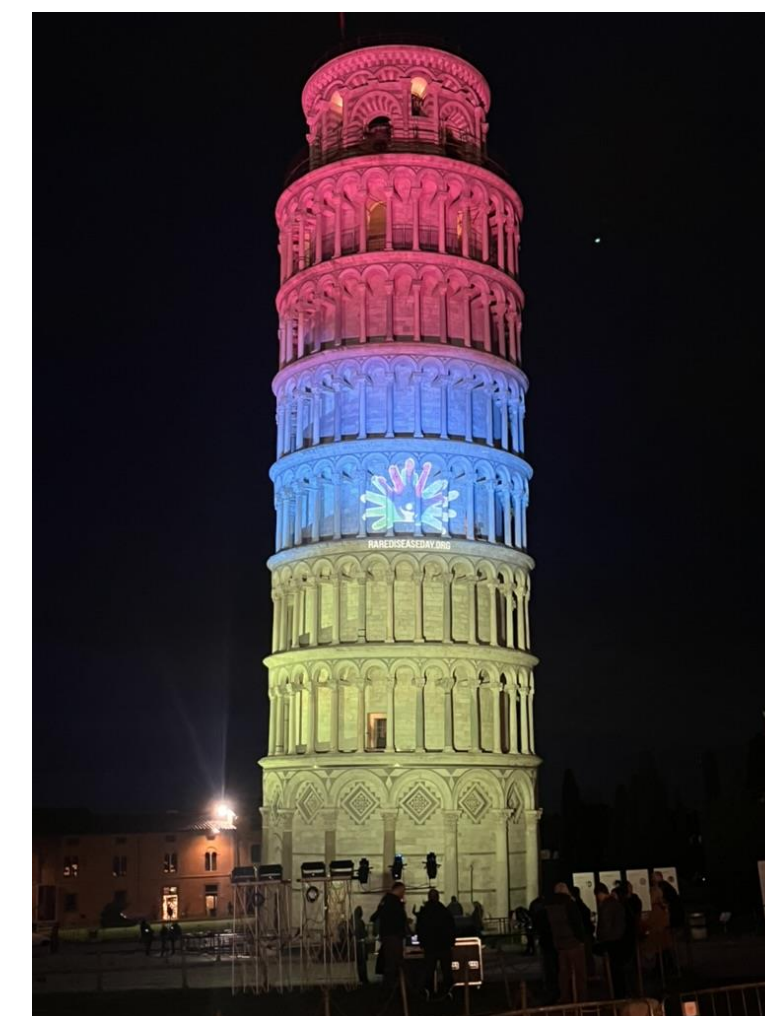




8th ERN EURO-NMD Annual Meeting

**Patient reported outcome measures
PROMMY the new app in the PROMs' ecosystem**

**Michelangelo Mancuso, MD, PhD, Prof.
Azienda Ospedaliera Universitaria Pisana,
Pisa (Italy)**



ERN EURO-NMD

- EURO-NMD includes 84 healthcare entities from 25 EU Member State
- An estimated number of 100,000 patients with rare neuromuscular diseases is followed every year
- Over 200 different forms of NMDs frequently with multi-system involvement
- Multiple symptoms (i.e. muscle weakness, muscle pain, fatigue, difficulties in swallowing and breathing, sleeping problems....), not in the clinical registry
- Not only neuromuscular involvement....

**There are some symptoms that have a critical impact on patient's daily life →
“Patients’ symptom burden”**

How will we manage those challenges?

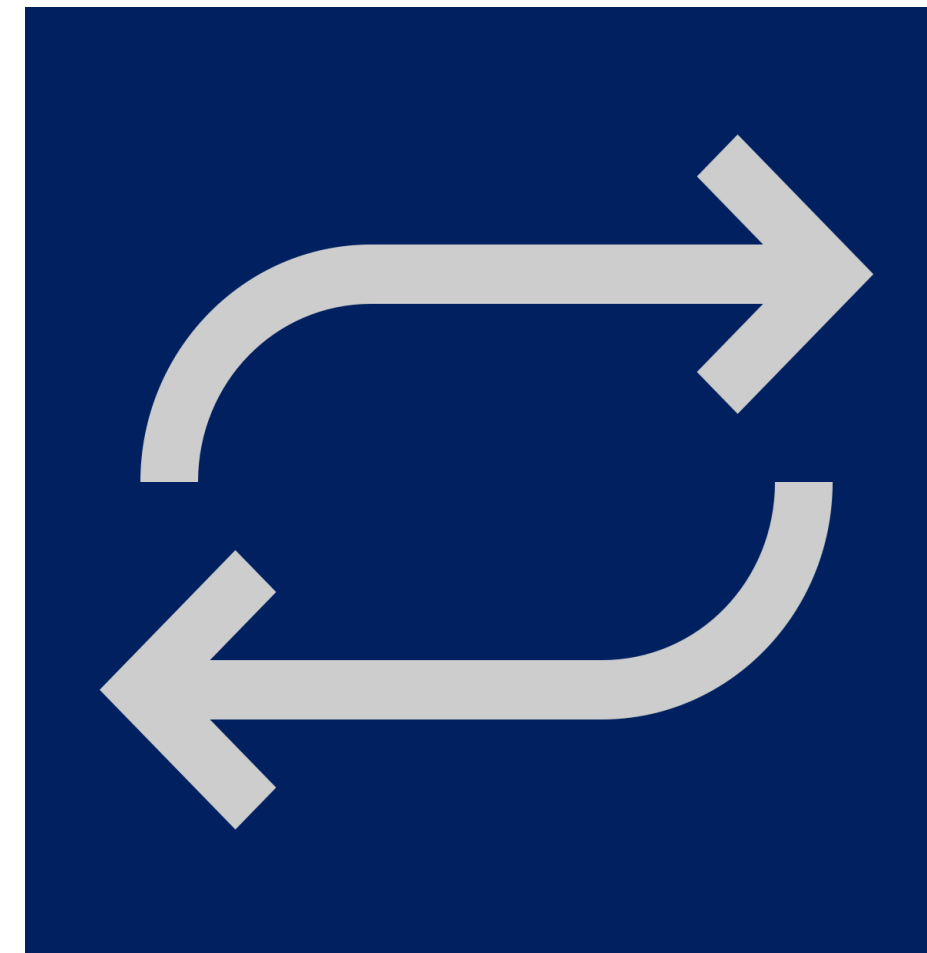


Disease progression

Biomarkers

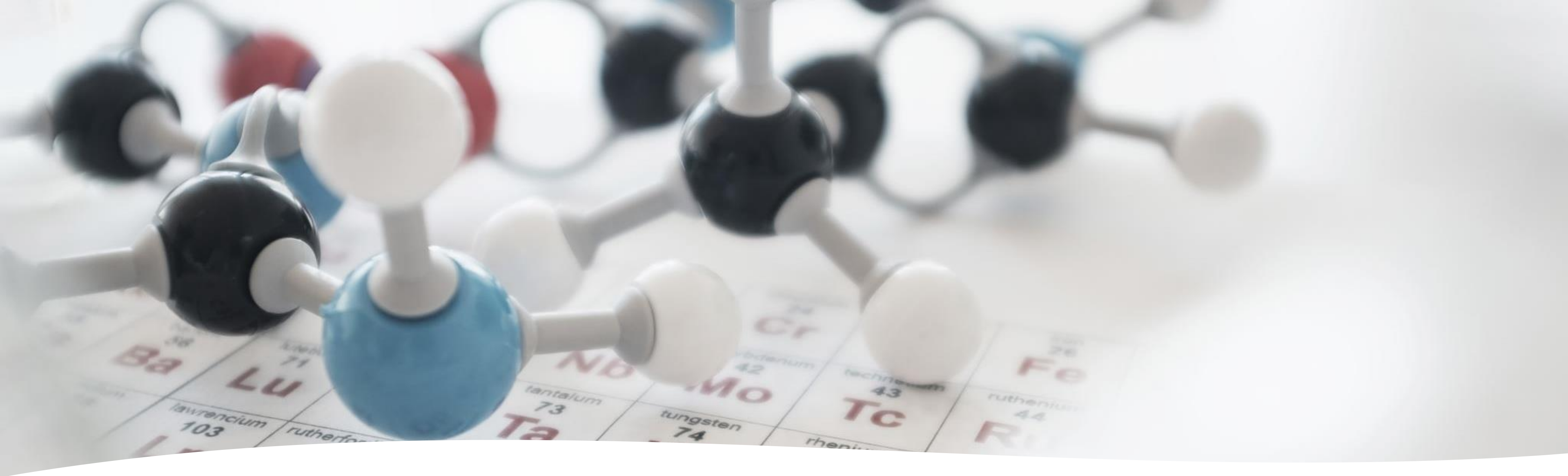
NATURAL HX; RWD,
RWE; REGISTRIES

NEW TECHNOLOGIES



Genetic rel'ships

Treatment effects

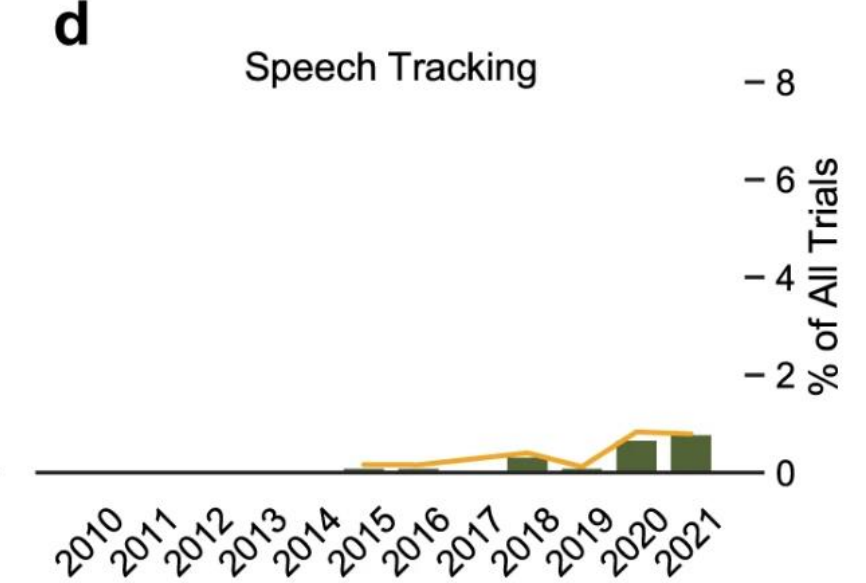
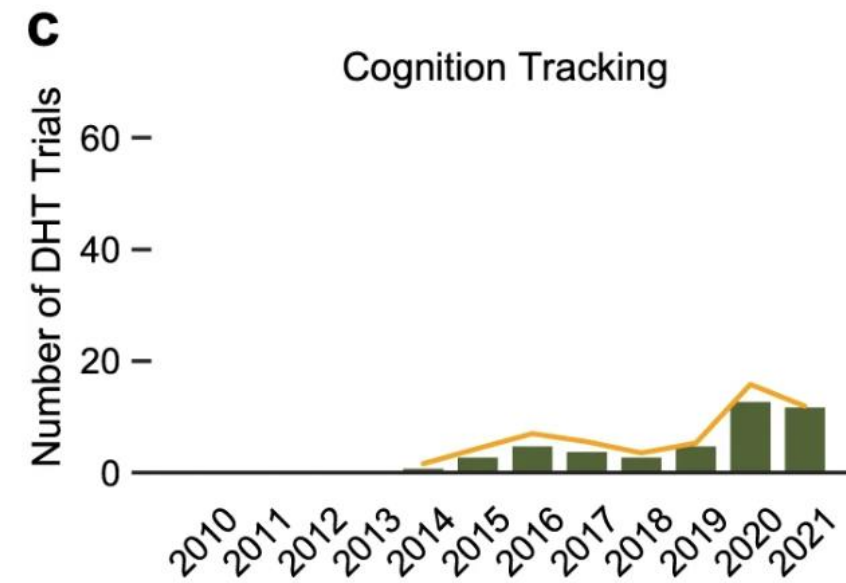
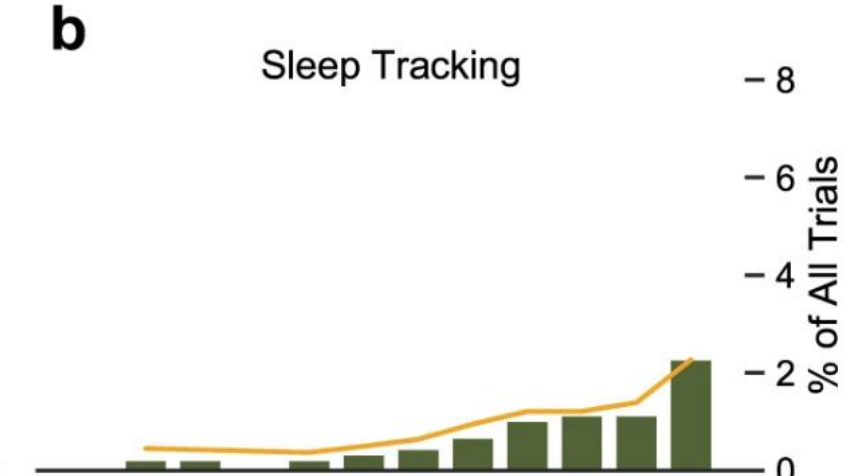
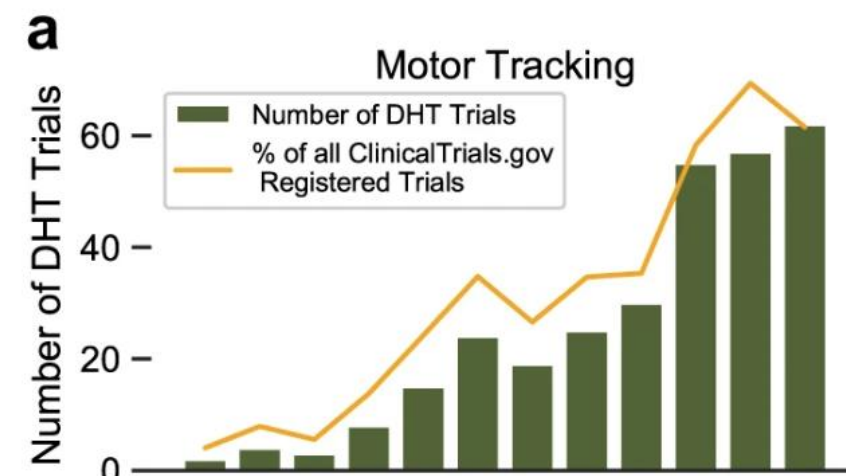
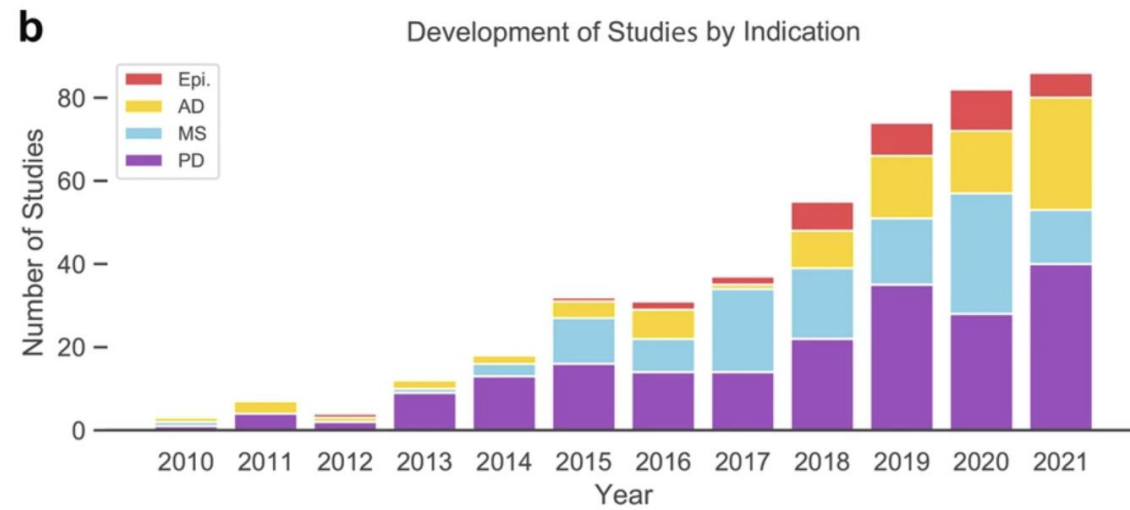
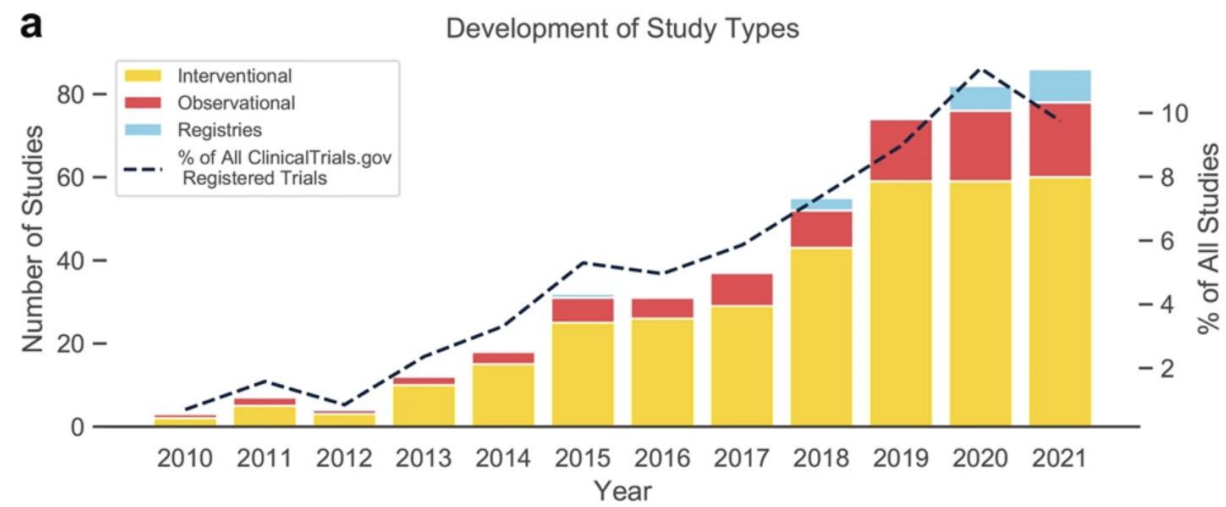


Looking at the future

- AI and ML in NMDs
- Digital Health Technologies (DHTs)
- NMDs specific OMs?
- NMDs specific PROMs?
- Digital biomarkers?
- Telemedicine



AI and DHTs in neurology



ML & Digital Health Technologies in clinical care



Clinical care: To improve the efficiency and efficacy of disease management



Providing earlier diagnoses & delivering more useful clinical phenotyping for prognostication



Enabling greater precision and more personalization of treatment



Monitoring response to treatment and disease trajectory



Motivating and engaging patients in their care and in their environment

Digital biomarkers

Can patient-generated health data from wearable and other mobile/electronic devices supplement or even replace study visits and their associated traditional data collection?



Wearable devices and smartphones

Data acquisition and analysis

Visualizing patient outcomes
Proving drug values
Understanding diseases

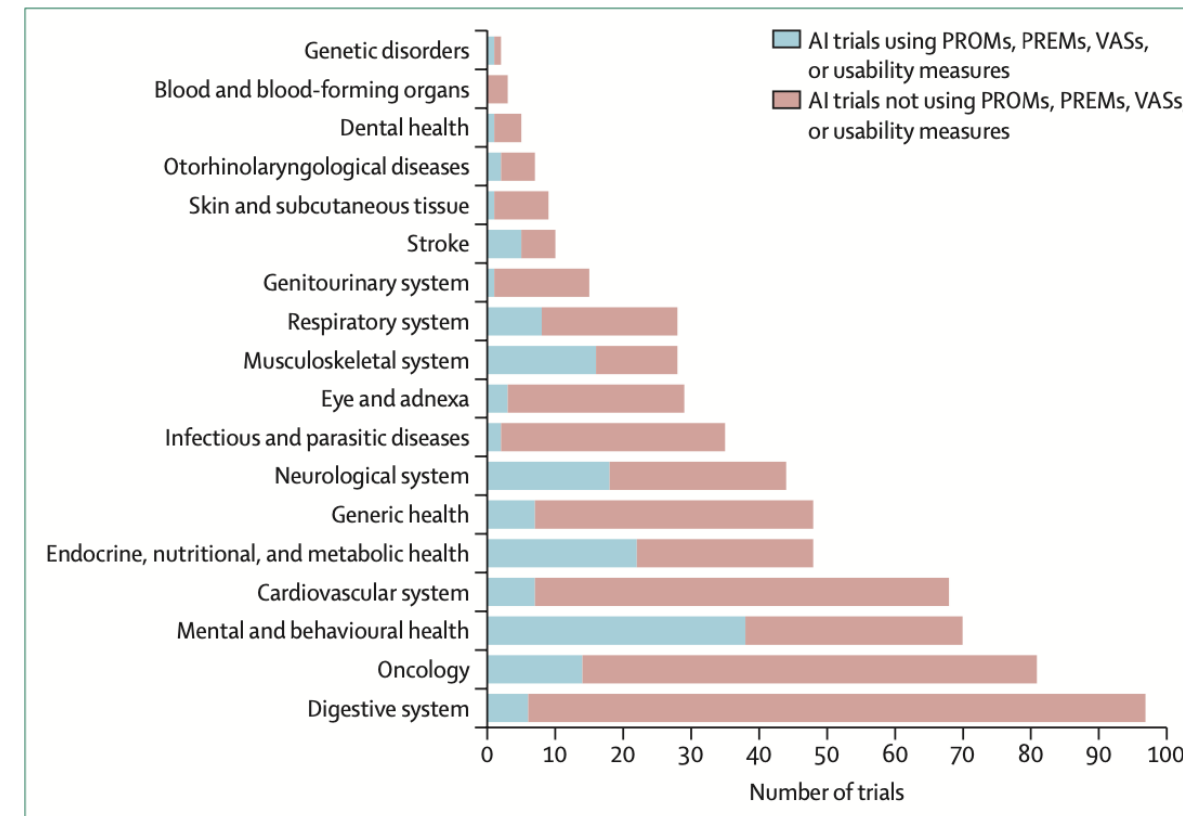
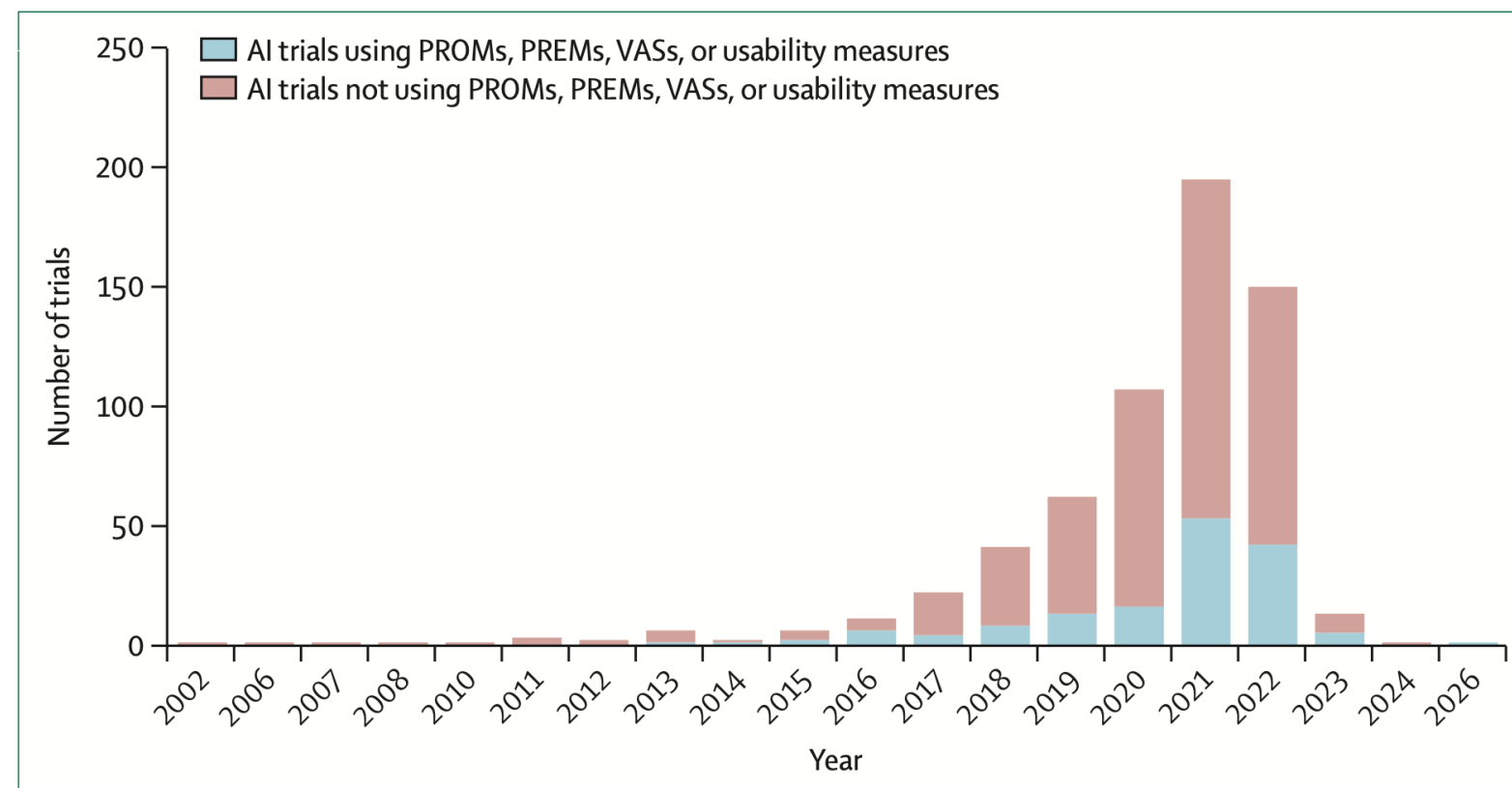
Patient Reported Outcome Measure(s)

PROMs deal with aspects of health that cannot be observed objectively and can therefore only be measured by asking the patient, for example, symptoms or complaints such as pain or mood disorders, and work, sport or housekeeping performances





AI in clinical research: focus on PROMs



Overall, the use of PROMs in the function and assessment of AI health technologies is not only possible, but is a powerful way of showing that, even in the most technologically advanced health-care systems, **patients' perspectives remain central.**

Electronic PROMs

Advances:

- Increased completion rates. In the case of surveys that are to be completed when the patient is at home, and not in hospital, there is an added benefit that electronic PROMs don't need to be posted back to the clinician or researcher
- Easy to remind participants to complete surveys (i.e. pop-up)
- Less risk of secondary data entry errors and more accurate and complete data

Why do we need PROMs and a NMD PROM?

- *There is no PROM that uses a unique cross-sectional approach to accumulate information about the symptomatology of patients with*

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Review

Patient-Reported Outcome Measures in Neuromuscular Diseases: A Scoping Review

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Abstract. Patient-reported outcome measures (PROMs) are valuable in comprehensively understanding patients' health experiences and informing healthcare decisions in research and clinical care without clinicians' input. Until now, no central resource containing information on all PROMS in neuromuscular diseases (NMD) is available, hindering the comparison and choice of PROMs used to monitor NMDs and appropriately reflect the patient's voice. This scoping review aimed to present a comprehensive assessment of the existing literature on using PROMs in children and adults with NMD. A scoping methodology was followed using Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) and Consensus-based Standards for the selection of health Measurement INstruments (COSMIN) guidelines to assess the literature on PROMs in NMDs. Eligibility criteria encompassed articles describing psychometric development or evaluation of generic or disease-specific PROM-based instruments for adults and children with specific NMDs. The data charting process involved extracting measurement properties of included PROMs, comprising validity, reliability, responsiveness, and interpretability information. **The review identified 190 PROMs evaluated across 247 studies in individuals with NMDs. The majority of PROMs were disease specific. The physical functioning domain was most assessed. Validity was the most frequently investigated measurement property, with a limited number of PROMs sufficiently evaluated for a range of psychometric characteristics. There is a strong need for further research on the responsiveness and interpretability of PROMs and the development of PROMs on social functioning in NMD.**

CONTROL THEIR EVOLUTION OVER TIME
(/rehab)

Improvement of diagnostics, therapies,
use natural history

WP7 parallel projects

- *Development of a PROM for the most bothersome symptoms in patients with NMD*
- *Development of the APP for patients engagement*



European
Reference
Network

for rare or low prevalence
complex diseases

 Network
Neuromuscular
Diseases (ERN EURO-NMD)

PROJECT PLAN

Starting point: which one is the most critical symptom for NMD patients?

How do we get this information from patients?

List of NMD symptoms (28), developed with PAGs and the ERN ExeC


LIST OF SYMPTOMS

- 1) Muscle fatigue
- 2) Mental fatigue
- 3) Muscle weakness
- 4) Muscle stiffness
- 5) Coordination e/o unbalance problems
- 6) Muscle pain
- 7) Impaired physical function/activity
- 8) Joint pain and/or swollen joints
- 9) Symptoms suggestive of cardiac impairment
- 10) Involuntary muscle contraction
- 11) Neuropathic pain
- 12) Vision impairment
- 13) Hearing impairment
- 14) Chewing and swallowing difficulties
- 15) Breathing difficulties
- 16) Speech problems
- 17) Headache
- 18) Cognitive impairment
- 19) Mental health issues
- 20) Behavioural impairment
- 21) Tingling and/or numbness
- 22) Dizziness
- 23) Sleep disturbance
- 24) Sexual dysfunction
- 25) Gastrointestinal dysfunction
- 26) Urinary dysfunction
- 27) Subjective sensory loss or extreme sensitivity to touch, temperature and/or pain
- 28) Autonomic symptoms



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 **Network**
Neuromuscular
Diseases (ERN EURO-NMD)

EURO-NMD

Building bridges and breaking barriers
in rare neuromuscular diseases

ERN NMD PROM FOR ADULTS

Welcome to the Assessment of the Neuromuscular Disease (NMD) patients' symptom burden

Thank you for participating in our survey. Your feedback is important.

This survey will allow us to better identify your symptom burden!

This survey is only for adult patients (18 years and older)!

**The survey must be completed by the patient only! If you are not able to complete it,
please ask help to your caregiver!**

Data protection. This is an anonymous survey.

**We are not collecting any personal data and we will not share or make public
information that can link you to individual responses presented in our final report.**

Please continue the survey if you agree on that thank you

SURVEY – ERN-NMD FOR ADULTS

- Survey in English and Italian
- General information: Gender, age-range, country, name of disease
- List of 28 symptoms with their explanation and a severity scale

ERN NMD PROM FOR ADULTS

In this page, you should provide an answer to all queries, quantifying how much a specific symptom (or a group of symptoms) is affecting your daily life

* 5. **Muscle Fatigue** (i.e., overwhelming sense of tiredness, lack of energy and feeling exhausted)

0 (None)

1 (Mild)

2 (Moderate)

3 (Severe)

- **1108 answered obtained for all NMDs**

LIST OF PATHOLOGIES

Have you been diagnosed with one of the following diseases?

- Mitochondrial Diseases
- Duchenne or Becker Muscular Dystrophy
- Facioscapulohumeral Muscular Dystrophy (FSHD)
- Myotonic Dystrophies
- Other Muscular Dystrophies (excluding Duchenne, Becker, FSHD, myotonic dystrophie)
- Metabolic Myopathies
- Idiopathic Inflammatory Myopathies
- Myofibrillar Myopathies
- Congenital Myopathies and Congenital muscular dystrophies
- Skeletal Muscle Channelopathies
- Amyotrophic Lateral Sclerosis and other motor neuron diseases (excluding SMA)
- Spinal Muscular Atrophy (SMA)
- Myasthenia gravis
- Congenital Myasthenic Syndromes
- Charcot-Marie Tooth and related neuropathies (HNNP, HSAN, dHMN)
- Hereditary Amyloid Neuropathy
- Neuropathies associated with haematological disease and monoclonal gammopathy (MGUS, POEMS, ETC)
- Inflammatory and Dysimmune Neuropathies
- Small Fibre Neuropathies
- Idiopathic Neuropathies
- I do not know the name of my disease
- Other

PRELIMINARY DATA: Prevalent conditions

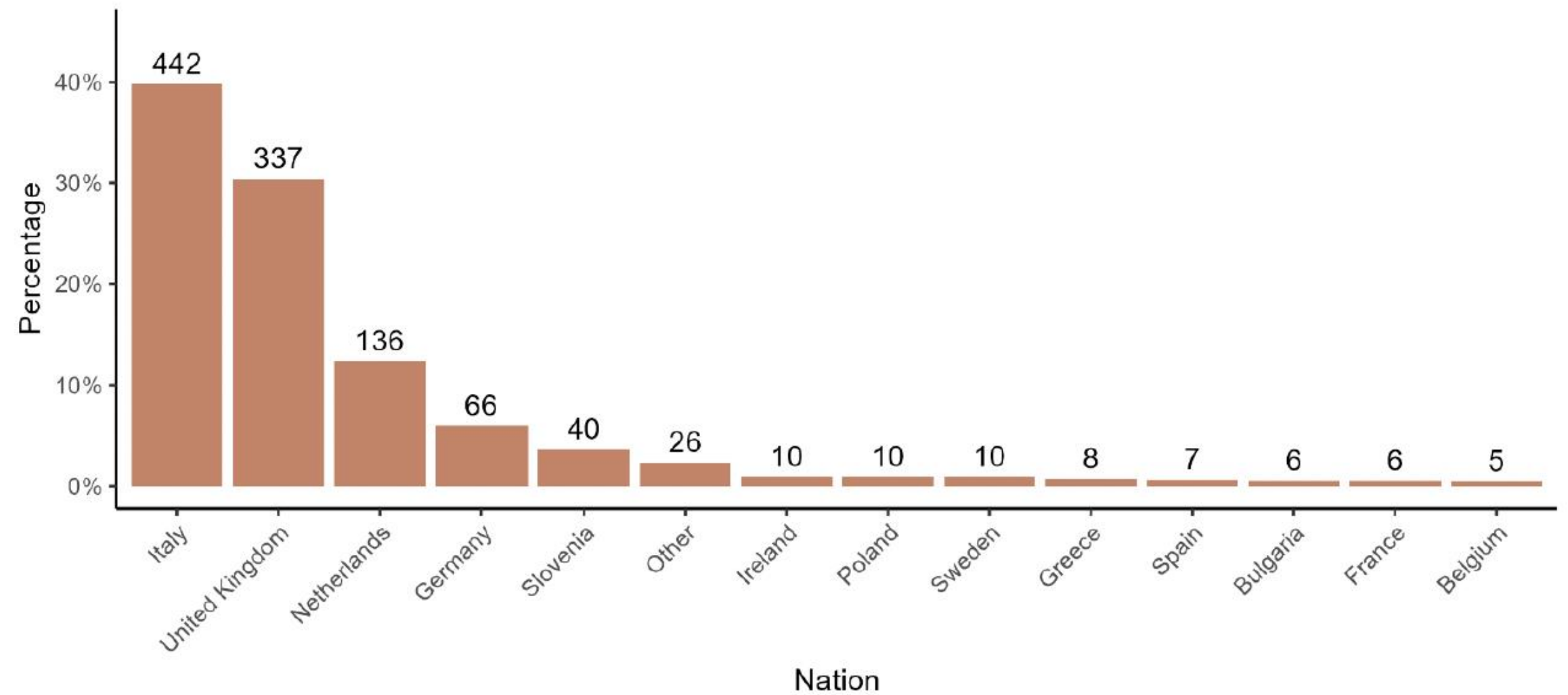
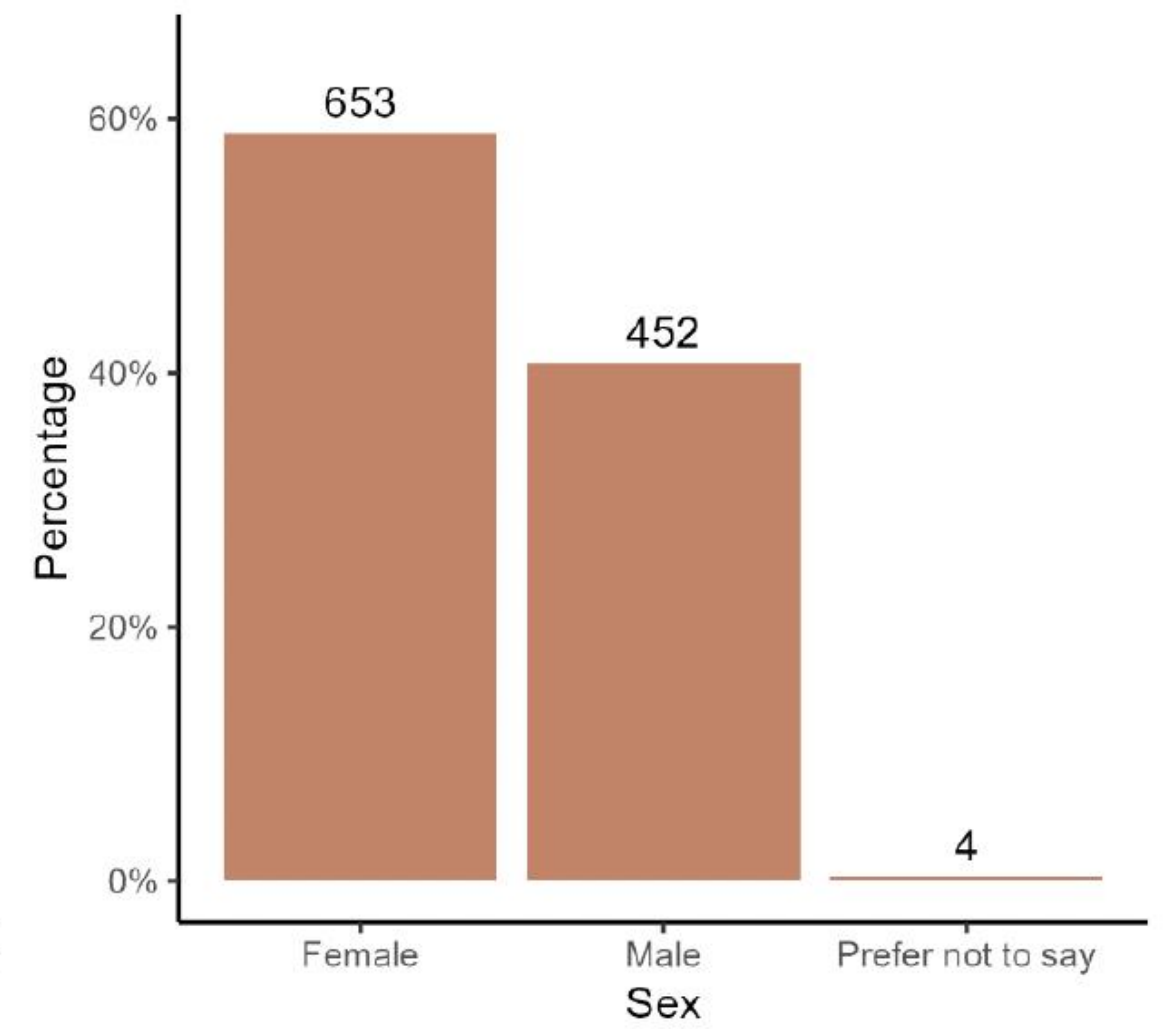
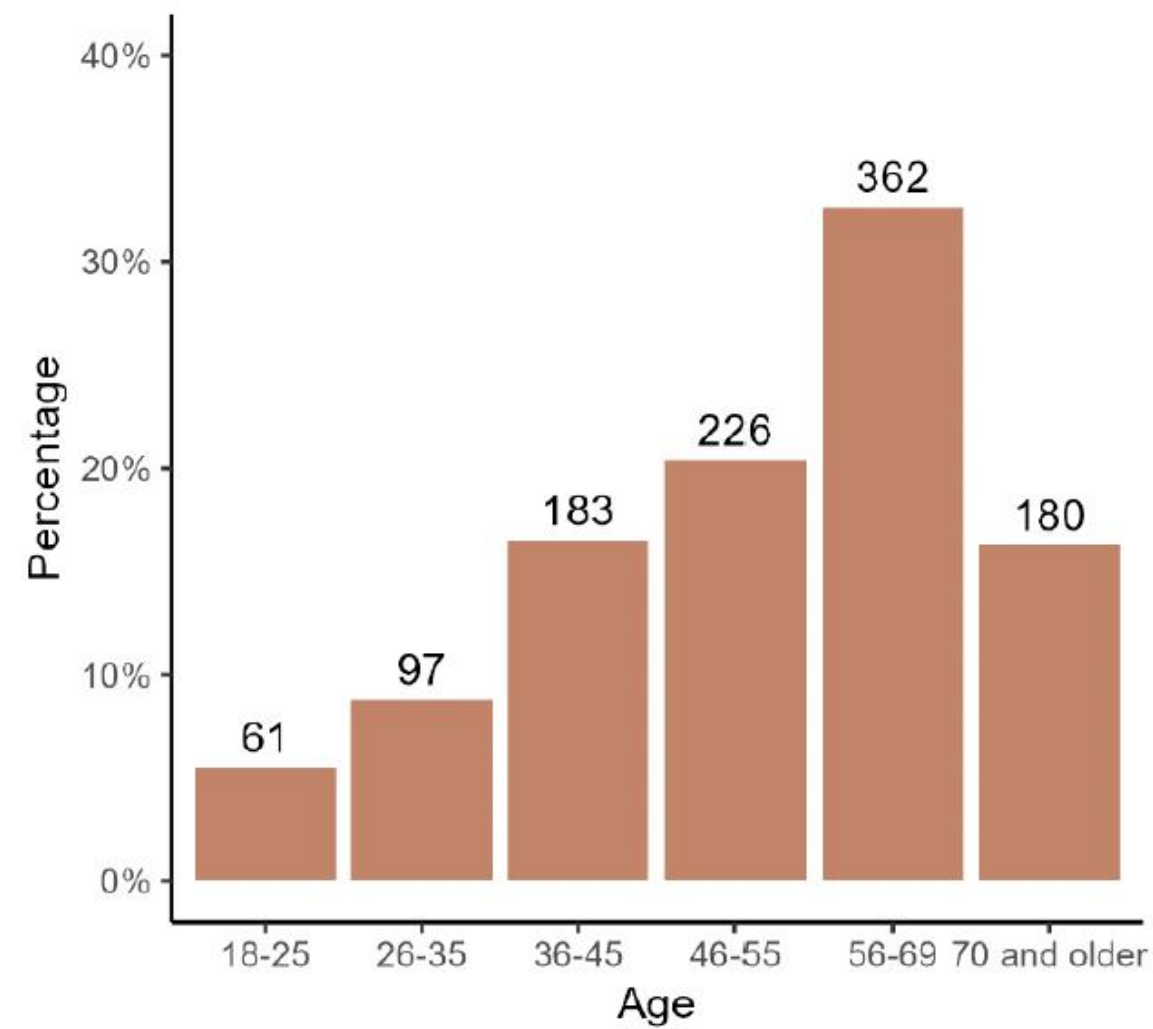
Have you been diagnosed with one of the following diseases?	
Answer Choices	%
Mitochondrial Diseases	18
Duchenne or Becker Muscular Dystrophy	4
Facioscapulohumeral Muscular Dystrophy (FSHD)	6
Myotonic Dystrophies	4
Other Muscular Dystrophies (excluding Duchenne, Becker, FSHD, myotonic dystrop	6
Metabolic Myopathies	2
Idiopathic Inflammatory Myopathies	3
Myofibrillar Myopathies	0
Congenital Myopathies and Congenital muscular dystrophies	2
Skeletal Muscle Channelopathies	0
Amyotrophic Lateral Sclerosis and other motor neuron diseases (excluding SMA)	1
Spinal Muscular Atrophy (SMA)	7
Myasthenia gravis	4
Congenital Myasthenic Syndromes	1
Charcot-Marie Tooth and related neuropathies (HNNP, HSAN, dHMN)	25
Hereditary Amyloid Neuropathy	0
Neuropathies associated with haematological disease and monoclonal gammopathy (0
Inflammatory and Dysimmune Neuropathies	1
Small Fibre Neuropathies	2
Idiopathic Neuropathies	1
I do not know the name of my disease	2
Other	12

- Charcot-Marie Tooth (25%)
- Mitochondrial diseases (18%)
- SMA
- FSHD
- Other dystrophies

Confidential data

Mancuso et al, submitted to OJRD,
under review

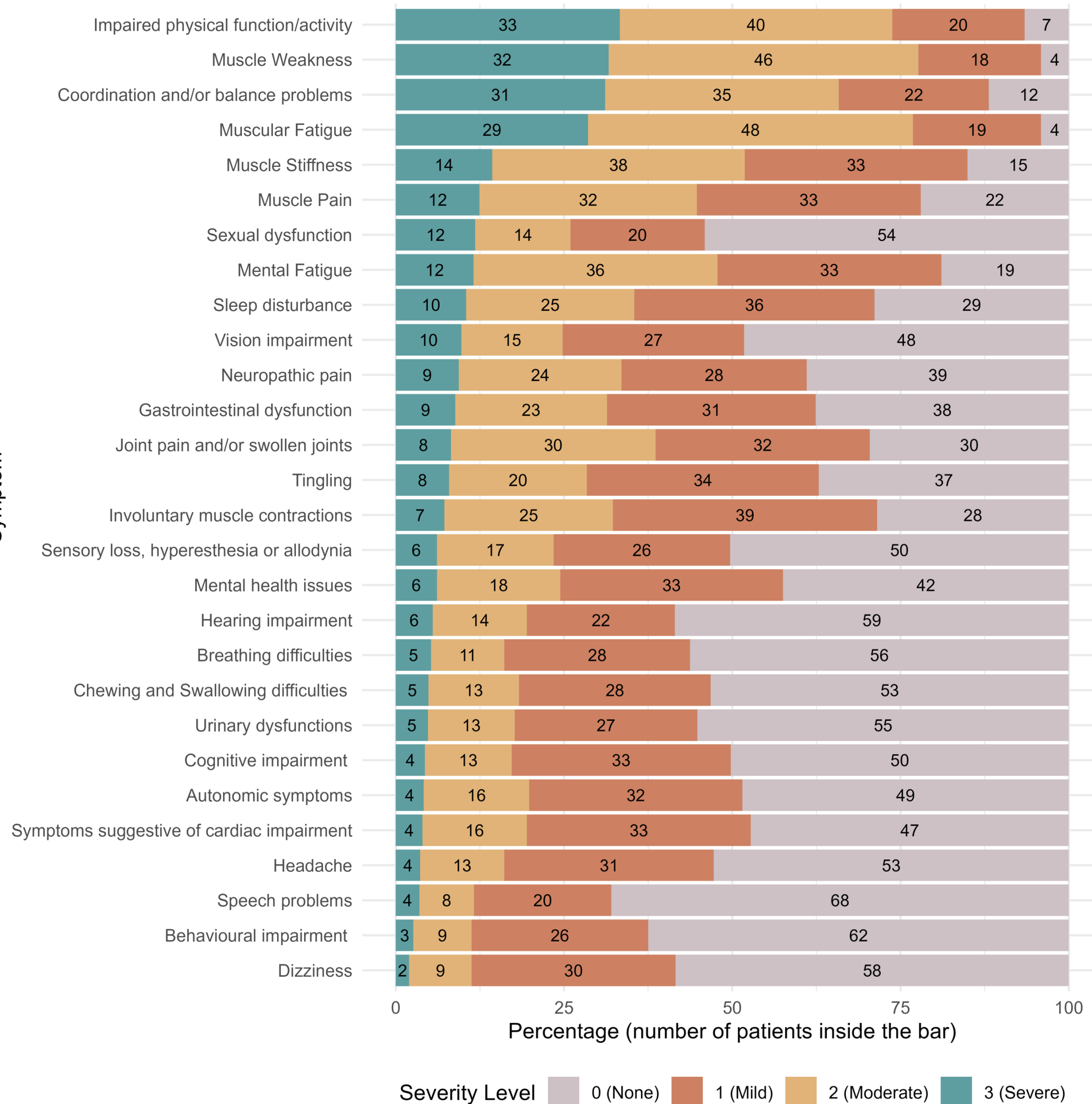
Demographic data



Confidential data

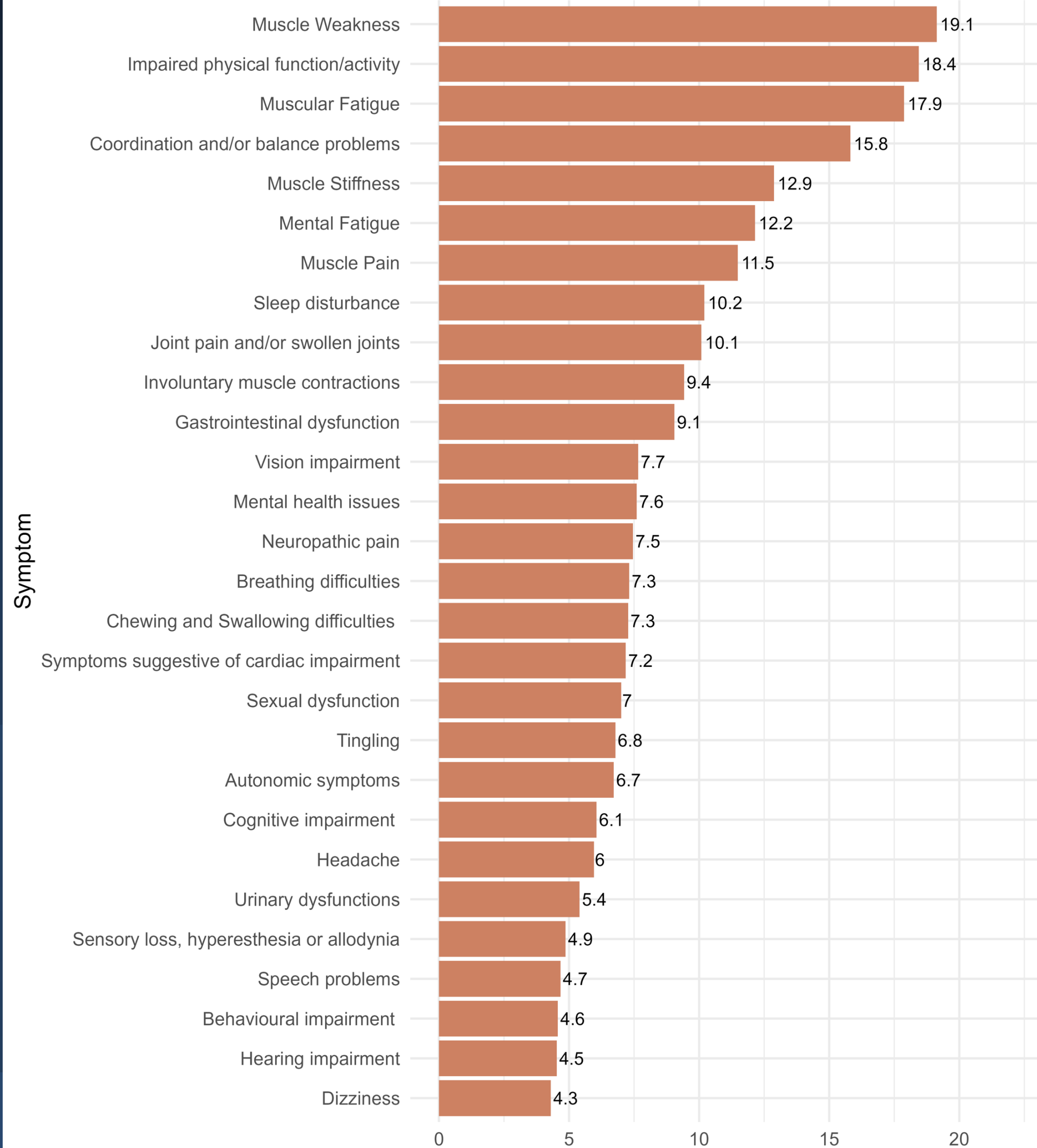
Symptoms quantification: severity scale

Symptom



Confidential data

Symptoms quantification: MDCA severity score

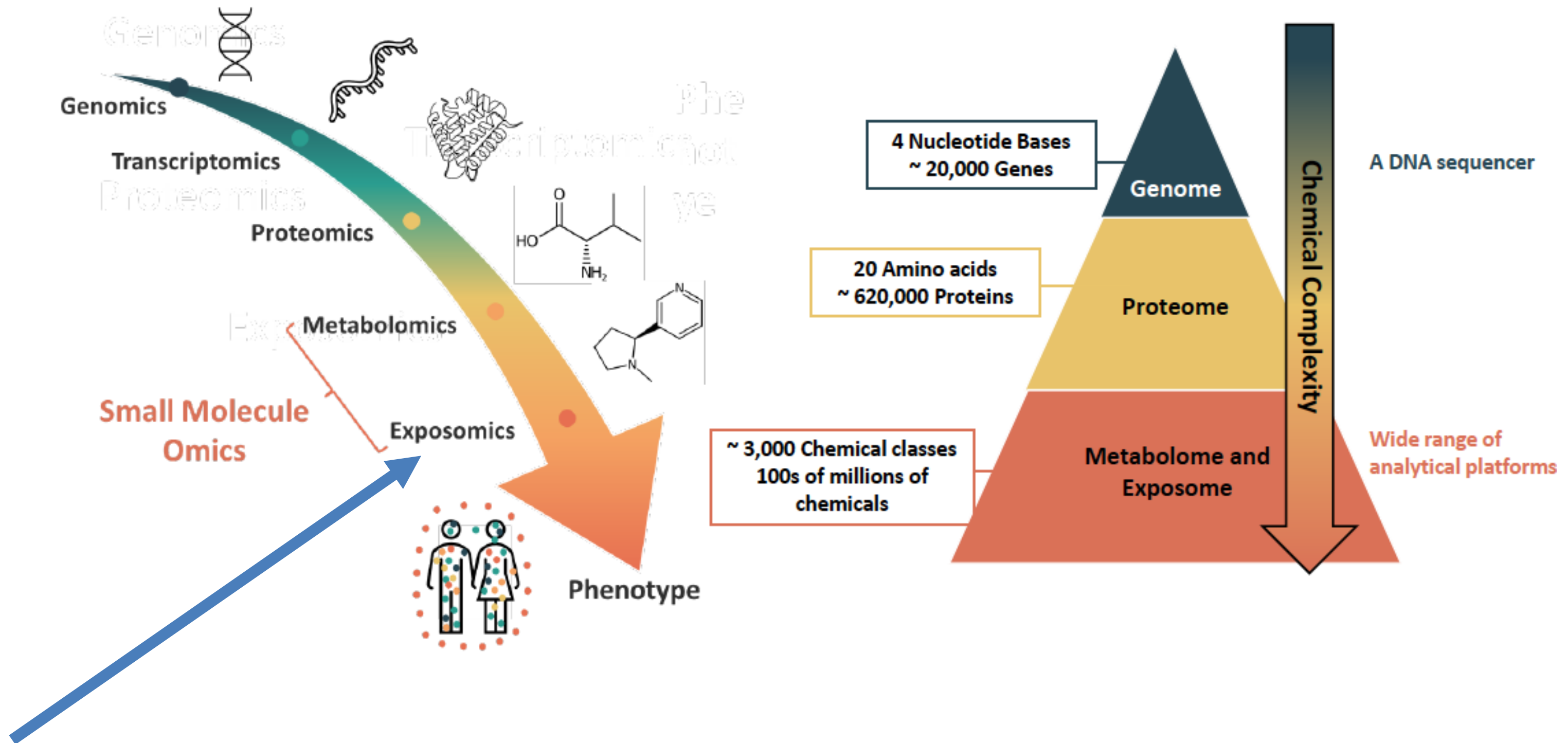


Confidential data

PROMMY APP

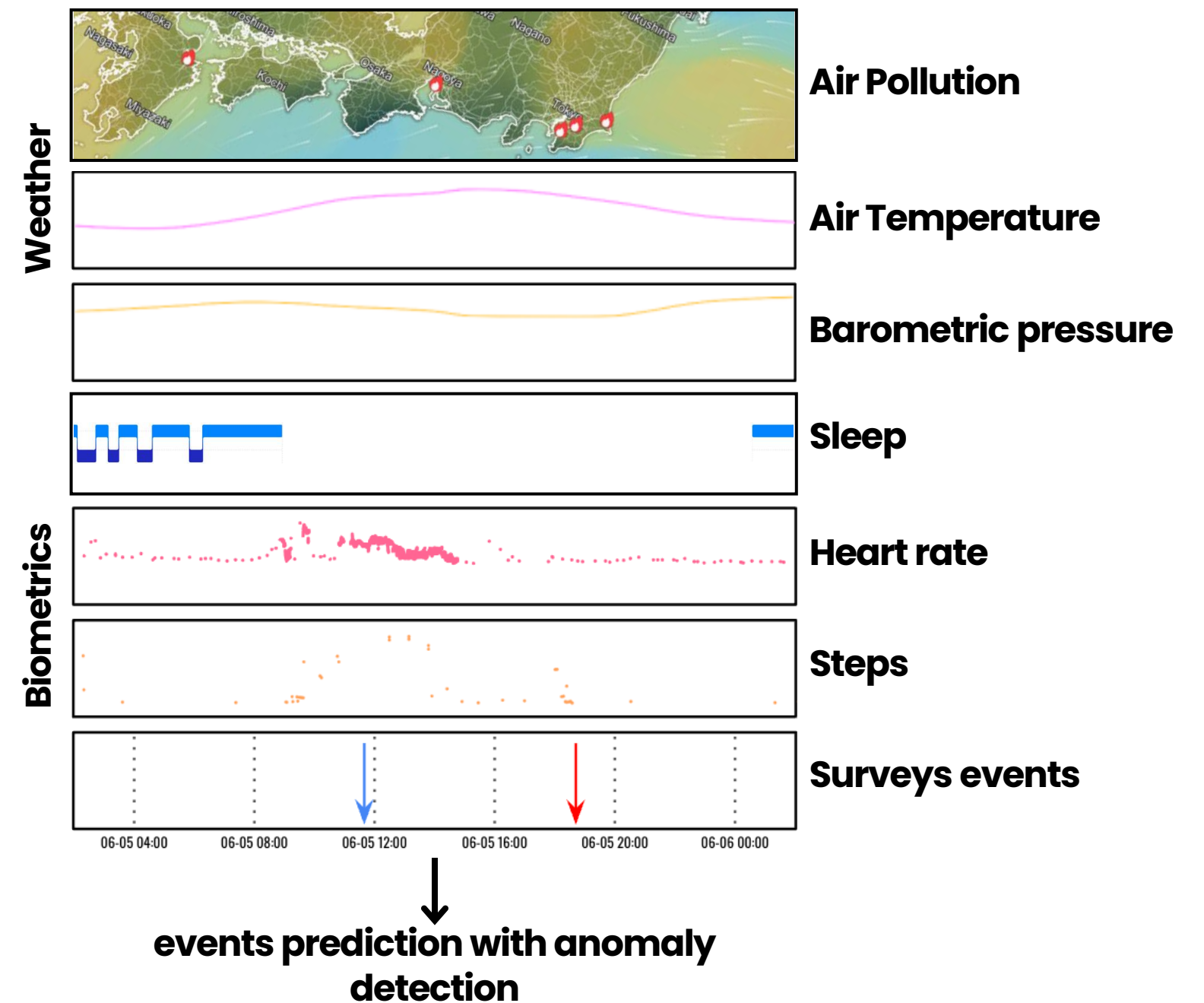
- ▶ Patient activation
- ▶ Patient data sharing
- ▶ Security aspects
- ▶ Data Gathered by the Prommy App
 - › Self evaluation
 - › PROMS

The "Omics" Cascade



Courtesy of Prof. Dr.Emma L. Schymanski

Digital Biomarker & Environmental Triggers for Pain, Fatigue or.....



Data Gathered by the Prommy App

- The Prommy app allows patients to periodically assess their health status in relation to their disease and its symptoms.
- This is achieved through two types of interactions: Self-Evaluations and PROMs.

Self-Evaluation

How do you feel today (at the installation and *weekly* pop-up, but also when needed/desired)



If sad.... What is the annoying symptom that makes you sad (multiple choices allowed)?



Muscle Fatigue

Muscle Weakness

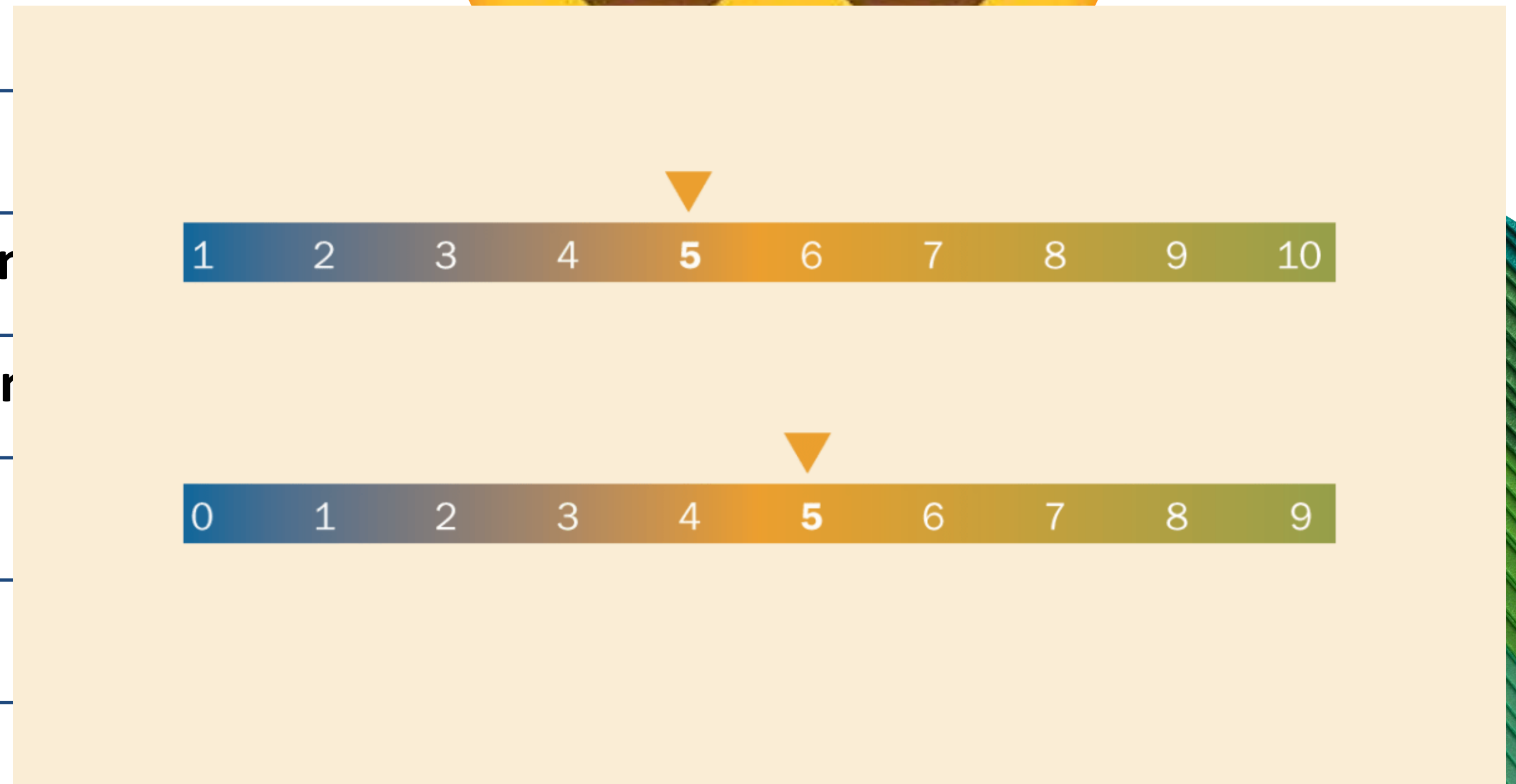
Impaired physical function

Coordination and/or balance

Muscle Stiffness

Muscle Pain

Other



The most bothersome symptoms. Orphanet J, submitted

PROMs

- Every 6 months, the patient will receive a pop-up asking him/her to fill in disease-related PROMs and the new PROM (under development)
- Self evaluation and PROMs may be exported as PDF and share with the physician and the ERN EURO-NMD Clinical registry
- Under consideration: personal wallet for patients

Conclusions and future directions

- ✓ We have developed a robust questionnaire that allowed us to understand the 5 most critical symptoms in all neuromuscular diseases
- ✓ Developed PROMMY (in collaboration with Devitalia SRL): Data safety, Unilateral communication from Prommy to the Registry, easy to use
 - Ready to be launched in both Android and iOS
 - Multilanguage will follow (now set fo ENG and ITA)

8th ERN EURO-NMD ANNUAL MEETING

Essen University Hospital, Germany

5th - 7th March 2025



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THANK YOU

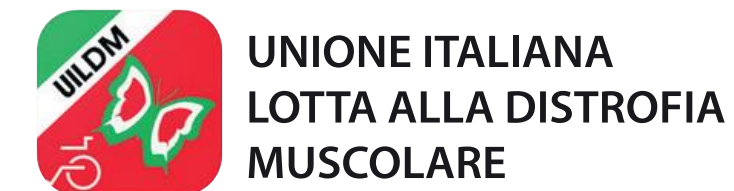


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Network
Neuromuscular Diseases (ERN EURO-NMD)



Grateful to FL & all patients and to the ERN ExeC



and all other patient associations involved in the project!