# HD-med: A longitudinal, observational study to assess medication use, medication efficacy and the role of pharmacogenetics in Huntington*s Disease.

Published: 26-11-2019
Last updated: 08-02-2025

Primary objective: To classify the effect of the pharmacogenetic profile of CYP2C19 and CYP2D6 in HD gene carriers, compared to more classic medication prescribing parameters (such as age and comorbidities) on negative medication effects of HD-...

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| **Ethical review** | Approved WMO |
| **Status** | Completed |
| **Health condition type** | Chromosomal abnormalities, gene alterations and gene variants |
| **Study type** | Observational invasive |

## Summary

### ID

NL-OMON55123

**Source**
ToetsingOnline

**Brief title**
HD-med: Pharmacogenetics in Huntington*s Disease

### Condition

- Chromosomal abnormalities, gene alterations and gene variants
- Movement disorders (incl parkinsonism)

**Synonym**
Huntington's Disease; Huntington's chorea (outdated terminology)

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Leids Universitair Medisch Centrum
**Source(s) of monetary or material Support:** Ministerie van OC&W,Geldelijke donatie particulier en algemene onderzoeksgelden vanuit de afdeling

## Intervention

**Keyword:** CYP2C19, CYP2D6, Huntington's Disease, Pharmacogenetics

## Outcome measures

### Primary outcome

Percentage definite prescription changes in HD gene carriers with a divergent

PGx CYP2C19 or CYP2D6 phenotype (poor and ultra-rapid metabolizers) versus

those with a PGx phenotype in more normal range (extensive and intermediate

metabolizers).

### Secondary outcome

Secondary study parameters/endpoints:

- Overview of medication use by HD gene carriers in one year.

- Accuracy of a one-year medication diary compared to pharmacy medication

history surveys.

Exploratory study parameters/endpoints

- Identify potentially new genetic polymorphisms with pharmacogenetic action in

HD gene carriers.

# Study description

### Background summary

Rationale: Huntington*s disease (HD) is a hereditary, neurodegenerative disorder characterized by motor, cognitive and psychiatric symptoms. Currently, HD can only be managed symptomatically, including a large variety in prescribed drugs. Many HD patients experience negative medication effects (e.g. side-effects or non-response). Pharmacogenetic (PGx) studies show how individual genetic differences affect medication efficacy and toxicity, and holds the potential to explain and resolve these negative medication effects. This study aims to characterize which part of negative medication effects can be resolved by implementing PGx testing. The ultimate goal is to better guide the long-term pharmacological management of HD in a more personalized manner by predicting the individual patient*s risk of negative medication effects.

## Study objective

Primary objective: To classify the effect of the pharmacogenetic profile of CYP2C19 and CYP2D6 in HD gene carriers, compared to more classic medication prescribing parameters (such as age and comorbidities) on negative medication effects of HD-related medication. Negative medication effects are classified as non-response or side effects of the prescribed drug, which lead to definite prescription changes in that drug. Definite prescription changes are classified as; discontinuation of the drug, switching to another type of drug or adding another drug to treat the same symptom.

Secondary objectives:
- To assess and categorize current medication use in HD gene carriers.
- To determine the eligibility of a one-year medication diary compared to pharmacy medication history surveys in HD patients.
- To classify the effect of the pharmacogenetic profile of CYP2C19 and CYP2D6 in HD gene carriers who are on HD-related medication and who either use a relatively low or a relatively high drug dose with regard to the symptom the drug is prescribed for.

Explorative objective:
- To explore potential new genetic polymorphisms with pharmacogenetic action in HD gene carrier subgroups with an extra-ordinary side effect profile or lack of medication response.

## Study design

Longitudinal, observational, mulit-center study.

## Study burden and risks

During baseline visit at the outpatient clinic, subjects are asked to fill in a medication questionnaire and have a neurological and neuropsychologic examination. Furthermore, a single blood sample (4 ml) for pharmacogenetic

analysis will be drawn. During follow-up, subjects record their medication changes in a diary. Five telephone calls are performed to map any changes in medication use or general health. At baseline and after one year, a medication verification scheme is requested at subjects* local pharmacy. A negligible risk is attached to blood drawing, furthermore no risks are attached to this study and patient burden is considered to be low.

## Contacts

**Public**
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## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

### Inclusion criteria

- A capacitated individual, aged >= 18 years.
- Genetically confirmed CAG-repeat expansion of >= 36 in the Huntingtin gene.
- Either about to start with prescribed medication related to HD or already using one or more HD related drugs. HD-related drugs are drugs considered to

treat symptoms that either are related to manifest HD or are prescribed in pre-motor manifest or prodromal HD stage for symptoms that may be attributed to HD.
- Sufficient knowledge of the Dutch language to understand the subject information letter and sign the IC.

### Exclusion criteria

Any medical condition, in the view of the investigator, which might endanger subject*s safety and/or satisfactory participation in the study.

## Study design

### Design

**Study type:** Observational invasive

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| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Other |

### Recruitment

NL

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|---|---|
| Recruitment status: | Completed |
| Start date (anticipated): | 15-01-2020 |
| Enrollment: | 391 |
| Type: | Actual |

## Ethics review

Approved WMO

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| Date: | 26-11-2019 |
| Application type: | First submission |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br><br>metc-ldd@lumc.nl |

Approved WMO

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|---|---|
| Date: | 05-10-2021 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br><br>metc-ldd@lumc.nl |

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

ID: 23607
Source: Nationaal Trial Register
Title:

## In other registers

| Register | ID |
|---|---|
| CCMO | NL70391.058.19 |
| Other | NTR-nummer: NL8251 |