

## Safety and tolerability of research lumbar puncture in Huntington's disease: the HDClarity cohort and community bioresource

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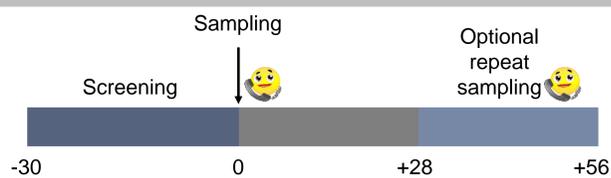
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### Background

With clinical trials ongoing and in planning to evaluate novel therapeutic approaches for Huntington's disease (HD), biomarkers are needed to measure disease progression, target engagement and efficacy. Cerebrospinal fluid (CSF) is an ideal medium to assess HD biomarkers and pathobiology in humans due to its proximity to the brain. There is a pressing need for a high-quality, international, open repository of CSF samples from well-characterized controls and HD gene-expansion carriers (HDGECs) spanning the disease spectrum.

HDClarity is the first such project and aims to expedite HD research and therapeutic development. Its guiding principles are open collaboration, consistency in sample collection and processing, rigorous quality control, and the gathering of standardized, detailed phenotypic data via the Enroll-HD platform.

### Study Design



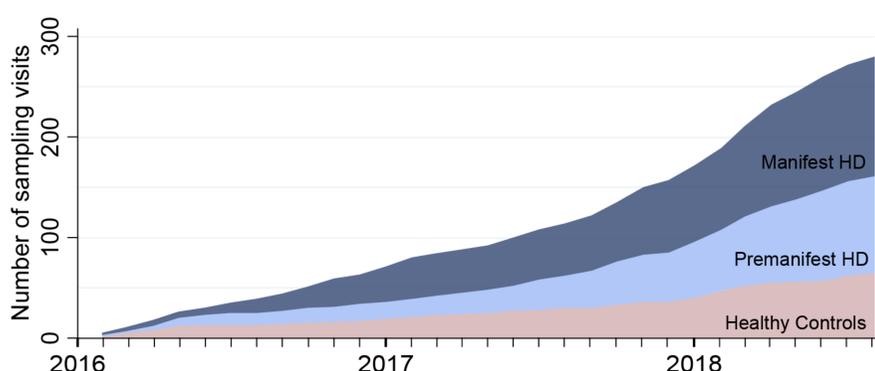
HDClarity is international multicentre observational study. Participants attend two study visits (screening and sampling) and may attend an optional third visit 4-8 weeks later. A subset of participants presented here attended 2-year follow up screening and sampling visits. During screening, medical history, clinical and phenotypic data are collected, including the Unified Huntington's Disease Rating Scale (UHDRS). During sampling, CSF and blood are collected after an overnight fast. Standard operation procedures, and sample collection and processing kits are followed/used in visits. Here we report on fully monitored data from participants recruited until October 2018.

### Participants

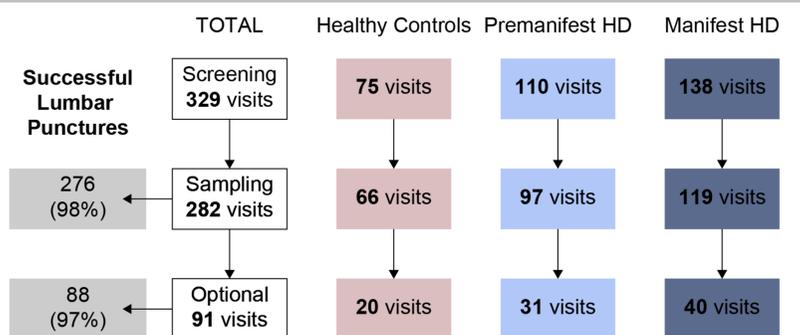
- |                                |                              |
|--------------------------------|------------------------------|
| <b>1. Healthy Controls</b>     | DCS < 4; CAG ≥ 40; BOP < 250 |
| <b>2. Early Premanifest HD</b> | DCS < 4; CAG ≥ 40; BOP ≥ 250 |
| <b>3. Late Premanifest HD</b>  | DCS = 4; CAG ≥ 36; TFC 7-13  |
| <b>4. Early Manifest HD</b>    | DCS = 4; CAG ≥ 36; TFC 3-6   |
| <b>5. Moderate Manifest HD</b> | DCS = 4; CAG ≥ 36; TFC 0-2   |
| <b>6. Advanced Manifest HD</b> |                              |

DCS, Unified Huntington's Disease Rating Scale Diagnostic Confidence Score; BOP, burden of pathology score ((CAG - 35.5) × age); TFC, Total Functional Capacity Score.

### Recruitment



### Visit description\*



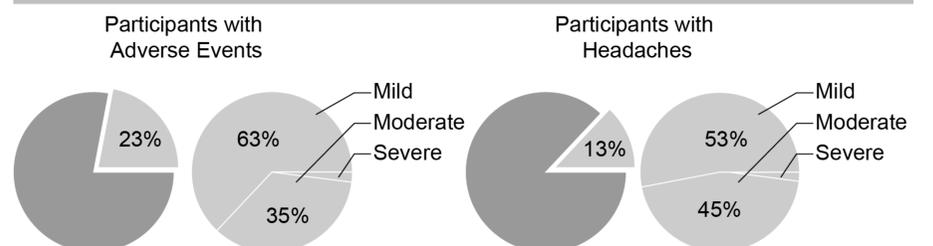
\*Unit of analysis: visit

### Participant characteristics\*

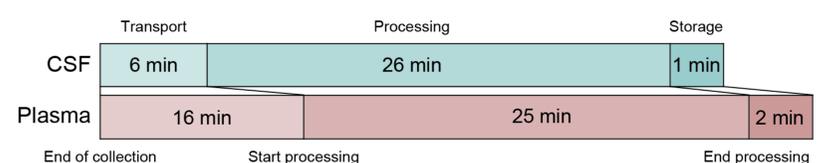
	Total	Healthy Controls	Premanifest HD	Manifest HD
n (%)	269	60 (22%)	91 (34%)	118 (44%)
Age mean (SD)	49 (13)	50 (12)	40 (12)	55 (10)
Female n (%)	132 (49%)	33 (55%)	48 (53%)	51 (43%)
Caucasian n (%)	264 (98%)	60 (100%)	89 (98%)	115 (97%)
Right handed n (%)	235 (87%)	55 (92%)	80 (89%)	100 (85%)
CAG mean (SD)	n/a	n/a	43 (2)	43 (3)
DBS mean (SD)	n/a	n/a	280 (±82)	395 (105)
TMS mean (SD)	16 (21)	1 (2)	2 (3)	33 (22)

\*Unit of analysis: participants who underwent 1 or more sampling visits

### Adverse events

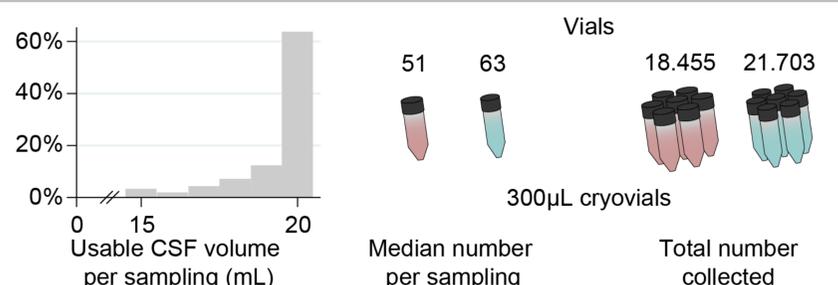


### CSF and blood quality



CSF contamination	Median	IQR	Min	Max
Red blood cells	1	7	0	2,131
White blood cells	0	1	0	8
Haemoglobin (%<2µg/mL)			91%	

### Volume and sample distribution



Sample requests	CSF vials	Plasma vials
13	748	416