

# REiNS Patient Reported Outcomes (PRO) Working Group

REiNS Committee Meeting

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Paris, France

Pam Wolters, PhD  
National Cancer Institute

On behalf of the REiNS PRO group



Response Evaluation In Neurofibromatosis Schwannomatosis  
INTERNATIONAL COLLABORATION

# 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

National Cancer Institute  
National Cancer Institute  
University of Toronto  
Johns Hopkins University  
NF Network  
Guy's Hospital  
Patient Advocate  
Patient Advocate  
MGH/Harvard  
University of Pittsburgh  
University Hospitals of Cleveland  
Indiana University  
Leiden University Medical Center  
National Cancer Institute  
MGH/Harvard  
Randall Children's Hospital  
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Patient Advocate  
Cincinnati Children's Hospital  
California Polytechnical Institute  
California State University  
University of Chicago  
MGH/ Harvard  
Children's National Medical Center  
National Cancer Institute



# 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
  - PRO-RATE form (6 criteria) Wolters, et al., 2013
- Determined four core domains for NF trials ( $\geq 8$  years)
  - 1) Pain
    - Pain intensity
    - Pain interference
  - 2) Physical Functioning
    - Mobility Wolters et al., 2016
    - Upper extremity
  - 3) General QOL
  - 4) Disease Specific QOL
    - NF1 Submission 2019
    - NF2
    - Schwannomatosis
- Further evaluate use of PROs in NF: modify tools for NF; conduct validation studies; assess feasibility in NF trials



# PRO Working Group

- PRO subgroups (specialized domains)

- 1) Vision-specific QOL measure

Fisher et al., 2013

- Staci Martin and Vanessa Merker

- 2) Hearing and communication PROs

- Heather Thompson

- 3) Pain PROs for young child pain

- Taryn Allen and Andrea Baldwin

# Current Work of the PRO Group

- 1) Completed reviews of general QOL domain; present group recommendations
- 2) Currently reviewing disease-specific PROs for NF
- 3) Communication Subgroup is working to review hearing measures



# General and Disease-specific QOL

- General QOL measures
  - Assess individual's perceived functioning and well-being in general health domains (physical, social, emotional, role functioning)
  - Pros:
    - Assess the effects of a disease across a set of general health domains
    - Compare QOL across healthy and disease populations
    - Primary outcome for psychosocial trials: goal is increased satisfaction and well-being despite symptoms; may include multiple types of NF
    - Secondary outcomes for medical trials: assess how treatment affects functioning in domains of everyday life
  - Cons:
    - Items less related to disease-specific treatment changes in a drug trial
    - FDA prefers more symptom-specific outcomes
    - May add to patient burden if adding to symptom-specific measures



# General and Disease-specific QOL

- General QOL measures
  - Challenges:
    - Numerous general QOL scales available
    - Focus on different general domains
      - Potential need for different tools for psychosocial and drug trials
    - Few assess children through adults
      - Potential need for PROs for different age ranges
        - » Adult only
        - » Children only
        - » Children through adults





# General and 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



# General QOL - Adults

## PRO measures reviewed:

- **FACT-G** (Cella et al., 1993)
- **WHO QOL BREF** (Skevington et al., 2004)
- **PROMIS Global Health** (Hays et al., 2009)
- **PedsQL Generic Core Scale** (Varni, et al., 1999)
- **SF-36** (J. E. Ware & Sherbourne, 1992)
- **SF-12** (J. Ware et al., 1996)
- **EURO-QOL** (The EuroQol Group, 1990)



# General QOL - Adults

Criteria	FACT-G	WHO QOL BREF
Patient Characteristics	2.75	2.75
Published Studies	2.75	2.75
Item/Domain Content	2.44	2.40
Scores Available	3	3
Psychometric Data	2.75	2.5
Feasibility	3	3
<b>MEAN (6)</b>	<b>2.782</b>	<b>2.775</b>
<b>MEAN (4)</b>	<b>2.735</b>	<b>2.725</b>

- FACT-G for adult-only drug trials
- WHO QOL BREF for adult-only psychosocial trials

# General QOL - Children

## PRO measures reviewed:

- **PROMIS Global Health** (Hays, Bjorner, Revicki, Spritzer, & Cella, 2009)
- **PedsQL Generic Core Scales** (Varni et al., 1999)
- **Child Health Questionnaire** (Landgraf et al., 1996)
- **Kidscreen** (Raven-Sieberer et al., 2014)
- **DISABKIDS** (Schmidt et al., 2006)
- **KINDL-R** (Raven-Sieberer et al., 1998)
- **ITQOL Questionnaire** (Langraf, 1994)

# General QOL - Children

Criteria	PedsQL	KINDL-R	DISABKIDS
Patient Characteristics	3	2.75	2.5
Published Studies	2.75	2.25	2
Item/Domain Content	2.75	2.5	2
Scores Available	2.5	2.75	2.75
Psychometric Data	2.5	2.5	2.5
Feasibility	2.5	2.75	2.75
<b>MEAN (6)</b>	2.67	2.58	2.42
<b>MEAN (4)</b>	2.6875	2.625	2.4375

- PedsQL Generic Core Scales including infant form

# General QOL - Children to Adults

## PRO measures reviewed:

- PedsQL includes infant scale (Varni, Seid, & Rode, 1999)
- PROMIS Global Health (Hays, Bjorner, Revicki, Spritzer, & Cella, 2009)

# General QOL - Children to Adults

Criteria	PedsQL Generic Core	PROMIS Global Health
Patient Characteristics	2.9	2.5
Published Studies	3	1.75
Item/Domain Content	2.75	1.75
Scores Available	2.5	3
Psychometric Data	2.75	2.5
Feasibility	2.75	2.75
<b>MEAN (6)</b>	2.775	2.375
<b>MEAN (4)</b>	<b>2.7875</b>	<b>2.375</b>

- PedsQL Generic Core Scales including infant form

# Recommendations for General QOL

- Adult only
  - FACT-G for adult-only drug trials
  - WHO QOL BREF for adult-only psychosocial trials
- Child only
  - PedsQL Generic Core Scales (including infant form)
- Child to adult
  - PedsQL Generic Core Scales (including infant form)



# Future Directions

- Review final NF disease-specific QOL scales and make recommendations
  - Previous recommendation for NF2: NFTI-QOL (Ferner et al., 2017)
    - Exploratory outcome in NF2 trials for VS: PANQOL (Shaffer, 2010)
  - Finish review of NF1 measures: NF1 PedsQL module, Plexi-QOL, PROMIS battery for NF1, INF1-QOL, Skindex
- Publish recommendations for general and disease-specific QOL
- Continue subgroups work for specialized domains
- Increase use of electronic PRO measures
- Transition to a new leader: Vanessa Merker, PhD

If interested in being an active member of the REiNS PRO working group: Contact Pam Wolters at [woltersp@mail.nih.gov](mailto:woltersp@mail.nih.gov) or Vanessa Merker at [VMERKER@mgh.harvard.edu](mailto:VMERKER@mgh.harvard.edu)



