

# REiNS functional working group

---

Winter 2017 Meeting

December 4, 2017



Response Evaluation In Neurofibromatosis Schwannomatosis  
INTERNATIONAL COLLABORATION

# Goal

- To identify standardized functional measures appropriate for use as endpoints in NF clinical trials
- Functional measure outcomes
  - Outcomes that focus on a patient's ability to perform specified activities that are a meaningful (to the patient), part of typical (e.g., daily) life
- Our group reviews measures for types of physical functioning that can be affected by NF
  - hearing, facial function, pulmonary function (breathing), walking and sleep



# Completed projects

Hearing and facial function outcomes for neurofibromatosis 2 clinical trials

- For hearing endpoints, the functional group endorsed the use of maximum word recognition score as a primary endpoint, with the 95% critical difference as primary hearing outcomes
- The group recommended use of the scaled measurement of improvement in lip excursion (SMILE) system for studies of facial function.

Correspondence to  
Dr. Plotkin:  
plotki@stanford.edu

endpoints for use in clinical trials of patients with NF2. The use of common endpoints should improve the quality of clinical trials and foster comparison among studies for hearing loss and



# Completed projects

Sleep and pulmonary outcomes for clinical trials of airway plexiform neurofibromas in NF1

Scott R. Plotkin, MD,  
PhD

ABSTRACT

- For patients with airway PNs, polysomnography, impulse oscillometry, and spirometry should be performed to identify abnormal function that will be targeted
- The functional group endorsed the use of the AHI as the primary sleep endpoint, and pulmonary resistance at 10 Hz (R10) or forced expiratory volume in 1 or 0.75 seconds (FEV1 or FEV0.75) as primary pulmonary endpoints

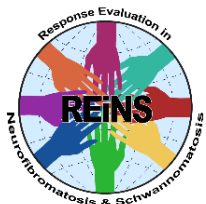
Response Evaluation in  
Correspondence to  
Plotkin:

**Conclusions:** These recommended sleep and pulmonary evaluations are intended to provide re-



# Overview of ongoing projects

- Outcome measures for assessing muscle strength
  - Srivandana Akshintala, David Stevenson
- Dysphagia outcome measures
  - Heather Thompson, Ann Blanton



# Assessing muscle strength

- A pilot study of using hand held dynamometry for muscle strength testing in children and adults with NF
  - Primary objective: To assess the reliability of measuring muscle strength using HHD
- Muscle weakness has been described in NF
  - primary myopathy, central nervous system dysfunction, abnormalities of peripheral nerves, spinal tumors
- Clinical trials targeting PNs in children with NF1 have anecdotally shown to decrease functional impairments including muscle weakness
- Functional outcome measures are therefore needed to assess clinical benefit, in particular, muscle strength



# Methods for strength testing

- Manual Muscle Testing
- Isokinetic dynamometers
- Hand held dynamometry
- Handgrip strength



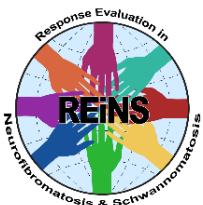
Douma et al 2014

## HHD

- Has been validated against isokinetic dynamometers
- Reliability studied in many patient populations with performance varying based on patient population and muscle group being tested
- Has been used as an efficacy measure in clinical trials for amyotrophic lateral sclerosis

# Study design

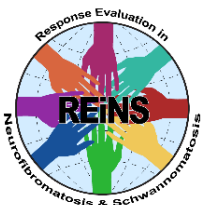
- Key eligibility
  - Patients  $\geq 5$  years with clinically confirmed NF1 or NF2 or a known NF mutation
  - At least 1 muscle group that is weak per MMT ( $<5/5$  strength) out of a list of pre-selected potential muscle groups
- Study design
  - Evaluate muscle strength in 20 patients using HHD
  - Assess strength in 2 muscle groups 3 times each
  - Obtain clinical data such as age, sex, weight, height, handedness, muscle strength by MRC scale, and h/o NF manifestations
  - Assess reliability of strength measurement using ICC





# Dysphagia outcome measures

- Dysphagia refers to disorders related to swallowing
  - Occurs in individuals with Neurofibromatosis
- Extensive literature search performed (Spring 2017)
- Outcome measures considered
  - Bedside swallowing screen (3oz water test)
  - Endoscopic Evaluation of Swallowing (FEES)
  - Videofluoroscopic Evaluation of Swallowing (VFSS)
- Recommendations
  - Three ounces of water test + pulse oximetry for screening
  - Videofluoroscopic Study for further evaluation following a failed screening
    - Modified Barium Swallow Tool (MBSImp, Martin-Harris et al., 2008)
    - Penetration-aspiration scale (Coyle, 2017)



# Acknowledgements

## **REiNS**

## **CTF**

- Scott Plotkin
- Brigitte Widemann
- Kaleb Yohay
- Andrea Gross
- Jaishri Blakeley
- Michael Fisher
- Judith Goldberg
- Nashwa Khalil
- Barbara Johnson
- Heather Thompson
- Ann Blanton
- Simone Ardern-Holmes
- Dusica Babovic
- Andrea Baldwin
- Fred Barker
- Rebecca Betensky
- Joni Doherty
- Rachel Ershler
- Gareth Evans
- Rosalie Ferner
- Kathy Gardner
- Tessa Hadlock
- Chris Halpin
- Trent Hummel
- Allen Julian
- Chris Moertel
- Rebecca Mullin
- Kent Robertson
- Betty Schorry
- Carolyn Sidor
- William Slattery
- James Tonsgard
- David Viskochil
- Ute Wahllander
- Brad Welling
- David Wolf

