Why CHDI reached out to C-Path

- or -

How learning to play chess can inform efforts to bring effective treatments for HD to patients

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evotec

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Psychogenics

Redefining Drug Discovery Through Innovation
## Acknowledgements

<table>
<thead>
<tr>
<th>Science</th>
<th>Admin</th>
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<tbody>
<tr>
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<td>Ruth Basu</td>
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<tr>
<td>Cristina Sampaio</td>
<td>David Rankin</td>
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<td>Celia Dominguez</td>
<td>Eileen Neacy</td>
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<td>Ignacio Munoz-Sanjuan</td>
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<td>Thomas Vogt</td>
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<td>Andrew Wood</td>
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Estimates for a group that is all gene-expanded, with CAG lengths known

CAG age Model, 80% power, alpha = .05, 5% annual censoring

Magnitude of Therapeutic Effect

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<th>Years followed</th>
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circa 2004
Guidance for Industry

Qualification Process for Drug Development Tools

Additional copies are available from:
Office of Communication
Division of Drug Information, WO51, Room 2201
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave.
Silver Spring, MD 20993
DBT-HD

Clinical

Surrogate

Pharmacodynamic

Predictive

Prognostic

? ← CAR  → ?

? ← Furt 1.0  → TFC

? ← Furt 2.0  → ?

? ← "Subclinical HD"  → "Clinical HD"

18 yrs  ← Age  → "Disease Border"  → Motor Diagnosis

CHDI
Validation of a Prognostic Index for Huntington’s Disease

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ABSTRACT: Background: Characterizing progression in Huntington’s disease is important for study the natural course and selecting appropriate participants. Components of the index included total motor score, Symbol Digit Modalities Test, baseline age, and cytosine-adenine-guanine expansion. External predictive performance was very good for the
Phenotype progression through States 1 - 9

1. Motor, cognition, GCI + occupation
2. Motor, cognition & GCI
3. Function, SF & Caregiver survey
4. Cognition, motor & function
5. Motor, cognition + MMSE
6. Motor, cognition + MMSE
7. Function, cognition, motor, physio & MMSE
8. Cognition, motor + moderate activities (walking, climbing)
9. Cognition, motor + moderate activities (walking, climbing)

abc: new outcome measures

Distance between states proportional to empirical durations in years
A word on strategy... and hope

10^{20}

10^{120}
Number of half moves played

Expected half moves remaining