

ABSTRACT

Whole exome sequencing (WES) has proven to increase the diagnostic rate of genetic disorders; however, testing can produce uncertainty, regardless of the test result. This study aims to explore the psychological outcomes, specifically uncertainty, that parents may experience when their child has WES for a variety of clinical indications, with varying WES results. Parents of children who had WES at Columbia University Medical Center (CUMC) were contacted for potential enrollment to complete a survey about their experiences with WES. Significant differences in MICRA scores were found between test results on total MICRA scores, distress subscale scores, and uncertainty subscale scores. Parents do experience some degree of uncertainty, and thus psychological impact, when their children undergo WES.

BACKGROUND

The field of genetics and genomics is continuing to expand as technology becomes more accessible in a clinical setting. The development of next-generation sequencing (NGS) created the platform for affordable large-scale genomic sequencing. Whole exome sequencing (WES) uses NGS technology to analyze the coding region (exons) of the 20,000 genes, collectively referred to as the exome. WES is a valuable technique that has led to improved genetic diagnostic rates, which will potentially impact the time to development of novel therapeutic methods. Despite the increasing use of WES in clinical genetics, little research has focused on the psychological impact of WES on patients and their families. There are many factors that contribute to the psychological outcome of individuals undergoing genetic testing, including uncertainty. Uncertainty can arise from WES through many different outlets. Although a positive result will lead to a diagnosis, the condition may be newly discovered, which will leave the individual with uncertainty in regards to the course of the condition and prognosis. If a negative test result is identified, the individual remains on their diagnostic odyssey and the underlying cause of the condition remains uncertain. Finally, if a variant of unknown significance (VUS), or variant that is unknown if it is disease causing or not, is identified, uncertainty presents for both the patient and the provider.

OBJECTIVES

We aim to identify if parents of children undergoing WES for a variety of clinical indications experience uncertainty, and the degree to which WES diagnostic testing impacts them psychologically. It is predicted that these parents will experience some degree of uncertainty regardless of the test result, and that there will be some differences in uncertainty between test results.

METHODS

This study population is a retrospective population, comprised of parents of pediatric patients who had previously been evaluated at Columbia University Medical Center (CUMC) and had undergone clinical WES testing. Participants were identified through an existing clinical database of all patients who received WES results at CUMC from April 2012 to October 2015. This study only examines information regarding the psychological impact of WES from the Multidimensional Impact of Cancer Risk Assessment (MICRA) Questionnaire, adjusted to capture the experience of all types of genetic test results. The scale is divided into three subscales, which measure distress, uncertainty, and positive experiences. Higher MICRA scores indicate higher test specific distress.

RESULTS

Three hundred seventy-eight unique individuals were invited to participate in the study and 370 parents consented to complete the survey, from 184 unique families. Two hundred eighteen surveys were completed from 124 unique families for a response rate of 59% of consented individuals and a consented family response rate of 67%.

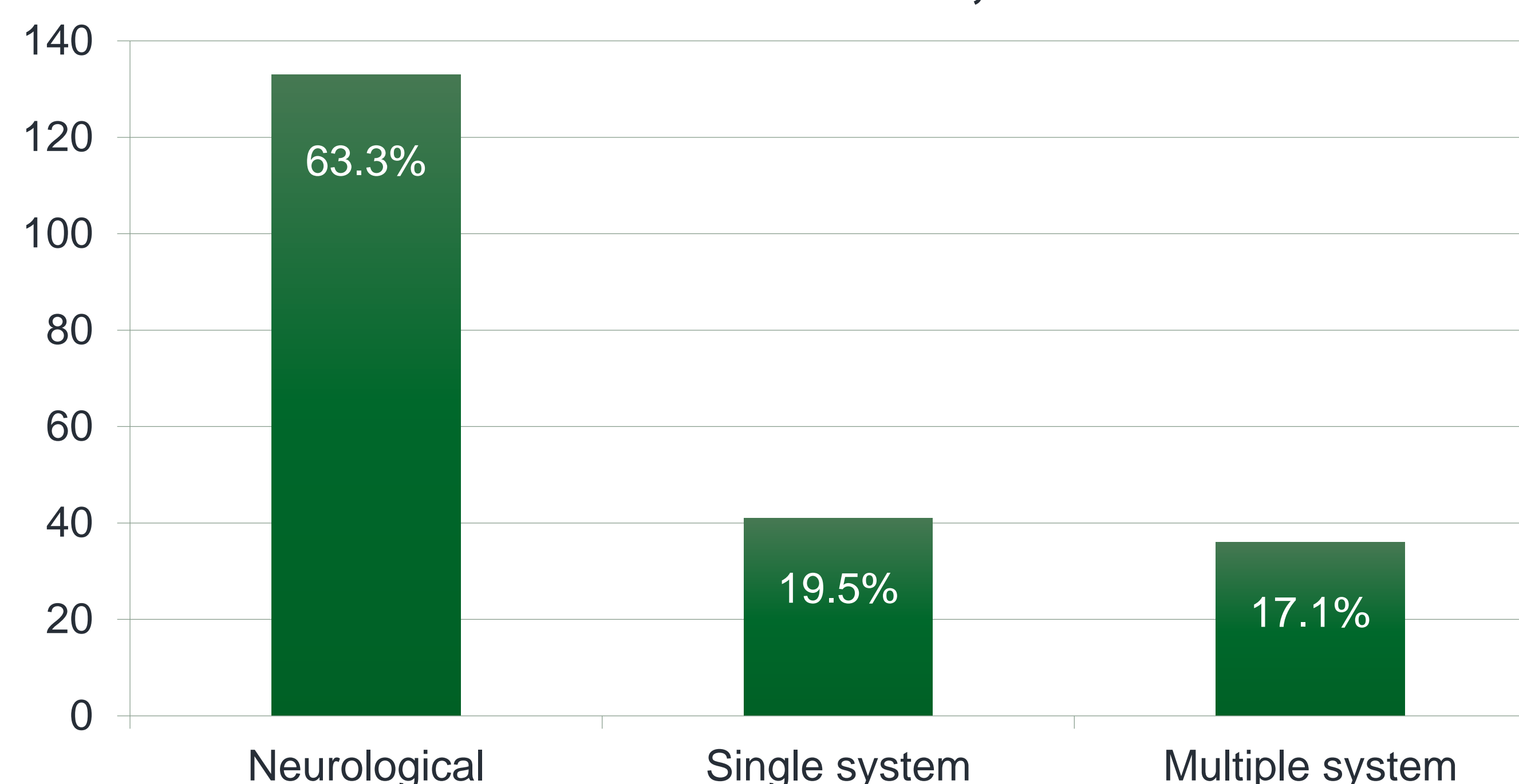
After exclusion criteria (incomplete surveys) were applied, results from 210 surveys were analyzed for this study. The majority of the participants were female (67.6%), married (84.3%), white non-Hispanic (76.7%), college educated (69.2%), and employed (68.1%). The mean age of the participants was 39 (range 20 – 67) years.

Raw mean scores of MICRA Questionnaire

	No. of items	Group 1	Group 2	Group 3	Total
		M (SD)	M (SD)	M (SD)	M (SD)
Distress	6	14.05 (8.97)	5.71 (6.61)	8.21 (7.07)	9.70 (8.54)
Uncertainty	9	13.32 (11.71)	6.98 (7.47)	9.54 (7.96)	10.12 (9.71)
Positive Experiences	4	8.23 (5.18)	7.71 (6.36)	9.20 (4.89)	8.31 (5.54)
Total	25	45.26 (25.37)	27.05 (17.34)	33.58 (15.58)	35.75 (21.94)

M = mean; SD = standard deviation; Group 1 = positive WES results; Group 2 = negative WES results; Group 3 = uncertain WES results. Because of a small amount of missing data, not all cells have the same sample size

Indications for referral, n = 210



One-way ANOVA of test results by MICRA scores

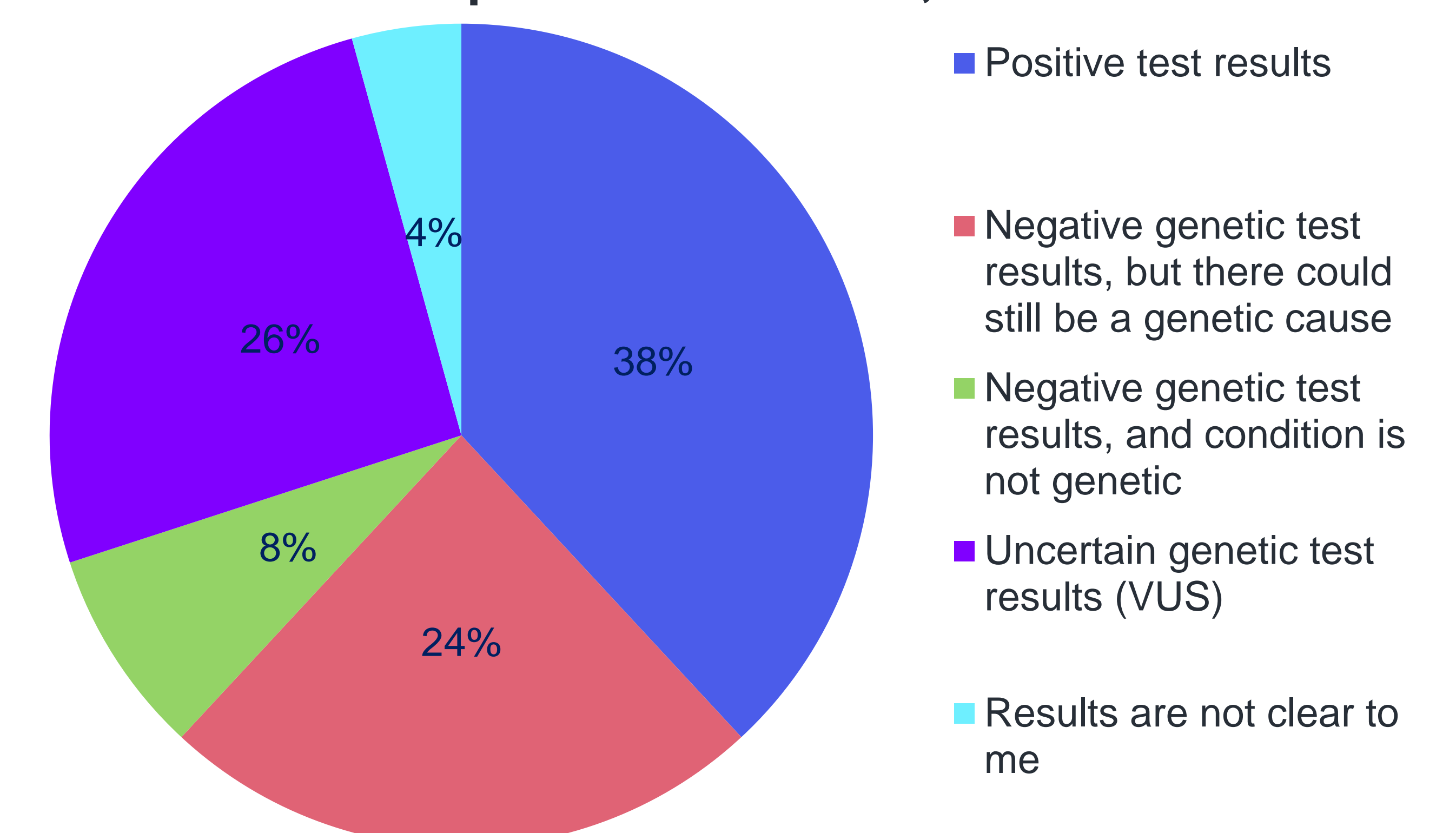
	F	p
Total MICRA	13.27	<0.001
Distress subscale	21.92	<0.001
Uncertainty subscale	7.99	<0.001
Positive experiences subscale	1.04	0.35

RESULTS

Post hoc Tukey tests

	p
Total MICRA scores between positive and negative results	<0.001
Total MICRA scores between positive and uncertain results	<0.001
Distress scores between positive and negative results	<0.001
Distress scores between positive and uncertain results	<0.001
Uncertainty scores between positive and negative results	<0.001

Self-reported test results, n=210



CONCLUSIONS

Significant differences were found among groups when looking at total MICRA scores, distress scores, and uncertainty scores. Individuals who reported a positive WES result had significantly higher MICRA scores than the individuals who reported a negative result and an uncertain result. When looking at the distress and uncertainty subscales, significantly higher scores were found among individuals who reported a positive result than individuals who reported a negative result. Parents who reported receiving a positive result showed the greatest amount of psychological impact from WES when examining total and subscale scores. The increased psychological impact from a positive WES result may be attributed to many sources and further research is needed to identify this. These results demonstrate that genetic counselors and other health providers should be cognizant of the potential impacts WES testing has on parents. Understanding the risk for psychological impact could help better prepare parents cope with the uncertainty that WES may bring and potentially lower overall psychological impact from testing.

ACKNOWLEDGEMENTS

- Long Island University – Post Genetic Counseling Graduate Program
- Columbia University Medical Center, Division of Molecular Genetics