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Caregiver-Care Recipient Relationship Closeness is Associated with Neuropsychiatric Symptoms in Dementia

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Abstract

OBJECTIVE—Closer caregiver-care recipient (CG-CR) relationships are associated with better cognitive and functional abilities, activities of daily living (in persons with dementia), and lower informal care costs.

METHODS—Due to the difficulty in treating neuropsychiatric symptoms (NPSs) and their detrimental effects on caregivers and care recipients, we examined whether closeness of CG-CR relationships was associated with overall NPS severity or with specific NPS symptom domains in care recipients. In a longitudinal population-based study in Cache County, Utah, the 12-item Neuropsychiatric Inventory (NPI-12) was assessed in 300 CG-CR dyads. Caregivers reported current relationship closeness using the Whitlatch Relationship Closeness Scale. Linear mixed models examined associations between CG-CR closeness and NPI-12 total score or selected symptom domains over time (observation period: 2002–2012).

RESULTS—In unadjusted linear mixed models, higher closeness scores were associated with a five-point lower NPI-12 score and a one-point lesser increase in NPI-12 per year. NPI scores also showed lower affective cluster scores (two points) and lesser increase in psychosis cluster

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(approximately 0.5 points per year) and agitation/aggression (0.16 points per year) for each unit increase in closeness. When controlling for NPI caregiver distress, associations between closeness and NPSs diminished to a 0.5-point lesser increase in total NPI-12 score per year. Adjusted models for NPI domains/clusters showed -0.32 points per year for the psychosis cluster, -0.11 points per year for agitation/aggression, and -0.67 overall for the affective cluster.

CONCLUSION—Higher CG-CR closeness, a potentially modifiable factor, is associated with lower NPS severity and may provide a target for intervention.

Keywords

Dementia; Alzheimer's Disease; Neuropsychiatric Symptoms; Caregiver and Care-Recipient; Relationship closeness

Objective

Approximately 5 million Americans have dementia and 1 million additional individuals are diagnosed each year (1). Nearly 98% of persons with dementia will experience at least one clinically significant neuropsychiatric symptom (NPS) in the course of their disease (2;3). NPS include depression, anxiety, agitation/aggression, apathy/indifference, dysphoria, elation/euphoria, disinhibition, irritability/lability, hallucinations, and delusions (4), the most common of which are depression, apathy, psychosis, agitation, and sleep disturbances. However, the prevalence and trajectories of NPS vary throughout the course of dementia with higher occurrences typically in mild and moderate stages. NPS appear to also co-vary or occur together within clusters, and this can vary by populations (5). Clusters that have been proposed include behavioral problems (agitation/aggression, disinhibition, irritability, and aberrant motor behavior), psychosis (delusions and hallucinations), mood (depression, anxiety, sleep, appetite, and apathy), and euphoria (6). Behavioral clusters have also been proposed and include negative valence (e.g., depression), positive valence (e.g., euphoria), cognitive systems (e.g., delusions, hallucinations), processes of social systems (e.g., apathy), and arousal or regulatory systems (e.g., agitation, aggression, sleep and appetite disturbance) (7). In prior work, we have also reported clusters of NPS, for example in mild Alzheimer's disease (AD) of psychosis and affective symptoms (8) and in work examining risk factors for NPS and symptom clusters (9). In AD, NPS are associated with worse cognitive functioning (4), severity of dementia (10; 11; 12), increased informal costs (13), and increased rates of institutionalization (14; 15). NPS are also associated with caregiver outcomes including reports of greater burden, worse health (12), higher prevalence of depression (16), and increased risk of AD (17).

NPS have been associated with neurodegenerative changes corresponding with brain regions involved in affect, behavior, motivation, and/or perception (7). For example, psychotic symptoms have been associated with reduced neuronal density, increased neocortical neurofibrillary tangles, disruption in serotonin signaling among other changes whereas agitation has been linked to abnormalities in frontal, anterior and posterior cingulate cortex, amygdala and the hippocampus (7). Neurobiological vulnerabilities may further be impacted by environmental challenges (noisy or confusing surroundings) leading to overload. Unmet care-recipient needs and mismatches between caregiving and care-recipient's abilities may

further elicit NPS (18). Although non-pharmacologic approaches (e.g., educating caregivers, changing the physical environment, exercise, etc.) have had some success (7;18), NPS are difficult to treat (17) and given their negative impact on both members of the care dyad, it is important to identify modifiable risk factors for their occurrence.

Closeness in the caregiver-care-recipient (CG-CR) relationship has been associated with better cognitive (executive functioning, memory, etc.) and functional outcomes for the care-recipient (19; 20). Specifically, closer CG-CR relationships are predictive of better quality of life and psychological well-being, increased problem-solving abilities (19), lower informal costs (13), slower rates of cognitive and functional decline (20) and better adjustment to nursing homes for the care-recipient with dementia (14). Caregiver-reported relationship closeness may reflect both the emotional aspects of the care environment (e.g. caregiver's emotional investment and/or sensitivity to the care recipient) and the behavioral aspects of the care environment (intensity and quality of care provided). Given that closeness would impact factors associated with the care environment, we hypothesized that closer CG-CR relationships would be associated with less severe NPS over time. Furthermore, we hypothesized that specific NPS that are more likely affected by the care environment (i.e., agitation/aggression and affective cluster) would show greater associations with CG-CR relationship closeness.

Methods

Participants.

Dementia care-dyads were enrolled in the Cache County Dementia Progression Study (DPS; 21), a longitudinal, population-based study assessing individuals who had been newly diagnosed with dementia from the Cache County Study on Memory in Aging (CCSMA) (19). The procedures of the CCSMA are described in prior publications (22; 23). Briefly, 5,092 residents of Cache County, Utah were enrolled in Wave 1 (1995 – 1996) and underwent stages of dementia screening and evaluation; those without dementia at each wave were invited to participate in subsequent triennial waves that occurred between 1998–2007. A total of 942 individuals with dementia were identified in the CCSMA. Dementia diagnoses were based on a clinical assessment that included a brief physical and neurological exam, clinical history provided by an informant and neuropsychological testing. Data from the clinical assessment were reviewed by a study physician, clinical neuropsychologist, and the clinical assessment team who assigned preliminary diagnoses of cognitive status as applicable. Diagnoses of dementia were assigned based on Diagnostic Statistical Manual Third Edition-Revised (DSM-III-R) criteria. Those participants suspected of having dementia or its prodrome were asked to complete a physician examination, brain MRI scan and standard laboratory tests to rule out other causes of dementia (22). The results of all of the aforementioned assessment and lab results were reviewed by an expert panel (geropsychiatrists, neurologists, neuropsychologists and a cognitive neuroscientist), who determined the presence of dementia and the likely underlying cause. Diagnoses of type of dementia followed standard research protocol at the time, for example, criteria for AD followed NINCDS-ADRDA criteria (24) and vascular dementia followed NINDS-AIREN

criteria (25). Surviving individuals identified with new onset (incident) dementia at each wave were enrolled along with their caregivers in the DPS between 2002-2009.

Procedures.

Three hundred twenty-eight dementia-caregiver dyads were enrolled in the DPS and evaluated approximately every six months at their place of residence (21). At each visit, the person with dementia (PWD) underwent a brief clinical assessment with neuropsychological testing similar to the CCMSA clinical assessment. Caregivers provided an update regarding the PWD's cognitive and functional limitations, NPS, health status, and daily activities. Caregivers also reported on aspects of the care environment as well as information regarding the nature of their relationship with the care recipient at alternating (odd numbered) visits (21). Informed consent was obtained at each visit and study procedures were approved by the Institutional Review Boards at Utah State University and the John Hopkins University.

Measures.

Primary predictor variable—The Relationship Closeness Scale, completed by the caregiver, assessed the closeness of the caregiver-care recipient relationship with six items (26; 14). The instrument assesses the caregiver's agreement (4= strongly agree, 3= agree, 2=disagree, 1=strongly disagree) with each of the following six statements: 1) My relative always understands what I value in life, 2) My relationship with my relative has always been close, 3) My relative always makes me feel that whatever I do for him/her is not enough, 4) My relative always makes me feel like a special person, 5) My relative is often critical of me, and 6) My relative and I can always discuss things together (26;14). Scores were summed (with items 3 and 5 reverse coded) and a mean score was calculated to retain the original scaling of the instrument. Closeness scores were available at each odd-numbered visit. Chronbach's alpha for the Whitlatch has been reported previously as .90 (14) and as 0.89 in the Cache County DPS sample (27).

Outcome variable

Neuropsychiatric Inventory-12 (NPI-12).: The NPI-12, administered at baseline and subsequent visits, assessed NPS in 12 domains: delusions, hallucinations, agitation/aggression, depression/dysphoria, anxiety, elation/euphoria, apathy/indifference, disinhibition, irritability/lability, aberrant motor behavior, nighttime behavioral disturbances, and appetite/eating changes (28). If a symptom was endorsed by the caregiver, they were asked to rate the frequency and severity of each symptom domain, which were then multiplied to yield a domain score (maximum=12). Scores were summed across each domain to yield a total NPI-12 score (maximum=144). Factor or latent class analyses indicate that NPI domains are correlated or frequently co-occur (29, 30, 31). Thus, to explore specific NPS domains/symptoms, cluster scores for affective behavior (depression, anxiety, and irritability; score range = 0 – 36) and psychosis (hallucinations and delusions; score range = 0 – 24) were calculated. Individual symptom domain scores for agitation/aggression and apathy (score range 0 – 12) were also selected for analyses. The NPI also includes a rating of how distressing the caregiver finds each endorsed symptom (with 0 representing not at all to 5 representing very severely/extremely). For domains not endorsed,

a score of 0 was imputed. A total distress score was calculated by summing across distress ratings across the 12 symptom domains and cluster distress scores as a sum of distress ratings of the specific behaviors making up the cluster. Distress scores for apathy and agitation/aggression were obtained from the individual domains.

Other Variables.: Caregiver and care-recipient demographic information was collected at each visit, including age, gender, education, co-residency status (with caregiver), and kin relationship (spouse, adult child, and other). Duration of dementia at baseline was based on the age of dementia onset from the CCSMA. Severity of dementia at baseline and at subsequent visits were based on a Clinical Dementia Rating (CDR). The CDR provides a global rating of dementia based on an individual's abilities in the following domains: memory, orientation, judgment and problem-solving, community affairs, home and hobbies, and personal care. Each domain is rated from; 0=no dementia, 0.5=questionable dementia, 1= mild, 2= moderate, 3= severe dementia, and in older versions, 4=profound, and 5=terminal. The global CDR is determined from a standard algorithm (32). The Brief Psychiatric Rating Scale (BPRS) consists of 18 symptoms and provides a global indicator of psychiatric symptoms. Intraclass correlation is $r = .78$ (33). In the DPS, the rating was based on interview and observation of the PWD.

Statistical Analyses.: To examine the association between CG-CR closeness and NPS in the care-recipient, we estimated separate linear mixed-effects models using relationship closeness (time-varying) as the predictor for NPI-12 total score, cluster score (affective or psychosis) and individual symptom domain score (agitation/aggression, and apathy). Caregiver and care-recipient demographics (age at baseline, gender, education) and characteristics (time-varying dementia severity (CDR), dementia duration and caregiver co-residency at baseline, and kin relationship) were tested in each model. As an indicator of caregiver burden associated with NPS, caregiver distress rating was also tested as a covariate. Each predictor (or covariate) was added to each model (Maximum Likelihood Estimates) sequentially to examine change in the specific NPI outcome. A predictor was retained in the model if the likelihood ratio (LR) χ^2 test of models with and without the predictor improved model fit at a significance of $p = .05$. Interactions between relationship closeness and time were tested to examine effects on the slope of NPI-12 score (or symptom cluster or domain) over the period of observation. To display the parameter estimates and Wald statistics, all models were re-run using Restricted Maximum Likelihood Estimates. Finally, as the NPI-12 was based on caregiver report which may reflect the effects of other caregiver factors on the report, for example caregiver burden or stress, we examined the correlation (visit 1 only) between the NPI-12 total and the BPRS. We further examined whether closeness was also associated with the BPRS. All models were run in SPSS version 25 (34).

Results

Our analysis included 300 dyads (91%) out of a total 328 who met the inclusion criteria of completing the Relationship Closeness Scale, completion of the NPI-12, and available data on covariates. Table 1 provides baseline demographics and significant differences between those included vs. excluded in the current analyses. Those who were excluded were more

often female (85.7% vs. 55.3%), were rated as more severe in their dementia (CDR) at baseline than those included. The caregivers of those excluded were younger and less likely to live with their CR than those included in the analyses.

Relationship Closeness and Neuropsychiatric Symptoms.

In the unadjusted model, CG-CR relationship closeness was associated with NPI-12 score and change in NPI-12 score over time, with each unit of closeness being associated with a 5.4-point lower total score and a 1-point less increase in NPI-12 score per year. This diminished to approximately 0.5-point less increase in NPI-12 total score per year at marginal significance level (refer to Table 2). Higher caregiver distress ratings and global dementia severity were each associated with approximately 1- and 3-point increase in NPI-12 score, respectively. To illustrate the association between CG-CR relationship closeness and NPS, Table 3 displays the Total NPI-12 score for selected Relationship Closeness scores at each year post baseline. Figure 1 presents plots for selected mean CG-CR closeness score and changes in NPI-12 total score over time (from the fully adjusted model).

With respect to NPI symptom clusters, higher closeness scores were associated with lower affective cluster scores (2 points), but not with rate of change (refer to Table 4, unadjusted model). Higher closeness scores were also associated with less increase in psychosis cluster and agitation/aggression scores over time (refer to Tables 5 and 6, unadjusted models). With the inclusion of covariates (refer to adjusted models in Tables 4, 5, and 6), the associations between closeness and NPI clusters and symptom domains diminished, with agitation/aggression being of marginal significance. Note that the model for apathy did not converge. Figures 2 and 3 display the trajectories of the psychosis and agitation/aggression severity scores by selected closeness scores across time (from fully adjusted models).

BPRS and NPI-12 and Closeness.

BPRS total and NPI-12 scores were moderately correlated ($r = .41$, $df = 239$, $p < .0001$). In an unadjusted linear mixed-effects model, closeness score was significantly associated with the BPRS, such that a one unit increase in closeness was associated with a 1 point lower score on the BPRS ($t [df = 518.30] = -2.749$; $b = -1.00$; $p = 0.006$).

Conclusions

In this population-based sample of persons with dementia and their caregivers, we found that closer caregiver-care recipient relationship closeness (reported by the caregiver) was associated with smaller increases in NPS severity over time. Higher CG-CR closeness was specifically associated with lower affective symptom score and with change in psychosis and agitation/aggression over time.

Closeness in the caregiver-care recipient relationship, as perceived by the caregiver, may reflect emotional closeness, intimacy, relationship quality among other characteristics (27). The current findings align with prior research on the positive impact of CG-CR relationship closeness on improved care recipient outcomes, including better cognitive (19,20) and

functional (20) outcomes as well as reduced informal costs of care (13). While the underlying mechanisms are unclear, we hypothesize that caregivers feeling closer to their care recipient engage in care management strategies that are tailored to the care recipient and result in better care recipient outcomes. Our previous work suggests that certain care activities such as providing a cognitively stimulating environment (35), maintaining good nutritional status (36) and ensuring fewer acute or unstable health concerns (29), are related to better outcomes in the care recipient. It is also possible that a closer relationship between the care dyad fosters improved care-related behaviors.

As a modifiable factor, CG-CR relationship closeness may be targeted for modification along side other nonpharmacologic approaches in dementia care to reduce NPSs.³⁶ (37). In fact, caregivers who feel closer to their care recipient may provide valuable insights to individually tailor non-pharmacological interventions that maximize care recipient engagement, resulting in greater beneficial effects. Along these lines, skills training for caregivers may conceivably help caregivers in managing NPS in persons with dementia, including learning simpler and more effective communication styles that may reduce bouts of agitation/aggression and psychosis (18) and enhance relationship closeness. Training in activity planning and environmental redesigns may provide more appropriate levels of stimulation for the care-recipient and reduce affective symptoms (18). Caregivers with closer relationships may also be better equipped to identify specific activities and environments that are enjoyable and acceptable to the care recipient. Modifying the care recipients' physical (reduced noise and structured schedules) and social environments (social engagement) may also help reduce agitation/aggression and affective symptoms (18). Interventions that enhance the quality of the CG-CR relationship may improve the quality of the care environment through the aforementioned factors, all of which are hypothesized to benefit the care recipient as well as the caregiver through reduced stress/burden. Of note however, in our prior work on caregiver outcomes, CG-CR closeness has been associated with both positive and negative outcomes for the caregiver (27). Thus, it is suggested that interventions consider *both* members of the care dyad and aspects of the care environment for optimizing outcomes.

There are limitations to the current study. First, we relied solely on caregiver report of relationship closeness; care-recipient reports were not systematically collected due to concerns of reporting validity. Furthermore, the caregiver reported NPS of the care recipients; thus it is possible that a social desirability reporting bias in the direction of higher closeness and lower NPS may have affected our results. While we cannot rule out this possibility, the results of the current study are consistent with our previous findings with objectively assessed outcomes [e.g, cognition; (20)] and thus lessen these concerns. Additionally, correlations between the BPRS score, which was based more heavily on care-recipient report and nurse observations, were modestly correlated with caregiver reports on the NPI ($r = .41$), providing support for the validity of caregiver report on NPS. Furthermore, in an ancillary analysis, relationship closeness was also significantly associated with BPRS, similar to the direction of the effect with the NPI. Finally, the Cache County population is predominantly White with high religious affiliation in the Latter-Day Saints religion, therefore findings may not generalize to other populations.

Among the strengths of the study are the population and community based-sample of older adults with dementia, the high initial enrollment (85%) and follow-up (95 – 100%) participation rates, thorough characterization of both CG and CRs, and the duration of follow-up extending up to 12 years. Additionally, in statistical analyses, we controlled for potential confounders in the relationship between CG-CR relationship closeness, namely dementia severity and caregiver distress. Indeed, inclusion of both variables in the fully-adjusted models diminished the magnitude of the effect of closeness on NPS. The relationship among these factors (dementia severity, closeness, and caregiver distress) and NPS are likely complex and dynamic with probable bi-directional effects, for example where closeness may predict NPS, but also where NPS may predict closeness through caregiver distress. Examination of such complex interactions between CG-CR factors is beyond the scope of the present paper, though may be a topic of future investigation.

In summary, we found that caregiver perceptions of closer CG-CR relationships are associated with lower NPS and lesser increases in NPS severity in dementia over time. Implications include consideration of quality of the CG-CR relationship as a target for nonpharmacological interventions of NPS.

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Figure 1.

The plot shows the average NPI-12 Total trajectories associated with CG-CR closeness for individuals with a caregiver distress score of one and a care-recipient dementia severity rating of one.

Figure 2.

The plot shows the average NPI agitation/aggression trajectories associated with CG-CR closeness for individuals with a caregiver distress score of one and a care-recipient dementia severity rating of one.

Figure 3.

The plot shows the average NPI psychosis trajectories associated with mean CG-CR closeness for individuals with a caregiver distress rating of one and care-recipient dementia severity of one.

Table 1.

Presents the Baseline Demographics for those included and excluded from the analyses for both Care-Recipient and Caregiver.

	Included in Analyses (N=300) ²	Missing data, excluded from Analyses (N=28)	df	Statistic (t or X ²)
Care-Recipient				
Age in years [Mean (SD)]	85.90 (5.6)	86.50 (6.90)	326	0.53
Female N (%)	166 (55.3%)	24 (85.7%)		9.70 **
Education in years [Mean (SD)]	13.33 (2.88)	13.30 (3.59)	325	-0.06
CDR [Mean (SD)]	1.23 (0.77)	1.90 (1.23)	24.45	3.86 **
Asst. Liv/NH [N (%)]	92 (31.0%)	13 (46.4%)	1	2.79
Dementia Duration in years [Mean (SD)]	3.49 (1.87)	4.32 (2.07)	326	2.22
NPI-12 Total (max = 144) [Mean (SD)]	11.59 (10.98)	12.58 (11.33)	304	0.49
NPI-Agitation (max = 12) [Mean (SD)]	0.67 (1.65)	1.17 (2.17)	75.33	1.66
NPI-Apathy (max = 12) [Mean (SD)]	2.21 (3.30)	2.33 (3.33)	321	0.27
NPI-Affective (max = 36) [Mean (SD)]	3.26 (4.02)	3.42 (4.28)	318	0.27
NPI-Psychosis (max = 24) [Mean (SD)]	1.37 (3.13)	1.86 (2.70)	319	1.10
Caregiver				
Age in years [Mean (SD)]	68.25 (13.82)	58.77 (15.18)	288	3.07 *
Female N (%)	228 (76.0%)	20 (83.3%)	1	0.67
Co-Reside N (%)	149 (50.3%)	3 (15.0%)	1	1.08 *
Spousal Relationship N (%)	126 (42.0%)	4 (19.0%)	1	4.29 *
Whitlatch ¹ (max=4); [Mean (SD)]	3.15 (0.63)	2.94 (0.64)	301	1.14
Whitlatch Categories			3	0.45
Strongly Disagree N (%)	6 (2.28)	1 (2.5)		
Disagree N (%)	36 (13.69)	7 (1.75)		
Agree N (%)	141 (53.61)	20 (50)		
Strongly Agree N (%)	80 (30.42)	12 (30)		
CG burden (max=10); [Mean(SD)]	3.72 (1.73)	3.71 (2.08)	295	0.03
CG NPI Total Distress (max = 60); [Mean(SD)]	5.34 (5.88)	5.04 (5.60)	326	-0.37
CG NPI-Agitation Distress (max = 5); [Mean(SD)]	0.39 (0.99)	0.63 (1.21)	86.7	1.66
CG NPI-Apathy Distress (max = 5); [Mean(SD)]	0.80 (1.31)	0.69 (1.24)	326	-0.59
CG NPI-Affective Distress (max = 15); [Mean(SD)]	2.10 (2.68)	1.83 (2.60)	326	-0.74
CG NPI-Psychosis Distress (max = 10); [Mean(SD)]	0.65 (1.55)	0.88 (1.64)	326	1.06

¹Whitlatch Closeness Scores are to be interpreted as the extent to which the caregiver agrees or disagrees with 6 statements that describe the caregiver-care recipient relationship. Higher mean scores (i.e., agree, strongly agree), reflect higher closeness (with two items reversed coded in scoring). Asst. Liv= Assisted Living; NH=Nursing Home; N=Total Number of individuals; CG= Caregiver; NPI= Neuropsychiatric Inventory; SD=Standard Deviation.

* significant at the p < .05;

** significant at the p < .01

²Note: Sum of included and excluded participants will not equal 328 for all variables due to some participants missing baseline values.

Also as different N's were included in analyses depending on the outcome (NPI-total 12 or NPI cluster scores), all statistics reported in Table 1 reflect those included in the NPI-total 12 analyses.

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Table 2.

Unadjusted and Adjusted Linear Mixed Models of Neuropsychiatric Inventory

<i>Parameter</i>	Unadjusted Model							Adjusted Model						
	<i>Est.</i>	<i>Std. Error</i>	<i>df</i>	<i>t</i>	<i>p</i>	95% CI Lower Bound	95% CI Upper Bound	<i>Est.</i>	<i>Std. Error</i>	<i>df</i>	<i>t</i>	<i>p</i>	95% CI Lower Bound	95% CI Upper Bound
Intercept	28.64	2.94	366.85	9.74	<.001	22.85	34.42	2.34	2.68	385.39	1.07	0.28	-2.03	6.89
Time	4.21	1.49	167.73	2.83	.005	1.27	7.15	2.69	1.10	202.66	2.06	0.04*	0.10	4.44
Whitlatch Score	-5.37	0.92	370.61	-5.86	<.001	-7.17	-3.57	-0.49	0.65	354.57	-0.75	0.46	-1.77	0.80
Whitlatch*Time	-1.02	0.47	178.63	-2.15	.033	-1.95	-0.08	-0.63	0.35	212.64	-1.80	0.07	-1.31	0.06
Dementia Severity								3.36	0.38	487.32	8.74	<0.001	2.61	4.12
CG Distress								1.27	0.05	599.72	23.12	<0.001	1.16	1.38

The table shows unstandardized slope estimates from linear mixed models using Restricted Maximum Likelihood Estimates.

CG=Caregiver; Est=Estimate; Std=Standard; df=Degrees of Freedom; 95% CI= 95% Confidence Interval.

Table 3.

Estimated Values of Neuropsychiatric Inventory Total Scores by Relationship Closeness Over Time

Relationship	NPI	NPI	NPI	NPI	NPI	NPI	NPI	NPI	NPI	NPI
Closeness	Total	Total	Total	Total	Total	Total	Total	Total	Total	Total
Average	Baseline	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Year 9
Score										
1	6.57	8.21	9.85	11.49	13.13	14.77	16.41	18.05	19.69	21.33
2	6.08	7.09	8.10	9.11	10.12	11.13	12.14	13.15	14.16	15.17
3	5.59	5.97	6.35	6.73	7.11	7.49	7.87	8.25	8.63	9.01
4	5.10	4.85	4.60	4.35	4.10	3.85	3.60	3.35	3.10	2.85

NPI=Neuropsychiatric Inventory

Table 4.

Unadjusted and Adjusted Linear Mixed Models of Affective Cluster and its Association with Relationship Closeness

<i>Parameter</i>	Unadjusted Model						Adjusted Model							
	<i>Est.</i>	<i>Std. Error</i>	<i>df</i>	<i>t</i>	<i>p</i>	<i>95% CI Lower Bound</i>	<i>95% CI Upper Bound</i>	<i>Est.</i>	<i>Std. Error</i>	<i>df</i>	<i>t</i>	<i>p</i>	<i>95% CI Lower Bound</i>	<i>95% CI Upper Bound</i>
Intercept	9.69	0.82	520.38	11.84	<.001	8.08	11.30	2.58	0.65	490.21	3.99	<.001	1.31	3.85
Time	−0.09	0.10	125.85	−0.91	.363	−0.28	0.10	−0.06	0.07	175.72	−0.88	.378	−0.20	0.07
Whitlatch Score	−2.05	0.25	522.11	−8.15	<.001	−2.54	−1.55	−0.67	0.18	471.91	−3.78	<.001	−1.02	−0.32
CG Does not Co Reside								0.45	0.21	363.40	2.13	.034	0.04	0.87
Dementia Severity								0.22	.12	447.69	1.77	.077	−0.02	0.47
CG Distress								1.11	0.04	600.76	26.88	<.001	1.03	1.19

The table shows unstandardized slope estimates from linear mixed models using Restricted Maximum Likelihood Estimates.

CG=Caregiver; Est=Estimate; Std=Standard; df=Degrees of Freedom; 95% CI= 95% Confidence Interval

Table 5.

Unadjusted and Adjusted Linear Mixed Models of Psychosis Cluster and its Association with Relationship Closeness

<i>Parameter</i>	Unadjusted Model						Adjusted Model							
	<i>Est.</i>	<i>Std. Error</i>	<i>df</i>	<i>t</i>	<i>p</i>	<i>95% CI Lower Bound</i>	<i>95% CI Upper Bound</i>	<i>Est.</i>	<i>Std. Error</i>	<i>df</i>	<i>t</i>	<i>p</i>	<i>95% CI Lower Bound</i>	<i>95% CI Upper Bound</i>
Intercept	2.53	0.87	386.22	2.93	.004	0.83	4.24	-1.51	0.66	370.72	-2.26	0.02	-2.81	-0.21
Time	1.64	0.44	381.80	3.71	<.001	0.77	2.51	1.05	0.33	325.05	3.16	<0.001	0.40	1.71
Whitlatch Score	-0.36	0.27	391.01	-1.34	.18	-0.89	0.17	0.33	0.20	347.42	1.69	0.92	-0.05	0.72
Whitlatch*Time	-0.47	0.14	400.03	-3.41	.001	-0.75	-0.20	-0.32	0.10	334.47	-3.09	<0.001	-0.53	-0.12
Dementia Severity								0.78	0.11	369.02	7.36	<0.001	-0.57	0.98
CG Distress								1.34	0.06	547.90	21.94	<0.001	1.22	1.46

The table shows unstandardized slope estimates from linear mixed models using Restricted Maximum Likelihood Estimates.

CG=Caregiver; Est=Estimate; Std=Standard; df=Degrees of Freedom; 95%=95% Confidence Interval

Table 6.

Unadjusted and Adjusted Linear Mixed Models of Agitation/Aggression Score and its Association with Relationship Closeness

<i>Parameter</i>	Unadjusted Model						Adjusted Model							
	<i>Est.</i>	<i>Std. Error</i>	<i>df</i>	<i>t</i>	<i>p</i>	<i>95% CI Lower Bound</i>	<i>95% CI Upper Bound</i>	<i>Est.</i>	<i>Std. Error</i>	<i>df</i>	<i>t</i>	<i>p</i>	<i>95% CI Lower Bound</i>	<i>95% CI Upper Bound</i>
Intercept	2.64	0.46	365.94	5.68	<.001	1.72	3.55	-0.45	0.36	417.69	-1.24	0.22	-1.16	0.26
Time	0.65	0.26	313.83	2.51	.013	0.14	1.16	0.34	0.18	240.15	1.90	0.06	-0.01	0.70
Whitlatch Score	-0.62	0.14	371.01	-4.26	<.001	-0.90	-0.33	0.06	0.11	393.54	0.56	0.57	-0.15	0.27
Whitlatch* Time	-0.16	.08	331.96	-1.95	.052	-0.32	0.002	-0.11	0.06	251.37	-1.91	0.058	-0.22	0.00
Dementia Severity								0.41	0.06	462.55	6.67	<0.001	0.29	0.53
CG Distress								1.11	0.05	641.24	23.59	<0.001	1.01	1.20

The table shows unstandardized slope estimates from linear mixed models using Restricted Maximum Likelihood Estimates.

CG=Caregiver; Est=Estimate; Std=Standard error; 95% CI=95% Confidence Interval