Huntington's Disease Society of America

Putting HD patient data to work

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Presenter Disclosures

Amrita Mohan

The following personal financial relationships with commercial interests relevant to this presentation existed during the past 12 months:

No relationships to disclose

Key takeaways

1. HD research participant data is absolutely critical to clinical research

2. A cool example of how HD individuals' data is being used

3. YOU are important to the success of clinical research

Background: HD observational studies

HD observational studies are VERY important

Guide clinical development

- Understand course of disease
- Design better drug trials
- Improve patient care

Credit: Rob Sinclair

Thank You

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Data gathered in HD observational studies

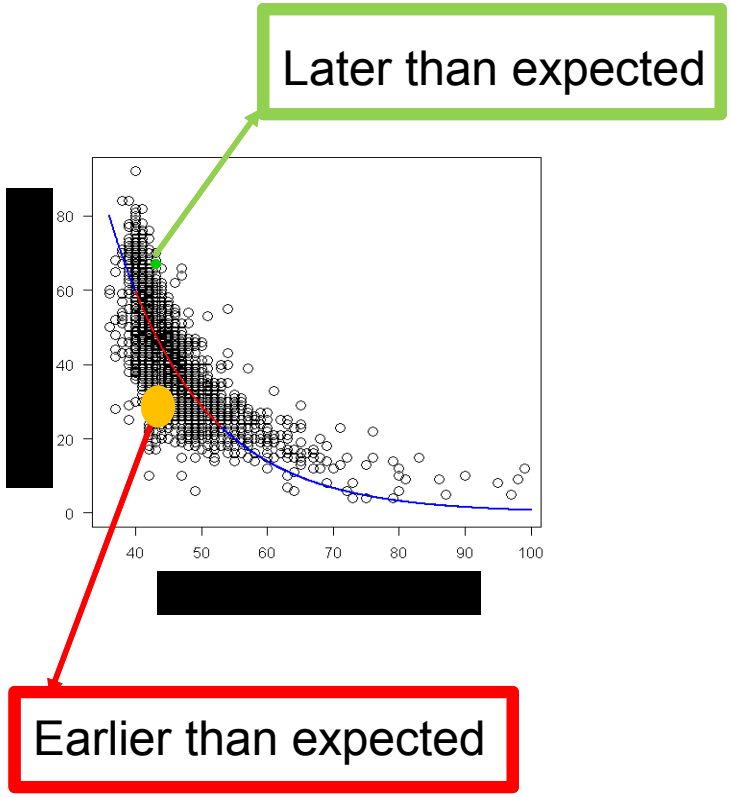
- ~15 studies known so far
  - Variety of data
    - clinical assessments (e.g. UHDRS)
    - neuro-imaging
    - molecular (through biosamples)
  - Visit-based
    - each visit spanning a few hours, by participants

Recent example: Use of biosamples from different HD observational studies

Huntingtin gene is important in HD but other genes are involved as well

- CAG length good predictor of age of motor onset
- However a wide range exists!

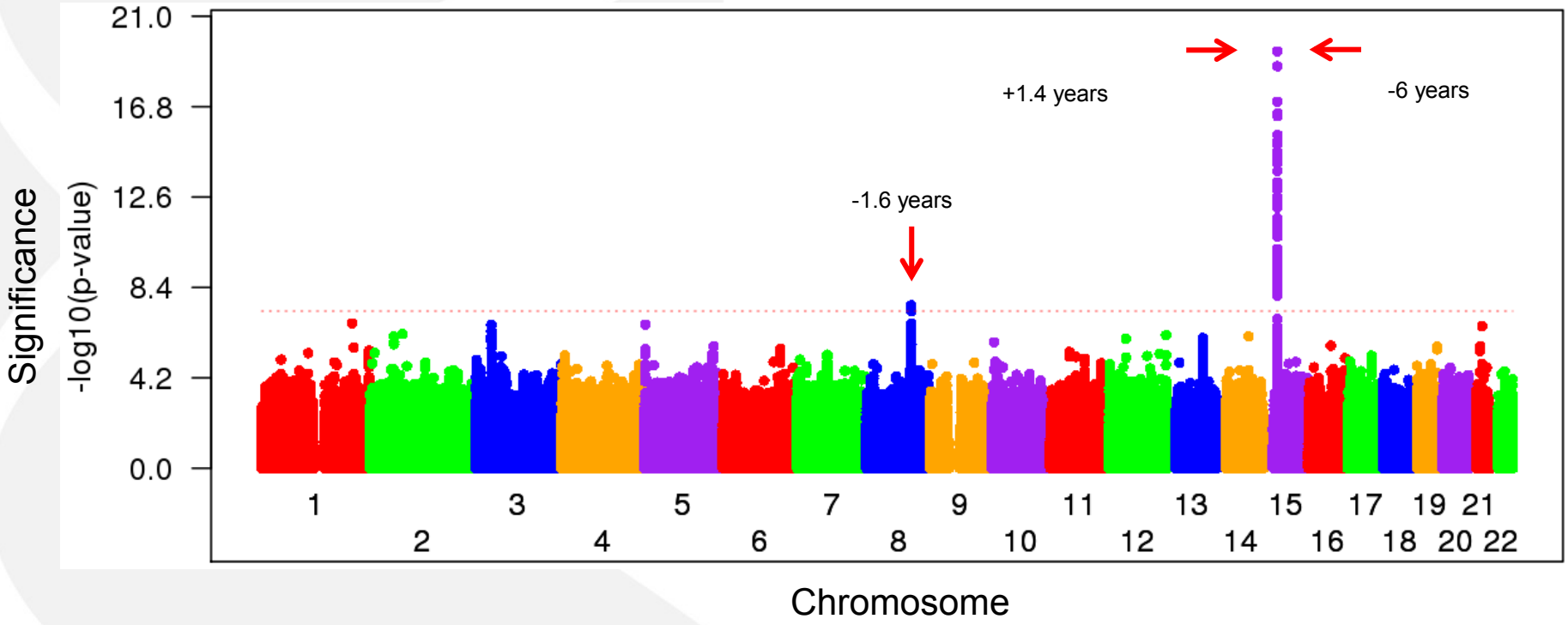
Other genes that affect age of motor onset?



Other genes that affect motor onset in HD

Using DNA from ~7000 HD research participants spanning Enroll-HD, Registry, Predict-HD and COHORT

More genes identified



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Genetic Modifiers of HD (GeM-HD) Consortium *Cell 2015*
Modifier of HD onset at *MLH1* locus *HMG 2017*

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1. Not only is the *huntingtin* gene critical

2. Other genes are also involved that affect age of motor onset

3. Such findings are now possible due to new technologies and data collected through HD observational studies

Pooling biosamples from multiple HD studies is powerful

What about clinical measurements in HD observational studies?

Clinical measurement types gathered

- Motor
- Function
- Cognitive
- Psychiatric
- Quality of Life
- Medical History
- CAG
- Family
- Physical Treatment
- Health & Disability
- Health Economics
- Q-motor/TMS
- Nutrition
- Medication & Co-morbidity

Enroll-HD

PREDICT-HD

REGISTRY

TRACKHD

TrackOnHD

A lot of HD clinical measurement data now available

Cohort study	# Participants	CAG	Max visits	Mean visits	Motor	Functional	Psychiatric	Cognitive	QoL	Family	Medical History	Comorbid & medication	Health Economics	Q-motor Oculomotor/TMS	Health and Disability	Physical Treatment/Nutrition
Enroll-HD	7,614	✓	4	1	✓	✓	✓	✓	✓	✓	✓	✓	✓			✓
Registry	12,108	✓	15	3	✓	✓	✓	✓	✓	✓	✓	✓	✓			
Track-HD/ON	466	✓	7	4	✓	✓	✓	✓	✓	✓	✓	✓		✓		
PREDICT-HD	1,481	✓	14	5	✓	✓	✓	✓							✓	

A lot of HD clinical measurement data now available

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Registry-HD	12,108	✓	15	3	✓	✓	✓	✓	✓	✓	✓	✓	✓			
Track-HD/ON	466	✓	7	4	✓	✓	✓	✓	✓	✓	✓	✓		✓		
PREDICT-HD	1,481	✓	14	5	✓	✓	✓	✓							✓	

A lot of data!!

200 million data points

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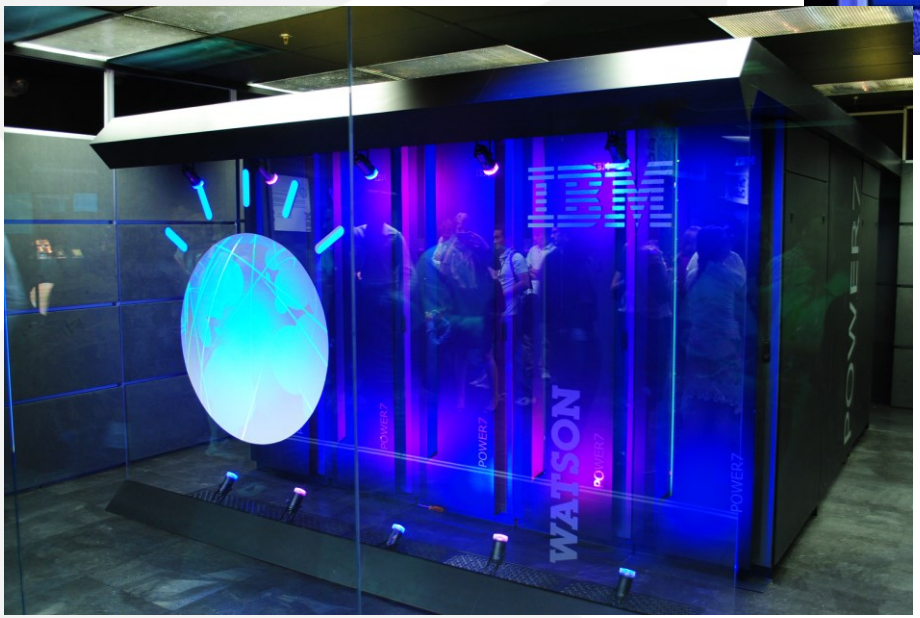
CHDI-IBM partnership 2015 -

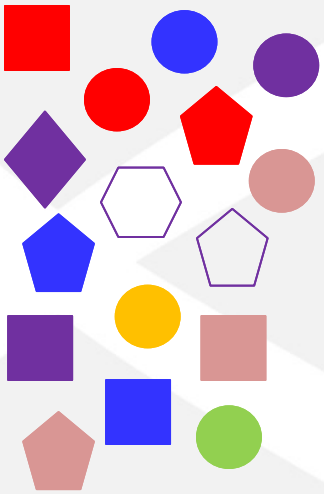


IBM

A 3-step data crunching cartoon

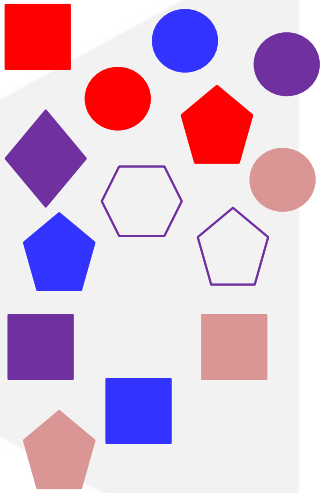
1

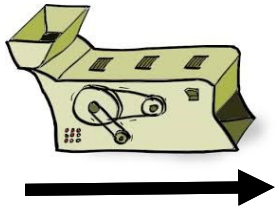
Collect data



2

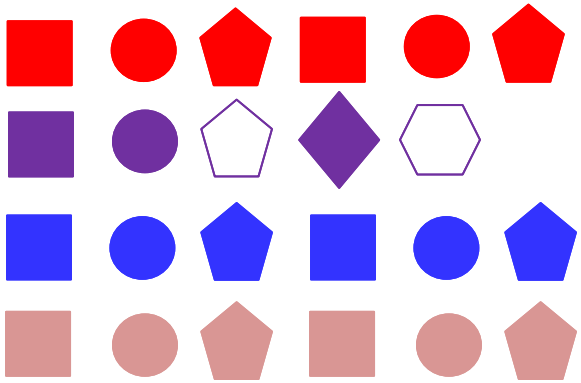
Clean up



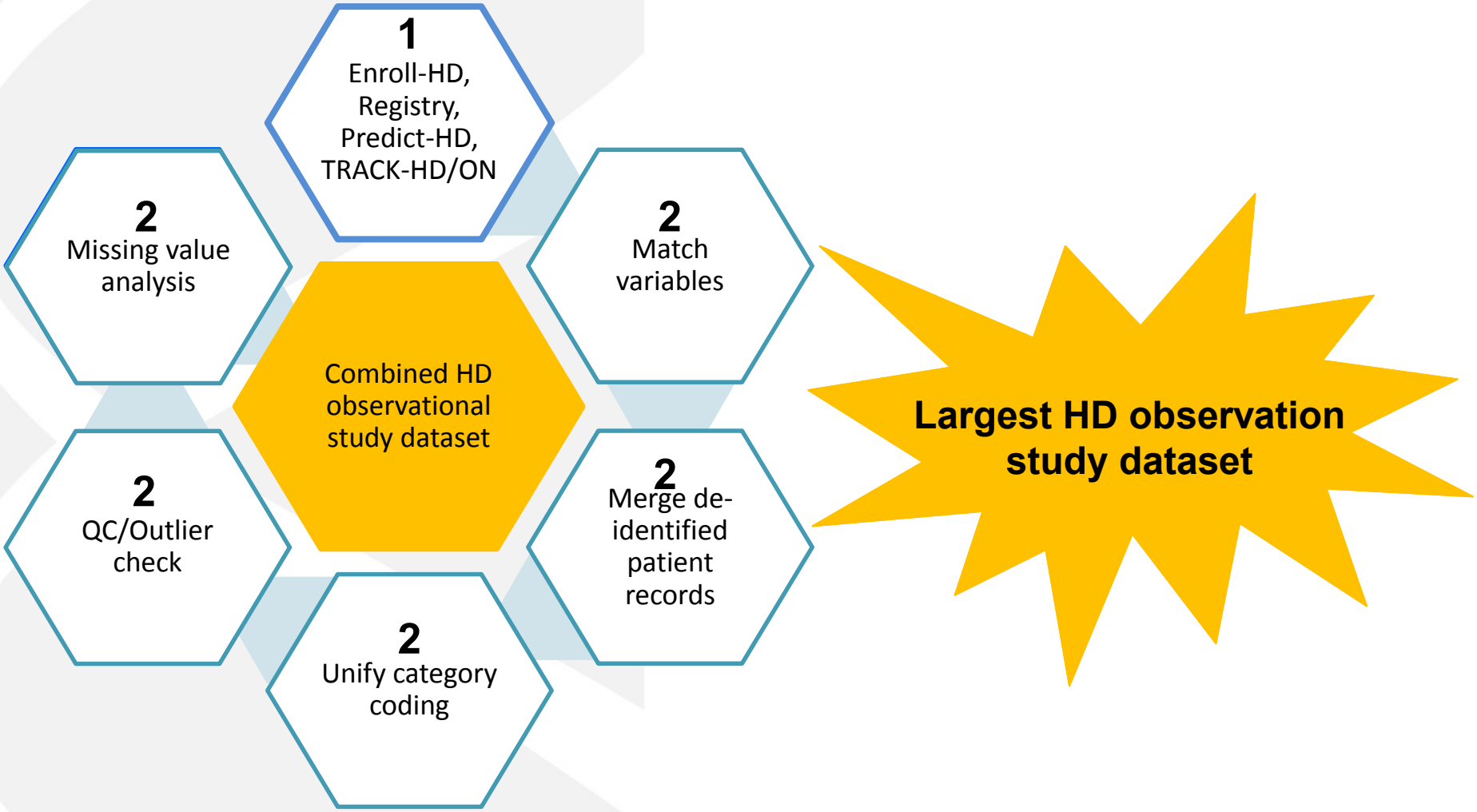


3

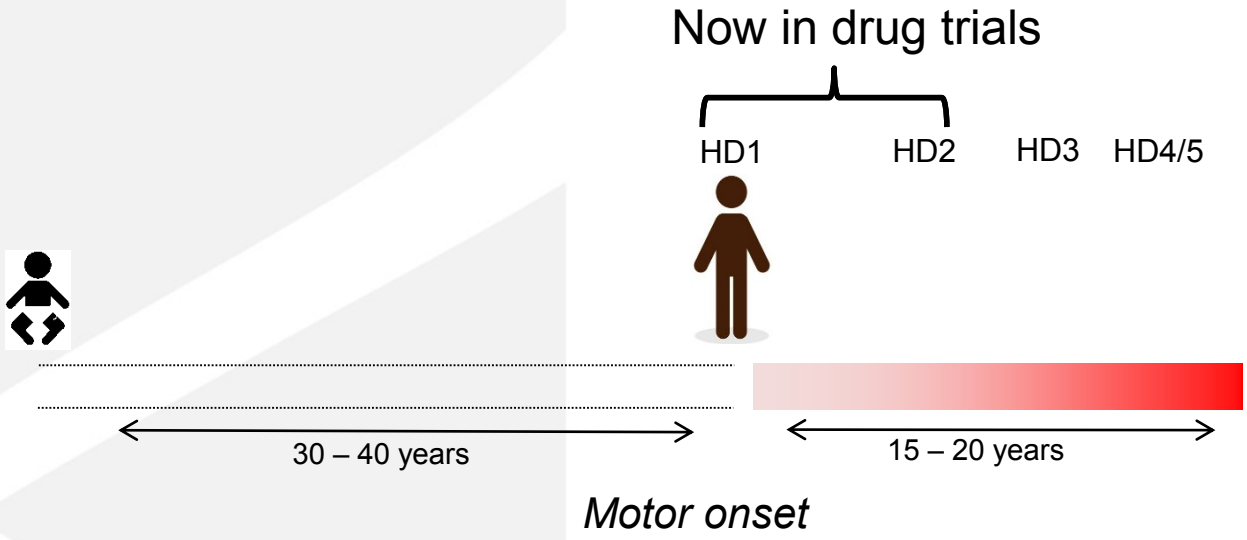
Identify patterns & predict



Data crunching process at IBM



Current clinical understanding of HD



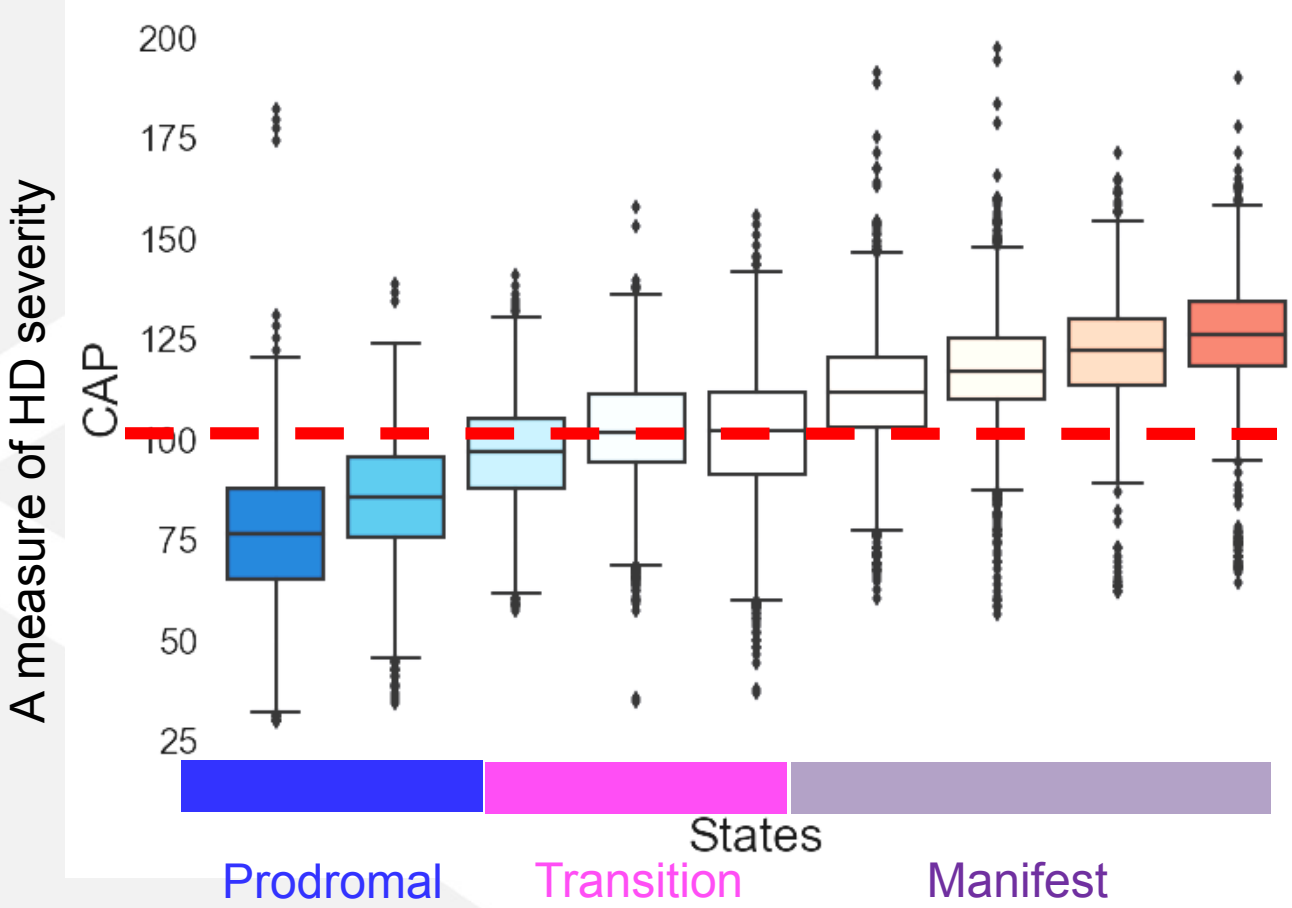
- Practical understanding of course of disease after motor onset
- HD staging begins after clinical diagnosis

- No clear understanding of preceding decades: Difficult to bring therapies earlier

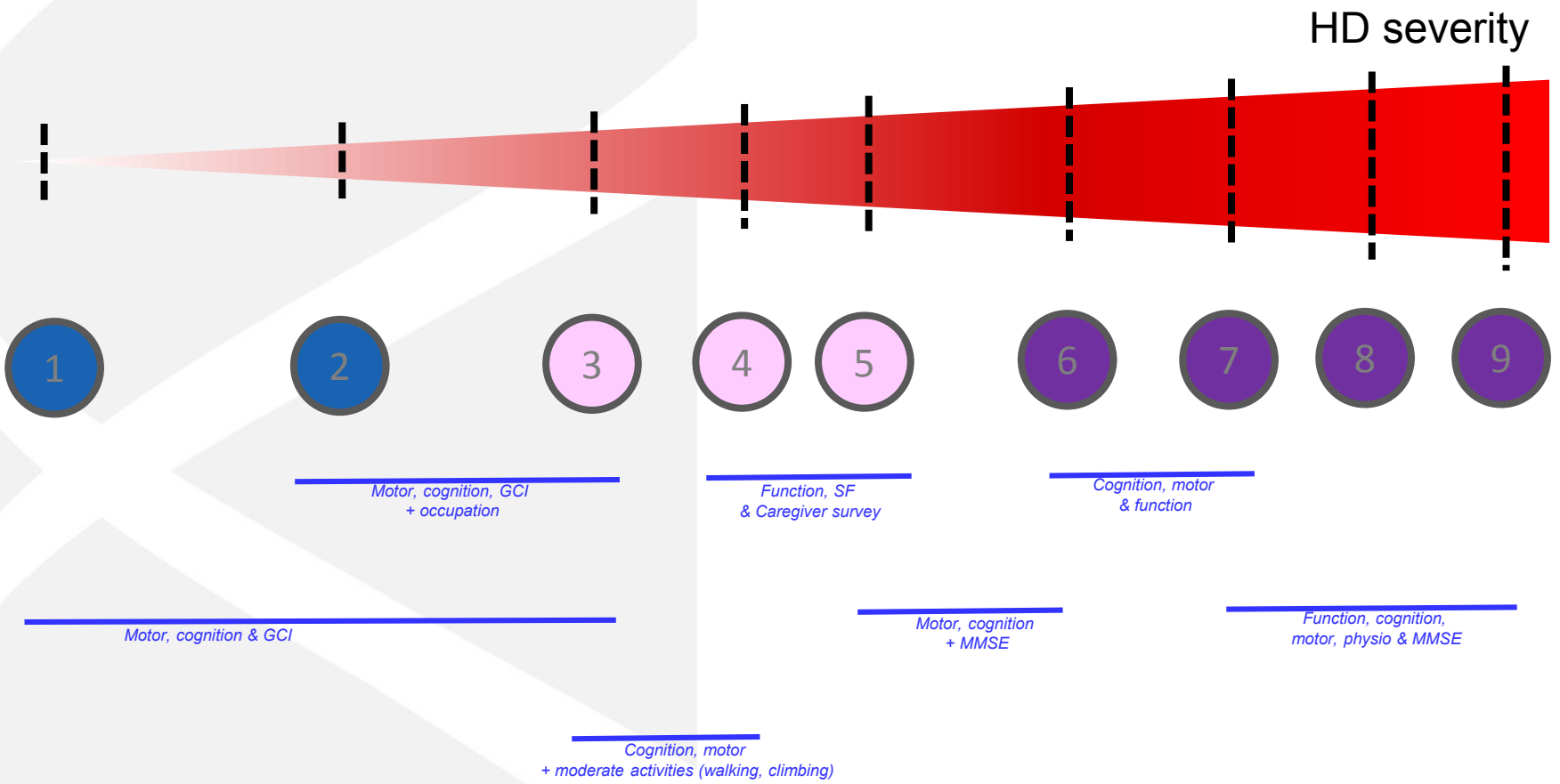
Can we improve our understanding of the course of HD using combined observational study data?

Using the combined HD observational study dataset

A 9-state HD progression/staging model



Distinct changes tracked over the course of HD



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Distance between states proportional to expected durations in years

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Why is this research exciting?

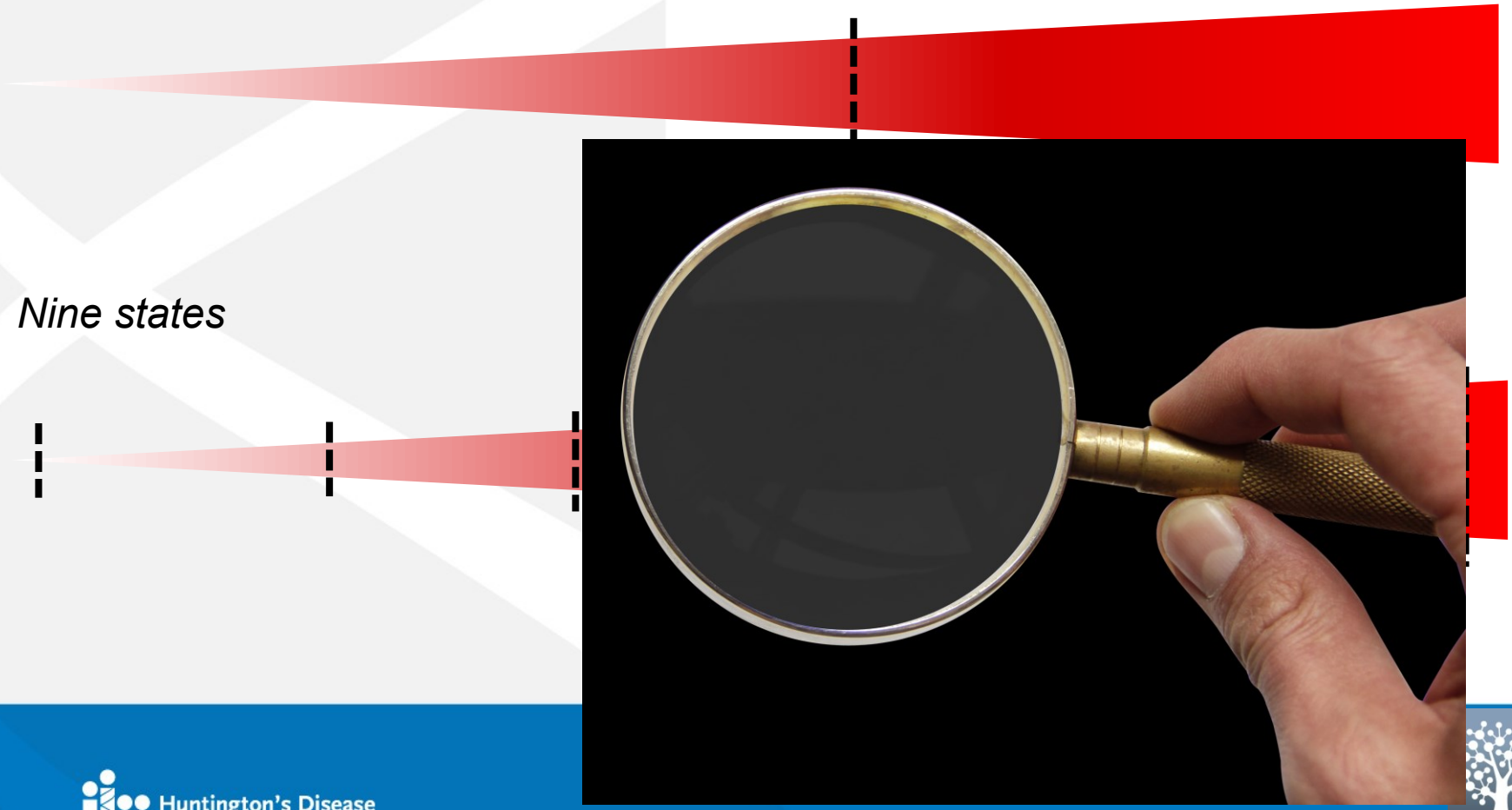
1. More detailed picture of the course of HD

Two states

HD severity

Premanifest

Manifest



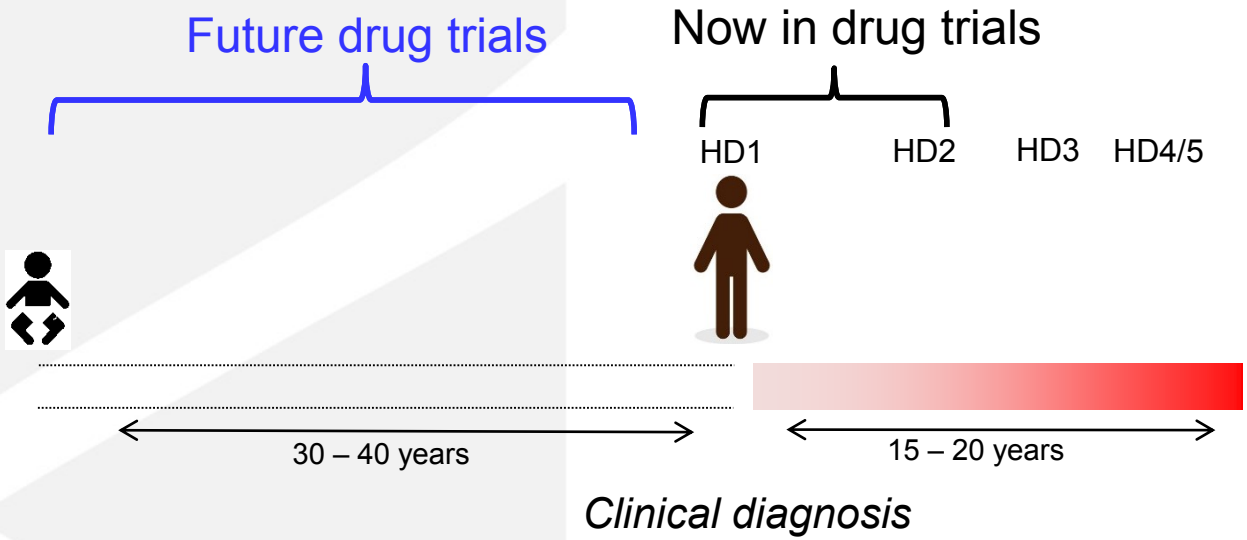
Nine states

2. Will enable targeted clinical decision making

What's next?
How long?

Better trials

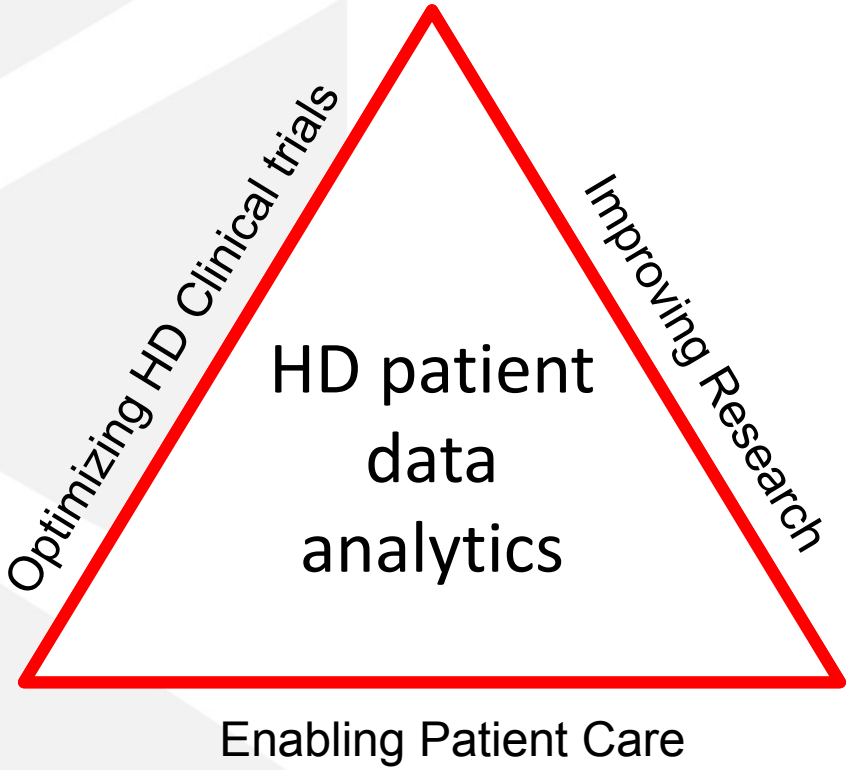
3. A way to bring therapies earlier



~~• No clear understanding of preceding decades: Difficult to bring therapies earlier~~

To wrap up

HD patient data is absolutely essential to gain fast, new insights



Other collaborative efforts that are using HD patient data

A number of other projects currently supported by CHDI that are striving to learn new insights

IBM

Neuroimaging & speech analysis

Neuroimaging HD staging

GNS HEALTHCARE

Progression changes

THE UNIVERSITY OF IOWA

Enroll-HD data analysis

AIDFM
Associação para Investigação e Desenvolvimento da Faculdade de Medicina

RAND HEALTH

Environmental factors affecting HD

Participants & Investigators

Thank You

Enroll-HD — *Bernhard Landwehrmeyer*

TRACK-HD

TrackOn-HD — *Sarah Tabrizi*

COHORT Cooperative Huntington's Observational Research Trial — *Ira Shoulson*

PREDICT-HD — *Jane Paulsen*

HD REGISTRY — *Jean Marc Burgunder*

IBM

CHDI ***and collaborators***

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Zhaonan Sun	Seung Kwak	Jan Tuschoff	

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