Enroll-HD is a worldwide clinical research platform and observational study for Huntington's disease that has three main goals:

- To improve the design of clinical trials to rapidly provide clear outcomes - better, smarter, faster clinical trials will identify effective treatments as quickly as possible
- To better understand HD as it happens in people to give insight into developing new drugs
- To improve clinical care for HD patients by identifying the best clinical practices across all Enroll-HD sites around the world and ensure that all families receive that standard of care

In support of these goals, Enroll-HD is helping coordinate and expedite experimental medicine studies and the development of biomarkers and clinical assessment tools for HD.

July 2019 Quarterly News Bulletin

Dear Enroll-HD Investigators and Site Staff,

With this second bulletin of 2019, we would like to express our appreciation of your continued commitment and dedication to the Enroll-HD platform. As mentioned in our last bulletin, we would like to emphasize on Enroll-HD recruitment strategy of focusing on the recruitment of **at risk**, **premanifest and early stage participants.** Some metrics on the recruitment strategy are provided in this news bulletin.

Here are the study updates:

Plasma Collection
- We are thrilled to share that **the first Enroll-HD plasma collection was completed** on July 23rd, 2019 at Center for Movement Disorders in Toronto, Canada. Based on the study criteria and site selection, thus far total **of 22 Enroll-HD sites** have been invited to participate in a longitudinal collection of plasma, which will continue to start up in the coming months.

- As we have more than **20,000 participants** that are enrolled into Enroll-HD and **over 1 million aliquots** of DNA, lymphoblastoid cell lines and PBMCs that are available for research, the demand for high quality plasma samples for biomarker research is increasing. Therefore, the biosample collection is now **refocusing on collecting PMBCs and plasma.** To create a **high-quality longitudinal plasma collection from 2000-3000 HD gene expansion carriers at all** disease stages but with a primary focus on **pre-manifest and early manifest participants.** In addition, **10-15% gene negatives and family controls** will be included. Ideally the same participants would contribute plasma annually for a minimum of **5 years.**

Enroll-HD Newsletter
- Enroll-HD Newsletter will be published in Summer 2019. It will introduce you to some of the people including research participants that make this study a success. The newsletter aims at bringing updates to the wider HD community regarding the study's progress and explore the practical aspects of how the study is put together and what keeps it running smoothly.

General Reminder
- Friendly reminder for the Enroll-HD sites to ONLY include Lab IDs when responding to BioRep inquiries for biosamples related communications.

- For any issues concerning biosamples (e.g. you would like to request the destruction of a sample collected in the study) please contact your Lanco/Site Manager. Do not contact BioRep directly.

- Change in Sample Collection and biokit ordering after EDC 1.10 Release: ***Maximum of 2 ACD tubes should be collected at Baseline/Follow-up visit.*** *With this change, there will only be one standard kit (both for Baseline and Follow-up) available for Enroll-HD samples in the EDC for ordering.* If a third blood tube was collected accidentally, please include the third tube in the shipment and include a comment for the first barcode field in the Sample Form in the EDC, specifying the bar code of the third tube. **Reminder**: The collection of the third ACD tube has been stopped altogether. Site should only enter comments in "Bar code" comment fields, as BioRep can only see comments that are stated under "Bar code" comment field.

Recruitment update

- As of **July 1st,** there are 18,845 active **participants** enrolled at **174 sites** (158 sites still active) in 19 **countries** around the world.

Regional startup and enrollment updates

EUROPE:
- 11,618 active participants have been enrolled at 99 sites (92 are still active) in Austria, Belgium, Denmark, France, Germany, Ireland, Italy, The Netherlands, Poland, Portugal, Spain, Switzerland, and the UK.
- 17 additional European sites that will participate in Enroll-HD are in start-up.

  NORTH AMERICA:
- 6,288 active participants have been enrolled at 66 sites (58 are still active) in the US and Canada.
- An additional 3 sites are in start-up.

  AUSTRALASIA:
- 706 active participants have been enrolled at 6 sites (all sites are still active) in Australia and New Zealand.
- 1 additional site is in start-up.

  LATIN AMERICA:
- 235 active participants have been enrolled at 3 sites (2 are still active) in Argentina and Chile.
- 5 sites in Argentina, Colombia and Peru are in start-up.

Enroll-HD datasets and website information
- The recent periodic dataset is available at: https://www.enroll-hd.org/for-researchers/access-data/
- You can find on the Enroll-HD website information about how the study is structured and the people who keep it running, from site staff to participants to clinicians to researchers. Please share the link with your colleagues and your participants and check back often for new articles, updates and announcements. https://www.enroll-hd.org
- Please also check that the information listed on the website for your site (https://www.enroll-hd.org/participate/clinic-locations/) is current and correct; please email any corrections to your site manager or language coordinator.

Top Enrolling Sites - Since Study Start (Active Participants)
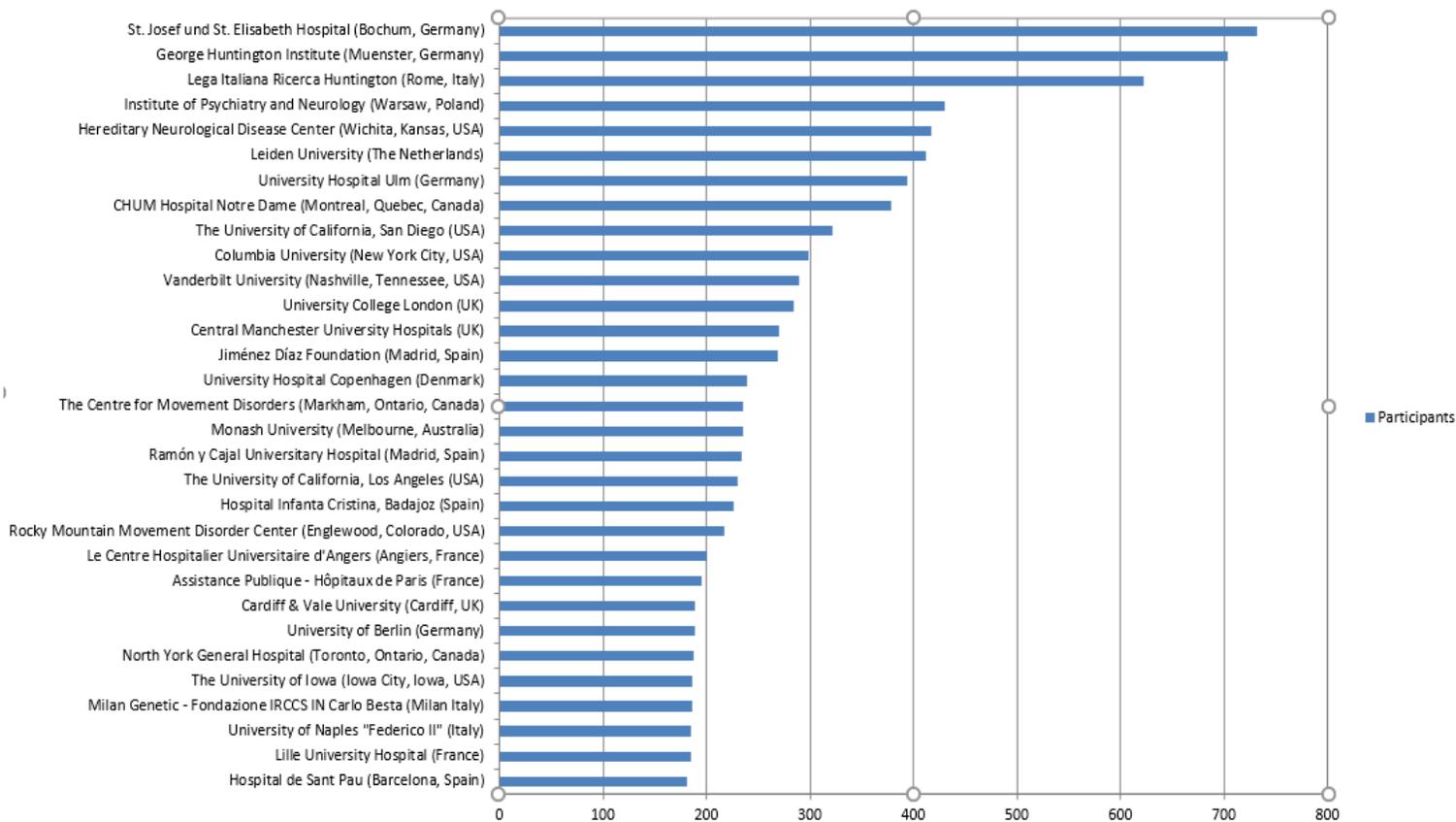
☆ The top enrolling site is St. Josef und St. Elisabeth Hospital (Bochum, Germany) with **732 active participants** enrolled!

Top Recruiting Sites of Genotype Unknown, Premanifest and Early Manifest Participants (disease stages 1-2) recruited since January 2018
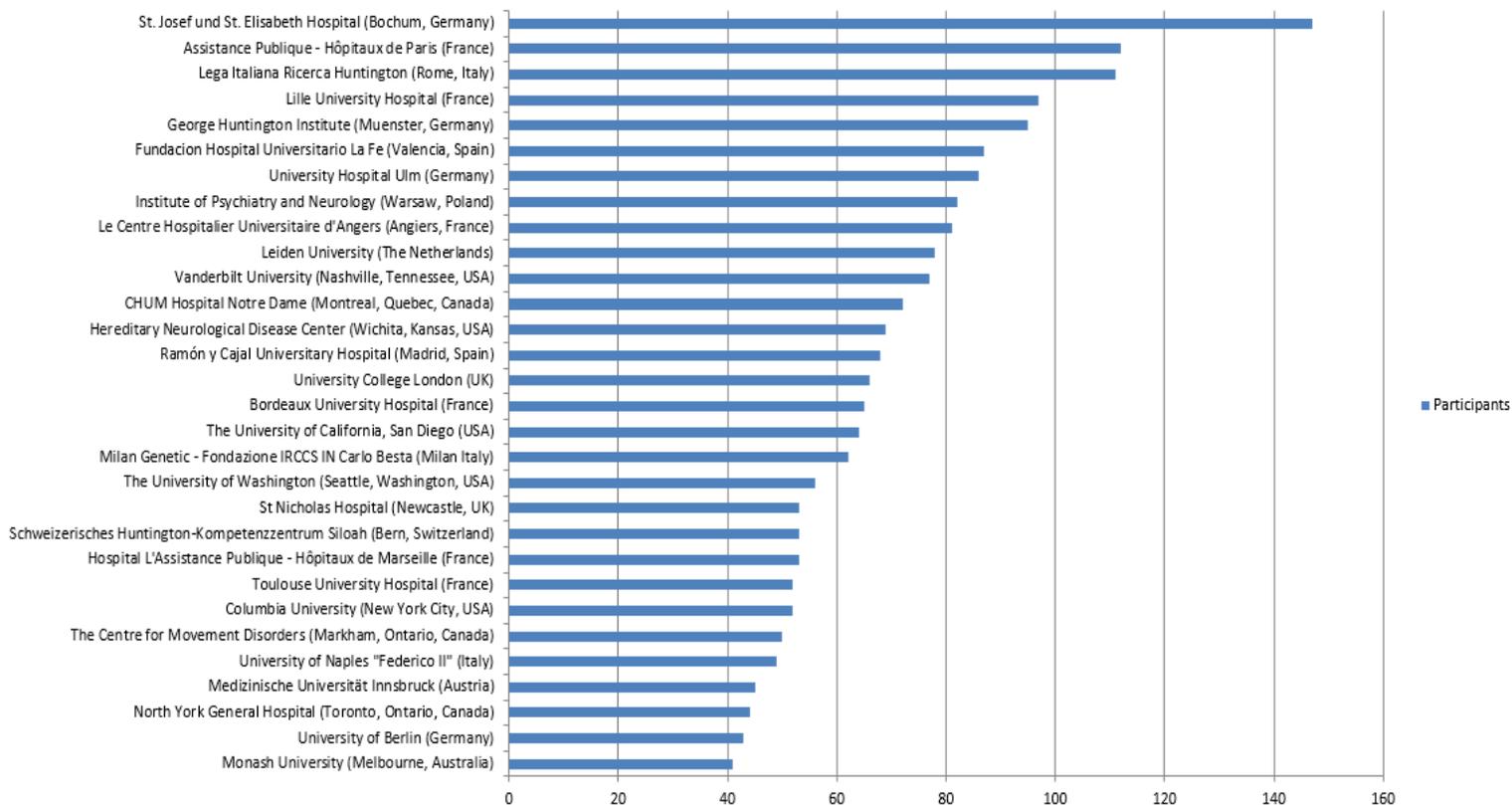
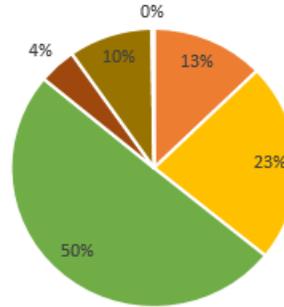# Distribution of participant categories at enrollment

* After 2017 the recruitment strategy had been changed to focus only on participants who are genotype unknown, premanifest, early manifest or family controls

HD category distribution at Baseline visit before January 2018 – (Cut off date: June 30, 2019)
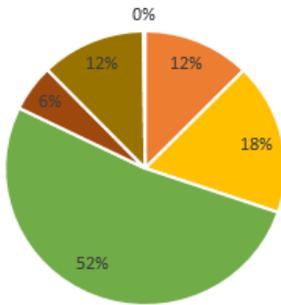
0%
12% 12%
6%
18%
52%

- genotype unknown
- premanifest
- manifest
- genotype negative
- family control
- community control

HD category distribution at Baseline visit after January 2018 – (Cut off date: June 30, 2019)

0%
4% 10% 13%
23%
50%

- genotype unknown
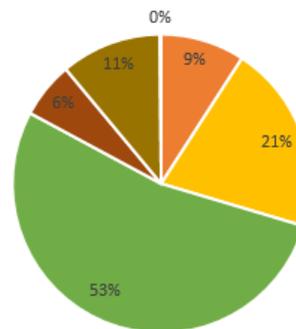- premanifest
- manifest
- genotype negative
- family control
- community control

Distribution of participant categories at their latest visit

### HD category distribution at last visit – before January 2018
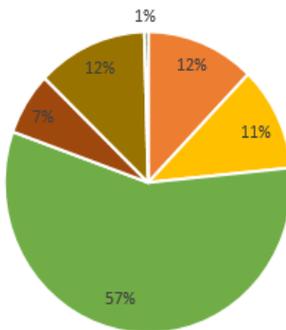
1%
12% 12%
7%
11%
57%

- genotype unknown
- premanifest
- manifest
- genotype negative
- family control
- community control

HD category distribution at last visit – Last visit after January 2018

0%
11% 9%
6%
21%
53%

- genotype unknown
- premanifest
- manifest
- genotype negative
- family control
- community control

Disease Stage distribution at the last visit (Manifest participants only)
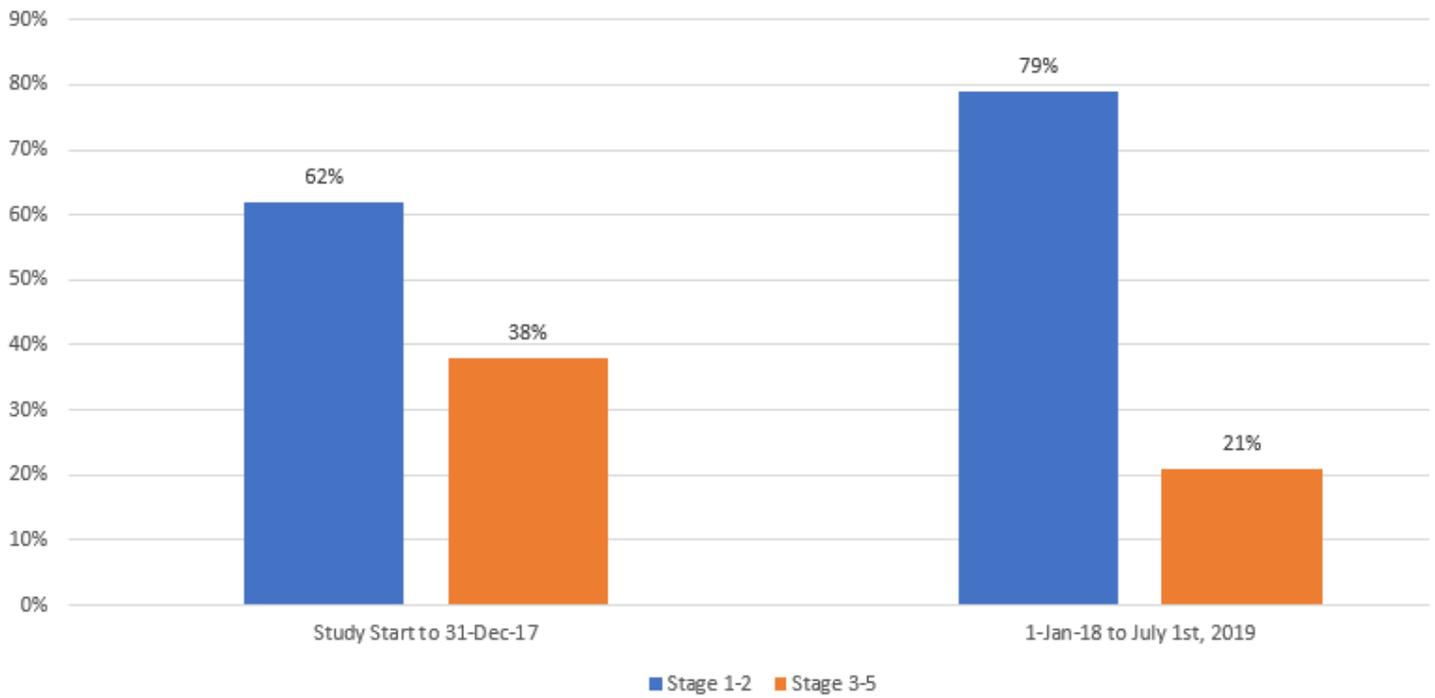
Thank you for your support in helping Enroll-HD achieve its goals.

The Enroll-HD Study Team