Family caregiving in dementia and its impact on quality of life and economic burden in Japan-web based survey

Ataru Igarashi a, Ayako Fukuda a, Lida Teng b, Fan-Fan Ma b, Julie Dorey b and Yoshie Onishi c

aDepartment of Drug Policy and Management, The University of Tokyo, Tokyo, Japan; bCreativ-Ceutical SARL, Paris, France; cCreativ-Ceutical K.K., Tokyo, Japan

ABSTRACT
Background: Dementia has become a growing health-care problem in the rapidly ageing Japanese population. This study assesses the impact of dementia on quality of life, economic burden, and productivity loss.

Objective: The objective of this study was to assess the impact of dementia on the Quality of Life (QoL), economic burden, and productivity loss among families living with dementia.

Methods: An online survey was conducted among families who lived with relatives with dementia. Demographic data and information about health condition and costs of long-term care and treatment were collected. Participants were asked to answer the EuroQol (EQ-5D-5L) questionnaire, Zarit Burden Interview (ZARIT-8), and Work Productivity and Activity Impairment Questionnaire (WPAI). Multivariate analyses were conducted to assess factors associated with burden by families living with dementia.

Results: Six hundred and thirty-five participants completed the survey. Of these participants, 50.5% were primary caregivers. Overall, 78.7% of dementia patients suffered from Alzheimer, and 43.9% needed long-term care. Compared to non-primary caregivers, primary caregivers had lower health utility scores (0.896 vs 0.873; p = 0.02), higher burden of caregiving (ZARIT-8: 21.1 vs 24.5; p < 0.0001), and higher overall work impairment (40.2% vs 20.8%; p < 0.0001), absenteeism (15.3% vs 5.7%; p < 0.0001), and presenteeism-related impairment (33.2% vs 17.3%; p < 0.0001).

Conclusion: Families living with dementia caring for a person with dementia experience increased burden. Health policies related to dementia need to be considered not only for patients, but also for their families living with dementia to improve their QoL.

Introduction
Dementia is one of the major causes of disability and dependency among older people with pathologies such as Alzheimer disease (AD), vascular cognitive impairment (VCI)/vascular dementia (VaD), and dementia with Lewy bodies (DLB). It is estimated that 47.5 million people suffer from dementia worldwide, and 7.7 million new cases emerge yearly [1]. The prevalence of dementia is expected to double every 20 years from 35.6 million in 2010 to 65.7 million in 2030, reaching 115.4 million in 2050 [2].

In Japan, the prevalence of dementia in people aged 65 years or older, is estimated to be 15% and is expected to increase as the Japanese society ages. The number of elderly with mild cognitive impairment (MCI) was estimated to be 4 million in 2012 and to reach 7 million in 2025 [3].

Dementia has a major impact on the lives, families, and careers of those with the condition. It is a disorder that poses many challenges to health professionals throughout the entire pathway of care, from early diagnosis to the end of life. More than 95% of people in nursing care homes have dementia and 68% of elderly need caregiving (over level III by governmental criteria of long-term care support/needed [youkaigo/youshien]) [4].

Shortage of nursing care and caregiving services are considered serious issues in Japan. There is over 3.6 million elderly over 75 years of age qualified as needing care as of 2013 estimates. The number of nursing personnel who works for long-term care is relatively small to the share of the aged population. The government aims at establishing a community based comprehensive care system by 2025, which could provide a care package of housing, health care,
long-term care, preventive care, and support for living [5,6].

Dementia impacts not only the patient’s quality of life (QoL) but also that of the caregivers [7,8]. The 2011 National Health and Aging Trends Study (NHATS) and National Study of Caregiving (NSOC) revealed that caregivers providing substantial help with health care were significantly more likely to experience emotional, physical, and financial difficulties than caregivers providing no help with healthcare in USA [7]. It was also reported that there is a strong relationship between mental health and health-related quality of life (HRQoL) among caregivers of dementia patients in Columbia [8].

The objective of this study was to assess, via a web-based survey, the impact of dementia on QoL, economic burden, and productivity loss among families living with dementia.

**Methods**

**Study design**

We conducted an online web-based survey between February 2016 and March 2016 among families who were living with patients afflicted by dementia. The survey was a self-administered, self-reported, internet-based questionnaire for adults 18 years of age or older. Respondents were recruited through a panel of Japanese residents who agree to participate regularly to online surveys. (Anterio Inc., Japan). Online survey was sent to 1,319 panel members who responded living with a family member diagnosed with dementia and 635 (48.1%) were responded to the survey. The protocol of the study was approved by the Ethics Review Committee of the Health Outcome Research Institute.

**Study sample and procedures**

The families living with dementia were divided into primary caregivers and non-primary caregivers. Primary caregivers were defined as families living with dementia who were mainly taking care of persons with dementia, whereas, non-primary caregivers were defined as families living with dementia providing secondary care or family members without caregiving activities. The questionnaire was composed of two sections which focused on the burden of families living with dementia patients and the burden of persons with dementia.

The questionnaire for families living with dementia included questions on demographics (age, gender, marital status, annual income, education level, number of children, and comorbidities), and employee status (full-time, non-full-time (part time, self-employed, unemployed, or student). Further questions addressed caregiving status (primary-caregiver, supportive caregivers, or no caregiving), health utility score (EQ-5D-5L), burden of caregiving (ZARIT-8), monthly direct medical cost (yen) of families living with dementia, work productivity and activity impairment (WPAI).

The questionnaire for persons with dementia included questions on demographics (age, gender, and current living situation of the patient) and type of dementia (Alzheimer, cerebrovascular dementia, DLB, Pick’s disease, juvenile Alzheimer’s disease, others, or unknown). The questionnaire also included questions on EQ-5D-5L, Barthel index for activities of daily living (ADL), monthly medical care, and level of care (care-support level I or II and care-need level I, II, III, IV and V). People with the care-need level 1 are least disabled, and with care-need level V are most disabled. People classified with care-need level III, IV, and V require long-term care services [9].

EQ-5D-5L questionnaire was developed by EuroQol Group as a standardized non-disease specific instrument to describe and value health-related quality of life [10]. Utility values were derived using Japanese EQ-5D-5L tariffs developed by Shiroiwa et al [11]. ZARIT-8 questionnaire was validated for the Japanese population by Arai et al [12]. The total score ranges from 0 to 88 with the higher score indicating the greater burden.

WPAI is a six–item validated questionnaire that measures metrics of problems with work during the past 7 days [13]. The score shows the percentage of hours missed due to problems and degree health affected productivity. The greater percentage of absenteeism indicates the greater burden, while the greater percentage of presenteeism indicates more time spent at work.

ADL questionnaire consists of 10 items: feeding, transfers, grooming, toilet use, bathing, mobility, stair use, dressing, and bowel and bladder movement. A score of 100 indicates independence while 0 describes patients who totally dependent on his/her caregivers [14].

**Statistical analysis**

The statistical analyses were performed using the SAS 9.3 statistical package (SAS Institute Inc., Cary, NC, USA).

Descriptive statistics were computed to describe burden of families living with dementia and patients with dementia living with these families. Data with normal distribution were compared using the Student’s t-test or ANOVA; the Mann-Whitney-Wilcoxon test or the Kruskal-Wallis test were used for groups with non-
normal distribution. The level of significance was set at p < 0.05.

Identification of risk factors of outcomes of interest, i.e., QoL, caregiving burden [Zarit-8 total score], overall WPAI, and medical cost of families living with dementia was performed in two steps.

The first step consisted in identification of potential risk factors looking at the association between each outcome of interest and included variables comprising demographical characteristics of families living with dementia and dementia patients, QoL and ADL of dementia patients. Associations were determined using unadjusted bivariate analyses. Variables were qualified as potential risk factors when p-value of tested associations were lower than 0.1.

The second step consisted in identification of risk factors of the outcomes of interest, using generalised linear models (GLMs) with potential risk factors as covariates. Several distributions were tested including normal, Poisson, negative binomial, log-normal, zero-inflated Poisson, and zero-inflated negative binomial distributions. Zero-inflated Poisson, and zero-inflated negative binomial distributions are two-part regression models. Those models are useful when proportion of zeros of the outcome of interest is high. These models are constructed with two different components: – one drives whether the value is 0 or not, and – the other one drives the value of the strictly positive count (amount part). The best fitted model was selected based on the minimization of the Akaike Information Criterion (AIC) [15,16]. Covariates were qualified as risk factors when p-value of tested associations were lower than 0.05.

**Results**

**Socio-demographical characteristics and burden description**

A total of 635 families living with dementia patients were identified, as the cohort panel of families living with a dementia patient through Anterio inc. Japan, with a mean age of 51.2 ± 11.3 years and 49.1% were women. 50.6% of the families living with dementia were primary caregivers, and 42.7% were full-time employees. Among the working families living with dementia, 40.9% were primary caregivers. Detailed information is given in Table 1.

Patients with dementia totalled to 635 with a mean age of 82.5 ± 7.6 years, and 75.4% were women. The majority of patients were suffering from Alzheimer’s disease (78.7%), followed by 4.1% with juvenile Alzheimer’s disease, 3.9% DLB, and 1.6% with Pick’s disease. The mean ADL score was 39.3 ± 32.6. The proportion of long-term care level over III, IV, and V were 43.9%. The average monthly cost was estimated to 215,862 ± 369,959 yen; however, the long-term care cost was 34,925 ± 33,239 yen. The average score of EQ-5D-5L was 0.559 ± 0.236. The demographic characteristics of dementia patients are presented in Table 2.

**Outcomes by caregiver status**

The analysis of health outcomes by caregiver status revealed an average score of 0.885 ± 0.126 of EQ-5D-5L for families living with dementia. However, the EQ-5D-5L score of primary caregivers was significantly lower compared to non-primary caregivers (0.896 vs 0.873; p = 0.021). The mean Zarit-8 score was 22.8 ± 8.5 for families living with dementia, and it was significantly higher for primary caregivers compared to non-primary caregivers (24.5 vs 21.1; p < 0.001). Detailed information is given in Table 1 in supplementary materials.

For WPAI, the mean overall work impairment was 28.9%±32.8; while absenteeism and presenteeism were 9.7%±18.6 and 23.8%±30.2, respectively. The comparison between the two groups showed that overall work impairment and absenteeism were significantly higher in primary caregivers (40.2% vs 20.8%; p < 0.0001 and 15.3% vs 5.7%; p < 0.001, respectively). A significant difference in presenteeism was also observed between the two groups (33.2% vs 17.3%; p < 0.001). Detailed information is given in Table 1 in supplementary materials.

The analysis of monthly medical cost showed an average cost of 21,242 ± 41,743 yen for families living with dementia, yet no significant difference was observed between primary caregivers and non-primary caregivers. The outcomes by caregiver status are presented in Table 3.

**Factors associated with outcomes of interest**

Comorbid hyperlipidaemia (p = 0.001), hypertension (p = 0.006), asthma (p < .0001), and osteoporosis (p = 0.004) of families living with dementia, lower dementia patients QoL, no full-time employment of caregiver, being a primary caregiver, and lower annual household income were identified as potential factors using bivariate analyses. Based on the best fitted model, families living with dementia with comorbid hypertension, stroke, asthma, osteoporosis, diabetes, hyperlipidaemia, not having full-time jobs, and relatives living with families living with dementia having hyperlipidaemia were considered negative predictors of families living with dementia on QoL. Higher patients’ EQ-5D
Table 1. Demographical characteristics of families living with dementia.

| Characteristics of families living with dementia | Primary Caregivers (N = 321) | Non-Primary Caregivers (N = 314) | Overall (N = 635) |
|---|---|---|---|
| Gender [n (%)] | Male 137 (42.7) 186 (59.2) 323 (50.9) | Female 184 (57.3) 128 (40.8) 312 (49.1) | | |
| Age, years [Mean ± SD] | 55.2 ± 9.9 | 47.8 ± 11.0 | 51.2 ± 11.3 |
| Age group, years [n (%)] | 20-39 17 (5.3) 83 (26.4) 100 (15.8) | 40-59 204 (63.6) 193 (61.5) 397 (62.5) | ≥60 100 (31.2) 38 (12.1) 138 (21.7) |
| Employment status [n (%)] | Full time employee 95 (29.6) 176 (56.1) 271 (42.7) | Part time job 36 (11.2) 37 (11.8) 73 (11.5) | Self-employee 45 (14.0) 41 (13.1) 86 (13.5) |
| No job or other 145 (45.2) 60 (19.1) 205 (32.3) | | |
| Status of caregivers [n (%)] | Primary caregivers 321 (100) 0 (0.0) 321 (50.6) | Secondary caregiver 0 (0.0) 197 (62.7) 197 (31.0) | Non-caretaker 0 (0.0) 117 (37.3) 117 (18.4) |
| No. of children of family member [n (%)] | One 297 (92.5) 298 (94.9) 595 (93.7) | Two 18 (5.6) 11 (3.5) 29 (4.6) | Three or more 6 (1.9) 5 (1.6) 11 (1.7) |
| Comorbidity [n (%)] | Diabetes 21 (6.5) 18 (5.7) 39 (6.1) | Hyperlipidemia 24 (7.5) 13 (4.1) 37 (5.8) | Parkinson disease 0 (0.0) 0 (0.0) 0 (0.0) |
| Hypertension 65 (20.3) 38 (12.1) 103 (16.2) | Stroke 3 (0.9) 2 (0.6) 5 (0.8) | Asthma 13 (4.1) 15 (4.8) 28 (4.4) |
| Rheumatoid arthritis 1 (0.3) 4 (1.3) 5 (0.8) | Osteoporosis 5 (1.6) 0 (0.0) 5 (0.8) | Cancer 13 (4.1) 6 (1.9) 19 (3.0) |
| Other disease 74 (23.1) 57 (18.2) 131 (20.6) | Household annual income [n (%)] | < 6 million yen 172 (53.6) 119 (37.9) 291 (45.8) |
| 6.9-9.9 million yen 55 (17.1) 83 (26.4) 138 (21.7) | ≥10 million yen 27 (8.4) 44 (14.0) 71 (11.2) | Don’t want to answer 67 (20.9) 68 (21.7) 135 (21.3) |
| Education level [n (%)] | Elementary/junior high school 9 (2.8) 9 (2.9) 18 (2.8) | | |
| High school 116 (36.1) 95 (30.3) 211 (33.2) | Professional school 46 (14.3) 46 (14.7) 92 (14.5) | Two-year college 39 (12.2) 24 (7.6) 63 (9.9) |
| College (4 years) 100 (31.2) 121 (38.5) 221 (34.8) | Graduate school 4 (1.3) 12 (3.8) 16 (2.5) | Don’t want to answer or other 7 (2.2) 7 (2.2) 14 (2.2) |
| Marital status [n (%)] | Never married 113 (35.2) 139 (44.3) 252 (39.7) | Married 157 (48.9) 151 (48.1) 308 (48.5) | Divorced 42 (13.1) 21 (6.7) 63 (9.9) |
| Widow/or other 9 (2.8) 3 (1.0) 12 (1.9) | Number of children [n (%)] | 0 237 (73.8) 209 (66.6) 446 (70.2) | 1 51 (15.9) 55 (17.5) 106 (16.7) |
| 2 25 (7.8) 35 (11.2) 60 (9.5) | 3 or more 8 (2.5) 15 (4.8) 23 (3.6) | Comorbidities of dementia patients [n (%)] |

Table 2. Characteristics of dementia patients.

| Characteristics of dementia patients | Overall (N = 635) |
|---|---|
| Gender [n (%)] | Male 156 (24.6) | Female 479 (75.4) |
| Age, years [Mean ± SD] | 82.5 ± 7.6 | | |
| Dementia type [n (%)] | Alzheimer’s dementia 500 (78.7) | Multiinfarct dementia 19 (3.0) | Dementia with Lewy bodies 25 (3.9) |
| Frontotemporal dementia (Pick’s disease) 10 (1.6) | Juvenile Alzheimer disease 26 (4.1) | Unknown or other 55 (8.7) |
| Place of relative with dementia living in [n (%)] | Hospital 53 (8.4) | Nursing home 91 (14.3) | Living at home 491 (77.3) |
| Visiting a medical institution for following diseases [n (%)] | | | |
| Diabetic 93 (14.7) | Hyperlipidemia 24 (3.8) | Parkinson disease 18 (2.8) |
| Hypertension 198 (31.2) | Stroke 42 (6.6) | Asthma 14 (2.2) |
| Rheumatoid arthritis 15 (2.4) | Osteoporosis 101 (15.9) | Cancer 36 (5.7) |
| Other disease 101 (15.9) | No disease for visiting a medical institution 196 (30.9) | Level of care [n (%)] | |
| Assist level 40 (6.3) | Nursing care level 1 115 (18.1) | Nursing care level 2 133 (20.9) |
| Nursing care level 3 110 (17.3) | Nursing care level >3 169 (26.6) | Not qualified or unknown 68 (10.7) |
| EQ-SD utility scores [Mean ± SD] 0.559 ± 0.236 | Barthe index [Mean ± SD] 39.3 ± 32.6 | Monthly medical cost, JPY [Mean ± SD] 215,863 ± 369,959 |
| Monthly nursing cost, JPY [Mean ± SD] 257,672 ± 369,959 | | Monthly nursing cost, JPY [Mean ± SD] 34,925 ± 33,239 |

Based on the best fitted model, being primary caregivers and caregivers with two relatives with dementia were associated with higher caregiving burden. Higher dementia patients QoL and relatives living together scores, higher annual household incomes, and better ADL of dementia patients were associated with higher QoL of families living with dementia. Detailed information is given in Table 2 in supplementary materials.
with families living with dementia having rheumatoid arthritis were associated with lower caregiving burden.

Factors associated with overall WPAI of families living with dementia were assessed using the bivariate analysis. The proportion of zero was estimated to be 37.6% using the two-part regression model. Being primary caregivers, divorced, and widowed families living with dementia were associated with higher overall work impairment.

The proportion of zeros of the monthly medical cost was estimated to be 28.5% using the 2-part regression model. Families living with dementia with diabetes, hypertension, stroke, cancer, and asthma, and dementia patients with rheumatoid arthritis, and those living in nursing homes were found as factors of higher costs. Better QoL of families living with dementia was associated with lower monthly medical cost. Detailed information is given in Table 2 in supplementary materials.

**Discussion**

Caregiving is a source of distress and poses a significant burden on families living with dementia. It has been shown that caregiving burden is higher in dementia than in other diseases [17], highlighting the importance of research in this field for the development of solutions in the reduction of the burden of caregiving by identifying factors associated with QoL for caregiving. Our study showed that the burden of caregiving was significantly higher in primary caregivers than in non-primary caregivers. We also found that the level of QoL was significantly lower in primary caregivers compared to non-primary caregivers with chronic diseases, contributing to the reduction in QoL, in both caregivers and care recipients. Being a primary caregiver significantly determined high overall work impairment.

The burden of caregiving depends on many factors related to the severity of care recipients’ disease and their general health condition as well as socioeconomic factors. The presence of dementia contributes significantly to the increase in caregiving burden [18]. Behavioural and psychological symptoms that appear in the course of dementia have been shown to increase the caregiving burden among families living with dementia [19]. Although not all symptoms contribute equally to the burden of caregiving, they significantly affect relationships among families living with dementia. The study by Matsumoto et al. showed that agitation and aggression, as well as irritability and lability, had the highest impact on the distress among informal caregivers [20]. The study conducted by Miyamoto et al. confirmed this relationship among formal caregivers. Behavioural and psychological symptoms manifested by patients with dementia staying in psychiatric hospitals, nursing homes, or geriatric care facilities significantly increased the caregiver burden [21]. Reduced QoL is strongly associated with the burden of caregiving. Santos et al. investigated the caregiving burden and QoL among primary caregivers of relatives with mild to moderate dementia. They found that caregivers’ QoL was negatively correlated with depressive symptoms (r = −0.638; p = 0.001), anxiety (r = −0.359; p = 0.001) and burden (r = −0.547; p = 0.001); this association was similar in both dementia groups [22]. Takai et al. confirmed the presence of reduced QoL in families living with dementia but highlighted that patient-related variables were less important for QoL than subjective experiences of caregivers. In their study, depressive symptoms appeared to be the strongest predictors for caregivers’ QoL followed by burnout and the cognitive impairment of dementia patients [23]. Results of our study are in line with previous reports. We found that QoL measured with EQ-5D-5L score was significantly lower in primary caregivers than in non-primary caregivers. Interestingly, working part-time was associated with lower QoL, which may be explained by the need for a longer time spent on caregiving translating into an increased burden of caregiving. Further

**Table 3. Health outcomes by caregiver status.**

| Characteristics                  | Primary Caregivers (N = 321) | Non-Primary Caregivers (N = 314) | P value | Overall (N = 635) |
|----------------------------------|------------------------------|----------------------------------|---------|-------------------|
| EQ-5D utility scores [Mean ± SD] | 0.873 ± 0.117               | 0.896 ± 0.133                    | 0.021   | 0.885 ± 0.126     |
| Zarit-8 scores [Mean ± SD]      | 24.5 ± 8.5                   | 21.1 ± 8.3                       | <0.0001 | 22.8 ± 8.5        |
| WPAI- Overall impairment [Mean ± SD] | 40.2% ± 35.3%              | 20.8% ± 28.3%                    | <0.0001 | 28.9% ± 32.8%     |
| WPAI- Absenteeism [Mean ± SD]   | 15.3% ± 22.0%               | 5.7% ± 14.5%                     | <0.0001 | 9.7% ± 18.6%      |
| WPAI- Presenteeism [Mean ± SD]  | 33.2% ± 33.7%               | 17.3% ± 25.7%                    | <0.0001 | 23.8% ± 30.2%     |
| Monthly medical cost, JPY [Mean ± SD] | 23,475 ± 40,359             | 18,504 ± 43,336                  | 0.235   | 21,242 ± 41,743   |

SD: Standard deviation.
investigation is needed for evaluating the association between QoL and longer time spent on caregiving. We also found that comorbidities such as hypertension, stroke, asthma, osteoporosis, diabetes, and hyperlipidaemia in dementia patients served as negative predictors for QoL among caregivers. Greater independence of dementia subjects was associated with higher QoL among their caregivers, which is directly related to lower burden.

Reports on the association between work impairment in primary caregivers and caregiving burden are scarce. Farre et al. investigated indirect costs related to loss of labour productivity in families living with dementia of dementia relatives and the caregiving burden in a prospective observational study of costs and resource use. They found that 28.3% of working caregivers had to reduce working hours, which was particularly evident among those who cared for relatives with more severe dementia. Factors such as caregiver burden, health status, or psychological well-being, increased the likelihood of reducing working hours [24]. Michalowski et al. found that caring for dementia patients includes mostly the use of informal care (85.1%). One in 7 caregivers experienced productivity loss. Factors such as the low daily living activity of dementia patients, living alone, and employment of a caregiver shift costs of care and are associated with greater use of formal care [25]. Reese et al. noted that long-term care consumes about 43% of the total costs of caregiving of dementia patients. The indirect cost of caregiving was almost entirely composed of productivity loss of caregivers [26]. The present study showed that the overall work impairment of primary caregivers was significantly higher than non-primary caregivers. Moreover, primary caregivers who lived alone (divorced and widow) reported higher overall work impairment, which can be explained by a greater number of reduced working hours due to patient care.

Our study has some limitations. In this survey, the sampled population may not be representative of the families with dementia patients since respondents were from a panel of Japanese residents who agree to participate regularly to online surveys. We reported outcomes on the Japanese population of patients with dementia and their caregivers. In Japan, the percentage of older people with dementia is high, with half of them living at home with their relatives. Cultural and social differences, as well as differences in health care systems, do not allow the results to be generalised to other populations. In our statistical analysis, the interactions and collinearity between variables were not tested.

Conclusion
The relationship between patients with dementia and their families living with dementia is complex and multidimensional. The severity of dementia and socioeconomic factors decrease QoL, particularly in primary caregivers who experience higher caregiving burden and overall work impairment compared to non-primary caregivers. Health policies related to dementia need to be developed, not only for dementia patients, but also for their families living with dementia to improve their QoL and productivity. Further investigation is needed to develop tailored interventions aimed at reducing the caregiving burden and its consequences.

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ORCID
Lida Teng http://orcid.org/0000-0001-5879-9060
Yoshie Onishi http://orcid.org/0000-0003-3519-4733

References
[1] Organization WH. Dementia. 2016 [cited 2016 May 4]. Available from: http://www.who.int/en/news-room/factsheets/detail/dementia
[2] Prince M, Guerchet M, Prina M. Policy brief for heads of government: the global impact of dementia 2013–2050. Alzheimer’s Disease International; 2013.
[3] Ninomiya T. Study of estimating future dementia population in Japan, health labour sciences research grant; 2014.
[4] Ministry of Health LaWM. Survey of institutions and establishments for long-term care. 2013 [cited 2017 Oct 17]. Available from: http://www.mhlw.go.jp/toukei/saikin/hw/kaigou/service13/
[5] Ministry of Health LaWM. 15th committee for the social security council of welfare. 2015 [cited 2017 Oct 17]. Available from: http://www.mhlw.go.jp/file/05-Shingikai-12601000-Seisakoutoukatsukan-Sanjikanshitsu_Shakaihoshoutantuou/0000075711.pdf
[6] Association JN. Nursing for the older people in Japan. 2016.
[7] Wolff JL, Spillman BC, Freedman VA, et al. A national profile of family and unpaid caregivers who assist older adults with health care activities. JAMA Intern Med. 2016;176(3):372–379.
[8] Moreno JA, Nicholls E, Ojeda N, et al. Caregiving in dementia and its impact on psychological functioning and health-related quality of life: findings from a colombian sample. J Cross Cult Gerontol. 2015;30(4):393–408.

[9] Iwagami M, Tamiya N. The long-term care insurance system in Japan: past, present, and future. JMA J. 2019;2(2):67–69.

[10] EUROQOL. EQ-5D. [cited 2019 Jul 08]. Available from: https://euroqol.org/euroqol/

[11] Shiroiwa T, Fukuda T, Ikeda S, et al. Japanese population norms for preference-based measures: EQ-5D-3L, EQ-5D-5L, and SF-6D. Qual Life Res. 2016;25(3):707–719.

[12] Arai Y, Tamiya N, Yano E. The short version of the Japanese version of the zarit caregiver burden interview (J-ZBI_8): its reliability and validity. Nihon Ronen Igakkai Zasshi Jpn J Geriatrics. 2003;40(5):497–503.

[13] Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. PharmacoEconomics. 1993;4(5):353–365.

[14] Mahoney FI, Barthel DW. FUNCTIONAL EVALUATION: THE BARTHEL INDEX. Maryland state Med J. 1965;14:61–65.

[15] Akaike H Information theory as an extension of the maximum likelihood principle. In: Petrov B, Csaki F, eds. Second International Symposium on Information Theory. Budapest: Akademiai Kiado, 1973:p. 267–281.

[16] Cavanaugh J. Lecture II: the akaike information criterion [unpublished PowerPoint slides]; 2012.

[17] Pinquart M, Sorensen S. Differences between caregivers and noncaregivers in psychological health and physical health: a meta-analysis. Psychol Aging. 2003;18(2):250–267.

[18] Leroy I, McDonald K, Pantula H, et al. Cognitive impairment in Parkinson disease: impact on quality of life, disability, and caregiver burden. J Geriatr Psychiatry Neurol. 2012;25(4):208–214.

[19] Black W, Almeida OP. A systematic review of the association between the behavioral and psychological symptoms of dementia and burden of care. Int Psychogeriatr. 2004;16(3):295–315.

[20] Matsumoto N, Ikeda M, Fukuhara R, et al. Caregiver burden associated with behavioral and psychological symptoms of dementia in elderly people in the local community. Dement Geriatr Cogn Disord. 2007;23(4):219–224.

[21] Miyamoto Y, Tachimori H, Ito H. Formal caregiver burden in dementia: impact of behavioral and psychological symptoms of dementia and activities of daily living. Geriatric nurs (New York, NY). 2010;31(4):246–253.

[22] Santos RL, Sousa MF, Simoes-Neto JP, et al. Caregivers’ quality of life in mild and moderate dementia. Arq Neuropsiquiatr. 2014;72(12):931–937.

[23] Takai M, Takahashi M, Iwamitsu Y, et al. Subjective experiences of family caregivers of patients with dementia as predictive factors of quality of life. Psychogeriatrics. 2011;11(2):98–104.

[24] Farre M, Kostov B, Haro JM, et al. Costs and burden associated with loss of labor productivity in informal caregivers of people with dementia: results from Spain. J Occup Environ Med. 2018;60(5):449–456.

[25] Michalowsky B, Thyrian JR, Eichler T, et al. Economic analysis of formal care, informal care, and productivity losses in primary care patients who screened positive for dementia in Germany. J Alzheimers Dis. 2016;50(1):47–59.

[26] Reese JP, Hessmann P, Seeberg G, et al. Cost and care of patients with Alzheimer’s disease: clinical predictors in German health care settings. J Alzheimers Dis. 2011;27(4):723–736.