



## Short Communication

## Genetic testing experiences and genetics knowledge among families with inherited metabolic diseases

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## ABSTRACT

We surveyed individuals with inherited metabolic diseases (IMDs) or their caregivers to explore experiences with genetic testing. Pursuit of knowledge, benefit to science, clinician recommendations, cascade testing, and cost were important considerations for pursuing genetic testing. Knowledge about inheritance patterns was limited, even for those who had received genetic testing. Future studies should further examine knowledge of IMDs and genetic testing among families, and factors that impact clinicians' decisions to offer genetic testing for IMDs.

## 1. Introduction

Inherited metabolic diseases (IMDs) are genetic disorders which affect the way nutrients are metabolized. Although biochemical testing is standard of care for the diagnosis and management of IMDs, practice guidelines and publications support an increasing role for genetic testing. Genetic testing for IMDs may be recommended to confirm diagnosis [1], inform treatment [2], or to inform the individualized treatment [3]. Identification of pathogenic genetic variants can also impact the broader family [4–6], including the feasibility of carrier testing [7]. Despite these recommendations, only approximately two-thirds of individuals with an IMD report having received genetic testing with testing rates varying across condition, ranging from 34% to 100% [8]. Genetic testing should be accompanied by genetic counseling to ensure appropriate informed consent prior to testing, comprehension of test results, and understanding of implications for medical care and genetic risk of other family members [9–11].

## 2. Materials and methods

This study surveyed individuals with an IMD, or their parents or caregivers, in the United States. This project was approved by the Emory University Institutional Review Board. Participants were recruited from, the 2018 National Maple Syrup Urine Disease (MSUD) Family Support Group Symposium and the National Phenylketonuria (PKU) Alliance Conference. Additional participants were recruited from the Newborn Screening (NBS) Connect patient registry [12] until 50 completed surveys were received. All survey responses were

anonymous and not linked to the registry data. At the time of the survey, the NBS Connect Registry focused primarily on MSUD, PKU, and tyrosinemia, and included 585 registrants.

Survey questions included demographics, if genetic testing had been obtained or offered, whether or not insurance covered the cost of testing, satisfaction with decision to receive genetic testing, sharing genetic testing results with family members, reasons for choosing not to share results with family members, carrier testing of family members, and knowledge of autosomal recessive inheritance.

A *t*-test was used to compare the difference in genetic knowledge test scores between those who received genetic testing and those who had not received or were unsure if they received genetic testing, and fisher's exact test was used to compare the frequency of correct answers for each question between the two groups. A *p*-value threshold of 0.05 was used to indicate statistical significance, with no correction for multiple comparisons.

## 3. Results

The survey was completed by 50 individuals: 15 from the MSUD Family Support Group Symposium, 12 from the National PKU Alliance Conference, and 23 from the NBS Connect Registry. Of the 50 respondents, 13 were adult individuals with an IMD and 37 were parents or caregivers. The diagnoses of the affected person were: PKU (46%), MSUD (42%), tyrosinemia (4%), other (6%), and not listed (2%). In total, 27 (54%) of the individuals with an IMD had received genetic testing, 19 (38%) had not received genetic testing, and four (8%) were unsure.

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Of the 19 participants who had not received genetic testing, four reported that they had been offered genetic testing and 13 reported that they were interested in genetic testing. Two participants had insurance coverage for genetic testing, four had insurance that would not cover genetic testing, and the remainder were unsure of their coverage. The most commonly reported factor in deciding not to have genetic testing was “concern about the financial cost of genetic testing,” which was endorsed by 57.8% of participants who had not received genetic testing.

Among the 27 individuals who had received genetic testing, the most commonly endorsed factor affecting their decision was “knowledge” (94.7%). Other factors supporting testing included “recommended by doctor” (78.9%), “results may impact the affected person's treatment options” (78.9%), “benefit to science” (78.9%), and “benefit to future generations” (73.7%). Of those who received genetic testing, 17 reported that they shared the results with family members, six had not shared results, three were unsure, and one did not answer. Of those who had not shared their results with family, the reasons given included: did not have access to results ( $n = 4$ ), believed that their relatives already understood their carrier risk ( $n = 3$ ), not close to or do not speak to relatives ( $n = 2$ ), did not believe relatives are at risk ( $n = 1$ ), told by relatives that they already understand their risk ( $n = 1$ ), and relatives did not want to know the information ( $n = 1$ ). Eight participants indicated that unaffected members of the family had received genetic carrier testing.

Forty-five participants with a personal or family history of the autosomal recessive conditions MSUD, PKU, or tyrosinemia answered the knowledge of genetics questions (Table 1). Among those who had experience with genetic testing for an IMD, the score on the genetic knowledge quiz ranged from 0 to 83.3%, with a mean of 54.3%. Among those who had not received genetic testing for an IMD or did not know, the score ranged from 33.3% to 83.3%, with a mean of 52.3%. There was no statistical difference between the two groups in total score ( $p = 0.7961$ ), or in the frequency of correct answers for each question (Table 1).

#### 4. Discussion

While cascade testing was important to the families in this study, knowledge about the carrier probability of extended family members was limited. In our analysis of genetic knowledge, most answered Q1 and Q2 correctly, indicating an understanding of the basic concepts of parental carrier status and recurrence probability for a subsequent pregnancy. However, fewer correct responses were received for the more nuanced questions about inheritance patterns (Q4 and Q5). Correct answers for these two questions assumed full sibship, so individual responses may have been skewed if they based their answers

**Table 1**  
Percent of participants who answered each genetic knowledge question correctly.

Question	Percent Correct Responses		P-value
	Have received genetic testing ( $n = 26$ )	Have not received genetic testing or do not know ( $n = 19$ )	
Q1. If a child has an inherited metabolic disorder such as PKU, MSUD or tyrosinemia, then parents are carriers of the disorder. (True/False)	92%	95%	1
Q2. If two carriers have a child together, what is the chance that the child will be affected? (multiple choice)	88%	100%	0.2515
Q3. If an affected individual has a child with a carrier, what is the chance that the child will be affected? (multiple choice)	42%	58%	0.3726
Q4. Unaffected brothers and sisters of a child with a metabolic disorder have a ___ chance of being a carrier. (multiple choice)	15%	5%	0.3783
Q5. Brothers and sisters of a carrier have a ___ chance of also being a carrier. (multiple choice)	23%	47%	0.1158
Q6. If no mutations are found during genetic testing, then the child does not really have the disorder. (True/False)	46%	42%	1

on other family structures. Other limitations of this study include our inability to verify whether or not genetic testing took place. Also, genetic testing is not always accompanied by adequate patient education, and we did not ask if genetic counseling had been received.

Further investigations should evaluate individual knowledge of IMDs and genetic testing more deeply, including how this knowledge influences decisions among individuals with IMDs and their families. Additional research also is needed to understand factors that impact clinicians' decisions to offer genetic testing for IMDs and whether benefits outside of clinical utility are considered (e.g., knowledge, cascade testing of family). It also is not known how many families with IMDs have been counseled about the potential benefits and risks of genetic testing, although a study by Stein and colleagues found that genetic counseling rates were high among families with IMDs [8]. While our study focused on families with IMDs, expanded carrier screening programs that include genes for IMDs leads to the identification of additional families in need of genetics education.

Further research also is needed to clarify who provides education around genetic disorders and testing, what type of genetics education families with IMDs receive, and when they receive counseling. Ideally, patient education about genetics should be an ongoing process, rather than limited to pre- and post-genetic testing counseling, and may include innovative approaches beyond traditional in-person genetic counseling sessions, such as web-based education for both clinicians [13] and patients [14].

#### 5. Conclusions

In conclusion, drivers that influence of genetic testing among adults with IMDs and parents/caregivers of affected minors include the desire for knowledge, a benefit to science, recommendations by doctors and cascade testing. Financial considerations can be a barrier to genetic testing. While participants demonstrated knowledge about the basics of recurrence risk, they were less likely to correctly answer questions about the more nuanced aspects of carrier probability among family members. Genetic counselors can play a key role in educating clinicians and supporting family decision making about genetic testing with discussions of clinical utility and education about carrier probabilities for other family members.

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