

Predictors of Caregiver Burden in Aged Caregivers of Demented Older Patients

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Abstract

Background

Dementia in the oldest-old is projected to increase exponentially as is the burden of their caregivers who may experience unique challenges and suffering. Thus, we aim to investigate which factors are associated with older caregivers' burden in caring demented outpatients in a multicenter cohort.

Methods

Patients and their caregivers, both aged ≥ 65 years, in the National Dementia Registry Study in Taiwan (T-NDRS) were included in this study. Caregiver burden was measured with the short version of the Zarit Burden Interview (ZBI). The correlations between the ZBI scores and characteristics of caregivers and patients, including severity of dementia, physical comorbidities, instrumental activities of daily living (IADL), neuropsychiatric symptoms assessed by the Neuropsychiatric Inventory (NPI), and family monthly income, were analyzed.

Results

We recruited 328 aged informal caregiver-patient dyads. The mean age of caregivers was 73.7 ± 7.0 years, with female predominance (66.8%), and the mean age of patients was 78.8 ± 6.9 years, with male predominance (61.0%). Multivariable linear regression showed that IADLs ($\beta=0.83$, $p<0.001$) and NPI subscores of apathy ($\beta=3.83$, $p<0.001$) and irritability ($\beta=4.25$, $p<0.001$) were positively associated with ZBI scores. The highest family monthly income ($\beta= -10.92$, $p=0.001$) and caregiver age ($\beta= -0.41$, $p=0.001$) were negatively correlated with ZBI scores.

Conclusions

Older caregivers of older demented patients experience a higher care burden when patients had greater impaired functional autonomy and the presence of NPI symptoms of apathy and irritability. Our findings provide the direction to identify risky older caregivers, and we should pay more attention to and provide support for these exhausted caregivers.

Background

Dementia is characterized by irreversible and progressive impairments in cognition, behavioral function and activities of daily living (ADL). The growing numbers of people affected by dementia, with the number expected to double every 20 years worldwide, makes caring in dementia a global public health issue (1). Because the symptoms of dementia interfere with patient function and increase their dependency, patients with dementia require more support in daily living and long-term care from their caregivers, which often results in substantial financial and health distress of their caregivers (2). The obligation to care for dementia patients is often shifted to their original family, mainly the spouse, children or siblings of the patients. Many of them have to cut back on work to take the role as caregivers

and face additional expensive medical services. Dementia patient caregivers encounter extra household expenditure, which has been shown to be associated with their caring role (3). As family is expected to be the primary source of care going forward, especially in Asian populations, understanding the burden suffered by family caregivers of dementia patients is of great importance.

Dementia caregiving has negative associations with the caregiver's physical and mental illness (4-6). Previous research has found that various factors, such as neuropsychiatric symptoms (NPS) and abnormal behaviors of demented patients, more severe dementia severity, higher functional dependence, cognitive impairment, low level of education and family income, and impaired health status of the caregivers are significantly associated with higher caregiver burden (7, 8). Although studies have tried to investigate the factors associated with caregiver burden, there is a lack of research focusing on older caregivers of patients with dementia. The age of most caregivers in past studies is often mixed, ranging from 50 to 65 years old (9-12).

Taiwan has entered the stage of an aged society as people over 65 years old accounted for more than 15.3% of the country's total population (13), and this group includes a large number of demented patients and their caregivers. However, the increase in dementia in the older adults coincides with a dramatic decline in the potential support ratio, namely, the number of persons aged 20–64 per person aged 65 or older (12). According to the population projections reported by the National Development Council of Taiwan, the potential support ratio is predicted to drop from 5.9 in 2015 to approximately 2.7 by 2030 (14), with similar declines expected in most countries worldwide (12, 15). In recent years, there has been an increase in the number of older people who have become caregivers for their elderly relatives. There is a need to examine the social context in which an older individual must take care of a centenarian one with dementia, although this emerging problem has been overlooked, and few studies have emphasized this collateral issue.

The aim of this study was to investigate factors that may be associated with informal caregiver burden for those who provide “elderly-for-elderly care”. We examined the associations among caregiver burden and demographic variables of patients and caregivers, NPS, cognitive impairments, physical dependencies, underlying medical conditions, and contextual factors in a large multicenter cohort of aged caregiver-patient dyads.

Methods

The National Dementia Registry Study in Taiwan (T-NDRS) is an ongoing collaborative study conducted by the Institute of Population Health Sciences, Taiwan National Health Research Institute since 2017. Eight hospitals (three in northern Taiwan, two in middle Taiwan and three in southern Taiwan) participated in this project. All patients with dementia received clinical examinations, including a thorough survey of medical history, physical and neurological evaluations, laboratory tests (complete blood counts, serum B12 and folic acid, thyroid hormone levels, syphilis serology, routine biochemical tests) and brain image evaluations (computed tomography or magnetic resonance imaging). The T-NDRS

aimed to investigate the baseline characteristics (including demographics, cognitive status, and other measures), cognitive and functional changes in patients with dementia and their caregivers' burden. The T-NDRS study was approved by the ethics committees of the hospital sites. Written informed consent and permission for interviews were received from all study participants and their main adult caregivers.

Study overview and inclusion criteria

All participants received assessments, and their caregivers reported patients' NPS and their own caregiver burden. General demographics and clinical information, such as history of major psychiatric diseases, neuropsychological and neuropsychiatric disturbances, functional disability, ADLs, and monthly income, physical activity per week were collected (16). For inclusion, patients in the age range between 65 and 90 years must have had a diagnosis of dementia with a clinical dementia rating (CDR) score ≥ 0.5 (covering from very mild to severe dementia) and had at least one main caregiver defined as the person who frequently took care of/talked to/interacted with the dementia patient for at least 10 hours a week. The caregivers should accompany the dementia patients for the interview and annual follow-ups. The exclusion criteria for all participants included having any other central nervous system disease other than dementia, having psychosis not due to dementia, having alcohol use disorder or hepatic encephalopathy, or having expected life expectancy less than six months. Only caregiver-patient dyads aged ≥ 65 years old were analyzed in this study. From 2017 to 2019, 328 elderly patient-caregiver dyads (19.2%) were retrieved from the T-NDRS database (Figure 1).

Diagnostic Criteria

The diagnosis of dementia type was made according to any of the following criteria: (1) NIA-AA criteria for Alzheimer's disease (AD) (17), (2) NINDS-AIREN criteria for vascular dementia (18), (3) Lund-Manchester criteria of frontotemporal dementia (19), (4) 2015 International Dementia with Lewy Bodies (DLB) conference criteria for dementia with Lewy bodies (20), and (5) The Movement Disorders Society (MDS) criteria for dementia from Parkinson's disease (21).

Assessment of questionnaire and scores

Mini-mental Status Exam (MMSE)

The MMSE is one of the widely used instruments for dementia. It provides a total score ranging from 0 - 30, with lower scores indicating greater cognitive impairment. It was administered to patients to obtain a global level of current cognitive function (22).

Clinical Dementia Rating Scale (CDR)

The severity of dementia was defined according to the CDR (23). The CDR is based on inquiries of patients or informants concerning six areas of cognitive function. Each cognitive ability was scored as 0 = normal, 0.5 = questionable, 1 = mild impairment, 2 = moderate impairment, and 3 = severe impairment, from which an overall stage of dementia was derived.

Neuropsychiatric Inventory Questionnaire (NPI-Q)

The NPI-Q is a caregiver-based questionnaire in which the caregiver indicated the presence or absence of NPS in the demented patient during the last few weeks (24). The severity scale has scores ranging from 1 to 3 (1=mild; 2=moderate; and 3=severe). A total score for the NPI-Q was generated by summing all the individual severity scores.

Instrumental Activities of Daily Living Scale (IADL)

The Lawton Instrumental Activities of Daily Living Scale was used to evaluate independent living skills of the patients with dementia, which consisted of 8 domains of functions (25). Persons are scored according to their highest level of functioning in that category. A summary score ranges from 0 (low function, dependent) to 8 (high function, independent).

Zarit Burden Interview (ZBI)

The ZBI is a 22-item, self-report measure of perceived burden among caregivers. The instrument measures the caregiver's emotion, psychological health, well-being, social and family life, finances, and degree of control over one's life (26). Each question is scored on a 5-point Likert scale. Total scores can range from 0 (low burden) to 88 (high burden).

Statistical analysis

Categorical variables were presented by numbers with percentages, and continuous variables were presented by means with standard deviations. Chi-square tests and independent t-tests were used to compare categorical and continuous variables, respectively. Multivariable linear regression analysis was conducted to assess the associations between covariates and ZBI scores (caregiver burden). β values and their 95% confidence intervals (95% CIs) were calculated after adjustments in different models. Multivariable linear regression model 1 was adjusted for all variables listed in Table 1 except NPI total scores and NPI severity scores for the 12 items. Model 2 and model 3 were model 1 plus adjusting for the total summed NPI severity scores or the severity score for each NPI item, respectively. Finally, the approaches of stepwise selection were applied in model 2 and model 3 to identify significant covariables for caregiver burden. All statistical analyses were performed using SPSS version 21.0 (IBM, Armonk, NY, USA) with 2-tailed statistical tests. P values less than 0.05 were considered statistically significant.

Results

The demographics and clinical characteristics of the patients and their caregivers are presented in Table 1. A total of 328 patients (61% male, mean age=78.8, mean education=9.5 years) were included. Their caregivers were mostly female (66.8%), with a mean age of 73.7 years and a mean education of 10.1 years. The mean ZBI score was 26.7 ± 18.1 . The majority of caregivers were spouses (87.0%) or offspring (8.8%). Most caregivers lived with the patients (91.5%) and had earnings in the middle family income class. The caregivers had a similar age distribution to the patients with dementia, with the exception that

the caregivers aged over 95 years mostly took care of patients aged 75-84 years (Table 1). Regarding the relationships between the patients and caregivers, the spouses (n=285) were in dyads with patients aged 78.1 ± 6.7 years, and caregivers aged 74.6 ± 7.0 years; the offspring (n=29) were in dyads with patients aged 88.0 ± 2.1 years, and caregivers aged 67.0 ± 1.6 years. With regard to the dementia severity of patients, the average scores were 17.8 on the MMSE, 1.2 on the CDR, and 4.3 on the IADL. Each NPI item demonstrated similar averaged severity with the exception of relatively lower severity of euphoria and relatively higher severity of sleep/nighttime behavior change.

In multivariable model 1 (Table 2), the ZBI scores were negatively associated with the highest income class but positively associated with IADLs. Physical diseases, psychiatric disorders such as major depressive disorder and anxiety, physical activities and life habits such as drinking and smoking did not show an influence on the ZBI scores. After the total NPI score was added to the analysis (model 2, Table 2), the NPI total scores were positively associated with increases in the ZBI scores (β : 1.09, 95% CI: 0.68 to 1.49, $p < 0.001$). We further analyzed each NPI item in model 3 (Table 2). The NPI scores for the apathy, depression and irritability domains were significantly associated with ZBI scores. For every additional unit of severity for the aforementioned NPI domains, there was a 3.7-point increase in the ZBI score for apathy (95% CI: 1.5 to 5.9, $p = 0.001$), a 3.3-point increase for irritability (95% CI: 0.3 to 6.3, $p = 0.03$) and a 3.0-point decrease for depression (95% CI: -6.0 to -0.0, $p = 0.047$). In addition, the NPI anxiety and euphoria domains delivered trend-like positively related influences (Table 2).

In the stepwise multivariable regression (Table 3), the model that included total NPI severity scores showed that IADLs, the highest class of family income, caregiver age and total NPI severity scores were significantly correlated with the ZBI scores. In detail and listed by the order of importance, another model including the 12 NPI items demonstrated that IADLs, NPI_irritability/lability, NPI_apathy/indifference, the highest family income, and caregiver age had significant influences on the ZBI scores. Other NPI domains did not have a significant impact on caregiver burden.

Discussion

This nationwide multicenter study included informal caregivers of patients who, for the most part, suffered from mild or moderate probable or possible AD and exhibited, on average, mild NPS (Table 1). The study was performed in 8 memory clinics of medical centers and local hospitals in both urban and rural areas. Among our aged patient-caregiver dyads, most patients were male and cared for by female family caregivers. This corresponds to international findings that have shown that caregiving for dementia patients is usually informal and a female dominant (9, 27-31). Spouses played a major role (86.9%) in caregiving in these old-old dyads, rather than offspring, such as middle-aged daughters or daughters-in-law (32, 33).

We found that family monthly income, IADL functional impairment, NPS, and caregiver age emerged as independent predictors of elderly caregiver burden in the present cohort regarding after adjusting for severity of dementia, medical comorbidities, education, relationship between patients and caregivers, and

physical activities per week. Many studies have consistently found that both NPS and functional impairment caused more distress to family caregivers than other care demands, such as cognitive deficits (8).

Our findings corroborate previous research that IADL deficits in patients with dementia were associated with more caregiver burden and depression (34, 35). In addition to the physical burden of the caregivers, the ADL dependency of the patient is also correlated with the number of care hours, and it has been shown to be the only factor independently associated with missing more hours at work for those who were employed (29).

By conducting multiple regression analysis using different NPS as individual predictors of caregiver burden, we found that the NPI apathy and NPI irritability subscores were independent factors for caregiver burden. Comparably, Dauphinot et al found the presence of apathy, agitation/aggression, aberrant motor behavior, appetite changes, and irritability to be significantly and independently associated with caregiver burden in 548 French caregivers, without mention of the mean value of caregiver's age (34). Studies on older adult caregivers, one in the USA and the other in Taiwan, showed that delusions, agitation/aggression and irritability of demented patients caused the most distress to their caregivers (10, 36). In dementia, the burden of providing care for ADLs is often exacerbated by NPS (37). Fauth and colleagues found that NPS that occurred in the context of ADL assistance (i.e., care refusal) mainly accounted for the associations between ADL impairments and measures of caregiver burden (38).

Dementia creates a substantial burden on human and financial resources, and unpaid assistance is the costliest component of the total cost of home care (39). It is common for family caregivers to experience financial strain as a result of providing care during the long disease course of dementia, both when the relative is cared for at home or in nursing homes (40). Adult caregivers with low incomes experience more distress than caregivers with higher incomes (11, 41), and low levels of financial resources have been shown to predict depression in dementia patient caregivers (42). Caregivers with higher financial resources probably have more access to supportive services (home health aides, adult day care) that may reduce their burden (42). Compared with adult caregivers, most elderly caregivers are retired or unemployed. Developing policies such as programs that pay family caregivers, providing financial compensation, and special tax deductions for caregivers may be helpful. Further larger-scale follow-up cohort studies are required to verify this opinion.

Similar to several publications (27, 30, 43, 44) but in contrast to other studies (45-47), our study revealed an inverse relationship between caregiver burden and caregiver age among those aged 65 and older. Young-old caregivers may still be employed, and caregiving-related interference with occupation and leisure time activities might explain the more severe burden in young-old than old-old caregivers.

Our findings may help to identify elderly caregivers who are at risk of caregiver burden and serve to take targeted steps to alleviate their suffering, such as effective management of IADL functional decline and NPS of the client, personal and psychological support for the caregiver, and presumably, better financial funding of informal care.

This study had several limitations. First, information about caregiver-related health problems, social support, and cumulative duration of care was not available in the T-NDRS. Without these, we cannot evaluate their impacts. Second, this study only recruited caregiver-patient dyads who had sought medical services. In addition, most of the eight participating hospitals were medical centers, and our findings may not be generalizable to those visiting community clinics alone or those not seeking medical help.

Conclusion

Older caregivers of aged demented patients experience higher caregiver burden, which may be positively associated with impairments in functional autonomy and more severe NPS of apathy and irritability and negatively correlated with higher family income.

Abbreviations

AD: Alzheimer's disease

ADL: activities of daily living

CDR: clinical dementia rating

DLB: Dementia with Lewy Bodies

IADL: Instrumental Activities of Daily Living Scale

MDS: Movement Disorders Society

MMSE: Mini-mental Status Exam

NPI-Q: Neuropsychiatric Inventory Questionnaire

NPS: neuropsychiatric symptoms

T-NDRS: National Dementia Registry Study in Taiwan

ZBI: Zarit Burden Interview

Declarations

Ethics approval and consent to participate:

Written informed consent and permission for interviews and publication were received from all study participants and their main adult caregivers. The National Dementia Registry Study was approved by the ethics committees of the eight participated hospital sites.

Availability of data and materials:

The data that support the findings of this study are available from National Dementia Registry Study group (T-NDRS) but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of T-NDRS study group (National Health Research Institutes, Taiwan) via corresponding author.

Consent for publication:

Not Applicable

Competing interests:

The authors declare that they have no competing interests.

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Authors' contributions:

Study concept and design: Tsai CF, Hwang WS, Hsu CC, Fuh JL. Data acquisition:

Tsai CF, Lee JJ, Wang WF, Huang LC, Huang LK, Lee WJ, Sung PS, Liu YC, Fuh JL

Data analysis: Tsai CF, Hwang WS, Fuh JL. Interpretation of data: all authors.

Drafting of the manuscript: Tsai CF, Hwang WS. Critical revision of the manuscript:

all authors. Fuh JL had full access to all data in this study and takes responsibility for

the integrity of data and the accuracy of data analysis.

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Tables

Table 1 Demographic data of patients with dementia (n=328) and their caregivers

	Mean (SD) / n(%)		Mean (SD) / n(%)
Patient_Age	78.82 (6.92)	Physical diseases	
Patient_Sex, Male	200 (61.0%)	Hypertension	205 (62.5%)
Patient_Education, yr	9.45 (5.20)	Diabetes	92 (28.0%)
Caregiver_Age	73.65 (6.99)	Hyperlipidemia	101 (30.8%)
Caregiver_Sex, Male	109 (33.2%)	Ischemic stroke	41 (12.5%)
Caregiver_Education, yr	10.08 (4.74)	Hemorrhagic stroke	12 (3.7%)
Relationship		Transient Ischemic Attack	30 (9.1%)
Spouse	285 (86.9%)	Head trauma	17 (5.2%)
Offspring	29 (8.8%)	CAD	17 (5.2%)
Others	14 (4.3%)	Heart failure	7 (2.1%)
		MDD	16 (4.9%)
Live together, yes	300 (91.5%)	Anxiety	23 (7.0%)
Family income		NPI_severity_Total	4.45 (5.16)
<30,000 NTD	104 (31.7%)	NPI severity_Delusion	0.38 (0.81)
30000~100000 NTD	192 (58.5%)	NPI severity_Hallucination	0.31 (0.75)
>100000 NTD	28 (8.5%)	NPI severity_Agitation	0.38 (0.77)
MMSE	17.78 (7.07)	NPI severity_Depression	0.39 (0.77)
CDR	1.16 (0.78)	NPI severity_Anxiety	0.40 (0.78)
IADL	4.33 (5.76)	NPI severity_Euphoria	0.08 (0.34)
Drinking, yes	8(2.4%)	NPI severity_Apathy	0.55 (0.91)
Smoking, yes	26 (7.9%)	NPI severity_Disinhibition	0.29 (0.70)
ZBI score	26.65 (18.12)	NPI severity_Irritability	0.48 (0.84)
Physical activity in 7 days		NPI severity_Aberrant	0.25 (0.63)
Vigorous activities,yes	29 (8.8%)	NPI severity_ Sleep/nighttime behavior change	0.61 (1.00)
Moderate activities,yes	67 (20.4%)	NPI severity_Appetite	0.32 (0.72)
Walking,yes	234 (71.3%)		
Sitting,yes	327 (99.7%)		

Abbreviations: SD=standard deviation; NTD=new Taiwan dollar; MMSE= mini-mental state examination; CDR= clinical dementia rating Scale, IADL= instrumental activities of daily living, ZBI=Zarit Burden Interview, CAD=coronary artery disease; MDD=major depressive disorder; NPI=Neuropsychiatric Inventory.

Table 2. Multivariable linear regressions for ZBI scores of different models

	Model 1		Model 2 (NPI_severity_total)		Model 3(NPI_severity)	
	β (95% C.I)	P value	β (95% C.I)	P value	β (95% C.I)	P value
Pt_Age	-0.34 (-0.72 to 0.04)	0.080	-0.34 (-0.71 to 0.02)	0.066	-0.27 (-0.63 to 0.10)	0.151
Pt_Sex, Male	2.25 (-5.26 to 9.77)	0.555	0.47 (-6.75 to 7.69)	0.899	0.45 (-6.76 to 7.67)	0.902
Pt_Education, yr	-0.33 (-0.86 to 0.21)	0.232	-0.34 (-0.86 to 0.17)	0.185	-0.37 (-0.88 to 0.14)	0.157
Caregiver_Age	-0.23 (-0.62 to 0.16)	0.253	-0.15 (-0.53 to 0.22)	0.417	-0.24 (-0.62 to 0.14)	0.211
Caregiver_Sex, Male	-4.99 (-13.06 to 3.08)	0.225	-6.58 (-14.32 to 1.16)	0.095	-5.62 (-13.35 to 2.11)	0.153
Caregiver_Education, yr	0.47 (-0.07 to 1.02)	0.088	0.39 (-0.13 to 0.92)	0.141	0.32 (-0.21 to 0.85)	0.241
Relationship						
Spouse	0.00 (reference)		0.00 (reference)		0.00 (reference)	
Offspring	7.08 (-4.46 to 18.61)	0.228	6.69 (-4.35 to 17.73)	0.234	4.19 (-6.92 to 15.29)	0.459
Others	-5.80 (-16.91 to 5.30)	0.305	-7.79 (-18.44 to 2.87)	0.151	-7.44 (-18.17 to 3.30)	0.174
Live together, yes	7.25 (-1.30 to 15.80)	0.096	4.81 (-3.42 to 13.05)	0.251	3.80 (-4.47 to 12.08)	0.367
Family income						
<30,000 NTD	0.00 (reference)		0.00 (reference)		0.00 (reference)	
30000~100000 NTD	2.05 (-2.35 to 6.46)	0.360	2.38 (-1.84 to 6.60)	0.268	2.34 (-1.84 to 6.53)	0.271
>100000 NTD	-9.54 (-17.02 to -2.06)	0.013*	-9.29 (-16.45 to -2.14)	0.011*	-8.99 (-16.08 to -1.90)	0.013*
MMSE	-0.22 (-0.65 to 0.22)	0.329	-0.22 (-0.64 to 0.19)	0.294	-0.28 (-0.70 to 0.14)	0.185

	Model 1		Model 2 (NPI_severity_total)		Model 3(NPI_severity)	
	β(95% C.I)	P value	β(95% C.I)	P value	β(95% C.I)	P value
CDR	-0.75 (-4.47 to 2.97)	0.692	-2.81 (-6.45 to 0.83)	0.130	-3.91 (-7.62 to -0.20)	0.039*
IADL	0.96 (0.50 to 1.41)	<0.001*	0.94 (0.51 to 1.38)	<0.001*	1.00 (0.55 to 1.45)	<0.001*
Drinking, yes	-5.18 (-17.57 to 7.21)	0.411	-3.36 (-15.23 to 8.51)	0.578	-4.13 (-15.87 to 7.61)	0.489
Smoking, yes	-0.84 (-8.18 to 6.51)	0.823	-1.26 (-8.29 to 5.77)	0.725	-0.30 (-7.43 to 6.83)	0.934
Physical activity in 7 days						
Vigorous activities, yes	0.63 (-6.60 to 7.87)	0.863	0.71 (-6.21 to 7.63)	0.840	1.58 (-5.38 to 8.53)	0.656
Moderate activities, yes	-3.20 (-8.67 to 2.27)	0.251	-1.69 (-6.95 to 3.58)	0.528	-1.25 (-6.49 to 4.00)	0.640
Walking, yes	1.23 (-3.68 to 6.14)	0.622	2.29 (-2.43 to 7.00)	0.341	1.30 (-3.52 to 6.13)	0.595
Sitting, yes	7.94 (-26.57 to 42.44)	0.651	-1.75 (-34.95 to 31.45)	0.917	2.65 (-30.83 to 36.13)	0.876
Physical diseases						
Hypertension	-1.75 (-5.90 to 2.40)	0.407	-1.03 (-5.01 to 2.95)	0.611	-1.79 (-5.76 to 2.18)	0.375
Diabetes	0.87 (-3.50 to 5.23)	0.696	1.52 (-2.67 to 5.70)	0.476	1.93 (-2.32 to 6.19)	0.371
Hyperlipidemia	-0.06 (-4.77 to 4.64)	0.979	0.82 (-3.69 to 5.34)	0.719	0.37 (-4.13 to 4.86)	0.872
Ischemic stroke	0.22 (-6.71 to 7.15)	0.951	0.01 (-6.62 to 6.64)	0.998	-0.42 (-7.05 to 6.20)	0.900
Hemorrhagic stroke	0.03 (-10.16 to 10.22)	0.995	0.69 (-9.06 to 10.44)	0.889	-1.05 (-10.76 to 8.66)	0.831

	Model 1		Model 2 (NPI_severity_total)		Model 3(NPI_severity)	
	β(95% C.I)	P value	β(95% C.I)	P value	β(95% C.I)	P value
Transient Ischemic Attack	1.09 (-5.71 to 7.88)	0.753	0.91 (-5.59 to 7.42)	0.782	1.38 (-5.08 to 7.83)	0.675
Head trauma	4.01 (-4.81 to 12.84)	0.371	1.44 (-7.05 to 9.94)	0.738	-0.97 (-9.71 to 7.77)	0.828
CAD	2.58 (-6.35 to 11.52)	0.570	1.94 (-6.62 to 10.49)	0.656	2.89 (-5.84 to 11.61)	0.516
Heart failure	-3.76 (-17.79 to 10.27)	0.599	-2.59 (-16.02 to 10.84)	0.704	-5.97 (-19.40 to 7.46)	0.382
MDD	-1.34 (-13.32 to 10.65)	0.826	-5.62 (-17.20 to 5.95)	0.340	-6.08 (-17.90 to 5.73)	0.312
Anxiety	6.54 (-3.58 to 16.66)	0.205	3.37 (-6.38 to 13.13)	0.496	5.32 (-5.12 to 15.75)	0.317
NPI_Total			1.09 (0.69 to 1.49)	<0.001*	N/A	
NPI_Delusion					1.26 (-1.57 to 4.10)	0.380
NPI_Hallucination					-2.03 (-5.21 to 1.15)	0.211
NPI_Agitation					0.99 (-2.09 to 4.08)	0.526
NPI_Depression					-3.03 (-6.00 to -0.06)	0.046*
NPI_Anxiety					2.84 (-0.16 to 5.84)	0.063
NPI_Euphoria					5.82 (-0.28 to 11.91)	0.061
NPI_Apathy					3.70 (1.47 to 5.93)	0.001*
NPI_Disinhibition					0.63 (-2.83 to 4.09)	0.721
NPI_Irritability					3.33 (0.30 to 6.36)	0.031*

	Model 1		Model 2 (NPI_severity_total)		Model 3(NPI_severity)	
	β (95% C.I.)	P value	β (95% C.I.)	P value	β (95% C.I.)	P value
NPI_Aberrant motor activity					-0.83 (-4.35 to 2.70)	0.644
NPI_Night					1.25 (-0.72 to 3.22)	0.214
NPI_Appetite					1.97 (-0.76 to 4.69)	0.157

*p<0.05

Abbreviations: NTD=new Taiwan dollar; MMSE= mini-mental state examination; CDR= clinical dementia rating Scale, IADL= instrumental activities of daily living CAD=coronary artery disease; MDD=major depressive disorder;

Table 3. Multivariable linear regression in a stepwise manner

NPI_Severity_total model	β (95% C.I.)	P value
NPI_Severity_Total	1.03 (0.68 to 1.37)	<0.001
IADL	0.79 (0.48 to 1.10)	<0.001
Family income: >100000 NTD vs <30,000 NTD	-10.50 (-16.74 to -4.26)	0.001
Caregiver_Age	-0.40 (-0.65 to -0.15)	0.002
NPI_severity_12 items model		
IADL	0.83 (0.52 to 1.13)	<0.001
NPI_irritability_severity	4.25 (2.11 to 6.39)	<0.001
NPI_Apathy_severity	3.83 (1.85 to 5.81)	<0.001
Family income: >100000 NTD vs <30,000 NTD	-10.92 (-17.06 to -4.77)	0.001
Caregiver_Age	-0.41 (-0.65 to -0.16)	0.001
NPI_Euphoria_severity	5.76 (0.62 to 10.90)	0.028

Abbreviations: IADL= instrumental activities of daily living; NPI=Neuropsychiatric Inventory.

Figures

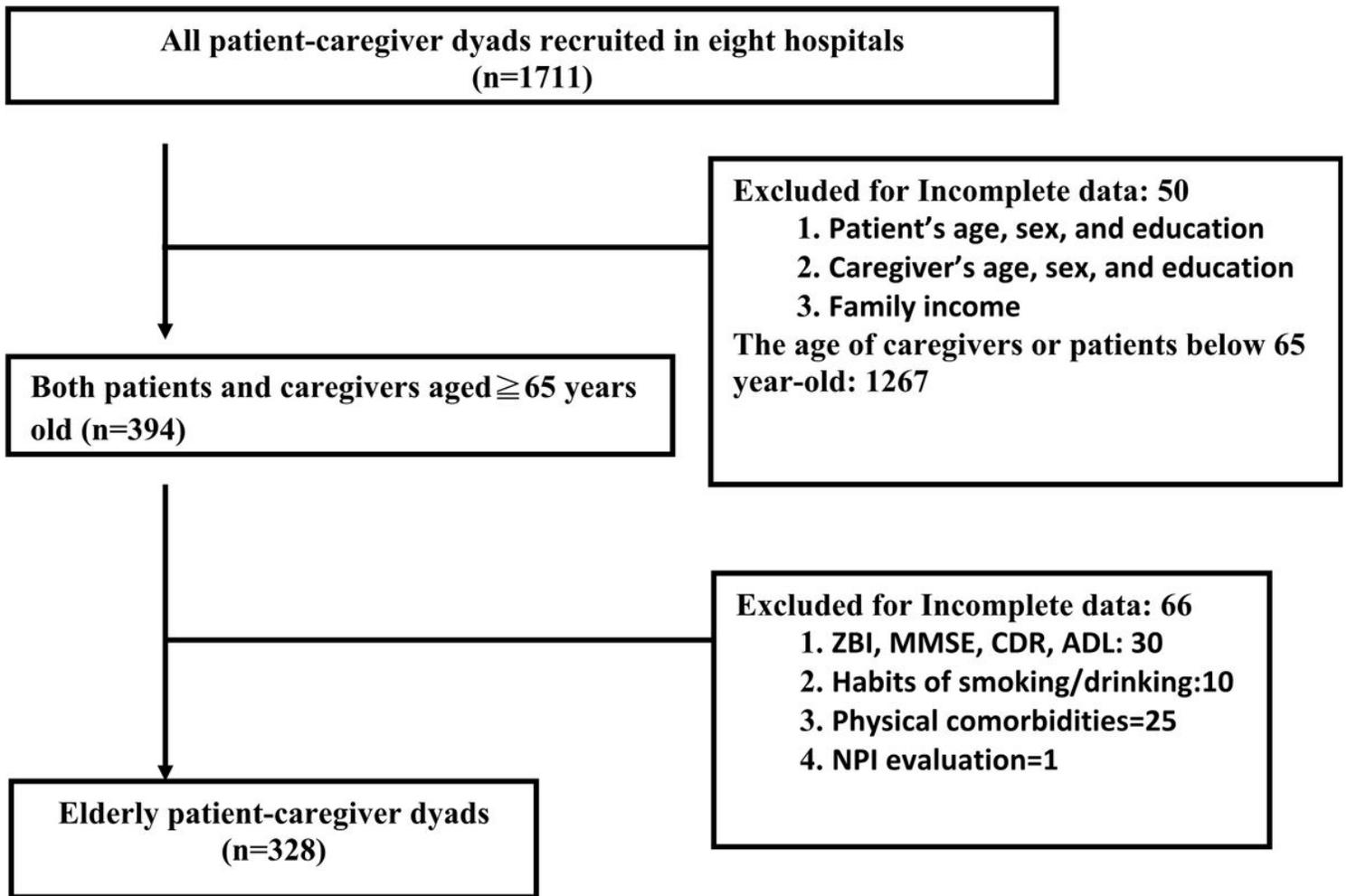


Figure 1

Flow chart of the enrollment of study participants