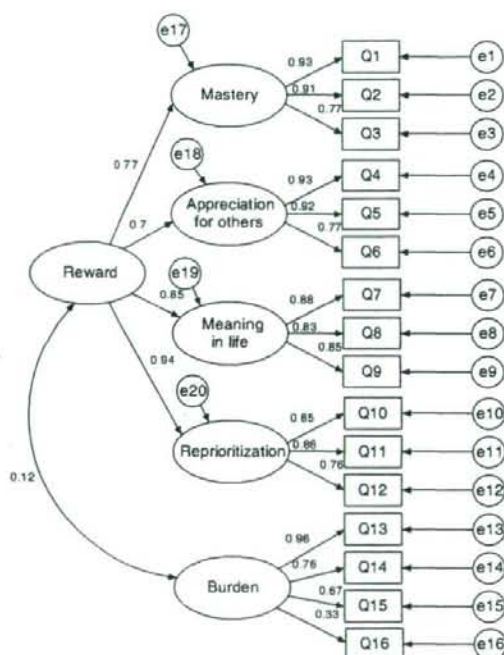


**Table 4.** Known-group validity of Caregiving Consequence Inventory

	Faith				P-value	Education				P-value	Optimism				P-value
	Less faith		More faith			Less educated		More educated			Less optimistic		More optimistic		
	Means	SD	Means	SD		Means	SD	Means	SD		Means	SD	Means	SD	
<i>Perceived reward domains</i>															
Mastery	4.8	1.2	5.2	1.0	0.02*	5.1	1.1	4.6	1.3	0.01*	4.8	1.1	5.2	1.2	0.03*
Appreciation for others	5.5	1.1	5.6	1.0	0.63	5.6	1.0	5.4	1.2	0.32	5.5	1.0	5.7	1.1	0.15
Meaning in life	4.8	1.2	5.4	0.9	<0.001***	5.2	1.0	4.6	1.3	0.001**	4.9	1.1	5.1	1.3	0.13
Reprioritization	5.4	1.1	5.8	0.8	0.03*	5.7	0.9	5.4	1.2	0.06	5.4	1.0	5.9	1.1	0.003**
Total reward score	5.1	1.0	5.5	0.7	0.01*	5.4	0.8	5.0	1.0	0.01*	5.1	0.9	5.5	1.0	0.03*

\* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ .**Figure 1.** Confirmatory factor analysis of Caregiving Consequence Inventory (Part I).  $\chi^2 262.333$  (DF = 99),  $P < 0.001$ ; GFI = 0.919; AGFI = 0.848; CFI = 0.792; RMSEA = 0.094

The four reward domain scores were highly correlated with each other ( $0.47 < r < 0.69$ ) (Table 5). We tested the factor structure of reward further by conducting confirmatory factor analyses, comparing the 4-reward domain and 1-reward domain approaches. The analysis revealed that the 4-reward domain model fit the data significantly better than the 1-reward domain model ( $\chi^2 699.4$  [df = 103],  $P < 0.001$ ; GFI = 0.692; AGFI = 0.652; CFI = 0.541; RMSEA = 0.186).

Table 6 shows the known group validity and shows that no significant correlation exists between each domain score and psychological distress,

except for a slight correlation with mastery ( $r = -0.19$ ,  $P = 0.05$ ) and burden ( $r = 0.24$ ,  $P = 0.01$ ).

#### Reliability

Table 7 shows the internal consistency and test-retest reliability. Cronbach's  $\alpha$  ranged from 0.78 to 0.93. The Cronbach's  $\alpha$  coefficient of the total reward domain was 0.93 and of the burden domain was 0.78. The ICC ranged from 0.60 to 0.73. The ICC of the total reward domain was 0.73 and of the burden domain was 0.60.

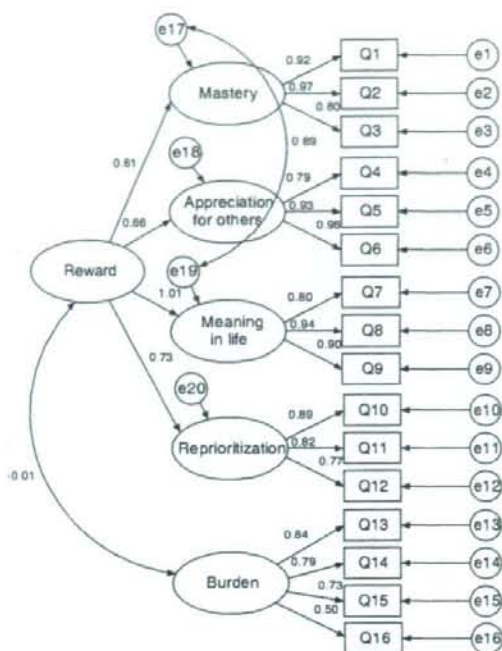


Figure 2. Confirmatory factor analysis of Caregiving Consequence Inventory (Part 2).  $\chi^2 191.6$  (DF = 98),  $P < 0.001$ ; GFI = 0.929; AGFI = 0.819; CFI = 0.749; RMSEA = 0.097

Table 5. The association with each other domain score of CCI

	Mastery	Appreciation for others	Meaning in life	Reprioritization
Mastery	1.00			
Appreciation for others	0.47***	1.00		
Meaning in life	0.63***	0.49***	1.00	
Reprioritization	0.60***	0.60***	0.69***	1.00
Burden	0.07	0.06	0.12	0.07

Figures are Pearson's correlation coefficients. \* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ .

Table 6. The association between caregiving consequence and psychological distress

	Psychological distress
Perceived reward domains	
Mastery	-0.19*
Appreciation for others	0.11
Meaning in life	-0.13
Reprioritization	-0.01
Total reward score	-0.07
Perceived burden domain	
Burden	0.24*

Figures are Pearson's correlation coefficients. \* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ .

Discussion

The most important result of this study was the development of an instrument to measure the bereaved family's perceptions about the caregiving experience in Japan. The instrument showed good

internal consistency and test-retest reliability, and known group validity was also consistent with a previous study [52,53]. The CCI is 16 items and takes less than 10 min to complete. Plain terms are used for these items, so the deficit rate is low 2% or less. Thus, we believe that this scale can assess caregiving consequences with few demands placed on the bereaved family.

Exploratory factor analysis and confirmatory factor analysis revealed 5 domains consisting of 4 sub-domains of perceived rewards and 1 domain of perceived burden: mastery, appreciation for others, meaning in life, reprioritization, and burden. The themes of the domains are consistent with our prior hypothesized concepts.

Items selected for the 'mastery' domain represented the extent to which the respondent felt in control over his or her life [35,36,56]. Although the operationalization of 'meaning' varied widely across studies and sometimes represented overall

**Table 7.** Reliability of Caregiving Consequence Inventory

	$\alpha$	ICC
<i>Perceived reward domains</i>		
Mastery	0.90	0.73
Appreciation for others	0.90	0.60
Meaning in life	0.89	0.62
Reprioritization	0.86	0.67
Total reward score	0.93	0.73
<i>Perceived burden domain</i>		
Burden	0.78	0.60

$\alpha$ , Cronbach's alpha coefficient; ICC, intra-class correlation coefficient.

positive aspects of caregiving [34,57], items selected for 'meaning' in life domains assessed the sense of purpose in life and task [57]. The 'appreciation for others' domain included items about gratitude for relationships and compassion [52], and the 'reprioritization' domain assessed changes in values and attitudes about living life to the fullest [23,52]. These 4 reward domains are similar to those identified in other studies of post-traumatic growth [39,40], and the burden domain included the items identified important for assessing caregiver burden [2,3,12,14]. Thus, content validity is assured.

It was not surprising that the 4 reward domain scores were highly correlated with each other because a sense of mastery may occur through the development of new capabilities and finding a sense of meaning or purpose [32]. In addition, caregivers described their deeper appreciation for relationships for one of the changes in values [31]. On examining concurrent validity, each reward domain of the CCI and overall perceived rewards were only moderately correlated, and the comparisons between the 4-domain and 1-domain models of perceived rewards revealed the superiority of the 4-domain model. We thus believe that a comprehensive assessment of rewards by one overall item is difficult and evaluation of every domain is recommended.

As for discriminant validity, almost none of the reward domains correlated with psychological distress. Only mastery and burden showed slight correlation with psychological distress, however these correlations were very weak. Therefore, we believe that mastery and burden were not clinically correlated with psychological distress.

This means that the caregiver considered reward to be an entity distinct from psychological distress, and it is important to use perceived reward as a measure for evaluation of caregiving consequences, as well as the caregiving burden, for improving the quality of the caregiving and bereavement experience.

Although the domains of the CCI demonstrated sufficient internal consistency, reliability measured by ICC was of moderate value [58]. Possible reasons for the moderate reliability are (1) the test-retest period was longer than 1 month and (2)

the family member's assessment of the CCI may have changed over time. However, the sufficient internal consistency as a measure of reliability for a cross-sectional study is appreciated; therefore, these moderate ICCs are not considered critical limitations of the CCI.

#### Limitations and future perspectives

The limitations of this study are as follows: first, the response rate in Part 1 of the survey was 57%. We think that this was low because the response rate of the bereaved families receiving care on the general wards was low (47% on general wards vs 62% in PCU). We believe, however, that the effect on this study was not crucial because (1) the objective was to validate a scale, not to survey actual conditions and (2) comparing the backgrounds of respondents and non-respondents revealed no differences in age, gender, the length of patient's hospital stay, or time since patient's death. Second, we identified the bereaved family members of patients who died from lung or gastrointestinal cancer on the general wards in Part 1 of the survey. We believe, however, that the effect on this study was not crucial because (1) the proportion of deceased patients on the general wards who died from other types of cancers was only 12% (23/188) in Part 1 and (2) we identified the bereaved family members of patients who died of all types of cancer on the PCU in Parts 1 and 2 of the survey. Third, we were unable to examine concurrent validity sufficiently in this study because we did not have scales to examine the details of positive aspects of caregiving consequences when this survey was conducted. Fourth, we set only one correlation between errors in the confirmatory factor analysis in Part 2 because of insufficient sample size. However, we believe this is not a fatal flaw because the fit indices for this final model in Part 1 were acceptable. We are going to perform further confirmation with a larger sample size in the next step. Fifth, this validation was executed in Japan, a culturally and ethnically homogeneous country. It is necessary to examine whether the structure of CCI can be reproduced in different cultures.

In the future, we would like to conduct a national survey on the actual positive and negative aspects of caregiving consequences in Japan. To decide the focus of the intervention, it is necessary to clarify factors related to positive and negative experience, and to explore the mechanisms that maintain and increase positive experiences, as well as those that decrease negative experiences. This CCI provides a good base for further exploration of these mechanisms. We also would like to conduct a prospective survey to clarify factors related to the change of perceived rewards using this tool, and hope that this effort will lead to the

## Caregiving consequence inventory

development of intervention programs that focus on specific aims and examine the effects on caregiver outcomes.

## Conclusions

We validated the CCI in Japanese bereaved family members. The CCI was a valid scale having sufficient factor validity, internal consistency, test-retest reliability, and acceptable construct validity. The CCI comprises four perceived reward domains: 'mastery', 'appreciation for others', 'meaning in life', and 'reprioritization', and one perceived burden domain, evaluating both positive and negative aspects of caregiving consequences from the bereaved family member's perspective. As for discriminate validity, reward has little or no correlation with psychological distress. Thus, it is important to use perceived rewards as a measure for evaluation of caregiving consequences, as well as the caregiving burden, for improving the quality of the caregiving and bereavement experience.

## Acknowledgements

This research was supported by a Health and Labor Sciences Research Grant for a third term comprehensive control research for cancer.

## Appendix

### Caregiving Consequences Inventory

How do you feel about your caregiving experience with your family member? Please check the appropriate number. 1: absolutely disagree, 2: disagree, 3: somewhat disagree, 4: unsure, 5: somewhat agree, 6: agree, 7: absolutely agree.  
Through caring for your family member,

#### Mastery

I feel confident enough to manage future life changes.  
I have learned to cope better with my life.  
I came to accept some of the changes in my life.

#### Appreciation for others

I came to have more appreciation for others.  
I became more aware of love from other people.  
I came to place greater value on relationships.

#### Meaning in life

I came to find purpose and sense of meaning in my life.  
I have a better outlook on my life.  
I came to believe that there was meaning in life no matter what happened.

#### Reprioritization

I came to understand the brevity of life and appreciate each day.

I came to notice what is really important in my life.  
I have learned the importance of being alive.

#### Burden

I felt a physical burden.  
I sacrificed my own time and schedule.  
I felt a mental burden.  
I felt a financial burden.

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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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<sup>a</sup>See Appendix for list of members.

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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 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

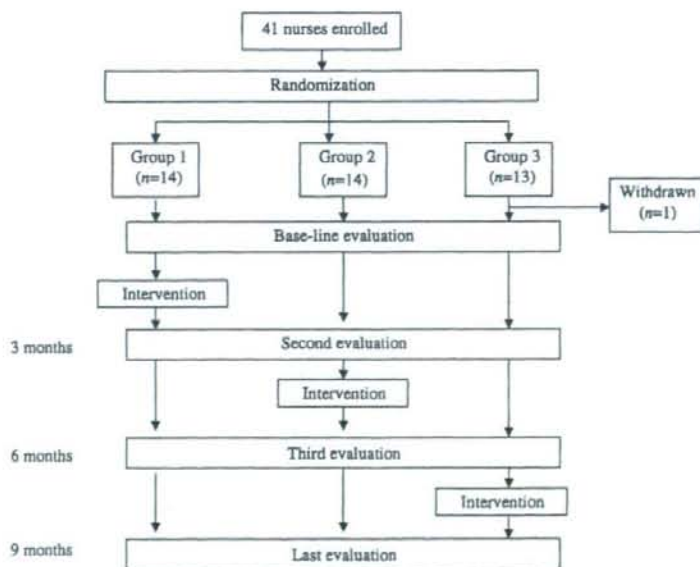


Fig. 1. Study protocol.



Table 1  
Participants' Backgrounds

	Group 1	Group 2	Group 3	P
	(n = 14)	(n = 14)	(n = 13)	
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 ± 5.9	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)	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.	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 listen attentively to maintain a relationship with others.
Temporality	P5(underlined)	Mr. A felt supported by someone listening to him.	Encourage him to reflect on his past life, to regain the meaning supported by his past and relationships, not by the future.
Autonomy	"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 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 and dependence causes meaningless from temporality and autonomy. However, he could reflect on his past of meaningful 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.	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.

Circumstances:  
I visited Mr. A during a round of the Palliative Care Team. According to a ward nurse, he had undergone painful and distressing tests the day before and was depressed, saying, "I'm finished. There is no sense in living."  
Mr. A was supine in the bed on the hall side of a 3-bed room. I sat on a chair beside his bed.

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 38. 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?  
P6: 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>17,22,23</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 meaningless; 2) helping in self-discussing nurses' personal beliefs, values, and life goals; and 3) helping in learning how to provide care for patients feeling meaningless 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

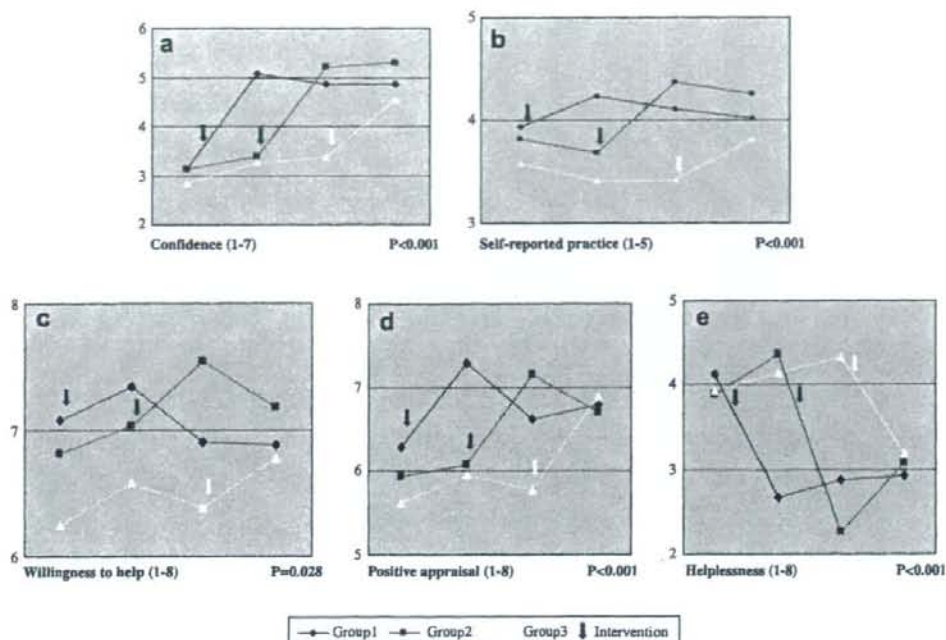


Fig. 3. Primary end points.

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 meaninglessness), 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 meaninglessness).

#### 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

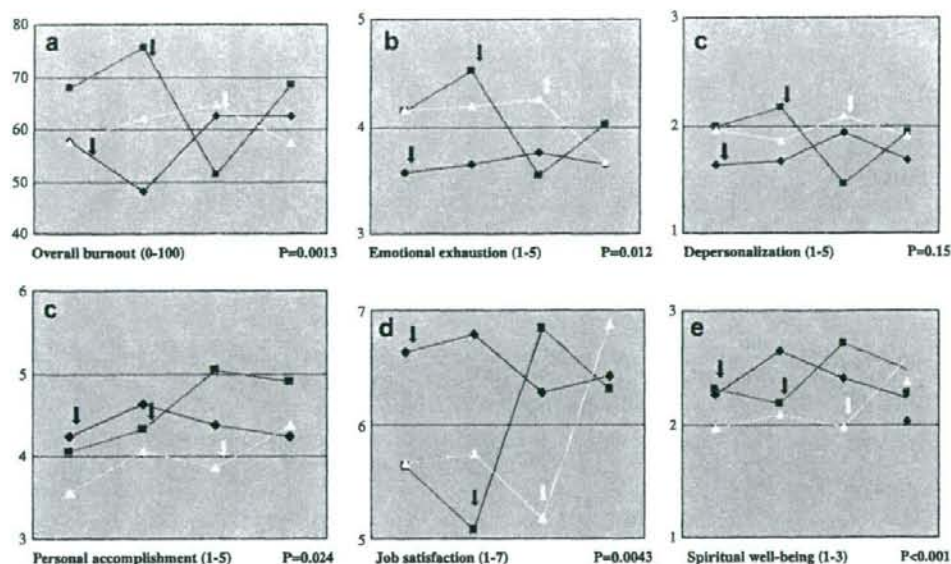


Fig. 4. Secondary end points.

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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## Original Article

# Symptom Prevalence and Longitudinal Follow-Up in Cancer Outpatients Receiving Chemotherapy

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**Abstract**

Palliative care for cancer patients receiving chemotherapy in the outpatient setting is important. The aims of this study were 1) to identify symptom prevalence and intensity in cancer patients receiving chemotherapy and 2) to describe longitudinal follow-up data obtained from repeated assessment using the distress thermometer (DT). Questionnaires were distributed to consecutive cancer outpatients newly starting chemotherapy at the first appointment and at every hospital visit. The questionnaire included the severity of 11 symptoms (M. D. Anderson Symptom Inventory [MDASI], Japanese version), the DT, and the need for help in four psychosocial areas (decision-making, economic problems, nutrition, and daily activities). In total, 4000 questionnaires were returned by 462 patients. The frequently identified problems were oral problems (21%), insomnia (19%), psychological distress (defined as the DT score of 6 or more; 15%), help with information and decision-making (14%), severe fatigue (8.2%), and severe appetite loss (6.3%). Cluster analysis identified four symptom clusters: 1) fatigue and somnolence; 2) pain, dyspnea, and numbness; 3) nausea, appetite loss, and constipation; and 4) psychological distress. Of 165 patients with a DT of score 6 or more, 115 patients (70%) demonstrated a DT score below 6 at a median of 17 days' follow-up. 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 at 7 or more on an 11-point numeric rating scale. Compared with patients with a DT score below 6 at follow-up, patients with a DT score of 6 or more at follow-up had higher levels of all physical symptoms. Frequent symptoms experienced by cancer outpatients receiving chemotherapy may be 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 score may be highly influenced by coexisting physical symptoms, and future studies to develop an appropriate

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system to identify patients with psychiatric comorbidity are necessary. *J Pain Symptom Manage* 2008;■■■-■■■. © 2008 U.S. Cancer Pain Relief Committee. Published by Elsevier Inc. All rights reserved.

### Key Words

Palliative care, neoplasms, chemotherapy, outpatient

## Introduction

Increasing numbers of cancer patients receive chemotherapy in the outpatient setting,<sup>1</sup> and symptom palliation for these outpatients is urgently required. The recent literature suggests a broad range of palliative care needs, including physical symptoms, psychological distress, help with decision-making, and economical and practical support.<sup>2-7</sup>

Knowledge of symptom prevalence is important in clinical practice: 1) to anticipate problems and needs of patients; 2) to plan care for patients; and 3) to educate clinical staff to focus on particular symptoms.<sup>8</sup> To clarify symptom prevalence and understanding patient needs are the first steps to establish an effective palliative care system for patients.

Although many studies have addressed symptom prevalence in cancer patients, their findings may not generalize to cancer outpatients receiving chemotherapy, because: 1) most studies include cancer patients receiving no anticancer treatments,<sup>9-15</sup> and few have specifically addressed cancer patients receiving chemotherapy; 2) sample sizes are usually small and nonrepresentative (i.e., limited to a certain specialty or patients consenting to a research intervention); and 3) no systematic survey has been performed in Japanese patients. In addition, cancer patients often have multiple concurrent symptoms,<sup>14-18</sup> and symptom management has shifted from individual symptoms to symptom clusters,<sup>19-21</sup> but a few empirical studies have examined clustering symptoms in outpatient cancer patients receiving chemotherapy. To address these limitations, the first aims of this study were 1) to clarify the prevalence of physical and psychological symptoms and concerns among a representative sample of cancer patients receiving chemotherapy in the outpatient setting and 2) to evaluate symptom clusters in this study population.

One of the most important symptoms is psychiatric comorbidity, including major depression and adjustment disorders. Despite the importance of early diagnosis and treatment, psychiatric comorbidity is difficult to identify and is often overlooked.<sup>22,23</sup> Recent empirical studies suggested that the distress thermometer (DT) can be an appropriate method to identify cancer patients with major depression and adjustment disorder.<sup>24-27</sup> The study populations in these studies, however, were limited to cancer patients referred to a psychiatric consultation service or a palliative care unit, or awaiting bone marrow transplantation, and only cross-sectional assessments were obtained. Longitudinal data from the outpatient chemotherapy setting, where the patient often experiences short-term deterioration and improvement of physical symptoms related to chemotherapy, are lacking. Clarifying longitudinal changes and the effects of physical symptoms on the DT can contribute to better understanding of the DT as a tool to identify psychiatric comorbidity in outpatient chemotherapy settings. The second aim of this study was thus to explore longitudinal change and the effects of physical symptoms on the DT.

## Patients and Methods

This study included all cancer patients newly starting chemotherapy, with primary tumor sites of the lung, stomach or intestine, pancreas, bile duct, breast, ovary, and uterus from April 2006 to December 2007. At the appointment regarding chemotherapy, pharmacists handed out a self-report questionnaire, with coaching on how to complete it.<sup>28</sup> This intervention was part of general instruction for outpatient chemotherapy, and required 10 to 20 minutes for completion. All pharmacists received an hour of educational instruction by the second author. Questionnaires were

thereafter distributed at every hospital visit. If the patients refused to complete the questionnaire or recognized no need, they were not obliged to complete it.

Demographic and medical variables (age, sex, primary cancer site, and opioid consumption) were obtained from medical charts. Opioid consumption was calculated as the daily amounts (mg) of oral morphine using the standard calculation ratio (transdermal fentanyl, 25 µg/hour = oral oxycodone, 40 mg = oral morphine, 60 mg).

The Institutional Review Board approved the ethical and scientific validity of a retrospective analysis of the questionnaire data obtained as part of routine clinical activity. Admitted patients gave written consent that their clinical information could be used for clinical research.

#### Questionnaire

The study group developed the questionnaire on the basis of existing validated instruments<sup>24,29-32</sup> (available in our previous report<sup>28</sup>). The questionnaire included 1) an open-ended question about the patient's greatest concerns; 2) 0-10 numeric rating scales of eight physical symptoms (pain, dyspnea, nausea, appetite loss, somnolence, fatigue, constipation, numbness) adopted from the Japanese version of the M. D. Anderson Symptom Inventory (MDASI)<sup>29</sup>; 3) presence or absence of oral problems, fever, and insomnia; 4) a 0-7 numeric rating scale of overall quality of life adopted from item 29 of the European Organization for Research and Treatment of Cancer (EORTC)-C30 questionnaire<sup>30</sup>; 5) the DT<sup>24,31</sup>; 6) presence or absence of a need for help in four areas, i.e., information about treatment and decision-making, economic problems, nutrition, and daily activities<sup>7,32</sup>; wish for help from the specialized palliative care service.

#### Analyses

The prevalence of problems was calculated for each questionnaire. Analyses of opioid consumption were performed only for patients receiving opioids. For calculations, we adopted the definition of moderate and severe symptom intensity for MDASI items as 4-6 and 7-10, respectively. We used cutoff points on the DT of 6 or more based on previous findings,<sup>24,31</sup> and follow-up data of the DT was

defined as the score obtained at a visit closest to two weeks after the initial assessment and within four weeks. We determined that a patient had problems if s/he had MDASI symptoms score as 7 or more, an oral problem, fever, insomnia, a DT score of 6 or more, or an expressed need for any help with information and decision-making, nutrition, economic problems, or daily activities.

For comparisons, age was classified into two groups (less than 60 and 60 or more years), and primary tumor sites were classified into three groups (chest, breast, and gastrointestinal). Univariate analysis was performed by the Mann-Whitney test or Kruskal-Wallis test, where appropriate. The effect of age was estimated with adjustment for gender and primary tumor site, and the effect of gender was estimated with adjustment for age and primary tumor site.

We performed cluster analysis and displayed a dendrogram using average linkage. Clusters were formed based on the distance between symptom ratings, which were calculated using squared Euclidian distances.

To explore the longitudinal change and effects of physical symptom on the DT, we initially identified all patients who had a DT score of 6 or more at any time during the study period. We then classified them into two groups: those with a DT score that declined to less than 6 at the follow-up and those with a DT score of 6 or more at the follow-up. We compared their demographic factors and the intensity of all physical symptoms.

For statistical analysis, SPSS for Windows (version 11.0) was used.

#### Results

During this study period, 472 patients newly started chemotherapy, and 10 refused to complete the questionnaire. In total, we obtained 4000 questionnaires from 462 patients (compliance rate, 98%). Each patient completed a median of six questionnaires during the study period. The percentages of missing values ranged from 2.8% (appetite loss) to 4.8% (dyspnea). Table 1 summarizes the patient characteristics. Forty-seven patients received opioid, with a mean of 36 mg oral morphine equivalent/day (range, 5.0-170;

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 2.2 ± 2.5 (1.0)
Appetite loss	6.3	11 1.6 ± 2.4 (0.0)
Constipation	4.9	11 1.5 ± 2.2 (0.0)
Somnolence	4.6	9.1 1.7 ± 2.2 (1.0)
Pain	3.6	11 1.5 ± 2.0 (1.0)
Dyspnea	3.5	9.0 1.2 ± 2.0 (0.0)
Numbness	5.3	6.9 1.2 ± 2.2 (0.0)
Nausea	2.4	6.2 9.0 0.9 ± 1.7 (0.0)
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*	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.

\*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>35-38</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

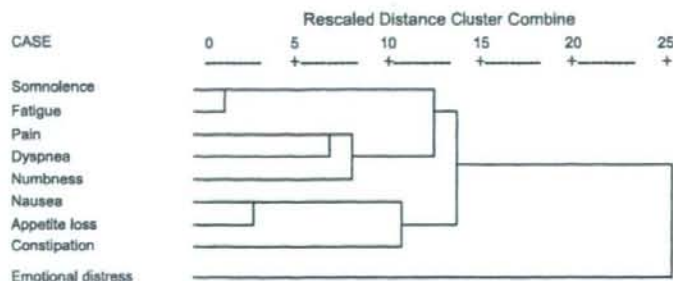


Fig. 1. Symptom cluster.