# Genetic Testing in Dyslipidemia

NATIONAL LIPID ASSOCIATION

## When to Consider Genetic Testing

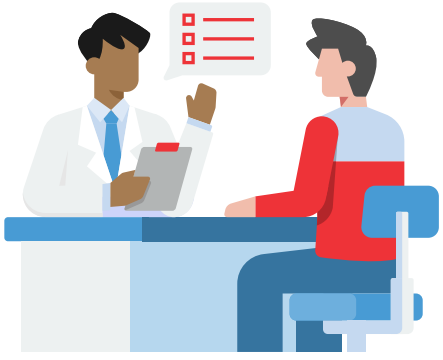
The decision to undergo genetic testing in a dyslipidemia patient should weigh the following factors:

- Strong clinical suspicion of a genetic dyslipidemia
- Strong family history of dyslipidemia or its complications
- Presence of characteristic syndromic features
- Evidence that testing might change management
- Available and effective early interventions exist
- Eligibility for new or investigational drugs
- Patient preference
- Family planning

## Positive Genetic Testing Results Can...

- Aid in clinical diagnosis and targeted treatment for specific disorders
- Guide optimal management and prevention strategies
- Increase patient adherence and motivation
- Provide early identification of affected family members through cascade screening

## Genetic Counseling



### What to do before ordering a genetic test:

- Obtain informed consent
- Counsel the patient about the benefits and risks of genetic testing

### You've ordered a genetic test – now what?

- Test results should be disclosed by a clinician with expertise in genetics or by a certified genetic counselor
- Genetic counseling should be provided to the patient and their family, even if test results are negative
- Definitive incidental findings in certain genes that are unrelated to lipids should also be communicated to the patient
- Results should be tailored to the patient's specific circumstances, level of understanding, and literacy

## Genetic Testing Considerations

- Not all genetic tests are created equal
- Review analytic and clinical validity of a test prior to medical management decisions
- Attributing pathogenicity to a DNA variant can differ between laboratories
- Direct-to-consumer genetic testing may provide both false positive and false negative results; confirmation using a clinical genetic test is recommended
- Currently polygenic scores for dyslipidemia are not standardized and not recommended or appropriate for clinical use in dyslipidemia
- Intensity of treatment for familial hypercholesterolemia should be guided by LDL-C elevation rather than the underlying genotype

Brown, Emily E., et al. "Genetic Testing in Dyslipidemia: A Scientific Statement from the National Lipid Association" *Journal of Clinical Lipidology*, May 2020, doi: 10.1016/j.jacl.2020.04.011

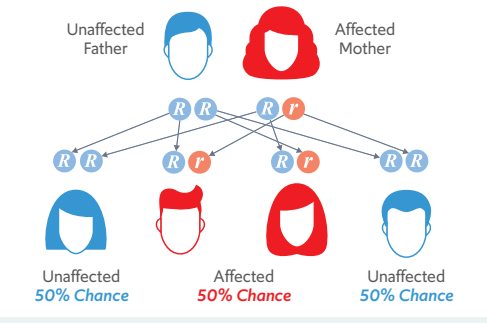
## What are Monogenic and Polygenic Dyslipidemias?

### *Monogenic Dyslipidemias:*

- Rare, large-effect DNA variants (mutations) that cause monogenic or Mendelian dyslipidemias
- Characteristic clinical features are variably present
- Familial Hypercholesterolemia (FH) is the most common monogenic dyslipidemia

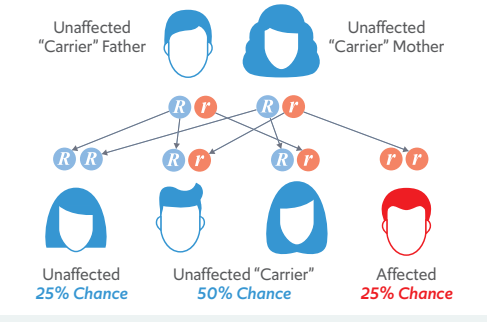
### *Autosomal Dominant*

*As seen in Heterozygous Familial Hypercholesterolemia (HeFH)*




### *Autosomal Recessive*

*As seen in Familial Chylomicronemia Syndrome (FCS) and LCAT deficiency*




### *Polygenic Dyslipidemias:*

- Results from concurrent contributions of multiple common variants whose aggregate effect on lipoprotein levels can resemble a large-effect rare variant
- Inheritance does not follow Mendelian rules
- Impact of such common variants is quantified using a polygenic score
- The clinical utility of polygenic scores is not clear