Published in final edited form as:

J Am Geriatr Soc. 2010 May ; 58(5): 880–888. doi:10.1111/j.1532-5415.2010.02819.x.

Daily Medication Use in Nursing Home Residents with Advanced Dementia

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Abstract

Objectives—Many medications commonly used to treat chronic conditions have unclear benefits for nursing home (NH) residents with advanced dementia. This study describes the pattern and factors associated with daily medication use in this population.

Design, Setting, Participants—Residents with advanced dementia (N=323) from 22 Boston-area NHs were followed prospectively for 18 months.

Measurements—Data from residents' records were used to determine the number of daily medications, specific drugs prescribed, and use of drugs deemed 'never appropriate' in advanced dementia. Resident characteristics associated with the use of more daily medications and drugs deemed inappropriate were examined.

Results—Residents were prescribed a mean of 5.9 ± 3.0 daily medications, and 37.5% received at least one medication considered 'never appropriate' in advanced dementia. Acetylcholinesterase inhibitors (15.8%) and lipid-lowering agents (12.1%) were the most common inappropriate drugs. Twenty-eight percent of residents took antipsychotics daily. Modest reductions of most daily medications only occurred during the last week of life. Factors independently associated with taking more daily medications included older age, male, non-white, dementia not due Alzheimer's, better cognition, cardiovascular disease, acute illness, and hospice referral. Factors independently associated with greater likelihood of taking inappropriate medications included male, shorter NH

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Author contributions: Dr Mitchell had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Rothman, Mitchell. **Acquisition of data:** Mitchell. **Analysis and interpretation of data:** Tjia, Rothman, Kiely, Shaffer, Holmes, Sachs, Mitchell. **Drafting of manuscript:** Tjia, Rothman, Mitchell. **Critical revision of manuscript for important intellectual content:** Tjia, Rothman, Kiely, Shaffer, Holmes, Sachs, Mitchell. **Statistical analysis:** Tjia, Kiely, Shaffer, Mitchell. **Obtained funding:** Mitchell. **Study supervision:** Mitchell.

Conflict of Interest

All other authors have no conflict of interest of any kind to report.

stay, better functional status, and diabetes, while a do-not-hospitalize order was associated with a lower likelihood.

Conclusion—Questionably beneficial medications are common in advanced dementia, even as death approaches. Several characteristics can help identify residents at risk for greater medication burden. Medication use in advanced dementia should be tailored to the goals of care.

Keywords

end-of-life care; dementia; inappropriate medication use; nursing homes; polypharmacy

INTRODUCTION

Over 50% of the 1.6 million nursing home (NH) residents in the United States have dementia,^{1, 2} the majority of whom suffer from other chronic conditions common among the elderly.³ The average NH resident is prescribed 7 to 8 separate medications daily,^{4, 5} many of which target chronic conditions. However, the potential benefits of continuing many of these drugs are questionable in the final stages of dementia.

Treatment in advanced dementia should be guided by the goals of care. For some patients, life prolongation remains a priority. However, the ability of many medications to meaningfully meet this goal is mitigated by the fact that these patients are already near the end-of-life. Similarly, some medications may be of limited benefit among those whose primary goal of care is to maintain their current functional or cognitive status, as these patients already are severely impaired. For the majority of advanced dementia patients whose primary goal of care is palliation,⁶ it is reasonable to continue medications that avoid or reduce suffering.

The potential benefits of daily medication use must be weighed against possible harmful effects and burdens.^{7,8} An estimated 760,000 preventable adverse drug events occur in NHs annually.⁷ Polypharmacy, resulting in part from the indefinite use of medications beyond their original indications, is a main contributor to these events.⁹ The oral administration of multiple medications in end-stage dementia patients with feeding problems, and repeated venipunctures needed to monitor certain drugs (e.g. warfarin) are additional burdensome consequences of polypharmacy in this population. Finally, prescribing medications of questionable benefit utilizes considerable resources, both in terms of the direct costs of the medications, as well as the staff-time to administer them.

Prior work has examined approaches to medication use in other terminal conditions (e.g., cancer)¹⁰ and the frail elderly.^{8, 11-14} In one model, prescribing is guided by weighing the patient's estimated life expectancy against the time required to achieve benefit from the medication.¹¹ There are few studies examining drug use in advanced dementia and these are limited by small sample sizes,^{15,16} cross-sectional design,¹⁶ or focus only on anti-dementia agents.¹⁷ Recently, an expert consensus panel attempted to classify certain medications as 'never appropriate' in advanced dementia when the goal of treatment is palliation.¹⁶ The degree to which medications inappropriate in advanced dementia are prescribed has not been examined in a rigorous fashion.

The main objective of this study was to examine daily medication use in advanced dementia, particularly near the end-of-life. To achieve this objective, this report describes the quantity, pattern, and types of medications prescribed to a cohort of 323 NH residents with end-stage dementia followed prospectively over 18 months. In addition, the study examines use of medications considered 'never appropriate,'¹⁶ and factors associated with daily medication burden in these residents.

METHODS

Study Population

NH residents with advanced dementia living in 22 Boston-area facilities were recruited from February 1, 2003 until September 30, 2006, as part of the Choices, Attitudes, and Strategies for Care in Advanced Dementia at the End-of-Life (CASCADE) study.¹⁸ Follow-up was completed in February 2009. The over-riding goal of the CASCADE study was to describe multiple facets of the end-of-life experience of NH residents with advanced dementia and their families. Details of the complete CASCADE study protocol are provided elsewhere.¹⁸

Briefly, to identify a cohort with advanced dementia, the residents' most recent Minimum Data Set assessments identified those with a Cognitive Performance Scale score of 5 or 6, indicating severe to very severe cognitive impairment.¹⁹ These residents then underwent screening for full eligibility, which included (1) age of 60 years or older, (2) length of stay of > 30 days, (3) cognitive impairment due to dementia (from chart), (4) Global Deterioration Scale (GDS) score of 7 (by nurse interview)²⁰ and (5) an appointed health care proxy (HCP) who could communicate in English. A GDS score of 7 indicates very severe memory deficits (cannot recognize family members), minimal verbal communication, incontinence of urine and stool, complete functional dependence and loss of the ability to walk.²⁰ Participant facilities had at least 60 beds and were located within a 60-mile radius of Boston.

Data Collection and Elements

Data were obtained from the residents' medical records, a brief mental status examination, and interviews of nurses and health care proxies. Assessments were conducted at baseline and quarterly thereafter up to 18 months. If the resident died, an assessment was obtained within 14 days of death.

Variables were selected for analyses from the CASCADE study dataset if they were considered 'a priori' to be associated with daily medication use based on the literature^{2, 5} and our clinical experience. The following resident characteristics were obtained from a baseline chart review: age, gender, race (white vs non-white), whether the resident lived in a special-care dementia unit, length of NH stay (years), and cause of dementia (Alzheimer's disease, vascular, or other). Cognitive disability was determined by resident examination at each assessment using the Test for Severe Impairment (TSI) (range 0-24, lower scores indicate greater impairment).²¹ The Bedford Alzheimer's Nursing Severity-Subscale (BANS-S) was quantified by the resident's nurse at each assessment (range 7 to 28, higher scores indicate greater functional disability).²² All comorbid health conditions were identified at baseline.

At each follow-up assessment, the following variables were obtained from the record: whether the resident has experienced an acute illness in the prior 90 days (e.g., infectious episode, myocardial infarction, stroke, any bone fracture, gastrointestinal bleed, seizure); hospitalizations in the prior 90 days; number of physician, nurse practitioner or physician assistant visits in the past 90 days; whether the resident had a do-not-hospitalize (DNH) order; feeding tube use; and whether the resident was referred to hospice. HCP's were asked at the baseline interview whether or not the primary goal of care was comfort (versus life prolongation).

Daily Medication Use

All medications prescribed to residents on a daily basis at the time of each follow-up assessment were ascertained from the medication administration record. Drugs administered

on an as needed basis, topical preparations for skin conditions, vitamins (except vitamin D), and antimicrobials were excluded from the analyses. Antimicrobial use in this cohort are described elsewhere.²³ Medications were recorded verbatim from the medication administration record and then categorized into the following classes: analgesics, scopolamine, hypoglycemics, cardiovascular agents, lipid-lowering agents, diuretics, urinary incontinence agents, prostate agents, gastrointestinal agents, oral corticosteroids, respiratory agents, hematological agents, thyroid agents, osteoporosis agents, estrogen, antiparkinsonian agents, antidepressants, antipsychotics, anti-dementia agents, anticonvulsants, benzodiazepines and non-benzodiazepine hypnotics. Medications classified as ‘never appropriate’ in advanced dementia when palliation is the goal of care included: lipid-lowering agents, antiplatelet agents (excluding aspirin), leukotriene receptor antagonists, anti-dementia agents (acetylcholinesterase inhibitors, N-methyl-D-aspartate receptor antagonists [memantine]), antiestrogens, hormone antagonists, immunomodulators (e.g. etanercept), and cytotoxic chemotherapy.¹⁶ Aspirin is not included with other antiplatelets agents because, unlike other antiplatelets agents that are used solely for secondary prevention in cardiovascular disease, aspirin may be appropriate in advanced dementia when used as an analgesic.

The protocol of the CASCADE study was approved by the Institutional Review Board at Hebrew SeniorLife. The residents’ HCPs provided written consent for their participation.

Analysis

Descriptive statistics were used to present the resident characteristics. The following outcomes were described for all residents during the 18 month follow-up period and, for those who died, during the last week of life: i. mean number of daily medications, ii. the proportion of residents receiving each medication, and iii. the proportion of residents receiving at least one ‘never appropriate’ medication.

In order to examine patterns of daily medication use during the last year of life, the proportion of decedents taking selected agents was quantified during the following intervals prior to death: 0-7 days, 8-90 days, 91-180 days, 181-270 days, and 271-365 days. In these analyses, we aimed to capture a heterogeneous group of drugs representing various aspects of medication use in advanced dementia, including: drugs of particularly questionable benefit (lipid-lowering, anti-dementia, osteoporosis agents), highly prevalent medications (proton-pump inhibitors [PPIs], antidepressants), agents associated with serious adverse effects (antipsychotics, benzodiazepines), and agents whose cessation (hypoglycemics, ACE inhibitors) or initiation (opioids) could indicate a shift in goals of care towards comfort. For purposes of presentation, drugs analyzed over the last year of life were grouped into non-psychotropic and psychotropic/opioid medications.

To examine factors associated with drug burden in advanced dementia, two outcomes were examined: i. total number of daily medications, and ii. the use of ≥ 1 ‘never appropriate’ drug. These analyses included all assessments obtained from residents during the follow-up period, and were conducted at the assessment level. Fixed independent variables (e.g., gender) were brought forward from baseline across all assessments, and dynamic variables (e.g., DNH status) were derived from the same assessment from which the medication data were obtained. For both outcomes, all aforementioned resident characteristics were included as independent variables. Bivariable analyses were used to examine unadjusted associations between each independent variable with the outcome, and those associated at a p-value of 0.10 or below were included in multivariable models. A stepwise approach was used to select the final set of variables independently associated with each outcome. Negative binomial regression via generalized estimating equations was used to identify factors associated with the number of daily medications,²⁴ where follow-up time (days) was used as

the measure of exposure. For residents who died, follow-up was defined as the number of days between baseline and death. For residents who survived, follow-up time was 18 months (540 days). The measure of association derived from the generalized negative binomial regression is a rate ratio, representing the number of daily medications per day of follow-up. Logistic regression via generalized estimating equations was used to examine factors independently associated with the dichotomous outcome of use of at least one 'never appropriate' drug. All bivariable and multivariable analyses accounted for clustering at the resident level. All analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, NC).

RESULTS

Study Population

Among 572 eligible NH residents with advanced dementia, 323 (56.5%) were recruited. A total of 177/323 residents (54.8%) died during the 18 months follow-up. Medication use in the last week of life could not be ascertained from 13 residents who died outside the NH. Therefore, analyses of drug use in the last week of life include 164 residents.

The residents' mean age was 85.3 years [standard deviation (SD) 7.5]; 14.6% were male; and 89.5% were white (African-American, 10.2%; Asian, 0.3%). Alzheimer's disease was the most common cause of dementia (72.4%), followed by vascular dementia (17.0%) and other causes (12.7%), and most residents were severely cognitively impaired with 72.1% scoring 0 on the TSI. The mean length of stay was 3.8 (SD) $\pm$ 3.3 years and 43.6% of residents lived in a special care dementia unit. The most common comorbid conditions were: hypertension (58.5%), osteoporosis (24.8%), coronary artery disease (18.6%), and diabetes (18.9%). HCP's stated that the primary goal of care was comfort for 90% of residents.

Daily Medication Use

Residents took a mean of $5.9 \pm$ (SD) 3.0 (range, 0-18) daily medications over the follow-up period. Similarly, residents who died were prescribed a mean of $6.3 \pm$ (SD) 3.3 (range, 0-18) daily medications during the last week of life.

Table 1 presents daily medication use for all 323 residents during the entire follow-up period and among decedents during the last week of life (N=164). Among all residents, gastrointestinal agents were the most commonly prescribed daily medication, followed by: analgesics, antidepressants, cardiovascular agents, hematological agents, osteoporosis agents, diuretics, antipsychotics, anticonvulsants, anti-dementia agents, hypoglycemics and lipid-lowering agents. The general pattern of drug use was similar among decedents during the last week of life, although the proportion of residents taking each drug was lower, with the exception of analgesics and scopolamine.

Figures 1 and 2 illustrate the change in daily medication use as residents approached death. Among non-psychotropic medications (Figure 1), the use of osteoporosis agents steadily declined from 32.8% to 18.9% over the last year of life. In contrast, there was little change in use of proton pump inhibitors (20.9% to 18.3%), ACE inhibitors (13.4% to 10.4%) and lipid-lowering agents (9.0% to 7.9%), and any reductions of these drugs occurred very close to death. Among psychotropic medications (Figure 2), antidepressant use was very common throughout the last year of life, and although the proportion of residents on antidepressants declined as they approached death, 37.2% remained on these drugs when they died. Antipsychotic use was also common during the last year of life, but did not decline as death approached (20.9% to 20.1%). While there was a relatively large reduction in the use of anti-dementia agents (14.9% to 7.9%), this primarily occurred very close to death. Opioid use rose dramatically as the residents approached the end-of-life (6.0% to 34.1%).

A large proportion (37.5%) of residents with advanced dementia were prescribed at least one ‘never appropriate’ medication at some point during the follow-up period, of which anti-dementia agents (acetylcholinesterase inhibitor [15.8%] and memantine [9.9%]) were the most common. Over one in ten residents (12.0%) used two or more ‘never appropriate’ medication during the follow-up period. During the last week of life, 18.3% of residents remained on at least one ‘never appropriate’ medication, of which lipid-lowering agents were the most common (7.9%).

Factors Associated with Daily Medication Burden

Table 2 presents the associations between resident characteristics with the number of daily medications taken at each assessment over the follow-up period. The measure of association represents the ratio of rates expressed as the number of medications taken per day of follow-up. For example, males were taking 1.36 times as many medications per day as females. In unadjusted analysis, characteristics associated with a higher number of daily medications use at the $p < 0.1$ level included: older age, male, non-white race, not living in a special care dementia unit, dementia not due to Alzheimer’s disease, a TSI score > 0 (better cognitive status), cardiovascular disease, diabetes, an acute illness in the prior 90 days, hospitalization in the prior 90 days, and having a hospice referral. After multivariable adjustment accounting for clustering at the resident level, factors most strongly associated with being on more daily medications were having a hospice referral (adjusted risk ratio [aRR] = 1.58, 95% confidence interval [95% CI] 1.24, 2.02) and having an acute illness in the prior 90 days (aRR = 1.57, 95% CI 1.38, 1.78). Other variables independently associated with a greater daily medication burden included: older age, male, non-white race, dementia not due to Alzheimer’s disease, a TSI score > 0 , and cardiovascular disease.

Table 3 presents the associations between the resident characteristics with the likelihood of being on at least one medication deemed “never appropriate” for advanced dementia with the goal of care is palliation. In unadjusted analyses, factors were associated with being on a never appropriate drug were: younger age, male, shorter length of NH stay, TSI score > 0 (better cognitive status), lower BANS-S score (higher functional ability), cardiovascular disease, diabetes, hospitalization in the prior 90 days, physician or nurse practitioner visit in the prior 90 days, and lack of a do-not-hospitalize order. After multivariable adjustment and accounting for clustering at the resident level, factors independently associated with being on an inappropriate medication included: male, shorter length of NH stay, lower BANS-S (higher functional ability), diabetes. Having a DNH order was independently associated with a lower likelihood of using an inappropriate medication.

DISCUSSION

This prospective study demonstrates that daily medications for chronic conditions are commonly and persistently prescribed to NH residents with advanced dementia. Although some medications of questionable benefit were discontinued towards the end-of-life (e.g., anti-dementia drugs), reductions often occurred only when death was imminent, and some drugs with unclear benefits (e.g. lipid-lowering agents) or potential harmful side effects (e.g., antipsychotics) did not decline. In addition, although the stated primary goal of care was comfort for 90% of residents, up to 40% were prescribed drugs deemed “inappropriate” in end-stage dementia when palliation is the goal of care. These findings raise concerns not only about the burden of medication use in advanced dementia, but also about how decisions regarding drug treatment are made for these residents.

This study supports previous work demonstrating that the on-going use of daily medications to treat chronic conditions is common among terminally ill patients, and extends these findings to NH residents with end-stage dementia. Our cohort took an average of 6 daily

medications, which is comparable to the general NH population (mean, 7-8),⁴ and at the lower range reported for patients with terminal conditions (6.5 to 14.6).^{10, 15, 16} Blass et al. reported that NH residents with advanced dementia took a mean of 15 daily medications, but that study's medication inclusion criteria were broader (e.g., measured all medications, including antimicrobials and as needed medications). Our study further corroborates that the total number of daily medications remains unchanged as residents with advanced dementia approach death, and mirrors previously reported shifts away from medications for comorbid medical conditions (e.g. osteoporosis) toward palliative and symptom-specific medications (e.g., opioids, scopolamine).^{10, 15}

The determination that a drug is unambiguously inappropriate in advanced dementia is hampered by limited outcome data and variability in individual patient preferences. Despite these challenges, a recent expert panel concluded that a small number of medications are "never appropriate" in advanced dementia when the primary goal of care is palliation.¹⁶ In a cross-sectional examination of 34 NH residents with advanced dementia, the panel reported that 29% were prescribed at least one of these drugs.¹⁶ In this much larger prospective cohort, almost 40% of residents were prescribed at least one "never appropriate" medication over 18 months, and 18% remained on these drugs at death. Anti-dementia and lipid-lowering agents were the most common "never appropriate" medications. Although acetylcholinesterase inhibitors were approved for the treatment of severe dementia after the consensus panel established the "never appropriate" list, and limited evidence suggests that anti-dementia drugs may improve outcomes in moderate dementia,²⁵ to date there still remains a lack of convincing data to support on-going use in end-stage disease. Continued lipid-lowering treatment is hard to justify in end-stage dementia patients when comfort is the goal of care, as the sequelae of hyperlipidemia are no longer relevant.

Two drugs not on the "never appropriate" list warrant further comment. First, antipsychotics were taken by almost one-third of residents and did not diminish as death approached. Several studies, including a randomized trial²⁶, fail to support the off-label use of antipsychotics to treat behavior problems in dementia. Moreover, these drugs have serious adverse sequelae in dementia patients, including extrapyramidalism and increased mortality.²⁷ Second, proton pump inhibitors were taken by one-fifth of residents and did not diminish as death approached. Although PPIs are often used for gastrointestinal prophylaxis in NSAID users, PPI use far exceeded NSAID use in our study. As one of the most frequently prescribed classes of drugs in the world, PPIs are well-known to be over-prescribed.²⁸ Often initiated during hospitalization and continued upon discharge without clear indication²⁹, PPIs are prime candidates for reconsideration in NH residents with advanced dementia, particularly upon return from the hospital.

Our findings suggest some factors may help identify NH residents with advanced dementia who are at higher risk for greater medication burden. Male residents were at increased risk for both being on inappropriate and a greater number of daily medications. The fact that a recent acute illness was associated with taking more medications may reflect the addition of new drugs necessary to treat that episode. The variable capturing recent acute illness was also collinear with recent hospitalization. Taken together, our findings suggest that acute illnesses and healthcare transitions may lead to the initiation of medications that are not indicated in advanced dementia on an ongoing basis, and highlights the need for careful medication review following such events. The fact that residents with DNH orders were less likely to be on an inappropriate medication further suggests that advance care planning which directs care toward comfort may be an important step in reducing inappropriate medication use in advanced dementia. The finding that residents referred to hospice took more daily medications does not necessarily contradict this notion, as a shift towards

palliation may require the addition of new drugs appropriately needed for symptom control (e.g., opioids and scopolamine).

It is important to consider our findings in light of the study's limitations. First, the study population was drawn from NHs in the Boston area and the cohort was predominately white, thus potentially limiting the generalizability of our findings. Second, while NH characteristics may influence end of life care, this study was not designed and lacks adequate power to identify NH factors influencing prescribing patterns at the facility level.

Finally, the “never appropriate” categorization by Holmes et al¹⁶ remains subject to interpretation and a more rigorous consensus process should be pursued as a next step towards establishing physician prescribing guidelines for advanced dementia.

To date, this is the largest study of daily medication use in advanced dementia. Our findings indicate that many NH residents with this condition receive drug treatment that is no longer appropriate given their advanced disability and limited life expectancy. The burden, costs and risks of polypharmacy are considerable, particularly in this frail population. Our results underscore the need for shared decision-making between providers and families of patients with end-stage dementia, in order to ascertain the goal of care, review the advantages and disadvantages of each ongoing medication, and to align treatment with stated preferences. When palliation is identified as the goal of care, the use of medications of questionable benefit should be reconsidered in favor of treatment that promotes comfort.

Acknowledgments

This study was supported by NIH-NIA R01 AG024091.

Dr. Tjia was supported by NIH-NIA K08AG021527. Dr. Holmes is supported by a Hartford Geriatrics Health Outcomes Research Scholars Award. Dr. Mitchell is supported by NIH-NIA K24AG033640.

Role of the sponsor: The funding sources had no role in the design and conduct of the study; in the collection, management, analysis and interpretation of the data; or in the preparation of the manuscript.

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Figure 1.

Proportion of nursing home residents with advanced dementia using selected non-psychotropic medications during the last year of life. The number of residents available for analysis at each interval were: 0-7 days, N=164 (7 decedents were outside the nursing home during the last week of life); 8-90 days, N=177; 91-180 days, N=128; 181-270 days, N=81 and 271-365 days, N=67.

Figure 2.

Proportion of nursing home residents with advanced dementia using selected psychotropic medications and opioids during the last year of life. The number of residents available for analysis at each interval were: 0-7 days, N=164 (7 decedents were outside the nursing home during the last week of life); 8-90 days, N=177; 91-180 days, N=128; 181-270 days, N=81 and 271-365 days, N=67.

Table 1
Daily Medication Use among Nursing Home Residents with Advanced Dementia

Medication	No. (%) of all residents who took medication ever during follow-up period (n=323)	No. (%) of decedents who took medication during last week of life (n=164)
Analgesics	190 (58.8)	98 (59.8)
Acetaminophen	161 (49.9)	59 (36.0)
NSAID	16 (5.0)	6 (3.7)
Opioid	77 (23.8)	56 (34.2)
Tramadol	8 (2.5)	4 (2.4)
Scopolamine	26 (8.1)	18 (11.0)
Hypoglycemics	48 (14.9)	12 (7.3)
Metformin	12 (3.7)	2 (1.2)
Insulin	27 (8.4)	9 (5.5)
Sulfonylurea	18 (5.6)	1 (0.6)
Thiazolidinedione	5 (1.6)	0 (0)
Cardiovascular agents	150 (46.4)	72 (43.9)
Beta blocker	97 (30.0)	48 (29.3)
Angiotensin-converting enzyme inhibitor	49 (15.2)	17 (10.4)
Calcium channel blocker	38 (11.8)	13 (7.9)
Digoxin	22 (6.8)	8 (4.9)
Nitrate	15 (4.6)	9 (5.5)
Alpha blocker	11 (3.4)	5 (3.1)
Angiotensin II receptor blocker	4 (1.2)	2 (1.2)
Antiarrhythmic	4 (1.2)	3 (1.8)
Hydralazine	2 (0.6)	1 (0.6)
Lipid-lowering agents	39 (12.1)	13 (7.9)
Diuretics	96 (29.7)	31 (18.9)
Urinary Incontinence	1 (0.3)	0 (0)
Prostate agents	2 (0.6)	1 (0.6)
Gastrointestinal agents	290 (90.1)	129 (78.7)
Laxative	259 (80.2)	115 (70.1)
Proton pump inhibitor	88 (27.2)	30 (18.3)
Histamine-2 receptor Blocker	56 (17.3)	18 (11.0)
Hyoscyamine	13 (4.0)	7 (4.3)
Metoclopramide	9 (2.8)	3 (1.8)
Antacid	20 (6.2)	3 (1.8)
Corticosteroid (oral)	21 (6.5)	9 (5.5)
Respiratory agents	56 (17.3)	28 (17.1)

Medication	No. (%) of all residents who took medication ever during follow-up period (n=323)	No. (%) of decedents who took medication during last week of life (n=164)
Hematological agents	149 (46.1)	50 (30.5)
Aspirin	119 (36.8)	42 (25.6)
Other non-aspirin antiplatelet agent	16 (5.0)	4 (2.4)
Warfarin	15 (4.6)	3 (1.8)
Heparin	6 (1.9)	2 (1.2)
Erythropoietin	2 (0.6)	0 (0)
Thyroid agents		
Thyroid hormone	55 (17.0)	24 (14.6)
Antithyroid agent	4 (1.4)	3 (1.8)
Estrogen	3 (0.9)	1 (0.6)
Osteoporosis agents	103 (31.9)	31 (18.9)
Calcium	99 (30.7)	29 (17.7)
Raloxifene	5 (1.6)	2 (1.2)
Calcitonin	9 (2.8)	3 (1.8)
Bisphosphonate	6 (1.9)	1 (0.6)
Antiparkinsonian agents	26 (8.1)	7 (4.3)
Antidepressants	173 (53.6)	61 (37.2)
Selective serotonin reuptake inhibitor	82 (25.4)	32 (19.5)
Trazadone	62 (19.2)	16 (9.8)
Mirtazapine	56 (17.3)	19 (11.6)
Stimulant	8 (2.5)	1 (0.6)
Tricyclic antidepressant	5 (1.6)	3 (1.8)
Serotonin-norepinephrine reuptake inhibitor (venlafaxine)	3 (0.9)	3 (1.8)
Bupropion	2 (0.6)	0 (0)
Antipsychotics	90 (27.9)	33 (20.1)
Anti-dementia	68 (21.1)	13 (7.9)
Acetylcholinesterase inhibitor	51 (15.8)	7 (4.3)
N-methyl-D-aspartate receptor antagonist (memantine)	32 (9.9)	8 (5.5)
Anticonvulsants	81 (25.1)	36 (22.0)
Benzodiazepines	39 (12.1)	16 (9.8)
Non-benzodiazepine hypnotics	3 (0.9)	1 (0.6)

Abbreviation: NSAID, non-steroidal anti-inflammatory drug

Table 2
Factors Associated with a Greater Number of Daily Medications among Nursing Home Residents with Advanced Dementia N=1381 assessments)*

<i>Characteristic</i>	<i>Values</i>	<i>Unadjusted Rate Ratio[‡](95% CI[§])</i>	<i>Adjusted[†] Rate Ratio[‡](95% CI[§])</i>
Age, mean ± SD [¶] (years)	84.9 ± 7.5	1.02 (1.01, 1.02)	1.02 (1.01, 1.03)
Male, No. (%)	172 (12.5)	1.36 (1.04, 1.67)	1.34 (1.08, 1.66)
Non-white race (vs. white), No. (%)	140 (10.1)	1.24 (0.98, 1.59)	1.28 (1.05, 1.58)
Does not live in special care dementia unit, No. (%)	795 (57.6)	1.15 (0.99, 1.34)	#
Shorter length of stay, mean ± SD (years)	4.5 ± 3.2	1.02 (0.99, 1.04)	-
Dementia not due to Alzheimer's disease, No. (%)	348 (25.2)	1.37 (1.16, 1.63)	1.24 (1.06, 1.46)
Test for Severe Impairment score >0 ^{**} , No. (%)	209 (15.2)	1.18 (0.99, 1.42)	1.22 (1.04, 1.44)
Lower BANS-S score ^{††} , mean ± SD	21.6 ± 2.2	1.00 (0.96, 1.03)	-
Cardiovascular disease ^{‡‡} , No. (%)	458 (33.2)	1.29 (1.11, 1.50)	1.21 (1.05, 1.39)
Diabetes, No. (%)	264 (19.1)	1.21 (1.02, 1.43)	-
No cancer, No. (%)	1361 (98.5)	1.38 (0.68, 2.81)	-
Acute illness in prior 90 days ^{§§} , No. (%)	428 (31.0)	1.62 (1.42, 1.85)	1.57 (1.38, 1.78)
Hospitalization in prior 90 days, No. (%)	61 (4.4)	1.29 (1.07, 1.55)	-
Physician, nurse practitioner or physician assistant visit prior 90 days, No. (%)	1300 (94.1)	1.08 (0.87, 1.33)	-
Do-not-hospitalize order, No. (%)	803 (58.1)	0.94 (0.82, 1.08)	-
Feeding tube, No. (%)	106 (7.7)	1.18 (0.93, 1.50)	-
Hospice referral, No. (%)	157 (11.4)	1.62 (1.25, 2.09)	1.58 (1.24, 2.02)
Goal of care is comfort			

* The mean number of daily medications were 5.9 ± (SD) 3.0, range 0-18

[†] Adjusted for clustering at the resident level

[‡] Represents the ratio of rates expressed as the number of medications used per day of follow-up. For example, males were on 1.36 times as many medications per day as females.

[§] CI= Confidence interval

[¶] SD = Standard deviation

Dash (–) under the adjusted RR indicates that the variable was not carried over to the adjusted analysis from the unadjusted analysis.

** Test for Severe Impairment, possible range 0-24, lower scores indicate greater cognitive impairment

^{††} BANS-S=Bedford Alzheimer Nursing Scale – Severity Subscale, possible range 7-28, higher scores indicate greater functional disability

^{‡‡} Cardiovascular disease includes history of coronary artery disease and cerebrovascular accident

^{§§} Acute illnesses include infectious episodes myocardial infarction, stroke, any bone fracture, gastrointestinal bleed, and seizures

Table 3
Factors Associated with ‘Never Appropriate’ Medication Use* among Nursing Home Residents with Advanced Dementia (N=1381 assessments)

Characteristic	All assessments No. (%) N =1381	Residents taking at least one never appropriate medication at each assessment among those with and without characteristic N (%)	Unadjusted Odds ratio (95% CI [‡])	Adjusted [†] Odds ratio (95% CI [‡])
Age, mean ± SD [§] (years)	84.9 ± 7.5	-	0.95 (0.92, 0.98)	- [¶]
Male				
Yes	172 (12.5)	80/172 (46.5)	3.35 (1.75, 6.41)	2.52 (1.21, 5.27)
No	1209 (87.5)	249/1209 (20.6)	referent	
Non-white race (vs. white)				
Yes	140 (10.1)	47/140 (33.5)	1.72 (0.75, 3.92)	-
No	1241 (89.9)	282/1241 (22.7)	referent	
Lives in special care dementia unit				
Yes	586 (42.4)	129/586 (22.0)	0.84 (0.50, 1.40)	-
No	795 (57.6)	200/795 (25.2)	referent	
Shorter length of stay, mean ± SD (years)	4.5 (3.2)	-	1.22 (1.10, 1.35)	1.14 (1.02, 1.27)
Dementia due to Alzheimer’s disease				
Yes	1033 (74.8)	263/1033 (25.5)	1.46 (0.79, 2.69)	-
No	348 (25.2)	66/348 (19.0)	referent	
Test for Severe Impairment score >0 [#]				
Yes	209 (15.2)	74/209 (35.4)	1.98 (1.23, 3.20)	-
No	1168 (84.8)	253/1168 (21.7)	referent	
Lower BANS-S score ^{**} , mean ± SD	21.6 (2.2)	-	1.23 (1.12, 1.37)	1.16 (1.04, 1.28)
Cardiovascular disease ^{††}				
Yes	458 (33.2)	139/458 (30.4)	1.68 (1.00, 2.83)	-
No	923 (66.8)	190/923 (20.6)	referent	
Diabetes				
Yes	264 (19.1)	101/264 (38.3)	2.42 (1.31, 4.45)	2.31 (1.21, 4.41)
No	1117 (80.9)	228/1117 (20.4)	referent	
Cancer				
Yes	20 (1.5)	11/20 (55.0)	4.01 (0.84, 19.0)	-
No	1361 (98.5)	318/1361 (23.4)	referent	
Acute illness in prior 90 days ^{‡‡}				
Yes	428 (31.0)	113/428 (26.4)	1.22 (0.87, 1.71)	-
No	953 (69.0)	216/953 (22.7)	referent	
Hospitalization in prior 90 days				
Yes	61 (4.4)	21/61 (34.4)	1.73 (0.92, 3.22)	-
No	1320 (95.6)	308/1320 (23.3)	referent	

Characteristic	All assessments No. (%) N =1381	Residents taking at least one never appropriate medication at each assessment among those with and without characteristic N (%)	Unadjusted Odds ratio (95% CI [‡])	Adjusted [†] Odds ratio (95% CI [‡])
Physician or nurse practitioner visit in prior 90 days				
Yes	1300 (94.1)	319/1300 (24.5)	2.31 (1.12, 4.75)	-
No	81 (5.9)	10/81 (12.4)	referent	
Do-not-hospitalize order				
Yes	803 (58.1)	131/803 (16.3)	0.37 (0.23, 0.60)	0.45 (0.27, 0.72)
No	578 (41.9)	198/578 (34.3)	referent	
No feeding tube				
Yes	1275 (92.3)	306/1275 (24.0)	1.14 (0.45, 2.91)	-
No	106 (7.7)	23/106 (21.7)	referent	
No hospice referral				
Yes	1224 (88.6)	300/1224 (24.5)	1.43 (0.76, 2.69)	-
No	157 (11.4)	29/157 (18.5)	referent	

* Never appropriate drug in advanced dementia as classified by Holmes et al¹⁶ includes lipid-lowering agents, antiplatelet agents (excluding aspirin), leukotriene receptor antagonists, anti-dementia agents (acetylcholinesterase inhibitors, N-methyl-D-aspartate receptor antagonists [memantine]), antiestrogens, hormone antagonists, immunomodulators, and cytotoxic chemotherapy

[†] Adjusted for clustering at the resident assessment level

[‡] CI= Confidence interval

[§] SD = Standard deviation

[¶] Dash (–) under the adjusted RR indicates that the variable was not carried over to the adjusted analysis from the unadjusted analysis.

[#] Test for Severe Impairment, possible range 0-24, lower scores indicate greater cognitive impairment

^{**} BANS-S=Bedford Alzheimer Nursing Scale – Severity Subscale, possible range 7-28, higher scores indicate greater functional disability

^{††} Cardiovascular disease includes history of coronary artery disease and cerebrovascular accident

^{‡‡} Acute illnesses include infectious episodes myocardial infarction, stroke, any bone fracture, gastrointestinal bleed, and seizure