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An observational study providing new insights into lifestyle and genetic risk factors in Huntington's disease

Submission date
06/08/2020

Recruitment status
No longer recruiting

Registration date
20/08/2020

Overall study status
Completed

Last Edited
26/07/2023

Condition category
Nervous System Diseases

[X] Prospectively registered
[X] Protocol
[X] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Huntington's Disease (HD) is an inherited brain disease where people suffer from increasing problems with movement, thinking, and behavioural changes. At the moment there are no treatments that can slow down or stop the disease. Recent research studies have shown that there are some promising treatments being developed, however, there is also evidence that the rate at which people with HD gets worse can be affected by the environment and by how people live their lives. This study aims to investigate the relationship between lifestyle and disease progression and to gain an understanding on how the way people with HD live their lives may affect the way in which their disease progresses.

Who can participate?
Adults (aged over 18 years) with a diagnosis of Huntington's Disease (HD) confirmed by genetic testing, who are able to walk unassisted and are participating (current or newly enrolled) in the Enroll-HD study.

What does the study involve?
The study is split into two phases; phase 1 is looking at methods for reliably measuring lifestyle factors (physical activity, sleep, diet) in people with HD in a way that disrupts their normal life as little as possible. Phase 2 will use the information gathered in phase 1 to measure these lifestyle factors in people with HD over 12 months.

Phase 1 will investigate in more detail various lifestyle factors and how reliably these can be measured in people with HD across a number of different studies:
1. How well do standard activity trackers or smart watches measure physical activity and heart rate in people with HD? People with HD will be asked to wear these devices in a laboratory setting whilst doing simple tasks that people do everyday, such as walking up stairs. Video recordings of these tasks being done will be used to compare with the information recorded by the activity tracker to see how good the tracker is at recording those particular movements. Participants will be asked to wear these trackers at home for about a week to allow further assessment how well they work. The people taking part in the study will be asked what they

think about using these devices.
2. How can the clinical tests, which are normally used by doctors to judge how much a person is affected by HD, be made more sensitive? Very detailed measurements of these commonly performed tests will be made. This would make it easier for doctors and researchers working with people with HD to measure small changes in the person's disease.
3. How well can standard activity trackers measure sleep in people with HD? Participants will be asked to wear an activity monitor in a sleep laboratory where sleep can be measured accurately by recording brain waves. The participants will then be asked to wear the activity tracker at home and complete a diary recording their sleep so that measurement can be made of how well the tracker records sleep in a real-world setting and to better understand how sleep is affected by HD.
4) Nutrition in people with HD. Participants will complete questionnaires about their diet and lifestyle, have a DEXA scan which measures the make up of the body (bone, muscle, and fat), and give blood samples for the measurement of nutrients in the blood. It is hoped that this will provide a better understanding of the relationship between nutrition and HD progression
5) How well can an activity tracker measure how much energy a person with HD uses? To do this participants will be asked to perform certain activities in a laboratory setting wearing an activity monitor and some other sensors that measure movement and that are used to measure how much energy is used during movement. Participants will then be asked to wear the activity tracker and some of the other sensors at home to see how well the activity tracker works in a real-world setting.

Phase 2 will measure lifestyle factors (physical activity, sleep and diet) in 300 people with HD for 12 months. Exactly how and what will be measured will depend on the information collected in the first part of this study. This information will be taken and combined with other information about the participant's disease status to look for lifestyle factors that may affect disease progression. It is hoped that this information will be used to design a programme of lifestyle recommendations to try and improve the quality of life for people with HD.

What are the possible benefits and risks of participating?
It is not expected that taking part in this research will have any specific benefit or increase in risk for participants. Adverse events will not be monitored during the 12-month observational study but will be monitored and recorded during participant assessments.

Where is the study run from?
1. Institute of Psychiatry and Neurology (Poland)
2. UniversitätsSpital Zürich (Switzerland)
3. Hospital Universitario Burgos (Spain)
4. Ulm University (Germany)
5. Cardiff University (UK)

When is the study starting and how long is it expected to run for?
April 2019 to March 2023

Who is funding the study?
1. Alzheimer's Society (UK)
2. Jacques und Gloria Gossweiler-Stiftung (Switzerland)
3. Schweizerischer Nationalfonds zur Förderung der Wissenschaftlichen Forschung (Switzerland)
4. Deutsches Zentrum für Luft- und Raumfahrt (Germany)
5. National Center for Research and Development (Jordan)
6. Health Research Board (Ireland)

Who is the main contact?
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Additional identifiers

Integrated Research Application System (IRAS)
274100

Study information

Scientific Title
Multi DOMain lifestyle targets for Improving progNOsis in Huntington's Disease (DOMINO-HD)

Acronym
DOMINO-HD

Study objectives
DOMINO-HD is a Consortium led observational study of behaviour and lifestyle in people with early-to-mid stage Huntington's Disease (HD). Which aims to:
1. Assess the feasibility and acceptability of using digital technologies to consistently collect information directly from people with HD about their physical activity, sleep, and diet
2. Assess the appropriateness of commercially available activity trackers to measure physical activity and sleep in people with HD
3. Design lifestyle and/or behavioural interventions aimed at improving the quality of life of people with HD.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 13/01/2020, Wales REC 3 (Health and Care Research Support Centre, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff CF11 9AB; +44 029 2078 573; REC3@wales.nhs.uk), ref: 19 /WA/0329

Primary study design
Observational

Study design
Consortium-led longitudinal observational study

Study type(s)
Quality of life

Health condition(s) or problem(s) studied
Huntington's Disease (HD)

Interventions
DOMINO will be conducted in two phases. Individual consortium partners will be responsible for performing phase 1 sub-studies within their site and /or in collaboration with other partners. The phase 2 study will be conducted across all clinical sites.

Phase 1 sub study 1 (performed by Cardiff University and University College Dublin partners) will involve validation of Fitbit Charge 4 physical activity metrics in Huntington’s Disease (HD). This study will explore the performance of the Fitbit charge 4 smartwatch as a physical activity monitoring device in people with Huntington’s disease and the use of wrist and thigh worn accelerometers to describe physical activity characteristics in HD. This study will comprise of two parts. Firstly, people with HD will be invited to the motion analysis lab where they will perform a range of physical activities whilst wearing commercially available activity trackers and motion

sensing devices. The measures provided by these devices will be analysed against the amount of activity each person actually performed to see how well they compare and whether the devices provide useful information about activity levels. Participants may also be asked to take some activity tracking devices home to collect free-living data and again assess the suitability of the devices for long term activity monitoring in HD. Having worn an activity tracker, participants will be asked to give feedback on how user-friendly the devices were and whether they were happy wearing them.

Phase 1 sub study 2 (performed by Cardiff University and University College Dublin partners) will involve development of novel objective clinical assessments in Huntington's Disease. A number of recommendations have been made outlining a range of clinical assessments that should be performed by any research team investigating the progression of HD. Whilst this provides consistency across the research literature, it remains very challenging to sensitively measure the symptoms of HD. Additional sensitive, reliable, and objective assessments that can take place in the clinical setting are vital in order to measure subtle changes in disease progression and to determine the success of therapeutic interventions. DOMINO-HD will develop new assessment methods that allow sensitive, objective assessments of HD symptoms. This will include the novel assessment of parameters believed to be clinically important:
1. Upper limb function will be measured using motion sensing devices (accelerometers) and sensors that measure muscle activity (electromyography).
2. Speech will be measured using audio-recordings and sensors that measure muscle activity (electromyography) and acceleration.

Phase 1 sub study 3 (performed by Cardiff University, University College Dublin, and University Hospital Zurich partners) will involve validation of Fitbit Charge 4 sleep metrics in Huntington's disease. This study will explore the performance of the Fitbit Charge 4 smartwatch as a sleep monitoring device in people with HD. The study will comprise two parts. Firstly, the smartwatch will be compared to the gold standard for sleep monitoring, polysomnography (PSG), during an overnight sleep assessment in a supervised clinical environment. Secondly, the smartwatch sleep metrics will be compared to a self-reported diary and questionnaires related to sleep during an unsupervised seven-night in-home study. Specific characteristics of sleep in HD will be assessed in relation to PSG data.

Phase 1 sub study 4 (perfomed by Hospital Universitario Burgos, Ulm University, Institute of Psychiatry and Neurology, Warsaw, and University College Dublin) will involve investigating the impact of nutrition on disease progression and quality of life in those with Huntington's disease. This study will investigate the impact of nutrition on disease progression and quality of life in those with HD . This study will collect additional nutrition information on a subset of 180 participants recruited as part of the 12 month longitudinal study (see below). These additional measures include baseline blood samples to enable metabolomics analyses and a baseline Dexa Scan to enable the assessment of body composition and bone mineral density.

Phase 1 sub study 5 (performed by Hospital Universitario Burgos, Ulm University, Cardiff University, and University College Dublin partners) will involve validation of the Fitbit Charge 4 energy expenditure metrics in Huntington's disease. This study will explore the performance of the Fitbit charge 4 smartwatch as a physical activity monitoring device in people with Huntington's disease (with specific focus on the ability estimate energy expenditure) and the use of wrist and thigh worn accelerometers to describe energy expenditure characteristics in HD. This study will comprise of two parts. Firstly, people with HD will be invited to the exercise laboratory where they will perform a range of physical activities whilst wearing commercially available activity trackers, motion sensing devices, and equipment capable of providing gold standard measures of energy expenditure. Calories burnt, metabolic equivalent of task (MET),

and activity intensity Fitbit Charge 4 metrics will be compared to the gold standard energy expenditure to determine whether these metrics are suitable when monitoring energy expenditure in HD. Participants may also be asked to take some activity tracking devices home to collect free-living data and again assess the suitability of the devices for long term activity monitoring in HD.

Phase 2 study will involve the longitudinal data collection of physical activity, sleep and dietary intake data in up to 300-450 people with HD across all clinical partner sites. Participants will be recruited from Enroll-HD (a global research platform and core longitudinal observational study of people with HD) over a period of 10 months, with a follow-up period of 12 months. On recruitment into this study, baseline DOMINO-HD measures will be collected in addition to the routine annual Enroll-HD visit. Participants will then be provided with a Fitbit Charge 4 to take home for continuous data collection for the follow-up period. During this time, participants may be asked to complete an additional 7 day/night activity assessment in the home involving additional wearable sensors to track their physical activity and sleep. DOMINO-HD assessments will be repeated at 12 months in line with the next annual Enroll-HD visit.

Intervention Type
Other

Primary outcome(s)
Feasibility of linking lifestyle factors and genetic risk factors to explore their interplay with HD symptom severity assessed through the linking of: physical activity data (from Fitbit charge 4) measured continuously from baseline for 12 months; and genotyping and clinical assessment data (in motor, cognitive and behavioural domains to include measures of symptom severity, collected via Enroll-HD) at baseline and 12 months.

Key secondary outcome(s)
1. Feasibility and acceptability of using digital technologies to consistently collect information directly from people with HD about their physical activity, sleep, and diet using a combination of questionnaires and semi structured interviews. These will be completed at baseline, 12 months and after 7 day in home assessments.
2. Appropriateness of commercially available activity trackers to measure physical activity and sleep in people with HD using data obtained from activity trackers and other specific activity and sleep recording devices in combination with video analysis and participant self-report diaries during phase 1 study assessments.

Sub study 1:
1. Accuracy of physical activity and heart rate metrics provided by the Fitbit Charge 4 compared to ground truth information on number of steps performed whilst in the motion analysis lab setting using summary metrics obtained from the activity trackers and compared to movement analysis from video recordings and participant self-reported diaries obtained during the visit to the motion lab or during the 7-day in-home assessment
2. Influence of device location on the quantification of physical activity metrics in people with HD using summary metrics obtained from the activity trackers and compared to movement analysis from video recordings and participant self-reported diaries obtained during the visit to the motion lab or during the 7-day in-home assessment
3. Difference in physical activity metrics obtained from different devices worn on the wrist and thigh using summary metrics obtained from the activity trackers and compared to movement analysis from video recordings and participant self-reported diaries obtained during the visit to the motion lab or during the 7-day in-home assessment

4. Movement signatures of people with HD performing physical activities/during sleep measured during the visit to the motion lab or during the 7-day in-home assessment, in order to inform the development of HD specific activity trackers using accelerometer devices

Sub study 2:
1. Ability to objectively measure motor symptoms in HD (namely chorea, dystonia and bradykinesia and speech abnormalities) using electromyography, accelerometer data and audio recordings obtained at the study visit

Sub study 3:
1. Accuracy of the sleep metrics provided by the Fitbit Charge 4 compared with the gold standard, polysomnography (PSG) measured during the sleep lab assessment
2. Performance of the Fitbit Charge 4 for assessing sleep-wake architecture and distinct behavioural states during a seven night in-home study using Fitbit Charge 4 data obtained across the 7 days of the in-home assessment
3. To understand the limitations of the Fitbit Charge 4 as a sleep monitor in HD and to develop methods to improve the accuracy of sleep metrics in this cohort.
5. Describe the sleep architecture of people diagnosed with HD using metrics obtained via PSG in the sleep lab assessment.
6. To investigate relationships between sleep metrics (as determined by PSG and Fitbit Charge 4 obtained during the sleep lab assessment) and genetic biomarkers from analysis of DNA samples provided by Enroll-HD
7. Associations between genotype and sleep by through comparison of identified genetic modifiers of disease progression and sleep parameters measured by PSG during sleep lab assessment.

Sub study 4:
1. Relationship between nutrition and the progression of HD using nutrition data collected using the Food Frequency questionnnaire and clinical assessment data obtained at 0 and 12 months
2. Develop nutritional interventions aimed at improving the quality of life of people with HD.

Sub study 5:
1. Accuracy of accelerometer-based activity monitors which are frequently used in research to objectively quantify energy expenditure (EE) in free-living settings using data from activity monitors compared to gold standard EE measurement devices during in-home assessment
2. Best anatomical location of the accelerometer to analyse EE using data from activity monitors and gold standard EE measurement devices during the in-lab activity assessment
3. EE for different activities using data from activity monitors and gold standard EE measurement devices during the in-lab activity assessment
4. Quantify EE, nutrition, and its relationship with functional capacity in HD using data obtained from activity monitors, the Food frequency questionnaire, total functional capacity assessment captured at 0 and 12 months

Completion date
31/03/2023

Eligibility

Key inclusion criteria
1. Diagnosis of Huntington's Disease (HD) confirmed by genetic testing
2. Aged ≥18 years

3. Diagnostic confidence level (DCL) 3 and 4 (which can include both pre-motor [late prodromal] or motor manifest HD)
4. Self-ambulatory
5. Participating (current or newly enrolled) in the Enroll-HD study (with a preference for those who have been genotyped in GWAS3-5 or are to be genotyped in GWAS6)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
97

Key exclusion criteria
1. Diagnosis of juvenile onset Huntington's Disease (HD)
2. History of co-morbid neurological conditions such as multiple sclerosis or stroke
3. Acute (within 1 month) orthopaedic conditions such as an ankle sprain or fracture
4. Severe medical conditions such as unstable or progressive heart disease, uncontrolled diabetes, severe liver, kidney or thyroid dysfunction, or similar medical conditions
5. Any acute or unstable psychiatric condition
6. Unable to tolerate long-term wear of activity monitor
7. Inability or unwillingness to give written informed consent
8. No access to a smartphone
9. Not willing to allow the research team to install Apps on their smartphone related to the study

Date of first enrolment
01/11/2020

Date of final enrolment
31/03/2022

Locations

Countries of recruitment
United Kingdom

Wales

Germany

Poland

Spain

Switzerland

Study participating centre
Cardiff University
Neuadd Meirionydd
Heath Park
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United Kingdom
CF14 4YS

Study participating centre
Ulm University
Ulm University Hospital
Department of Neurology
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45/189081

Study participating centre
Hospital Universitario Burgos
Neurology Department, Avda Islas Baleares 3
Burgos
Spain
09006

Study participating centre
UniversitätsSpital Zürich
Klinik für Neurologie
Frauenklinikstrasse 26 (Anreise)
Zurich
Switzerland
CH-8091

Study participating centre
Institute of Psychiatry and Neurology
Jana III Sobieskiego 9

Warszawa
Poland
02-957

Study participating centre
Southmead Hospital
Southmead Rd
Bristol
United Kingdom
BS10 5NB

Sponsor information

Organisation
Cardiff University

ROR
https://ror.org/03kk7td41

Funder(s)

Funder type
Research organisation

Funder Name
Alzheimer's Society

Alternative Name(s)
alzheimerssoc

Funding Body Type
Private sector organisation

Funding Body Subtype
Associations and societies (private and public)

Location
United Kingdom

Funder Name

Jacques und Gloria Gossweiler-Stiftung

Alternative Name(s)
Jacques and Gloria Gossweiler Foundation, Gossweiler Foundation, Jacques & Gloria Gossweiler Foundation, Jacques und Gloria Gossweiler Stiftung, Fondation Jacques und Gloria Gossweiler, JGGF

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Switzerland

Funder Name
Deutsches Zentrum für Luft- und Raumfahrt

Alternative Name(s)
German Centre for Air and Space Travel, German Aerospace Center, DLR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Germany

Funder Name
Schweizerischer Nationalfonds zur Förderung der Wissenschaftlichen Forschung

Alternative Name(s)
Schweizerischer Nationalfonds, Swiss National Science Foundation, Fonds National Suisse de la Recherche Scientifique, Fondo Nazionale Svizzero per la Ricerca Scientifica, Fonds National Suisse, Fondo Nazionale Svizzero, Schweizerische Nationalfonds, The Swiss National Science Foundation (SNSF), SNF, SNSF, FNS

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Switzerland

Funder Name
National Center for Research and Development

Alternative Name(s)
NCRD

Funding Body Type
Private sector organisation

Funding Body Subtype
Associations and societies (private and public)

Location
Jordan

Funder Name
Health Research Board

Alternative Name(s)
Health Research Board, Ireland, An Bord Taighde Sláinte, HRB

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Ireland

Results and Publications

Individual participant data (IPD) sharing plan
The integrated dataset will be shared back with Enroll-HD and will be shared once the intended analyses of the consortium are completed and published. The anonymised dataset will be available to any researcher on request through the Enroll-HD specific data request process. As part of this, all applications to use the data will need to outline the analyses they intend to perform and the release of data is pursuant to a data sharing agreement. All participants will be informed of this data sharing at the point of registration and will be asked to provide consent for this.

Raw sensor data will be made available on request to CTR@cardiff.ac.uk. All requests need to specify the intention for use of the data and will be judge on their individual merits. All requests will be pursuant to a data sharing agreement and participants will be asked to provide consent for data sharing on entry to the study,

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Protocol file	version 1.2	08/02/2021	27/03/2023	No	No
Statistical Analysis Plan	version 1.0	18/07/2023	26/07/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes