

Prescribing Patterns of Antipsychotics in Dementia-Related Psychosis: A National Alzheimer's Coordinating Center Analysis

Ali Abdullah, HBS¹, Harani Uthayakumar^{1,2}, Neda Rashidi-Ranjbar^{1,4}, Nathan Churchill¹, Luis Fornazzari^{1,5}, Vincenzo De Luca⁶, Zahinoor Ismail⁷, Simon Graham^{8,9}, David Munoz^{10,12}, Tom A. Schweizer^{1,11}, Corinne E. Fischer, MD, FRCPC^{1,3}

¹ Keenan Research Centre for Biomedical Science, Li Ka Shing Knowledge Institute, St. Michael's Hospital, Toronto, ON, Canada, ² Temerty Faculty of Medicine, Institute of Medical Science, University of Toronto, Toronto, Ontario, Canada, ³ Department of Psychiatry, Temerty Faculty of Medicine, University of Toronto, Toronto, ON, Canada, ⁴ University of Toronto, Toronto, ON, Canada, ⁵ Faculty of Medicine, Department of Neurology, University of Toronto, Toronto, ON, Canada, ⁶ Division of Geriatric Psychiatry, Centre for Addiction & Mental Health, Toronto, ON M5T 1R8, Canada, Toronto, ON, Canada, ⁷ Department of Psychiatry, Hotchkiss Brain Institute, University of Calgary, Calgary, AB, Canada, ⁸ Temerty Faculty of Medicine, Department of Medical Biophysics, University of Toronto, Toronto, ON, Canada, ⁹ Hurvitz Brain Sciences Program, Sunnybrook Research Institute, Toronto, ON, Canada, ¹⁰ Temerty Faculty of Medicine, Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, ON, Canada, ¹¹ Temerty Faculty of Medicine, Division of Neurosurgery, University of Toronto, Toronto, ON, Canada, ¹² Division of Pathology, St. Michael's Hospital, Toronto, ON, Canada

Introduction

- Psychosis in Alzheimer's Disease (AD) is typically defined by delusions and/or hallucinations and is associated with greater patient distress, caregiver burden, clinical complexity, and disease severity (Lanctôt et al., 2017).
- Prescription of antipsychotics (AP) occur when symptoms are severe or unsafe, but usage remains controversial due to concerns about cognition, physical harm, and mortality (Rogowska et al., 2022).
- A known effect remains limited surrounding the cognitive trajectory of patients prescribed AP

Objective: To determine the natural history and clinical trajectory of AP exposed AD patients with psychosis relative to non-exposed patients

Hypothesis: Antipsychotic exposure will be associated with greater psychosis, behavioral, cognitive, and dementia-related burden, reflecting the greater clinical severity of individuals who receive antipsychotic treatment.

Methods

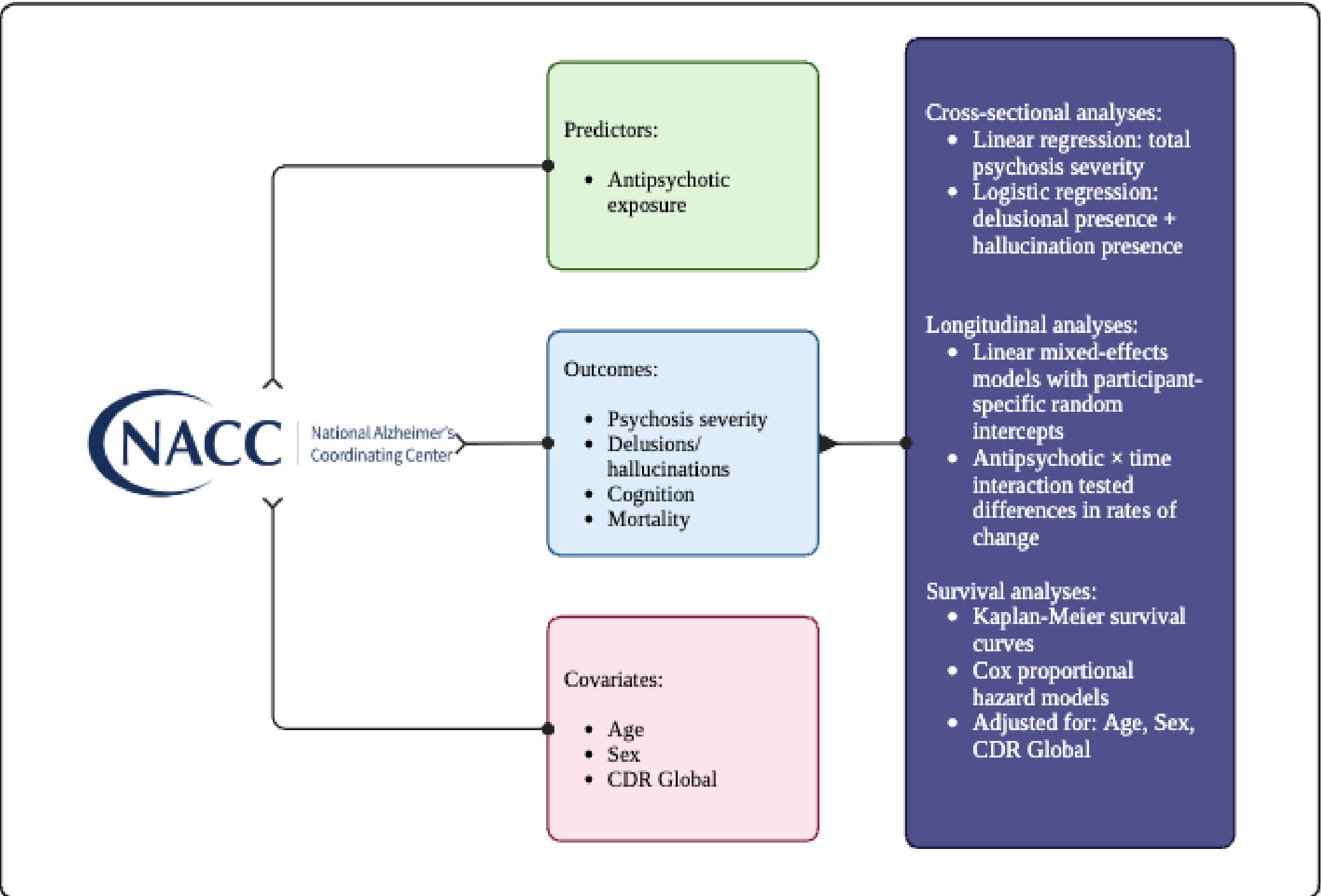


Figure 1. Flowchart indications predictors, outcomes, and covariates employed in the statistical analysis process of antipsychotic exposure among individuals with Alzheimer's in the NACC dataset

Results

	Overall N = 34,005	No AP N = 32,951	AP N = 1,054	p-value
Characteristics				
Age, years	71.1 ± 10.0	71.2 ± 10.0	70.2 ± 10.5	
Sex				
Male	14,622 (43.0%)	14,114 (42.8%)	508 (48.2%)	
Female	19,383 (57.0%)	18,837 (57.2%)	546 (51.8%)	
Number of visits	4 [2, 6]	4 [3, 6]	3 [2, 5]	
Follow-up duration, years	3.81 [2.01, 6.48]	3.87 [2.02, 6.57]	2.56 [1.28, 4.63]	
Death during follow-up	10,294 (30.3%)	9,738 (29.6%)	556 (52.8%)	
Clinical Characteristics				
Delusions present	1,851 (5.7%)	1,576 (5.0%)	275 (27.6%)	<0.001
Hallucinations present	1,025 (3.2%)	813 (2.6%)	212 (21.3%)	<0.001
Delusions and hallucinations present	471 (1.4%)	337 (1.1%)	134 (13.5%)	<0.001
MoCA score	25.0 [21.0, 27.0]	25.0 [21.0, 27.0]	21.0 [16.0, 25.0]	<0.001
NPI total burden	3.0 [2.0, 6.0]	3.0 [2.0, 5.0]	6.0 [3.0, 9.0]	<0.001

Table 1. Participant Demographics and Clinical Characteristics by Antipsychotic Exposure. Compared with participants not receiving antipsychotics (AP), AP-exposed participants had a significantly higher prevalence of delusions (27.6% vs. 5.0%), hallucinations (21.3% vs. 2.6%), and co-occurring delusions and hallucinations (13.5% vs. 1.1%; all $p < .001$). AP-exposed participants also had significantly lower median MoCA scores (21.0 vs. 25.0, $p < .001$), greater NPI total burden (6.0 vs. 3.0, $p < .001$).

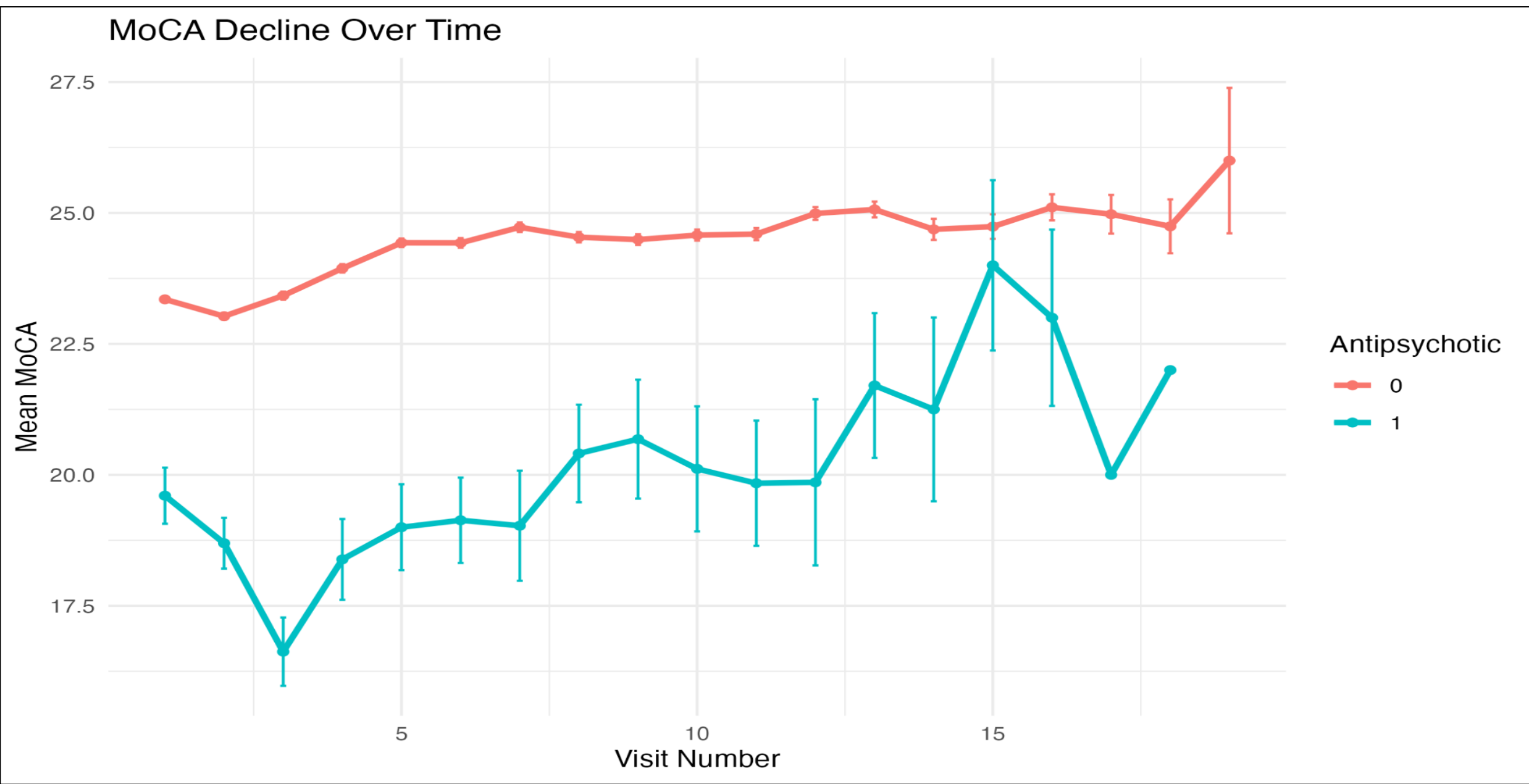


Figure 2. MoCA Scores Over Time by Antipsychotic Exposure. Antipsychotic-exposed participants demonstrated significantly lower overall MoCA scores than non-exposed participants ($\beta = -0.81$, $p < .001$). The antipsychotic-by-time interaction was not significant ($\beta = 0.013$, $p = .609$), indicating no evidence that the rate of MoCA change differed between exposure groups.

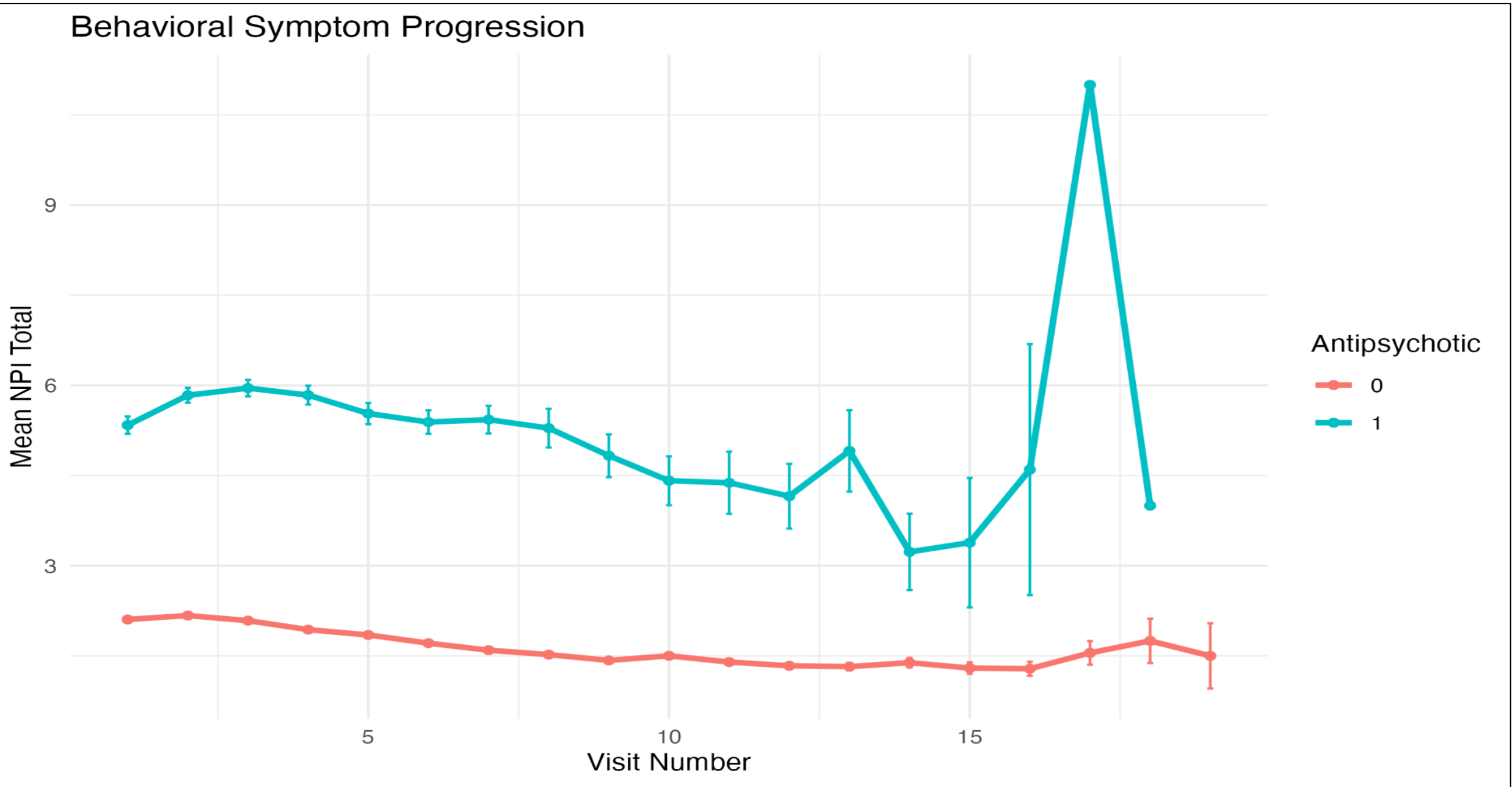


Figure 3. NPI Symptom Progression Over Time by Antipsychotic Exposure. Antipsychotic-exposed participants demonstrated significantly greater overall neuropsychiatric symptom burden than non-exposed participants ($\beta = 1.36$, $p < .001$). The significant negative antipsychotic-by-time interaction ($\beta = -0.156$, $p < .001$) indicated that the difference in NPI burden between groups decreased over time.

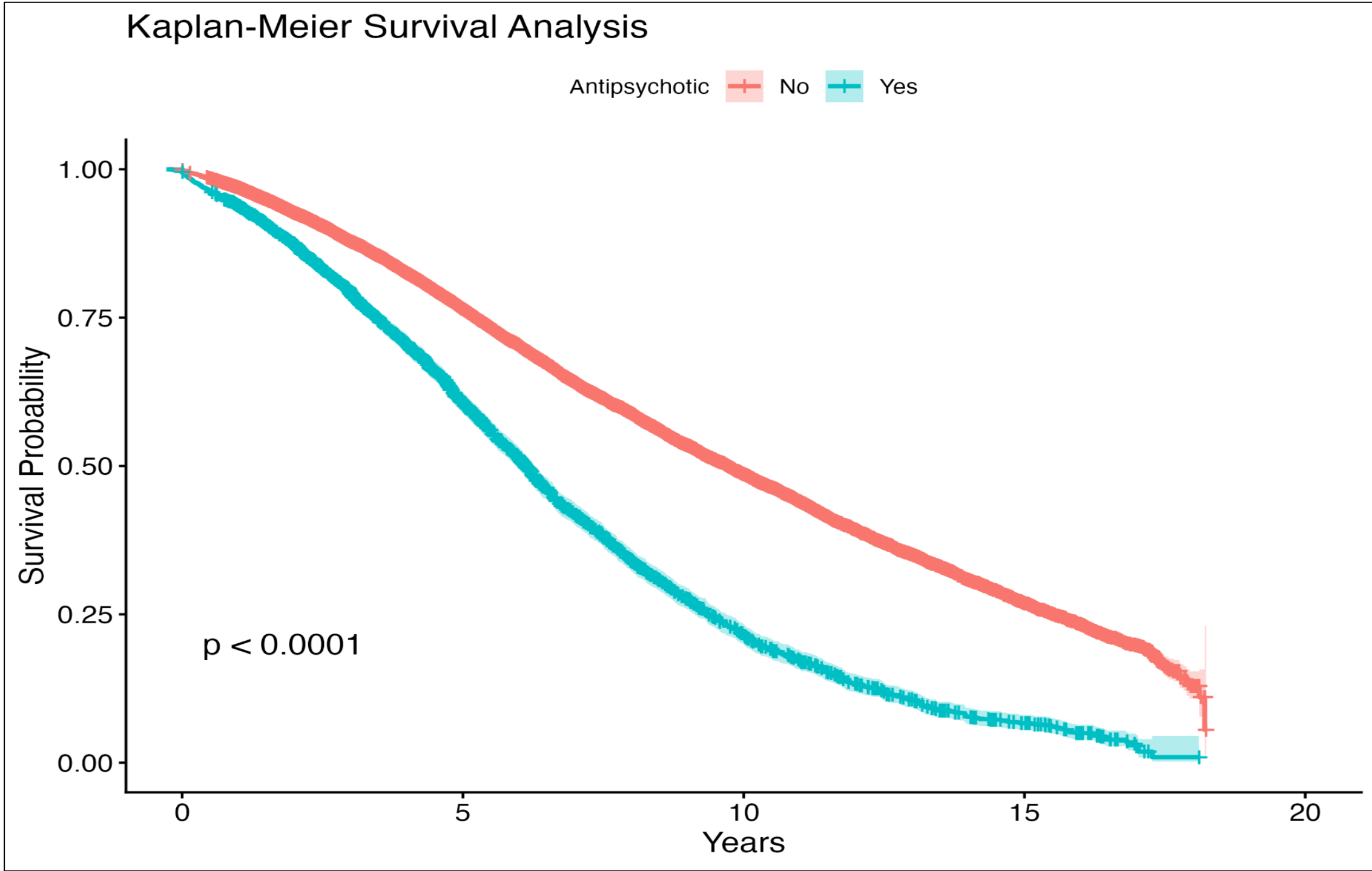


Figure 4. Kaplan-Meier Survival by Antipsychotic Exposure. Antipsychotic-exposed participants demonstrated significantly poorer unadjusted survival than non-exposed participants (log-rank $p < .001$); however, antipsychotic exposure was not independently associated with mortality after adjustment for age, sex, and CDR Global score (HR = 0.99, 95% CI: 0.94–1.04, $p = .587$).

Discussion

- Across domains, AP exposure appears to mark a clinically complex subgroup with greater psychosis, greater behavioral symptom burden, lower MoCA scores, and worse CDR-rated dementia severity.
- The survival analyses highlight confounding by severity: the KM curve shows worse unadjusted survival, but the adjusted Cox model shows no independent mortality association for AP exposure.
- Cognitive results remain ambiguous because MMSE findings were inconsistent with MoCA/CDR outcomes and affected by instability/outliers.

Acknowledgments

This project was supported by the Heather and Eric Donnelly Endowment through the St. Michael's Hospital Foundation. Data used in this study were obtained from the National Alzheimer's Coordinating Center (NACC), which is funded by the National Institute on Aging (NIA/NIH Grant U24 AG072122). The data were contributed by the NIA-funded Alzheimer's Disease Research Centers (ADRCs).



ST. MICHAEL'S
UNITY HEALTH TORONTO



National Alzheimer's
Coordinating Center

