

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.



# Developing Endpoints Across Multiple Cognitive Domains

---

Karin Walsh, PsyD  
(for Jennifer Janusz, PsyD)



Response Evaluation In Neurofibromatosis Schwannomatosis  
INTERNATIONAL COLLABORATION

# Members

## Chair

Jennifer Janusz

## Committee Members

- Cynthia Campen
- Pete de Blank
- Deborah Gold
- Kristina Haebich
- Kristi Hardy
- Matt Hocking
- Kelly Janke
- Bonnie Klein-Tasman \*
- Staci Martin
- Jonathan Payne \*
- Carlos Prada
- Natalie Pride
- Tena Rosser
- Pete Stavinoha
- Heather Thompson
- Karin Walsh \*
- Nicole Ullrich
- Hannah Weisman
- Pam Wolters

## Patient Representatives

- Maureen Hussey
- Jessica Samblanet
- Connie Sorman
- Tracy Wirtanen

\* Steering Committee



# History and Mission of Neurocognitive Group

- Started 2011, led by Karin Walsh
- Goal to identify measures of cognition and psychosocial functioning for use in clinical trials
  - Well-designed measures (good psychometrics)
  - Easily administered in clinical trials setting
  - Previous use in clinical trials
  - Previous use with NF1
  - Availability in other languages
- Preschool subcommittee 2016
  - Lead: Bonnie Klein-Tasman



# Relevant Domains

- Cognition
- Language
- Visual-spatial
- Memory
- Attention
- Executive functions
- Adaptive skills
- Academics
- Psychosocial
- Social skills
- Social cognition
- Computerized measures
- Global outcome measures

2016 Neurology supplement

Preschool - 2021 Neurology supplement

2021 Neurology supplement



# Is there a better way to do this?

- Traumatic Brain Injury Common Data Elements (CDE) Initiative
- Co-sponsored by NNDS, VA, NIDRR, DCoE, and DVBIC
- 8 working groups, including one focused on cognitive and psychological outcomes



# TBI CDE Workgroup Method

- Subgroups for each cognitive domain working simultaneously
- Standardized search and review process
  - Each subgroup used similar search terms to find measures
  - Measures reviewed on same properties (similar to our CogRATE Form)
- For each cognitive domain, recommended measures organized into three tiers
  - Core: single, well-established measure
  - Supplemental: more in-depth assessment
  - Emerging: promising measures under development



# Recommendations for outcome measures in pediatric TBI

Cognitive Domain	Core	Supplementary	Emerging
<b>IQ</b>	Wechsler Abbreviated Scale of Intelligence (WASI)	None	None
<b>Executive Function</b>	Delis-Kaplan Executive Function System (DKEFS) Verbal Fluency	<ol style="list-style-type: none"> <li>1. DKEFS Trail Making Test</li> <li>2. Behavior Rating Inventory of Executive Function (BRIEF)</li> <li>3. Contingency Naming Test</li> </ol>	<ol style="list-style-type: none"> <li>1. Test of Executive Control</li> <li>2. Test of Strategic Learning</li> <li>3. NIH Toolbox</li> </ol>
<b>Attention/Processing Speed</b>	WISC/WPPSI Processing Speed	<ol style="list-style-type: none"> <li>1. Conners Continuous Performance Test</li> <li>2. Test of Everyday Attention (TEA-Ch)</li> </ol>	<ol style="list-style-type: none"> <li>1. Flanker Test</li> <li>2. NIH Toolbox</li> </ol>





# Advantages of TBI CDE Model

- Efficient
- Tier groupings gives more guidance for primary and secondary study aims measures
- Future work will focus on updating recommendations



# “All Domains” Paper

- Subgroups reviewing multiple domains concurrently
- Currently focusing on pediatric measures
- Each subgroup will use same search terms and rating forms
- Timeline
  - January 2021- August 2021
    - Adaptive
    - Psychosocial
    - Academics
    - Social Cognition
  - September 2021-April 2022
    - Language
    - Cognition
    - Executive Functions
    - Memory
  - May 2022- December 2022
    - Attention
    - Computerized Measures
    - Global Outcome Measures



# Subgroups

- Psychosocial
  - Karin Walsh (lead)
  - Pam Wolters
  - Nicky Ullrich
  - Pete de Blank
  - Hannah Weisman
  - Maureen Hussey
- Social Cognition
  - Jonathan Payne (lead)
  - Kristina Haebich
  - Natalie Pride
- Adaptive
  - Bonnie Klein-Tasman (lead)
  - Heather Thompson
  - Pete Stavinoha
  - Cynthia Campen
  - Tena Rosser
  - Connie Sorman
- Academics
  - Kelly Janke (lead)
  - Kristi Hardy
  - Staci Martin
  - Deborah Gold
  - Jennifer Janusz



# Review Process

- Literature search to identify measures used in clinical trials (conducted by subgroup leader)
- Measures identified are divided up amongst group members to lead review
- Lead reviewer provides summary of measure and a few key articles for committee members to read
- Each committee member rates the measure prior to the meeting
- Lead reviewer leads discussion of measure
- Lead reviewer enters ratings into Excel spreadsheet
- All information uploaded to Dropbox
- Focus is on use in clinical trials, not clinical utility



# Definition of Core, Supplemental, and Emerging

- Core
  - Established use in NF1
  - Good Psychometrics
  - Brevity and ease of administration
  - Multiple languages
- Supplemental
  - Specific topics or more in-depth assessment
  - Example TBI Group: For Psychological Functioning, CBCL Problem Behaviors is Core and specific anxiety measures are supplemental
- Emerging
  - Instruments under development, in the process of validation, or nearing point of published findings with NF1



# Search Terms

- PubMed and ClinicalTrials.gov
- From social skills paper: Combining the social terms of “social,” “social skills,” “social function,” or “social behavior” with disorder specific terms, including [“ADHD” or “Attention deficit hyperactivity disorder”] or [“autism,” “Asperger,” “ASD,” or “autism spectrum disorder”] or [“neurofibromatosis,” “neurofibromatosis type 1,” or “NF1”].
- Additional searches were conducted with the previous terms and including “clinical trial,” “randomized controlled trial,” “RCT,” or “intervention”.
- Also considered measures used frequently with NF1

