Work-related Stress, Caregiver Role and Depressive Symptoms among Japanese Workers

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#### **Abstract**

Background: In Japan, more than 60% of employees are reported to suffer from anxiety and stress. Consequently, Japanese society has begun to address such important issues as psychogenic disability and job-related suicide. Furthermore, given the aging of society and the surge in the number of elderly people requiring care, it is necessary to adequately and proactively support employees who care for their elderly relatives. The purpose of the present study was to investigate caregiver burden in caring for elderly relatives and work-related stress factors associated with mental health among employees.

**Methods:** We studied 722 men and women aged 18-83 years in a cross-sectional study. The K10 questionnaire was used to examine mental health status.

**Results:** The proportion of participants with a high K10 score was 15% (n=106). Having little conversation with their supervisor and/or co-workers significantly increased the risk of depression (odds ratio, OR 1.8), as did high job overload (OR 2.7) and job dissatisfaction (OR 3.8), compared with employees who frequently conversed with their supervisor and/or co-workers. Caring for elderly relatives as a prominent characteristic of an employee was a significant risk factor for depression (OR 2.1).

**Conclusions:** The present study demonstrated that employees who were caring for elderly relatives were significantly associated with an increased risk of depression. To prevent depressive disorders, it may be important to focus on reducing the work-caregiving role

conflict, as well as enhancing employees' job control and better rewarding their efforts in the workplace.

**Key words:** work-related stress, caregiving, depression

#### Introduction

In Japan, more than 60% of employees are reported to suffer from anxiety and stress [1]. Consequently, Japanese society has begun to address important mental health issues such as psychogenic disability and job-related suicide.

The average life expectancy in Japan has increased dramatically as the mortality rate has decreased, resulting in growth of the elderly population. In 2009, 22.8% of the population was aged 65 years or older; this proportion has been projected to increase to more than 30% by 2025 [2]. This has led to an increase in the number of elderly people requiring care as a result of being bedridden or having cognitive impairment. Because caregivers who live in smaller households have consistently low support and caregivers whose household size is largest describe a pattern of high support, the increasing need for care of elderly relatives is caused by the familial structure having changed from an extended family to a nuclear one.

Based on this social background, the Long-Term Care Insurance (LTCI) Act was enacted in 2000. Its purpose was to provide care for elderly people with the support of society as a whole. In 2000, 2,180,000 people were certified for LTCI, and 1,490,000 used it [3]. By April 2009, these figures had increased dramatically, with 4,690,000 people certified and 3,840,000 users [3].

In general, research studies have reported that providing care has a detrimental effect on emotional well-being [4-6] and social activity [7], and that caregivers of the elderly are more likely to experience physical and psychological burdens and suffer from anxiety and depression than non-caregivers [8-10]. A large majority of family caregivers are traditionally non-working spouses, daughters, or daughters-in-law of elderly people in need of care. However, the recent trend shows an increasing number of primary caregivers who maintain paid employment due to fewer family members per household. In 2010, the Child Care and Family Care Leave Act was enacted to realize a society in which all workers who are eager to work while raising their children or taking care of family members can continue to work. According to a previous study, working family caregivers tend to adjust their working hours to allow them to provide care if they obtain support from their workplace colleagues and/or supervisor [11]. In addition, reduced work-related stress and increased job satisfaction are associated with better physical health and higher quality of life among caregivers [12-14]. Given the aging of society and the surge in the numbers of elderly people requiring care, it is important to adequately and proactively support employees who care for their relatives. However, many of the studies above were conducted in Western countries, with little of this research having been performed in Japan.

The purpose of this study was to investigate caregiver burden among employees who care for their elderly relatives and analyze work-related stress factors associated with mental health condition in employees.

## **Participants and Methods**

### **Participants**

We conducted a self-administered questionnaire survey in Nagasaki Prefecture, Japan, from December 2009 to February 2010. First, a letter was sent to the directors of three workplaces. The letter explained the aims, procedures, and ethical considerations of the study. The directors of all three workplaces agreed to participate. The questionnaire was distributed to 844 employees. The purpose and ethical aspects of the study were described at the beginning of the questionnaire, and only employees who agreed to participate and who provided informed consent were enrolled as study participants. The participants were requested to fill out the questionnaire and return it in a sealed envelope to the researchers by mail. Of the 844 questionnaires distributed, 787 were returned (response rate 93.2%). After eliminating respondents whose sex or age were unknown and those who did not complete all questions of the K10, 722 participants (355 men and 367 women) remained for analysis.

The present study was reviewed and approved in October 2009 by the institutional ethics committee of Nagasaki University School of Medicine.

## Questionnaire

The questionnaire included questions on demographic characteristics, self-rated health, quality of sleep, satisfaction with daily life, employment status (working hours, work environment) and caregiving status regarding elderly people (aged 65 years and older)

requiring assistance or supervision. Mental health condition was assessed using the K10, while occupational stress was assessed using the National Institute for Occupational Safety and Health Generic Job Stress Questionnaire (NIOSH-GJSQ).

#### Measures

The K10 has been widely used to measure psychological distress. It was developed as a convenient and reliable self-rating scale to screen for psychological distress [15]. The K10 was found to have high screening performance for psychological distress [15-18]. The Japanese version of the K10 also has high internal consistency, with a Cronbach's  $\alpha$  of 0.91 [19]. Receiver operating characteristic (ROC) curve analysis showed good discrimination of DSM-IV mood and anxiety disorders, as assessed by the area under the curve of 0.94 [20]. The K10 is a 10-item scale. Subjects were asked to indicate how frequently they had experienced symptoms or feelings during the past month using a 5-point Likert scale ranging from none of the time (0), a little of the time (1), some of the time (2), most of the time (3), to

The NIOSH-GJSQ was developed to measure occupational stress, particularly the relationship between job-related psychosocial stressors and mental health condition [22]. The NIOSH-GJSQ has acceptable reliability, with Cronbach's  $\alpha$  coefficients ranging from 0.65 to

all of the time (4). The total score is the sum of all responses, and ranges from 0 to 40. Higher

scores reflect more severe psychological distress. A score of 15 or higher on the K10 indicates

increased risk for psychological distress [21].

0.90 (mean = 0.81), and is widely used in the field of occupational health [22]. The Japanese version of the NIOSH-GJSQ was developed as a convenient and reliable self-rating scale to screen for job-related stress [23]. It has demonstrated consistently high levels of internal consistency (Cronbach's  $\alpha$ , 0.68-0.95) [24]. Domains indicating occupational stress in the Japanese version of the NIOSH-GJSQ used in this study were "job overload" (7 items, score range 0-7), "job control" (3 items, score range 0-3), "intra-/inter- group conflict" (3 items, score range 0-3), and "job satisfaction" (2 items, score range 0-2). The proposed cut-off point score of each domain was as follows: 2 points over for job control, 2 points over for intra-/inter- group conflict, and 2 points over for job satisfaction. Different cut-off point scores by sex were set for job overload: 6 points over in males and 5 points over in females.

The associations between the frequency of subjects with high K10 score and demographic, lifestyle, caregiving status, work environment and work-related stress factors were analyzed. The chi-square test was used for nominal scale data such as sex, while the Cochran-Armitage test was used for ordinal scale data such as self-rated health.

Furthermore, the simultaneous effect of factors on the frequency of subjects with a high K10 score was analyzed using a linear logistic model. The most appropriate model was selected on the basis of the Akaike Information Criterion (AIC). The AIC is a measure of goodness of fit of a statistical model, and provides a means for model selection. Starting from

a model including sex, age, self-rated health, quality of sleep, satisfaction with daily life, working hours per day, conversation with supervisor and co-workers, support from supervisor and co-workers, job overload, intra-/inter-group conflict, job control, job satisfaction, and caring for elderly relatives as covariates, the final model with minimum AIC value was selected as the most appropriate. The variables of age, self-rated health, quality of sleep, conversation with supervisor and co-workers, satisfaction with daily life, job overload, job satisfaction and caring for elderly relatives were included in the final model, while the variables of sex, working hours per day, support from supervisor and co-workers, intra-/inter-group conflict, and job control were excluded. The maximum likelihood estimation of the final model parameters was carried out, followed by calculation of the odds ratio (OR) and its 95% confidence interval (CI) for each covariate in the model.

#### **Results**

Table 1 shows the characteristics of the study participants. Their mean age was 40.4 (standard deviation 10.7) years. Among the 722 respondents, 112 (15.5%) were caregivers. Approximately 40% of the participants rated their health as good (31.9%) or very good (5.1%), while 5.5% rated it as poor. The proportion of participants with a high K10 score was 14.7%.

Characteristics of the work environment and work-related stress of the participants are

shown in Table 2. More than half of the participants worked 8 hours or more per day. The proportion of those who conversed with their supervisor and/or co-workers "a lot" to "some" was 56.7%, while the proportion of workers who felt supported by their supervisor and/or co-workers was 48.3%. In terms of occupational stress, 379 employees (52.5%) had high job overload, 290 (40.2%) reported low job control, and 166 (23.1%) had high intra-/inter-group conflict.

The associations between K10 score and demographic and lifestyle factors, work environment, and work-related stress factors are shown in Table 3. Regarding the association between K10 score and participant characteristics, the proportion of respondents with a high K10 score was significantly higher in women (17.7%) than in men (11.5%) (p = 0.019). Moreover, in people aged 18 to 40 years, depression was approximately twice as common in women (21.1%) than in men (11%) (p = 0.011). Poor self-rated health (p < 0.001), poor quality of sleep (p < 0.001), and dissatisfaction with daily life (p < 0.001) were also associated with high K10 score.

Regarding K10 score and work environment, participants who had little to no conversation with their supervisor and/or co-workers, and those who experienced little to no support at work, had significantly greater K10 scores than their counterparts. Employees who experienced a high level of job overload (i.e., "there is a great deal to be done") were significantly more likely to have a high K10 score than those reporting a low level of job

overload (20.6% vs. 8.1%, p < 0.001). Employees who experienced a high level of intra-/inter-group conflict (i.e., "there are differences of opinion within my group," "there are personality clashes between my group and another group") were more likely to have a high K10 score than those who experienced little intra-/inter-group conflict (27.7% vs. 10.9%, p < 0.001). In addition, employees who experienced low job control (i.e., "I can't work at my own pace," "I'm not allowed to decide which tasks to perform at work") were significantly more likely to have a high K10 score than those who experienced a high level of job control (21%) vs. 10.1%, p < 0.001). Furthermore, employees who were not satisfied with their job were more likely to have a high K10 score than those who were satisfied (36.7% vs. 10.8%, p < 0.001). Lastly, employees who were engaged in caregiving showed a non-significant tendency for a high K10 score compared with those who were not (19.6% vs. 13.8%, p = 0.107). However, quantity and quality of conflict of job with caregiving may depend on working hours or age. We conducted a stratified analysis by age group (18-40 years and 41-83 years) and by working hours group (8 hours or more per day and less than 8 hours per day). The stratified analysis did not show any substantial differences between age groups and between working hours groups (data not shown).

Table 4 shows independent variables related to depression using multiple logistic regression analysis to examine simultaneous effects. Having little conversation with one's supervisor and/or co-workers significantly increased the risk of depression (OR: 1.77; 95% CI:

1.08-2.90), as did high job overload (OR: 2.66; 95% CI: 1.59-4.44) and job dissatisfaction (OR: 3.75; 95% CI: 2.19-6.41). However, neither low job control nor high intra-/inter-group conflict were associated with depression in this model. Poor self-rated health and poor quality of sleep were significant risk factors for depression (OR: 1.81; 95% CI: 1.02-3.22 and OR: 3.29; 95% CI: 1.93-5.61, respectively). Caring for elderly relatives was also a significant risk factor for depression (OR: 2.11; 95% CI: 1.14-3.91). Although the odds ratios were not statistically significant, the risk of depression tended to be higher in employees aged 18 to 40 years (OR: 1.60; 95% CI: 0.97-2.63) than in those who were older, and also tended to be higher in those who felt dissatisfied with their daily life (OR: 1.89, 95% CI: 0.96-3.70) than in those who were satisfied.

### **Discussion**

The present study aimed to reveal caregiver burden in caring for elderly relatives and work-related stress factors associated with mental health condition in working people. Of the 722 respondents, 106 (14.7%) demonstrated depression, as defined by a high K10 score. The logistic regression analysis (Table 4) showed several risk factors for depression: young age, poor self-rated health, poor sleep, little or no conversation with others in the workplace, dissatisfaction with daily life, high job overload, dissatisfaction with job, and caregiver status. In the logistic regression analysis, we found that the risk of depression was increased (OR,

1.6) in people aged 18 to 40 years when compared with their older counterparts. Moreover, in this younger age group, depression was approximately twice as common in women than in men. This is consistent with a study by Birnbaum et al. [25], who found a significantly greater risk of depression (a three-fold increase) in people aged 18 to 44 years when compared with those aged 60 years and older, and a prevalence of depression in women nearly twice as high as that in men. Several studies have reported that young employees more frequently have stressful experiences early in their career, including reality shock and unsuccessful occupational socialization [26,27]. Consequently, we considered that the risk of depression was higher in young employees, compared with those aged 41 years and older.

Poor self-rated health significantly increased the risk of depression (OR, 1.8 compared with good self-rated health). Mavaddat et al. [28] reported similar results in a population-based cohort study (European Prospective Investigation of Cancer Study). Another study reported that self-rated health moderated the relationship between physical functional impairment and depressive symptoms, and that people with poor self-rated health and severe physical functional impairment had more depressive symptoms [29]. Joling et al. [30] investigated depressive symptoms among caregivers of dementia patients, and found that poor self-rated health was significantly associated with caregiver depression. People engaged in caring for older relatives are thought to be at increased risk of depression because of the associated physical and mental burden and poor self-rated health.

We also found that employees with poor quality of sleep were at significantly increased risk of depression (OR, 3.3). Some studies have reported that insomnia is considered a symptom of depression [31-33]. Szklo-Coxe et al. [34] found a dose-response relationship between the number of insomnia symptoms, including difficulty falling asleep, repeated nocturnal awakening and early morning awakening, and incidence of depression. In addition, Szklo-Coxe et al. reported that employees with 3 or 4 insomnia symptoms were at significantly increased risk of depression (OR, 3.23 compared to employees without insomnia symptoms). In the present study, 38% of employees at high risk of depression reported insomnia symptoms.

Consistent with the findings of several studies, our study showed that workers at high risk of depression experienced job-related stress and high intra-/inter-group conflict such as poor communication with supervisor and/or co-workers, high job overload, and low job satisfaction [35-37]. High job overload and work-family conflict are thought to be closely related to burnout [38,39]. In the field of occupational health, job strain, effort-reward imbalance, and work-family conflicts are widely considered aspects of job-related stress [35-37,40]. Saijo et al. [41] reported that lack of supervisor support was significantly associated with depressive disorders.

The present study found that support from supervisor and/or co-workers was not associated with reduced risk of depression. However, multiple logistic regression analysis revealed that

risk of depression was significantly increased in employees who had little conversation with their supervisor and/or co-workers (OR, 1.7 compared with those who had a lot to some conversation). Furthermore, a chi-square test revealed that employees who had little workplace conversation also experienced little support from supervisor and/or co-workers (p<0.001, data not shown). Our results suggest that support in the workplace was associated with smooth communication and mitigation of depression. Hence, employees with adequate support in the workplace may be able to avoid depression. However, those who are not able to obtain such support and who have little conversation with their supervisor and/or co-workers may be at increased risk of both depression and intra-/inter-group conflict. We therefore consider that low support in the workplace is a predictor of adverse outcomes such as job-related stress and depressive disorders.

The risk of depression increased significantly in employees with high job overload (OR, 2.6 compared with those with low job overload). The burden of job overload includes not only high variance in workload, but also high perceived demands, and considerable physical strain. The present results are consistent with those of recent studies reporting that job overload leads to fatigue and deteriorates mental and physical health [42], and that it significantly increases the risk of depression [41,43-45]. The present findings suggest that high job overload was associated with depression, although enough communication with and support from supervisor and/or co-workers are psychosocial factors that may mitigate job-related stress.

Caring for elderly relatives is time-consuming and is associated with physical and psychological burden. In the present study, we separated employees into two groups according to whether or not they cared for elderly relatives; we found that the risk of depression increased significantly in caregivers (OR, 2.1 compared with non-caregivers). Some previous studies have also reported an association between caregiving and depression. Anthony-Bergstone et al. [46] found that the frequency of depression was higher in caregivers than in non-caregivers. Hirst [9] used the British Household Panel Survey to examine the association between time spent caring for elderly relatives and depression in the caregiver, and reported that the proportion of people with a high General Health Questionnaire-12 (GHQ-12) score was significantly increased in caregivers providing 16 hours or more of care per day compared with non-caregivers. Waite et al. [8] found that 43% of caregivers who care for elderly relatives with dementia had depression, while McConaghy & Caltabiano [47] reported that almost 60% of caregivers of elderly relatives with dementia had Center for Epidemiologic Studies-Depression scale (CES-D) scores of 16 and above. Consistent with prior research findings, we found a strong association between caring for elderly relatives and caregiver depression, although factors such as amount of time per day spent providing care and characteristics of the elderly relatives in need of care were not taken into account in the present study.

Our study had several limitations. First, because the design was cross-sectional, the

relationships found in the present study cannot be interpreted as causal. Second, because the participants in this study were limited to the employees of three workplaces in Nagasaki Prefecture, Japan, generalization of the findings should be made with caution. Finally, the quality of relationships between caregivers and care recipients has emerged as an important variable in caregiving research; however, this was not assessed in the present study. The strengths of this study were that: 1) the response rate was relatively high at 93.2% (787 responses from 844 questionnaires distributed); and 2) it is one of few studies focusing on a working population exposed to conflict between the roles of employee and caregiver of elderly relatives.

#### **Conclusions**

The present study demonstrated that employees who were caring for elderly relatives were significantly associated with an increased risk of depression. As the Japanese population ages, employees will increasingly need to provide elder care services. Occupational health nurses are in an ideal position to help employees better manage their work and their caregiving responsibilities.

To prevent depressive disorders, it may be important to focus on reducing work-caregiving role conflict, as well as enhancing job control and improving the effort-reward balance in the workplace. This requires the development of public health and occupational health policies

and interventions directed toward addressing the mental health problems of employees. This is one of the most important challenges for the workplace in the coming years.

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Table 1. Characteristics of the study participants

Characteristic	Number	Percentage
Sex		
Female	367	50.8
Male	355	49.2
Age (years)		
18-40	367	50.8
41-83	355	49.2
Self-rated health		
Very good	37	5.1
Good	230	31.9
Intermediate	412	57.1
Poor	40	5.5
Unknown	3	0.4
Quality of sleep		
Very good	60	8.3
Fairly good	230	31.9
Intermediate	312	43.2
Fairly poor	106	14.7
Very poor	14	1.9
Satisfaction with daily life		
Very satisfied	11	1.5
Fairly satisfied	239	33.1
Intermediate	333	46.1
Fairly unsatisfied	124	17.2
Very unsatisfied	13	1.8
Unknown	2	0.3
Caring for elderly relatives		
Yes	112	15.5
No	610	84.5
K10 score		
Low (0-14)	616	85.3
High (15-40)	106	14.7

Table 2. Characteristics of the work environment and work-related stress

Characteristic	Number	Percentage
Working hours per day		
Less than 3	1	0.1
3-4.9	10	1.4
5-7.9	326	45.2
8 or more	382	52.9
Unknown	3	0.4
Conversation with supervisor and		
co-workers		
A lot	85	11.8
Some	324	44.9
A little	298	41.3
None	5	0.7
Unknown	10	1.4
Support from supervisor and co-workers		
A lot	74	10.2
Some	275	38.1
A little	349	48.3
None	12	1.7
Unknown	12	1.7
Job overload		
Low	335	46.4
High	379	52.5
Unknown	8	1.1
Intra-/inter- group conflict		
Low	542	75.1
High	166	23.1
Unknown	14	1.9
Job control		
High	424	58.7
Low	290	40.2
Unknown	8	1.1
Job satisfaction		
Satisfied	603	83.5
Unsatisfied	109	15.1
Unknown	10	1.4

Table 3. Associations between demographic and lifestyle factors, work environment and work-related stress factors, and  $K10\ score$ 

Factor	K10 s	K10 score	
Factor	Low	High	P value
Sex			
Female	302 (82.3)	65 (17.7)	$0.019^{a}$
Male	314 (88.5)	41 (11.5)	
Age (years)			
18-40	305 (83.1)	62 (16.9)	$0.088^{a}$
41-83	311 (87.6)	44 (12.4)	
Self-rated health			
Very good	35 (94.6)	2 (5.4)	
Good	212 (92.2)	18 (7.8)	-0.001h
Intermediate	341 (82.8)	71 (17.2)	<0.001 <sup>b</sup>
Poor	26 (65)	14 (35)	
Unknown	2 (66.7)	1 (33.3)	
Quality of sleep			
Very good	55 (91.7)	5 (8.3)	
Fairly good	208 (90.4)	22 (9.6)	-0.001h
Intermediate	273 (87.5)	39 (12.5)	<0.001 <sup>b</sup>
Fairly poor	75 (70.8)	31 (29.2)	
Very poor	5 (35.7)	9 (64.3)	
Satisfaction with daily life			
Very satisfied	10 (90.9)	1 (9.1)	
Fairly satisfied	227 (95)	12 (5)	
Intermediate	295 (88.6)	38 (11.4)	<0.001 <sup>b</sup>
Fairly unsatisfied	77 (62.1)	47 (37.9)	
Very unsatisfied	5 (38.5)	8 (61.5)	
Unknown	2 (100)	0 (0)	
Working hours per day			
Less than 3	0 (0)	1 (100)	
3-4.9	7 (70)	3 (30)	0.025 <sup>a</sup>
5-7.9	285 (87.4)	41 (12.6)	
8 or more	321 (84)	61 (16)	
Unknown	3 (100)	0 (0)	

Conversation with supervisor a	nd co-workers			
A lot	78 (91.8)	7 (8.2)	<0.001 <sup>b</sup>	
Some	295 (91)	29 (9)		
A little	233 (78.2)	65 (21.8)		
None	2 (40)	3 (60)		
Unknown	8 (80)	2 (20)		
Support from supervisor and co	o-workers			
A lot	69 (93.2)	5 (6.8)	0.001 <sup>b</sup>	
Some	242 (88)	33 (12)		
A little	291 (83.4)	58 (16.6)		
None	6 (50)	6 (50)		
Unknown	8 (66.7)	4 (33.3)		
Job overload				
Low	308 (91.9)	27 (8.1)	-0.0018	
High	301 (79.4)	78 (20.6)	<0.001 <sup>a</sup>	
Unknown	7 (87.5)	1 (12.5)		
Intra-/inter- group conflict				
Low	483 (89.1)	59 (10.9)	<0.001 <sup>a</sup>	
High	120 (72.3)	46 (27.7)		
Unknown	13 (92.9)	1 (7.1)		
Job control				
High	381 (89.9)	43 (10.1)	<0.001a	
Low	229 (79)	61 (21)	<0.001	
Unknown	6 (75)	2 (25)		
Job satisfaction				
Satisfied	538 (89.2)	65 (10.8)	∠0.001a	
Unsatisfied	69 (63.3)	40 (36.7)	<0.001ª	
Unknown	9 (90)	1 (10)		
Caring for elderly relatives				
Yes	90 (80.4)	22 (19.6)	$0.107^{a}$	
No	526 (86.2)	84 (13.8)		

<sup>&</sup>lt;sup>a</sup>Chi square test excluding unknown category

<sup>&</sup>lt;sup>b</sup>Cochran-Armitage test excluding unknown category

Table 4. Analysis of logistic regression model assessing the odds ratios and 95% confidence intervals for demographic and lifestyle factors and work-related stress factors

Factor variable		Odds ratio estimate	95%CI <sup>a</sup>	P-value
Age				
	18-40	1.60	0.97-2.63	0.064
	41+	1.00	Referent	
Self-rated health				
	Intermediate or poor	1.81	1.02-3.22	0.043
	Very good or good	1.00	Referent	
Quality of sleep				
	Fairy poor or very poor	3.29	1.93-5.61	< 0.001
	Very good or fairly good	1.00	Referent	
Conversations	with			
supervisor and co-work	ers			
	A little or none	1.77	1.08-2.90	0.023
	A lot or some	1.00	Referent	
Satisfaction with daily	life			
	Intermediate or fairly unsatisfied or very unsatisfied	1.89	0.96-3.70	0.066
	Very satisfied or fairly satisfied	1.00	Referent	
Job overload				
	High	2.66	1.59-4.44	< 0.001
	Low	1.00	Referent	
Job satisfaction				
	Unsatisfied	3.75	2.19-6.41	< 0.001
	Satisfied	1.00	Referent	
Caring for elderly relati	ives			
	Yes	2.11	1.14-3.91	0.018
	No	1.00	Referent	

<sup>&</sup>lt;sup>a</sup>95% confidence interval