

Response Evaluation In Neurofibromatosis Schwannomatosis
INTERNATIONAL COLLABORATION

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REiNS Patient Reported Outcomes (PRO) Working Group

REiNS Committee Meeting

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Heather Thompson, PhD CCC-SLP
California State University, Sacramento

On behalf of the REiNS PRO group



Response Evaluation In Neurofibromatosis Schwannomatosis
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REiNS PRO Working Group

Taryn Allen, PhD
Andrea Baldwin, CRNP
Caroline Barnett
Amanda Bergner, MS CGC
Kim Bischoff
Rosalie Ferner, MD
Barbara Franklin, BS
Krista Frederick
Chris Funes, MS
Kathy Gardner, MD
Deborah Gold, MD
Cynthia Hingtgen, MD, PhD
Kimberley Koetsier
Staci Martin, PhD
Vanessa Merker, BS
Drea Peterson
Melissa Reider-Demer, NP
Stephanie Reeves
Betty Schorry, MD
Taylor Smith, PhD
Heather Thompson, PhD. CCC-SLP
Jim Tonggard, MD
Ana-Maria Vranceanu, PhD
Karin Walsh, PsyD
Pam Wolters, PhD
Ann Blanton, PhD CCC-SLP
Kevin Franck, PhD MBA CCC-A
Brad Welling, MD, PhD, FACS

National Cancer Institute
National Cancer Institute
University of Toronto
Johns Hopkins University
NF Network
Guy's Hospital
Patient Representative
Patient Representative
MGH/Harvard
University of Pittsburgh
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Patient Representative
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National Cancer Institute
SUNY Cortland
MEEI/Harvard
MEEI/Harvard



PRO Working Group

- Goal: To identify PRO measures appropriate for assessing clinical outcomes in NF trials
- Context of Use:
 - Treatment trials for tumors: FDA is requiring a reduction in tumor volume *in conjunction* with demonstrated clinical benefit
 - PRO as a co-primary or secondary endpoint
 - Psychosocial interventions to reduce NF symptoms or to improve quality of life: Studies need to show clinical benefit to indicate efficacy
 - PRO as a primary endpoint



PRO Working Group

- Developed a systematic methodology to review PROs
 - PRO-RATE form (6 criteria) Wolters, et al., 2013
- Determined four core domains for NF trials (≥ 8 years)
 - 1) Pain
 - Pain intensity
 - Pain interference
 - 2) Physical Functioning
 - Mobility Wolters et al., 2016
 - Upper extremity
 - 3) General QOL
- PRO subgroups (specialized domains)
 - 1) Vision-specific QOL measure Fisher et al., 2013
 - Staci Martin and Vanessa Merker

Current Work of the PRO Group

1. Finalized reviews for disease-specific PROs
2. Finalized reviews for hearing PROs for NF2
 - Hearing functioning
 - Quality of life related to hearing

Disease-specific QOL

- Disease-specific QOL measures
 - Assess individual's perceived functioning and well-being in domains typically affected by a specific disease
 - Pros:
 - Provide a more detailed description of specific problems of a disease
 - More sensitive to disease/treatment related changes of specific disease
 - Useful for assessing change in disease-specific symptoms in drug trials
 - Cons:
 - More suited to drug trials than psychosocial trials due to focus on assessing disease-related symptoms
 - Cannot use across different types of NF (e.g., psychosocial trial)
 - Challenges:
 - Limited current tools for NF
 - Some still under development or peer review; all relatively new



Disease-specific QOL

- NF1
 - INF1-QOL
 - PedsQL-NF1 module
 - PROMIS & Neuro-QOL
 - Skindex
- NF2
 - NF2 QOL
 - NFTI-QOL
 - Neary scale
 - PANQOL



Disease-Specific QOL

NF1

Criteria	INF1-QOL	Peds QL NF Module	PROMIS & Neuro-QOL	Skindex
Patient Characteristics				
Published Studies				
Item/Domain Content				
Scores Available				
Psychometric Data				
Feasibility				
MEAN				

Disease-Specific QOL

NF1

Criteria	INF1-QOL	Peds QL NF Module	PROMIS & Neuro-QOL	Skindex
Patient Characteristics				
Published Studies				
Item/Domain Content				
Scores Available				
Psychometric Data				
Feasibility				
MEAN (4)				

Disease-Specific QOL

NF1

Criteria	INF1-QOL	Peds QL NF Module	PROMIS & Neuro-QOL	Skindex
Patient Characteristics	1.00	2.75	1.50	2.50
Published Studies	1.00	1.75	2.25	2.75
Item/Domain Content	1.50	2.75	2.00	1.50
Scores Available	1.75	2.50	3.00	2.25
Psychometric Data	2.00	2.50	1.00	2.50
Feasibility	2.00	2.00	3.00	2.50
MEAN (4)	1.625	2.50	1.875	2.25

Disease-Specific QOL NF1

Peds QL NF module

Pros

- Covers a wide age range (5+)
- Items cover many domains
(16 for adult; 18 for child/adolescent)
- Simple wording of items;
format is clear
- Domain-specific total scores
available

Cons

- New – limited studies
- Long to complete
(74 items for adults; 104 for
child/adolescent)

Disease-Specific QOL

NF2

Criteria	NF2 Questions (Neary)	NFTI-QOL (Hornigold)	NF2 QOL (Cosetti)	PANQOL (Shaffer)
Patient Characteristics				
Published Studies				
Item/Domain Content				
Scores Available				
Psychometric Data				
Feasibility				
MEAN				

Disease-Specific QOL

NF2

Criteria	NF2 Questions (Neary)	NFTI-QOL (Hornigold)	NF2 QOL (Cosetti)	PANQOL (Shaffer)
Patient Characteristics				
Published Studies				
Item/Domain Content				
Scores Available				
Psychometric Data				
Feasibility				
MEAN (4)				

Disease-Specific QOL

NF2

Criteria	NF2 Questions (Neary)	NFTI-QOL (Hornigold)	NF2 QOL (Cosetti)	PANQOL (Shaffer)
Patient Characteristics	2.0	2.25	1.75	1.75
Published Studies	1.25	2.75	1.0	2.0
Item/Domain Content	2.5	1.75	1.625	2.25
Scores Available	1.0	1.75	1.875	2.25
Psychometric Data	1.0	2.25	.75	1.75
Feasibility	2.0	2.5	1.875	2.25
MEAN (4)	1.875	2.1875	1.5	2

Disease-Specific QOL NF2

NFTI-QOL

Pros

- Developed by group experienced in NF2 with recent publications (Shukla et al., 2019; Quambry et al., 2019)
- Covers the main complications of NF2
- Useful for clinical trials - yields a single score
- Good preliminary reliability (IC and test-retest) and validity (construct and discriminative)
- Excellent feasibility

Cons

- Only 16± years; no parent proxy
- Limited in scope (8 items) with no items in several areas (e.g., social/communication, eating/swallowing, energy/fatigue, cognition)
- Some items assess more than one construct (e.g., anxiety & depression)
- Different recall periods on some items
- 4 point likert-type scale across items (0-3)
- No published trials data



Disease-Specific QOL NF2

PANQOL

Pros

- Developed for individuals with VS
- Useful for clinical trials targeting VS
- Good preliminary reliability and validity
- Excellent feasibility

Cons

- No version for < 18 years (or parent proxy)
- Not used in NF2
- No published clinical trial data

Disease-Specific QOL Recommendations

- NF1
 - Peds QL NF1 module
- NF2
 - NFTI-QOL
 - PANQOL – use as an exploratory outcome measure in NF2 clinical trials targeting VS

PROs in Hearing

Assesses an (1) individual's perceived functioning in the area of hearing and (2) perceived quality of life related to hearing

- Pros:

- Provides information specifically concerning how a patient feels they are functioning separate from data obtained from audiological evaluations
- Assess the effects of a disease within one specific health domain
- Can be used to assess outcomes of medical, instrumentation, and behavioral interventions

- Cons:

- Perception of disability associated with hearing is not always associated with degree of hearing loss (Ventry & Weinstein, 1982)

- Challenges:

- Presence of communication disorder + visual impairment in NF2
- Questionnaires developed for adults with presbycusis and/or use of HAs
- Limitations in research and use of PROs in the clinical world of audiology



Domain of Hearing

Adult measures reviewed:

- Hearing Functioning
 - SAC (Schow & Nerbonne, 1982)
 - AIADH(m) (Kramer et al., 1995)
 - SHQ (Tyler et al., 2009)
 - SSQ (Gatehouse & Noble, 2004)
 - ELQ2 (Goldring & Gault, 2007)
 - HMS (Noble & Atherley, 1970)

Domain of Hearing

Adult measures reviewed:

- Quality of Life

- SAC (Schow & Nerbonne, 1982)
- HHIE (Ventry & Weinstein, 1982)
- ALHQ (Saunders & Cienkowski, 1996)
- CHPI/STHP (Demorest & Erdman, 1982)
- HBQ (Saunders et al., 2013)
- HMS (Noble & Atherley, 1970)
- PANQL (Shaffer et al., 2010)



Domain of Hearing

Child measures reviewed (Communication subgroup work):

- Hearing Functioning
 - SAC-A (Elkayam & English, 2003)
 - SSQ (Gatehouse & Noble, 2004)
 - LIFE (Anderson and Smaldino, 1996)
 - ABEL (Purdy et al., 2002)

Domain of Hearing

Child measures reviewed (Communication subgroup work):

- Quality of Life
 - SAC-A (Elkayam & English, 2003)
 - HEAR-QL (Umansky et al., 2011)
 - GCBI (Kubba et al., 2004)
 - CPQ (Garrison et al., 1994)

PROs for Hearing in Adults

Criteria	SAC/SAC-A	SSQ	SHQ
Patient Characteristics	2.50	2.75	2.50
Published Studies	2.00	2.75	2.50
Item/Domain Content	2.75	2.75	1.30
Scores Available	1.75	1.50	1.00
Psychometric Data	2.50	2.50	3.00
Feasibility	2.75	2.25	3.00
MEAN (6)	2.30	2.42	2.06
MEAN (4)	2.6250	2.5625	2.450



PROs for Hearing in Adults

Criteria	SAC/SAC-A	SSQ	SHQ
Patient Characteristics	2.50	2.75	2.50
Published Studies	2.00	2.75	2.50
Item/Domain Content	2.75	2.75	2.50
Scores Available	1.75	1.50	1.00
Psychometric Data	2.50	2.50	3.00
Feasibility	2.75	2.25	3.00
MEAN (6)	2.30	2.42	2.06
MEAN (4)	2.6250	2.5625	2.450



PROs for Hearing in Adults

Criteria	SAC/SAC-A	SSQ
Patient Characteristics	2.50	2.75
Published Studies	2.00	2.75
Item/Domain Content	2.75	2.75
Scores Available	1.75	1.50
Psychometric Data	2.50	2.50
Feasibility	2.75	2.25
MEAN (6)	2.30	2.42
MEAN (4)	2.6250	2.5625

PROs for Hearing in Adults

SAC

Pros

- Self-report form ages 11-19 (SAC-A); 25+ (SAC); SO proxy form ages 11+
- Item content
- Covers hearing related QOL and hearing functioning
- Likert-type raw and composite scores available
- Clinically significant difference (15% change)
- Reliability and validity

Brief (11 items)

Free

Cons

- No studies in NF
- No form for children under 11
- Only available in English



SELF ASSESSMENT OF COMMUNICATION (SAC)

Name _____

Date _____

Raw Score ____ x 2 = ____ - 20 = ____ x 1.25 ____ %

Please select the appropriate number ranging from 1 to 5 for the following questions. Circle only one number for each question. If you have a hearing aid, please fill out the form according to how you communicate when the hearing aid is not in use.

Various Communication Situations

1. Do you experience communication difficulties in situations when speaking with one other person? (for example, at home, at work, in a social situation, with a waitress, a store clerk, with a spouse, boss, etc.)

- | | | | | |
|-------------------------------|---|------------------------------|---|---|
| 1) almost never
(or never) | 2) occasionally
(about 1/4 of
the time) | 3) about half of
the time | 4) frequently
(about 3/4
of the time) | 5) practically
always
(or always) |
|-------------------------------|---|------------------------------|---|---|

2. Do you experience communication difficulties in situations when conversing with a small group of several persons? (for example, with friends or family, co-workers, in meetings or casual conversations, over dinner or while playing cards, etc.)

- | | | | | |
|-------------------------------|---|------------------------------|---|---|
| 1) almost never
(or never) | 2) occasionally
(about 1/4 of
the time) | 3) about half of
the time | 4) frequently
(about 3/4
of the time) | 5) practically
always
(or always) |
|-------------------------------|---|------------------------------|---|---|

3. Do you experience communication difficulties while listening to someone speak to a large group? (for example, at church or in a civic meeting, in a fraternal or women's club, at an educational lecture, etc.)

- | | | | | |
|-------------------------------|---|------------------------------|---|---|
| 1) almost never
(or never) | 2) occasionally
(about 1/4 of
the time) | 3) about half of
the time | 4) frequently
(about 3/4
of the time) | 5) practically
always
(or always) |
|-------------------------------|---|------------------------------|---|---|

4. Do you experience communication difficulties while participating in various types of entertainment? (for example, movies, TV, radio, plays, night clubs, musical entertainment, etc.)

- | | | | | |
|-------------------------------|---|------------------------------|---|---|
| 1) almost never
(or never) | 2) occasionally
(about 1/4 of
the time) | 3) about half of
the time | 4) frequently
(about 3/4
of the time) | 5) practically
always
(or always) |
|-------------------------------|---|------------------------------|---|---|



Recommendations for Hearing

- The SAC and the SAC-A were recommended for the assessment of (1) hearing functioning and (2) hearing related QOL
- No child-specific measures were recommended as the SAC/SAC-A is for 11+
- For investigators seeking a hearing related QOL measure for children aged 7-11, the HEAR-QL is recommended

Current and Future Directions

- Publish recommendations for general and disease-specific QOL and hearing PROs
 - Disease Specific QOL
 - NF1
 - NF2
 - Schwannomatosis
 - Hearing and Communication PROs for NF2
 - Heather Thompson & Ann Blanton
- Continue subgroup work for specialized domains
- Determine new PRO domains to review

Submission 2020

Submission 2020

Current and Future Directions

- Further evaluate use of recommended PROs in NF; modify tools if needed; conduct validation studies
- Finalize and conduct patient engagement survey to assist planning patient-centered psychosocial trials
- Increase use of electronic PRO measures

If interested in being an active member of the REiNS PRO working group: Contact Vanessa Merker at Vanessa.Merker@va.gov



