



Longitudinal Adaptive Behavioral Outcomes in Ogden Syndrome by Seizure Status and Therapeutic Intervention

Makwana, Rikhil¹; Christ, Carolina¹; Marchi, Elaine¹; Harpell, Randie; Lyon, Gholson J.^{1,2,3}

¹Department of Human Genetics, New York State Institute for Basic Research in Developmental Disabilities, Staten Island, New York, United States of America; ²George A. Jervis Clinic, New York State Institute for Basic Research in Developmental Disabilities, Staten Island, New York, United States of America; ³Biology PhD Program, The Graduate Center, The City University of New York, New York, United States of America.

Introduction

Ogden syndrome (OS), also known as NAA10-related neurodevelopment syndrome, is a rare X-linked genetic syndrome associated with pathogenic variants in the NAA10 N-terminal acetylation family of proteins. OS is associated with characteristic neurologic phenotypes including seizures and developmental delays.

Objective

To characterize the behavioral deficits, present in OS, determine the incidence of seizures, and identify the most effective non-pharmaceutical therapies for managing the developmental delays associated with the disorder.

Methods

Data Collection

Participants responded to survey about seizure incidence and therapy use. Participants were also administered the Vineland Adaptive Behavioral Scales assessment, Third Edition (Vineland-3) and were tested longitudinally over a period of multiple years.

Data Analysis

A natural history analysis was conducted using the Vineland data and by comparing participants and the Vineland domains considering age of administration. Two-tailed students t-tests of unequal variance were performed with a presumed p-value of <.05 to determine if there were any differences in Vineland adaptive domains, seizure status, and therapy utilization.

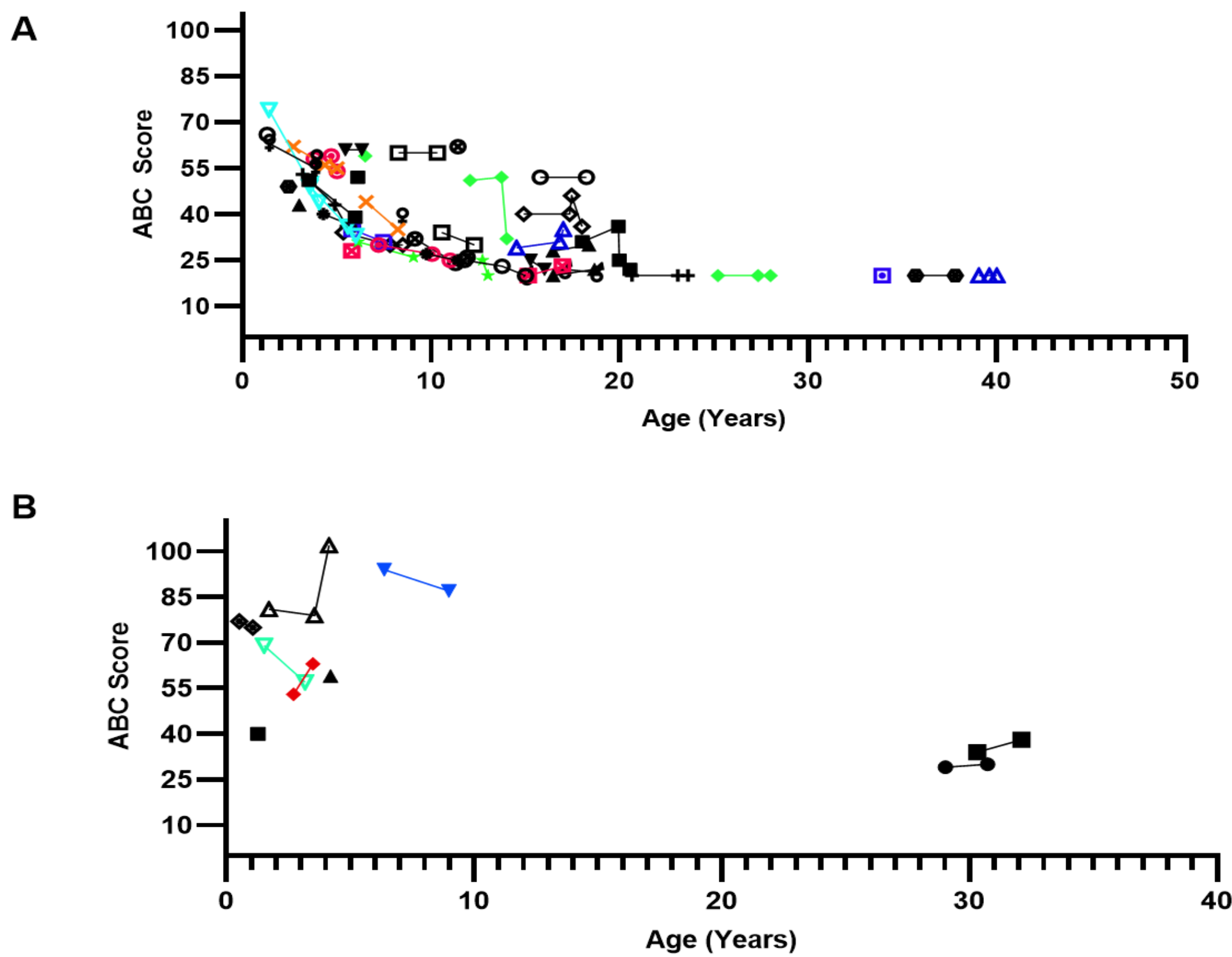


Figure 2. Vineland Standard Scores vs Age of Vineland Assessment **A. Females** Mean score 36.5 (SD = 14.6) **B. Males** Mean score 62.8 (SD = 22.9) All participants with Vineland data were included in analysis. The average age at time of most recent assessment was 12.4 years old (age range 11 months to 40.2 years old).

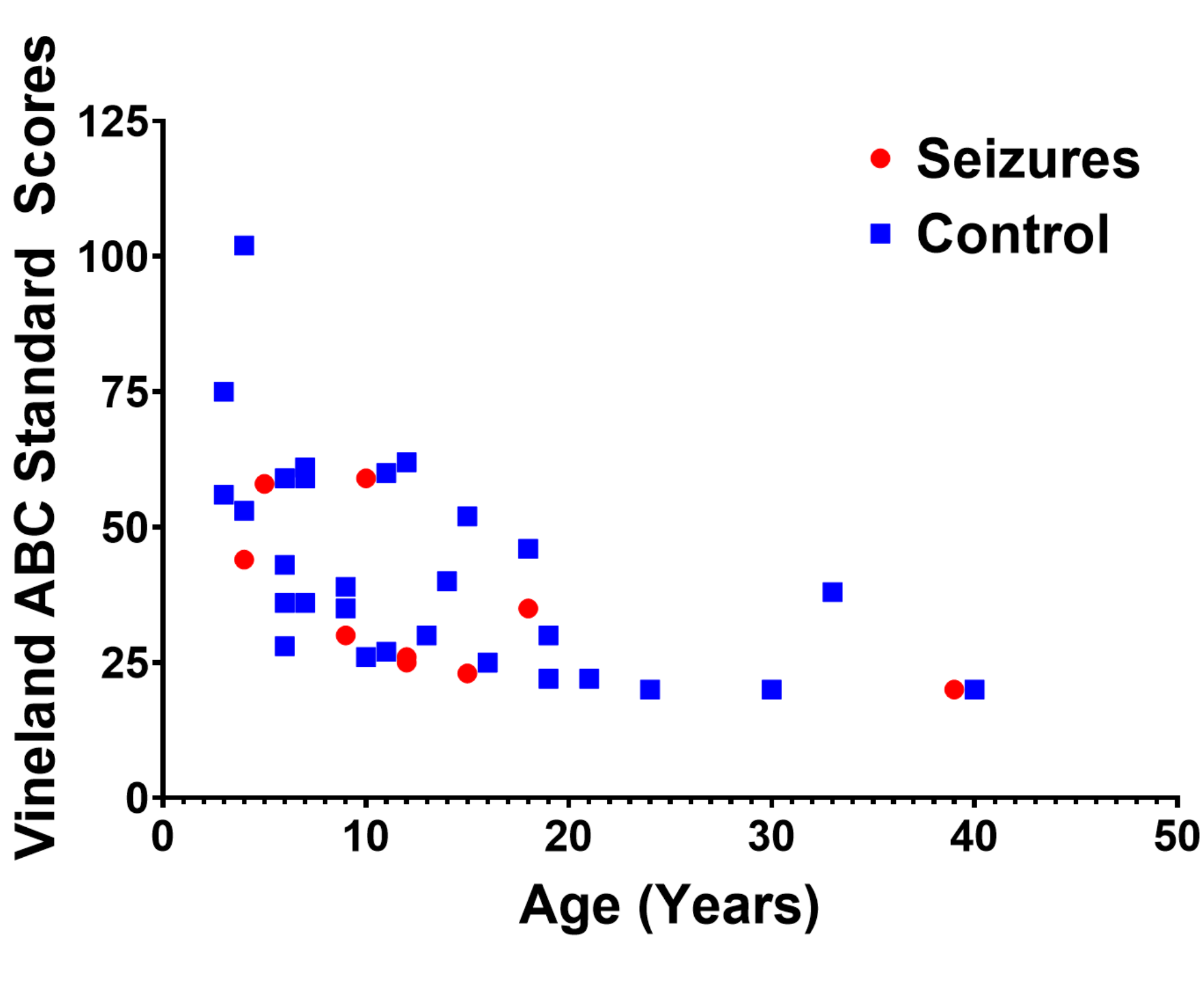


Figure 3. ABC Standard Score vs Age at time of Vineland Assessment based on Participant Seizure Status The mean ABC SS in the Seizure group was 35.6 (SD 14.0). The mean ABC SS in the non-seizure group was 42.1 (SD = 19.0) There was no significant difference in the Vineland ABC standard scores between groups.

Results

Participants

58 participants including (n=48 females, n=10 males), 48 of whom were administered the Vineland and answered the survey. **Figure 1** illustrates all the NAA10 pathogenic variants.

Natural History

Males and females performed significantly worse than the normalized population scores. Females performed worse than males and both sexes showed a decrease in adaptive functioning with age. **Figure 2** shows Vineland ABC standard scores over time. **Figure 3** compares Vineland ABC scores between individuals with (n = 9) and without (n=39) the seizure phenotype. Over time, both groups appear to be declining in function while following similar trajectories.

Therapeutic Interventions

Figure 4 shows the therapies

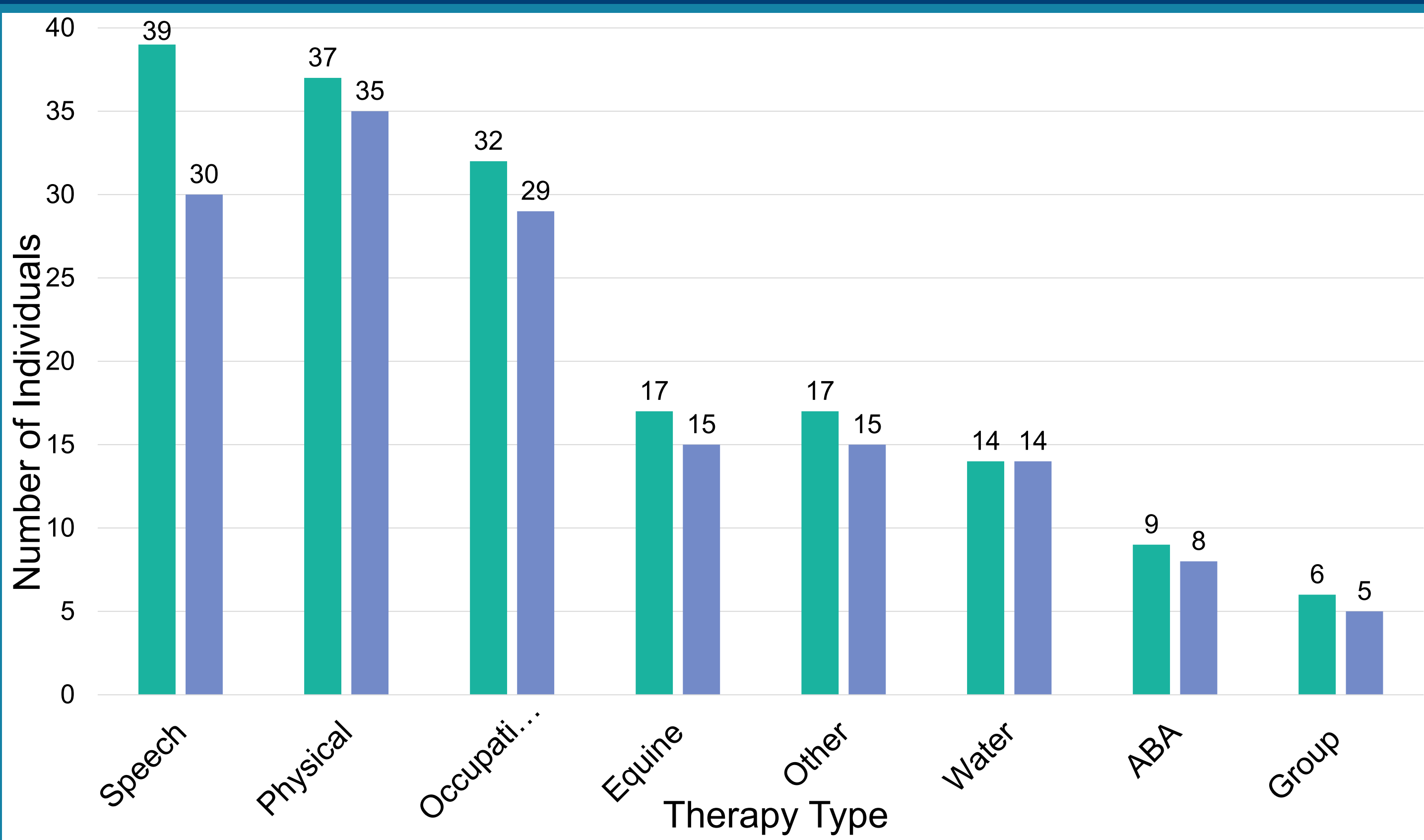


Figure 4. Therapy Utilization and Reported Helpfulness. Speech therapy was the most utilized intervention (n = 39). Water and physical therapy had the greatest satisfaction rates.

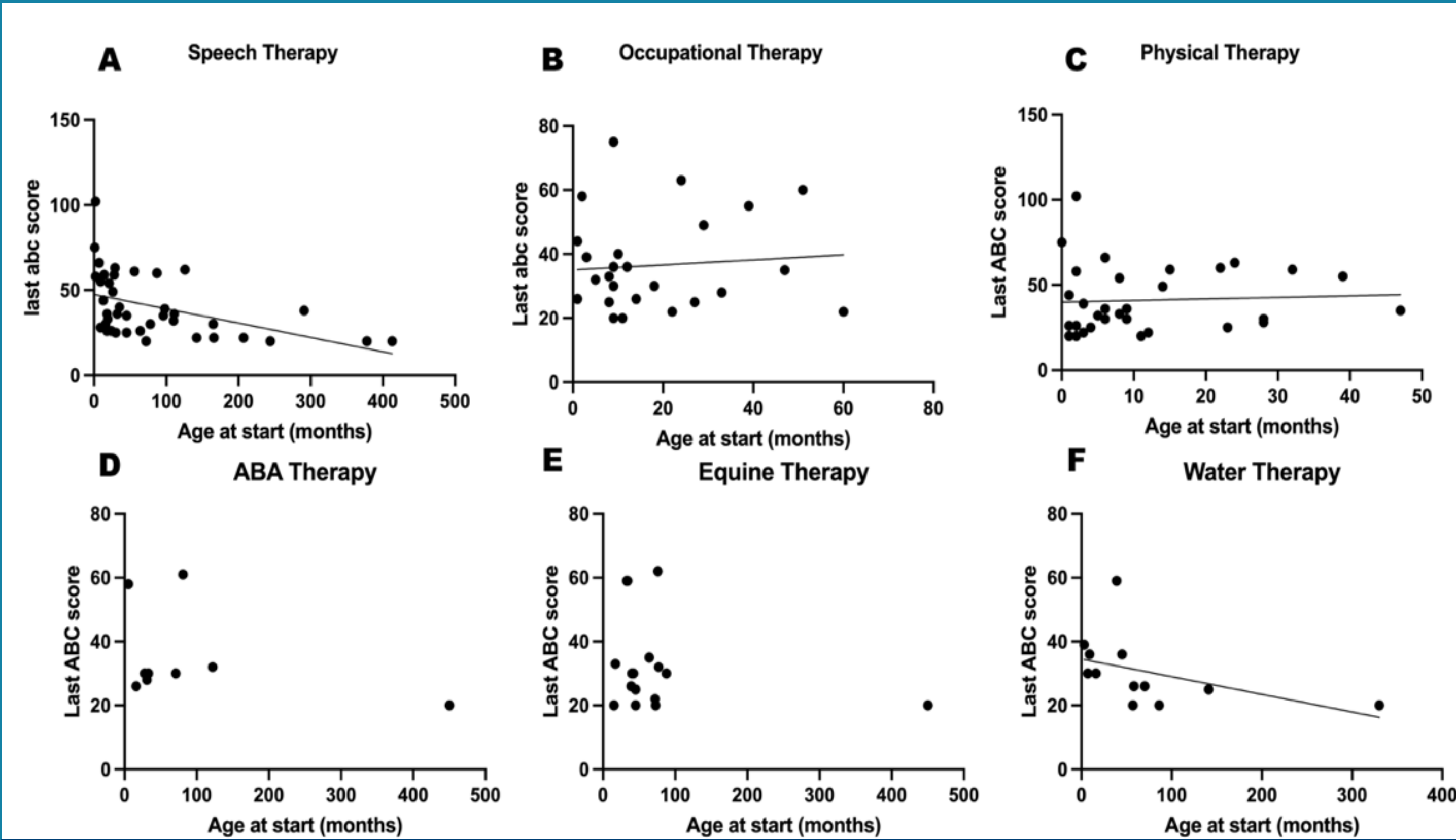


Figure 5. ABC Standard Score vs Age at time of Starting Therapy. Age converted to months to allow for inclusion of therapies started in infancy.

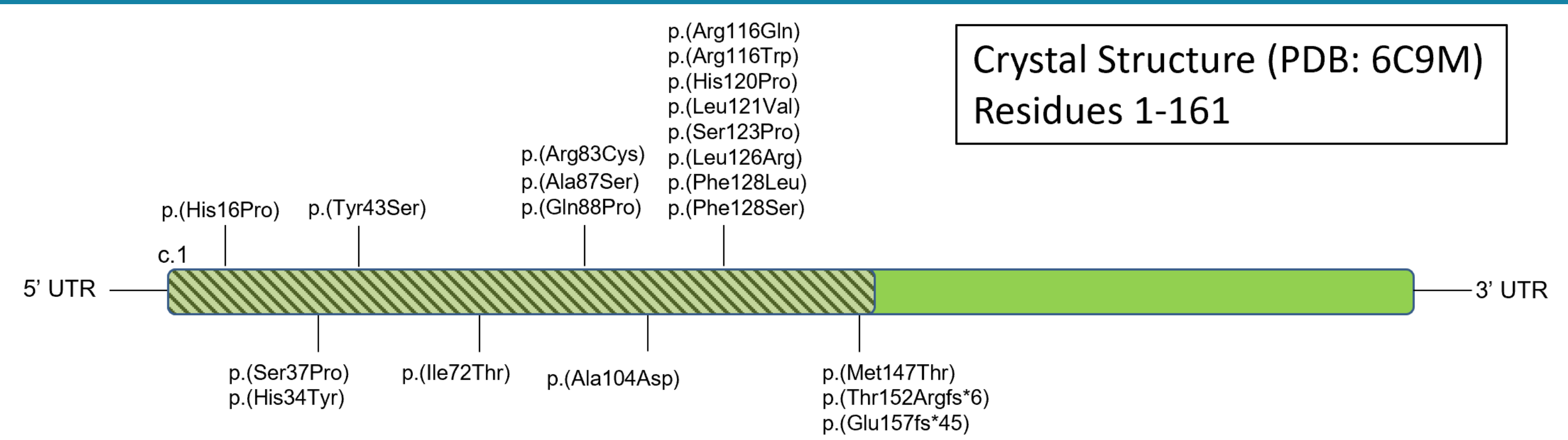


Figure 1. NAA10 pathological variants. Arg83Cys was the most common pathologic variant (n=23). Phe128Leu was the second most common (n=7). Several variants appeared only in a single proband.

Randomized controlled trials comparing intervention types, age at start of intervention, and number of contiguous interventions need to be performed before specific recommendations for guiding care can be made.

utilized and subjective helpfulness. There was an inverse relationship between number of therapies used and ABC score (p=0.0069). **Figure 5** shows the ABC standard score at the age at which the therapy was started. There was a significant association between the age at which speech therapy was started and participant outcomes (p=0.0031).

Conclusion

Seizures are not a significant phenotypic component of OS. Both sexes experience a decline in adaptive function with age.