

### INTRODUCTION

The University of Rochester Batten Center has engaged in research on the Natural History of all forms of Batten Disease. "Natural History" refers to the usual course of development of a disease. High quality natural history data are important for evaluating treatments in rare diseases. This poster summarizes our work in CLN3 disease (JNCL; Juvenile Batten Disease)

### RATING SCALE: THE UBDRS

Beginning in 2002, we developed and have used the Unified Batten Disease Rating Scale (UBDRS) to measure key features of Batten Disease. The UBDRS was designed to be used in all forms of Batten Disease.

The UBDRS consists of 4 domains:

- 1) Physical Impairment
- 2) Seizures
- 3) Mood and Behavior
- 4) Functional Capability

It also captures information about age-at-onset of different symptoms.

Cognition is assessed with separate tools.

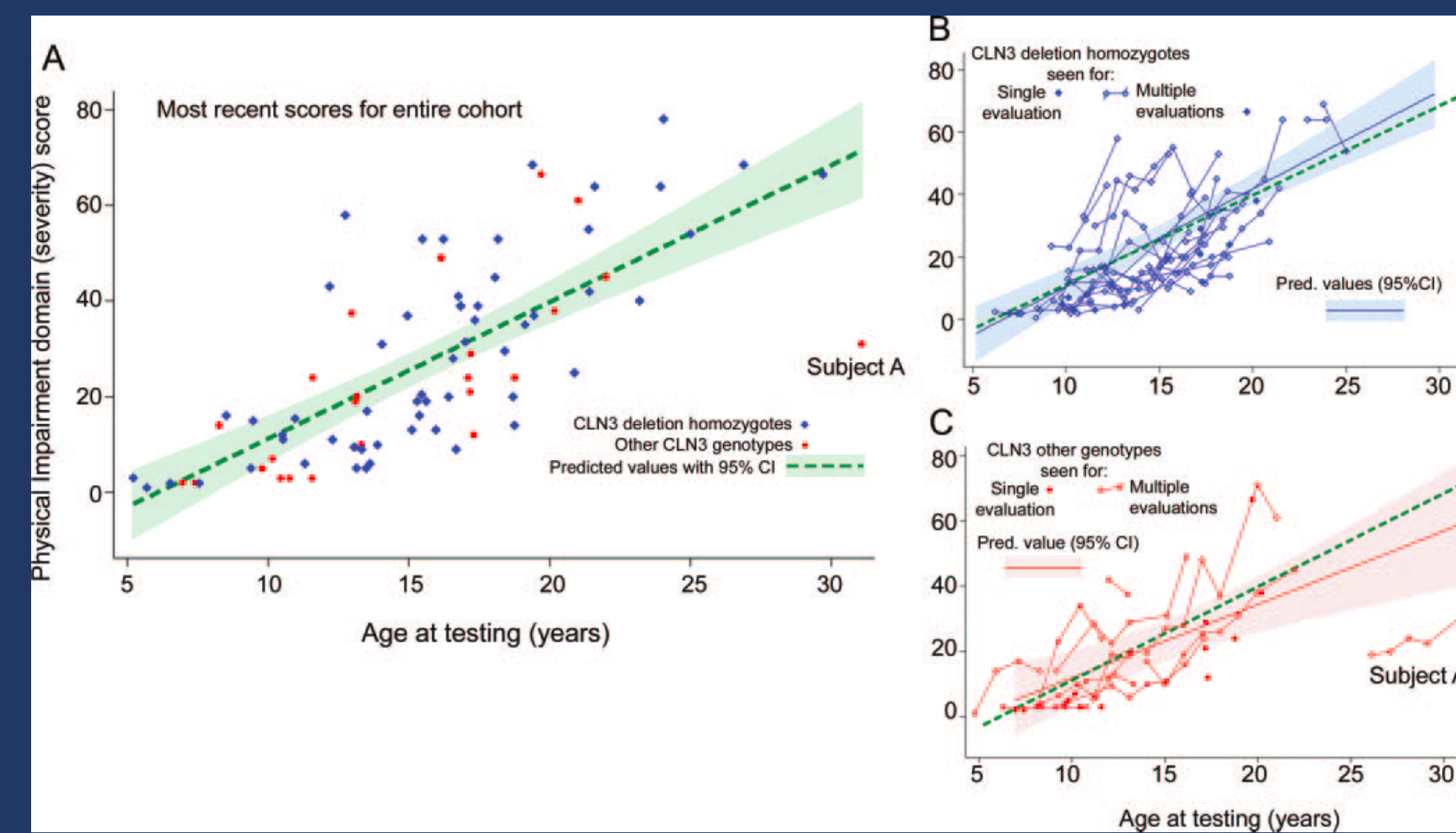
The UBDRS has allowed us to measure key features of Batten Disease in order to determine how affected individuals change with age and which aspects contribute most to disability.

We have used the UBDRS to evaluate over 150 individuals with some form of NCL, including 110 individuals with CLN3 disease. We have performed a total of 400 evaluations, with as many as 15 annual evaluations in an individual.

In addition, we have used data from our natural history work to develop a staging system for potential use in CLN3 disease.

### PHYSICAL IMPAIRMENT

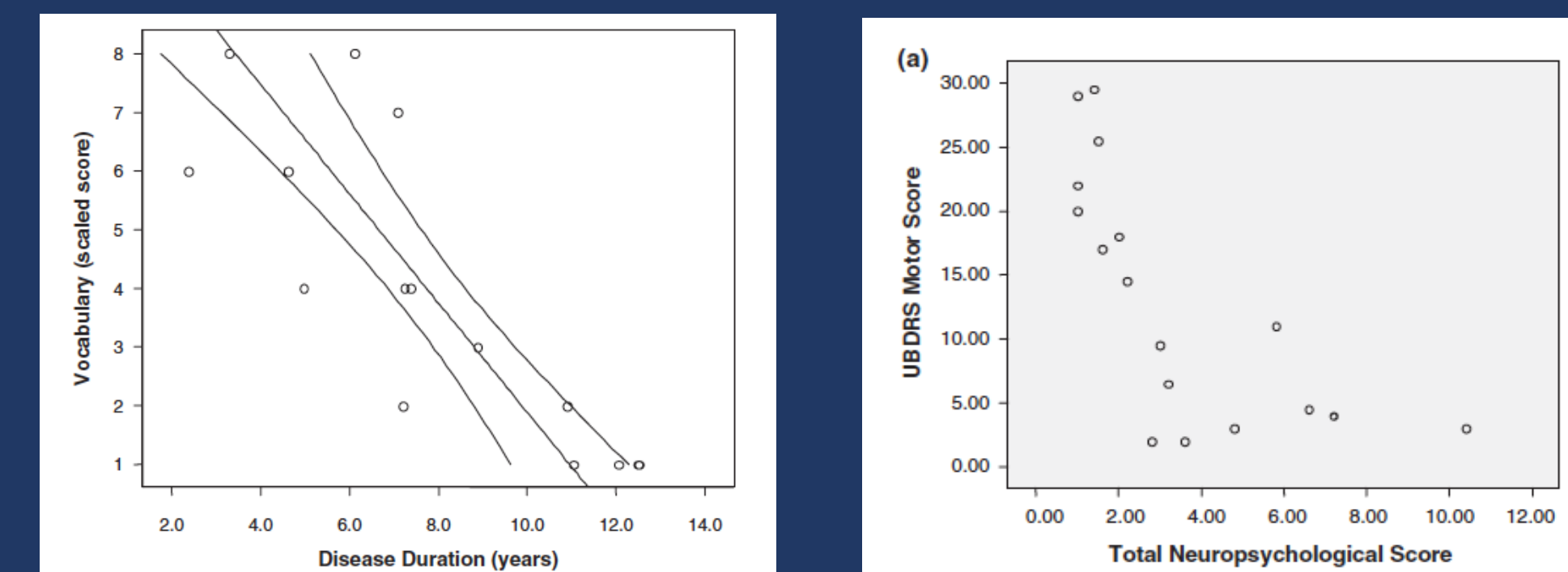
Physical impairment progresses continuously over the course of the disease



Physical Impairment scores at the most recent time of testing for all subjects are shown. The colored labels indicate the subject's CLN3 genotype (B) Physical Impairment scores of the subset who are homozygous for the common CLN3 deletion. When subjects participated for multiple evaluations, their scores are marked by connected blue diamonds. C) Physical Impairment scores of those with other CLN3 genotypes. When subjects participated for multiple evaluations, their scores are marked by connected red circles. Subject A is the only clear outlier from an otherwise consistent pattern. (From Kwon et al., 2011)

### COGNITION

Cognitive decline progresses over the course of the disease and may precede physical impairment.



Vocabulary score declines with age in CLN3 disease (higher scores are better).

Adams et al., 2007

Cognitive decline precedes motor CLN3 disease (higher Neuropsychological scores are better; higher Motor scores are worse).

### SYMPTOM ONSET AGES

Typical CLN3 disease starts with vision loss, followed by cognitive and behavior problems, then seizures and finally motor decline.

	Vision Loss	Behavior Problems	Cognitive Problems	Seizures	Motor Problems
Males	5.4 ± 1.5	7.0 ± 3.4	8.2 ± 4.0	9.8 ± 2.7	10.9 ± 4.4
Females	6.3 ± 1.4	9.5 ± 4.4	8.7 ± 2.9	9.4 ± 2.5	11.8 ± 3.6

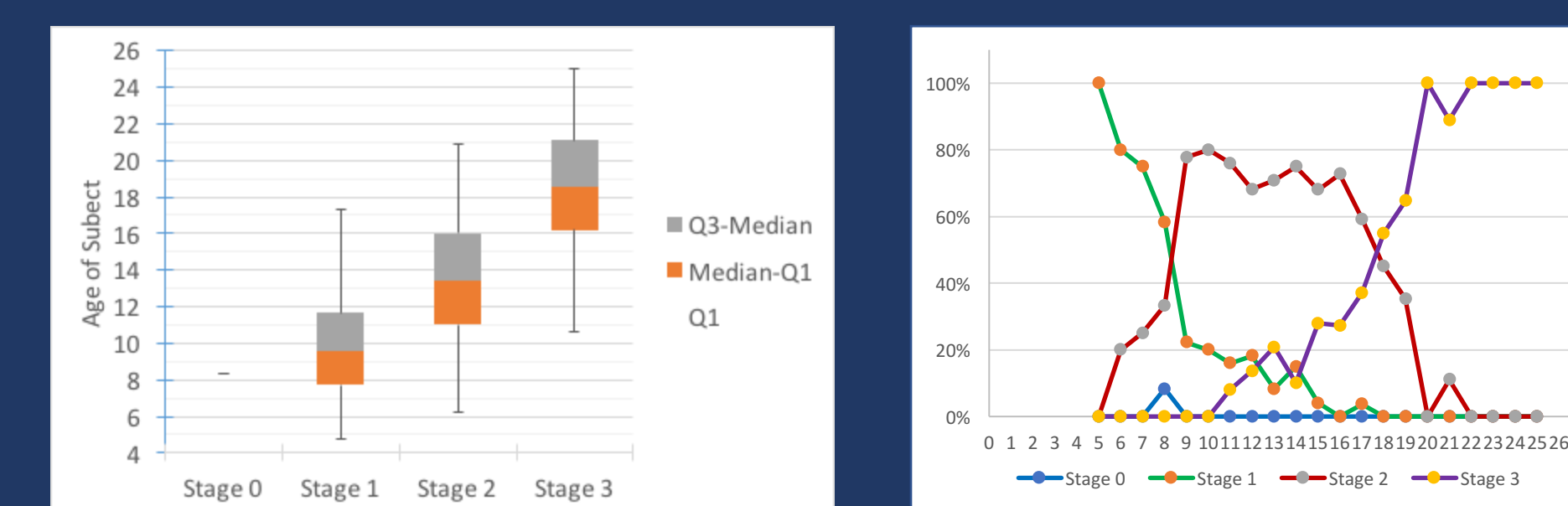
Age at onset in years. On average girls have onset of vision loss one year later than boys.

Cialone et al., 2012

### PROPOSED STAGING SYSTEM

Staging can facilitate division into groups for possible clinical trials and provides a broad sense of disease progression

Stage	Defining Event	UBDRS Item and Score
0	Asymptomatic	Genetic Confirmation Required
1	Vision Loss	Physical Assessment item 3 > 0
2	Seizure Onset	NCL History Seizure Item > 0
3	Assistance Required for Ambulation	Physical Assessment item 12 > 2



Our staging system is based on readily identified, meaningful milestones in the progression of CLN3 disease. There is little overlap between stages and the crossover from one stage to the next is relatively discrete.

Unpublished data

### SEIZURES

In most individuals with CLN3 disease, most seizures are "grand mal" (generalized tonic-clonic), are relatively infrequent, and respond well to medications. Other types of seizures do occur. Fewer than 10% of individuals are on >2 medications for seizures.

**Table III: Clinical characteristics according to seizure type**

Seizure type	n (%)	Mean seizure frequency (SD)	Mean total seizure subscale score (SD)	Mean age at assessment (SD)
Generalized tonic-clonic	67 (78)	2.3 (1.3)	18.7 (11.6)	16.9 (4.8)
Complex partial/absence	31 (38)	2.9 (1.9)	22.7 (14.9)	16.5 (4.1)
Myoclonic	14 (16)	3.8 (2.2)	29.3 (16.9)	18.2 (5.2)
Atonic*	5 (6)	2.2 (2)	25.9 (6.9)	18.8 (4.4)
Simple partial	5 (6)	3.5 (2)	40.5 (15.1)	19.5 (4.3)

#### Seizure frequency score:

- 0=none
- 1=fewer than one per 6 months
- 2=between one per 3 to 6 months
- 3=between one per 1 to 3 months
- 4=between one per week and one per month
- 5=between one per day and one per week
- 6=more than one per day

**Table IV: Medication use and seizure severity**

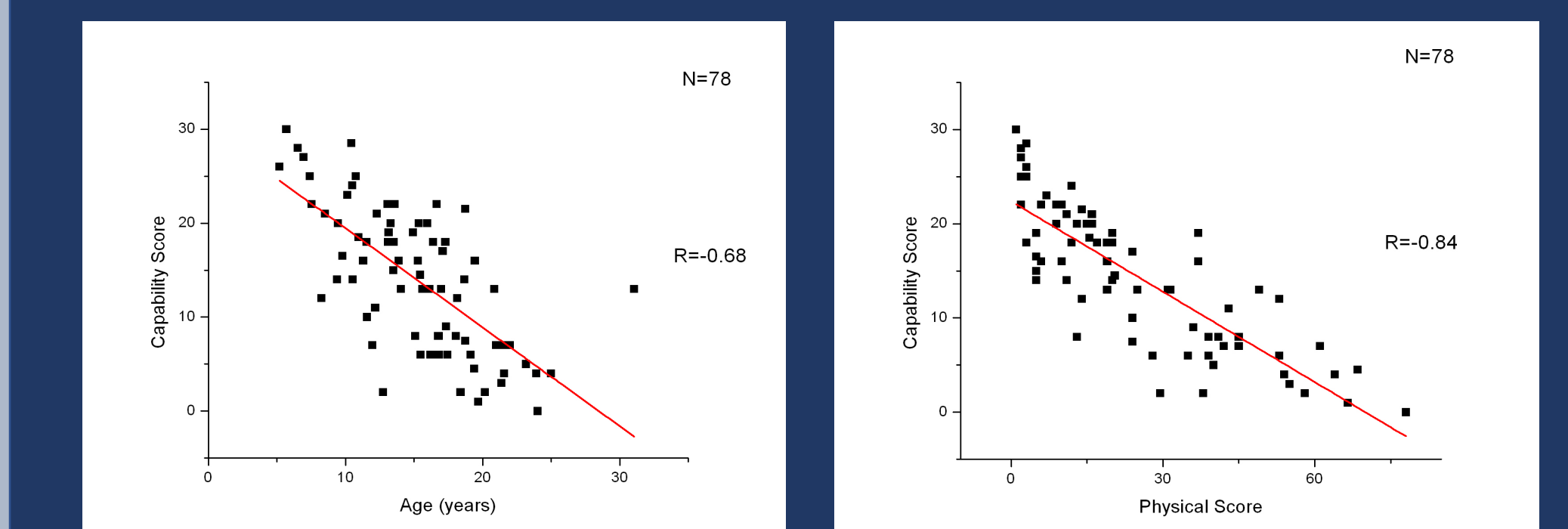
Number of medications used concurrently	n (%)	Mean total seizure subscale score (SD)
0	3 (4.1)	8.1 (4.7)
1	32 (43.8)	14.6 (8.6)
2	27 (37)	17.2 (11.5)
3	7 (9.6)	25.9 (14.3)
4	3 (4.1)	35.7 (22.7)
5	1 (1.4)	27.8 (N/A)

\*Represents the value for a single participant.

From Augustine et al., 2015

### FUNCTIONAL CAPABILITY

Functional capability declines with age and correlates with Physical Impairment. Functional capability assessed included school, chores, game playing, and activities of daily living.



Higher capability scores are better; Lower physical scores are better. As physical impairment worsens, so does functional capability. The capability assessment includes impact of visual loss, cognitive function, and physical function.

Unpublished data

### URBC Contributors to this work

- Heather Adams, PhD
- Erika Augustine, MD
- Chris Beck, PhD
- Jennifer (Cialone) Vermilion, MD
- Jennifer Kwon, MD MPH
- Frederick Marshall, MD
- Jonathan Mink, MD, PhD
- Paul Rothberg, PhD
- Alyssa Thatcher
- Amy Vierhile, DNP
- Justin Williams

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