RESEARCH ARTICLE

Care Needs and Clinical Outcomes of Older People with Dementia: A Population-Based Propensity Score-Matched Cohort Study

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Abstract

Objective  
To explore the healthcare resource utilization, psychotropic drug use and mortality of older people with dementia.

Design  
A nationwide propensity score-matched cohort study.

Setting  
National Health Insurance Research database.

Participants  
A total of 32,649 elderly people with dementia and their propensity-score matched controls (n=32,649).

Measurements  
Outpatient visits, inpatient care, psychotropic drug use, in-hospital mortality and all-cause mortality at 90 and 365 days.

Results  
Compared to the non-dementia group, a higher proportion of patients with dementia used inpatient services (1 year after index date: 20.91% vs. 9.55%), and the dementia group had more outpatient visits (median [standard deviation]: 7.00 [8.87] vs. 3.00 [8.30]). Furthermore, dementia cases with acute admission had the highest psychotropic drug utilization.
both at baseline and at the post-index dates (difference-in-differences: all <0.001). Demen-
tia was associated with an increased risk of all-cause mortality (90 days, Odds ratio (OR) 
=1.85 [95%CI 1.67-2.05], p<0.001; 365 days, OR=1.59 [1.50-1.69], p<0.001) and in-hospit-
tal mortality (90 days, OR=1.97 [1.71-2.27], p<0.001; 365 days, OR=1.82 [1.61-2.05], 
p<0.001) compared to matched controls.

Conclusions

When older people with dementia are admitted for acute illnesses, they may increase their 
use of psychotropic agents and their risk of death, particularly in-hospital mortality.

Introduction

Dementia, a neurodegenerative disorder characterized by cognitive impairment, has attracted 
broad international attention due to its high prevalence and profound health effects in the el-
derly population.[1] The annual incidence of dementia is approximately 2–7% in people aged 
65 years and older across all countries and is expected to increase sharply as populations age. 
[2] With the expected increase in people with dementia, various healthcare challenges related 
to dementia care may become important issues within the healthcare system. The majority of 
people with dementia go unrecognized when searching for healthcare services across the 
healthcare settings. Empirical data describing the healthcare utilization and clinical outcomes 
for these patients are scarce, and limitations in study design also limit clinical interpretations. 

Although dementia has been reported to increase healthcare utilization and related medical 
costs, most studies were performed in the 1990s; these studies did not include modern health-
care patterns and were focused primarily on inpatient services.[3–6] The disease burden of de-
mentia on the primary care sector remains unknown. This may limit the possibility for proper 
healthcare resource allocation because a large number of older people with dementia live in 
communities. Furthermore, studies have shown that the comorbidities of older people with de-
mentia are significantly higher than those without dementia:[7] indeed, the increased hospital 
admissions of these patients may result from a failure of outpatient management of comorbidi-
ties rather than dementia per se.[8–11]

We know little about the utilization of specific drug categories, such as psychotropic agents 
(i.e., anxiolytics or antipsychotics) among demented people. This is concerning because behav-
ioral and psychotic symptoms are common among people with dementia; these symptoms 
may be managed by pharmaceutical intervention.[12–15] According to The Alzheimer's Socie-
ty, 77% of nurses who were surveyed reported treating people with dementia in the hospital set-
ting with antipsychotic drugs[16] despite strong evidence of harmful adverse effects of these 
drugs. In particular, existing studies have raised significant concerns regarding the potential 
harms and adverse events associated with psychotropic drug use, such as dependency[17], road 
traffic accidents[18,19], accidental falls[20,21], fractures[22,23], or impaired cognitive func-
tion.[24–26] Furthermore, it remains unclear whether people with dementia are discharged 
with these medications, which may result in negative outcomes after potential long-term use. 

The most significant knowledge gap regarding caring for people with dementia lies within 
the potential interactions between acute hospital admissions and dementia. In addition to the 
increased use of inpatient services among people with dementia, the long-term effects of acute 
hospital admissions and dementia care remain uninvestigated. When compared to people 
without dementia, people with dementia may have various healthcare needs during or after an
acute admission. Moyle et al. suggested that the physical layout, particularly the busy environment, in hospital wards can be disorientating for people with dementia[27] and can trigger the occurrence of delirium. Kurrle et al. further reported that a period of hospitalization has an adverse effect on frail older people, particularly among people with dementia.[28] Without appropriate caution, people with dementia may suffer from more severe negative effects of hospitalizations than patients without dementia. However, there is a lack of empirical studies to test these hypotheses.

To overcome the above-mentioned knowledge gaps, the aim of this study was to evaluate healthcare utilizations, with a specific focus on medication use, in a cohort consisting of people with dementia and their propensity score-matched controls. Moreover, this study also aimed to explore the potential interaction between dementia and acute admission on the medication use and survival of people with dementia.

**Material and Methods**

**Data sources**

This is a population-based cohort study that utilized the National Health Insurance Research database (NHIRD). The NHIRD is a nationwide database consisting of anonymous eligibility and enrollment information as well as claims for visits, procedures, and prescription medications of more than 99% of the entire population in Taiwan (23 million). Individual patients are recorded as entering the NHIRD when they were covered by Taiwan’s mandatory National Health Insurance (NHI) program (from 1996), and individuals are recorded as leaving the program at death. For each visit, the NHIRD records the dates of the visits (outpatient visits, admissions and discharges) and up to 5 diagnoses coded by physicians according to the *International Classification of Disease, 9th Edition* (ICD-9 CM codes).[29] The completeness and accuracy of the NHIRD are ensured by the Ministry of Health and Welfare and the National Health Insurance Administration of Taiwan. The database has been described in detail elsewhere[30] and has been a source for numerous epidemiological studies published in peer-reviewed journals.[31–33]

We used the 2001–2009 Longitudinal Health Insurance Database, which contains the claims data of two million beneficiaries (approximately 10% of the total population) randomly sampled from the NHIRD, as our data source. The age and gender distributions of the LHID are not significantly different from those of the original NHIRD cohort. The longitudinal nature of the LHID permits the identification of a cohort based upon diagnoses, health services, drug utilization, track medical history, and the establishment of a prescription drug profile and can determine the endpoint of drug treatment.

**Ethical statement**

Because the identification numbers of all subjects in the NHIRD were encrypted to protect individual privacy, this study was exempted from full review by the Institution Review Board of the National Taiwan University Hospital, and the requirement for informed consent was waived. The Institution Review Board of the National Taiwan University Hospital approved this study.

**Dementia cases and controls**

From the LHID between January 1, 2001 and December 31, 2009, we identified people who were older than 65 years and who were first diagnosed with dementia, according to the following *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM)
codes: 290.0 (senile dementia, uncomplicated), 290.1× (presenile dementia), 290.2× (senile dementia with delusional or depressive features), 290.3× (senile dementia with delirium), and 290.4× (arteriosclerotic dementia). We did not include 331.0 (Alzheimer’s disease) and 331.1 (frontotemporal dementia) to define dementia in our study because the prevalence of outpatient or inpatient visits when using these diagnostic codes was less than 5% in the NHIRD. To increase the identification of dementia cases, only those who had at least three outpatient or inpatient claim records of dementia-related diagnosis codes were selected as our dementia cases [34]. The date of the first diagnosis of dementia was designated as the index date for all identified dementia cases.

For each dementia case, a matched control was randomly selected from the NHIRD using the propensity score matching technique to account for baseline differences between the demented and non-demented groups.[35,36] The propensity score was estimated from a multivariable logistic regression model. Covariates included in the model were age, sex, and concomitant diseases (diabetes mellitus, hypertension, heart failure, stroke, transient ischemic attack, osteoporosis, osteoarthritis, chronic obstructive pulmonary disease and depression). This approach enables the determination of whether dementia was an independent predictor of outcomes.

**Outcome measures**

The primary endpoint was the health-related resource use between the demented and non-demented groups. We focused on hospitalizations (number of admissions, length of stay, and primary diagnosis on admission) and outpatient services (number of visits and primary diagnosis on admission) during the one-year follow-up period after the index date. Additionally, we examined pharmacotherapies with known cognitive effects, including the use of antipsychotics (as defined by the Anatomical Therapeutic Chemical [ATC] classification system released by the WHO Collaborating Centre for Drug Statistics Methodology[37] [ATC code: N05A-], such as lithium, perphenazine, or fluphenazine), anxiolytics (N05B-, such as hydroxyzine), hypnotics (benzodiazepine derivatives [N05CD-, such as estazolam] and z-drugs [N05CF-, such as zolpidem]), and antidepressants (N06A-, such as paroxetine or mirtazapine) one year before and after the index date. Based on this approach, most mood stabilizers (e.g., lithium) or drugs with anticholinergic effects (such as paroxetine or mirtazapine) were included in our measurement of “psychotropic drug” use. The secondary outcomes were all-cause mortality and in-hospital mortality at 90 and 365 days.

**Statistical analyses**

McNemar tests were performed to compare categorical variables, and paired t-tests were used to compare continuous variables of both baseline characteristics as well as the health-related resource use. One pre-planned analysis was performed to further investigate the interactions between dementia and acute admission in relation to the use of psychotropic agents. The reason we mainly used pairwise comparisons was because of our “propensity score-matched cohort” study design. When outcomes were binary, propensity score methods allowed estimation of differences in proportions as most comorbid diseases were balanced between people with dementia and people without dementia in our study[38]. A difference-in-difference estimation was adopted to examine the difference in the use of psychotropic agents one year before and after the index date between the two study groups.[39] Conditional logistic regression models were used to examine the effects of dementia on 90-day and 365-day mortality (all-cause mortality, in-hospital mortality and in-hospital mortality associated with pneumonia) in our study subjects. All analyses were performed using SAS version 9.1.3 (SAS Institute Inc., Cary, NC, USA).
Results

The study subjects consisted of 32,649 people with dementia and their propensity score-matched non-dementia controls (n = 32,649). The age and gender distributions in the dementia cases and controls were well matched. The dementia cases were slightly more likely to have a transient ischemic attack than the non-dementia group (dementia case: 2.27% vs. non-dementia control: 1.92%). In contrast, the dementia cases were slightly less likely to have hypertension (dementia case: 45.09% vs. non-dementia control: 42.70%) than the non-dementia group. Other comorbid diseases were balanced between the groups (Table 1).

Compared to the non-dementia group, a higher proportion of patients with dementia used inpatient services (1 year after index date: 20.91% [7,829 admissions] vs. 9.55% [3,209 admissions]). For both groups, pneumonia was the most common condition for hospital admissions. Patients with dementia also had higher use of outpatient visits than the non-dementia group (1 year after the index date, number of outpatient visits, median [standard deviation] 7.00 [8.87] vs. 3.00 [8.30]). Dementia was the most common diagnosis for outpatient visits among the dementia group, while essential hypertension was the most common diagnosis for outpatient visits among non-dementia subjects (Table 2).

We further divided our study subjects into two groups: those with and those without acute admission 1 year after the index date. Our results showed that subjects with dementia were more likely to be prescribed study medications, including antipsychotics, anxiolytics, hypnotics (benzodiazepine and z-drugs), and antidepressants. Furthermore, acute admissions had a significant effect on drug utilizations, particularly in subjects with dementia. Among these subjects, dementia cases with acute admissions had the highest drug utilization both at baseline

| Table 1. Dementia cases and their propensity-score matched cohort. |
|---------------------------------------------------------------|
| **Propensity-score matched cohort** (n = 51,384)              |
| **Dementia cases** (n = 25,692)                                |
| n                | %      | n                | %      | p-value |
| Age group (in 5-yr increments)                                |
| 65–74            | 8021   | 31.22            | 8362   | 32.55   |
| 75–84            | 12683  | 49.37            | 12797  | 49.81   |
| ≥85              | 4988   | 19.41            | 4533   | 17.64   |
| Female           | 12418  | 48.33            | 12415  | 48.32   |
| Concomitant diseases                                      |
| Diabetes mellitus                                         |
| 5129            | 19.96  | 5345            | 20.80  |
| Hypertension                                             |
| 10971          | 42.70  | 11584          | 45.09  |
| Heart failure                                            |
| 12253          | 4.77   | 1124             | 4.37   |
| Stroke                                                   |
| 2796            | 10.88  | 2910             | 11.33  |
| Transient ischemic attack                                 |
| 582             | 2.27   | 493              | 1.92   |
| Osteoporosis                                             |
| 1552            | 6.04   | 1566             | 6.10   |
| Osteoarthritis                                           |
| 3926            | 15.28  | 4029             | 15.88  |
| COPD                                                      |
| 1263            | 4.92   | 1191             | 4.64   |
| Depression                                               |
| 1538            | 5.99   | 1546             | 6.02   |

Propensity score: age, gender, diabetes, hypertension, heart failure, stroke, transient ischemic attack, osteoporosis, osteoarthritis, COPD, depression

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Table 2. Hospitalization and outpatient service utilization 1 year after the index date.

|                          | Propensity-score matched cohort (n = 51,384) |
|--------------------------|-------------------------------------------|
|                          | Dementia cases (n = 25,692) | Controls (n = 25,692) | p-value |
|                          | n         | %         | n         | %         |          |
| **Hospitalizations**     |           |           |           |           |          |
| Hospitalizations per individual |           |           |           |           |          |
| 0                        | 20321     | 79.09     | 23239     | 90.45     | <0.0001  |
| 1                        | 3694      | 14.38     | 1929      | 7.51      |          |
| 2                        | 1122      | 4.37      | 367       | 1.43      |          |
| 3+                       | 555       | 2.16      | 157       | 0.61      |          |
| **Total number of hospitalizations** | 7829     | 3209      |           |           |          |
| **Length of stay**       |           |           |           |           | <0.0001  |
| Median [Std]             | 9.00      | 35.20     | 8.00      | 37.23     |          |
| <= 7                     | 3414      | 43.61     | 1548      | 48.24     |          |
| 8–30                     | 3473      | 44.36     | 1276      | 39.76     |          |
| 31–90                    | 750       | 9.58      | 298       | 9.29      |          |
| 91+                      | 192       | 2.45      | 87        | 2.71      |          |
| **Primary diagnosis (Top 5)** |           |           |           |           |          |
| Pneumonia (ICD-9-CM: 486) |           |           |           |           |          |
| Other urethra and urinary tract disorders (599) |           |           |           |           |          |
| Occlusion of cerebral arteries (ICD-9-CM: 434) |           |           |           |           |          |
| Other lung diseases (ICD-9-CM: 518) |           |           |           |           |          |
| Dementia (ICD-9-CM: 290) |           |           |           |           |          |
| Chronic bronchitis (ICD-9-CM: 491) |           |           |           |           |          |
| **Outpatient visits**    |           |           |           |           | <0.0001  |
| Outpatient visits per patient |           |           |           |           |          |
| Median [Std]             | 7.00      | 8.87      | 3.00      | 8.30      |          |
| 0                        | 3685      | 14.34     | 9309      | 36.23     |          |
| 1–5                      | 6677      | 25.99     | 6281      | 24.45     |          |
| 6–10                     | 6165      | 24.00     | 4267      | 16.61     |          |
| 11–15                    | 4026      | 15.67     | 2657      | 10.34     |          |
| 16+                      | 5139      | 20.00     | 3178      | 12.37     |          |
| **Primary diagnosis (Top 5)** |           |           |           |           |          |
| Dementia (ICD-9-CM: 290) |           |           |           |           |          |
| Essential hypertension (ICD-9-CM: 401) |           |           |           |           |          |
| Diabetes mellitus (ICD-9-CM: 250) |           |           |           |           |          |
| Acute upper respiratory infections (465) |           |           |           |           |          |
| Occlusion of cerebral arteries (ICD-9-CM: 434) |           |           |           |           |          |
| Osteoarthrosis and associated disorders (715) |           |           |           |           |          |
| General symptom (ICD-9-CM: 780) |           |           |           |           |          |
| Hypertensive heart disease (ICD-9-CM: 402) |           |           |           |           |          |
and at the post-index dates (difference-in-differences: all <0.001). Among all of the drugs investigated, anxiolytics were the most frequently prescribed to our study subjects (dementia with acute admission: 30.12% [baseline] vs. 35.56% [post-index date]; control without acute admission: 10.74% [baseline] vs. 20.17% [post-index date]). Specifically, more than one-third (35.13%) of dementia cases with an acute admission were prescribed antipsychotics compared to only 4.79% in controls without acute admission (Table 3).

We found that dementia was associated with an increased risk of all-cause mortality (90 days, OR = 1.85 [95%CI 1.67–2.05], p<0.001; 365 days, OR = 1.59 [1.50–1.69], p<0.001) compared to matched controls. Moreover, dementia was associated with a two-fold increased risk of in-hospital mortality compared to matched controls (90 days, OR = 1.97 [1.71–2.27], p<0.001; 365 days, OR = 1.82 [1.61–2.05], p<0.001). Specifically, we found an increased risk of in-hospital mortality associated with pneumonia among dementia cases (90 days, OR = 1.62 [1.13–2.32], p = 0.01; 365 days, OR = 1.47 [1.08–2.00], p = 0.02) (Table 4).

**Discussion**

Our study is the first to use the propensity score-matched cohort approach to quantify the healthcare utilization associated with dementia. Compared to previous studies, which only accounted for demographics (usually age and gender) or a few comorbid conditions, we provided credible estimates of the independent effects of dementia on healthcare utilization. Our most important finding was the identification of significant care needs for people with dementia who were discharged after an acute admission; these people had the highest use of psychotropic agents, both at baseline and at the post-index dates. Additionally, dementia was associated with an increased risk of death, particularly in-hospital mortality. Consistent with previous studies,[1,3–5] we found that the use of inpatient services by people with dementia was doubled when compared to non-dementia people. This may be because older people with dementia are more likely to have multiple comorbid conditions that place them at a higher risk to be hospitalized in general medical wards, which has been suggested in previous studies.[8] However, a recent review clearly reported the drawbacks and challenges of acute care for older people with dementia.[40] Older people with dementia are considered to be highly vulnerable to acute hospital admissions. It has been reported that disruption from the usual home routine may be the primary problem encountered by older people with dementia during acute hospital admissions.[41] Moreover, the hospital staff may be not experienced in dementia care, which may result in inappropriate physical and chemical restraints; additionally, this may result in unmet needs in such patients due to poor communication with older people with dementia.[42] Furthermore, clinicians may focus on acute care within their own specialties and ignore the potentially inappropriate medications for older people with dementia, which may lead to a worsening of their psychiatric symptoms.[27,43–45] Taken together, older people with dementia may be placed at a higher risk of adverse outcomes, which may occur during and after acute admission. This hypothesis is supported by our study because people with dementia had increased associated risks of in-hospital (all-cause and pneumonia-associated) and overall mortality.

However, there has been very little attention towards addressing and improving the quality of acute care for older people with dementia in acute care settings. Because people with dementia were usually admitted to acute hospitals for diseases other than dementia,[8] the greatest challenge in improving the quality of dementia care for older people is the management of the causes of acute admissions. In our study, the top five conditions of admissions among people with dementia were mainly preventable ambulatory care-sensitive conditions (ACSCs),[8] such as pneumonia and urinary tract infections. Early detection and management of acute
### Table 3. Use of psychotropic agents 1 year before and after the index date, with or without acute admission.

| Drug utilization                | Dementia cases (n = 25,692) | Controls (n = 25,692) | Difference-in-difference^b | Difference^a |
|--------------------------------|-----------------------------|-----------------------|----------------------------|--------------|
|                                | w/ acute admission          | w/o acute admission   | w/ acute admission         | w/o acute admission |
|                                | n = 5,391                  | n = 20,321            | n = 2,453                  | n = 23,239    |
|                                | (21.00%)                   | (79.00%)              | (9.50%)                    | (90.50%)      |
|                               | n  | %     | Difference^a | n  | %     | Difference^a | n  | %     | Difference^a | n  | %     | Difference^a |
| Antipsychotics                 | 729 | 13.57 | +21.56%      | 1933 | 9.51 | +15.28%      | 76  | 3.10 | <0.01       | 604 | 2.60 | <0.01       |
| 1 year before index date      | 1887| 35.13 | +21.56%      | 5038 | 24.79 | +15.28%      | 205 | 8.36 | +5.26%      | 1114| 4.79 | +2.19%      |
| 1 year after index date       | 1910| 35.56 | +5.44%       | 6086 | 29.95 | +3.16%       | 687 | 28.01| +15.90%     | 4687| 20.17| +9.43%      |
| Anxiolytics                    | 552 | 10.28 | +5.62%       | 1677 | 8.25  | +2.21%       | 84  | 3.42 | <0.01       | 700 | 3.01 | <0.01       |
| 1 year before index date      | 854 | 15.90 | +5.62%       | 2125 | 10.46 | +2.21%       | 213 | 8.68 | +5.26%      | 1232| 5.30 | +2.29%      |
| 1 year after index date       | 731 | 13.61 | +7.54%       | 2388 | 11.75 | +3.52%       | 141 | 5.75 | <0.01       | 988 | 4.25 | <0.01       |
| Hypnotics, benzodiazepine     | 1136 | 21.15 | +7.54%       | 3104 | 15.27 | +3.52%       | 329 | 13.41| +7.66%      | 1677| 7.22 | +2.97%      |
| 1 year before index date      | 1190 | 22.16 | +9.63%       | 3858 | 18.99 | +8.16%       | 263 | 10.72| +5.34%      | 1473| 6.34 | +1.75%      |
| 1 year after index date       | 1190 | 22.16 | +9.63%       | 3858 | 18.99 | +8.16%       | 263 | 10.72| <0.01       | 1473| 6.34 | +1.75%      |

Difference^a: The proportion of patients who used specific a drug category (1 year after index date-1 year before index date)
Difference-in-difference^b: The proportion of patients who used a specific drug category (1 year after index date-1 year before index date); dementia vs. control; after adjustment of the impact of acute admission

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illnesses in their early phase may minimize the need for hospitalizations. Furthermore, similar conditions were observed among non-demented people; therefore, ACSCs should be the main focus when caring for an aged population. Therefore, this may be considered as a universal approach in improving the quality of acute care for patients with and without dementia.

Our results raise a significant concern regarding the use of psychotropic agents among people with dementia. In particular, we observed an approximately three-fold increase in antipsychotic use one year after the diagnosis of dementia, which was independent of whether the patient suffered an acute admission event (with admission: 13.57% at baseline vs. 35.13% 1 year after diagnosis; without admission: 9.51% at baseline vs. 24.79% 1 year after diagnosis). People with dementia who experienced acute admissions after the diagnosis of dementia were more likely to be exposed to hypnotics (both benzodiazepine and z-hypnotics) compared to those without acute admissions after the diagnosis of dementia. The increased use of psychotropic agents during and after acute hospital admissions may also have resulted from the deterioration of the behavioral and psychotic symptoms of dementia, particularly when patients were unable to cope with unfriendly acute care environments.[27] This finding is supported by Banerjee, who indicated that physicians too often prescribe antipsychotics as a first-line response to managing the challenging behaviors of people with dementia.[46] These prescriptions may further result in admissions related to fractures or other associated adverse outcomes.[26] This finding also echoes the experience of caregivers who reported that the physical and mental conditions of demented people significantly deteriorated after acute hospital admissions.[41] Although non-pharmacological intervention should be prioritized in the management of behavioral and psychotic symptoms for dementia, these treatments are usually only available in specific units in acute hospitals.

### Table 4. Conditional logistic regression on the risk of mortality.

|                  | n    | %    | Odds Ratio (95% CI) | P      |
|------------------|------|------|---------------------|--------|
| **90 days**      |      |      |                     |        |
| All-cause mortality |      |      |                     |        |
| Dementia         | 1144 | 4.45 | 1.85 (1.67–2.05)    | <0.0001|
| Control          | 678  | 2.64 | 1.00 (reference)    |        |
| In-hospital mortality |      |      |                     |        |
| Dementia         | 614  | 2.39 | 1.97 (1.71–2.27)    | <0.0001|
| Control          | 339  | 1.32 | 1.00 (reference)    |        |
| In-hospital mortality (pneumonia) |      |      |                     |        |
| Dementia         | 86   | 0.33 | 1.62 (1.13–2.32)    | 0.01   |
| Control          | 55   | 0.21 | 1.00 (reference)    |        |
| **365 days**     |      |      |                     |        |
| All-cause mortality |      |      |                     |        |
| Dementia         | 3345 | 13.02| 1.59 (1.50–1.69)    | <0.0001|
| Control          | 2187 | 8.51 | 1.00 (reference)    |        |
| In-hospital mortality |      |      |                     |        |
| Dementia         | 799  | 3.11 | 1.82 (1.61–2.05)    | <0.0001|
| Control          | 474  | 1.84 | 1.00 (reference)    |        |
| In-hospital mortality (pneumonia) |      |      |                     |        |
| Dementia         | 113  | 0.44 | 1.47 (1.08–2.00)    | 0.02   |
| Control          | 78   | 0.30 | 1.00 (reference)    |        |

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Another safety concern regarding the higher utilization of antipsychotics among people with dementia than control is the risk of stroke. Previous studies have suggested that dementia itself could be an independent risk factor for stroke and the use of antipsychotics may further increase the risk of stroke in people with dementia.[47,48] Liu et al reported use of antipsychotics increased a 1.17-fold risk of stroke (hazard ratio 1.17, 95% CI 1.01–1.40; p<0.05) among people with dementia [47] while Imfeld et al reported a 4.5-fold increase of odds (OR 4.5, 95% CI 2.1–9.2) of transient ischemic attack for patients with Alzheimer disease treated with atypical antipsychotics.[48] Our study also found that people with dementia were slightly more likely to have a transient ischemic attack than the non-dementia group (dementia case: 2.27% vs. non-dementia control: 1.92%) and they had higher utilization of antipsychotics than control even before the index date.

The results of this study clearly demonstrate the long-term adverse outcomes in older people with dementia. Dementia itself was associated with an increased risk of all-cause, in-hospital and pneumonia-related in-hospital mortality. However, there is little information regarding the time of discharge to the end of life among older people with dementia. A study performed by Bradshaw et al. demonstrated that the outcomes for older people who were discharged from an acute hospital were very poor. More than half of the survivors did not recover their physical independence after an associated acute illness, and more than 70% of the survivors presented with significant behavioral and psychological symptoms.[49] This finding was also consistent with our findings regarding the sharp increased use of psychotropic agents among people with dementia and patients who experienced acute admissions. Therefore, more efforts should be placed on the long-term management of these people after they are discharged from an acute hospital.[50]

Despite the efforts in this study, there were several limitations. First, the dementia diagnosis in this study was determined using the claim data of NHIRD. As with all observational studies based on claim databases, we were not able to include variables not routinely captured in claim databases, such as social histories (cigarette or alcohol consumption), measurements of functional scales (e.g., MMSE), results of radiographs (e.g., CT/MRI) or laboratory tests. We were also not able to differentiate between dementia and other dementia-like etiologies. Nevertheless, we adopted a published algorithm to increase the identification of dementia cases. Additionally, we adopted a “newly diagnosed dementia cohort” study design to attenuate the potential effect of the severity of dementia. Second, we could not confirm whether the patients had adhered to the instructions for taking their prescriptions of psychotropic medications. However, this is a common challenge in most studies. Third, indications for the increased use of psychotropic agents were unknown from the claim data, such that we were not able to presume that these prescriptions were given as chemical restraints. Nevertheless, there is a generalized consensus that psychotropic agents should be terminated whenever possible. Therefore, the rising trends of psychotropic agent use for older patients with and without dementia in this study deserve further attention.

**Conclusion**

Our study suggested that specific attention should be paid when older people with dementia are admitted to general medical wards. A few models have been developed to improve the quality of acute care for older people with dementia, including a special unit or shared-care model. However, improving the awareness of hospital staff regarding dementia is of great importance because the negative effect of acute care on older people with dementia may only be the tip of the iceberg. The cognitive impairments in elderly patients admitted to general medical wards may be overlooked by hospital staff, which may lead to a significant functional decline in these
patients. Taken together, improving the awareness and understanding of dementia among general hospital staff is important in order to optimize the care for older people with dementia. The quality of dementia care in general hospitals has been regarded as an important indicator of the quality of acute care in general hospitals.

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Author Contributions

Conceived and designed the experiments: FYH LNP LKC. Performed the experiments: FYH YWW. Analyzed the data: FYH YWW. Contributed reagents/materials/analysis tools: FYH YWW. Wrote the paper: FYH LNP CKL PNW LKC.

References

1. van der Ploeg ES, Bax D, Boorsma M, Nijpels G, van Hout HP (2013) A cross-sectional study to compare care needs of individuals with and without dementia in residential homes in the Netherlands. BMC Geriatr 13: 51. doi: 10.1186/1471-2318-13-51 PMID: 23706150
2. Prince M, Bryce R, Albanese E, Wimo A, Ribeiro W, Ferri CP (2013) The global prevalence of dementia: a systematic review and metaanalysis. Alzheimers Dement 9: 63–75 e62. doi: 10.1016/j.jalz.2012.11.007 PMID: 23905823
3. Leibson C, Owens T, O'Brien P, Waring S, Tangalo E, Hanson V, et al. (1999) Use of physician and acute care services by persons with and without Alzheimer's disease: a population-based comparison. J Am Geriatr Soc 47: 864–869. PMID:10404933
4. Richards KM, Shepherd MD, Crismon ML, Snyder EH, Jermain DM (2000) Medical services utilization and charge comparisons between elderly patients with and without Alzheimer’s disease in a managed care organization. Clin Ther 22: 775–791. PMID: 10929924
5. Weiner M, Powe NR, Weller WE, Shaffer TJ, Anderson GF (1998) Alzheimer’s disease under managed care: implications from Medicare utilization and expenditure patterns. J Am Geriatr Soc 46: 762–770. PMID: 9625195
6. Albert SM, Costa R, Merchant C, Small S, Jenders RA, Stern Y (1999) Hospitalization and Alzheimer’s disease: results from a community-based study. J Gerontol A Biol Sci Med Sci 54: M267–271. PMID: 10362011
7. Zhao Y, Kuo TC, Weir S, Kramer MS, Ash AS (2008) Healthcare costs and utilization for Medicare beneficiaries with Alzheimer’s. BMC Health Serv Res 8: 108. doi: 10.1186/1472-6963-8-108 PMID: 18498638
8. Phelan EA, Borson S, Grothaus L, Balch S, Larson EB (2012) Association of incident dementia with hospitalizations. JAMA 307: 165–172. doi: 10.1001/jama.2011.1964 PMID: 22235087
9. Zuliani G, Galvani M, Sioulis F, Bonetti F, Prandini S, Boari B, et al. (2012) Discharge diagnosis and comorbidity profile in hospitalized older patients with dementia. Int J Geriatr Psychiatry 27: 313–320. doi: 10.1002/gps.2722 PMID: 21595539
10. Natalwala A, Potluri R, Upal P, Heun R (2008) Reasons for hospital admissions in dementia patients in Birmingham, UK, during 2002–2007. Dement Geriatr Cogn Disord 26: 499–505. doi: 10.1159/000171044 PMID: 19005254
11. Saver BG, Wang CY, Dobie SA, Green PK, Baldwin LM (2014) The central role of comorbidity in predicting ambulatory care sensitive hospitalizations. Eur J Public Health 24: 66–72. doi: 10.1093/eurpub/ckd018 PMID: 23543676
12. Miu DKY, Szeto SSL (2012) Sleep disturbances among a group of dementia participants. Journal of Clinical Gerontology and Geriatrics 3: 105–109.
13. Lyketsos CG, Lopez O, Jones B, Fitzpatrick AL, Breitner J, DeKosky S (2002) Prevalence of neuropsychiatric symptoms in dementia and mild cognitive impairment: results from the cardiovascular health study. JAMA 288: 1475–1483. PMID:12243634

14. Lu JH, Zhou AH, Li F, Hao ZH, Li WJ, Cui ZJ, et al. (2013) Risk factors and characteristics of the recurrence of behavioral and psychological symptoms of Alzheimer’s disease. Journal of Clinical Gerontology and Geriatrics 4: 115–118.

15. Verhoeven V, Hartmann ML, Wens J, Sabbé B, Dieleman P, Tsakitzidis G, et al. (2014) Happy pills in nursing homes in Belgium: A cohort study to determine prescribing patterns and relation to fall risk. Journal of Clinical Gerontology and Geriatrics.

16. Alzheimer’s Society (2009) Counting the cost: Caring for people with dementia on hospital wards. London, England.

17. Rojas-Fernandez CH, Carver D, Tonks R (1999) Population trends in the prevalence of benzodiazepine use in the older population of Nova Scotia: A cause for concern? Can J Clin Pharmacol 6: 149–156. PMID: 10495367

18. Gustavsen I, Bramness JG, Skurtveit S, Engeland A, Neutel I, Mørland J. (2008) Road traffic accident risk related to prescriptions of the hypnotics zopiclone, zolpidem, flunitrazepam and nitrazepam. Sleep Med 9: 818–822. doi: 10.1016/j.sleep.2007.11.011 PMID: 1826959

19. Orriols L, Philip P, Moore N, Castot A, Gadegbeku B, Delorme B, et al. (2011) Benzodiazepine-like hypnotics and the associated risk of road traffic accidents. Clinic PharmacoTher 89: 595–601. doi: 10.1038/cpt.2011.3 PMID: 21368756

20. Panneman MJ, Goettsch WG, Kramarz P, Herings RM (2003) The costs of benzodiazepine-associated hospital-treated fall Injuries in the EU: a Pharma study. Drugs Aging 20: 833–839. PMID: 12964889

21. Chang CM, Chen MJ, Tsai CY, Ho LH, Hsieh HL, Chau YL, et al. (2011) Medical conditions and medications as risk factors of falls in the inpatient older people: a case-control study. Int J Geriatr Psychiatry 26: 602–607. doi: 10.1002/gps.2569 PMID: 21480377

22. Finkle WD, Der JS, Greenland S, Adams JL, Blaschke T, et al. (2011) Risk of fractures requiring hospitalization after an initial prescription for zolpidem, alprazolam, lorazepam, or diazepam in older adults. J Am Geriatr Soc 59: 1883–1890. doi: 10.1111/j.1532-5415.2011.03591.x PMID: 22091502

23. Kang DY, Park S, Rhee CW, Kim YJ, Choi NK, Lee J, et al. (2012) Zolpidem use and risk of fracture in elderly insomnia patients. J Prev Med Public Health 45: 219–226. doi: 10.3961/jpmph.2012.45.4.219 PMID: 22880153

24. Koyama A, Steinman M, Ensrud K, Hillier TA, Yaffe K (2014) Long-term cognitive and functional effects of potentially inappropriate medications in older women. J Gerontol A Biol Sci Med Sci 69: 423–429. doi: 10.1093/gerona/glt192 PMID: 24293516

25. Koyama A, Steinman M, Ensrud K, Hillier TA, Yaffe K (2013) Ten-year trajectory of potentially inappropriate medications in very old women: importance of cognitive status. J Am Geriatr Soc 61: 258–263. doi: 10.1111/jgs.12093 PMID: 23320787

26. Hsiao FY, Peng LN, Lin MH, Chen LK (2014) Dose-Responsive Effect of Psychotropic Drug Use and Subsequent Dementia: A Nationwide Propensity Score Matched Case-Control Study in Taiwan. J Am Med Dir Assoc 15:509–513. doi:10.1016/j.jamda.2014.02.009 PMID: 24685407

27. Moyle W, Borbasi S, Wallis M, Olorenshaw R, Gracia N (2011) Acute care management of older people with dementia: a qualitative perspective. J Clin Nurs 20: 420–428. doi:10.1111/j.1365-2702.2010.03521.x PMID: 21029231

28. Kurrle SE (2006) Improving acute care services for older people. Med J Aust 184: 427–428. PMID: 16646738

29. World Health Organization (2011) International Classification of Diseases, Ninth Revision (ICD-9).

30. Hsiao FY, Yang CL, Huang YT, Huang WF (2007) Using Taiwan’s national health insurance research databases for pharmacoepidemiology research. Journal of Food and Drug Analysis 15: 99–108.

31. Chen YM, Chen DY, Lin MH, Chen LK (2014) Alendronate and risk of oesophageal cancer: a nationwide population-based study in Taiwan. J Am Med Dir Assoc 15:509–513. doi:10.1016/j.amed.2014.02.009 PMID: 24685407

32. Moyle W, Borbasi S, Wallis M, Olorenshaw R, Gracia N (2011) Acute care management of older people with dementia: a qualitative perspective. J Clin Nurs 20: 420–428. doi:10.1111/j.1365-2702.2010.03521.x PMID: 21029231

33. Hsiao FY, Huang WF, Chen YM, Chen LK, Tai YW, Chang LC, et al. (2011) Hip and subtrochanteric or diaphysal femoral fractures in alendronate users: a 10-year, nationwide retrospective cohort study in Taiwanese women. Clin Ther 33: 1659–1667. doi:10.1016/j.clinthera.2011.09.006 PMID: 22018450

34. Huang WF, Tsai YW, Wen YW, Hsiao FY, Kuo KN, Tsai CR (2010) Osteoporosis treatment and atrial fibrillation: alendronate versus raloxifene. Menopause 17: 57–63. doi:10.1097/gme.0b013e3181b34749 PMID: 19680161
34. Lin CF, Wu FL, Lin SW, Bai CH, Chan DC, Gau CS, et al. (2012) Age, dementia and care patterns after admission for acute coronary syndrome: an analysis from a nationwide cohort under the national health insurance coverage. Drugs Aging 29: 819–828. doi: 10.1007/s40266-012-0011-6 PMID: 23018581

35. Austin PC (2008) The performance of different propensity-score methods for estimating relative risks. J Clin Epidemiol 61: 537–545. doi: 10.1016/j.jclinepi.2007.07.011 PMID: 18471657

36. Austin PC, Grootendorst P, Normand SL, Anderson GM (2007) Conditioning on the propensity score can result in biased estimation of common measures of treatment effect: a Monte Carlo study. Stat Med 26: 754–768. PMID: 16783757

37. Austin PC, Grootendorst P, Anderson GM (2007) A comparison of the ability of different propensity score models to balance measured variables between treated and untreated subjects: a Monte Carlo study. Stat Med 26: 734–753. PMID: 16708349

38. Austin PC (2011) A Tutorial and Case Study in Propensity Score Analysis: An Application to Estimating the Effect of In-Hospital Smoking Cessation Counseling on Mortality. Multivariate Behav Res 46: 119–151. PMID: 22287812

39. Donald SG, Lang K (2007) Inference with difference-in-differences and other panel data. Review of Economics and Statistics 89: 221–233.

40. Dewing J, Dijk S (2014) What is the current state of care for older people with dementia in general hospitals? A literature review. Dementia (London).

41. Goldberg SE, Whittamore KH, Pollock K, Harwood RH, Gladman JR (2014) Caring for cognitively impaired older patients in the general hospital: A qualitative analysis of similarities and differences between a specialist Medical and Mental Health Unit and standard care wards. Int J Nurs Stud.

42. Jurgens FJ, Clissett P, Gladman JR, Harwood RH (2012) Why are family carers of people with dementia dissatisfied with general hospital care? A qualitative study. BMC Geriatr 12: 57. doi: 10.1186/1471-2318-12-57 PMID: 23006826

43. Draper B, Hudson C, Peut A, Karmel R, Chan N, Gibson D (2013) Hospital Dementia Services Project: Aged care and dementia services in New South Wales hospitals. Australas J Ageing.

44. Bail K, Hudson C, Grealish L, Shannon K, Ehsern S, Peut A (2013) Characteristics of rural hospital services for people with dementia: findings from the Hospital Dementia Services Project. Aust J Rural Health 21: 208–215. doi: 10.1111/ajr.12041 PMID: 24033521

45. Draper B, Karmel R, Gibson D, Peut A, Anderson P (2011) The Hospital Dementia Services Project: age differences in hospital stays for older people with and without dementia. Int Psychogeriatr 23: 1649–1658. doi: 10.1017/S1041610211001694 PMID: 21902861

46. Banerjee S (2009) The use of antipsychotic medication for people with dementia: Time for action. A report for the Minister of State for care services. London, England.: Department of Health.

47. Liu ME, Tsai SJ, Chang WC, Hsu CH, Lu T, Hung KS, et al. (2013) Population-based 5-year follow-up study in Taiwan of dementia and risk of stroke. PLoS One 8: e61771. doi: 10.1371/journal.pone.0061771 PMID: 23626726

48. Imfeld P, Bodmer M, Schuerch M, Jick SS, Meier CR (2013) Risk of incident stroke in patients with Alzheimer disease or vascular dementia. Neurology 81: 910–919. doi: 10.1212/WNL.0b013e3182a35151 PMID: 23902701

49. Bradshaw LE, Goldberg SE, Lewis SA, Whittamore K, Gladman JR, Jones RG, et al. (2013) Six-month outcomes following an emergency hospital admission for older adults with co-morbid mental health problems indicate complexity of care needs. Age Ageing 42: 582–588. doi: 10.1093/ageing/aft074 PMID: 23800454

50. Yeh KP, Lin MH, Liu VK, Chen LY, Peng LN, Chen LK (2014) Functional decline and mortality in long-term care settings: Static and dynamic approach. Journal of Clinical Gerontology and Geriatrics 5: 13–17.