Published in final edited form as:

Am J Geriatr Psychiatry. 2017 October ; 25(10): 1074–1082. doi:10.1016/j.jagp.2017.02.025.

Distress Associated with Dementia-related Psychosis and Agitation in Relation to Healthcare Utilization and Costs

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Abstract

Objectives—Explore the relationship between behavioral and psychological symptoms of dementia (BPSD; specifically delusions, hallucinations, and agitation/aggression) and associated caregiver distress with ED utilization, inpatient hospitalization, and expenditures for direct medical care.

Design/Setting/Participants—Retrospective cross-sectional cohort of participants with dementia (n=332) and informants from the Aging, Demographics, and Memory Study, a nationally-representative survey of US adults >70 years old.

Measurements—BPSD of interest and associated informant distress (trichotomized as none/low/high) were determined by the Neuropsychiatric Inventory (NPI). Outcomes were determined from one year of Medicare claims and examined according to presence of BPSD and associated informant distress, adjusting for participant demographics, dementia severity, and comorbidity.

Results—58 (15%) of participants with dementia had clinically significant delusions, hallucinations, or agitation/aggression. ED visits, inpatient admissions, and costs were not significantly higher among the group with significant BPSD. In fully adjusted models, a high level of informant distress was associated with all outcomes: ED visit incident rate ratio (IRR) 3.03 (95% CI, 1.98–4.63; p<0.001), hospitalization IRR 2.78 (95% CI, 1.73–4.46; p<0.001), and relative cost ratio 2.00 (95% CI, 1.12–3.59; p=0.02).

Conclusions—A high level of informant distress related to participant BPSD, rather than the symptoms themselves, was associated with increased healthcare utilization and costs. Effectively

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Conflicts of Interest: The authors report no competing interests.

Previous presentation: This work previously presented at the 2015 Annual Meeting of the American Association for Geriatric Psychiatry; Washington, DC, March 17–20, 2016.

identifying, educating, and supporting distressed caregivers may help reduce excess healthcare utilization for the growing number of older adults with dementia.

Keywords

dementia; behavioral and psychological symptom; caregiver

OBJECTIVE

Older adults with dementia are at increased risk of hospital admission for reasons that are not clear (1–3). Potential contributing factors that have been largely unaddressed are the behavioral and psychological symptoms of dementia (BPSD [also referred to as neuropsychiatric symptoms]) and associated caregiver distress. These symptoms, such as depression, psychosis, agitation, apathy, and sleep disturbances (4, 5), occur in dementia of all types, are exceedingly common, and often dominate disease presentation (5, 6). Thirty percent of the cost of caring for community-dwelling patients with dementia is directly attributable to BPSD management (7), with just 1 or 2 symptoms associated with double the hours of active caregiver help (8). Such symptoms, as opposed to core cognitive symptoms like declines in memory and executive function, create the most difficulties for caregivers and providers and lead to earlier nursing home placement (9–12).

Despite the large influence of BPSD on clinical presentation and caregiver strain, there has been little investigation specifically focused on the role of these symptoms in healthcare utilization and direct medical costs. Previous analyses have found an association between BPSD and medical costs, although BPSD were simply categorized as “high” (13) or “present” (14) in those studies, and the role of caregiver distress was not considered. In addition, costs were estimated from a caregiver survey and emergency department (ED) utilization was not considered, although ED use is known to be elevated in patients with dementia (3). A recent prospective Scottish cohort study found high overall BPSD to be associated with hospital admission, although overall caregiver distress was not significant; ED utilization was not considered (15).

Intervention studies to prevent hospitalization of older adults with dementia have had minimal impact (16), which may reflect a limited ability to target high-risk patient-caregiver dyads. Given both the wide variety of and pervasiveness of non-cognitive dementia symptoms, a more focused analysis of the role of *specific* BPSD to risk-stratify patient-caregiver dyads with dementia is critical. For example, while apathy is common and can be distressing to caregivers (17), it is not typical clinical experience that this specific symptom prompts ED visits. By comparison, psychotic symptoms or agitation often prompt caregivers to seek medical attention for patients, either to evaluate for an underlying medical cause or because the caregiver feels unable to safely manage the patient in the home. Connecting specific BPSD to utilization is likely key to identifying patient-caregiver dyads in high distress that might benefit most from intervention, which is particularly important as Medicare shifts to population-based and bundled payment strategies (18).

We used the Aging, Demographics, and Memory Study (ADAMS) (19), a sub-study of the Health and Retirement Study (HRS), to test the association of specific BPSD with healthcare

utilization. ADAMS was a survey of US adults over the age of 70 designed to derive nationally-representative estimates of both prevalent and incident dementia, which also included an inventory of BPSD and associated informant distress for all participants. While other BPSD such as irritation and apathy are associated with a high burden of caregiving hours (8) and distress (20), respectively, it is unlikely that informants would interpret these symptoms as the ADAMS participant needing acute medical attention. Based on clinical experience, we hypothesized that, when controlling for informant distress and participant characteristics, symptoms of psychosis (delusions or hallucinations) and agitation or aggression (hereafter referred to as "agitation") would, however, be associated with higher ED and inpatient utilization and overall direct medical costs, as determined from participants' Medicare claims.

METHODS

Data Sources

The ADAMS sample was drawn from the larger Health and Retirement Study (HRS), an ongoing, nationally-representative cohort of individuals >50 years that began in 1992. ADAMS was designed to provide nationally representative data on the antecedents, prevalence, outcomes, and costs of dementia and began with a stratified random subsample of 1,770 individuals selected from HRS respondents >70 years who completed the 2000 or 2002 HRS wave (19). Of those HRS respondents selected for participation, 856 (56% of eligible, living participants) consented to the ADAMS baseline assessment (Wave A) that was conducted from 2001 to 2003. As part of the purpose of ADAMS was to understand incident dementia, three follow-up waves (Waves B–D) were completed at approximately two-year intervals through 2008, with the same information collected as in Wave A. Participants selected for follow-up were generally patients not yet been diagnosed with dementia; once diagnosed with dementia, ADAMS participants *did not* undergo follow-up. The sample for the present analysis was those participants with prevalent or incident dementia who consented to linkage of their study data with Medicare claims (n=332). Data were from the single Wave at which dementia was diagnosed.

Participants completed a 3- to 4-hour assessment by a nurse and neuropsychology technician in their residence. The ADAMS protocol also required the participation of an informant familiar with the participant's daily activities and medical history in order to provide a detailed history and assessment of the participant's current cognition, function, and burden of BPSD (21). The informant was a spouse or a child in most cases and, among those included in this analysis, 40.7% lived with the participant. Each participant completed neuropsychological measures and a neurological examination. The ADAMS multi-specialty consensus panel reviewed all information from the in-person evaluation and relevant medical records.

The institutional review boards at the University of Michigan and Duke University Medical Center approved all study procedures; study participants or surrogates provided informed consent.

Measurements

Dementia Assessment and Diagnosis—Dementia diagnosis was made using criteria from the *Diagnostic and Statistical Manual of Mental Disorders (DSM)-III-R* and *DSM-IV* (22), with severity classified using the Clinical Dementia Rating Scale (CDR) (23). As in prior studies, mild dementia was defined as a CDR stage of 0.5–1.0, moderate as CDR 2.0, and severe as CDR 3.0–5.0 (24, 25). Testing included the Mini-Mental State Examination (MMSE) (26); details of the full neuropsychological battery have been previously described (19).

Demographic and Clinical Characteristics—We included participant age, sex, ethnicity, education, informant relationship, and characteristics of the living situation in our analysis. We calculated the Charlson Comorbidity Index score (27) based on the presence of 18 medical comorbidities (excluding dementia) identified in Medicare claims, and then categorized participants as 0, 1, and >1.

Behavioral and Psychological Symptoms of Dementia—BPSD were assessed using the 10-item Neuropsychiatric Inventory (NPI) (28). Informants were asked whether, in the past month, the participant exhibited symptoms from 10 domains: delusions, hallucinations, agitation/aggression, depression, apathy, elation, anxiety, disinhibition, irritability, and aberrant motor behaviors. If informants answered “yes” to the domain-specific screening item, they were then asked follow-up questions to confirm presence of the symptom. If confirmed, informants were asked to rate frequency on a 4-point scale and severity on a 3-point scale. Each NPI domain then received a score equal to frequency × severity, yielding a domain range of 0–12; a score ≥4 is considered clinically significant (29, 30). After describing each NPI domain over the past month, the informant was asked, “How emotionally distressing do you find this behavior?” on a scale from 0 to 5, yielding a total NPI informant distress score of 0–50 across all 10 domains.

Costs and Utilization—We measured total Medicare expenditures including all claims for inpatient, outpatient, skilled-nursing facility, hospice, home care, and durable medical equipment, adjusted to 2009 U.S. dollars. In addition, we determined the number of emergency department (ED) visits and acute inpatient hospitalizations. Following Unützer et al.’s analysis of depressive symptoms and cost (31), we used 6 months of Medicare claims before and after the ADAMS assessment to measure cost and utilization, as BPSD may fluctuate over time (32) and the ADAMS assessment captures participants at different points in their symptom trajectory. Finally, given the marked increase in healthcare costs at the end of life (33), we censored observation 2 months before death (n=47 deceased participants during 6 months post-interview observation window) to eliminate this large potential source of confounding.

Analyses

Population sample weights were utilized to account for probability of selection into ADAMS and to adjust for differential participation and non-response in ADAMS for each assessment wave (34). Using the longitudinal weight allows the ADAMS sample to be nationally representative of older adults >70 years old with dementia from 2002–2008. We compared

those participants with clinically significant (i.e., domain score ≥4) delusions, hallucinations, and/or agitation to those without such symptoms. This domain score threshold was selected as it has been used in antipsychotic trials as the minimum severity for pharmacological treatment (29). We calculated informant distress *associated with those three BPSD domains* by summing the respective NPI distress scores (range: 0–15 combining the three domains). 231 (74.5%) informants reported no distress; we divided the remainder into two roughly equal groups: low (1–3; n=59 [13.2%]) and high (≥4; n=42 [12.4%]).

We compared groups on demographic and clinical characteristics using t-tests and Chi-square. We adjusted Medicare costs for inflation based on the medical care Consumer Price Index and used 2-sided t-tests to compare annualized and mean log costs (in 2009 US dollars). Costs were modeled using a generalized linear model (GLM) with a gamma distribution and a log link. The gamma distribution (variance proportional to the square of the mean) was selected based on the modified Park test, while the log link provides coefficients interpretable as multiplicative of costs and avoids the need for log-transformation and subsequent retransformation back to dollars (35). The counts of ED visits and inpatient hospitalizations were modeled using negative binomial regression, allowing for overdispersion. For all dependent variables, censoring in the post-interview period was accounted for through the inclusion of an exposure variable. The analyses are weighted to be representative of the reference population, and all confidence intervals and associated significance tests are adjusted to account for the complex sample design (34).

In the regression models, we first tested the association of the presence of any clinically significant BPSD of interest (delusions, hallucinations, and/or agitation) and associated informant distress with utilization and costs. Our second model adjusted for patient demographic characteristics and living situation, and the final model also adjusted for medical comorbidity and dementia severity.

RESULTS

Characteristics of ADAMS participants with dementia are presented in Table 1. 58 participants (15.0%) had significant BPSD (hereafter, “significant BPSD” will refer specifically to presence of clinically significant symptoms in the NPI domains of psychosis [delusions and/or hallucinations] or agitation). Overall, this group had more impaired cognition and more severe dementia than the group without significant BPSD. The group with significant BPSD had a higher total NPI score than participants without significant BPSD in the three domains of interest (25.4 [95% CI, 16.3–34.5] v. 3.8 [95% CI, 3.0–4.6], $p<0.001$), and their informants reported significantly higher overall distress on the NPI (12.5 [95% CI, 7.9–17.2] v. 2.1 [95% CI, 1.7–2.5], $p<0.001$). Among the group with these significant BPSD, 92.6% (n=52) of informants reported at least some associated distress. Among informants of participants without the significant BPSD, or with symptoms that did not meet the clinically significant threshold, 13.4% (n=49) still reported at least some informant distress related to the three domains.

ED visits, inpatient utilization, and Medicare expenditures are presented in Table 2. The annualized total expenditures of participants without significant BPSD were lower ($16,973

[interquartile range $1,764–$21,687]) than among those participants with significant BPSD ($33,571 [interquartile range, $1,626–$44,595]), although this difference was not statistically significant. Log-transformed costs were also not significantly different. ED visits and inpatient admissions were slightly higher among participants with significant BPSD, although this was not statistically significant.

In the final adjusted models (Table 3), the highest level of informant distress (≥4 NPI distress score on the three combined items) was associated with increased ED utilization (incidence rate ratio [IRR] 3.03 (95% CI, 1.98–4.63, p<0.001), hospitalization (IRR 2.78 [95% CI, 1.73–4.46], p<0.001), and expenditures (relative cost ratio 2.00 [95% CI, 1.12–3.59], p=0.02). Relative to no informant distress, a low level of informant distress was also associated with ED visits (IRR 2.31 [95% CI, 1.24–4.31]), though no other outcomes. In contrast to informant distress, the presence of significant BPSD in participants had no association with hospitalization or expenditures but was associated with reduced ED utilization (final model IRR 0.39 [95% CI, 0.25–0.61], p<0.001).

We completed several *post hoc* analyses to further explore our findings, which were not consistent with our original hypothesis that *participant* symptoms would be associated with increased outcomes. First, in our fully adjusted models we tested whether the association of significant symptoms with utilization or cost was moderated by dementia severity. Among those with significant symptoms, increased dementia severity was associated with fewer ED visits than experienced by those with less severe dementia (p=0.024), but this moderating effect was not seen for costs nor inpatient stays. Next, we tested if the association between informant distress and outcomes was moderated by whether the informant lived with the respondent;; this had no effect on the outcomes.

Lastly, to test the robustness of our informant distress findings, we tested the distress variable in 2 additional ways (eTable 1): 1) total NPI distress from all 10 domains (trichotomized, as in the main model, as none, low, and high; and 2) NPI distress on the psychosis and agitation domains as a continuous measure. A high overall level of informant distress on all NPI domains was not associated with increased utilization or cost. Increased informant distress on the domains of interest as a continuous measure was associated with higher rates of all outcomes.

CONCLUSIONS

Using the only nationally-representative sample of patients with dementia in the U.S., which we have linked with Medicare claims, our main finding is that informant distress related to psychosis or agitation in persons with dementia is associated with increased ED utilization, inpatient hospitalization, and Medicare expenditures. Contrary to our hypothesis, the NPS burden among ADAMS participants was not independently associated with utilization or cost in either unadjusted or adjusted models, with one exception: in the fully adjusted model of ED use, the presence of clinically significant symptoms was actually associated with a lower rate of utilization.

While these results are not consistent with our initial hypothesis, the finding that higher informant distress is associated with all three outcomes is important and understandable, since patients with dementia typically receive health care through the efforts of another person. While the burden of NPS to caregivers is driven in part by characteristics of the person with dementia, its magnitude varies related to caregiver characteristics and may not reflect patient symptom severity (36, 37). Since the informant serves as a gatekeeper to healthcare utilization, the threshold for seeking healthcare likely also depends on informant features.

The ED utilization results help illustrate this. When comparing ADAMS participants with and without the BPSD of interest, there was no difference in ED utilization. However, in the first model that only added informant distress, the highest level of distress was associated with double the rate of ED utilization. In other words: without any additional information about *participant characteristics such as age or medical comorbidity that would normally influence ED visits*, a highly distressed informant is associated with ED visits. In contrast, informant distress was not associated with hospitalization or cost until the final models that included all patient characteristics. Since an ED encounter may depend on a caregiver as gatekeeper, such visits are then only limited by the caregiver's threshold for seeking medical attention for the participant. In contrast, hospital admission and medical expenditures require not only the caregiver to seek medical attention, but physicians and other healthcare providers to pursue medical testing and treatment, which should be driven primarily by patient characteristics. Since these outcomes depend on more than just the caregiver, the association with caregiver distress is less apparent until after patient factors such as dementia severity and medical comorbidity are taken into account.

The final model's finding that participant psychosis and agitation were associated with lower ED utilization was unexpected. In our sensitivity analyses, this was limited to those with severe dementia. Perhaps in patients with more advanced disease, the symptoms are not as worrying because of caregivers' experience managing them or patients' limited physical function makes them less threatening.

Putting our findings into context requires a brief return to the Neuropsychiatric Inventory (28). As noted in the Methods, the version used in ADAMS assessed 10 different BPSD domains, yielding a continuous score of 0–120, with informant distress items for each domain yielding a score of 0–50. While each individual domain has a score of 0–12, a threshold of 4 is considered "clinically significant "(29, 30). In Russ et al.'s recent analysis of time-to-hospitalization, they used the total NPI patient and caregiver scores, considering one standard deviation above the mean as "high" and finding that high patient NPI but not caregiver distress was associated with earlier time to hospitalization. While using total NPI as the primary predictor is potentially appealing, given the variety of symptoms captured by the NPI, it is unlikely that additional NPI points for anxiety and apathy, for example, would have the same effect on ED utilization as the same number of points for hallucinations or agitation. And while apathy may be distressing to caregivers, it is unlikely that apathy-related distress would prompt a caregiver to seek emergency medical attention for a person with dementia, in contrast to psychosis-related distress. The two other primary analyses of

the association of BPSD with costs and utilization used a similarly broad conceptualization of BPSD that used all NPI domains and did not include caregiver distress (13, 14).

The primary limitation of our analysis is its cross-sectional nature, which limits us to establishing association rather than suggesting causation. We used 6 months before and after the date of the ADAMS assessment to determine outcomes in order to capture utilization most proximal in time to the NPI scoring. Given that BPSD change significantly over time (32), it would be difficult to assert that outcomes occurring 12 months distant from the ADAMS assessment might be associated with the baseline NPI score, though others have used this approach (13–15). In addition, it is possible that higher utilization in the 6 months before the ADAMS assessment may be stressful for informants and therefore contribute to higher distress reported by informants on the NPI. However, the correlation between individual NPI items and overall caregiver quality of life is limited (38). In addition, after informants scored each separate NPI domain, they were asked about distress *specifically caused by that symptom*. In addition, while the ADAMS informant had to know the respondent well to participate, they may not have been the respondent's primary caregiver. Finally, our analysis is limited to Medicare fee-for-service beneficiaries, whose utilization may differ from those in Medicare Advantage.

Our findings suggest an association between specific BPSD and healthcare utilization that appears to arise through caregiver distress rather than the absolute level of patient symptoms. A recent review of intervention studies to prevent hospitalization among adults with dementia found minimal impact (16), which may reflect the difficulty of identifying the most high-risk population (39). While the expanding population of patients with dementia and the spread of population-based and bundled payment strategies make identifying high-risk patient-caregiver dyads especially important, our findings suggest that identifying this high-risk group based solely on patient characteristics will not be successful. Rather than paying for psychotropic medications that achieve minimal benefit, Medicare should expand investment in programs that teach caregivers strategies to manage challenging behaviors (40, 41). Identifying, educating, and supporting dementia caregivers with high levels of distress might potentially reduce patient costs and utilization, while limiting medication expenditures that also expose patients to potential harms.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Source of Funding: DTM was supported by the Beeson Career Development Award Program (NIA K08AG048321, AFAR, The John A. Hartford Foundation, and The Atlantic Philanthropies). KML was supported by National Institute on Aging (NIA) grant P30 AG024824. The Health and Retirement Study is funded by the NIA (U01 AG009740) and performed at the Institute for Social Research, University of Michigan, Ann Arbor.

References

1. Bynum JP, Rabins PV, Weller W, et al. The relationship between a dementia diagnosis, chronic illness, medicare expenditures, and hospital use. J Am Geriatr Soc. 2004; 52:187–194. [PubMed: 14728626]

2. Phelan EA, Borson S, Grothaus L, et al. Association of incident dementia with hospitalizations. JAMA. 2012; 307:165–172. [PubMed: 22235087]
3. Feng Z, Coots LA, Kaganova Y, et al. Hospital And ED Use Among Medicare Beneficiaries With Dementia Varies By Setting And Proximity To Death. Health Aff (Millwood). 2014; 33:683–690. [PubMed: 24711331]
4. Lawlor B. Managing behavioural and psychological symptoms in dementia. Br J Psychiatry. 2002; 181:463–465. [PubMed: 12456513]
5. Lyketsos CG, Carrillo MC, Ryan JM, et al. Neuropsychiatric symptoms in Alzheimer's disease. Alzheimers Dement. 2011; 7:532–539. [PubMed: 21889116]
6. Geda YE, Roberts RO, Knopman DS, et al. Prevalence of neuropsychiatric symptoms in mild cognitive impairment and normal cognitive aging: population-based study. Arch Gen Psychiatry. 2008; 65:1193–1198. [PubMed: 18838636]
7. Schnaider Beeri M, Werner P, Davidson M, et al. The cost of behavioral and psychological symptoms of dementia (BPSD) in community dwelling Alzheimer's disease patients. Int J Geriatr Psychiatry. 2002; 17:403–408. [PubMed: 11994927]
8. Okura T, Langa KM. Caregiver burden and neuropsychiatric symptoms in older adults with cognitive impairment: the Aging, Demographics, and Memory Study (ADAMS). Alzheimer Dis Assoc Disord. 2011; 25:116–121. [PubMed: 21192239]
9. Kales HC, Chen P, Blow FC, et al. Rates of clinical depression diagnosis, functional impairment, and nursing home placement in coexisting dementia and depression. Am J Geriatr Psychiatry. 2005; 13:441–449. [PubMed: 15956263]
10. Yaffe K, Fox P, Newcomer R, et al. Patient and caregiver characteristics and nursing home placement in patients with dementia. JAMA. 2002; 287:2090–2097. [PubMed: 11966383]
11. Covinsky KE, Newcomer R, Fox P, et al. Patient and caregiver characteristics associated with depression in caregivers of patients with dementia. J Gen Intern Med. 2003; 18:1006–1014. [PubMed: 14687259]
12. Buhr GT, Kuchibhatla M, Clipp EC. Caregivers' reasons for nursing home placement: clues for improving discussions with families prior to the transition. The Gerontologist. 2006; 46:52–61. [PubMed: 16452284]
13. Murman DL, Chen Q, Powell MC, et al. The incremental direct costs associated with behavioral symptoms in AD. Neurology. 2002; 59:1721–1729. [PubMed: 12473759]
14. Herrmann N, Lanctot KL, Sambrook R, et al. The contribution of neuropsychiatric symptoms to the cost of dementia care. Int J Geriatr Psychiatry. 2006; 21:972–976. [PubMed: 16955429]
15. Russ TC, Parra MA, Lim AE, et al. Prediction of general hospital admission in people with dementia: cohort study. Br J Psychiatry. 2015; 206:153–159. [PubMed: 25395686]
16. Phelan EA, Debnam KJ, Anderson LA, et al. A systematic review of intervention studies to prevent hospitalizations of community-dwelling older adults with dementia. Med Care. 2015; 53:207–213. [PubMed: 25588136]
17. Kaufer DI, Cummings JL, Christine D, et al. Assessing the impact of neuropsychiatric symptoms in Alzheimer's disease: the Neuropsychiatric Inventory Caregiver Distress Scale. J Am Geriatr Soc. 1998; 46:210–215. [PubMed: 9475452]
18. Maust DT, Oslin DW, Marcus SC. Mental health care in the accountable care organization. Psychiatr Serv. 2013; 64:908–910. [PubMed: 23771432]
19. Langa KM, Plassman BL, Wallace RB, et al. The Aging, Demographics, and Memory Study: study design and methods. Neuroepidemiology. 2005; 25:181–191. [PubMed: 16103729]
20. Landes AM, Sperry SD, Strauss ME, et al. Apathy in Alzheimer's disease. J Am Geriatr Soc. 2001; 49:1700–1707. [PubMed: 11844006]
21. Plassman BL, Langa KM, McCammon RJ, et al. Incidence of dementia and cognitive impairment, not dementia in the united states. Ann Neurol. 2011; 70:418–426. [PubMed: 21425187]
22. McKhann G, Drachman D, Folstein M, et al. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. Neurology. 1984; 34:939–944. [PubMed: 6610841]
23. Morris JC. The Clinical Dementia Rating (CDR): current version and scoring rules. Neurology. 1993; 43:2412–2414.

24. Okura T, Plassman BL, Steffens DC, et al. Prevalence of Neuropsychiatric Symptoms and Their Association with Functional Limitations in Older Adults in the United States: The Aging, Demographics, and Memory Study. J Am Geriatr Soc. 2010; 58:330–337. [PubMed: 20374406]
25. Lyketsos CG, Steinberg M, Tschanz JT, et al. Mental and behavioral disturbances in dementia: findings from the Cache County Study on Memory in Aging. Am J Psychiatry. 2000; 157:708–714. [PubMed: 10784462]
26. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state" A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975; 12:189–198. [PubMed: 1202204]
27. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987; 40:373–383. [PubMed: 3558716]
28. Cummings JL. The Neuropsychiatric Inventory: assessing psychopathology in dementia patients. Neurology. 1997; 48:S10–16.
29. Schneider LS, Tariot PN, Lyketsos CG, et al. National Institute of Mental Health Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE): Alzheimer disease trial methodology. Am J Geriatr Psychiatry. 2001; 9:346–360. [PubMed: 11739062]
30. Lyketsos CG, Lopez O, Jones B, et al. Prevalence of neuropsychiatric symptoms in dementia and mild cognitive impairment: results from the cardiovascular health study. JAMA. 2002; 288:1475–1483. [PubMed: 12243634]
31. Unutzer J, Patrick DL, Simon G, et al. Depressive symptoms and the cost of health services in HMO patients aged 65 years and older. A 4-year prospective study. JAMA. 1997; 277:1618–1623. [PubMed: 9168292]
32. Ryu SH, Katona C, Rive B, et al. Persistence of and changes in neuropsychiatric symptoms in Alzheimer disease over 6 months: the LASER-AD study. Am J Geriatr Psychiatry. 2005; 13:976–983. [PubMed: 16286441]
33. Lubitz JD, Riley GF. Trends in Medicare payments in the last year of life. N Engl J Med. 1993; 328:1092–1096. [PubMed: 8455667]
34. Heeringa, SG., Fisher, GG., Hurd, MD., et al. Aging, Demographics, and Memory Study (ADAMS). Sample design, weighting, and analysis for ADAMS. 2009. http://hrsonline.isr.umich.edu/sitedocs/userg/ADAMSSampleWeights_Jun2009.pdf. Accessed October 15, 2014
35. Buntin MB, Zaslavsky AM. Too much ado about two-part models and transformation? J Health Econ. 2004; 23:525–542. [PubMed: 15120469]
36. Meiland FJ, Kat MG, van Tilburg W, et al. The emotional impact of psychiatric symptoms in dementia on partner caregivers: do caregiver, patient, and situation characteristics make a difference? Alzheimer Dis Assoc Disord. 2005; 19:195–201. [PubMed: 16327346]
37. Pearlin LI, Mullan JT, Semple SJ, et al. Caregiving and the stress process: an overview of concepts and their measures. Gerontologist. 1990; 30:583–594. [PubMed: 2276631]
38. Shin IS, Carter M, Masterman D, et al. Neuropsychiatric symptoms and quality of life in Alzheimer disease. Am J Geriatr Psychiatry. 2005; 13:469–474. [PubMed: 15956266]
39. Reuben DB. Better care for older people with chronic diseases: an emerging vision. JAMA. 2007; 298:2673–2674. [PubMed: 18073365]
40. Kales HC, Gitlin LN, Lyketsos CG, et al. Management of neuropsychiatric symptoms of dementia in clinical settings: recommendations from a multidisciplinary expert panel. J Am Geriatr Soc. 2014; 62:762–769. [PubMed: 24635665]
41. Callahan CM, Sachs GA, Lamantia MA, et al. Redesigning systems of care for older adults with Alzheimer's disease. Health Aff (Millwood). 2014; 33:626–632. [PubMed: 24711324]

Table 1

Characteristics of ADAMS participants with dementia, without and with significant symptoms of psychosis or agitation

	Significant psychosis or agitation[a]							
	No (n=274)			Yes (n=58)				
Variable	**n**	**%[b]**	**95% CI**	**n**	**%[b]**	**CI**	**F**	**p-value**
Age, mean, y		84.7	83.7–85.7		83.5	81.1–85.8	0.840	0.37
70–79	47	20.3	13.2–29.8	13	27.3	8.1–61.5	0.6486	0.46
80–89	139	60.0	49.6–69.7	35	63.1	32.2–86.1		
≥90	88	19.7	13.7–27.6	10	9.6	4.6–18.9		
Gender								
Female	184	67.5	59.9–74.2	42	77.0	55.4–90.0	1.0051	0.33
Male	90	32.5	25.8–40.1	16	23.1	10.0–44.6		
Ethnicity								
Non-Hispanic white	188	83.6	73.6–90.3	46	91.5	84.2–95.5	2.2833	0.12
Non-Hispanic black	63	10.5	6.0–17.3	10	6.4	2.6–14.7		
Hispanic	23	5.9	2.0–16.2	2	2.2	0.6–8.0		
Years of education								
0–11	170	43.9	34.8–53.4	32	51.0	32.2–69.5	0.3106	0.71
12	55	30.2	20.6–41.8	12	21.9	7.1–50.8		
≥13	49	25.9	15.7–39.7	14	27.1	15.3–43.3		
Living situation								
Community-dwelling	200	78.2	69.6–84.9	37	54.1	27.8–78.4	4.5516	0.04
Nursing home	74	21.8	15.1–30.4	21	45.8	21.6–72.2		
Informant co-residency								
Lives elsewhere	161	55.8	45.1–67.0	35	78.8	65.3–88.1	10.4021	.003
Lives with respondent	113	44.2	33.0–56.0	23	21.2	12.0–34.8		
Informant relationship								
Spouse	51	20.3	13.8–28.8	9	12.0	6.4–21.4	0.4541	0.57
Child	143	53.2	40.3–65.6	28	55.5	30.5–78.1		
Other	80	26.6	16.4–40.0	21	32.5	12.4–62.1		

	Significant psychosis or agitation[a]							
	No (n=274)			Yes (n=58)				
Variable	**n**	**%[b]**	**95% CI**	**n**	**%[b]**	**CI**	**F**	**p-value**
Clinical Dementia Rating (CDR) Scale[c]								
Mild (CDR 0–1)	187	78.8	69.6–85.7	16	36.9	19.5–58.6	8.483	<0.001
Moderate (CDR 2)	41	9.3	5.5–15.2	19	30.4	13.3–55.6		
Severe (CDR 3–5)	45	12.0	7.2–19.3	23	32.6	16.2–54.8		
Mini-Mental State Examination, mean		17.9	16.4–19.3		11.7	7.6–15.8	6.700	0.02
Medical comorbidity (Charlson)								
0	94	34.0	24.4–45.2	18	30.7	15.7–51.1	0.5376	0.53
1	63	22.7	17.3–29.3	17	16.5	8.4–29.7		
≥2	117	43.3	32.4–54.9	23	52.9	30.3–74.4		
NPI[d] total score (range 0–120), mean		3.8	3.0–4.6		25.4	16.3–34.5	23.18	<0.001
NPI informant distress (range 0–50), mean		2.1	1.7–2.5		12.5	7.9–17.2	19.92	<0.001

[a] "Yes" means ADAMS participant had significant BPSD (domain score ≥4) on at least one of the following domains: delusions, hallucinations, agitation/aggression. Participants in the "No" group had no significant BPSD in any of those three domains.

[b] Percentages are weighted percentages derived using the Aging, Demographics, and Memory Study (ADAMS) sample weights to adjust for the complex sampling design.

[c] n=1 respondent from the "No" group missing CDR

[d] NPI: Neuropsychiatric Inventory

Table 2

Emergency department visits, hospitalization, and Medicare costs among ADAMS participants without and with significant symptoms of psychosis or agitation

	Significant psychosis or agitation[a]					
	No (n=274)		Yes (n=58)			
Variable	**Estimate**	**95% CI**	**Estimate**	**95% CI**	**F**	**p-value**
Annualized ED visits, n, mean	1.0	0.7–1.3	1.1	0.4–1.8	0.07	0.79
Annualized inpatient stays, n, mean	0.6	0.3–0.9	0.9	0.2–1.6	0.59	0.45
Annualized total Medicare costs, 2009 $, mean	16,973	10,684–23,262	33,571	0–67,443	0.93	0.34
25th percentile	1,764		1,626			
Median	8,546		15,682			
75th percentile	21,687		44,595			
Annualized total Medicare costs, 2009 log $, mean	8.7	8.3–9.0	9.0	7.7–10.2	0.13	0.72

[a]"Yes" means ADAMS participant had significant BPSD (domain score ≥4) on at least one of the following domains: delusions, hallucinations, agitation/aggression. Participants in the "No" group had no significant BPSD in any of those three domains.

Table 3

The relationship of significant psychosis or agitation and associated informant distress with utilization and Medicare costs among ADAMS participants with dementia

	Model 1 (unadjusted)			Model 2[a]			Model 3[b]		
	Outcome[c]	95% CI	p-value	Outcome[c]	95% CI	p-value	Outcome[c]	95% CI	p-value
Emergency Department visits									
Significant psychosis or agitation[d]									
No (ref.)	1.00	–	–	1.00	–	–	1.00	–	–
Yes	0.56	0.31–1.00	0.05	0.57	0.32–1.02	0.06	0.39	0.25–0.61	<0.001
Associated informant distress[e]									
None (ref.)	1.00	–	–	1.00	–	–	1.00	–	–
Low	1.32	0.64–2.73	0.43	1.68	0.90–3.13	0.10	2.31	1.24–4.31	0.01
High	2.10	1.11–3.95	0.02	2.30	1.24–4.28	0.01	3.03	1.98–4.63	<0.001
Acute inpatient hospitalization									
Significant psychosis or agitation									
No (ref.)	1.00	–	–	1.00	–	–	1.00	–	–
Yes	0.88	0.42–1.86	0.73	1.06	0.55–2.02	0.86	0.63	0.36–1.09	0.09
Associated informant distress									
None (ref.)	1.00	–	–	1.00	–	–	1.00	–	–
Low	0.50	0.26–0.98	0.04	0.54	0.29–1.01	0.05	0.78	0.37–1.62	0.49
High	1.71	0.86–3.41	0.12	1.81	0.98–3.32	0.06	2.78	1.73–4.46	<0.001
Medicare expenditures									
Significant psychosis or agitation									
No (ref.)	1.00	–	–	1.00	–	–	1.00	–	–
Yes	1.23	0.62–2.44	0.54	1.69	0.79–3.58	0.17	0.88	0.43–1.80	0.72
Associated informant distress									
None (ref.)	1.00	–	–	1.00	–	–	1.00	–	–
Low	0.65	0.37–1.16	0.14	0.77	0.52–1.12	0.16	1.17	0.73–1.87	0.51

	Model 1 (unadjusted)			Model 2[a]			Model 3[b]		
	Outcome[c]	95% CI	p-value	Outcome[c]	95% CI	p-value	Outcome[c]	95% CI	p-value
High	1.89	0.74–4.81	0.17	1.43	0.63–3.25	0.38	2.00	1.12–3.59	0.02

[a] adjusted for age, age^2, gender, race/ethnicity, education, nursing home residency, and informant coresidency.

[b] adjusted for Model 2 covariates as well as Charlson comorbidity score and dementia severity.

[c] for emergency department and acute inpatient hospitalization, the outcome is incidence rate ratio; for Medicare expenditures, the outcome is relative cost ratio.

[d] "Yes" means ADAMS participant had significant BPSD (domain score ≥4) on at least one of the following domains: delusions, hallucinations, agitation/aggression. Participants in the "No" group had no significant BPSD in any of those three domains. The models did not otherwise adjust for the severity of BPSD, only whether clinically significant symptoms were present.

[e] Summed Neuropsychiatric Inventory informant distress score for domains of delusions, hallucinations, and agitation/aggression (total range 0–15), trichotomized as: none (score 0, n=231 [74.5%]), low (score 1–3, n=59 [13.2%]), and high (score ≥4, n=42 [12.4%]).