DISEASE BURDEN IN PATIENTS WITH HUNTINGTON'S DISEASE FROM A NATIONWIDE SWEDISH REGISTRY COMPARED WITH THE GENERAL POPULATION (2002–2019)

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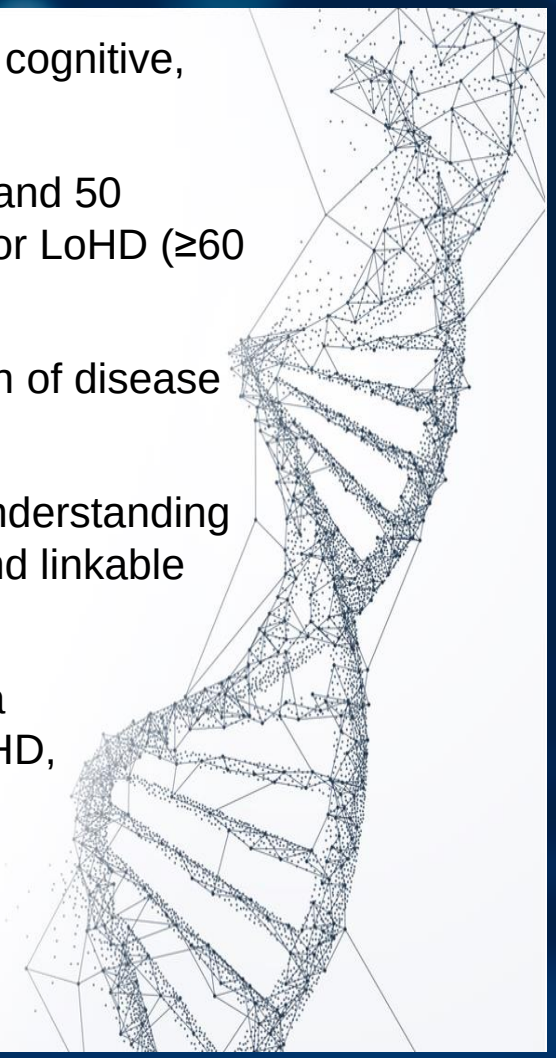
Background

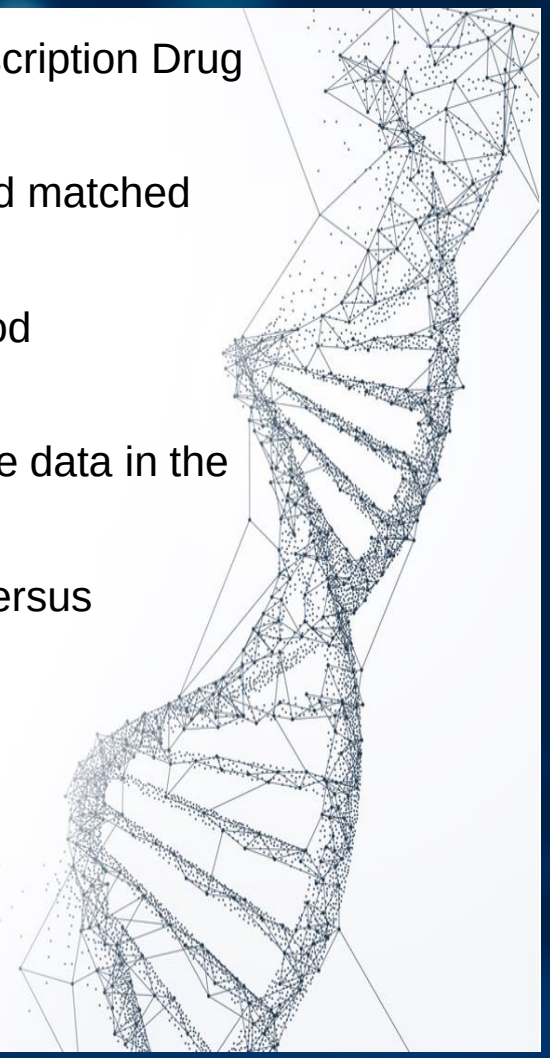
- HD is a rare, genetic, neurodegenerative and ultimately fatal disease[1] characterised by a triad of cognitive, behavioural and motor symptoms[2,3]
- Mean age of symptom onset can occur at any time, but typically occurs between the ages of 30 and 50 years.[2] JoHD (≤20 years) is much rarer and manifests slightly differently to AoHD (>20 years)[4,5] or LoHD (≥60 years)[6]
- Given the rarity of HD, large cohort studies are warranted to better understand the clinical burden of disease over extended periods of time in routine clinical practice relative to those without HD
- Electronic medical records such as the National Swedish Registries are ideal data sources for understanding the natural history of rare diseases like HD, due to the nationwide coverage, lifelong follow-up and linkable databases
- This study aimed to describe the incidence of clinical events in patients with HD compared with a matched cohort from the general population, and to describe differences between JoHD and AoHD, defined in this study as HD onset at <20 years and ≥20 years, respectively



AoHD, adult-onset HD; HD, Huntington's disease; JoHD, juvenile-onset HD; LoHD, late-onset HD. 1. Bates GP, et al. *Nat Rev Dis Primers*. 2015; 1:15005; 2. Roos RA. *Orphanet J Rare Dis*. 2010; 5:40; 3. Ross CA, et al. *Nat Rev Neurol*. 2014; 10:204–216; 4. Quarrell O, et al. *PLoS Curr*. 2012; 4:e4f8606b8742ef8603; 5. Ajikumar A and De Jesus O. Huntington's Disease. StatPearls Publishing; 2021. Available from: https://www.ncbi.nlm.nih.gov/books/NBK559166/ (Accessed August 2021); 6. Chaganti SS, et al. *J Huntingtons Dis*. 2017; 6:95–103.

Methods

- This was a nationwide cohort study linking data from the Swedish National Patient Registry, Prescription Drug Registry and Cause of Death Registry
- Patients of all ages with a first diagnosis of HD (ICD-10: G10) from 2002–2018 were included and matched 1:4 (on age and sex) to a control cohort without HD
- Index date was defined as the first instance of an HD diagnosis during the cohort enrolment period (ICD-10: G10)
- The follow-up period started the day after the index date, and lasted until the last date of available data in the NPR, death or emigration, whichever occurred first
- IRRs and 95% CI approximated the relative risk of clinical events occurring in patients with HD versus controls during the time after first HD diagnosis
- IRs of cases were described overall and in those aged <20 years (JoHD) or ≥20 years (AoHD) at first diagnosis



AoHD, adult-onset HD; CI, confidence interval; HD, Huntington's disease; ICD-10, International Classification of Diseases, 10th Revision; IR, incidence rate; IRR, incidence rate ratio; JoHD, juvenile-onset HD; NPR, National Patient Registry.

Demographics and clinical characteristics

1,492 individuals with HD were matched to 5,946 controls:

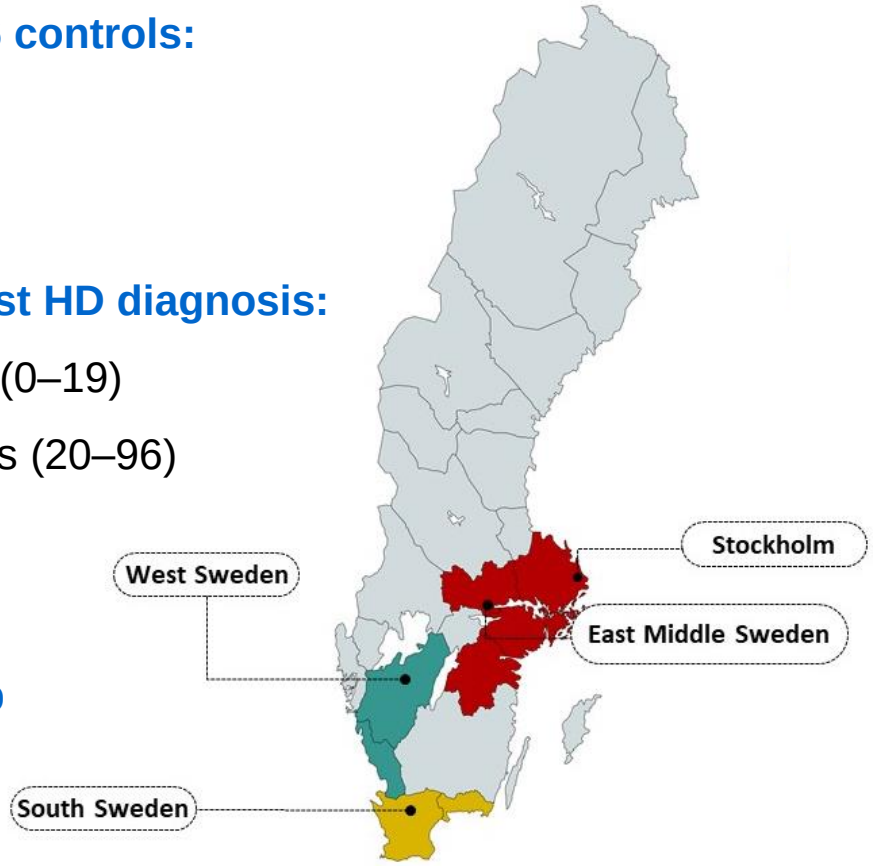
- AoHD=1,447
- JoHD=45

Median age at first HD diagnosis:

- JoHD=8 years (0–19)
- AoHD=57 years (20–96)

Females: 50%

Median follow-up period: 6 years



CCI, mean (SD):

- AoHD versus matched controls: 0.6 (1.4) versus 0.3 (0.9)
- JoHD versus matched controls: 0.2 (0.5) versus 0.09 (0.4)

Geographical location	AoHD, n (%)	JoHD, n (%)
Stockholm	359 (24.8)	15 (33.3)
West Sweden	302 (20.9)	13 (28.9)
East Middle Sweden	223 (15.4)	3 (6.7)
South Sweden	185 (12.8)	6 (13.3)
Other region	378 (26.1)	8 (17.8)

AoHD, adult-onset HD; CCI, Charlson Comorbidity Index; HD, Huntington's disease; JoHD, juvenile-onset HD; SD, standard deviation.

Higher IRs of a number of clinical outcomes were observed in individuals with HD compared with controls

- The IRs of most clinical outcomes were higher in individuals with HD versus controls, with the greatest differences observed for acute psychiatric episodes, subdural haematoma, communication and speech problems, depression, obsessive compulsive disorder and anxiety disorders
- The IRs of asthma, thrombocytopenia, thyroid disorders, cancer, chronic renal impairment, hypertension and liver failure/hepatic impairment were somewhat higher in the controls

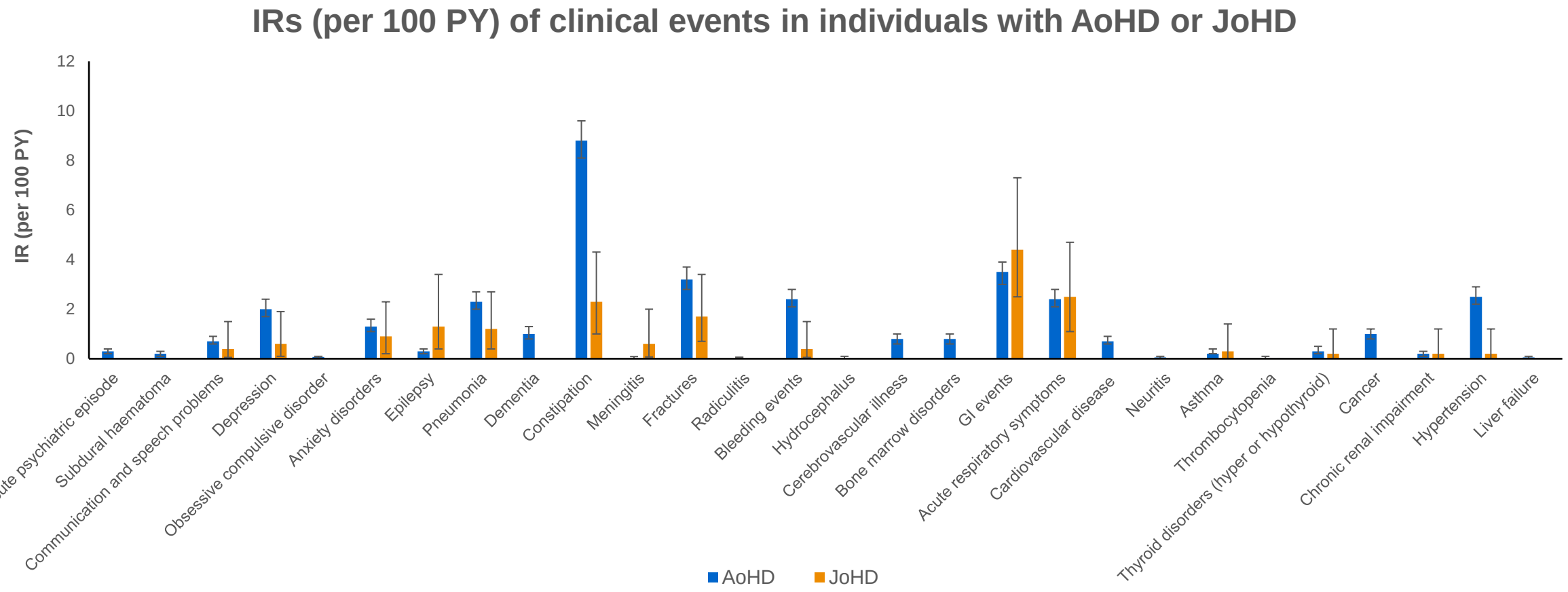
Clinical events	All patients	Control	HD cases	
	IR per 100 PY (95% CI)			IRR (95% CI)
Acute psychiatric episode	0.06 (0.05–0.09)	0.02 (0.009–0.04)	0.3 (0.2–0.4)	14.4 (13.6–15.2)
Subdural haematoma	0.06 (0.04–0.09)	0.03 (0.02–0.05)	0.2 (0.1–0.3)	7.5 (7.1–7.9)
Communication and speech problems	0.2 (0.2–0.3)	0.1 (0.09–0.1)	0.7 (0.6–0.9)	6.4 (6.1–6.8)
Depression	0.6 (0.5–0.6)	0.3 (0.3–0.4)	1.9 (1.7–2.3)	6.0 (5.7–6.4)
Obsessive compulsive disorder	0.02 (0.01–0.04)	0.01 (0.004–0.03)	0.07 (0.03–0.1)	5.7 (5.4–6.0)
Anxiety disorders	0.5 (0.4–0.5)	0.3 (0.2–0.3)	1.3 (1.1–1.6)	4.4 (4.2–4.7)
Epilepsy	0.1 (0.1–0.2)	0.08 (0.06–0.1)	0.3 (0.2–0.5)	4.2 (3.9–4.4)
Pneumonia	0.9 (0.9–1.0)	0.7 (0.6–0.8)	2.3 (2.0–2.6)	3.4 (3.2–3.6)
Dementia	0.4 (0.4–0.5)	0.3 (0.3–0.4)	1.0 (0.8–1.2)	2.8 (2.7–3.0)
Constipation	4.4 (4.2–4.6)	3.7 (3.6–3.9)	8.4 (7.7–9.1)	2.2 (2.1–2.4)
Meningitis	0.03 (0.01–0.04)	0.02 (0.01–0.04)	0.05 (0.02–0.1)	2.2 (2.1–2.4)
Fractures	1.9 (1.7–2.0)	1.6 (1.5–1.7)	3.2 (2.8–3.6)	1.9 (1.8–2.1)
Radiculitis	0.007 (0.002–0.02)	0.006 (0.001–0.02)	0.01 (0.0002–0.05)	1.6 (1.5–1.7)
Bleeding events	1.6 (1.5–1.7)	1.5 (1.4–1.6)	2.3 (2.0–2.7)	1.6 (1.5–1.7)
Hydrocephalus	0.03 (0.01–0.04)	0.02 (0.01–0.04)	0.04 (0.01–0.1)	1.6 (1.5–1.7)

Clinical events	All patients	Control	HD cases	
	IR per 100 PY (95% CI)			IRR (95% CI)
Cerebrovascular illness	0.5 (0.5–0.6)	0.5 (0.4–0.5)	0.7 (0.6–0.9)	1.5 (1.5–1.6)
Bone marrow disorders	0.6 (0.5–0.6)	0.5 (0.5–0.6)	0.7 (0.6–0.9)	1.4 (1.3–1.5)
GI events	2.9 (2.7–3.0)	2.8 (2.6–2.9)	3.5 (3.1–3.9)	1.3 (1.2–1.3)
Acute respiratory symptoms	2.1 (2.0–2.2)	2.0 (1.9–2.2)	2.4 (2.1–2.8)	1.2 (1.1–1.3)
Cardiovascular disease	0.7 (0.6–0.8)	0.7 (0.6–0.8)	0.7 (0.5–0.9)	1.0 (1.0–1.1)
Neuritis	0.05 (0.03–0.07)	0.05 (0.03–0.07)	0.05 (0.02–0.1)	1.0 (1.0–1.1)
Asthma	0.3 (0.2–0.3)	0.3 (0.2–0.3)	0.2 (0.2–0.4)	0.9 (0.8–0.9)
Thrombocytopenia	0.05 (0.03–0.07)	0.05 (0.03–0.07)	0.04 (0.01–0.1)	0.8 (0.8–0.9)
Thyroid disorders (hyper or hypothyroid)	0.4 (0.3–0.4)	0.4 (0.4–0.5)	0.3 (0.2–0.5)	0.8 (0.8–0.8)
Cancer	1.3 (1.2–1.4)	1.4 (1.3–1.5)	0.9 (0.8–1.1)	0.7 (0.6–0.7)
Chronic renal impairment	0.3 (0.3–0.3)	0.3 (0.3–0.4)	0.2 (0.1–0.3)	0.7 (0.6–0.7)
Hypertension	4.0 (3.8–4.2)	4.3 (4.1–4.6)	2.4 (2.0–2.7)	0.5 (0.5–0.6)
Liver failure	0.09 (0.06–0.1)	0.09 (0.07–0.1)	0.05 (0.02–0.1)	0.5 (0.5–0.5)

IRR>1 reflects an increased rate of events in the HD group; IRR<1 indicates a higher rate in controls.
CI, confidence interval; GI, gastrointestinal; HD, Huntington's disease; IR, incidence rate; IRR, incidence rate ratio; PY, person years.

Only a few IRs were higher in JoHD compared with AoHD

- IRs for most studied clinical events were higher in AoHD (N=1447) compared with JoHD (N=45), except for epilepsy, asthma, GI events, meningitis, and acute respiratory symptoms in which incidence was higher in patients with JoHD



AoHD, adult-onset HD; HD, Huntington's disease; GI, gastrointestinal; IR, incidence rate; JoHD, juvenile-onset HD; PY, person years.

Conclusions

- This nationwide study demonstrates the considerable disease burden in HD compared with the general population
- Burden of illness was already higher in patients with HD than matched controls at the time of first diagnosis
- In addition to the psychiatric burden of disease, which has been well reported, these findings also describe a higher physical burden e.g. pneumonia, epilepsy, meningitis and constipation
- Individuals with JoHD have a higher incidence of some clinical events when compared with individuals with AoHD, which sheds light on the clinical profile of this rare HD group

We would like to thank the patients and families who have participated and who are currently still participating in our research, and the ongoing partnership of the whole HD community

AoHD, adult-onset HD; HD, Huntington's disease; JoHD, juvenile-onset HD.