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HD Clinical Research Overview & Getting Involved

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Getting involved in clinical research is a personal decision. This guide is designed to provide you with the tools and information you need to make the most informed decision regarding study participation.
This document is designed to help you understand what clinical research is, the types of research studies that may be available, some of the participation requirements, and your rights as a research participant.
Any questions specific to a certain clinical research study such as age criteria, length of study visits, or compensation should be directed to study staff before agreeing to participate.

Clinical research IS NOT medical care. The main purpose of clinical research is to contribute to general scientific knowledge and NOT to guide your medical needs, even if your doctor and the researcher are the same person.

What is clinical research?

Clinical research is the study of health and illness in people. Clinical research studies teach us how to prevent, diagnose and treat illness. These studies help take laboratory research and translate it into new treatments and information to benefit patients. There are 2 main types of clinical studies:

Observational Research

- Does NOT include intervention or treatment option.
- Usually 1 visit per year over a set time period.
- Information and bio-specimens collected are centrally stored in repositories, which can be accessed by investigators worldwide. This helps speed up interventional trials and allows for researchers to make new discoveries without having to collect the data on their own.
- Observation Trials allow researchers to evaluate: *Disease progression and progression rate; Patient symptoms; Disease markers provided by brain scans or blood tests, and other aspects of HD.*

Interventional Research

- Commonly referred to as clinical trials
- Participants are given 1 or more new medical interventions.
- Used to evaluate the effects of these interventions on pre-defined outcome measures this may include Drugs, Devices, and/or Procedures
- These new interventions may be compared to:
  - An intervention that is already available
  - Placebo (contains no active ingredients)
  - No intervention

Methods of Interventional Research: Many factors can complicate clinical trials including bias on the part of the investigator or research subject. Here are some methods used to minimize bias:

Blinding

knowledge of the assigned treatment is hidden from one or more people involved with the study

Single-blind

- one party does not know assigned treatment. Usually this is the participant. This can also mean that the participant AND investigator are unaware of treatment assignment, which is a bit misleading

Double-blind

- The name is misleading. In double-blinded studies the participant, investigator, and study sponsor are all unaware of the treatment assignment

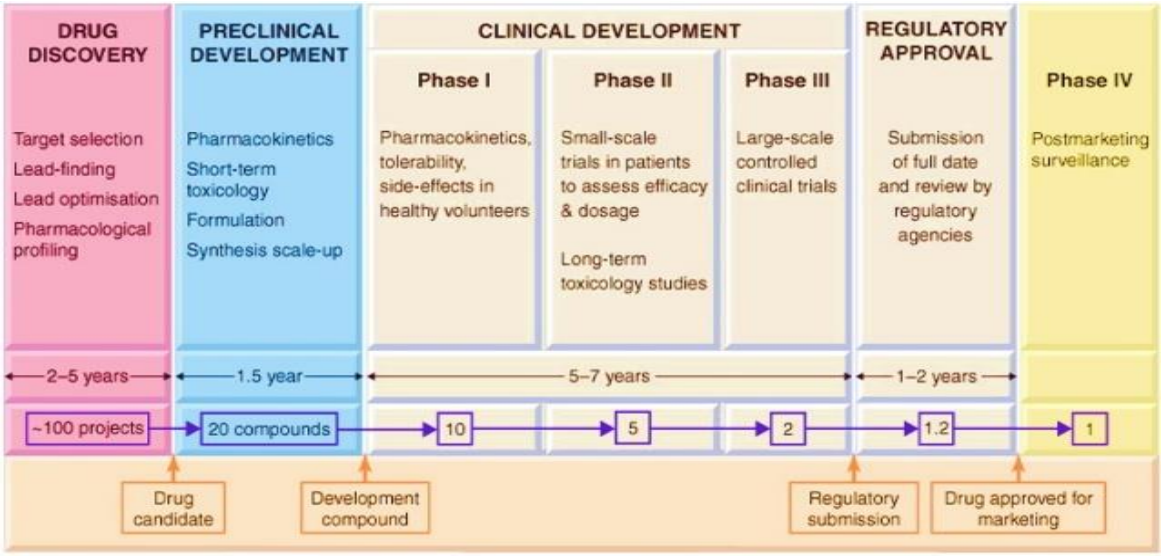
Triple-blind

- These studies are double-blinded AND the data analysis is done blinded

Randomization

- the study participant is assigned randomly to receive one of the study treatment assignments
  - Ensures each participant has an equal opportunity to receive the new intervention
  - Equally distributes participant attributes amongst all treatment groups
  - Prevents investigators from choosing the "better" treatment for certain patients over others

Interventional (Clinical) Trial Phases to drug development:

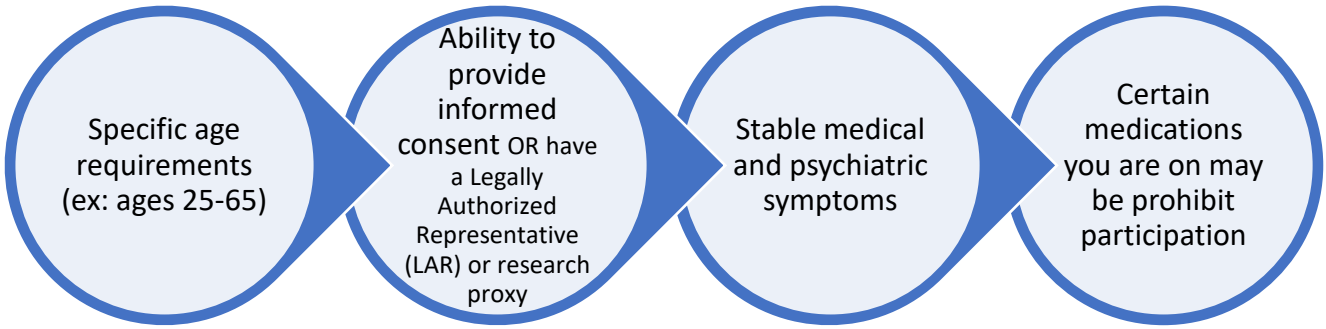


As you see, this process is long and not all products will make it to market. Getting and keeping study participants is essential to help move this process along as quickly as possible. That's where we hope YOU will come in!

Who can participate in research studies?

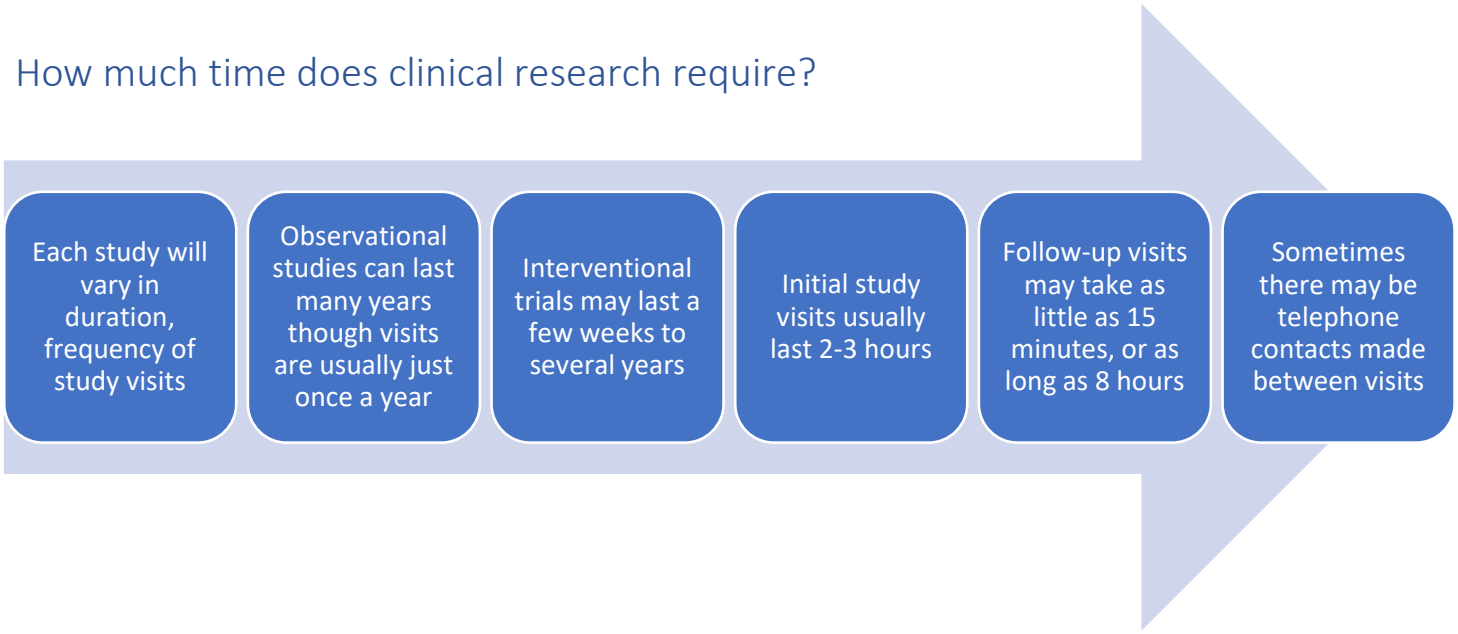
The study protocol is a research plan or roadmap designed to best answer the question posed by the study. The protocol includes criteria for who is eligible to maintain patient safety and to try to ensure the study sponsor can collect the data they need to answer their research question. Each study will have specific criteria, so while you may qualify for one study you may not qualify for another.

Inclusion criteria may include, but is not limited to:



For HD studies, researchers may wish to include people of a certain HD status such as all or some of the following groups:

How much time does clinical research require?



What happens during a clinical trial visit?

Informed Consent:

Before any study procedures can take place, study staff will provide you with a consent form that details all the information about what it means to be a volunteer for the study, the criteria for participating in the study, and the possible risks and benefits associated with participating. It details what you can expect at study visits, how long the study will be, and all the contact information for study staff, the primary researchers, and the institutional review board for any questions/issues during the study. After thoroughly reviewing the document and discussing all questions and concerns, you can decide whether you would like to proceed with participating in the study. **Informed consent is a process that should continue throughout the study as you, as a voluntary research participant, have the right to withdraw consent at any point without negative consequences.**

Study Procedures

Each study is different and exact study procedures will var. The exact procedures for each study is detailed in the informed consent. Some common study procedures include, but are not limited to the following:

- Vital signs: blood pressure, pulse, weight
- Discussion of medical history and current medications
- Evaluation of any health changes since the last study visit
- Physical and neurological exam
- Take blood samples (the amount of blood depends on the study)
- MRI imagining (depends on study)
- Study tasks (surveys and questionnaires)
- Cognitive assessments

Where will clinical research visits take place?

For clinical trials with the UC Davis HDSA Center of Excellence there are several locations where patients may be required to go, many located on the main hospital campus. The study staff will provide directions and parking information as needed for each study visit. On occasion, study visits can be scheduled concomitantly with clinic visits, which will take place off main campus at the UC Davis Health Midtown Neurology Clinic.

How are research participants protected?

Federal Agencies

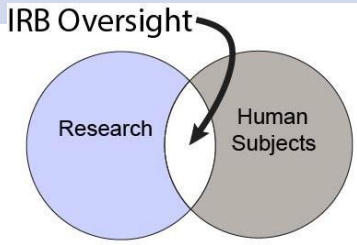
- Protect rights and well-being of research participants
- In the United States the NIH and FDA oversee much of the medical research conducted.

Institutional Review Boards (IRB)

- consist of a combination of scientists and community members.
- They oversee research studies at the centers where clinical research takes place.
- NO research study can begin without review by the IRB.
- They ensure that the safety, rights, and well-being of research participants are protected.

Informed Consent

- What IS required for inclusion in the Informed Consent document is mandated by federal regulations
- It must include all necessary information for the participant to make a fully informed and voluntary decision on whether to participant or not.
- This process is ongoing and is reviewed often.



Confidentiality and Subject Rights' are prime concerns to researchers. Participant identities are known to study site personnel and select people who must oversee the study at each site. Participants are assigned a unique ID code at the time of enrollment, used for coding all study documents, blood samples and communication with parties outside the institution. Study staff will keep a document connecting the IDs with study participant name, but this document is only available to study staff. Despite these contingencies we can never 100% guarantee confidentiality and thus loss of confidentiality will always be listed as a risk of participation in clinical research. **The California Experimental Subjects Bill of Rights** is below and will be shared with you at the start of study participation.

- Be informed of the nature and purpose of the experiment.
- Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized.
- Be given a description of any attendant discomforts and risks reasonably to be expected from the experiment.
- Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.
- Be given a copy of the signed and dated written consent form.
- Be given a disclosure of any appropriate alternative procedures, drugs or devices that might be advantageous to the subject, and their relative risks and benefits.
- Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation in the medical experiment without prejudice.
- Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the subject's decision
- Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.
- Be given an opportunity to ask any questions concerning the experiment or the procedures involved.

How is participating in clinical research different from seeing my doctor?

As discussed earlier, clinical research should never be confused with medical care even when the researcher and your doctor are the same person.

Participating in Clinical Research	Seeing Your Doctor
The researcher's goal is to learn about your illness and contributing to general scientific knowledge	Your doctor's goal is to treat your condition
The researcher must use standardized procedures. You may be removed from the study if your illness worsens	Your doctor will change your treatment as necessary and will see you even as your illness worsens
You will be randomly assigned to a group to take either: • a standard treatment • placebo, a treatment with no active ingredient • a group taking a new treatment The researcher will NOT be allowed to choose which you get and may not know which group you end up in	Your doctor will usually offer standard treatment for your Illness and will be allowed to choose whatever standard treatment they think is best to treat you
The results from your participation may help researchers develop new treatments and may be published so that other researchers can learn	Your treatment is designed to help you, and not to help the doctor learn how to treat other people with your same illness
In some cases, costs of the study may be covered, and you may receive additional compensation	You will likely need to pay or use insurance for treatment
With your permission, researchers may check in with your doctors to learn about your conditions and past treatments	Your doctor usually won't share your information with researchers (In some cases, he or she may ask permission to share information)

Source: U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES National Institutes of Health NIH Publication No. 09-4379 Reprinted 2009

Who FUNDS research?

Each study will have a specific funding source. Some examples of funding sources can include:

Government Agencies	Pharmaceutical Companies	Private Foundations
NIH National Institutes of Health CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE CIRM	Genentech A Member of the Roche Group TEVA CNS	CHDI FOUNDATION

Do I get paid for research?

In order to avoid participants becoming involved in research for the compensation (this is called coercion) many studies will only reimburse participants for the costs they may incur to participate in the study. This can include reimbursement for travel, food expenses, etc. Reimbursement is study specific and will be detailed in the consent form.

Should participate in research?

There are reasons for and against participating in research. It will always depend on the individual and the nature of the research. If approached for study participation, it is important to ask any questions you may have about Participating with research staff.

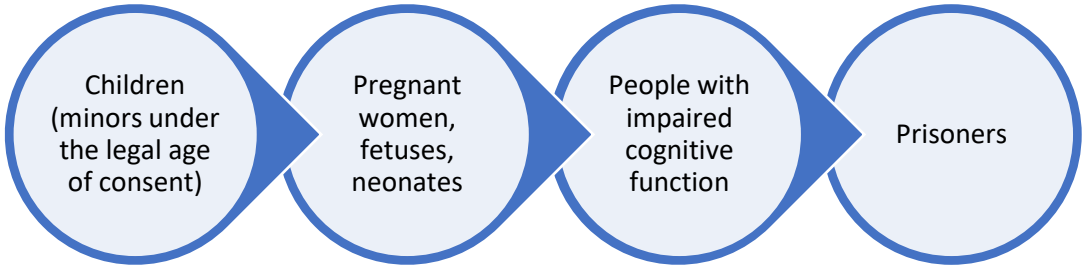
Possible reasons to participate:
- You've always wanted to 'help'
- You want to contribute to the efforts for a cure/effective treatment
- You have time
- You care about HD research and future generations
- Being in research makes you feel like you are 'doing something' about HD

Possible reasons NOT to participate:
- I don't have enough time due to other responsibilities
- I'm concerned about my privacy
- I prefer not to think about HD
- I don't want to have physical exams or thinking tests
- Fear of needles
- Not wanting to drive that far
- I don't want to be on a placebo

QUESTIONS about participating:
- research is VOLUNTARY, you can change your mind at any time.
- You will not be treated differently or receive different care by NOT participating
- **Contact UC Davis Research Coordinator,** Becky Craig, rscraig@ucdavis.edu , Phone: 916-734-3541

Research and Vulnerable Populations

There are certain populations of participants which the federal regulations define as "vulnerable populations." These participants are groups of people who may require greater protection than normal as they may be at higher risk for negative outcomes, they may have reduced capacity to consent, they are more prone to coercion, etc. These groups include, but are not limited to:



Children and Research: Children and young adults can also volunteer to participate in research opportunities. As stated above, children are a protected population, meaning that IRBs require additional protections to be included in studies, to protect their wellbeing and safety as research volunteers.

Things to consider IF your child wants to participate in research:

- Children UNDER 18 years old will need agree to participate, AND
- Get one OR both parents or legal guardian permission for participation. The requirement of one or both parents will depend on the study.
- Research involving children and adolescents include a form called an ASSENT form. This provides information about study participation tailored specifically to participates age/development.
- ALWAYS, describe the study expectations to them in detail, at a level appropriate to their understanding.
- Children and adolescents interested in research participation should ask questions prior to deciding whether to participate. Parents/guardians should also ask questions, raise concerns prior to deciding to agree to participation.
- If a child turns 18 during a study, they will have to sign a consent form as an adult participant before continuing participation in the study.

For more information on research, visit:

HDSA.org | HDSA Center of Excellence, UC Davis | Help4HD

HDBuzz.net | Clinical Trials.gov

Glossary

Assent: Children cannot legally consent to research prior to the age of 18. In research that involves children under 18, they are asked to provide assent. Assent means that they agree to take part. They may also dissent, which means they do not agree. Unlike informed consent, assent is not always required by law, though IRBs may require it.

- To take part in the assent process, your child must be mature enough to understand the trial and what they are required to do.
- Some children as young as 7 years old may be able to take part. This age varies depending on the child and the group running the trial.

Blinding: also known as *masking*, this is the process of keeping the study group assignment hidden after allocation. Blinding is often used in research and is intended to help reduce the risk of bias in trials that have two or more study groups.

Clinical Research: clinical research examines people, or data or samples of tissue from people, which is studied to help understand health and disease processes. This type of research is intended to help find new and better ways to detect, diagnose, treat, and prevent disease.

Clinical Trial: A clinical trial is a type of study that where new medical approaches, such as new drug treatments or medical devices are examined to see how they work in people. Also called *clinical study*. There are four phases of clinical trials:

- Phase I: The main purpose of Phase I studies is to determine if the medical drug or device being studied is safe. Phase I trials have about 20-100 healthy volunteers and can take several months. This phase helps researchers assess how the drug or device effects humans (for example, in what way the human body absorbs, metabolizes and excretes the drug).
- Phase II: The main purpose of Phase II trials is to determine the efficacy of the drug or medical device. This phase may last several months or several years. There can be several hundred participants in Phase II trials, and most often phase II trials are randomized and include a control group.
- Phase III: Phase III drug studies are randomized and blinded studies, which can include hundreds to several thousands of participants. This phase can last several years and is intended to give the drug company and the FDA more information about how effective the drug or medical device is. This phase can last several years and helps drug companies and researchers clarify the benefits and possible adverse reactions of a drug.
- Phase IV: Phase IV trials are done after the drug is approved by the FDA for sale. In Phase IV trials drug companies may want to:
    - compare a drug with other already available treatments
    - monitor the efficacy of a drug over a period of time
    - determine the cost-effectiveness of a drug therapy as compared to already available treatments and/or therapies

Consent Form: A document with important information about a medical procedure or treatment, clinical trial, or genetic testing. It includes information on possible risks and benefits. If a person chooses to take part in the treatment, procedure, trial, or testing, he or she signs the form to give official consent. Even if a participant signs this document, they have the right to stop participating at any time they choose during the course of a study.

Control Group: In a clinical trial, the control group is the group that does not receive the new treatment being studied. This is the group which is compared to the group that receives the new treatment. This is done to examine if the treatment is effective.

Double-Blind Study: A type of clinical trial in which neither the participants nor the researcher knows which treatment or intervention participants are receiving until the clinical trial is over. This makes results of the study less likely to be biased. This means that the results are less likely to be affected by factors that are not related to the treatment or intervention being tested.

Eligibility Criteria: Describe characteristics that must be shared by all participants. The criteria differ from study to study. Examples may include age, gender, medical history, and current health status.

Informed Consent: A process in which patients are given important information, including possible risks and benefits, about a medical procedure or treatment, genetic testing, or a clinical trial. This is to help them decide if they want to be treated, tested, or take part in the trial. Patients are also given any new information that might affect their decision to continue. Also called consent process.

Institutional Review Board: An institutional review board, often referred to as an IRB, is an administrative body created to protect the rights and welfare of human research subjects. Institutions typically have a local IRB which oversees any affiliated research activities. The IRB must review and approve all research involving human subjects, before any research activities can take place. In addition to approving the initiation of research with human subject, IRBs also review any proposed modifications to research activities. The IRB can approve, deny, request more information, or request changes to any proposed modifications submitted by researchers after the study is initially approved. IRBs are made of at least 5 members of diverse backgrounds to consider all possible consequences of the proposed research. IRBs include at least one member not affiliated with the institution, as well as one community member.

Interventional Study: An interventional study is one in which researchers administer and observe the effects of an intervention, such as a new medicine, in order to evaluate its efficacy and the effects. Clinical trials are a type of interventional study.

Observational Study: An observational study is one in which researchers observe the effect of a risk factor or disease, diagnostic test, treatment or other intervention without trying to change who is or is not exposed to it.

Placebo: A placebo is an inactive treatment. A placebo may be in a pill or tablet form, or it may be an injection or a medical device depending on the study. Placebos often look like the real medical treatment that is being studied except they do not contain the active medication. Placebos are used in clinical research to help scientists establish if a new treatment or medication is more beneficial that no treatment at all.

Principal Investigator: The principal investigator (PI) is the primary researcher for a given study. The PI is responsible for overseeing the entirety of the study including managing study staff and ensuring all activities adhere to the study protocol.

Sponsor: A person, company, institution, group, or organization that oversees or pays for a clinical trial and collects and analyzes the data.