

# Widely Used Clinical Endpoints Applications for JNCL

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# Clinical Trial endpoints

- Clinically relevant, measurable, accurate, reliable, sensitive to change, interpretable
- Direct measure of how a patient “feels, functions, or survives”
- Determined by the setting



## Direct Clinical Outcome Assessments

*Patient Reported  
Outcomes*

*Observer Reported  
Outcomes*

*How a person  
feels, functions,  
survives*

*Performance  
Outcomes*

*Clinician Reported  
Outcomes*

# Endpoint content

- Forms the basis of drug labeling
- Disease specific clinical features
- Occurrence of disease-related-events
- Impact of symptoms on adaptive function
- Impact of symptoms on Quality of Life

Wang, et al. Clinical Trials – A Practical Guide to Design, Analysis, and Reporting. 2006

L Burke. Clinical Trial Endpoints: Development and Validation of Measures to Support Claims in Labeling. 2010. FDA



# Disease specific clinical features

- Vision impairment
- Motor impairment
- Cognitive and behavioral impairment
- Epilepsy




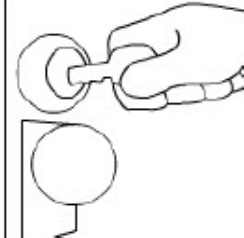


# Pediatric Evaluation of Disability (Adaptive Function)







- Ages 0-20years
- Physical and/or behavioral conditions
- Domains
  - daily activities
  - mobility
  - social/cognitive
  - responsibility
- Computer-administered



# PEDI-CAT Daily Activity

Item Number	Content Area	Item	Illustration
DA008	Eating & Mealtime	Drinks liquids using a straw	
DA067	Getting Dressed	Puts on socks	
DA044	Keeping Clean	Shaves face using electric or safety razor	
DA092	Home Tasks	Opens door lock using key	

# PEDI-CAT Mobility

Item Number	Content Area	Item	Illustration
MB016	Basic Movement & Transfers	Sits on floor without support of pillow or couch	
MB046	Standing & Walking	Walks while wearing a light backpack	
MB074	Steps & Inclines	Walks up a flight of stairs without holding onto handrail	
MB092	Running & Playing	Pumps legs and swings on playground swing	
MB121D	Wheelchair	Goes up and down ramp with wheelchair	
MB111D	Steps & Inclines	Walks with walking aid (e.g. cane, crutches, walker) up and down ramp	



# PEDI-CAT Social/Cognitive

## Sample Social/Cognitive Items

Item Number	Content Area	Item
SC011	Everyday Cognition	Follows directions given by adult leader of a small group (4-5 children or teenagers)
SC012	Interaction	Asks permission before using someone else's property
SC032	Everyday Cognition	Recognizes his/her printed name
SC057	Self-Management	When upset, responds without punching, hitting, or biting



# PEDI-CAT Responsibility

## Sample Responsibility Items

Item Number	Content Area	Item	Includes
RS001	Organization & Planning	Getting ready in the morning on time	Getting up; Getting dressed; Grooming and hygiene activities; Eating breakfast; Completing on time
RS009	Health Management	Taking care of minor health needs	Caring for minor cuts and burns; Taking over the counter medication for fever, cold, and flu when appropriate
RS023	Taking Care of Daily Needs	Selecting clothing that is appropriate given the weather, daily schedule, and activities	Identifying dress codes or expectations for different events; Seeking information about weather for the day
RS040	Staying Safe	Taking precautions to protect the privacy of personal information	Providing personal information (e.g. social security number, address) only when appropriate



# PEDI-CAT Challenges

- Not previously used for neurodegenerative disorders



# 6-Minute Walk Test (Performance outcome)

- Used by many disciplines
- Measure of functional exercise capacity
- Simple, no specialized equipment



# 6-Minute Walk Test Challenges

- Floor effects
- Minimal Clinically Important Difference
  - variability
- Significance?



# PedsQL (Quality of Life)

- physical, emotional, social well-being
- Subjective
- **Allows for a broader assessment of intervention impact on study subject**
- Health related QoL
- Brief
- Variety of conditions



<b>PHYSICAL FUNCTIONING</b> ( <i>problems with...</i> )	<b>Never</b>	<b>Almost Never</b>	<b>Some-times</b>	<b>Often</b>	<b>Almost Always</b>
1. Walking more than one block	0	1	2	3	4
2. Running	0	1	2	3	4
3. Participating in sports activity or exercise	0	1	2	3	4
4. Lifting something heavy	0	1	2	3	4
5. Taking a bath or shower by him or herself	0	1	2	3	4
6. Doing chores around the house	0	1	2	3	4
7. Having hurts or aches	0	1	2	3	4
8. Low energy level	0	1	2	3	4

<b>EMOTIONAL FUNCTIONING</b> ( <i>problems with...</i> )	<b>Never</b>	<b>Almost Never</b>	<b>Some-times</b>	<b>Often</b>	<b>Almost Always</b>
1. Feeling afraid or scared	0	1	2	3	4
2. Feeling sad or blue	0	1	2	3	4
3. Feeling angry	0	1	2	3	4
4. Trouble sleeping	0	1	2	3	4
5. Worrying about what will happen to him or her	0	1	2	3	4

<b>SOCIAL FUNCTIONING</b> ( <i>problems with...</i> )	<b>Never</b>	<b>Almost Never</b>	<b>Some-times</b>	<b>Often</b>	<b>Almost Always</b>
1. Getting along with other children	0	1	2	3	4
2. Other kids not wanting to be his or her friend	0	1	2	3	4
3. Getting teased by other children	0	1	2	3	4
4. Not able to do things that other children his or her age can do	0	1	2	3	4
5. Keeping up when playing with other children	0	1	2	3	4

<b>SCHOOL FUNCTIONING</b> ( <i>problems with...</i> )	<b>Never</b>	<b>Almost Never</b>	<b>Some-times</b>	<b>Often</b>	<b>Almost Always</b>
1. Paying attention in class	0	1	2	3	4
2. Forgetting things	0	1	2	3	4
3. Keeping up with schoolwork	0	1	2	3	4
4. Missing school because of not feeling well	0	1	2	3	4
5. Missing school to go to the doctor or hospital	0	1	2	3	4





# PedsQL Challenges

- Reflective of JNCL concerns?
- Floor effects



# Challenges – new measures

- Validity
  - content
  - construct
- Reliability
  - test-retest
  - inter-rater
- **Sensitivity to change**



# Challenges – selecting endpoints

- **Vision**
- Duration of follow-up
- Efficiency
- Variety of evaluators
- Key disease-related events
- Single versus composite outcome



# Endpoint goals

- Represents direct assessment of present or future clinical status of patient
- Clinically meaningful
- Meaningful to patients and families



# Opportunity – Common measures

- NCLs
- Pediatric neurodegenerative disorders



