

DMD testing in males unknown to have a dystrophinopathy – A retrospective analysis from a sponsored DMD testing program



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1. Parent Project Muscular Dystrophy; 2. Revvity Omics

Background

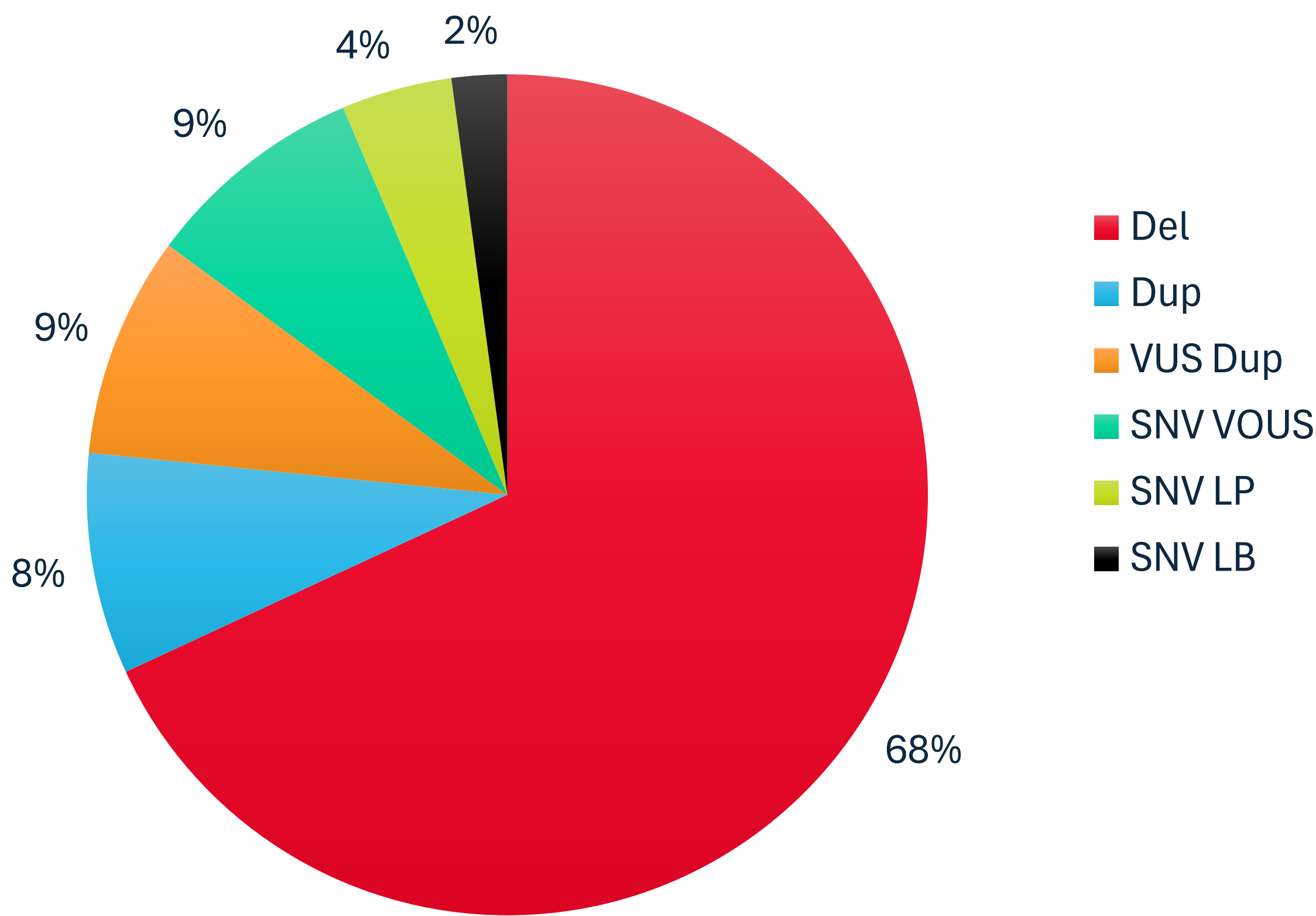
Dystrophinopathies are a spectrum of disorders associated with variants in the *DMD* gene. Historically, confirmatory genetic testing has been completed on those who exhibit a classic clinical picture. However, broader testing, either through familial cascade testing or increased recognition of “milder” phenotypes, seems to be identifying additional hemizygous individuals who receive a diagnosis or possible positive result later in life.

Methods – Retrospective Analysis

Inclusion criteria

- XY male undergoing targeted variant testing through sponsored genetic testing program
- ≥18 years old at the time of testing
- Found to have a *DMD* variant classified as pathogenic or a variant of uncertain significance at the time of reporting
- Not known to have a clinical suspicion or diagnosis of dystrophinopathy

Results – Variant Types and Classifications



- All deletions in-frame
- 38/47 (84%) classified as pathogenic or likely pathogenic

Of 47 individuals meeting criteria, 42 (89%) reported no clinical symptoms

Indication for testing in 25 individuals (53%) was a daughter’s positive test result

Acknowledgements

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# in Cohort	Variant Type	Location	Age Range at Testing
1	Del	E14-16	29
1	Del	E26-44	62
1	Del	E27-29	57
1	Del	E30	68
1	Del	E31-41	69
1	Del	E42-44	35
3	Del	E45-48	23-33 ₃
1	Del	E45-51	28
2	Del	E45-55	45-74 ₃
1	Del	E47	64
1	Del	E47-51	31
2	Del	E48	20-29
1	Del	E48-51	70
4	Del	E48-55	55-69 ₃
1	Del	E49	41
7	Del	E49-51	18-72 ₃
1	Del	E49-55	72
1	Del	E51-52	41
1	Del	E56-59	49
1	Dup	E13	50
1	Dup VUS	E17-30	58
2	Dup VUS	E45-51 ₁	59
1	Dup	E54-74	22
2	Dup/Dup VUS	E55; E55 ₁	48-65
1	Dup	E56-60	61
1	SNV LP	c.30T>A (p.Cys10Ter)	66
1	SNV LP	c.2949+909C>T	21
2	SNV VUS	c.1812+1G>A	37-84
1	SNV VUS	c.1812+2T>A	62
1	SNV VUS	c.10262C>T (p.Ala3421Val)	60
1	SNV LB ₂	c.9749A>C (p.Glu3250Ala)	68

- 1.Suspected or confirmed extragenic dup
- 2.Originally reported as VUS, and later reclassified
- 3.At least one participant reported with symptoms

Symptoms reported included isolated hCK, gait issues, muscle weakness, cardiomyopathy, and other general non-specific cardiac issues

Scan for additional details on the cohort



Conclusion:

- This cohort provides insight into variants identified in individuals who historically may not have been tested for dystrophinopathy.
- Half of the cohort pursued testing following a daughter’s results, which emphasizes the importance of cautious evaluation of variants identified without a family history of dystrophinopathy.
- We look to this new era of testing utilization to further explore the variability of the spectrum, as well as pathogenicity of variants identified on broad screening mechanisms.