Newsletter

Jan 22 Issue 27

7 Nations Participating

28 Clinical Sites Worldwide

618 Participants Screened (including longitudinal visits)

Dear HDClarity Teams,

Firstly, we would like to wish you all a Happy New Year and well wishes for 2022!! Last year was extremely challenging for many; however, the dedication of our clinical sites and the determination of the HD community ensured that HDClarity had a successful year and we would like to thank everyone for all your hard work. We have now completed 657 sampling visits, including longitudinal and optional repeat sampling visits.

- Since the last newsletter (October 2021) HDClarity sites have conducted 28 new screening visits, 28 sampling visits and 1 optional repeat sampling visit.
- Special thanks are given to GHI, Rome and Houston for prioritising longitudinal recruitment and we have now obtained longitudinal samples from 47 participants. This is a fantastic number, and we are confident that it will continue to rise!!
- We would like to congratulate Birmingham & Solihull Mental Health Trust for their successful restart following the UK COVID19 lockdown. We are excited for additional UK sites to reopen soon.

REMINDERS

- Clinical sites operating on protocol V3 can invite participants back for repeat HDClarity visits. These visits must occur >11 months after the previous enrolment and are open to all participant categories. Sites operating on Protocol V3 should attempt to prioritise longitudinal visits, if possible.
- Please contact CC when you intend to restart HDClarity. We will provide you with detailed instructions on how to proceed.
- When shipping samples, it is important that the shipment notification on the EDC is completed accurately (e.g., quantity and type of samples, site name/ID, LabID) and corresponds to the samples in the shipment.
- Please always check HDClarity biokits expiry dates and do not use or discard expired items as replacements can usually be provided. Please contact CC to arrange replacements for expired components at least 14 days in advance. Expired components may include:
  - Spinal needles – kits containing 22G Whitacre spinal needles should be replaced with new kits that include the 24G needle, introducer, and aspiration syringe.
  - Polypropylene pipette tips – have expired in many CSF and blood processing kits.
  - Vacutainers – have expired in many blood collection kits. You may use a locally sourced

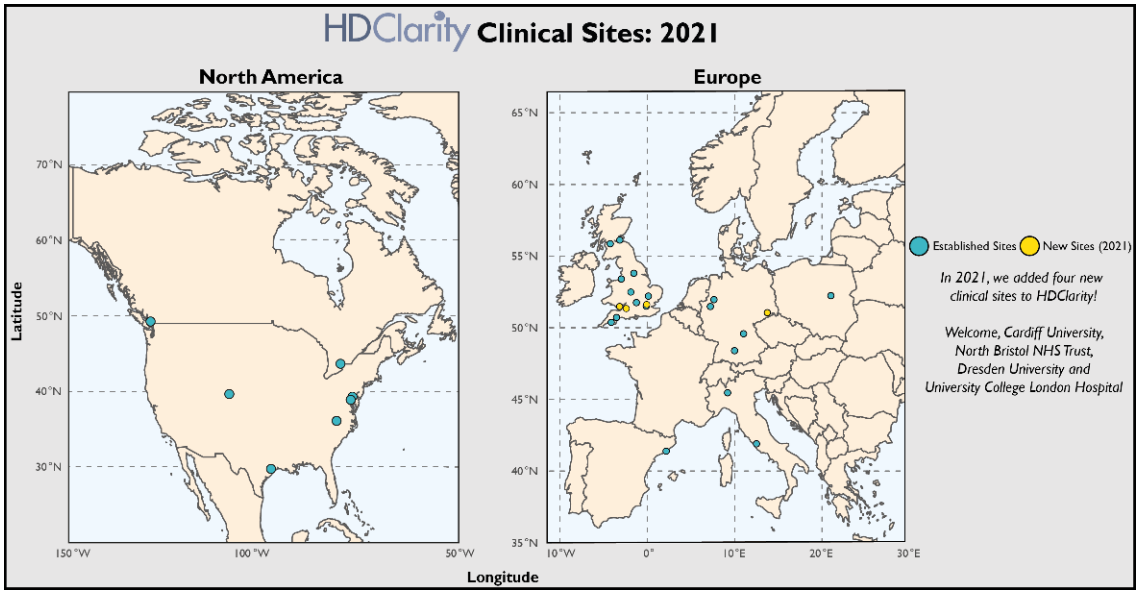
As a new year of HDClarity has begun, this edition of the newsletter will review last year's activities and provide key facts and figures concerning the advancement of HDClarity throughout the last 12 months.

New Clinical Sites Added in 2021

We added 4 new clinical sites in 2021, bringing the total number to 29:

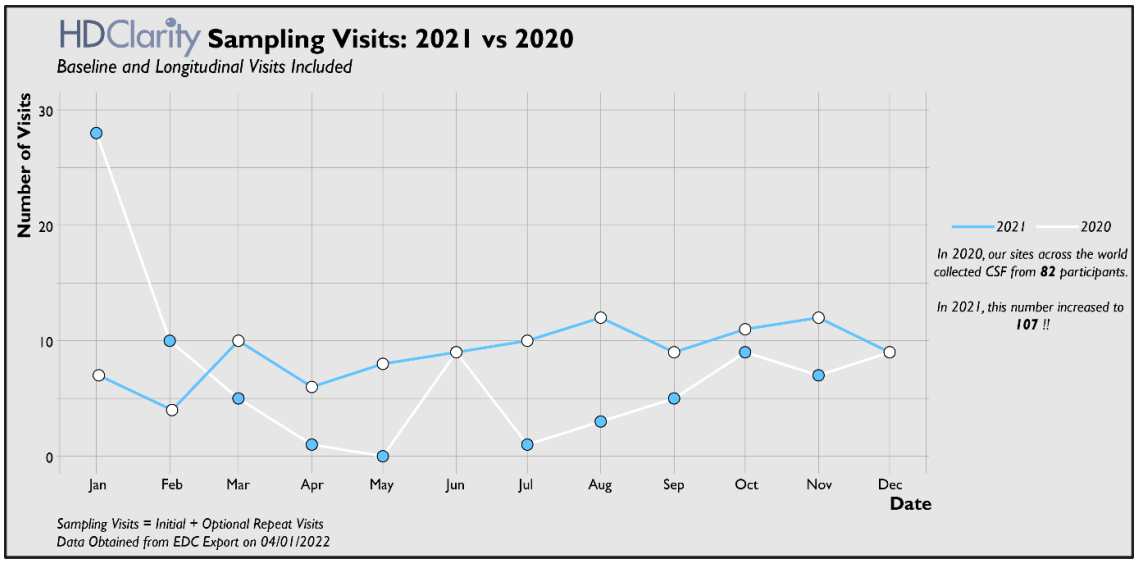
- Cardiff University
- North Bristol NHS Trust
- Dresden University
- University College London Hospital

We are confident this number will continue to grow in 2022, starting with a site Initiation visit with Hospital Ramón y Cajal, Madrid in January.



HDClarity Sampling Visits: 2021 vs 2020

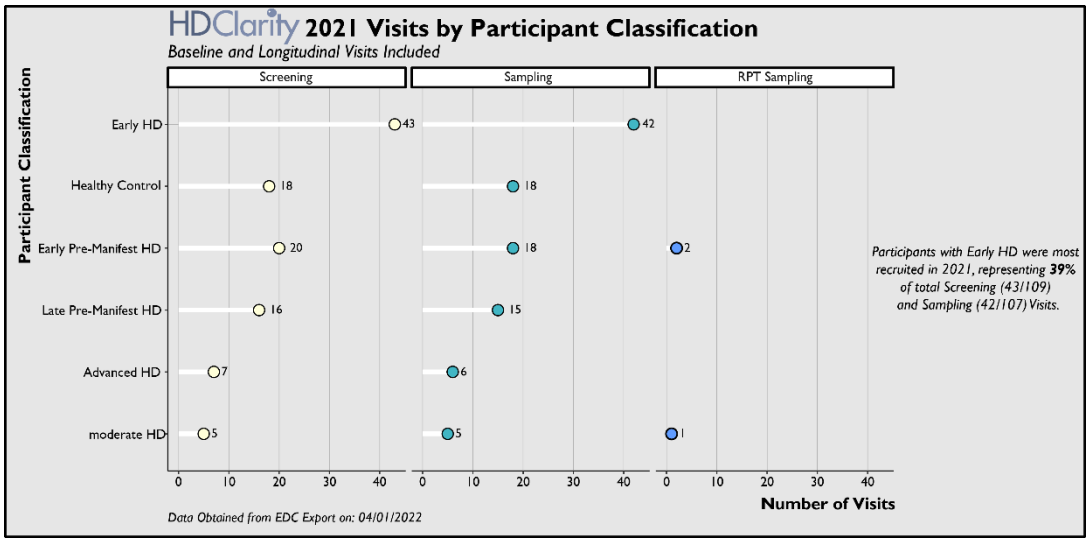
Last year we collected CSF and plasma from 107 participants in total, an increase of 25 compared to 2020. Crucially, 36 of these samples were collected from longitudinal visits, representing a 200% increase from the previous year (2020).



Who Was Recruited in 2021?

As part of HDClarity, participants are classified into one of six categories: Healthy Control, Early Pre-Manifest HD, Late Pre-Manifest HD, Early HD, Moderate HD, and Advanced HD.

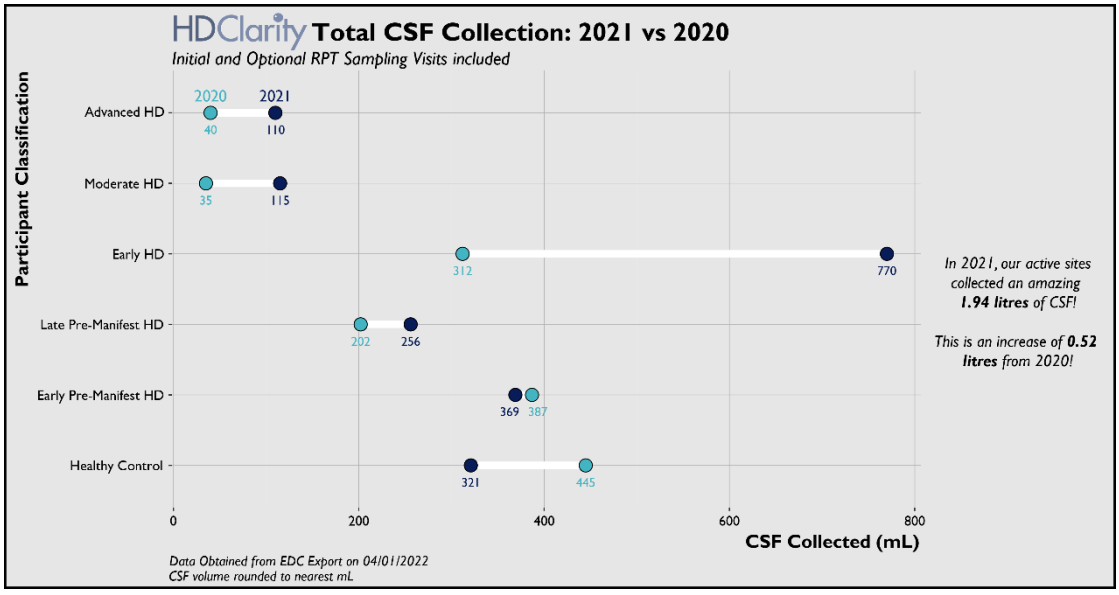
Recruiting participants across all categories allows researchers to study HD across the entire disease spectrum, providing valuable insight into disease progression and efficacy of potential treatments.



HDClarity CSF Collection: 2021 vs 2020

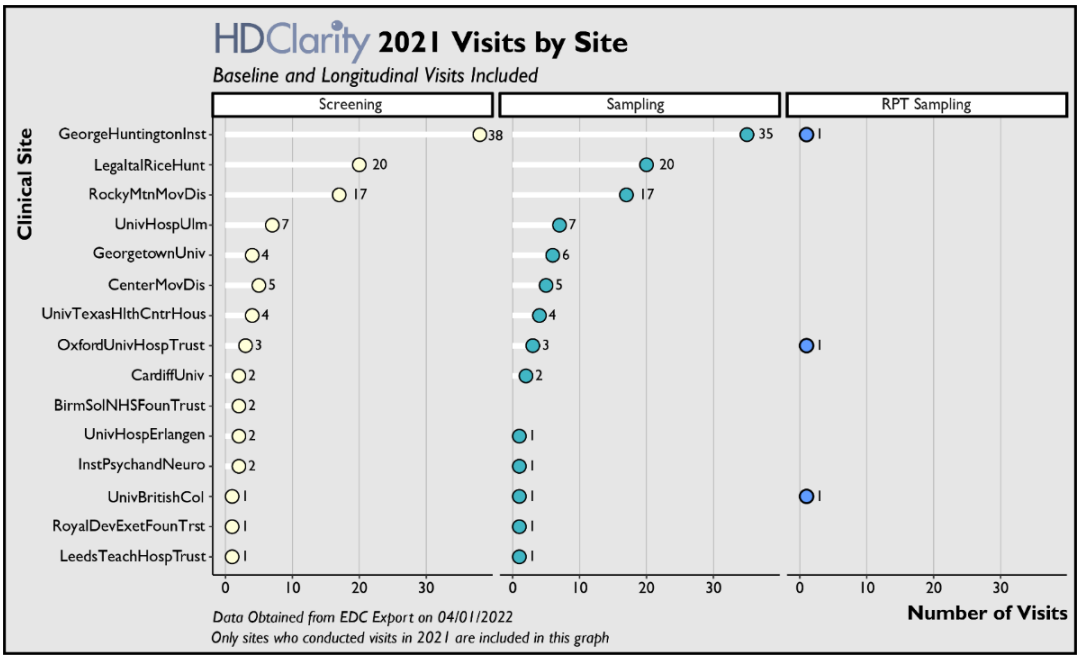
Given that Early HD recruitment was the highest in 2021, it is no surprise that we collected the most CSF from participants in this category!

Compared with 2020, more CSF was collected in 4 out of 6 participant categories. The total volume collected from those with Early HD was considerably higher than the previous year, with 458mL more CSF collected in 2021. Importantly, the volume of CSF collected was also higher in both Moderate and Advanced HD categories, this is a fantastic achievement and will help provide insight into part of the disease spectrum which can be challenging to study.



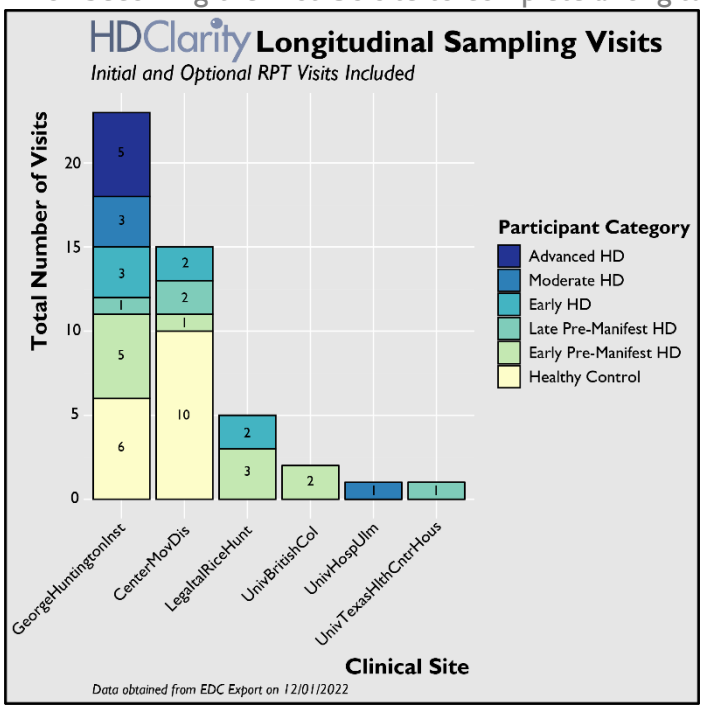
Clinical Site Performance: 2021

Many sites were still facing research restrictions last year and were unable to recruit to HDClarity. When combined, the visits conducted at GHI, Rome and Rocky Mountain accounted for 69% of total Screening visits and 67% of total Sampling (including RPT Sampling) visits conducted in 2021. A special thanks goes to Dr Ralf Reilmann and his team in Münster (GHI) who completed 38 Screening, 35 Sampling and 1 Optional RPT Sampling visit.



HDClarity Longitudinal Recruitment

Currently, we have 6 sites that have successfully completed a total of 45 longitudinal initial sampling visits and 2 Optional RPT sampling visits. We are encouraging our sites to prioritise longitudinal recruitment wherever possible, as the samples collected will provide valuable insight into the dynamics and prognostic potential of biomarkers derived from blood and CSF. We would like to offer our congratulations to Prof Furr-Stimming and her team in Houston, TX for becoming the first US site to complete a longitudinal screening and sampling visit!



HDClarity Longitudinal Sample Use

"*Longitudinal samples are of critical importance to understand how the biomarker under study relates with disease progression. Typically, the annual individual changes of biomarker are relatively small. When cross-sectional groups are compared, as it is done when longitudinal samples are not available, the mean differences for the biomarker under study tend to be large if they are present. These group differences over-estimate the true change and are likely to lead to misleading conclusions regarding the value of the biomarker to detect changes over time*" (*Cristina Sampaio, MD, PhD: CHDI Chief Clinical Officer*).

To date, there are two planned CHDI projects which intend to utilise longitudinal HDClarity samples to facilitate novel biomarker research in HD:

1. HDClarity Core Analysis Data Set

Certain types of analysis are being performed as part of many research projects, and thus, samples are being used for duplicate work. To prevent the use of samples for duplicate work and provide consistent high-quality data sets, this project aims to create a core sample analysis dataset for key analytes, such as NfL, mHTT and total HTT, derived from CSF and blood.

2. HDClarity: Proteomics Discovery of HD Biomarkers

This project aims to conduct a robust quantitative proteomics analysis of the HDClarity sample set using the Somalogic validated proteomics panels (Somapanel). Somapanel enables 7000+ analytes to be measured, allowing for an in-depth exploration of biomarker potential.

The above projects will result in the production of two proteomic datasets that will be made available for HD researchers to facilitate the discovery of biomarker signatures and analyse individual proteins of interest, thus not only supporting HD research, but also preserve the HDClarity biosample inventory for other types of analyses. This concept of providing data to external researchers, as opposed to samples, was spearheaded by the previous CHDI Science Director Anka Ehrhard and represents a fantastic open-science initiative that will accelerate therapeutic developments in Huntington's disease.