November 16, 2019

Huntington's Disease Society of America Center of Excellence
University of South Carolina School of Medicine

2019 SC Family Education Day

University of South Carolina College of Social Work

Huntington's Disease Society of America
South Carolina Affiliate

Genentech
A Member of the Roche Group

Huntington's Disease Society of America
Center of Excellence
University of South Carolina
School of Medicine

SC 2019 Family Education Day

SPEAKER:

Kimberly Osborne

Kimberly Austin Osborne has worked in healthcare and information technology since 1996. She is currently an Interface Analyst for the Regional Medical Center in Orangeburg, SC. She received her Bachelor's degree with dual specialization in Management and Management Information Systems from Saint Leo University in 2001. Kimberly began her work with the Huntington's Disease Society of America in February 2013 with peer support group training and then moved on to SC's first Team Hope Walk in October 2014. She is currently a co-chair for the SC HDSA Affiliate.

- Affiliate Website:

https://southcarolina.hdsa.org/

Facebook Affiliate Page:
https://www.facebook.com/HDSASouthCarolina

Facebook Closed Support Group:

Put in Search Bar--HD in SC →Hope for a Cure

Twitter: @CureHDinSC

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SPEAKER:
Martha Nance, MD

Martha Nance received her MD from the Medical College of Virginia; completed her residency in Neurology and a fellowship in clinical genetics at the University of Minnesota; and a fellowship in clinical genetics at the University of Minnesota. She is board certified in neurology and clinical genetics. Dr. Nance has a special interest in movement disorders and has been the medical director of the Huntington's Disease Center at Hennepin County Medical Center since 1991 and is currently the Director of the HDSA Center of Excellence there.

Dr. Nance wears many hats. In addition to the care of patients and families with HD she is involved in clinical research to develop better treatment. She is interested in education for both patients and medical professionals.

Dr. Nance received the Lifetime achievement Award from the Huntington Study Group at the annual meeting last week in Sacramento California

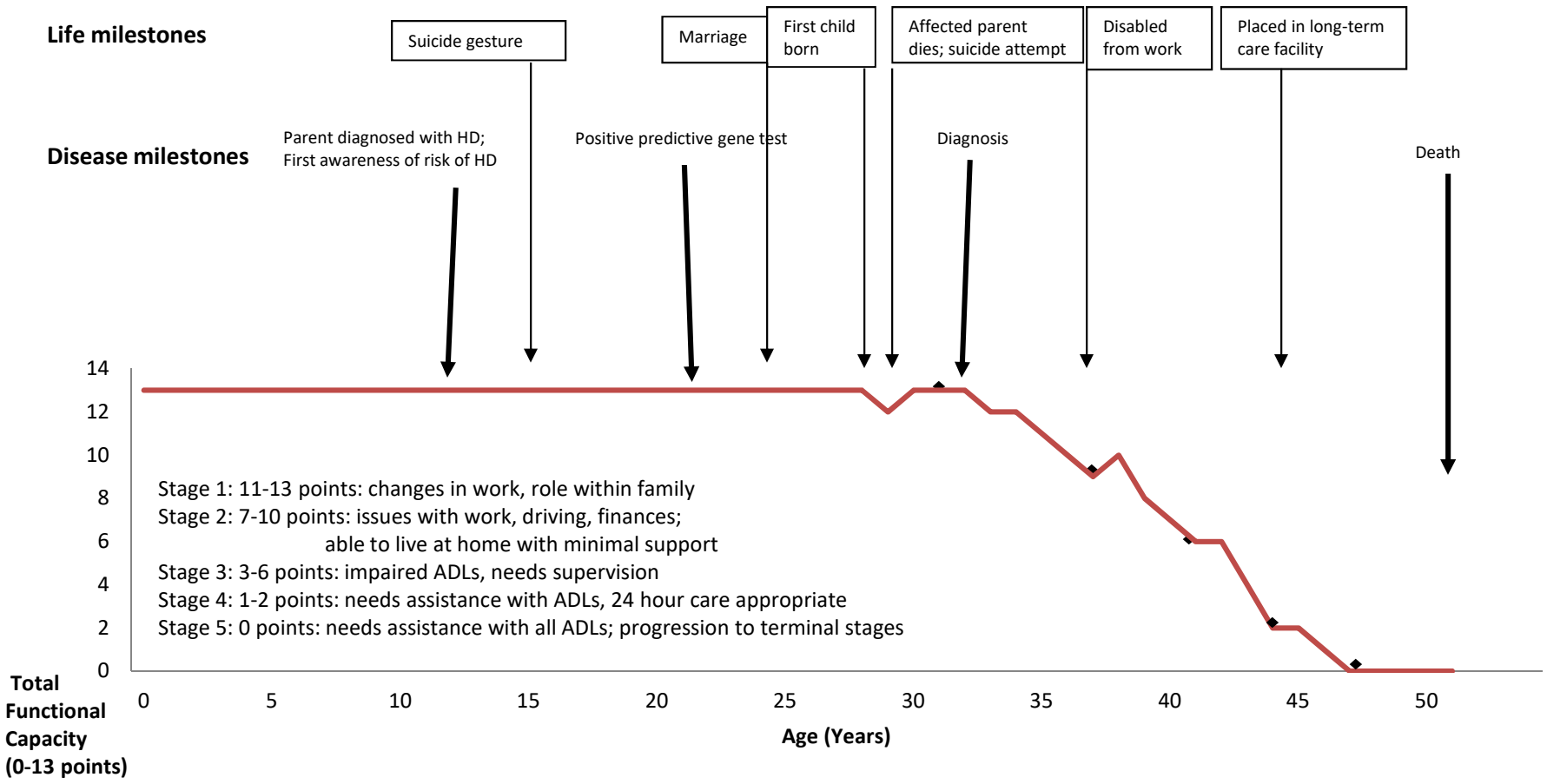
Huntington's disease—the long view

Martha A. Nance MD
Hennepin County Medical Center
HDSA Center of Excellence

Disclosures

- Consultant: Roche, Voyager, Uniqure
- Steering Committee: KINECT-HD
- Grant support: CHDI, HDSA
- Chair, Family Education Committee, HSG
- Member, Scientific and Bioethics Advisory Committee, EHDN

Progression of symptoms and disability in a typical patient with Huntington's disease



HD lasts a lifetime

- The “HD gene” is there from conception
- The impact of HD on a person often begins long before any symptoms
- Changes in the brain appear up to 20 years before there are definite motor symptoms

On a long life with HD,

- Plan ahead, so you can have the stuff that you like and need
  - (and so that the inevitable changes do not come as a surprise)
- Eat right
- Drink enough fluids
- Do things! Life is to be lived!
- Bring family/friends with you

- Oh yeah, and…stay fit! Exercise!


MARATHON
FINISHER

OPC-1147
Coenzyme Q10
Creatine
Ethyl-EPA
Riluzole
Dimebon/Latrepirdine
Laquinimod
Minocycline
Phenylbutyrate
Pridopidine
Remacemide
VX-15 (Signal)

Tetrabenazine
Deutetrabenazine

PREDICT
PHAROS
COHORT
ENROLL-HD

2019: trials of treatments directed at the HD gene itself

RG6042 (HD Generation 1) (Roche)

PRECISION HD-1 and
PRECISION HD-2
(Wave Life Sciences)

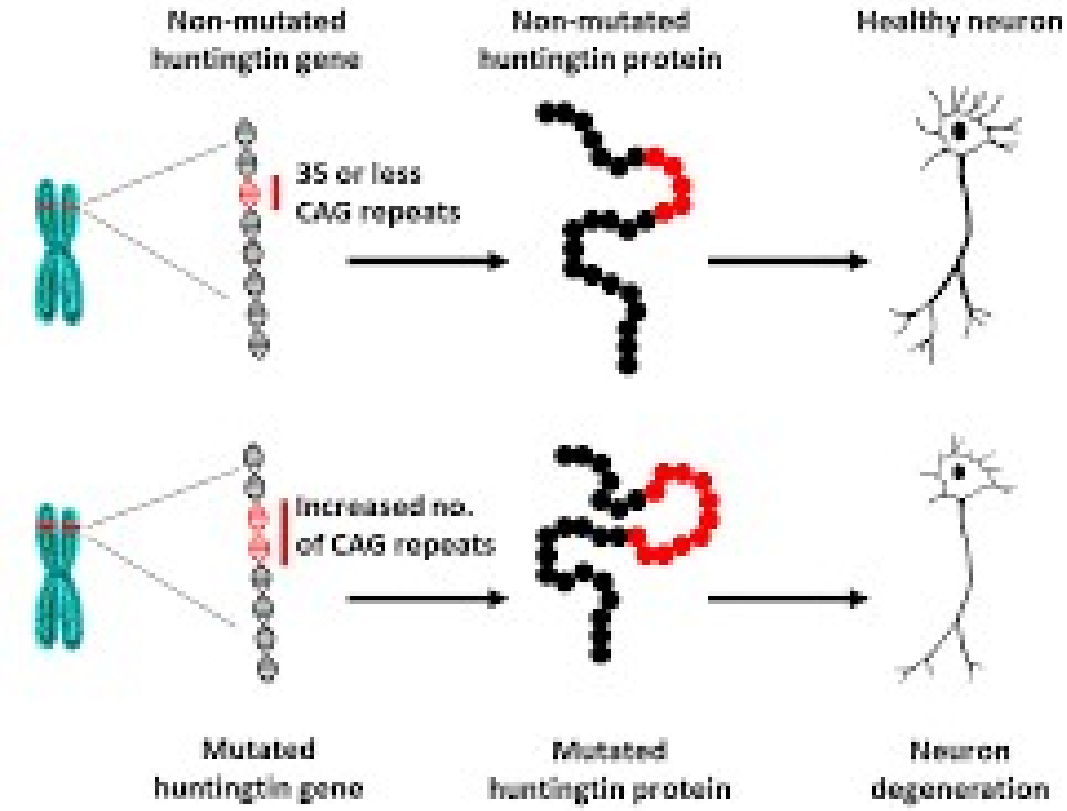
AMT-130 (UniQure)

GENE SILENCING

Gene silencing, in words

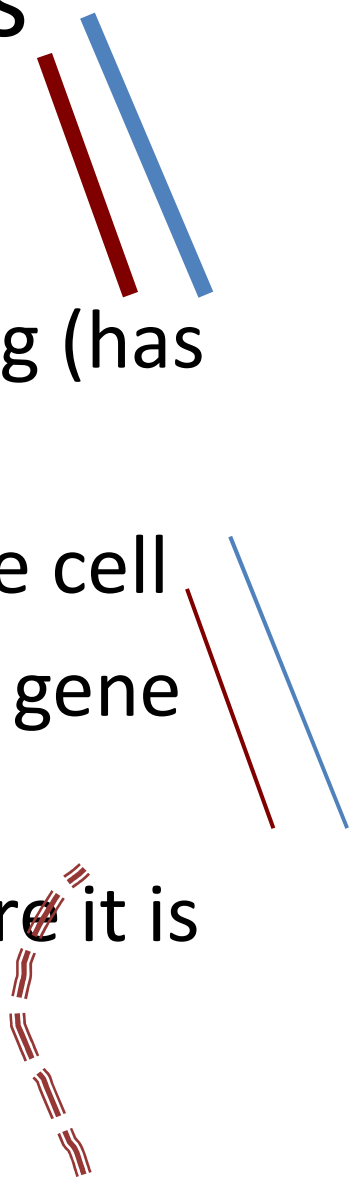
- You have two HD genes

CAG repeats in the HD gene



Gene silencing, in words

- You have two HD genes
- In people with HD, one gene is too long (has too many CAG repeats)
- Genes are located in the nucleus of the cell
- When it is time to make a protein, the gene makes a copy of itself, called mRNA
- The mRNA goes to the ribosome, where it is “read” to make the huntingtin protein



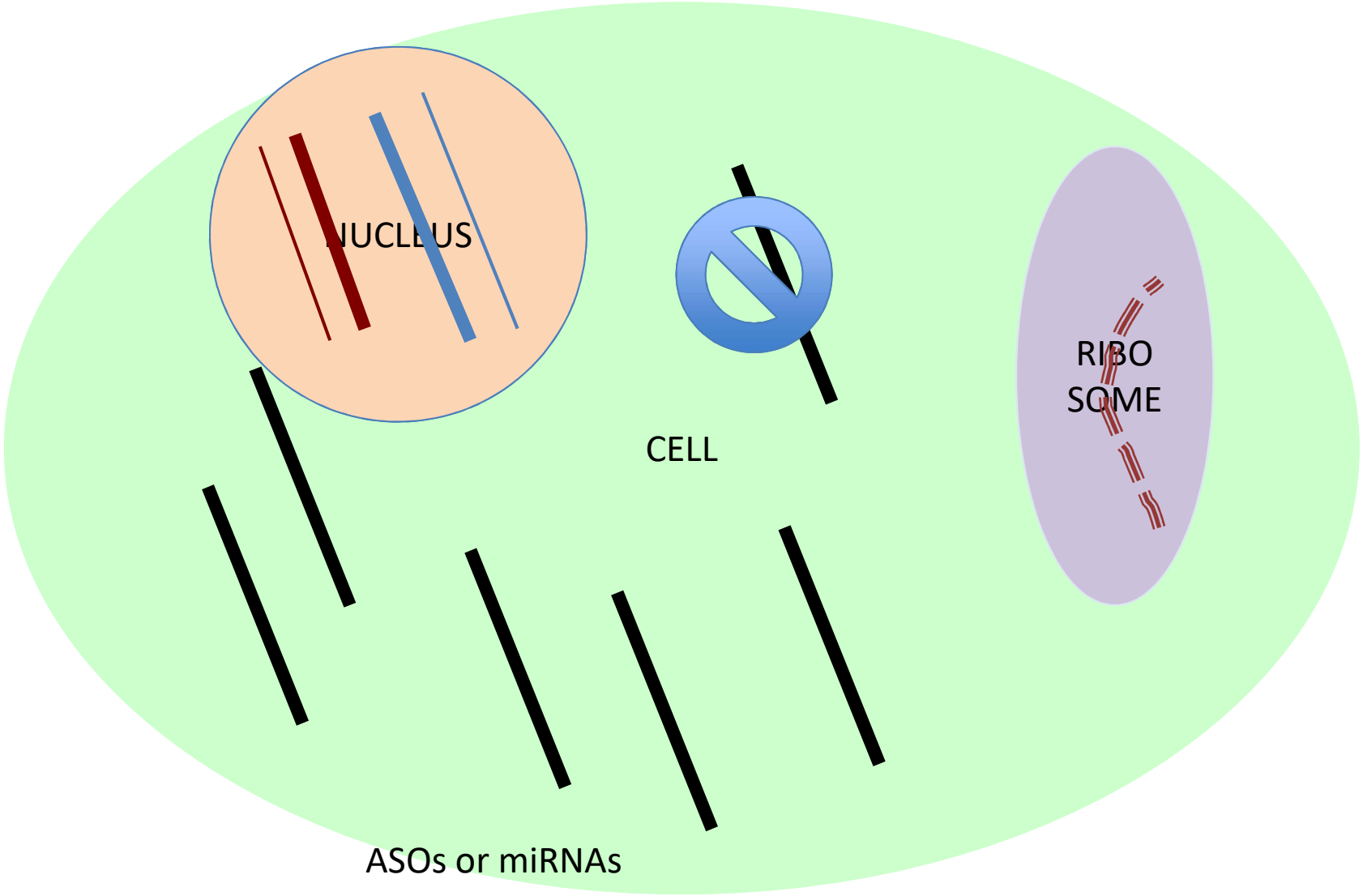
Gene silencing, in words

- If the normal gene makes RNA, it will make a normal protein
- If the abnormally long gene makes RNA, then the resulting protein will be too long and will not work properly/fall apart too easily
- Too much abnormal huntingtin protein in the (nerve) cell leads to damage and death of the cell

Gene silencing, in words

- Insert an “antisense oligonucleotide” (ASO) or “microRNA”)miRNA)into the cell, which recognizes mRNA made by the abnormal gene
- The mRNA will stick to the ASO, and will be discarded by the cell/not used to make a protein
- If you only make normal protein, then you shouldn’t get HD

Gene silencing



Different approaches

	Kind of molecule	Targets	Administration	Phase	Enrolling
Roche	ASO	Both HD genes	Repeated intrathecal injections	3	yes!
Wave	ASO	Two “flags” found on 70% of abnormal HD genes	Repeated Intrathecal injections	1-2	In Canada and Europe
UniQure	miRNA/viral vector	Both HD genes	Single surgical treatment	1-2	4th Q 2019?

Challenges

- ASOs don’t silence the abnormal gene completely
  - Huntingtin levels in CSF reduced by 40-60% (Roche)
- Is it OK to silence both copies of the gene?
  - So far, so good
  - But mice without an HD gene do not live long enough to be born

Questions

- Does intrathecal (by spinal tap) administration get the ASO where it needs to go (where does it need to go?)
- All treatments so far are targeting the brain
- How about surgical administration—both sides of the brain? What locations?
- How long will a miRNA persist in the brain?

Other things to think about

- The Wave products target 2 “flags” that are present near about 70% of abnormal HD genes (in Caucasians) (and could be present near normal genes in some people)
- Understand that this is research…some participants will receive placebos
- What if the treatment works, but is reallly expensive…

HD lasts a lifetime

- The “HD gene” is there from conception
  - Why don’t the symptoms start at birth?

The new genetics of HD

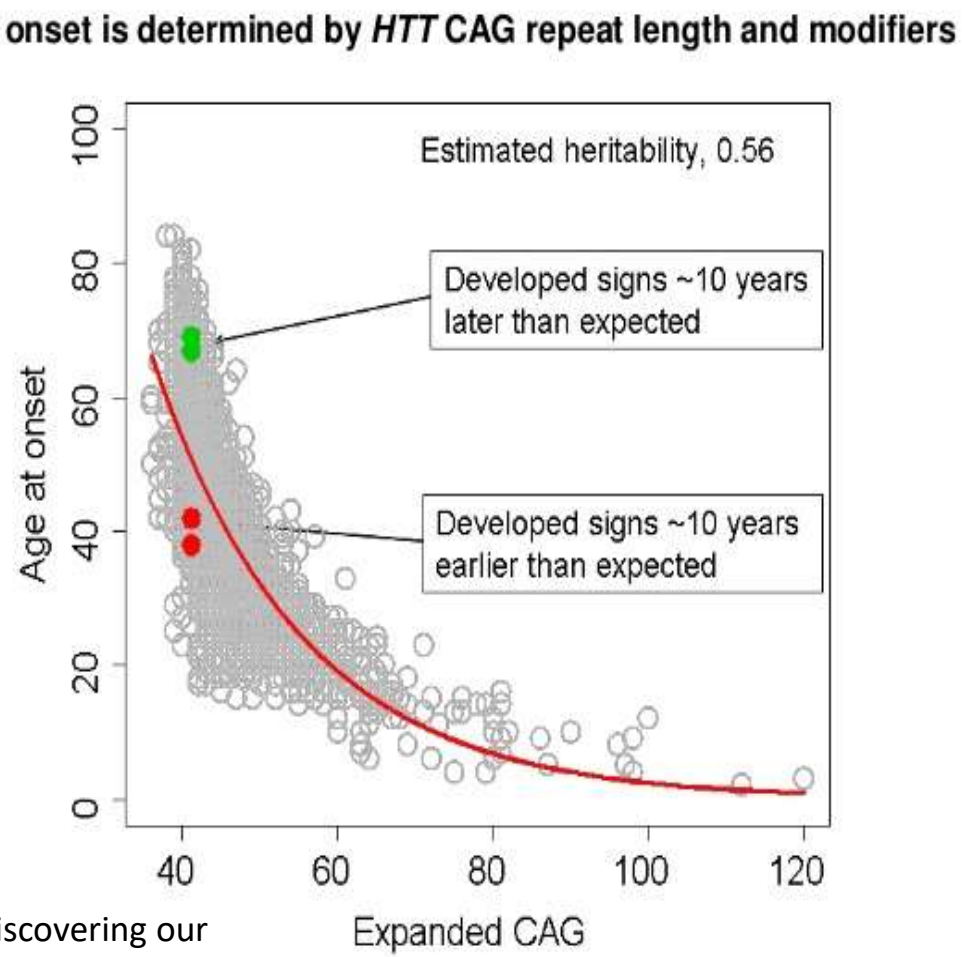
- The old genetics:
  - How many CAG repeats in the huntingtin (HD) gene
- The new genetics:
  - Up to 5% of CAG repeat sequences may be counted incorrectly using the current gene test (usually +/- 2 of the actual CAG length)
  - CAG repeat lengths can change during lifetime—in the brain cells
  - Onset of HD may be related to when/how much the CAG repeat length increases in the brain cells

Say what?

- Increases in CAG repeat length in brain cells may be related to
  - Whether there is an “interruption” in the CAG repeat sequence (the same thing that might cause the repeat number to be counted incorrectly)
  - The function of other genes (in particular, genes involved in DNA repair)
- This has not (yet) led to new tests

Relationship between CAG Repeat Number and Onset Age

- Related to length of the CAG repeat sequence
- And (possibly) whether that sequence is “interrupted”
- And to increases in CAG length in brain cells
- Which is related to the function of some DNA repair genes?

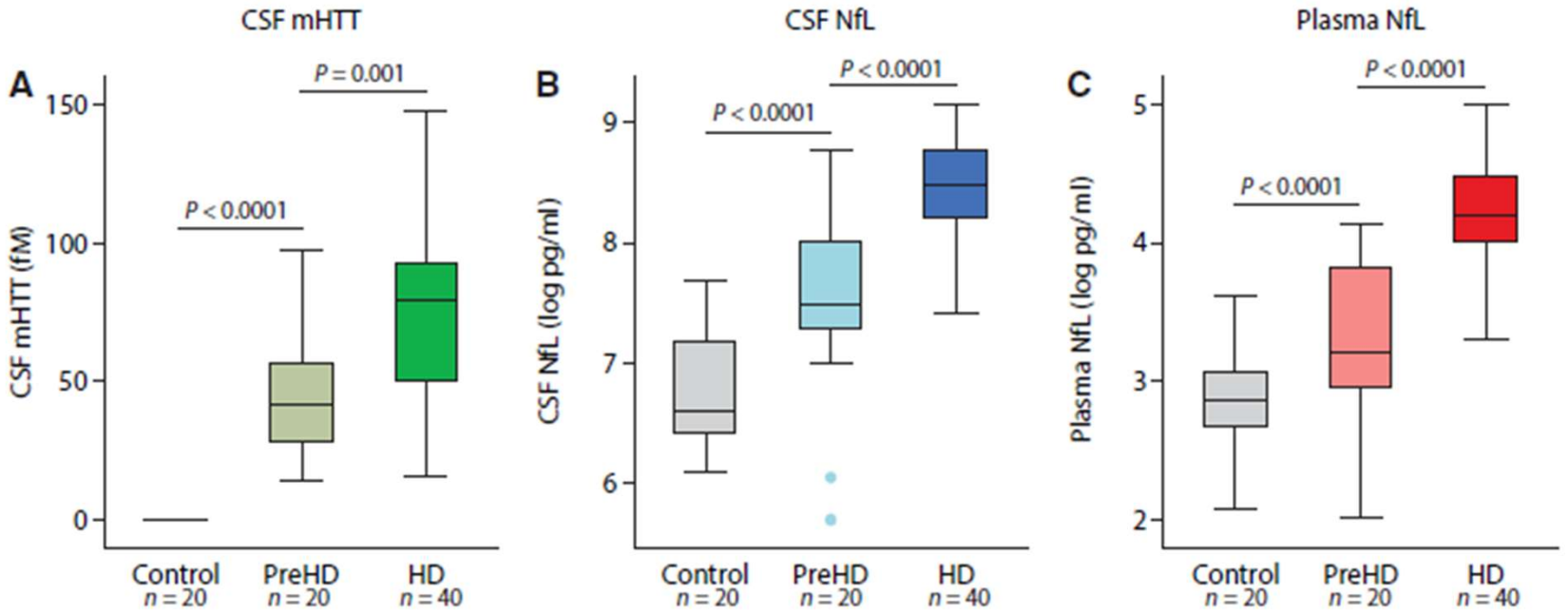


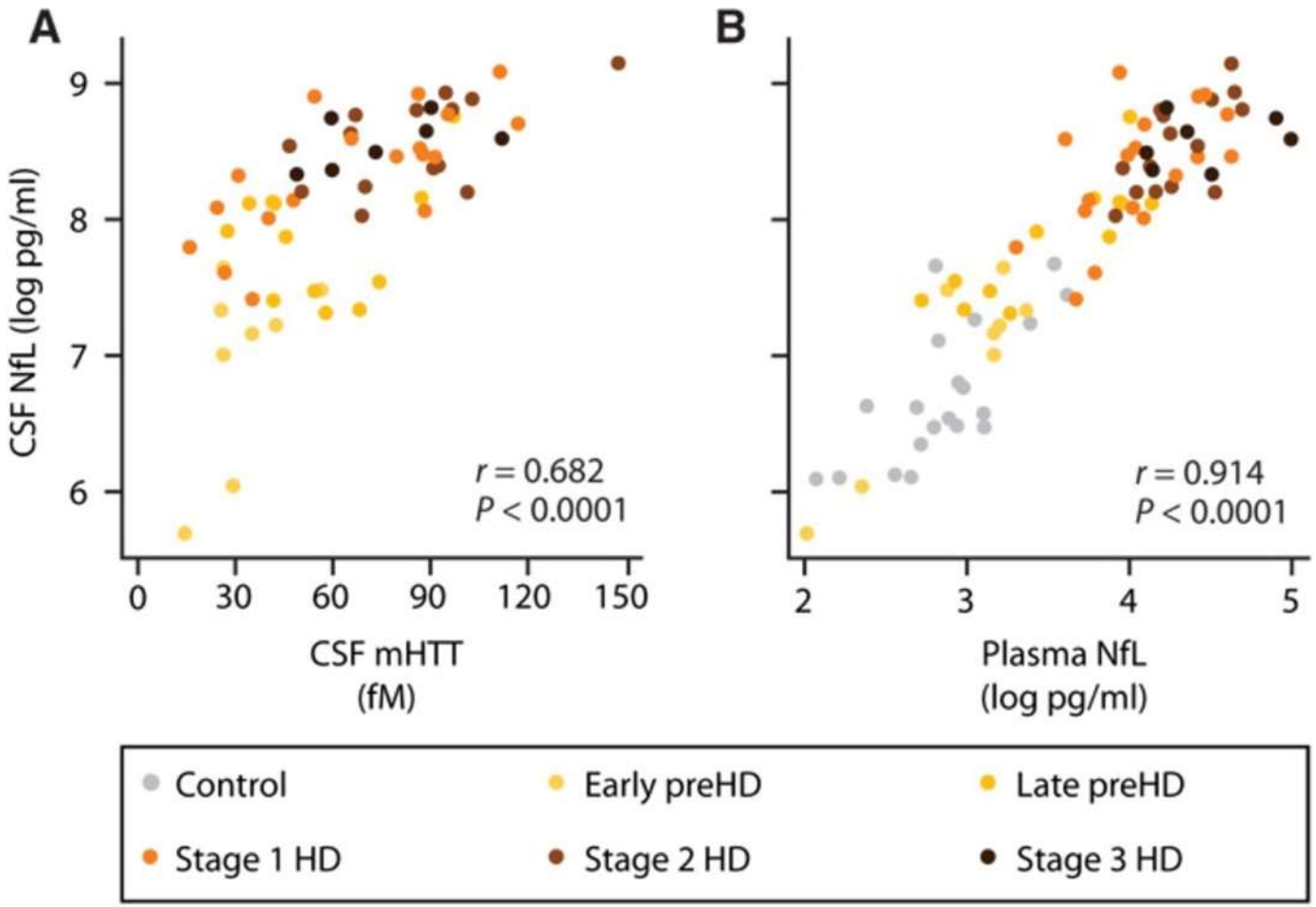
Geschwind, M. 2016 HD Insights of the Year, HSG 2016:Discovering our future. https://www.slideshare.net/HeatherHare/hd-insights-of-the-year-niccolini

HD lasts a lifetime

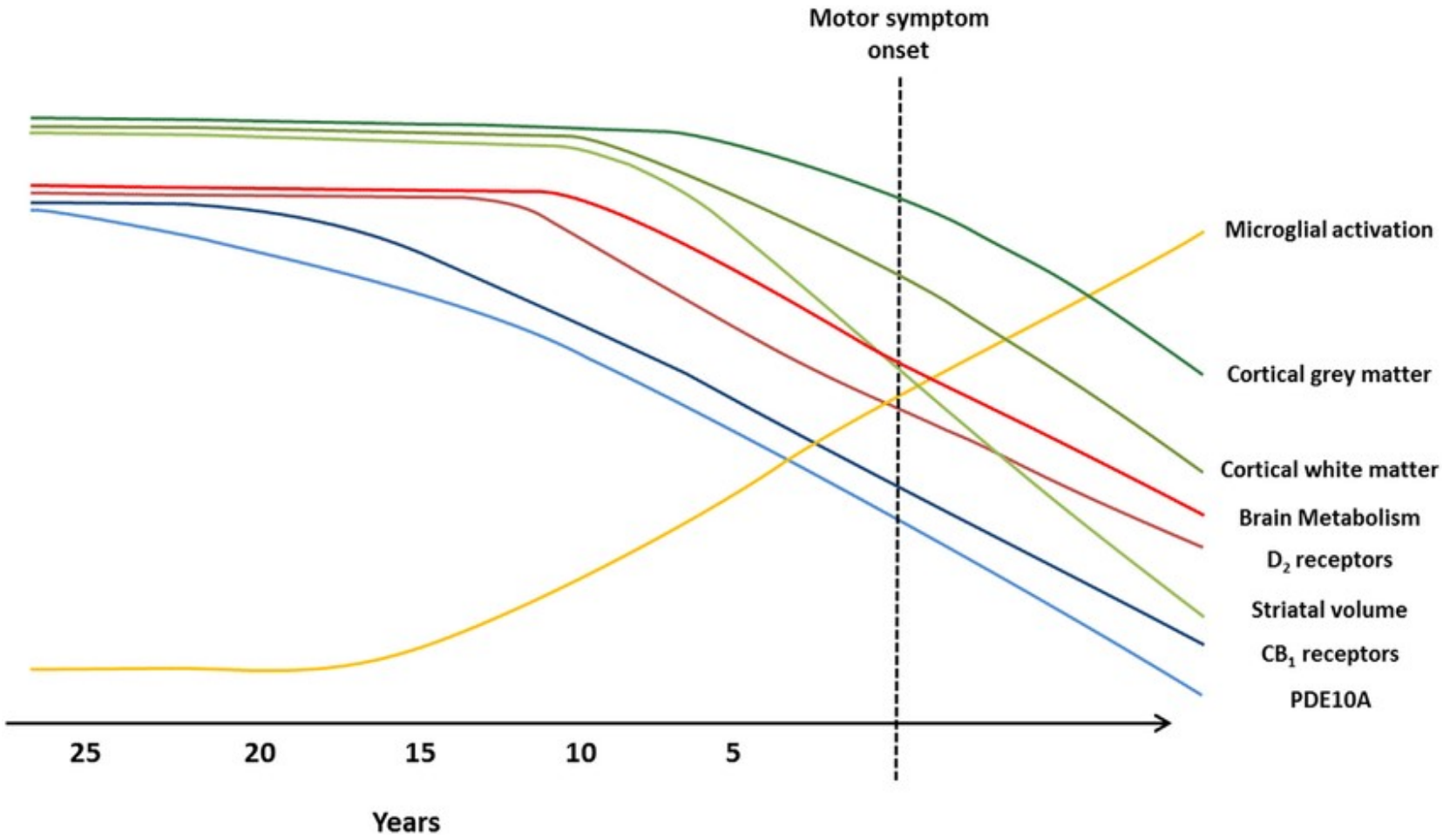
- What are the earliest changes in the brain?
- Biomarkers may tell us when the disease process has begun (CSF htt levels, MRI markers)
  - Maybe in the future at-risk/gene-positive people will come in for periodic (2 year? 5 year?) spinal taps

HTT and NfL proteins increase as HD symptoms develop

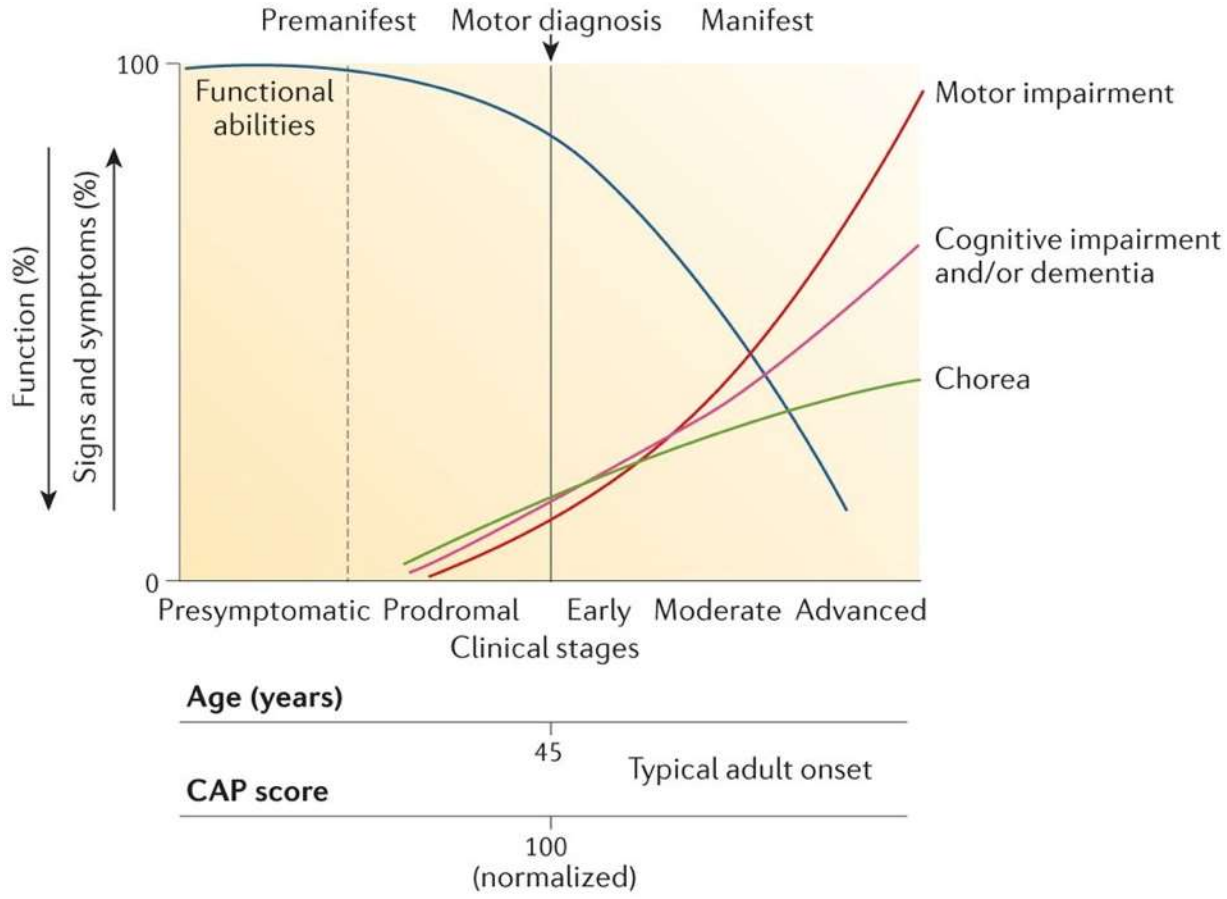



A
B
CSF NfL (log pg/ml)
9
8
7
6
0
30
60
90
120
150
CSF mHTT
(fM)
r = 0.682
P < 0.0001
2
3
4
5
Plasma NfL
(log pg/ml)
r = 0.914
P < 0.0001
Control
Early preHD
Late preHD
Stage 1 HD
Stage 2 HD
Stage 3 HD

MRI changes are detectable before clinical symptoms of HD



The course of HD



Nature Reviews | Disease Primers

If we “diagnose” HD earlier, then we need to work on…

- Insurability
- Employability
- Self-image
- Status within the family
- Our attitudes about what it means to “have HD”

BJ Viau—from hoopathons…

To international leadership

Even if “disease-modifying therapies” (DMTs) work…

- There will still be people who have HD who won’t or can’t get ASO treatment
  - Who will need the best care
- And people realizing they are at risk or affected
  - Who will need support, counseling, testing, reproductive/life/career decisionmaking, medical care

Advances in HD care

- Guidelines for physical therapy
  - (we now know that you SHOULD be exercising!)
- Guidelines for doing predictive genetic testing
- Algorithms for managing a number of psychological/psychiatric symptoms
- Two FDA-approved medications for chorea (and a third one being studied in the KINECT-HD trial)

Sonshine and Hope

Huntington's Disease Society of America
Center of Excellence
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SC 2019 Family Education Day

SPEAKER:
Miroslav Cuturic, MD

Dr. Miroslav Cuturic joined University of South Carolina School of Medicine in 2003. He earned his medical degree from the University of Zagreb School of Medicine, and completed postdoctoral research at the Center for Biomedical Research within the fields of virology and immunology in Zagreb, Croatia. He attended a psychiatry residency at Connecticut Valley Hospital in Middletown, CT, followed by a neurology residency at St. Louis University in St

Louis, MO. He completed neuromuscular/EMG fellowship training at Tulane University, New Orleans, LA. He has been director of our Huntington's disease (HD) clinic since 2009. He is board certified in Neurology, Clinical Neurophysiology and Electrodiagnostic medicine. Currently, he is our site HSG investigator, site primary investigator for Enroll-HD and the director of the SC HDSA Center of Excellence.

Huntington's Disease Society of America

Huntington's Disease Research Update

Miroslav Cuturic, MD
Assistant Professor of Clinical Neurology
HDSA Center of Excellence
University of South Carolina School of Medicine
HD Education Day
Columbia, SC, November 16, 2019

Huntington's Disease Society of America
50 YEARS OF SERVICE

Huntington's Disease Society of America

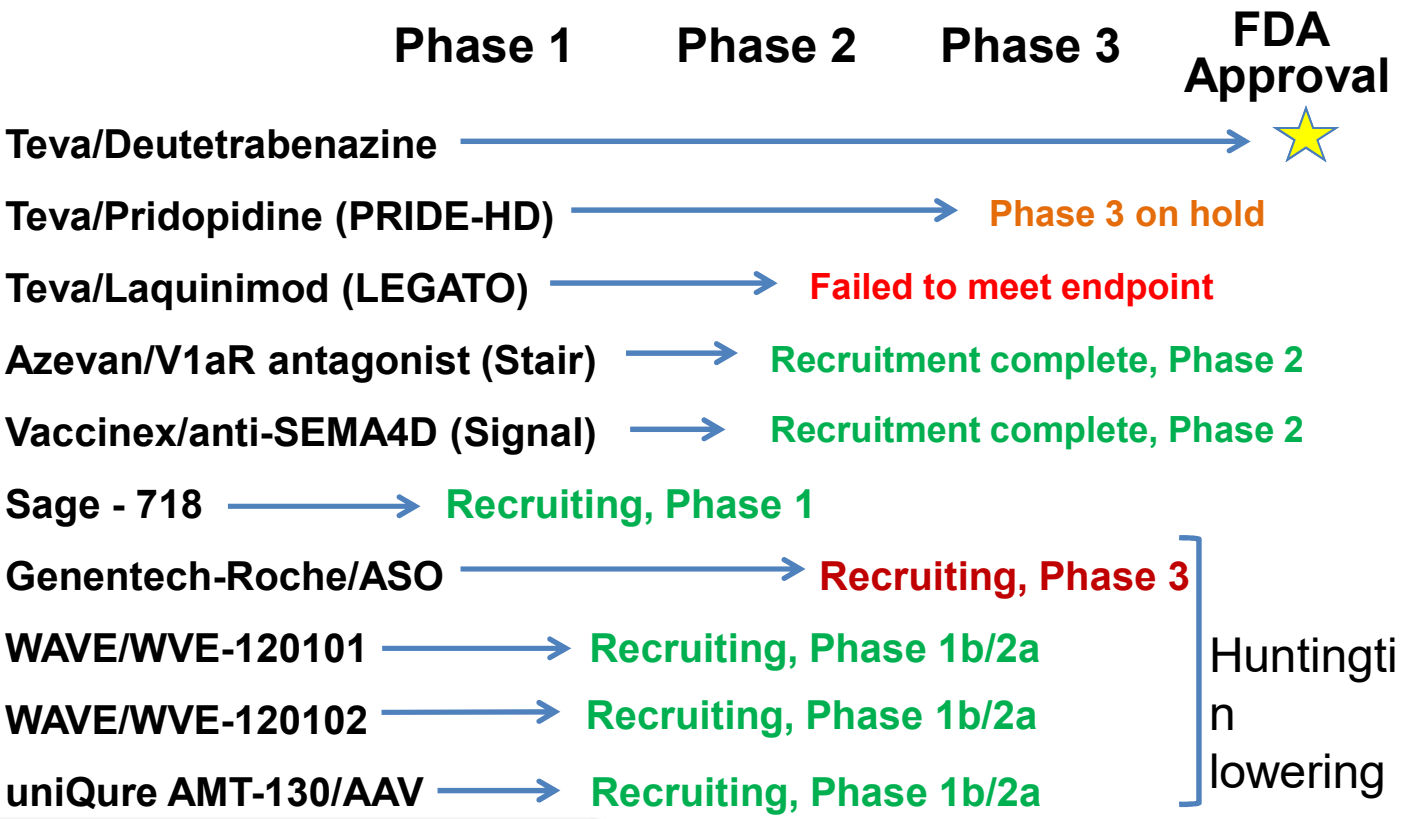
HD clinical studies and trials

Huntington's Disease Society of America

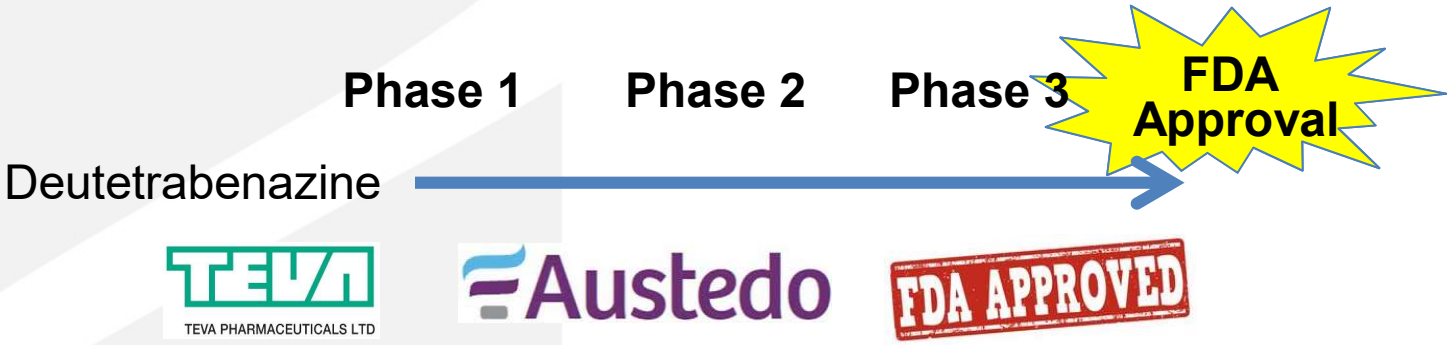
What are the phases of a clinical trial?

	Phase 1	Phase 2	Phase 3
Who?	Patients or healthy volunteers	Patients	Patients
What?	Safety (dangerous side effects)	Other side effects & body effects	Efficacy (helping symptoms)
How many?	20-100	100-300	300-600 or more

HD drug pipeline: completed and ongoing trials



HD drug pipeline: Austedo approved by FDA!



- Oral drug that controls movements; similar to tetrabenazine
- In the Phase III trial called FIRST-HD it showed benefits for chorea and day to day function
- Longer lasting = fewer side effects than tetrabenazine

HD drug trials: ongoing, not currently recruiting

Phase 1 **Phase 2** **Phase 3** **FDA Approval**

Pridopidine →

TEVA PHARMACEUTICALS LTD

Pride-HD
PRIDOPIDINE

- An oral medication to stabilize dopamine, a neurotransmitter that controls movement and mood
- Did not improve movements, but improved total functional capacity, a measure of how people function in their daily lives
- The Phase III study is currently on hold

OCCUPATION
0 = unable
1 = marginal work only
2 = reduced capacity for usual job
3 = normal

FINANCES
0 = unable
1 = major assistance
2 = slight assistance
3 = normal

DOMESTIC CHORES
0 = unable
1 = impaired
2 = normal

ADL
0 = total care
1 = gross tasks only
2 = minimal impairment
3 = normal

CARE LEVEL
0 = full time skilled nursing
1 = home or chronic care
2 = home

HD drug trials: ongoing, not currently recruiting

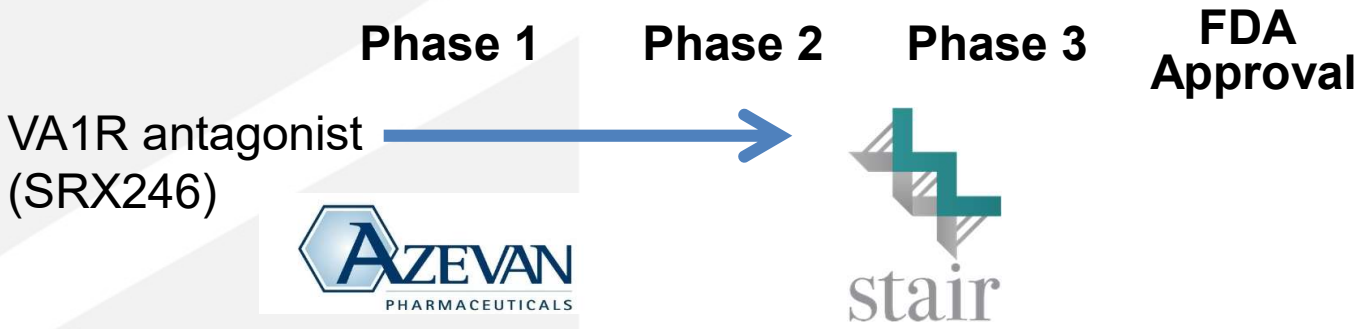
	Phase 1	Phase 2	Phase 3	FDA Approval
Laquinimod	→			

TEVA PHARMACEUTICALS LTD

LEGATO-HD
THE LAQUINIMOD HD STUDY

- An oral medication targeting brain inflammation
- Looking mainly at effects on movements but also other symptoms
- In August 2018 this trial unfortunately did not meet its primary endpoint – it did not improve motor symptoms
- However, brain volume shrinkage was slowed somewhat

HD drug trials: just finished recruiting



- A 2x daily oral medication to treat irritability in HD
- Blocks vasopressin receptor 1a which plays a role in anxiety and aggression
- Test in early symptomatic HD patients (108 patients)
- Trial began May 2016 and finished recruiting in Sept 2018

HD drug trials: enrollment completed

- An antibody given as a monthly IV infusion
- Could modulate brain inflammation and increase growth and health of nerve cells
- Enrollment completed in January 2019
- Effect on the volume of the brain as measured by MRI and other imaging, awaiting report on efficacy.

Recruiting now

Phase 1

Sage-718, a drug to treat cognitive changes in HD

- Looking for participants age 18-65 with diagnosed early HD
- Pill taken by mouth 1x/day
- Early safety study involving close monitoring: blood draws, heart and brain wave tracing, urine samples
- Two sites: Long Beach CA and Berlin NJ
- Study lasts 36 days and includes an 18-day hospital stay
- Goal is to address the thinking/behavioral symptoms of HD

www.hdtrialfinder.org

Recruiting now

Kinect-HD Neurocrine Biosciences

Phase 3 **Valbenazine**, a drug to treat chorea in HD

- Looking for 120 participants, age 18-75, diagnosed with HD
- Pill taken by mouth 1x/day for 12 weeks
- Evaluating efficacy, safety and tolerability
- Recruitment started this month, 50-60 sites (3 in SC)
- Already FDA approved for chorea with tranquilizers, similar to tetrabenazine and deutetrabenazine, but less adverse effects

www.hdtrialfinder.org

Huntington's Disease Society of America

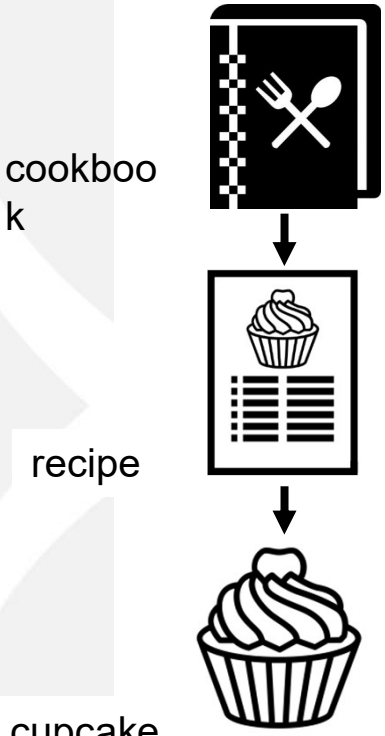
Huntingtin-lowering

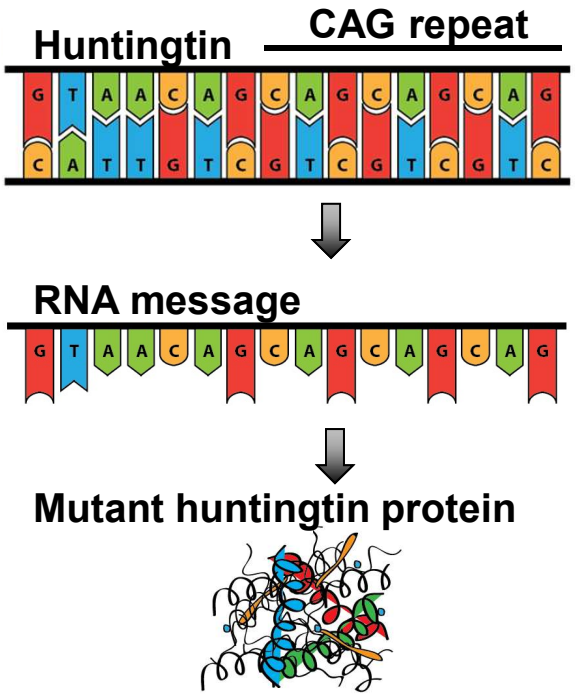
Huntington's Disease Society of America

Gene therapy

- Promising molecular approach that can impact disease progression by modulating gene expression, either by suppressing deleterious gene or increasing expression of beneficial genes.
- Gene expression can be silenced with anti-sense oligonucleotides (ASO) or small interfering RNA (siRNA).
- In vivo delivery of siRNA and ASO has been shown to be effective in animal models of HD, AD, ALS, SCA.

The HD gene and huntingtin lowering





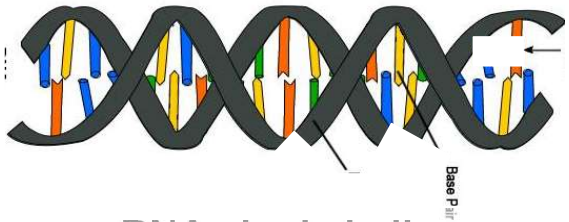
Zinc finger Proteins
nanomolecules
CRISPR-cas9

Antisense oligonucleotides (ASO)
AAV-siRNA
AAV-miRNA

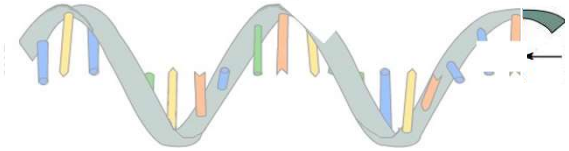
Autophagy inducers
HDAC4 inhibition
Post-translational modifications (PTM)
PET Ligand

Huntingtin lowering: antisense oligonucleotides

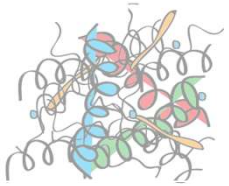
DNA double helix



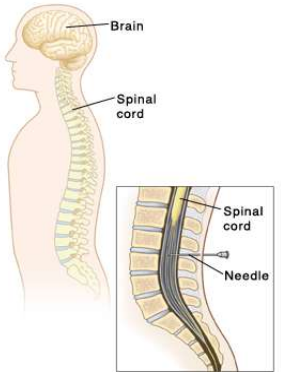
mRNA single helix



Protein 3D structure



Antisense oligonucleotide (ASO)



Less huntingtin RNA = less harmful protein

Slow or stop disease progression?

Huntingtin lowering ASO: Roche / Genentech

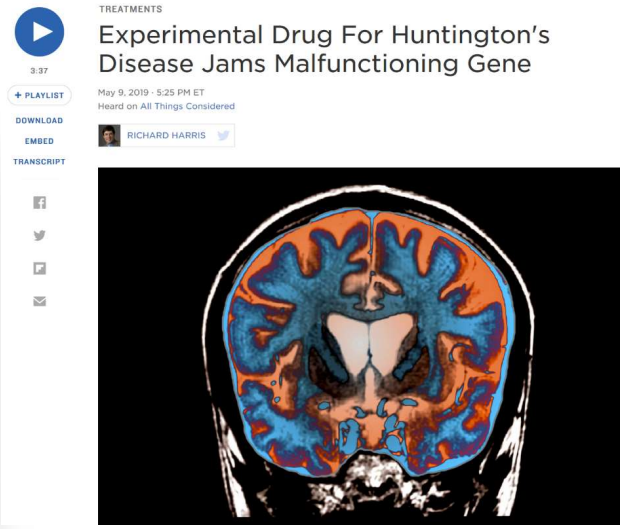
- Small Phase 1/2 trial in 2015-2017 found that this ASO drug (RG6042) was SAFE and lowered huntingtin in participants' spinal fluid.
- Published in May 2019 in NEJM and highlighted on NPR

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Targeting Huntingtin Expression in Patients with Huntington's Disease

Sarah J. Tabrizi, M.B., Ch.B., Ph.D., Blair R. Leavitt, M.D., C.M., G. Bernhard Landwehrmeyer, M.D., Edward J. Wild, M.B., B.Chir., Ph.D., Carsten Saft, M.D., Roger A. Barker, M.R.C.P., Ph.D., Nick F. Blair, M.B., B.S.,* David Craufurd, M.B., B.S., F.R.C.Psych., Josef Priller, M.D., Hugh Rickards, M.D., Anne Rosser, M.B., B.Chir., Ph.D., Holly B. Kordasiewicz, Ph.D., Christian Czech, Ph.D., Eric E. Swayze, Ph.D., Daniel A. Norris, Ph.D., Tiffany Baumann, B.S., Irene Gerlach, Ph.D., Scott A. Schobel, M.D., Erika Paz, B.S., Anne V. Smith, Ph.D., C. Frank Bennett, Ph.D., and Roger M. Lane, M.D.



3:37

+ PLAYLIST

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EMBED

TRANSCRIPT

TREATMENTS

Experimental Drug For Huntington's Disease Jams Malfunctioning Gene

May 9, 2019 · 5:25 PM ET

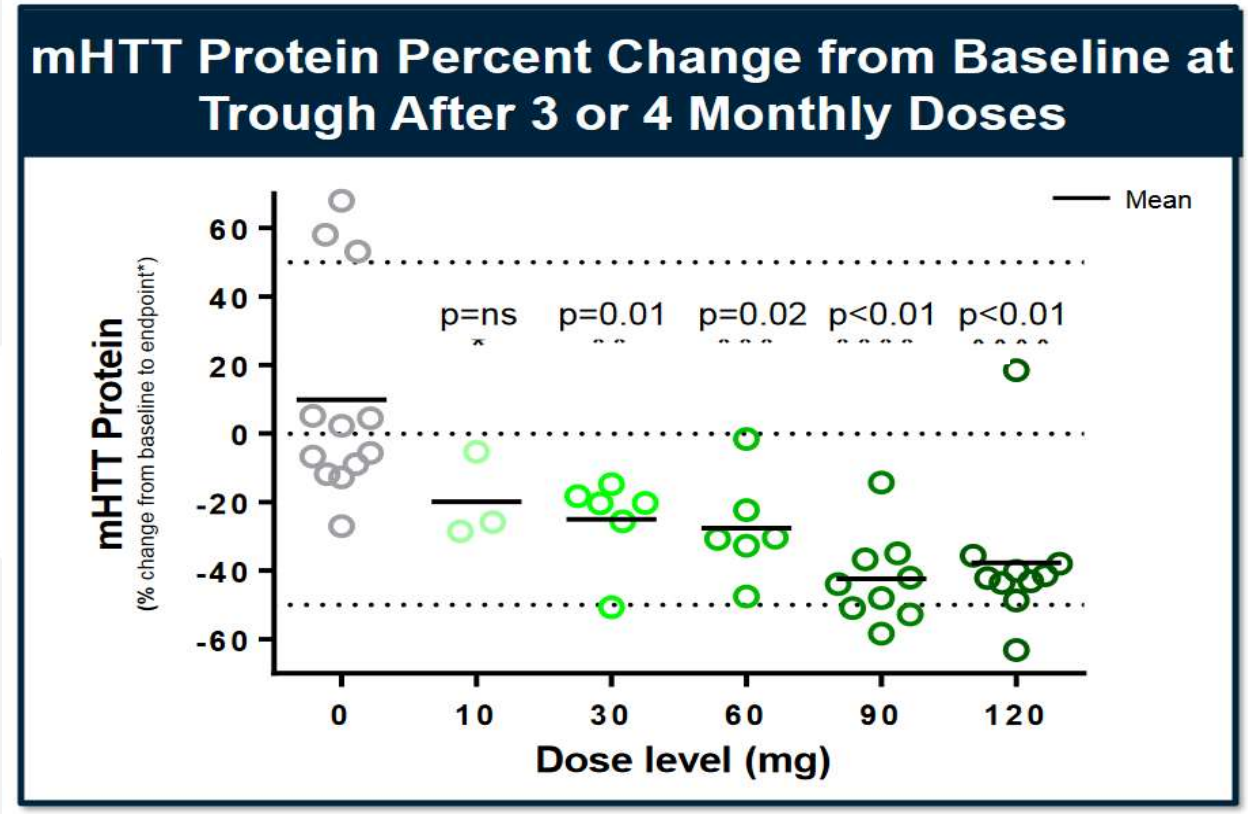
Heard on All Things Considered

RICHARD HARRIS

Ionis-HTTrx: intrathecal application well tolerated

Side effect or event	Placebo group (12 people)	Drug group (34 people)
Pain during the procedure	50%	56%
Post lumbar puncture syndrome	42%	35%
Headache	50%	18%
Cold symptoms	17%	21%
Falls	25%	21%

Demonstrates Dose-dependent Reduction in CSF mHTT



Huntingtin lowering ASO: Generation-HD1

- A **Phase 3** trial of **RG4062** is underway, called **GENERATION-HD1**.
- There will be 660 participants, aged 25-65, with diagnosed manifest HD.
- All sites in the United States have finished recruiting.
- Each person participates for 2 years. It could take 3-4 years or more to find out the results.

Important questions to answer about RG6042

DOSING

What is the optimal dosing strategy for efficacy, safety and tolerability?

SAFETY

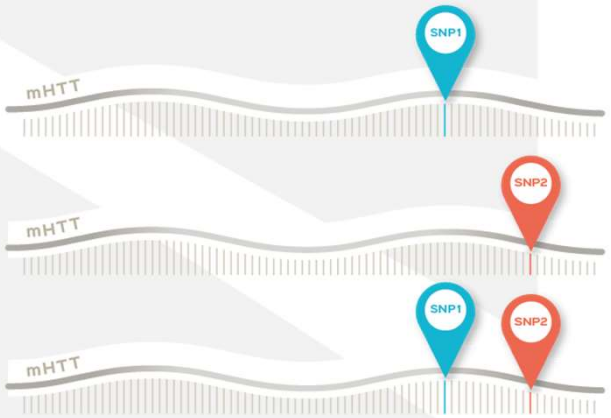
Do any safety concerns emerge when we treat a larger group of people for a longer time?

CLINICAL BENEFIT

Does sustained treatment slow or stop the progression of Huntington's disease?

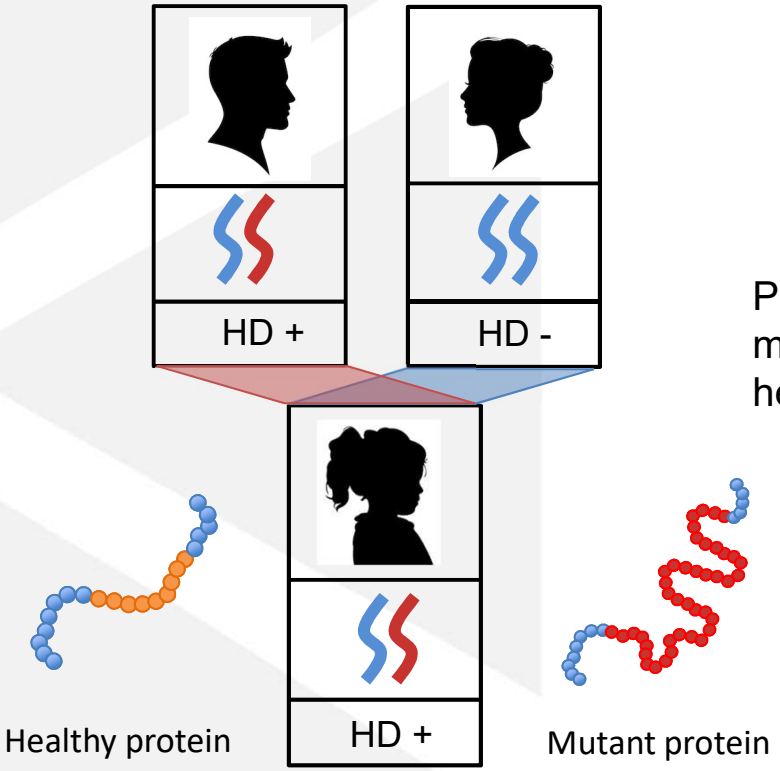
Huntingtin lowering: WAVE LIFE SCIENCES PRECISION HD 1 PRECISION HD 2

- Phase 1/2 trial to understand whether this ASO drug is SAFE.
- There are two separate trials of the Wave drug underway, called **PRECISION-HD1** and **PRECISION-HD2**.
- 60 early manifest HD patients per trial; US sites have finished recruiting.
- Results from these studies are expected in late 2019.



- Only people with either of two genetic markers (SNPs) in their HD gene could receive this drug
- The SNP is like a GPS signal directing the drug to the right spot.
- Around 70% of people with the HD gene have SNP1, SNP2, or both.

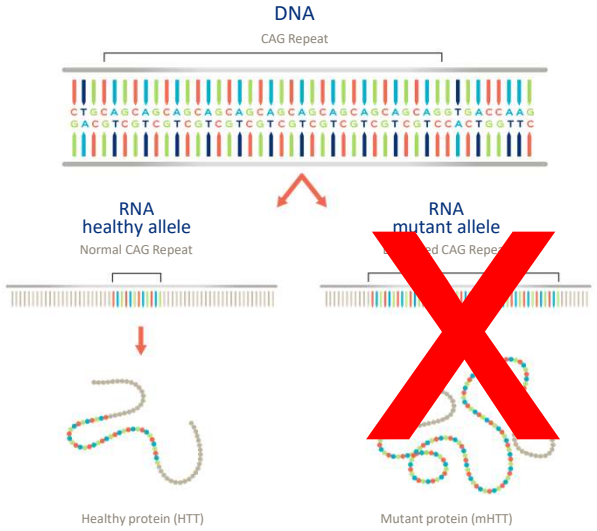
Huntingtin lowering ASO: Precision HD

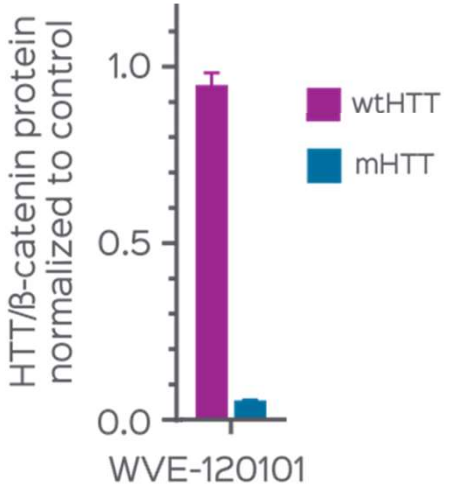


Precision HD1&2 ASO targets mutant huntingtin, leaving the healthy RNA and protein intact

A targeted approach to mutant huntingtin lowering:

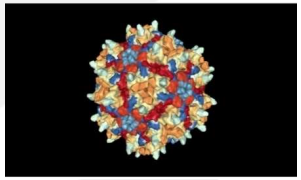
PRECISION HD





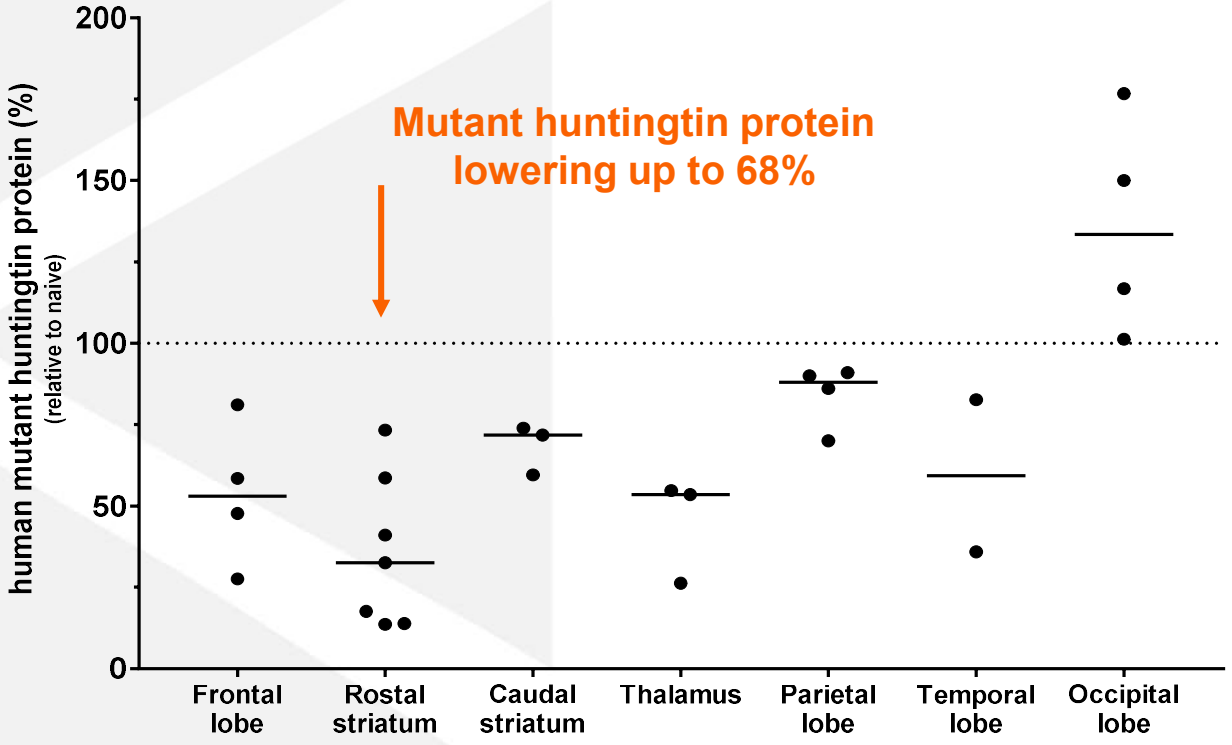
Thse ASOs targets mutant huntingtin, leaving the normal RNA and protein intact

Huntingtin lowering: treating HD with RNA interference by using AAV vector

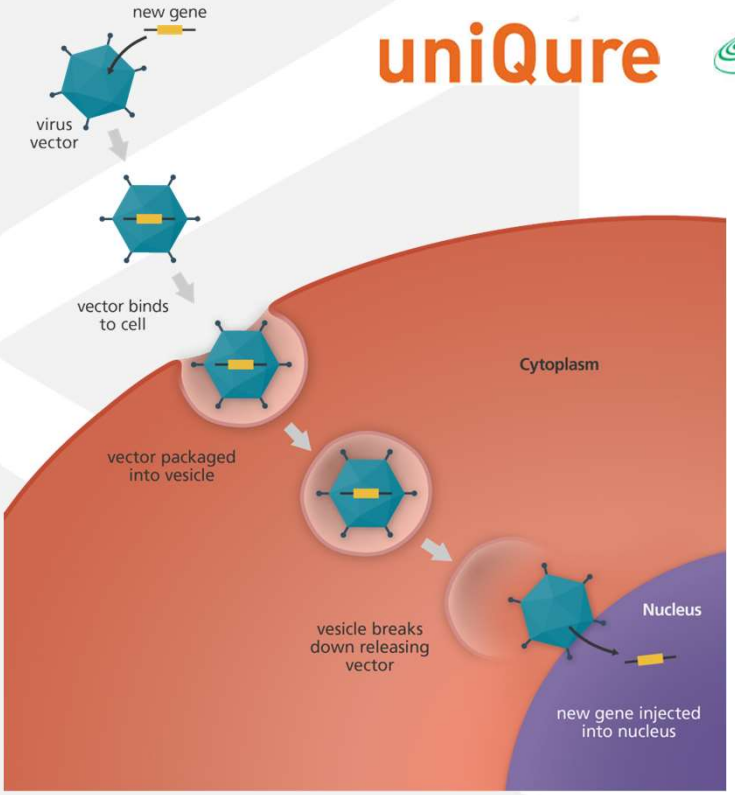


- AMT-130 consists of benign adeno associated virus (AAV) vector carrying an artificial small RNA tailored to silence the huntingtin gene and mutant protein production (mHTT)
- In animal models have demonstrated promising effects
- In April 2019 Fast Track designation by the USFDA;
- Phase 1b/2a trial started this month
- POSSIBLY ONE TIME TREATMENT, WITH LIFELONG EFFECT

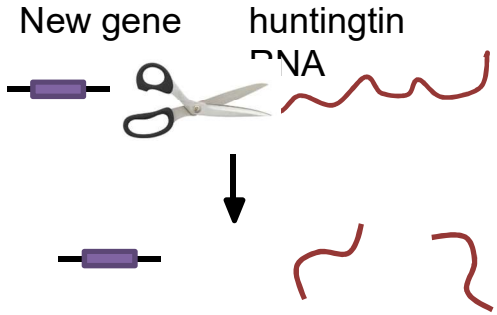
shows promising data (in minipigs)



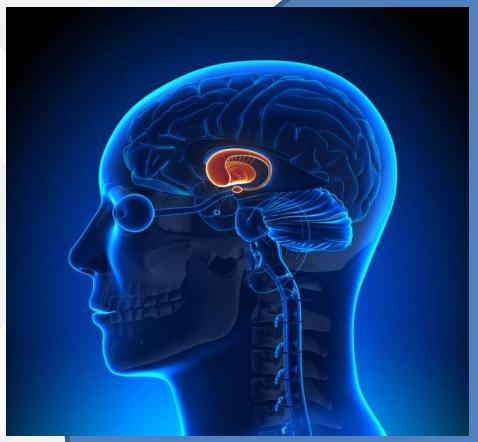
Huntingtin lowering: RNA interference using viruses



- Gene therapy
- Single intervention (brain surgery)
- Permanent
- Potent silencing



Treating HD with RNA interference by using AAV



Huntingtin mRNA

siRNA

siRNA

siRN
A

Huntingtin gene

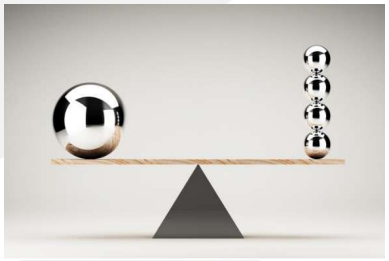
Huntingtin protein

Huntingtin mRNA

RNA interference using AAV viruses: first HD gene therapy trial underway

- Phase 1/2 trial to understand whether this gene therapy drug is **SAFE.**
  - Only 26 participants, 16 will receive drug, 10 placebo
  - Will require surgery to deliver the virus directly to the brain
  - 18 month study with 5 year follow-up
  - Neurological exams, MRI, blood and spinal fluid collection
  - Current sites in Columbus OH, Richmond VA, and Houston TX
- Eligibility:
  - Diagnosed, early manifest HD
  - 44 CAG repeats or more in HD gene
  - Ages 25-65
- Enrollment began late October 2019
- Updates on sites and enrollment at www.hdtrialfinder.org and www.clinicaltrials.gov.

Obstacles to Human Gene Silencing in HD



- Delivery requires intrathecal approach (LP, surgery).
- ASO effects are time limited and require repeated dosing.
- siRNA AAV application requires stereotactic brain application.
- **Need to ensure that siRNA selectively suppresses the mutated gene and avoid “off target” (lifelong) effects.**
- Entire brain needs to be treated, across all brain regions.

Huntingtin lowering: small molecules

The holy grail of HD treatments:

- A pill taken by mouth
- No needles or surgery
- Adjustable dose
- Gets into the brain
- Lowers huntingtin all over the body

Work in HD mice suggests this is possible

Novartis clinical trial to begin ___

HD Clinical Research: Enroll-HD

Enroll-HD is a global observational study open to people who have HD or who are at risk.

What's involved?

- Annual visits (about 1-2 hours)
- Health questions (thinking, behaviors, feelings, lifestyle)
- Neurological exam
- Blood sample for genotyping and bio-banking
- Family history (optional)
- Travel support is available

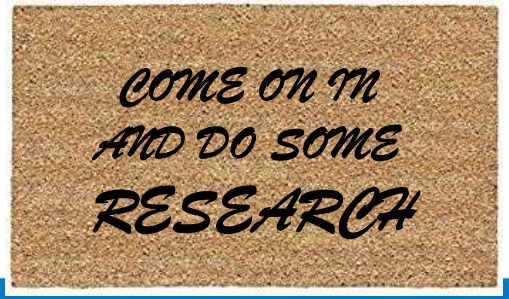
More than 18,800 participants worldwide

What are the goals of Enroll-HD ?

- To increase our understanding of HD in people by monitoring how symptoms appear and change over time
- To study the best clinical practices for HD care
- To improve the design of clinical trials to give us clear answers more quickly
- To accelerate the discovery and development of new treatments

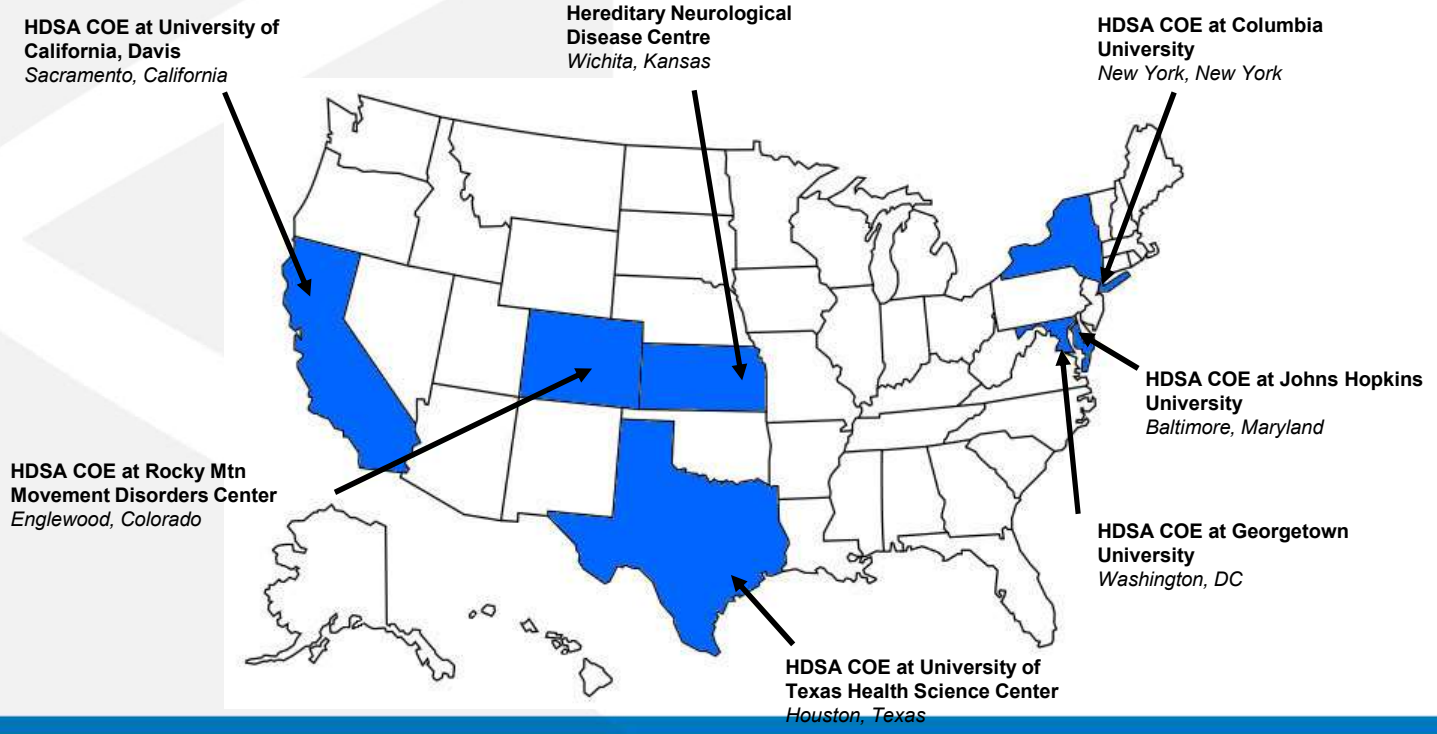
How does Enroll-HD accelerate research?

- **More people undergoing the exact same evaluations** means greater likelihood to uncover new things about HD.
- **More scientists around the world working on HD:** the data is available to any scientist with a legitimate research project devoted to understanding HD
- **Research platform for future trials:**
  - It lays out a "welcome mat" for researchers and pharmaceutical companies to study HD
  - Enroll-HD creates a database of potential volunteers for future studies, including drug trials



How does Enroll-HD drive site selection?

Example: Roche Natural History Study Sites

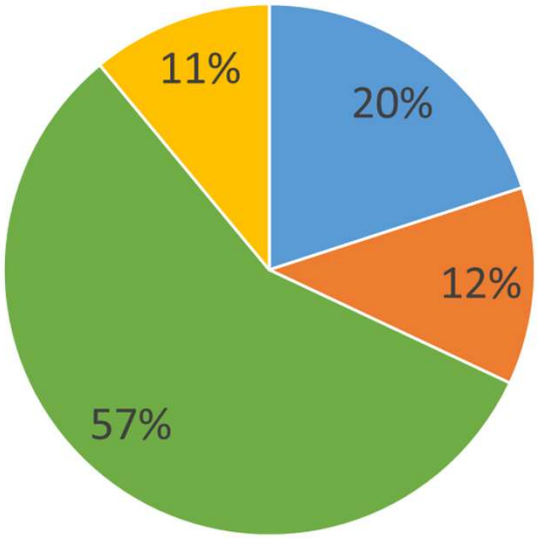


Roche-Genentech Announce the 20 "Expected" Generation HD1 US Trial Sites

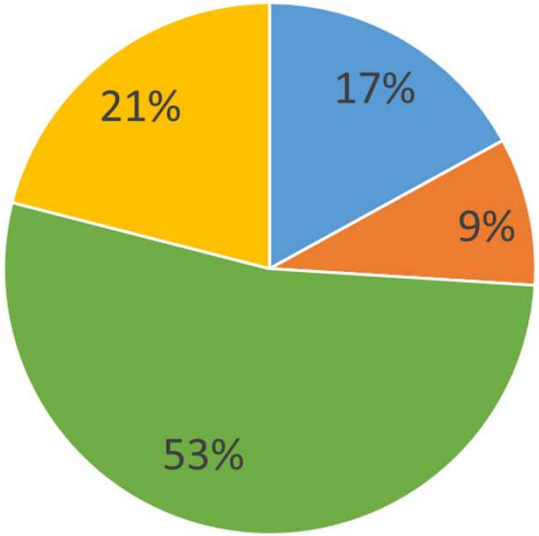
- Alabama, Birmingham - University of Alabama
- Arizona, Phoenix - Barrow Neurological Clinic
- California, Davis - University of California, Davis
- California, Palo Alto - Stanford University
- California, Pasadena - Arcadia Neurology Center
- California, San Diego - University of California, San Diego
- Colorado, Englewood - Rocky Mountain Movement Disorders Center
- District of Columbia, Washington - Georgetown University
- Florida, Tampa - University of South Florida
- Illinois, Evanston - Northwestern University
- Maryland, Baltimore - John Hopkins University
- Massachusetts, Amherst - Dent Institute
- Massachusetts, Boston - Beth Israel Deaconess Medical Center
- Missouri, St Louis - Washington University
- New York, New York - Columbia University
- Pennsylvania, Pittsburgh - University of Pittsburgh Medical Center
- Tennessee, Nashville - Vanderbilt University Medical Center
- Texas, Houston - University of Texas Health Science Center
- Utah, Salt Lake City - University of Utah
- Washington, Kirkland - Evergreen Health

Enroll-HD is focusing on premanifest HD

Before January 2018



Today



negative/control unknown manifest premanifest

Huntington's disease: Enroll-HD contribution

Relationship Between CAG Repeat Number and Disease Expression

No. of CAG repeats	Outcome
≤ 28	Normal range; individual will not develop Huntington's disease
29-34	Individual will not develop Huntington's disease but the next generation is at risk
35-39	Some, but not all, individuals in this range will develop Huntington's disease; next generation is at risk (incomplete penetrance)
≥ 40	Individual will develop Huntington's disease

Huntington's Disease: Enroll-HD contribution

Environmental Modifiers

- Substance abuse hastens onset of motor symptoms:
- tobacco abuse: 2.3 years (males 2.0, females 2.7)
- alcohol abuse: 1 year (males 0.9, females 1.3)
- illicit drug abuse*: 3.3 years (males 2.5, females 4.6)
- effects more pronounced in women

*40 % only marijuana abuse

Neurology. 2017 Feb 28;88(9):909-915

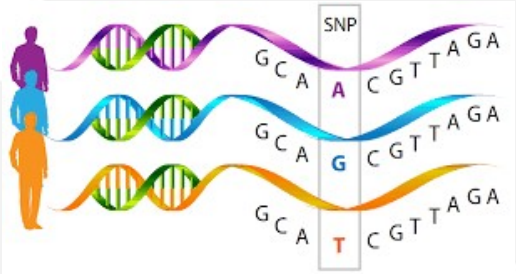
Huntington's Disease: Enroll-HD contribution

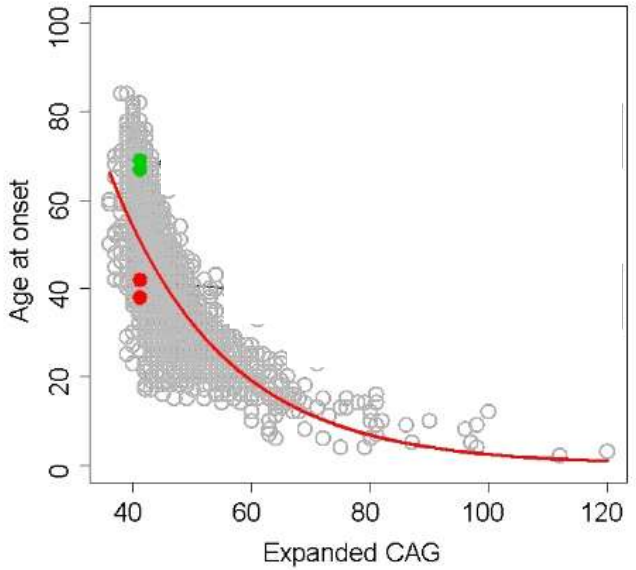
Genetic Modifiers

- Genes other than Huntingtin gene that affect onset of HD
- Genome-wide association (GWA) analysis by using single nucleotide polymorphisms (SNPs) in the DNA as genetic markers

Why does age of onset vary?

- Genome-wide association studies (GWAS)
- **What o**ther genes matter?
- Can we harness or block these pathways to delay symptoms?

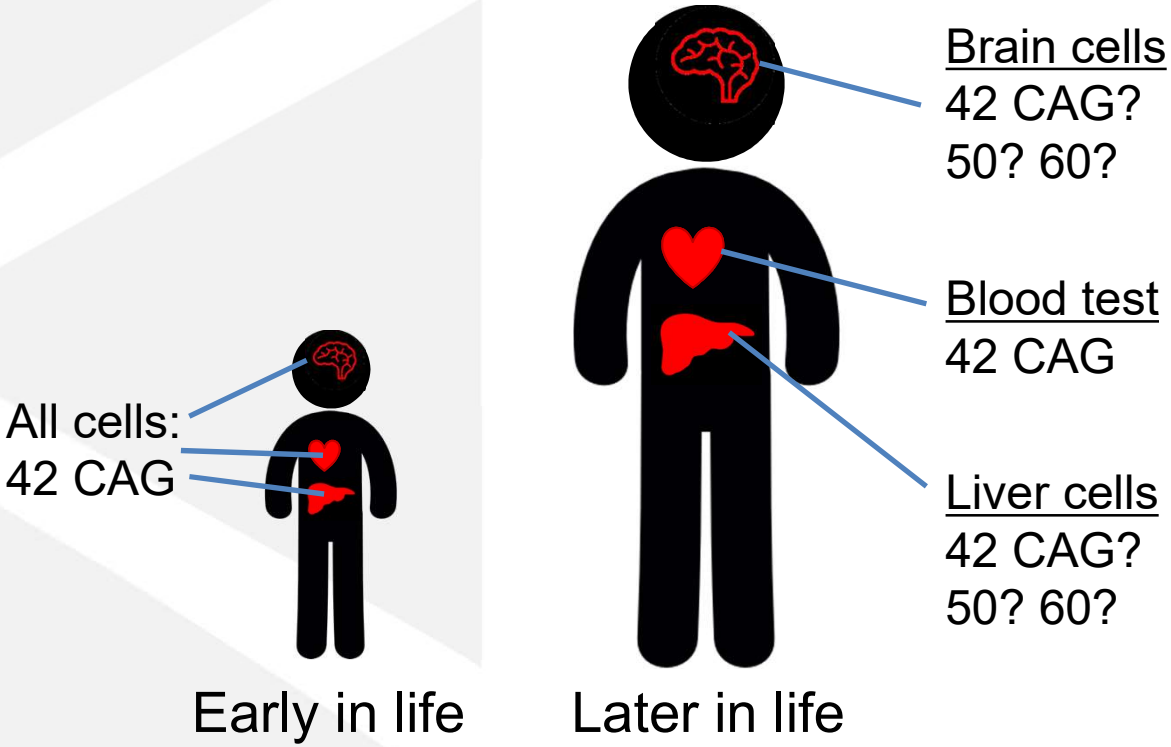




New therapeutic target: DNA repair proteins

Michael Geschwind, HSG meeting 2016

Importance of DNA repair: CAG repeat instability

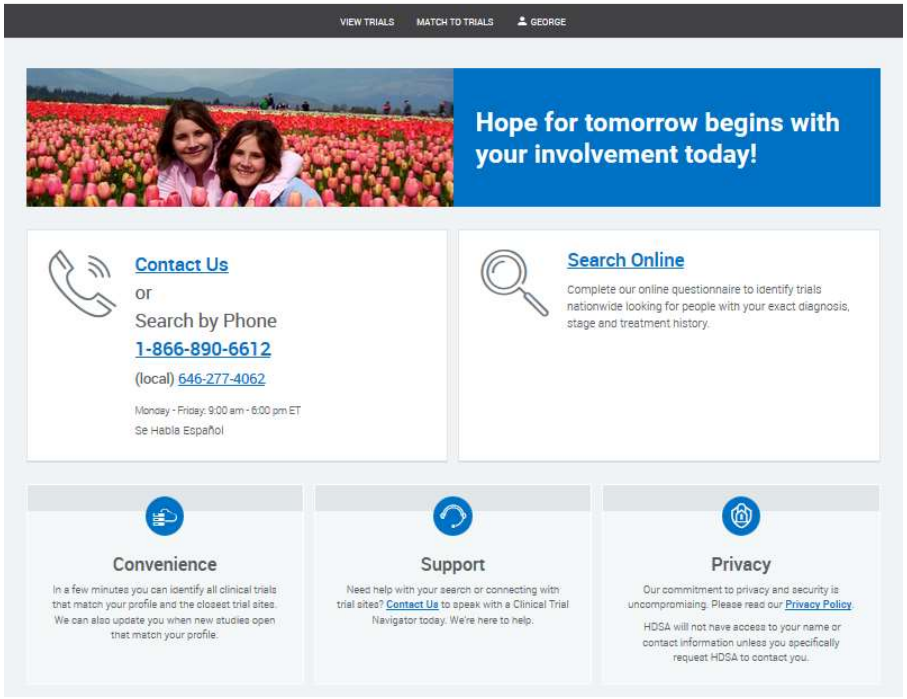


Genetic analysis of 9000 patients in Enroll-HD

CAG-CAG-CAG-CAG-CAG-CAG-CAG-CAG-
CAG-CAG-CAG-CAG-CAG-CAG-CAG-CAG-
CAG-CAG-CAG-CAG-CAG-CAG-CAG-CAG-
CAG-CAG-CAG-CAG-CAG-CAG-CAG-CAG-
CAG-CAG-CAG-CAG-CAG-CAG-CAG-CAG-
CAA-CAG.

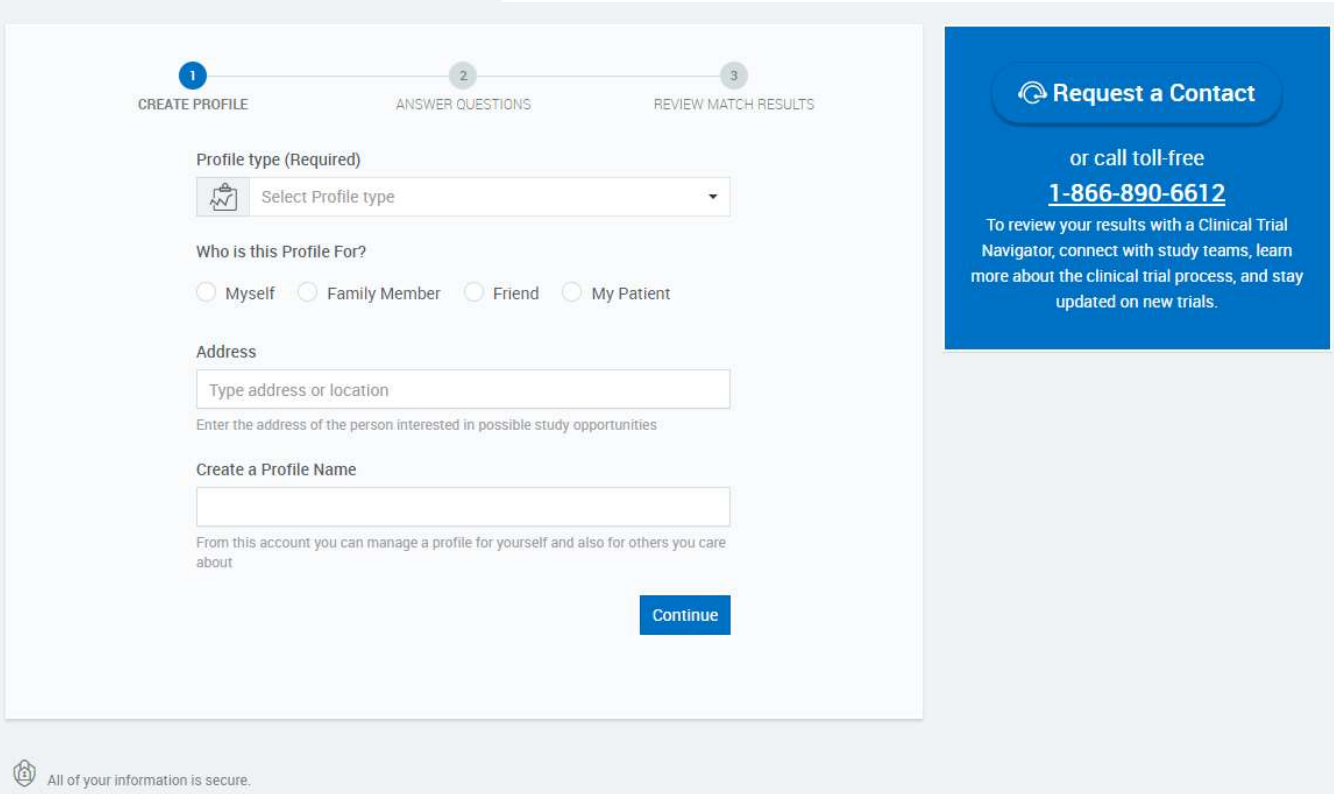
- Glutamine can be coded either with CAG or CAA triplet (codon)
- In most people CAG tract in HD gene contains one CAA codon
- One in 300 cases; CAG tract misses CAA codon, resulting in significantly earlier onset of HD symptoms
- One in 100 cases; CAG tract has 2 CAA codons, and significantly delayed onset of HD symptoms

Huntington's Disease Society of America HDTrialfinder: Find a Clinical Trial near you



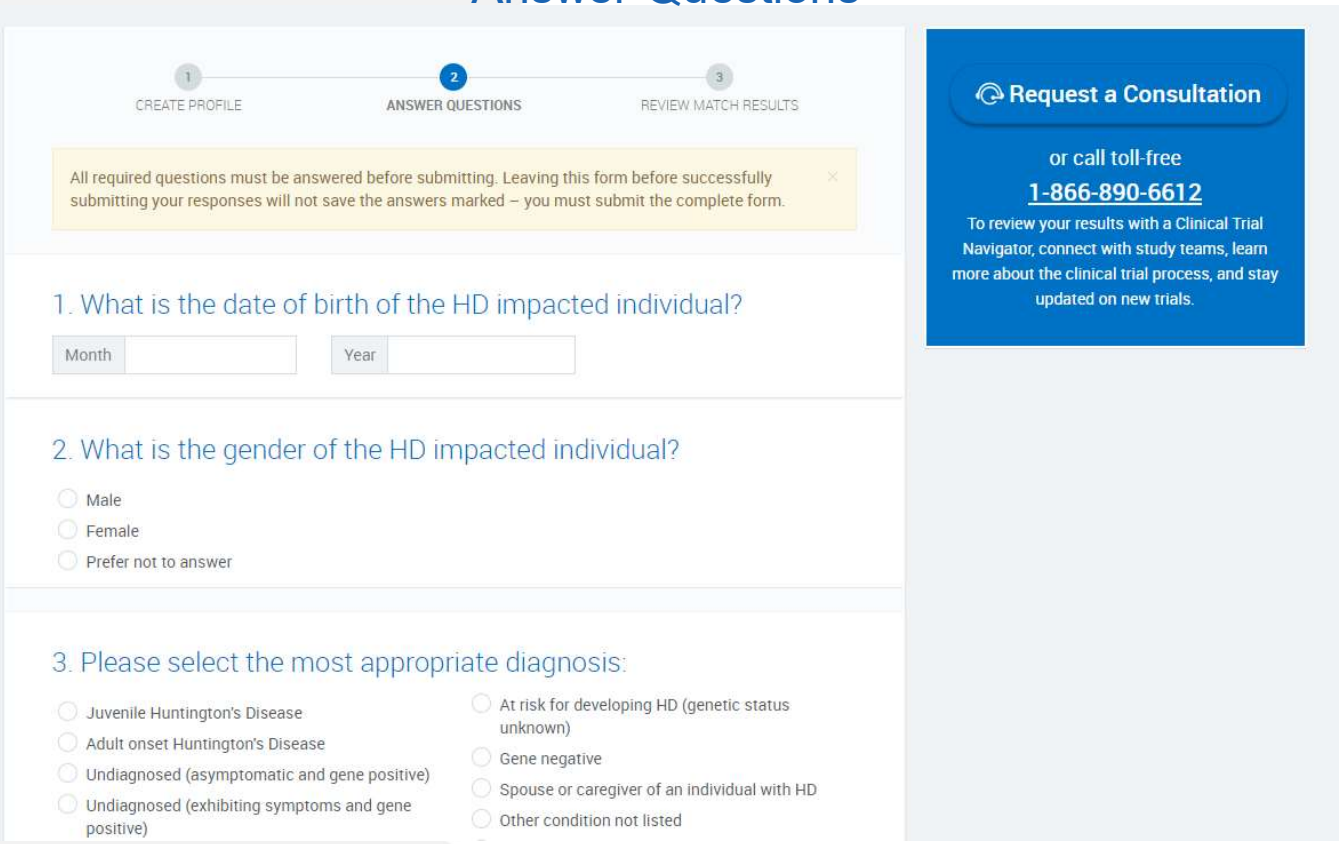
- New look, new features and extended call center hours (9-6 EST)
- >3,500 individual profiles signed up
- Most up to date database of North American HD research opportunities

Create a Profile

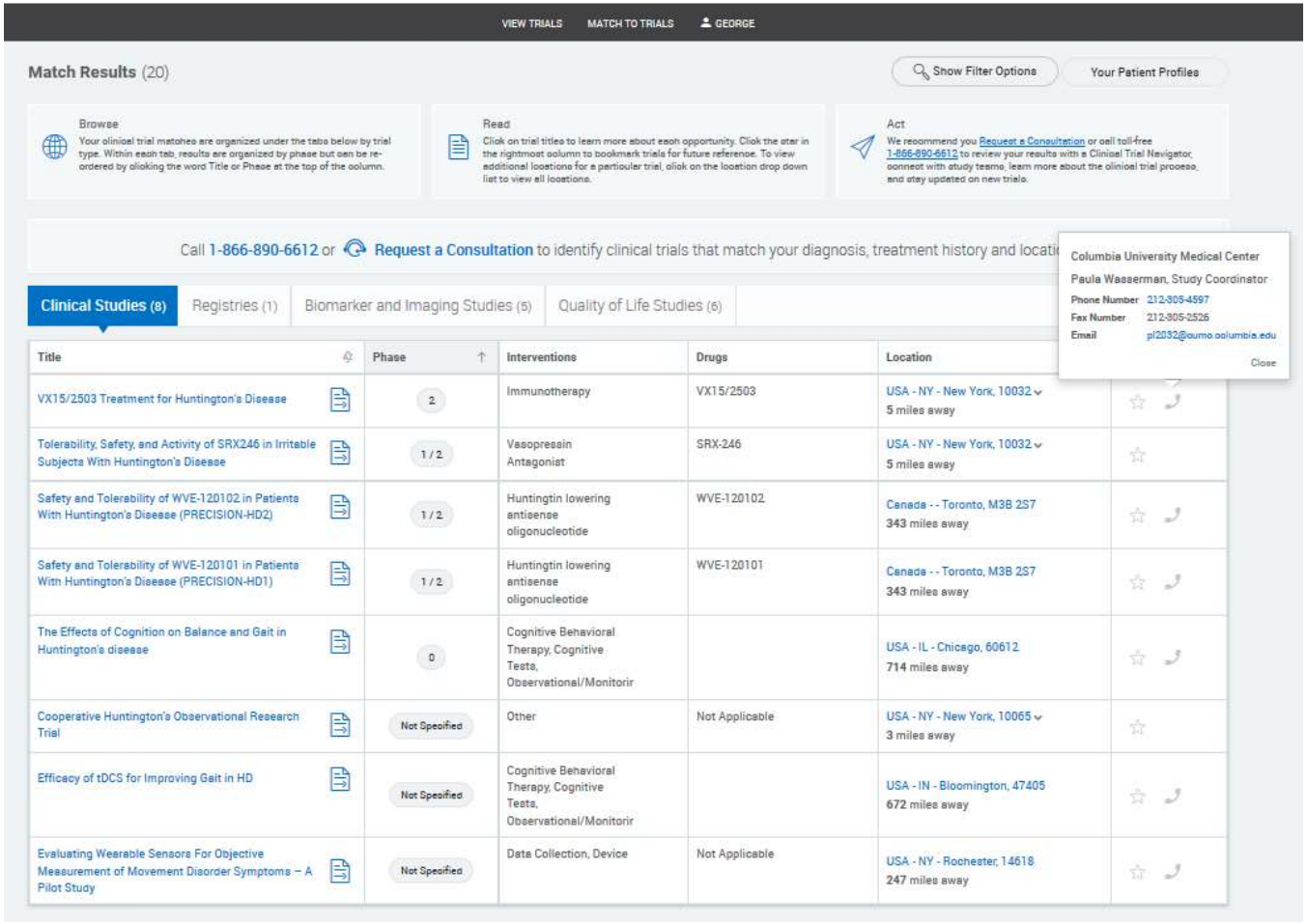


Huntington's Disease Society of America

Answer Questions



Personalized Trial Info Now at Your Fingertips



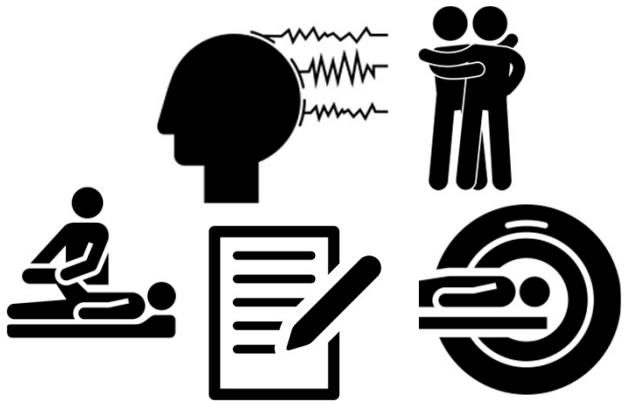
Local and observational studies: Huntington's Disease Society of America HDTrialfinder

Enroll-HD

HDClarity

CHDI FOUNDATION

HDLEGACY ORGAN DONATION FOR RESEARCH



Worldwide registries
Global observational studies
Sample collection initiatives
Brain and organ donation

Smaller local trials
Exercise and imaging studies
Non-drug interventions
Nationwide surveys

Learn

HDBuzz

Huntington's Disease Society of America

THIS WEEK IN HUNTINGTON'S DISEASE RESEARCH

Participate

Enroll-HD

HDTrialfinder

Centers of Excellence

THANK YOU!!!

Huntington's Disease Society of America Center of Excellence
University of South Carolina School of Medicine

SC 2019 Family Education Day

Lunch Break:

Until 1:30

Huntington's Disease Society of America Center of Excellence
University of South Carolina School of Medicine

SC 2019 Family Education Day

SPEAKER:
Celena Brown, MA, CCC-SLP

Celena Brown has a BA in Biology and her MA in Speech Language Pathology from SC State University. She has 23 years of experience, the majority of that time with adults in long term care. She is currently an outpatient specialist with Prisma. She is experienced in the evaluation and treatment of dysphagia, including modified barium swallow and fiber optic endoscopic swallow evaluation, cognition, and communication. Celena Brown has joined the SC HDSA Center of Excellence and serves as the primary speech and language disorder specialis

The Role of the Speech-Language Pathologist with Huntington's Disease Patients

CELENA BROWN, MACCC-SLP

Points of Interest

- Dysphagia management for patients with Huntington's Disease (HD).
- Assisting with communication skills to make wants/needs known.
- Identifying cognitive deficits in patients with HD.
- The Speech-Language Pathologist as an interdisciplinary team member for the HD patient.

Speech-Language Pathologist

- Speech–Language Pathologist(SLP) works to prevent, assess, diagnose, and treat speech, language, social communication, cognitive-communication, and swallowing disorders in children and adults, as defined by American Speech-Language Association (ASHA).

REFFERAL

- -Receipt of information
- -Identify risk factors
- -Discussion of management
- -Build relationships

Types of Evaluations

Swallowing

Communication

Cognitive

BEDSIDE SWALLOW EVALUATION

A **BEDSIDE SWALLOW EVALUATION IS COMPLETED TO IDENTIFY, IF YOU HAVE DYSPHAGIA. DYSPHAGIA IS THE MEDICAL TERM USED TO DESCRIBE DIFFICULTY SWALLOWING.**

Go to PDF

Postures to Enhance Safe Eating

- Sit as close to table as possible-place elbows on the table to stabilize the upper body.
- Place a pillow or wedge cushion at the back to support the body to stay forward.
- Be sure feet are flat on the floor, or place a box or stool under the feet for support.

Strategy: Pay attention to texture

- **Particulates:** little pieces of food or foods that break into particles/pieces in the mouth. *ie: peanuts, rice, popcorn, peanut M & M's, corn*
- **Crunchy:** raw vegetables like carrots, broccoli, apples, some crackers or chips
- **Chewy:** might be difficult to chew it completely. *Ie., dense breads/bagels, dense meat like steak or pork chops*
- **Stringy:** celery, lettuce, pineapple, fruit with skins like grapes or apples

Strategy: Diet modifications

- Eliminate certain foods from the diet

- Change from a Regular diet to a Soft diet
  - Cut meats into small pieces
  - Grind and moisten meats
  - Cook all vegetables
  - Limited options with fresh fruit
  - Introduce canned fruit, applesauce, baked fruit

Strategy: Diet Modifications in Later Stages

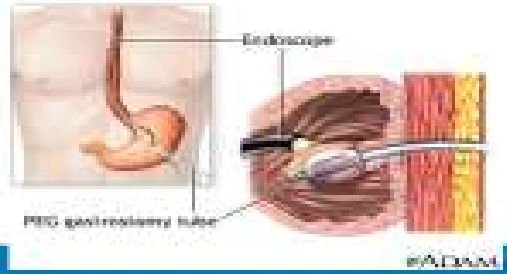
- Transition from a Soft diet to a Ground or Pureed diet
  - Dysphagia Diet - Levels 1, 2, 3 may be recommended by a Speech Pathologist
  - People with HD will have increased dependence on others for assistance with feeding
  - Might be a struggle to get enough calories each day
  - Supplements, high calorie shakes, 1000 Calorie Shake, Super Cereal, etc. can help

Alternate Means Of Nutrition

Indications

- Tube feeding is used when someone is unable to consume an adequate amount of food.
- Tube feeding can be used as a supplement to oral intake of foods and/or fluids, or as a sole means of providing nutrition.
- Tube feeding can be used on a temporary basis, when a medical condition does not allow the person to eat normally

Talk to your loved one and a medical professional about the different options before they become necessary.



A pastry cutter or potato masher

A blender and/or food processor

Dishes with sides

A “keep warm” dish

Sports Cups

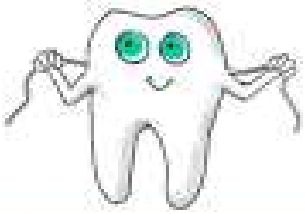
Utensils with larger handles

SWALLOW STRATEGIES

- POSITIONING
- BOLUS SIZE
- RATE OF SPEED
- UTENSILS/DEVICES
- ENVIRONMENT
- LEVEL OF SUPERVISION

Dental Care

- See your dentist regularly
- Brush after meals and snacks
- Remember to floss
- Talk to your dentist about special issues and problems like dry mouth.



Key Points

- ✓ See a Speech Pathologist (SLP) for a baseline exam and tips/ strategies for safe swallowing
- ✓ See an Occupational Therapist for ideas for adaptive equipment
- ✓ Look out for signs of trouble swallowing
- ✓ Changing the texture of the food can help.
- ✓ Tube feeding can be an option when someone is unable to consume an adequate amount of food, as well as in other situations like medical crises.

Back to Module list

Communication Evaluation

COMMUNICATION IS THE IMPARTING OR INTERCHANGE OF THOUGHTS, OPINIONS, OR INFORMATION BY SPEECH, WRITING, OR SIGNS.

Dysarthria

A speech disorder caused by muscle weakness. It can make it hard for you to talk. People may have trouble understanding what you say.

Characteristics

- SLURRED SPEECH WITH POOR SPEECH INTELLIGIBILITY
  - A. IMPAIRED LIP AND TONGUE POSTURING
  - B. DISCOORDINATION OF MOVEMENTS
  - C. DECREASED RESPIRATORY CONTROL FOR VOCAL LOUDNESS AND SUSTAINED PHONATION

Treatment

1. ORAL MOTOR EXERCISES TO INCREASE ROM/STRENGTH/COORDINATION
2. BREATHING EXERCISES
3. COGNITIVE DEFICITS MAY LEAD TREATMENT TOWARDS AWARENESS, SELF MONITORING AND IMPULSIVITY.
4. USE OF AUGMENTATIVE AND ALTERNATIVE COMMUNICATION WITH PROGRESSION OF THE DISEASE.

Cognitive Evaluation

COGNITION IS THE MENTAL ACTION OR PROCESS OF ACQUIRING KNOWLEDGE AND UNDERSTANDING THROUGH THOUGHT, EXPERIENCE, AND THE SENSES.

Domains of Cognitive Skills

- Attention
- Memory
- Problem solving
- Reasoning
- Executive Function
- Visuospatial Function

Strategies to Assist with Cognitive Function

1. SPEAK SLOWLY, CONCISE, AND CLEAR.
2. ALLOW TIME TO RESPOND.
3. ASK SHORT MUTLIPLE CHOICE QUESTIONS.
4. ASK YES/NO QUESTIONS
5. IDENTIFY NON VERBAL BEHAVIORS AS CUES TO NEEDS.
6. ANTICIPATE NEEDS.

Resources

Amazon.com

- For keep warm dishes

Dentist.com

- For Dr. Barmans and other adaptive toothbrushes

For More Information

Huntington's Disease Society of America

Website: www.hdsa.org

E-mail: hdsainfo@hdsa.org

National Helpline: (888)HDSA-506

References

- Cassiday, J., Imbriglio, S., and Cerrillo, L. (2007). A Primer for Speech-Language Pathologists Managing Clients with Huntington's Disease in a Residential Care Facility. *Perspectives on Gerontology*, *12*(1), 22-26.
- Hamilton, A., Heemskerk, A.-W., et al. (2012). Oral Feeding in Huntington's Disease. A Guideline Document For Speech and Language Therapists. *Neurogegen. Dis. Manage.* *2*(1), 45-53.

References

HDSA Family Guide Series: Nutrition & HD

Available at www.hdsa.org/publications

We Are HDSA: February 2012 (eating well with HD); May 2011 (Food Away from Home)

Available at: http://www.hdsa.org/articleconnect

EHDN Guidelines (Nutrition, oral feeding, oral healthcare) Available at: http://www.hdsa.org/ehdnpubs

Huntington's Disease Society of America Center of Excellence
University of South Carolina School of Medicine

SC 2019 Family Education Day

SPEAKER:

Sydney Phillips, MSW

Sydney Phillips has a degree in Social Work from the University of South Carolina. She is a Licensed Master's level Social Worker. She currently works at Prisma with the Geriatrics and Palliative Care Teams. She currently focuses on Advance Directives and patients with Serious Illnesses.

PRISMA HEALTH SM

Having Conversations That Matter

Sydney Phillips, LMSW

Objectives

- To understand the importance of Advance Care Planning
- To think about health care choices that reflect your values and beliefs
- To make plans to talk about your decisions with loved ones
- To understand the Health Care Power of Attorney Document

What is Advance Care Planning (ACP)?

ACP is a process that enables individuals to make plans about their future health care choices. It allows individuals to take part and be in charge of their health care plan.

What is Advance Care Planning?

Advance Care Planning is about preplanning the following:

- **Knowing** available future treatment plan for individuals
- **Determining** an individual's future treatment plan goals that align with his/her values
- **Sharing** their decision with their physicians and loved ones
- **Completing** Advance Directive for future reference

Everyone **over the age of 18-years-old** should have ACP conversations and an advance directive completed.

Why is Advance Care Planning Important?

- The completed Advance Directive will be an **individual's voice**
- The completed Advance Directive will **guide clinicians and families** to honor a person's wishes regarding treatment plans when he/she is too ill to make decisions
- It is a **gift** for loved ones, as it will **ease the burden of decision-making**

Advance Directives available in South Carolina

(1)South Carolina Health Care Power of Attorney (HCPOA)

(2)Living Will (Declaration of a Desire for a natural death)

(3)Five Wishes

(4)EMS DNR (Do Not Resuscitate) Order

(5)POST (not active yet)

*Adult Health Care Consent: If you did not have one or any of the advance directives listed above your health care professionals would then move to the health care consent act to guide the clinician for decision making.

Who makes Health Care decisions for you, when you cannot provide consent?

(1)A **Guardian** appointed by the court

(2)An **attorney-in-fact** appointed by the patient in a durable power of attorney , if the decision is within the scope of his/ her authority

(3)Appointed Health Care Power Of Attorney **(HCPOA)**

(4)A **spouse** of the patient

(5)An **adult child** of the patient

(6)A **parent** of the patient

(7)An **adult sibling** of the patient

(8)A **grandparent** of the patient

(9)Any other **adult relative** by blood or marriage

South Carolina Health Care Power of Attorney (HCPOA)

This document only comes into effect if, **and only if**, a person is unable to make decisions for themselves.

The HCPOA document allows a person to make **4 important decisions:**

(1) The first decision that will be made is about **appointing an agent**

(2) The second decision is about **organ donation**

The third and fourth decisions pertain to a situation **where an individuals life expectancy is limited or they are permanently unconscious.**

(3) The third decision is about **life-sustaining treatment**

(4) The final decision is about **artificial nutrition and hydration**

This document may be altered or changed at ANY TIME. We suggest that you review this document each year with your loved ones and health care providers because your values, beliefs and wishes may change. You may complete a new document at any time and dispose of the previous one.

Evidence-Based Benefits of Advance Care Planning Conversations

- Adequate time to make informed decisions and fulfill personal goals
- Higher patient satisfaction
- Enhanced goal-oriented care
- Fewer hospitalizations
- Increased and earlier hospice care
- Improved quality of life
- Better patient and family coping
- Improved bereavement outcomes

Choosing an Agent

- What should you think about when choosing an agent?
  - Will this person put my values, beliefs and wishes above their own
  - Do they know me well and understand what is important to me
  - Could they handle this responsibility
  - Will they be readily available if something happens/will they be able to get to me in a timely manner
- Who can be an agent?
  - Anyone may be your agent if they are over the age of 18. Ex: Neighbors whom you are close too, Long-Term Partners, Family or Friends
  - Doctors or Health Care Providers who are currently providing you treatment MAY NOT be your agent (Page 2 Section 7)
- What is the agents role?
  - The agents role is to ultimately act as if they are you when making medical decisions for you
  - The agent will speak for you if you are unable to speak for yourself for whatever reason

Choosing an Agent
Continued

- When does this come into effect?
  - The Health Care Power of Attorney only comes into effect if you do not have the capacity to make decisions for yourself EX: Coma
- When should I tell that person they are my Health Care Agent?
  - Before you make them your Health Care Agent
  - That person may not feel comfortable making those decisions or they may feel like their value system does not align with what you want

ACP is appropriate for which of the following people?

A. A 22 year old female healthy new college graduate who comes to your clinic for birth control and annual physical.
B. An 88 year old male with end stage COPD who comes to your clinic for medication refills.
C. A 45 year old female with hypothyroid, obesity, and diabetes who comes to your clinic for routine follow-ups.
D. All of the above

ACP is appropriate for which of the following people?

A. A 22 year old female healthy new college graduate who comes to your clinic for birth control and annual physical.
B. An 88 year old male with end stage COPD who comes to your clinic for medication refills.
C. A 45 year old female with hypothyroid, obesity, and diabetes who comes to your clinic for routine follow-ups.
D. All of the above

Who would be the legal health care proxy for an unconscious, unmarried patient with no advanced directive or legal guardian and five adult children?

A. Live in girlfriend for two years
B. The majority of his adult children
C. Eldest son who is 40 years old from out of town
D. Youngest daughter, who lives locally and goes to all of the patient's appointments and has the most knowledge about his health
E. Ex-wife

Who would be the legal health care proxy for an unconscious, unmarried patient with no advanced directive or legal guardian and five adult children?

A. Live in girlfriend for two years
B. The majority of his adult children
➡ C. Eldest son who is 40 years old from out of town
D. Youngest daughter, who lives locally and goes to all of the patient's appointments and has the most knowledge about his health
E. Ex-wife

Who would be the legal health care proxy for an unconscious, married patient with no advanced directive or legal guardian and two adult children?

A. Live in girlfriend for two years
B. Spouse, from whom he has be separated for four years
C. Eldest son, who is 40 years old from out of town
D. Youngest daughter
E. Sister, who lives locally and goes to all of patient's appointments and has the most knowledge about his health

Who would be the legal health care proxy for an unconscious, married patient with no advanced directive or legal guardian and two adult children?

A. Live in girlfriend for two years
B. Spouse, from whom he has be separated for four years
➡ C. Eldest son, who is 40 years old from out of town
D. Youngest daughter
E. Sister, who lives locally and goes to all of patient's appointments and has the most knowledge about his health

Tips and Tricks:

- Remember that you will move onto your next patient. This family has to live with their decision forever. Be kind. Reserve judgement.
- These discussions are an ongoing process, not a one time event.
- Remember Ask-Tell-Ask.
- Remember hope/worry, wish/worry language.
- “Tell me more.”
- Warning shots: “I have some serious news to tell you.”
- Do not to give more than three pieces of information at a time.
- You are not responsible for the outcome, only how you show up.

Communication

Communication is KEY

- Having these conversations with your loved ones and health care providers are extremely important!
- These conversations can help bridge the gap between what is important to YOU and what is important to your loved ones!
- We understand these conversations are hard and we can assist with having these conversations if you are uncomfortable!

Where should I keep my HCPOA Document?

- File Cabinet
- Give one to your primary doctor and if you go to the hospital have them scan a copy into your chart
- Give a copy to your HCPOA
- You could keep one in the glove box of your car
- Keep a copy in a book or a bible

Do NOT

- Keep a copy in a safe that only you know the password too
- Do not keep it in a safety deposit box at the bank

Questions

Contact Information:

- Prisma Health Home Health and Prisma Health Hospice
- Please Contact: Sydney Phillips, LMSW
- sydney.phillips@prismahealth.org
- 803-296-3353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November 16, 2019

Huntington's Disease Society of America Center of Excellence
University of South Carolina School of Medicine

2019 SC Family Education Day

University of South Carolina College of Social Work

Huntington's Disease Society of America
South Carolina Affiliate

Genentech
A Member of the Roche Group

Huntington's Disease Society of America Center of Excellence
University of South Carolina School of Medicine

University of South Carolina College of Social Work

Education Day:
Resources for Persons and Families Living with Huntington's Disease

MELISSA REITMEIER, LMSW, PHD

NOVEMBER 16, 2019

Objectives

1. Share my role as the HD Social Worker for our Center of Excellence
2. Share resources we through website to launch January 1, 2019
3. http://www.schd.info

Goals

- One of the goals of the Huntington's Disease Center of Excellence at Palmetto Health Medical Group and the University of South Carolina School of Medicine is to promote education about Huntington's disease.
- Our aim is to help patients and families better understand the disease and its progression in order to plan and prepare for the future.
- Promote access to needed resources

RESOURCES

New Website

- https://mcreitme.wixsite.com/hdsc
- LAUNCHING/LIVE
  Jnuary 1, 2019

Huntington's Disease Society of America Center of Excellence
University of South Carolina School of Medicine

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UNIVERSITY OF SOUTH CAROLINA
College of Social Work