Case Study on Neurological degenerative disease

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Preference study perspective

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Patient preference information guidance

Study qualities:

Study sample	Study design	Study conduct and analysis
Well-informed patients	Questions are meaningful and relevant to patients	Well-documented instrument development process and study conduct
Representative sample for generalizable results	Minimize cognitive bias	Logical soundness
Capturing heterogeneity	Effective benefit-risk communication	Robustness of study results
	Demonstrated comprehension by patients	

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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*

JOHNS HOPKINS
BLOOMBERG SCHOOL
of PUBLIC HEALTH

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

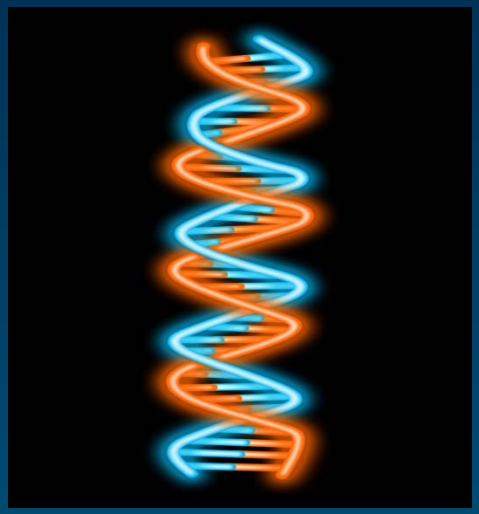
Patient Preference Research Approaches

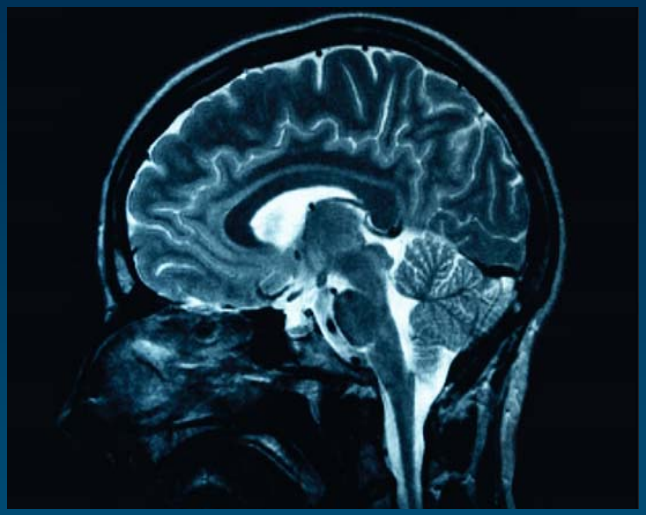
- Clinical experience (anecdotal)
- Focus groups and longitudinal research platforms (transcription, qualitative analysis, natural language processing, machine learning)
- Choice, tradeoff, and allocation preferences
- Clinical trials

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

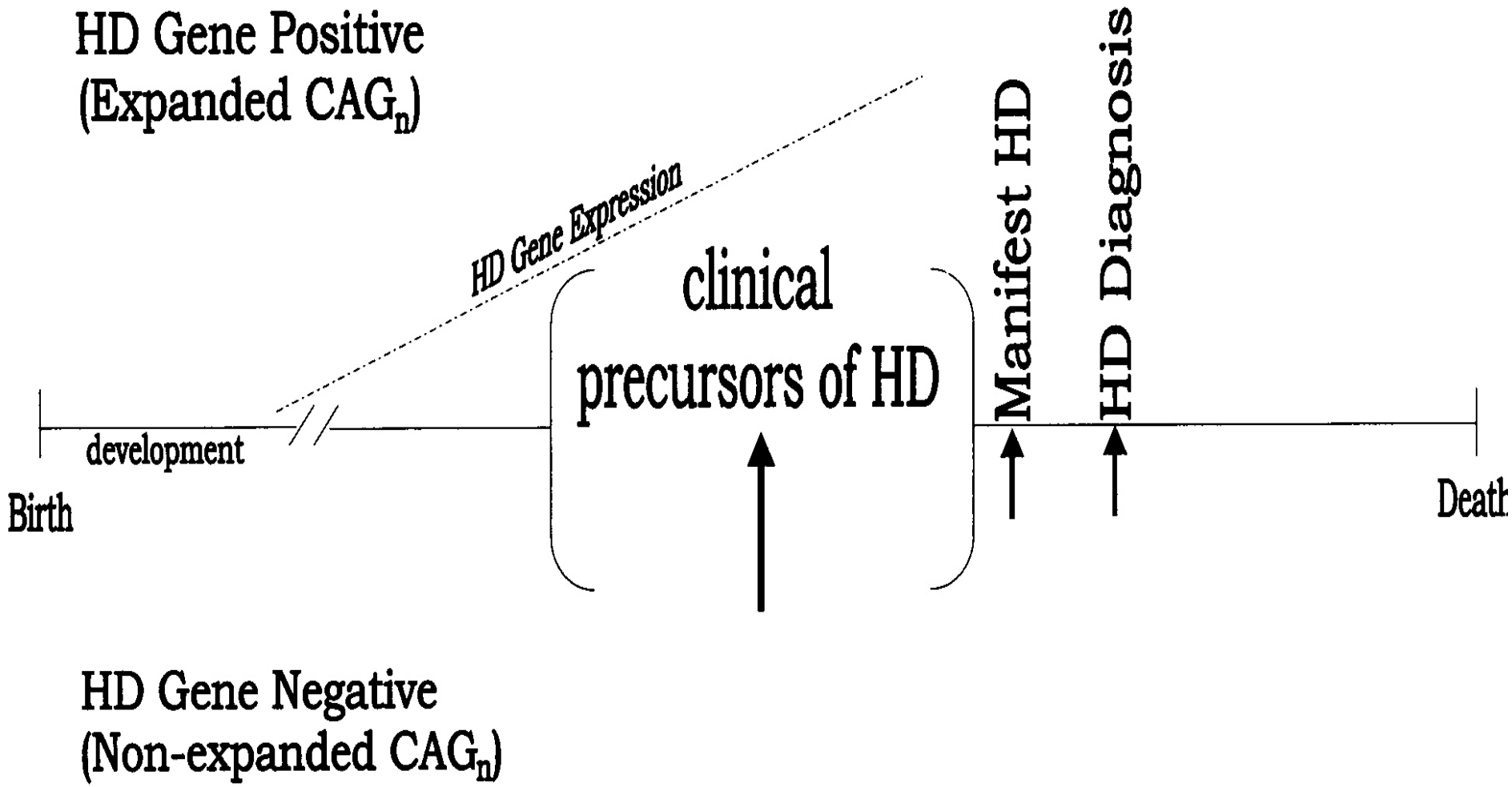
Selective Neuronal Degeneration

Brain Phenotype & Pathogenesis

Clinical Consequences

Clinical Phenotype

Clinical Precursors and Manifest Huntington's Disease (HD)



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

Respondent Groups	Sample Size	Genetic Risk	Manifest HD Symptoms / Signs	Current Opportunities for HD Clinical Trial Participation
1. Adult HD patients, early stages 1-3 of illness	N=30	100%	Mild-Moderate	Widely Available
2. Clinically unaffected adults, unknown gene status	N=20	50%	Subtle or Absent	Under Development
3. Clinically unaffected adults who carry HD gene (DNA tested)	N=20	100%	Subtle or Absent	Under Development
4. Clinically unaffected adults who do not carry HD gene (DNA tested)	N=20	0%	Absent	N.A.
5. Adult family members or care partners	N=20	0%	Absent	N.A.

(Prototype Question)

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)