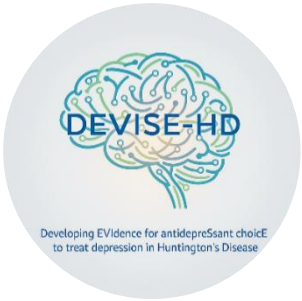

Developing EVIdence for AntidepreSsant ChoicE to Treat Depression in Huntington's Disease

Participant Information Sheet V4.1, 27/04/2026

You are being invited to take part in a research trial on the impact of anti-depressants in Huntington's Disease.

TRIAL SUMMARY

- This trial is for people that carry the gene mutation that causes Huntington's Disease (HD), and your doctor has recently diagnosed you with a new episode of depression
- HD causes difficulty with movement and thinking that get worse over time. Many individuals with HD also have depression
- Research has shown that depression in people with HD is different and anti-depressants may work differently because of that.
- We want to know how well anti-depressants do or don't work to improve depression in HD
- To do this we want to understand whether it is possible to run a Randomised Control Trial (RCT) looking at the effect of anti-depressants in people with HD.
- In this study, half of the people will receive the anti-depressant Sertraline, or a version without the antidepressant medication (placebo). You will take the treatment daily for 6 months.
- You will be asked to give some small samples of blood, but this is optional
- Throughout the trial we will ask about your feelings of depression and how the disease is progressing.

WE WOULD LIKE TO INVITE YOU TO TAKE PART IN A RESEARCH TRIAL

- Before you decide to take part it is important you know why the research is being done and what it will involve.
- You can discuss with family, friends, and clinical staff before making a decision.
- You are free to decide whether you would like to take part.
- If you choose to take part and then decide you no longer want to be involved you can stop taking part without giving a reason. Your care will not be affected.
- Please let us know if there is anything in this leaflet that is not clear or if you would like more information. A member of our team will answer your questions.
- If you decide to take part, we will offer you a copy of this information sheet and ask you to sign a consent form. If you believe you may have physical difficulties signing a consent form, please let us know and we will provide an alternative method for you to confirm your consent.

We know that living with HD can be challenging, the research team is here to support you, or you can reach out Samaritans or Shout.

There are two sections to this information sheet:

Section 1: Tells you the purpose of the trial and what will happen to you if you take part

Section 2: Gives you more detailed information about the conduct of the trial

PART 1. PURPOSE OF THE TRIAL AND WHAT WILL HAPPEN

WHY ARE WE DOING THIS TRIAL?

Huntington's Disease (HD) causes problems with movement and thinking which worsen over time. Depression is very common in HD and has effects on quality of life and people's ability to do things. We think that by properly treating depression, we can improve the quality of life for people with HD and their families.

Observational data shows that depression in HD is different from depression in people without HD. This means anti-depressant medicines might work differently in people with HD. We do not know how well anti-depressants work in HD or what is the best way of measuring depression in HD.

We want to know how well anti-depressants do or don't work to improve depression in HD. The first step in answering this question is to test how well a Randomised Controlled Trial (RCT) of anti-depressants may work.

WHY HAVE I BEEN INVITED TO TAKE PART?

You have been invited to take part because you carry the gene mutation that causes HD and your doctor has recently diagnosed you with a new episode of depression. The trial will involve 40 adults with HD who also meet the criteria for a diagnosis of depression, in 3 HD clinics across the UK.

DO I HAVE TO TAKE PART?

No. It is up to you if you decide to take part in this trial. Participation is entirely voluntary. A member of the team will describe the trial and go through this information sheet. If you decide to take part, you will be given the information sheet to keep and you will be asked to sign a consent form. Please feel free to talk about the trial with your family, friends or others before you decide to take part.

You are free to withdraw from the trial at any time, without giving a reason. A decision to withdraw at any time or a decision not to take part will not affect the standard of medical care you receive.

WHAT WILL HAPPEN TO ME DURING THE TRIAL?

If you decide to take part in the trial you may be given a course of Sertraline (the most commonly prescribed anti-depressant) or product that is identical (a placebo), but which does not contain the active medication. This will be decided at random by a computer-like picking a name from a hat. This is so that neither you, your doctor, nor the research team, can choose whether you receive Sertraline or not. Neither you nor your doctor will know whether you have received the Sertraline or not during the trial.

Half of the people in the trial will receive Sertraline and half will receive the placebo. We use a placebo in trials like this so we can accurately see what effects are caused by the drug and what effects happen by chance or are unrelated to the drug. The placebo in this trial will be microcrystalline cellulose, a common anti-caking agent used in food production. It will look like the trial medication but will not contain the active ingredient. The trial treatment (Sertraline or placebo) will be given as a 50mg capsule. You will need to take the treatment orally every day for 6 months. All pill bottles will need be returned to help us to understand how often you take the medication. The treatment will need to be collected from the hospital. If you lose the medication, please contact the research team as soon as possible.

After 6 months you will be told if you were taking Sertraline or the placebo. You will then be given the option to continue Sertraline or asked if you want to start taking it. If you decide to stop taking Sertraline, you will need to gradually stop taking the medication. During this period, we will need to monitor you to make sure you are not experiencing any significant side effects.

WHAT TESTS WILL BE DONE IF I TAKE PART?

When you join the study	Day 7 Telephone call	4 Weeks	8 Weeks Telephone Call	6 Months In person clinic visit	6-12 Month	12 Months
Clinical assessment Questionnaires Blood sample Lumbar puncture if part of HDClarity	Check to see if you are experiencing any side effects	Collect Medication	Questionnaires	Clinical assessment Questionnaires Blood sample	Monitor Sertraline withdrawal (if appropriate)	Data collected from ENROLL-HD, if part of ENROLL-HD HDClarity Samples if relevant

SAMPLES

When you were told about this study you were also asked if you wanted to join a study called HDClarity. As part of HDClarity you will have a lumber puncture to collect some fluid (cerebrospinal Fluid or CSF), and have a blood sample taken. You will be invited to provide consent for the lumber puncture and CSF sample as part of the HDClarity study. If you do not want to join HDClarity, you can choose to give a blood sample as part of DEVISE-HD at the start of the study and then again 6 months later. The samples will be collected when you visit the clinic for your health assessments. We will collect about 12 mls (or 2 teaspoons) of blood each time you donate a sample. These samples will be used to measure the progression of HD. Joining HDClarity is completely up to you. You can still take part in DEVISE-HD even if you choose not to take part in the HDClarity trial. You can also take part in DEVISE-HD without giving any blood samples

ASSESSMENTS

We will be assessing your experience of depression, and how the disease is progressing. All together the assessments will take around two hours and 45 min to complete. When completing the assessments, you can take as many breaks as you need. You will be asked to complete the assessments when you first join the study, 8 weeks later, and then again 6 months later.

We want to understand how different questionnaires assess the depression in individuals with HD. To do this we will ask you to complete a series of different questionnaires that are used to measure depression. It will take approximately one hour and 15 minutes to complete all the questionnaires. For some of the questionnaires, we will ask if it's ok for your Study Partner to be present with you to help answer some of the questions. Some of the questionnaires will need to be completed with the medical team responsible for your HD care.

Some of these questionnaires will involve questions about sensitive and potentially upsetting topics such as suicide and self-harm. You can ask to take a break from completing the questionnaires if you need to.

We also want to see if computer-based assessments can be used effectively to measure how people with HD think and reason. This means we will ask you to complete a series of tasks on the computer. These tasks are optional. It will take you about an hour to complete all the tasks.

Many people in the UK with HD are also part of ENROLL-HD. We will ask for the results of the disease progression assessments that you regularly do as part of ENROLL-HD. We will ask for those results when you first join DEVISE-HD, 6 months and then 12 months later. To do this we will collect your ENROLL-HD ID number (HD-ID). You can still take part in the DEVISE-HD trial without joining ENROLL-HD but if you are interested in joining ENROLL-HD, please speak to your clinical team who can provide you with more information.

The ENROLL-HD clinical assessment looks at your motor function, ability to work and care for yourself, your memory, visual association and how well you can stop automatic thoughts or behaviours. These tasks will take about 30 minutes to complete over the phone, in addition to the DEVISE-HD questionnaires and assessments listed above.

We will also be asking someone close to you to act as a study partner. We will collect their contact details including their name, email address and telephone number and with your permission we will contact them in the event that we are not able to contact you. They can help you complete to assessments, if you choose or need support.

WHAT WILL HAPPEN TO THE SAMPLES COLLECTED?

All samples will be taken at your hospital and then transported to the Welsh Neuroscience Research Tissue Bank laboratories (WNRTBL) (at Cardiff University) supporting the trial. These samples will be analysed to tell us more about the disease and how the drug is working. You will not be told the results of any of the tests performed on your samples. No genetic testing will be done on the samples. You'll be given the option on the consent form to allow your blood samples to be stored long-term in the WNTBL after the study has finished. If you choose to do this, the WNTBL will be allowed to share your anonymised blood samples with other researchers (including those from the commercial sector). Your anonymised blood samples will be looked after by Cardiff University in line with the Human Tissue Act (HTA) and with strict legal and ethical codes of practice and governance structures.

The samples will not have any of your personal information written on them, but they may be linked back to your clinical data. Both your samples and clinical data will be identified by your unique trial reference number only. They will be stored in a secure building.

WILL YOU ANALYSE MY DNA?

No, this study will not involve the analysis of DNA.

WHAT HAPPENS TO MY SAMPLES AT THE END OF THE STUDY?

With your consent, your anonymised blood samples will be deposited into the WNTBL at Cardiff University for distribution to researchers in the UK and abroad for further research according to ethically approved procedures. At this stage we do not know what the research will involve but some of it could include DNA analysis, animal research or use in the commercial sector. We will share some clinical data like your HD diagnosis with WNTBL. They will not share any information that could directly identify you with other researchers.

On the consent form you will be given the option to exclude your samples from the WNTBL if you choose.

WHAT ARE THE POSSIBLE BENEFITS OF TAKING PART?

There is no guarantee that this trial will help you. You may benefit from receiving Sertraline, however we will not know this until the end of the trial. You will receive reimbursement for travel costs to attend the follow up visits.

The information we get from this trial will help us understand more about the role of Sertraline to treat depression in individuals who have Huntington's Disease. We hope that this will benefit patients in the future.

WHAT ARE THE POSSIBLE DISADVANTAGES AND RISKS OF TAKING PART?

The disadvantage in taking part in this trial may be the risk of having the side-effects of Sertraline (this will not be the case if you are in the group that does not have Sertraline).

The adverse events of Sertraline are well-known. Normally these reactions will occur within the first few days of your first dose. We will monitor carefully for these but please tell the research team or your GP if you experience any of them.

Common Side Effects (affecting somewhere between 1/10 and 1/100 people):

- Nausea, vomiting, and constipation
- Fatigue
- Respiratory infections
- Changes in appetite and weight gain
- Difficulty sleeping
- Increased feelings of depression and anxiety
- Decreased libido and sexual dysfunction
- Menstrual irregularities
- Headaches
- Difficulty concentrating
- Abnormal heart rhythms and hot flushes

- Back pain
- Tremors, teeth grinding or difficulty moving
- rashes

Uncommon side effects (affecting somewhere between 1/100 and 1/1000 people)

- Inflammation and pain of the stomach or intestines
- Ear infections and pain
- Tumour growths
- Swollen lymph nodes and low platelet count
- Increased allergic reactions
- Decreased thyroid activity, and increased hormone activity
- Changes in blood sugar levels and metabolisms
- Increased suicidal ideation and self-harm behaviour
- Sleepwalking, and night terrors
- Amnesia, migraines, dizziness, motor restlessness, or coma
- Vision difficulties
- Abnormal bleeding
- Difficulty breathing
- Mouth ulcers, irritation of the throat that leads to bleeding
- Difficulty going to the bathroom and incontinence
- Decreased drug tolerance
- Abnormal clinical laboratory tests
- Increased cholesterol tests

You can also reach out to Samaritans, SHOUT, or another organisation who can help you by talking through your thoughts and feelings

Samaritans by calling 116 123

Shout by texting 85258

[INSERT LOCAL TRUST SERVICES OR LOCAL SUPPORT ORGANISATIONS]

Please tell your research nurse or doctor about any prescribed or other medications you are taking at any stage of the trial as there are some restrictions regarding other medications which might make you unsuitable for this trial. Your Trial Doctor will discuss these with you. When taking the treatment, it is important you do not eat grapefruit, or take St John's wort and take care when drinking alcohol. Sertraline can reduce your alcohol tolerance.

There is also the discomfort of potentially having additional blood tests. The side effects are well known and generally only last a short time. These could include pain, bruising, and fainting but you don't need to give blood samples if you don't want to.

If you are pregnant or become pregnant during the trial, there is a small chance that anti-depressants can have a negative impact on your baby's development. This risk is low and anti-depressants are regularly given during pregnancy. During the trial, your baby's development and health will be closely monitored. You should make sure to discuss the risks and benefits to joining the trial with the treating physician before you make a decision.

£ WILL I BE PAID FOR TAKING PART IN THE TRIAL?

No but you will receive reimbursement for travel costs to attend the follow up visits.

This completes Part 1 of the Information Sheet

If the information in Part 1 has interested you and you are considering taking part, please continue to read the additional information in part 2 before making any decision.

PART 2. DETAILED INFORMATION ON TRIAL CONDUCT

WHAT WILL HAPPEN IF I DON'T WANT TO CARRY ON TAKING PART IN THE TRIAL?

Taking part in the trial is entirely voluntary. If you decide to take part you may withdraw from the trial, at any time, without affecting the standard of care you receive. You can withdraw from different parts of the trial, like withdrawing from trial treatment, or from provision of samples for future research, or from provision of questionnaires only. Your care team will go through these options with you.

If you wish to stop taking part in the trial completely, we may need to see you one last time for an assessment and tests. The trial doctor will look to see if you were receiving the Sertraline or the placebo. **If you were receiving the Sertraline, you must not suddenly stop taking it.** Your doctor will discuss with you how to safely stop taking the medication if that is what you want. This will be for your own safety. We will need to monitor you while you gradually stop taking the medication to make sure you are not experiencing any significant side effects.

If you are suffering a serious reaction to the trial treatment when you decide to stop, we will need to continue to collect information about you for as long as the reaction lasts.

The trial doctor may decide to withdraw you from the trial if he/she feels it is in your best interests or if you have experienced a serious side effect.

Even if you stop taking part in the trial, the information we have recorded about you and the samples you have provided whilst you were in the trial will still be used.

WHAT IF RELEVANT NEW INFORMATION BECOMES AVAILABLE?

Sometimes over the course of a research trial, new information about the treatment becomes available. If this happens, your trial doctor will tell you

about it as soon as reasonably possible and discuss whether you should continue in the trial. If you decide not to carry on, your trial doctor will make arrangements for your care to continue. If you decide to continue in the trial, they may ask you to sign a new consent form.

WHAT IF THERE IS A PROBLEM AND I WISH TO COMPLAIN?

If you have a concern about any aspect of this trial, you should contact the researchers who will do their best to answer your questions DEVISEHD@Cardiff.ac.uk or the Director of the Brain Health and Mental Wellbeing Division, Rachel McNamara (McNamara@cardiff.ac.uk). If you remain unhappy and wish to complain formally, you can do this by contacting an NHS complaints advocate. Details can be obtained from https://www.nhs.uk/using-the-nhs/about-the-nhs/how-to-complain-to-the-nhs/]

In the event that something does go wrong, and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against Cardiff University but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

WILL MY TAKING PART BE KEPT CONFIDENTIAL?

All information collected about you will be kept strictly confidential in accordance with applicable Data Protection laws. Once you have been registered onto the trial, you will be assigned a unique trial number and this number will be used for the collection and recording of all trial related information to preserve your anonymity.

The information collected will be primarily to do with the treatment you receive, any side effects that you have during treatment and your long-term state of health. The personal data collected will be kept separate from any data about your condition, treatment, and recovery. It may become necessary to discuss your condition, recovery, and trial participation with a relative or

friend if you are no longer able to make decisions about your continued involvement in the trial.

Information recorded in your medical records may need to be seen by authorised members of the research team (including staff from the trials co-ordination unit), and the sponsor organisation to verify the data collected. In addition, different regulatory bodies such as the Medicines and Healthcare products Regulatory Agency (MHRA) may require access to your medical records to ensure that the trial is being run in accordance with UK law. They will only look at data that is relevant to the trial. All trial data will be kept securely with restricted access.

WILL MY GP BE INFORMED I AM TAKING PART?

If you decide to take part in the trial, with your consent your GP will be notified that you are taking part. We may also contact your GP if we are not able to contact you or your study partner and we have concerns about your wellbeing. We will discuss our concerns about your wellbeing and ask them to help us get in touch with you.

HOW WILL WE USE INFORMATION ABOUT YOU?

We will need to use information from you and from your medical records for this research project.

This information will include your:

- Name and contact details;
- Initials;
- NHS Number;
- Information about your health and wellbeing, HD diagnosis, and any medications you are taking.

People will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

Cardiff University is the Sponsor of this research. Cardiff University is responsible for looking after your information. Cardiff University will share your information related to this research project with the following types of organisations:

- Representatives of organisations providing services in connection with this study (For example WNTBL and CHDI Foundation), or organisation contracted to collect, maintain, and manage the information collected in this study alongside Cardiff University;
- Service providers engaged to check the accuracy of the information collected (for example, auditors, monitors) and regulatory authorities (where we are required to as part of a regulatory inspection)

We will keep all information about you safe and secure by:

- Only storing it on password-protected, secure servers (for electronic data);
- Only storing it in locked cabinets in secured-accessed buildings (for physical data).

HOW WILL WE USE INFORMATION ABOUT YOU AFTER THE STUDY ENDS?

Cardiff University will keep your study data for the minimum period of time required by the UK Clinical Trial Regulations, which is 25 years. The study data will then be fully anonymised and securely archived or destroyed.

The coded information collected from you during this trial may be used by DEVISE-HD partners, with their research team members, other academic, not-for-profit and/or commercial research organisations and their respective service providers also engaged in conducting research on HD and further shared by these individuals/ organizations for the following purposes:

- To generate results of the DEVISE-HD trial and publish those results in academic journals, conference presentations and relevant websites.
- To design and guide future research studies and clinical trials.

- To support and enable scientific discussion and research, including the addition of your coded information to one or more electronic databases; (1) to better understand HD or other diseases being studied, (2) that furthers the development of treatments and/or rating scales for HD or other diseases or (3) that furthers biomedical research.

We may share or provide access to data about you outside the UK for research related purposes to:

- To support and enable scientific discussion and research.

If this happens, we will only share the data that is needed. We will also make sure you can't be identified from the data that is shared where possible. This may not be possible under certain circumstances – for instance, if you have a rare illness, it may still be possible to identify you. If your data is shared outside the UK, it will be with the following sorts of organisations:

- Other universities or companies

We will make sure your data is protected. Anyone who accesses your data outside the UK must do what we tell them so that your data has a similar level of protection as it does under UK law. We will make sure your data is safe outside the UK by doing the following

- We need other organisations to have appropriate security measures to protect your data which are consistent with the data security and confidentiality obligations we have. This includes having appropriate measures to protect your data against accidental loss and unauthorised access, use, changes or sharing.

The information collected about you during this study will be used only for research purposes and will not be sold.

WHAT ARE YOUR CHOICES ABOUT HOW YOUR INFORMATION IS USED?

- You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.
- If you choose to stop taking part in the study, we would like to continue collecting information about your health from your hospital. If you do not want this to happen, tell us and we will stop
- you have the right to ask us to access, remove, change or delete data we hold about you for the purposes of the study. You can also object to our processing of your data. We might not always be able to remove, change

or delete the data, if it means we cannot use your data to do the research. If so, we will tell you why we cannot do this. If we have collected any information that could potentially identify you such as your name, address, phone number or email address, you can request that we destroy this within 28 days of you telling us that you no longer want to continue in the study however we will delete this information as standard at the end of the trial.

- In the event of your withdrawal, we will attempt to contact you to ascertain your written wishes regarding use of samples you have already provided. If we are unable to obtain your wishes in writing, we will keep your samples and use them as described in this information sheet. If you don't want your samples stored for future use, they will be destroyed at the end of the study after the analysis has been completed.
- **Data will be used for future research:** If you agree to take part in this study, you will have the option to agree for the data collected during the study to be shared with other organisations involved in the project or other researchers or organisations in the UK, or abroad, for example other universities or companies. Your name, address or other information could directly identify you will not be shared. The researchers and other organisations may publish the results of their research, including coded information, in medical journals or present such results at meetings.

WHERE CAN YOU FIND OUT MORE ABOUT HOW YOUR INFORMATION IS USED?

You can find out more about how we use your information, including the specific mechanism used by us when transferring your personal data out of the UK:

- By speaking with a member of the DEVISE-HD Trial Management Team (contact details on p.12)
- By having a look at the Cardiff University Data Protection Policy: www.cardiff.ac.uk/public-information/policies-and procedures/data-protection

- by contacting the Cardiff University Data Protection Officer by email- inforequest@cardiff.ac.uk or in writing to:
  Data Protection Officer
  Compliance and Risk, University Secretary's Office
  Cardiff University
  42 Park Place
  Cathays, Cardiff
  CF10 3BB

WHAT WILL HAPPEN TO THE RESULTS OF THE RESEARCH?

At the end of the trial the results will be analysed and published in recognised medical journals and presented at scientific meetings. You will not be identified in any publication or presentation about the trial. We will use the results to help design and guide future research studies and clinical trials. At the end of the trial, you will be able to see a summary of the results here: https://www.cardiff.ac.uk/centre-for-trials-research/research/studies-and-trials/view/devise-hd.

Details of the trial will be made publicly available on the UK Clinical Trial Registry: ISRCTN . Nothing that could identify you will ever be included on ISRCTN.

WHO IS ORGANISING AND FUNDING THE RESEARCH?

This trial is sponsored by Cardiff University and is being organised and monitored by the Centre for Trials Research at Cardiff University. Funding for the trial has been provided by Health and Care Research Wales.

WHO HAS REVIEWED THE TRIAL?

All research is looked at by an independent group of people, called a Research Ethics Committee to protect your interests. This trial has been reviewed and approved by Wales REC 5.

CONTACT FOR FURTHER INFORMATION

If you have any questions or would like further information about the trial please contact DEVISEHD@Cardiff.ac.uk or your hospital trial team

We understand that taking part in research can feel overwhelming. If you ever feel unsure or distressed, please speak to your trial team — your wellbeing matters.

<LOCAL SITE CONTACT DETAILS, including PI name>

Thank you for reading this information and considering taking part in this trial.