

Exome- and Genome-Based Testing Have Lower VUS Rates than Multi-Gene Panel Testing

STUDY BASICS BY THE NUMBERS



19 Institutions



1.5 Million
Samples



96%
Multi-Gene Panels



90% Exome
10% Genome

4% Whole Exome
and Whole Genome
Sequencing

THE MORE GENES YOU TEST, THE MORE VUS YOU REPORT...RIGHT? WRONG!

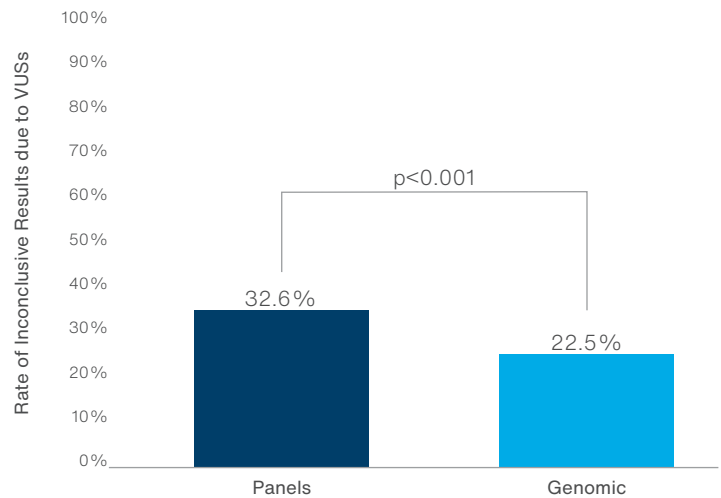
When making decisions about which test to order, the balance between positive yield and VUS rate can be an important consideration.

Many clinicians and payors are cautious about whole exome and genome sequencing (WES/WGS) because of the possibility of a higher VUS rate compared to multi-gene panel (MGP) testing.

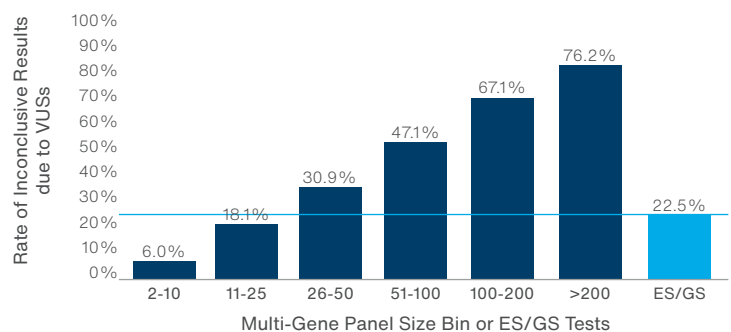
In this multi-institutional study of 1.5 million genetic tests, researchers found that the VUS rate was actually higher and the positive rate was lower in MGP tests compared to genomic testing, especially in the setting of trio-based WES/WGS.

Study investigators suggest that a shift towards WES/WGS as a first tier test may be beneficial for some indications to reduce VUS burden.

VUS rate in MGP is 10% higher than WES/WGS

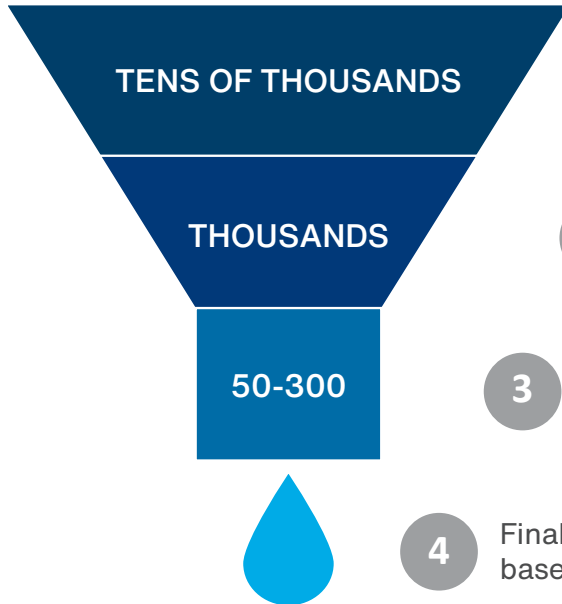


VUS rate for WES/WGS similar to 25 gene panel



HOW DOES ES/GS MAXIMIZE POSITIVES AND LIMIT VUS?

Ambry uses genotype-first filtering, which protects pathogenic and reduced penetrance variants, lowering the false negative rate. Through our Classifi program, we reduce the chance of uncertain results and focus on the most relevant details for your patient.

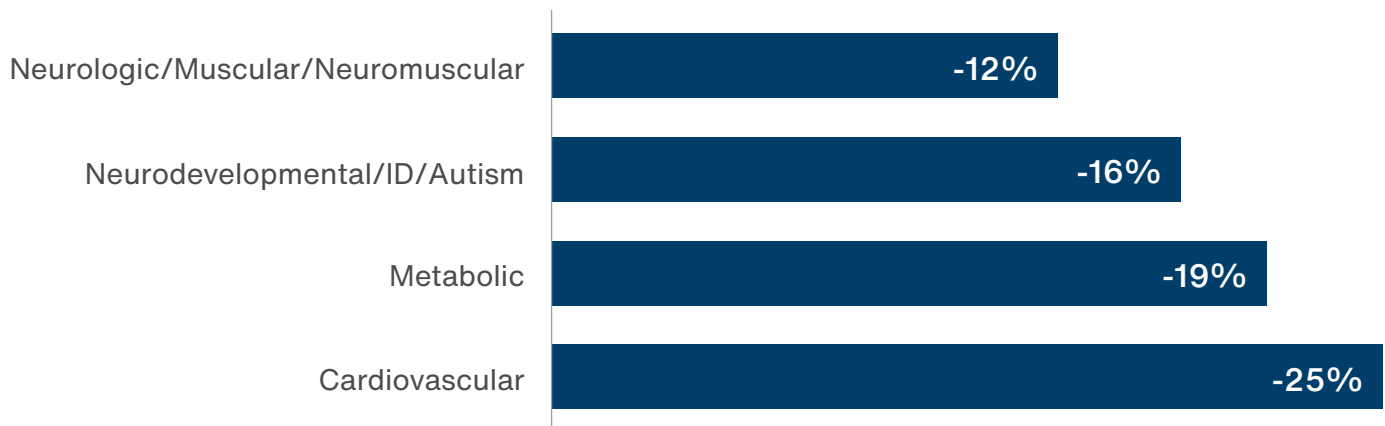


- 1 All variations detected are compared to reference genome
- 2 Bioinformatics filters assess the quality of the call; the number of times a base pair was sequenced and the ratio of variant to wild type calls
- 3 Variants seen at relatively high frequencies in population databases are removed; known pathogenic variants are protected
- 4 Final list of variants evaluated by an analyst for clinical relevance based on inheritance, clinical overlap, and variant pathogenicity

THE DIFFERENCE IN VUS RATE VARIES BY TESTING INDICATION

WES/WGS may be especially useful in specific clinical settings.

Decrease in VUS rate in WES/WGS compared to MGP



Genomic based testing has higher positive and lower VUS rates compared to panels

Benefits of WES/WGS were observed across a variety of indications

These data support a shift towards WES/WGS as a first-tier test