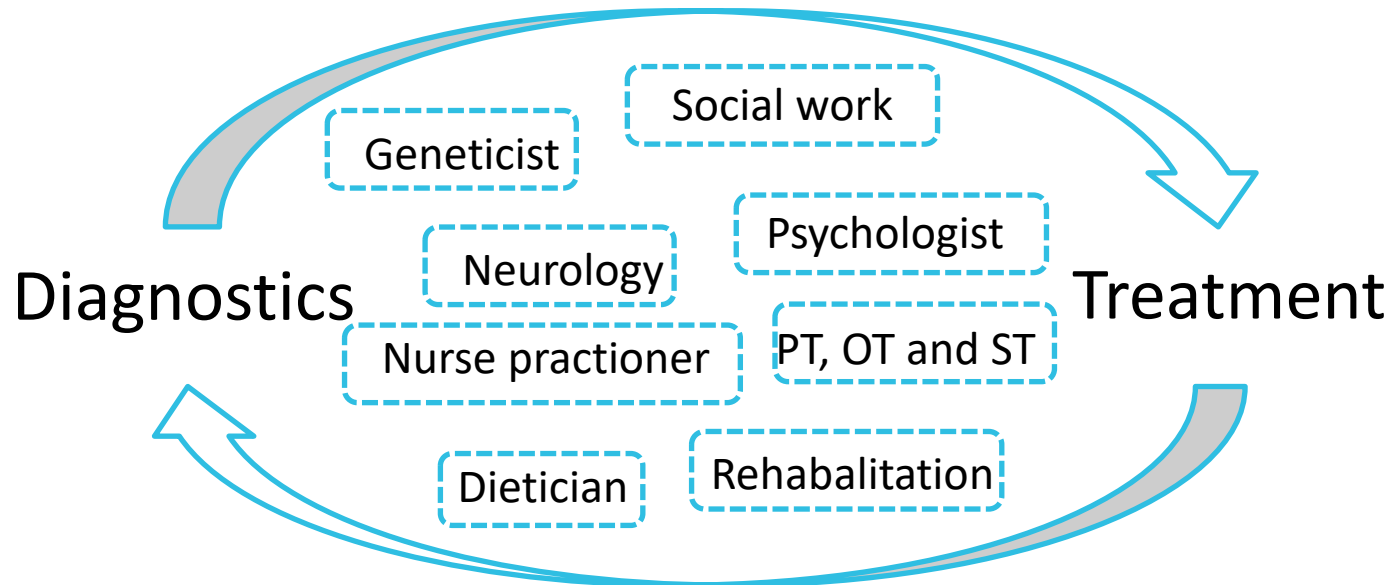


TREATMENT FOR FSHD – A BROADER VIEW

Nicol Voermans, neurologist

Radboudumc

Neuromuscular Centre Radboudumc



European Reference Network

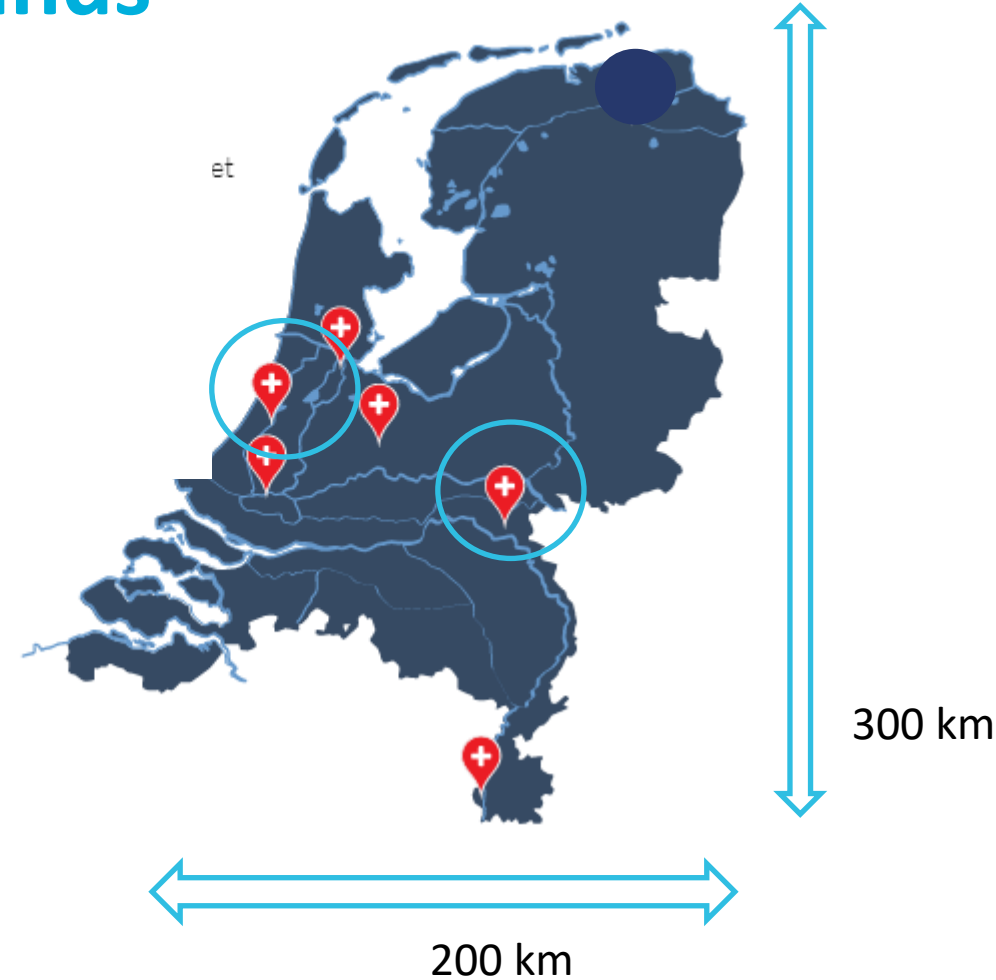
for rare or low prevalence complex diseases

Network
Neuromuscular Diseases (ERN EURO-NMD)



Neuromuscular Centre the Netherlands

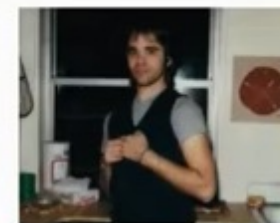
- Netherlands:
 - 17 million people
 - 2000 patients with FSHD
- 6 Neuromuscular centers



2022 IRC Keynote: Patient Perspective on Living with FSHD by Lexi Pappas - YouTube



FSHD in our family



FSHD clinic

Are my symptoms caused by a muscle disease?

Do I have the same disease as my father or mother?

What is the cause of the pain in my back?

How can I contribute to research?

Can I become a mother?

Diagnostics

Treatment

Orthotics

Tricycle

Keep fit

Reduction of pain

Reduction of fatigue

Improvement of social participation

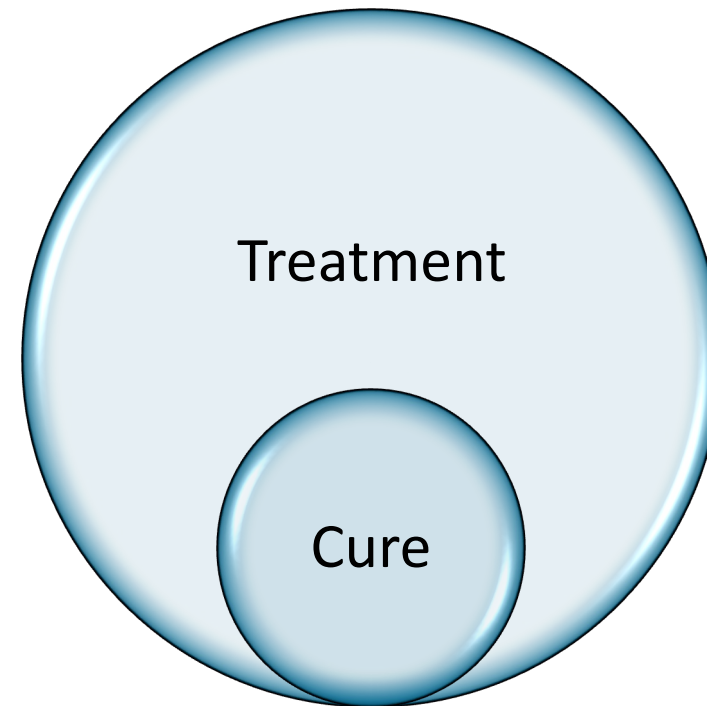
Cure and treatment



FACT:

Currently, there is no cure for FSHD.

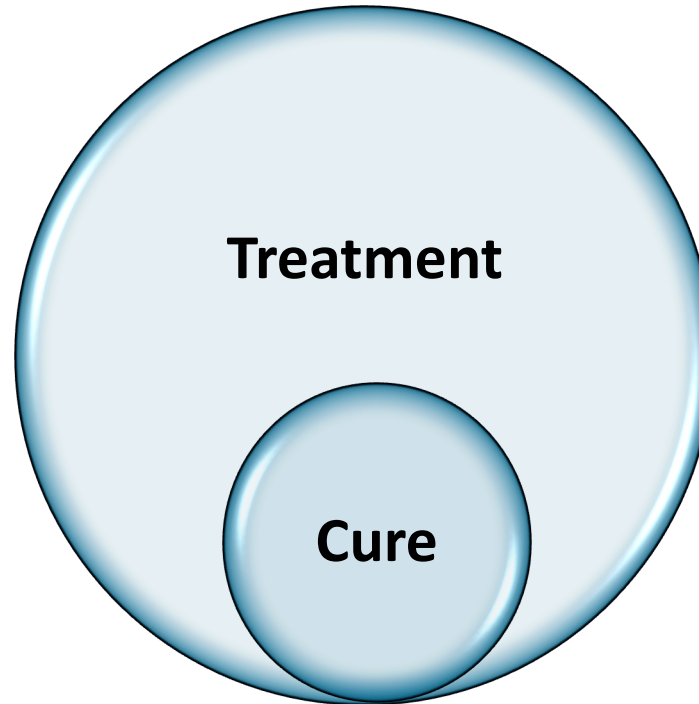
Cure and treatment



Cure and treatment

Treatment

A treatment is a process that leads to an improvement in health, but it may not eliminate the disease. When a disease can't be cured (or a cure doesn't exist yet) medical professionals use medicine, therapy, surgery, and other treatments to help lessen the symptoms.

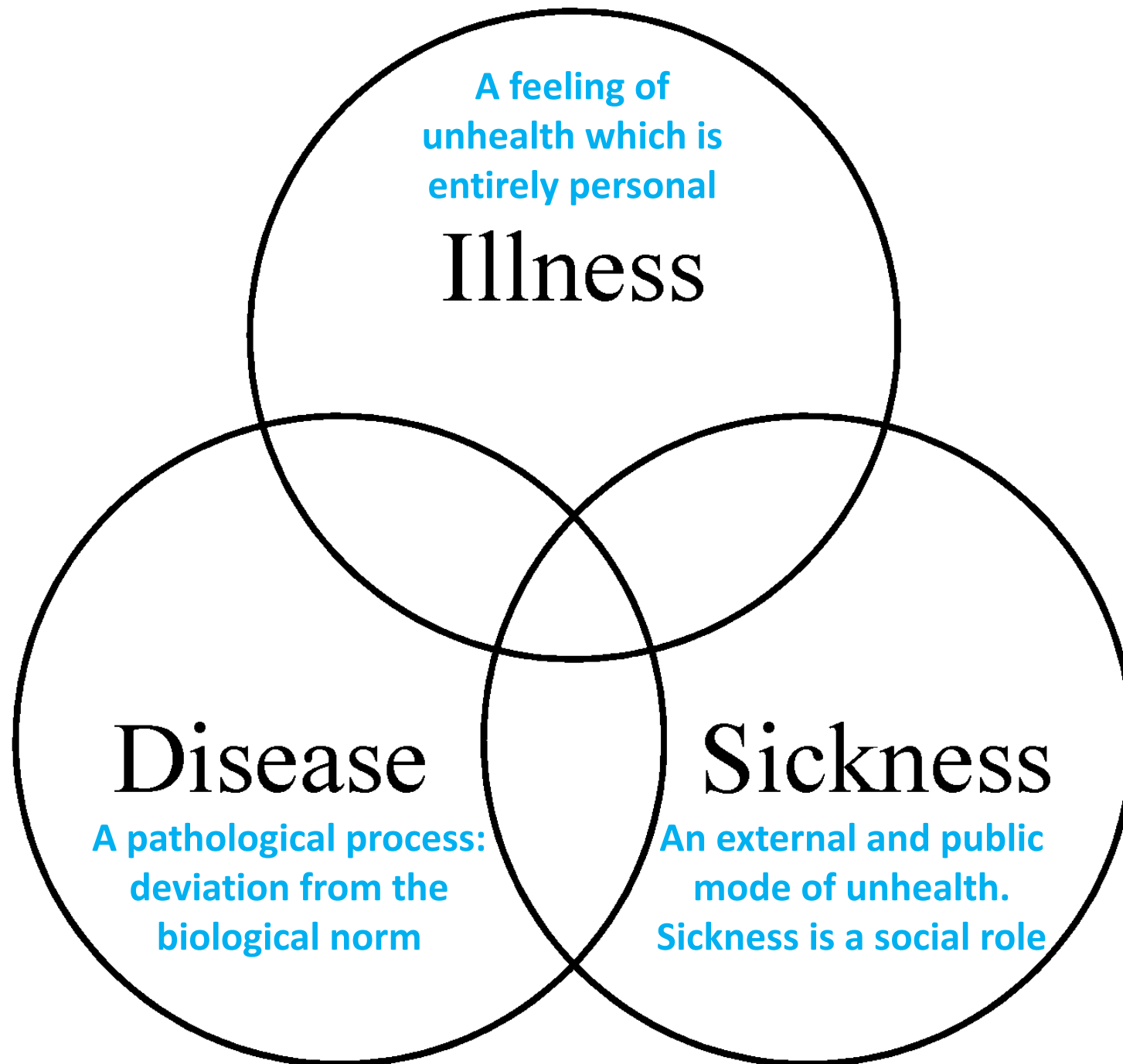


Cure

A "cure" usually refers to a complete restoration of health. After medical treatment, the patient no longer has that particular condition anymore.

(Sub)acute, acquired diseases (fracture, infection)

Chronic, inherited diseases (inherited myopathy)



A feeling of
unhealth which is
entirely personal

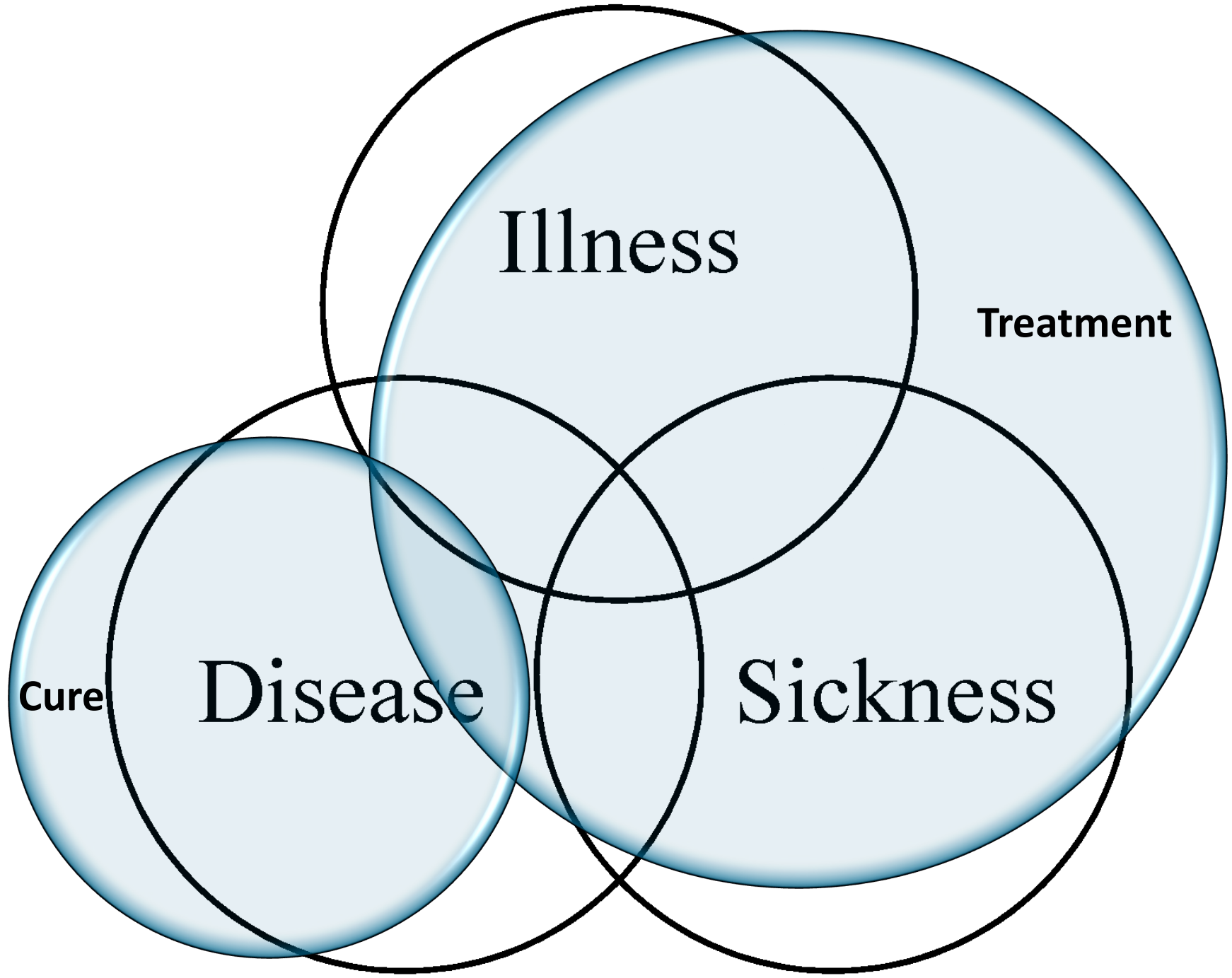
Illness

Disease

A pathological process:
deviation from the
biological norm

Sickness

An external and public
mode of unhealth.
Sickness is a social role



Illness

Treatment

Cure

Disease

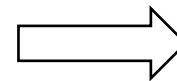
Sickness

FSHD Cure

Cure is targeted at the **disease process in muscle cells**
(gene, RNA or toxic protein (DUX4))

Cure

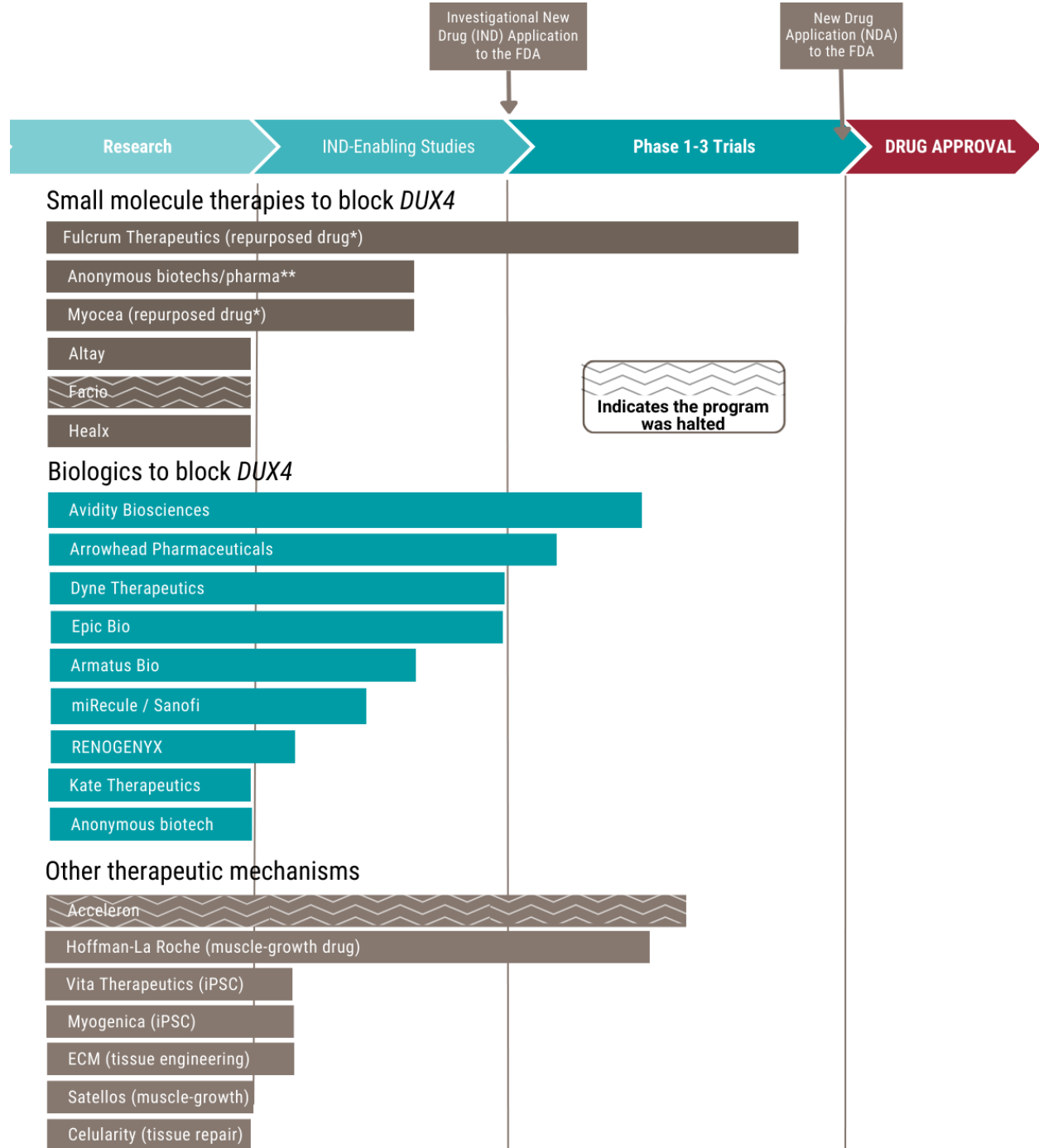
A "cure" usually refers to a complete restoration of health. After medical treatment, the patient no longer has that particular condition anymore.



Dystrophy in muscle cells ->
Muscle weakness

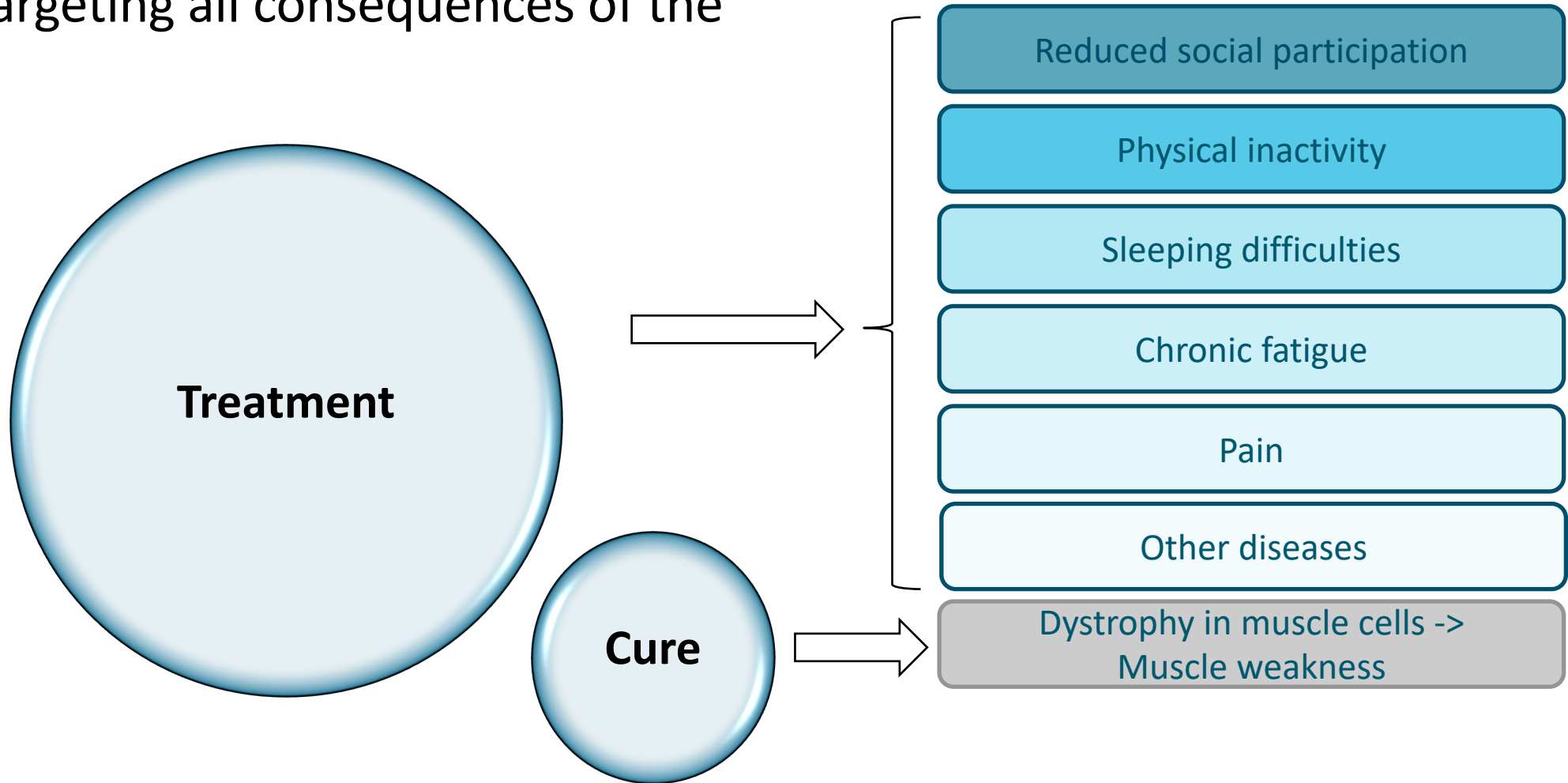


Annual Drug Development Update
with Nicholas Johnson



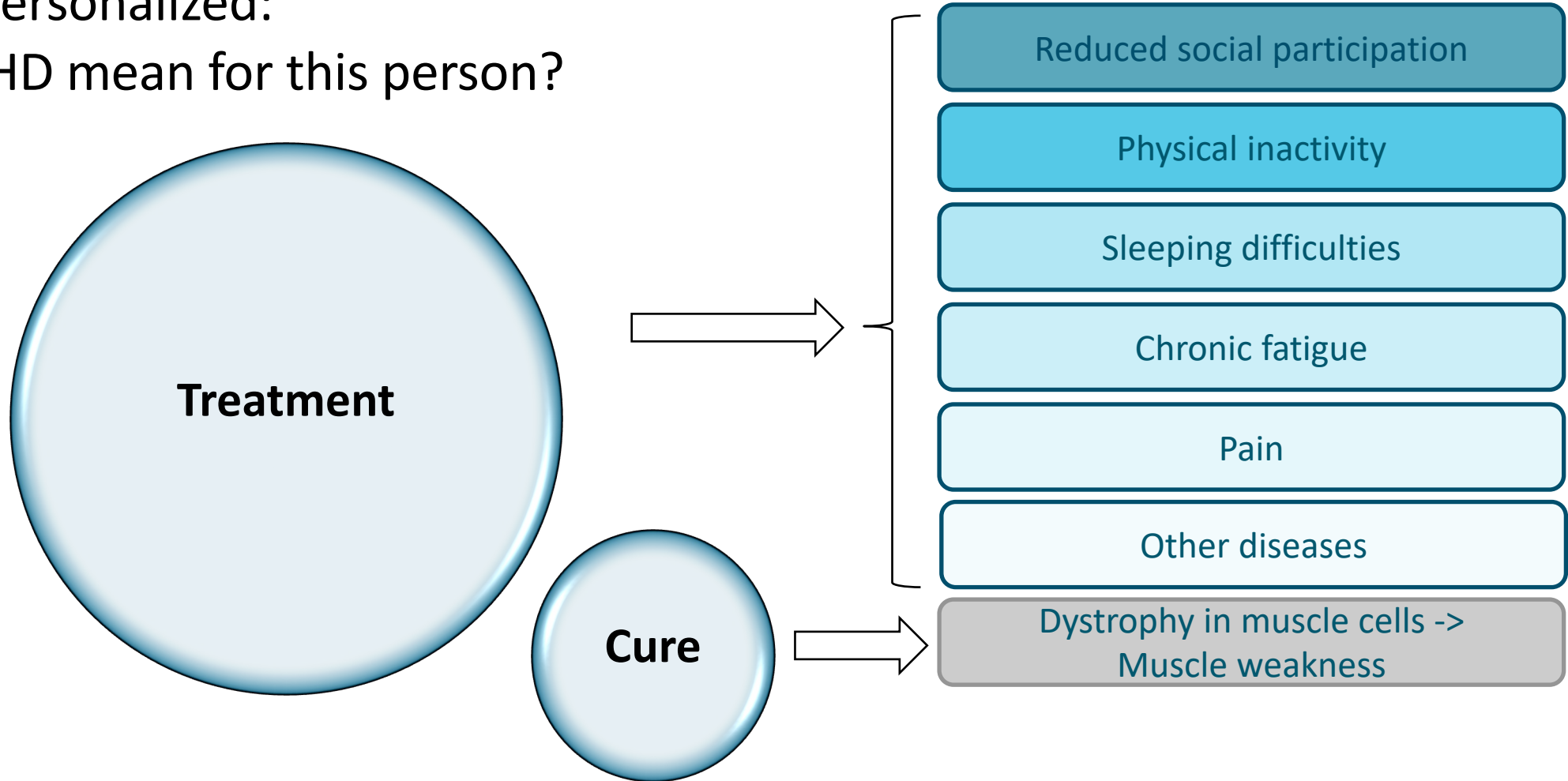
FSHD Treatment

Treatment is targeting all consequences of the disease



FSHD Treatment

Treatment is personalized:
What does FSHD mean for this person?

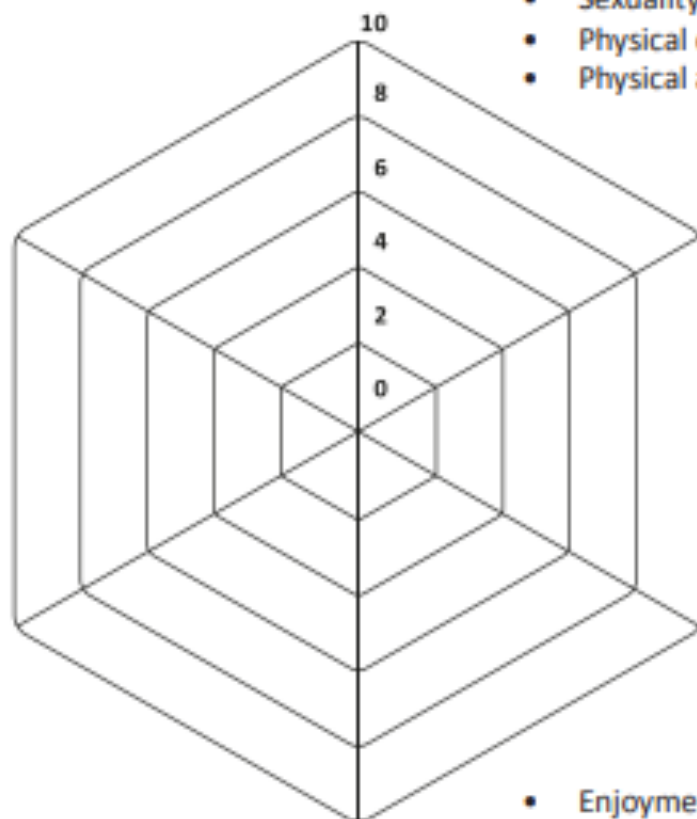




MY POSITIVE HEALTH

- Taking care of yourself
- Knowing your limitations
- Knowledge of health
- Managing time
- Managing money
- Being able to work
- Being able to ask for help

- Social contacts
- Being taken seriously
- Doing fun things together
- Having the support from others
- Sense of belonging
- Doing meaningful things
- Being interested in society



- Feeling healthy
- Feeling fit
- No physical complaints and/or pain
- Sleeping
- Eating
- Sexuality
- Physical condition
- Physical activity



- Enjoyment
- Being happy
- Feeling good
- Feeling well-balanced
- Feeling safe
- Intimacy
- Housing circumstances
- Having enough money

- Being able to remember things
- Being able to concentrate
- Being able to communicate
- Being cheerful
- Accepting yourself
- Being able to handle change
- Feeling in control

- Having a meaningful life
- Having a zest for life
- Pursuing ideals
- Feeling confident
- Accepting life
- Being grateful
- Lifelong learning



Medical Issues

Home / Physical Health / Medical Issues

FSHD brings with it several important health issues, We're here to help you learn and understand more. In addition to the information below, follow our blog for regular updates and information on [Living with FSHD](#).

Anesthesia	+
Breathing	+
Emergency Medical Considerations for FSHD Patients	+
Facial Surgery	+
Heart problems	+
Occupational Therapy and Assistive Technology	+
Pain Management	+
Physical Therapy	+
Scapular Fixation Surgery	+

FSHD Treatment

Symptomatic treatment

- Genetic testing
- Respiratory strength assessment and home mechanical ventilation
- Cardiac screening
- Screening of ear and eye function
- Treatment of chronic pain and fatigue
- Strength training

SPECIAL ARTICLE



Evidence-based guideline summary: Evaluation, diagnosis, and management of facioscapulohumeral muscular dystrophy

Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the Practice Issues Review Panel of the American Association of Neuromuscular & Electrodiagnostic Medicine



FSHD Treatment

Symptomatic treatment

- Genetic testing
- Respiratory strength assessment and home mechanical ventilation
- Cardiac screening
- Screening of ear and eye function
- Treatment of chronic pain and fatigue
- Strength training

General neuromuscular care

Specific

SPECIAL ARTICLE



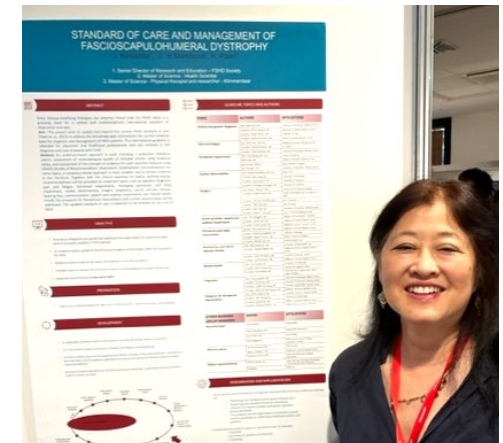
Evidence-based guideline summary:
Evaluation, diagnosis, and management of
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Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the Practice Issues Review Panel of the American Association of Neuromuscular & Electrodiagnostic Medicine



FSHD Treatment

Update of standard of care



P7.07 **Developing an updated standard of care and management for facioscapulohumeral muscular dystrophy**
June Kinoshita, Sarah Elmarkhous, Ronne Pater

FSHD Treatment

Genetic testing

- Complex genetic test
 - only few laboratories
 - deletion (number of units) and A allele
 - FSHD2 and rare genetic causes
- Update of standard of genetic testing



10:10 a.m.

S4.02 Clinical variability in FSHD: The importance of robust clinical information for reliable interpretation of genetic data

Richard Lemmers, *Leiden University Medical Center*

Richard Lemmers and Emiliano Giardina

FSHD Treatment

Genetic testing

- Challenges in interpretation:
 - kB / units
 - small deletions in the normal populations (9-10 units)
 - importance of family history

Table 1

Confirmation table of D4Z4 repeat lengths in units and kb with the different techniques.

For registries it is recommended to document the D4Z4 repeat size in repeat units including the genetic background irrespective of the technology used.

Size D4Z4 fragment (in basepair) after digestion

units	4A161S		4A161L	
	EcoRI	EcoRI/BlnI	EcoRI	EcoRI/BlnI
1U	10,2	7,0	11,8	8,6
2U	13,5	10,3	15,1	15,1
3U	16,8	13,6	18,4	18,4
4U	20,1	16,9	21,7	21,7
5U	23,4	20,2	25,0	25,0
6U	26,7	23,5	28,3	28,3
7U	30,0	26,8	31,6	31,6
8U	33,3	30,1	34,9	34,9
9U	36,6	33,4	38,2	38,2
10U	39,9	36,7	41,5	41,5
11U	43,2	40,0	44,8	44,8
12U	46,5	43,3	48,1	48,1
13U	49,8	46,6	51,4	51,4

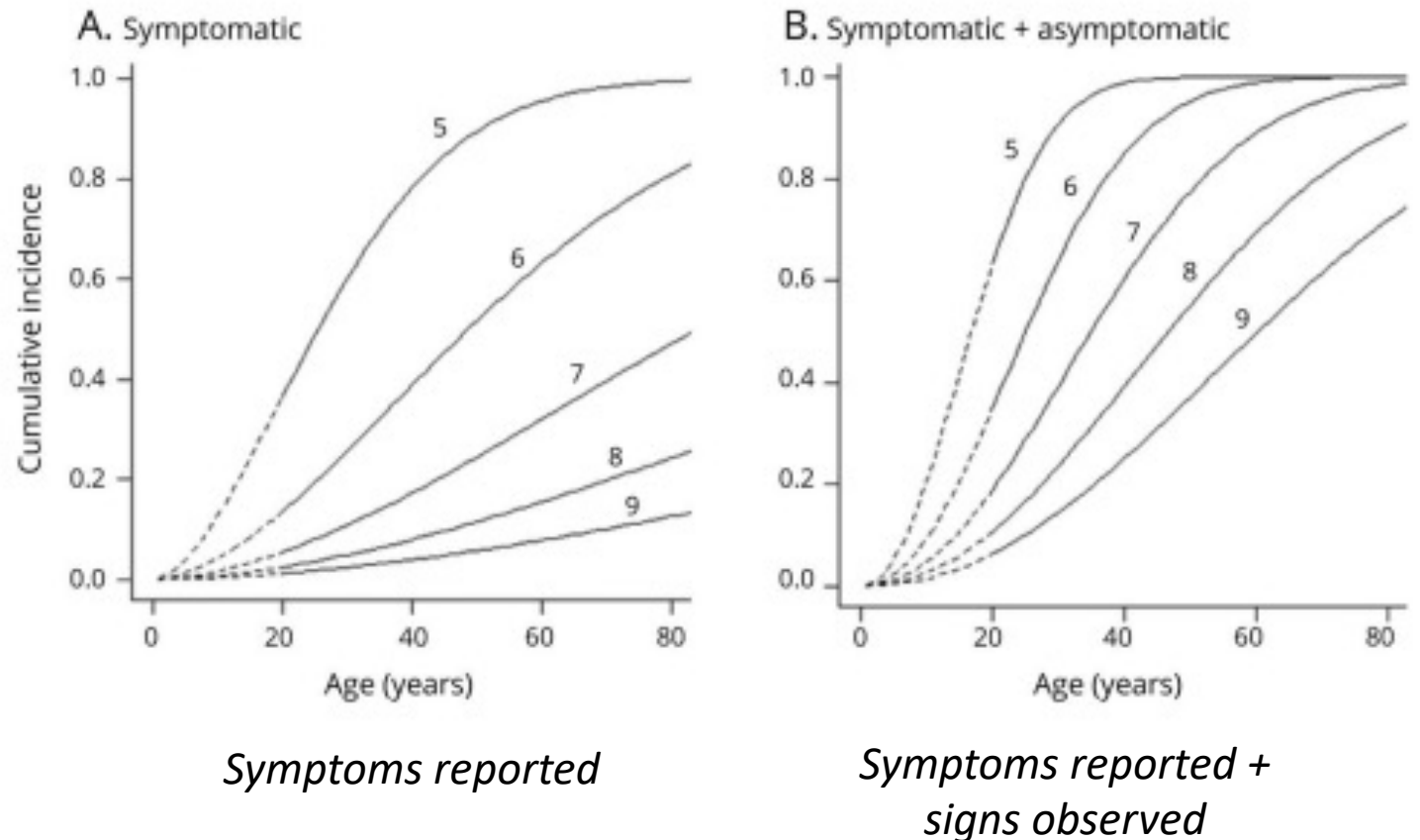
1 unit fragments (4A161S = short variant); 4A161L = long variant

FSHD Treatment

Genetic testing

- Challenges in interpretation:
 - incomplete penetrance

Figure 3 Maximum likelihood curves of the penetrance



Genetic counseling and reproductive options

Facioscapulohumeral muscular dystrophy—Reproductive counseling, pregnancy, and delivery in a complex multigenetic disease

Sanne C. C. Vincenten¹ | Nienke Van Der Stoep² | Aimée D. C. Paulussen³ |
Karlien Mul¹ | Umesh A. Badrising⁴ | Marjolein Kriek² |
Olivier W. H. Van Der Heijden⁵ | Baziel G. M. Van Engelen¹ | Nicol C. Voermans¹ |
Christine E. M. De Die-Smulders³ | Saskia Lassche^{1,6}

TABLE 1 Reproductive options

Reproductive options	FSHD1	FSHD2
Prenatal diagnostic trajectory using chorionic villus testing or amniocentesis (PND)	X	
Preimplantation genetic testing (PGT)	X	
Refrain from having (biological) children	X	X
Adoptive or foster children	X	X
Egg- or sperm donation	X	X
Accepting the risk of having a child affected with FSHD	X	X

FSHD Treatment

Symptoms of Hypercapnia



Headaches.



Shortness of breath.



Seizures.



Persistent tiredness or sluggishness during the day.



Neurological symptoms (disorientation, confusion, altered mental state, depression).

Respiratory strength assessment

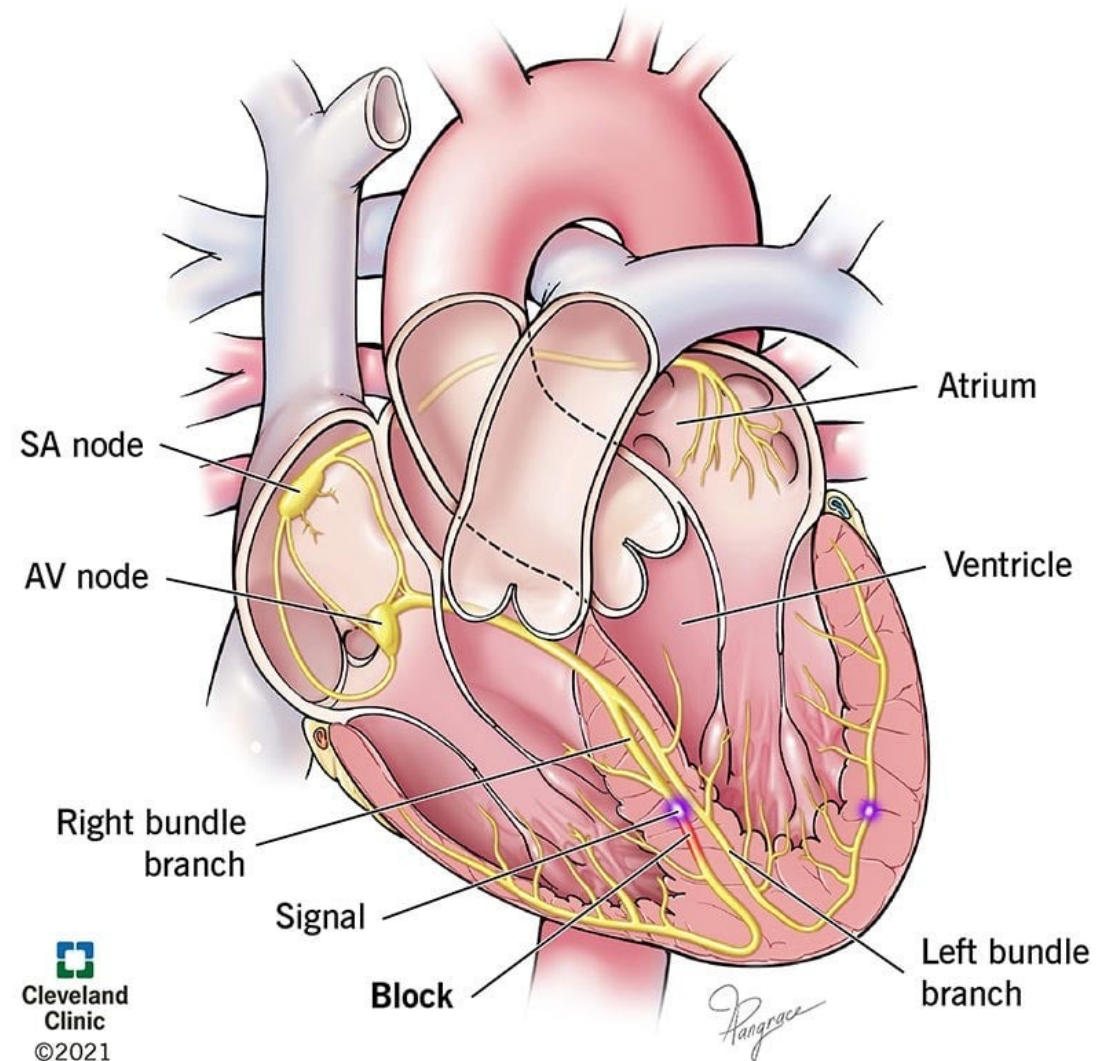
- Hypoxia = low oxygen
- Hypercapnia = high carbon dioxide
- Spirometry:
 - Reduction of vital capacity from sitting to lying down



FSHD Treatment

Cardiac screening

- Cardiac ultrasound:
 - No / few abnormalities in heart muscle
- ECG:
 - Rythm abnormalities in 10%:
 - Right bundle branch block
 - mostly not symptomatic
 - mostly not progressive
- Presence of cardiac abnormalities cannot be predicted from phenotype nor genotype



FSHD Treatment

Screening of ear and eye function

- Audiometry (hearing test):
 - hearing loss only in patients with severe mutations (large deletions: ≤ 20 kB): 32%
- Fundoscopy (view on retina):
 - 25% has abnormalities on test
 - 0.6% has symptoms



FSHD Treatment

Treatment of chronic pain and fatigue



Who We Are ▾

Understanding FSHD ▾

Get Involved ▾

Research ▾

News ▾

JOIN US ✉

DONATE ❤

FSHD brings with it several important health issues, We're here to help you learn and understand more. In addition to the information below, follow our blog for regular updates and information on [Living with FSHD](#).

Physical Therapy



Occupational Therapy and Assistive Technology



Pain Management



FSHD Treatment

Overall approach to pain management in FSHD



- Is there a clear modifiable cause (ex. it only hurts when I sit in this chair)?
- Treatments
 - Pharmacologic (medication)
 - Non-pharmacologic (physical and cognitive treatments)
 - Recall, pain occurs in the brain. If the brain is not involved (anesthesia) you don't feel pain
- Treatment is a process, there is no magic wand
 - Pain is complex and different for each person



Aerobic exercise and cognitive behavioral therapy reduces fatigue

Both aerobic exercise and cognitive-behavioral therapy reduce chronic fatigue in FSHD

An RCT



Design:

- FSHD patients with severe chronic fatigue
- 16 weeks intervention:
 - 28 patients aerobic training (hometrainer and PT)
 - 25 patients cognitive behavioral therapy (increase of physical activity)
- Measurements before, directly after and 12 weeks after intervention

Conclusion

- More physically active
- Better sleep
- Less fatigue
- Better social participation

Self-management improves participation

ARTICLE CLASS OF EVIDENCE

Self-management program improves participation in patients with neuromuscular disease

A randomized controlled trial

Yvonne Veenhuizen, MSc, Edith H.C. Cup, PhD, Marianne A. Jonker, PhD, Nicoline B.M. Voet, MD, PhD, Bianca J. van Keulen, MSc, Daphne M. Maas, MSc, Anita Heeren, MD, Jan T. Groothuis, MD, PhD,* Baziel G.M. van Engelen, MD, PhD,* and Alexander C.H. Geurts, MD, PhD

Neurology® 2019;93:e1720-e1731. doi:10.1212/WNL.00000000000008393

Correspondence
Mrs. Veenhuizen
Yvonne.Veenhuizen@
radboudumc.nl



Gold Coin
ENERGY SELF-MANAGEMENT
Ria de Haas, PhD, project manager, FSHD
Europe/FSHD European Trial Network



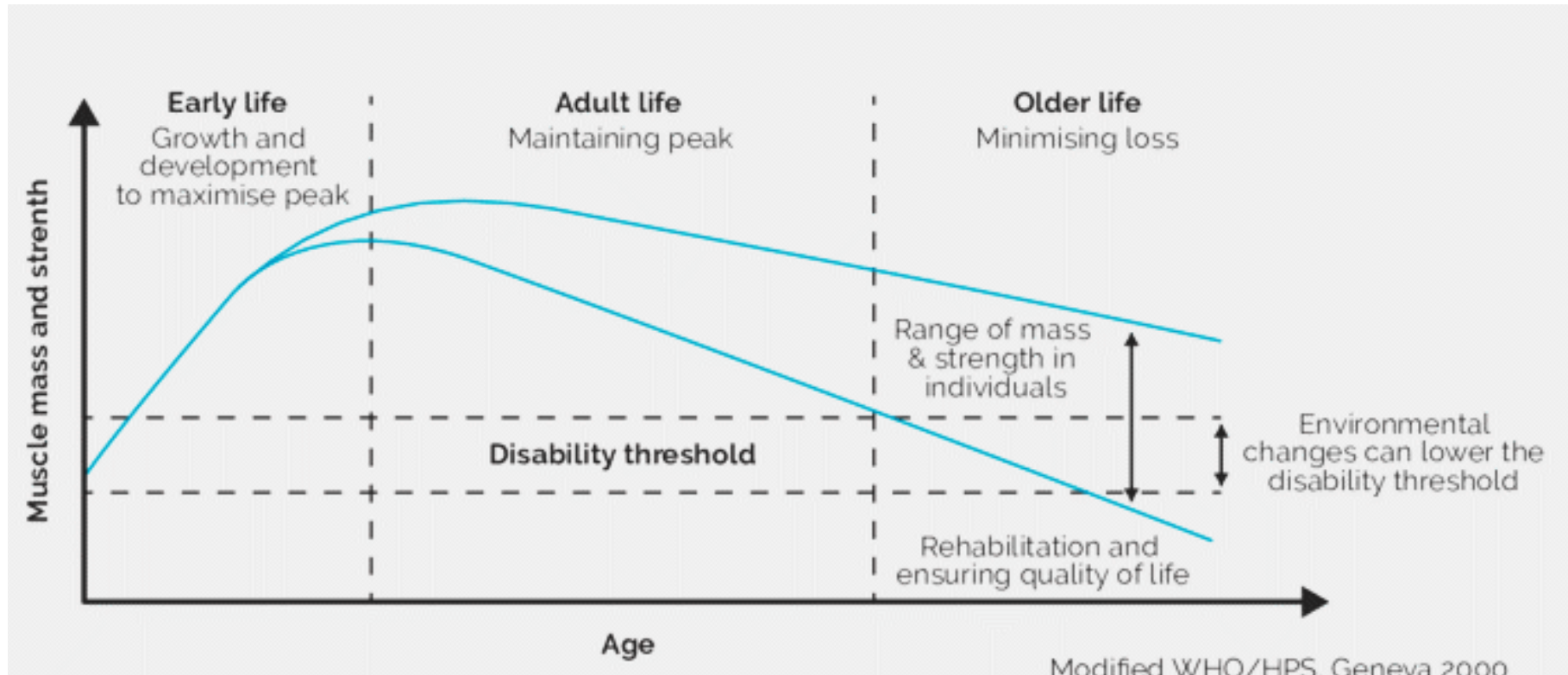
Design:

- 53 patients with different neuromuscular disorders and severe fatigue
- 16 weeks intervention:
 - 29 patients self-management group training (aerobic training and energy management)
 - 24 patients usual care
- Measurements before, 3 and 11 months after intervention

Conclusion

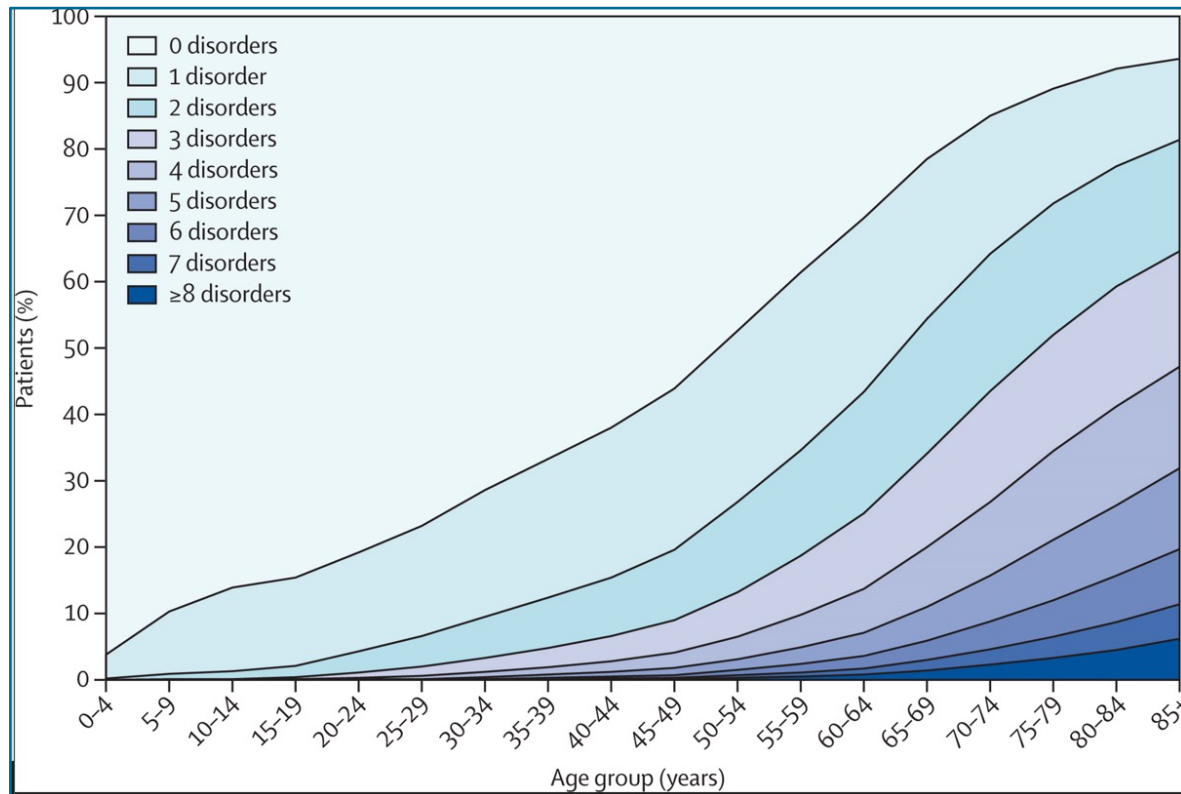
- Improvement of walking: longer distance on 6MWT
- Better endurance of physical activity
- Better social participation
- Sustainable improvements

Muscle mass and strength

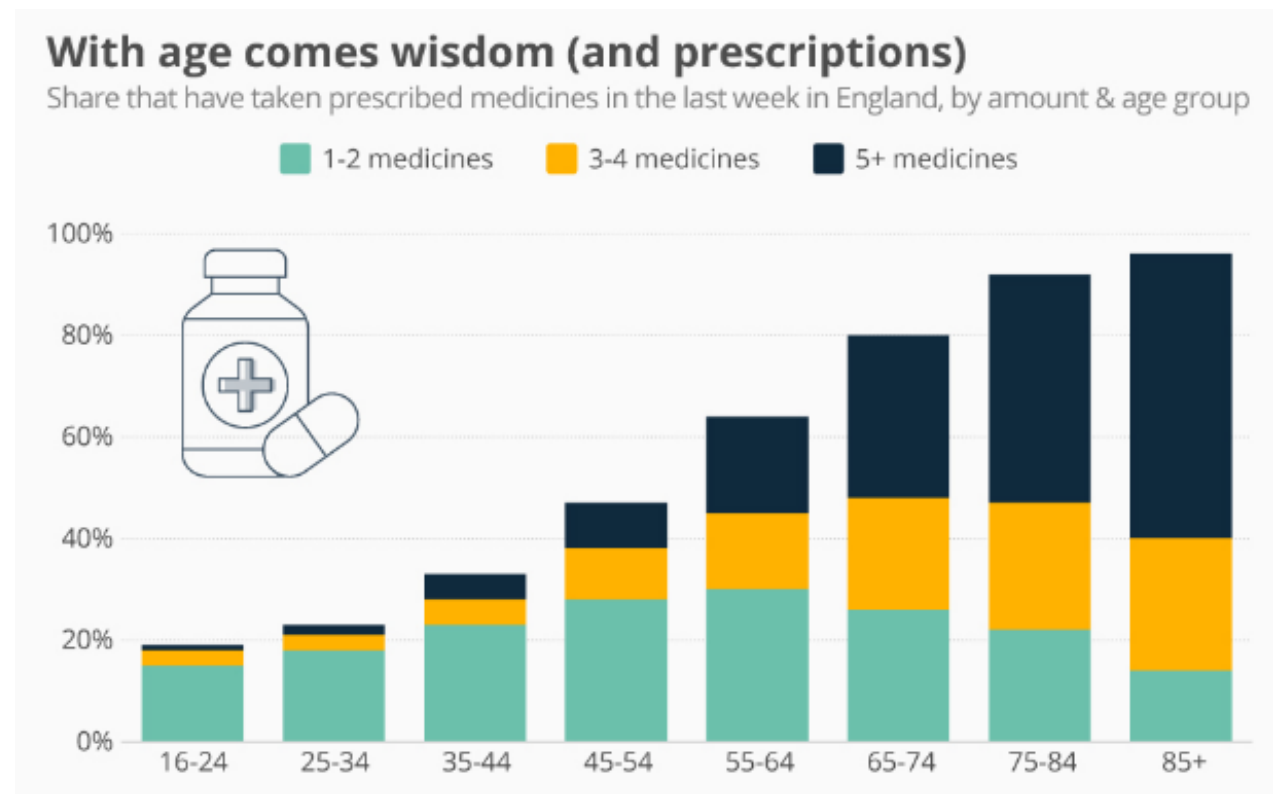


Healthy lifestyle is essential

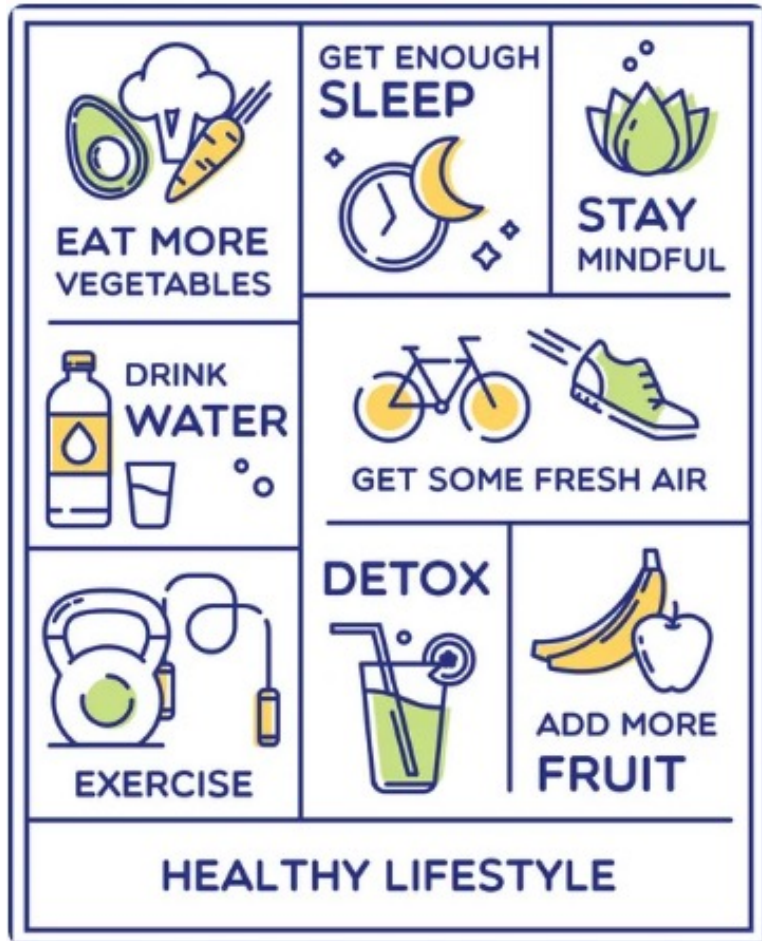
Age – number of disorders



Age – number of prescribed drugs

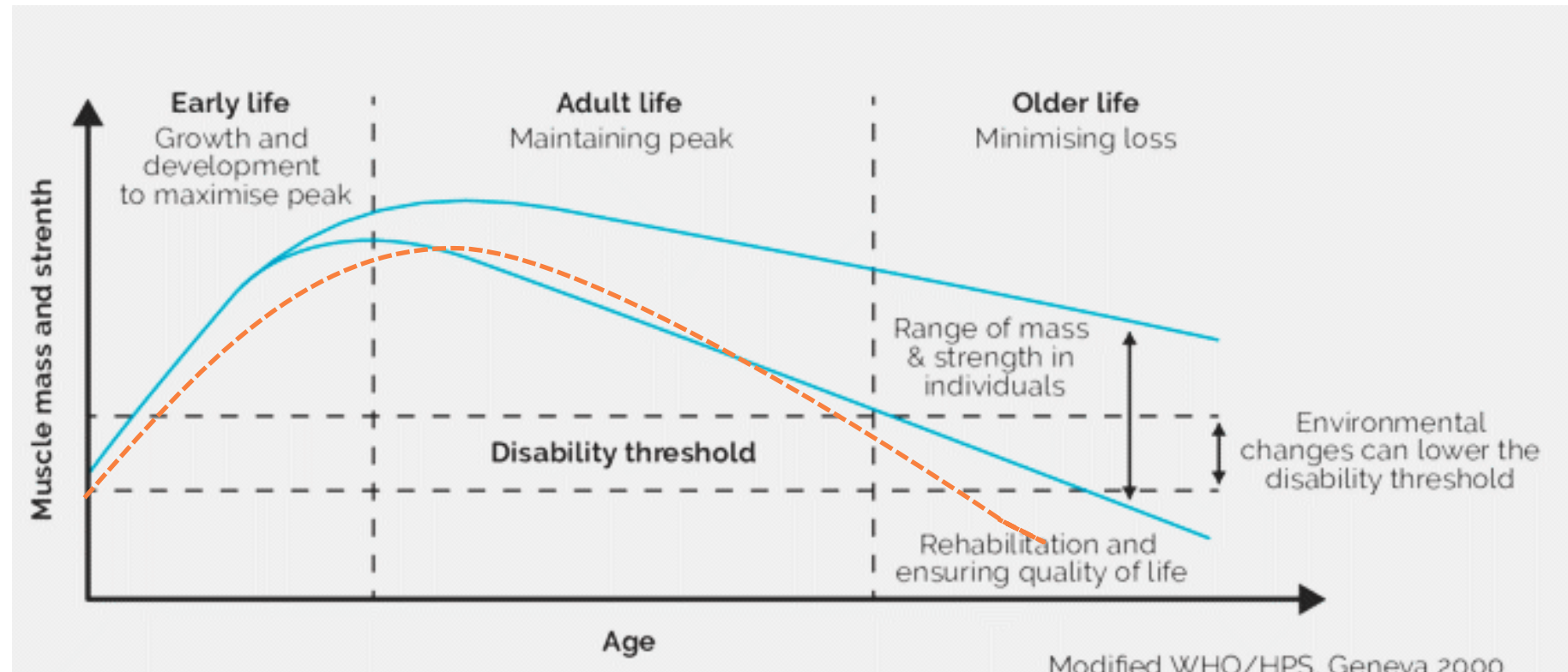


Lifestyle intervention



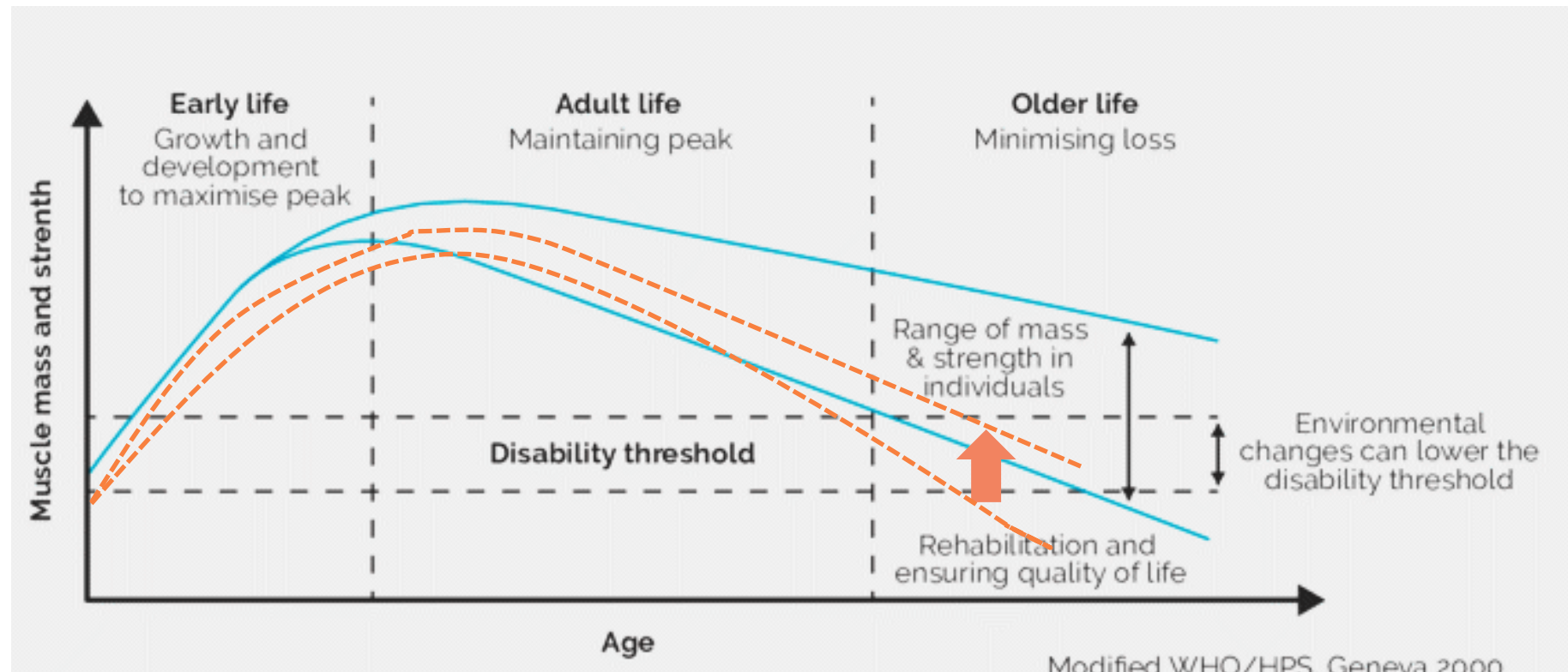
Lifestyle intervention

FSHD patients:
Muscle mass and
strenght in ageing

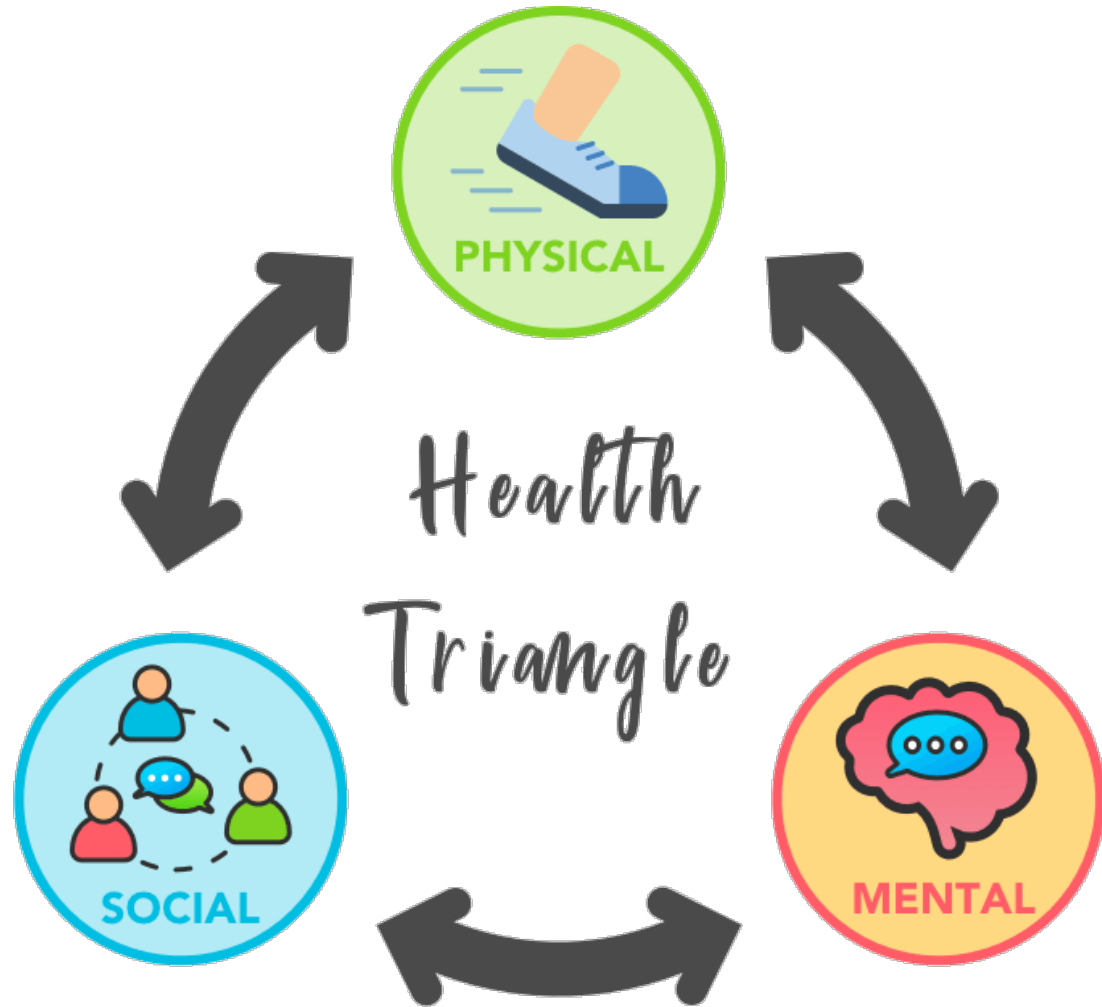


Lifestyle intervention

FSHD patients:
Muscle mass and
strenght in ageing



Mental strength training



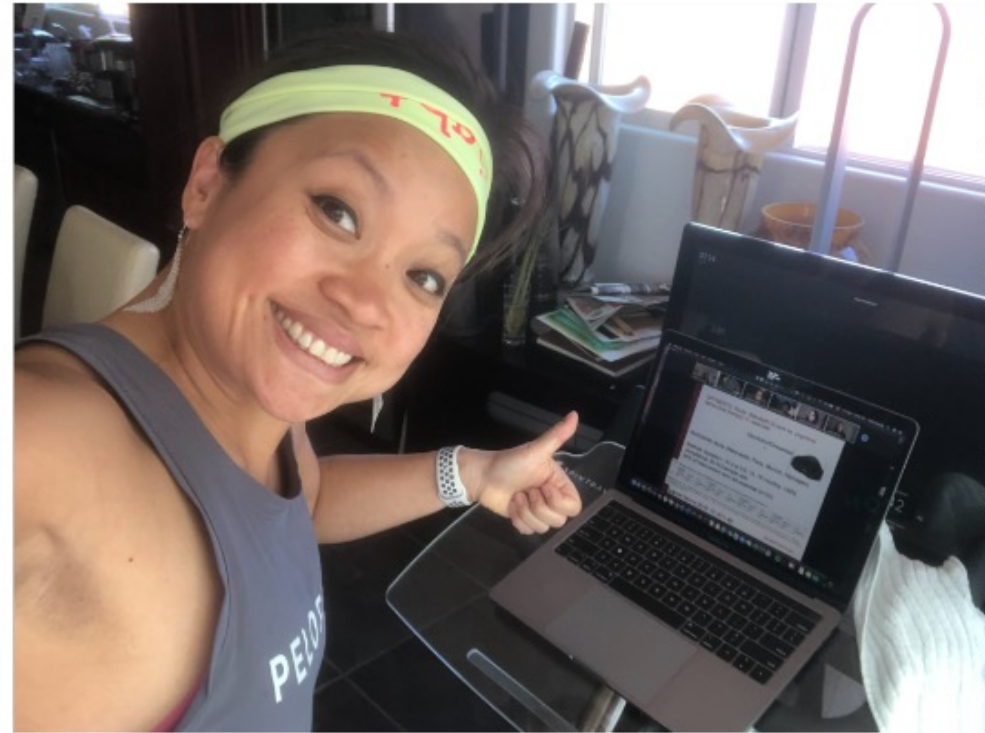
Physical Health

Home / Physical Health

As an individual or family member affected by FSH muscular dystrophy, you are going to find that most doctors, therapists, and fitness trainers have little to no experience with FSHD. That's just the reality of living with any rare disease, but you have the power to make a difference. Learn all you can about FSHD so you can take care of yourself and guide your health care providers on how to help you maintain the best possible fitness and health.

Our downloadable brochure [About FSHD](#) provides valuable guidance. A physician or licensed therapist should be your source for specific health care recommendations, but being a knowledgeable patient makes a huge difference.

Click on the links below for a deeper dive...

[HEALTH AND MEDICINE](#)
[EXERCISE AND FITNESS](#)


ACT to improve quality of life

Home / FSHD Research / ACT to improve quality of life

Posted on: Apr 11, 2022

by Kent Drescher, PhD, Bay Area Chapter Co-Director

I've had FSHD symptoms for over 50 years. It seems like I've spent much of that time waiting. Waiting for treatment. Waiting to see what precious physical ability I will lose next. Waiting for a cure. Along with physical symptoms of FSHD (e.g. weakness, pain, fatigue) there are large mental and emotional costs. These range from hopelessness and depression to worry about one's future. It also **brings** struggles with self-worth as we fall prey to societal expectations about body image and implicit bias about disability. Unfortunately, little research has examined those costs.

I am excited to share positive results from a recent clinical trial of a psychological treatment for the mental and emotional costs of FSHD and other neuromuscular diseases. Michael Rose, Christopher Graham, and their team found large positive improvements in quality of life and mood within the group of patients who completed four weekly self-help modules at home using Acceptance and Commitment Therapy (ACT). Their study randomized 139 patients with neuromuscular disease (50% had FSHD) into two groups, comprising standard medical care (SMC) and ACT plus SMC.



Five Things I Wish I'd Known Before My Chronic Illness

Finding out you have a chronic illness — one that will, by definition, never go away — changes things, both for you and those you love.



Share full article



By Tessa Miller

Feb. 18, 2019

Communication training



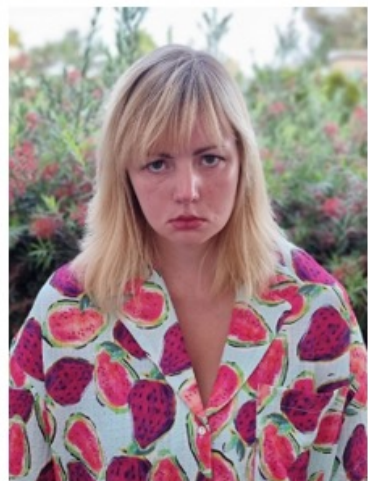
Neutral facial expression



Happy facial expression



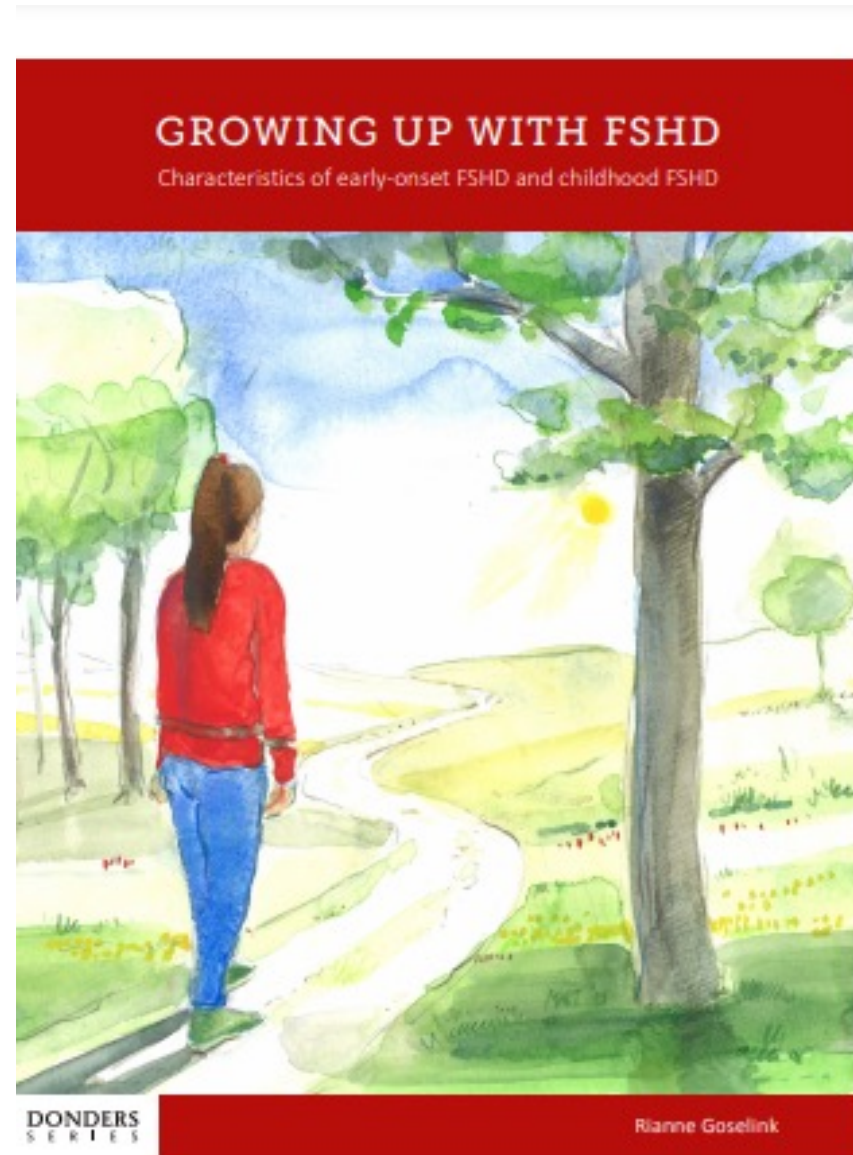
Sad facial expression



Angry facial expression

- How does facial weakness influence communication?
- What does it mean to have a different facial expression in different phases of your life?
- How do you create the right “ subtitles”?

FSHD in childhood



Precautions in emergency situations / for anesthesia



Zorgverleners

Centrum voor Thuisbeademing
Ziekenhuis:

Telefoonnummer:

• Kantooruren:

• Buiten kantooruren:

Belangrijkste arts:

Praktijk/ziekenhuis:

Telefoonnummer:

FSHD Expertisecentrum voor
ziektespecifieke vragen:
www.fshdexpertisecentrum.nl

In samenwerking met:



FSHD
EXPERTISECENTRUM



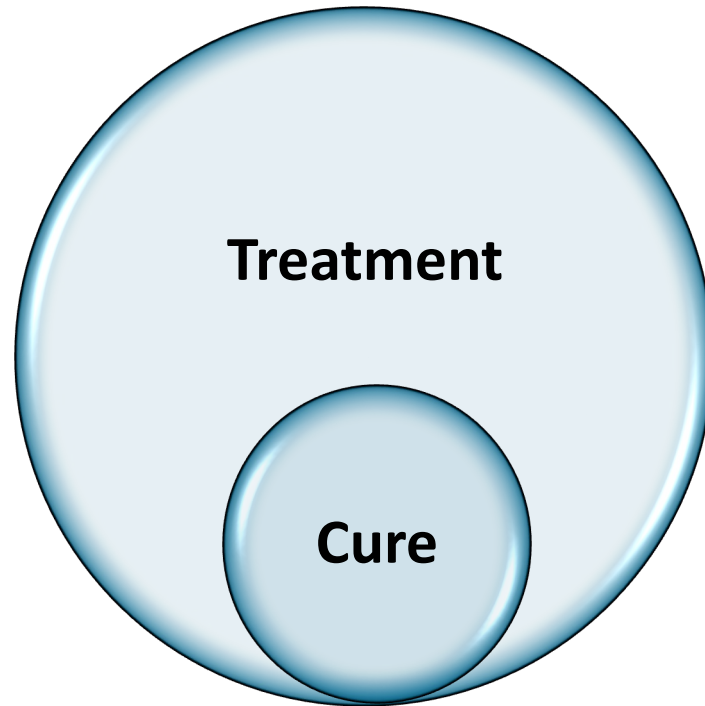
SOS

Medische
informatiekaart

Ik heb de spierziekte:

FSHD
Facioscapulohumerale dystrofie

Treatment is a required start for cure



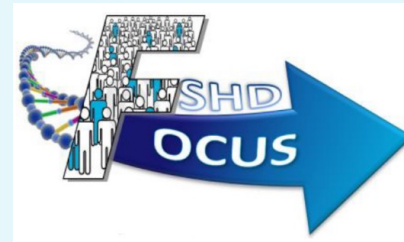
What is needed in clinical trials?



Patients:
Adequate
diagnostics
Registration



**Clinical
outcome
measures:**
PROM, functional,
imaging



**Natural
history:**
Disease course
without cure

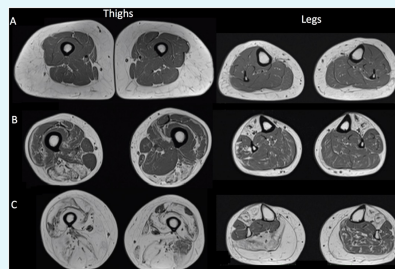


**Personnel and
facilities**
Trial sites

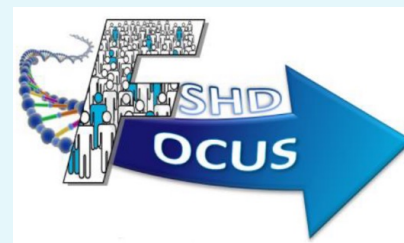
Treatment



Patients:
Adequate
diagnostics
Registration



**Clinical
outcome
measures:**
PROM, functional,
imaging



**Natural
history:**
Disease course
without cure



**Personnel and
facilities**
Trial sites

Questions?

Thanks

