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Cognitive Decline and Polypharmacy in an Elderly Population

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To the editor: The Department of Health & Human Services estimates that by 2030 there will be 72.1 million individuals 65 or older in the U.S.[1] The prevalence of Mild Cognitive Impairment (MCI) in the elderly population is between 3% and 19%, with an incidence of 8–58 per 1000 per year, and a risk of developing dementia of 11–33% over 2 years.[2] The higher prevalence of chronic diseases makes this population at a higher risk of taking multiple medications. Polypharmacy, defined most commonly as the concomitant use of 5 or more medications, is a poorly studied factor in relation with MCI, but may also play an important role.[3] Jyrkkä et al. performed a follow-up study in a Finnish population of 294 elderly people between 2004 and 2007, recording the use of medications and the cognitive function of participants.[3] The authors observed that excessive polypharmacy, defined as the concomitant use of 10 or more medications, was associated with a decline in the cognitive capacity measured by the Mini-Mental State Examination (MMSE) compared with the non-polypharmacy group. Considering the dearth of scientific studies analyzing the effects of polypharmacy on cognitive decline, particularly in the American population, this study examines data from the New Mexico Aging Process Study (NMAPS) to further investigate the effects of polypharmacy on cognitive status changes.

We developed a longitudinal cohort study using the data from 572 participants from NMAPS to measure the impact of polypharmacy on MMSE scores and risk of MCI. Mixed linear regression multivariable models and generalized estimating equations were used to estimate these associations, adjusting for gender, age at baseline, Charlson Comorbidity Index (CCI), presence of ApoE ε4 allele, body mass index (BMI), and hypertension.

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Author Contributions: X. Oyarzun-Gonzalez conceived the study objectives, performed data cleaning and analysis, interpreted the results, and drafted the manuscript; K. Taylor assisted with data analysis, interpretation of results and drafting of the manuscript; S. Muldoon was involved in oversight of data analysis and interpretation of data, and with preparation of manuscript; S. Myers assisted with interpretation of results and manuscript preparation; R. Baumgartner was the Principle Investigator of the study in which the data analyzed were collected and contributed to the preparation of the manuscript.

Most of the study subjects were female (63.6%), white (88.5%), and married (66.6%). In addition, 47.2% of the study population had between 12 and 16 years of education and 36.2% had more than 16 years of education. Polypharmacy was associated with a 0.11±0.09 decrease in MMSE scores (P=0.23) and an increased risk of MCI (odds ratio=1.95, 95% CI 0.40–9.43) (Table 1). Thus, even though the sample size was small and the associations were not statistically significant, the results suggest that polypharmacy could be an important factor in cognitive decline. Other notable findings included the detrimental effects of male gender, CCI greater than 0 and the presence of the ApoE ε4 allele on cognitive decline, although only the CCI reached statistical significance. Furthermore, hypertension (treated) was significantly associated with higher MMSE scores. These results were consistent with the analyses done for MCI and for change in MMSE scores over time.

The sampled population was unusually healthy and educated compared with the general American population. The prevalences of diabetes, hypertension, and obesity in the studied sample (0.53%, 34.5% and 10.5%, respectively) were much lower than the 26.9%, 71.6% and 35% prevalences described for those diseases in Americans older than 65 years.[4–5] According to the U.S. Department of Health and Human Services, the percentage of older people that completed high school rose from 28% to 71% between 1970 and 2003.[6] Approximately 83% of the sample studied had completed a high school education, and taking into consideration that the recruitment process was between 1979 and 2003, it is possible to establish that this sample was unusually highly educated. These characteristics may limit the generalizability of these results to the American population.

Anticholinergic drugs and other drugs categorized as potentially inappropriate medication (PIM) have been found to be strongly associated with cognitive impairment, whereas other categories of drugs have not shown an association.[7] In addition, the more drugs the patient is receiving, the more likely it is to observe an adverse drug event, such as cognitive impairment.[8–10] It was not possible to look at specific drug types or PIM use in this study, which are possible underlying mechanisms for this association; however, it would be important that future research takes into consideration that specific drugs can have a negative or positive impact on the cognitive performance of a subject, or not have any impact at all, which makes it even more important to incorporate the specific type of drugs in future research. Nevertheless, the results obtained suggest that it is important for health professionals to thoroughly evaluate medication use in the elderly and try to limit the number of medications (both prescription and over-the-counter), not only to avoid possible adverse drug reactions and interactions but also to achieve a good treatment compliance.

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Table 1

Multivariable Models Results for the Effects of Polypharmacy on MMSE or MCI (N=439 Individuals)

	Model 1[a] (MMSE)			Model 2[b] (ΔMMSE)			Model 3[c] (MCI)	
Covariates	**β**	**SE[d]**	**P-value**	**β**	**SE[d]**	**P-value**	**OR[e]**	**95% CI[f]**
Polypharmacy	−0.11	0.092	0.23	−0.12	0.092	0.20	1.94	(0.40, 9.43)
Gender								
Male	−0.15	0.10	0.14	−0.14	0.10	0.17	2.50	(0.52, 12.12)
Female*	0			0			1.0	(1.0, 1.0)
Age at baseline	−0.045	0.0079	<0.001	−0.047	0.0079	<0.001	1.11	(0.98, 1.25)
Charlson Comorbidity Index								
≥2	−0.22	0.11	0.043	−0.23	0.10	0.031	1.4	(0.21, 9.26)
1	−0.065	0.13	0.62	−0.065	0.13	0.62	0.90	(0.05, 3.32)
0*	0			0			1.0	(1.0, 1.0)
ApoEε4 allele	−0.17	0.10	0.099	−0.17	0.10	0.093	2.18	(0.48, 9.96)
BMI								
Obese	0.048	0.15	0.76	0.046	0.15	0.77	0.78	(0.08, 7.29)
Overweight	0.16	0.096	0.096	0.16	0.096	0.10	0.21	(0.04, 1.09)
Normal*	0			0			1.0	(1.0, 1.0)
Treated Hypertension	0.22	0.10	0.033	0.22	0.10	0.031	0.12	(0.02, 0.65)
Years since baseline	−0.024	0.016	0.13	−0.024	0.016	0.14	1.27	(0.91, 1.78)
MMSE score at baseline	0.34	0.027	< 0.001	−0.67	0.027	<0.001	−0.40	(0.30, 0.52)

[a] Model 1: Mixed multivariable linear model results examining the effect of polypharmacy on MMSE score

[b] Model 2: Mixed multivariable linear model results examining the effect of polypharmacy on the change in MMSE score.

[c] Model 3: Multivariable GEE model results examining the effect of polypharmacy on probability of MCI.

[d] SE=Standard error

[e] OR=Odds Ratio

[f] CI=Confidence Interval

* Reference group