

Longitudinal Trajectories of Cognitive Functioning in Adults with Down Syndrome based on Residence

Dasoo Milton Yoon^{1,2}, Courtney Brothers^{1,2}, Ashlyn Barry^{1,3}, Emily K. Schworer¹, Melissa Jenkins¹, Benjamin L. Handen⁴, Christy L. Hom⁵, Lauren Ptomey⁶, Sigan L. Hartley^{1,2} and the Alzheimer Biomarker Consortium - Down syndrome

¹Waisman Center, University of Wisconsin-Madison, Madison, Wisconsin, 53705, USA
²Department of Human Development and Family Studies, University of Wisconsin-Madison, 53705, USA
³Department of Kinesiology, University of Wisconsin-Madison, Madison, Wisconsin, 53705, USA
⁴Department of Psychiatry, University of Pittsburgh, Pittsburgh, Pennsylvania, 15213, USA
⁵Department of Psychiatry & Human Behavior, University of California, Irvine, Orange, California, 92868, USA
⁶Department of Neurology, University of Kansas Medical Center, Kansas City, Kansas, 66160, USA



INTRODUCTION

- Genetic Foundation:** Triplication of chromosome 21 causes *APP* over-expression, leading to near-universal Alzheimer’s Disease (AD) neuropathology by midlife (Wiseman et al., 2015; Rafii et al., 2025).
- Heterogeneity:** While average decline begins in the 40s or 50s, symptom onset spans a 30-year range, suggesting lifestyle factors could influence timing (Fortea et al., 2021; McCarron et al., 2017).
- Residence & Cognitive Reserve:** Living arrangements heavily dictate daily routines and social engagement, directly shaping the cognitive reserve required to compensate for underlying AD pathology. (Mihaila et al., 2020).
- Transition:** Residential moves are major life stressors associated with functional decline and increased mortality, potentially overwhelming remaining reserve (Aneshensel et al., 2000; Melrose, 2019).

CURRENT STUDY

- Aim:** To compare cognitive trajectories across residential settings and evaluate the impact of residential transitions using a large, multi-site cohort.
- Hypothesis:** Residential transitions will act as significant stressors, leading to accelerated cognitive decline compared to stable living arrangements.

METHODS

Participants

- N = 529 adults with DS (age > 25)
- Residential Groups
 - With Parent (n = 220)
 - With Sibling (n = 32)
 - Independently (n = 66)
 - Group Home/Facility (n = 161)
 - Transition (n = 50)

Variable	Overall (N = 529)
Age	43 ± 10
Premorbid Intellectual Impairment	
Mild	253 (47.8%)
Moderate	225 (42.5%)
Severe	51 (9.6%)
Sex	
Male	282 (53.3%)
Female	247 (46.7%)
Race	
White	516 (97.5%)
Black	9 (1.7%)
Asian	4 (0.8%)

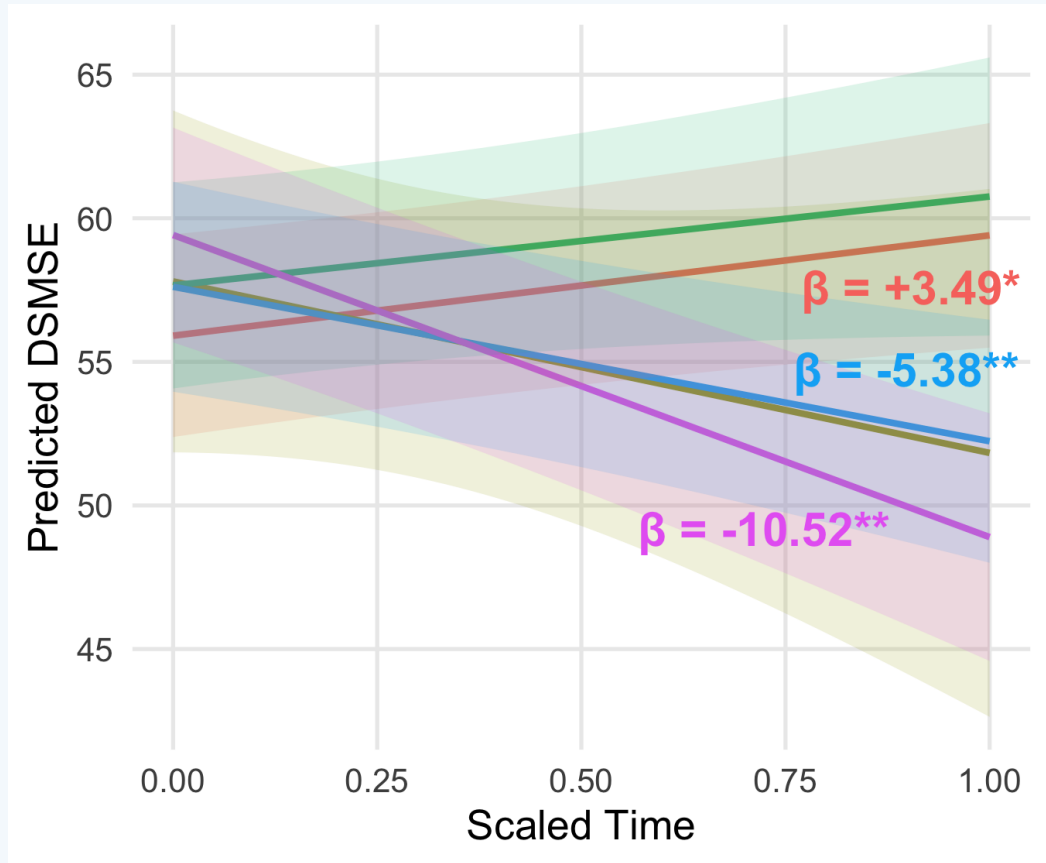
Variable	Overall (N = 529)
Karyotype	
Trisomy	479 (90.5%)
Mosaicism	24 (4.5%)
Translocation	26 (4.9%)
Dementia Consensus	
No MCI/Dementia	388 (73.3%)
MCI	60 (11.3%)
Dementia	58 (11.0%)
Unable to Determine	23 (4.3%)
DSMSE	59 ± 17
MCRT	28 ± 10
DLD-Cognitive	7 ± 9
NTG	6 ± 10

Key Measures

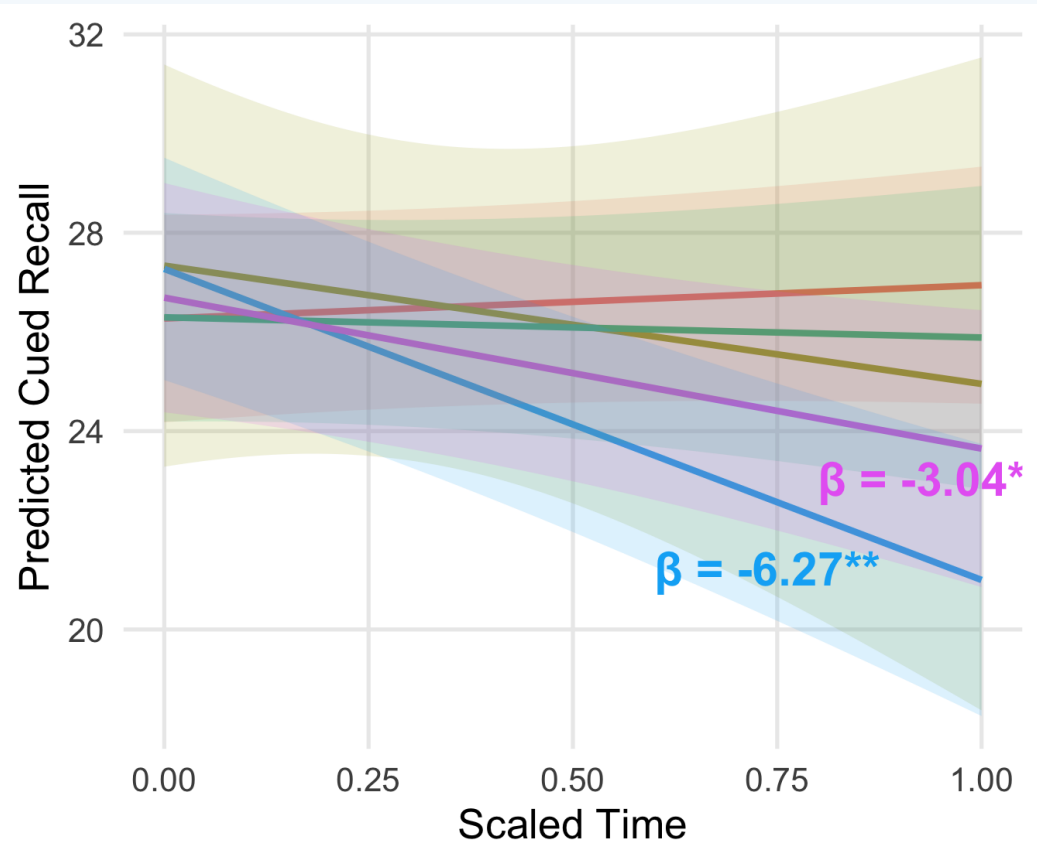
Measure	Domain	Direction of Interpretation
Down Syndrome Mental Status Examination (DSMSE; Haxby, 1989)	Cognitive Functioning	↓ Lower scores = Greater overall cognitive impairment
Modified Cued Recall Test (mCRT; Devenny et al., 2002)	Episodic Memory	↓ Lower scores = Greater memory impairment
Dementia Questionnaire for People with Learning Disabilities Scale, Cognitive Subscale (DLD; Evenhuis et al., 1992)	Dementia Symptoms	↑ Higher scores = Greater challenges with daily functional skills
National Task Group–Early Detection Screen for Dementia (NTG; Esralew et al., 2013)	Dementia Symptoms	↑ Higher scores = Greater dementia symptom burden

LONGITUDINAL CHANGE BY RESIDENCE GROUP

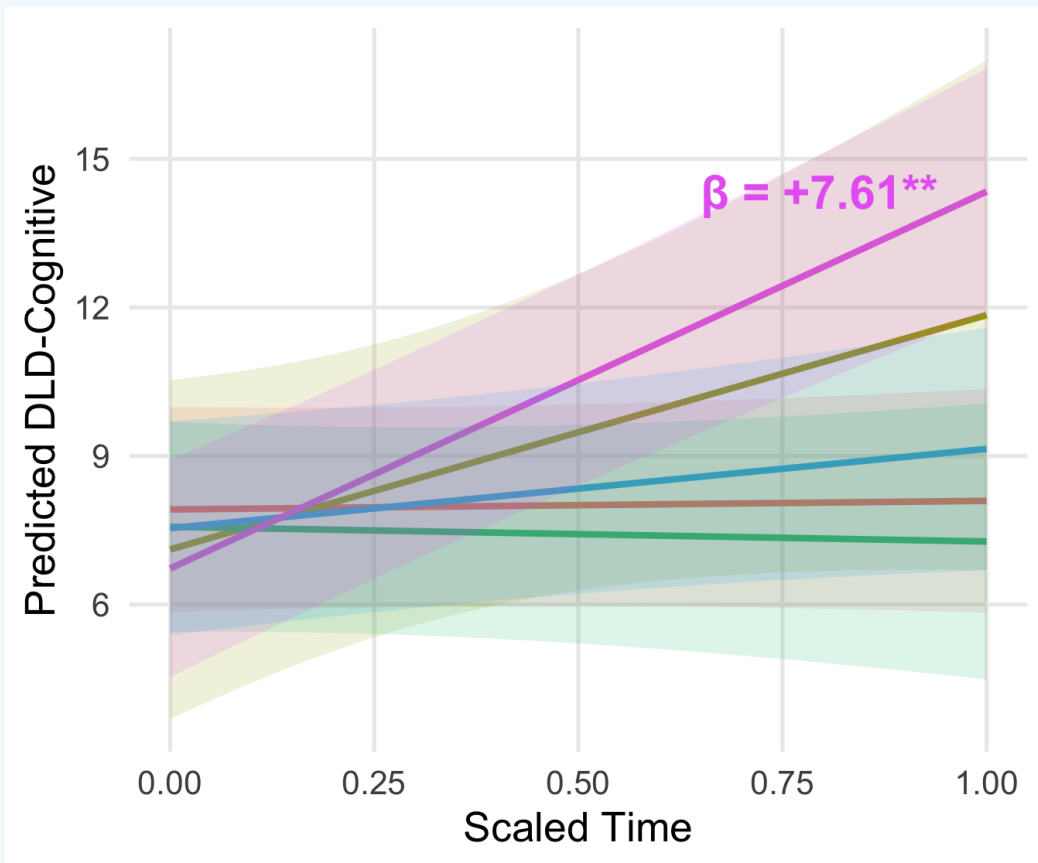
DSMSE



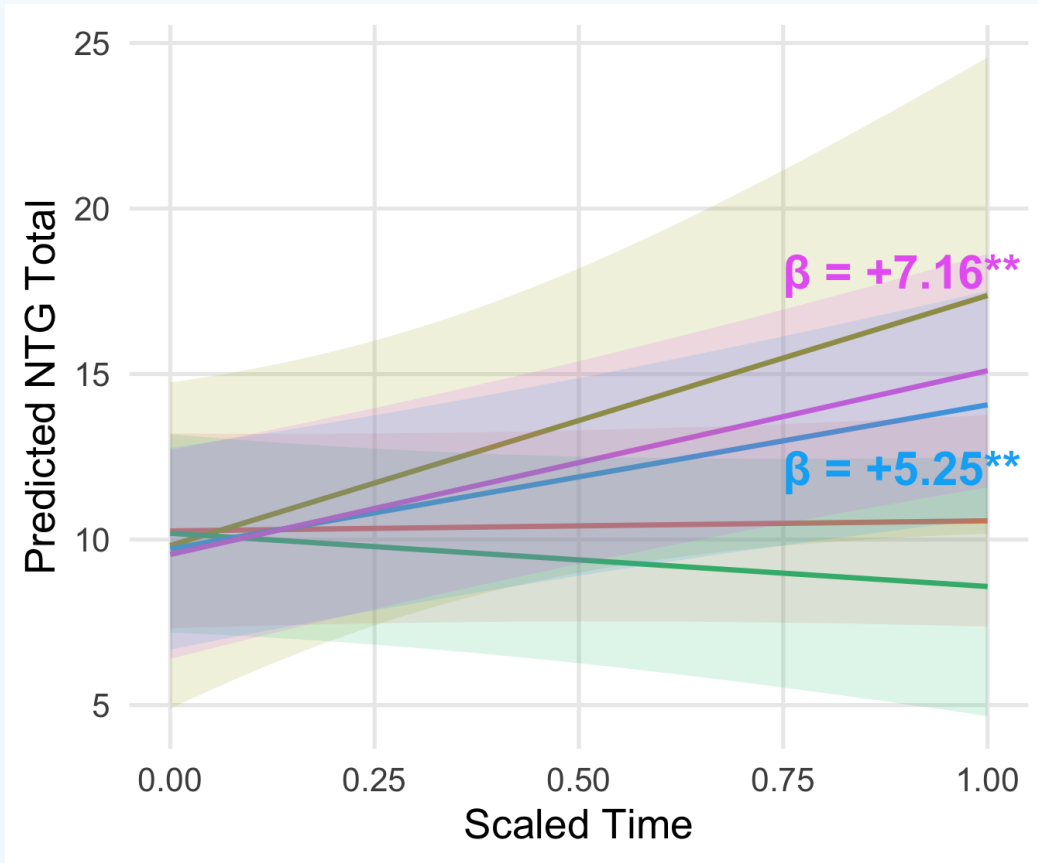
mCRT



DLD-Cognitive



NTG



Residential group — With Parent — Sibling — Independent — Group Home — Transition p < .05*, p < .001**

What the Data Shows

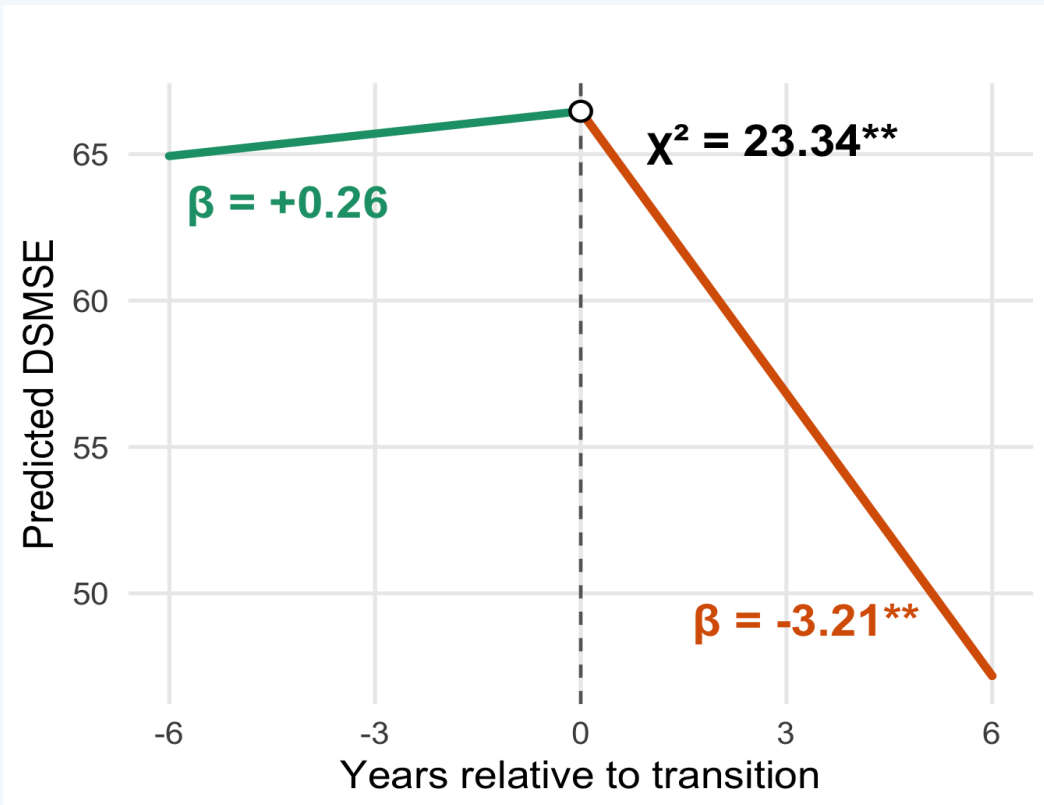
Stable parental and independent living are associated with cognitive and functional stability, whereas individuals in group homes or those undergoing residential relocations exhibit significant decline, with transitioning cohorts experiencing the sharpest, most rapid deterioration across all metrics.

Interpretation

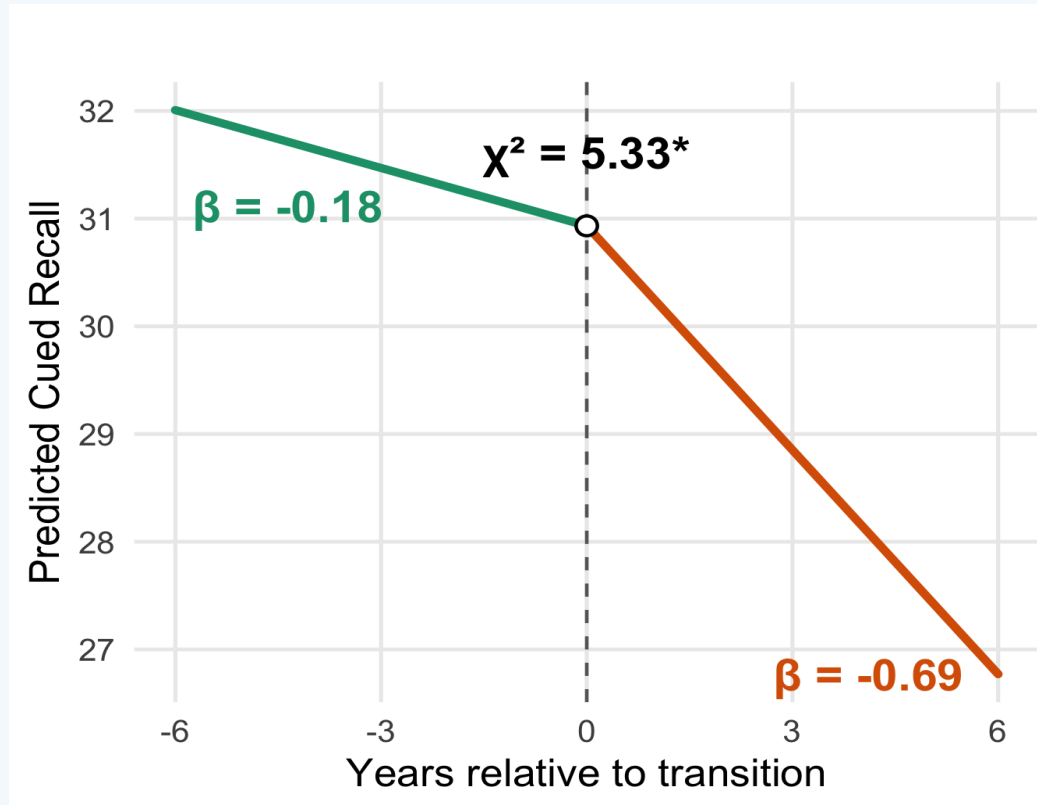
Disparities are dual-driven: "selection effects" reflect pre-existing medical conditions, baseline functioning, or changes in parental care capacity that dictate placement, while "environmental effects" capture variations in daily social, cognitive, and physical activities that build or deplete cognitive reserve.

TRANSITION GROUP: THE “MOVE EFFECT”

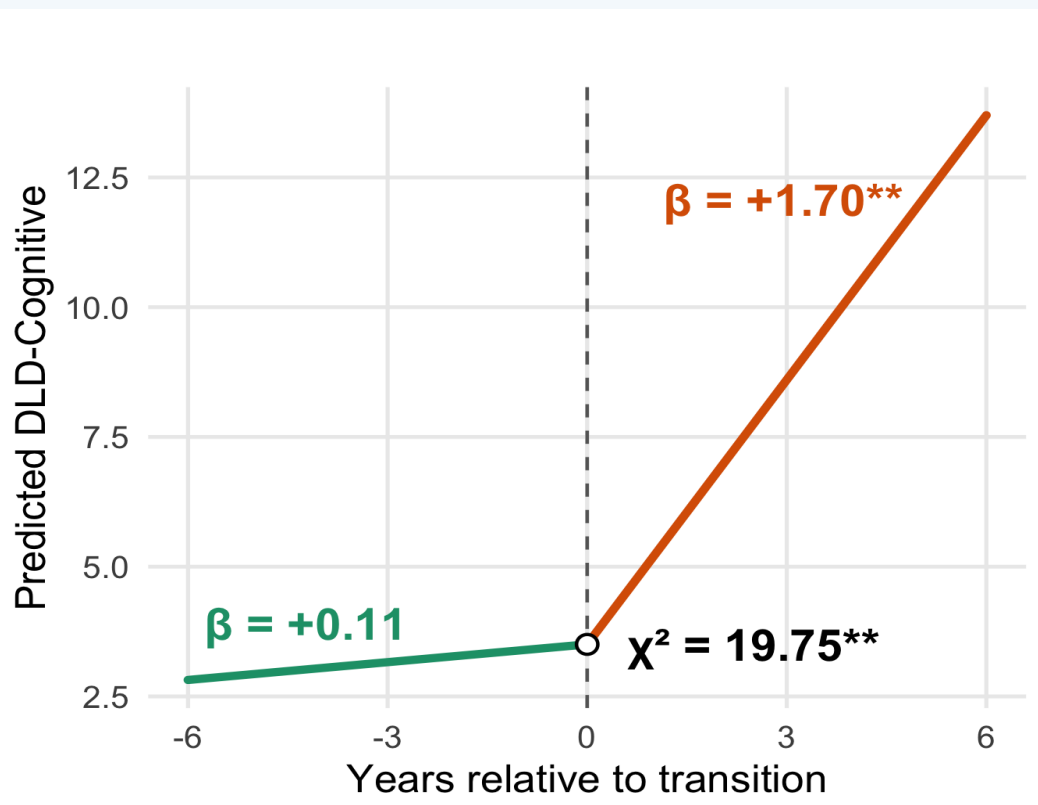
DSMSE



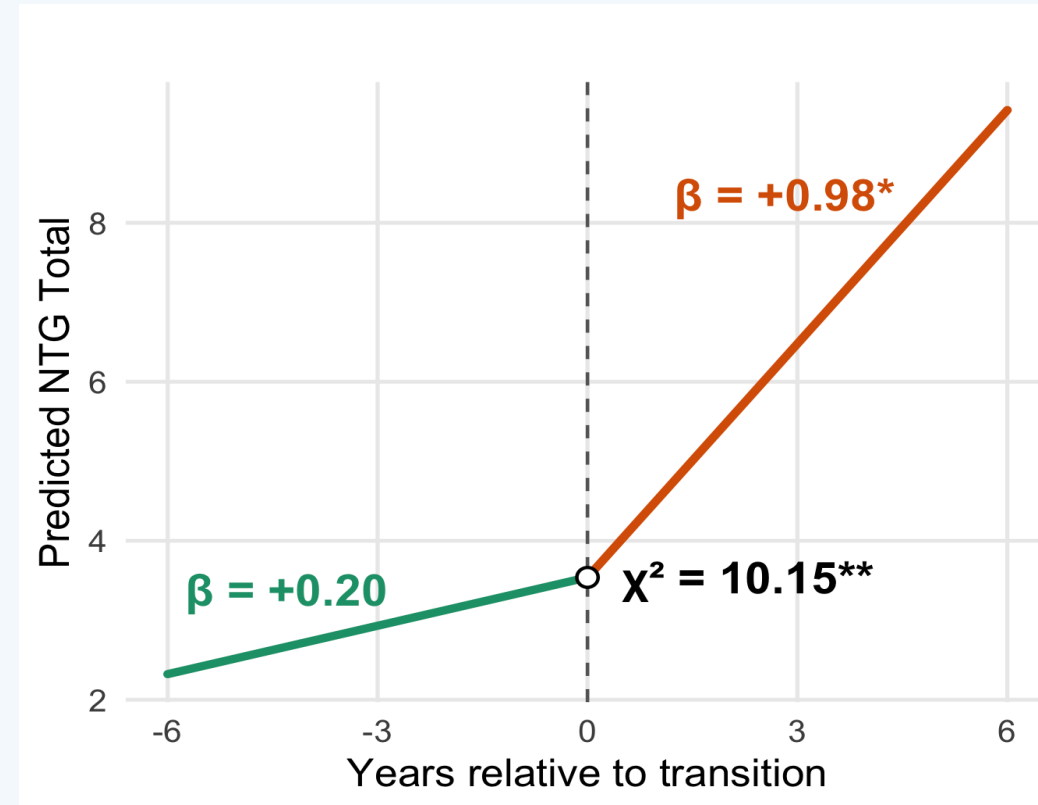
mCRT



DLD-Cognitive



NTG



Residential group — With Parent — Sibling — Independent — Group Home — Transition p < .05*, p < .001**

What the Data Shows

Piecewise models reveal statistical stability immediately prior to relocation followed by a sharp, abrupt post-move drop across all outcomes, occurring universally regardless of move direction.

Interpretation

This inflection point represents a dual dynamic: relocation may act as a stressor whose high cognitive and adaptation demands exhaust remaining reserve (causality), or the transition itself is a reactive measure prompted by early, subtle functional changes preceding formal clinical detection (reaction).

DISCUSSION

Reserve vs. Disruption: Stable family settings provide a protective "environmental reserve" that preserves cognitive function longer. Conversely, relocation disrupts automatic routines and introduces intense adaptation demands that exhaust remaining cognitive reserve, though moves can also be reactive to early, unmeasured functional shifts.

Clinical Action: Clinicians must flag residential transitions as periods of acute cognitive risk requiring proactive monitoring. Structural mitigation should utilize "phased integration" (e.g., visual schedules, reminders) alongside targeted resource toolkits for sibling caregivers.

Future Directions: Future research must examine specific move triggers (e.g., parental health) and contexts (planned vs. crisis) to refine clinical risk profiles.

ABC-DS



REFERENCES



HARTLEY LAB



CORRESPONDENCE

D. Milton Yoon, dmyoon@wisc.edu

ACKNOWLEDGEMENTS

NIA R01 AG070028; U01 AG051406; U01 AG051412; U19AG068064