

# Timing and Impact of Psychiatric, Cognitive, and Motor Abnormalities in Huntington Disease

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## Study Question

What are the prevalence, timing, and functional impacts of psychiatric, cognitive, and motor symptoms in carriers of the expanded CAG repeat in the Huntingtin gene that causes Huntington disease (HD)?

## What Is Known and What This Paper Adds

Motor abnormalities are the most noticeable clinical features of HD, but patients may also experience psychiatric and cognitive symptoms. This large, retrospective study shows that psychiatric and cognitive abnormalities are very common in HD patients, often occur before motor problems, and are associated with significantly worse functional outcomes.

## Methods

The investigators analyzed retrospective, cross-sectional data from the observational REGISTRY study, which collected data from 6,316 individuals with clinical HD onset through 161 sites in 17 European countries between June 2004 and February 2016. These individuals had confirmed CAG repeat lengths of 36–93. Data came from Clinical history and the patient-completed HD Clinical Characteristics Questionnaire (HD-CCQ) that assessed 8 symptoms: motor, cognitive, apathy, depression, perseverative/obsessive behavior, irritability, violent/aggressive behavior, and psychosis. Logistic regression analyses were used to test for associations between symptoms and functional outcomes.

## Results and Study Limitations

As the age at onset increased, motor presentations became more likely, and non-motor presentations less likely. Overall, 42.4% of the patients with HD reported experiencing at least 1 psychiatric or cognitive symptom before the onset of motor symptoms, with depression being the most common. The presence of each non-motor symptom predicted worse

**Table** Lifetime Prevalence of Psychiatric Symptoms in HD

Psychiatric symptom	Lifetime prevalence in men	Lifetime prevalence in women	p Value for difference
Apathy	53.63%	52.11%	$2.56 \times 10^{-1}$
Depression	58.23%	70.36%	$2.57 \times 10^{-21}$
Irritability	62.91%	56.85%	$4.03 \times 10^{-6}$
Violent or aggressive behavior	34.87%	27.01%	$1.99 \times 10^{-10}$
Psychosis	11.75%	11.31%	$6.06 \times 10^{-1}$

Sex-specific lifetime prevalence rates for selected psychiatric symptoms.

functional capacity scores. The study's limitations include its retrospective nature and the dependency of HD-CCQ data on the interpretation of questions. In addition, it remains impossible to distinguish confidently between those non-motor symptoms arising from HD and those from primary psychiatric disorders.

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