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Dementia neuropsychiatric symptom frequency, severity, and correlates in community-dwelling Thai older adults

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Abstract

Background: Thailand is experiencing a rapid increase in the number of older people with dementia (PWD). We examined the frequency, severity, and correlates of dementia neuropsychiatric symptoms (NPS) among community-dwelling Thai older adults.

Methods: This study was based on analysis of baseline data from a larger clinical trial comparing two different implementation approaches of an evidence-based exercise intervention for people with dementia. To be eligible, participants needed to be age 60 and above, have probable dementia, have 1 or more NPS, be ambulatory, and have an adult (age 18+) family caregiver. In the 353 eligible participants, we examined the correlation between NPS severity and caregiver distress (assessed by the Neuropsychiatry Inventory Questionnaire or NPI-Q) and used ordinary least

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squares (OLS) regression to examine associations between PWD and caregiver characteristics and NPS severity.

Results: NPS frequency varied from 18% for appetite/eating changes to 42% for delusions. NPS severity was significantly ($p < 0.05$) associated with caregiver stress for all individual NPS. Among PWD characteristics, higher ADL score (less functional impairment) was inversely associated with NPS total severity ($b = -0.16$, $p < 0.05$). More physical role limitation was significantly associated with higher NPS total severity ($b = 0.77$, $p < 0.001$). Among caregivers' characteristics, higher burden was significantly associated with higher NPS total severity ($b = 0.19$, $p < 0.001$).

Conclusion: Our study found NPS to be common among community dwelling PWD in Thailand and have adverse impacts on both the PWD and family caregivers. These findings highlight the clinical importance of NPS symptoms among Thai older adults.

Keywords

dementia; Thailand; non-pharmacological interventions; caregiving

INTRODUCTION

Thailand and other low- and middle-income countries (LMIC) are experiencing a rapid increase in the number of older people with dementia (PWD).^{1, 2} Alzheimer's disease and related dementias (ADRD) are among the most disabling conditions to affect older adults and put significant strain on families. In addition to progressive disability, one of the most challenging aspects of in the provision of care to people with dementia is the associated neuropsychiatric symptoms (NPS), also referred to as psychological and behavioral symptoms of dementia.³⁻⁵ While there is growing recognition of the public health significance of NPS in LMIC, relatively little is known about the nature and consequences of these symptoms in Thailand and other LMIC.

In studies conducted largely in the United States (U.S.) and other high-income countries (HIC), NPS have been shown to adversely impact both PWD and their family caregivers.⁶ Adverse impacts include increased disability and poorer quality of life in PWD as well as increased psychological distress and burden in family caregivers. Multiple factors can contribute to the development or worsening of NPS, including characteristics of PWD, caregiver, and environment.⁷ Prior studies of Thai elderly in specialty clinics, hospitals, and nursing homes have found that neuropsychiatric symptoms are common and associated with functional disability and caregiver burden (e.g., Sananrong et al, 2005).⁸⁻¹⁰ However, there is a lack of studies from community settings that are more representative of the general population.

To address this knowledge gap, we conducted analyses of baseline data from the NIMH funded Partnership in Implementation Science for Geriatric Mental Health (PRISM) study in Thailand. This study is a cluster randomized controlled study examining the relative effectiveness of an implementation support strategy to enhance delivery of the Reducing Disability in Alzheimer's Disease (RDAD) program,¹¹ an evidence-based multicomponent

exercise plus behavioral/psychosocial intervention for older adults with dementia and their family caregivers. Because the PRISM sample was recruited from the Thailand's long-term care (LTC) system, which provides primary health and social care to community-dwelling older adults, it presented a unique opportunity to examine NPS in a non-specialty clinic setting in Thailand. The specific goals of this study were to examine the frequency, severity, and correlates of NPS, including correlation with family caregiver burden and distress, among community-dwelling, ambulatory Thai older adults with probable dementia. To our knowledge, this is the first study in Thailand conducted in a community setting to examine the frequency and correlates of NPS.

METHODS

Overview of the study:

As previously described,¹² the parent study is a hybrid type III cluster randomized design comparing 8 geographical districts (intervention arm) that receive training to implement both the Reducing Disabilities in Alzheimer's Disease (RDAD) clinical intervention and GTO (Getting to Outcomes) implementation support strategies vs. 8 districts (control arm) that received the same RDAD training without training in GTO implementation support strategies. GTO is an evidence-based intervention designed to provide implementation support for implementers to better plan, implement, and evaluate innovative intervention programs in a novel setting.^{13, 14} The parent study will test the hypothesis that the group receiving GTO will show better implementation and clinical outcomes compared to usual implementation. Primary outcomes will be assessed at baseline, 3 months (post-treatment), and 6 months, including implementation outcomes and clinical outcomes.

Study setting:

This study was conducted in Khon Kaen province, in Northeast Thailand, which has 26 districts, each of which has up to 3–18 subdistricts. Khon Kaen province was chosen because it includes both rural and urban areas (broadly representative of Thailand), has relatively mature and well-functioning LTC programs, and has the capacity to participate in research. Each subdistrict has one long-term care program, led by a Care Manager (CM), typically a trained nurse, along with several Community Caregivers (CCGs), typically a community health worker with additional training in elder care, who provide health and social care to non-institutionalized older adults residing in the community.

Inclusion and exclusion criteria:

To be eligible, participants needed to be age 60 and above, have probable dementia, have 1 or more NPS and have an adult (age 18+) family caregiver who lives with or spends a minimum of 4 hours every day with the PWD. An additional criterion was the ability to walk independently or with assistive device (such as canes or walkers) but without physical assistance for support from another person. Older adults were excluded from the study if they or their family caregivers did not consent to study participation or their CM and/or primary care providers did not recommend the PWD participate in the intervention due to concerns about medical conditions (e.g., severe/unstable cardiovascular disease) and/or frailty.

Recruitment process (see Figure 1 for consort diagram):

The study used a three-step process for recruiting participants including 1) referral of Thai elderly with cognitive impairment from LTC system, 2) screening for study eligibility, and 3) clinical case confirmation of likely degenerative dementia. This process was put in place because many Thai elderly in the LTC system have not been formally diagnosed with dementia.

Referral of cognitively impaired Thai elderly from LTC: To identify older adults with cognitive impairment who might be good candidates for the study, participating CMs from the LTC system reviewed their caseloads for older adults who had scored below the threshold of 17 on the Thai Mini-Mental State Examination (TMMSE), an instrument that is routinely administered and recorded in the charts of patients in the LTC system.

Screening of Thai elderly with cognitive impairment: Next, LTC patients who scored below the TMMSE threshold for cognitive impairment were referred to the study along with their family caregivers, who participated in screening with the IQCODE, NPI-Q, and Ambulatory test to determine study eligibility (see below under Measures for additional details on instruments). Elderly with IQCODE score above 3.47, presence of one or more NPS on NPI-Q, and ability to ambulate independently on the Ambulatory Walk Test were invited to participate in case confirmation.

Case confirmation: The final step in the recruitment was a case adjudication process to identify persons with probable dementia. A team consisting of the Research Assistant, Research Director, Care Manager, and Study Physician reviewed the screening results and history of medical conditions (e.g., cardiac disease, hypertension) to 1) determine if the person met clinical criteria for a degenerative dementia (according to DSM-5), and 2) identify any medical contraindications to the exercise intervention. Older adults with probable dementia and their family caregivers were then invited to participate and, if both the caregiver and person with dementia agreed to participate, they were enrolled in the study.

Measures:

Data for these analyses were collected during the screening process and/or at the time of baseline assessment. All instruments were administered by a trained research staff to either the family caregiver or the person with dementia (PWD). Specific measures included:

IQCODE (screening): The Informant Questionnaire on Cognitive Decline in the Elderly, or IQCODE, is a locally validated short questionnaire completed by a family member or friend who is familiar with the person's cognitive functioning.^{15, 16} A score of greater than or equal to 3.47 is indicative of probable dementia. The IQCODE was to identify cases/persons "at high risk" for dementia, referred to hereafter as "probable dementia."

Neuropsychiatric Inventory Questionnaire or NPI-Q (screening and baseline): The NPI-Q is a widely informant-based instrument¹⁷ based on the NPI¹⁸ which has been previously used in several studies in Thailand.⁸⁻¹⁰ The instrument is administered to an informant (usually a family caregiver or another person who knows the person with

dementia well) who reports the presence or absence of 12 different NPS in the person with dementia in the past month. For symptoms that are present, the informant also rates their level of severity (on a scale of 1–3 with 3 being very severe) and the degree to which the informant is distressed by the symptom (on a scale of 0–5 with 5 being extremely distressed). An NPI-Q total severity score is generated by calculating the sum of individual symptom severity scores (NPI-Q symptoms administered at screening; NPI-Q symptoms, severity, and caregiver distress administered at screening, baseline, and 3 and 6 months after baseline). The NPI-Q is a secondary outcome for the intervention study and was administered at screening to determine the presence or absence of NPS and again at baseline to determine the presence/absence of NPS as well as their severity and associated distress.

Ambulatory Walk Test (screening): The validated Ambulatory Walk Test tests the person's ability to walk independently or with an assistive device and was used to assess ensure participants could participate in the physical activity component of the RDAD without putting themselves at risk.¹⁹ This was administered to all participants.

Medical history questionnaire (screening): Family caregivers were administered a questionnaire that collected information on whether the participant had common chronic diseases.

Thai Mental State Examination or MSE (baseline): Based on the mini-mental status examination, the Thai version assesses multiple domains of cognitive functioning and is scored on a scale of 0–30, with lower scores indicating more cognitive impairment.²⁰ As noted above, this instrument is also administered routinely by staff in the LTC service system and was used by CCG to identify potential participants for the study.

Disability (baseline): The Barthel ADL Index relied on caregiver-proxy report, to assess level of participant's impairment in activities of daily living. For this 10-item scale, a higher score indicates better functioning.²¹

Physical role functioning (baseline): Physical role functioning, assessed by caregiver-proxy report, is one component of the SF-36 scale, and includes 4 items that assess role limitations due to physical health during the prior month, with higher scores indicated more impairment (range 0–1 for each item).²²

Caregiver burden (baseline): Caregiver burden was assessed with the 12 item version of the Zarit Burden Interview, with higher scores (individual item range is 0–4) indicating higher levels of burden.²³

Sociodemographic questionnaire (baseline): Basic sociodemographic information was collected from both the participant and the family caregiver.

Ethical:

This study was approved by IRB in Thailand and at Harvard University. The parent study has been registered on [clinicaltrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT03264378) (NCT03264378).

Statistical analysis:

First, we used descriptive statistics to summarize the baseline characteristics for both PWD and caregivers. Second, we summarized the distribution of severity levels for NPS and examined the correlation between neuropsychiatric symptom severity and caregiver distress using Spearman's correlation. Third, we used ordinary least squares (OLS) regression to examine the associations between PWD and caregiver characteristics and neuropsychiatric symptom severity. Our choice of variables to include in the multiple regression was based on a theoretical framework specifying PWD, caregiver, and environmental factors that may trigger or worsen behavioral symptoms of dementia.^{4, 7} This theoretical framework was based on a review and synthesis of the literature and was developed to help inform intervention approaches.

RESULTS

Recruitment (see Figure 1):

LTC CMs referred 942 participants to the study for initial screening. Of the 942, 396 were excluded based on the screening instruments and an additional 120 for other reasons, leaving 426 who were eligible and available for case confirmation. At case confirmation, 17 persons were ineligible based on medical history and an additional 56 were eligible but were excluded for other reasons prior to enrollment, leaving 353 in the final sample.

Sociodemographic and clinical characteristics (see Table 1):

The mean age of PWD was 81 years, more than 70% were women, and about one-third are married. Family caregiver's mean age was 55 (range from 18 to 90) and over 80% were women, usually an adult child or spouse.

Neuropsychiatric symptom prevalence, severity, and association with caregiver distress (see Table 2):

The prevalence of individual NPS varied from 18% for appetite/eating changes (least frequent symptom) to 42% for delusions (most frequent symptom). The mean number of NPS was 3.6. When present, NPS severity ranged from 1.64 for elation/euphoria to 2.12 for motoric disturbance. Caregiver distress associated with specific NPS ranged from 1.14 for elation/euphoria to 2.34 for disinhibition. Results of Spearman's correlation test show that severity of individual NPS was significantly associated with caregiver stress for all 12 NPS with all symptoms associated at the $p < 0.001$ level except for elation/euphoria ($p < 0.05$). Spearman's r ranged from 0.30 to 0.74 for the 12 NPS.

Ordinary Least squares regression predicting NPI-Q severity (see Table 3):

Among PWD characteristics, higher ADL score (less functional impairment) was inversely associated with NPI-Q total severity (unstandardized regression coefficient $b = -0.16$; standardized regression coefficient $\beta = -0.13$, $p < 0.05$). More physical role limitation was significantly associated with higher total NPI-Q severity ($b = 0.77$; $\beta = 0.24$; $p < 0.001$). Among caregivers' characteristics, higher caregiver burden was significantly associated with higher NPI-Q severity ($b = 0.19$, $\beta = 0.30$; $p < 0.001$).

DISCUSSION

To our knowledge, this is the first study in a community setting in Thailand examining the frequency and correlates of NPS. In our study, many of the older adults with dementia had multiple NPS as reported by their family caregivers. After controlling for sociodemographic and other factors, these symptoms were associated with increased functional impairment and with family caregiver burden and distress. Our study, conducted in a widely used community-based and publicly funded program to support older adults, adds to the existing literature based largely on specialty clinics and institutional settings in Thailand. Together our findings underscore the public health importance of NPS among Thai elderly with dementia and the need to strengthen supports and services to better support families in the community.

Our study demonstrates the high prevalence of NPS among community dwelling PWD in Thailand. In addition, the majority of PWD in our study had multiple NPS as reported by their family caregivers. Not surprisingly, the prevalence of NPS was in general lower compared with prior studies of Thai PWD in clinical settings^{8, 24} and long-term care facilities,⁹ even though our sample was selected based on having at least one NPI-Q symptom. The notable exception is the high prevalence of psychotic symptoms reported in our sample relative to other NPS. In other studies of PWD in clinical and nursing home settings in Thailand,^{8-10, 24} psychotic symptoms are generally among the less frequently reported NPS. In our study psychotic symptoms were most frequently reported symptoms and the prevalence was as high or higher compared with both prior clinic studies in Thailand. One possible explanation is that participants in our study may have a higher prevalence of types of dementia (i.e., vascular or Lewy Body) more commonly associated with psychotic symptoms in PWD. Further attention is needed to better understand the high levels of psychotic symptoms in Thai elderly found in this study.

We found that certain PWD and caregiver factors were significantly associated with total severity of NPS. PWD functioning, as assessed by either the ADL scale or in terms of physical role functioning, was significantly associated with severity of NPS. Caregiver burden was also significantly associated with total severity of NPS. The cross-sectional nature of this study limits our ability to draw conclusions about the meaning of these associations in terms of directional of causality. Our findings with respect to functioning and caregiver burden suggest potential negative impacts of NPS on both persons with dementia and caregivers. While NPS may contribute to disability associated with dementia and may also be stressful and burdensome for family caregivers, PWD functional disability may also play a role in triggering or worsening NPS.⁷

This study has several important limitations. First, because our sample was selected based on inclusion criteria for the larger study, including the presence of 1 or more NPS and participation in the LTC system, our sample is not representative of the general population of Thai elders with dementia. Second, the cross-sectional nature of this study limits our ability to determine the directional of causality in terms of the association of characteristics of PWD and caregivers with NPS. Third, our study did not include assessment to determine type of degenerative dementia which may have helped to characterize the sample and

explain the high levels of psychotic and other reported NPS. Finally, our choice of factors to include in our multivariate analysis predicting NPI-Q was limited by the available data collected as part of the parent intervention study. In addition, the effects sizes for the variables included in the multivariate analysis were small but of potential theoretical interest.

In conclusion, this community-based study of Thai PWD found high levels of NPS and evidence of significant family burden and distress associated with their occurrence. Our findings may help inform quality improvements in the LTC for PWD and their family caregivers, including routine screening for NPS using instruments such as the NPI-Q and enhanced education and support for caregivers. Longitudinal studies are needed to better identify potential causal pathways as well as intervention studies to understand how best to support Thai PWD and their family caregivers. These issues are more urgent given growing numbers of PWD in Thailand and other LMIC.

DISCLOSURE/CONFLICT OF INTEREST:

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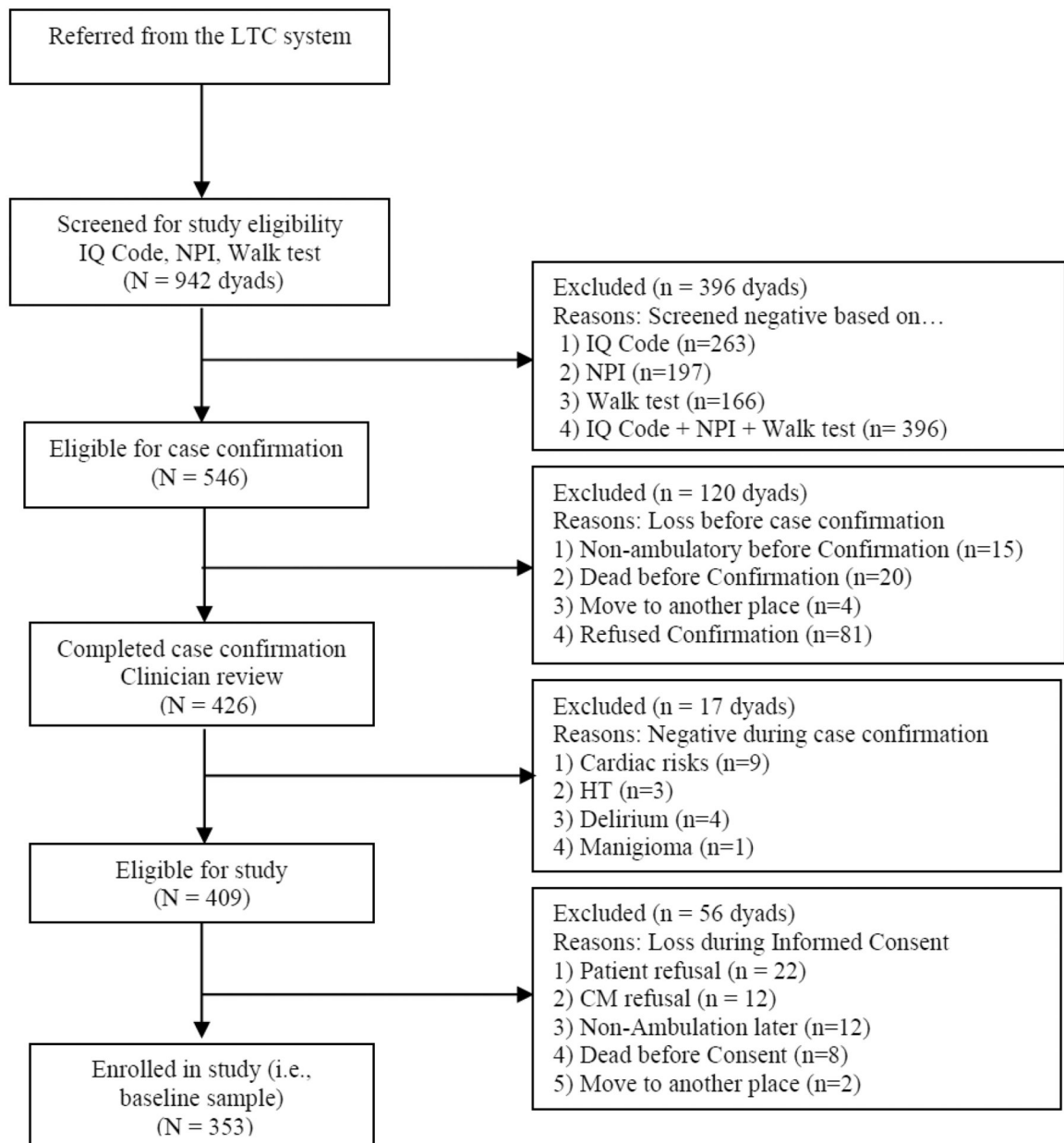


Figure 1:
Flow Diagram of Participant Selection

Table 1.

Sociodemographic and clinical characteristics of baseline sample (N= 353)

Variables	n (%) / mean (SD)
Patients' characteristics	
Age in years, mean (SD)	81.27 (7.97)
Sex	
Male, n (%)	94 (27%)
Female, n (%)	252 (73%)
Married (%)	122 (35%)
Education level (%)	
None, n (%)	35 (10%)
Primary school, n (%)	300 (85%)
Above primary school, n (%)	18 (5%)
Family size, mean (SD)	4.41 (1.75)
ADL, mean (sd)	14.82 (5.17)
TMSE, mean (sd)	12.14 (7.00)
SF-36: physical role limitation	2.28 (1.89)
NPI severity	6.81 (6.04)
Caregivers' characteristics	
Age in years, mean (SD)	55 (12.18)
Sex	
Male, n (%)	60 (17%)
Female, n (%)	293 (83%)
Relationship with patients	
Child, n (%)	246 (70%)
Spouse, n (%)	59 (17%)
Relative, n (%)	41 (11%)
Neighbor, n (%)	7 (2%)
Caregiver burden, mean (SD)	10.35 (9.25)

Table 2.

Prevalence and severity of neuropsychiatric symptoms in baseline sample & correlation of caregiver distress and NPI symptom severity (n varies) (N=353)

NPI symptoms	Present	Severity score n (% among patients having the symptom)			Symptom severity	Caregiver distress	Spearman Correlation
	n (%)	1	2	3	Mean (SD)	Mean (SD)	(r)
Delusions	149 (42%)	45 (30%)	50 (34%)	54 (36%)	2.06 (0.82)	2.09 (1.57)	0.49 ***
Hallucinations	126 (36%)	40 (32%)	39 (31%)	47 (37%)	2.06 (0.83)	2.42 (1.49)	0.59 ***
Agitation	109 (31%)	57 (52%)	27 (25%)	25 (23%)	1.71 (0.82)	2.02 (1.52)	0.60 ***
Depression	72 (20%)	33 (46%)	25 (35%)	14 (19%)	1.74 (0.77)	2.15 (1.41)	0.45 ***
Anxiety	105 (30%)	46 (44%)	39 (37%)	20 (19%)	0.75 (0.76)	2.04 (1.29)	0.61 ***
Elation	72 (20%)	36 (50%)	26 (36%)	10 (14%)	1.64 (0.72)	1.14 (1.26)	0.30 *
Apathy	99 (28%)	38 (38%)	40 (41%)	21 (21%)	1.83 (0.76)	2.03 (1.45)	0.49 ***
Disinhibition	91 (26%)	31 (34%)	44 (48%)	16 (18%)	1.84 (0.70)	2.34 (1.43)	0.66 ***
Irritability	121 (34%)	50 (41%)	47 (39%)	24 (20%)	1.79 (0.76)	2.10 (1.46)	0.67 ***
Motor	140 (40%)	39 (28%)	45 (32%)	56 (40%)	2.12 (0.82)	2.18 (1.59)	0.53 ***
Sleep/nighttime	132 (38%)	52 (40%)	36 (27%)	44 (33%)	1.94 (0.85)	2.26 (1.52)	0.74 ***
Appetite	64 (18%)	31 (48%)	23 (36%)	10 (16%)	1.67 (0.76)	1.81 (1.32)	0.61 ***

Note: (1) The mean of number of NPI symptoms was 3.63 (SD = 2.76). (2) *: $p < 0.05$; ***: $p < 0.001$. (3) Given responses for each NPI symptom and caregiver distress did not follow normal distribution, Spearman's correlation r between each NPI symptom score (range: 1–3) and corresponding distress score (range: 0–6) was used to examine their association.

Table 3

Ordinary Least square regression predicting total NPI-Q severity score in baseline sample (N = 353)

Variables	Unstandardized coefficients (<i>b</i>)	95% CI	Standardized coefficient (β)
<i>Patients' characteristics</i>			
Age in years	0.04	(-0.04, 0.12)	0.05
Female (ref: male)	1.08	(-0.32, 2.48)	0.08
Married	-0.04	(-1.67, 1.58)	-0.01
Education (ref: none)			
Primary school	1.65	(-0.18, 3.48)	0.10
Above primary school	1.00	(-2.52, 4.52)	0.04
Family size	0.10	(-0.24, 0.48)	0.03
ADL	-0.16 *	(-0.29, -0.02)	-0.13
TMSE	0.02	(-0.08, 0.11)	0.02
SF-36: Physical role limitation	0.77 ***	(0.42, 1.12)	0.24
<i>Caregivers' characteristics</i>			
Age in years	-0.02	(-0.09, 0.04)	-0.04
Female (male)	0.44	(-1.26, 2.14)	0.03
Relationship with patients (ref: child)			
Spouse	0.01	(-2.91, 2.93)	0.01
Relative	0.15	(-1.41, 1.70)	0.01
Neighbor	2.71	(-2.67, 8.08)	0.06
Caregiver burden	0.19 ***	(0.12, 0.26)	0.30

Note: (1) As results of Breusch-Pagan/Cook-Weisberg test revealed the assumption of homoskedasticity was violated ($\chi^2 = 17.36$, $p < 0.001$), we applied robust standard errors to the model. (2) Variance of Inflation Factors (VIFs) ranged from 1.04 to 2.76, indicating no severe multicollinearity. (3) Degrees of freedom: The total variance had 352 degrees of freedom; the model had 15 degrees of freedom; the residuals had 337 degrees of freedom. (4) *: $p < 0.05$; ***: $p < 0.001$; otherwise, $p > 0.05$. p -values were calculated based on two-tailed t-tests.