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Cognitive Impairment and Medication Complexity in Community-Living Older Adults: The Health, Aging and Body Composition Study

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CONFLICT OF INTEREST

All authors report no conflicts of interests

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ABSTRACT

Background

Medication complexity is a large determinant of adherence. Few studies have explored the relationship between cognitive impairment and medication complexity.

Objective

To evaluate whether cognitive impairment is associated with medication complexity for prescription and over-the-counter (OTC) medications.

Methods

In this cross-sectional analysis, we studied the association between cognitive impairment and the complexity of prescriptions and OTC drug regimens. Baseline participants were from the Health, Aging and Body Composition study, consisting of 3,075 well-functioning 70 to79 year old black and white men and women. Cognitive impairment was defined by having a Modified Mini-Mental State Examimation score <80. The complexity of prescription and OTC (including supplements/herbals) medications was assessed using a modified version of the Medication Regimen Complexity Index (mMRCI). The mMRCI score increases with complexity of dosage forms, number of medications, pill burden, and non-daily dosing.

Results

The mean (SD) age was 74 (2.9) years old (n=3,055; 52% female, 41% black). The median prescription mMRCI score was 6 (range: 0-66). The median OTC mMRCI score was 4 (range: 0-71). Adjusting for health status, demographics, and access to care, medication complexity was lower in participants with cognitive impairment for prescription (adjusted RR 0.89; 95% CI 0.80 to 0.99) and OTC medications (adjusted RR 0.76; 95% CI, 0.64 to 0.93) compared to those

without cognitive impairment. The number of prescription medications was not different, but the number of OTC drugs was lower for those with cognitive impairment.

Conclusions

In this cohort of well-functioning older adults, those with cognitive impairment had lower prescription complexity due to less-complex dosage forms, pill burden, or daily dosing. OTC complexity was also lower, primarily due to a lower number of OTC drugs. The results of this study show that further research on medication complexity and adherence and health outcomes in cognitively impaired individuals is warranted.

INTRODUCTION

According to a World Health Organization (WHO) 2003 report, poor medication adherence is the primary reason for suboptimal clinical benefit, affecting morbidity and mortality for various chronic diseases such as hypertension and diabetes.[1] Poor adherence is commonly seen in older adults for a variety of reasons, including managing multiple chronic diseases, polypharmacy and medication regimen complexity.[2] Poor adherence accounts for 33-69% of all medication-related hospital admissions, costing approximately $100 billion per year.[3] Medication complexity was one of the therapy-related factors that affects adherence to therapy that was identified in the WHO report and in other studies.[1,2]

Several factors affect the complexity of medication regimens, including polypharmacy, pill burden and dosage form.[4] Persons with more complex medication regimens are less likely than those with simpler regimens to adhere to treatments.[5] Cognitive impairment is a known risk-factor for medication-related problems in older adults. In addition, adherence is often poor in patients with cognitive impairment.[6] Interventions to improve adherence by decreasing complexity in individuals with normal cognitive function were successful.[5] However, limited data exist regarding the relationship between decreased cognitive status and medication complexity.

The objective of this study is to evaluate whether cognitive impairment is related to medication regimen complexity for both prescription and over-the-counter (OTC) medications. This study uses a validated instrument to assess medication complexity in a large cohort of community-living older adults. Medication complexity is assessed for both prescription and OTC medications.

METHODS:

Study Design

This cross-sectional study included baseline participants who were enrolled in the Health, Aging, and Body Composition (Health ABC) Study. The Health ABC Study is a prospective cohort study sponsored by the National Institute of Aging. The Health ABC Study recruited 3,075 men and women aged 70-79 years at 2 clinical centers in Memphis, TN or Pittsburgh, PA between April 1997 and June 1998. At baseline, participants had to be well-functioning: the participants had to be free of functional limitations, that is, had no difficulty in walking a quarter of a mile, walking up 10 steps without resting, getting in and out of bed or chairs, bathing or showering, dressing, or eating. They also could not use a cane, walker, crutches, or other assistive device to ambulate. The participants also had to be free of any life-threatening illnesses, such as cancer.

Participants with missing medication data (n=20) were excluded from this analysis, leaving 3,055 participants in the analytic sample. All participants signed an informed written consent form and study protocols were approved by the institutional review boards of University of Tennessee and University of Pittsburgh. The analysis protocol was approved by the institutional review board of Yale University, where this analysis was performed.

Data Collection and Management

Participants underwent a baseline home visit followed by a clinic visit. At the home visit, participants were given a bag and asked to bring in all medications to a clinic visit. Reminder calls were made the day before the clinic visit, and they were reminded again to bring their medications. Information about the medications was collected at the clinic visit and additional questions were asked to elicit information on any missing or forgotten medications. If any

medications were missing at the clinic visit, a follow-up phone interview was performed to collect the medication information.

Cognitive Impairment

There were no entry criteria based on cognitive impairment, but the participants had to be considered well-functioning to be enrolled in the study. Cognitive impairment was assessed by the Teng Modified Mini-Mental State Examination (3MS).[7,8] The 3MS was administered by a trained technician during the clinic visit. The 3MS is a rescaling of the Folstein Mini-Mental State Examination with scores ranging from 30-100 and is more sensitive than the Folstein Mini-Mental State Examination in older adults. Cognitive impairment was defined as a dichotomous variable, with a score < 80 on the 3MS indicating cognitive impairment.[7,8]

Covariates

At the home and clinic visits, the baseline questionnaire assessed demographic and health history information. Clinical assessments included vital measurements and blood analysis. Presence of disease was assessed by self-report of a physician-diagnosed condition, use of a medication specific to that disease, and/or by physiologic or psychological measures.[9-12] Low self-perceived health status was defined as the participants self-rating their health as poor or fair, compared to good, very good, or excellent. The demographic variables included age,sex, race and education. Access to health care was defined by dichotomous variables for supplemental medication insurance (self-report), greater than 2 outpatient visits in the last year, and prior hospitalization in the last 5 years; outpatient visits and prior hospitalization were determined by administrative or fiscal records.

Medication use was determined through examination of all prescription and non-prescription medications used by participants in the 2 weeks preceding the baseline clinic visit.

Self-reporting of medications by older adults has been validated by several different methods, including comparison of serum concentrations of cardiovascular medications,[13] pharmacy data,[14] and pharmaceutical claims data.[15] The short recall period was designed to limit recall bias. The medication name, strength, and dosage form were recorded. Additional information obtained included categorizing the drug as either prescription or an OTC and whether it was taken on an "as-needed basis". OTC medications included herbals and supplements. The dosage frequency was recorded as the total number of doses taken on a daily, weekly, or monthly basis.

Outcome Measure

Drug-therapy complexity was assessed using a modified version of the Medication Regimen Complexity Index (MRCI), originally developed by George et al.[16] The main modification was that we did not have information about additional preparation instructions, e.g., mixing the medication with apple juice. The modified MRCI (mMRCI) score was calculated using the number of medications, dosage forms, pill burden and increased complexity for non-daily dosing. The modifications to the MRCI resulted in a more conservative (lower) complexity score compared to the full MRCI score since additional instructions were not included. Higher mMRCI scores indicate greater medication complexity.

Dosage forms were scored as described by George et al.[17] In short, oral tablets and capsules were scored a "one"; topical creams were scored a "two"; inhalers were scored a "three"; and injections were scored a "four". For dosage frequency, medications taken on a daily basis were scored a "one", medications taken on a weekly and monthly basis were scored a "two", i.e., medications taken less often than daily were more complex to administer. To account for pill burden, if more than one tablet was taken in a day, "one" was added to the score.

If the medication was taken on an as-needed basis, the dosage frequency and pill burden scores were divided by half.

The medication complexity was scored by a computer algorithm as described above. A random sample of 250 medications was reviewed by the pharmacist co-authors with geriatrics training (D.S.H.L., S.M.J., and J.T.H.) to insure the fidelity of the mMRCI scores. In short, the dosage form, daily pill burden and non-daily dosing schedule were printed for the 250 medications along with the score generated by the algorithm and manually checked for the correct score being assigned.

The mMRCI scores for all prescription medications were summed for a total prescription complexity score. This was repeated for OTC medications. Thus, the total participant mMRCI score is a composite of the number of medications, complexity of dosage forms, daily pill burden and non-daily dosing. If the dosage form was not recorded, the three pharmacist coauthors assigned a dosage form score based on known dosage forms (n=49). If multiple dosage forms exist, the more conservative (lower) score was assigned. In the analysis, the mMRCI was used as a continuous variable.

Statistical analysis

Multivariable linear models with a negative binomial distribution were used to estimate the relative risk (RR) of medication complexity by cognitive impairment. The dependent variable was cognitive impairment. The first primary independent variable was prescription medication complexity. We present four linear models to examine the association between cognitive impairment and prescription complexity. The first model presents the unadjusted RR (and 95% CIs) for the association of cognitive impairment and prescription mMRCI; model 2 presents RR adjusted for health status (hypertension, CVD, diabetes, arthritis, pulmonary

disease, depressive symptoms, heart failure and self-perceived health status); model 3 estimates the RR adjusted for health status and demographics (age, race, gender and education); model 4 presents RR adjusted for all potential confounding variables by including access to health care (supplemental medication insurance, more outpatient visits, hospitalization in the last 5 years). RR greater than one is associated with higher medication complexity, and RR less than one is associated with lower medication complexity. The same analysis was performed on OTC complexity, the second primary independent variable.

Since the coexistence of a cognitive impairment and chronic condition may alter medication complexity, we also examined all two-way interactions between cognitive impairment and any chronic condition left in the final model. The two-way interaction was to test if any chronic condition changed the association of mMRCI with cognitive impairment. If no two-way interactions were observed, this would suggest that the other chronic conditions did not change the association between mMRCI and cognitive impairment.

Since the number of medications can increase complexity, we conducted a second analysis to assess the association between the number of medications and cognitive impairment. All statistical analyses were performed with SAS Statistical Software, version 9.2 (SAS Institute, Cary, NC).

RESULTS

Participant's Characteristics

Baseline characteristics are listed in **Table 1**. The mean age was 74 (± 2.9) years, 52% were female and 41% were black; 10% of the participants had cognitive impairment. Hypertension was the most prevalent disease (61%) followed by cardiovascular disease (25%). Approximately a quarter of the participants had more than two outpatient visits in the last year, and 38% were hospitalized in the last five years. The number of prescription medications ranged from 0 to 23, and the median and interquartile range were 3 and [1, 5], respectively. The number of OTC medications ranged from 0 to 27, and the median and interquartile range were 2 and [1, 4], respectively.

Cognitive Impairment and Prescription Complexity

The prescription complexity score ranged from 0 to 66 and the median and interquartile range were 6 and [2, 11.5], respectively. **Table 2** shows the results of the association between cognitive impairment and prescription complexity. Cognitive impairment was associated with lower prescription complexity adjusting for other health status, demographics and access to healthcare in the fully adjusted model (RR, 0.89: 95% CI, 0.80-0.99). In contrast to complexity, the number of prescription medications was not significantly different between cognitively impaired and cognitively normal individuals controlling for health status, demographic and access to care variables. The two-way interaction between cognitive impairment and each of the chronic conditions was not significant and indicates that the decrease in prescription complexity was observed regardless of which chronic condition was present.

Cognitive Impairment and OTC Complexity

The complexity score for OTC medications ranged from 0 to 71 and the median and interquartile range were 4 and [1.5, 8], respectively. **Table 3** shows the results of multivariable regression model for the OTC medications. Cognitive impairment was associated with lower OTC complexity and remained significant when controlled for health status, demographics and access to healthcare in the fully adjusted model (RR, 0.76; 95% CI, 0.64-0.93). The number of nonprescription medications was also lower for those with cognitive impairment when controlled for health status, demographics and access to healthcare (RR, 0.76; 95% CI, 0.66-0.88). Thus, the decreased OTC complexity likely reflects the decreased number of OTC medications, rather than complexity. The only remaining health status characteristic was arthritis. The two-way interaction between cognitive impairment and arthritis was not significant and indicates that the decrease in OTC complexity was observed regardless of whether arthritis was present or not.

DISCUSSION

This report is, to the best of our knowledge, the first study to describe the relationship between medication complexity and cognitive impairment in a community-living older population. Cognitive impairment was associated with lower prescription and OTC complexity. The lower prescription complexity was not due to lower prescription usage, but rather due to decreased complexity in dosage form, daily pill burden, and non-daily dosing. In contrast, the decreased OTC complexity was primarily due to decreased OTC usage, and is consistent with other reports.[18] These decreases are observed regardless of which chronic condition was present.

Medication complexity may be lower in the presence of cognitive impairment for a variety of reasons. Clinicians may simplify regimens once patients demonstrate functional impairments resulting from cognitive decline. This could occur either by decreasing the number of medications in a patient's regimen (e.g. reducing polypharmacy) or by adopting strategies that reduce complexity (e.g. decrease pill burden). Furthermore, as cognitive impairment worsens, clinicians may re-evaluate the need for certain medications, thereby reducing complexity. Prior reports have indicated both increased[19] and decreased[20] prescription use in cognitively impaired persons, but neither was seen in this study. This study shows the number of prescription medications used was not different for those with cognitive impairment, suggesting that the complexity was lower due to simpler dosage forms, decreased pill burden, or dosing daily rather than weekly or monthly. Additionally, patients and/or their caregivers may request a less complex prescription regimen in response to subclinical or overt cognitive impairment.

On the other hand, the number of OTC medications was lower for those with cognitive impairment, suggesting that those with cognitive impairment simply took less OTC medications, similar to what has been reported previously.[18] OTC medications, by Food and Drug

Administration definition, must be easy to administer. Thus, taking less OTCs is one of the only ways to decrease OTC complexity and therefore is expected.

The implications of this research are two fold: first, prescription complexity may be decreased for older adults with cognitive impairment, possibly in an attempt to improve adherence or decrease pill burden. However, the number of prescriptions may not be decreased. Pharmacists should be aware that because the number of prescriptions was not decreased, and each chronic condition increases medication complexity, even if the patient had cognitive impairment, this would suggest that they are still being treated and quality of care has not compromised. Second, the number of OTC medications used was decreased in participants with cognitive. Therefore, pharmacists should pay extra attention to those with cognitive impairment to be sure that OTC symptomatic treatment is still received, such as for pain.

This study is also among the first to describe other key covariates important to prescription MRCI. Not surprisingly, other diseases increased the complexity of prescription medications, but this study shows that conditions with complex therapies, such as pulmonary disease, diabetes and heart failure were more strongly associated with higher prescription complexity. Hypertension was also strongly associated with higher prescription complexity most likely due to multiple agents being used to control blood pressure. Female participants had more complex prescription regimens, perhaps due to greater utilization of health services.[21] Access to care variables, such as more outpatient visits, most likely increased complexity by increasing the number of prescribed medications. Finally, the prescription regimens for participants in Pittsburgh were associated with lower complexity, perhaps reflecting better health status and a different demographic.

OTC medication complexity was only associated with arthritis, most likely due to increased OTC analgesic use.[20] Being a black participant was associated with lower OTC complexity, which may indicate less use of OTC medications in this population.[22] Similar to prescription complexity, being female was associated with higher OTC complexity because of more OTC usage.[21] A prior hospitalization was associated with lower OTC complexity.

This study had several potential limitations. This study was cross-sectional and did not explore the change in medication complexity over time. There may be some historical differences in treatments, which may limit the results; overall, while specific treatment choices have changed over time, the complexity of treatments have not dramatically changed and many complex diseases, such as pulmonary diseases, are still complex to treat. Some diseases and other factors used to control for confounding were self-reported by the participants. Due to limitations of available data, the complete medication complexity score could not be calculated: thus the modified complexity score did not account for additional instructions but represents an estimate that incorporates the number of medications, dosage form, daily pill burden and non-daily dosing. Additional instructions could not be included, so the mMRCI would be a conservative measure of medication complexity. Further, there may be residual confounding not accounted for in the model, such as acute medical problems, injuries or infections that may affect medication complexity. The study sample consisted of well-functioning older adults, and may represent only mild cognitive impairment, and may not be representative of the general population of 70-79 year old adults because they are well-functioning with higher education levels. Despite these limitations, this study describes how prescription and OTC complexity is associated with cognitive impairment in a large cohort of well-functioning older adults using

multivariable linear regression to control for potential confounders by other diseases, demographic factors and access to care.

In conclusion, this study found that prescription complexity was lower in cognitively impaired older adults compared to those without impairment, and was independent of the number of prescription medications. Chronic conditions, especially those with complex therapies such as pulmonary disease and heart failure, had the most influence on prescription complexity. The implication is that prescription complexity may be decreased, but not the number of medications, which may affect the both the adherence and quality of care, but more research is needed in this area. OTC complexity was also lower in cognitively impaired older adults but appeared to be primarily due to less use of OTC medications. This result is expected since OTCs are generally not complex to administer, thus the only way to decrease complexity for OTCs is to use fewer of them. The implication for OTCs is that cognitively impaired older adults may be using fewer OTCs, and may not be treating symptoms as readily as cognitively normal older adults.

Our next area of research is to explore the effect of medication complexity on medication adherence in community-living older adults with and without cognitive impairment. Additional longitudinal analyses will explore the effect of complexity on clinically relevant outcomes, such as falls and cardiovascular events.

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REFERENCES

1. World Health Organization. Adherence to long-term therapies: Evidence for Action. 2003. ISBN 92 4 154599 2.

2. Ingersoll KS, Cohen J. The impact of medication regimen factors on adherence to chronic treatment: a review of literature. J Behav Med 2008;31:213-24. doi: 10.1007/s10865-007-9147-y.

3. Osterberg L, Blaschke T. Adherence to medication. N Engl J Med 2005;353:487-97. doi: 10.1056/NEJMra050100.

4. Conn VS, Taylor SG, Kelley S. Medication regimen complexity and adherence among older adults. Image J Nurs Sch 1991;23:231-5. doi: 10.1111/j.1547-5069.1991.tb00677.x

5. Choudhry NK, Fischer MA, Avorn J, et al. The Implications of therapeutic complexity on adherence to cardiovascular medications. Arch Intern Med 2011;171:814-22. doi: 10.1001/archinternmed.2010.495.

6. Ownby RL. Medication adherence and cognition. Medical, personal and economic factors influence level of adherence in older adults. Geriatrics 2006;61:30-5. url: http://geriatrics.modernmedicine.com/geriatrics/data/articlestandard/geriatrics/062006/305670/article.pdf

7. Teng EL, Chui HC. The Modified Mini-Mental State (3MS) examination. J Clin Psychiatry 1987;48:314-8. url: http:// psycnet.apa.org/journals/pas/8/1/48.pdf

8. Bland RC. Mild Dementia or Cognitive Impairment: The Modified Mini-Mental State Examination (3MS) as a Screen for Dementia. Canadian Journal of Psychiatry 2001;46:506. url: https://ww1.cpa-apc.org/Publications/Archives/CJP/2001/August/PDF/dementia.pdf

9. Rooks RN, Simonsick EM, Miles T, et al. The association of race and socioeconomic status with cardiovascular disease indicators among older adults in the health, aging, and body composition study. J Gerontol B Psychol Sci Soc Sci 2002;57:S247-56. doi: 10.1093/geronb/57.4.S247.

10. Diagnosis and classification of diabetes mellitus. Diabetes Care 2009;32 Suppl 1:S62-7.

11. Radloff LS. The CES-D Scale. Applied Psychological Measurement 1977;1:385-401. doi: 10.1177/014662167700100306

12. Butler J, Kalogeropoulos A, Georgiopoulou V, et al. Incident Heart Failure Prediction in the Elderly: The Health ABC Heart Failure Score. Circ Heart Fail 2008;1:125-33. doi: CIRCHEARTFAILURE.108.768457

13. Smith NL, Psaty BM, Heckbert SR, Tracy RP, Cornell ES. The reliability of medication inventory methods compared to serum levels of cardiovascular drugs in the elderly. J Clin Epidemiol 1999;52:143-6. doi: 10.1016/j.bbr.2011.03.031.

14. Caskie GI, Willis SL, Warner Schaie K, Zanjani FA. Congruence of medication information from a brown bag data collection and pharmacy records: findings from the Seattle longitudinal study. Exp Aging Res 2006;32:79-103. doi: 10.1080/03610730500326341.

15. Pit SW, Byles JE, Cockburn J. Accuracy of telephone self-report of drug use in older people and agreement with pharmaceutical claims data. Drugs Aging 2008;25:71-80. url: http://adisonline.com/aging/Fulltext/2008/25010/Accuracy_of_Telephone_Self_Report_of_Drug_Use_in.8.aspx

16. George J, Phun YT, Bailey MJ, Kong DC, Stewart K. Development and validation of the medication regimen complexity index. Ann Pharmacother 2004;38:1369-76. doi: 10.1345/aph.1D479

17. George J, Vuong T, Bailey MJ, Kong DC, Marriott JL, Stewart K. Regimen Complexity and Medication Adherence in Patients at Risk of Medication Misadventure. Journal of Pharmacy Practice and Research 2006;36:99-102. url: http://jppr.shpa.org.au/scripts/cgiip.exe/WService=SHPAJP/ccms.r?pageid=6010&CallerID=10022

18. Schmader KE, Hanlon JT, Fillenbaum GG, Huber M, Pieper C, Horner R. Medication use patterns among demented, cognitively impaired and cognitively intact community-dwelling elderly people. Age Ageing 1998;27:493-501. doi: 10.1093/ageing/27.4.493.

19. Crentsil V, Ricks MO, Xue QL, Fried LP. A pharmacoepidemiologic study of community-dwelling, disabled older women: Factors associated with medication use. Am J Geriatr Pharmacother 2010;8:215-24. doi: 10.1016/j.amjopharm.2010.06.003.

20. Hanlon JT, Landerman LR, Wall WE, Jr., et al. Is medication use by community-dwelling elderly people influenced by cognitive function? Age Ageing 1996;25:190-6. doi: 10.1093/ageing/25.3.190.

21. Payne J, Neutel I, Cho R, DesMeules M. Factors Associated with Women's Medication Use. BMC Women's Health 2004;4:S29, doi:10.1186/472-6874-4-S1-S29.

22. Hanlon J, Fillenbaum G, Burchett B, et al. Drug-use patterns among black and nonblack community-dwelling elderly. The Annals of Pharmacotherapy 1992;26:679-85.

Table 1. Baseline characteristics of the analytic sample (N=3055)

Characteristic	*Mean (±SD), Number (%), or Median [interquartile range]*
Cognitive Impairment	**303 (10%)**
Health Status	
Hypertension	1854 (61%)
Cardiovascular Disease	744 (25%)
Diabetes	575 (19%)
Osteoarthritis	513 (17%)
Pulmonary	355 (12%)
Depressive Symptoms	144 (5%)
Heart Failure	40 (1%)
Low Self-perceived Health Status	493 (16%)
Number of chronic conditions, c	
0	645 (21%)
1	1188 (38%)
2	844 (28%)
3	315 (10%)
≥4	63 (2.1%)
Demographics	
Age (years)	74 (± 2.9)
Female Gender	1574 (52%)
Black Race	1266 (41%)
High school education or greater	2281 (75%)
Pittsburgh, a	1516 (49%)
Access to Care	
Supplemental Medication Insurance	1873 (63%)

Characteristic	*Mean (±SD), Number (%), or Median [interquartile range]*
>2 Outpatient Visits in last year	834 (27%)
Prior Hospitalization in last 5 years	1159 (38%)
Prescription medications	3 [1, 5]
OTC medications	2 [1, 4]

a, Pittsburgh, Pennsylvania, compared to Memphis Tennessee.

b, unless otherwise indicated

c, conditions include hypertension, cardiovascular disease, diabetes, osteoarthritis, pulmonary disease and heart failure

Table 2. Association of cognitive impairment with prescription medication complexity adjusted for key covariates (N=3055).

	Cognitive impairment alone		Cognitive impairment and health status		Cognitive impairment, health status and demographics		Fully adjusted model	
	Relative Risk [95% CI]		Relative Risk [95% CI]		Relative Risk [95% CI]		Relative Risk [95% CI]	
Cognitive Impairment	**1.00**	**[0.89, 1.12]**	**0.87**	**[0.78, 0.96]**	**0.89**	**[0.89, 0.99]**	**0.89**	**[0.80, 0.99]**
Health Status								
Hypertension			1.45	[1.36, 1.56]	1.46	[1.36, 1.56]	1.45	[1.35, 1.55]
Cardiovascular Disease			1.48	[1.39, 1.57]	1.54	[1.44, 1.64]	1.40	[1.31, 1.50]
Diabetes			1.45	[1.40, 1.56]	1.50	[1.40, 1.64]	1.46	[1.36, 1.56]
Arthritis			1.28	[1.18, 1.38]	1.25	[1.135 1.35]	1.21	[1.12, 1.31]
Pulmonary			1.73	[1.59, 1.89]	1.75	[1.60, 1.91]	1.71	[1.57, 1.88]
Depressive Symptoms			1.20	[1.10, 1.38]	1.18	[1.03, 1.35]	1.15	[1.01, 1.31]
Heart Failure			1.64	[1.43, 1.87]	1.68	[1.48, 1.93]	1.53	[1.36, 1.73]
Lower self-perceived health			1.26	[1.16, 1.37]	1.29	[1.18, 1.40]	1.28	[1.17, 1.40]
Demographics								
Age (in years)						NS		NS
Female					1.22	[1.14, 1.30]	1.18	[1.12, 1.27]
Black					0.92	[0.86, 0.98]	0.93	[0.87, 0.99]

	Cognitive impairment alone	Cognitive impairment and health status	Cognitive impairment, health status and demographics	Fully adjusted model
	Relative Risk [95% CI]	Relative Risk [95% CI]	Relative Risk [95% CI]	Relative Risk [95% CI]
High school education or greater			NS	NS
Pittsburgh, a			0.87 [0.82, 0.92]	0.80 [0.75, 0.85]
Access to Care				
Supplemental Medication Insurance				1.23 [1.14, 1.30]
More outpatient visits, b				1.17 [1.10, 1.26]
Prior Hospitalization, c				1.21 [1.13, 1.30]

Adjusted relative risk [95% Confidence Interval (CI)] in generalized linear models with negative binomial error distribution fit by backwards elimination.

NS: Not significant with a two-sided p-value of <0.05

a, Pittsburgh, Pennsylvania, compared to Memphis Tennessee.

b, More than two outpatient visits in the last year,

c, Hospitalization in the last five years.

Table 3. Association of cognitive impairment with OTC medication complexity adjusted for key covariates (N=3055)

	Cognitive impairment alone	Cognitive impairment and health status	Cognitive impairment, health status and demographics	Fully adjusted model
	Relative Risk [95% CI]	Relative Risk [95% CI]	Relative Risk [95% CI]	Relative Risk [95% CI]
Cognitive Impairment	**0.55 [0.46, 0.65]**	**0.59 [0.49, 0.70]**	**0.77 [0.64, 0.93]**	**0.76 [0.64, 0.93]**
Health Status				
Hypertension		NS	NS	NS
Cardiovascular Disease		NS	NS	NS
Diabetes		0.79 [0.71, 0.88]	0.90 [0.81, 1.00]	NS
Arthritis		1.29 [1.18, 1.41]	1.17 [1.07, 1.28]	1.19 [1.06, 1.31]
Pulmonary		NS	NS	NS
Depressive Symptoms		NS	NS	NS
Heart Failure		NS	NS	NS
Lower self-perceived health		NS	NS	NS
Demographics				
Age (in years)			NS	NS
Female			1.27 [1.17, 1.38]	1.26 [1.16, 1.37]
Black			0.63 [0.58, 0.69]	0.62 [0.57, 0.68]

	Cognitive impairment alone Relative Risk [95% CI]	Cognitive impairment and health status Relative Risk [95% CI]	Cognitive impairment, health status and demographics Relative Risk [95% CI]	Fully adjusted model Relative Risk [95% CI]
High school education or greater			1.10 [1.01, 1.20]	1.11 [1.03, 1.21]
Pittsburgh, a			NS	NS
Access to Care				
Supplemental Medication Insurance				NS
More outpatient visits, b				NS
Prior Hospitalization, c				0.87 [0.80, 0.94]

Adjusted relative risk [95% Confidence Interval (CI)] in generalized linear models with negative binomial error distribution fit by backwards elimination.

NS: Not significant with a two-sided p-value of <0.05

a, Pittsburgh, Pennsylvania, compared to Memphis Tennessee.

b, More than two outpatient visits in the last year,

c, Hospitalization in the last five years.