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for rare or low prevalence complex diseases
Network Neurological Diseases (ERN-RND)

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Webinar

’Learning by example:

HD-JUNIOR a national registry for patients with juvenile onset Huntington's Disease’

by Hannah Bakels,

Leiden University Medical Center, the Netherlands

01. February 2022

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Speaker

Hannah Bakels

- Training: Neurosciences (MSc(res)), Medicine (MD)
- Current position: Research physician, PhD-candidate
- Research: translational research to juvenile-onset Huntington‘s Disease

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Learning objectives

- By the end of this webinar you will be able to:

  - recognize the importance of patient registries for rare (neurological) disorders
  - differentiate various forms of patient registries
  - build a registry on your own
  - choose a registry form based on your patient population and problem definition

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Webinar outline

- Huntington‘s Disease
- HD in the Netherlands
- Juvenile-onset HD
- Problem definition
- Patient Registries
- Patient population
- Study design and datasets
- Collaborations
- Privacy regulations and IRB review
- Recruitment and informed consent
- Data sharing
- Acknowledgements
- Q&A

Huntington's Disease

AD brain disorder caused by an CAG-repeat expansion (≥36) in *HTT*

Average prevalence in Europe 4 per 100.000[1]

Age at clinical onset of disease : 1.5 – 87 years

Mean 30 – 50 years

<21 years: 4 – 10%[2]

Reverse relationship CAG-repeat length and age at onset[3]

Trias of movement disorder – cognitive dysfunction – psychiatric disturbances

1. Rawlins MD, Wexler NS, Wexler AR, Tabrizi SJ, Douglas I, Evans SJ, et al. The Prevalence of Huntington's Disease. Neuroepidemiology. 2016;46(2):144-53.
2. Quarrell O, O'Donovan KL, Bandmann O, Strong M. The Prevalence of Juvenile Huntington's Disease: A Review of the Literature and Meta-Analysis. PLoS Curr. 2012;4.
3. Squitieri F, Frati L, Ciarmiello A, Lastoria S, Quarrell O. Juvenile Huntington's disease: does a dosage-effect pathogenic mechanism differ from the classical adult disease? Mech Ageing Dev. 2006;127(2):208-12.

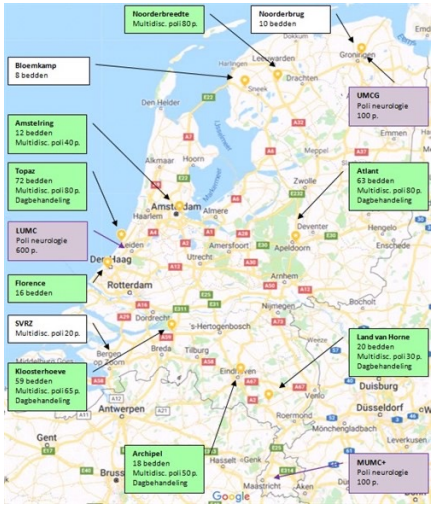
HD in the Netherlands

Population: 17 million inhabitants

Prevalence HD

±2000 HDEGC – 75% manifest disease

±6000-9000 HD risk carriers (50%)



Centered HD diagnostics and care

3 academic medical centers

University Medical Center Groningen (UMCG)

Leiden University Medical Center (LUMC)

Maastricht University Medical Center (MUMC+)

8 care facilities / nursery homes

Juvenile-onset HD

Juvenile-onset HD is arbitrary defined as having symptoms before the age of 21 years

New terminology in clinical practice and for research purposes[1,2]

Childhood-onset HD

Adolescent-onset HD

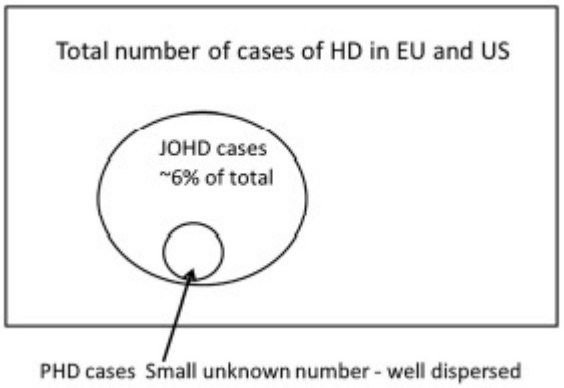
Pediatric HD

1. Fusilli C, Migliore S, Mazza T, Consoli F, De Luca A, Barbagallo G, et al. Biological and clinical manifestations of juvenile Huntington's disease: a retrospective analysis. The Lancet Neurology. 2018;17(11):986-93.
2. Quarrell OWJ, Nance MA, Nopoulos P, Reilmann R, Oosterloo M, Tabrizi SJ, et al. Defining pediatric huntington disease: Time to abandon the term Juvenile Huntington Disease? Movement disorders : official journal of the Movement Disorder Society. 2019.

Problem definition

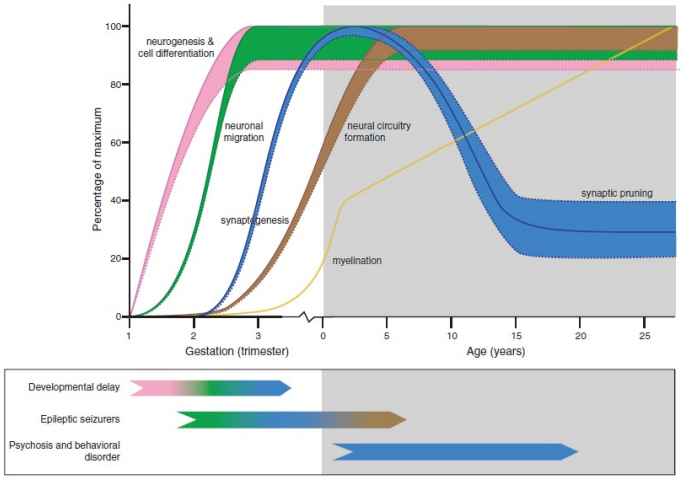
Removal class waiver EMA for PHD patients[1]

- Identification and number of patients
- Disease burden and progression
- Legal and ethical issues



Differences in JHD phenotype and development[2]

- Pathophysiology
- Outcome measures
- Therapeutic strategies
- Needs and care



1. Quarrell OWJ, Nance MA, Nopoulos P, Reilmann R, Oosterloo M, Tabrizi SJ, et al. Defining pediatric huntington disease: Time to abandon the term Juvenile Huntington Disease? Movement disorders : official journal of the Movement Disorder Society. 2019.
2. Bakels HS, Roos RAC, van Roon-Mom WMC, de Bot ST. Juvenile-Onset Huntington Disease Pathophysiology and Neurodevelopment: A Review. Movement disorders : official journal of the Movement Disorder Society. 2021.

Patient Registries

Data collection of large numbers of similar patients

- Retrospective vs prospective
- Cross-sectional vs longitudinal
- National vs international
- Patient association vs medical center

Leiden University Medical Center

Enroll-HD

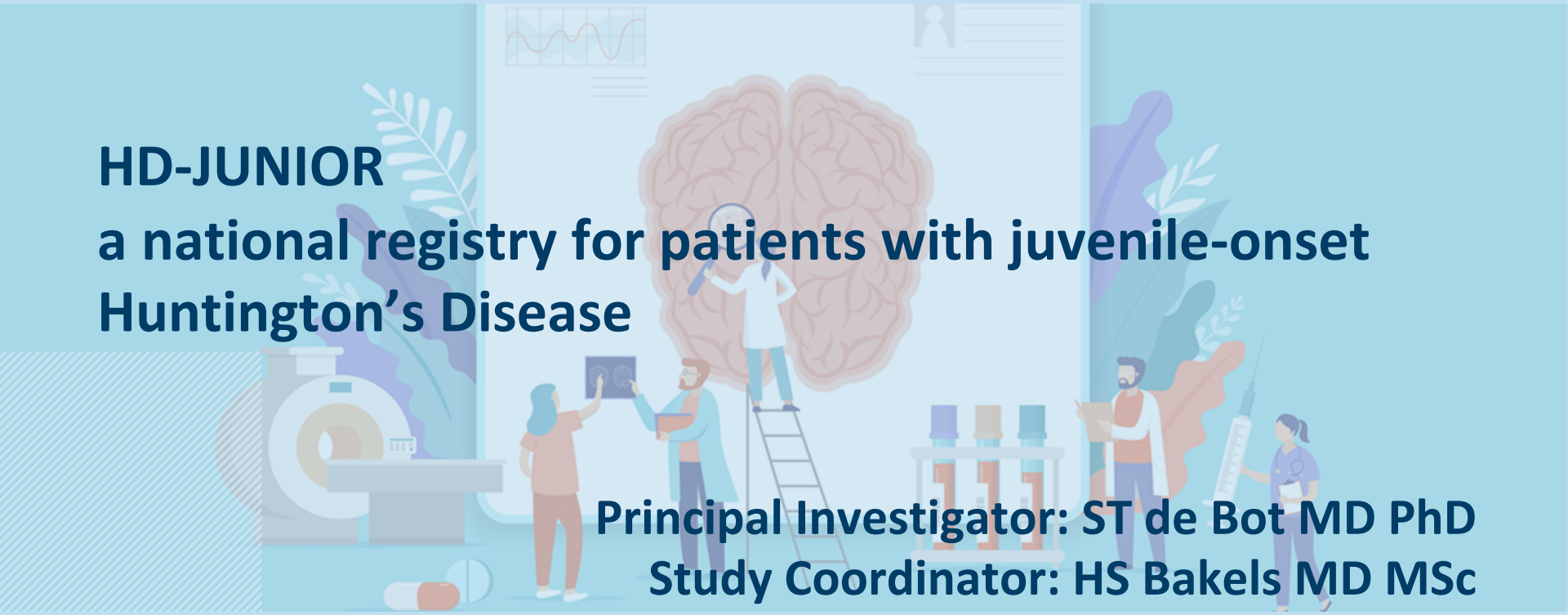
Vereniging van Huntington

JOIN-HD
The Juvenile-Onset Initiative for Huntington's Disease

Goals

- Localization and identification
- Epidemiological characterization
- Clinical characterization
- Therapeutic characterization
- Determining special and/or unmet needs in clinical care

HD-JUNIOR
a national registry for patients with juvenile-onset Huntington's Disease



Principal Investigator: ST de Bot MD PhD
Study Coordinator: HS Bakels MD MSc

Study design and datasets

Study design

- Retrospective vs prospective
- Cross-sectional vs longitudinal
- Patient/care taker reported vs physician reported
- Data mining vs specified data

Considerations

- Study design can differ between datasets
- Study goals determine your most optimal datasets
- Take your patient population into account
- Take other registries within your field into account

Demography

Clinic

Registry

Survey

Patient population

Determining your patient population

- Age criteria
- Classification phenotype
- Genetic criteria
- Survival status

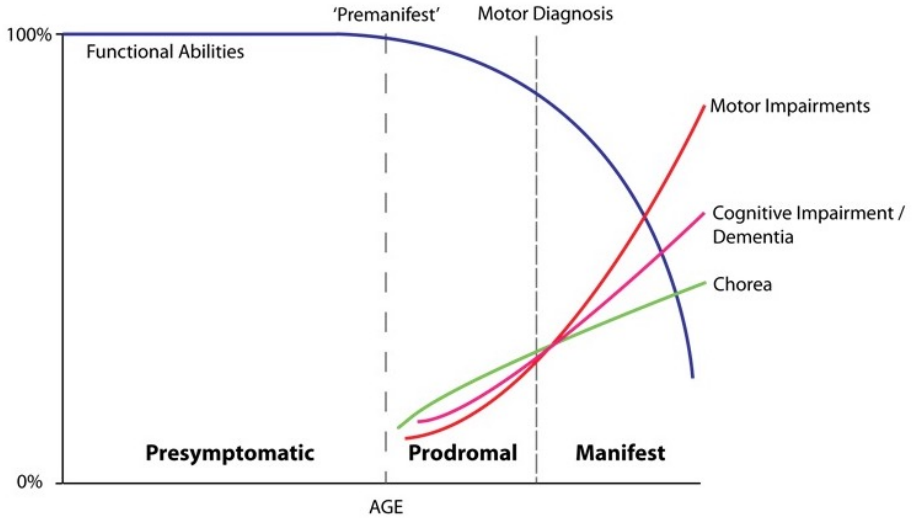
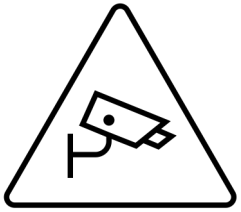


Table 16 Conditional Probability of Onset for an Individual with 51 CAG Repeats

Current age (years)	Conditional Probability (95% CI) within 5 years	10 years	15 years	20 years	25 years
0	0 (0-0)	0 (0-0)	0.01 (0.01-0.02)	0.05 (0.04-0.07)	0.20 (0.17-0.23)
1	0 (0-0)	0 (0-0.01)	0.02 (0.01-0.02)	0.07 (0.06-0.09)	0.25 (0.22-0.28)
2	0 (0-0)	0.01 (0-0.01)	0.02 (0.02-0.03)	0.09 (0.07-0.11)	0.31 (0.27-0.34)
3	0 (0-0)	0.01 (0-0.01)	0.03 (0.02-0.04)	0.12 (0.10-0.15)	0.37 (0.34-0.41)
4	0 (0-0)	0.01 (0.01-0.01)	0.04 (0.03-0.05)	0.15 (0.13-0.18)	0.44 (0.40-0.48)
5	0 (0-0)	0.01 (0.01-0.02)	0.05 (0.04-0.07)	0.20 (0.17-0.23)	0.52 (0.48-0.55)
6	0 (0-0)	0.02 (0.01-0.02)	0.07 (0.06-0.09)	0.25 (0.22-0.28)	0.59 (0.55-0.63)
7	0 (0-0.01)	0.02 (0.02-0.03)	0.09 (0.07-0.11)	0.31 (0.27-0.34)	0.66 (0.62-0.69)
8	0.01 (0-0.01)	0.03 (0.02-0.04)	0.12 (0.10-0.14)	0.37 (0.34-0.41)	0.72 (0.68-0.75)
9	0.01 (0.01-0.01)	0.04 (0.03-0.05)	0.15 (0.13-0.18)	0.44 (0.40-0.48)	0.77 (0.74-0.81)
10	0.01 (0.01-0.01)	0.05 (0.04-0.07)	0.20 (0.17-0.23)	0.51 (0.48-0.55)	0.82 (0.79-0.85)
11	0.01 (0.01-0.02)	0.07 (0.05-0.08)	0.25 (0.21-0.28)	0.59 (0.55-0.62)	0.86 (0.83-0.88)
12	0.02 (0.01-0.02)	0.09 (0.07-0.11)	0.30 (0.27-0.34)	0.65 (0.62-0.69)	0.89 (0.87-0.91)
13	0.02 (0.02-0.03)	0.11 (0.09-0.14)	0.37 (0.33-0.40)	0.72 (0.68-0.75)	0.92 (0.89-0.93)
14	0.03 (0.02-0.04)	0.15 (0.12-0.17)	0.44 (0.40-0.47)	0.77 (0.74-0.80)	0.94 (0.92-0.95)
15	0.04 (0.03-0.05)	0.19 (0.16-0.22)	0.51 (0.47-0.55)	0.82 (0.79-0.85)	0.95 (0.94-0.96)
16	0.05 (0.04-0.07)	0.23 (0.21-0.27)	0.58 (0.54-0.62)	0.86 (0.83-0.88)	0.96 (0.95-0.97)
17	0.07 (0.06-0.09)	0.29 (0.26-0.32)	0.65 (0.61-0.69)	0.89 (0.86-0.91)	0.97 (0.96-0.98)
18	0.09 (0.08-0.11)	0.35 (0.32-0.39)	0.71 (0.67-0.75)	0.91 (0.89-0.93)	0.98 (0.97-0.99)
19	0.12 (0.10-0.14)	0.42 (0.38-0.46)	0.76 (0.73-0.80)	0.93 (0.91-0.95)	0.98 (0.98-0.99)
20	0.15 (0.13-0.17)	0.49 (0.45-0.53)	0.81 (0.78-0.84)	0.95 (0.93-0.96)	0.99 (0.98-0.99)
21	0.19 (0.17-0.21)	0.56 (0.52-0.60)	0.85 (0.82-0.88)	0.96 (0.95-0.97)	0.99 (0.99-0.99)

Privacy regulations and IRB review

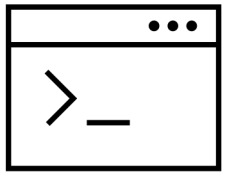
General Data Protection Regulation (GDPR)



owner ship data

pseudonymized vs anonymized use of data

Database



software

metadata

data management and - roles

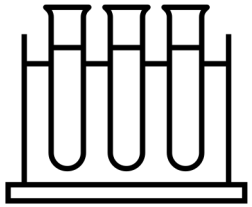
IRB review

national differences

more is less

Collaborations

Genetic laboratory



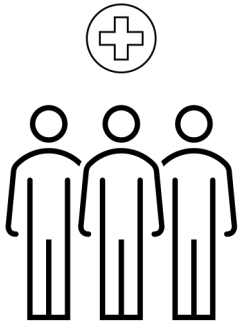
sharing data

Physicians / care facilities

sharing data

recruitment

Patient associations



recruitment

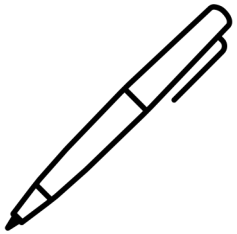
advisory board

Recruitment and informed consent

Recruitment

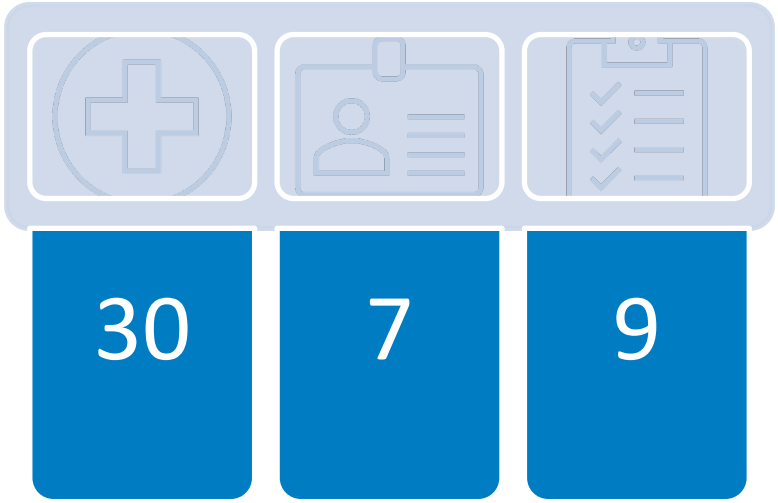
- Physicians
- Patient associations
- (Social) media
- Patient survey

Informed consent



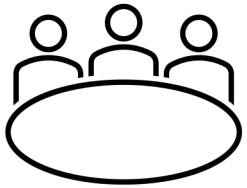
- Registration options
- On site vs at home

HD-JUNIOR



Data sharing

Advisory board

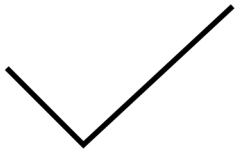


Board member patient association

Physician

Care taker

Type of data



Clinical data

Registry

Survey

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M Losekoot
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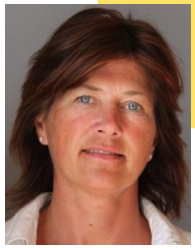
R Haselberg
Board of Dutch HD patient association



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Key conclusions

- JHD and PHD are a small and dispersed group of patients that need to be better defined
- Patient registries can serve for many purposes and exist in many forms
- Various registries for the same patient population can serve different goals and do not exclude each others relevance
- Think well of your most optimal datasets and patient population
- Study design can differ between datasets
- Invest in collaborations
- Share your data – this will move the field and patient care forward!