Preferences for Genetic Tests: Trading off Speed of Diagnosis, Availability of Treatment, and Cost

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OBJECTIVES

- Rare diseases can be difficult to diagnose, and the diagnosis can take years and involve multiple doctors and invasive diagnostic testing[1,2]
- Pompe disease is an inherited neuromuscular disease caused by mutations in the acid alpha-glucosidase (GAA) gene or a deficiency in the GAA enzyme that leads to the accumulation of glycogen in the patient's muscle tissue[3]
- Discovery of the GAA (glucosidase alpha, acid) gene has advanced the treatment of Pompe disease and introduced the possibility of genetic testing to allow for earlier diagnosis of Pompe disease
- Genetic testing can provide significant benefits to patients with rare diseases, and there is a need for patients, physicians, and other stakeholders to understand the benefits of genetic tests
- This study evaluates the relative importance to patients of the features of genetic tests for rare muscle weakness diseases

METHODS

Study Design

- We designed an online discrete-choice experiment (DCE) survey with six test attributes (see Table 1)
  - Attributes and levels used in the DCE were based on genetic tests for Pompe disease and adapted to represent a broader set of genetic tests
  - The survey instrument was pretested in 15 semistructured, face-to-face interviews
- Respondents were asked to assume they were experiencing unexplained muscle weakness and were offered choices between pairs of hypothetical diagnostic genetic tests (Figure 1)
- A follow-up question presented a choice between two tests defined by the DCE attributes but with different costs (not included in the DCE questions); respondents were randomly assigned to one of two cost ranges (see Table 2)

Table 1. Attributes and Levels for the Choice Questions

Attribute	Level
Number of rare muscle diseases tested for (chance of getting a final diagnosis from the test)	100 diseases (60% chance) 34 diseases (30% chance) 1 disease (5% chance)
Treatment availability for diseases covered by the test[a]	Treatment is available for 100 diseases Treatment is available for 34 diseases Treatment is available for 1 disease Treatment is not available
Time until results from the test	1 month 2 months 6 months
Test results may contain information about unrelated health risks	Yes No
A muscle biopsy is needed to confirm results	Yes No
Average time until final diagnosis, if the first test is negative	2 years 4 years 7 years

[a] The experimental design was created using 3 levels: treatment is available for all diseases tested for by the genetic test, treatment is available for 1 of the diseases tested for by the genetic test, and treatment is not available for any of the diseases tested for by the genetic test. The text in the survey instrument used the 4 levels listed in Table 1. For example, if the number of rare muscle diseases tested for was 34 and treatment availability for diseases covered by the test was "all," respondents saw "Treatment is available for 34 diseases."

Figure 1. Example of Choice Question

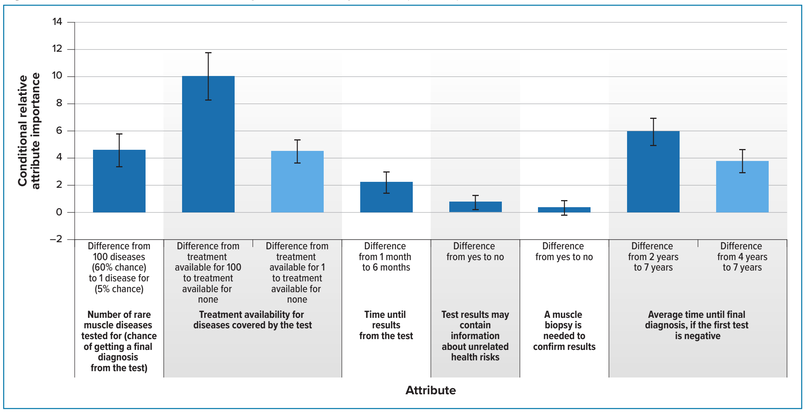
Test Feature	Start With Genetic Test A	Start With Genetic Test B
Number of rare muscle diseases tested for	1 disease	34 diseases
Chance you get a final diagnosis from the test	5 out of 100 people (5%)	30 out of 100 people (30%)
Time until you get results from the test	1 month	6 months
Treatment available for diseases covered by the test	Treatment is available for 1 disease	Treatment is available for 34 diseases
Test results may contain information about unrelated health risks	No	Yes
A muscle biopsy is needed to confirm results	Yes	No
If the first test is negative: Average time until you get a final diagnosis after testing for more diseases	**2 years** and unknown if treatment available for the final diagnosis (will be true for 95% of people who did not get a diagnosis from the first test)	**4 years** and unknown if treatment available for the final diagnosis (will be true for 70% of people who did not get a diagnosis from the first test)
Which test would you choose?	○	○

DATA ANALYSIS

- Choice data were analyzed using random-parameters logit (RPL)[4]
- RPL results were used to calculate relative preference weights for each attribute level
- Preference heterogeneity was further explored using subgroup analysis to compare men and women
- RPL estimates were used to calculate predicted-choice probabilities for the average respondent selecting one hypothetical genetic screening test over another, based on the genetic test profiles presented in Table 2, without cost
- Predicted-choice probabilities for test profiles in Table 2 were compared with the percentage of the sample that selected each profile when cost was included in the survey instrument

RESULTS

Figure 2. Conditional Relative Attribute Importance for Respondents (N = 600)



Note: The vertical bars surrounding each relative importance weight estimate denote the 95% confidence interval (computed by the delta method). Reducing the chance of long-term health complications by 50% is set to 10, and the relative importance of each of the other attributes is scaled relative to the conditional importance of this attribute

Sample

- 600 adults aged 18 to 50 years were recruited from the general population through an online panel
- The average (standard deviation) age of respondents was 36.6 (10.2) years, and 51.5% of the sample were female
- One-quarter of the sample (24.8%) had ever had a genetic test of any kind
- 86.7% of the sample had heard of genetic testing before taking the survey

Preference Results

- Respondents preferred tests that included more diseases with a higher probability of diagnosis, tests for diseases with treatments, tests that might provide information about unrelated health risks, and faster diagnosis
- Figure 2 shows the conditional relative attribute importance of changing each attribute from the least-preferred level to the most-preferred level, as well as change between intermediate levels for a test that included at least one disease with a treatment compared with a test for disease(s) with no treatment and an increase from 4 years to 7 years in the average time to final diagnosis if the first test is negative
- Over the ranges presented in the survey, the relative importance of the largest change in each attribute from most to least important was as follows
  - The difference between a test where no treatments are available compared with a test for 100 diseases with treatment for all diseases
  - Reducing time until final diagnosis by 5 years, if the first test is negative
  - The difference between a test for one disease (5% probability of diagnosis) and a test for 100 diseases (60% probability of diagnosis)
  - A 5-month decrease in the time until results from the first genetic test are available
  - A test that might contain information about unrelated health risks
  - Whether the test needed a muscle biopsy was not statistically significantly different from zero, indicating that it did not have an impact on choice relative to the other attributes
- Looking at changes between intermediate levels, the relative importance of a test that included at least one disease with a treatment compared with a test for disease(s) with no treatment was as important as the relative importance of testing for 1 disease compared with testing for 100 diseases
- Similarly, an increase from 4 years to 7 years in the average time to final diagnosis if the first test is negative was about two times more important than the increase from 1 month to 6 months in the amount of time it takes to get the results from the test

Subgroup Analysis

- Compared with women, men placed relatively more importance on tests for diseases with treatments
- Women had a statistically significant higher preference for tests that might provide unrelated health information compared with tests that would not, while men were indifferent

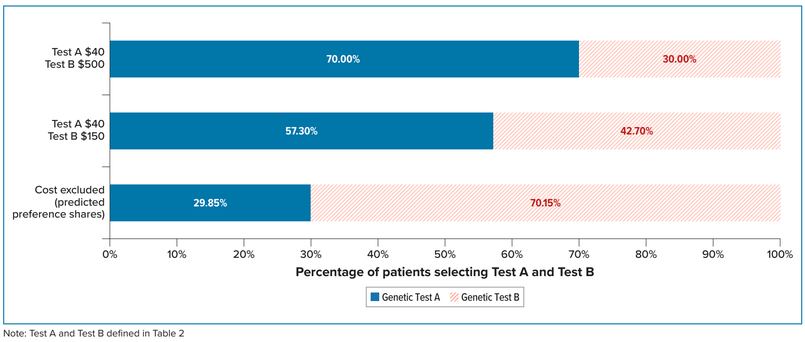
Predicted-Choice Probabilities and the Impact of Cost on Choice

- Figure 3 compares predicted preference shares for the profiles in Table 2 with the proportion of people who selected Test A or Test B in the question that included cost
- The model predicts that the average respondent in the sample has a 70% probability of selecting Test B when cost is not included
- When asked to select between Test A and Test B in Table 2 but including cost, 43% of respondents selected Test B when Test B cost $150 and Test A cost $40, while 30% of respondents selected Test B when Test B cost $500 and Test A cost $40
- Respondents were sensitive to cost, but 30% of the sample assigned to the highest cost were willing to pay $500 for a test that provided a diagnosis almost 2 years earlier

Table 2. Profiles for Preference Share Prediction With Cost

Attribute	Genetic Test A	Genetic Test B
Number of rare muscle diseases tested for (chance of getting a final diagnosis from the test)	1 disease (5% chance)	34 diseases (30% chance)
Treatment availability for diseases covered by the test	Treatment is available for 1 disease	Treatment is available for 1 disease
Time until results from the test	2 months	6 months
Test results may contain information about unrelated health risks	No	No
A muscle biopsy is needed to confirm results	No	Yes
Average time until you get a final diagnosis, if the first test is negative	4 years	2 years
Cost (only included in direct choice question presented after DCE)	$40	$150/$500 (respondents randomly assigned to one cost)

Figure 3. Probability of Selecting Test A and Test B (N = 600)



Note: Test A and Test B defined in Table 2

CONCLUSIONS

- Overall, respondents preferred tests that tested for more diseases and had a higher probability of diagnosis, tests for diseases that had treatments available, and tests that led to a final diagnosis sooner
- The results from this survey serve as a starting point for additional research on the value of genetic testing for other populations and for other conditions, including conditions for which there is no treatment
- The results support a desire for faster diagnosis of rare, unexplained muscle weakness and diagnosis of diseases with treatments. Faster diagnosis can provide earlier access to treatment and an end to the diagnostic journey, which patients highly value

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