



Accelerating therapeutic
development for
Huntington's disease

Success in sharing data from HD natural history studies

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Thought structure

- Rationale for natural history (NH) studies in HD
- HD NH studies
- Evolution of study data
- HD NH data sharing process

- Data application
 - Approach
 - Select findings

- Key takeaways

HD natural history studies : Why?

Guiding clinical development

- Specific challenges
 1. Subtle symptoms, early on
 2. Sparse population
 3. Disease progression & progression biomarkers



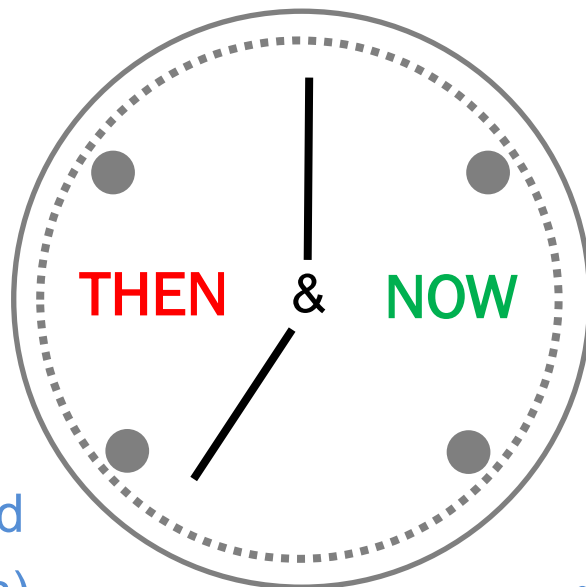
Credit: Rob Sinclair

HD natural history studies

- ~15 studies known so far
 - Enroll-HD largest in terms of participant pool
 - Early studies focused on clinical assessments (e.g. UHDRS)
 - More recent focusing on neuroimaging and molecular measurements



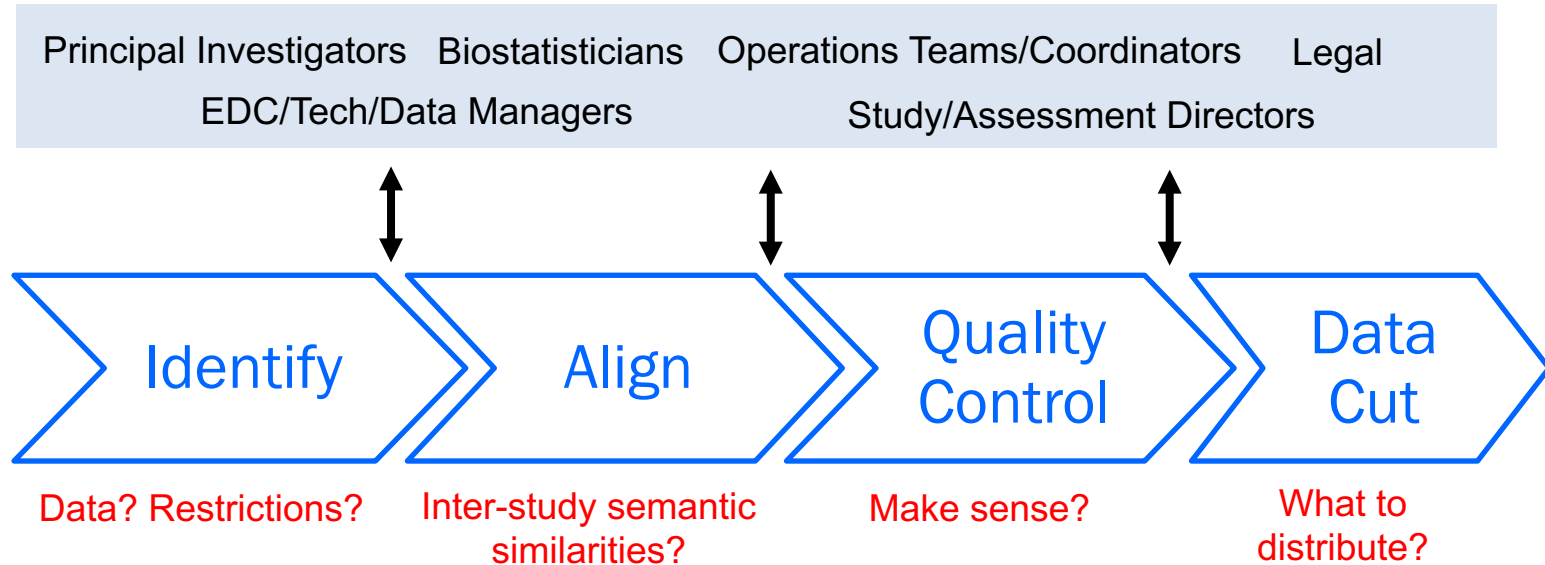
Evolution of study data



- Paper based
- Largely unstructured
- Siloed (no synthesis)
- Smaller studies/fewer measures
 - Simple analysis

- EMR & Big data
- More structured
- On the fly digestion
- Multi-variable studies
 - Patient privacy/de-identification
- Transparency mandates

Preparing to share HD natural history dataset



Duration: 1 – 1.5yrs
Need for data standards

Application

Can we learn about HD progression trajectories?

..covering entire HD gene expansion carrier population



Largest HD natural history Dataset

Cohort study	# Approx. Participants	CAG	Max visits	Mean visits	Motor	Functional	Psychiatric	Cognitive
Enroll-HD	7,500	✓	4	1	✓	✓	✓	✓
Registry-HD	12,000	✓	15	3	✓	✓	✓	✓
Track-HD/ON	450	✓	7	4	✓	✓	✓	✓
PREDICT-HD	1,500	✓	14	5	✓	✓	✓	✓

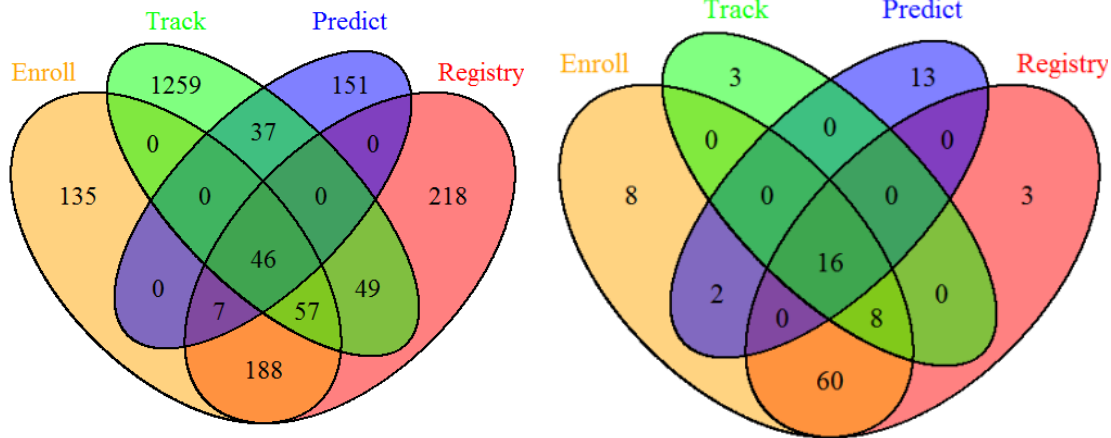


- Criteria

- Large participant base
- Longitudinal visit data
- Clinical assessment data

Characterizing HD-NH Data

Clinical Variables

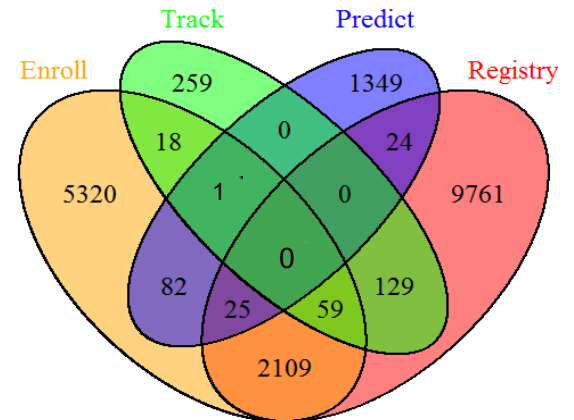


~2000 outcome measurements

~100 fixed measurements

- Shared
- Fixed
 - CAG length, age, gender, BMI, education level, region, subject status, CAP, disease burden score, year to onset
 - Shared Outcomes
 - UHDRS Motor, Functional, SDMT, SWRT, Trail making, among others

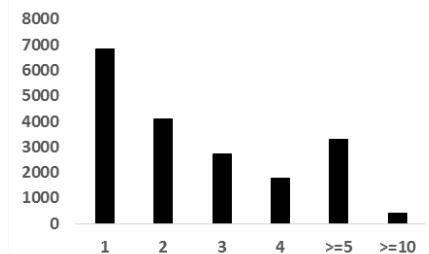
Participants



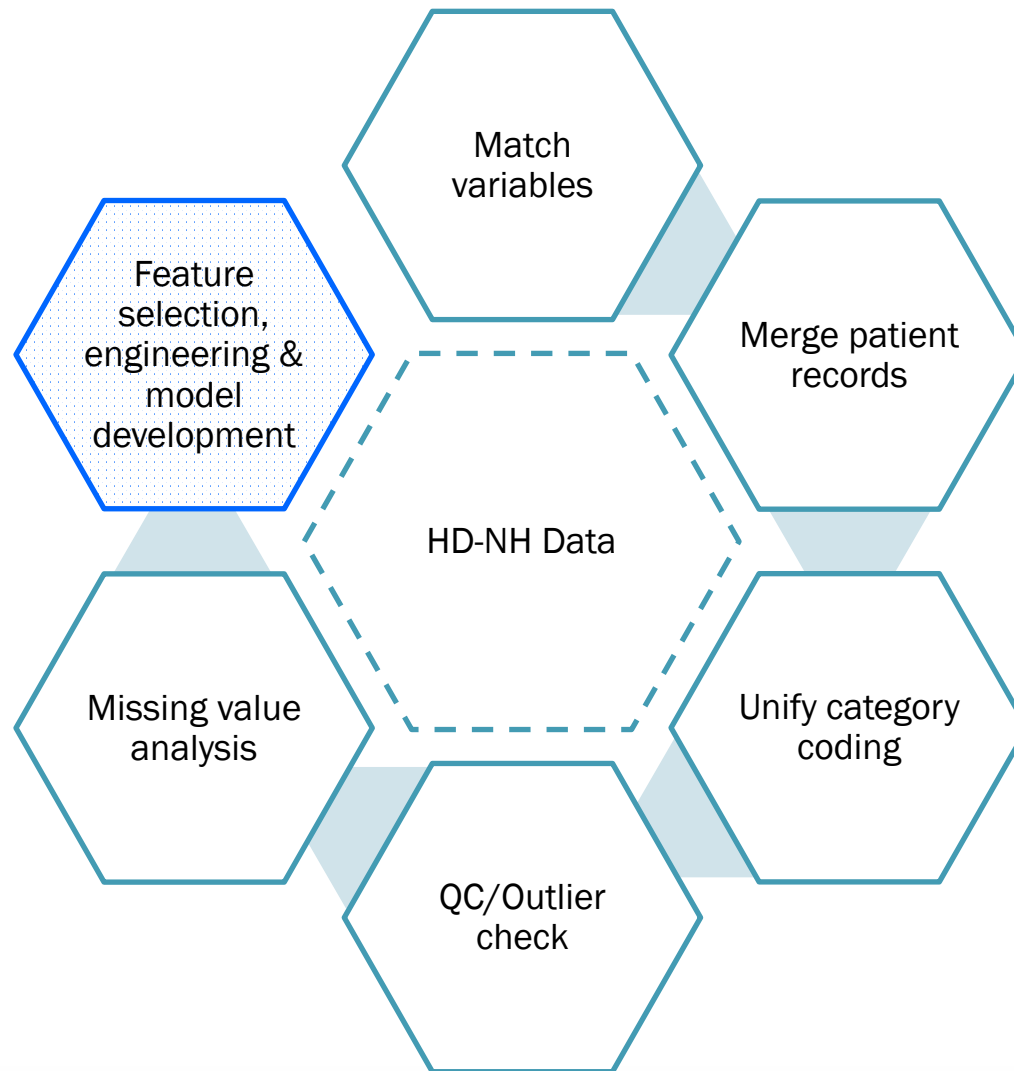
~20,000 participants

Visit statistics

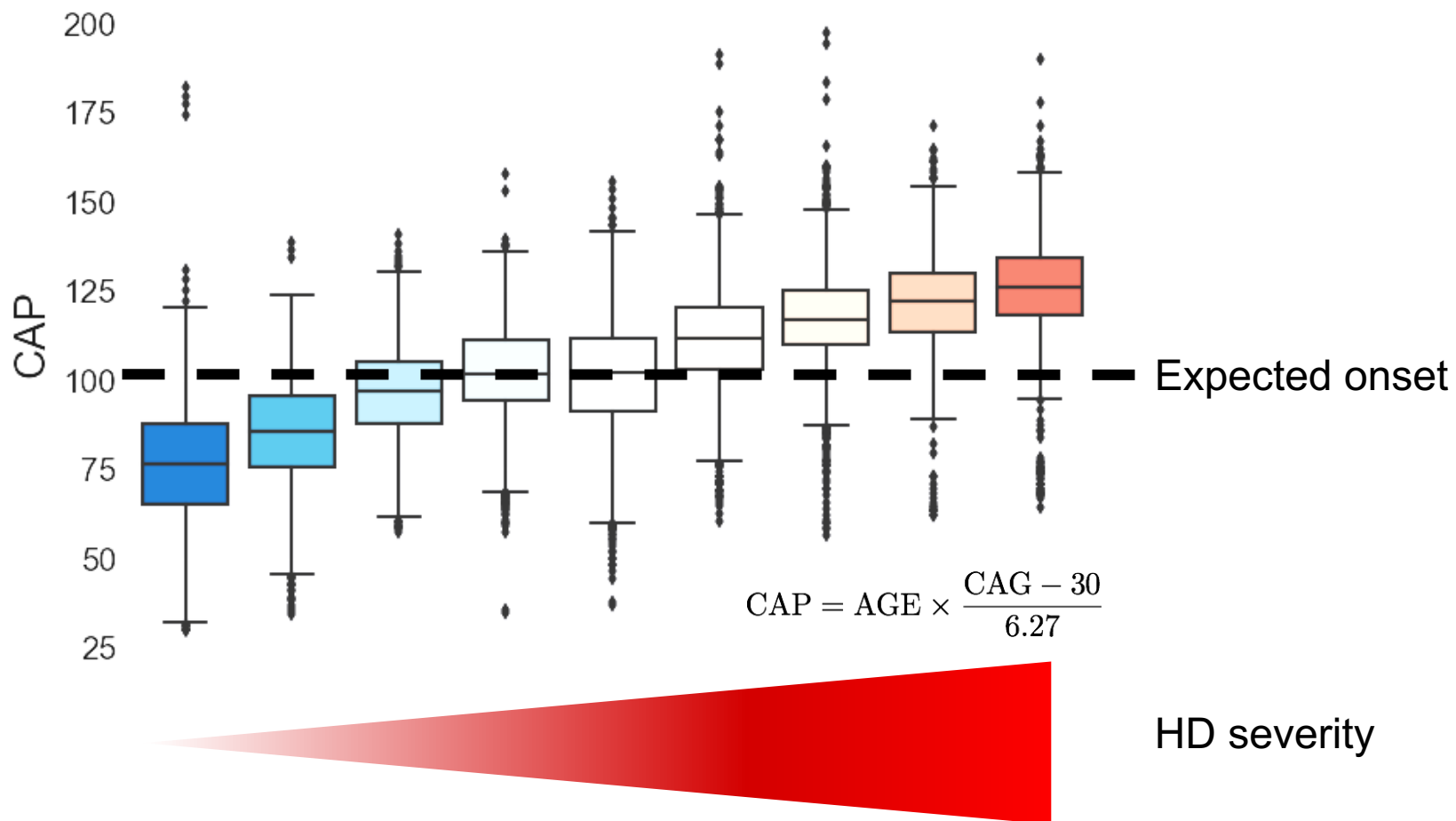
min	median	mean	max
1	2	3	17



Leveraging HD-NH Data



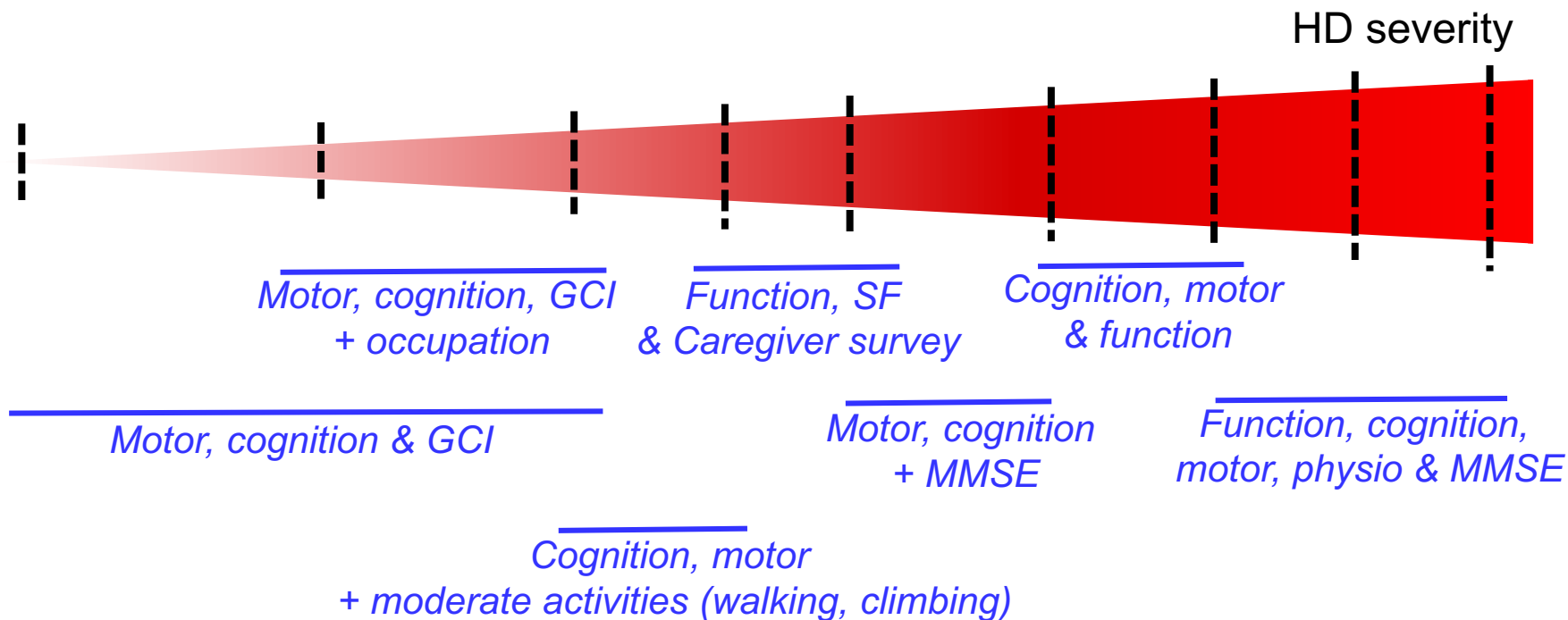
Observation: HDGEC population-wide trend...



**Using clinical outcome measures only;
without CAG/CAP score**

Observation:

Distinct clinical events spanning 4 decades...



- **Population-wide**
- **Measurable using standard battery of tests**
 - **Can be brought to clinical practice**

Key takeaways

- Multi-source, heterogeneous HD clinical datasets integrated and analyzed to understand complex, population-wide phenotypes
- A clear set of HD data standards can expedite leveraging clinical trials datasets
- New knowledge can improve HD clinical practice; transform patient journey



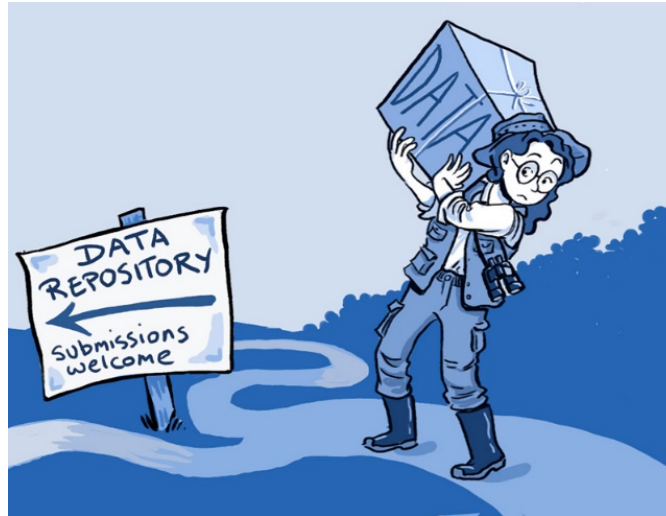


Image credit: Ainsley Seago, PLoS Biology

Thank you