

Response Evaluation In Neurofibromatosis Schwannomatosis INTERNATIONAL COLLABORATION

- 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.

Patient reported outcomes for NF1-related scoliosis: domains of interest

REiNS 2021 Winter Meeting

Webinar

March 22nd, 2021

Vanessa Merker, PhD

Massachusetts General Hospital

&

Heather Thompson, PhD CCC-SLP

California State University, Sacramento

on behalf of the REiNS PRO group



Response Evaluation In Neurofibromatosis Schwannomatosis
INTERNATIONAL COLLABORATION

Patient Reported Outcome Measures (PROs or PROMs)

- “Any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else.”
 - A questionnaire administered on paper or a computer
 - Assesses patients’ perception of specific symptoms, their day-to-day functioning, or their quality of life
 - Focus on analyzing within-patient change to demonstrate benefits of treatment

Note: Our group evaluates both patient self-report and proxy report (usually for young children)



Scoliosis PROMs

- Studies investigating scoliosis in NF1 are in need of PROMs
 - Need to demonstrate clinical benefit in addition to radiographic change
 - Symptoms not explained by degree of curvature alone

Scoliosis PROMs

- Challenges to assessing scoliosis with PROMs in NF1 trials
 - Measures developed for idiopathic scoliosis may not be appropriate for NF1
 - Need measures that cover a wide age range; but these are rare
 - Patient burden from completing multiple measures

Roadmap for Presentation

- Review previously recommended REiNS PROs and how the content relates to scoliosis
- Briefly review potential additional scoliosis measures and their pros/cons
- Discuss PRO endpoint strategy for scoliosis and next steps for PRO review

REiNS Recommend PROMs

- Pain Intensity: NRS-11
- Pain Interference: Pain Interference Index or PROMIS Pain Interference scale
- Physical Functioning: PROMIS Physical Functioning Scale
- NF1-Specific Quality of Life: PedsQL NF1 Module
- General Quality of Life: FACT-G or PedsQL Generic Core Scales

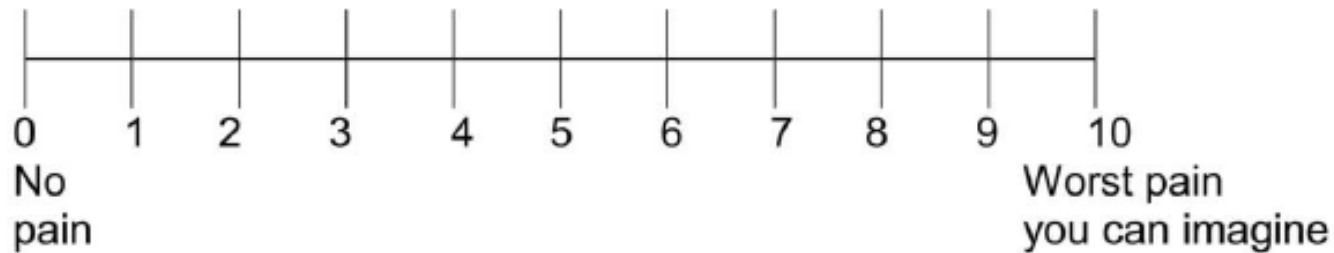


Pain Intensity

A Numeric Rating Scale (NRS-11)

Example:

Please circle the one number that best shows how strong your worst pain was during the past week.



- Pain intensity extremely relevant to scoliosis
- Could ask one question about all pain or ask separate questions for tumor-related and scoliosis- (or spine-) related pain

Pain Interference Index

Pain Interference Index

Below you will find a list of questions about you and your situation. Please answer each question by circling a number between 0 and 6.

Please note that we are asking about your situation during the last 2 weeks.

Has Your Pain:	Not at All			Some			Completely
1. Made it difficult for you to do schoolwork?	0	1	2	3	4	5	6
2. Made it difficult for you to do activities outside school (leisure activities)?	0	1	2	3	4	5	6
3. Made it difficult for you to spend time with friends?	0	1	2	3	4	5	6
4. Affected your mood?	0	1	2	3	4	5	6
5. Affected your ability to do physical activities (like run, walk up stairs, play sports)?	0	1	2	3	4	5	6
6. Affected your sleep?	0	1	2	3	4	5	6

- Can briefly assess pain interference on scoliosis relevant domains (leisure, physical activity, sleep, etc.) for ages 6-24 years



PROMIS Pain Interference

Pain Interference – Short Form 8a

Please respond to each question or statement by marking one box per row.

In the past 7 days...

		Not at all	A little bit	Somewhat	Quite a bit	Very much
PAINING	How much did pain interfere with your day to day activities?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
		1	2	3	4	5

In the past 7 days...

How much did pain interfere with your day to day activities?

How much did pain interfere with work around the home?

How much did pain interfere with your ability to participate in social activities?

How much did pain interfere with your household chores?

How much did pain interfere with the things you usually do for fun?

How much did pain interfere with your enjoyment of social activities? ...

How much did pain interfere with your enjoyment of life?

How much did pain interfere with your family life?

- Not scoliosis specific but could briefly assess pain interference on scoliosis-relevant domains for ages 8+ (with proxy report ages 5-17)



PROMIS Physical Functioning (Adults)

Physical Function – Short Form 20a

Please respond to each question or statement by marking one box per row.

	Without any difficulty	With a little difficulty	With some difficulty	With much difficulty	Unable to do
PFA11 Are you able to do chores such as vacuuming or yard work?.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1

- Push open a heavy door
- Wash your back
- Dry your back with a towel
- Sit on the edge of the bed
- Wash and dry your body
- Get into and out of a car
- Run a short distance, such as to catch a bus
- Sit on and get up from the toilet
- Transfer from a bed to a chair and back
- Dress yourself, including tying shoelaces and buttoning clothes
- Squeeze a new tube of toothpaste
- Hold a plate full of food
- Shampoo your hair



PROMIS Physical Functioning (Adults)

	Not at all	Very little	Somewhat	Quite a lot	Cannot do
Does your health now limit you in doing vigorous activities, such as running, lifting heavy objects, participating in strenuous sports?.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1

- Bending, kneeling, or stooping
- Lifting or carrying groceries
- Doing two hours of physical labor
- Walking more than a mile
- Climbing one flight of stairs

* Can briefly assess physical functioning on scoliosis-relevant domains for adults (ages 18+)



PROMIS Physical Functioning (Kids)

- Two separate forms: upper extremity and mobility

Pediatric Mobility – Short Form 8a

Please respond to each question or statement by marking one box per row.

In the past 7 days...		With no trouble	With a little trouble	With some trouble	With a lot of trouble	Not able to do
235R1r	I could do sports and exercise that other kids my age could do	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1

- I could get up from the floor
- I could keep up when I played with other kids
- I could move my legs
- I could stand up by myself
- I could stand on my tiptoes
- I could walk up stairs without holding on to anything
- I have been physically able to do the activities I enjoy most

* Unclear if assessment of mobility is relevant to scoliosis; measure is for ages 8-17 (with proxy report ages 5-17)



PedsQL NF1 module

- Detailed assessment of many NF1 symptoms
 - 74 items for adults (ages 18+)
 - 16 domains, with domain specific scores

Potentially relevant to scoliosis

Pain and Hurt	Emotional Functioning
Physical Functioning	Social Functioning
Movement and Balance	Sexual Functioning*
Daily Activities	Worry*
Fatigue	Treatment Anxiety
Perceived physical appearance*	Communication (Talking with medical personnel and others)

Not relevant to scoliosis

Paresthesias (?)
Skin Irritation
Cognitive functioning
Sensation (vision, hearing, speech)

*Some questions in scale specific to other NF issues, but majority could apply to scoliosis



PedsQL NF1 module

- Detailed assessment of many NF1 symptoms
 - 104 items for kids/adolescents (ages 5-17)
 - 18 domains, with domain specific scores

Potentially relevant to scoliosis

Pain
Pain Impact
Pain Management
Balance (?)

Worry
Treatment Anxiety
Communication (Difficulty
talking about NF with others)

Not relevant to scoliosis

Perceived physical appearance
Skin sensations
Skin itch bother
Cognitive functioning
Speech
Fine Motor
Vision
Medicines (Adherence/Tolerability) (?)
Stomach Discomfort
Constipation
Diarrhea

←
2 of 3 questions
specific to
neurofibromas/
café-au-lait spots

General QoL Measures

- PedsQL Core Scales
 - Self-report ages 8+, with proxy report for infants through adults
 - 23 items assessing functioning in 4 domains: physical, emotional, social, & work/school

Physical	Emotional	Social	Work/School
Physical functioning	Sad/Angry/ Scared	Friendships	Cognitive (attention, forgetting)
Pain	Worry	Teasing	Missing work/school due to illness
Fatigue	Sleep	Comparison with peers	

General QoL Measures

- **FACT-G**
 - Self-report for adults
 - 27 items assessing well-being in 4 domains: physical, emotional, social/family, & functional

Physical	Emotional	Social/Family	Functional
Feeling ill, having side effects	Sad/Anxious	Support from friends/family	Work and leisure
Pain	Worry	Satisfaction with sex life	Satisfaction with/enjoyment of life
Fatigue	Coping		Sleep

Summary of Recommended PROM Applicability to Scoliosis

- Adults: pain, physical functioning, and NF1-specific quality of life well-covered by existing measures
 - NRS-11, PedsQL NF1 module, PROMIS PI/PF scales (probably as computer adaptive tests)
- Kids & adolescents: pain well-covered; physical functioning and QOL only partially covered
 - NRS-11, PII, PedsQL Core module; but more specific scoliosis scale might be needed
- PRO group recommendations for appearance are pending
 - Severity of disfigurement + satisfaction with appearance/distress caused by appearance
 - Latter may only have suitable adult forms available

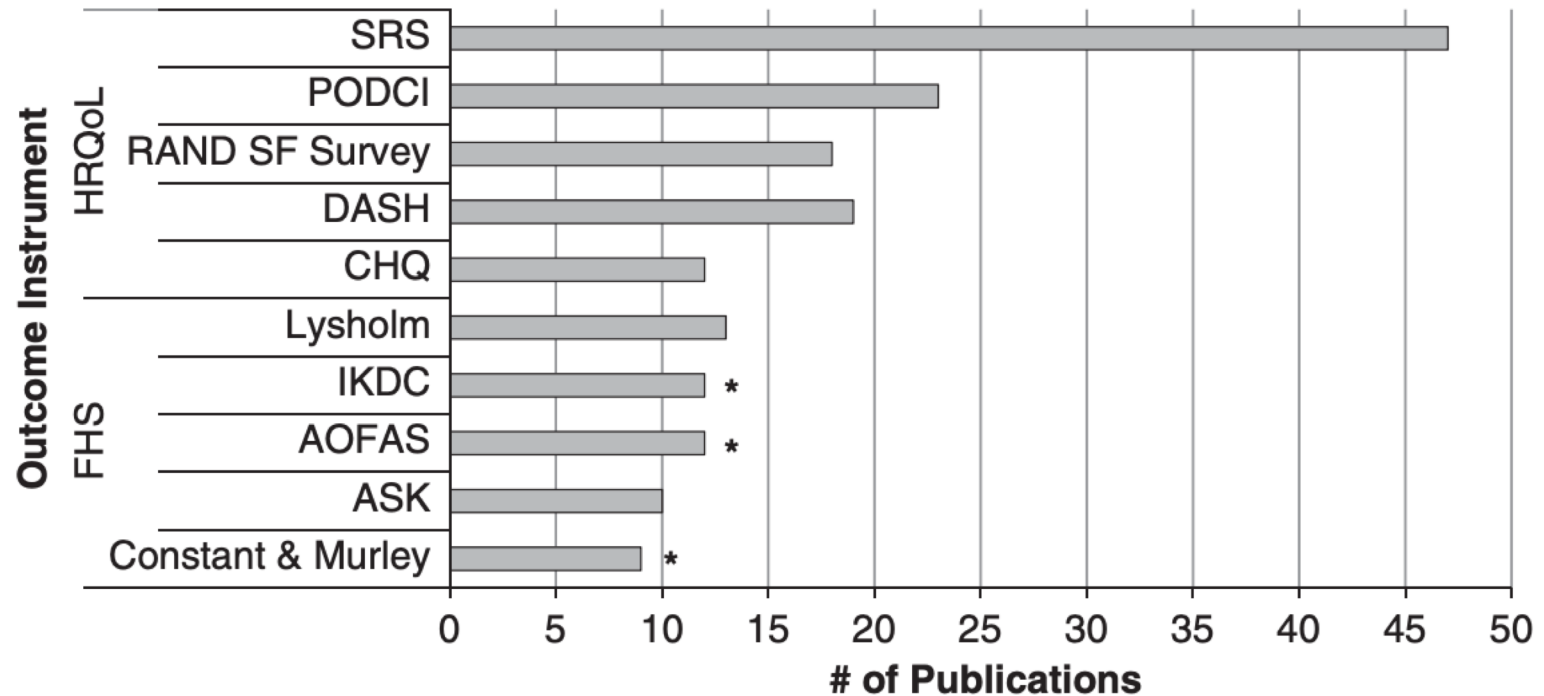
Scoliosis/Orthopedic PROMs

- Age range
- Item content overlap with generic QoL measures
 - Studies often include FHS as opposed to HRQoL tools (Phillips et al., 2018)
- Scoring scale
- Languages available

Scoliosis/Orthopedic PROMs

Pediatric Literature

Most Frequently Used Patient-Based Outcome Measures



Phillips et al., 2018



*Tool has not been validated in a pediatric population. AOFAS = American Orthopaedic Foot and Ankle Society; ASK = Activities Scale for Kids; CHQ = Child Health Questionnaire; DASH = Disabilities of the Arm, Shoulder, & Hand Questionnaire; IKDC = International Knee Documentation Committee Score; PODCI = Pediatric Outcomes Data Collection Instrument; SRS = Scoliosis Research Society. RAND = Research & Development (SF-36); Lysholm Knee Questionnaire

Scoliosis Measures

1. Scoliosis Research Society (SRS-22r)
2. Pediatric Outcomes Data Instrument (PODCI)
3. Italian Spinal Youth Quality of Life Scale (ISYQOL)

SRS-22r

- Standard measure for QoL assessing physical functioning
- Assessment for adults + children
- 22 items

Potentially relevant to scoliosis

- Pain (5 items)
- Self-image/appearance (5 items)
- Function/activity (5 items)
- Mental health (5 items)

Not relevant to scoliosis

- Satisfaction with management (2 items)

Example Items

During the past 6 months have you been a very nervous person?

Do you experience back pain when at rest?

If you had to spend the rest of your life with your back shape as it is right now, how would you feel about it?

Pediatrics Outcomes Data Collection Instrument (PODCI)

- Proxy and self-report form used to document changes in functional status pre-post intervention
 - Parent report for children birth-10 and adolescents 11-18 years
 - Self-report 11-18 years
- Uses IRT (Allen et al., 2008); variable response formats; lengthy
- Has been used in NF (e.g., Johnson et al., 2015)
- 5 languages

Potentially relevant to scoliosis

- Mobility
- Comfort

Not relevant to scoliosis

- Upper extremity function (UEF)
- General health (CGH)
- Self-worth

Example Items

Open a jar that has been opened before?

How much pain have you had during the last week?

Bend over from a standing position and pick up something off the floor?



PODCI

Adolescent Health Assessment (self-reported)

Some kind of problems can make it hard to do many activities, such as eating, bathing, school work, and playing with friends. We would like to find out how you are doing. (Circle one response on each line.)

During the **last week** was it easy or hard for you to:

	Easy	A little hard	Very hard	Can't do at all
1. Lift heavy books?	1	2	3	4
2. Pour a half gallon of milk?	1	2	3	4
3. Open a jar that has been opened before?	1	2	3	4
4. Use a fork and spoon?	1	2	3	4
5. Comb your hair?	1	2	3	4
6. Button buttons?	1	2	3	4
7. Put on your coat?	1	2	3	4
8. Write with a pencil?	1	2	3	4



Italian Spine Youth Quality of Life questionnaire (ISY-QOL)

- Used to assess QoL in youth with spinal concerns
- 20 items
- Two languages
- Satisfactory correlation between the ISY-QOL and the SRS-22

ISY-QOL

We want to evaluate your well-being with regards to your back problem (scoliosis, kyphosis or something else). Try to answer all of the following questions yourself.

1	Are you afraid that your back problem may get worse?	<input type="checkbox"/> never	<input type="checkbox"/> sometimes	<input type="checkbox"/> often
2	Are you worried about having back pain as an adult because of your back problem?	<input type="checkbox"/> never	<input type="checkbox"/> sometimes	<input type="checkbox"/> often
3	Do you feel that having your back problem is a big deal?	<input type="checkbox"/> never	<input type="checkbox"/> sometimes	<input type="checkbox"/> often
4	Are you worried that, despite all your efforts to treat your back, it will not get better?	<input type="checkbox"/> never	<input type="checkbox"/> sometimes	<input type="checkbox"/> often
5	Do you think that there are other health conditions affecting other people that are more serious than your back problem?	<input type="checkbox"/> never	<input type="checkbox"/> sometimes	<input type="checkbox"/> often
6	Despite your back problem, do you think you lead a normal life?	<input type="checkbox"/> never	<input type="checkbox"/> sometimes	<input type="checkbox"/> often
7	Are you suffering because of your back problem?	<input type="checkbox"/> never	<input type="checkbox"/> sometimes	<input type="checkbox"/> often
8	Does the appearance of your back make you feel uncomfortable?	<input type="checkbox"/> never	<input type="checkbox"/> sometimes	<input type="checkbox"/> often
9	Are you worried about your back problem?	<input type="checkbox"/> never	<input type="checkbox"/> sometimes	<input type="checkbox"/> often
10	Do you think that your back problem is not a big concern to you?	<input type="checkbox"/> never	<input type="checkbox"/> sometimes	<input type="checkbox"/> often
11	Does it bother you to show your physical appearance?	<input type="checkbox"/> never	<input type="checkbox"/> sometimes	<input type="checkbox"/> often
12	Are you worried that your back problem is very visible?	<input type="checkbox"/> never	<input type="checkbox"/> sometimes	<input type="checkbox"/> often
13	Despite your back problem, do you live a happy life?	<input type="checkbox"/> never	<input type="checkbox"/> sometimes	<input type="checkbox"/> often

+ 7 questions asking about wearing a brace

Caronni et al., 2017



Summary of Pros/Cons of Scoliosis Specific Measures

- SRS-22r and PODCI
 - Used widely but the SRS-22r is missing items that ask about self-care and mobility (Du et al., 2018)
 - PODCI has overlap with recommended measures and is not specific to scoliosis
- ISY-QOL
 - More specific to scoliosis or back problems
 - Not as well used/validated in adult and young child populations

Discussion Questions

- Given anticipated trial design, do we need additional scoliosis-specific PROMs or can we use multiple symptom-specific PROMs?
- What additional domains do we need to assess (if any) to capture the impact of treatment on scoliosis?
- Can we, and do we want to, separate scoliosis-related symptoms from other symptoms of NF?

REiNS PRO Working Group

Taryn Allen
Andrea Baldwin
Carolina Barnett-Tapia
Belinda Barton
Kim Bischoff
Ann Blanton
Frank Buono
Kevin Franck
Barbara Franklin
Deborah Gold
Diana Haberkamp
Cynthia Hingtgen
Kim Koetsier
Staci Martin
Vanessa Merker
Renie Moss

Drea Peterson
Melissa Reider-Demer
Claas Rohl
Carlos Romo
Tena Rosser
Betty Schorry
Taylor Smith
Heather Thompson
James Tonsgard
Ana-Maria Vranceanu
Karin Walsh
Pam Wolters
Brad Welling

*Thank you to
Shawna Garayalde

If interested in being an active member of the REiNS PRO
working group: Contact Vanessa Merker at
vmerker@mgh.harvard.edu

