November 2021 · Issue 44

EHDN *News*

EUROPEAN **HUNTINGTON'S DISEASE** NETWORK

Onwards and Upwards:

New Frontiers and the New Normal

On 9 September, more than **480 eager delegates** virtually 'tuned in' to the warm welcome to the 2021 Remote Meeting by Anne Rosser [EHDN Executive Committee (EC) Chair], Jean-Marc Burgunder (former EHDN EC Chair) and Astri Arnesen [President of the European Huntington's Association (EHA)]. Over the course of the meeting, an impressive **865 participants** out of the 1,065 who had registered attended for at least part of the proceedings. And they weren't disappointed – the stimulating presentations and discussions provided fascinating insights into the latest research that is opening up new frontiers in HD treatment and care.

OUR PHOTO EXPERIMENT CONTINUES – SHARE YOUR OWN! SEE PAGE 18

CONTENT — Click the Page

www.ehdn.org

Subscribe to EHDN *News*:
Please go to the URL below and fill out the online form:
http://www.ehdn.org/news-events/
Please send us your comments, suggestions and overall feedback:
newsletter@euro-hd.net

Imprint:
Editorial Board of EHDN *News*:
Catherine Deeprose, Editor
Gabriele Stautner Artifox Communication Design (Ulm, Germany).

Anne Rosser

EHDN Business Meeting: Key Updates from Anne Rosser

The EHDN has remained highly active in most areas despite the pandemic, with the EC and the Scientific and Bioethics Advisory Committee (SBAC) continuing to meet regularly by Zoom.

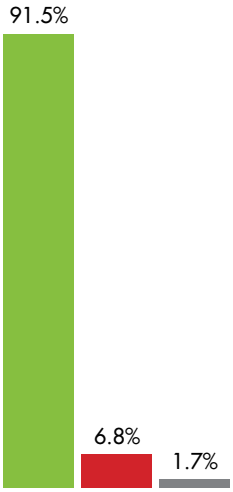
Endorsement of clinical studies: Since the last plenary meeting, seven major clinical studies have been endorsed and several study protocols have been reviewed.

Seed Funds, data mining and sample use: Over the last two years, the SBAC and EC have granted access to ten legacy registry data and samples requests and 16 Seed Funds have been awarded in response to the twice-yearly application rounds for funding.

Working groups (WGs) and task forces (TFs): The majority of WGs and TFs have managed to remain active through Zoom networking. These groups are a testament to the commitment and the generosity of the EHDN membership and this work is recognised and very much appreciated.

Think Tank (TT): Key activities include liaising with WG and TF lead facilitators to help identify potential collaborations and funding opportunities, as well as holding discussions on scientific ideas. The TT also provides a forum for discussion with internal groups such as the Communications Group, and also internal and external collaborators in identifying important questions for HD research.

Clinical Trial Site Certification Scheme: Managed by the Enroll-HD Clinical Trial Committee, this scheme supports the recording of key information about sites relating to personnel, facilities and trial populations which can be made available to sponsors preparing to run clinical trials. There have been 162 applications, 131 of which are certified.



Constitution amendments and voting outcomes: A summary of changes to the constitution was presented. Most of these changes were proposed to better align the constitution with current practices or to make semantic edits to improve clarity. Prompted by the COVID-19 pandemic, the provision to extend the terms of the EC due to unforeseen circumstances was highlighted, and also the proposed increased flexibility in the appointment of individuals to other EHDN committees. At the close of voting, an overwhelming majority of 91.5% of voters agreed with the proposed changes, 6.8% disagreed and 1.7% abstained.

EHDN 2022 Plenary Meeting: The next EHDN Plenary Meeting will be held face-to-face in Bologna in September 2022. The Programme Committee will be jointly chaired by Patrick Weydt (University Hospital Bonn, Germany, and EHDN EC Deputy Chair) and Åsa Petersén (Lund University, Sweden). Elections for the EC will be held and new SBAC members will be appointed at this meeting.

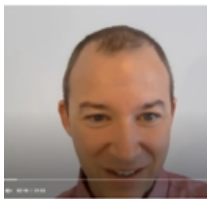
From Fruitfly Biorhythm Genetics to HD: A Personal Journey

The first keynote session by **Charalambos P. Kyriacou** provided a personal account of his extraordinary career, starting at Brandeis University (USA) where he conducted his early work to the University of Leicester (UK), where he is now Chair of Behavioural Genetics. We heard how early in his career, he discovered the rhythmic components of the Drosophila courtship display and how mutations of the period gene influence this. With others, he then started molecularly identifying the period gene leading to the demonstration in the 1980s that a piece of DNA from the period locus could restore circadian rhythms in mutant, arrhythmic Drosophila. This work culminated in a model of the Drosophila circadian clock. Later, the key findings were replicated in mammals, confirming the relevance to understanding human sleep and circadian rhythms. Kyriacou shared with us how his interest in HD had been prompted due to a family connection with the disease, and explained how work with colleagues later confirmed the role of the metabolic kynurenine pathway in modulating neurodegeneration in a Drosophila model of HD. Kyriacou elaborated how this work has been subsequently developed to explore therapeutic targets in HD.

FIRST PLENARY SESSION

Genetic Modifiers of HD: DNA Damage and Somatic Expansion of Repeats

The first plenary session was chaired by Lesley Jones (EHDN Executive Committee) and Davina Hensman Moss (St George's University of London, UK).



Vincent Dion of Cardiff University, UK, presented a novel gene-editing approach to contract CAG/CTG repeats. Reminding us that longer repeats cause more severe disease at an earlier age, he noted that if we can take a long repeat and shrink it down to a non-pathogenic size then this should bring benefits to patients. To try to achieve this, researchers have removed the repeat track altogether although some difficulties are associated with this. Dion described his alternative approach of using a Cas9 nickase that cuts only one of the two strands of DNA to specifically target only the repeat track. Striking data from Dion and his colleagues have confirmed the utility and safety of this approach and ongoing research aims to identify the underlying molecular mechanisms of CRISPR-Cas9-induced contractions.

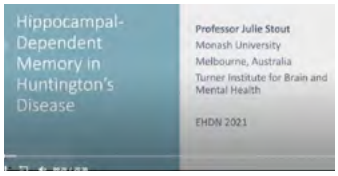
Bob Lahue of the National University of Ireland, was next to speak on his work identifying the role of histone deacetylase 3 (HDAC3) enzymes in modifying other target proteins. Specifically, Lahue explained, HDAC3 seems to work on a very important protein called MutSβ which drives the repeat CAG expansions that occur in HD. Work in Lahue's laboratory has shown that RGFP966 inhibits HDAC3, and in doing so, can block the activation of MutSβ and thus block expansions. Lahue provided the analogy of thinking about the expansion mutations in HD as an 'out of control genetic train', arguing that if we can slow down that train, we can slow down the deterioration of the brain in HD. He ended the presentation by showing that administration of RGFP966 in mice before the onset of symptoms of HD suppresses huntingtin (HTT) expansions in the brain, pointing to the potential for RGFP966 as a therapy in HD.

The third speaker was **Vanessa C. Wheeler** of the Center for Genomic Medicine, Massachusetts General Hospital, USA. She began with the observation that genome-wide association studies have provided significant insight into the pathogenesis of HD in recent years. She described how longer somatic expansions in the brain are associated with earlier onset of HD, and how quantification of somatic expansion reveals common patterns of instability. Wheeler presented a two-step theoretical model of pathogenesis in HD that involves a repeat expansion component and a toxicity component. Wheeler provided evidence in support of this model and concluded that further work, including the dissection of human modifier alleles, is now needed to better understand mechanisms and optimal therapeutic approaches.

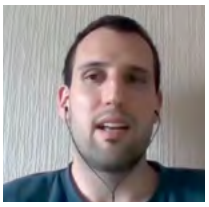
Key Advances in Cognition Research

The second plenary session was chaired by Jaime Kulisevsky and Saul Martinez-Horta, both of the Biomedical Research Institute Sant Pau, Spain.

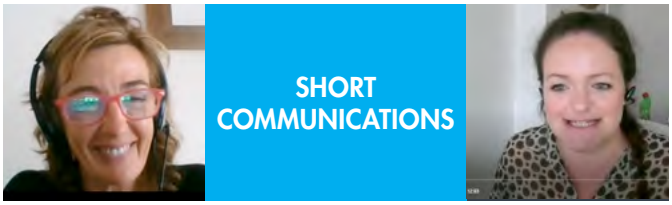
Michael Orth (EHDN Science Director and of the University of Bern, Switzerland) spoke about visual cognition in HD. In patients, information transfer to the primary visual cortex appears intact, and neuronal density of the primary visual cortex is similar to controls. Nonetheless, a large number of studies point to abnormalities of further information processing in HD as well as structural and functional abnormalities of the visual cortex. Visual cognition is of immense practical importance (consider, for example, the impacts on social cognition, movement and balance, and driving capability). Orth concluded that future research should focus more specifically on visual cognition, selecting appropriate neuropsychological measures, and integrating data from several modalities (e.g., imaging, functional and behavioural assessment).



Next, **Julie Stout** of Monash University in Australia presented on hippocampal-dependent memory. While impairments in learning and retrieving information present the biggest problem, closer inspection also indicates problems with storage. Stout discussed two studies, the first being on autobiographical memory, defined as 'recollections of personally experienced events'. She found that individuals with HD are poorer at autobiographical event recall. The second study on spatial memory and navigation identified deficits in early HD on the navigation component of a computerised task compared to healthy controls, but not in pre-manifest HD. In the object location component, both the HD groups showed deficits. How overall functioning in HD is impacted by these deficits requires further investigation.



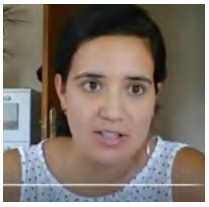
After the second plenary session, **Matthew Ellison** of the Huntington's Disease Youth Organization (HDYO) provided an announcement on the global work of the HDYO in providing support for young people and their families. He explained this is achieved in part through the HDYO website, where supportive information is available in 14 languages. HDYO also organises youth camps to provide experiences for teenagers and young adults. Although these services have been provided for free, HDYO would gladly welcome donations to support this work and encouraged delegates to contribute.



From Research Participation to Rehabilitation

The next session consisted of brief presentations on a wide range of topics, chaired by Esther Cubo of the Hospital Universitario Burgos in Spain, and Lauren Byrne of University College London in the UK.

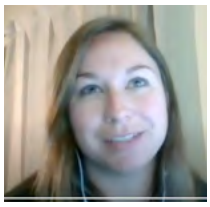
Filipa Júlio of the EHA spoke first on the factors that influence research participation. Her findings from an online survey indicate that motivation to take part in research is high, despite limited research experience and literacy. This work is providing a knowledge base for the latest EHA project 'Moving Forward' aiming to increase participation in HD research, and Júlio noted the key role of patient organisations in fostering engagement.



Next, **Idaira Rodriguez Santana** of HCD Economics in the UK presented the Huntington's Disease Burden of Illness study. Data on patients were collected from physicians in the USA, Germany, Italy, Spain, France and the UK, and indicated that the pandemic has negatively impacted patients and caregivers, particularly in relation

to health resource use and mental health. These novel data on health resource use by HD stage increase the evidence base of the HD community.

Peter Holmans of Cardiff University, UK, explained that the influence of CAG length on recorded HD age at onset (AOO) means that the power to detect other risk factors is increased by statistically modelling AAO as accurately as possible. Using the Enroll-HD PDS5 dataset, he compared the Langbehn (2004) model with that by Kaplan (2007) in predicting AOO. Both models were similarly accurate when CAG 40–55 but the Kaplan model had greater accuracy when CAG >56, offering a preferable approach for use in genome-wide association studies.



Emma Burnip of the University of Canterbury, New Zealand, explained that dysphagia is highly prevalent in HD and associated with aspiration pneumonia. To address this difficulty, skill-based training aims to enhance cortical modulation to improve the safety and efficiency of swallowing. Burnip reported on a study of 12 adults with HD and dysphagia who had completed two weeks of training, confirming the feasibility and benefits of the intervention on swallowing-related quality of life.

Rebecca Mason of the HDYO presented on JOIN-HD – the Juvenile Onset Initiative for Huntington's Disease. The aim of this registry is to identify patients with juvenile onset of HD, further insight into e.g. their phenotypes, facilitate future research and identify unmet needs. Since pre-registration opened in March 2021, 17 registrations from six countries have been received and the team are busy preparing a platform for stage 1, establishing a family advisory group, obtaining EHDN approval, increasing recruitment and securing additional funding.

Anne Rosser, Jean-Marc Burgunder, Sandrine Humbert (Grenoble Institute Neuroscience, France) and Bernhard Landwehrmeyer (Ulm University, Germany) reconvened at the end of the day to share their perspectives and insights following this exciting first day of presentations.

Updates in Ongoing Clinical Trials

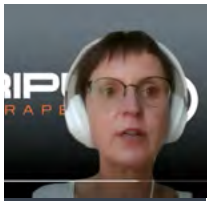
Day 2 opened with the third plenary session which was dedicated to clinical trials, chaired by Ralf Reilmann of the George Huntington Institute in Germany and Dina de Sousa of the EHA.

Scott Schobel of F. Hoffmann-La Roche A.G. recapped on the IDMC's decision to stop tominersen dosing in the GENERATION-HD1 trial, noting that ~85% of patients currently remain in the study for clinical and safety follow-up. He also reminded us that 120 mg tominersen given once every 8 weeks had an unfavourable safety profile and while the same dose given once every 16 weeks was safer, showed no clear benefit. Schobel updated that simple analyses recently commenced and more interesting and complex analyses are yet to be completed. Questions regarding the future for tominersen will be answered and shared with the HD community in due course.

Maurice Zauderer of Vaccinex Inc explained that SIGNAL was a randomised, placebo-controlled trial of pepinemab (VX15) in cohorts of early manifest and prodromal HD. There were minimal treatment effects in the prodromal group but in early manifest HD patients, significant benefits were seen for the cognition composite scores across all study time points (months 2–17). Benefits were also seen to apathy. For patients with more advanced progression of HD, post-hoc analyses showed benefits for treatment on the Clinical Global Impression of Change score. Finally, imaging data demonstrated significantly reduced caudate atrophy for treatment and a trend in the same direction for ventricular expansion.

An update on WVE-003 (an allele-selective mutant (m)HTT-lowering oligonucleotide) was the focus for **Vissia Viglietta** of Wave Life Sciences Ltd. Wave's dual aim is to preserve the neuroprotective effects of non-mutated wildtype HTT while reducing toxic, mutant HTT. Allele-selectivity is achieved by targeting single nucleotide polymorphisms (SNPs) associated with the long CAG repeat responsible for the production of toxic, mutant HTT. In a mouse model of HD, potent and durable effects are observed for WVE-003 in the cortex and striatum. Preclinical data have informed the starting dose for human testing in the Phase Ib/IIa SELECT-HD trial which has now commenced.

David Cooper of uniQure Inc., updated on the HD-GeneTRX-1 and HD-GeneTRX-2 clinical trials of AMT-130, which targets toxic huntingtin exon 1 following implantation into the striatum. The ultimate goal is to focus neurosurgical delivery to the most relevant brain regions and critically, slow disease progression in patients. The CT-AMT-130-01 Phase I/II study is the first FDA-approved clinical study for gene therapy in HD and in addition to safety and tolerability, the duration of AMT-130 persistence in the brain will be assessed. Treatment in this randomised, imitation-surgery controlled study of early manifest HD patients commenced in the USA in June 2020 and the planned Phase Ib/II open-label study (no control group) in the EU and UK will augment these data.



Irina Antonijevic of Triplet Therapeutics Inc., presented on the antisense oligonucleotide TTX-3360 which aims to stop somatic expansion (rather than lower HTT) to halt HD onset and progression. Intracerebroventricular injection of TTX-3360 in non-human primates has shown a good safety margin as well as sustained MSH3 lowering in the targeted brain areas, and Triplet states that intracerebroventricular injection is preferable to intrathecal injection for both safety and efficacy reasons. The data from SHIELD HD will be used to inform the planning and augment the control group of their planned Phase I/IIa study, for which CTA/IND submission is on track for mid-2022.

The final speaker in this session was **Michael R. Hayden** of Prilenia Therapeutics B.V., on PROOF-HD, a Phase III

clinical trial of pridopidine. He said that in HD, pridopidine activation of the sigma-1 receptor positively influences multiple pathways that lead to neuroprotection. Decreased functional capacity places a heavy burden on the daily lives of patients and their families and follows a stable pattern of decline. In earlier clinical trials pridopidine was assessed to have maintained functional capacity and stabilise neurofilament light levels (a marker of progressing neurodegeneration in HD). Hayden reported that 570 patients have been screened or reserved for screening in their current Phase III study and that completion is on target for October 2021.

The session was concluded with the speakers and chairs taking forward a lively panel discussion focused on what we have learnt in the drug development process in recent times.

Driving Forward Multidisciplinary Care and Treatment

This parallel session was opened (and co-chaired) by **Marleen van Walsem** (of Oslo University Hospital, Norway) on challenges and practice-based approaches in professional advanced care. Her qualitative research provides important insight into how the challenges facing healthcare professionals in HD affect their care of patients and how various approaches are available to confront these challenges.

Fellow co-chair **Ruth Veenhuizen** (of Atlant, Huntington Centre of Expertise in the Netherlands) then spoke on the characteristics, functioning and gender differences of patients with HD based in a nursing home. We heard how her quantitative research findings emphasise the highly variable and complex care needs of patients, and the need for person-centred, flexible approaches to care and treatment.

She was followed by **Manon van Kampen** (also of Atlant) on 'Passivities of Daily Living'. This multidisciplinary approach focuses on stabilisation and dealing with disabilities from which recovery is not possible, with increased attention directed towards the needs of the patient. A case study has provided preliminary positive results for the approach and a further study is in progress looking at the impact in late-stage HD.

PARALLEL SESSION

Investigating Neurodevelopment

The parallel session on neurodevelopment was chaired by Silvia Gines of the University of Barcelona and Sandrine Humbert.

Monia Barnat of the Université Grenoble Alpes, France, opened by explaining the potential impact of HD on neuro-development and presented data from different mouse models demonstrating the consequences of HTT mutation/deletion on cortical development, noting the convergence of these findings with some recent human studies.

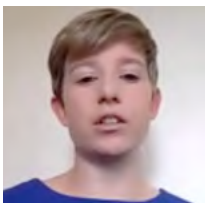
Ferdinando Squitieri of IRCCS Casa Sollievo della Sofferenza and Istituto CSS Mendel, Italy, continued on this theme with his presentation on paediatric onset HD. Reminding us of the links between neurodegeneration and neurodevelopment, Squitieri shared data supporting his assertion that HD differs in children, juveniles/young adults and finally adults/late-onset HD in terms of impact on the brain as well as expected disease length.

The final presentation was by **Josep M. Canals** of the University of Barcelona, Spain. His laboratory works to characterise the molecular alterations that occur at embryonic stages and changes in the homeostasis of neuronal progenitor cells during the development of medium spiny neurons, and has confirmed specific changes occurring during the embryonic period of development in HD.

SHORT COMMUNICATIONS

From Cognitive Flexibility to Brain Energy

The last session of the day was another series of short communications, chaired by Ahmad Aziz of the German Center for Neurodegenerative Diseases and Bonn University Hospital, Germany, and Maria Björkqvist of Lund University, Sweden.



First to speak was **Christelle Langley** of the University of Cambridge, UK. Cognitive flexibility is vital for adaptive decision making but specific impairments are found in premanifest HD patients, accompanied by an alternative fronto-striatal circuit associated with attentional set-shifting compared to controls, potentially representing functional reorganisation.

Chiara Casella of Cardiff University, UK, presented on white matter pathology. In a comparison of HD patients and controls, she used tractometry to assess tract-specific changes across the callosum, and found significant alterations in callosal apparent myelin. Noting that alterations follow a topologically specific pattern of degeneration, she speculated that the HD mutation leads to excessive myelin production early in disease progression, and this leads to the detrimental effects observed.

Also from Cardiff University was speaker **Duncan McLauchlan**. Unfortunately, clinical depression is common in HD and has major effects on quality of life. In his first study, propensity scoring in the Enroll-HD

dataset was used to determine the efficacy of different antidepressant classes, showing that SSRIs and NDRI classes outperformed other agents. In his second study, he found that motivational anhedonia is the core process underlying depression in HD, and thus, drugs acting to improve this outperform other drug classes.

Anne Rosser of Cardiff University explained that while stem cell-derived products show promise as treatments for HD, significant challenges remain for clinical translation. Stem Cells for Huntington's Disease and the EHDN Advanced Therapies WG are global platforms created to combine expertise in addressing these. Their work has recently culminated in a position paper on translating cell therapies for neurodegenerative disease using HD as a model. The next steps include creating task forces to work on the specific areas identified in the paper.

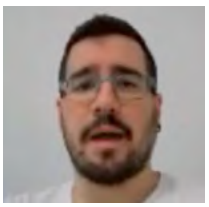
Next to present was **Fanny Mochel** of the Paris Brain Insitute in France. Noting the importance of brain energy deficiency in HD, she explained that triheptanoin is an anaplerotic drug that improves brain energy in HD patients after one month of treatment. She then presented the larger TRIHEP3 study of triheptanoin compared to placebo, which showed stabilisation at 1 year compared to the assessments at baseline and 6 months in the Unified Huntington's Disease Rating Scale score, as well as improvements relative to placebo. Further analyses showed a decrease in caudate atrophy. Based on these encouraging data, plans are now underway for a potential Phase III study.

The meeting was concluded for the day with a round-up and reflective discussion by Anne Rosser, Jean-Marc Burgunder, Ahmad Aziz and Dina de Sousa.

From CAG Repeat Expansion to Psychological Intervention

The final day opened with another series of short communications, this time chaired by Kathrin Reetz of RWTH Aachen University in Germany and Jean-Marc Burgunder.

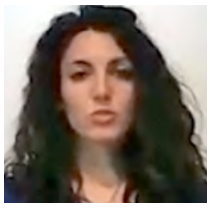
Joseph Hamilton of University College London, UK, noted that although the importance of the somatic expansion of CAG repeats in HD is well established, how the endonuclease FAN1 inhibits this process has been unclear. He provided data supporting a dual function of FAN1 in CAG repeat stabilisation, and proposed that promotion of specific FAN1 interactions may modify the age of onset in HD and/or the progression of the disease.



Rafael Alcalá-Vida of the Centre National de la Recherche Scientifique and Université de Strasbourg in France focuses on transcriptional dysregulation, chromatin alterations, and the consequences of these. Using a mouse model of HD, he has assessed striatal procedural memory across a series of studies and this work is elucidating the critical role of epigenetic alterations in the cognitive symptoms of HD.

Vittoria Bocchi of the University of Milan and Istituto Nazionale di Genetica Molecolare in Italy described work in which human foetal striatum single-cell atlas was used as a reference. Most critically, this work in vivo and in vitro single-cell datasets will

hopefully act as benchmarks to quantify and refine current stem cell engineering protocols, allowing better understanding of HD pathophysiology and an acceleration of the development of therapies.



Alice Migazzi of the University of Trento in Italy has sought to elucidate precisely how HTT mediates axonal transport and why this is disrupted in HD. Presenting a series of findings from in vitro and in vivo studies, she explained the newly discovered role of the arginine methyltransferase PRMT6 in recovering axonal transport defects and promoting neuronal health.

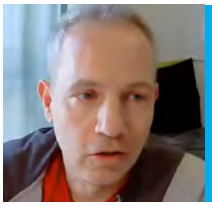
Lucienne van der Meer of Leiden University Medical Center in the Netherlands then described the 'Hold me Tight' relationship programme for couples facing HD. This 8-session intervention is based on the psychological attachment theory of human relationships, adapted for the HD population. It has been well-received by couples and brings positive outcomes, presenting a useful adjunct to standard care.

PARALLEL SESSION

Digital Technologies to Advance Assessment and Care

This parallel session was chaired by Alzbeta Mühlbäck of the University of Ulm, Germany, and Monica Busse of Cardiff University, UK.

Ralf Reilmann presented on the IDEA-FAST consortium and explained the scientific rationale for the use of quantitative measures in clinical development, noting that among several benefits, they provide greater sensitivity than standard clinical scales. Next to speak was Pearl van Lonkhuizen of Leiden University Medical Center in the Netherlands. Quoting the belief that the knowledge rather than the patient should travel, she explained the development process of the European eHealth Platform for HD patients and their families. Finally, Philippa Morgan-Jones of Cardiff University, UK, provided an overview of embedding Fitbit activity trackers in the European-wide consortium DOMINO-HD, a longitudinal observational study of multi-domain lifestyle and genetic factors in HD. The speakers and two chairs then reconvened for a stimulating panel discussion on the ethical and practical challenges of using digital technologies in clinical assessment and care.



PARALLEL SESSION

Sleep, Circadian Rhythm and Metabolism

This parallel session was chaired by Patrick Weydt and Åsa Petersén.

Roger Barker of the University of Cambridge, UK, presented data showing that sleep problems are one of the earliest abnormalities in HD and coincide with some of the earliest cognitive deficits. He concluded that sleep difficulties may be part of a bigger circadian rhythm problem in HD, leading us on to the presentation by Charalambos P. Kyriacou. Pointing to the utility of the fly as a useful model for sleep/circadian studies in HD, he noted the potential avenues of therapeutic development arising from such work. Kyriacou concluded by proposing a new model accounting for the potential interactions between sleep, sleep need, the circadian clock and autophagy in HD.

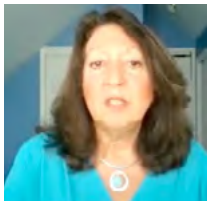
The last presentation in this session was by **Sandrine Betuing** of Sorbonne Université/Institut de Biologie Paris Seine/Neuroscience Paris Seine, France. She presented a theoretical model of cholesterol metabolism in HD and incorporated a discussion of the enzyme CYP46A1 as a potential therapy. The session was concluded by the chairs with a summary of the key findings arising from the presentions with a specific focus on practical tips to overcome issues such as sleep difficulties in HD.

FOURTH PLENARY SESSION

Exciting Developments in Ongoing and Future Clinical Research

This informative plenary session was chaired by Jean-Marc Burgunder and Bernhard Landwehrmeyer.

First to speak was **Catherine Scart-Grès**. Developed in the 1980s, SOM3355 is commercialised for the treatment of hypertension but has now been identified by Som Biotech S.A., to be a potential vesicular monoamine transporter type 2 (VMAT2) inhibitor, supported by their in vitro studies showing inhibitory activity at VMAT2 and in vivo studies showing adequate brain penetration without adverse effects. A proof of concept study in HD has demonstrated improvement on chorea symptoms with active treatment compared to placebo. The next trial will be an international Phase IIb study to assess the efficacy of SOM3355 in reducing chorea in two parallel doses followed by an open-label extension. Currently, site selection is ongoing and the study is due to start by the end of 2021.



Beth Borowsky on behalf of Novartis Pharmaceuticals presented on the investigational oral HTT-lowering therapy branaplam. Noting that HTT-lowering therapies are among the most promising in HD, Borowsky added that branaplam will be the first to be given orally to patients. Mechanistically, branaplam decreases the expression of HTT mRNA and HTT protein as confirmed in a Phase I study. The protocol for a Phase IIb study in early manifest HD patients has now been finalised, with the goal to identify a safe and well-tolerated dose of branaplam that lowers mHTT sufficiently to achieve a clinical benefit. Part 1 will be a staggered, dose-finding study and then Part 2 will be an open-label extension of the selected dose. It is planned that 11 countries will participate, and the first patient first visit is expected at the end of 2021. Given the potential advantages of oral administration of HTT-lowering therapies, this is an exciting move forward.

G. Bernhard Landwehrmeyer of Ulm University, Germany, provided an overview of current gene therapeutic efforts. Starting with the 'promise of fixing the root cause of monogenetic disorders', he noted that current in vivo approaches differ in several important respects before summarising the specific development programmes of uniQure, Spark Therapeutics, Takeda Pharmaceutical Company Ltd and Voyager. Landwehrmeyer then considered the challenges facing gene therapy in HD. In particular, he pointed to the recent FDA focus on the toxicity risks and the further concerns that lie with delivery. Looking further to the future, Landwehrmeyer emphasised the utility of capsid engineering to allow precise in vivo targeting of vectors (carriers) in gene therapy.

An update from PTC Therapeutics, Inc., was provided by **Brian Pfister**. He explained their objective of developing a disease-modifying HTT-lowering small molecule that is orally bioavailable and penetrates the blood-brain barrier. Turning our attention to the example of PTC518, he noted that years of research and development have contributed to the achievement of key milestones to date. The Phase I study of PTC518 in healthy volunteers consisting of single dose, multiple ascending dose, food effect and cerebrospinal fluid (CSF) sampling components is currently ongoing. However, the single and ascending dose studies have already confirmed the proof of mechanism and PTC518 will make the exciting move from Phase I to Phase II evaluation across multiple countries and centres later in 2021.

Next to speak was EHDN's **Olivia Handley** with an update on the Enroll-HD platform studies. She opened by recapping the platform aims, namely, to enhance the design and expedite the conduct of clinical trials, to improve our understanding of the phenotypic spectrum and disease mechanisms of HD in humans, and to foster good clinical care and improve health outcomes. At the core of the platform is the global, observational, longitudinal study of HD, Enroll-HD. This is a family study, recruiting gene positive, gene not known, gene negative individuals, as well as companions/caregivers and community controls. Since 2012, 21 countries have signed up and 26,161 participants have been recruited. Handley continued to note that Enroll-HD releases periodic datasets as well as biosamples, providing an invaluable research resource for the research

community. Currently, the Enroll-HD platform is supporting studies looking at brain imaging, health economics, and outcome measures, to cite just a few examples of the input into advancing knowledge of HD.

HDClarity is one of the studies supported by the Enroll-HD platform and was the focus of the presentation that followed by **Ed Wild** of University College London, UK. HDClarity is the largest multi-site, observational cerebral spinal fluid collection initiative to date, and has been running for four years. Samples are requested by researchers for further analysis and already, over 600 samples have been collected from more than 500 participants. Globally, there are seven participating nations and 25 clinical sites. To date, 15 requests for the distribution of samples and data have been approved for projects aiming to identify new biomarkers or to research further already identified HD biomarkers. Despite the challenges of the pandemic, Wild noted that recruitment and collection progressed, and the recruitment target has increased from 1,200 to 2,500 participants as momentum continues to gather strength.

This session was wrapped up with a panel discussion including the chairs and speakers to address questions arising from the stimulating presentations.

FINAL KEYNOTE SESSION

A New Staging System in HD: Extending the Window of Testing and Treatment

Giorgos Papantoniou of the Huntington's Disease Association of Cyprus and Dina De Sousa chaired the final session of the meeting.

It opened with a keynote address by **Cristina Sampaio**, Chief Medical officer at the CHDI Management/CHDI Foundation, USA. As explained by Sampaio, in all clinical research and epidemiology, we need to be able to identify the cases of interest using specific, standardised criteria and be able to define stages of disease. As such, the HD scientific community identified the need for a 'standardised definition of HD that allows for a case definition comprising the totality of the temporal course of disease, i.e., from birth to death'. This led to the establishment of the HD-RSC Regulatory Science Forum Working Group (RSF), which comprises researchers, clinician-scientists and representatives from pharmaceutical and biotech companies. Their approach has been one of formal consensus and the use of systematic methodologies for evidence gathering and analysis, culminating in the HD-ISS – the integrated staging system in HD (HD-ISS). Undoubtedly, the future developments and implications of the HD-ISS are considerable, and Sampaio justifiably reminded us of the value this evidence-based staging system will have on advancing therapeutic development and paving the way for trials and treatments earlier in the progression of HD.

As the meeting drew to a close, it was fitting at this point that **Tom Bird** of the University of Washington presented a historical account of his five decades of work in the HD field. He recounted his early-career interactions with an inmate at Walla Walla Penitentiary who had HD, noting the frequency with which HD patients come to the attention of the legal and mental health care system. He noted that lack of judgement and impulsivity, for example, are features of the disease that may increase the risk of not only criminal behaviour in HD but also the risk of harm from others. Bird noted the difficulties for health care systems in caring for individuals, who many years ago, would have been institutionalised. He then turned to the issues surrounding embarrassment, injury (such as through falls) and neglect that affect individuals with HD. In summing up his fascinating and productive career, Bird reflected on his experiences with patients and their families, sharing how impressed he has been by their compassion, determination, patient and 'gaman', which he explained is the Japanese term for 'enduring the seemingly unbearable with patience and dignity'.

At the close of the virtual meeting, Anne Rosser extended her thanks to all those who had worked endlessly hard to make the conference such a success, the speakers and chairs who had driven the extremely high standard of presentations and discussions, and of course, the meeting sponsors.

Presentations, discussions, posters and full report of the EHDN 2021 Remote Meeting can now be found on the EHDN website: ehdn.org/ehdn2021.

Photo: Jenny Townhill

Photo: G. Stautner, Artifox.com

Update: Clinical Trials

Jenny Townhill and Tim McLean, Central Coordination

The following studies have been endorsed by EHDN. Endorsement of a study protocol follows review by the EHDN SBAC, which makes its recommendations to the EC. If endorsed, a formal letter of endorsement is then issued to the study sponsor, allowing them to inform relevant regulatory authorities and/or ethics committees that the study protocol has been reviewed and endorsed by a group of expert HD scientists and clinicians. The endorsement may also be posted on the EHDN website, signalling the same message to the HD community.

Key updates are provided below for the EHDN endorsed trials and studies that are active or in start-up; please refer to Table 1 for a summary of the main study information.

LMI070 (Novartis)

This global Phase IIb trial of branaplam (LMI070) will recruit 75 Stage I and Stage II participants with HD at multiple sites in Europe and North America and is expected to be initiated by the end of 2021. The study will run in two parts: Part 1 is dose-range finding; branaplam/placebo will be administered as an oral liquid once per week, starting with a low dose and moving to higher doses for subsequent participants, for a minimum of 16 weeks until all participants complete this treatment period. In Part 2, participants will transition to an open-label extension.

The primary goal of this study is to identify a safe and well-tolerated dose of branaplam that lowers mHTT to a sufficient level in CSF to predict a clinical benefit (35–50%). The selected dose from this Phase IIb study is then planned for study in a larger Phase III study.

SOM3355 (SOM Biotech S.A.)

SOM Biotech are planning an international multicentre Phase IIb trial of SOM3355 (bevantalol), a VMAT2 inhibitor. Bevantalol is currently marketed for use in hypertension and has been shown to have an acceptable safety and tolerability profile.

The study is planned to start at the end of this year and recruit 129 HD participants with chorea at ~20 sites in Europe. Bevantalol or placebo, administered via oral capsules, will be given for a duration of 12 weeks. The primary goals of the study are to assess efficacy in treating chorea and the safety of the two doses that will be administered vs placebo.

SELECT-HD (Wave Life Sciences Ltd)

Wave announced in September 2021 that the first participant has been dosed in their Phase Ib/IIa international study of the allele selective ASO WVE-003. The study is recruiting participants with early-manifest HD who carry SNP3, one of the SNPs more frequently found in association with the HD gene.

GENERATION-HD1 and GENEXTEND (F. Hoffmann-La Roche A.G.)

Although dosing for these trials has been stopped (GENERATION-HD1) and paused (GEN-EXTEND) following a decision by the IDMC in March 2021, participants continue to attend follow-up visits for both studies. A full unblinded analysis of the data is in progress, including a detailed review in collaboration with HD experts to understand what factors may impact how people respond to treatment, e.g., disease stage, treatment duration/dose, and results will be released to the community as soon as they are available (safety data are expected at the end of 2021 and the full study analysis in early 2022).

HD-DBS (Heinrich-Heine University, Duesseldorf)

This multi-centre trial exploring the safety and efficacy of deep brain stimulation in HD has completed recruitment, bringing the total number recruited to 48. The last participant is expected to complete the study in December 2021. The final study report is expected during 2022.

DOMINO-HD (Cardiff University)

This study aims to explore how digital technologies, such as wearable fitness trackers, can be used to support people with HD, and is open to recruitment in Austria, Poland, UK and Spain, with a site in Germany expected to be activated in the coming months. For more information visit: https://www.cardiff.ac.uk/centre-for-trials-research/research/studies-and-trials/view/domino-hd

PROOF-HD (Prilenia Therapeutics B.V.)

This ongoing Phase III trial of pridopidine is expected to complete recruitment in October 2021, ahead of target. Participants receive pridopidine/placebo for 65–78 weeks then have the option to enter an open-label extension period, where all participants are given pridopidine. For more information visit: https://huntingtonstudygroup.org/proof-hd/

HDGeneTRX2/AMT-130-2 (uniQure Inc.)

The European gene therapy trial of AMT-130 in early manifest participants is expected to start recruitment by the end of 2021. This open label surgical trial is linked to and will be run in parallel to the North American uniQure HDGeneTRX1/AMT-130-1 randomised, double-blind, sham-controlled trial.

Table 1: EHDN-endorsed Trials and Studies

(Active or in Start-up)

Registration ID (CT.gov)	Sponsor	Trial name	Phase	Intervention	Mechanism of Action	Target Enrolment	Location(s)	Status
TBC	Novartis	LMI070/ branaplam	IIb	LMI070/ branaplam	mRNA splicing modifier	75	USA, Canada, UK, Germany, France, Spain, Lithuania, Russia, Italy, Belgium, Hungary	In start-up
TBC	SOM Biotech S.A.	SOM3355	IIb	SOM3355/ bevantolol	VMAT2 inhibition	129	Europe	In start-up
NCT02535884	Heinrich-Heine University, Duesseldorf	HD-DBS	II	Deep brain stimulation	High-frequency stimulation of the Globus Pallidus	50	Austria, Germany, Switzerland	Participant follow-up
NCT03761849	F. Hoffmann-La Roche A.G.	GENERATION-HD1	III	RG6042/ tominersen	Allele-nonselective ASO	801 (completed enrolment: 791 participants)	Australasia, Canada, Europe, Japan, USA, Latin America	Participant follow-up
NCT03842969	F. Hoffmann-La Roche A.G.	GEN-EXTEND	OLE	RG6042/ tominersen	Allele-nonselective ASO	1,100	USA, Canada, Europe	Participant follow-up
NCT04120493	uniQure Inc.	HD GeneTRX2/ AMT-130-02	Ib/II	rAAV5-miHTT	miRNA nonselective (gene therapy)	26	UK, Germany, Poland	In start-up
NCT04556656	Prilenia Therapeutics B.V.	PROOF-HD	III	pridopidine	Sigma-1 receptor agonist	480	USA, Canada, Europe	Recruiting
NCT05032196	Wave Life Sciences Ltd.	SELECT-HD	Ib/IIa	WVE-003	Allele-selective ASO	36	Australia, Canada, Europe	Recruiting
NCT04406636	Triplet Therapeutics Inc.	SHIELD-HD	N/A	N/A	N/A	60 (completed enrolment: 70 participants)	USA, Canada, Europe	Participant follow-up
N/A	Cardiff University	DOMINO-HD	N/A	N/A	N/A	300	Poland, Spain, Switzerland, UK	Recruiting

Note. ASO = antisense oligonucleotide; OLE = open label extension; VMAT2 = vesicular monoamine transporter 2


Photo: G. Stautner, Artifox.com

Update: Enroll-HD – Status and Recent Milestones

Olivia Handley, Enroll-HD Global Platform Manager

Since Enroll-HD recruited its first participant in July 2012, it has gone on to become the largest longitudinal observational study of HD. Here we reflect on a number of recent milestones for the study (see also Figure 1) as well as describe some examples of how Enroll-HD can be used for other research activities.

Towards the end of 2020, Enroll-HD released its fifth and largest dataset with a total of **21,116** Enroll-HD participants included. Some participants data included in this PDS have up to **8 Enroll-HD annual visits**. The PDS is available to the research community via a straightforward application process. To date, there have been more than **230 downloads** of PDS data since the first release in 2016 along with over **80 peer-reviewed publications**. It's clear to see how Enroll-HD's datasets are making a significant contribution to our understanding of the disease.

In November 2020, Enroll-HD recruited its **25,000**th participant – this achievement represents the remarkable continued commitment and partnership that exists between the HD families, the study sites, and the Enroll-HD team. Despite all the challenges and restrictions brought on by the COVID-19 pandemic, over **1,000** new Enroll-HD participants were recruited during the first 6 months of 2021; this took place in addition to sites continuing their follow-up visits with existing Enroll-HD participants.

Enroll-HD is also seeing an increase in the number of studies looking to use Enroll-HD data to add to their own study data. In other words, standardised clinical assessment data such as the UHDRS '99, cognitive measures, behavioural interviews, collected in Enroll-HD can be shared with other studies for inclusion into their own datasets. The advantage here is that participants are not asked to repeat assessments, therefore reducing participant burden and at the same time, reducing the amount of time required by site staff to complete those assessments, removing any redundant duplication. One study, now completed, adopted this approach successfully, a further **four studies that are active are linking with Enroll-HD data**, and an additional five to seven studies are in the pipeline and will be using a similar approach.

Enroll-HD continues to grow year on year, surpassing previous milestones and enabling a broader range of opportunities within the research community. We very much look forward to further progress in 2022!

Figure 1: Key Enroll-HD data as of 01 July 2021

Update: HDClarity

Seema Maru, HDClarity Study Coordinator and
Alex Lowe, HDClarity Research Assistant

Current Site Status

Since HDClarity began in 2016, the study has opened at 27 clinical sites, across seven nations worldwide, and has over 500 participants. The study was designed to address the rapidly growing demand for CSF samples and all participants are included from Enroll-HD. The study is expanding to further sites in Australasia, Europe and North America.

Total Recruitment

As of September 2021, HDClarity sites have successfully completed over 600 sampling visits, including optional repeat, longitudinal and longitudinal repeat visits across all participant groups.

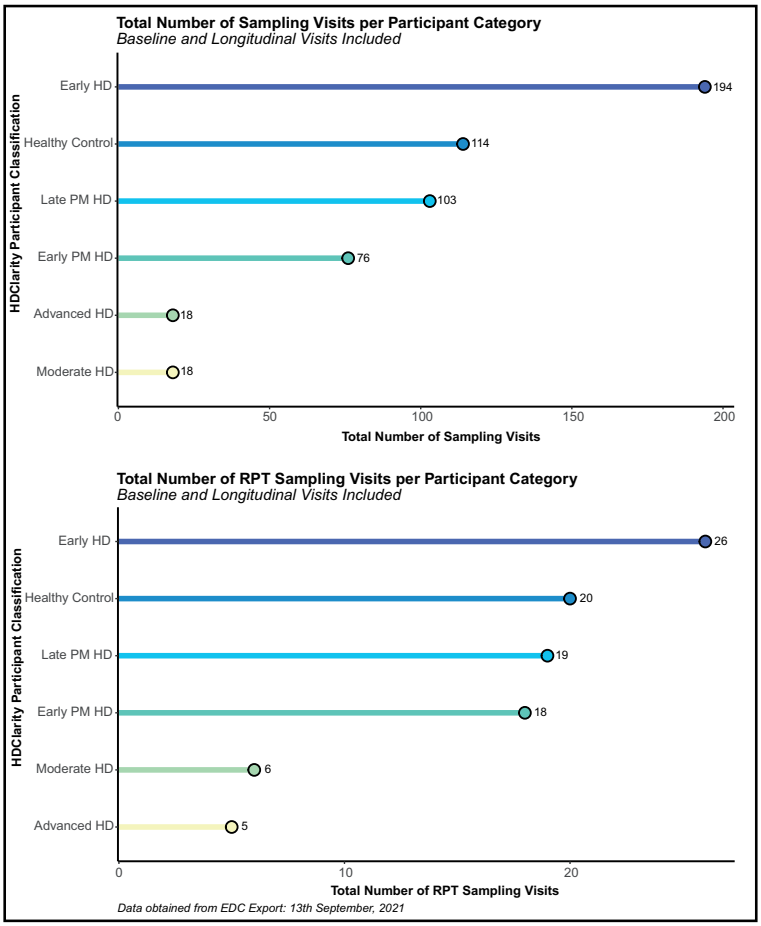


Figure 2: Total number of Initial and Repeat (RPT) Sampling Visits Across Participants in All Diagnostic Categories Note: PM = Pre-manifest.

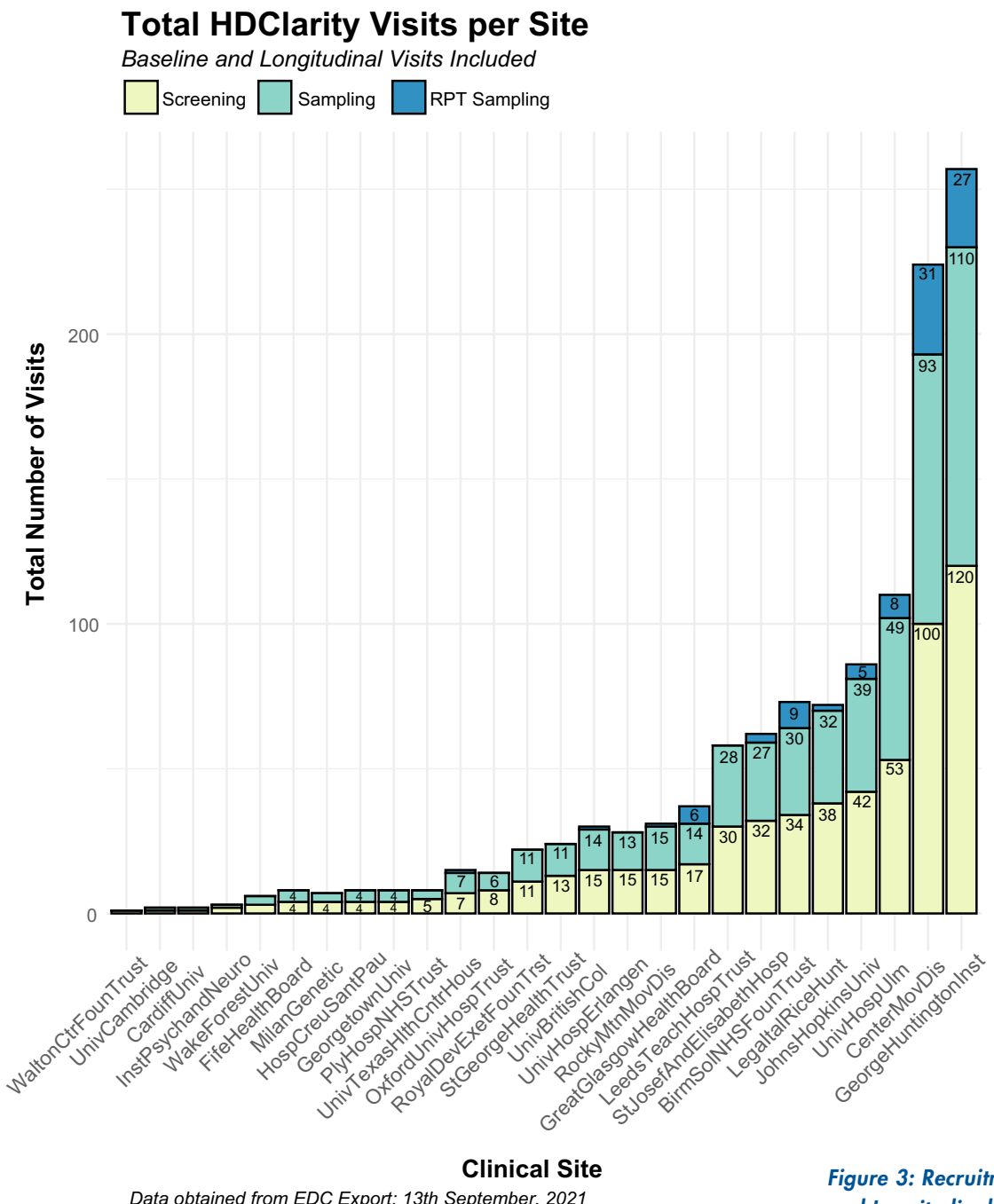
Diagnostic Category	Screening	Longitudinal Screening	Sampling	RPT Sampling	Longitudinal Sampling	Longitudinal RPT Sampling
Early PM HD	72	10	68	17	8	1
Late PM HD	109	3	100	19	3	0
Early HD	216	4	190	26	4	0
Moderate HD	20	2	16	6	2	0
Advanced HD	14	5	13	5	5	0
Healthy Control	107	15	99	20	14	0
Total	**538**	**39**	**486**	**93**	**36**	**1**

Table 2: Recruitment by HDClarity Participant Category (as of 13 September, 2021) Note. PM = Pre-manifest; RPT = Repeat.

Sampling Visits and CSF Collection

During HDClarity sampling visits, CSF and plasma samples are collected from the participant and clinical data is taken from a recent Enroll-HD visit. Participants may also be invited to attend an optional repeat sampling visit, which allows researchers to explore the short-term stability of biomarkers. Participants may also choose to enrol again in the study after 11 months to provide samples for longitudinal analysis. Such visits are extremely valuable, allowing researchers to assess the stability of identified biomarkers as the disease progresses, ultimately helping to facilitate therapeutic advances in HD.

Throughout the pandemic, HDClarity sites and participants have remained committed and have continued providing valuable samples, including those collected from secondary (longitudinal) enrolments. We are hoping that within the next few months, many more active sites will be able to resume screening and sampling visits.



Data obtained from EDC Export: 13th September, 2021

Figure 3: Recruitment Data (Baseline and Longitudinal) by Initiated Sites (as of 13 September, 2021)
Note. RPT = Repeat.

Future Plans

Due to the success of the study and the increasing demand for CSF and plasma samples for HD research, we are currently in the process of submitting a protocol amendment which will include the following changes:

- Four Annual Screening and Sampling Visits (i.e., at 1, 2 and 3 years after the first initial visit), after which participants can consent to take part again.
- Recruitment target increased from 1,200 to 2,500 participants
- Inclusion of juvenile participants and gene expansion carriers with CAG <40.

For more information and details on participating in HDClarity, please email hdclarity-cc@enroll-hd.org. Researchers can request samples by visiting https://enroll-hd.org/for-researchers/technical-support/.

Update: New Seed Funds Awarded

Catherine Deeprose

The EHDN has recently awarded seed funding for two exciting new projects.

Philipp Capetian at the University of Würzburg, Germany, has been awarded funding for his project aiming to establish and validate a methodology for conducting state-of-the-art post-mortem analyses of foetal grafts in HD patient brains.

While replacing lost cells in HD via stem cell transplantation seems like an intuitive treatment, it is unfortunate that some large studies have failed to confirm the efficacy of this approach. The underlying reasons for this are unknown, particularly as analyses of the brains of HD patients who had received transplant have demonstrated viable transplanted neural cells. We propose that expanding our knowledge on graft integration will help us understand how transplantation therapy can be made more effective. More specifically, we will extend our knowledge on graft integration by analysing post-mortem HD brains using magnetic resonance imaging and pioneering histological techniques to identify if – and if so, how strongly – grafted neurons have been integrated into the hosts' brains. We hope that findings from this work will help the important effort towards making transplantation a more effective intervention for HD.

Rana Soylu Kucharz at Lund University, Sweden, has been awarded funding for her project aiming to investigate calcium transients in HD-affected muscles.

Intracellular calcium acts as a signalling molecule in all cell bodies. Calcium transients, for example, fluxes, spikes, and other changes in calcium concentrations regulate many aspects of cell life. It is a precise messaging system that tells cells how to develop, function, or even when to die. When this messaging system is dysregulated, slow but progressive changes ultimately result in an avalanche of devastating consequences for the cells. This is of special relevance for muscles, where calcium regulates the primary muscle function: the ability to constrict and relax. Detrimental changes in intracellular calcium signalling accompany many chronic diseases, but their contribution to HD pathology is not well understood. We will establish a quantitative imaging approach to investigate intracellular calcium signalling in muscles, correlate the changes in signalling patterns with HD disease progression, and determine its impact on muscle dysfunction observed in HD. This, in turn, may push the HD field in a new direction, pointing at previously unknown underlying mechanisms.

Seed funds are intended to support pilot studies that will eventually kickstart larger projects. The next deadline for applications is 1 March 2022. More information about the programme and how to apply can be found here or you can contact Christine Capper-Loup (Christine.Capper-Loup@siloah.ch) for further information.

Update: Funding Opportunities

Fionnuala Margreiter,
Grants & Collaborations Manager

Horizon Europe Funding Call (Topic ID: HORIZON-HLTH-2022-DISEASE-06-04-two-stage) Development of Effective Therapies for Rare Diseases

This two-stage, collaborative call opened on 6 October 2021 and the first deadline is 1 February 2022.

For more information on grant opportunities, please see the EHDN website which is updated on a regular basis: http://www.ehdn.org/hd-clinicians-researchers/grant-manager/

Follow our Grants and Collaborations Manager on Twitter @EHDN_GRANTM for the latest news on EU funding and events and policy developments in the domain of rare diseases.

Photos: Gregory Youdan

Send Us Your Photos!

These photos are of Kristen Hokenson (who is gene positive) and me performing the dance DUET, choreographed by Heidi Latsky at the Huntington's Disease Society of America (HDSA) Hope Walk in 2019.

These pictures are important because 'Dance for HD' is a burgeoning field and one that is growing in research and programming. There is increasing evidence that physical activity and dance may be beneficial for people with HD.

It is also noteworthy that the founder of the HDSA was professional modern dancer Marjorie Guthrie, principal dancer with the Martha Graham Dance Company and the wife of Woody Guthrie, American folk singer, activist and songwriter.

Our photo experiment continues!

Whether you're affected by HD personally, or you're a carer, clinician or scientist working in the field, we'd like to publish your images in the newsletter. If you have a photo that provides an insight into your daily life, that you think might interest or inspire other EHDN members – or make them think differently about the disease – please send it to us along with a few words explaining who you are and what the image shows: **newsletter@euro-hd.net**

European Huntington Association: The 'Moving Forward' and 'Let us Talk' Initiatives

Filipa Júlio, EHA Project Manager

We have recently launched the 'Moving Forward – Toward a Future with Effective Disease-Modifying Therapies for Huntington's Disease' project, aiming to be a useful educational and supportive resource for persons at risk and with premanifest HD. As discussed in our recent webinar, presentation at the EHDN 2021 Remote Meeting, and also documented in our published article, the focus of Moving Forward is to mobilise the HD community to show an active, informed, and lasting commitment to research. Moving Forward is already operating in Russia, in close collaboration with the national HD organisation, the Orphan People. Soon the project is going to start in Spain, together with the Asociación Corea De Huntington Española and partnerships are currently being discussed with the Flemish and the Dutch HD Associations.
The EHA team is also preparing a communication skills course for HD professionals, 'Let Us Talk: Building Up the Communication Skills of HD Professionals to Empower HD Families'. This initiative was one of the awardees of the European Federation of Neurological Associations grants 2021.

• • •

'The Broken Doll: A Story About Huntington Disease' is a touching and poignant cartoon made for children affected by HD.

It was created by the Italian Youth HD Association (www.noihuntington.it) and officially launched on 28 September 2021. You can watch the video here.

• • •

Huntington's Disease Youth Organization: An Exciting Research Initiative and Recent News

Jenna Heilman, HDYO Executive Director

In March 2021, we launched our global patient registry JOIN-HD: The Juvenile-Onset Initiative for Huntington's Disease. As discussed at the recent EDHN Remote Meeting, the primary aim is to identify and locate people affected by Juvenile Onset HD (JoHD), while also increasing the understanding of JoHD, facilitating future research, identifying unmet needs, and improving advocacy, care, and support for patients with JoHD.

In other news, we've embarked on new programmes including Breaking Down Barriers – An Insight into Drug Development and Clinical Trials, monthly Ambassador Top Tips, partnered Research Videos with HD Buzz and recently unveiled details of our Youth Mentorship Program in partnership with HDSA.

We welcome requests for further information about these programs or how you can support our work – click here for our website or email info@hdyo.org.

International Parkinson and Movement Disorder Society

Celebrating Achievement: Congratulations to Cristina Sampaio

Catherine Deeprose

The International Congress of Parkinson's Disease and Movement Disorders named Cristina Sampaio, CHDI's Chief Medical Officer, as a winner of their 2021 President's Distinguished Service Award at the MDS Virtual Congress Opening Ceremony in September this year, in recognition of her contributions to the development of evidence-based medicine within the society.

Cristina obtained her MD in 1986 and her PhD in clinical pharmacology in 1997 from the University of Lisbon. She is a board-certified Clinical Pharmacologist and completed neurological training in the Neurology Department of the Hospital St Maria in Lisbon. She was a staff member of the Movement Disorders Clinic from 1988 to 2011, President of the Portuguese Movement Disorders Society from 2008 to 2012, and Chair of the Evidence-based Medicine Committee of the International Parkinson and Movement Disorder Society from 2010 to 2014.

In 2011, Cristina joined CHDI Foundation as Chief Clinical Officer. Here, she oversees an extensive portfolio of clinical projects ranging from experimental medicine, through biomarker and rating scale development to support drug development activities, to the development and maintenance of Enroll-HD. Before this, she had spent 25 years of her career in academia where her primary research interests centred on clinical research methodology, clinical trial design, and related aspects of meta-research applied to movement disorders. Together with several colleagues she founded the Cochrane Movement Disorders Group (MovDisCRG) and became its Coordinating Editor in 1996, a position that she shared with Professor Joao Costa from 2013 to 2018. She is now an Editor of the MovDisCRG. In addition, she was a member of the Committee on Human Medicinal Products and the Scientific Advice Working Party at the European Medicines Agency from 1998 to 2011. During this period, she had a very active role in the development of the standards of regulatory science for CNS medicinal products in the EU. She was rapporteur, coordinator, or assessor of over 400 medicinal products files submitted to the European Medicines Agency for licensing or scientific advice and she coordinated the first clinical biomarker qualification in the EU. To date, Cristina has published more than 170 peer review papers and book chapters.

This summary provides just a snapshot of Cristina's illustrious career to date. We are thrilled to see her work and achievements in HD and movement disorders recognised in this way – congratulations!

Get in touch with the Think Tank!

The EHDN's HD Science Think Tank brings together EHDN members and staff who are closely involved in supporting scientific research – including members of the Executive Committee, Central Coordination and the working groups – and it engages with the HD research community in three ways:

- Researchers may contact the Think Tank for help in identifying potential collaborators or funding opportunities, or to discuss scientific ideas
- The Think Tank welcomes suggestions of research topics, and has provided a contact form on its website via which these can be submitted
- The Think Tank may occasionally propose specific research topics that could be addressed by a dedicated task force working for a defined period of time

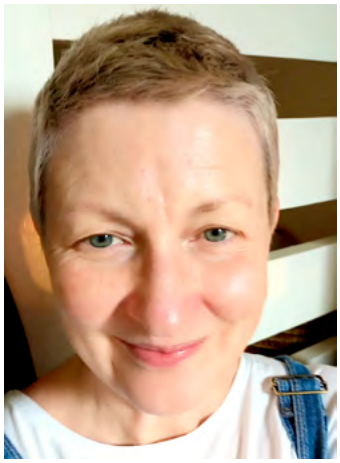
For more information about the Think Tank, please contact Kristina Bečanović: kristina.becanovic@euro-hd.net

Photo provided by Kristina Bečanović

The New Normal: How the Pandemic Has Changed the Way We Work

Within only a few months, the COVID-19 pandemic had demanded that we dramatically change the way we live and work. In this issue, we speak with three professionals working in different ways in the HD field to hear about their experiences and their perspectives on the new normal in our increasingly connected world.

Alex Fisher: Senior Occupational Therapist at Birmingham and Solihull Mental Health NHS Foundation Trust, based in the West Midlands, UK.



Tell us briefly about your day to day work pre-COVID-19?

I work as part of the West Midlands Regional Neuropsychiatry Service, where as a team we look after at least 350 HD families. Because of the geographical spread, we work at a number of levels, seeing patients in outpatient settings as part of our multidisciplinary team. This includes medics, dieticians, speech and language therapists, occupational therapists and physiotherapists. We refer to local services as and when needed. We also visit patients residing in nursing homes according to need (such as medical review, change of equipment, and so on). If local services are struggling, then we visit patients 'on the ground' to provide support.

Before COVID-19, clinics were regularly held for patients and families as part of our service. The social element is a valuable aspect of this, and due to the various interactions between patients, families and staff, these can feel much like a tea party! As we have known many of these patients for several years, I would describe this event as sad but joyous at the same time – and patients often comment how much they enjoy it. We work closely with the HDA and usually have an HDA Adviser present as part of the multidisciplinary team.

As a team, much of our work is face-to-face. As HD is, of course, a lifetime diagnosis, we don't discharge patients from our service.

How has this changed during the pandemic?

The pandemic brought overnight change and suddenly we were having to deal with the unknown, doing the best we could with advice from infection control colleagues. Microsoft Teams and telephones became the predominant methods of communication between professionals and with patients.

Professor Hugh Rickards (Consultant in Neuropsychiatry) and the team agreed our main priority should be keeping people out of hospital. To this end, we generated a spreadsheet and adopted a 'traffic light system' to allow us to focus on patients designated as 'red'. These were the challenging patients, for example, those who were not cognitively able to understand the situation, those with swallowing difficulties making them particularly vulnerable.

What changes do you think might be here to stay?

Much of what I have described is what we've been doing ever since the pandemic began and will continue to do. However, the nature of occupational therapy and speech and language therapy means that we need to see people. We need to balance the assessment of risk with the impact of not seeing patients to ensure adequate care.

Our clinics stopped for just over 15 months but have recently restarted. We have adopted a hybrid model for this (a mix of telephone, video and face to face), and limit the number of patients and families who can attend each session due to the limits in space and ongoing social distancing. Now, we hold monthly multidisciplinary team meetings and plan approaches for specific patients using the variety of methods we have available. I believe this hybrid model is here to stay for the foreseeable future at least.

And how do you feel about that?

We all quite like it! For example, it is much easier for professionals to meet up using communication technology than travelling long distances. Cohesive working has also improved and our systems are more robust and flexible.

However, we need to remember that for some patients, embracing telemedicine is simply not possible. There can be many reasons for this, such as executive function and complex language difficulties, or lack of support to

use the technology required or even having the access to tech. Patients can also feel pressured and/or worried about participating in an approach they are unfamiliar with.
As clinicians, we need to remember the importance of gut feel and clinical instinct in guiding much of our practice, and this requires face-to-face interaction. There are things that telemedicine can't provide and we need to break down the metaphorical 'fourth wall' to really understand the full richness of patient and family experiences and perspectives. In the current times, we remain dynamic, flexible and fluid – we have to.

> *'In the current times, we remain dynamic, flexible and fluid – we have to.'*

Jerry Turner: Meeting & Event Manager at CHDI Management/CHDI Foundation, based in New York, USA

Tell us briefly about your day to day work pre-COVID-19?

Before COVID-19, my day-to-day work routine consisted of overseeing the administrative organisation of CHDI's meetings and events – the annual conference, workshops, seminars, symposiums, joint steering committee meetings, advisory meetings, internal all company events, and so on. My tasks included liaising with all participants, venue sourcing, travel and lodging arrangement, food and beverage arrangement, and cocktail and dinner arrangement, among other things.

How has this changed during the pandemic?

The pandemic essentially shut down all in-person meetings and events. As you can imagine, my job was dramatically affected by this as planning these in-person events is the core of my duties. Most of the in-person meetings and events that were being planned at that time were cancelled with the rest being converted to virtual meetings. The good news is that this has provided me and my colleague in the Meetings and Events Department, Kristin Jenkins, with a valuable new skill set.

What changes do you think might be here to stay?

Although you can't truly replicate the in-person experience in a virtual setting, having the option to still host meetings and gather virtually has been utterly invaluable during the pandemic. Our goal is to return to in-person meetings and events as soon as possible, but my feeling is that having a virtual attendance option in addition to an in-person attendance option will be the standard going forward. Participants for sure will appreciate the flexibility, especially those with limited travel budgets.

And how do you feel about that?

I feel very optimistic about the 'hybrid' future of meetings and events!

> *'Although you can't truly replicate the in-person experience in a virtual setting, having the option to still host meetings and gather virtually has been utterly invaluable during the pandemic.'*

Sina Bartosch: EHDN Event Manager based at the University Hospital of Ulm in Germany

Tell us briefly about your day to day work pre-Covid-19?

As the event manager of the EHDN, my work before the pandemic consisted largely of organising our employee meetings in changing European cities, planning our plenary meeting which takes place every two years with around 1,000 participants in a European metropolis and also designing our trade fair appearances. I also personally supervised many of the events on-site and selected the

locations on the basis of site visits, which is why I travelled a lot and was in direct contact with all participants and partners.

How has this changed during the pandemic?

Due to the travel restrictions, it was no longer possible for us to hold our meeting in person on-site, which is why we decided to organise all meetings via Zoom in order to continue to enable the exchange. For this, it was necessary to familiarise ourselves with the new approach, the functions as well as the possibilities of such a meeting. All of the meetings that were previously held by phone were now also carried out using Zoom, and we found that personal contact through the video function greatly strengthened togetherness. Since our team stretches across the whole world, my working hours also changed, as meetings often took place in the evening due to different time zones. My colleagues would say I've been Queen of Zoom ever since!

The biggest change came with the decision to also host our Plenary Meeting online. For this purpose, an online platform had to be selected first and then brought closer to the participants and speakers. It was important to us to maintain the character of the event, to bring the presentations to our participants, but also to offer the possibility of interaction.

There were many challenges but the feedback after the Remote Meeting shows that all the work has led to success.

What changes do you think might be here to stay?

It's safe to assume that those event organisers and marketers who are able to adapt to change will be the ones that survive the COVID-19 challenge.

The excitement of being able to meet people again, combined with all the possibilities we didn't have online, will surely generate new ideas, concepts and visions. Different combinations or hybrids, where physical encounters are combined with modern technology through which you can connect with people on the other side of the world, will be interesting alternatives to implement. The power of change and the possibilities it offers us is truly something to put our trust in.

And how do you feel about that?

I'm not worried about the future. Things will continue to happen in the world, things that are bigger than us. It's our job to adapt and do the best we can. The most important thing is that we don't rest on our laurels. It's amazing to see how this has brought people together, created unity and given us perspective. Now is the time for doing and creating – to lose heart is not an option.

> *'It's amazing to see how this has brought people together, created unity and given us perspective.'*

• • •

Website Survey:
Tell Us What You Think Of The EHDN *website*

Follow us on Twitter:
@EHDN_*News*

Dates for your diary

- The Huntington Study Group Annual Meeting for researchers, health care providers, industry representatives and members of the HD community takes place this year 4–6 November 2021. Click here to register: HSG 2021: UNMASKING HD
- The MDS 1st Movement Disorders Clinical Practice Conference consisting of live interactive sessions for clinicians and MDS members takes place 18–19 November 2021.
- And finally, the EHDN Plenary Meeting will take place in Bologna, Italy, 16–18 September 2022. Registration and abstract submission will open in May 2022.

Would you like to share an upcoming event with our readers?
Please email the details to newsletter@euro-hd.net