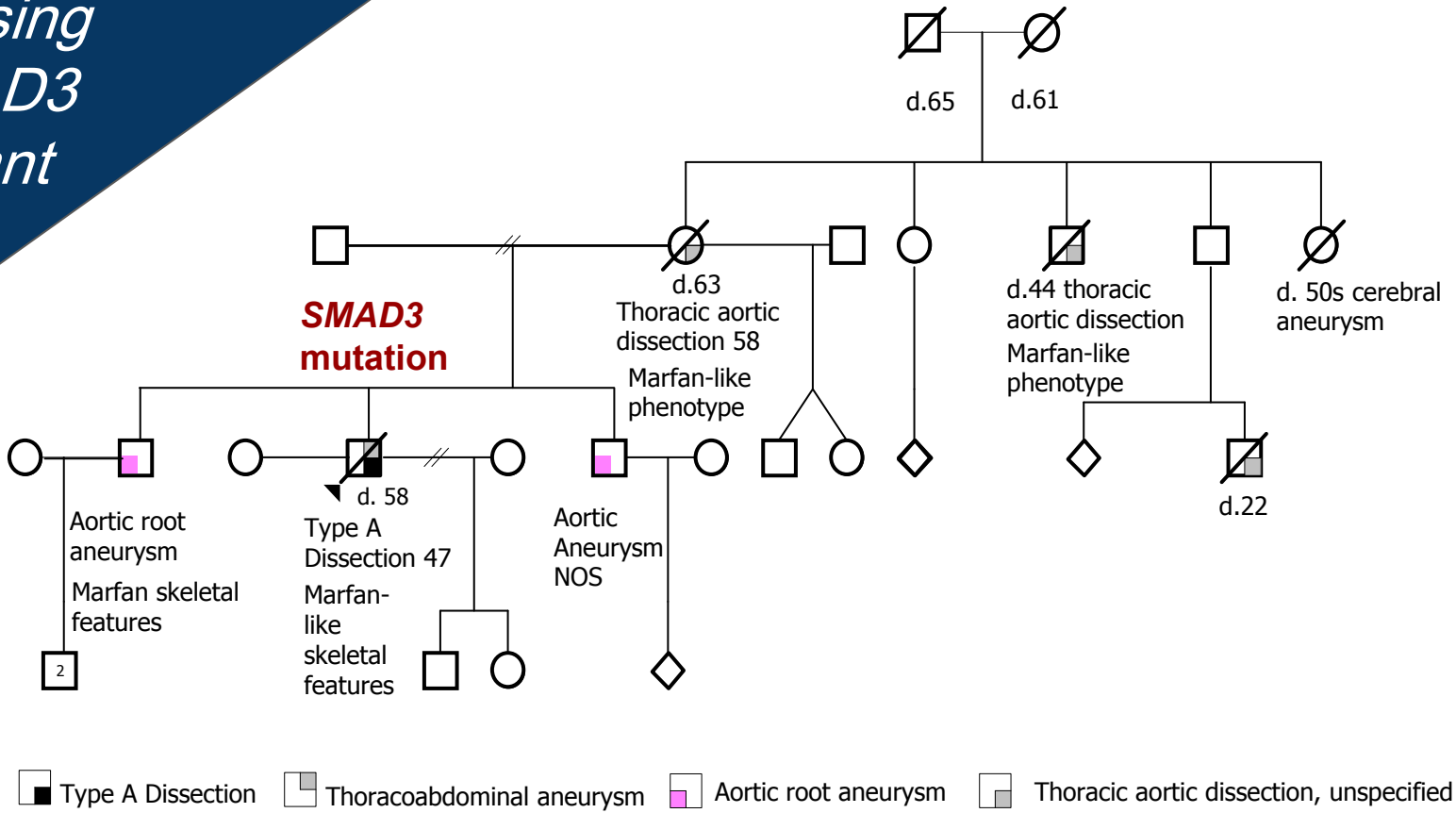
FBN1

TGFBR2

Incorrect Marfan Diagnosis

- Male acute type A aortic dissection at 47 years > diagnosed Marfan syndrome
- Marfan-like skeletal features: scoliosis, pectus carinatum, joint hypermobility, hernias, flat feet
- Cerebral aneurysm dx 50 years
- Thoracoabdominal aortic aneurysm repair at 51 years
- In his 50's, **negative** genetic testing for *FBN1* gene (Marfan) and *TGFBR1/2* genes > **what's the diagnosis?**

Disease Causing SMAD3 variant



Indications for Genetic Testing & Counseling Apply to a Broad Range of Patients

Personal history TAAD or multiple aneurysms

If isolated, consider age of onset ≤ 60

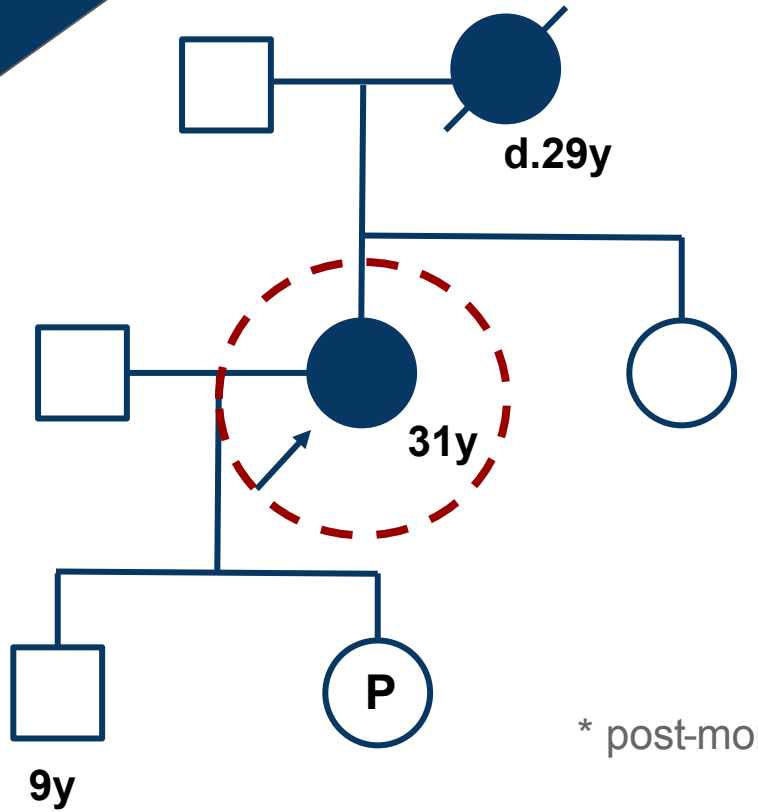
Family history TAAD or other arteriopathy

aneurysms/ruptures, sudden death, CAD...

Known disease-causing gene variant in family

"genetic mutation"

Genetic Testing Strategy



Most informative to test affected individual first

* post-mortem genetic testing is a possibility

The Test Result

Interpretation of Results Is Not Always Straightforward

RESULTS

FBN1 **Pathogenic Mutation: c.6590delA**

SUMMARY

POSITIVE: Pathogenic Mutation Detected

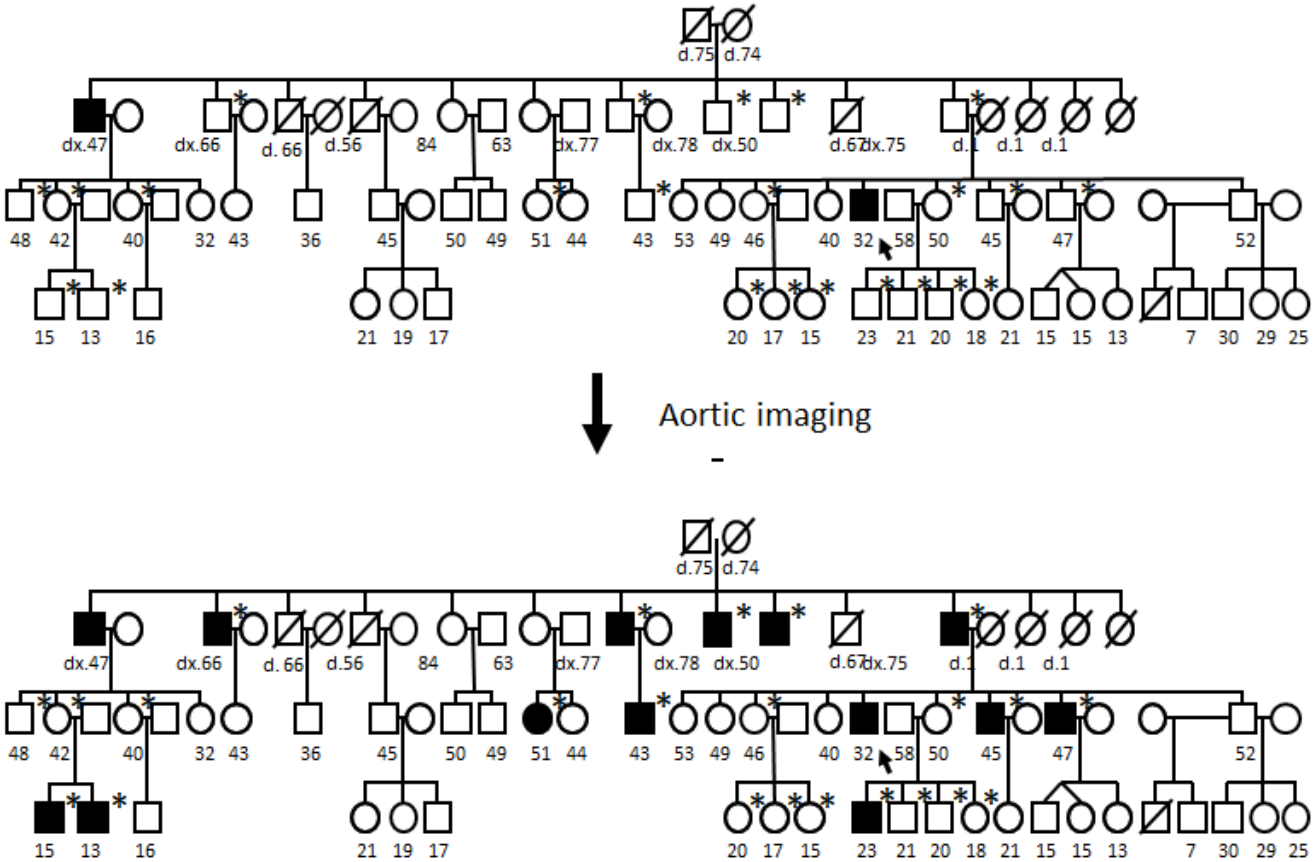
→ Confirms Marfan diagnosis

Summary

Variant of Uncertain Significance identified in FBN1.

→ “VUS” > uncertain

TAA254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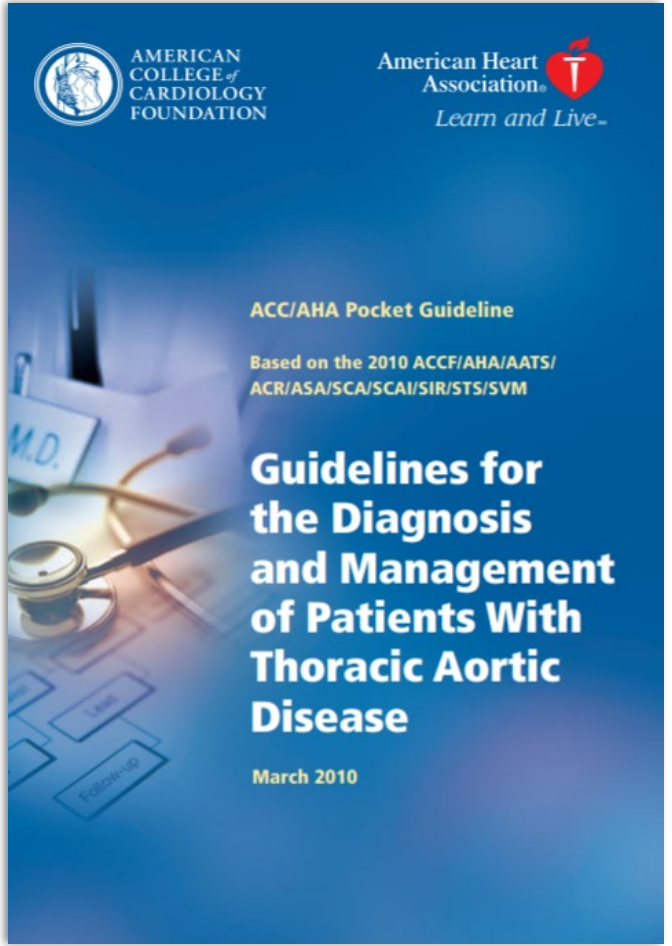
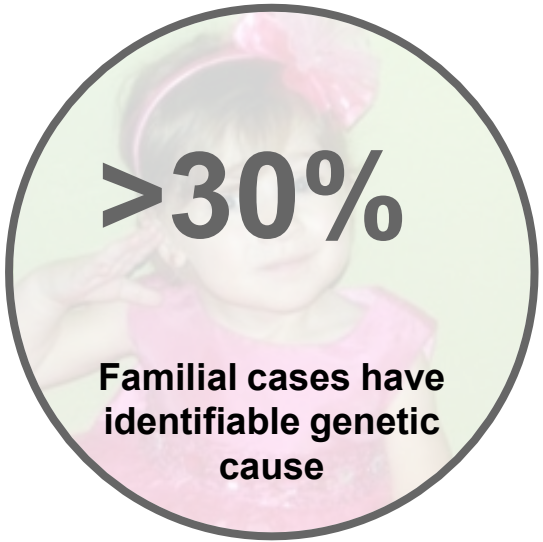
Aortic imaging

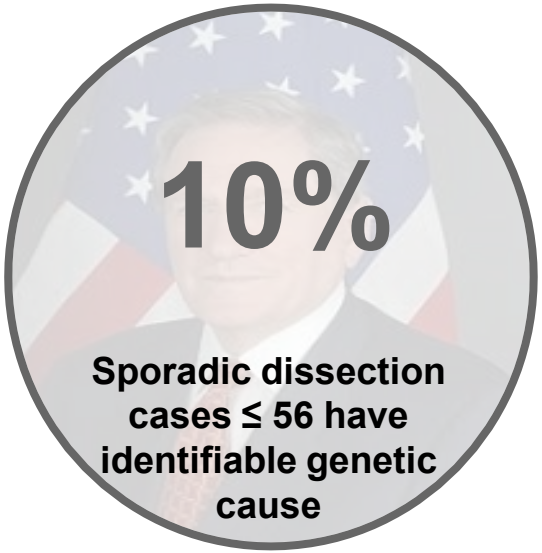
Imaging Family Members is Recommended

"Given the familial risk of thoracic aortic aneurysms, **screening the proband's first-degree relatives** with appropriate imaging studies is indicated in the absence of identification of the defective gene leading to the disease."



The Patients and Families Who **Benefit** From Testing





Some things to remember...

- Identifying disease-causing gene variant is powerful
- May inform **timing of surgery** and **risk for other diseases**
- Multi-gene panel testing preferred - **cost not prohibitive**
- Negative clinical genetic testing does NOT rule out hereditary predisposition
- Screening recommended for first-degree relatives
- Family history is important

"Identification of the underlying gene triggering HTAAD is **powerful** information that can be used not only to **identify family members at risk** for the disease, but also to **inform thoracic aortic disease surveillance and management**, including timing of surgical repair, risk for additional vascular diseases, and systemic complications."

Renard M. et al, *Clinical Validity of Genes for Heritable Thoracic Aortic Aneurysm and Dissection*, JACC 2018

Thank You, and Many Thanks to...

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- Department of Cardiothoracic and Vascular Surgery at UTHealth
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