# A comparative study of caregiver strain in Parkinson's disease between Japan and the United States

by

Haruko Tanji, MD

Department of Neurology, Hematology, Metabolism, Endocrinology and Diabetology

(DNHMED), Yamagata University School of Medicine, Yamagata, Japan

# TABLE OF CONTENTS

Co	ver Page
Tal	ble of Contents1
Lis	t of Abbreviations2
Ab	stract3
Th	esis
A.	Introduction6
B.	Methods9
C.	Results14
D.	Discussion20
E.	Acknowledgements32
F.	References33
G.	Tables42

# LIST OF ABBREVIATIONS

BDI	Beck Depression Inventory
BSI	Brief Symptom Inventory
CIRS-G	Cumulative Illness Rating Scale-Geriatric Version
CSI	Caregiver Strain Index
GH	General health perception
HY stage	Hoehn and Yahr stage
LTCI	Long term care insurance
MCS	Mental component summary
MMSE	Mini-Mental State Examination
PCS	Physical component summary
PD	Parkinson's disease
QoL	Quality of life
S&E ADL Scale	Schwab and England Activities of Daily Living Scale
UPDRS	Unified Parkinson's Disease Rating Scale
US	United States

#### ABSTRACT

Background: Japan and the United States (US) have different backgrounds of caregiving with regard to culture, family structure, and social support system, which could differentially affect caregiver strain and quality of life (QoL) in each country.
Objectives: This study compared (1) caregiver strain in spouses of Parkinson's disease (PD) patients, (2) QoL of PD patients, and (3) QoL of spouses of PD patients in Yamagata, Japan and in Maryland, US, and determined patient and spousal factors associated with caregiver strain.

**Methods**: In Yamagata and in Maryland, spouses of PD patients completed questionnaires assessing caregiver strain (Caregiver Strain Index). Patients and spouses completed scales assessing health related QoL (SF12v2), mental health (Beck Depression Inventory in Yamagata, Brief Symptom Inventory-18 in Maryland), and medical comorbidity (Cumulative Illness Rating Scale-Geriatrics Version). PD severity and disability were assessed with the Unified Parkinson's Disease Rating Scale and the Schwab and England Activities of Daily Living Scale. The results in Yamagata and in Maryland were compared using the Student t-test and Chi-square test. The relationships between caregiver strain and patient and spousal variables were analyzed with univariate correlations and multivariate regression. **Results**: One hundred seventy eight spouse-patient pairs were assessed. Couples with PD in Yamagata were older, had less education and employment, and had more advanced disease than patients in Maryland. PD patients in Yamagata had less comorbidity and their spouses received more help from others for caregiving than in Maryland. There was no significant difference between Yamagata and Maryland on the level of caregiver strain, but spouses in Yamagata felt physical, time and financial pressure, while spouses in Maryland felt more emotional distress than physical and social pressure. Patient depression was highly correlated with caregiver strain in Maryland. In both locations, spousal depression was a significant contributor to caregiver strain. A component of SF-12v2 (general health perception) of patients with PD and their spouses in Yamagata was lower than that of patients and spouses in Maryland.

**Conclusion**: More physical support for longer hours might be attained by using the Japanese Long Term Care Insurance more effectively, which could be helpful for couples in Yamagata. In Maryland, interventions to improve patient depression could have a positive impact on caregiver strain. In both countries, spousal mental health was strongly correlated with caregiver strain, and interventions to enhance mental health of not only PD patients but also their spouses could reduce caregiver strain.

#### **INTRODUCTION**

Parkinson's disease (PD) is the second most common neurodegenerative disease with wide-ranging impairments such as gait disturbance, bradykinesia, postural instability, tremor, rigidity, depression, cognitive impairment, and autonomic dysfunction<sup>1</sup>. Despite all medical and surgical efforts, the diverse impairments of PD reduce mobility and affect social interaction, leading to disability and dependence on their caregivers in the advanced stages.

Caregiving is important in the management of PD. Support from caregivers, including physical assistance, support for depression, and management of anti-parkinsonian medications, is essential for the patient. Simultaneously, multi-dimensional impairments of PD oblige caregivers to make major adjustments to their daily lives. Disability and emotional debilitation of patients with PD often result in physical and psychosocial strain in caregivers<sup>2</sup>. Caregiver strain is significantly correlated with patient disability, mental health problems and axial symptoms such as falls<sup>2</sup>. Caregiver psychological wellbeing, depression, and problems with social support also significantly correlate with caregiver strain in PD<sup>3,4,5</sup>.

Zarit et al. gave an operational definition of the burden of caregiving, which they

 $\mathbf{5}$ 

defined as the extent to which caregivers perceived their emotional or physical health, social life and financial status as suffering as a result of caring for their relatives<sup>6</sup>. Caregiving is based on a set of subjective assumptions about need, security, and self-sufficiency, limited by objective aspects such as societal and social support systems<sup>7</sup>. The perceptions and expectations of caregiving influence our vision of caregiver strain, and they vary from one culture to another. Also, objective aspects of caregiving are limited by available resources which are defined by medical and social support systems. Caregiver strain is such a complex of multifactorial variables that it is difficult to assess, interpret, and intervene.

Quality of life (QoL) also has a multidimensional nature, including clinical, psychological, and socio-demographic factors<sup>8</sup>. Spouse caregivers are at high risk of reduced QoL because of the energy involved in providing the required care. However, not only the stress of caregiving but also social support, education, communication, and length of marriage influence caregiver QoL<sup>9</sup>. QoL of patients and spouse caregivers are intertwined since the patient-caregiver dyad functions as a unit at home<sup>8</sup>. Cultural and social aspects of QoL of both patients and spouses could be influenced by differences between two different countries.

Comparing the similarities and differences on caregiver strain and QoL between two

different societies offers an opportunity to explore caregiver strain and QoL from a different point of view and to add new sights to it. In 2000, Japan implemented a Long Term Care Insurance Plan (LTCI) for the elderly over 65, in addition to the existing universal coverage of public health insurance for Japanese citizens of all ages<sup>10</sup>. Furthermore, in Japan, the Specified Disease Treatment Research Program subsidizes medical care for patients with rare and intractable diseases including PD<sup>11</sup>. In the United States (US), there are only private long term insurance plans available and no universal national health insurance. The differences between the social support systems in the two countries may have important implications for caregiver strain and QoL of patients with PD and their spouses in each country; however, such differences have rarely been considered in the assessment of caregiver strain and QoL in PD.

The objective of this study was to compare (1) caregiver strain in spouses of PD patients (2) QoL of PD patients and (3) QoL of spouses of PD patients in Japan and the US. Also, the correlations between caregiver strain and PD symptoms, disability, cognitive impairment, mental problems, comorbidity, medications, social support, and QoL are examined.

This study draws on data from two sites: Yamagata Prefecture, in Japan and the State of Maryland in the US. These two areas are different in terms of size, population, social

class, and ethnicity. Maryland is a service-oriented urban state located close to Washington D.C.. Yamagata is an agricultural prefecture with a high proportion of traditional three-generation families<sup>12</sup>. The comparison between two areas in different countries offers the advantage of exploring the effect of diverse social and cultural conditions on caregiver strain and QoL and how we should interpret and intervene in them in each country.

#### **METHODS**

#### **Subjects**

PD patient-spouse pairs seen at the University of Maryland School of Medicine Parkinson Disease and Movement Disorders Center between April 2004 and November 2005, and PD patient-spouse pairs seen at the Department of Neurology in the Yamagata University School of Medicine and the general hospitals in Yamagata Prefecture, Japan between June 2008 and August 2011 consented to participate in the study. The study was approved by the Institutional Review Board of all participating institutions. Inclusion criteria for participation were: diagnosis of PD [by neurologists using the following criteria: asymmetrical onset of at least two of the three cardinal signs (resting tremor, rigidity, and bradykinesia) with no atypical signs or exposure to dopamine blocking medications], patient and spouse living together, and patient and spouse able to complete questionnaires, with supervision if necessary.

#### Measures

# Spouse Variables

Caregiver strain was assessed with the Caregiver Strain Index (CSI) with higher scores

indicating greater caregiver burden<sup>13</sup>. In Yamagata, a validated Japanese version of CSI was used<sup>14</sup>.

# **Patient Variables**

Disease impairment and disability were assessed with the Unified Parkinson's disease rating scale (UPDRS)<sup>15</sup>, Hoehn and Yahr (HY) staging<sup>16</sup>, the Mini-Mental State Examination (MMSE)<sup>17</sup>, and Schwab and England Activities of Daily Living Scale (S&E ADL Scale)<sup>18</sup> by either the treating neurologist or a trained examiner (HT) during the office visit. Demographic data including current medications and duration of PD was reported by the treating neurologist or obtained from the medical record of each patient. Social support was defined as help that patients received from others apart from primary caregivers, such as support from other family members, relatives, friends, and professional caregivers including the LTCI services in Yamagata. For Japanese patients, the level of mandatory public LTCI received was reported by the spouses. In Japan, everyone aged 40 years and older pays premiums, and everyone aged 65 years and older is eligible for benefits from this system. Eligibility is assessed by use of a questionnaire based on ADL, with a categorization into one of seven levels (not certified, support required, care level 1, 2, 3, 4, and 5, defined by the total amount of care assistance time required, as estimated by a 67-item assessment). Each level sets the ceiling amount of services that can be purchased as benefits. Elderly beneficiaries contribute 10% of the payment for services received. Higher levels indicate more severe disability<sup>10,19</sup>.

### Variables of spouses and patients

Demographic data including age and years of marriage were collected from patient and caregiver questionnaires. Medical comorbidity of both patients and spouses was assessed with the Cumulative Illness Rating Scale-Geriatrics Version (CIRS-G)<sup>20</sup>. Higher scores indicated greater medical comorbidity. CIRS-G was translated into Japanese and used to calculate a total score of CIRS-G for the subjects in Yamagata. Mental health of both patients and spouses was assessed with the Beck Depression Inventory (BDI)<sup>21,22</sup> in Yamagata and the Brief Symptom Inventory 18 (BSI)<sup>23</sup> in Maryland. The BDI is a widely used self-report instrument for measuring the severity of depression, translated into many languages including Japanese with high levels of reliability and validity across cultures. The BSI has three subscales (depression, anxiety, and somatization), and a global psychiatric symptom index. Psychiatric ratings are represented as T-scores with a mean of 50 and standard deviation of 10 for the general population in the US. Higher scores indicate greater psychiatric morbidity in both scales.

Health-related QoL was assessed with the SF12v2 health status survey,<sup>24</sup> which consists of the following subscales: "physical functioning"(PF), "role physical"(RP), "bodily pain"(BP), "general health perception"(GH), "vitality"(VT), social functioning"(SF), "role emotional"(RE), and "mental health"(MH). The SF12v2 also has both physical health summary score (Physical Component Summary, PCS) and mental health summary scores (Mental Component Summary, MCS). The summary scores are reported as T-scores which are normalized against the general population to have a mean of 50 and standard deviation of 10 with higher scores indicating better QoL. The validated Japanese version was used in Yamagata<sup>25</sup>. Age-matched national norms of each country were used for comparison<sup>25,26</sup>.

# Statistical Analysis

Differences between Japan and the US on disease severity, disability, cognitive impairment, and medications for patients, caregiver burden for spouses, and demographics, comorbidity, and QoL for both patients and spouses were examined using the Student t-test. Spearman's correlations between caregiver strain and predictor variables were performed. The impact of predictor variables on caregiver strain and health related QoL was examined using multivariate regression. To adjust for multiple comparisons on the t-tests and correlations, the Benjamin-Hochberg False Discovery Rate was used<sup>27</sup>. A modified *P* value of 0.03 (0.026-0.028) was calculated using the formula: [Modified P=P (m+1) / 2m [P= 0.05, m = number of tests].

#### RESULTS

One hundred and twenty US patient-spouse pairs were asked to participate in the present study. Twelve spouses and 10 patients declined due to time constraints, and two pairs were excluded due to incomplete answers on study questionnaires resulting in a sample of 96 US patient-spouse pairs (192 subjects).

Ninety nine Japanese patient-spouse pairs were asked to participate. Five spouses and five patients declined due to time constrains, two patients could not participate because of the exacerbation of their comorbidity, and five were excluded because of incomplete answers on study questionnaires, resulting in a sample of 82 Japanese patient-spouse pairs (164 subjects).

#### 1. Comparison between Japan and US patient-spouse pairs

Patients and spouses in Yamagata were older, less well-educated, and had lower employment than their counterparts in Maryland, and the patients in Yamagata had less comorbidity than patients in Maryland (Table 1). Patients in Yamagata had more advanced disease at a shorter time after diagnosis than patients in Maryland. The MMSE scores of patients were lower in Yamagata than in Maryland. Every type of anti-parkinsonian medication except entacapone (data not shown) was used more frequently in Yamagata than in Maryland. Benzodiazepines were used more frequently in Japan and antidepressants were used more often in Maryland (Table 1).

More couples in Yamagata received help from others for caregiving than in Maryland. Indeed, 41.3% of spouses received help from others in Yamagata, while only 4.3% of spouses received assistance on caregiving from others in Maryland (Table 1). The utilization of the LTCI by each HY stage is shown in Table 2. The mean level of the LTCI in the Yamagata subjects was 2.5 (total estimated assisting care time by the LTCI: about 70 min per day) with usage 2.1 days per week on average.

There was no significant difference on CSI total score between the two areas (CSI:  $4.2\pm3.6$  in Yamagata vs.  $3.7\pm3.4$  in Maryland, P=0.34) (Table 1). The comparison on mean score of each item in CSI showed a significant difference on items 3, 7, 9, 10, and 12 (Table 3). This result showed that spouses in Yamagata scored higher on items related to time demand and physical and financial distress and that those in Maryland scored higher on items asking about their emotional distress. In Japan, there was no significant difference on CSI between the group using LTCI and the group not using LTCI (Table 4).

Table 5 shows scores for each domain of SF12v2 for patients and spouses in the two locations. Patients in Yamagata attained lower scores in the subscale of GH, VT, and RE,

and spouses in Yamagata attained lower scores in the subscales of GF, VT, RE, and SF than their counterpart in Maryland. The PCS and MCS scores of health-related QoL are shown in Table 6. In both areas, physical and mental health QoL of PD patients were substantially worse than the age-matched national standard in each country (Table 6). In Yamagata, mental health QoL of PD spouses was also found to be compromised compared to the norm (Table 6).

# 2. Correlations of caregiver burden with patient and spouse variables

Increased disease severity, lower ADL, and greater comorbidity of patients were correlated with higher caregiver strain in both countries (Table 7). More severe cognitive impairment of patients was associated with higher caregiver strain in Yamagata, while higher patient depression scores were correlated with higher caregiver strain in Maryland (Table 7).

Worse spousal mental health was associated with higher caregiver strain in both communities (Table 7). In the Maryland sample, it was found that patient depression and more frequent utilization of antidepressants and benzodiazepines were correlated with higher CSI (Table 7). Severe axial symptoms such as gait impairment, postural instability, and fall in patients were correlated with high caregiver strain in both locations (Table 8).

#### 3. Multivariate regression analysis on caregiver strain (CSI)

To determine which variable contributed the most to caregiver strain (CSI), multivariate linear regression was performed by entering variables that were correlated with CSI into the regression in blocks of patient and spousal variables for subjects in Yamagata and Maryland. In the case of variables within similar domains, the highest correlated variable was chosen due to the potential for multicollinearity. For example, HY stage and postural instability were excluded due to high inter-correlations with gait (r > 0.70) and number of years of marriage was excluded due to high inter-correlation with age (r > 0.70). The country where the patient and spouse lived was entered as a dichotomous variable (Japan=0, US=1) to assess the contribution of cultural and social differences between the countries to caregiver strain. In this analysis, spousal mental health was represented with spousal mental health QoL (MCS), instead of BDI or subtotal score of the BSI, which was only available in the subjects either in Yamagata or in Maryland.

When variables of both patients and spouses were included, 40% of the variance in CSI was accounted for (Table 9). In the analysis with both patient and spousal variables, the most predictive variables were spousal mental health QoL (MCS), followed by patient fall and patient comorbidity (Table 9). In this model, the country was not a significant

predictor of CSI.

To examine which variable contributed the most to CSI in each location, multivariate linear regressions were performed with the subjects in Yamagata and in Maryland, separately. When variables of both patients and spouses in Yamagata were included, 23% of the variance in CSI was accounted for (Table 10, Model A). In the analysis with both patient and spousal variables, the most predictive variables were patient fall, followed by spousal depression in Yamagata. When variables of couples in Maryland were analyzed, 57% of the variance in CSI could be accounted for (Table 10, Model B). In the analysis with both patient and spousal variables, the most predictive variables were patient depression, followed by help from others for caregiving and spousal depression in Maryland.

#### 4. Multivariate Regression Analysis on QoL

To examine which variables contributed to health related QoL, multivariate regression was performed by entering variables that correlated with each subscale score of SF12v2 into the regression. Original subtotal scores of SF12v2 were used for the regressions instead of t-scores, to assess the effect of the difference between the countries on QoL without the influence of national standardization. In the case of variables within similar

domains, the highest correlated variable was chosen because of the potential for multicollinearity. In the regression, the country where the patient and spouse lived was entered as a dichotomous variable (Japan=0, US=1) to assess the contribution of cultural and social differences between countries to QoL. In the analysis with both patient and spousal variables, the most significant predictor of spousal general health perception (GH of SF12v2) was spousal comorbidity (CIRS-G), followed by country (Japan/US) and spousal education (Table 11, Model A). The most significant predictor of patient GH was the country (Japan/US), followed by employment status, postural instability, and motivation (Table 11, Model B). The country (Japan/US) was not a significant predictor for other subtotal scores of SF12v2 (data not shown).

#### DISCUSSION

This is the first investigation to compare caregiver strain in communities in Japan and the US focusing on patients with PD and their spouses. Couples in Yamagata were older, were less well-educated, had lower employment, and had more advanced disease, but they had less comorbidity and their spouses had more help from others for caregiving than their counterparts in Maryland. There was no difference between Yamagata and Maryland on the level of caregiver strain, but spouses in Yamagata felt physical, time and financial constraint, while spouses in Maryland felt more emotional distress than physical and social constraint. In Maryland, patient depression (depression subtotal score of the BSI) was highly correlated with caregiver strain. In both locations, spousal depression (BDI in Yamagata and the depression subtotal score of the BSI in Maryland) was a significant contributor to caregiver strain. A subscale of health related QoL (general health perception on SF12) was lower in the patients and spouses in Yamagata than in patients and spouses in Maryland.

# Comparison of patients and their spouses in Yamagata and in Maryland

It is notable that significantly more spouses in Yamagata received help from others for

caregiving than spouses in Maryland (Table 1). In fact, 67.6% of spouses who received help from others utilized the LTCI in Yamagata. This result suggests that the LTCI contributes to the availability of support for caregivers in Yamagata. In Japan, greater service utilization under the LTCI was reported to be associated with a lower caregiver burden<sup>28</sup>. In this study, however, 27.3% of patients with PD in HY stage 4 did not utilize the LTCI at all despite their severe disability (Table 2). Also, 80% of those utilizing the LTCI only used services for 1 to 2 days per week, although some of them were certified as "care level 4", such that they were entitled to use services for up to 110 minutes per day. This means that these couples utilized only a small proportion of the available supports from the LTCI. A study of a community-dwelling Japanese elderly revealed that utilization of daycare included in the LTCI services tended to decrease the risk of institutionalization, but to a non-significant degree<sup>29</sup>. Further studies are necessary to examine the distribution of resources and the longitudinal effect of the LTCI on caregiver strain in Yamagata. More public awareness of the LTCI, especially for the elderly with limited access to the relevant information should be promoted.

In the present study, patients in Yamagata had more advanced disease at a shorter time after diagnosis than patients in Maryland (Table 1). This result suggests that PD patients in Maryland visit hospitals at an earlier stage of the disease than their counterparts in

Yamagata. One explanation of the difference could be the attitudes towards health problems with aging in each country. Hashimoto showed in her sociological comparative study between Japan and the US that the perceptions of health problems and aging are different between the two countries<sup>7</sup>. The Japanese elderly tend to accommodate their health problems, considering their impairment as "due to aging". Contrarily, the American elderly try to overcome their health problems regardless of age, thus maximizing their independence. The differences in attitudes towards their own health problems between the two communities might influence the timing of their first attendance at the clinic. Also, antidepressants were prescribed more frequently in Maryland than in Yamagata, which might be associated with more reluctance to visit psychiatrists in Japan than in the US. An international comparative study showed that there was a significant difference in the prevalence of depression between Japan (3%) and the US  $(16\%)^{30}$ . However, the difference might be associated with underdiagnosis of depressive disorders in Japan, according to the report by Mino et al<sup>31</sup>. Underdiagnosis and undertreatment of depression in PD are possible in Yamagata. Differences in the diagnosis and treatment for depression in PD between Japan and the US should be further examined.

# Caregiver strain in Japan and in Maryland

There was no significant difference in caregiver strain between spouses of patients with PD in Yamagata and in Maryland (Table 1). Previous studies have found that higher caregiver strain was correlated with many variables such as more severe patient impairment in ADL, worse patient mental problems, more severe patient axial symptoms, more severe caregiver depression, more caregiver comorbidity, and less social support<sup>3-5,32,33</sup>. In our study, patients in Yamagata were older and had more axial symptoms with less comorbidity and more social support than their counterparts in Maryland. It is suggested that more readily available social supports and less comorbidity in patients in Yamagata might offset the negative effect factors such as older age and more advanced disease, resulting in a similar level of CSI in Yamagata to the level of CSI in Maryland. Another explanation of the similar level of caregiver strain despite the difference in demographics and disease severity between Yamagata and Maryland could be a perception of caregiver strain in each society. In Japan, elderly patient vulnerability is considered as inevitable, and caregiving is perceived as an obligation of families and society<sup>7,34</sup>. In contrast, vulnerability is thought to be something which might happen, and caregiving is perceived as a voluntary choice for caregivers in the US. Therefore, Japanese caregivers may be unlikely to reveal a feeling of having a burden until they do much more caregiving than, they think, they are supposed to do as an obligation. On the other hand, American

caregivers may be more likely to disclose their feelings of having a burden more openly, because caregiving is seen not as an obligation for caregivers, but as a right for patients. This difference in the perception of caregiver strain between the countries might partially explain why caregiver strain is relatively suppressed in Yamagata despite older age and more advanced disease. The perception of caregiving as an obligation in Japan might also be related to the hesitation in the usage of the LTCI in Yamagata. The possibility that spouse caregivers in Yamagata might shoulder the burden of caregiving without complaining of any distress should be acknowledged.

Spouses in Yamagata felt more physical, financial and time constraints rather than emotional distress (Table 3). Spouses in Maryland scored on more items regarding emotional distress than the counterparts in Yamagata (Table 3). In Yamagata, the LTCI is available for all people over 65<sup>10</sup>. Moreover, couples with PD in Yamagata may have more assistance at home because of the high proportion of three-generation families<sup>12</sup>. Utilization of the LTCI and these extended families are likely to enable spouse caregivers to cope with their emotional distress. Couples in Yamagata were older with more advanced disease, and these characteristics might explain spouses in Yamagata feeling more physical strain than the spouses in Maryland. Miyashita et al. reported that caregivers of PD patients in Japan had more of a time and physical burden than emotional burden<sup>35</sup>. Our results are consistent with their reports.

With regard to financial burden, Japanese pairs with PD have more benefits than their counterparts in the US from the social support system in Japan including the National health insurance, the LTCI, and the Specified Disease Treatment Research Program. The latter subsidizes medical care for patients with rare and intractable diseases including PD. Although a 30% patient contribution is required for insurance-covered medical care in most cases, the national government and prefectures partly cover the patients' share of medical expenses by this program. PD patients over HY stage 3 are allowed exemption from medical expenses for PD with this program<sup>11</sup>. In this study, however, spouses in Yamagata revealed more financial distress than spouses in Maryland (Table 3). The difference in economic status anticipated by the difference in education and employment status between the Yamagata and Maryland subjects might result in greater financial burden in Yamagata than in Maryland despite the benefits from the multifold social support system in Japan. The financial impact of PD in both countries should be further examined in a different setting with the subjects who have similar levels of income.

In the multivariate regression analysis of subjects in both locations, spousal mental health and fall of patients with PD were significantly correlated with caregiver strain (Table 9). Mental health and depression of caregivers caring for PD patients have been reported to be correlated with caregiver burden<sup>36</sup>. O'Reilly et al. reported an almost fivefold increase in psychiatric morbidity in spouses who took care of their partners with PD as compared with those who did not <sup>37</sup>. The high correlation between caregiver strain and spousal mental health supports the results of these previous reports<sup>36,37</sup>. Falls and fear of falling could compel patients to restrict their mobility and independence, leading to higher caregiver strain<sup>38,39</sup>. Exercise programs targeting leg muscle strength, balance, and freezing were shown to reduce fall risk in PD<sup>40</sup>. Interventions to enhance spousal mental health and safety programs specific to PD impairments to reduce falls, such as weight-bearing balance and strength exercises along with cueing strategies<sup>41</sup>, would be effective in alleviating caregiver burden in both countries.

Multivariate regression of data of subjects in Maryland showed that the most significant predictor of caregiver strain was patient depression (Table 10, Model B). Generally, most households in the US are small nuclear families where elderly couples usually live by themselves<sup>42</sup>, compared with Yamagata where extended families living together are not uncommon<sup>12</sup>. In the US, when a partner is affected by a health problem, the spouse might provide much of the caregiving alone. In particular, a chronic progressive disease such as PD which encompasses mental and behavioral problems could have a serious effect on the quality of the relationship and communication between the couples in Maryland. Americans tend to form their primary bonds with their husbands or wives, while the Japanese do so with their children<sup>43</sup>. The quality of the marital relationship in couples with PD is highly correlated with caregiver strain in the US<sup>44</sup>. This impact of mental health problems in PD patients on the marital relationship may be one of the explanations for the greater impact on spousal emotional distress in Maryland. Perhaps special attention should be paid to spouses caring for PD patients when these patients exhibit mental health problems. This may be particularly true in Maryland.

Over the past 60 years, the percentage of older people residing with their children has been consistently decreasing in Japan<sup>45</sup>. This suggests that the problems currently faced by the American elderly could be a problem that the Japanese elderly will face in the near future, and could be a problem that the Japanese elderly in urban areas are now facing. Current Japanese LTCI includes few services targeting mental health problems of the elderly. Such services for mental health might become increasingly needed in Yamagata to reduce caregiver strain as the number of small nuclear households, where an elderly person cares for his/her elderly partner, increases.

# QoL of PD patients and their spouses in Japan and in the US

The results of our study suggest that PD had substantial adverse effects on the physical wellbeing, and to a lesser extent, on the mental wellbeing of patients when compared with population norms in both areas (Table 6). On the other hand, spousal physical health was not substantially different from that of the general population. In Yamagata, spousal mental wellbeing appeared slightly worse than the general population while spousal mental wellbeing in Maryland was not substantially different from that of the general population. The physical health wellbeing of PD patients was reported to be lower than that of the general population<sup>5</sup>. Previous research has suggested a link between caregiver wellbeing and patient disease severity and presence of key symptoms<sup>2,3</sup>. More advanced disease and more severe axial symptoms in Yamagata might be associated with lower spousal mental wellbeing than in Maryland.

Multivariate regression of SF12v2 subtotal scores showed that the scores of the general health perception of both patients and spouses were lower in Yamagata than in Maryland, even when the differences in demographics and disease severity between the two areas were taken into account (Table 11). General health perception in SF12 refers to the response to a simple question: "In general, would you say your health is excellent / very good / good / fair / poor ?". The difference in general health perception between the two locations might be related to the attitudes towards their own health in each community.

Generally, the Japanese elderly tend to accept their health status, even though it is impaired, considering their impairment as age related health problems<sup>7</sup>. In contrast, US elderly try to overcome their health problems regardless of age<sup>7</sup>. The differences in attitudes towards their own health problems between the two communities might influence the self-reports of their own health. Positive attitudes towards their health in the US might give the patients a confidence for their health, leading to a better self-assessment of their own health, while passive attitudes towards their health in Yamagata might lead to a negative assessment of their health. Indeed, Lyons et al. reported that pessimism was an early warning sign of compromised health for caregivers of patients with PD<sup>45</sup>. Chang and Asakawa also reported in their comparative study between European Americans and Japanese that European Americans held an optimistic bias with self-enhancement, whereas Japanese held a pessimistic bias with self-criticism<sup>46</sup>. These cultural variations on pessimism and optimism might influence self-reports of health in each country. The lower general health perception on SF12 in Yamagata could be an early warning sign of compromised health or reflect pessimism and self-criticism specific to the Japanese. Attention should be paid to the difference in the self-perception of health between the two countries.

There are some limitations of this study. First, since this study is cross-sectional, we

cannot formulate conclusions about cause and effect. We do not know whether high caregiver strain results from patient psychiatric symptoms or whether caregiver strain influences mental health and QoL. To clarify this issue, longitudinal studies are needed. Second, Yamagata and Maryland are different in terms of culture, ethnicity, social class, urbanization, and social support systems. Thus, we were not able to show exactly which aspect of cultural and social differences contributed to caregiver strain in this study. Third, we used two different questionnaires to assess mental health in patients and spouses in each country. This prevented patient and spousal mental health from being compared directly between Yamagata and Maryland. Since the mental health of both patients and spouses were important determinants for caregiver strain, the same validated scales in two different languages should be used in the future. Similarly, comorbidity of patients and their spouses was assessed by the Japanese translation of the CIRS-G, which has not been validated. Total CIRS-G scores of Japanese subjects should be considered as preliminary comparative data in this report. Finally, the results of multivariate regressions performed separately in Yamagata and in Maryland did not lead to a direct comparison between predictor variables because of the difference between the populations.

In conclusion, the degree of caregiver strain did not differ between Yamagata and Maryland, despite the couples being older and patients having more severe PD in

Yamagata. In Yamagata, more available help from others including the utilization of the Japanese LTCI might have a positive impact on caregiver strain. It is suggested by the results of our study that differences in caregiver strain between Japan and the US arose from different cultural backgrounds and social support systems. Spouses in Yamagata felt physical, time and financial constraint on caregiving, while spouses in Maryland felt more emotional distress than physical and social constraints, and they were especially distressed by patient depression. Underestimation of caregiver strain and under-utilization of the social support system in Yamagata, possibly based on the perception of caregiving specific to Japan should be considered in the assessment and the intervention for caregiver strain. Vulnerability of spouses in Maryland to patient emotional distress, which might be related to family structures in the US, should also be considered. It is possible that more physical support for longer hours might be attained by using the LTCI more effectively, which could be helpful for couples in Yamagata. In Maryland, interventions to improve patient depression could have a positive impact on caregiver strain. In both countries, spousal mental health was strongly correlated with caregiver strain, and interventions to enhance mental health of not only PD patients but also their spouses could reduce caregiver strain.

# ACKNOWLEDGEMENTS

I deeply thank the following doctors for their assistance of the present study.

Prof. Takeo Kato<sup>1</sup>, Dr. Keiji Kurita<sup>1</sup>, Dr. Toru Kawanami<sup>1</sup>, Dr. Manabu Wada<sup>1</sup>, Dr. Shingo

Koyama<sup>1</sup>, Prof. Kyoko Suzuki<sup>2</sup>, Dr. Naohiro Saito<sup>2</sup>, Prof. Gen Tamiya<sup>3</sup>

<sup>1</sup>Department of Neurology, Hematology, Metabolism, Endocrinology and Diabetology (DNHMED), Yamagata University School of Medicine, Yamagata, Japan

<sup>2</sup>Department of Clinical Neuroscience, Yamagata University School of Medicine, Yamagata, Japan <sup>3</sup>Advanced Molecular Epidemiology Research Institute, Yamagata University School of Medicine, Yamagata, Japan

Prof. Lisa M. Shulman<sup>4</sup>, Prof. William J. Weiner<sup>4</sup>, Prof. Stephen G. Reich<sup>4</sup>, Prof. Paul S.
Fishman<sup>4</sup>, Prof. Ann L. Gruber-Baldini<sup>5</sup>, Dr. Karen E. Anderson<sup>4,6</sup>
<sup>4</sup>Department of Neurology, University of Maryland School of Medicine, Baltimore, USA
<sup>5</sup>Division of Gerontology, Department of Epidemiology and Public Health, University of Maryland School of Medicine, Baltimore, USA

<sup>6</sup>Department of Psychiatry, University of Maryland School of Medicine, Baltimore, USA

#### REFERENCES

- de Lau LM, Breteler MM. Epidemiology of Parkinson's disease. Lancet Neurol. 2006;
   5: 525-35
- Schrag A, Hovris A, Morley D, Quinn N, Jahanshahi M. Caregiver-burden in parkinson's disease is closely associated with psychiatric symptoms, falls, and disability. Parkinsonism Relat Disord. 2006; 12: 35-41
- Martínez-Martín P, Forjaz MJ, Frades-Payo B, Rusiñol AB, Fernández-García JM, Benito-León J, Arillo VC, Barberá MA, Sordo MP, Catalán MJ. Caregiver burden in Parkinson's disease. Mov Disord. 2007; 22: 924-31
- Martinez-Martin P, Arroyo S, Rojo-Abuin JM, Rodriguez-Blazquez C, Frades B, de Pedro Cuesta J. Longitudinal Parkinson's disease patient study. Burden, perceived health status, and mood among caregivers of Parkinson's disease patients. Mov Disord. 2008 ; 23: 1673-80

- Peters M, Fitzpatrick R, Doll H, Playford D, Jenkinson C. Does self-reported well-being of patients with Parkinson's disease influence caregiver strain and quality of life? Parkinsonism Relat Disord. 2011; 17: 348-52
- Zarit SH, Reever KE, Bach-Peterson J. Relatives of the impaired elderly: correlates of feelings of burden. Gerontologist. 1980; 20: 649-55
- Hashimoto A. The gift of generations. Japanese and American perspectives of aging and the social contract. Cambridge University Press, Cambridge; UK: 1996
- 8. Glozman JM. Quality of life of caregivers. Neuropsychol Rev. 2004; 14: 183-96
- Berry RA, Murphy JF. Well-being of caregivers of spouses with Parkinson's disease. Clin Nurs. 1995; 4:373-86
- Tsutsui T, Muramatsu N. Care-needs certification in the Long-Term Care Insurance System in Japan. J Am Geriatr Soc. 2005; 53: 522-7
- 11. Japan Intractable Diseases Research Foundation/Japanese Intractable Diseases Information Center. What is an intractable disease? The Specified Disease Treatment Research Program. Available from: http://www.nanbyou.or.jp/english/index.htm

- 12. Ministry of Internal Affairs and Communications. Statistics Bureau, Director-General for Policy Planning & Statistical Research and Training Institute. About 2010 Population Census of Japan · Outline of the Survey. Available from: http://www.stat.go.jp/english/data/kokusei/index.htm
- 13. Robinson B. Validation of a caregiver strain index. J Gerontol. 1983; 38: 344-8
- 14. Iida N, Kobashi N. An Assessment of the Care Burden and the Quality of Life on At-Home Caregivers: Employing the Care Strain Index and the Questionnaire for QOL revised. Japanese Journal of Psychosomatic Medicine 2001; 41: 11-8
- 15. Fahn S, Elton RL.Members of the UPDRS development committee. Unified Parkinson's disease rating scale. In: Fahn S, Marsden CD, Calne DB, Goldstein M, editors. Recent developments in Parkinson's disease. Florham Park, NJ: Macmillan HealthCare Information; 1987. 153–64
- Hoehn MW, Yahr MD. Parkinsonism: onset, progression, and mortality. Neurology 1967; 17: 427–42
- 17. Folstein MF, Folstein SE, McHugh PR. "Mini-Mental State" a practical method for grading the cognitive state of patients for the clinician. J Psychiat Res 1975; 12:

- Schwab JF, England AC. Projection technique for evaluating surgery in Parkinson's disease. In: Gillingham FJ, Donaldson MC, editors. Third symposium on Parkinson's disease. Edinburgh: Livingston; 1969. 152–7
- 19. Imahashi K, Kawagoe M, Eto F, Haga N. Clinical status and dependency of the elderly requiring Long-Term Care in Japan. Tohoku J. Exp. Med. 2007; 212: 229-38
- 20. Miller MD, Paradis CF, Houck PR, Mazumdar S, Stack JA, Rifai AH, Mulsant B, Reynold CF, III. Rating chronic medical illness burden in geropsychiatric practice and research: application of the cumulative illness rating scale. Psychiatry Res 1992; 41: 237–48
- Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch. Gen. Psychiatry 1961; 4: 561–71
- 22. Kojima M, Furukawa TA, Takahashi H, Kawai M, Nagaya T, Tokudome S.
  Cross-cultural validation of the Beck Depression Inventory-II in Japan. Psychiatry Res.
  2002; 31: 291-9

- 23. Derogatis LR. The brief symptom inventory (BSI): administration, scoring and procedures manual, 3rd ed. Minneapolis, MN: National Computer Systems; 1993
- 24. Ware JE, Jr, Kosinski M, Keller SD. A 12-item short-form health survey: construction of scales and preliminary tests of reliability and validity. Med Care 1996; 34: 220–33
- 25. Fukuhara S, Suzukamo Y. Manual of SF-36v2 Japanese version: Institute for Health Outcomes &Process Evaluation Research, Kyoto, 2004
- 26. Jenkinson C. The SF-36 physical and mental health summary measures: an example of how to interpret scores. J Health Serv Res Policy 1998; 3: 92-6
- 27. Benjamini, Y; Hochberg, Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. J Roy Statistical Society 1995; 57: 289-300
- 28. Kumamoto K, Arai Y, Zarit SH. Use of home care services effectively reduces feeling of burden among family caregivers of disabled elderly in Japan: Preliminary results. Int J Geriatr Psychiatry 2006; 21: 163-70
- 29. Ohwaki K, Hashimoto H, Sato M, Tamiya N, Yano E. Predictors of continuity in home care for the elderly under public long-term care insurance in Japan. Aging Clin Exp

Res. 2009; 21:323-8

- 30. Andrade L, Caraveo-Anduaga JJ, Berglund P, Bijl RV, De Graaf R, Vollebergh W, Dragomirecka E, Kohn R, Keller M, Kessler RC, Kawakami N, Kiliç C, Offord D, Ustun TB, Wittchen HU. The epidemiology of major depressive episodes: results from the International Consortium of Psychiatric Epidemiology (ICPE) Surveys. Int J Methods Psychiatr Res. 2003; 12: 3-21
- Mino Y, Aoyama H, Froom J. Depressive disorders in Japanese primary care patients. Family Practice 1994; 11:363-7
- 32. Aarsland D, Larsen JP, Karlsen K, Lim NG, Tandberg E. Mental symptoms in Parkinson's disease are important contributors to caregiver distress. Int J Geriat Psychiatry 1999; 14: 866-74
- 33. Miller E, Berrios GE, Politynska BE. Caring for someone with Parkinson's disease: factors that contribute to distress. Int J Geriat Psychiatry 1996; 11: 263-8

- 34. Long SO, Hashimoto A. Introduction, Cultural meanings of "security" in aging policies.In: Long SO, editor. Caring for the elderly in Japan and the U.S. Routledge, Abington, Oxton; USA: 2001. 1-27
- 35. Miyashita M, Narita Y, Sakamoto A, Kawada N, Akiyama M, Kayama M, Suzukamo Y, Fukuhara S. Care burden and depression in caregivers caring for patients with intractable neurological diseases at home in Japan. J Neurol Sci. 2009; 15: 148-52
- 36. Caap-Ahlgren M, Dehlin O. Factors of importance to the caregiver burden experienced by family caregivers of Parkinson's disease patients. Aging Clin Exp Res. 2002 ;14: 371-7
- 37. O'Reilly F, Finnan F, Allright S, Smith GD, Ben-Shlomo Y. The effects of caring for a spouse with Parkinson's disease on social, psychological and physical well-being. Br J Gen Pract 1996; 46: 507–12
- 38. Martignoni E, Godi L, Citterio A, Zangaglia R, Riboldazzi G, Calandrella D, Pacchetti C, Nappi G; Parkinson's Disease Comorbidity Study Group. Comorbid disorders and

hospitalisation in Parkinson's disease: a prospective study. Neurol Sci. 2004 ;25: 66-71

- Murphy SL, Williams CS, Gill TM. Characteristics associated with fear of falling and activity restriction in community-living older persons. J Am Geriatr Soc. 2002; 50: 516-20
- 40. Allen NE, Canning CG, Sherrington C, Lord SR, Latt MD, Close JC, O'Rourke SD, Murray SM, Fung VS. The effects of an exercise program on fall risk factors in people with Parkinson's disease: a randomized controlled trial. Mov Disord. 2010; 25: 1217-25
- 41. Canning GC, Sherrington C, Lord SR, Fung V, Close J, Latt MD, Howard K, Allen NE, O'Rourke SD, and Murray SM. Exercise therapy for prevention of falls in people with Parkinson's disease: A protocol for a randomized controlled trial and economic evaluation. BMC Neurology 2009; 9:1-7
- U.S. Census Bureau. State & County Quickfacts. Maryland. 2010. Available from: http://quickfacts.census.gov/qfd/states/24000.html

- Yanagisako, S.J. Transforming the past: Tradition and kinship among Japanese Americans. 1985. Stanford: Stanford University Press.
- 44. Tanji H, Anderson KE, Gruber-Baldini AL, Fishman PS, Reich SG, Weiner WJ,
  Shulman LM. Mutuality of the marital relationship in Parkinson's disease. Mov Disord.
  2008; 23: 1843-9
- 45. National institute of population and social security research. Household projections of Japan by prefectures: 1995-2020 reported on March 2000 Available from: http://www.ipss.gp.jp/pp-ajsetai/e/chk2000/chk.html
- 46. Lyon KS, Stewart BJ, Archbold PG, Carter JH, Perrin NA. Pessimism and optimism as early warning signs for compromised health for caregivers of patients with Parkinson's disease. Nurs Res. 2004; 53: 354-62
- 47. Chang EC, Asakawa K. Cultural variations on optimistic and pessimistic bias for self versus a sibling: is there evidence for self-enhancement in the west and for self-criticism in the east when the referent group is specified? J Pers Soc Psychol. 2003; 84: 569-81

	Var	iable	Scale	Yamagata, Mean (SD), or N (%)	Maryland, Mean (SD), or N(%)	р
	Age			68.9 (9.4)	63.7 (9.7)	<0.001*
	Edu	cation (>high school)		14 (17.9)	68 (70.8)	<0.001*
	Em	ployment status (employed)		18 (23.1)	37 (39.4)	0.049†
ıse	Cor	norbidity	CIRS-G	3.7 (2.4)	3.2 (2.8)	0.21
Spouse	Yea	rs of marriage		44.4 (10.6)	39.1 (12.9)	0.004*
	Hel	p from others		33 (41.3)	4 (4.3)	<0.001*
	Car	egiver strain	CSI	4.2 (3.6)	3.7 (3.4)	0.34
	Phy	sical health QoL	SF12 PCS	46.3 (13.0)	51.6 (14.1)	0.01*
	Me	ntal health QoL	SF12 MCS	47.1 (11.1)	51.5 (10.1)	0.01*
	Age			69.5 (8.5)	65.7 (8.9)	0.004*
	Ger	nder (male)		47 (57.3)	64 (66.7)	0.26
	Education (>high school)			13 (16.7)	67 (71.3)	<0.001*
	Employment status (employed)			11 (13.9)	29 (31.2)	0.01*
t	Comorbidity		CIRS-G	3.6 (2.6)	5.0 (3.5)	0.01*
Patient	Dise	ease severity	HY stage	2.8 (0.7)	2.4 (0.8)	0.003*
Pê	RS	UPDRS mentation	UPDRS part1	2.5 (1.9)	2.0 (1.8)	0.04†
	UPDRS	UPDRS ADL	UPDRS Part2	14.5 (8.0)	12.8 (6.9)	0.13
		UPDRS Motor	UPDRS Part3	26.6 (10.3)	27.0 (11.6)	0.81
		UPDRS complications	UPDRS Part4	2.2 (2.7)	2.1 (2.5)	0.85
		Total UPDRS		43.3 (17.0)	42.2 (18.1)	0.68
	PD	duration( years)		7.8 (6.0)	10.7 (6.6)	0.006*
	Disa	ability	S&E ADL scale	76.6 (15.8)	76.8 (15.6)	0.95
	Cog	nition	MMSE	25.9 (3.8)	28.4 (2.2)	<0.001*
	nt	L-dopa		77 (93.9)	59 (61.5)	<0.001*
	Treatment	Dopamine agonist		62 (75.6)	44 (45.8)	<0.001*
	Trei	Benzodiazepine		25 (30.5)	15 (15.6)	0.03*
		Anti-depressant		3 (3.7)	28 (29.2)	<0.001*
		Deep Brain Stimulation		4 (4.9)	3 (3.1)	0.83
	Phy	rsical health QoL	SF12PCS	28.2 (16.0)	30.8 (16.9)	0.33
	Me	ntal health QoL	SF12MCS	44.5 (9.3)	50.3 (11.0)	0.001*

Table 1. Demographics and ratings of patients and spouses

\*: p<0.03, †: 0.03<=p<0.05. CIRS-G: Cumulative Illness Rating Scale-Geriatrics Version, CSI: Caregiver Strain Index, HY stage: Hoehn & Yahr stage, PCS: Physical Component Summary, MCS: Mental Component Summary, UPDRS: Unified Parkinson's Disease Rating Scale. S&E ADL Scale: Schwab and England Activities of Daily Living Scale

#### Table 2. Utilization of the LTCI and HY stage

	LTCI (+), Number of patients (%)	LTCI (-), Number of patients (%)	Total
HY 2	9 (19.6)	37 (80.4)	46
HY3	7 (33.3)	14 (66.6)	21
HY4	8 (72.7)	3 (27.3)	11
HY5	1 (100)	0	1
Total	25	54	79

LTCI: the Long Term Care Insurance, HY stage: Hoehn & Yahr stage

CSI	Question	Yamagata, n=82 Number of "yes" (%)	Maryland, n=96 Number of "yes" (%)	р
1	Sleep is disturbed	27 (32.9)	34 (35.4)	0.81
2	It is inconvenient	13 (15.9)	20 (20.8)	0.49
3	It is a physical strain	28 (34.1)	9 (9.4)	<0.001*
4	It is confining	19 (23.2)	27 (28.1)	0.53
5	There have been family adjustments	26 (31.7)	23 (24.0)	0.35
6	There have been changes in personal plans	24 (29.3)	34 (35.4)	0.45
7	There have been demands on my time	44 (53.7)	27 (28.1)	0.001*
8	There have been emotional adjustments	37 (45.1)	35 (36.5)	0.34
9	Some behavior is upsetting	18 (17.1)	42 (43.8)	0.003*
10	It is upsetting to find patient has changed so much	27 (32.9)	46 (47.9)	0.049†
11	There have been work adjustments	21 (25.6)	18 (18.8)	0.40
12	It is a financial strain	29 (35.4)	19 (19.8)	0.03†
13	Feeling completely overwhelmed	28 (34.1)	27 (28.1)	0.54

### Table 3. Comparison on each item of CSIbetween Yamagata and Maryland

\*: p<0.03, +: 0.03<=p<0.05. CSI: Caregiver Strain Index

	LTCI (+),	LTCI (-),	р
	Mean (SD)	Mean (SD)	
HY2.5	6.0 (3.8), n=9	3.9 (3.5) , n=25	0.14
НҮЗ	4.8 (3.4) <i>,</i> n=6	4.4 (3.7) , n=14	0.79
HY4	6.4 (4.0) <i>,</i> n=8	3.7 (5.5) , n=3	0.39

# Table 4. Comparison on CSI between users and non-users of LTCI in Yamagata

CSI: Caregiver Strain Index, LTCI: Long Term Care Insurance, HY stage: Hoehn & Yahr stage

	SF12 subscale	Yamagata	Maryland	р
	Physical functioning	82.0±24.3	86.1±22.4	0.25
	Role- Physical	79.2±23.6	84.7±20.4	0.10
	Bodily pain	74.7±24.5	82.1±21.8	0.04†
Spouse	General health	53.8±21.0	75.8±23.0	<0.001*
Spc	Vitality	51.3±29.5	67.2±20.3	<0.001*
	Social functioning	81.1±23.2	90.9±17.8	0.003*
	Role- Emotional	80.6±23.2	88.2±17.3	0.02*
	Mental health	67.9±20.8	71.2±20.0	0.28
	Physical functioning	46.6±34.2	51.1±36.3	0.40
	Role- Physical	51.5±36.3	46.4±28.8	0.25
ent	Bodily pain	59.9±28.1	66.1±30.5	0.17
Patient	General health	28.4±21.4	50.9±25.5	<0.001*
	Vitality	33.8±25.8	42.3±23.8	0.02*
	Social functioning	62.5±27.8	68.9±31.3	0.16
	Role- Emotional	60.3±28.2	75.1±26.2	0.001*
	Mental health	60.6±19.8	63.8±22.1	0.32

# Table 5. Comparison on SF12 subscale scores between Yamagata and Maryland

\*: Modified p<0.03, +: 0.03<=p<0.05

#### Table 6. Physical component summary (PCS) and Mental component summary (MCS) for a general population sample and PD patients and spouses

		Yamagata		Maryland	
		Mean (SD)	N (Age:60-69)	Mean(SD)	N (Age: 55-65)
PCS	Age-matched norm	47.6(9.9) <sup>a</sup>	n=438,	48.1 (10.3) <sup>b</sup>	n=1402,
	Spouses	49.3 (11.2)	n=27	52.5 (14.2)	n=36
	Patients	34.9 (16.1)	n=24	30.0 (16.0),	n=31
MCS	Age-matched norm	52.4(9.8) <sup>a</sup>	n=438,	49.2 (10.6) <sup>b</sup>	n=1402
	Spouses	47.4 (12.4)	n=27	51.7 (8.8)	n=36
	Patients	45.8 (8.9)	n=24	46.3 (11.0)	n=31

<sup>a</sup> Fukuhara S, Suzukamo Y. Manual of SF-36v2 Japanese version: Institute for Health Outcomes &Process Evaluation Research, Kyoto, 2004 <sup>b</sup> Jenkinson C. The SF-36 physical and mental health summary measures: an example of

how to interpret scores. J Health Serv Res Policy 1998; 3(2): 92-6

	Variable	Scale	r (p)	
			Yamagata	Maryland
	Age		0.07(0.54)	-0.09(0.44)
	Education		-0.17(0.14)	0.01(0.90)
se	Years of marriage		0.08(0.48)	-0.07(0.52)
Spouse	Help from others		-0.22(0.049†)	-0.26(0.01*)
	Employment status		0.07(0.57)	0.01(0.92)
	Medical comorbidity	CIRS-G	0.26(0.02*)	0.1(0.35)
	Mental health	BDI/BSI	0.44(<0.001*)	0.57(<0.001*)
	Age		0.11(0.34)	-0.12(0.29)
	Gender		0.04(0.72)	0.01(0.92)
	PD duration		0.14(0.21)	0.44(0.001)*
	Cognitive function	MMSE	-0.25(0.02*)	-0.17(0.11)
Patient	Disability	S&E ADL scale	-0.35(0.002*)	-0.31(0.005*)
Pati	PD severity	HY stage	0.30(0.006*)	0.30(0.005*)
	Medical comorbidity	CIRS-G	0.31(0.004*)	0.35(0.004*)
	Mental health	BDI/BSI	0.15(0.20)	0.56(<0.001*)
	L dopa		0.01(0.95)	0.19(0.07)
	Dopamine agonist		0.13(0.25)	0.07(0.55)
	Antidepressant		-0.16(0.16)	0.36(0.001*)
	Benzodiazepine		0.11(0.32)	0.23(0.03*)

Table 7. Correlations between caregiver strain (CSI) and spouse and patient variables

\*: p<0.03, †: 0.03<=p<0.05. CSI: Caregiver Strain Index, CIRS-G: Cumulative Illness Rating Scale-Geriatrics Version, BDI: Beck Depression Inventory, BSI: Brief Symptom Inventory, HY stage: Hoehn & Yahr stage, PCS: Physical Component Summary, MCS: Mental Component Summary, S&E ADL scale: Schwab and England Activities of Daily Living Scale

Table 8. Correlations between caregiver strain and patient impairment

Variable	Scale	r (p)	
		Yamagata	Maryland
UPDRS subscales	UPDRS mental	0.27(0.02*)	0.29(0.006*)
	UPDRS ADL	0.29(0.008*)	0.33(0.002*)
	UPDRS motor exam	0.13(0.25)	0.18(0.11)
	UPDRS complications	0.16(0.16)	0.28(0.009*)
UPDRS total	UPDRS Part 1-3	0.19(0.10)	0.27(0.02*)
Thought disorder	UPDRS no.2	0.17(0.13)	0.14(0.18)
Depression	UPDRS no.3	0.07(0.49)	0.22(0.04†)
Motivation	UPDRS no.4	0.11(0.32)	0.13(0.23)
Speech impairment	UPDRS no.18	0.17 (0.13)	0.23(0.04†)
Freezing	UPDRS no. 14	0.16 (0.17)	0.29(0.008*)
Fall	UPDRS no. 13	0.44 (<0.001*)	0.29 (0.007*)
Gait impairment	UPDRS no.29	0.25(0.03*)	0.41(<0.001*)
Postural instability	UPDRS no.30	0.32(0.004*)	0.25(0.02*)
Dyskinesia	UPDRS no.32	0.01(0.94)	0.06(0.55)
Tremor	UPDRS nos.20,21	-0.10(0.39)	-0.003(0.98)
Rigidity	UPDRS no.22	0.01(0.94)	0.01(0.90)
Bradykinesia	UPDRS no.23-27	0.06(0.60)	0.14(0.18)
Motor fluctuations	UPDRS no.39	0.13(0.25)	0.25(0.02*)
Facial expressions	UPDRS no.19	0.14(0.21)	0.09(0.40)

\*: p<0.03, †: 0.03<=p<0.05. UPDRS: Unified Parkinson's Disease Rating Scale

Yamagata an	d Maryland, R <sup>2</sup> =0.40, N	=99			
	Variables	Unstandard	ized coefficient	Standardized coefficient	р
		В	Standard error	Beta	
	Constant	10.27	1.48		
Spouse	Mental health QoL (MCS)	-0.16	0.03	-0.48	<0.001
Patient	Fall (UPDRS no.13)	0.88	0.28	0.26	0.002
	Comorbidity (CIRS-G)	0.30	0.10	0.24	0.005

Table 9. Predictors of caregiver strain by multiple regression analysis

Independent variables: country, thought disorder, motivation, falling, freezing, speech impairment, gait, fluctuation, S&E ADL scale, MMSE, antianxiety, antidepressant, spousal age, spousal education, spousal employment status, help from others, patient MCS, spousal MCS, patient CIRS-G, spousal CIRS-G

MCS: Mental Health Summary, CIRS-G: Cumulative Illness Rating Scale-Geriatrics Version, UPDRS: Unified Parkinson's Disease Rating Scale

Table 10. Predictors of caregiver strain by multiple regression analysis
with couples in Yamagata and in Maryalnd

Model A. Yama	gata, R <sup>2</sup> =0.23 N=62				
	Variables	Unstandard	ized coefficient	Standardized coefficient	р
		В	Standard error	Beta	
	Constant	1.24	0.79		
Spouse	Depression (BDI)	0.17	0.06	0.35	0.003
Patient	Fall	1.10	0.35	0.36	0.003
Model B. Mary	land, R <sup>2</sup> =0.57 N=54				
	Variables	Unstandard	ized coefficient	Standardized coefficient	р
				coenicient	
		В	Standard error	Beta	
	Constant	B 2.39	Standard error 4.53		
Spouse	Constant Help from others				0.001
Spouse		2.39	4.53	Beta	0.001 0.03

Independent variables in the model A: fall, speech, gait, postural instability, S&E ADL scale, MMSE, patient CIRS-G, help from others, spousal CIRS-G, spousal BDI, spousal age

Independent variables in the model B: patient BSI, fall, freezing, gait, fluctuation, S&E ADL scale, amantadine, antianxiety, patient CIRS-G, help from others, spousal CIRS-G, spousal age. spousal BSI

BDI: Beck Depression Inventory, BSI: Brief Symptom Inventory

#### Table 11. Predictors of patient and spousal self-reported general health perception by multiple regression analysis

	Variables	Unstanda	dized coefficient	Standardized coefficient	Р
		b	Standard error	Beta	
	Constant	67.74	8.7		
	Japan/US (Japan=0)	14.09	3.43	0.31	<0.001
Spouse	Total CIRS	-4.29	0.58	-0.48	<0.001
	Education	8.70	3.45	0.19	0.01
Model B. D	ependent variable: Patient : Variables			1	1
	Valiables	Unstanda	dized coefficient	Standardized coefficient	Р
	Variables	b	dized coefficient Standard error		Ρ.
	constant			coefficient	Ρ
		b	Standard error	coefficient	P <0.001
Patient	constant Japan/US	b 67.74	Standard error 2.67	coefficient Beta	
Patient	constant Japan/US (Japan=0)	b 67.74 13.90	Standard error 2.67 3.79	coefficient Beta 0.28	<0.001
Patient	constant Japan/US (Japan=0) Employment status	b 67.74 13.90 -14.61	Standard error           2.67           3.79           4.61	coefficient Beta 0.28 -0.24	<0.001 0.002

Independent variables in the model A: country, patient education, patient employment status, freezing, postural instability, S&E ADL scale, MMSE, amantadine, L-dopa, dopamine agonist, antidepressant, spousal age, spousal education, help from others, spousal CIRS-G

Independent variables in the model B: country, patient education, patient employment status, thought disorder, depression. motivation, fall, speech, freezing, postural instability, S&E ADL scale, MMSE, anticholinergic, L-dopa, dopamine agonist, antianxiety, spousal age, spousal education, help from others, spousal CIRS-G, bradykinesia