

Table 1  
Patient Characteristics (n = 462)

	n (%)
Age (yr ± SD)	62 ± 11
Sex	
Male	209 (45)
Female	253 (55)
Primary sites	
Lung, chest	150 (33)
Breast	113 (25)
Colon, rectum	65 (14)
Stomach	74 (16)
Uterus, ovary	33 (7.1)
Pancreas, bile duct	19 (4.1)
Others	8 (1.7)
Chemotherapy regimens	
Carboplatin and taxanes	100 (21)
Oral tegafur, gimeracil, oteracil with/without taxanes	80 (17)
Taxanes	76 (16)
Doxorubicin and cyclophosphamide	75 (16)
Fluorouracil	47 (10)
Gemcitabine	20 (4.3)
Oxaliplatin and 5-fluorouracil/leucovorin	10 (2.1)
Irinotecan (with/without taxanes)	9 (1.9)
Trastuzumab (with/without taxanes)	8 (1.7)
Gefitinib	7 (1.5)
Low-dose cisplatin and 5-fluorouracil	3 (0.6)
Vinorelbine	2 (0.4)
Oral capecitabine	2 (0.4)
Others	23 (7.1)

oral oxycodone, n = 25; transdermal fentanyl, n = 11; and oral morphine, n = 11).

#### Symptom Prevalence and Symptom Clusters

Frequently identified problems were oral problems (21%), insomnia (19%), psychological distress (defined as the DT score of 6 or more; 15%), needing help with information and decision-making (14%), severe fatigue (8.2%), and severe appetite loss (6.3%) (Table 2). As a whole, problems were identified in half of all questionnaires.

Table 3 summarizes the effects of age and gender on each symptom. Younger patients reported significantly higher intensity of pain and nausea, and male patients reported significantly higher intensity of fatigue, dyspnea, appetite loss, and somnolence, after adjustment for other demographic variables. Opioid consumption was significantly higher in male patients.

Four symptom clusters emerged in this population (Fig. 1): 1) fatigue and somnolence; 2) pain, dyspnea, and numbness; 3) nausea, appetite loss, and constipation; and 4) psychological distress.

Table 2  
Problems Identified in 4000 Questionnaires

	Prevalence (%) <sup>a</sup>	Mean ± SD (median) <sup>b</sup>
Physical problems		
MDASI items		
Fatigue	8.2	15
Appetite loss	6.3	11
Constipation	4.9	11
Somnolence	4.6	9.1
Pain	3.6	11
Dyspnea	3.5	9.0
Numbness	5.3	6.9
Nausea	2.4	6.2
Oral problems		21
Fever		6.8
Psychological problems		
Insomnia		19
DT		15
Concern		
Information and help with decision-making		14
Nutrition		5.6
Daily activities		4.6
Economic problems		2.4

<sup>a</sup>The percentages of responses with moderate (4–6) and severe (7–10) symptom intensity for MDASI items; the percentages of score of 6 or more for the DT; the percentages of problem presence for other items.

<sup>b</sup>Mean values calculated for only MDASI items.

#### Longitudinal Change in the DT

Of 462 patients, 170 patients (37%) had a DT score of 6 or more at any time during the study period. Owing to a lack of follow-up data in five patients, we used 165 patients for follow-up analyses, and the median interval from the initial assessment was 17 days (range, 7–28 days).

Of 165 patients with a DT score of 6 or more, 115 patients (70%) had a score below 6 at follow-up (Fig. 2). In the remaining 50 patients who had a DT score of 6 or more at follow-up, 34 patients (68%) had one or more physical symptoms rated as 7 or more, and an additional 12 patients (24%) had one or more physical symptoms rated at 4 to 6.

Compared with patients with a DT score below 6 at follow-up, patients with a continuing DT score of 6 or more had higher levels of all physical symptoms at follow-up, including pain, dyspnea, nausea, appetite loss, somnolence, fatigue, constipation, and numbness (Table 4). The level of the DT and all physical symptoms in the initial assessment

Table 3  
Association between Symptom Intensity and Age, Gender, and Primary Tumor Site

	Age			Gender			Primary Tumor Sites			
	<60	>60	P	Male	Female	P	Abdominal	Chest	Breast	P
Fatigue	2.2 ± 2.3	2.2 ± 2.6	0.51	2.3 ± 2.6	2.1 ± 2.4	<0.001	2.5 ± 2.7	1.5 ± 2.1	2.3 ± 2.3	<0.001
Pain	1.7 ± 1.9	1.5 ± 2.0	0.003	1.5 ± 2.0	1.7 ± 2.1	0.70	1.6 ± 2.0	1.3 ± 2.0	1.9 ± 2.1	<0.001
Numbness	1.4 ± 2.2	1.1 ± 2.1	0.71	0.9 ± 1.8	1.5 ± 2.5	0.16	1.1 ± 1.8	0.7 ± 1.7	2.2 ± 3.0	<0.001
Dyspnea	1.2 ± 1.9	1.3 ± 2.0	0.41	1.3 ± 2.0	1.1 ± 1.9	<0.001	1.2 ± 1.8	1.3 ± 2.1	1.2 ± 2.0	0.15
Appetite loss	1.6 ± 2.3	1.7 ± 2.4	0.33	1.8 ± 2.5	1.5 ± 2.2	0.004	1.9 ± 2.5	1.4 ± 2.3	1.3 ± 2.1	<0.001
Nausea	1.1 ± 2.0	0.8 ± 1.6	<0.001	0.9 ± 1.8	0.9 ± 1.8	0.84	1.2 ± 1.8	0.6 ± 1.8	0.8 ± 1.7	<0.001
Somnolence	1.7 ± 2.0	1.8 ± 2.3	0.62	1.8 ± 2.3	1.7 ± 2.1	<0.001	2.0 ± 2.3	1.3 ± 2.0	1.8 ± 2.1	<0.001
Constipation	1.5 ± 2.1	1.6 ± 2.3	0.50	1.7 ± 2.4	1.4 ± 2.1	0.042	1.9 ± 2.3	1.2 ± 2.2	1.2 ± 2.0	<0.001
Psychological distress	3.2 ± 2.5	3.0 ± 2.8	0.066	2.9 ± 2.8	3.2 ± 2.6	0.32	3.2 ± 2.7	2.6 ± 2.7	3.5 ± 2.6	<0.001
Opioid consumption <sup>a</sup>	29 ± 27	28 ± 20	0.20	33 ± 25	18 ± 13	0.019	37 ± 28	23 ± 13	18 ± 15	<0.001

P values for age were adjusted for gender and primary tumor sites. P values for gender were adjusted for age and primary tumor sites.  
<sup>a</sup>Oral morphine equivalent (mg/day).

demonstrated no significant difference between the groups.

### Discussion

This is, to our knowledge, the first large study to identify symptom prevalence and intensity in cancer patients receiving chemotherapy, in addition to providing longitudinal follow-up data from the DT, in the outpatient setting of a general hospital, a typical regional cancer center in Japan.

The first important finding of this study was the clarification of the types of symptoms and concerns observed in cancer outpatients receiving chemotherapy. In this study, the predominant problems were psychosocial issues (insomnia, psychological distress, concern about information, and decision-making), nutrition-related issues (oral problems and appetite loss), and fatigue. Furthermore, four distinct symptom clusters were identified: 1) fatigue and somnolence; 2) pain, dyspnea, and numbness; 3) nausea, appetite loss, and

constipation; and 4) psychological distress. From these findings, the outpatient chemotherapy department should establish a palliative care program targeting: 1) psychosocial issues (insomnia, psychological distress, decision-making support); 2) nutrition-gastrointestinal issues (oral problems, appetite loss, nausea); 3) fatigue; and 4) pain, dyspnea, and numbness. Pharmacological treatments, collaboration with mental health care professionals and dentists, and cognitive-behavioral nursing interventions are promising, and should be tested in future intervention trials of Japanese cancer patients.<sup>39-58</sup>

The second important finding of this study was longitudinal follow-up data from patients receiving outpatient chemotherapy who were repeatedly assessed using the DT. This is the first study to explore longitudinal changes in the DT in the outpatient chemotherapy setting. In this setting, 11% of all patients had a DT score of 6 or more at any time of treatment. The majority (70%), however, demonstrated the DT score below 6 within four

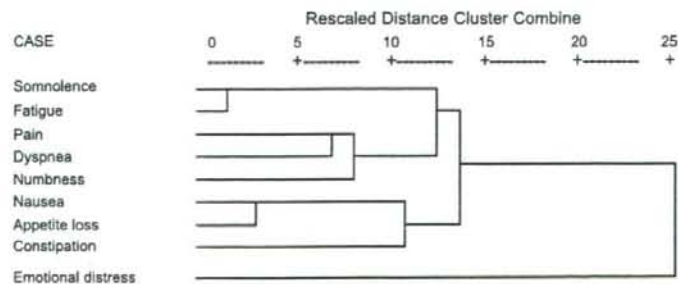


Fig. 1. Symptom cluster.

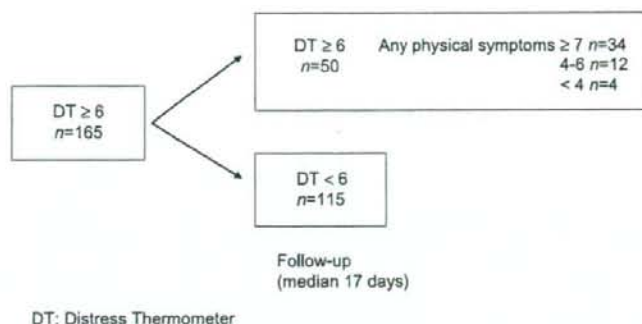


Fig. 2. Changes in the DT.

weeks, and the change in a DT was strongly associated with changes in physical symptoms. This result suggests that chemotherapy-related physical symptoms may highly influence the DT and result in rapid changes within several weeks in the outpatient chemotherapy setting. Future study is required to assess the usefulness of the DT as a clinical tool to identify patients with psychiatric comorbidity. Modifying the procedure, such as two-point follow-up, or encouraging symptom control to be

maximized before rating the DT, may be necessary. In the meantime, clinicians should note that a high score in the DT is not simply the indicator of psychiatric comorbidity. DT often indicates the need of palliating co-existing physical symptoms.

Age and gender differences in the symptoms of cancer patients are a focus of some researches.<sup>39-45</sup> Consistent with previous findings from a systematic review of symptom prevalence,<sup>44</sup> higher pain intensity was significantly associated with younger age. This result indicates that younger patients need special attention in terms of pain management and active monitoring of pain. We also observed gender differences in some symptoms: male patients reported a higher intensity of fatigue, dyspnea, appetite loss, and somnolence, in addition to a higher dose of opioids, after adjustment for age and primary tumor sites. This result is not consistent with a large-scale study of patients receiving no anticancer treatments that revealed a gender difference in the prevalence of nausea.<sup>44,45</sup> Potential interpretations of these differences include: 1) different measurement methods (i.e., symptom intensity vs. frequency); 2) different treatment settings (receiving chemotherapy in the outpatient setting vs. palliative phase); and 3) analyses with or without adjustment for other factors. To determine the effects of age and gender on symptom intensity in this population, more pooled data from this setting is necessary.

This was a descriptive study of clinical experience and thus had considerable limitations. First, as the patients were a heterogeneous sample of primary tumor sites, stages, and

Table 4  
Comparison of Patients with a DT of 6 or More and Below 6 at Follow-up

	Patients with DT of 6 or More at Follow-up (n = 50)	Patients with DT below 6 at Follow-up (n = 115)	P Value
Age	63 ± 9.6	63 ± 11	0.26
Sex (male)	56% (n = 28)	44% (n = 51)	0.17
At initial assessment			
Pain	3.2 ± 2.6	2.8 ± 2.8	0.63
Dyspnea	2.3 ± 2.6	1.8 ± 2.5	0.49
Nausea	2.1 ± 2.8	2.2 ± 3.0	0.11
Appetite loss	3.4 ± 3.1	3.4 ± 3.3	0.38
Somnolence	3.0 ± 2.5	2.5 ± 2.4	0.89
Fatigue	4.6 ± 3.0	3.5 ± 2.8	0.56
Constipation	2.4 ± 2.6	2.9 ± 3.2	0.027
Numbness	2.8 ± 3.0	1.8 ± 2.7	0.16
DT	7.4 ± 1.2	7.6 ± 1.3	0.15
At the follow-up			
Pain	3.5 ± 2.7	1.5 ± 1.8	0.001
Dyspnea	3.1 ± 2.8	1.1 ± 1.8	<0.001
Nausea	2.2 ± 2.7	0.48 ± 1.0	<0.001
Appetite loss	3.7 ± 3.0	1.1 ± 1.8	<0.001
Somnolence	3.9 ± 2.7	1.3 ± 1.6	<0.001
Fatigue	5.0 ± 3.0	1.9 ± 2.3	0.005
Constipation	3.1 ± 2.9	1.4 ± 2.3	<0.001
Numbness	3.0 ± 3.1	1.0 ± 1.7	<0.001

Analyses were performed on patients who had a DT score of 6 or more at any time in this study period (n = 165).

chemotherapy regimens, the results cannot be automatically generalized to specific target populations. We believe that this is not a fatal flaw of this study, but rather can be a strength, because we need to develop a useful system for heterogeneous outpatients receiving chemotherapy. Second, this was a single-institution study. We believe, however, that the results are generalizable to other institutions, as our hospital is a typical general hospital functioning as a regional cancer center. Third, we adopted the single-item DT to increase patients' compliance. The combined use of the DT and impact thermometer (i.e., the degree of interference to daily activity) might decrease the influence of physical symptoms. Finally, we did not analyze the effects of chemotherapy cycle of each regimen on symptom intensity, and this should be explored in a future study.

In conclusion, frequent symptoms of cancer outpatients receiving chemotherapy are categorized as: 1) psychosocial issues (insomnia, psychological distress, decision-making support); 2) nutrition-gastrointestinal issues (oral problems, appetite loss, nausea); 3) fatigue; and 4) pain, dyspnea, and numbness. Developing a systematic intervention program targeting these four areas is urgently required. The DT might be an effective tool to monitor psychological distress but can be highly influenced by coexisting physical symptoms. Future studies are required to determine the intervention effects in the above four areas and to develop more appropriate procedure to identify patients with psychiatric comorbidity.

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## Original Article

## Meaninglessness in Terminally Ill Cancer Patients: A Randomized Controlled Study

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**Abstract**

Although recent empirical studies reveal that fostering patients' perception of meaning in their life is an essential task for palliative care clinicians, few studies have reported the effects of training programs for nurses specifically aimed at improving these skills. The primary aim of this randomized controlled trial was to determine the effects of an educational workshop focusing on patients' feelings of meaninglessness on nurses' confidence, self-reported practice, and attitudes toward caring for such patients, in addition to burnout and meaning of life. The study was designed as a single-institution, randomized controlled trial using a waiting list control. The intervention consisted of eight 180-minute training sessions over four months, including lectures and exercises using structured assessment. A total of 41 nurses were randomly allocated to three groups, which were separately trained, and all were evaluated four times at three-month intervals (before intervention, between each intervention, and after the last intervention). Assessments included validated Confidence and Self-Reported Practice scales, the Attitudes Toward Caring for Patients Feeling Meaningless Scale (including willingness to help, positive appraisal, and helplessness items), the Maslach Burnout Scale, job satisfaction, and the Functional Assessment of Chronic Illness Therapy-Spiritual (FACIT-Sp). One participant withdrew from the study before the baseline evaluation, and the remaining 40 nurses completed the study. The nurses were all female and had a mean age of  $31 \pm 6.4$ , and mean clinical experience of  $8.9 \pm 5.5$  years. There were no significant differences in background among the groups. The intervention effects were statistically significant on the Confidence Scale, the Self-Reported Practice Scale, and the

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willingness to help, positive appraisal, and helplessness subscales, in addition to the overall levels of burnout, emotional exhaustion, personal accomplishment, job satisfaction, and the FACIT-Sp. The change ratio of each parameter ranged from 5.6% (willingness to help) to 37% for the helplessness score and 51% on the Confidence Scale. The percentages of nurses who evaluated this program as "useful" or "very useful" were 85% (to understand the conceptual framework in caring for terminally ill patients with meaninglessness), 80% (to foster nurses' personal values), and 88% (to know how to provide care for patients with meaninglessness). This educational intervention had a significant beneficial effect on nurse-perceived confidence, practice, and attitudes in providing care for patients feeling meaninglessness, in addition to the levels of burnout and spiritual well being of the nurses. *J Pain Symptom Manage* 2008;■:■-■. © 2008 U.S. Cancer Pain Relief Committee. Published by Elsevier Inc. All rights reserved.

#### Key Words

Palliative care, neoplasms, education, spiritual care, suffering, meaning, nurse

### Introduction

Recent empirical studies reveal that fostering patients' perception of meaning in their life is an essential task for palliative care clinicians.<sup>1-4</sup> In Japan, multiple surveys have identified that terminally ill cancer patients experience considerable levels of meaninglessness.<sup>5,6</sup> Our group recently proposed a conceptual framework for psycho-existential care for Japanese patients.<sup>7</sup> We defined psycho-existential suffering as pain caused by extinction of the being and the meaning of the self. We assumed that psycho-existential suffering is caused by the loss of essential components of meaning for human beings: loss of relationships with others, loss of autonomy, and loss of future (temporality). In this model, sense of meaning is interpreted as a main outcome, as consistent with some psychometric instruments measuring sense of meaning as a core concept of the state of spiritual well being.<sup>7</sup>

In fostering a sense of meaning in terminally ill cancer patients, nurses play a major role. Nurses often experience difficulty and emotional stress when facing terminally ill cancer patients with unrelieved suffering.<sup>8-10</sup> One of the sources of nurses' stress is the lack of an adequate training system to improve the skills required to care for such patients.<sup>8-10</sup> General training in communication skills has been described and evaluated.<sup>11,12</sup> A few studies also have reported the effects of training programs for nurses, specifically aimed at improving skills to relieve meaninglessness in terminally

ill cancer patients.<sup>13-16</sup> These pioneer studies have major limitations, however, including no control groups, a nonstructured intervention, and the use of nonvalidated measurement tools.

In our previous work,<sup>17</sup> we validated measurement tools to quantify nurses' self-reported practice and attitudes toward caring for terminally ill cancer patients feeling meaninglessness, and explored the effects of a five-hour educational workshop focusing on meaninglessness on nurses' self-reported practice, attitudes toward caring for such patients, confidence, burnout, death anxiety, and meaning of life. After the short-term educational session, the nurses' self-reported practice and confidence significantly improved, and helplessness, emotional exhaustion, and death anxiety significantly decreased. The percentage of nurses who evaluated this program as "useful" or "very useful" was about 80%. This result suggested that the five-hour workshop has a beneficial effect on nurse-reported practice, attitudes, and confidence in providing care for terminally ill cancer patients feeling meaninglessness. Lack of control group in the pilot study, however, limited the determination of the effects of the intervention as compared with conventional care.

The primary aim of this randomized controlled trial was thus to determine the effects of an educational workshop focusing on patient meaninglessness on nurses' confidence, self-reported practice, and attitudes toward

caring for such patients, in addition to nurses' burnout and meaning of life.

### Methods

This study was designed as a randomized controlled trial using a waiting list control (Fig. 1). The nurses were recruited from a single general hospital. A total of 41 nurses were randomly allocated to three groups using the envelope method. One participant (Group 3) withdrew from the study before the baseline evaluation, but we tried no supplementary recruitment because of adequate sample size. The remaining 40 nurses completed the study. We evaluated the nurses four times at three-month intervals (before intervention, between each intervention, and after the last intervention).

The Institutional Review Board approved the scientific and ethical validity of this study, and the nurses gave written consent.

### Subjects

The nurses were all female and had a mean age of  $31 \pm 6.4$  years (median, 29; range, 21–47), and mean clinical experience of

$8.9 \pm 5.5$  years (median, 8.0; range, 1 to 22). Eleven nurses worked in the palliative care unit. All nurses were general practice nurses, including those working in palliative care units (none of the nurses had formal certification in palliative care, such as clinical nurse specialists). There were no significant differences in the participants' backgrounds among the groups (Table 1).

### Interventions

The workshop was principally based on Murata and Morita's conceptual framework, and specifically focused on the care of terminally ill cancer patients feeling meaninglessness.<sup>7</sup> The intervention was the same throughout the study periods. The second author (H. M.) provided all lectures.

The workshop consisted of eight sessions over four months, and each session took 180 minutes. Table 2 summarizes the program contents. In the first three introductory sessions, participants were educated about basic communication skills through lectures and exercises. In the exercise section, each participant was requested to report short, typically 20 to 30 sentences, verbatim records of their actual

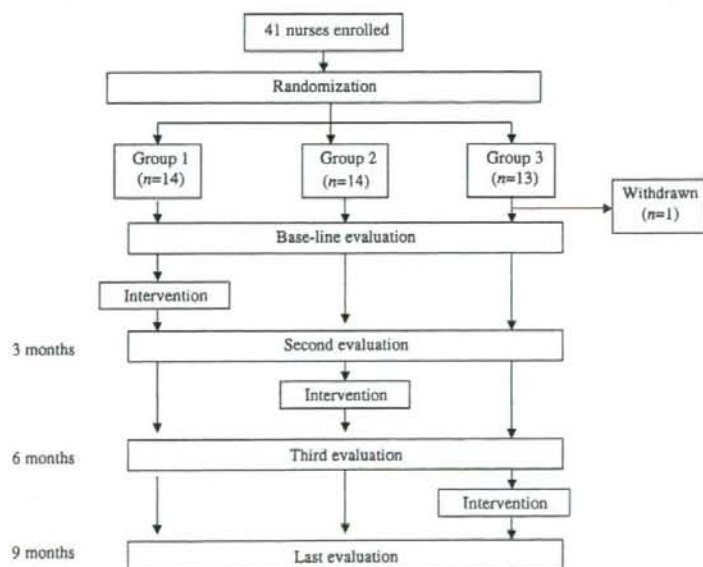


Fig. 1. Study protocol.



Table 1  
Participants' Backgrounds

	Group 1	Group 2	Group 3	P
	(n = 14)	(n = 14)	(n = 15)	
Age, years (mean ± SD)	31 ± 5.2	32 ± 8.5	31 ± 5.3	0.94
Clinical experience, years (mean ± SD)	8.1 ± 3.7	9.8 ± 7.1	8.6 ± 5.3	0.73
Working in the palliative care unit, n (%)	3 (21)	4 (29)	4 (31)	0.77

experiences in their routine practice, and received face-to-face feedback based on group discussion about appropriate listening skills.

In the following two sessions, participants were educated about the conceptual framework of meaninglessness used in this practice, and how to use the Spiritual Conference Summary Sheet. In the last three sessions, participants were requested to complete the Spiritual Conference Summary Sheet for actual patients: to identify which of the patient's statements are expressions of meaninglessness from the verbatim record as the origin of the patient's meaninglessness (temporality, relationships, or autonomy), and to establish a care plan to alleviate the patient's sense of

Table 2  
Program Contents

Session	Contents
1	Lecture (overview and what is "helping others"? (90 minutes) Exercise: read and discuss three verbatim case records (90 minutes)
2	Lecture (sympathy and active listening) (90 minutes) Exercise: read and discuss three verbatim case records (90 minutes)
3	Lecture (communication) (90 minutes) Exercise: read and discuss three verbatim case records (90 minutes)
4	Lecture (conceptual framework of meaninglessness) (90 minutes) Exercise: read and discuss three verbatim case records (90 minutes)
5	Lecture (how to use the Spiritual Conference Summary Sheet) (90 minutes) Exercise: read and discuss three verbatim case records (90 minutes)
6	Exercise: case discussion based on four Spiritual Conference Summary Sheets (180 minutes)
7	Exercise: case discussion based on four Spiritual Conference Summary Sheets (180 minutes)
8	Exercise: case discussion based on four Spiritual Conference Summary Sheets (180 minutes)

meaninglessness in daily nursing practice by strengthening the factors supporting meaning and alleviating the factors causing meaninglessness. In these sessions, four Spiritual Conference Summary Sheets were discussed under supervision from the second author, and all participants received additional individual, written feedback.

Assessment and care planning based on the Spiritual Conference Summary Sheet is an essential part of this intervention. The Spiritual Conference Summary Sheet (Fig. 2) was designed to respectively assess the source of meaning for each patient (i.e., temporality, relationships, or autonomy) from patients' actual dialogue.

#### Measurement Instruments

We adopted the Confidence and Self-Reported Practice scales, and the Attitudes toward Caring for Patients Feeling Meaningless Scale (willingness to help, positive appraisal, and helplessness) as primary end points for this study. The rationale and scale development process were described in detail in our previous article.<sup>17</sup> In addition, we measured the levels of burnout (Maslach Burnout Scale<sup>18,19</sup>) and the nurses' own spiritual well being (Functional Assessment of Chronic Illness Therapy-Spiritual [FACIT-SP]<sup>20,21</sup>) as secondary end points.

**Confidence.** Confidence in caring for terminally ill cancer patients with meaninglessness was evaluated on a single Likert-type scale from 1: "not confident at all" to 7: "very confident" for the question "With what degree of confidence can you communicate with terminally ill cancer patients saying, 'I can see no meaning in life?'"<sup>17</sup>

**Self-Reported Practice Scale.** The Self-Reported Practice Scale quantifies the level of self-reported adherence to recommended clinical practice in helping terminally ill patients to find meaning in their lives.<sup>17</sup> Self-reported practice was evaluated by the level of adherence to six recommended practice statements on a Likert-type scale from 1: "not do at all" to 5: "always": "I try to know what make the patient's life meaningful," "I try to know what strengthens or weakens the meaning of life for the patient," "I try to know how the

Dimension	Patient dialog	Assessment	Care plan
Relationships	P4(underlined)  P5(underlined)	Mr. A reflected on his past and gave a positive meaning to his bitter experience, whereby his feelings changed from repentance to gratefulness and reconciliation.  Mr. A felt supported by someone listening to him.	Listen to Mr. A's reflections on his life and encourage him to talk to strengthen the meaning from his relationships with family and relatives. Continue to listens attentively to maintain a relationship with others.
Temporality	"I'm finished. There is no sense in living."	Mr. A sensed the ineffectiveness of treatment and felt that there was no hope of cure. This caused him to feel that he had no future and that his life was meaningless from temporality.	Encourage him to reflect on his past life, to regain the meaning supported by his past and relationships, not by the future.
Autonomy		He stays in bed all day due to paralysis of the bilateral lower limbs and dependence causes meaningless from autonomy.	Encourage reflections on life to divert their patients' value from dependency to the meaningful past.
Assessment and Planning	Mr. A feels his treatment to be ineffective and suffers from feelings of having no future, and physical dependence. No future relationships. The care plan therefore would be to continue listening carefully to his reflections on life to increase the meaningfulness of his past experiences and relationships, rather than the future and physical autonomy.		

Verbatim record N: nurse P: patient

N1: How are you, Mr. A?  
 P1: ... at night. I get up in the middle of the night, and I can't help thinking of one thing after another.  
 N2: You think of many things?  
 P2: Yeah. (After being silent for a while) You visit other patients and listen to them, too?  
 N3: Yes, there are others, too.  
 P3: I guess it's pretty hard for a mother with small children. (Silent for a while)...  
 N4: (Waiting)  
 P4: I lost my mother, too, when I was 6. She was 36. Then, I was taken care of by a stepmother, but it was difficult to get used to her. We were never on good terms. (Weeps) I was raised by 3 mothers: My own mother, nurse, and stepmother. But, when my father died, I said at his funeral, "I was brought up by 3 mothers, and this was my greatest fortune," showing my thanks to relatives. That was good, because everyone thanked me for saying it. (Weeps)  
 N5: At your father's funeral, you said you were very lucky to have been brought up by 3 mothers and thanked your relatives? And you felt good, because it made everybody grateful?  
 P5: Yes. (Weeps) (Looking straight at me) I thank you for coming today. I really do. You are coming again to listen to me? It makes me feel relieved.  
 N6: Yes, I am. I am looking forward to listening to you again. (Leaves the room)

Fig. 2. Spiritual conference summary sheet.

patient's life is supported," "I try to know what meaning the disease has for the patient," "I try to understand the patient's wishes," and "I try to know what is important to the patient." We defined the scale score as the mean of the total score of the responses, and thus the score ranged from 1 to 5, with a higher score indicating a higher level of performance of recommended practices. Reliability was high, and convergent validity was examined by moderate correlation with self-reported practice about general communication.<sup>17</sup>

*Attitudes Toward Caring for Patients Feeling Meaningless: Willingness to Help, Positive Appraisal, and Helplessness.* Willingness to help, positive appraisal, and helplessness quantify the degree of willingness to make an effort to help patients feeling meaningless, nurses' positive appraisal of their experience of encountering patients feeling meaningless, and nurses' perception of helplessness when facing patients feeling meaningless, respectively. These were evaluated by levels of agreement with several statements on a Likert-type scale from 1: "never" to 7: "very much." The instructions specifically presented a situation in which the nurse faced a terminally ill cancer patient suffering from meaninglessness. The item questions were: "I feel willing to do something to relieve the patient's suffering," "I think how I can support the patient effectively," and "I wish to relieve the patient's suffering as much as possible" (willingness to help; three items, range = 1-3); "I feel grateful that the patient has told me," and "I feel that the patient trusts me" (positive appraisal; two items, range = 1-3); "I feel helplessness," "I feel like escaping," and "I feel willing to be involved (reversed item)" (helplessness; three items, range = 1-3), respectively. Higher scores indicated higher levels of nurses' willingness to help, positive appraisal of their experience, and perception of helplessness, respectively. Reliability was high, construct validity was confirmed using confirmatory factor analysis, and convergent validity was examined by moderate correlation with the Frommelt Scale.<sup>17,22,25</sup>

*Burnout.* Professional burnout was measured using the Maslach Burnout Inventory,<sup>18,19</sup> which measures three components of burnout syndrome: emotional exhaustion, depersonalization,

and lack of personal accomplishment, in addition to overall levels of burnout (visual analog scale, range = 0-100).<sup>18</sup> The psychometric properties of the Japanese version have been confirmed.<sup>19</sup> In addition, job satisfaction was measured on a 0-10 rating scale following the previous study.<sup>14</sup>

*Spiritual Well Being.* Nurses' own spiritual well being was measured using the FACIT-SP.<sup>20,21</sup> The psychometric property of the Japanese version has been confirmed.<sup>21</sup>

*Overall Evaluation.* Finally, we asked the respondents to rate their overall evaluation about the usefulness of this program in terms of: 1) understanding the conceptual framework in caring for terminally ill patients feeling meaninglessness; 2) helping in self-disclosing nurses' personal beliefs, values, and life goals; and 3) helping in learning how to provide care for patients feeling meaninglessness in clinical practice.<sup>17</sup> We used the second question, given the possibility that nurses' own spirituality might change through this educational session about patient suffering,<sup>17</sup> although the intervention itself did not deal with nurses' own spirituality. The choices were "not useful," "slightly not useful," "slightly useful," "useful," and "very useful."

#### Statistical Analysis

We first compared participants' backgrounds (age, clinical experience, and working setting) among groups by analysis of variance or Chi-square test, as appropriate. We then calculated the change ratio of each score from the mean value of each score at the baseline and just after intervention for all end points. Finally, we tested the statistical significance of treatment effect using the mixed effect model for all end points. In all analyses, the significance level was set at  $P < 0.05$  and a two-sided test was used. All analyses were conducted using statistical package SAS (SAS Institute, Cary, NC).

## Results

### Primary End Points

As shown in Fig. 3, the intervention effects were statistically significant for all primary end points: Confidence and Self-Reported Practice scales, and Attitudes toward Caring for Patients

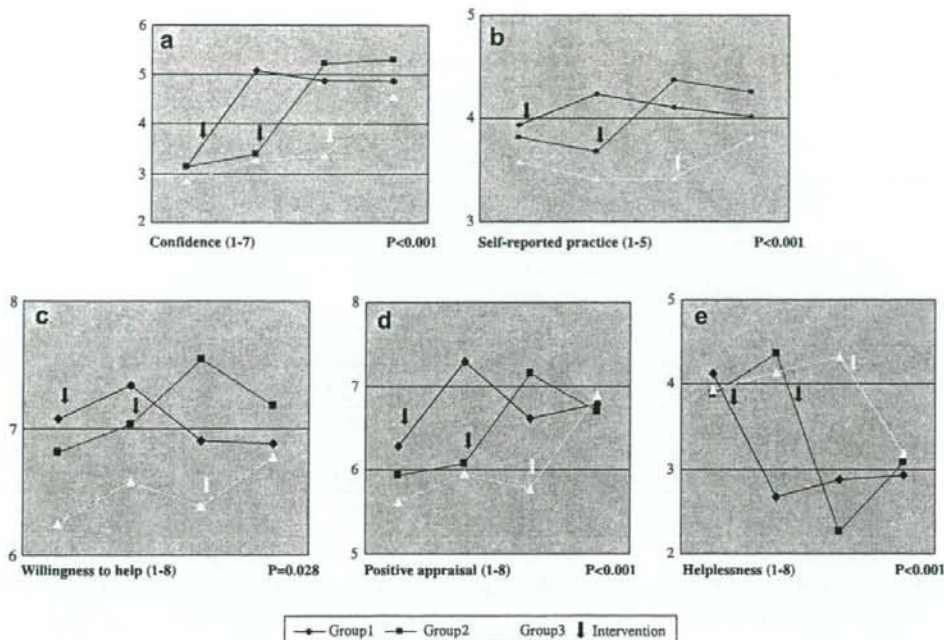


Fig. 3. Primary end points.

Feeling Meaningless (willingness to help, positive appraisal, and helplessness). The changes in these primary end points were: 5.6% (willingness to help), 12% (self-reported practice), 18% (positive appraisal), 37% (helplessness), and 51% (Confidence Scale) (Table 3).

#### Secondary End Points

As shown in Fig. 4, the intervention effects were statistically significant for the overall levels of burnout, emotional exhaustion, personal accomplishment, job satisfaction, and nurses' own spiritual well being. The changes in these parameters were: 12% (emotional exhaustion), 13% (personal accomplishment), 15% (depersonalization), 21% (overall burnout, job satisfaction), and 23% (spiritual well being) (Table 3).

#### Overall Evaluation

The percentages of nurses who evaluated this program as "useful" or "very useful" were 85% (to understand the conceptual framework in caring for terminally ill patients feeling meaningless), 80% (to help in self-disclosing nurses' personal beliefs, values, and life goals),

and 88% (to help in learning how to provide care for patients feeling meaningless).

#### Discussion

The most important finding of this study is a significant and clear beneficial effect of an educational intervention focusing on patient

Table 3  
Changes in Primary and Secondary End Points

	Before	After	Change (%)
Confidence (1-7)	3.29	4.97	51
Self-Reported Practice score (1-5)	3.70	4.16	12
Attitudes toward caring for patients feeling meaningless			
Willingness to help (1-8)	6.85	7.24	5.6
Positive appraisal (1-8)	6.06	7.12	18
Helplessness (1-8)	4.27	2.68	-37
Maslach Burnout Inventory			
Overall burnout (0-100)	66.1	52.1	-21
Emotional exhaustion (1-7)	4.11	3.62	-12
Personal accomplishment (1-7)	4.16	4.70	13
Depersonalization (1-7)	1.96	1.67	-15
Job satisfaction (0-10)	5.65	6.84	21
Spiritual well being (FACIT-Sp, 0-4)	2.15	2.65	23

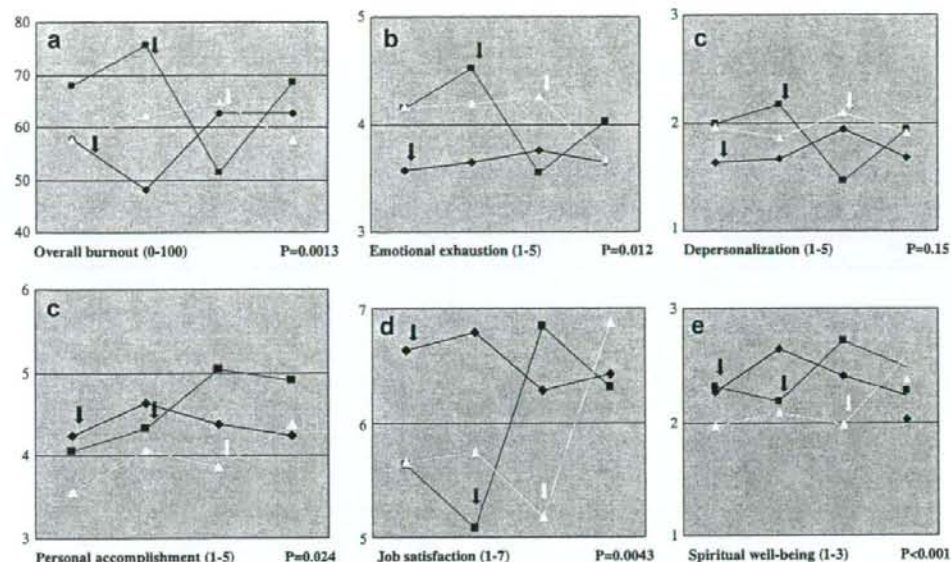


Fig. 4. Secondary end points.

meaninglessness on nurses' confidence, nurse-reported practice, and attitudes in providing care for such patients. This finding confirms our preliminary study that the intervention could provide considerable benefits for confidence, nurse-reported practice, and attitudes. Of note was the great change in nurses' confidence (51%) and helplessness (37%), in addition to the high evaluation of the overall usefulness of the workshop in learning how to provide care in clinical practice compared with a previous study (80% vs. 34%).<sup>15</sup> This result strongly suggests that this educational program can provide nurses with clinically useful specific strategies for caring for patients feeling meaninglessness.

From the fact that the change rate of willingness to help was much smaller than other variables, it could be interpreted that the participating nurses had voluntarily participated in this program and had higher motivation to help such patients. As for nurse-reported burnout, job satisfaction, and spiritual well being, our preliminary study failed to demonstrate beneficial effects,<sup>17</sup> but the present study, in addition to Wasner et al.'s pioneer work, showed positive results.<sup>14</sup> This discrepancy could be explained by the intensity of

the intervention: our preliminary work was only a five-hour workshop, whereas the two positive studies consisted of at least three month continuing education. The greater difference in the scores in the present study vs. Wasner et al.'s study could indicate that our intervention has a stronger role in preventing nurses' burnout: 21% vs. 6.6% (overall burnout), 21% vs. 9.7% (job satisfaction), and 23% vs. 7.8% (spiritual well being on the FACIT-Sp) 14. From the fact that intervention effects on burnout items in Group 1 was relatively lower compared with Groups 2 and 3, it could be interpreted that the instructor became more skillful in preventing nurses' burnout through the study periods.

A concern about this intervention is the possibility that the intervention effect may not be maintained, because some variables returned to the baseline levels after six to nine months. The finding suggests that this intervention may require periodic exposure or "maintenance therapy," and this should be a main focus of future research.

This study has several limitations. First, as this study measured nurse-reported outcomes, a future study should examine patient outcomes and/or observer-rating behavior of nurses.

Second, as the intervention was performed by one facilitator (the second author) and at a single institution, the generalizability might be limited. This shortcoming should be overcome in the next study by using different instructors and a multicenter design. Third, the intervention effects might be nonspecific effects, such as the supportive environment of a group session. We believe, however, that this possibility is low because specific outcomes, not only general burnout, significantly changed.

In conclusion, this educational intervention had a significant and clear beneficial effect on nurse-perceived confidence, practice, and attitudes in providing care for patients feeling meaninglessness, in addition to their levels of burnout and spiritual well being. Further intervention trials with patient-oriented end points using trained instructors are promising.

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## Care burden and depression in caregivers caring for patients with intractable neurological diseases at home in Japan<sup>☆</sup>

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### ABSTRACT

**Objectives:** The aims of this study are to describe the care burden on caregivers of individuals with intractable neurological diseases and to clarify the prevalence of depression in caregivers and factors related to the presence of depression.

**Methods:** A cross-sectional survey was conducted among caregivers who provide home care to patients with neurological diseases such as Parkinson disease (PD), spinocerebellar degeneration (SCD), multiple system atrophy (MSA), and amyotrophic lateral sclerosis (ALS), using a mailed, self-administered questionnaire. We used the Burden Index of Caregivers to measure multi-dimensional care burden and the Center for Epidemiologic Studies Depression scale to determine the presence of depression among caregivers.

**Results:** A total of 418 questionnaires were analyzed. Although several domains of care burden for caregivers were significantly different among the four diseases, the intensity of caregiving and hours spent caregiving were the main definitive variables. In addition, we described different aspects of the care burden using the multi-dimensional care burden scale. The prevalence of depression in caregivers was high (PD, 46%; SCD, 42%; MSA, 63%; ALS, 61%). Hours required for close supervision of the patient ( $P=0.015$ ), intensity of caregiving ( $P=0.024$ ), and low household income ( $P=0.013$ ) were independently-related variables for depression in caregivers.

**Conclusions:** The care burden of caregivers was mainly explained by the intensity of caregiving and hours spent caregiving per day, not only according to the disease. The high prevalence of depression indicates the need for effective interventions, especially for caregivers of patients with MSA and ALS.

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### 1. Introduction

The concept of burden of care was defined in 1980 by Zarit, an American gerontologist, as the physical, psychological, financial, and social discomfort and disruption experienced by the principal caregiver of an older family member [1]. In 1999, Shultz showed in a prospective study in the United States that care burden is an independent risk factor for mortality among elderly spousal caregivers [2]. Since then, many studies focusing on care burden have been

conducted and numerous instruments measuring care burden have been developed [1,3–12]. In addition, it has been shown that many caregivers experience depression during the caregiving period and care burden is correlated with depression in caregivers [13–20].

Japanese health policy now provides various preferential treatment conditions to patients with certain neuromuscular diseases, including Parkinson disease (PD), spinocerebellar degeneration (SCD), multiple system atrophy (MSA), and amyotrophic lateral sclerosis (ALS), under the framework of “intractable diseases.” Despite increased subsidization of costs, however, the heavy burden of home care for these patients has remained [21,22]. However, a quantitative evaluation of the care burden and depression among caregivers of individuals with intractable neurological disease has not been conducted in Japan. In addition, although the care burden and quality of life of caregivers for patients with PD [13,14,23,24] and ALS [25–29] have been well investigated worldwide, little research has

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been done on caregivers for patients with SCD and MSA until now [30,31].

Therefore, we conducted a cross-sectional study using a multi-dimensional instrument to clarify the care burden and depression among caregivers of patients with intractable neurological diseases including PD, SCD, MSA, and ALS in Japan. The aims of this study are (1) to clarify the care burden of caregivers of patients with such intractable neurological diseases, (2) to explore factors related to the multiple dimensions of the care burden of caregivers, (3) to clarify the prevalence of depression in caregivers of such intractable neurological diseases, and (4) to explore factors related to depression in caregivers.

## 2. Methods

### 2.1. Participants and procedures

Participants were caregivers providing home health care to patients with intractable neurological diseases between November 2003 and May 2004. A self-rating questionnaire was mailed to all caregivers of patients registered as having PD, SCD, MSA, and ALS in Mie Prefecture, Japan. The participants were asked to complete the questionnaire and return the answer sheets.

### 2.2. Measurements

#### 2.2.1. Burden Index of Caregivers (BIC-11) [32]

The BIC-11 is a multi-dimensional scale that measures the care burden on caregivers. The BIC-11 was developed through qualitative research and a validation study in accordance with Japanese cultural characteristics. The BIC is composed of 10 questions with 5 domains, "time-dependent burden," "emotional burden," "existential burden," "physical burden," and "service-related burden." Each domain consisted of two questions. Each question was assessed using a 5-point Likert scale (0: never, 1: almost never, 2: sometimes, 3: often, 4: always) and one item for overall burden, i.e., "How burdensome do you think providing care is to you?" The validity and reliability of the BIC-11 have been confirmed [32].

**Table 1**  
Participant characteristics (N=418)

	n (%)
Patient age, years (mean +/-SD)	70 +/-9
Patient gender (female)	218 (52)
Diagnosis	
Parkinson disease	273 (65)
Spinocerebellar degeneration	77 (18)
Multiple system atrophy	39 (9)
Amyotrophic lateral sclerosis	29 (7)
Intensity of caregiving <sup>a</sup>	
0	117 (30)
1	90 (23)
2	84 (22)
3	77 (20)
4	54 (14)
5	56 (14)
Caregiver age, years (mean +/-SD)	65 +/-11
Caregiver gender (female)	253 (61)
Relationship to patient (spouse)	315 (76)
Caregiver's chronic illness	331 (80)
Working caregivers	103 (25)
Household income (yen, millions)	
<=3	186 (47)
<=5	113 (29)
<=7	46 (12)
<=9	29 (7)
>9	21 (5)
Duration of caregiving, years (mean +/-SD)	5.6 +/-4.6
Hours spent caregiving per day (mean +/-SD)	5.4 +/-5.7
Hours required for close supervision of the patient (mean +/-SD)	4.8 +/-6.3
Number of other persons who help with caregiving (mean +/-SD)	1.1 +/-1.0

<sup>a</sup> Japanese intensity of caregiving grading for the long-term care insurance system.

**Table 2**

Care burden among caregivers of patients with intractable neurological diseases (Burden Index of Caregivers)

	PD		SCD		MSA		ALS		P value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Time-dependent burden	2.4	(1.1)	2.2	(1.1)	2.5	(1.0)	2.4	(1.2)	0.356
Emotional burden	1.4	(1.0)	1.2	(1.0)	1.6	(1.4)	1.6	(1.2)	0.153
Existential burden	1.4	(1.0)	1.3	(1.0)	1.7	(1.1)	1.9	(1.2)	0.046
Physical burden	1.6	(1.1)	1.2	(1.0)	1.6	(1.1)	1.9	(1.2)	0.017
Service-related burden	0.9	(0.9)	0.9	(0.9)	1.1	(1.0)	1.2	(1.0)	0.489
Total care burden	2.0	(1.1)	1.6	(1.0)	2.2	(1.2)	2.0	(1.1)	0.047
BIC total	1.6	(0.8)	1.3	(0.8)	1.8	(0.9)	1.8	(1.0)	0.015

Each question was rated 0: never, 1: almost never, 2: sometimes, 3: often, or 4: always. P values were calculated by analysis of variance.

PD, Parkinson disease; SCD, spinocerebellar degeneration, MSA, multiple system atrophy; ALS, amyotrophic lateral sclerosis.

#### 2.2.2. The Center for Epidemiologic Studies Depression scale (CES-D) [33,34]

The CES-D, developed by the National Institute of Mental Health, USA, is a self-report scale to identify individuals at risk for depression. It has been translated into Japanese by Shima. It is a self-assessment of 20 symptoms associated with depression. The responses to the questions indicate the number of days per week the subject is affected by the symptoms (0 days with a score of 0, 1 to 2 days with a score of 1, 3 to 4 days with a score of 2, and 5 or more days with a score of 3). Scores can range from 0 to 60, with a higher score representing a stronger tendency toward depressive feelings. A score of 16 or higher indicates depression [34].

#### 2.2.3. Participant demographics

Regarding demographic factors, we collected information on patient's age, gender, diagnosis, intensity of caregiving, caregiver's age, gender, relationship to patient, presence of chronic illness, working status, household income, duration of caregiving, hours spent caregiving per day, hours required for close supervision of the patient, and number of other persons who help with care. The intensity of caregiving score was determined according to the Japanese intensity of caregiving grading for the long-term care insurance system (0: none or needs only social support, 1: needs part-time caregiving, 2: needs slight caregiving, 3: needs moderate caregiving, 4: needs frequent caregiving, and 5: needs constant caregiving). The intensity of caregiving score was determined by local authorities in accordance with the needs of caregiving and the opinion of the primary physician. In the Japanese long-term care insurance system, the medical and welfare services, including financial support, were defined by the intensity of caregiving score.

### 2.3. Statistical analysis

We first described the mean values of the BIC and compared them among diseases by analysis of variance. Second, we explored factors related to each domain of the BIC using multiple regression analysis. The dependent variables were the mean score of each domain of the BIC, total care burden, and the total BIC score (mean of 11 questions); explanatory variables were participant characteristics. The multiple regression analyses were conducted with a backward variable selection method ( $P < 0.05$ ). We included the diagnosis in the models. Third, we calculated the prevalence of depression among caregivers and compared its presence among the four diseases by the chi-square test. Finally, we explored factors related to the prevalence of depression by logistic regression analysis. The dependent variable was the presence of depression in caregivers and explanatory variables were participant characteristics. Logistic regression analysis was also conducted with the backward variable selection method ( $P < 0.05$ ). We included the diagnosis in the model. The significance level was set at 0.05 and two-sided tests were conducted. All analyses

were carried out with the statistical package SAS Version 9.1 (SAS Institute, Cary, NC).

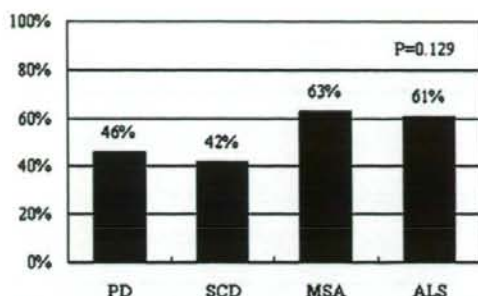
#### 2.4. Ethical considerations

Before implementing this study, the ethical and scientific validity was approved by ethics committees at Mie University Hospital in

**Table 3**  
Factors related to the domains and total score of the Burden Index of Caregiver

	Regression coefficient	Standard error	P value
<b>Time-dependent burden (<math>R^2=0.442</math>)</b>			
PD (reference)	–	–	–
SCD	–0.06	0.13	0.615
MSA	–0.06	0.18	0.725
ALS	–0.13	0.21	0.536
Hours spent caregiving per day	0.05	0.01	<0.0001
Hours required for close supervision of the patient	0.04	0.01	0.001
Intensity of caregiving	0.19	0.04	<0.0001
<b>Emotional burden (<math>R^2=0.133</math>)</b>			
PD (reference)	–	–	–
SCD	–0.12	0.16	0.443
MSA	0.04	0.22	0.874
ALS	0.13	0.25	0.620
Hours spent caregiving per day	0.03	0.01	0.008
Intensity of caregiving	0.16	0.05	0.001
<b>Existential burden (<math>R^2=0.171</math>)</b>			
PD (reference)	–	–	–
SCD	–0.08	0.15	0.592
MSA	0.06	0.21	0.774
ALS	0.40	0.24	0.099
Caregiver's age	0.01	0.01	0.021
Hours spent caregiving per day	0.04	0.01	0.001
Intensity of caregiving	0.10	0.04	0.028
<b>Physical burden (<math>R^2=0.425</math>)</b>			
PD (reference)	–	–	–
SCD	–0.23	0.13	0.086
MSA	–0.21	0.19	0.273
ALS	–0.01	0.22	0.948
Caregiver's age	0.01	0.01	0.013
Duration of caregiving	0.03	0.01	0.021
Hours spent caregiving per day	0.05	0.01	<0.0001
Hours required for close supervision of the patient	0.03	0.01	0.019
Patient gender (male)	0.46	0.10	<0.0001
Intensity of caregiving	0.15	0.04	0.000
Relationship to patient (spouse)	–0.29	0.14	0.037
<b>Service-related burden (<math>R^2=0.056</math>)</b>			
PD (reference)	–	–	–
SCD	0.01	0.13	0.941
MSA	0.22	0.20	0.291
ALS	0.52	0.22	0.019
Hours spent caregiving per day	0.02	0.01	0.016
<b>Total care burden (<math>R^2=0.379</math>)</b>			
PD (reference)	–	–	–
SCD	–0.16	0.15	0.265
MSA	–0.23	0.21	0.257
ALS	0.04	0.24	0.860
Hours spent caregiving per day	0.03	0.01	0.022
Hours required for close supervision of the patient	0.04	0.01	0.001
Patient gender (male)	0.23	0.11	0.039
Intensity of caregiving	0.20	0.04	<0.0001
<b>BIC total (<math>R^2=0.399</math>)</b>			
PD (reference)	–	–	–
SCD	–0.12	0.10	0.251
MSA	–0.14	0.15	0.348
ALS	0.03	0.16	0.838
Hours spent caregiving per day	0.05	0.01	<0.0001
Intensity of caregiving	0.13	0.03	<0.0001
Caregiver gender (male)	–0.18	0.08	0.025

The analyses were conducted by the multiple regression analysis with backward variable selection method ( $P<0.05$ ). PD, Parkinson disease; SCD, spinocerebellar degeneration; MSA, multiple system atrophy; ALS, amyotrophic lateral sclerosis.



**Fig. 1.** Prevalence of depression (CES-D). PD, Parkinson disease; SCD, spinocerebellar degeneration; MSA, multiple system atrophy; ALS, amyotrophic lateral sclerosis.

accordance with the Helsinki Declaration. Each subject was informed in writing that participation in the study was voluntary and that privacy would be strictly protected.

### 3. Results

#### 3.1. Participant characteristics

The questionnaire was sent to all 1577 families of patients with intractable neurological diseases and answer sheets were received from 785 (50%). The 1577 families included caregivers of patient who did not need caregiving. Therefore, we asked families to return the questionnaire only if the patient needed caregiving. Therefore, the nominal response rate was underestimated. The number of total respondents (analysis set) who provided valid final responses was 418 (PD, 273; SCD, 77; MSA, 39; ALS, 29).

We show participant characteristics in Table 1. The mean age of the patients was 70+/-9 years and 52% were female. As for level of caregiving, 48% was equal to or greater than grade 3. The mean age of caregivers was 65+/-11 years and 61% were female. The proportion of caregivers who were spouses was 76%. Annual household income was less than 3 million yen (US \$25,000) for 47% of the respondents. Average duration of caregiving was 5.6+/-4.6 years, and average time spent on care was 5.4+/-4.7 h daily.

#### 3.2. Care burden among caregivers of patients with intractable neurological diseases (BIC-11)

We show the care burden among caregivers of patients with intractable neurological diseases according to the BIC-11 score in Table 2. The time-dependent burden was high for all the diseases (PD, 2.4; SCD, 2.2; MSA, 2.5; ALS, 2.4). As for comparison among diseases, the existential burden ( $P=0.046$ ), physical burden ( $P=0.017$ ), total care burden ( $P=0.047$ ), and BIC total ( $P=0.015$ ) were significantly different. The existential and physical burdens tended to be higher for MSA and ALS compared to PD and SCD. In addition, the total care burden and BIC total were higher for PD, MSA, and ALS compared to SCD.

#### 3.3. Factors related to the domains and total score of the BIC-11

In Table 3, we show factors related to each domain and total score of the BIC-11. The intensity of caregiving and hours spent caregiving per day were related to the care burden domains. In addition, all participant characteristics were related to the different domains. As for the BIC total, hours spent caregiving per day ( $P<0.0001$ ), intensity of caregiving ( $P<0.0001$ ), and caregiver's gender (male,  $P=0.025$ ) were significant variables affecting care burden. Moreover, after adjustment for participant characteristics, the diagnoses were not related to domains of the BIC-11 and total score of the BIC-11. However, for time-dependent burden, physical burden, total care

**Table 4**  
Factors related to depression in caregivers (CES-D)

	Odds ratio	95% confidence interval	P value
PD (reference)	–	–	–
SCD	0.85	0.42–1.71	0.645
MSA	2.20	0.78–6.23	0.139
ALS	3.14	0.87–11.36	0.081
Hours required for close supervision of the patient	1.06	1.01–1.12	0.015
Intensity of caregiving	1.26	1.03–1.55	0.024
Household income	0.76	0.61–0.94	0.013

$R^2=0.127$ , max-rescaled  $R^2=0.169$ .

PD, Parkinson disease; SCD, spinocerebellar degeneration, MSA, multiple system atrophy; ALS, amyotrophic lateral sclerosis.

burden, and BIC total, the  $R^2$ s were high ( $R^2=0.442, 0.425, 0.379$ , and  $0.399$ , respectively). The  $R^2$ s for emotional burden and existential burden were low ( $R^2=0.133$  and  $0.171$ , respectively).

#### 3.4. Depression among caregivers of patients with intractable neurological diseases (CES-D)

In Fig. 1, we show the prevalence of depression among caregivers of patients with intractable neurological diseases measured by the CES-D. The prevalence of depression was high for caregivers of patients with all diseases surveyed (PD, 46%; SCD, 42%; MSA, 63%; ALS, 61%). But there were no statistically significant differences among diseases ( $P=0.129$ ).

#### 3.5. Factors related to depression in caregivers

We show factors related to depression in caregivers of patients with intractable neurological diseases in Table 4. Hours required for close supervision of the patient (odds ratio [OR]=1.06,  $P=0.015$ ), intensity of caregiving (OR=1.26,  $P=0.024$ ), and household income (OR=0.76,  $P=0.013$ ) were significant independently-related variables for depression in caregivers. The  $R^2$  was 0.127 and max-rescaled  $R^2$  was 0.169.

## 4. Discussion

This is the first large-scale quantitative study to investigate the care burden among caregivers of patients with intractable neurological diseases in Japan. This study is unique due to the use of the multi-dimensional care burden scale (BIC-11)[32]. We examined different features of the care burden according to the domains of the BIC-11. In addition, we showed that there is a high prevalence of depression in home caregivers of patients with intractable neurological diseases and we explored the factors related to depression in these caregivers.

Although several care burden domains of the BIC-11 were significantly different among diseases, we found that there were no significant differences after adjustment for participant characteristics (Table 3). The care burden of caregivers was mainly due to the intensity of caregiving and hours spent caregiving per day, not only by the diseases. The results indicated that the intensity of caregiving is different among diseases. Therefore, it is reasonable that the long-term care insurance system is dependent on the intensity of caregiving.

As for emotional and existential burden, the  $R^2$ s were low. The personality of caregivers, which was not measured in this study, might affect these two domains [6]. The caregiver's age was significantly related to the existential care burden. As for the physical burden, the caregiver's age, duration of caregiving, and patient's gender (male) significantly increased the care burden, whereas the relationship to the patient (spouse) significantly decreased the burden. These results were easily interpretable. The multi-dimensional approach of measuring the care burden revealed these different features of caregiving.

We found a high prevalence of depression in caregivers for all the diseases. Although statistically not significant, the prevalence of

depression in caregivers for MSA (63%) and ALS (61%) was very high. Interventions to alleviate depression are needed especially for caregivers of patients with these two diseases. In addition, we showed the factors that were related to depression in caregivers. The significant variables were the hours required for close supervision of the patient, intensity of caregiving, and household income. This is concordant with the results of Edwards's report [24]. The results of multiple logistic regression analysis were adjusted according to the intensity of caregiving and the availability of social financial support by the health authority. Low income is an independent risk factor for depression in caregivers.

The  $R^2$  for the logistic regression exploring factors related to depression was low. This result might be linked with the low  $R^2$ s obtained for the results of multiple regressions to the emotional and existential burdens. The caregiver's personality or depressive characteristics might be related to these outcomes [6,7]. Further research is needed to explore factors related to depression among caregivers.

In addition, previous research has reported on problem behavior, such as delirium, in patients with PD [23], the emotional effect of the heritability of SCD [30], the multitude of different symptoms of MSA DEL id="del69" orig=""; [31], and respirator-dependent patients and burden of caregiving [27]. Further study including these disease-specific topics would be beneficial.

#### 4.1. Limitations and future perspectives

The limitations of this study are as follows. First, the response rate was low (50%). We suspect that this is related to the patient register used, which included a considerable number of people who do not require care. Thus, the true response rate might be greater than the nominal value. However, it is a fact that there is a lack of external validity in this study. Therefore, we compared the patients' characteristics between participants and non-participants. The mean age of non-participants was 67 compared to participants' mean age of 70. In addition, the proportion of females among non-participants was 55% compared to 52% among participants. The participants were slightly older and had a higher proportion of males. Therefore, we assume that older patients require more care and that males could receive care at home from female caregivers. Moreover, we consider that in comparison with the non-participating caregivers, the participating caregivers are slightly older and comprise a higher proportion of females. However, the difference between participants and non-participants was so small that the non-responder bias is not considered to be a serious limitation. Second, we should note that participants in this study were the caregivers in the homes of patients with certain neurological diseases. The results of this study are not generalizable to institutional caregivers of patients or to caregivers of patients with other intractable neurological diseases.

## 5. Conclusion

We concluded that although several domains of care burden for caregivers of patients with intractable diseases were significantly different among diseases, the intensity of caregiving and hours spent caregiving were the main variables related to the care burden. In addition, the multi-dimensional approach to exploring care burden is effective. The prevalence of depression in caregivers of patients with intractable neurological disease was high. The significant independently-related variables related to depression were hours required for close supervision of the patient, intensity of caregiving, and low household income.

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