

# The Differential Impact of Unique Behavioral and Psychological Symptoms for the Dementia Caregiver: How and Why Do Patients' Individual Symptom Clusters Impact Caregiver Depressive Symptoms?

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**Objective:** *The behavioral and psychological symptoms associated with dementia (BPSD) are highly burdensome to caregivers. While BPSD consist of a wide variety of patient behaviors including depression, physical aggression, and paranoid delusions, it remains unclear whether specific symptoms have a differential impact on caregivers. The aims of this study were 1) to assess how individual BPSD, categorized based on how they may affect caregivers, impact depressive symptoms for dementia patient caregivers and 2) to test the pathways by which BPSD clusters impact caregiver depressive symptoms.*

**Design:** *Cross-sectional analysis of data from a longitudinal study of patients with Alzheimer disease and dementia with Lewy bodies. Setting:* *Multiple U.S. dementia clinics. Participants:* *One hundred sixty patient–caregiver dyads. Methods:* *Using multivariate generalized estimating equation logistic models, we analyzed the relationship between four BPSD clusters (patient depressive symptoms, accusatory/aggressive behaviors, nontreating psychotic symptoms, and difficult to manage behaviors) and caregiver depressive symptoms and assessed mediators of these relationships. Results:* *Only the presence of patient depressive symptoms was associated with caregiver depression (odds ratio: 1.55; 95% confidence interval: 1.14–2.1). This relationship was mediated by caregiver report of both the symptom's impact on the patient and perceived burden to caregivers. Conclusion:* *Patient depressive symptoms may be the most important driver of the relationship between BPSD and caregiver depression. Research in this field should further test the effects of individual BPSD and also consider how symptoms may negatively impact caregivers by increasing burden and evoking empathy for the patient. (Am J Geriatr Psychiatry 2013; 21:1277–1286)*

**Key Words:** Alzheimer dementia, BPSD, caregiver depression

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Although cognitive decline is considered the clinical hallmark of dementia, an extensive body of literature suggests that noncognitive domains, commonly referred to as the behavioral and psychological symptoms associated with dementia (BPSD), are more burdensome to caregivers and have the greatest impact on decisions to institutionalize patients.<sup>1-3</sup> Although BPSD are composed of wide-ranging symptoms including depression, physical aggression, and paranoid delusions, it remains unclear whether specific individual symptoms, or symptom clusters (one or more symptoms grouped together, e.g., mood symptoms), differentially impact caregivers. The majority of research studies that have concluded that BPSD negatively impact caregivers have solely examined cumulative scores of BPSD.<sup>4-7</sup> By grouping together all BPSD as one construct, it is impossible to determine whether there are individual symptoms/symptom clusters that are most stressful for caregivers, a potential missed opportunity to target interventions to better meet the clinical needs of patients and caregivers.

The limited research that differentiates individual symptoms is largely exploratory and does not simultaneously control for the impact of multiple BPSD.<sup>8-11</sup> Furthermore, when differentiated, BPSD are categorized broadly on the basis of patient's clinical manifestations. While this system of categorization is appropriate for monitoring symptom progression and making appropriate treatment recommendations *for patients*, it fails to conceptualize BPSD from the perspective of their impact on *caregivers*. Different types of symptoms are likely to exert differential impact on caregivers. Aggressive behavior including physical violence cannot be easily dismissed by caregivers and may make the caregiver fearful of the patient and weaken the caregiver's commitment to ongoing at-home care. On the contrary, behaviors that are very difficult to manage, but not directed at the caregiver (e.g., wandering at night), may feel less threatening to the caregiver and result in fewer depressive symptoms. Patient depression has been repeatedly reported as a predictor of caregiver depression<sup>9,12,13</sup> and may be particularly difficult to handle for the caregiver who perceives the patient as suffering. Determining whether individual BPSD differentially impact caregiver outcomes and examining the mechanisms by which individual symptoms impact caregivers can help target intervention and prevention efforts for caregivers.

According to the stress process model,<sup>5,14</sup> caregiving is a chronic stressor that gives rise to strains from multiple domains and ultimately leads to increased risk for psychiatric distress and diagnosable disorder. The model differentiates between objective stressors (the occurrence of care demands or symptoms related to disease severity of the patient), the caregiver's subjective experience of those stressors, and background and contextual factors that impact the stressor and caregiver outcomes. Using this model, studies report that the association between objective stressors such as BPSD and mental and physical health outcomes of caregivers is mediated by subjective stress appraisal.<sup>15-17</sup> Suffering may be another pathway by which BPSD result into depression in caregivers,<sup>18</sup> suggesting that perception of the patient's quality of life and his or her ability to function daily may affect the caregiver by evoking empathy for the patient.

The aims of this study were to assess how distinct BPSD, or clusters, impact depressive symptoms for caregivers of patients with dementia. We examined the relationship between caregiver depressive symptoms and four symptom clusters of patients with dementia: accusatory and aggressive symptoms, depressive symptoms, nonthreatening psychotic behaviors, and difficult to manage behaviors. We hypothesized that while each behavior cluster negatively impacts caregivers, accusatory and aggressive behaviors would have a stronger relationship with caregiver depressive symptoms than with other BPSD clusters. In addition, we hypothesized that the relationship between BPSD and caregiver depressive symptoms was mediated by both caregiver perceived burden of behavior and perceived impact of behavior on patient functioning.

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## METHODS

### Sample

In the Predictors 2 Study, a cohort of patients with probable Alzheimer disease (AD) and dementia with Lewy bodies was followed prospectively from early stages of patient illness. Patients were recruited from memory disorder centers or private physician offices in three sites between 1997 and 2008: Columbia

University College of Physicians and Surgeons; Johns Hopkins University School of Medicine; and Massachusetts General Hospital. The inclusion and exclusion criteria and evaluation procedures of the Predictors Study have been fully described elsewhere.<sup>19</sup> Briefly, following an initial evaluation, all patients' conditions were diagnosed in a consensus conference by at least two faculty physicians specializing in dementia (neurologist or psychiatrist) including the patients' treating physician and one faculty neuropsychologist. All AD patients met National Institute of Neurological and Communicative Disorders and Stroke—AD and Related Disorders Association criteria for probable AD.<sup>20</sup> At entry into study, each AD participant was required to have relatively mild dementia operationalized as a modified Mini-Mental State Examination (MMSE)<sup>21</sup> score  $\geq 30$ , equivalent to a score of 16 or more on the standard Folstein MMSE.<sup>22</sup> Patients' dementia with Lewy bodies was diagnosed according to the 1996 consensus guidelines for the disease.<sup>23</sup> Participants were also required to have at least one family member/informant available. Exclusion criteria were parkinsonism, stroke, alcoholism, schizophrenia, schizoaffective disorder, and electroconvulsive treatments.

During an initial visit, the following data were collected about the patient via clinical assessment: patient and caregiver demographic data, medical history, neurologic evaluation, presenting features of cognitive impairment, functional status, family history of dementia, onset date and features, and psychiatric history. Follow-up data were collected at 6-month intervals via in-person visit, thereafter until dropout or death including: neurologic evaluation, functional and cognitive status, medical and psychiatric history, and quality of life. If patients were unable to travel to the outpatient clinic for evaluation, they were visited at their homes, nursing homes, or healthcare facilities. There is 94% follow-up of patients.

The Predictors Caregiver Study was initiated 6 years after the launch of the Predictors 2 study cohort. A total of 169 patients were active in the Predictors Study at the time of, or subsequent to, the launching of the Predictors Caregiver Study. Of these patients, six did not have an eligible informal caregiver to complete the study (3.6%). Three did not have caregiver data available for at least one assessment. Detailed data on the mental health status of the informal caregivers of

the patient cohort were collected for 160 patient–caregiver dyads. On average, each dyad completed 4.2 assessments (range: 1–12).

## Measures

*Outcome measure.* Caregiver depressive symptomatology was measured by the six-item depression subsection of the Brief Symptom Inventory.<sup>24</sup> Caregivers were asked how much during the past week they were bothered by the following: feeling lonely, feeling blue, feeling no interest in things, feeling hopeless about the future, feelings of worthlessness, and thoughts of ending your life using a 5-point Likert scale response for each item ranging from “not at all” to “extremely.” A higher score indicates higher depressive symptoms. The mean score across six symptoms was 1.44 (SD: 0.56). The standardized Chronbach coefficient  $\alpha$  was more than 0.80, indicating acceptable reliability.<sup>25</sup> Mean Brief Symptom Inventory score was dichotomized as no depressive symptoms ( $< 2$ ) and depressive symptoms ( $\geq 2$ ). Caregivers categorized as having depressive symptoms were 1) 1 SD above the mean depressive symptom score and 2) indicated that on average each of the six symptoms bothered or impacted them from a minimal to extreme level.

*Exposure measures.* The Columbia University Scale for Psychopathology in Alzheimer's Disease (CUSPAD)<sup>26</sup> was used to measure patient BPSD at baseline and at subsequent 6-month intervals. The CUSPAD is a semistructured rating scale administered to the informant regarding the presence of 26 patient symptoms during the last month before each interview. Interrater reliabilities for individual symptoms range from  $\kappa$  coefficients of 0.61–0.73.<sup>26</sup> Existing clinical grouping of symptom clusters in the CUSPAD were not maintained. Instead, we created four nonoverlapping symptom clusters on the basis of our hypotheses that certain individual patient symptoms or symptom clusters may have greater negative mental health consequences for the caregiver than for others. For example, delusions of abandonment may be particularly disturbing to caregivers who are being accused of not helping the patient despite all their efforts, whereas other psychotic behaviors that do not involve the caregiver (e.g., auditory hallucinations) may be less threatening

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to the caregiver, therefore resulting in less negative consequences for the caregiver.

Dichotomous variables were created to characterize the presence or absence of each of the following clusters:

- 1) *Accusatory and aggressive symptoms* were measured on the basis of six CUSPAD items designed to assess paranoid and abandonment delusions as well as aggression: for example, beliefs that people are stealing things, engaging in threatening behavior.
- 2) *Nonthreatening psychotic symptoms* consisted of 13 items that constitute the remainder of the psychotic symptoms (hallucinations, illusions, misidentification delusions, and somatic delusions) measured in the CUSPAD: for example, belief that people are in the house when nobody is there, belief that someone else is in the mirror. These items are categorized as nonthreatening because, while they are by definition psychotic and likely disturbing to the caregiver because they are nonnormative, they are not directly threatening the caregiver.
- 3) *Depressive symptoms*: Patient depressive symptoms were defined as having 1) depressed mood and 2) either any difficulty sleeping or change in appetite.
- 4) *Difficult to manage behaviors*: Difficult to manage behaviors were defined as having one or more of the following four behaviors: wandering away from home or from the caregiver, showing agitation or restlessness, making verbal outbursts, and sundowning.

*Potential confounding variables.* We examined a variety of 1) non-BPSD objective stressors and 2) background and contextual variables as potential confounding variables.

*Objective stressors.* Patient cognitive status was assessed at each visit using the MMSE,<sup>22</sup> in which higher MMSE score indicates better cognitive status. Patient functional status was assessed at each visit using Parts I and II of the Blessed Dementia Rating Scale.<sup>27</sup> Patients' medical histories were used to construct a modified version of the Charlson Index of Comorbidity.<sup>28</sup> A modified Unified Parkinson's Disease Rating Scale<sup>29</sup> was administered at each visit to measure the presence or absence of extrapyramidal signs (e.g., tremors, rigidity).

*Background and contextual factors.* Patient age, ethnicity, sex, and highest level of education were

recorded at the baseline visit; marital status was recorded at each visit. Whether or not the patient had a home health aide was recorded annually. Duration of illness in years was estimated by a neurologist during baseline interviews with the patient and the caregiver. Caregiver age, sex, ethnicity, highest level of education, and relationship to the patient were recorded at the start of the Predictors Caregiver Study. Whether the caregiver lived with the patient, frequency of contact with the patient, and length of time the caregiver had known the patient were recorded at each visit. Whether the caregiver assists with basic and instrumental activities of daily living, the amount of hours the patient spends per day with the caregiver, whether a paid attendant assisted with care, and caregiver's employment status were reported annually.

*Mediator variables.* Symptom-specific perceived burden to the caregiver (i.e., subjective stress) was measured by asking the caregiver the following after the presence of a symptom/cluster of behaviors was reported: "How difficult or disturbing do *you* find these behaviors to manage or deal with?" Response options were dichotomized as not difficult and difficult to easily conceptualize these variables in our models. Similar single-item measures of burden have been validated for screening burden.<sup>30</sup> Patient impact was measured on the basis of caregiver response to the following question: "To what extent would you say these behaviors have affected *the patient's* daily activities and functioning?" Response options were dichotomized as "no effect" and "affected patient."

### **Analysis**

We examined the concurrent association between patient BPSD and caregiver depressive symptoms at any given time point for all patient-caregiver dyads. To account for repeated observations within dyads, we used a generalized estimating equation (GEE) extension of logistic regression using an exchangeable correlation structure with a robust standard error estimator. We conducted unadjusted analyses to examine the association between each symptom cluster and caregiver depression and multivariate models that simultaneously tested each symptom cluster while controlling for confounders. To determine which variables would be included in the final model, bivariate associations between 1) caregiver

depressive symptoms and potential confounders and 2) individual BPSD and potential confounders were assessed. Variables that showed a statistically significant effect on the outcome at the 0.10 level, were associated with at least one symptom cluster, and were not highly correlated with other variables (correlation >0.5) in the bivariate analysis were included in the final model. Subsequent models were tested to control for the impact of patient antidepressant and neuroleptic use on the BPSD–caregiver depression relationship.

Mediational analyses were restricted to symptom clusters that had significant impact on the main exposure outcome. We used techniques outlined by Baron and Kenny<sup>31</sup> to formally test for mediation. First, we examined the unadjusted relationship between two mediator variables (patient impact and burden to caregiver) and caregiver depression, using logistic regression GEE models. Next, we determined the unadjusted relationship between BPSD clusters and each mediator using  $\chi^2$  analysis. Finally, we considered the effect of each mediator on the relationship between individual symptom clusters and caregiver depression in full GEE logistic models. Beta estimates derived from logistic models for the role of symptom clusters in individual adjusted models that controlled for mediation were compared with models that did not control for the effect of a mediator. All analyses were completed using SAS version 9.2.

## RESULTS

Baseline descriptive and clinical characteristics of the study sample are depicted in Table 1. Mean patient age was 75.4 years, slightly more than half were women, and most were white. The vast majority (92%) had at least a high school education, and almost two thirds were married. Most patients had AD (86.3%). Consistent with study enrollment criteria, patients were at early stages of illness with relatively mild cognitive impairment. Average dependence score was 5.0 and functional status score was 3.7, indicating a mild level of dependence and high physical function. Accordingly, very few patients lived in a nursing home (3.8%) and only 12% required any home healthcare assistance.

Caregiver characteristics at the time of first caregiver assessment are summarized in Table 2.

Caregivers were on average 65 years old, women (76%), predominantly white, highly educated, and just less than half worked outside of the home. More than half of caregivers (55%) were spouses of patients and 36.3% were children of patients. The vast majority (89%) lived with the patient and reported being very involved with patient activities.

As summarized in Table 3, BPSD of any kind were common at baseline (57.96%) and were almost universally reported by the end of the study period (up to 12 years of follow-up). Each of the four symptom clusters was common at study baseline, with depression least common (17.95%) and difficult behaviors the most frequently reported (41.94%).

We examined the association of each of the four symptom clusters with 1) caregiver depression unadjusted, 2) after simultaneously adjusting for all

**TABLE 1. Patient Characteristics at Baseline (N = 160)**

Characteristic	
Age, mean $\pm$ SD, years	75.4 $\pm$ 7.4
Sex (female)	54.4
Ethnicity	
White	90
Other	10
Years of schooling, mean $\pm$ SD	14.7 $\pm$ 3.1
Less than high school	8.1
High school	26.3
More than high school	65.6
Marital status	
Married	63.1
Widowed	28.1
Other	8.8
Living status	
Home	89.4
Retirement home	6.9
Nursing home	3.8
Site	
Columbia University	44.4
Johns Hopkins	29.4
Mass General	26.3
Diagnosis	
Alzheimer disease	86.3
Dementia with Lewy bodies	13.7
Neurologist estimation of duration of illness, mean $\pm$ SD (range: 1–18), years	4.8 $\pm$ 2.5
Mini-Mental State Examination score, mean $\pm$ SD (range: 9–30)	22.7 $\pm$ 3.7
Blessed Functional Activity Scale score, mean $\pm$ SD (range: 0–13)	3.7 $\pm$ 2.3
Total dependence, mean $\pm$ SD (range: 0–12)	5.0 $\pm$ 2.4
Home health aide in last 3 months, yes	11.9
Modified Comorbidity Index	
0	51.6
$\geq$ 1	48.4
Extrapyramidal signs, yes	17.2

Notes: Values given are percentages unless reported otherwise.

**TABLE 2. Caregiver Characteristics at Initial Caregiver Assessment (N = 160)**

Characteristic	
Age, mean ± SD, years	65.3 ± 14.4
Sex (female)	76
Ethnicity	
White	91
Other	9
Years of schooling, mean ± SD	15.8 ± 3.3
Less than high school	5.0
High school	18.4
More than high school	76.6
Work at least part-time for pay, yes	44.7
Relationship to patient	
Spouse	55
Child	36.3
Other relative/friend	8.7
Years caregiver has known patient, mean ± SD (range: 10–91)	49.6 ± 12.9
Lives with patient, yes	89.4
Time spent daily with patient	
None	2
Up to 3 hours	29.4
3–5 hours	11.8
6–9 hours	9.8
9–12 hours	8.5
>12 hours	38.6
Assists patient with ADL, yes	44.9
Time spent daily assisting with IADL	
None	18.9
Up to 3 hours	52
3–5 hours	20.3
6–9 hours	4.1
9–12 hours	1.4
>12 hours	3.4

Notes: Values given are percentages unless reported otherwise. ADL: activities of daily living and include bathing, eating, etc; IADL: instrumental activities of daily living and include shopping, housekeeping, etc.

other symptom clusters, and 3) after simultaneously controlling for all relevant confounders and symptom clusters (Table 4). In our final model, each cluster had a positive, yet weak, association with caregiver depression, with patient depressive symptoms showing the strongest effect (odds ratio: 1.55, z: 2.78,  $p < 0.01$ ). Only patient depressive symptoms had a statistically significant impact on the likelihood of caregiver depression. We also controlled for patient antidepressant and neuroleptic use and found that the effect of patient depressive symptoms on caregiver depression was of highest magnitude and statistically significant (odds ratio: 1.76; 95% confidence interval: 1.26–2.45;  $p < 0.05$ ).

To explicitly test whether the effects of patient depression symptoms were significantly different from the effects of other BPSD clusters on caregiver

**TABLE 3. Proportion of Patients Experiencing Symptom Clusters (N = 160)**

	Prevalence of Patient Symptoms at Baseline	Study Period Prevalence (0–12 years)
Patient depressive symptoms	17.95	43.13
Patient accusatory/aggressive	22.58	47.50
Patient nonthreatening psychotic behavior	24.84	61.88
Patient difficult behaviors	41.94	85.00
Any symptom cluster	57.96	93.13

Notes: Values given are percentages.

depression, we compared logistic regression models in which the parameter estimates for patient depression and each of the other symptom clusters are forced to be equal with a model where patient depression is allowed to differ. Using methods described by Rindskopf,<sup>32</sup> we found that the two models were significantly different ( $p < 0.05$ ) by comparing differences in the likelihood ratio  $\chi^2$  statistics for the restricted and unrestricted models.

Because the magnitude of effects among symptom clusters was all positive and in relatively close range, we further examined these relationships in subsequent models. First, we treated the outcome variable, depressive symptoms, as a continuous outcome using GEE Poisson regression analysis (data not shown) and replicated our findings using continuous measures of each BPSD cluster, for example, the more nonthreatening psychotic symptoms the patient exhibited, the higher the BPSD score (data not shown). Our findings continued to suggest that patient depression has the largest effect and remained the only statistically significant ( $p < 0.05$ ) predictor of caregiver depression.

Both the mediators tested, patient impact and perceived burden to caregiver, were significantly associated with caregiver depressive symptoms. In separate multivariate models, each mediator reduced the effect estimate of patient depressive symptoms on caregiver depressive symptoms (Table 5). These results remained unchanged when mediator variables were treated as continuous (data not shown).

## DISCUSSION

In this study, we examined the association of caregiver depression with a wealth of clinical

variables, using validated clinician-administered scales for a range of dimensions including extrapyramidal signs, cognitive status, functional status, and the presence of other medical comorbidities. The only clinical features of dementia that were consistently associated with caregiver depressive symptoms were functional status and one component of BPSD, the presence of patient depressive symptoms.

While we hypothesized that accusatory and aggressive symptoms would result in the most depressive symptoms for caregivers, we consistently found that patient depressive symptoms had a greater magnitude of effect on caregiver depression while remaining statistically significant. Our findings are supported in the literature,<sup>9,12,13</sup> although existing studies do not simultaneously control for the impact of other possible BPSD and important confounders. The potential for a negative effect of depression above and beyond other BPSD on caregivers is especially important, given that depression is highly prevalent among patients with AD, with estimates ranging up to 40%.<sup>33,34</sup> While pharmacologic treatment efforts for depression in dementia are common,

their efficacy is not proven<sup>35</sup> and usage remains complicated due to polypharmacy and difficulty assessing symptom change in patients due to cognitive impairment.<sup>36</sup> Developing and testing more effective strategies for treating depression in patients with dementia may improve outcomes for the patient and the caregiver.

Depression may be especially challenging for caregivers to handle not only because of the difficulty it causes caregivers in dealing with the patients but also because of the negative impact it has on the patient's quality of life.<sup>37,38</sup> In our examination of mediators of the patient depression-caregiver depression relationship, both impact on patient's functioning and burden to caregiver were important. While caregiver burden has been previously shown to mediate the relationship between patient objective behavior and caregiver outcomes,<sup>15,17,39</sup> the role of impact on patient functioning in the causal pathway has not been previously explored. Our findings suggest that caregivers recognize the difficulty that patients face due to depressive symptoms and that this mechanism may independently result in

**TABLE 4. Associations Between Symptom Clusters and Caregiver Depression (N = 160)**

	Model 1 <sup>a</sup>			Model 2 <sup>b</sup>			Model 3 <sup>c</sup>		
	OR	95% CI	z Test (p)	OR	95% CI	z Test (p)	OR	95% CI	z Test (p)
Depressive symptoms	1.77	1.28–2.44	3.47 (<0.01)	1.58	1.15–2.17	2.84 (<0.01)	1.55	1.14–2.11	2.78 (<0.01)
Accusatory/aggressive behavior	1.42	0.99–2.01	1.95 (0.05)	1.15	0.79–1.68	0.73 (0.47)	1.17	0.82–1.69	0.87 (0.38)
Nonthreatening psychotic behavior	1.76	1.22–2.53	3.05 (<0.01)	1.59	1.07–2.37	2.28 (0.02)	1.39	0.93–2.08	1.62 (0.10)
Difficult behaviors	1.28	0.85–1.94	1.18 (0.24)	1.10	0.72–1.70	0.44 (0.66)	1.03	0.67–1.58	0.12 (0.90)

Notes: Includes multiple assessments (mean: 4.2) per 160 patient-caregiver dyads. CI: confidence interval; OR: odds ratio.

<sup>a</sup>Unadjusted.

<sup>b</sup>Adjusted for other patient symptom clusters.

<sup>c</sup>Simultaneously adjusted for other patient symptom clusters, patient functional status, whether caregiver is the spouse.

**TABLE 5. The Mediating Effect of Patient Impact and Perceived Caregiver Burden on the Association Between Patient Depressive Symptoms and Caregiver Depression (N = 160)**

	Model 1			Model 2			Model 3		
	OR	95% CI	z Test (p)	OR	95% CI	z Test (p)	OR	95% CI	z Test (p)
Depressive symptoms	1.56	1.14–2.13	2.79 (<0.01)	1.09	0.71–1.69	1.89 (0.06)	1.04	0.67–1.63	1.42 (0.16)
Spousal relationship	2.22	1.24–3.97	2.68 (<0.01)	2.22	1.27–3.90	2.69 (<0.01)	2.18	1.22–3.90	2.62 (<0.01)
Patient functional status	1.07	1.01–1.12	2.41 (0.02)	1.06	1.01–1.11	2.28 (0.02)	1.06	1.02–1.12	2.53 (0.01)
Accusatory/aggressive behavior	1.18	0.83–1.68	0.92 (0.36)	1.14	0.81–1.60	0.70 (0.49)	1.09	0.76–1.57	.40 (0.69)
Nonthreatening psychotic behavior	1.40	0.94–2.07	1.66 (0.10)	1.46	0.98–2.17	1.67 (0.10)	1.37	0.92–2.05	1.56 (0.12)
Mediator 1: patient impact	–	–	–	2.05	1.24–3.39	4.21 (<0.01)	–	–	–
Mediator 2: perceived caregiver burden	–	–	–	–	–	–	2.12	1.22–3.67	4.55 (<0.01)

Notes: Includes multiple assessments (mean: 4.2) per 160 patient-caregiver dyads. CI: confidence interval; OR: odds ratio.

caregiver depression. New approaches are likely required for caregiver interventions that minimize impact of symptoms for the patient, thus helping the caregiver to cope with the effects of the symptoms and suffering experience of the patient.

Our lack of strong positive findings surrounding the association between accusatory and aggressive symptoms and caregiver depressive symptoms was unexpected. We hypothesized that these symptoms would be most challenging because they represent aberrant behavior (because of their psychotic nature) and are difficult to ignore because they are largely directed at the caregiver (e.g., accusations of infidelity). While caregiver depressive symptoms may not be associated with such symptoms, other outcomes such as caregiver burden or desire for institutionalization may be associated with these types of symptoms, and these relationships should be explored further. Future research should continue to examine which elements of psychotic symptoms are most disturbing to caregivers, especially given the trend for these symptom clusters to be associated with caregiver depression in this study.

Furthermore, as etiology of dementia may influence the way that caregivers experience BPSD, we recommend that future studies with larger samples should explore the role of dementia subtype diagnosis when examining BPSD–caregiver depression relationships.

This study does have several limitations. While we had sufficient power to detect meaningful effect estimates between BPSD and caregiver depression, we may not have had sufficient power to detect more subtle differences after controlling for the effects of other symptoms. Furthermore, as in almost all studies of BPSD, this study relies on caregiver report of BPSD, which may itself be affected by the caregiver's mental health status. Given the cross-sectional nature of these analyses, we cannot rule out the possibility that caregiver depression itself impacted report of patient depressive symptoms. While the caregiving component of the Predictors 2 Study was initiated when patients were at various stages of illness, we were able to test the effects of length of time with illness and cognitive status that had no effect on caregiver depression outcomes.

Depression is difficult to recognize in patients with dementia due to the overlapping nature of depressive symptoms with dementia and the inherent nature of

cognitive impairment. Caregiver reports of patients' depression, which was relied upon in this study, is known to be underreported by caregivers regardless of their depression status.<sup>40</sup> Nondifferential underreporting of depression by all caregivers suggests that the true association between patient depression and caregiver depression may be even stronger than we have concluded. In addition, while the study used validated measures for caregiver and patient depressive symptoms, this study did not incorporate measures of depressive disorder, which may be of greater concern to clinicians. Furthermore, while we examined the effects of severity of patient BPSD on caregiver outcomes in post hoc analyses by examining frequency of total symptoms exhibited, we were unable to examine the impact of individual symptom frequency or severity based on symptom type and persistence. Future research should ascertain whether severity and frequency of BPSD, in particular, patient depression, impact caregiver outcomes while examining other BPSD.

We also relied on unvalidated single-item measures of caregiver symptom–specific burden and patient impact. The development of more extensive scales to measure patient impact is important, given that no other assessments exist for this measure. Finally, this clinical sample of predominantly white patients with dementia may not be generalizable.

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## CONCLUSION

BPSD clusters may not impact caregivers uniformly. Patient depressive symptoms may have the most consistent negative impact on caregivers and may be driving research findings that suggest that BPSD impact caregiver depression. Given the high prevalence of BPSD among patients with dementia, it may be more useful to consider the effect of specific symptoms on caregivers rather than focusing on the cumulative effect of a wide range of behaviors. For example, effective behavioral therapies have been developed to specifically control depressive symptoms in patients with dementia.<sup>41</sup> Many such psychosocial interventions involve caregivers to directly alleviate symptoms for patients while helping caregivers deal with management of the symptoms (e.g., via support groups).<sup>42,43</sup>



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