

Patient-Reported Walking Capacity (WC) in Children with Ataxia Telangiectasia (AT) From Global AT Family Data Platform

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INTRODUCTION

- Ataxia telangiectasia (AT) is a rare neurodegenerative disorder manifesting with cerebellar ataxia, oculomotor apraxia, slurred speech, involuntary movements, telangiectasias, delayed growth and sexual maturation, sensitivity to ionizing radiation, immunodeficiencies, and an increased risk of malignancy.
- Premature loss of walking capacity (WC) is an important component of this disease which affects patients’ independence and quality of life.
- AT Children’s Project is an organization supporting research and it maintains a large database (Global AT Family Data Platform) comprising genetic, medical, and data on walking capacity, provided directly by AT participants and their families.

OBJECTIVE

- Describe the pattern of age-related WC loss as reported to the Global AT Family Data Platform by participants and families, using subjective WC scale.
- Compare subjective WC scale to the two scales used in clinical trials: International Cooperative Ataxia Rating Scale (ICARS) and Rescored modified ICARS (RmICARS).

METHODS

- Between 2016 and 2024, 624 AT participants completed the Global AT Family Data Platform questionnaire. Inclusion criteria comprised age (≤18 years at the time of WC reporting) and presence of the first neurological symptom at ≤5 years of age. Each participant contributed only one WC datapoint.
- Walking categories of ICARS and RmICARS were mapped to the subjective scale categories, as described in Table 1
- The relationship between categories of the three WC scales and age was assessed using Spearman’s Rank correlation. Linear regression was used in 5-14-year-olds, who had fast disease progression (N=220), to estimate disease progression with increasing age.
- We use graphical displays to demonstrate change in WC scores with age, and the R² to describe the proportion of variability in WC scores which is explained by age.

Table 1: Subjective WC scale scores, and mapped Scales

Subjective walking capacity scale	ICARS Original and a mapped score	RmICARS Original and a mapped score
Walks independently Score 1	Walks without support Mapped Score 1.5 0 = normal 1 = almost normal naturally, but unable to walk with feet in tandem position 2 = walking without support, but clearly abnormal and irregular	Walks without support Mapped score 0.5 0 = walking normal but unable to walk with feet in tandem position 1 = walking without support, but clearly abnormal and irregular
Walks independently most of the time Score 2	Walks without support but with difficulties Mapped score 3 3 = walking without support but with considerable staggering; difficulties in half turn	Walks without support but with difficulties Mapped score 2 2= walking without support but with considerable staggering; difficulty with half turn
Needs assistance for long trips (may use wheelchair or stroller when fatigued or on extended trips) Score 3	Walks with support Mapped score 4.5 4 = walking with autonomous support no longer possible; the patient uses episodic support of a wall for a 10-meter test 5 = walking only possible with one stick	Walks with support Mapped score 3 3 = walking with autonomous support no longer possible; the patient uses episodic support 3 = walking only possible with one stick 3 = walking only possible with two special sticks or a stroller or accompanying person
Uses bilateral support (walker) most of the time Score 4	Walks with bilateral support Mapped score 6.5 6 = walking only possible with two special sticks or a stroller 7 = walking only with accompanying person	
Uses wheelchair without assistance Score 5	Uses wheelchair Mapped score 8 8 = walking impossible even with accompanying person (wheelchair)	Uses wheelchair Mapped score 4 4 = walking impossible even with accompanying person (wheelchair)
Uses wheelchair with assistance Score 6		

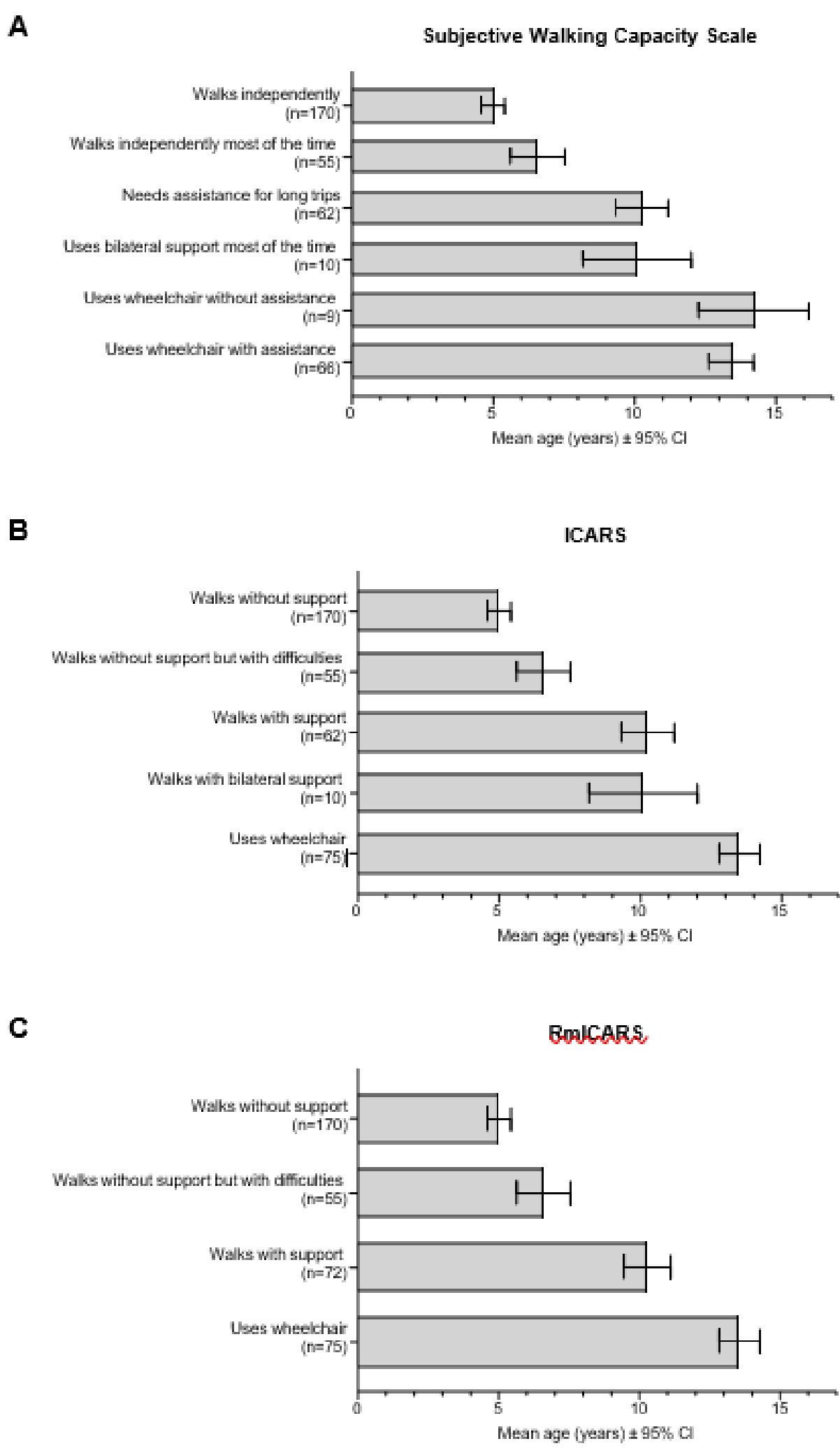


Figure 1: Mean age and walking capacity categories

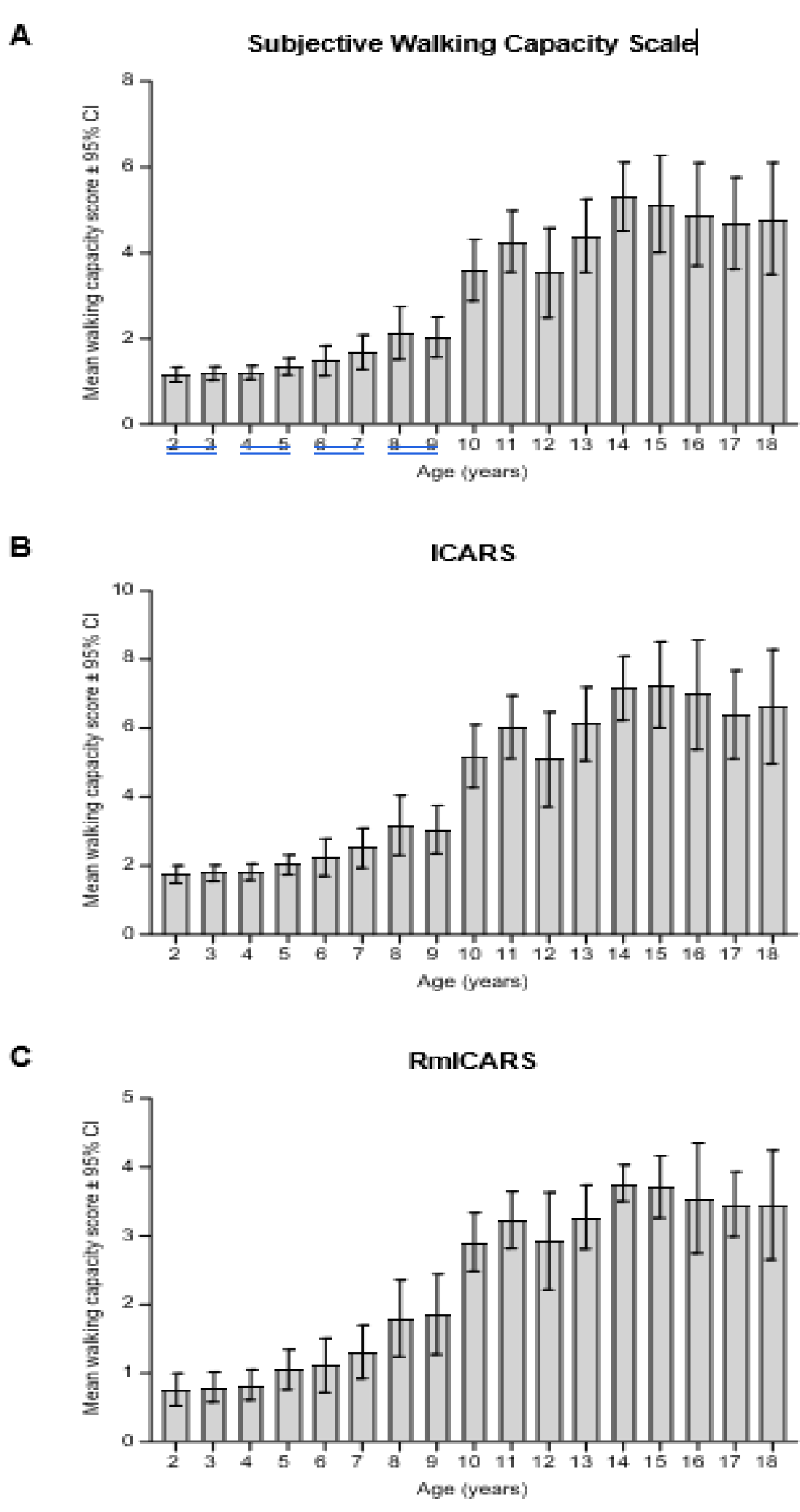


Figure 2: Mean walking capacity score by each year of age

RESULTS AND DISCUSSION

- Figures 1A-C depict the mean age (years ± SD) at reporting of each walking capacity category, for the three scales.
- The two least frequently chosen categories “uses walker” and “uses wheelchair without assistance” did not reflect a clear pattern of age-related progression.
- Figures 2A-C describe change in WC with age by three different scales. Three age-related stages of change in WC can be distinguished:
 - 2-4 years of age with stable WC,
 - 5 to ~12-14 years of age, fast loss of WC, with peak scores being reached at the age of 14 years, and
 - persistently high scores indicating loss of walking ability.
- Spearman’s rho correlation coefficients were 0.711 for the subjective walking capacity scale, 0.713 for ICARS, and 0.714 for RmICARS, showing consistently strong association with age across the three scales.
- Linear regression estimated times to a one-point change in each scale of 2.3 years (subjective scale), 1.7 (ICARS) and 3.0 years (RmICARS), with corresponding R² values (proportion of variability explained by the regression line) of 0.45, 0.46 and 0.45, respectively (all p<0.001).
- The R² values indicated that age accounted for just under half of the total variability in WC progression in this population. Other factors, such as disease phenotype, or participants’ inability to distinguish the categories of assisted walking, contributed to observed variability.

CONCLUSIONS

- Subjective WC scale was comparable to ICARS and RmICARS after mapping the categories across the 3 scales.
- All scales described an approximately linear age-related change in WC with age explaining approximately half of variability in WC progression.
- Although a simplified scale, RmICARS retains changes in age-related disease progression. This was likely due to its ability to capture detail categories of walking without assistance, making it suitable for use in younger children with AT.

Disclosures: BH, MR, DT are employees of Quince Therapeutics Inc. AS, AD, TS, and WW received consulting fees from Quince Therapeutics Inc. for other projects related to ataxia telangiectasia. JT is the Executive Director of Ataxia Telangiectasia Children’s Project.