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Incident Antipsychotic Use in a Diverse Population with Dementia

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To the Editor

Antipsychotic drugs have significant risks of side effects, especially increased risk of death, in elderly people with dementia [1]. Emerging research on racial and ethnic disparities in the treatment of Alzheimer's Disease (AD) and other dementias has further driven the need to identify groups at greater risk of using these medications. We examined patterns of antipsychotic use in African American, Hispanic, and non-Hispanic White patients with dementia, in the National Alzheimer's Coordinating Center (NACC) [2]. The objectives of this study were to characterize the incident use of antipsychotics participants, overall and by race/ethnicity, and to assess whether differences in time to antipsychotic use across race/ethnic groups persisted after accounting for demographic and clinical variables.

METHODS

We conducted a retrospective review of prescription medication records for community dwelling NACC participants diagnosed with dementia. The study sample consists of NACC participants (2008–2014) who had a diagnosis of dementia and indicated no current use of antipsychotic medications at their index visit. An index visit was determined by the participant's first available prescription information starting in 2008. A total of 4,741 participants fit this description: African American (n=401), Hispanic (n=337), and Non-Hispanic White (n=3,389). Demographic information included age, gender, education, and

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race/ethnicity. Clinical information included informant-reported neuropsychiatric symptoms (NPS) measured by the Neuropsychiatric Inventory Questionnaire (NPI-Q) [3, 4] and a clinician assessment of dementia severity using the Clinical Dementia Rating (CDR) [5,6,7]. The primary outcome was the time until either first record of antipsychotic use or censoring (last follow-up visit.) For a full list of medications included in this study please see the NACC Derived Variables documentation [8]. To estimate differences between racial/ethnic groups and to assess the additional effects of other demographic and clinical variables, we fitted Cox proportional hazard regression models. The effects of race/ethnicity were assessed in a series of three multivariate Cox regression models. The first model assessed whether likelihood of use of antipsychotic medications differed by race/ethnicity, taking account of the demographic variables. The second model added the NPI-Q sum of severity scores at index visit to assess the impact of NPS on future antipsychotic use and determine whether differences across race/ethnic groups might be accounted for by differences in NPS. In the third model, the CDR sum of boxes score at baseline was added to the model to assess the impact of dementia severity. For the purpose of these analyses we assumed that time of censoring was non-informative and independent of later antipsychotic use. All reported p-values were those of two-sided tests; significance was defined as $p<0.05$.

RESULTS

Of 4,741 participants, 614 (12.95%) went on antipsychotics during the study period. For many participants, data collection ended with the end of study period (10%), or death (25%). We compared rates and causes of censoring across race/ethnicities to see if non-Hispanics White and/or African Americans might not be followed as long for reasons related to decisions about antipsychotic medications, and found no significant difference between the three groups..

A series of multivariate Cox regression analyses examined the association of race/ethnicity with likelihood of future antipsychotic use, adjusted for age, education, and gender (Model I) and sequentially adding NPS (Model II) and CDR (Model III), in participants with dementia (Table 1).

Hispanics were significantly more likely to go on antipsychotics after adjusting for age, education, and gender (Hazard ratio (HR)=1.72). In Models II and III, the odds for Hispanics of being on antipsychotics continued to be elevated and remained significant with the Hispanic group about 60% more likely to go on antipsychotics (HR=1.58, 95%CI (1.19,2.11)) in the final model.

DISCUSSION

To our knowledge this analysis is the first to study incident use of antipsychotics in a community setting of elderly patients with dementia, across demographics. Hispanics but not African Americans had an increased likelihood of going on antipsychotics in NACC participants with dementia compared to non-Hispanic Whites. This difference is not accounted for by higher dementia severity and NPS in Hispanic participants either at baseline or during follow-up. By analyzing incidence rather than prevalence, our results can

better reflect use of antipsychotics following the diagnosis of dementia, and thus likely attributable to dementia-related concerns rather than to prior issues such as a preexisting psychotic disorder. Further studies are needed to clarify ethnic differences on how families and physicians address dementia progression and neuropsychiatric symptoms in community dwelling patients with dementia.

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Table 1

Multivariate Cox Proportional Hazard Analysis of Incident Anti-psychotic Drug Use Among Socio-Demographic Factors, Level of Cognitive Impairment as Measured by CDR, and Severity of Neuropsychiatric Symptoms.

	Model I		Model II		Model III	
	HR	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**
Primary Predictor of Interest						
Race/Ethnicity						
Hispanic: White	**1.72**	**(1.29, 2.29)**	**1.58**	**(1.18, 2.09)**	**1.58**	**(1.19, 2.11)**
African American: White	1.13	(0.86, 1.51)	1.17	(0.88, 1.55)	1.20	(0.90, 1.59)
Key Predictors						
Sociodemographic						
Age from 70						
Effect of 1 year increase	**0.97**	**(0.97, 0.98)**	**0.98**	**(0.97, 0.99)**	**0.98**	**(0.97, 0.98)**
Sex						
Female compared to male	**0.73**	**(0.62, 0.86)**	**0.80**	**(0.68, 0.94)**	**0.73**	**(0.62, 0.86)**
Education						
<HS compared to HS	0.87	(0.63, 1.20)	0.89	(0.65, 1.22)	0.89	**(0.65, 1.23)**
College compared to HS	0.96	(0.78, 1.19)	0.95	(0.77, 1.17)	0.93	**(0.75, 1.14)**
Graduate education compared to HS	1.06	(0.87, 1.30)	1.07	(0.87, 1.3)	1.04	(0.85, 1.28)
NeuroPsych SymptomsSeverity						
NPS Sum of Boxes			**1.08**	**(1.06, 1.09)**	**1.07**	**(1.05, 1.08)**
Clinical Dementia Rating						
CDR Sum of Boxes					**1.06**	**(1.04, 1.08)**

*Results in bold are significant at p<0.05, CI= confidence interval, HS= high school, HR= hazard ratio, NPS = NeuroPsych Symptom Severity, CDR = Clinical Dementia Rating

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