



Juvenile Huntington's Disease

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Outline:

- Definitions
- Genetics
- Symptom profile
- Management
- Future directions



HDSA Center of Excellence at UC Davis

JP Roberson Foundation
Charles and Margaret Pue Foundation

Our Mission:

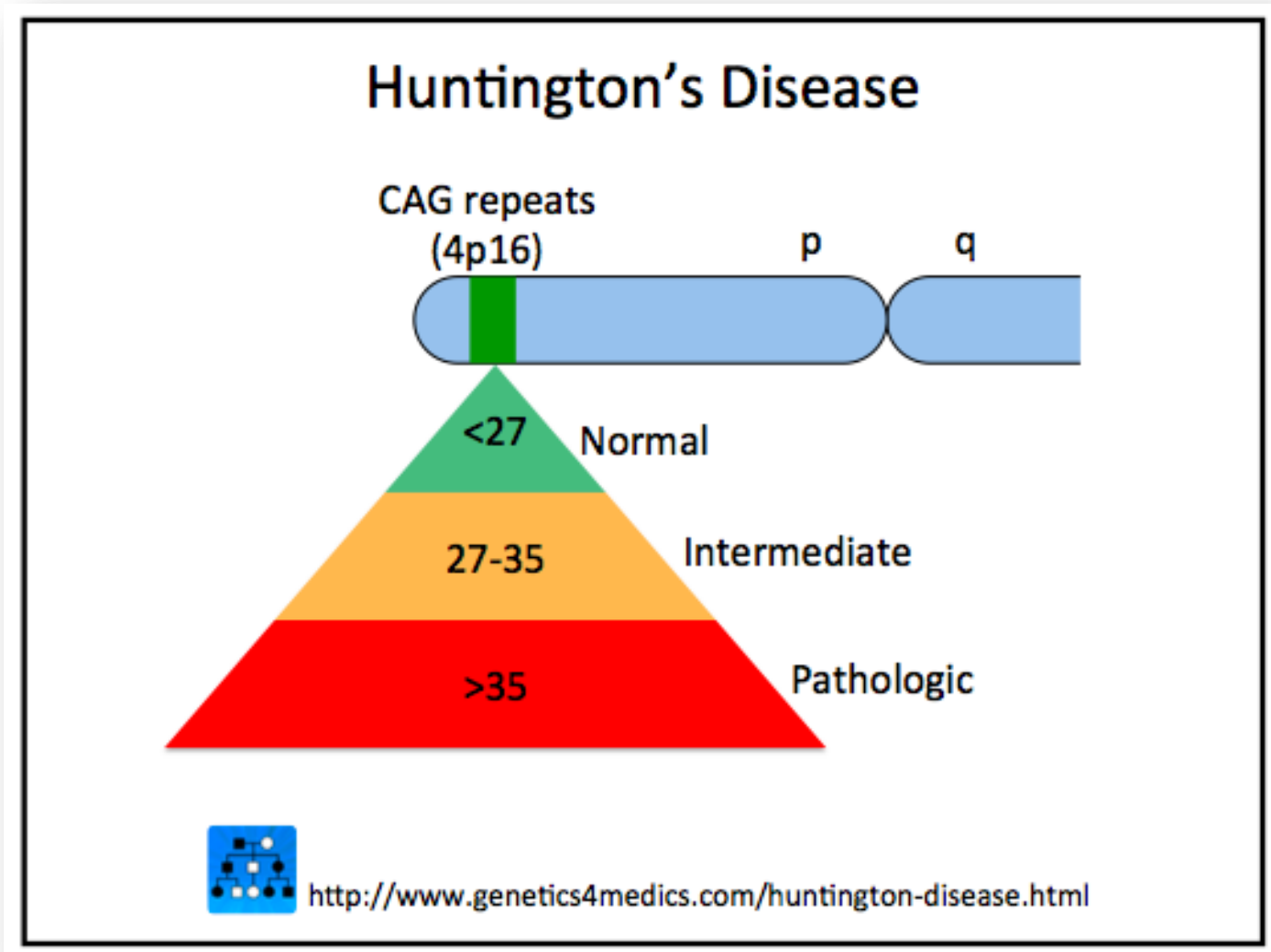
- *To provide excellent, comprehensive and compassionate care and outreach to HD families*
- *To provide expert education about HD to families, researchers and health care providers*
- *To advance HD research*



JHD Definition

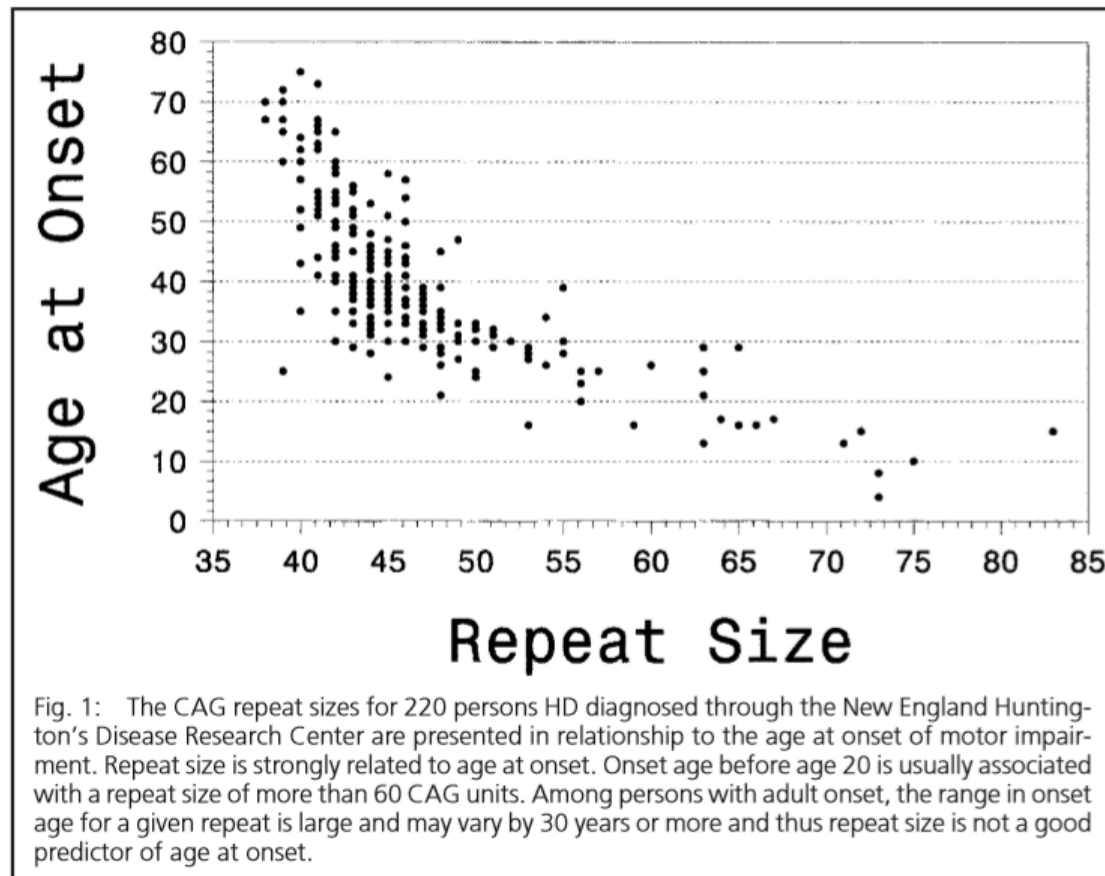
- Huntington's disease is an inherited neuropsychiatric degenerative disease caused by a mutation in the Huntingtin gene.
- Juvenile HD is defined as HD onset before age 21
- Only 5-10 % of cases of HD have juvenile onset
- Only 1-2% of cases have childhood onset, defined as onset before age 10 years
- The onset and symptoms of JHD differ significantly with those seen in adult-onset HD

Genetics



Relationship between CAG repeat length and age at onset

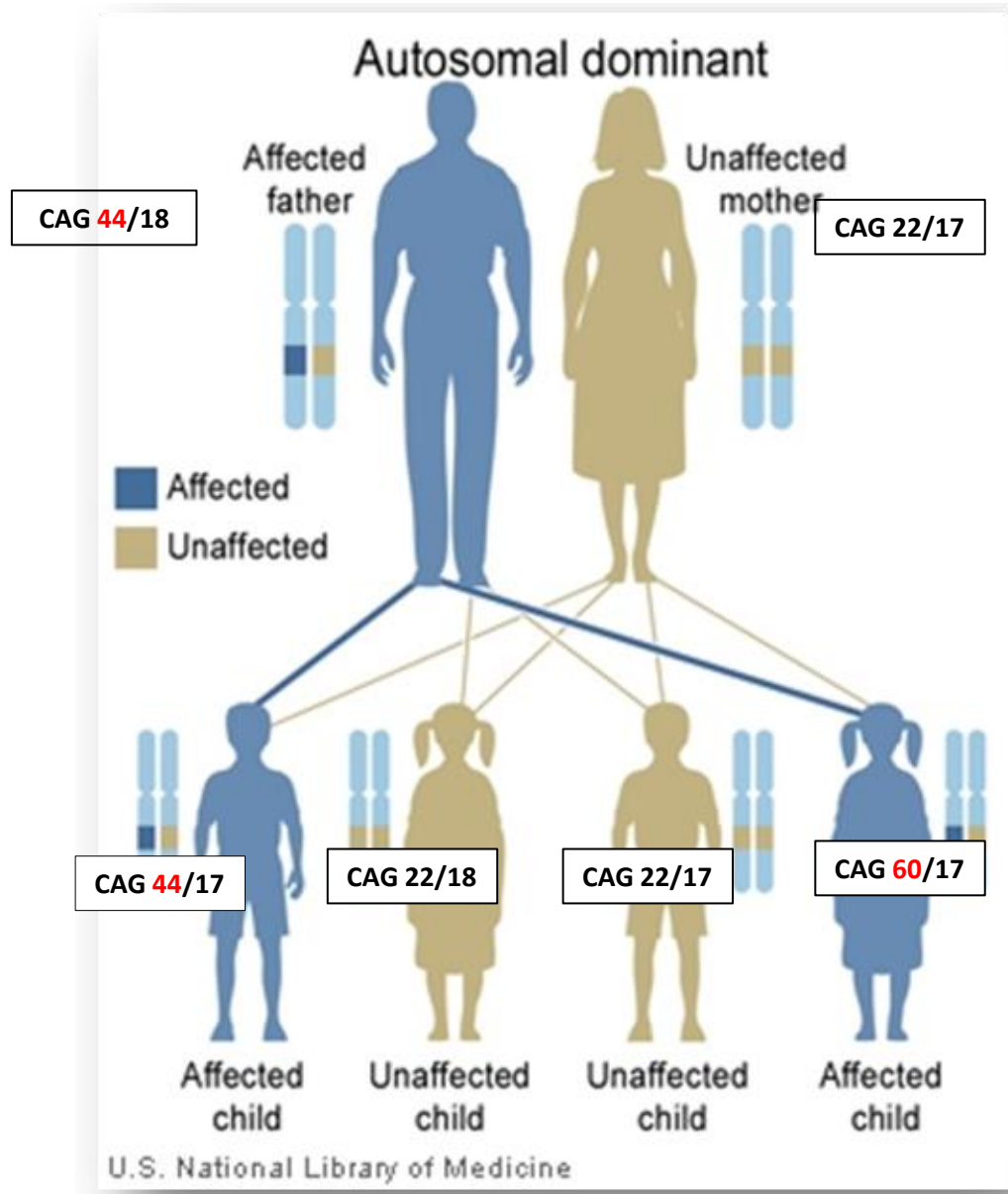
Nance and Meyers, MRDD Research Reviews 2001;7:153–157.



JHD genetics

- Typically, CAG repeats are > 60
- More likely to occur with inheritance from father (75%)
 - The CAG repeat length is “mutable” in spermatozoa and may increase from one generation to the next
 - This can also occur with maternal inheritance, but is less likely
- The range can be as low as 45 repeats, and can overlap the range seen in adult HD
- The longest CAG repeat length reported is >250 , associated with JHD in a child with onset during their second year of life

Genetics



How common is JHD?

- Review of JHD from Salpêtrière Hospital in Paris
 - 29/1452 referrals had JHD, or 2%
 - Symptom onset 14.5 yr (range 5-20)
 - Mean delay in diagnosis: 9 years
 - Initial symptoms: psychiatric or behavioral in 65%
 - CAGn 62 ± 11 (range 45-89)
 - All cases with onset < age 10 had paternal inheritance
- Review of HD prevalence by UK group showed ranges of 1-15% of all HD case series world-wide, but with average of 5% overall.

JHD Symptoms

- Usually, one parent has HD
 - In childhood-onset HD, sometimes the child may develop symptoms before their affected parent
- Cognitive decline, reduced school performance
- Behavioral disturbances
- Rigidity of limbs and trunk
- Oral motor dysfunction: difficulty with speech, swallow or drooling
- Seizures in 25%
- There is slow progression of symptoms over time

Features of Cognitive decline

- Change in learning trajectory in school performance/regression
- Impaired memory
- Impaired concentration and attention
- Slowness in thinking

Behavioral and psychiatric symptoms

- Carelessness
- Irritability
- Aggression
- Disinhibition and inappropriate behaviors
- Social withdrawal
- Anorexia
- Depression and suicide attempts
- Substance abuse
- At times, severe and requiring medical or legal intervention

Motor symptoms: different than adult HD

- Slowness, stiffness and rigidity are common
 - Dystonia: a sustained pattern of rigidity, often with twisting pattern
 - Parkinsonism: rigidity and slowness
- Chorea is less common, more prevalent with onset over age 10
- Impaired voluntary motor control: dexterity, coordination
- Speech and swallow difficulties
- Impaired balance
- Gait disorders

Seizures in JHD

- Reported in about 25% of patients
- There are multiple types of seizures reported in JHD
 - Generalized tonic-clonic: sudden loss of consciousness, fall to ground, stiffness and repetitive spasms, altered breathing for minutes followed by drowsy/confusional state
 - Absence: sudden, brief staring- off spell with rapid recovery
 - Complex partial: sudden alteration in feelings, sensation or movement, often with altered awareness
 - Partial seizures: sudden alteration in feelings, sensation or movement without any loss of awareness
 - Electroencephalogram (EEG) may show various patterns of seizure-related activity
 - Treatment available with medications

Diagnosis: when to test

- Diagnosis is made when there is evidence of cognitive decline and/or motor features suggestive of HD
- Presymptomatic testing of minors at risk for HD is not advised
- Sometimes children and teens in HD families have school issues, symptoms of ADHD, and/or behavioral difficulties that may raise the question of possible JHD.
- “The greatest challenge to the clinician is the 10- to 20-year-old patient presenting with behavioral symptoms or cognitive changes, ***as attentional difficulties, depression, and anxiety are common disorders in the general population.***”
- Symptoms that do NOT suggest JHD: Tics, tremors and spasticity

Lehman and Nance, Neurology® 2013;80:976–977

- “In order to avoid both a failure to diagnose HD in a teenager with predominantly behavioral symptoms and a premature or incorrect attribution of symptoms to HD, we advocate an intermediate approach to children who present with atypical or nonspecific symptoms: a brief period of watchful waiting, roughly a year in duration, to confirm a progressive course.”
- “This observation period need not be a time of sitting by idly; rather, it can be used to document the patient’s cognitive baseline through neuropsychological testing, treat the motor or behavioral symptoms, and optimize psychosocial factors.”
- It’s important to seek evaluation by a child neurologist or movement disorders neurologist.
 - It is sometimes advisable to have cognitive testing (neuropsychological testing) and a movement disorders exam looking to establish a baseline for the child or adolescent.
 - Assessments can then be repeated in 6-12 months to look for changes

Lehman and Nance, Neurology® 2013;80:976–977

Decision to seek evaluation

- Symptoms in a child or teen that worry parents may be due to psychological factors such as stress, adjustment reaction, mood disorders.
- These symptoms should be identified and treated in order to help the child's quality of life and function
- Delay in the diagnosis of JHD leads to lack of assessment and initiation of treatments that can help the child or teen at the start of the symptoms and through the course of the disease
- This may be especially true for psychiatric and behavioral symptoms....delay may limit the potential for a therapeutic effect of medications and therapy.

Staging of JHD

A. School attendance

- 3 – attends school, no special assistance needed
- 2 – attends school, some regular classes, some special or modified classes
- 1 – attends school, few or no regular classes
- 0 – unable to attend school or work program

B. Academic/developmental performance

- 3 – reading/writing/math skills appropriate to age
- 2 – mild decrease in academic performance but still able to take a test or to write
- 1 – unable to write legibly but able to communicate orally
- 0 – unable to read/write/communicate orally

C. Chores

- 2 – able to assist in age-appropriate manner with household chores
- 1 – occasionally assists with chores
- 0 – unable to participate in household chores

D. Activities of daily living

- 3 – performs self-cares in an age-appropriate manner
- 2 – requires some assistance for bathing, dressing, grooming, or feeding
- 1 – assists others who bathe, dress, or feed him/her
- 0 – unable to assist in self-cares

E. Lives

- 2 – at home with only family assistance
- 1 – at home/group home/foster care with assistance from non-family members
- 0 – living in a long-term care facility

Stages of JHD (total points in all areas)

11-13 points: Stage 1

7-10 points: Stage 2

3-6 points: Stage 3

1-2 points: Stage 4

0 points: Stage 5

Source: JHD by M. Nance, *A Physician's Guide to the Management of HD*, 3rd edition, 2011

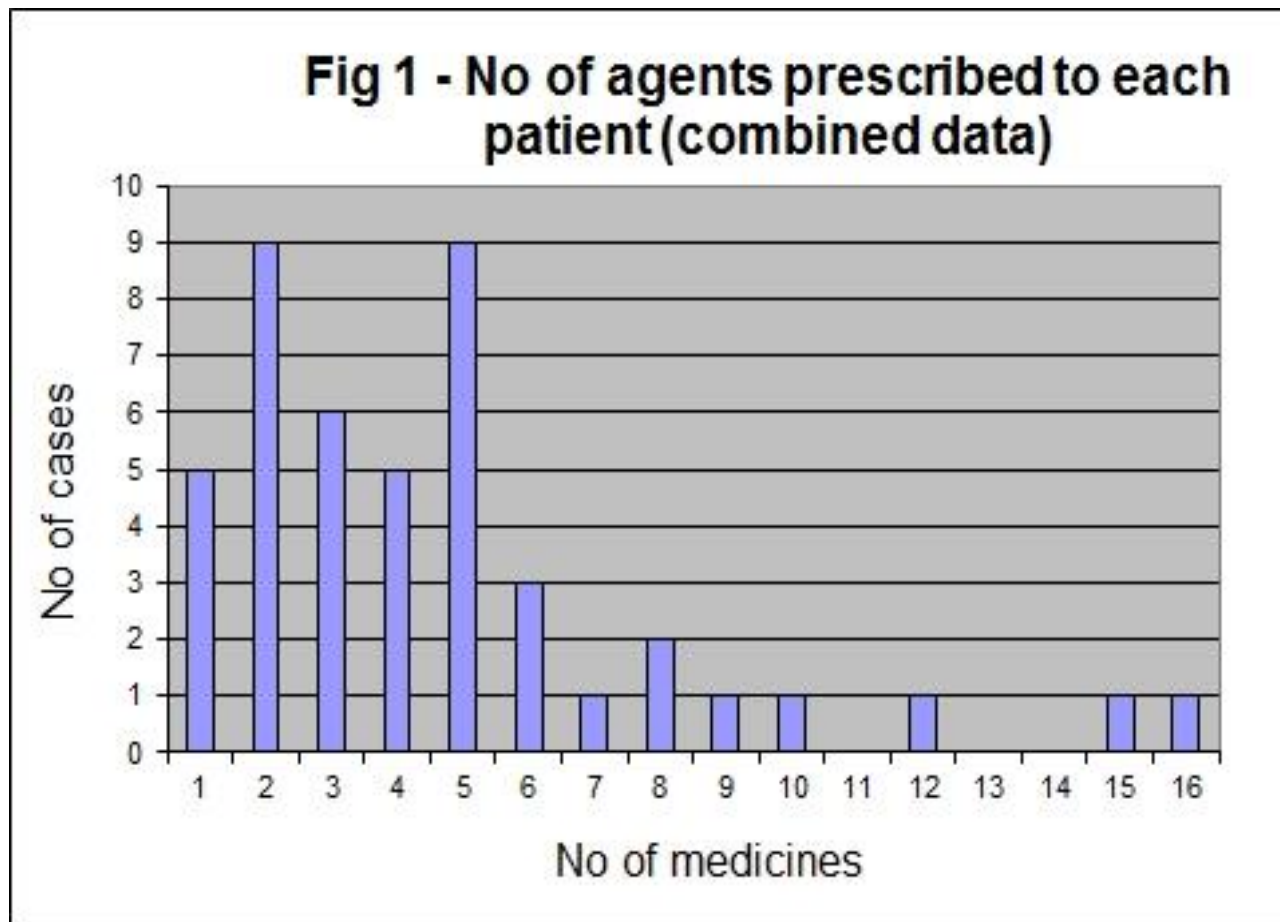
Management

- Treatment is symptomatic
- Focuses on cognitive, behavioral, motor and functional symptoms
- Medications can help mood, behavior and motor symptoms
- Therapies: physical, occupational and speech
- Management of seizures: safety education and medications
- Psychiatric care may be needed: medications and counseling
- School must be involved in treatment plan

Medications used for JHD: Review from Europe

N = 45 patients

Robertson et al, . PLoS Curr. 2012 February 15 [revised 2012 March 26];



**Fig 2 - Classes of medicines prescribed
(European Data)**

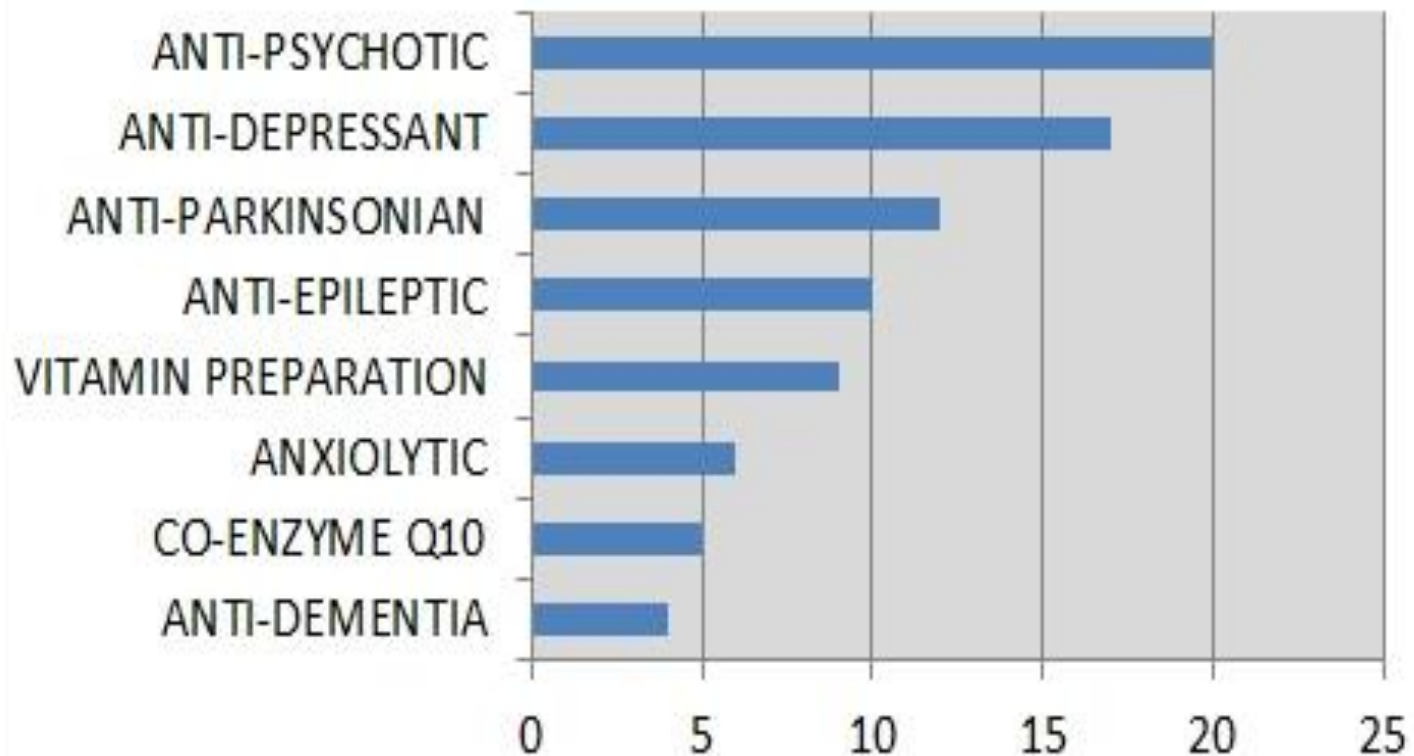


Fig 3 - Classes of medicines prescribed (UK data)

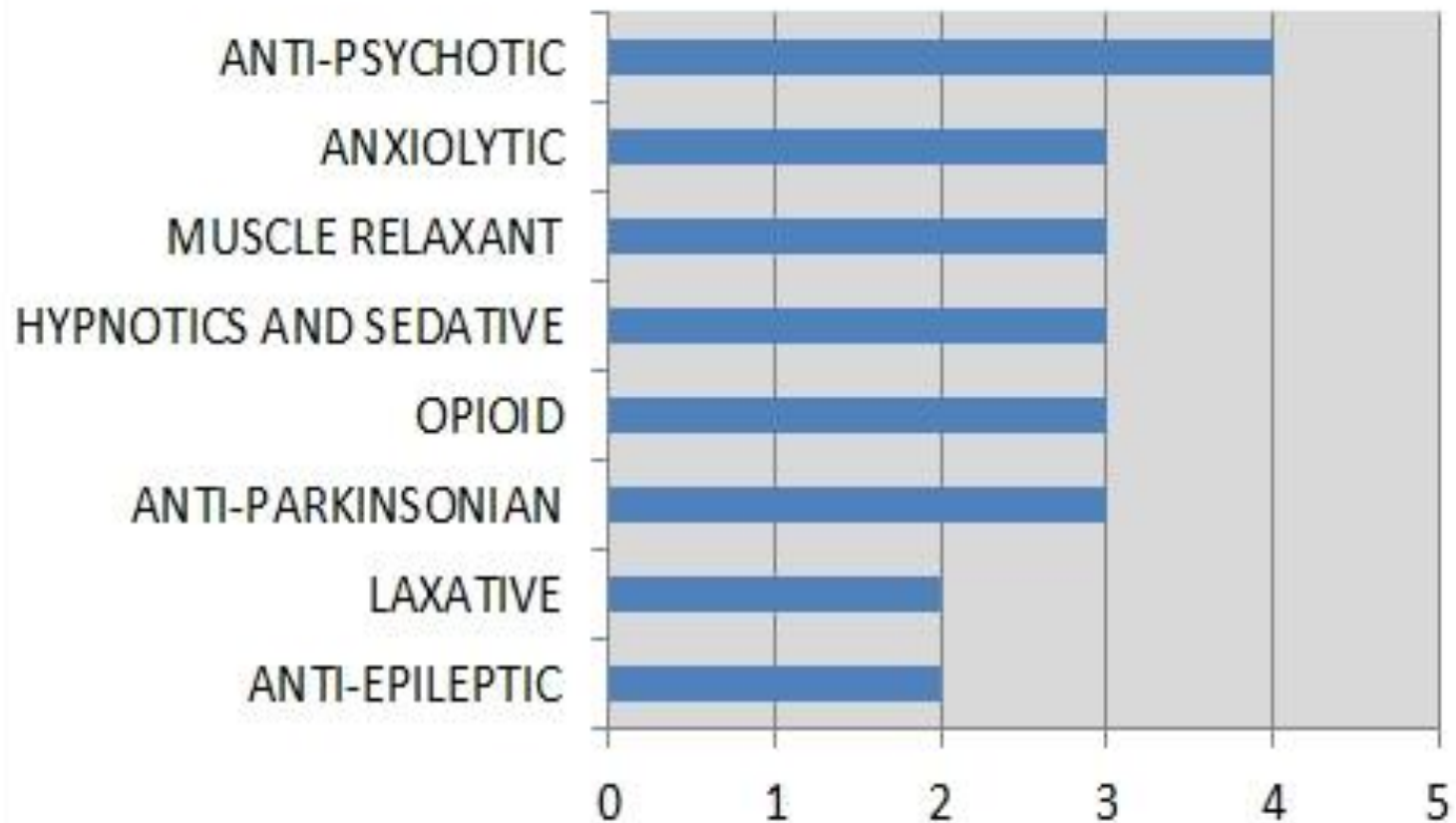


Fig 4 - The most commonly prescribed medicines, arranged by group

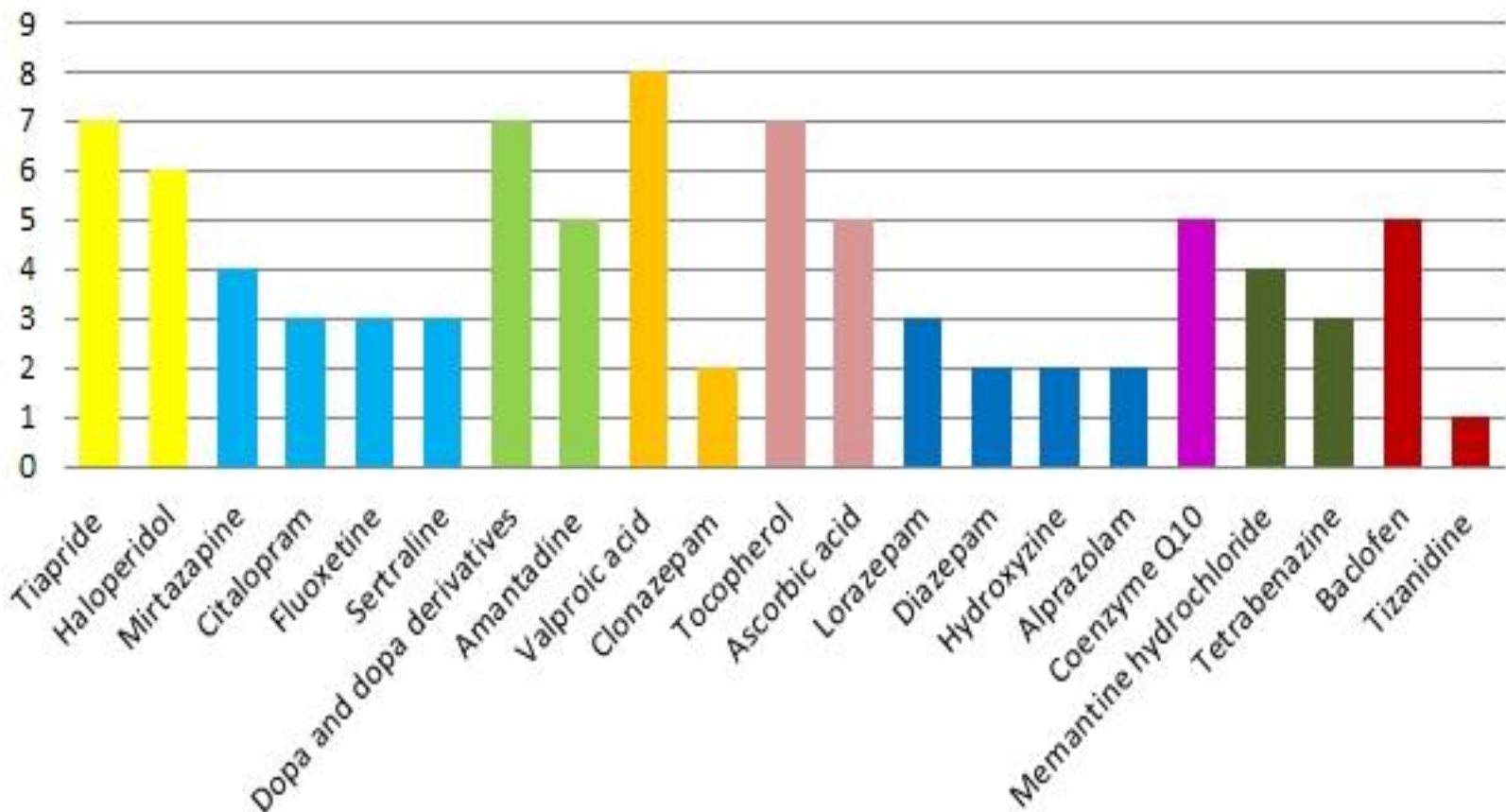
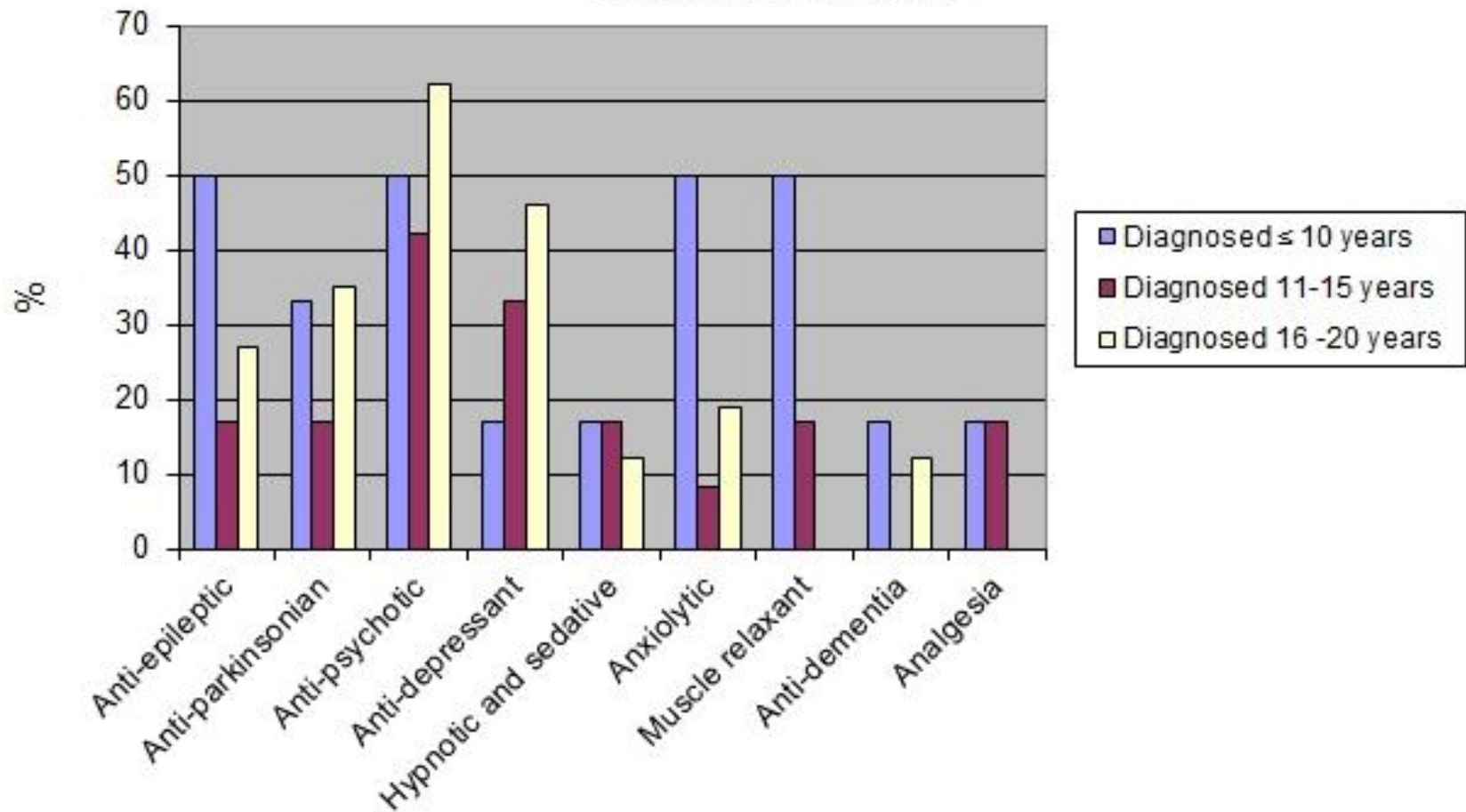


Fig 5 - Comparison of medications prescribed in JHD at different ages



Management of late-stage JHD

- Feeding difficulties and nutritional support: feeding tube
- Loss of mobility: wheelchair and bed-bound status
- Loss of speech and communication ability
- Increased rigidity, stiffness, spasms
- Crying
- Agitation
- Seizures
- Palliative care team approach
- Hospice referral

Special challenges

- When to consider JHD.....
- Effects of JHD diagnosis on siblings
- Family stress when both parent and child are affected
- “All children in an HD family, whether they have the disease or not, are at-risk for depression or stress-related problems.” – M. Nance
 - Seek support from pediatrician, counselors, school personnel, support groups

Future directions

- Hope through research
- To date, only children age 16 and older have been included in clinical trials for HD.
- University of Iowa study of children from HD families: observational study to examine neurological function, thinking, mood and MRI brain scans.

Thank you: HD patients and families

Your courage, generosity of spirit and hope are unparalleled

You have taught medical and health care professionals about HD and JHD

You inspire researchers to double their efforts to find a cure

You are invited.....



JHD Kids Walk Schedule



June 13, 2015- McKinley Park, Sacramento, CA

8:30 am

Registration Opens

\$25 covers vendors & entertainment

THANK YOU to Katie Jackson for your vision to hold this walk of HOPE for children and families affected by JHD!

For more information, see
<http://help4jhd.org/Walk.html>

