Case Study on Neurological degenerative disease - Preference study perspective

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## Patient preference information guidance

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Special aspects of case study

• **Existing product**
  - Tailor the instrument to the product’s benefits and risks
  - Ensure instrument is broad enough to be meaningful outside narrow scope of the existing product

• **Progressive disease**
  - Include patients at different levels of progression
  - Instrument needs to be relevant for patients at different levels of progression

• **Cognitive impairment**
  - Balance between cognitive burden and benefit-risk relevance
  - Consider strategies to elicit preferences of patients in late stages of disease
Protecting Health, Saving Lives—
Millions at a Time
Patient-Preference Information
FDA-CERSI Collaborative Workshop:
December 7, 2017
Silver Spring, MD

Neurodegenerative Disease Case Study
Research Approaches to Generating
Patient Preference Data

Ira Shoulson MD
Karen E Anderson MD
Georgetown University Medical Center
Washington, DC
http://regulatoryscience.georgetown.edu
Patient Preference
Research Approaches

• Clinical experience (anecdotal)
• Focus groups and longitudinal research platforms (transcription, qualitative analysis, natural language processing, machine learning)
• Choice, tradeoff, and allocation preferences
• Clinical trials
Neurodegenerative Diseases: Patient Preferences

• Neurodegeneration does not affect single domain or function (motor, cognition, behavior); multiple outcomes and maintenance of functional capacity are most relevant and clinically meaningful.

• Genetic risk factors are key in assessing preferences of unaffected individuals at high genetic risk as well as affected patients and their family members

• Demographics, education, health literacy, numeracy, and socioeconomic status help inform how genetic risk and covariates influence preferences and tradeoffs for experimental therapeutic risks and benefits

• ‘Informed’ consent is more nuanced than ‘can’ or ‘cannot’
HUNTINGTON DISEASE

- Movement Disorders
- Cognitive Impairment
- Behavioral Disorders

Expanded CAG$_n$ (polyglutamine repeats) on Chromosome 4

- Genetic Etiology
- Selective Neuronal Degeneration
- Brain Phenotype & Pathogenesis

Clinical Consequences
- Clinical Phenotype
Clinical Precursors and Manifest Huntington’s Disease (HD)

HD Gene Positive (Expanded CAGₙ)

HD Gene Negative (Non-expanded CAGₙ)

HD Gene Expression

clinical precursors of HD

Manifest HD

HD Diagnosis

Birth

development

Death
Huntington Disease Respondent Groups for Risk-Benefit Preferences: Genetic Risk and Clinical Characteristics

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<tr>
<th>Respondent Groups</th>
<th>Sample Size</th>
<th>Genetic Risk</th>
<th>Manifest HD Symptoms / Signs</th>
<th>Current Opportunities for HD Clinical Trial Participation</th>
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<tr>
<td>1. Adult HD patients, early stages 1-3 of illness</td>
<td>N=30</td>
<td>100%</td>
<td>Mild-Moderate</td>
<td>Widely Available</td>
</tr>
<tr>
<td>2. Clinically unaffected adults, unknown gene status</td>
<td>N=20</td>
<td>50%</td>
<td>Subtle or Absent</td>
<td>Under Development</td>
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<td>3. Clinically unaffected adults who carry HD gene (DNA tested)</td>
<td>N=20</td>
<td>100%</td>
<td>Subtle or Absent</td>
<td>Under Development</td>
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<td>4. Clinically unaffected adults who do not carry HD gene (DNA tested)</td>
<td>N=20</td>
<td>0%</td>
<td>Absent</td>
<td>N.A.</td>
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<td>5. Adult family members or care partners</td>
<td>N=20</td>
<td>0%</td>
<td>Absent</td>
<td>N.A.</td>
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Computer Adaptive Testing:
Preferential Allocation of a Fixed Number of Tokens
(low valence)

Assume you have inherited the HD gene expansion, so you know you will get HD in the future, but you have no symptoms now.

You have the option of taking a research drug intended to delay onset of uncontrollable movement or thinking difficulties.

But the research drug may cause some side effects, such as dizziness (which may make it difficult to drive), nausea (which may make it difficult to eat), or anxiety (which may be uncomfortable for yourself or others).

In this situation, what is most important to you?
Assign all your nine tokens among the choices below:

- Delay uncontrollable movements
- Delay thinking difficulties
- Avoid dizziness
- Avoid nausea
- Avoid anxiety
(Prototype Question)

Computer Adaptive Testing:
Preferential Allocation of a Fixed Number of Tokens
(high valence)

Assume you have inherited the HD gene expansion, so you know you will get HD in the future, but you have no symptoms now.

You have the option of taking a research drug intended to delay onset of uncontrollable movement or thinking difficulties.

But the research drug may cause some potentially serious side effects, such as permanent liver damage (potentially leading to death), blindness, or earlier onset of illness that might otherwise occur.

In this situation, what is most important to you?

Assign all your nine tokens among the choices below:

- Delay onset of movements
- Delay onset of thinking
- Avoid permanent liver damage
- Avoid blindness
- Avoid earlier onset of illness
Patient Preference Study: Focus Group Considerations

• Achieving benefit and avoiding adverse effects
• Are benefits and risks temporary/fleeting or persistent/enduring?
• Patients facing progressive (fatal) decline are often more willing to choose and prefer major risks, especially if perceived as temporary and seemingly reversible
• Loss of independence is great fear; maintenance of functioning and independence are key outcomes
• Patient-Preference Information (PPI) should be more appropriately viewed as Patient-Preference Data (PPD)