Published in final edited form as:

J Alzheimers Dis. 2015 ; 48(2): 361–375. doi:10.3233/JAD-150228.

Nationwide inpatient prevalence, predictors and outcomes of Alzheimer's Disease among older adults in the United States, 2002–2012

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Abstract

In the inpatient setting, prevalence, predictors and outcomes (mortality risk (MR), length of stay (LOS) and total charges (TC)) of Alzheimer's Disease (AD) are largely unknown. We used data on older adults (60y+) from the Nationwide Inpatient Sample (NIS) 2002–2012. AD prevalence was ~3.12% in 2012 (total weighted discharges with AD±standard error: 474,410±6,276). Co-morbidities prevailing more in AD inpatient admissions included depression (OR=1.67, 95%CI: 1.63–1.71, p<0.001), fluid/electrolyte disorders (OR=1.25, 95%CI:1.22–1.27, p<0.001), weight loss (OR=1.26, 95%CI:1.22–1.30, p<0.001) and psychosis (OR=2.59, 95%CI:2.47–2.71, p<0.001), with mean total co-morbidities increasing over-time. AD was linked to higher MR, longer LOS but lower TC. TC rose in AD, while MR and LOS dropped markedly over-time. In AD, co-morbidities predicting simultaneously higher MR, TC and LOS (2012) included congestive heart failure, chronic pulmonary disease, coagulopathy, fluid/electrolyte disorders, metastatic cancer, paralysis, pulmonary circulatory disorders and weight loss. In sum, co-morbidities and TC increased over-time in AD, while MR and LOS dropped. Few co-morbidities predicted occurrence of AD or adverse outcomes in AD.

Keywords

Alzheimer's Disease; inpatient sample; co-morbidity; length of stay; health care cost; mortality; older adults

INTRODUCTION

With older adults projected to at least double over the next 30 years [¹, ²] and limited success in treating Alzheimer's disease (AD), the annual number of new cases of AD will double by 2050. [³, ⁴] For adults 65 and older, AD rates will increase 40% by 2025. [³]

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Since individuals diagnosed with AD can live with illnesses for relatively long times, [3] the health services needed to assist them in sustaining their quality of life can have a substantial impact on health care expenditures, especially if they have coexisting medical conditions. [3] As rates of AD and other dementias grow, health care expenditures are projected to increase from 2013 (\$203 billion) to 2050 (\$1.2 trillion) [3]. Given that the risk for hospitalization is high for AD patients with coexisting conditions, a significant percentage of health care expenditures associated with the disease may be accounted for by hospital care costs. [5] In fact, a recent study carried out among a cohort aged 65 years or older (N=3,019), and using a retrospective design for hospitalization and comparing dementia (N=494) to non-dementia cases (N=2,525) was able to show that incident dementia was significantly associated with increased risk of hospitalization (OR=1.41 (95% CI: 1.23–1.61; P=0.001), including hospitalization for ambulatory care-sensitive conditions (OR=1.78 (95% CI: 1.38–2.31; P=0.001). [6]

Despite the potential increases in hospital care costs due to increasing rate of AD, there is limited research estimating AD prevalence among inpatient admissions to assist projecting future needs of hospital services for this patient population. Most studies assessing AD incidence and prevalence used population-based surveys of healthy community-dwelling older adults. [7, 8] Moreover, inpatients are often designated a number of diagnoses and co-morbidities. It is of interest to estimate inpatient AD prevalence as principal diagnosis as well as “any” diagnosis (primary or secondary), examine trends over-time, and assess whether co-morbidities and other individual-level and hospital-level characteristics are related to AD diagnosis and outcomes of hospitalization.

Our study has five key objectives: **(A)** To assess over-time trends in AD prevalence among an inpatient sample of US older adults, overall and stratifying by age group and sex; **(B)** To compare co-morbidities in AD and non-AD patient admissions, admission-level and hospital-level characteristics in a recent period of time; **(C)** To compare hospitalization outcomes in AD and non-AD patient admissions, namely mortality risk (MR), length of stay (LOS) and total charges (TC) in a recent period of time; **(D)** To examine trends in co-morbidity prevalence and outcomes of hospitalization among AD patient admissions; **(E)** To assess the predictive value of patient-level and hospital-level characteristics on outcomes of hospitalization among recent AD patient admissions.

MATERIALS AND METHODS

Database and study participants

The Nationwide Inpatient Sample (NIS) is among a family of databases and software tools comprising the Healthcare Cost and Utilization Project (HCUP), a federal-state-industry partnership sponsored by the Agency for Healthcare Research and Quality (AHRQ). The NIS is the largest US nationwide all-payer hospital inpatient care database to date. Annually, NIS collects data on approximately seven to eight million hospital stays, reflecting all discharges from around 1000 hospitals, a probability sample from the HCUP State Inpatient Databases (SID) data. The sampling probability is ~20% and the design is stratified covering U.S. non-rehabilitation, community hospitals, with the target universe being all acute care hospital discharges in the United States. The NIS was developed to provide information on

hospital utilization, charges, and quality of care, nationwide. For instance, in 2002, 4,840 hospitals in the hospital universe were available, of which NIS recorded all discharges from around a 20% sample of hospitals in this target universe. [9]

With the objective of selecting a sample of hospitals representative of the target universe, NIS defined its sampling strata through five hospital characteristics contained in the AHA hospital files: (1) Geographic Region – Northeast, Midwest, West, and South; (2) Control – public, private not-for-profit, and proprietary; (3) Location – urban or rural; (4) Teaching Status – teaching or non-teaching, (5) Bed Size – small, medium, and large.

The NIS includes clinical and resource-use information usually contained within a typical discharge abstract, protecting the privacy of individual patients, physicians, and hospitals as required by data sources. Although NIS data are available since 1988, severity and comorbidity measures contained in the *severity* file were only made available from 2002 onwards. In addition, NIS did not add new states to its 35-state geographical coverage since 2002 providing more homogeneity in data acquisition over time. Therefore, we used NIS data from 2002 to 2012 (See Appendix I for details).

We aimed at selecting older persons aged 60y or older based on the United Nations definition of the older population (<http://www.who.int/healthinfo/survey/ageingdefnolder/en/>). Of 87,039,711 patient admissions were sampled from 2002 to 2012, NIS (weighted mean age $\pm$ SE: 47.9 $\pm$ 0.2, and weighted proportion female $\pm$ SE: 58.5% $\pm$ 0.1, weighted number of discharges: 411,487,801), 35,258,031 were aged 60y or older (weighted mean age $\pm$ SE: 75.37 $\pm$ 0.03, and weighted proportion female $\pm$ SE: 56.0% $\pm$ 0.1). The total weighted number of hospital discharges of older adults aged 60y or older between 2002 and 2012 was estimated at 166,871,086 nationwide. In 2012, the unweighted number of discharges over 60y of age was 2,825,130; the weighted number was 14,126,650.

Diagnostic criteria

Each year, the *core* file of NIS provided the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes for diagnosis and procedure. The latest changes to ICD-9-CM codes are provided for 2011: <http://www.cdc.gov/nchs/data/icd/ICD-9-CM%20TABULARADDENDAfy12.pdf>

Although diagnoses provided per patient admission varied by State, it was truncated at 15 for consistency, since w cases had more than 15 between the 2002 and 2008. Thus, even though up to 25 diagnoses were provided between 2009 and 2012, for equal opportunity of having a specific diagnosis, only the first 15 were considered for any year.

Among the possible 15 diagnoses, the first ranked diagnosis of AD, also termed “principal diagnosis” was of secondary interest. In our main analysis, trends, characteristics and outcomes of AD as “any diagnosis” was of primary interest. ICD-9-CM code used for AD was 331.0. (See Appendix II)

Co-morbidity measure

The AHRQ comorbidity measures identify coexisting medical conditions not directly related to the principal diagnosis or the main reason for admission, and are likely to have originated before the hospital stay. The AHRQ comorbidity measures were developed as one of the HCUP tools. Complete documentation on the comorbidity measures is available on the HCUP User Support Website under Tools & Software. (<http://www.hcup-us.ahrq.gov/toolssoftware/comorbidity/comorbidity.jsp>).

In the present study, 27 of 29 co-morbidities (http://www.hcup-us.ahrq.gov/toolssoftware/comorbidity/Table2-FY12-V3_7.pdf) were included in our analyses. In particular, we examined the likelihood of specific co-morbid conditions among AD patient admissions and how this likelihood changed over the years (excluding AIDS due to rare occurrence and neurological co-morbidity for likely redundancies with AD diagnosis). In addition, we created a co-morbidity index ranging between 0 and 27 by summing the individual co-morbidity measures. This index was further categorized into “0”, “1–2” “3–4” “5+”.

Outcome measures

Three outcome measures of hospitalization were considered, MR upon discharge (0=discharged alive, 1=discharged dead), LOS (days) and TC(\$). In particular, we were interested in comparing outcome measures in patient admissions with AD to those without AD in 2012 and examining changes over time among AD patient admissions between the years of 2002 to 2012. For TC trends, values were inflated to reflect the consumer price index of 2012.

Covariates

Patient-level characteristics—Among patient-level characteristics, we included age (continuous and categorized as 60–64, 65–69, 70–74, 75–79, 80–84 and 85+), sex, race (White, Black, Hispanic, Asian/Pacific Islander, Native American and Other), median household income for zip code of patient (expressed as quartiles), insurance status (Medicare, Medicaid, Private insurance, self-pay, no charge and other) and admission day (weekday vs. weekend).

Hospital-level characteristics—We examined hospital-level characteristics in relation to AD status (1=Yes, 0=No), and outcomes of healthcare utilization, which included bed size (Small, Medium, Large), ownership of hospital (Government/nonfederal, private non-profit, private investor-owned), location/teaching status of the hospital (rural, urban, non-teaching, urban teaching) and region of the hospital (Northeast, Midwest, South and West).

Statistical analysis

Using Stata 13.0 (StataCorp, College Station, TX), [10] analyses accounted for survey design complexity based on analytic guidelines outlined by HCUP NIS [9] by incorporating sampling weights, primary sampling units and strata. Consequently, population estimates of proportions, means and regression coefficients were made (*svy* commands). [10] Standard errors were estimated using Taylor series linearization. Multiple regression modeling was also conducted, mainly using linear and logistic regression models, while also accounting

for sampling design complexity whenever possible. When waves were incorporated to examine trends of AD prevalence and outcomes of hospitalization, trends weights were used to ensure the redesigned 2012 NIS could be incorporated into the analysis of trends. Following our key objectives: **(A)** We first explored proportions of older adults 60y or older who were diagnosed with AD either as principal diagnosis or as any of 15 possible diagnoses. This analysis was conducted from 2002 to 2012, stratifying by sex and age groups. Overall, within each sex and sex-age groups, we assessed trends by conducting logistic analyses with year as the only covariate and AD status the binary outcome (1=Yes, 0=No). In addition, fractional polynomials were used to determine which linear model best fit AD prevalence proportion, testing 44 models with term orders ranging from -2 to +3 and comparing the best two models to the linear model. **(B)** AD and non-AD patient admissions, using the “any diagnosis” criterion and for the year 2012 – the most recent available year in NIS – were compared by logistic regression with various predictors of AD status, including patient-level and hospital-level characteristics as well as patient co-morbidities; **(C)** Using the 2012 wave of data among older adults aged 60y or older, we also compared outcomes of hospitalizations for AD and non-AD patient admissions by logistic and linear regression models with AD status as the main predictor of those outcomes, controlling for patient-level, and hospital-level characteristics, and co-morbidities; **(D)** Using data from 2002 through 2012, we conducted a trends analysis of co-morbidities among AD patient admissions, by estimating proportions with their SE and conducting a logistic regression model for each co-morbidity with year being the only predictor. Similarly, we examined trends in MR, LOS and TC using the same methods (i.e. proportion estimation and multiple regression models with year as the only covariates) among AD patient admissions; **(E)** Finally, and using analyses similar to (C) but restricting the sample to AD patient admissions, we ran several regression models testing predictors of hospitalization outcomes in 2012 among older adults with AD. Due to the large number of hypotheses tested in each model, the type I error was corrected from 0.05 to 0.01.

RESULTS

Of the 35,258,031 older adults in the unweighted sample (2002–2012), 126,284 were admitted to a hospital with AD as a “principal diagnosis” (weighted discharges: 604,642) while 1,206,190 had AD as their primary or secondary diagnosis i.e. “any diagnosis” (weighted discharges: 5,755,688). In 2012 alone, out of 2,825,130 older adults in the unweighted sample (weighted discharges: 15,227,740), 99,260 had AD as “any diagnosis” (total weighted discharges with AD±standard error: 474,410±6,276).

Table S1 shows the trends in weighted prevalence of AD as a principal diagnosis (%), stratifying by sex and age group. Overall, this prevalence was increasing over time by around 1–2% annually. In most sex-age groups, the increasing trend was noted between the years 2002 and 2007, with subsequent leveling off or drop between the years 2011 and 2012. The same pattern of trends were observed for AD as “any diagnosis” among hospitalized older adults. Overall, this proportion increased from 3.17% in 2002 to 3.69% in 2008, with a steady drop noted beyond that point to reach 3.12% in 2012 (Table 1). Based on fractional polynomials, among both men and women, year raised to the powers 2 and 3 as two separate terms gave the best fit in a linear model predicting AD (“any diagnosis”), with a positive

quadratic term and a negative cubic term. This model had a significantly better fit than the linear model with first-order year entered alone suggesting that the relationship between AD prevalence and year was in fact non-linear (See Appendix III for details)

Table 2 shows the association of patient and hospital-level characteristics with AD status among hospitalized older adults. In general, AD status was positively associated with being female, belonging to an older age group, Black or Hispanic ethnicity, lower income, having Medicare as the primary expected insurance, admission on a weekend, and with rural hospitalizations. Geographically speaking, compared to the Northeast, the South had a higher likelihood of AD diagnosis whereas the West had a lower AD diagnosis prevalence. Most co-morbidities were more prevalent in non-AD admissions compared to AD, with the exception of depression which was 67% more likely in AD admissions compared to non-AD (OR=1.67, 95% CI: 1.63–1.71, $p<0.001$), fluid/electrolyte disorders (OR=1.25, 95% CI: 1.22–1.27, $p<0.001$), weight loss (OR=1.26, 95% CI: 1.22–1.30, $p<0.001$) and psychosis (OR=2.59, 95% CI: 2.47–2.71, $p<0.001$)

Table 3 displays findings from multiple regression models testing associations between AD status (1=Yes, 0=No) with MR, LOS and TC, controlling for patient-level and hospital-level characteristics. For mortality risk upon discharge, being diagnosed with AD (as any diagnosis) was associated with a 7% greater risk. In contrast, other factors included in the models were inversely related to MR and those were: female gender, a younger age group, higher income, Medicare coverage, <3 co-morbidities, small bed size hospital, a private hospital, or any hospital in the Midwest (vs. Northeast). Whites had higher MR than Hispanics but lower risk compared to Asian/Pacific Islander.

LOS, on the other hand, was extended by AD diagnosis by about 0.80 days on average. Other factors also extended LOS and those were: male gender, older age, Black or Asian/Pacific Islander ethnicity (vs. White), lower income, Medicaid and Self-pay (vs. Medicare), weekday admission, larger bed size hospital, governmental ownership of hospital, urban location, and Northeast geographical area. Moreover, the larger the number of co-morbidities, the longer was the stay, with a clear dose-response relationship.

In contrast, TC was inversely related to AD status. The same independent pattern of association was noted for female gender, older age groups and weekend admission. Conversely, Hispanics, Asians and “other” minority groups had significantly higher total charges compared to whites, whereas the reverse was true for Native Americans and no difference was noted among Blacks. Higher income and private insurance (vs. Medicare) was independently linked to higher TC. As expected, the greater the number of co-morbidities, the higher the TC, with a clear dose-response relationship. This dose-response was also noted for hospital bed size (Large>Medium>Small) rural-urban location and teaching status of the hospital (urban-teaching>urban, non-teaching>rural), with private, investor-owned hospital charging on average \$18,879 more than governmental hospitals ($p<0.001$). Compared to the Northeast, the Midwest and the South had lower charges whereas the West had higher TC, independently of the patient-level and hospital-level covariates, and independently of AD status.

Among hospitalized older adults who were diagnosed with AD, trends in co-morbidities from 2002 to 2012 are presented in Table 4. Overall, the average number of co-morbidities increased steadily from 1.95 in 2002 to 2.93 in 2012. Some of the most prevalent co-morbidities (>10% in 2012) in AD patient admissions included deficiency anemia (~16% in 2002 → 24% in 2012), congestive heart failure (13.6% in 2002 → 14.6% in 2012), chronic pulmonary disorder (15% in 2002 → 19% in 2012), depression (8% in 2002 → 16% in 2012), uncomplicated diabetes (~16% in 2002 → 23% in 2012), hypertension (45% in 2002 → 68% in 2012), hypothyroidism (13% in 2002 → 21% in 2012), fluid/electrolyte disorder (27% in 2002 → 37% in 2012) and renal failure (3% in 2002 → 17% in 2012). For most co-morbidities, the prevalence rose over-time.

In parallel with the rise in co-morbidities among AD patient admissions, TC rose steadily from an average of \$22,180/admission in 2002 to \$33,499/admission in 2012. However, both MR and LOS have been markedly reduced over-time. In particular, MR dropped steadily from 6.1% in 2002 to 4.4% in 2012 (Table 5).

Using data from 2012 on inpatient older adults with AD, we tested predictors of outcomes of hospitalization (Table 6). MR was lower among women who also had a shorter LOS and lower TC. Older age groups (specifically, 74y and older) compared to 60–64y had higher MR, but shorter LOS and lower TC. TC was also higher among Hispanics compared to Whites. Admissions belonging to the 4th quartile of income had significantly higher TC compared to the 1st quartile. Privately insured individuals as well as those categorized as “self-pay” or “other” had higher MR compared to Medicare. Medicaid inpatient admissions were hospitalized longer on average than those on Medicare. Private and “other” type of insurance incurred lower charges compared to Medicare. Weekend admissions had higher MR, shorter LOS and lower TC than weekdays. Co-morbidities which independently increased TC, MR and LOS included congestive heart failure, chronic pulmonary disease, coagulopathy, fluid/electrolyte disorders, metastatic cancer, paralysis, pulmonary circulatory disorders and weight loss.

DISCUSSION

This study is the first to comprehensively examine trends in AD diagnoses among US inpatient older adults and whether hospitalization co-morbidities and outcomes are related to AD status. Moreover, this study tested both patient-level and hospital-level predictors of AD status and outcomes of hospitalization. Among key findings, AD prevalence was ~3.12% in 2012 (total weighted discharges with AD±standard error: 474,410±6,276), increasing from 2002–2007 but leveling off or dropping thereafter. While most co-morbidities prevailed mainly in non-AD patient admissions, the reverse was true for depression (OR=1.67, 95%CI:1.63–1.71, p<0.001), fluid/electrolyte disorders (OR=1.25, 95%CI:1.22–1.27, p<0.001), weight loss (OR=1.26, 95%CI:1.22–1.30, p<0.001) and psychosis (OR=2.59, 95%CI:2.47–2.71, p<0.001). Average number of co-morbidities in AD patient admissions increased from 1.95 (2002) to 2.93 (2012). AD status was linked to higher MR, longer LOS but lower TC. TC rose in AD patient admissions, while both MR and LOS dropped markedly over time. In AD patient admissions, co-morbidities predicting simultaneously higher MR, TC and LOS in 2012 included congestive heart failure, chronic pulmonary

disease, coagulopathy, fluid/electrolyte disorders, metastatic cancer, paralysis, pulmonary circulatory disorders and weight loss.

Vascular disease is a potentially modifiable cause of cognitive decline and dementia in older adults. Stroke, cardiovascular disease, peripheral vascular disease, hypertension and diabetes have each been associated with cognitive deficits or dementia. [11–24] Although some of those diseases had markedly increased prevalence over time in AD patient admissions (e.g. type 2 diabetes (16% in 2002 to 23% in 2012), hypertension (45% in 2002 to 68% in 2012), peripheral vascular disease (4.7% to 7.6%)) and affected outcomes of hospitalization in adverse ways (e.g. congestive heart failure, pulmonary circulatory disorders), most were either unassociated with or inversely related to AD status among older patient admissions. Possibly, many vascular risk factors associated with AD incidence are influential only when present at mid-life. In fact, among those co-morbid conditions, obesity was inversely related to AD status whereas weight loss was positively associated with both AD status and adverse outcomes of AD. There is evidence of a U-shaped association between weight status and AD incidence whereby both obesity and underweight at mid-life are linked to AD onset, possibly with gender differentials [25–30] whereas weight loss in later-life predicts advanced stages of AD as is the case of hospitalized older adults. [31–35] Among studies of Medicare beneficiaries, a study which covered 195,024 fee-for-service ADRD beneficiaries aged 65 years and an equal number of matched non-ADRD controls, was able to show that Medicare beneficiaries with ADRD were significantly more likely to have potentially avoidable hospitalizations (PAHs) for diabetes short-term complications (OR=1.43; 95% CI: 1.31–1.57), diabetes long-term complications (OR=1.08; 95% CI : 1.02–1.14), and hypertension (OR=1.22; 95% CI: 1.08–1.38), but less likely to have PAHs for chronic obstructive pulmonary disease (COPD)/asthma (OR=0.85; 95% CI: 0.82–0.87) and heart failure (OR=0.89; 95% CI: 0.86–0.92). [36]

In contrast, AD status in our present study was predicted by co-morbid depression or psychosis upon admission to the hospital. While many previous studies found a positive relationship between elevated depressive symptoms and dementia, AD or cognitive decline [37–40], other studies failed to observe an association [38–42] while still others found relationships in sub-groups with baseline cognitive impairment [43] or relatively more education. [44] In a recent study of 2,425 initially non-demented older adults, depressive symptoms were found to precede memory decline in late-life, but not vice versa. [45] A review of 55 epidemiological studies published between 1990 and 2003 revealed that, on average, 41% of AD patient admissions reported psychosis, including delusions in 36% and hallucinations in 18%. [46]

The results also indicate significant racial disparities in patient admissions with AD. This finding is consistent with previous observations. [3] In addition, the results also indicate significant racial/ethnic disparities in TC and LOS. Interestingly, Gilligan and colleagues (2013) found significant differences between minorities and whites and among minority groups in Medicaid payments for health costs among patient admissions with AD. [47] Moreover, our findings support potential racial disparities in hospitalization characteristics among AD patient admissions, which may explain the racial disparities observed in care

costs. However, future research is needed to further investigate other socio-demographic factors that may explain why these differences are occurring.

Despite many of the study strengths including national representativeness, large sample size, and availability of extensive healthcare data that allow for trends analyses, the current study is not without limitations. First, it relied on administrative database using ICD-9-CM codes which may lead to diagnosis misclassification. However, the AHRQ periodically ensures quality checks with internal and external validation. Second, discharge abstracts are de-identified, thus precluding longitudinal analyses. Third, the structure of NIS limits our ability to detect multiple discharges from the same condition per patient, including those with AD. Thus, although clustering was adjusted for at the hospital level, the occurrence of several admissions per patient within a year or during the period of study could not be corrected for due to the lack of individual patient-level identifiers. In addition, detailed patient data are lacking such that individual medication regimens and laboratory results are missing. This precludes examining important covariates we would otherwise have included. Fourth, NIS is limited to AD inpatient admissions and thus trend results may not be similar in the community. As with any retrospective administrative data analysis, there is potential for bias from missing data; however, it is unlikely that missing data will have a large effect on the results because of the large sample size of the current study. A final limitation is the inability to compare AD and non-AD patient frequencies of hospitalization over pre-set periods of time (e.g. a month or a year).

In sum, and among key findings, co-morbidities and total charges are increasing over-time in AD, while MR and LOS are dropping. Some co-morbidities were higher in AD compared to non-AD while others predicted mortality and other outcomes in AD. Studies investigating temporal relationships between co-morbid conditions and occurrence of AD as well as mortality among AD patients beyond hospital discharge are needed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This study was supported in part by the NIA/NIH/IRP in collaboration with Johns Hopkins University School of Medicine. We would like to thank Ms. Danielle Shaked and Ms. Megan Williams for their internal review of the manuscript.

ABBREVIATIONS

AD	Alzheimer's Disease
AHRQ	Agency for Healthcare Research and Quality
CI	Confidence Interval
HCUP	Healthcare Cost and Utilization Project

ICD-9-CM	International Classification of Diseases, Ninth Revision, Clinical Modification
LOS	length of stay
MR	Mortality risk
NIS	Nationwide Inpatient Sample
OR	Odds Ratio
SE	Standard Error
SID	State Inpatient Databases
TC	total charges

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APPENDIX I

NIS contains clinical and nonclinical data elements for each hospital stay, including: Primary and secondary diagnoses and procedures; patient demographic characteristics (e.g., sex, age, race, median household income for ZIP Code); hospital characteristics (e.g., ownership); expected payment source; TC; discharge status; LOS; severity and comorbidity measures. Many of these variables were included in the NIS core file which contains discharge-level data along with AHA hospital file which contain hospital characteristics and weights data.

Noteworthy changes occurred to the sampling design of NIS as of 1998, which included the following: (1) Revising definitions of the strata variables; (2) Excluding rehabilitation hospitals from the NIS hospital universe; (3) Changing the calculation of hospital universe

discharges for the weights. Between 1998 and 2002, the number of hospitals included in the sample covered 13 more States, thus going from a 22-State to a 35-State geographical coverage. The initial number of States included in 1988 was limited to 8. After 2002, no new States were added.

2012 NIS was redesigned to improve national estimates, making them more precise. Three major changes were made to this wave forward: (a) Sample design was modified so that the NIS would be a sample of discharge records from all HCUP-participating hospitals, rather than sampling the hospitals themselves from which all discharges would be retained; (b) The 2012 NIS forward uses the definitions of hospitals and discharges supplied by the statewide data organizations that contribute to HCUP, as opposed to definitions used by the AHA Annual Survey; (c) The 2012 NIS forward removed State and hospital identifiers and other data elements to enhance confidentiality.

APPENDIX II

The International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) list three definitions and clinical criteria: (1) “A disabling degenerative disease of the nervous system occurring in middle-aged or older persons and characterized by dementia and failure of memory for recent events, followed by total incapacitation and death. Types of the Alzheimer syndrome are differentiated by the age of onset and genetic characteristics. The early onset form (the mean age of the onset of symptoms between the ages of 40 and 60y) and the late onset form (the onset of symptoms after the age of 60y). Three forms are identified: ad-1, ad-2, ad-3. Some of the clinical characteristics of the Alzheimer syndrome are similar to those of the pick syndrome.” (2) “A progressive, neurodegenerative disease characterized by loss of function and death of nerve cells in several areas of the brain leading to loss of cognitive function such as memory and language”. (3) Neurodegenerative disorder of the central nervous system resulting in progressive loss of memory and intellectual functions; begins in the middle or later years; characterized by brain lesions such as neurofibrillary tangles and neuritic plaques. [5]

APPENDIX III

Men:

```
fp <year>: regress ad_any <year> if selectpart2male==1
(fitting 44 models)
(...10%...20%...30%...40%...50%...60%...70%...80%...90%...100%)
```

Fractional polynomial comparisons:

```
-----
--
year | df Deviance Res. s.d. Dev. dif. P(*) Powers
-----
+-----
omitted | 0 -12101246 0.164 959.403 0.000
linear | 1 -12101272 0.164 932.939 0.000 1
```

```

m = 1 | 2 -12101273 0.164 932.280 0.000 -2
m = 2 | 3 -12102205 0.164 0.000 -- 2 3
-----
--
(*) P = sig. level of model with m = 2 based on F with 15480936 denominator
dof.
Source | SS df MS Number of obs =15480940
-----+-----
Model | 25.7058027 2 12.8529013 Prob > F = 0.0000
Residual | 414776.18615480937 .026792705 R-squared = 0.0001
-----+-----
Total | 414801.89115480939 .026794363 Root MSE = .16368
-----

-
ad_any | Coef. Std. Err. t P>|t| [95% Conf. Interval]
-----+-----
year_1 | .0001446 4.73e-06 30.54 0.000 .0001353 .0001539
year_2 | -4.80e-08 1.57e-09 -30.54 0.000 -5.11e-08 -4.49e-08
_cons | -194.1525 6.357035 -30.54 0.000 -206.6121 -181.6929
-----

-

Women

:
fp <year>: regress ad_any <year> if selectpart2female==1
(fitting 44 models)
(....10%....20%....30%....40%....50%....60%....70%....80%....90%....100%)
Fractional polynomial comparisons:
-----
--
year | df Deviance Res. s.d. Dev. dif. P(*) Powers
-----+-----
omitted | 0 -8361738 0.196 1468.398 0.000
linear | 1 -8361744 0.196 1462.417 0.000 1
m = 1 | 2 -8361744 0.196 1462.021 0.000 -2
m = 2 | 3 -8363206 0.196 0.000 -- 2 3
-----
--
(*) P = sig. level of model with m = 2 based on F with 19752715 denominator
dof.
Source | SS df MS Number of obs =19752719

```



```

-----+-----
                                F( 2,19752716) = 734.23
      Model | 56.2998538    2 28.1499269    Prob > F    = 0.0000
      Residual | 757311.13319752716 .038339595    R-squared    = 0.0001
-----+-----
                                Adj R-squared = 0.0001
      Total | 757367.43319752718 .038342441    Root MSE    = .1958
-----

-
      ad_any |   Coef.   Std. Err.      t    P>|t|    [95% Conf. Interval]
-----+-----
      year_1 | .000192  5.02e-06   38.24  0.000   .0001822   .0002019
      year_2 | -6.38e-08 1.67e-09  -38.24  0.000  -6.71e-08  -6.05e-08
      _cons | -257.8195 6.742119  -38.24  0.000  -271.0339  -244.6052
-----

-

```

Sex- and age-specific time trends AD (as any diagnosis) prevalence (% of all admissions) in the inpatient older adult population; NIS, 2002 to 2012

Table 1

	Unwt. N, 60+y, 2002–2012	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Men and women (All ages) P<0.004, ↑*	35,233,659	3.17±0.06	3.38±0.07	3.53±0.06	3.43±0.06	3.51±0.06	3.61±0.06	3.69±0.07	3.56±0.07	3.48±0.07	3.43±0.07	3.12±0.03
Men (all ages) P<0.001, ↑	15,480,940	2.52±0.05	2.67±0.06	2.79±0.06	2.73±0.05	2.79±0.06	2.91±0.06	2.98±0.06	2.88±0.06	2.79±0.06	2.75±0.06	2.51±0.03
60–64, P=0.49	2,661,411	0.28±0.02	0.28±0.02	0.33±0.02	0.31±0.02	0.29±0.02	0.30±0.02	0.32±0.02	0.31±0.02	0.27±0.01	0.29±0.02	0.30±0.01
65–69, P=0.23	2,770,518	0.57±0.02	0.67±0.03	0.70±0.03	0.66±0.03	0.69±0.03	0.75±0.03	0.75±0.03	0.71±0.03	0.71±0.03	0.68±0.03	0.58±0.02
70–74, P=0.002, ↑	2,720,460	1.37±0.04	1.46±0.05	1.55±0.05	1.50±0.05	1.53±0.05	1.68±0.06	1.66±0.05	1.62±0.05	1.58±0.05	1.54±0.05	1.37±0.03
75–79, P<0.001, ↑	2,732,201	2.59±0.06	2.84±0.07	3.03±0.08	2.92±0.07	3.00±0.07	3.20±0.08	3.25±0.08	3.05±0.08	3.05±0.08	3.05±0.08	2.85±0.05
80–84, P<0.001, ↑	2,363,202	4.56±0.09	4.87±0.11	4.99±0.11	4.85±0.10	4.96±0.10	5.26±0.12	5.29±0.12	5.29±0.12	5.16±0.12	4.99±0.11	4.69±0.07
85+, P=0.47	2,223,148	6.72±0.13	6.95±0.13	7.30±0.14	6.89±0.13	7.16±0.14	7.29±0.14	7.58±0.15	7.42±0.16	7.20±0.15	7.02±0.15	6.44±0.08
Women (all ages) P=0.014, ↑	19,752,719	3.67±0.06	3.93±0.08	4.11±0.07	3.97±0.07	4.08±0.07	4.16±0.08	4.25±0.08	4.11±0.08	4.03±0.08	3.99±0.08	3.62±0.04
60–64, P=0.003, ↑	2,668,244	0.29±0.02	0.29±0.01	0.30±0.02	0.31±0.02	0.34±0.02	0.35±0.02	0.34±0.02	0.33±0.02	0.34±0.02	0.33±0.02	0.29±0.01
65–69, P=0.031, ↑	2,878,202	0.64±0.02	0.72±0.03	0.78±0.03	0.73±0.03	0.75±0.03	0.79±0.03	0.77±0.03	0.77±0.03	0.76±0.03	0.73±0.03	0.70±0.02
70–74, P=0.003, ↑	3,034,203	1.58±0.04	1.78±0.05	1.88±0.05	1.68±0.04	1.78±0.05	1.92±0.05	1.90±0.05	1.87±0.05	1.87±0.06	1.76±0.05	1.65±0.03
75–79, P<0.001, ↑	3,372,112	3.29±0.07	3.56±0.08	3.72±0.08	3.49±0.07	3.64±0.08	3.74±0.09	3.76±0.08	3.71±0.08	3.66±0.09	3.70±0.10	3.42±0.05
80–84, P<0.001, ↑	3,390,851	5.53±0.10	5.88±0.12	6.23±0.12	5.95±0.10	6.16±0.11	6.23±0.13	6.40±0.13	6.20±0.13	6.11±0.13	6.13±0.13	5.53±0.07
85+, P<0.001, ↑	4,409,107	7.85±1.38	8.35±1.58	8.80±1.45	8.43±1.38	8.58±0.15	8.88±0.16	9.11±0.18	8.96±0.17	8.75±0.17	8.57±0.18	7.95±0.08

* Linear trends significance was determined using a logistic regression model with outcome being AD status (1=Yes, 0=No) among NIS admissions within age/sex group and the NIS year as the only predictor.

Table 2

Associations of patient and hospital characteristics with Alzheimer's Disease status (1=Yes, 0=No) among the US inpatient older adult population:
Multiple logistic regression models (Unweighted N=2,825,289; Weighted N=14,126,445), NIS 2012

	Unwt. N*	Wt. %±SE* 60+y, 2012	OR**	95% CI	P
Female	3,045,164	55.1±0.1	1.11	(1.08;1.12)	<0.001
Age group	3,045,675				
60–64	503,657	16.4±0.1	1.00		
65–69	531,122	17.3±0.1	2.01	(1.87;2.17)	<0.001
70–74	490,935	16.0±0.0	4.82	(4.50;5.16)	<0.001
74–79	470,935	15.4±0.0	10.09	(9.44;10.78)	<0.001
80–84	452,445	14.9±0.0	16.54	(15.47;17.68)	<0.001
85+	597,194	19.6±0.1	23.24	(21.72;24.86)	<0.001
Race	2,889,484				
1=White	2,232,525	77.3±0.5	1.00		
2=Black	312,331	10.8±0.3	1.47	(1.42;1.53)	<0.001
3=Hispanic	194,468	6.7±0.3	1.42	(1.33;1.51)	<0.001
4=Asian/Pacific Islander	58,023	2.0±0.1	1.08	(0.99;1.17)	0.08
5=Native American	15,399	0.5±0.1	1.08	(0.86;1.35)	0.52
6=Other	76,738	2.7±0.2	1.08	(1.00;1.16)	0.032
Median HH income for zip code of patient	2,985,656				
1 st quartile	873,930	29.3±0.5	1.00		
2 nd quartile	754,442	25.3±0.4	0.92	(0.88;0.95)	<0.001
3 rd quartile	710,554	23.8±0.3	0.96	(0.92;0.99)	0.016
4 th quartile	646,730	21.7±0.5	0.96	(0.92;1.00)	0.07
Insurance status	3,039,449				
Medicare	2,432,075	80.0±0.2	1.00		
Medicaid	100,551	3.3±0.1	0.91	(0.84;0.98)	0.015
Private insurance	409,617	13.5±0.2	0.78	(0.75;0.82)	<0.001
Self-pay	39,753	1.3±0.1	0.56	(0.49;0.64)	<0.001
No charge	3,441	0.1±0.0	0.32	(0.12;0.84)	0.021

	Unwt. N*	Wt. %±SE* 60+yr, 2012	OR**	95% CI	P
Other	54,012	1.8±0.1	0.86	(0.78;0.94)	0.001
Admission day	3,045,672				
Weekday	2,440,195	80.1±0.1	1.00		
Weekend	605,477	19.9±0.1	1.10	(1.08;1.12)	<0.001
Co-morbidity	3,045,675				
Alcohol Abuse		2.6±0.0	0.99	(0.92;1.06)	0.72
Deficiency Anemia		22.0±0.1	0.98	(0.96;1.00)	0.041
Rheumatoid arthritis/collagen vascular disease		3.6±0.0	0.62	(0.58;0.64)	<0.001
Chronic blood loss anemia		1.3±0.0	0.83	(0.78;0.88)	<0.001
Congestive heart failure		13.8±0.1	0.89	(0.87;0.91)	<0.001
Chronic pulmonary disease		23.7±0.1	0.78	(0.77;0.80)	<0.001
Coagulopathy		5.8±0.0	0.83	(0.80;0.86)	<0.001
Depression		11.7±0.1	1.67	(1.63;1.71)	<0.001
Diabetes, uncomplicated		26.3±0.1	0.96	(0.94;0.98)	<0.001
Diabetes, complicated		5.9±0.1	0.82	(0.94;0.98)	<0.001
Drug abuse		1.0±0.0	0.78	(0.67;0.89)	<0.001
Hypertension		69.3±0.1	0.86	(0.85;0.89)	<0.001
Hypothyroidism		16.8±0.1	1.02	(1.00;1.04)	0.027
Liver disease		2.4±0.0	0.63	(0.58;0.68)	<0.001
Lymphoma		1.1±0.0	0.48	(0.44;0.53)	<0.001
Fluid/electrolyte disorders		29.5±0.1	1.25	(1.22;1.27)	<0.001
Metastatic cancer		3.0±0.0	0.33	(0.30;0.35)	<0.001
Obesity		10.8±0.0	0.48	(0.46;0.50)	<0.001
Paralysis		2.9±0.0	0.83	(0.79;0.87)	<0.001
Peripheral vascular disorders		9.6±0.0	0.77	(0.75;0.79)	<0.001
Psychoses		3.7±0.0	2.59	(2.47;2.71)	<0.001
Pulmonary circulation disorders		3.2±0.0	0.71	(0.68;0.74)	<0.001
Renal failure		18.5±0.1	0.81	(0.79;0.82)	<0.001
Non-metastatic cancer		3.0±0.0	0.59	(0.56;0.62)	<0.001
Peptic ulcer		0.04±0.00	0.54	(0.34;0.85)	<0.001
Valvular disease		5.8±0.0	0.79	(0.76;0.81)	<0.001

	Unwt. N [*]	Wt. %±SE ^{**} 60+y, 2012	OR ^{**}	95% CI	P
Weight loss		6.4±0.0	1.26	(1.22;1.30)	<0.001
Bed size	3,045,675				
Small	458,999	15.1±0.3	1.00		
Medium	801,171	26.3±0.4	1.02	(0.96;1.09)	0.51
Large	1,785,505	58.6±0.5	0.94	(0.88;0.99)	0.038
Ownership of hospital	3,045,675				
Government, nonfederal	321,524	10.6±0.3	1.00		
Private, non-profit	2,275,706	74.7±0.4	1.01	(0.96;1.09)	0.72
Private, investor-own	448,445	14.7±0.3	1.10	(1.02;1.19)	0.017
Location/teaching status	3,045,675				
Rural	404,639	13.3±0.3	1.00		
Urban, non-teaching	1,232,393	40.5±0.5	0.88	(0.85;0.93)	<0.001
Urban, teaching	1,408,643	46.3±0.5	0.78	(0.73;0.83)	<0.001
Region of hospital	3,045,675				
Northeast	612,680	20.1±0.4	1.00		
Midwest	715,874	23.5±0.4	1.05	(0.98;1.12)	0.13
South	1,175,080	38.6±0.5	1.10	(1.04;1.17)	0.002
West	542,041	17.8±0.3	0.88	(0.82;0.94)	<0.001

* Sample sizes and % were based on data availability per covariate among older adults 60+y in the NIS 2012.

** Odds ratios (OR) are estimated from a multiple logistic regression model with their 95% confidence interval (CI) and thus are multivariate-adjusted for all covariates included in the model. OR are interpreted as the odds of being AD among the exposed group(s) relative to the odds of being AD among the unexposed group (referent category), controlling for all other covariates in the model.

Table 3

Outcomes of healthcare utilization (MR, LOS and TC) among older adults by Alzheimer's Disease status, patient-level and hospital-level characteristics: multiple logistic and OLS regression models, NIS 2012.

	Model 1: MR			Model 2: LOS (days)			Model 3: TC (\$)		
	OR ^{***}	95% CI	P	β^{***}	(SE)	P	β^{***}	(SE)	P
Alzheimer's Disease status									
Non-AD	1.00			—			—		
AD (any diagnosis)	1.07	(1.03;1.11)	<0.001	+0.80	(0.05)	<0.001	-5,900	(237)	<0.001
Female	0.78	(0.77;0.79)	<0.001	-0.19	(0.01)	<0.001	-4,927	(139)	<0.001
Age									
60–64	1.00			—			—		
65–69	1.39	(1.34;1.44)	<0.001	+0.00	(0.02)	0.89	+719	(263)	0.006
70–74	1.69	(1.62;1.76)	<0.001	+0.05	(0.02)	0.016	-617	(278)	0.027
74–79	2.03	(1.95;2.12)	<0.001	+0.13	(0.02)	<0.001	-2,187	(318)	<0.001
80–84	2.47	(2.37;2.58)	<0.001	+0.20	(0.02)	<0.001	-5,047	(343)	<0.001
85+	3.50	(3.35;3.66)	<0.001	+0.12	(0.03)	<0.001	-10,101	(384)	<0.001
Race									
1=White	1.00			—			—		
2=Black	0.97	(0.94;1.00)	0.06	+0.28	(0.03)	<0.001	-168	(725)	0.82
3=Hispanic	0.91	(0.88;0.95)	<0.001	-0.00	(0.06)	0.98	+4,751	(1,198)	<0.001
4=Asian/Pacific Islander	1.25	(1.18;1.32)	<0.001	+0.48	(0.07)	<0.001	+7,570	(1,986)	<0.001
5=Native American	1.01	(0.90;1.13)	0.68	-0.19	(0.12)	0.11	-9,580	(2,957)	0.002
6=Other	1.02	(0.94;1.11)	0.65	+0.34	(0.07)	<0.001	+5,806	(2,032)	0.004
Median HH income for zip code of patient									
1 st quartile	1.00			—			—		
2 nd quartile	0.96	(0.94;0.98)	<0.001	-0.10	(0.02)	<0.001	+263	(494)	0.59
3 rd quartile	0.94	(0.91;0.96)	<0.001	-0.17	(0.02)	<0.001	+1,401	(605)	0.021
4 th quartile	0.92	(0.89;0.95)	<0.001	-0.15	(0.03)	<0.001	+5,079	(979)	<0.001
Insurance status									
Medicare	1.00			—			—		
Medicaid	1.41	(1.35;1.48)	<0.001	+1.01	(0.07)	<0.001	+759	(614)	0.22

	Model 1: MR			Model 2: LOS (days)			Model 3: TC (\$)		
	OR ^{**}	95% CI	P	β^{**}	(SE)	P	β^{**}	(SE)	P
Private insurance	1.40	(1.32;1.49)	<0.001	-0.11	(0.02)	<0.001	1,679	(410)	<0.001
Self-pay	2.25	(1.97;2.56)	<0.001	+0.44	(0.08)	<0.001	-1,326	(958)	0.17
No charge	0.89	(0.64;1.24)	0.49	+0.15	(0.24)	0.53	-6,513	(2,006)	0.001
Other	2.94	(2.56;3.38)	<0.001	+0.06	(0.05)	0.24	-1,368	(818)	0.09
Admission day									
Weekday	—			—			—		
Weekend	1.23	(1.21;1.25)	<0.001	-0.12	(0.01)	<0.001	-4,387	(135)	<0.001
Co-morbid conditions									
None	1.00			—			—		
1-2	0.82	(0.76;0.88)	<0.001	+0.63	(0.03)	<0.001	+3,583	(257)	<0.001
3-4	1.27	(1.18;1.37)	<0.001	+1.86	(0.04)	<0.001	+10,673	(417)	<0.001
5+	2.23	(2.07;2.40)	<0.001	+3.73	(0.05)	<0.001	+25,530	(711)	<0.001
Bed size									
Small	1.00			—			—		
Medium	1.15	(1.10;1.20)	<0.001	+0.13	(0.05)	0.016	+4,908	(1,007)	<0.001
Large	1.20	(1.15;1.25)	<0.001	+0.59	(0.05)	<0.001	+14,124	(1,060)	<0.001
Ownership of hospital									
Government, nonfederal	1.00			—			—		
Private, non-profit	0.91	(0.86;0.95)	<0.001	-0.51	(0.07)	<0.001	552	(1,880)	0.77
Private, investor-own	0.88	(0.83;0.93)	<0.001	-0.37	(0.08)	<0.001	18,851	(1,958)	<0.001
Location/teaching status									
Rural	1.00			—			—		
Urban, non-teaching	0.94	(0.90;0.98)	0.004	+0.44	(0.04)	<0.001	+13,339	(894)	<0.001
Urban, teaching	1.08	(1.03;1.13)	0.001	+0.98	(0.05)	<0.001	+23,561	(1,218)	<0.001
Region of hospital									
Northeast	1.00			—			—		
Midwest	0.81	(0.77;0.85)	<0.001	-0.76	(0.05)	<0.001	-8,629	(1,519)	<0.001
South	0.95	(0.91;0.99)	0.012	-0.49	(0.05)	<0.001	-5,920	(1,560)	<0.001
West	0.96	(0.91;1.01)	0.08	-0.75	(0.06)	<0.001	+13,974	(2,189)	<0.001
Unwt. N	2,824,677			2,828,130		2,767,007			

Wt. N	Model 1: MR			Model 2: LOS (days)			Model 3: TC (\$)		
	OR**	95% CI	P	β^{***}	(SE)	P	β^{***}	(SE)	P
	14,123,385			14,125,650			13,835,035		

Abbreviations: TC=Total Charges; LOS=Length of stay; MR=mortality Risk.

** Odds ratios (OR) are estimated from a multiple logistic regression model with their 95% confidence interval (CI) and linear regression coefficients (β) are estimated from multiple ordinary least square (OLS) models with their standard errors (SE) and thus are multivariate-adjusted for all covariates included in the model. OR are interpreted as the odds of mortality among the exposed group(s) relative to the odds of mortality among the unexposed group (referent category), controlling for all other covariates in the model. β is the estimated adjusted difference in LOS or TC between referent and exposure category(ies).

Table 4

Trends in co-morbidity among Alzheimer's Disease patients; NIS, 2002 to 2012

	P-trend***	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
%±SE												
Alcohol Abuse	<0.001	0.99±0.05	0.88±0.05	0.90±0.04	0.91±0.04	0.98±0.05	1.07±0.05	1.03±0.05	1.07±0.05	1.14±0.06	1.21±0.05	1.25±0.04
Def. anemia	<0.001	15.5±0.3	16.0±0.3	16.4±0.3	17.0±0.3	18.2±0.3	20.3±0.4	22.1±0.4	23.0±0.4	23.1±0.4	24.5±0.4	23.9±0.2
Rh. Arthritis	<0.001	1.27±0.04	1.25±0.05	1.37±0.05	1.45±0.05	1.50±0.05	1.57±0.05	1.78±0.06	1.95±0.06	2.13±0.08	2.16±0.07	2.24±0.05
Blood loss anemia	<0.001*	1.79±0.06	1.78±0.07	1.90±0.07	1.81±0.06	1.82±0.07	1.77±0.06	1.49±0.05	1.40±0.05	1.29±0.04	1.23±0.04	1.18±0.04
CHF	0.014	13.6±0.2	13.7±0.2	14.5±0.2	14.5±0.2	14.2±0.2	14.2±0.2	13.8±0.2	13.9±0.2	14.1±0.2	14.7±0.2	14.6±0.2
Chronic pulmonary	<0.001	14.9±0.3	15.6±0.3	16.2±0.2	16.6±0.2	17.2±0.2	17.7±0.3	17.5±0.3	17.5±0.2	17.8±0.2	18.1±0.2	18.5±0.2
Coagulopathy	<0.001	1.68±0.06	1.82±0.06	1.89±0.06	2.01±0.06	2.08±0.06	2.45±0.08	2.71±0.08	3.10±0.08	3.81±0.11	4.20±0.11	4.51±0.08
Depression	<0.001	8.3±0.2	9.3±0.2	10.2±0.3	10.7±0.3	11.7±0.3	12.8±0.3	14.0±0.3	14.0±0.3	15.5±0.3	16.6±0.4	16.2±0.2
Diabetes, uncomp.	<0.001	16.2±0.2	17.1±0.2	17.4±0.2	17.7±0.2	19.0±0.2	20.1±0.2	20.7±0.2	21.1±0.2	21.6±0.2	21.9±0.2	22.9±0.2
Diabetes, comp.	<0.001	1.9±0.1	2.0±0.1	2.3±0.1	2.3±0.1	2.6±0.1	2.9±0.1	3.0±0.1	3.1±0.1	3.3±0.1	3.5±0.1	3.7±0.1
Drug abuse	<0.001	0.14±0.02	0.14±0.01	0.14±0.01	0.14±0.01	0.17±0.01	0.20±0.0	0.20±0.02	0.24±0.02	0.25±0.02	0.37±0.04	0.32±0.02
Hypertension	<0.001	44.8±0.3	50.4±0.4	53.3±0.3	55.0±0.3	58.1±0.4	60.5±0.4	62.8±0.4	65.3±0.3	66.4±0.4	67.6±0.3	68.2±0.2
Hypothyroidism	<0.001	12.5±0.2	12.8±0.2	13.6±0.2	14.4±0.2	14.9±0.2	15.9±0.2	17.2±0.2	18.1±0.3	18.8±0.2	20.0±0.3	20.6±0.2
Liver disease	<0.001	0.33±0.02	0.43±0.02	0.44±0.02	0.46±0.02	0.51±0.03	0.54±0.03	0.58±0.03	0.60±0.03	0.65±0.03	0.77±0.04	0.80±0.03
Lymphoma	<0.001	0.45±0.03	0.31±0.02	0.38±0.02	0.38±0.02	0.39±0.02	0.44±0.02	0.42±0.02	0.47±0.02	0.51±0.03	0.48±0.02	0.54±0.02
Fluid/electrolyte	<0.001	26.9±0.3	28.3±0.3	28.4±0.3	30.4±0.3	30.8±0.3	32.3±0.4	32.8±0.4	33.5±0.4	34.4±0.4	36.3±0.4	37.1±0.2
Metastatic cancer	0.08	0.80±0.03	0.72±0.03	0.74±0.03	0.73±0.03	0.75±0.03	0.82±0.03	0.83±0.03	0.77±0.03	0.77±0.03	0.77±0.03	0.83±0.03
Obesity	<0.001	0.66±0.04	0.78±0.04	0.92±0.05	1.00±0.05	1.21±0.06	1.44±0.06	2.02±0.08	2.24±0.08	2.32±0.08	2.75±0.09	3.19±0.07
Paralysis	<0.001	2.75±0.09	1.74±0.07	1.79±0.07	1.67±0.06	1.73±0.07	1.85±0.07	2.03±0.06	2.12±0.06	2.15±0.07	2.29±0.07	2.46±0.06
Peripheral vascular	<0.001	4.56±0.12	4.91±0.15	5.11±0.12	5.11±0.14	5.45±0.14	6.04±0.16	6.46±0.14	6.87±0.15	6.88±0.15	7.72±0.24	7.65±0.13
Psychoses	<0.001	3.74±0.19	4.34±0.26	4.34±0.20	4.44±0.21	5.13±0.23	5.36±0.25	5.53±0.22	6.11±0.28	6.25±0.27	7.04±0.31	7.01±0.16
Pulmonary circ.	<0.001	0.47±0.03	0.42±0.03	0.49±0.03	0.66±0.04	0.78±0.04	1.25±0.05	1.60±0.06	1.88±0.06	1.83±0.06	2.17±0.08	2.31±0.06
Renal failure	<0.001	3.41±0.10	3.46±0.10	3.69±0.10	5.03±0.12	9.04±0.18	11.08±0.22	12.16±0.23	14.28±0.25	15.07±0.28	16.69±0.30	17.10±0.17
Non-metastatic cancer	<0.001*	8.13±0.15	1.63±0.05	1.77±0.05	1.76±0.00	1.75±0.00	1.83±0.01	1.82±0.01	1.79±0.00	1.78±0.00	1.74±0.00	1.78±0.00
Peptic ulcer	<0.001*	1.36±0.05	0.05±0.01	0.05±0.08	0.05±0.0	0.04±0.00	0.04±0.00	0.04±0.00	0.04±0.00	0.04±0.00	0.04±0.00	0.02±0.00
Valvular disease	<0.001	3.79±0.12	3.85±0.12	3.93±0.11	4.44±0.15	4.73±0.13	4.92±0.16	4.82±0.15	5.10±0.15	4.87±0.14	5.58±0.15	5.59±0.09
Weight loss	<0.001	3.85±0.14	4.44±0.17	4.39±0.17	4.50±0.17	4.71±0.17	5.45±0.22	6.75±0.27	7.18±0.24	7.74±0.26	9.06±0.33	8.77±0.16

	P-trend***	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Total co-morbidities, Mean±SE	<0.001	1.95±0.01	1.98±0.01	2.06±0.02	2.15±0.02	2.29±0.02	2.45±0.02	2.56±0.02	2.67±0.02	2.75±0.02	2.89±0.02	2.93±0.01
Unwt. N**	93,356	101,131	111,298	111,298	110,206	112,462	113,097	123,637	111,573	108,429	115,021	94,882

* Descending trend;

**

For sample with complete data on all co-morbidities, 2002–2012;

Linear trend significance was based on a logistic regression model with outcome being the co-morbidity (1=Yes, 0=No) and the predictor variable being the NIS year (continuous). For total co-morbidities, linear trend significance was determined by an ordinary least square model with total number of co-morbidities as the outcome and NIS year as the only predictor.

Table 5

Trends in MR, LOS(days) and TC(\$) among Alzheimer’s Disease patients; NIS, 2002 to 2012

	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	$\beta^*\pm SE$	P-trend
Unwt. N**	98,766	107,335	111,182	108,614	112,369	113,012	123,530	111,536	111,993	114,839	94,860		
Wt. N**	463,207	500,641	521,713	515,356	532,868	542,126	581,222	547,658	528,604	540,627	474,300		
MR, % $\pm SE$	6.07 $\pm$ 0.12	5.72 $\pm$ 0.12	5.23 $\pm$ 0.10	5.02 $\pm$ 0.11	4.96 $\pm$ 0.10	4.60 $\pm$ 0.10	4.78 $\pm$ 0.11	4.52 $\pm$ 0.11	4.25 $\pm$ 0.11	4.31 $\pm$ 0.10	4.41 $\pm$ 0.08	-0.04 $\pm$ 0.00	<0.001
LOS(days), Mean $\pm SE$	6.29 $\pm$ 0.08	6.15 $\pm$ 0.07	6.16 $\pm$ 0.08	5.97 $\pm$ 0.07	5.99 $\pm$ 0.08	6.09 $\pm$ 0.10	5.89 $\pm$ 0.07	5.88 $\pm$ 0.09	5.92 $\pm$ 0.09	5.88 $\pm$ 0.10	5.85 $\pm$ 0.05	-0.04 $\pm$ 0.01	<0.001
TC(\$), Mean $\pm SE$	22,180 $\pm$ 1,120	22,932 $\pm$ 591	24,091 $\pm$ 639	24,875 $\pm$ 682	25,917 $\pm$ 616	27,772 $\pm$ 693	28,236 $\pm$ 688	30,010 $\pm$ 727	31,546 $\pm$ 813	32,203 $\pm$ 768	33,499 $\pm$ 400	+1,171 $\pm$ 81	<0.001

* Liner trend and its significance was determined by a logistic regression model for MR and ordinary least square models for LOS and TC where the only predictor is the NIS year. β =Log(odds ratio) from the logistic regression model in the case of mortality status.

** Sample of older adults with AD having complete data on mortality status. Other sample sizes were comparable per year.

Table 6

Outcomes of healthcare utilization (MR, LOS and TC) among older adults with Alzheimer's Disease, patient-level and hospital-level characteristics: multiple logistic and OLS regression models, NIS 2012.

	Model 1: MR				Model 2: LOS(days)				Model 3: TC (\$)			
	Unwt. N*	Wt. %±SE*	OR**	95% CI	P	β**	(SE)	P	β**	(SE)	P	P
Female	94,879	63.9±0.2	0.81	(0.76;0.87)	<0.001	-0.26	(0.05)	<0.001	-1,818	(297)	<0.001	<0.001
Age												
60–64	1,486	1.6±0.0	1.00			—			—			
65–69	3,423	3.6±0.1	1.20	(0.75;1.92)	0.45	-0.16	(0.33)	0.63	-3,136	(1,675)	0.06	
70–74	7,428	7.8±0.1	1.57	(1.03;2.41)	0.038	-0.49	(0.30)	0.09	-2,959	(1,477)	0.045	
74–79	14,885	15.7±0.1	2.02	(1.33;3.05)	0.001	-0.76	(0.29)	0.009	-5,946	(1,387)	<0.001	
80–84	23,392	24.7±0.1	2.41	(1.60;3.65)	<0.001	-1.04	(0.29)	<0.001	-7,362	(1,395)	<0.001	
85+	44,268	46.7±0.2	3.10	(2.06;4.68)	<0.001	-1.33	(0.29)	<0.001	-9,077	(1,389)	<0.001	
Race												
1=White	69,296	76.5±0.6	1.00			—			—			
2=Black	10,174	11.2±0.3	0.94	(0.85;1.04)	0.24	+0.11	(0.09)	0.19	+1,681	(789)	0.033	
3=Hispanic	6,989	7.7±0.5	0.99	(0.86;1.14)	0.87	-0.07	(0.13)	0.61	+8,710	(1,147)	<0.001	
4=Asian/Pacific Islander	1,637	1.8±0.1	1.22	(1.00;1.50)	0.06	+0.14	(0.29)	0.62	+4,837	(2,166)	0.026	
5=Native American	386	0.4±0.1	1.02	(0.63;1.65)	0.94	-0.63	(0.33)	0.06	-4,144	(2,945)	0.16	
6=Other	2,151	2.4±0.2	1.04	(0.83;1.30)	0.73	+0.44	(0.24)	0.07	+4,078	(1,595)	0.011	
Median HH income for zip code of patient												
1 st quartile	29,151	31.3±0.6	1.00			—			—			
2 nd quartile	22,434	24.1±0.5	0.94	(0.85;1.04)	0.24	-0.09	(0.08)	0.30	+3	(539)	1.00	
3 rd quartile	21,533	23.1±0.4	1.04	(0.94;1.15)	0.39	-0.12	(0.08)	0.14	+511	(627)	0.41	
4 th quartile	19,994	21.5±0.6	1.01	(0.91;1.13)	0.80	-0.13	(0.10)	0.22	+3361	(893)	<0.001	
Insurance status												
Medicare	88,085	93.0±0.2	1.00			—			—			
Medicaid	1,225	1.3±0.1	1.01	(0.70;1.44)	1.00	+1.96	(0.63)	0.002	+1,869	(1,840)	0.31	
Private insurance	4,204	4.4±0.1	2.06	(1.76;2.41)	<0.001	+0.14	(0.17)	0.43	-2,202	(776)	0.005	
Self-pay	287	0.3±0.0	4.19	(2.60;6.76)	<0.001	+2.34	(1.59)	0.14	-4,738	(2,703)	0.08	
No charge	11	0.0±0.0	5.12	(0.58;45.4)	0.14	+3.57	(5.90)	0.55	-9,496	(7,815)	0.22	

	Unwt. N*	Model 1: MR				Model 2: LOS(days)			Model 3: TC (\$)		
		Wt. %±SE*	OR**	95% CI	P	β**	(SE)	P	β**	(SE)	P
Other	854	0.9±0.0	4.42	(3.35;5.82)	<0.001	+0.06	(0.36)	0.86	-8,225	(1,253)	<0.001
Admission day											
Weekday	72,772	76.7±0.2	1.00			—			—		
Weekend	22,110	23.3±0.2	1.13	(1.05;1.22)	<0.001	-0.58	(0.05)	<0.001	-1,170	(289)	<0.001
Co-morbidity	94,882										
Alcohol Abuse	1,191	1.26±0.04	0.84	(0.59;1.20)	0.34	+0.86	(0.24)	<0.001	+2,404	(1376)	0.08
Deficiency Anemia	22,634	23.9±0.2	0.80	(0.73;0.87)	<0.001	+0.64	(0.06)	<0.001	+5,437	(393)	<0.001
Rheumatoid arthritis/collagen vascular disease	2,130	2.24±0.05	0.95	(0.75;1.20)	0.68	-0.27	(0.14)	0.043	-978	(817)	0.23
Chronic blood loss anemia	1,116	1.18±0.04	0.79	(0.58;1.07)	0.13	+0.70	(0.21)	0.001	+9,655	(1,328)	<0.001
Congestive heart failure	13,893	4.51±0.08	1.65	(1.52;1.79)	<0.001	+0.63	(0.07)	<0.001	+4,244	(449)	<0.001
Chronic pulmonary disease	17,554	18.5±0.2	1.18	(1.09;1.27)	<0.001	+0.12	(0.06)	0.032	+3,529	(398)	<0.001
Coagulopathy	4,282	4.5±0.1	1.44	(1.26;1.64)	<0.001	+0.61	(0.09)	<0.001	+11,404	(954)	<0.001
Depression	15,325	16.2±0.2	0.81	(0.74;0.89)	0.51	+0.07	(0.08)	0.39	-1,065	(350)	0.002
Diabetes, uncomplicated	21,700	22.9±0.2	0.99	(0.91;1.07)	0.82	-0.10	(0.05)	0.06	+943	(349)	0.007
Diabetes, complicated	3,467	3.7±0.1	0.94	(0.79;1.13)	0.51	+0.29	(0.17)	0.08	+2,504	(752)	0.001
Drug abuse	303	0.32±0.02	0.11	(0.02;0.78)	0.027	+1.04	(0.45)	0.022	-3,380	(2,023)	0.10
Hypertension	64,698	68.2±0.2	0.75	(0.70;0.80)	<0.001	+0.29	(0.17)	<0.001	+2,465	(278)	<0.001
Hypothyroidism	19,513	20.6±0.2	0.91	(0.84;0.99)	0.026	+0.19	(0.06)	0.002	+395	(312)	0.21
Liver disease	760	0.80±0.03	1.00	(0.68;1.46)	0.98	-0.68	(0.19)	<0.001	+162	(1,512)	0.92
Lymphoma	517	0.54±0.02	1.05	(0.68;1.63)	0.83	-0.11	(0.25)	0.66	+422	(1,792)	0.81
Fluid/electrolyte disorders	35,183	37.1±0.2	1.77	(1.66;1.90)	<0.001	+0.46	(0.06)	<0.001	+5,593	(335)	<0.001
Metastatic cancer	788	0.83±0.03	1.72	(1.29;2.28)	<0.001	+0.78	(0.21)	<0.001	+8,801	(1,716)	<0.001
Obesity	3,030	3.19±0.07	0.69	(0.55;0.87)	<0.001	+0.08	(0.14)	0.56	+4,045	(840)	<0.001
Paralysis	2,335	2.5±0.1	1.30	(1.08;1.58)	0.006	+0.82	(0.15)	<0.001	+8,279	(1,338)	<0.001
Peripheral vascular disorders	7,261	7.7±0.1	1.06	(0.94;1.19)	0.36	+0.12	(0.10)	0.22	+3,788	(547)	<0.001
Psychoses	6,652	7.0±0.2	0.56	(0.47;0.66)	<0.001	+2.05	(0.15)	<0.001	+562	(588)	0.34
Pulmonary circulation disorders	2,191	2.31±0.05	1.30	(1.08;1.57)	0.005	+0.80	(0.14)	<0.001	+10,473	(1,216)	<0.001
Renal failure	16,230	17.1±0.2	1.25	(1.14;1.36)	<0.001	-0.02	(0.07)	0.78	+151	(391)	0.70
Non-metastatic cancer	1,680	1.77±0.04	1.08	(0.85;1.38)	0.51	+0.04	(0.16)	0.81	+1,761	(902)	0.05
Peptic ulcer	21	0.02±0.01	—			+1.23	(1.55)	0.43	-297	(8,188)	0.97

	Model 1: MR				Model 2: LOS(days)			Model 3: TC (\$)			
	Unwt. N**	Wt. %±SE*	OR**	95% CI	P	β**	(SE)	P	β**	(SE)	P
Valvular disease	5,302	5.6±0.1	0.84	(0.73;0.97)	0.017	+0.05	(0.09)	0.59	+2,329	(705)	0.001
Weight loss	8,327	8.8±0.2	1.42	(1.29;1.57)	<0.001	+1.85	(0.10)	<0.001	+11,966	(762)	<0.001
Bed size											
Small	15,891	16.7±0.5	1.00			—			—		
Medium	26,679	28.1±0.6	1.08	(0.97;1.21)	0.18	-0.27	(0.17)	0.13	+3,547	(949)	<0.001
Large	52,312	55.1±0.7	1.09	(0.98;1.21)	0.12	-0.10	(0.16)	0.53	+9,038	(930)	<0.001
Ownership of hospital											
Government, nonfederal	9,727	10.3±0.4	1.00			—			—		
Private, non-profit	68,463	72.2±0.6	0.86	(0.74;0.92)	0.023	-0.74	(0.20)	<0.001	-432	(1,457)	0.77
Private, investor-own	16,692	17.6±0.5	0.73	(0.62;0.85)	<0.001	-0.18	(0.24)	0.45	+13,491	(1,633)	<0.001
Location/teaching status											
Rural	16,108	17.0±0.4	1.00			—			—		
Urban, non-teaching	40,945	43.2±0.6	0.82	(0.74;0.92)	0.001	-0.14	(0.17)	0.41	+8,967	(785)	<0.001
Urban, teaching	37,829	39.8±0.7	0.84	(0.75;0.95)	0.005	+0.08	(0.16)	0.61	+13,020	(1,013)	<0.001
Region of hospital											
Northeast	19,249	20.3±0.6	1.00			—			—		
Midwest	21,767	22.9±0.5	0.79	(0.70;0.92)	<0.001	-0.99	(0.13)	<0.001	-10,856	(1,171)	<0.001
South	39,553	41.7±0.7	0.91	(0.82;1.02)	0.10	-0.97	(0.13)	<0.001	-9,221	(1,244)	<0.001
West	14,313	15.1±0.4	1.02	(0.90;1.16)	0.74	-0.96	(0.17)	<0.001	+7,747	(1,747)	<0.001
Unweighted sample	94,882		88,748			88,771			86,934		
Weighted sample	474,410		443,740		443,855			434,670			

* Sample of older adults with AD in 2012 having complete data on each covariates entered in the model.

** Odds ratios (OR) are estimated from a multiple logistic regression model with their 95% confidence interval (CI) and linear regression coefficients (β) are estimated from multiple ordinary least square (OLS) models with their standard errors (SE) and thus are multivariate-adjusted for all covariates included in the model. OR are interpreted as the odds of mortality among the exposed group(s) relative to the odds of mortality among the unexposed group (referent category), controlling for all other covariates in the model. β is the estimated adjusted difference in LOS or TC between referent and exposure category(ies).