

Is Medication Use by Community-dwelling Elderly People Influenced by Cognitive Function?

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Summary

To determine whether medication use differs by cognitive status among community dwelling elderly, a survey was made of a stratified random sample of 4110 black and white participants, aged 65 or older from the Duke Established Populations for Epidemiologic Studies of the Elderly in five adjacent urban and rural counties in the Piedmont area of North Carolina.

Main outcome measures were usage of prescription medications, non-prescription medications, and medicines within therapeutic classes in the previous 2 weeks as determined during an in-home interview; and total number of prescription and non-prescription medications used in the previous 2 weeks. Multivariate analyses, using weighted data adjusted for sampling design, were conducted to assess the association between drug use patterns and cognitive status, as assessed by the Short Portable Mental Status Questionnaire, while adjusting for demographic, health status, and access to health care factors.

Participants with cognitive impairment (13.7% of sample) were less likely to use any prescription medications (Adjusted OR = 0.66, 95% CI = 0.48–0.90) or any non-prescription medications (Adjusted OR = 0.71, 95% CI = 0.56–0.89) than cognitively intact subjects. Both groups took a similar number of prescription and non-prescription medications. Those who were cognitively impaired were less likely to take analgesics (Adjusted OR = 0.66, 95% CI = 0.52–0.83), but were more likely to take central nervous system drugs (Adjusted OR = 1.55, 95% CI 1.18–2.04) than those who were cognitively intact.

We conclude that drug use patterns by community-dwelling elderly people differ with cognitive status. Future research needs to examine medication use by specific causes of cognitive impairment.

Introduction

Elderly people are substantial consumers of medications [1–7]. Community-based surveys reveal that they take an average of 2.7 to 3.9 prescription and non-prescription medications [3, 5–7]. While medications can be beneficial in palliation and treatment of disease, there is concern that elderly people are more prone to drug-related problems such as inappropriate prescribing, and adverse drug reactions [1, 8–10]. Health professionals, if knowledgeable about those factors associated with medication use patterns, can be more vigilant in their efforts to provide optimal pharmacotherapy for their elderly patients.

A number of factors are associated with increased drug use including advanced age, female sex, white race, poor health status and access to health care [1, 4, 7]. The association of cognitive impairment with drug

use by elderly people has not been thoroughly investigated. The few relevant published studies have focused primarily on people with cognitive impairment due to dementia, and were either limited to the use of medications by a select group of patients [11, 12] or failed to include an adequate control group for comparison [13].

There are several reasons why examination of the association between medication use patterns and cognitive impairment may be important. First, cognitive impairment is disabling, stressful to family and caregivers, costly, and common in the elderly population [14]. Among community-dwelling participants in the Epidemiologic Catchment Area Program, severe cognitive impairment was found in 4.9% of persons over the age of 65, and in 15% in those 85 and older [15]. Second, among known risk factors for cognitive impairment, one of the most common is medication

[14, 16–20]. Finally, there is concern that cognitively impaired individuals may be under- or over-medicated. Under-utilization of medications is of concern since those who are cognitively impaired may be less able to report symptoms that would lead to appropriate therapy. Moreover, appropriate therapy may not be initiated because physicians may be influenced by the knowledge that the patient is cognitively impaired. Over-utilization of medications by cognitively impaired elderly people is of concern owing to the risks associated with inappropriate prescribing and adverse drug reactions [10, 21–23].

Given these issues and the growing number of drugs under investigation for the treatment of dementia [24–26], documentation of the prescribing and self-medication patterns of cognitively impaired elderly people is needed to guide health policy and future clinical research. The purpose of this study was to determine whether drug use by community-dwelling elderly people differs with cognitive status. Specifically, we examined the use and total number of prescription, and non-prescription medications, and the use of medicines within therapeutic classes among cognitively impaired and intact elderly people.

Methods

Sample: The data used are from the in-home baseline survey (1986–87) of the Duke site of the Established Populations for Epidemiological Studies of the Elderly (EPESE). Details on the Duke EPESE study design and methodology are presented elsewhere [27]. Briefly, the Duke EPESE is a stratified probability household sample comprising 4162 participants who are representative of the approximately 28 000 persons over the age of 65 living in five adjacent counties in the Piedmont area of North Carolina. One county is urban and four are predominantly rural; 35% of the area population are black, 64% white and 1% of other races. This study was approved by the Duke University Medical Center Institutional Review Board and informed consent was obtained from each participant prior to data collection.

Data collection: Data were collected by trained interviewers who used a comprehensive structured questionnaire during in-person interviews to obtain information on various aspects of the participants' physical, mental and social health and use of health services [27]. To minimize potential problems with under-reporting, for participants too ill or unable to provide usable information, an appropriate proxy (i.e. the person most familiar with the participant) was asked to provide information. Participants were asked whether, during the previous 2 weeks, they had taken any medicines prescribed by a doctor, or any others obtained from a store [3, 4], and if so, to show the interviewer all these medications. The interviewer recorded the drug name, dosage form, and the number of dosage forms the respondent reported taking the previous day. In addition, for prescription drugs, the interviewer recorded from the label, the drug strength, whether the participant's name was on the label, and whether the medicine was prescribed to be taken regularly or as needed.

Medication data entry and management: All information was edited for accuracy and consistency before computer entry. Prescription drug data were coded using an updated and modified version of the Drug Product Information Coding System [28], and for non-prescription drugs the Iowa

Non-prescription Drug Product Information Coding System was used [5]. These data were entered using a locally developed computerized program [3]. The unique numeric generic code assigned to each drug during data entry was matched with a therapeutic category code. This therapeutic category code allowed drugs to be assigned to one of 15 major therapeutic classes and 75 subclasses [3, 5], that are based upon an expanded version of the American Hospital Formulary Services format [29]. Reliability of the drug use data entry system was assessed by re-entering a random 5% sample of participants, and was found to be highly satisfactory with an error rate of 1.6% (95% CI, 0.7%–2.6%).

Outcome measures: We examined several dependent variables. We created a dichotomous variable (1 = yes, 0 = no) to indicate any use or no use of: (1) prescription medications, (2) non-prescription medications, and (3) medicines within each of the major therapeutic classes and selected subclasses. We also created quantitative variables to indicate the total number of prescription and non-prescription medications used.

Independent variables: The primary independent variable was cognitive status as assessed by the ten-item, Short Portable Mental Status Questionnaire (SPMSQ) with scoring adjusted for race and education [30]. Participants were divided into two groups: cognitively impaired and cognitively intact, based on standard cut-off scores adjusted for education and race [30]. Specifically, for those with grade school education, whites with four or more and blacks with five or more errors were categorized as being cognitively impaired. Whites and blacks with any high school education are permitted one less error and those with more than high school education are permitted two fewer errors.

We adjusted for important covariates that may influence the relationship between cognitive status and drug use [1, 4, 7, 14]. Demographic factors were represented by dichotomous variables (1 = yes, 0 = no) for race, sex, and place of residence (i.e. whether living in an urban or rural area as defined by U.S. Bureau of the Census), and by quantitative variables for age and education in years. Health status factors were represented by quantitative variables that included a modified (three-item) version of the Rosow–Breslau scale [31], and a health index measure (higher score = poorer health) based on physician-assessed medical impact of five self-reported chronic conditions (heart problems, hypertension, diabetes, stroke, and cancer) [4]. Access to health care was represented by dichotomous variables (1 = yes, 0 = no) for participants' Medicaid coverage status, hospitalization in the previous year, and continuity of care (i.e. whether the same physician was usually seen when going for care), and a quantitative variable that measured the number of health care visits in the 12 months prior to the interview.

Statistical analysis: For purposes of analysis, all data were weighted to adjust for the sampling design and to allow inference to the five-county area. The analysis proceeded in three phases. In the first phase, the data were summarized by percentages for all covariates and those who were cognitively impaired were compared using the χ^2 statistic with those who were cognitively intact [32].

In the second phase, bivariate analyses were conducted using χ^2 and t tests to estimate the effects of cognitive status on the dichotomous and quantitative drug usage measures [32]. Then, multivariate analyses, adjusting for covariates, were conducted using logistic regression to estimate the effects of the independent variables on dichotomous drug usage measures, and ordinary least squares (OLS) regression for the quantitative drug usage measures [33]. No covariates had more than 4.2% missing data. For the multivariate

analyses, missing values were replaced with regression-predicted imputed scores generated using the BMDP AM procedure [34]. Final models were fitted to estimate the effect of cognitive status on medication usage controlling for all the demographic variables and statistically important health status and access to health care variables. Final models were derived in stages. In the first stage, health status and access to health care variables were entered into regression models as a group of variables independent of each other. In the second stage, the significant ($p < 0.05$) health status and access to health care variables were retained and entered simultaneously into regression models that included cognitive status and the demographic variables. All of the above-mentioned analyses were conducted using SAS[®] software [35].

In the final phase of analyses, because the Duke EPESE data are based on a complex, stratified survey design, we retested the significance of our final multivariate regression models using SUDAAN, a specialized software program developed for the analysis of complex sampling designs and which adjusts for the effects of clustering and stratification [36]. Significance tests reported for the multivariate models were also adjusted to reflect the number of non-missing cases prior to imputation.

Results

Table I shows the descriptive characteristics of the participants by cognitive status. Fifty-two participants (1.2%) with missing data on cognitive status were excluded, leaving a sample of 4110 participants of whom 139 (3.4%) had proxy informants. All but one of the 139 proxy interviews were for those participants subsequently determined to be cognitively impaired. Cognitive impairment, as assessed by the SPMSQ, was found for 13.7% of the total sample. Assessment of group differences provided evidence ($p < 0.05$) that those who were cognitively impaired were older, less educated, more functionally impaired, had greater chronic disease burden, were more likely to have many health visits, be hospitalized in the past year and be receiving Medicaid.

The majority of participants reported the use of one or more prescription drugs. Bivariate analyses revealed that the use of prescription drugs was similar for both cognitively impaired and intact participants (74.8 vs. 75.2%, respectively; $\chi^2 = 0.03$; $df = 1$; $p = 0.88$). Table II presents the multivariate analyses on the prevalence of prescription drug use by cognitive status. After controlling for important covariates, those who were cognitively impaired were 34% less likely to use prescription drugs than those who were cognitively intact. Covariates found to be positively associated ($p < 0.05$) with prescription drug use included being female, an urban resident, having one or more functional limitations, poorer health, one or more health visits in the previous year and seeing the same physician at health visits. Bivariate analyses revealed that mean prescription drug use was greater among those who were cognitively impaired than among those who were intact (2.60 ± 0.10 vs. 2.17 ± 0.04 , respectively; $t = 4.31$; $df = 1$; $p < 0.001$). Table II also presents the

Table I. Descriptive characteristics of participants by cognitive status

Variable	Cognitively impaired (n = 364)† (%)‡	Cognitively intact (n = 3546)† (%)‡	p Value*
<i>Demographic factors</i>			
Age (years)			
< 75	36.5	66.7	< 0.001
75–84	41.8	28.6	
85 +	21.7	4.7	
Black race	36.1	35.5	0.78
Female sex	66.2	61.8	0.05
Education (years)			
< 8	42.6	35.2	< 0.001
8–11	27.8	36.1	
12 +	28.8	28.8	
Urban residence	53.7	57.2	0.12
<i>Health status factors</i>			
Functional status			
≥ 1 limitation	71.0	41.4	< 0.001
Chronic disease status			
low	38.0	39.3	< 0.001
medium	20.7	26.9	
high	41.3	33.7	
<i>Access to health care factors</i>			
Health visits (no.)			
0	20.9	18.8	0.02
1–4	43.4	49.9	
5 +	35.7	31.3	
Hospitalized in past year	24.2	16.0	< 0.001
On Medicaid	10.2	5.0	< 0.001
Continuity of care	82.2	85.2	0.07

* Comparison of groups using bivariate χ^2 test.

† Unweighted.

‡ Weighted, may not add up to 100% owing to rounding.

multivariate analyses on the number of prescription drugs used by cognitive status. There were no differences ($p > 0.05$) between cognitive status groups in the total number of prescription drugs taken after controlling for other factors. Covariates found to be inversely associated with the total number of prescription drugs taken ($p < 0.05$) included being older, and black, whereas being female, an urban resident, having one or more functional limitations, poorer health, one or more health visits in the previous year, being hospitalized in the previous year and seeing the same physician at health visits were positively associated with the total number of prescription drugs.

Those who were cognitively impaired were less likely to use any non-prescription drugs than those who were cognitively intact (68.0 vs 73.3%, respectively; $\chi^2 = 7.02$; $df = 1$; $p < 0.01$). Table III presents the multivariate analyses on the prevalence of non-prescription drug use by cognitive status and reveals that, after adjusting for other factors, those who were cognitively impaired were 29% less likely to be

Table II. Multivariate analyses of prescription drug use by cognitive status

Variable	Any use		No. drugs	
	Odds ratio	95% CI	b coefficient	95% CI
Cognitively impaired	0.66	0.48, 0.90*	-0.02	-0.20, 0.16
Age (years)	1.01	0.99, 1.02	-0.02	-0.03, -0.01*
Black race	0.86	0.70, 1.05	-0.33	-0.46, -0.20*
Female sex	1.51	1.23, 1.84*	0.21	0.08, 0.35*
Education (years)	1.01	0.97, 1.03	0.01	-0.01, 0.02
Urban residence	1.40	1.13, 1.74*	0.18	0.04, 0.31*
Functional status	1.42	1.27, 1.59*	0.50	0.43, 0.58*
Limitations (no.)				
Chronic disease status	1.88	1.67, 2.13*	0.49	0.42, 0.56*
Health visits (no.)	1.33	1.26, 1.40*	0.12	0.11, 0.14*
Hospitalized in past year	-	-	0.45	0.25, 0.65*
Continuity of care	3.40	2.67, 4.34*	0.69	0.54, 0.85*

*p < 0.05.

non-prescription medication users than cognitively intact elderly people. Another covariate found to be inversely associated ($p < 0.05$) with the total number of non-prescription drugs was being black, whereas being female, having one or more functional limitations, poorer health, and one or more health visits in the previous year were positively associated with the total number of non-prescription drugs. Bivariate analyses revealed that those who were cognitively impaired took a similar mean number of non-prescription medications to those who were cognitively intact (1.27 ± 0.05 vs. 1.32 ± 0.02 , respectively; $t = 0.83$; $df = 1$; $p = 0.23$). Table III also presents the multivariate analyses on the number of non-prescription drugs used by the cognitive status groups. There were no differences ($p > 0.05$) with cognitive status in the total number of non-prescription drugs taken after controlling for other factors. Covariates that were positively associated ($p < 0.05$) with number of non-prescription drugs

included being female, an urban resident, having one or more functional limitations, poorer health, and one or more health visits in the previous year, whereas being black was inversely associated ($p < 0.05$) with the total number of non-prescription drugs.

Table IV reports the percentage of people taking either a prescription or non-prescription drug in any of the 15 major therapeutic drug classes by cognitive status. Bivariate analyses indicate that participants who were cognitively impaired were less likely ($p < 0.05$) to take analgesics and more likely ($p < 0.05$) to take central nervous system and nutritional supplements than those who were intact. However, after controlling for other factors, this association did not hold for nutritional supplements (Adjusted OR = 1.23, 95% CI 0.95–1.59) but did for analgesics (Adjusted OR = 0.66, 95% CI 0.52–0.83) and central nervous system (CNS) medications (Adjusted OR = 1.55, 95% CI 1.18–2.04).

Table V presents the bivariate analyses on the

Table III. Multivariate analyses of non-prescription drug use by cognitive status

Variable	Any use		No. drugs	
	Odds ratio	95% CI	b coefficient	95% CI
Cognitively impaired	0.71	0.56, 0.89*	-0.09	-0.22, 0.04
Age (years)	0.99	0.98, 1.01	-0.01	-0.02, 0.01
Black race	0.62	0.53, 0.72*	-0.29	-0.38, -0.20*
Female sex	1.53	1.28, 1.83*	0.27	0.18, 0.36*
Education (years)	1.02	0.99, 1.04	0.01	-0.01, 0.02
Urban residence	1.11	0.93, 1.32	0.19	0.10, 0.28*
Functional status	1.13	1.03, 1.24*	0.07	0.03, 0.12*
Limitations (no.)				
Chronic disease status	1.15	1.05, 1.27*	0.07	0.02, 0.12*
Health visits (no.)	1.03	1.01, 1.05*	0.02	0.01, 0.03*

*p < 0.05.

Table IV. Prevalence of therapeutic drug class use by cognitive status

Therapeutic class	Cognitively impaired (n = 564) Any use (%)	Cognitively intact (n = 3546) Any use (%)	p Value*
1. Cardiovascular	57	54	0.223
2. Analgesic	55	61	0.005
3. Central nervous system	32	20	<0.001
4. Nutritional	29	23	0.001
5. Gastro-intestinal	28	27	0.824
6. Endocrine/metabolic	21	24	0.115
7. Respiratory	17	16	0.758
8. Antibiotic	9	7	0.065
9. Ophthalmic	6	5	0.474
10. Unidentified	3	3	0.626
11. Dermatological	2	2	0.727
12. Lipid lowering	2	<1	<0.001
13. Miscellaneous	2	3	0.076
14. Urinary	1	1	0.831
15. Otic	0	<1	0.396

* Comparison of groups using bivariate χ^2 test.

proportion of people taking a medication in any one of the analgesic or CNS subclasses by cognitive status. The most commonly used analgesic subclass was nonsteroidal anti-inflammatory drugs (NSAIDs) which were less likely ($p < 0.05$) to be taken by those who were cognitively impaired than by those who were intact. Use of other analgesic subclasses was similar ($p > 0.05$) for both groups. The most commonly used CNS subclass was benzodiazepines and their use and the use of miscellaneous CNS drugs was similar ($p > 0.05$) for the two groups. Those who were cognitively impaired were more likely ($p < 0.05$) to take antidepressants, anti-emetics, anticonvulsants, neuroleptics, other sedative/hypnotics, and antiparkinson drugs than those who were cognitively intact. These CNS subclasses were further collapsed into either psychotropic (i.e. benzodiazepines, antidepressants, neuroleptics, sedative/hypnotics) or non-psychotropic CNS medications. Bivariate analyses revealed that those who were cognitively impaired were more likely than cognitively intact individuals to take both psychotropic (22% vs. 16%, respectively; $\chi^2 = 12.15$; $df = 1$; $p < 0.001$) and non-psychotropic CNS medications (14.6% vs. 6.2%, respectively; $\chi^2 = 51.07$; $df = 1$; $p < 0.001$).

Discussion

This is one of the first studies to describe drug use patterns among cognitively impaired community-dwelling elderly people. We found that after controlling

Table V. Prevalence of CNS and analgesic subclass use by cognitive status

Therapeutic class	Cognitively impaired (n = 564) Any use (%)	Cognitively intact (n = 3546) Any use (%)	p Value*
<i>Analgesic</i>			
NSAIDs	43.3	50.8	0.001
Acetaminophen (paracetamol)	15.6	14.8	0.649
Narcotics	6.0	4.4	0.087
Miscellaneous	0.5	0.6	0.917
<i>CNS</i>			
Benzodiazepines	11.7	11.8	0.907
Antidepressants	7.0	3.2	<0.001
Anti-emetics	6.8	2.8	<0.001
Anticonvulsants	5.7	1.8	<0.001
Neuroleptics	5.7	1.1	<0.001
Sedative/hypnotics	1.8	1.5	<0.001
Antiparkinson	1.8	0.6	0.003
Miscellaneous	0.7	1.2	0.283

* Comparison of groups using bivariate χ^2 test.

for potential confounders, cognitively impaired individuals were less likely to be users of prescription or over-the-counter medications than those who were cognitively intact. The lower utilization of prescription drugs is of potential concern since it may represent underuse of medications, as those who were cognitively impaired should have had at least as great a need given their greater chronic disease burden and poorer functional status. There are several possible explanations for this finding. It is possible that this group's greater need was not adequately recognized by their physicians. Alternatively, this group's greater need may have been recognized by physicians, but appropriate therapy was not initiated because doctors were influenced by the knowledge that the patient was cognitively impaired. Standard medical practice should include, when feasible, treatment of health conditions that may improve functional status and quality of life regardless of cognitive function. The importance of the lower utilization of non-prescription drugs by the cognitively impaired is less clear. This finding may be related to their impaired cognitive and functional status and corresponding inability to purchase these products. Moreover, care-givers may not recognize an impaired elderly person's need for help.

We found that those who were cognitively impaired were less likely to take analgesic medications, specifically NSAIDs, than those who were cognitively intact. This agrees with the study by Kumar *et al.* for dementia patients and the findings by Wolf-Klein *et al.* in a study that compared patients with normal and impaired mental status [11, 12]. There are several possible interpretations of these findings. Participants with

cognitive impairment may not be able to express pain symptoms in an interpretable fashion [37]. Alternatively, the higher use of analgesics by those who were cognitively intact may represent a protective effect of certain diseases or the medications used to treat them. For example, a lower than expected prevalence of Alzheimer's disease has been reported in patients with rheumatoid arthritis [38]. Unfortunately, we did not collect information from participants during the Duke EPESE first in-home interview about the presence or absence of arthritis. Moreover, a recent report by Breitner *et al.* suggested that there is an inverse association between Alzheimer's disease and anti-inflammatory drugs (including NSAIDs) [39]. In contrast, a large study of an ambulatory elderly sample from Florida found no association between NSAID use and cognitive decline [40].

We found that those who were cognitively impaired were more likely to take CNS medications than those who were cognitively intact. Overall, 32% of cognitively impaired participants took one or more CNS medications, with the most common type being benzodiazepines. Although high, the prevalence of CNS medication usage was less than the 37–50% rate reported by Semla *et al.* for 930 ambulatory patients with different types of dementia who came to medical attention [13]. There are several plausible explanations for our findings. The high use of CNS medications may reflect the appropriate use of psychotropics to treat behavioural and psychiatric complications associated with cognitive impairment due to dementia [21–23]. However, the usage level of benzodiazepines may be of concern given that comparative clinical trials have demonstrated greater efficacy with neuroleptics, especially for psychotic symptoms [21–23]. Alternatively, the higher use of both CNS psychotropic and non-psychotropic medications may be causing or exacerbating cognitive impairment [16–20]. In one notable study of 300 patients referred to a tertiary care clinic for evaluation of cognitive impairment, Larson *et al.* rated 46 drug therapies as the aetiology for this condition in 35 patients, with the most common drug class implicated being benzodiazepines [20].

We believe that these differences in drug use patterns are not likely to be due to under- or over-reporting by those who were cognitively impaired for several reasons. First, special procedures were used to collect medication data (i.e. interviewers actually seeing and recording medications and use of proxy informants). Second, among those who were cognitively impaired, drug use patterns were similar (data not shown) for those without and with proxy interviews. Finally, the total number of medications used was similar for both cognitive status groups and similar to that reported by previous studies of elderly people in the community [5–7].

There are several potential limitations to this study. It was cross-sectional and causal interpretations are hampered by lack of knowledge of time-order relationships. Other potential limitations include that lack of

knowledge about the specific causes for participants' cognitive impairment and cognitive status were based on a single evaluation with the SPMSQ. However, the SPMSQ has been shown to have substantial reliability [30] and good sensitivity and specificity in identifying community dwelling subjects diagnosed as having dementia [41]. Fourth, medications were categorized into broad therapeutic classes, which did not allow for examination of individual medications for specific indications. Finally, this is a study of community dwelling elderly people living in the southeastern US and may not be representative of other populations where drug prescribing and non-prescription drug use habits may be different.

Despite these limitations, our findings suggest that community dwelling elderly people who are cognitively impaired are less likely than those who are cognitively intact to use prescription or non-prescription medication. Further, the use of analgesics is less likely and CNS drugs more likely among those who are cognitively impaired. Future research is needed to examine longitudinal drug-use patterns, and the use of specific medication classes for specific diseases or conditions by cognitive status and associated causes, to clarify these findings.

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