- If sharing any data or information from these slides generated by the REiNS International Collaboration, please acknowledge the authors, group chairs, and specific working group.
- If using any information presented with a citation, please reference the primary source.

REiNS Patient Representative Membership and Activities

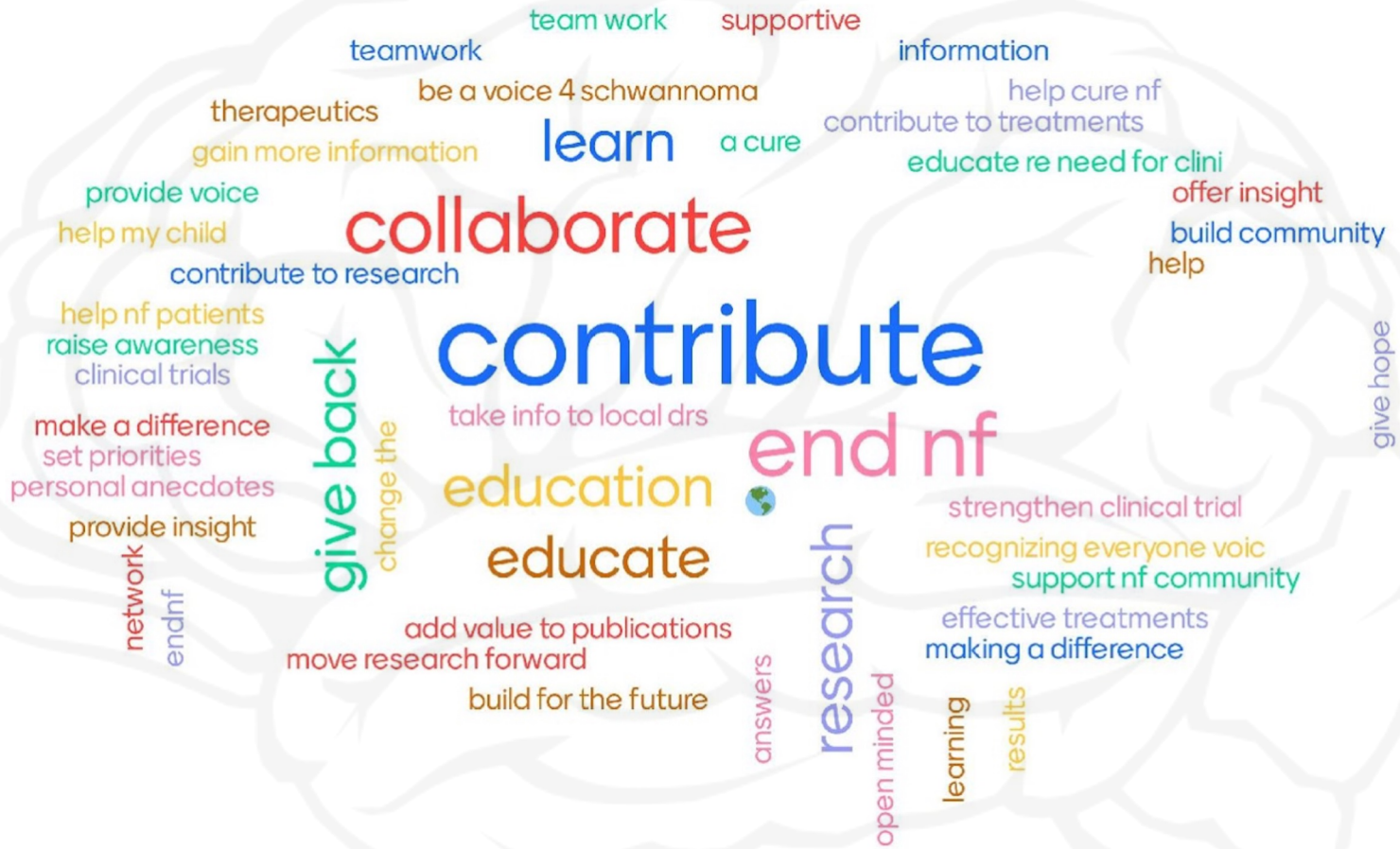
Vanessa Merker, PhD

on behalf of the REiNS Patient Representative Working Group

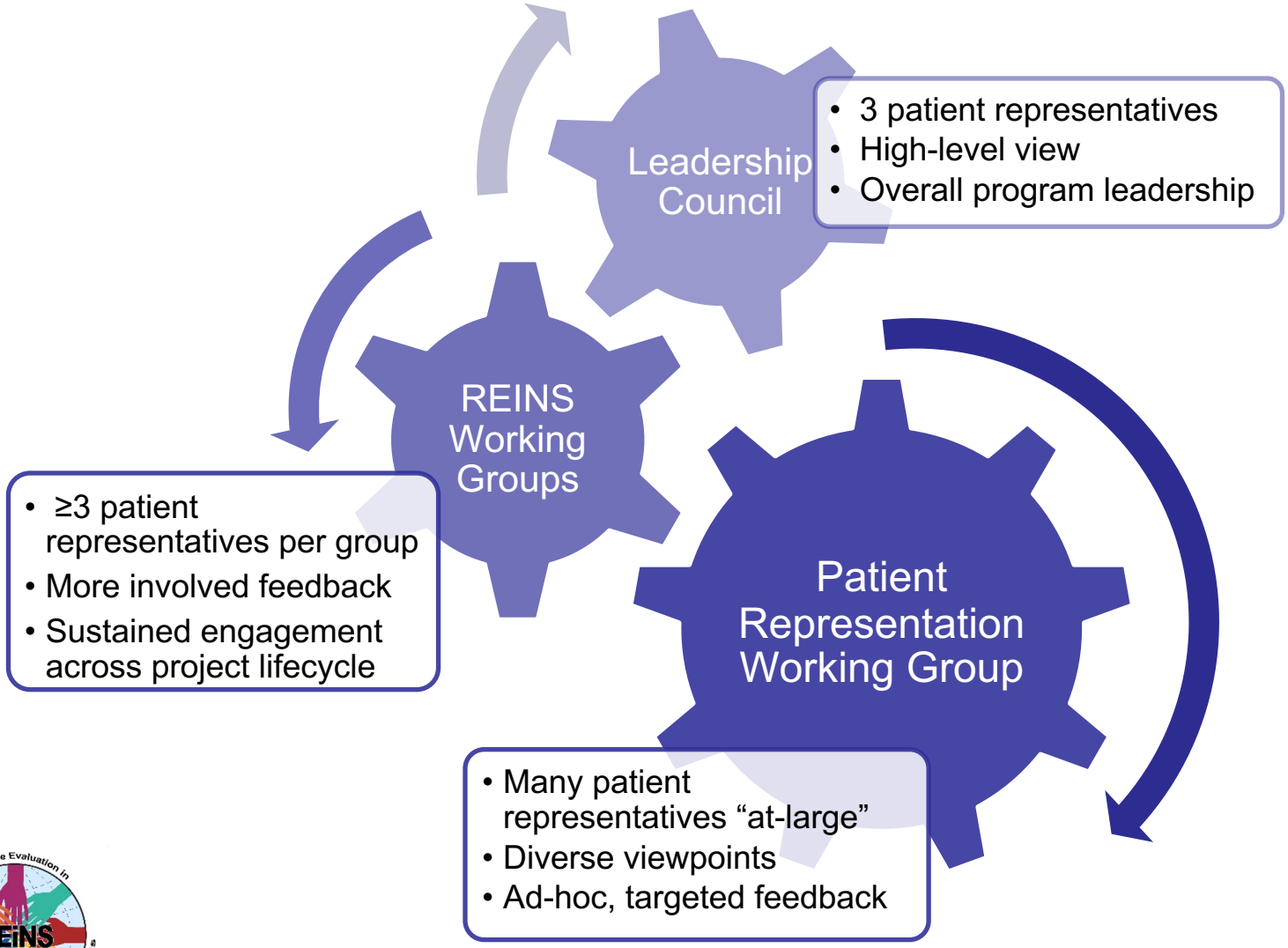
Response Evaluation In Neurofibromatosis Schwannomatosis
INTERNATIONAL COLLABORATION

June 2022

What do you hope to accomplish by being a REINS patient representative?



Patient Engagement in REiNS



REiNS Patient Representative Working Group

Researcher Chair: Vanessa Merker

Patient Representative Co-Chairs: Andrés Lessing, Claas Röhl

Scientific

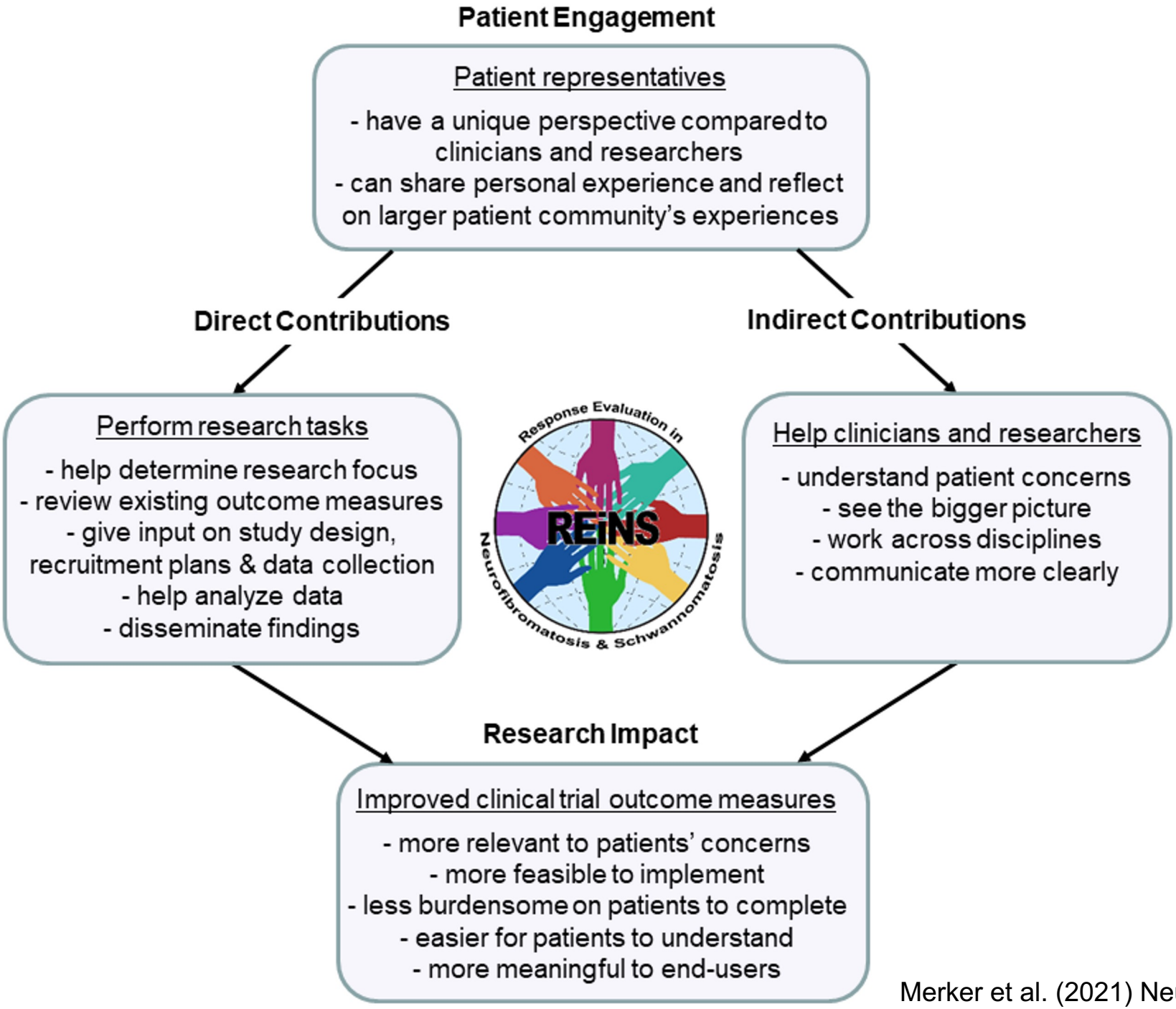
- REiNS Working Groups
- Clinical Trial Design Input
- Dissemination (Miranda McManus)

Operational

- Recruitment (Andrés Lessing)
- Education (Claas Röhl)
- Evaluation (Vanessa Merker)

Recruitment Updates

- Current membership: 55 representatives
  - From the US, Canada, UK, France, The Netherlands, Austria, Belgium, Denmark, & Australia
  - 42% people with NF/SWN, 58% family members/caregivers of someone with NF/SWN
  - 65.5% NF1, 25.5% NF2, 9% SWN
- Alternating meeting times and record meetings to facilitate participation across time zones
  - Second Saturday, 1-2pm ET
  - Second Wednesday, 7-8pm ET



Merker et al. (2021) Neurology

Patient Representative Feedback on Research Studies

Disfigurement rating scale (Observers & Patients)
Survey on communication difficulties
Survey on sleep
NF1: Plexiform neurofibroma trial MPNST triple combination drug trial MR-HiFU Trial for Atypical Neurofibromas Study of MEK inhibitors' effect on bone
NF2: Adding qualitative interviews to platform trial
SWN: Platform trial for pain
Vision restoration/vision preservation therapies

To present your NF research, email vmerker@mgh.harvard.edu. Open to all; REiNS participation not required.

Patient Representative Feedback on Research Studies

- 20 projects presented as of 8/2023
  - 14 NF1, 2 NF2, 2 SWN, and 2 applicable to all
- Clinical Trial Design
  - Secondary prevention for plexiform neurofibromas
  - MR-HiFU for Atypical Neurofibromas
  - MPNST triple combination therapy
  - NF2 hearing loss prevention
  - Platform trial for schwannomatosis pain
- Input on other studies (natural history, clinical outcome development studies, etc.)
- Feedback on surveys, PROs, and other patient-facing materials

To present your NF research, email vmerker@mgh.harvard.edu. Open to all; REiNS participation not required.

How to Join REiNS

We always accept new members on an ad-hoc basis.
We also run targeted rounds of recruitment every few years to onboard larger cohorts of diverse patient representatives simultaneously.

To join or refer a new member, email vmerker@mgh.harvard.edu

Onboarding steps:

- Fill out brief online application
- Get matched to a current patient representative ‘mentor’
- Review brief training materials to get oriented

Learn About Being
An NF Patient Representative

Next Steps

- Finish patient representative survey to update membership rolls & decide when/how to target next recruitment round
- Dissemination updates
- Increase feedback on research studies
  - Solicit more presenters
  - Develop presentation template and feedback forms
  - Conduct follow-up evaluation of patient representative program

Patient Representative Group

Disseminating REiNS Recommendations

Miranda McManus, MS
on behalf of the REiNS Patient Representative Dissemination subcommittee

Response Evaluation In Neurofibromatosis Schwannomatosis
INTERNATIONAL COLLABORATION

Dissemination updates

- Re-organization of the publication information on the REiNS website
- Development of 2-3 sentence summaries for all REiNS papers
- Creation of the REiNS Recommendations Toolbox
  - Advertising the Toolbox at this year's NF Conference

Home

Working Groups

Presentations

Publications

Recommendations

News & Meetings

Patient Representation

FDA Interactions

Member Info

Support

Photo Gallery

For Members Only

REiNS Publications

REiNS has published recommendations in three supplements in the journal *Neurology*. Click these links to access the full supplements:

Supplement I (2013)

Supplement II (2016)

Supplement III (2021)

Below is a list of the articles published in these supplements organized by topic. Click each topic to jump to the articles:

NF1—Neurofibromatosis type 1

NF2—*NF2*-related schwannomatosis (formerly called neurofibromatosis type 2)

SWN—*SMARCB1*-related schwannomatosis, *LZTR1*-related schwannomatosis, 22q-related schwannomatosis, schwannomatosis-NOS (not otherwise specified), or schwannomatosis-NEC (not elsewhere classified)

Home

Working Groups

Presentations

Publications

Recommendations

News & Meetings

Patient Representation

FDA Interactions

Member Info

Support

Photo Gallery

For Members Only

About REiNS

Achieving consensus for clinical trials: The REiNS International Collaboration

Plotkin SR, Blakeley JO, Dombi E, Fisher MJ, Hanemann CO, Walsh KS, Wolters PL, Widemann BC. Achieving consensus for clinical trials: the REiNS International Collaboration. *Neurology*. 2013;81(21 Suppl 1):S1-5; doi:10.1212/01.wnl.0000435743.49414.b6

> *Most early NF clinical trials used study designs similar to those used in cancer trials; however, because of differences in disease symptoms and tumor growth compared to solid cancers, there is a need for new designs that are better suited to NF. The Response Evaluation in Neurofibromatosis and Schwannomatosis (REiNS) International Collaboration was established in 2011 to reach agreement within the NF community about the design of future trials, with an emphasis on measures of response to treatment, also known as endpoints. This paper is an introduction to the first REiNS supplement published in 2013, which includes the first series of recommendations by the REiNS Collaboration.*

Abstract Full Text (Web) Full Text (PDF) **NF1 NF2 SWN**

Conclusions and future directions for the REiNS International Collaboration

Widemann BC, Blakeley JO, Dombi E, Fisher MJ, Hanemann CO, Walsh KS, Wolters PL, Plotkin SR. Conclusions and future directions for the REiNS International Collaboration. *Neurology*. 2013;81(21 Suppl 1):S41-4; doi:10.1212/01.wnl.0000435748.79908.c5

> *This paper is the conclusion to the first REiNS supplement published in 2013. It summarizes the first series of recommendations, addresses how they should be used in the context of NF clinical trials, and discusses future recommendations under development.*

Abstract Full Text (Web) Full Text (PDF) **NF1 NF2 SWN**

Consensus for NF clinical trials: Recommendations of the REiNS collaboration (Supplement II)

Widemann BC, Plotkin SR. Consensus for NF clinical trials: Recommendations of the REiNS collaboration (Supplement II). *Neurology*. 2016;87(7 Supplement 1):S1-S3; doi:10.1212/WNL.0000000000002930

> *This paper is an introduction to the second REiNS supplement published in 2016, which provides an update on clinical trials that have used the recommended measures from the first supplement. It also summarizes new recommendations for additional measures of response to treatment (endpoints) included in the rest of the supplement.*

Abstract Full Text (Web) Full Text (PDF) **NF1 NF2 SWN**

Wolters et al. (2013) Patient-reported outcomes in neurofibromatosis and schwannomatosis clinical trials.

REiNS developed a systematic process to rate existing patient-reported outcomes for use in NF clinical trials. Using this process, they reviewed measures of pain intensity and recommended using the NRS-11, a 0-10 pain scale.

Cannon et al. (2021) Perspectives of Adults with Neurofibromatosis 1 and Cutaneous Neurofibromas.

This paper presents a survey exploring the experiences of NF1 adults with cutaneous neurofibromas, taking into account tumor location, size, color, pain, and itchiness. The survey also asked patients' opinions about treatment options, what would be considered a successful treatment, and what side effects would be acceptable.

Home

Working Groups

Presentations

Publications

Recommendations

News & Meetings

Patient Representation

FDA Interactions

Member Info

Support

Photo Gallery

For Members Only

REiNS Recommendations

This table provides a summary of all current REiNS consensus recommendations for neurofibromatosis and schwannomatosis clinical trials. The peer-reviewed REiNS publications that discuss each of these recommendations are linked from the table. There are also links to each of the recommended outcome measures and/or to the relevant subsections of each paper.

	Clinical Trial Endpoint or Domain (full paper linked)	Recommended Primary Measure(s) or Key Points	Recommended Secondary/Exploratory Measure(s)
Biomarkers	Clinical annotation	· Minimal clinical dataset (Table 2)	· Recommendations for sample collection and methodology
	Cutaneous neurofibroma (cNF)	· Recommended sample collection for cNF trials · Recommended annotation for cNF biopsy samples (Table 2)	
	Genotype-phenotype correlation	· NF1—suggested that individuals with mutations p.Met992del and p.Arg1809Cys not be included in natural history studies or clinical trials investigating plexiform neurofibromas · NF2—genetic severity score	
Functional Outcomes	Hearing	· Maximum word recognition score (WRS) (Table 2)	· Pure-tone average (PTA)
	Facial function	· Scaled Measurement of Improvement in Lip Excursion (SMILE) analysis o Download FACEGRAM app (must be a member of the Sir Charles Bell Society)	· House-Brackmann scale

REiNS International Collaboration

Interested in helping the NF community reach consensus on outcome measures for clinical trials? Join REiNS! Email reinscollaboration@gmail.com for more info. ALL ARE WELCOME!

REiNS Working Groups:

- Patient Reported Outcomes
- Functional Outcomes
- Imaging
- Visual Outcomes
- Neurocognitive Outcomes
- Disease Biomarkers
- Cutaneous Neurofibromas
- Patient Representatives
- Gene-Targeted Therapy

Check out our NEW TOOLBOX to access all the REiNS recommendations in one place!
https://bit.ly/REiNSrec

SCAN ME

Future plans

- Papers from the upcoming REiNS supplement
- More extensive plain language summaries
  - Exploring the use of ChatGPT to expedite this process
  - Also exploring graphical abstracts
- Exploring ways to make it easier to update the website
  - Thanks to Pam Wolters for all of your help and putting up with us!!
  - Embedded files like Google Drive?

REiNS Dissemination subcommittee

- Miranda McManus, chair
- Andrea Gross
- Beverly Oberlander
- Diana Haberkamp
- Lara Mukabenov
- Madalyn Gibson-Williams
- Sharon Loftspring
- Steven Sheard
- Shannon Weaver
- Vanessa Merker