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Teaching Caregivers of Persons with Dementia To Address Pain

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Abstract

Objectives—To compare the efficacy of Preventing Aggression in Veterans with Dementia (PAVeD) with that of usual care in decreasing incidence of aggression (primary outcome) and pain and improving depression, pleasant events, caregiver burden and patient-caregiver relationship quality (secondary outcomes).

Design—Randomized controlled trial with assessments at baseline and 3, 6, 9 and 12 months

Setting—Houston, TX

Participants—203 community-dwelling veterans with pain and dementia and their caregivers

Intervention—PAVeD, 6 to 8 weekly sessions of 45-minute home visits with masters-level clinicians providing instruction to caregivers on recognizing pain, enhancing communication, making daily activities pleasant and enjoyable and at least 2 elective sessions.

Measurements—Cohen-Mansfield Agitation Inventory (primary outcome), Philadelphia Geriatric Pain Intensity Scale, Geriatric Depression Scale, Pleasant Events Schedule-AD, Burden Interview, Mutuality Scale (secondary outcomes), client Satisfaction Questionnaire

Results—There were no significant differences in aggression incidence between intervention and control groups; however, the PAVEd group had significantly better mutuality than controls.

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Conclusions—PAVeD may need to address a broader range and more in-depth coverage of aggression risk factors with person-centered tailoring to target certain types of distress. Interventions to prevent aggression may also need to address medical providers in addition to caregivers.

Keywords

pain; aggression; dementia; veterans; caregiving

Introduction

In the community setting, up to 50% of persons with dementia (PWD) develop aggression (1,2), lifetime risk of behavioral disturbances secondary to dementia is nearly 100% (1), and aggressive behavior doubles risk for earlier admission into an institution (3). Both PWD with aggression and their caregivers also have lower quality of life and are more likely to become depressed than PWD without aggression (4,5).

Although there is no current mainstay treatment for aggression in dementia, atypical antipsychotics are often used. Approximately 33% of nursing-home Medicare Part D enrollees with dementia are prescribed an antipsychotic (6), and 12% of all atypical antipsychotic use in nursing homes is for aggressive behavior in PWD (7); usage is poorly studied in the community setting. This is concerning, as clinical evidence for efficacy of antipsychotic use in aggression is mixed, with modest results at best (8). Conversely, risks for cardiovascular adverse events and general mortality are well-documented (9). Given the inconclusive evidence with available medications, best practice is widely recommended to be nonpharmacologic management (10).

Systematic literature reviews suggest promise for caregiver interventions, particularly those aiming to improve communication between caregivers and patients, which provide caregiver education and support and introduce meaningful activities (11). More work needs to identify successful setting-specific interventions, especially in community settings, where most PWD reside. A meta-analysis of 23 randomized controlled trials (RCTs) of caregiver interventions concluded that such interventions modestly reduce behavioral symptoms, but few focused on treating aggression, and no studies to date have primarily targeted prevention of aggression (11, 12).

Potential targets for preventing aggression include patient, caregiver, and environmental factors. Current literature primarily focuses on patient factors, suggesting that pain and depression are major risk factors (13,14). An acute medical condition, unmet needs, sensory changes, poor sleep hygiene, and male gender also independently predict aggression (15). Our own longitudinal epidemiologic work found that pain (pain factor), quality of patient-caregiver communication (caregiver factor), and low pleasant activity levels (environmental factor) were significant predictors of aggression (16). A multidisciplinary management approach to prevent aggression would include caregiver and patient factors, such as providing caregiver education, improving patient-caregiver communication and general care environment, and streamlining the caregiver's daily routine (15). Here, we describe the outcomes of an intervention to prevent aggression, focused primarily on the patient risk

factor of pain, with attention to patient-caregiver relationship and communication. In line with recommendations from Kales et al. (11), this intervention was delivered in a patient-education format and addressed the general care environment and caregiver routine. The aims of this RCT of a psychosocial intervention (i.e., PAVeD; Preventing Aggression in Veterans with Dementia) that builds unpaid caregiver skills to address pain were to compare its efficacy with that of usual care in decreasing incidence of aggression (primary outcome) and in decreasing pain and improving depression, pleasant events, caregiver burden, and patient-caregiver relationship quality (secondary outcomes).

Methods

Participants

This 4-year RCT included veterans with pain and dementia and their primary caregivers. Descriptions of trial design and methods are provided elsewhere (17). All participants had dementia and pain affecting their functioning enough to merit their interest in an 8-week psychosocial intervention (PAVeD). Participants were identified by a) a search of the Veterans Health Administration (VHA) outpatient data for persons with a diagnosis of dementia, or b) an active prescription of a medication indicated for dementia, or c) a provider referral. Inclusion criteria included (1) documented diagnosis of dementia; (2) receipt of primary care from the VHA; (3) residence outside a long-term care facility; (4) mild-to-moderate dementia (defined using the Functional Assessment Staging (18), a validated clinician-rated measure of functional decline in dementia, stages of 2-6); (6) no history of aggression in the past year, as assessed by the Cohen-Mansfield Agitation Inventory (CMAI) (19); (7) having an unpaid caregiver directly involved with the veteran at least 8 hours per week, seeing the veteran at least twice a week and willing to co-enroll; and (8) clinically significant pain, indicated either through self-report or a caregiver's affirmation of the person's pain through reporting level of 2 or higher (i.e., at least "moderate" overall pain over the last several weeks) on the Philadelphia Geriatric Pain Intensity Scale (20). Dyads meeting criteria and agreeing to participate completed consent/assent discussions and documentation forms. This study was approved by the Baylor College of Medicine Institutional Review Boards and the Michael E. DeBakey VA Medical Center Research and Development Committee.

Assessments

A phone-based baseline assessment elicited demographic information of both caregivers and PWD and included the following validated instruments: the CMAI; the Philadelphia Geriatric Pain Intensity Scale; the Geriatric Depression Scale (GDS); the Pleasant Events and Activities Schedule Alzheimer's Disease, short version; the Burden Interview; and the Mutuality Scale. Administration of these instruments was repeated at 3, 6, and 12 months postbaseline. All assessments were based on caregiver response with the exception of the pain scale, which was administered to both patient and caregiver. Assessments were performed by independent evaluators (IEs) blind to treatment group assignment.

Randomization

Caregiver-PWD dyads were randomly assigned to intervention groups (PAVeD or enhanced usual primary care [EU-PC]) in blocks of 10 immediately following the baseline evaluation, based on random numbers generated in SAS PROC PLAN. Participants were reminded not to reveal information about treatment being offered by the study during blinded IE assessment interviews. Clinicians providing the interventions were not involved in outcome data collection and were blind to IE assessments.

Interventions

The focus of PAVeD is to decrease incidence of aggressive behavior in PWD at increased risk of behavioral disturbance due to pain. PAVeD targets several areas of patient life known to cause aggression: pain and distress, including mood problems; lack of engagement in pleasurable activities; and difficulty in patient/caregiver communication. Dyads assigned to PAVeD (n=101) received 6 to 8 weekly sessions of 45-minute home visits. PAVeD consists of 4 weekly 45-minute “core” sessions (“Recognizing Pain”; “Recognizing and Responding to Pain and Distress”; “Enhancing Communication”; “Making Daily Activities More Pleasant and Enjoyable”) and 2 of 4 elective sessions (“Medical Treatments and Talking to Your Doctor,” “Rest and Relaxation Strategies,” “Communication Problems and Challenges,” and “Increasing Pleasant Activities”), chosen with the patient and/or caregiver through collaborative goal setting during the first session. The intervention includes didactics, skill-building, discussion, and role-playing guided by a clinician manual and caregiver workbook.

Dyads assigned to EU-PC (N=102) received 8 weekly 15-minute phone calls to query symptom severity, ascertain needs for immediate psychiatric care, and provide minimal support. Primary care physicians of patients assigned to both groups received American Medical Association Continuing Medical Education print material on treating pain in older adults, (21) as well as feedback progress notes documenting the PWD's level of pain and depression at baseline, 3 months, 6 months, and 12 months. Caregivers in both groups received the National Institute on Aging booklet, *Understanding Memory Loss* (22), as well as *Pain Management for Older Adults*, a self-help book (23).

The interventions were delivered by master's-level trained clinicians who each participated in both interventions. Fidelity was monitored through IE review of 20% of randomly selected visits.

Outcome Measures

Aggression Incidence—The CMAI is a 29-item caregivers' rating scale with Likert ratings of both frequency and disruptiveness of behaviors. We used the CMAI aggression subscale and derived the cut-point for defining aggression based on work done among community-dwelling veterans with dementia (24). Aggression is considered present if a participant scores over 1 on both frequency and disruptiveness (indicating that the event occurred and was at least “a little” disruptive) for spitting, cursing/verbal aggression, hitting, kicking, grabbing, pushing, throwing, biting, scratching, hurting self/others, tearing things/

destroying property, making inappropriate verbal sexual advances, or making inappropriate physical sexual advances.

Secondary Outcome Measures—Several instruments were used to assess secondary outcome measures. Pain was assessed via the Philadelphia Geriatric Pain Intensity Scale, which examines (1) the extent to which the patient has been bothered by pain over the past several weeks, and (2) the time when the pain was at its worst. Patient pain was rated by both the PWD and caregiver; other secondary outcomes were based on caregiver rating. Depression was assessed via the 30-item GDS (25), with scores ranging from 0 to 30 and scores above 10 suggesting depression. The Pleasant Events Schedule – AD (26) measured frequency and perceived enjoyment of participation in activity. The frequency with which one enjoys events was calculated by multiplying frequency and enjoyment scores for each item and then taking the sum across all 20 items. The resulting range of scores is between 0-40, with higher numbers representing greater frequency of pleasant activities over the last month. Caregiver Burden was measured via the Burden Interview (27), a 22-item instrument measuring the perceived impact of caregiving on the caregiver's financial status, physical status, physical health, emotional health, and social activities. Caregiver-patient relationship quality was assessed via the 15-item Mutuality Scale (28), which examines caregiver-PWD relationship. Whether the PWD had been moved to a long-term residential setting (a personal care home, assisted-living facility, skilled or nonskilled nursing facility, or other facility) was queried at each assessment.

Caregiver satisfaction and perceptions of usefulness of PAVeD and its components were assessed with an exit interview within 2 weeks postintervention. Caregiver satisfaction was assessed with 3 items from the Client Satisfaction Questionnaire (CSQ-8 (29). Caregivers were asked, “How would you rate the quality of the service you received ?” (1 = “Excellent”, 2 = “Good”, 3 = “Fair”, 4 = “Poor”), “Have the services you received helped you deal more effectively with your problems” (1 = “Yes, they helped a great deal”, 2 = “Yes, they helped somewhat,” 3 = “No, they really didn't help”, and 4 = “No, they seemed to make things worse”); and “In an over all, general sense, how satisfied are you with the service you received” (1 = “Very Satisfied”, 2 = “Mostly Satisfied”, 3 = “Indifferent or Mildly Dissatisfied”, 4 = “Quite Dissatisfied”). Additionally, caregivers were asked whether they found Pain Management for Older Adults: A Self-Help Guide helpful. Caregivers also rated the helpfulness (1 = “Not at all helpful and 4 = “Very helpful”) of skills learned. An open-ended question was asked: “When you think about your participation in the PAVeD program, what stands out?” and “What parts of the program were most useful in helping the PWD to manage his/her pain?”

Analysis

Before conducting outcome analyses, we evaluated differences in demographics and baseline clinical characteristics between study completers and noncompleters, using chi-square or Fisher Exact tests and independent samples *t*-tests when appropriate. Study completers were those who completed either the 6-or 12-month assessment or both. Furthermore, baseline differences between the PAVeD and EU-PC subgroups in demographics, as well as clinical characteristics, were evaluated with chi-square tests and

independent samples *t*-tests. However, when distributional assumptions were violated, a nonparametric Fishers Exact or Wilcoxon Mann-Whitney U test was conducted.

Univariate time-to-event analyses were performed, using discrete-time Cox regression models to evaluate differences between the PAVeD and EU-PC subgroups in the primary outcome of incidence of aggression (yes/no) over time. We separately examined differential incidence of overall aggression, verbal aggression, and nonverbal aggression. For participants who dropped out, their time until study attrition was used as the exposure period; and they were carried forward as part of the overall incidence count.

Between-group differences in change over time (baseline, and 3, 6 and, 12 months) for our secondary outcomes of caregiver-reported and patient-reported overall and worst pain, GDS, frequency of pleasant events, burden, and mutuality were evaluated using individual linear growth curve models (SAS Proc Mixed) with an autoregressive covariance structure type. Hierarchical linear models account for both various lengths of follow-up for each participant and missing observations not due to attrition. For each outcome, 2 models were conducted. The first included the main effects of time and treatment condition, as well as the respective baseline value. The second included all terms from the first model plus the interaction between treatment group and assessment time. A main effect of time indicates change over time on the dependent variable; a main effect of treatment group indicates differences between treatment groups on the dependent variable; and, importantly, a significant interaction between treatment group and time indicates that the way the dependent variable changes over time differs by treatment group. All analyses were conducted using SAS software Version 9.4.

Power calculations were based on the ability to detect a small-to-moderate difference (Cohen's $h = .4$) between treatment groups in rate of aggression onset (the primary outcome) over a 1-year period, assuming 80% power and type I error rate of 5%. This differential rate in aggression onset is comparable to a 37% rate of aggression onset over a 1-year period for the control group (anticipated based on estimated rates from prior work) versus 19% for the treatment group (16). Given this effect size and potential of up to 10% attrition, our goal was to include 220 total participants so that a minimum of 198 would be available after attrition. The randomized sample ($n = 101$ in PAVeD and $n = 102$ in EU-PC) exceeds the required 99 per group.

Results

Figure 1 summarizes participant flow during the study. Total attrition was 19.7% ($N = 40$), similar for PAVeD ($n = 23$, 22.8%) and EU-PC ($n = 17$, 16.7%), $X^2(1) = 1.20$, $p = .27$. Patient and caregiver demographics, as well as baseline clinical characteristics, did not differ between completers and noncompleters (all $ps > .05$, data not presented), except that completers were more likely to have a caregiver with at least a college degree ($n = 41$, 25.15% of completers versus $n = 3$, 7.5% of noncompleters), Fisher's $p = .014$.

Sample Characteristics

Table 1 presents patient and caregiver demographics overall and by treatment group. PAVeD and EU-PC dyads were similar in PWD and caregiver demographics.

Table 2 presents baseline clinical characteristics overall and by Treatment Group. Just over half of PWD were moderately impaired. Additionally, most PWD had mild depression ($N = 118$; 58.42%). Baseline clinical characteristics were similar among PWD in both groups, except that caregivers in PAVeD reported significantly greater patient overall pain than those in EU-PC (see Table 2). Patient-reported worst and overall pain was comparable, and both groups had comparable levels of cognitive impairment and similar usage of medication, burden severity and functional status. The mean number of sessions for those in the intervention group was 5.89 ($SD = 2.41$), and they reported practicing skills an average of 3.26 days a week ($SD = 1.67$).

Primary Outcome

Incidence of overall aggression was not different for participants in PAVeD compared with those in the EU-PC group ($n = 27$, 26.73% versus $n = 33$, 32.35%; $X^2(1) = 0.77$, $p = 0.38$). Similarly, no differences were found in verbal and nonverbal aggression in PAVeD compared with EU-PC (verbal: $N = 23$, 22.77% versus $N = 24$, 23.53% ($X^2(1) = .02$, $p = 0.90$); nonverbal: $N = 14$, 13.86% versus $N = 19$, 18.63% ($X^2(1) = 0.85$, $p = 0.36$)). Figure 2 presents incidence of overall (a), verbal (b), and nonverbal (c) aggression at each assessment, using the last observation carried forward method. Discrete time Cox regression analysis revealed no statistically significant difference in time until incidence of overall, verbal, or nonverbal aggression between groups (see Table 3).

Secondary Outcomes

Analysis of patient and caregiver-reported pain focused on worst pain and overall pain over the last several weeks. For each secondary outcome, we looked at the main effects of time and treatment group, as well as the interaction between time and treatment group. There were significant main effects of time for pain: there were decreases in pain over time (caregiver-reported worst pain: $F(3, 458) = 5.64$, $p = .001$; patient-reported worst pain: $F(3, 412) = 7.04$, $p = .001$; caregiver-reported overall pain: $F(3, 458) = 5.84$, $p = .001$; and patient-reported overall pain: $F(3, 412) = 4.59$, $p = .004$, but no differences between groups in pain or in change in pain over time (Table 4). There were no differences between treatment groups overall (no main effect of treatment group) or over time (no main effect of time) on depression or burden. Furthermore, changes in depression and burden over time did not differ between treatment groups.

Engagement in pleasant events decreased over time $F(3, 460) = 2.94$, $p = .03$, but there were no differences between groups in pleasant events or in change over time. The PAVeD group had significantly higher mutuality overall, $F(1, 200) = 6.63$, $p = .01$, and there was a significant decline in mutuality over time, $F(3, 459) = 11.63$, $p < .0001$. Importantly, there was a significant interaction between treatment condition and time, $F(3, 456) = 3.84$, $p = .01$, such that the significant decline in mutuality over time was only among those in the EU-PC group.

Long-term facility admissions were minimal during the study (N = 11; 5% overall), precluding statistical tests to evaluate differences between treatment groups over time. However, overall incidence of nursing-home admissions appeared to be higher and began earlier in EU-PC (n=7, 7% overall; the first admission for 3 (43%) of these occurred at 3 months) compared with PAVeD (N=4, 4% overall; the first admission for 2 (50%) of these occurred at 6 months postintervention and the other 2 (50%) occurred at 12 months).

Exit Interview

Upon completing the intervention, 72 caregivers in the PAVeD group completed a questionnaire containing quantitative and qualitative items regarding their experience. Most caregivers rated the quality of the service they received as “Excellent” (n = 62; 86.11%) or “Good” (n = 8; 11.11%), and most indicated that the services they received helped them to deal effectively with their problems a “Great Deal” (n = 53; 73.61%). Furthermore, all caregivers expressed overall satisfaction with the service they received, with 63 (87.50%) being “Very Satisfied” and 9 (12.50%) being “Mostly Satisfied.” Nearly all respondents (n = 64, 91.43%) expressed positive responses toward the pain-management resources, and the majority of respondents rated each intervention module “Very Helpful (between 52% for increasing pleasant activities and 79% for recognizing pain). The majority of participants indicated that they were very confident in their ability to use the skills (between 56% for increasing pleasant activities and 89.28% for medical treatments and talking to your doctor).

Responses to the question: “What parts of the program were most useful for you in helping (the PWD) to manage his/her pain,” aligned with ratings of the specific modules. Sixty-four percent of replies highlighted skills related to recognizing nonverbal and behavioral signs of pain and responding to pain through use of medication or other strategies covered in the highly rated pain modules. Almost 1 in 4 (24%) responses highlighted communication skills as most useful, while a smaller number (6%) reported that learning specific relaxation techniques (8%) or ways to engage in activities (6%) was most useful.

Discussion

Analysis of the primary outcome showed no significant differences in aggression incidence between intervention and control groups. On the basis of previous studies as well as pilot samples, we hypothesized a 40% aggression incidence in the control group and a 25% aggression incidence in the intervention group (1,2). One contributing factor to the lack of significance in aggression incidence between groups is that the control group had lower-than-expected incidences of aggression across all time points (14% at 3 months; 18% at 6 months; 21% at 12 months), while the PAVeD group's incidences were closer to expectations (8% at 3 months; 12% at 6 months; 20% at 12 months).

Evaluation of secondary outcome measures showed a significant decrease of pain over time but no difference in pain levels across treatment groups. The lack of differences between groups in pain reports may be attributed to the PAVeD group caregivers being better educated at identifying pain symptoms than their control-group counterparts, which may have led to a paradoxical increase in pain scores for this group. The PAVeD group received intensive instruction on how to identify nuances of pain manifestation through in-depth,

weekly home sessions. EU-PC participants learned only to better recognize pain through pain-management educational materials. We surmise there may have been an artificial underreporting of pain at baseline for both groups. As caregivers and patients learn to better identify symptoms of pain, the PAVeD group may have become more sensitive to and made more reports of pain, masking the intervention's impact in decreasing pain. In addition, our intervention almost exclusively focused on the patient-caregiver dyad but not the primary care provider. Other studies in long-term care with success in decreasing aggression have targeted providers, so this may be an important component to add in future interventions (30).

Mutuality was the sole secondary outcome significantly different between treatment groups. The nature of the PAVeD intervention likely increased mutuality by positively impacting multiple factors closely associated with mutuality (31) (e.g., improving communication) which created a significant difference in mutuality between treatment groups. This finding is promising because mutuality is a powerful predictor of psychosocial well-being between caregivers and PWD (28,31) and, thus, PAVeD has demonstrated itself as an effective intervention in positively impacting the relationship between the patient-caregiver dyad.

This study has several limitations. This sample, representative of a VHA demographic, limits generalizability. However, our prevalence of aggression is comparable to previous studies' (1). It is unclear through what mechanism our intervention targeted pain, as intervention sessions provided multifaceted pain education focused on the caregiver, PWD, their relationships, and their environments. Aggression, along with all of the other outcome measures except for pain, was based on caregivers' rating. Although caregiver ratings are common and have been validated in persons with dementia, arguments can be made for more objective or patient ratings. Finally, we were underpowered to detect small effects.

Overall, we did not observe significant effects on aggression incidence with this intervention. PAVeD may need to be modified to address a broader range and more in-depth coverage of aggression risk factors (pain, relationship, depression, caregiver unmet needs, dementia education), with person-centered tailoring to target certain types of distress

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Figure 1.
Flow of Participants through the Course of the Study

Figure 2.

a. Overall aggression incidence; b. Nonverbal aggression incidence; c. nonverbal aggression incidence. Corresponding results from discrete time cox regression analyses are presented in Table 3.

Table 1

Patient and Caregiver Demographics Overall and by Treatment Group.

	Overall (N = 203) [*]	PAVeD (N = 101)	EU-PC (N = 102)	Test statistic and degrees of freedom: <i>t</i> (df) or χ^2 (df)	P-value
Patient Demographics					
Males, N (%)	199 (98.03)	101 (100)	98 (96.08)	NA [†]	0.12
Age (years), mean (SD)	79.24 (8.27)	78.21 (8.46)	80.26 (8.00)	<i>t</i> (201) = 1.78 ^{**}	0.08
Education, N (%) (n = 201)				$\chi^2(2) = 0.96^{\dagger\dagger}$	0.62
Did not complete HS	35 (17.41)	15 (15.15)	20 (19.61)		
HS diploma or GED	64 (31.84)	34 (34.34)	30 (29.41)		
Some college or more	102 (50.75)	50 (50.51)	52 (50.98)		
Race/ethnicity, N (%)				NA [†]	1.00
Non-Hispanic White	94 (46.31)	47 (46.53)	47 (46.08)		
Black	73 (35.96)	36 (35.64)	37 (36.27)		
Hispanic	30 (14.78)	15 (14.85)	15 (14.71)		
Other	6 (2.96)	3 (2.97)	3 (2.94)		
Annual net income, N (%) (n = 189)				$\chi^2(2) = 1.27^{\dagger\dagger}$	0.53
< 20k	83 (43.92)	37 (39.78)	46 (47.92)		
20,000-49,999	93 (49.21)	49 (52.69)	44 (45.83)		
>=50,000	13 (6.88)	7 (7.53)	6 (6.25)		
Any psychotropic meds, N (%) (n = 202)	13 (6.44)	5 (4.95)	8 (7.92)	$\chi^2(1) = 0.74^{\dagger\dagger}$	0.39
Benzodiazepine, N (%)	7 (3.45)	3 (2.97)	4 (3.92)	NA [†]	1.00
Hypnotic, N (%)	3 (1.48)	0 (0.00)	3 (2.94)	NA [†]	0.25
Antipsychotic, N (%) (n = 202)	6 (2.97)	2 (1.98)	4 (3.96)	NA [†]	0.68
Caregiver Demographics					
Males, N (%)	16 (7.88)	6 (5.94)	10 (9.80)	$\chi^2(1) = 1.04^{\dagger\dagger}$	0.31
Age (years), mean (SD) (n = 202)	66.06 (12.61)	66.43 (12.54)	65.69 (12.72)	<i>t</i> (200) = -0.41 ^{**}	0.68
Education, N (%)				$\chi^2(2) = 6.05^{\dagger\dagger}$	0.05
Did not complete HS	20 (9.85)	5 (4.95)	15 (14.71)		
HS diploma or GED	60 (29.56)	29 (28.71)	31 (30.39)		
Some college or more	123 (60.59)	67 (66.34)	56 (54.90)		
Race/ethnicity, N (%)				NA [†]	0.99
Non-Hispanic White	89 (43.84)	43 (42.57)	46 (45.10)		
Black	71 (34.98)	36 (35.64)	35 (34.31)		
Hispanic	34 (16.75)	17 (16.83)	17 (16.67)		
Other	9 (4.43)	5 (4.95)	4 (3.92)		
Annual net income, N (%) (n = 193)				$\chi^2(2) = 0.01^{\dagger\dagger}$	1.00

	Overall (<i>N</i> = 203) *	PAVeD (<i>N</i> = 101)	EU-PC (<i>N</i> = 102)	Test statistic and degrees of freedom: <i>t</i> (<i>df</i>) or <i>X</i> ² (<i>df</i>)	<i>P</i> -value
< 20k	130 (67.36)	64 (67.37)	66 (67.35)		
20,000-49,999	47 (24.35)	23 (24.21)	24 (24.49)		
>=50,000	16 (8.29)	8 (8.42)	8 (8.16)		
Your relationship to your loved one/ care recipient, <i>N</i> (%)				NA [†]	0.79
Spouse	133 (65.52)	69 (68.32)	64 (62.75)		
Other family	66 (32.51)	30 (29.70)	36 (35.29)		
Nonfamily	4 (1.97)	2 (1.98)	2 (1.96)		

HS = high school; GED = graduate equivalency degree

* Unless otherwise specified

** Independent samples t-test when both samples are normally distributed (both *t* statistic and degrees of freedom are presented).

[†] Fisher's exact test when the expected frequency of any cell is less than five (no associated test statistic or degrees of freedom; marked as NA).

^{††} Chi-square test when the expected frequency for each cell is five or higher (both chi-square statistic and degrees of freedom are presented).

Table 2

Baseline Clinical Characteristics Overall and by Treatment Group

	Overall (N = 203) [*]	PAVeD (N = 101)	EU-PC (N = 102)	Test statistic and degrees of freedom: <i>t</i> (df) or χ^2 (df)	P-value
Mini Blessed, <i>mean</i> (SD)	14.95 (7.36)	15.21 (7.36)	14.70 (7.39)	<i>t</i> (201) = -0.49 ^{**}	0.62
Normal or minimally impaired (0-8), <i>N</i> (%)	40 (19.70)	18 (17.82)	22 (21.57)	χ^2 (2) = 1.12 ^{††}	0.57
Moderately impaired (9-19), <i>N</i> (%)	107 (52.71)	52 (51.49)	55 (53.92)		
Severely impaired (20-28), <i>N</i> (%)	56 (27.59)	31 (30.69)	25 (24.51)		
FAST stage, <i>N</i> (%) (<i>n</i> = 201)				NA [†]	1.00
Possible/mild cognitive impairment	7 (3.48)	3 (3.00)	4 (3.96)		
Mild dementia	47 (23.38)	23 (23.00)	24 (23.76)		
Moderate/moderately severe dementia	147 (73.13)	74 (74.00)	73 (72.28)		
GDS, <i>mean</i> (SD) (<i>n</i> = 202)	14.15 (6.21)	14.33 (6.22)	13.97 (6.22)	<i>t</i> (200) = -0.41 ^{**}	0.68
Enjoyment of Pleasant Events, <i>mean</i> (SD)	23.87 (6.67)	23.09 (5.78)	24.65 (7.39)	<i>t</i> (201) = 1.67 ^{**}	0.10
Burden severity, <i>mean</i> (SD)	28.78 (15.19)	28.94 (15.27)	28.63 (15.18)	<i>t</i> (201) = -0.15 ^{**}	0.88
Total mutuality, <i>mean</i> (SD)	2.96 (0.66)	2.93 (0.66)	2.99 (0.66)	<i>t</i> (201) = 0.60 ^{**}	0.55
Caregiver-reported pain, <i>mean</i> (SD)					
Worst pain	3.15 (1.34)	3.28 (1.37)	3.03 (1.29)	<i>t</i> (201) = -1.32 ^{**}	0.19
Overall pain	2.24 (1.05)	2.43 (1.13)	2.06 (0.94)	<i>t</i> (201) = -2.52 ^{**}	0.013
Patient-reported pain, <i>mean</i> (SD)					
Worst pain (<i>n</i> = 201)	2.93 (1.41)	3.01 (1.30)	2.84 (1.51)	<i>t</i> (199) = -0.85 ^{**}	0.40
Overall pain (<i>n</i> = 202)	2.04 (1.18)	2.13 (1.11)	1.96 (1.24)	<i>t</i> (199) = -1.02 ^{**}	0.31

FAST = Functional Assessment Staging; GDS = Geriatric Depression Scale

^{*} Unless otherwise specified^{**} Independent samples t-test when both samples are normally distributed (both *t* statistic and degrees of freedom are presented).[†] Fisher's exact test when the expected frequency of any cell is less than five (no associated test statistic or degrees of freedom; marked as NA).^{††} Chi-square test when the expected frequency for each cell is five or higher (both chi-square statistic and degrees of freedom are presented).

Table 3

Univariate discrete time Cox regression using LOCF method

Model	Treatment	df	χ^2	P-Value	Hazard Ratio	HR 95% CI	
Overall Aggression	Paved	1	2.31	0.13	0.71	0.45	1.11
	EU-PC			1.00	1.00		
Verbal Aggression	PAVeD	1	0.50	0.48	0.84	0.51	1.37
	EU-PC			1.00	1.00		
Non-verbal Aggression	PAVeD	1	0.75	0.39	0.77	0.43	1.39
	EU-PC			1.00	1.00		

Table 4

Results of Multilevel Models for Interval Secondary Outcomes

	Cg [†] -reported Worst Pain		Patient-reported Worst Pain		Cg [†] -reported Overall Pain		Patient-reported Overall Pain		GDS		Pleasant Events		Burden		Mutuality	
	F	p	F	p	F	p	F	p	F	p	F	p	F	p	F	p
Step 1: Main Effects																
Respective Baseline [*]	190.82	<.0001	256.80	<.0001	215.85	<.0001	208.00	<.0001	678.44	<.0001	783.07	<.0001	658.55	<.0001	829.87	<.0001
Tx Condition [*]	0.10	0.75	0.19	0.67	0.05	0.82	0.18	0.67	1.39	0.24	0.88	0.35	3.84	0.051	6.63	0.01
Assessment Time ^{**}	5.64	0.001	7.04	0.001	5.84	0.001	4.59	0.004	1.15	0.33	2.94	0.03	1.11	0.34	11.63	<.0001
Step 2: Interaction [#]																
Tx Condition × Assessment Time ^{***}	0.86	0.46	1.43	0.23	1.45	0.23	0.59	0.62	0.94	0.42	1.10	0.35	2.00	0.11	3.84	0.01

[†]Cg = caregiver

[#]Interaction models include all variable from Step 1.

^{*}Numerator df = 1, Denominator df = 201 (198 for patient-reported worst pain and patient-reported overall pain, 199 for GDS, 200 for Mutuality, PES, caregiver-reported worst pain, and caregiver-reported overall pain)

^{**}Numerator df = 3, Denominator df = 460 (412 for patient-reported worst pain and patient-reported overall pain, 456 for GDS, 458 for caregiver-reported worst pain and caregiver-reported overall pain, 459 for Burden and Mutuality)

^{***}Numerator df = 3, Denominator df = 457 (409 for patient-reported worst pain and patient-reported overall pain, 453 for GDS, 455 for caregiver-reported worst pain and caregiver-reported overall pain, 456 for Burden and Mutuality)