

## A multi-site cerebrospinal fluid collection initiative to facilitate therapeutic development for Huntington's disease

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### Background

With several clinical trials in progress and more expected to launch in the next few years exploring novel therapeutic approaches for treating Huntington's Disease, biomarkers are needed to evaluate target engagement, efficacy and disease progression.

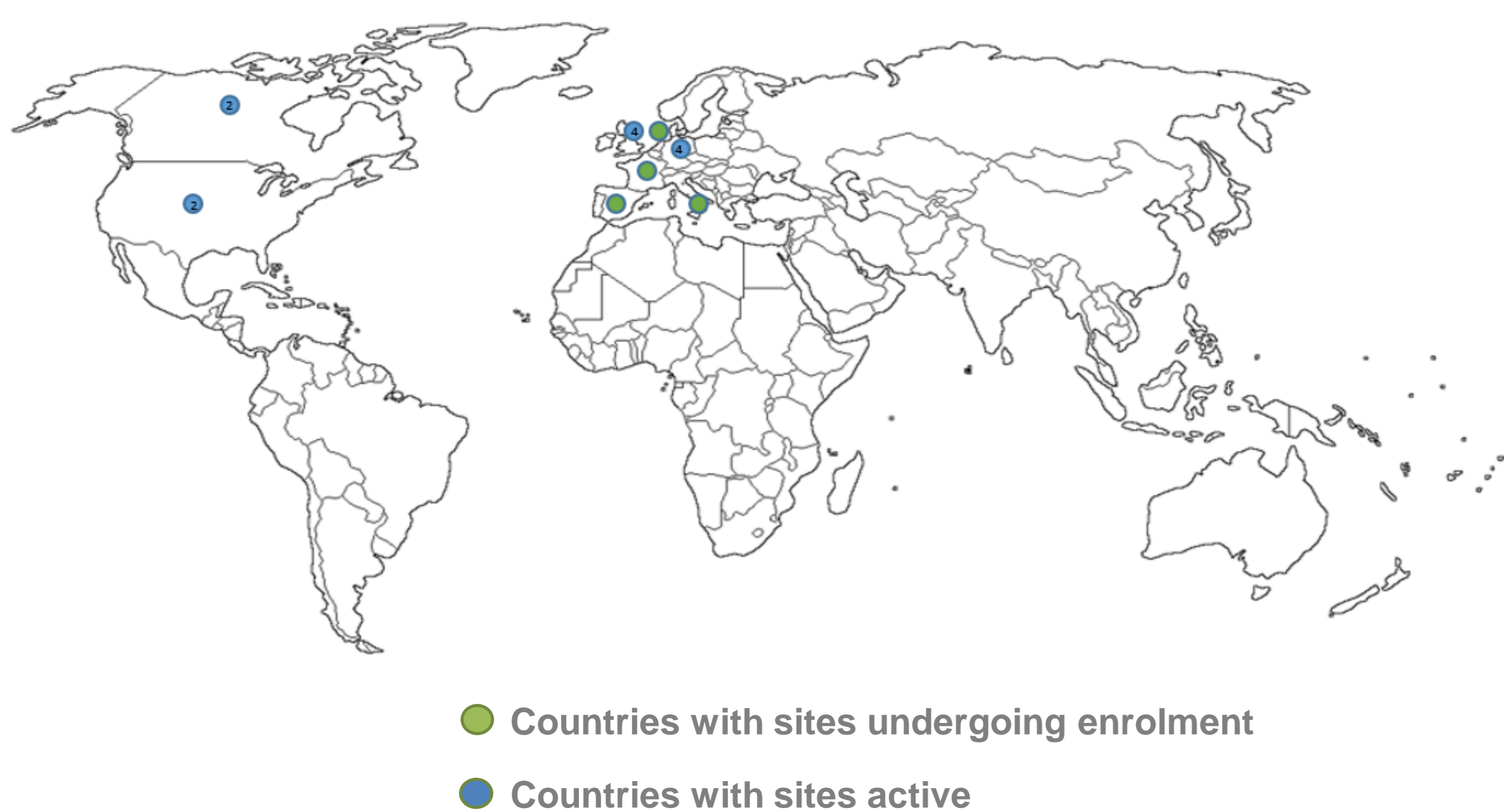
Cerebrospinal fluid (CSF) is an ideal fluid compartment for assessing HD biomarkers and pathobiology in humans, due to its proximity to the brain. There is currently no high-quality repository of CSF from well-characterized HD gene expansion carriers spanning the disease spectrum.

Now underway, HDClarity is building such a repository in order to expedite research into biomarkers for HD.

### Study Design

CSF and blood samples are already being collected at multiple sites. Careful collection of clinical and phenotypic data on each donor enable us to appropriately select subsets of samples for each set of experimental assays. HDClarity uses the Enroll-HD Platform to identify participants and collect standardized data. HDClarity will eventually include annual longitudinal collection and a larger sample size.

HDClarity is sponsored by University College London and coordinated by UCL Huntington's Disease Centre. It is funded and supported by CHDI Foundation, Inc.



### Participants

We will aim to recruit 1200 participants from approximately 30 sites:

1. Healthy controls
  2. Early Pre-manifest HD
  3. Late Pre-manifest HD
  4. Early Manifest HD
  5. Moderate Manifest HD
  6. Advanced Manifest HD
- DCS < 4; CAG ≥ 40; BOP < 250  
 DCS < 4; CAG ≥ 40; BOP ≥ 250  
 DCS = 4; CAG ≥ 36; TFC 7-13  
 DCS = 4; CAG ≥ 36; TFC 4-6  
 DCS = 4; CAG ≥ 36; TFC 0-3

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

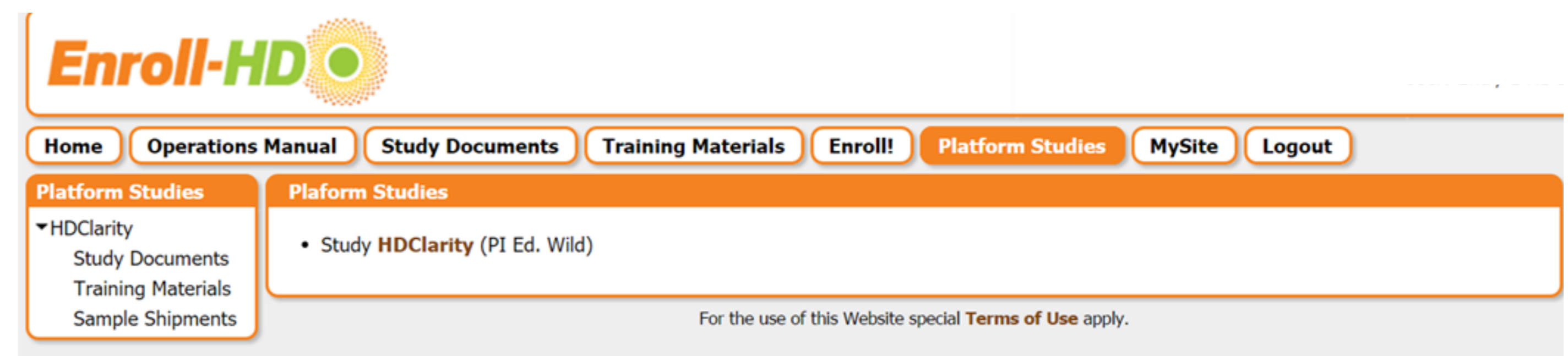
### Procedures

Participants attend two study visits (Screening and Sampling), and may attend an optional Repeat Sampling Visit. During the Screening Visit, medical history, and clinical and phenotypic data are obtained. Participants who meet the eligibility requirements of the study and are willing to continue in the study, return for a Sampling Visit. During that visit, biosamples will be collected following an overnight fast: blood is obtained via venipuncture and CSF is obtained via lumbar puncture. Some participants are invited to return for a Repeat Sampling Visit approximately 4-8 weeks later.

Custom biosample kits are supplied by BioRep to supply all equipment for standardised CSF and plasma collection and processing. BioRep is also the sample biorepository.



A bespoke electronic data capture (EDC) system built on the Enroll-HD platform is used to record all data, procedures and samples and handle site payments automatically.



### Analysis

Pre-planned analyses include quantification of kynurenine pathway metabolites and the development and application of novel assays to quantify various forms of huntingtin protein.

Any qualified investigator may request samples and data from HDClarity for uses relevant to the aims of the study. There have been 11 sample requests as of 22 February 2018. For more information, please visit the HDClarity website, [hdclarity.net](http://hdclarity.net).

Current Sample Collection by HDClarity category:

Visit	Premanifest HD		Manifest HD			Control	Total
	Early	Late	Early	Moderate	Advanced		
Sampling	22	40	69	7	3	46	187
Repeat Sampling	8	9	24	3	0	13	57