patterns; the facilitation clinical decisions; the ability to make clinical decisions explicit; and improvement the quality of treatment [21]. Furthermore, physicians may be unfamiliar about treatment of depression [22] and are not trained to treat it, and psychiatrists do not have much clinical experience and knowledge of evidence about depression among cancer patients. Thus, a pharmacological treatment algorithm for depression in cancer patients, which is based on evidence and expert opinion, is useful.

We have developed a pharmacological treatment algorithm for major depressive disorder in advanced cancer patients [23], and have used the revised version of the algorithm in clinical practices since August 2002. The objective of this study was to describe the applicability of this algorithm, the dropout rate, and the reasons for the choice of antidepressants within the framework of the algorithm and for dropout cases in this patient population. Problems related to the use of this algorithm are also identified and discussed.

Methods

Patients

This study was conducted by means of a retrospective chart review. The subjects of this study were cancer patients referred to the Psychiatry Division of the National Cancer Center Hospital (NCCH) and the Psycho-Oncology Division of the National Cancer Center Hospital East (NCCHE), Japan, between August 2002 and October 2003. The eligibility criteria for review were as follows: patients with advanced cancer, including clinical stage III or IV; patients with recurrent and systemic cancer; patients 18 years of age or older; patients diagnosed to have major depressive disorder based on the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition (DSM-IV); and patients considered to be a suitable candidate for pharmacotherapy of depression as determined by consultation-liaison psychiatrists. Patients already prescribed drugs in the algorithm for the current episode were excluded. Since this study was a retrospective review of using the algorithm in clinical practices, written consent and institutional review board approval were not obtained.

Treatment algorithm for major depressive disorder in advanced cancer patients

The algorithm is shown in Appendix [23]. It was developed on the basis of a systematic review of the literature, our own clinical experience, and advice from consultation-liaison psychiatrists. We assessed the feasibility [24], and developed a revised version taking into consideration the problems identified during the feasibility study and updated evidence. The algorithm was designed to determine the most appropriate medication for first administration, according to the severity of depression. The treatment course was determined by the drug delivery route. If the patients could not take medicines orally, amitriptyline or clomipramine, which were approved in Japan for parenteral administration, was administered. (Parenteral preparations of amitriptyline were withdrawn from the market in 2003.) Alprazolam and methylphenidate, which have a rapid onset of action, were available for mild depression. Antidepressants for moderate and severe depression were chosen based on the profiles of adverse effects of the drugs and drug interactions, for the following three reasons. First, while the drugs do not differ significantly in terms of their antidepressant efficacy, their adverse effect profiles differ among the various classes of antidepressants (e.g. serotonin re-uptake inhibitors (SSRIs): nausea, diarrhea, etc., tricyclic antidepressants (TCAs): dry mouth, constipation, etc.). Second, as advanced cancer patients also have various somatic symptoms and a compromised general condition, even minimal deleterious effects of medications can be serious. Third, advanced cancer patients take several medications. As there is no evidence yet that a combination of antidepressants is more effective than a single agent, and compliance and drug interaction are also an important consideration, this algorithm was based on the premise of monotherapy. Every drug was started at its low dose initially, with the dose being increased gradually thereafter, while watching carefully for the development of any adverse events.

Method

The applicability of the algorithm was estimated by calculating the proportion of patients for whom the algorithm was actually applied. Consultation-liaison psychiatrists treated major depressive disorder in eligible patients on the basis of the algorithm. The antidepressants were chosen according to the algorithm, in combination with appropriate psychosocial interventions and recommended physical symptom management. Psychosocial interventions mainly consist of psychotherapy and family support. These interventions and recommendations for physical symptom management are from the point of view of depression management. Psychotherapy is individualized and modified for each patient. The fundamental element of supportive psychotherapy consists of active listening with supportive verbal intervention and the occasional interpretation. Cognitive-behavioral interventions, such as relaxation and distraction with pleasant imagery are also used. For patients who feel anxious or hopeless due

to misunderstanding, a psycho-educational approach with realistic assurance is used [25]. Physical symptoms such as pain and fatigue are closely associated with depression. If we judge how a patient's physical symptoms affect depression, we recommend the primary physician to control the symptom, or sometimes to consult a specialist.

All the psychiatrists conducted weekly meetings to discuss the eligible patients and the implementation of the algorithm. We reviewed the reasons for non-application of the algorithm, the details of the treatment including the names of the drugs selected, dosage, drug delivery route, the reasons for the choice of the drug, and the reasons for any changes.

If the observation of a patient was interrupted, the reason was reviewed. Dropout was defined as discontinuation of the antidepressant within a week of initiation of treatment. If the reason for the dropout was the development of delirium, we reviewed the organic precipitating factors for the development of delirium using the approach used by Lawlor *et al.* [26] in their prospective study of advanced cancer patients. The status of involvement of each precipitating factor was classified as 'probable', 'possible', and 'comorbidity'. The most considerable precipitating factor of delirium was classified as 'probable'.

In an attempt to identify and discuss the problems associated with the implementation of the algorithm, we reviewed the reasons for non-application of the algorithm and also the reasons of dropout of patients from the treatment initiated based on the algorithm.

To identify the patient characteristics, we reviewed the computerized psychiatric consultation referral database of the Psychiatry and Psycho-Oncology Division of National Cancer Center, which included demographic variables (age, sex, marital status, education, and employment status) and medical information about the patient (primary cancer site, clinical stage of cancer, pain, and performance status as defined by Eastern Cooperative Oncology Group (ECOG) which is an objective index of a patient's physical functioning, ranging from 0 (no symptoms) to 4 (bedridden)). We recorded and reviewed the clinical estimation of the prognosis of the patent by the attending physicians at the first assessment.

Results

The total number of referrals to the Psychiatry Division of NCCH and the Psycho-Oncology Division of NCCHE between August 2002 and October 2003 was 1334, including 193 patients diagnosed as having major depressive disorder. Fifty-nine patients were diagnosed to have current major depressive disorder in advanced cancer and they were assessed by psychiatrists as being suitable candidates for pharmacotherapy.

Table 1. Demographic and clinical characteristics of the subjects ($N = 59$)

Characteristic	Mean	SD	Range
Age (years)	57	11	28–79
	N	%	
Female	38	64	
Outpatient	19	32	
Primary tumor site			
Lung	13	22	
Stomach	9	15	
Esophagus	8	14	
Breast	7	12	
Colon	7	12	
Pancreas	5	8	
Others	10	17	
Clinical stage			
III or IV	38	64	
Recurrence	18	31	
Others[a]	3	5	
Performance status (ECOG)[b]			
0	2	3	
1	19	32	
2	14	24	
3	20	34	
4	4	7	
Pain			
Present	40	68	
Absent	19	32	
Clinically estimated prognosis			
< 1 month	9	15	
1–3 months	12	20	
3–6 months	15	25	
6 months–1 year	13	22	
> 1 year	9	15	
Unknown	1	2	

[a] This includes bile duct, liver, skin, thymus, liposarcoma, malignant lymphoma, and unknown primary site.
[b] ECOG: Eastern Cooperative Oncology Group.

The demographic characteristics of the subjects are presented in Table 1. The most frequent site of cancer was the lung (22%), followed by the stomach (15%). Ninety-seven percent had physical impairment, with a performance status score of 1 or more, and 67% had pain. The clinically estimated prognosis was less than one month in 15% of the patients.

Applicability

The algorithm was applied in 54 cases (applicability rate, 92%) (54/59) (Figure 1). Among the 26 patients with mild depression, alprazolam was chosen for 19 cases, methylphenidate for 2 cases, intravenously administered amitriptyline for 4 cases, and intravenously administered clomipramine for 1 case. Among the 26 patients with moderate depression and 2 patients with severe

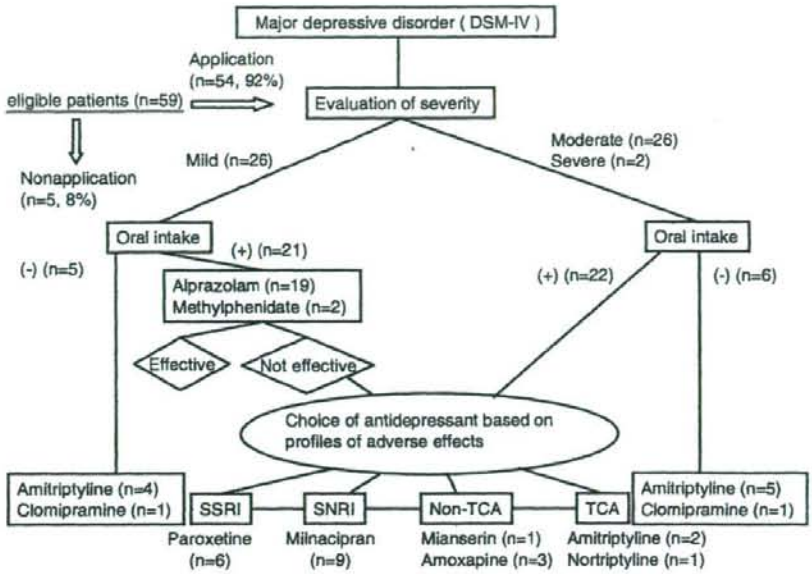


Figure 1. Pharmacological treatment algorithm for major depressive disorder in advanced cancer patients. SSRI: selective serotonin reuptake inhibitors; SNRI: serotonin noradrenalin reuptake inhibitors; TCA: tricyclic antidepressants

depression, intravenously administered amitriptyline was chosen for 5 cases, and intravenously administered clomipramine was chosen for 1 case. According to the 'choice of antidepressant based on the profiles of the adverse effects', paroxetine was chosen for 6 cases, milnacipran for 9 cases, amoxapine for 3 cases, mianserin for 1 case, nortriptyline for 1 case, and amitriptyline for 2 cases. The reasons for the selection of paroxetine were 'to prevent dry mouth and constipation' in 3 cases, 'to prevent urinary disturbances' in 2 cases, and 'to prevent delirium' in 1 case. The reasons for the selection of milnacipran were 'the presence of underlying hepatic impairment' in 3 cases, 'to prevent dry mouth and constipation' in 3 cases, and 'to prevent nausea' in 3 cases. The reasons for the selection of amoxapine were 'to prevent nausea' in 1 case, 'previously effective' in 1 case, and 'to provide an analgesic adjuvant' in 1 case. The reason for the selection of mianserin was 'to prevent arrhythmia'. The reason for the selection of nortriptyline was 'to prevent nausea' in 1 case. The reasons for the selection of amitriptyline were 'insomnia' in 1 case, and 'agitation' in 1 case. Initial doses and maximum doses are given in Table 2.

The psychiatrists did not apply the algorithm in 5 of the 59 cases. The reasons were the need to add a benzodiazepine to an antidepressant in 4 cases and the need to choose alprazolam, in spite of the diagnosis of moderate depression in order to obtain a rapid onset of action and reduce the anxiety of the patient in a case with a short prognosis. Of these 5 patients, 4 patients had moderate depression and 1 had severe depression. Because of high-anxiety level and agitation, we used antidepressants concomitantly with benzodiazepines in 4 cases.

Table 2. Initial and maximum doses ($N = 54$)

	N	Initial dose (mg)		Maximum dose (mg)	
		Median	Range	Median	Range
Mild cases					
Alprazolam	19	0.8	0.4–1.2	1.2	0.4–2.4
Methylphenidate	2	5	5	5	5
Amitriptyline[a]	4	10	5–10	12.5	10–15
Clomipramine[a]	1	6.25	6.25	6.25	6.25
Moderate and severe cases					
Milnacipran	9	30	15–50	30	15–100
Paroxetine	6	10	5–10	10	5–20
Amoxapine	3	25	25–75	25	25–75
Amitriptyline	2	25	20–30	30	30
Nortriptyline	1	10	10	10	10
Mianserin	1	10	10	10	10
Amitriptyline[a]	5	10	5–10	10	10–25
Clomipramine[a]	1	6.25	6.25	6.25	6.25

[a] Parenteral administration.

Dropout within a week

Nineteen of the 54 patients dropped out within a week of the start of treatment initiated based on the

algorithm: 8 manifested delirium; 3 showed deterioration of the general physical condition due to cancer; 2 showed adverse effects of the antidepressant treatment (fatigue after administration of milnacipran in 1 case and nausea after administration of paroxetine in one case); 2 were transferred to other hospitals; 1 showed resistance to the antidepressants; 1 suffered a brain hemorrhage; and 2 discontinued the treatment for unknown reasons. The antidepressants (alprazolam in 3 cases, amitriptyline in 1 case, and amoxapine in 1 case) were the probable precipitating factors of delirium in 5 out of the 8 cases who manifested delirium.

Discussion

In this report, we have described our experience with our algorithm-based pharmacological treatment of major depressive disorder designed especially for advanced cancer patients.

The applicability of the algorithm was 92%. This was adequate in view of the physical condition of the advanced cancer patients. As advanced cancer patients often have a wide range of physical symptoms, including pain, fatigue, weakness, anorexia, dry mouth, constipation, and nausea [10,11], some of which may limit the use of antidepressants, even minimal deleterious effects of medication can be serious in these patients. So we selected the antidepressant according to the profiles of adverse effects of the drugs for cases of moderate and severe depression. The physical symptoms and state, such as the potential development of dry mouth, constipation, urinary disturbances, nausea, delirium, hepatic impairment, and arrhythmia, were considered for the choice of the drug. Some other considerations in the choice of antidepressants were relief of symptoms such as insomnia, agitation, and pain.

As for the 11 cases which could not take medicine orally, amitriptyline and clomipramine were administered intravenously. Since the production of amitriptyline discontinued in Japan in 2003, only clomipramine is currently available for parenteral administration; therefore, such patients with depression are becoming more difficult to treat. While citalopram (SSRI), doxepin (TCA), and other antidepressants are available for intravenous administration in other countries [27], development of parenterally administrated antidepressants is needed in Japan.

In 4 cases, the algorithm was not applied because of the need to add a benzodiazepine to the antidepressant. As there was no evidence that a combination of some antidepressants was more effective than a single agent alone, and compliance and drug interaction were also important considerations, our algorithm was based on the premise of monotherapy. A previous meta-analysis revealed that the improvement of depression was more likely in the antidepressant–benzodiazepine combination group than in the antidepressant alone group at 4 weeks, but that the difference was no longer significant at 6 or 8 weeks [28]. In addition, the patients allocated to the combination group were less likely to dropout from the treatment due to the side effects than those receiving antidepressants alone [28]. Thus, the antidepressant–benzodiazepine combination may be considered in patients with high anxiety and agitation, or when dropout needs to be avoided.

In one case, the algorithm was not applied because of the selection of alprazolam in spite of the patient having moderate depression, in order to obtain a rapid onset action and reduce the anxiety for the patient who had a short prognosis. This is an issue that must be considered in the pharmacological treatment of patients with a short prognosis. It would be too difficult to conduct a randomized controlled trial of antidepressants for such a population, and there are only a few review articles and case reports [29–34]. In these reports, while no recommendations were made on the pharmacological treatment, it was suggested that psychostimulants may possibly have an effect and that alternative treatments with benzodiazepines and neuroleptics may be considered.

Delirium was the most frequent reason for dropout, and the antidepressants were the probable precipitating factor in 5 of the 8 cases. As delirium occurs in most terminally ill patients [26], it may be difficult to entirely prevent delirium based on the choice of pharmacological treatment of depression. It is known that TCAs sometimes induce delirium [35], and that benzodiazepines, including alprazolam, can also induce delirium. Therefore, the physical state should be assessed carefully, and the use of TCAs and bezodiazepines should be avoided in patients who are very vulnerable in terms of their physical condition and at a high risk of delirium. Though the reasons for the selection of amitriptyline were 'insomnia' in 1 case, and 'agitation' in 1 case, a combination of SSRI and neuloleptics may be a more safe way to treat such cases. Only clomipramine is available for parenteral administration currently, therefore, other antidepressants for parenteral administration are needed in Japan. Two patients dropped out because of the adverse effects of antidepressants. It was considered that dropouts due to adverse effects of antidepressants were few because the antidepressants were chosen based on the profiles of their adverse effects and drug interactions.

The applicability rate is high, but several problems related to the use of the algorithm were identified. Certain aspects require modification. The first issue is related to the combined use of antidepressants and benzodiazepines. The second

issue is pharmacological treatment of depression in patients with a short prognosis. The third issue is the development of delirium as an effect of the antidepressants. We are revising and developing the algorithm based on these considerations.

Appendix: Pharmacological treatment algorithm for major depressive disorder in patients with advanced cancer

Line 1

The diagnosis of major depressive disorder in patients with advanced cancer is based on the DSM-IV criteria. They include physical symptoms such as loss of appetite, insomnia, and loss of energy if they exist, whether the cause is depression, the treatment for cancer, or the cancer itself.

Line 2

Treatment is based on the severity of major depressive disorder. Cases are differentiated into mild and moderate to severe.

Line 3

The drug delivery route is evaluated. The presence of any intestinal obstruction or dysfunction of deglutition is a hindrance to oral administration.

Line 4

As rapid onset of the antidepressant effect is required with a poor prognosis, alprazolam and psychostimulants are the first choice for mild cases. Alprazolam is recommended for patients with anxiety and agitation, and psychostimulants are recommended for patients with somnolence and fatigue.

Line 5

Efficacy and adverse effects are evaluated by observation up to a week.

Line 6

Patients with advanced cancer have various physical symptoms and compromised conditions, and take several medications. So an antidepressant is chosen based on profiles of adverse effects and drug interactions.

Line 7

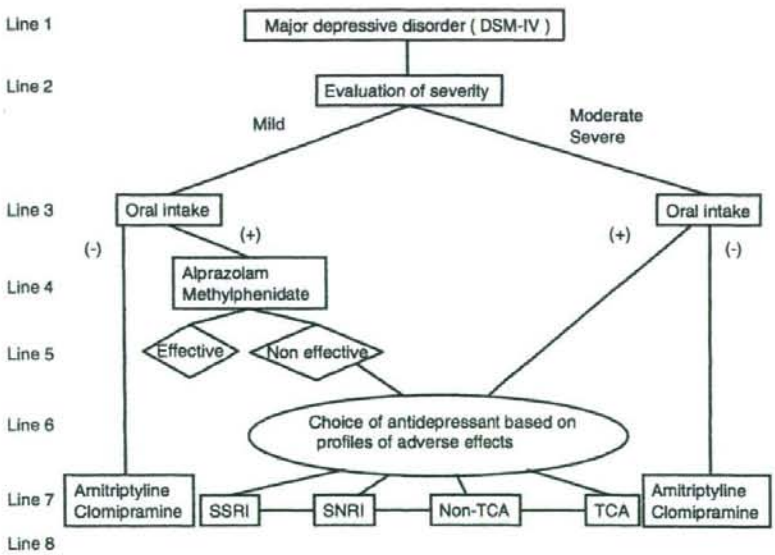
As there is no evidence yet that a combination of antidepressants is more effective than a single agent, and compliance and drug interaction are also an important consideration, this algorithm was based on the premise of monotherapy.

For patients who are unable to take medicine orally, clomipramine or amitriptyline, which are approved in Japan for parenteral administration, is administered.

SSRIs are recommended, except for patients with gastrointestinal symptoms such as nausea and a problem of drug interaction. SNRIs are recommended for patients with liver dysfunction and a problem of drug interaction, and when anticholinergic effects should be avoided. It is difficult to administer TCAs for patients with dry mouth, constipation, and fatigue which are similar symptoms as anticholinergic effects, but TCAs are recommended for agitated patients. As non-TCAs do not have the same specific effect, they should be used depending on each effect.

Line 8

Give every medication at a low dosage initially and increase it gradually, observing carefully for any adverse effects.



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References

1. Waraich P, Goldner EM, Somers JM, Hsu L. Prevalence and incidence studies of mood disorders: a systematic review of the literature. *Can J Psychiatry* 2005;**49**:124–138.
2. Hotopf M, Chidgey J, Addington-Hall J, Ly KL. Depression in advanced disease: a systematic review Part 1. Prevalence and case finding. *Palliat Med* 2002; **16**:81–97.
3. Grassi L, Indelli M, Marzola M *et al.* Depressive symptoms and quality of life in home-care-assisted cancer patients. *J Pain Symptom Manage* 1996;**12**: 300–307.
4. Okamura M, Yamawaki S, Akechi T, Taniguchi K, Uchitomi Y. Psychiatric disorders following first breast cancer recurrence: prevalence, associated factors and relationship to quality of life. *Jpn J Clin Oncol* 2005;**35**:302–309.
5. Cherny NI, Coyle N, Foley KM. Suffering in the advanced cancer patient: a definition and taxonomy. *J Palliat Care* 1994;**10**:57–70.
6. Breitbart W, Rosenfeld B, Pessin H *et al.* Depression hoplessness, and desire for hastened death in terminally ill patients with cancer. *J Am Med Assoc* 2000;**284**: 2907–2911.
7. Chochinov HM, Wilson KG, Enns M *et al.* Desire for death in the terminally ill. *Am J Psychiatry* 1995;**152**:1185–1191.
8. Henriksson MM, Isometsa ET, Hietanen PS, Aro HM, Lonnqvist JK. Mental disorders in cancer suicides. *J Affect Disord* 1995;**36**:11–20.
9. Cassileth BR, Lusk EJ, Strouse TB, Miller DS, Brown LL, Cross PA. A psychological analysis of cancer patients and their next-of-kin. *Cancer* 1985;**55**:72–76.
10. Conill C, Verger E, Henriquez I *et al.* Symptom prevalence in the last week of life. *J Pain Symptom Manage* 1997;**14**:328–331.
11. Vainio A, Auvinen A. Prevalence of symptoms among patients with advanced cancer: an international collaborative study. Symptom Prevalence Group. *J Pain Symptom Manage* 1996;**12**:3–10.
12. Ripamonti C. Management of bowel obstruction in advanced cancer patients. *J Pain Symptom Manage* 1994;**9**:193–200.
13. Costa D, Mogos I, Toma T. Efficacy and safety of mianserin in the treatment of depression of women with cancer. *Acta Psychiatr Scand* 1985;**72**:85–92.
14. Fisch MJ, Loehrer PJ, Kristeller J *et al.* Fluoxetine versus placebo in advanced cancer outpatients: a double-blinded trial of the Hoosier Oncology Group. *J Clin Oncol* 2003;**21**:1937–1943.
15. Heeringen KV, Zivkov M. Pharmacological treatment of depression in cancer patients. A placebo-controlled study of mianserin. *Br J Psychiatry* 1996;**169**:440–443.
16. Holland JC, Romano SJ, Heiligenstein JH, Tepner RG, Wilson MG. A controlled trial of fluoxetine and desipramine in depressed women with advanced cancer. *Psycho-Oncology* 1998;**7**:291–300.
17. Morrow GR, Hickok JT, Roscoe JA *et al.* Differential effects of paroxetine on fatigue and depression: a randomized, double-blind trial from the University of Rochester Cancer Center Community Clinical Oncology Program. *J Clin Oncol* 2003;**21**:4635–4641.
18. Pezzella G, Moslinger-Gehmayr R, Contu A. Treatment of depression in patients with breast cancer: a comparison between paroxetine and amitriptyline. *Breast Cancer Res Treat* 2001;**70**:1–10.
19. Razavi D, Allilaire JF, Smith M *et al.* The effect of fluoxetine on anxiety and depression symptoms in cancer patients. *Acta Psychiatr Scand* 1996;**94**:205–210.
20. Roscoe JA, Morrow GR, Hickok JT *et al.* Effect of paroxetine hydrochloride (Paxil) on fatigue and depression in breast cancer patients receiving chemotherapy. *Breast Cancer Res Treat* 2005;**89**:243–249.
21. Gilbert DA, Altshuler KZ, Rago WV *et al.* Texas medication algorithm project: definitions, rationale, and methods to develop medication algorithms. *J Clin Psychiatry* 1998;**59**:345–351.
22. Chochinov HM. Depression in cancer patients. *Lancet Oncol* 2001;**2**:499–505.
23. Akizuki N, Akechi T, Nakano T, Okamura M, Uchitomi Y. Major depression in advanced cancer patients. In *Pharmacological Treatment Algorithms for Affective Disorders*, Motohashi N (ed.). Jiho: Tokyo, 2003; 83–99.
24. Akizuki N, Okamura H, Akechi T *et al.* Clinical experience of the pharmacological treatment algorithm for major depression in advanced cancer patients: preliminary study. *Int J Psychiatry Clin Pract* 2002; **6**:83–89.
25. Wilson KG, Chochinov HM, Faye BJd, Breitbart W. Diagnosis and Management of Depression in Palliative Care. In *Handbook of Psychiatry in Palliative Medicine*, Chochinov HM, Breitbart W (eds). Oxford: New York, 2000; 25–49.
26. Lawlor PG, Gagnon B, Mancini IL *et al.* Occurrence, causes, and outcome of delirium in patients with advanced cancer: a prospective study. *Arch Intern Med* 2000;**160**:786–794.
27. Moukaddam NJ, Hirschfeld RM. Intravenous antidepressants: a review. *Depress Anxiety* 2004;**19**:1–9.
28. Furukawa TA, Streiner DL, Young LT. Is antidepressant-benzodiazepine combination therapy clinically more useful? A meta-analytic study. *J Affect Disord* 2001;**65**:173–177.
29. Block SD. Assessing and managing depression in the terminally ill patient. *Ann Intern Med* 2000;**132**:209–218.
30. Homsi J, Walsh D, Nelson KA, LeGrand S, Davis M. Methylphenidate for depression in hospice practice: a case series. *Am J Hosp Palliat Care* 2000;**17**:393–398.
31. Kugaya A, Akechi T, Nakano T, Okamura H, Shima Y, Uchitomi Y. Successful antidepressant treatment for five terminally ill cancer patients with major depression, suicidal ideation and desire for death. *Support Care Cancer* 1999;**7**:432–436.
32. Lloyd-Williams M. Difficulties in diagnosing and treating depression in the terminally ill cancer patient. *Postgrad Med J* 2000;**76**:555–558.
33. Macleod AD. Methylphenidate in terminal depression. *J Pain Symptom Manage* 1998;**16**:193–198.
34. Stiefel F, Die Trill M, Berney A, Olarte JM, Razavi D. Depression in palliative care: a pragmatic report from the Expert Working Group of the European Association for Palliative Care. *Support Care Cancer* 2001; **9**:477–488.
35. Degner D, Grohmann R, Kropp S *et al.* Severe adverse drug reactions of antidepressants: results of the German multicenter drug surveillance program AMSP. *Pharmacopsychiatry* 2004;**37**(Suppl 1):S39–S45.

original article

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Psychological and behavioral mechanisms influencing the use of complementary and alternative medicine (CAM) in cancer patients

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Background: This study explored the psychological and behavioral mechanisms of complementary and alternative medicine (CAM) use in Japanese cancer patients using two applied behavioral models, the transtheoretical model (TTM), and theory of planned behavior (TPB).

Patients and methods: Questionnaires were distributed to 1100 patients at three cancer treatment facilities in Japan and data on 521 cancer patients were used in the final analysis. The questionnaire included items based on TTM and TPB variables, as well as three psychological batteries.

Results: According to the TTM, 88 patients (17%) were in precontemplation, 226 (43%) in contemplation, 33 (6%) in preparation, 71 (14%) in action, and 103 (20%) in maintenance. The model derived from structural equation modeling revealed that the stage of CAM use was significantly affected by the pros, cons, expectation from family, norms of medical staff, use of chemotherapy, period from diagnosis, and place of treatment. The primary factor for the stage of CAM use was the expectation from family.

Conclusions: The findings revealed the existence of a number of psychologically induced potential CAM users, and psychological variables including positive attitude for CAM use and perceived family expectation greatly influence CAM use in cancer patients.

Key words: CAM, cancer patients, psychological adjustment, theory of planned behavior, transtheoretical model

original article

introduction

Cancer patients use nutritional supplements, psychological techniques, and natural medical approaches together with conventional medicine, or in replace of conventional therapy, which are so-called complementary and alternative medicine (CAM). Recent surveys have demonstrated the high prevalence of CAM use by cancer patients. Sixty-seven percent of Canadian respondents reported using CAM, most often in an attempt to boost the immune system [1]. The first national survey on the use of CAM in Japan revealed that 45% of Japanese cancer patients have used CAM [2].

CAM is defined by the National Center for Complementary and Alternative Medicine as 'a group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional medicine' [3] In addition, a new operational definition of CAM was proposed that it should include patients' perspectives, such as individual goals, objectives, and beliefs of the patients [4]. Therefore, it is important to consider psychological aspects such as patients' background, reasons or intentions for using CAM in oncology.

Several studies have explored the background and reasoning behind CAM use [1, 5–7]. CAM use in early-stage breast cancer patients was regarded as a marker of greater psychosocial distress and a worse quality of life [7] and advanced-stage cancer patients who used CAM had higher levels of anxiety and pain, lower satisfaction with conventional medicine, and a lower need for control over treatment decisions [8]. Alternatively, the use of CAM by cancer patients has not been associated with perceived distress or poor compliance with medical treatment [9]. However, the psychological and behavioral mechanisms of CAM use have not yet been clarified. Therefore, we carried out a multicenter cross-sectional survey to explore the psychological mechanism of CAM use in Japanese cancer patients from patients' perspectives, using the transtheoretical model (TTM), and the theory of planned behavior (TPB).

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The TTM [10] is useful for explaining changes in health behavior and has been used in various programs such as smoking cessation [11], genetic testing for colorectal cancer [12], and mammography adoption [13]. In the TTM, the decisional balance between pros and cons—positive and negative attitudes for the behavior—will account for the state of change observed during five stages: precontemplation, contemplation, preparation, action, and maintenance [10]. We adopted this classification to explain the behavioral intention of patients using CAM in cancer treatment. Moreover, self-efficacy, which acts as a mediating function for the psychological adjustment of cancer patients [14, 15], is an important factor affecting a person's movement from one stage to another.

The TPB [16] examines behavioral intentions based on three major components: the patient's attitude towards the behavior, perceived control, and subjective norms. In cases of cancer patients, attitude towards behavior may include perceived effectiveness of treatment, anxiety regarding side-effects, etc. Perceived control is the individual's perception of the extent to which performance of the behavior is easy or difficult, and is synonymous with the concept of self-efficacy [16]. Subjective norms in cancer CAM include expectation from family members, and norms of medical staff towards the patients.

Our hypotheses are as follows: (i) cancer patients are classified into five stages of CAM use, (ii) the stage of CAM use is explained by TTM and TPB variables, and (iii) perceived control positively correlates with CAM use and mediates between CAM use and psychological adjustment.

patients and methods

participants

This study was approved by the institutional review boards of the Kinki Chuo Chest Disease Center, National Kyushu Cancer Center, and National Shikoku Cancer Center. From April 2005 to August 2005, a total of 1100 questionnaires were distributed to patients at each institute. Patients were enrolled in the study after their attending physician assessed if they met the following conditions: were receiving medical treatment through the outpatient or inpatient units at any of the three cancer centers, had an Eastern Cooperative Oncology Group performance status [17] from zero to three, were physically able to fill in the questionnaires by themselves, and had no cognitive impairment. On the questionnaire, we explained the purpose of the study and the fact that returning the questionnaire would be regarded as consent for participation; though we asked the patients to return the questionnaires anonymously.

measures

For this study, we developed our own questionnaire to examine CAM use in cancer patients (available from the authors). The questionnaire contained 85 items and it took about 20 min to complete. On the cover page of the questionnaire, CAM was defined using same definition of our previous survey [2]: 'as any therapy is not included in the orthodox biomedical framework of care for patients, which includes remedies used without the approval of the relevant government authorities of new drugs after peer review of preclinical experiments and clinical trials regulated by law. Health insurance does not usually cover the cost of CAM, and patients are generally liable for all expenses incurred by CAM use. CAM may include use of natural products from mushrooms, herbs, green tea, shark cartilage, megavitamins, or other special foods, and may incorporate acupuncture, aromatherapy, massage, meditation, etc'. Additionally, a sheet containing 20 examples of CAM therapies and products was attached to the questionnaire. The first portion of the questionnaire asked for information on the patients' background, including type of disease, age at onset, current age, gender, educational level, economic status, type of cancer treatment, satisfaction with treatment, smoking, drinking, and social support measured by the single item Tangible Social Support Scale [18].

The second part of the questionnaire included items originally designed to evaluate the cancer CAM-specific TTM and TPB variables. To measure the patients' subjective intention with regard to CAM use, we additionally defined cancer CAM use as those 'using any supplements or dietary foods or receiving any therapy that appears to have anticancer effects or auxiliary effect to that of conventional cancer therapy'. Respondents were asked to rate themselves based on the five stages of the TTM [10]: precontemplation ("I have no interest in using CAM"), contemplation ("I have been thinking that I might want to use CAM"), preparation ("I am preparing to use CAM"), action ("I have already used CAM in the last 6 months"), and maintenance ("I have already used CAM for >6 months"). The next section was composed of 27 items measuring TTM and TPB variables. The items were measured on a five-point Likert-type scale that ranged from 'not at all' (1) to 'extremely' (5). They included following five categories, (i) positive attitudes for CAM; (ii) pros; (iii) cons; (iv) expectation from family; and (v) norms of medical staff. The items were developed in our previous study on CAM [2] and another study on dietary food intake [19]. We used 16 from 27 items using confirmatory factor analysis on the current data as structurally valid and reliable items (Table 1). Also, content validity of the all TTM and TPB items in this part was confirmed by experts of two physicians, one psychiatrist and two psychologists.

To assess psychological adjustment, we used the Japanese version [20] of the Hospital Anxiety and Depression Scale (HADS) [21], which has 14 questions on anxiety and depression with each question rated from 0 to 3. The validity and reliability of the Japanese HADS in cancer patients has been confirmed previously [22].

To assess perceived control in patients, we used the Self-Efficacy for Advanced Cancer (SEAC) scale, which was designed to evaluate self-efficacy of cancer patients [23]. The SEAC scale has 18 items with three subscales: symptom coping efficacy, activities of daily living efficacy (ADE), and affect regulation efficacy (ARE). The scale was formatted on an 11-point Likert-type scale ranging from 0 (not at all confident) to 100 (totally confident). The reliability and validity of this scale were also confirmed [23].

Finally, the Japanese version of the MD Anderson Symptom Inventory (MDASI-J) [24] was developed as a brief multiple-symptom assessment scale. It consisted of 13 symptom items [25], and its validity and reliability were confirmed [24]. We used 10 of the 13 physical symptom items for our statistical analyses since the items for distress, sadness, and remembrance were significantly and highly correlated with the HADS total score ($r = 0.0479$, $P < 0.001$; $r = 0.456$, $P < 0.001$; $r = 0.334$, $P < 0.001$, respectively).

statistical analyses

Descriptive analyses were carried out summarizing the participants' backgrounds and scores following psychological measurements. Those with >30% missing values on the questionnaire were excluded from the analyses. The factors predicting stage of CAM use were analyzed through univariate analysis using the analysis of variance. In order to carry out multivariate analyses, we transformed the participants' responses for the stage of CAM use into a numeric scale ranging from 1 to 5 points (1, precontemplation; 2, contemplation; 3, preparation; 4, action; and 5, maintenance), according to a previous study [15]. Next, structural equation modeling (SEM) using the maximum likelihood method was carried out to

Table 1. Items measuring TTM and TPB variables and factor definitions

Items	Factor loadings
Positive attitudes for CAM (Cronbach alpha = 0.83)	
Definition: The items represented the high-perceived availability and importance of CAM use for the patients.	
1. CAM is important to retain physical strength.	0.80
2. Hospital care alone is not enough.	0.68
3. Convenience is an important determinant of starting to use CAM.	0.84
4. The cost of CAM is important.	0.66
Pros (Cronbach alpha = 0.90)	
Definition: The items represeinted patients' perceived positive outcomes of CAM use.	
5. The use of CAM leads to the cure of disease.	0.90
6. The use of CAM halts the progression of disease.	0.89
7. The use of CAM boosts physical and immune strength.	0.90
8. CAM has fewer side-effects compared with medical care.	0.69
Cons (Cronbach alpha = 0.70)	
Definition: The items represented patients' perceived negative outcomes of CAM use.	
9. The use of CAM has bad influence on medical care.	0.79
10. The use of CAM deteriorates disease.	0.89
11. I am aware of the side-effects of CAM.	0.53
12. I am aware of the dependence liability of CAM.	0.53
Expectation from family (Cronbach alpha = 0.65)	
Definition: The items represented patients' perceived expectations and recommendations from family.	
13. My family/friends believe that I should be actively engaged in the use of CAM.	0.74
14. My use of CAM is influenced by the opinions of my family/friends.	0.65
Norms of medical staff (Cronbach alpha = 0.34)	
Definition: The items represented patients' perceived expectation, recommendation from patients' medical staff, or their norms.	
15. My doctors/nurses believe that I should be actively engaged in the use of CAM.	0.68
16. My use of CAM is influenced by the opinions of my doctors/nurses.	0.30

Fit indices from the confirmatory factor analysis for items and factors indicated above: chi-square (96) = 345.5; P = 0.001; GFI = 0.92; AGFI = 0.88; CFI = 0.94; RMSEA = 0.07.
TTM, transtheoretical model; TPB, theory of planned behaviour; CAM, complementary and alternative medicine.

test the model. Because the model needed a parsimonious structure, we used the mean scores of SEAC as 'self-efficacy', the total score of HADS as 'psychological distress', and the mean scores of 10 items of MDASI-J as 'physical sympotom'. We conducted all statistical analyses using SPSS (version 14.0) and AMOS (version 5.0.1) software packages.

results

response rate to questionnaire

Of the 1100 questionnaires, 750 were given to inpatients and 350 to outpatients. Out of the 651 questionnaires returned (response rate 59.2%), 521 were valid for statistical analyses. The rest (n = 130) were invalid because of the lack of major information such as disease name or stage of CAM use. Moreover, questionnaires from noncancer patients were excluded from the analyses. Thus, the rate of valid replies was 47.4%.

backgrounds of patients and distribution of CAM use

The participants consisted of 246 males and 270 females, and five unknowns. Table 2 summarizes the demographic and diagnostic information of the participants. For staging, 88 patients (16.9%) were in precontemplation, 226 (43.4%) in contemplation, and 31 (6.6%) in preparation among the 347 CAM nonusers (66.6%), with 71 (13.6%) in action and 103 (19.8%) in maintenance among the 174 CAM users (33.4%). Table 1 also shows the prevalence of the five stages of CAM use categorized by demographic and medical status variables. The prevalence of CAM use in the higher stages, including action and maintenance, was significantly higher in patients who received chemotherapy ($P < 0.001$), those dissatisfied with current conventional treatment ($P < 0.05$), and outpatients ($P < 0.001$).

psychosocial factors associated with the stages of CAM use

Table 3 shows the mean response and the results of the univariate analyses for psychological variables, physical symptom variables, and social support obtained from patients at each of the five stages of CAM use. There were significant differences amongst patients in the five stages based on pros ($P < 0.001$), cons ($P < 0.001$), positive attitude for CAM ($P < 0.001$), and expectation from family members ($P < 0.001$). There was a slightly higher response on ADE ($P < 0.10$) in patients who were in the action and maintenance stages.

structural model for stages of CAM use

We carried out SEM by first selecting 14 variables in the initial model because they were observed to be significant predictors in the univariate analysis or were essential components for the TTM and TPB theories: use of chemotherapy, period from diagnosis, whether need for treatment was met, treatment place, stage of CAM use, psychological distress, pros, cons, positive attitude, expectation from family members, norms of medical staff, self-efficacy, psychological distress, physical symptoms, and social support. Next, we drew all paths according to the results of the correlation analysis. Since there was a significantly strong correlation between the pros and a positive attitude ($r = 0.80$, $P < 0.001$), and since the explanation by the TTM is given a priority for our purposes, we dropped positive attitude from the initial model. We repeated the SEM and sequentially dropped paths that were not significant until all the paths in the model became significant ($P < 0.05$). The variable 'met need for treatment' was dropped from the model because all the paths from this variable became not significant.

Figure 1 represents the final model. The fit indices for this model were excellent and included the following: chi-square

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Table 2. Patients' background and CAM use stage

	Total	Precontemplation		Contemplation		Preparation		Action		Maintenance		P (χ^2 test)
	n	n	%	n	%	n	%	n	%	n	%	
Total	521	88	16.9	226	43.4	33	6.3	71	13.6	103	19.8	
Age years												
>60	262	47	17.9	120	45.8	13	5.0	31	11.8	51	19.5	0.446
£60	253	40	15.8	105	41.5	19	7.5	40	15.8	49	19.4	
Gender												
Male	270	43	15.9	112	41.5	22	8.1	35	13.0	58	21.5	0.336
Female	246	45	18.3	110	44.7	11	4.5	36	14.6	44	17.9	
Education												
High school	318	50	15.7	141	44.3	7.2	7.2	46	14.5	58	18.2	0.561
Posthigh school	174	34	19.5	67	38.5	10	5.7	25	14.4	38	18.2	
Period from diagnosis												
£1 year	261	56	21.5	118	45.2	20	7.7	46	17.6	21	8.0	0.000
>1 year	246	29	11.8	102	41.5	10	4.1	25	10.2	80	32.5	
Conventional treatment												
Chemotherapy	393	58	14.8	158	40.2	28	7.1	61	15.5	88	22.4	0.001
Nonchemotherapy	122	27	22.1	66	54.1	5	4.1	10	8.2	14	11.5	
Treatment met patient's needs												
Yes	371	72	19.4	161	43.4	18	4.9	49	13.2	71	19.1	0.045
No	150	16	10.7	65	43.3	15	10.0	22	14.7	32	21.3	
House income												
‡U7 000 000	113	17	15.0	48	42.5	5	4.4	13	11.5	30	26.5	0.438
<U7 000 000	334	53	15.9	144	43.1	23	6.9	50	15.0	64	19.2	
Treatment place												
Inpatient ward	360	67	18.6	167	46.4	27	7.5	53	14.7	46	12.8	0.000
Palliative care unit	24	2	8.3	8	33.3	5	20.8	3	12.5	6	25.0	
Outpatient clinic	161	21	13.0	59	36.6	6	3.7	18	11.2	57	35.4	
Cancer												
Lung	190	28	14.7	69	36.3	11	5.8	34	17.9	48	25.3	0.137
Breast	55	11	20.0	30	54.5	4	7.3	4	7.3	6	10.9	
Gastrointestinal	79	13	16.5	40	50.6	6	7.6	10	12.7	10	12.7	
Gynecological	61	8	13.1	28	45.9	2	3.3	7	11.5	16	26.2	
Other	121	24	19.8	54	44.6	9	7.4	13	10.7	21	17.4	

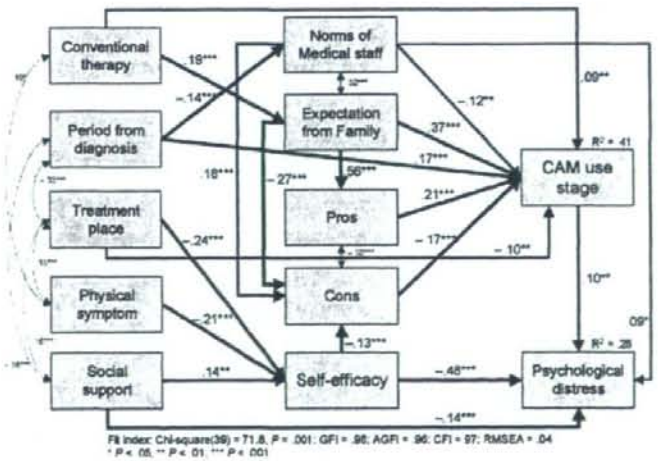

Figure 1. Structural model for the stage of CAM use and psychological adjustment.

Table 3. Descriptive data and ANOVA: mean comparison among CAM use stages

Measure	Precontemplation		Contemplation		Preparation		Action		Maintenance		P (F test)
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
TTM components[a]											
Pros	20.74	1.09	20.28	0.84	0.52	0.64	0.67	0.86	0.52	0.79	0.000
Cons	0.31	0.93	0.30	0.90	0.17	0.91	20.58	0.83	20.52	1.03	0.000
TPB components[a]											
Positive attitude	20.84	0.99	20.27	0.90	0.58	0.62	0.61	0.77	0.59	0.73	0.000
Expectation from family member	20.71	0.81	20.35	0.80	0.58	0.85	0.63	0.93	0.64	0.88	0.000
Norms of medical staff	20.10	1.06	0.05	0.92	0.08	1.11	0.12	0.95	20.14	1.09	0.335
Self-efficacy											
ARE	60.34	26.28	57.93	23.33	57.72	23.51	64.82	20.34	61.17	19.83	0.241
SCE	54.80	28.38	53.61	23.16	54.48	26.21	61.21	20.97	57.92	21.98	0.167
ADE	66.33	27.48	64.83	25.44	67.26	25.47	72.85	19.00	70.89	23.75	0.097
Total	60.49	26.44	58.79	23.18	59.82	23.87	66.30	19.01	63.33	20.68	0.139
HADS											
Anxiety	5.58	3.65	5.71	3.86	6.02	4.11	5.58	4.31	6.14	3.90	0.335
Depression	5.42	3.29	5.83	3.39	6.13	3.82	5.66	4.11	6.48	4.04	0.841
Total	11.00	6.26	11.54	6.66	12.15	7.30	11.24	8.05	12.62	7.26	0.533
Physical symptom											
Pain	29.01	33.68	28.13	31.88	37.42	32.66	32.50	34.09	23.70	30.61	0.227
Lack of appetite	33.61	34.56	27.41	30.30	31.43	29.15	32.35	32.97	24.00	30.48	0.219
Disturbed sleep	33.73	33.52	27.63	27.72	29.03	24.81	34.06	29.42	32.60	32.27	0.335
Nausea	20.95	32.51	22.57	30.67	18.71	27.78	22.65	32.07	20.10	32.28	0.937
Fatigue	38.10	29.76	32.80	27.59	37.74	28.37	34.06	30.06	37.92	29.71	0.461
Dyspnea	23.37	29.81	18.62	26.40	19.67	19.91	21.32	27.64	26.02	29.17	0.235
Numbness or tingling	28.80	32.25	25.79	29.21	27.33	30.16	28.26	31.85	30.30	33.53	0.800
Drowsy	34.88	26.86	28.69	26.86	37.00	26.67	31.76	26.26	35.54	27.62	0.140
Vomitting	20.85	32.93	18.97	30.53	16.00	28.96	20.00	30.71	20.70	31.92	0.944
Dry mouth	30.49	31.70	27.16	28.82	31.67	30.41	24.93	27.15	28.63	28.91	0.725
Physical symptom[b]	29.59	22.87	25.90	21.62	28.73	18.17	28.38	21.80	28.10	22.53	0.695
Social support											
Tangible assistance	6.09	5.27	5.57	4.37	6.71	4.90	6.12	3.85	5.12	2.88	0.307

[a]Z score.

[b]Average score among 10 physical symptom variables.

ANOVA, analysis of variance; CAM, complementary and alternative medicine; SD, standard deviation; TTM, transtheoretical model; TPB, theory of planned behaviour; ARE, affect regulation efficacy; SCE, symptom coping efficacy; ADE, activity of daily living efficacy; HADS, Hospital Anxiety and Depression Scale.

(39) = 71.8, P = 0.001; Goodness of fit index = 0.98; Adjusted goodness of fit index = 0.96; Comparative Fit Index = 0.97; and Root Mean Square Error of Approximation = 0.04. Overall, the final model accounted for 41% of the variance in the stage of CAM use and 28% of the variance in psychological distress. The parameter with the highest value that explained the stage of CAM use was expectation from family members (beta = 0.37, P < 0.001). Furthermore, norms of medical staff and pros and cons all had significant direct effects on the stage of CAM use (beta = −0.12, P < 0.01; beta = 0.21, P < 0.001; and beta = 20.17, P < 0.001, respectively). The demographic and medical status variables that significantly explained the stage of CAM use included receiving chemotherapy (beta = 0.09, P < 0.01), period from diagnosis (beta = 0.37, P < 0.001), and treatment place (beta = 20.10, P < 0.01). The parameter with the highest value that explained psychological distress was self-efficacy (beta = 0.17, P < 0.001). Moreover, social support significantly affected psychological distress (beta = 20.14, P < 0.001). Finally, the stage of CAM use significantly, though only partially, affected psychological distress (beta = 0.10, P < 0.01).

discussion

Our survey revealed that 33% of the participants used CAM as a replacement or an adjuvant to conventional cancer treatment. The rate of CAM use in this study approximately corresponded to the rate in a previous study [26], but was lower than the rate observed in a Japanese national survey [2]. This is likely due to the fact that our sample consisted of a much smaller number of patients from the palliative care unit (n = 24, 4.7%) compared with the previous study (n = 289, 9.3%). When we grouped participants into the five TTM stages of CAM use, the contemplation stage had the largest population (N = 226, 43.4%). Although these participants did not use CAM, they expressed interest in using it in the near future. Therefore, we concluded that a majority of our participants were potential CAM users.

Using SEM, we determined that 41% of the variance in advance of the CAM use stage was mainly due to the following TTM and TPB variables: expectation from family (positive), pros (positive), norms of medical staff (negative), and cons (negative). Three demographic and medical status variables were statistically significant in explaining CAM use, but their size was smaller than the other psychological variables. Therefore, we concluded that psychological variables are important factors promoting CAM use. With psychological variables, the pattern in which pros were positive predictors and cons were negative predictors of a person's stage, is consistent with the theoretical postulation of the TTM [10]. The most frequent pro notion regarding CAM was that it 'boosts physical and immune strength', while the most frequent con was that it had 'unpleasant side-effects' ['agree' and 'strongly agree' response: N = 272 (53%); N = 187 (38%), respectively]. Thus, beliefs regarding the positive outcome of CAM were strong motivations for CAM use, but patients simultaneously worried about the adverse effects. Therefore, if the patients' perceived balance between the pros and cons of CAM was to be changed by acquiring new information on CAM—e.g. the positive effect of a certain CAM product was empirically proven by a clinical trial—many patients in the contemplation stage would likely then use CAM. Therefore, it is important to provide evidence based and easy to understand information on CAM use in a systematic way, such as guidebooks or web resources, and to develop clinical guidelines on CAM use.

Another unique feature of CAM use that we determined is that the expectation from family in TPB explained the largest part of the variance in the CAM use stage. Previous studies have reported that family and friends of cancer patients generally provided information, supported the decision, or recommended the use of CAM [2, 27, 28], and that CAM users were not autonomous problem solvers [29]. Therefore, our result makes much clear of the critical role that patient recognition of family pressure plays during the decision-making process for CAM use.

Previous studies have indicated that the use of CAM was a marker of bad psychological adjustment [6] and had positive effects on patients' sense of control [30]. On our results, progressed stage of CAM use significantly but not strongly predicted psychological distress, which was mainly explained by self-efficacy, that is, perceived control, and it did not directly explain CAM use stage and mediated by cons. In summary, CAM use did not directly provide perceived control to patients but a little worse psychological adjustment. We could not obtain the evidence that perceived control had strongly mediated the relationship between CAM use and psychological adjustment.

The limitations to this study include the cross-sectional design and sample. Use of SEM could have made clear of multiple relationships among variables in the cross-sectional design. This study also used a convenient sample recruited from three cancer centers. In order to obtain epidemiological details of the CAM use, we need to carry out a large sample prospective study confirming the results of this study. The response rate of our study, 59% was slightly higher than that of our previous national survey, 57% [2]. However, the valid response rate was 47%, mainly due to the missing of a single item for stage of CAM use. These indicated that sampling was valid, however it will limit generality of our results. It might be needed to improve assessment for stage of CAM use in the questionnaire.

In conclusion, this study using two psychological model provided strong evidence that the existence of psychologically induced potential CAM users and psychological variables including positive attitude for CAM use and perceived family expectation greatly influence CAM use in cancer patients.

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references

1. Boon H, Stewart M, Kennard MA et al. Use of complementary/alternative medicine by breast cancer survivors in Ontario: prevalence and perceptions. J Clin Oncol 2000; 18: 2515–2521.
2. Hyodo I, Amano N, Eguchi K et al. Nationwide survey on complementary and alternative medicine in cancer patients in Japan. J Clin Oncol 2005; 23: 2645–2654.
3. National Center for Complementary and Alternative Medicine. What is Complementary and Alternative Medicine (CAM)?. http://nccam.nih.gov/health/whatiscam/ (28 July 2007, date last accessed).
4. Caspi O, Sechrest L, Pituk HC et al. On the definition of complementary, alternative, and integrative medicine: societal mega-stereotypes vs. the patients' perspectives. Altern Ther Health Med 2003; 9: 58–62.
5. Cassileth BR, Deng G. Complementary and alternative therapies for cancer. Oncologist 2004; 9: 80–89.
6. Paltiel O, Avitzour M, Peretz T et al. Determinants of the use of complementary therapies by patients with cancer. J Clin Oncol 2001; 19: 2439–2448.
7. Burstein HJ. Discussing complementary therapies with cancer patients: what should we be talking about? J Clin Oncol 2000; 18: 2501–2504.
8. Correa-Velez I, Clavarino A, Barnett AG, Eastwood H. Use of complementary and alternative medicine and quality of life: changes at the end of life. Palliat Med 2003; 17: 695–703.
9. Sollner W, Maislinger S, DeVries A et al. Use of complementary and alternative medicine by cancer patients is not associated with perceived distress or poor compliance with standard treatment but with active coping behavior: a survey. Cancer 2000; 89: 873–880.
10. Prochaska JO, DiClemente CC. Stages and processes of self-change of smoking: toward an integrative model of change. J Consult Clin Psychol 1983; 51: 390–395.
11. Prochaska JO, DiClemente CC. Self change processes, self efficacy and decisional balance across five stages of smoking cessation. Prog Clin Biol Res 1984; 156: 131–140.
12. Manne S, Markowitz A, Winawer S et al. Correlates of colorectal cancer screening compliance and stage of adoption among siblings of individuals with early onset colorectal cancer. Health Psychol 2002; 21: 3–15.
13. Lauver DR, Henriques JB, Settersten L, Bumann MC. Psychosocial variables, external barriers, and stage of mammography adoption. Health Psychol 2003; 22: 649–653.

14. Hirai K, Suzuki Y, Tsuneto S et al. A structural model of the relationships among self-efficacy, psychological adjustment, and physical condition in Japanese advanced cancer patients. Psychooncology 2002; 11: 221–229.
15. Honda K, Gorin SS. A model of stage of change to recommend colonoscopy among urban primary care physicians. Health Psychol 2006; 25: 65–73.
16. Ajzen I. The theory of planned behavior. Organ Behav Hum Decis Process 1991; 50: 179–211.
17. Le Chevalier T, Brisgand D, Douillard JY et al. Randomized study of vinorelbine and cisplatin versus vindesine and cisplatin versus vinorelbine alone in advanced non-small-cell lung cancer: results of a European multicenter trial including 612 patients. J Clin Oncol 1994; 12: 360–367.
18. Blake RL Jr, McKay DA. A single-item measure of social supports as a predictor of morbidity. J Fam Pract 1986; 22: 82–84.
19. Conner M, Kirk SF, Cade JE, Barrett JH. Why do women use dietary supplements? The use of the theory of planned behaviour to explore beliefs about their use. Soc Sci Med 2001; 52: 621–633.
20. Kitamura T. The hospital anxiety and depression scale [in Japanese]. Arch Psychiatr Diagn Clin Eval 1993; 4: 371–372.
21. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983; 67: 361–370.
22. Kugaya A, Akechi T, Okuyama T et al. Screening for psychological distress in Japanese cancer patients. Jpn J Clin Oncol 1998; 28: 333–338.
23. Hirai K, Suzuki Y, Tsuneto S et al. Self-efficacy scale for terminal cancer [in Japanese]. Jpn J Psychosom Med 2001; 41: 19–27.
24. Okuyama T, Wang XS, Akechi T et al. Japanese version of the MD Anderson Symptom Inventory: a validation study. J Pain Symptom Manage 2003; 26: 1093–1104.
25. Cleeland CS, Mendoza TR, Wang XS et al. Assessing symptom distress in cancer patients: the M.D. Anderson Symptom Inventory. Cancer 2000; 89: 1634–1646.
26. Eguchi K, Hyodo I, Saeki H. Current status of cancer patients' perception of alternative medicine in Japan. A preliminary cross-sectional survey. Support Care Cancer 2000; 8: 28–32.
27. Boon H, Brown JB, Gavin A et al. Breast cancer survivors' perceptions of complementary/alternative medicine (CAM): making the decision to use or not to use. Qual Health Res 1999; 9: 639–653.
28. Molassiotis A, Scott JA, Kearney N et al. Complementary and alternative medicine use in breast cancer patients in Europe. Support Care Cancer 2006; 14: 260–267.
29. Boon H, Westlake K, Deber R, Moineddin R. Problem-solving and decision-making preferences: no difference between complementary and alternative medicine users and non-users. Complement Ther Med 2005; 13: 213–216.
30. Sparber A, Bauer L, Curt G et al. Use of complementary medicine by adult patients participating in cancer clinical trials. Oncol Nurs Forum 2000; 27: 623–630.

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Discrimination between worry and anxiety among cancer patients: development of a brief cancer-related worry inventory

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Abstract

***Objectives*: A psychometric scale for assessing cancer-related worry among cancer patients, called the Brief Cancer-Related Worry Inventory (BCWI), was developed.**

***Methods*: A cross-sectional questionnaire survey for item development was conducted of 112 Japanese patients diagnosed with breast cancer, and test–retest validation analysis was conducted using the data from another prospective study of 20 lung cancer patients. The questionnaire contained 15 newly developed items for cancer-related worry, the Hospital Anxiety and Depression Scale, The Impact of Event Scale Revised, and the Medical Outcomes Study Short Form-8.**

***Results*: Exploratory factor analysis of the 15 items yielded a 3-factor structure including (1) future prospects, (2) physical and symptomatic problems and (3) social and interpersonal problems. A second-order confirmatory factor analysis identified a second-order factor called cancer-related worry and confirmed the factor structure with an acceptable fit (chi-square ($df = 87$) = 160.16, $P = 0.001$; GFI = 0.83; CFI = 0.92; RMSEA = 0.09). The internal consistency and test–retest reliability were confirmed with the lung cancer sample. Multidimensional scaling found that cancer-related worry is separate from anxiety, depression, and posttraumatic stress disorder (PTSD) symptoms.**

***Conclusion*: Our study succeeded in developing and confirming the validity and reliability of a BCWI. The study also confirmed the discriminable aspects of cancer-related worry from anxiety, depression, and PTSD symptoms.**

Keywords: worry; anxiety; stressor; cancer; oncology

Introduction

Being diagnosed with cancer is itself a major stressful event for cancer patients, and they subsequently experience other kinds of stressful events related to cancer and its treatment. As the first reaction to these negative events and cancer-related experiences, a number of cancer patients experience feelings of anxiety, and anxiety sometimes becomes a clinically important problem in its own right [1].

Anxiety in cancer patients is a concept for negative state of mind and has been defined as intrusive and unpleasant anxious thoughts; often involving recurrence of disease, death, or disability; and causing considerable disruption in concentration, decision-making, sleep, and social functioning [1]. Several anxiety-related measurement scales have been frequently used to assess anxiety-related moods or emotions of cancer patients. They include the State-Trait Anxiety Inventory and the Hospital Anxiety and Depression Scale (HADS). These scales mainly measure the patient's somatic symptoms caused by autonomic nervous activities, which correspond to a patient's level of anxiety, but do not evaluate what the patient is anxious or worried about. Therefore, the contents and types of causes, that is, the stressors that evoke anxiety have

not been clarified. In addition, there is a clinical need to evaluate the contents of patients' anxious status with convenient means to detect patients' needs or preferences in order to design individualized care for the patients.

For that purpose, several studies to evaluate stressors that would make the patients anxious have been undertaken in order to define unmet needs or concerns. The studies of unmet needs for cancer patients addressed psychological factors such as fear, anxiety, information about the medical system, physical factors, activity of daily living, disease itself, side effects of treatment, human relations, social support, social issues, and sexual issues [2–5]. The studies revealed types and contents of concerns of cancer patients. Domains of general concerns for cancer patients were cancer itself, disability, family, work, economic status, loss of independence, physical distress, psychological distress, medical uncertainty, and death [6–12].

The term worry has been used as a cardinal symptom in general anxiety disorder in *Diagnostic and Statistical Manual of Mental Disorders–Revised* (DSM-III-R) [13]. According to Wells' metacognitive theory, worry is a chain of catastrophic thoughts that are predominantly verbal, consists of the contemplation of potentially dangerous situations and of personal coping strategies and can become the focus of an individual's concern [14]. Therefore, worry is a predominantly cognitive activity, [15] which is characterized by negative thought and images about the outcome of events, particularly concerns about the future, and a part of anxiety but discriminable from it. In the cancer literature, worry indicates the fear of having cancer; several studies of cancer worry were investigated for cancer screening settings [16,17] such as mammography [18], ovarian cancer [19], and prostate cancer screening [20]. There are few studies concerning worry in cancer patients after their diagnosis. It was reported that the level of prediagnostic intrusive thoughts would provide a significant, useful, and practical method for clinicians to identify in advance those patients likely to worry excessively following a diagnosis of cancer [21]. A worry content scale was developed to assess multiple dimensions of worry in cancer patients [22].

However, the conceptual difference between worry and anxiety is unclear, especially from empirical perspectives, and it is necessary to confirm the validity of discrimination between the measures for worry and for anxiety. Therefore, we performed a cross-sectional study of breast cancer patients and a prospective observational study of lung cancer patients with the following aims: (1) to develop a scale to assess the variation in contents and strength of cancer-related worry thoughts; (2) to confirm the validity and reliability of the scale; and (3) to test discrimination between cancer-related worry and anxiety.

Methods

Participants

This study involved consecutive sampling and was composed of two different samples, which were breast cancer patients after surgery for the main phase of the study and lung cancer patients after surgery for the validation phase. The work was carried out in two university hospitals located in Osaka prefecture, Japan from July 2005 to August 2005 (breast cancer) and from February 2006 to April 2006 (lung cancer). Before initiation of this survey, the study protocol was examined and approved by the institutional review boards.

Both samples of breast cancer and lung cancer included patients with an Eastern Cooperative Oncology Group performance status of 1 or 2 and those who underwent surgery. On the face sheet of the questionnaire for the development phase, a single sentence explained that ethical notification and return of the questionnaire were regarded as consent to participate in our study, and patients were asked to return the questionnaires anonymously. For validation phase, we obtained written informed consent for participation in the study. Each patient was asked to complete two questionnaires in one month.

Instrument development

The questionnaire for cancer-related worry was developed by the authors and called the Brief Cancer-Related Worry Inventory (BCWI). We pooled items to describe patients' worries, concerns, unmet needs, and stressors by review of related articles [2–12]. The main domain of the items were *cancer itself, disability, effect of cancer treatment, side effects, physical distress, psychological distress, change of appearance, sexual issues, medical uncertainty, death, social support from family and medical staff, work, and economic status.* As we intended to develop a brief and clinically useful instrument, the developed items underwent intensive review of their content and clinical validity and modification of their verbal expressions by an oncologist, a nurse manager of a cancer ward, two psychiatrists, and two psychologists who were experienced in psycho-oncology practice and research. Finally, 15 items were selected through this procedure (see Table 2). The participants were asked to rate their degree of worry about the 15 items on an 11-point Likert-type scale, ranging from 0 (not at all worried) to 100 (extremely worried).

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Measures

We used the Japanese version [23] of the HADS [24] to assess patients' depression and anxiety. The HADS has 14 items in two question groups, one each on anxiety and depression, and each question is rated from 0 to 3.

The Japanese version of the Impact of Event Scale–Revised (IES-R) [25,26] was assessed for Posttraumatic Stress Disorder (PTSD) symptoms based on DSM-IV criteria. Respondents were asked to rate each item in relation to their cancer and its treatment, referring to their condition over the previous seven days. IES-R assesses three dimensions of PTSD symptoms: avoidance, intrusion, and hypertension.

Finally, the Japanese version of the Medical Outcomes Study Short Form-8 (SF-8) [27,28] was used to evaluate health-related quality of life. Each of the 8 items assesses a different dimension of health: general health, physical functioning, role physical, bodily pain, vitality, social functioning, mental health, and role emotional. The SF-8 provides summary scores for Physical Component Scales (PCS) and Mental Component Scales (MCS). Scores from each item or summary measurements range from 0–100, with higher scores indicating better health.

Table 1. Patients' background

	Development breast cancer $N = 109$		Validation lung cancer $N = 20$	
Age (years)				
Mean	54.5		65.6	
SD	11.4		8.8	
Gender				
Male	43	15.9%	16	41.5%
Female	45	18.3%	4	44.7%
Time since diagnosis (months)				
Mean	31.3		5.8	
SD	38.6		12.5	
Stage				
I	56	51.4%	12	60.0%
II	53	48.6%	0	0.0%
III			3	15.0%
Other			5	25.0%
Chemotherapy	58	14.8%	0	0.0%

Statistical analyses

Descriptive statistics were calculated for 15 items for the BCWI. As no largely skewed items were found, we performed an exploratory factor analysis using the maximum likelihood method and the promax rotation methods. After extracting factor structure, we performed the confirmatory factor analysis using the maximum likelihood method to test whether our factor structure fit the data. After calculating total scores of each subscale of the cancer-related worry scale, the correlation analyses were performed to evaluate convergence and validity of discrimination among subscales of cancer-related worry, HADS, IES-R, and SF-8. We used multidimensional scaling analysis based on the Euclidean distance model of stimulus configuration of measures to graphically describe and cluster multiple relations and similarities among cancer-related worry, HADS, and IES-R using their standardized scores. This statistical method can visualize similarities of endorsements by making a matrix of correlation coefficients. Kruskal's stress values were used as a badness-of-fit measure, and the two dimensional solution was adopted because of its simplicity, and ease of interpretation. To test the reliability of the BCWI, we calculated Cronbach's alpha on both the main and validation phase data and intra-class correlation coefficients of scores in the validation phase for test–retest reliability. We conducted all statistical analyses using the SPSS software package

Table 2. Factor loadings and mean score of Brief Cancer-Related Worry Inventory

	Factor 1 (future prospects)	Factor 2 (physical and symptomatic problems)	Factor 3 (social and interpersonal problems)	Mean	SD
(1) About whether cancer might get worse in the future	0.87	−0.09	0.05	53.70	31.70
(2) About cancer itself	0.84	0.09	−0.13	71.30	29.03
(3) About effect of current treatment	0.75	−0.26	0.27	38.50	28.99
(4) About life and death of oneself	0.69	0.21	−0.07	50.80	30.71
(5) About how to cope with cancer situation	0.57	0.32	0.05	41.00	25.35
(6) About mental status	0.55	0.34	−0.12	41.00	27.72
(7) About physical symptom	0.10	0.74	−0.08	37.60	29.93
(8) About side effect of cancer treatment	0.10	0.63	0.01	41.90	29.97
(9) About change of appearance	−0.03	0.62	0.23	37.80	31.19
(10) About sexual issues	−0.07	0.42	0.16	14.20	20.81
(11) About relationships with family members	−0.03	−0.06	0.88	18.40	25.50
(12) About doing job or house work	−0.18	0.34	0.65	31.80	31.19
(13) About relationships with medical staff	0.30	−0.03	0.48	20.00	23.01
(14) About the future of family members	0.35	0.04	0.42	39.50	30.74
(15) About economic problems	0.07	0.37	0.40	38.40	34.03

(version 11.0), except for the confirmatory factor analysis for which we used the EQS software package (version 5.6).

Results

Backgrounds of patients and distribution

Patients who satisfied the inclusion criteria and consented for enrollment in this study returned 112 responses in the development phase and 20 responses in the validation phase. Because 3 responses in the development phase were excluded due to more than 30% missing values, 109 responses in the development phase and 20 responses in the validation phase were finally analyzed. Table 1 summarizes the backgrounds of the patients in the development and validation phases.

Descriptive statistics of BCWI

Table 2 shows descriptive statistics of the 15 items in the BCWI. The item that had the highest mean score was 'worry for cancer itself' ($M = 71.3$), followed by 'worry for recurrence and metastasis' ($M = 53.7$) and 'worry for future life and death' ($M = 50.8$). The lowest scoring item was 'worry for sexual problems' ($M = 14.2$). The next lowest items were 'worry for family relationships' ($M = 18.4$) and 'worry for relationships with medical staff' ($M = 20.0$).

Factor structure of the BCWI

The exploratory factor analysis of the 15 items yielded a 3-factor structure. This solution was adopted because it was the only interpretable factor structure and its eigenvalue was >1.0. The subscales were interpreted as (1) future prospects, (2) physical and symptomatic problems, and (3) social and interpersonal problems (Table 2). We then adopted a second-order factor structure with 15 items and 4 factors including a second-order factor, cancer-related worry, due to moderate correlations among 3 factors, consistency with the hypothesized concepts, and clinical validity for a confirmatory factor analysis. The fit indices for this model were acceptable: chi-square ($df = 87$) $= 160.16$, $P = 0.001$; GFI $= 0.83$; CFI $= 0.92$; RMSEA $= 0.09$. Figure 1 presents the factor structure of BCWI.

Internal consistency and test–retest reliability of BWCI

Table 3 summarizes the internal consistency (Cronbach's alpha coefficients) and test–retest reliability of the BWCI on the data obtained from the test–retest phase for lung cancer patients. The BWCI had excellent internal consistency for both breast cancer and lung cancer samples and moderate and substantial test–retest reliability for the lung cancer sample.

Validity of the BCWI and discrimination form anxiety

Table 4 shows the correlations among BCWI, HADS, IES-R, and SF-8. There are significant and moderate correlations between subscales of BCWI, HADS, and IES-R ($r = 0.27$–0.59, $P < 0.01$), weak correlations between subscales of BCWI and PCS of SF-8 ($r = -0.28$ to -0.19, $p < 0.05$), and moderate correlations with MCS ($r = -0.42$ to -0.43, $P < 0.001$).

Figure 2 shows the structure of worry, anxiety, depression, intrusive, avoidance, and hyperarousal in BCWI, HADS, and IES-R using multidimensional scaling. The horizontal dimension and the vertical dimension successfully discriminate BCWI, HADS, and IES-R. The subscales of IES-R are located in the area defined by positive values both on the horizontal and vertical dimensions. The subscales of HADS were located in the negative area on the horizontal dimension and the positive area on the vertical. Three subscales of BCWI are located in the negative area on the vertical axis and the area near zero on the horizontal dimension. Kruskal's stress value ($= 0.14$) and proportion of variance of data ($= 0.89$) indicated that this solution was valid and accounted for more than 89% of the variance. The analysis showed that cancer-related worry is identifiable from anxiety, depression, and PTSD symptoms.

Discussion

We have successfully developed a brief instrument for the measurement of cancer-related worry of cancer patients (BCWI). The psychometric properties of the scale are acceptable. The reliability was shown by excellent internal consistency (overall Cronbach's alpha coefficient $= 0.87$) and fair test–retest reliability (intra-class correlation coefficient $= 0.69$). Construct validity was established by confirmatory factor analysis. In addition, the 15 items of the BCWI did not have any ceiling or floor effects. The feasibility of the scale was established with two different samples, breast cancer and lung cancer patients. Therefore, the BCWI has necessary and sufficient constructs for a useful compact scale with reliability and validity.

The scale has three subscales, namely future prospects, physical and symptomatic problems, and social and interpersonal problems. The themes of the subscales were consistent with previously identified domains in the concern or unmet need studies [2–12]. The future prospect subscale repre-

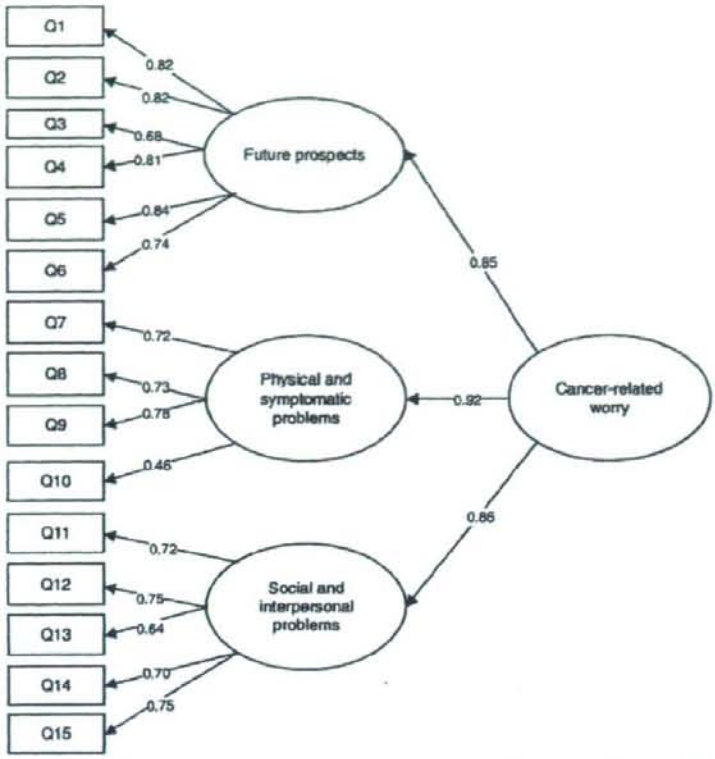

Figure 1. The factor structure of BCWI. Parameter estimates are standardized. Model Fit Index: Chi-square(87) = 160.16, $P = 0.00$; GFI = 0.83; CFI = 0.92; RMSEA = 0.09. Numbers of items correspond to those in Table 2

Table 3. Reliability of the Brief Cancer-Related Worry Inventory

	Cronbach alpha coecients[a]	Cronbach alpha coecients[b]	Test–retest ICC[c]
Future prospects	0.90	0.86	0.75
Physical and symptomatic problems	0.77	0.69	0.53
Social and interpersonal problems	0.83	0.75	0.54
Cancer-related worry	0.87	0.92	0.69

[a]Development phase (breast cancer).
[b]Validation phase (lung cancer).
[c]Intra-class correlation coefficients.

sents the worries for future events, outcomes, or uncertainty. The mean scores of the items in this subscale were higher than that of other subscales. A previous study reported that uncertainty of hospitalized patients was correlated with stress [29]. These studies indicated that future prospects including uncertainty and perceived negative outcomes or consequences of cancer comprise a central concept of cancer-related worry. Physical and symptomatic problems covered the domain of actual problems caused by cancer itself: physical symptoms, side effects of treatments, changes of appearance, and sexual issues. For our development data, test–retest reliability was lower than other subscales of BCWI. This indicates that this subscale is sensitive to physical and symptomatic changes of the patients and has content validity. Physical and symptomatic changes were found to be primary concerns of cancer patients in several studies [2–5], and controlling them was a primary purpose of palliative care or supportive care in ordinary medical treatment. Thus, changes of the score in this domain will correspond with the actual outcome of palliative treatments. *Social and interpersonal problems* covered secondary problems caused by cancer, including problems in interpersonal relationships with family members or medical staff, problems on the job, house work, and economic problems. Although these worries will not be influenced directly by cancer itself or cancer treatment, they may be very difficult issues for cancer patients to cope with or solve. Several forms of psychosocial intervention might be effective for these kinds of problems.

Table 4. Intercorrelations between Brief Cancer-Related Worry Inventory and other measures

	1	2	3	4	5	6	7	8	9
1. Future prospects (BCWI)	ξ								
2. Physical and symptomatic problems (BCWI)	0.65***	ξ							
3. Social and interpersonal problems (BCWI)	0.64***	0.66***	ξ						
4. Anxiety (HADS)	0.57***	0.48***	0.59***	ξ					
5. Depression (HADS)	0.27**	0.45***	0.39***	0.58***	ξ				
6. Intrusion (IES-R)	0.55***	0.56***	0.56***	0.58***	0.40***	ξ			
7. Avoidance (IES-R)	0.45***	0.40***	0.36***	0.35***	0.19*	0.65***	ξ		
8. Arousal (IES-R)	0.48***	0.56***	0.54***	0.57***	0.43***	0.77***	0.54***	ξ	
9. Physical component scales (SF8)	−0.19*	−0.28**	−0.18	−0.23*	−0.40***	−0.27**	−0.13	−0.31**	ξ
10. Mental component scales (SF8)	−0.41***	−0.34***	−0.42***	−0.55***	−0.42***	−0.58***	−0.32**	−0.60***	0.19*

*$P<0.05$, **$P<0.01$, ***$P<0.001$.

BCWI, Brief Cancer-related Worry Inventory; HADS, Hospital Anxiety and Depression Scale; IES-R, Impact of Event Scale Revised; SF8, Medical Outcomes Study Short Form-8.

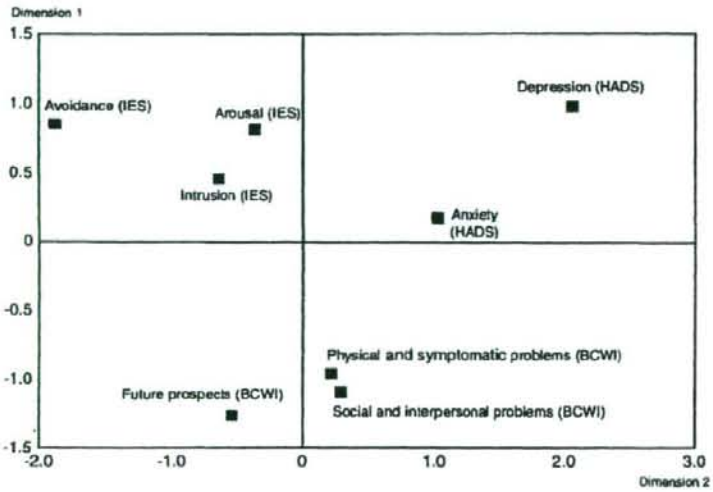

Figure 2. The structure of similarities among subscales of BCWI, HADS, and IES. Kruskal's stress value (= 0.14) and proportion of variance of data (= 0.89). BCWI, Brief Cancer-Related Worry Inventory; HADS, Hospital Anxiety and Depression Scale; IES-R, Impact of Event Scale Revised; SF8, Medical Outcomes Study Short Form-8

The finding that the BCWI was moderately correlated with HADS, IES-R, and SF-8 indicates that the scale has convergent validity. However, when we investigated the detailed differences and similarities among the scales by multidimensional scaling, we found that the distance between the subscales of BCWI and HADS-anxiety was similar to that between BCWI and HADS-depression and their directions were opposite (Figure 2). In addition to, the BCWI subscales were graphically different from the intrusion, avoidance, and arousal subscales of IES-R. If the distance between depression and anxiety in HADS is enough to discriminate two different emotional conditions, the subscales of BCWI were discriminable from HADS-anxiety and all the subscales of IES-R. Therefore, cancer-related worry that the BCWI measures is an interrelated but different and emotional construct discriminable from anxiety, depression, and PTSD symptoms.

Among discriminable aspects of the BCWI, the difference between worry and anxiety shows that patients with high cancer-related worry are not necessarily in a severely anxious status. In addition, the BCWI can evaluate the contents of each worry and their individual magnitudes, whereas the HADS-anxiety subscale can only measure the intensity of anxious states. This means that measurement of cancer-related worry by BCWI is valuable to clinical practice. For example, assessment of the type of cancer-related worry will contribute to formulation of a psychological intervention for the cancer patient, especially interventions using the problem-solving technique [30,31], because in the earlier stage of the problem-solving technique, making problem-lists is needed

for identifying the problem and setting a priority for solution. The BCWI will be helpful for patients to create their problem-list in a very structured and effective way.

The limitations to this study include the small and limited sample. We developed the items using a breast cancer sample ($N = 112$) and confirmed internal consistency and test–retest reliability using a lung cancer sample ($N = 20$). These samples are different from samples used in the development phase of this scale. As we used only two different cancer samples, this may limit validity for using the BCWI for patients with other kinds of cancer. However, we suppose that because the items of this scale were developed by reference to a broad range of the articles concerning unmet need, concerns, and stressors of cancer patients, the items in the scale are sufficiently general for application to other cancers.

In conclusion, our study succeeded in developing and confirming the validity and reliability of a scale for assessment of cancer-related worry, the so-called BCWI. The BCWI has only 15 items that enable a brief evaluation of the content and the magnitude of cancer-related worry of cancer patients. The study also confirmed that aspects of cancer-related worry are discriminable from anxiety, depression, and PTSD symptoms. However, to reach a final conclusion about differences in complicated emotions and usefulness for clinical practice in cancer care, further empirical work using the prospective design and academic discussion will be needed.

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References

1. Stark DP, House A. Anxiety in cancer patients. *Br J Cancer* 2000;83(10):1261–1267.
2. Sanson-Fisher R, Girgis A, Boyes A, Bonevski B, Burton L, Cook P. The unmet supportive care needs of patients with cancer. *Support Care Rev Group. Cancer* 2000;88(1):226–237.
3. Soothill K, Morris SM, Harman J, Francis B, Thomas C, McIllmurray MB. The significant unmet needs of cancer patients: probing psychosocial concerns. *Support Care Cancer* 2001;9(8):597–605.
4. Foot G, Sanson-Fisher R. Measuring the unmet needs of people living with cancer. *Cancer Forum* 1995;19: 131–135.
5. Steginga SK, Occhipinti S, Dunn J, Gardiner RA, Heathcote P, Yaxley J. The supportive care needs of men with prostate cancer (2000). *Psycho-Oncology* 2001;10(1):66–75.
6. Akechi T, Okuyama T, Sugawara Y, Nakano T, Shima Y, Uchitomi Y. Major depression, adjustment disorders, and post-traumatic stress disorder in terminally ill cancer patients: associated and predictive factors. *J Clin Oncol* 2004;22(10):1957–1965.
7. Hill KM, Amir Z, Muers MF, Connolly CK, Round CE. Do newly diagnosed lung cancer patients feel their concerns are being met? *Eur J Cancer Care (Engl)* 2003; 12(1):35–45.
8. Harrison J, Maguire P, Pitceathly C. Confiding in crisis: gender differences in pattern of confiding among cancer patients. *Soc Sci Med* 1995;41(9):1255–1260.
9. Farrell C, Heaven C, Beaver K, Maguire P. Identifying the concerns of women undergoing chemotherapy. *Patient Educ Couns* 2005;56(1):72–77.
10. Heaven CM, Maguire P. The relationship between patients' concerns and psychological distress in a hospice setting. *Psycho-Oncology* 1998;7(6):502–507.
11. Heaven CM, Maguire P. Disclosure of concerns by hospice patients and their identification by nurses. *Palliat Med* 1997;11(4):283–290.
12. Carver CS, Pozo-Kaderman C, Price AA *et al.* Concern about aspects of body image and adjustment to early stage breast cancer. *Psychosom Med* 1998;60(2): 168–174.
13. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn). APA: Washington, DC, 1987.
14. Wells A, Carter K. Preliminary tests of a cognitive model of generalized anxiety disorder. *Behav Res Ther* 1999;37(6):585–594.
15. Mathews A. Why worry? The cognitive function of anxiety. *Behav Res Ther* 1990;28(6):455–468.
16. Hay JL, Buckley TR, Ostroff JS. The role of cancer worry in cancer screening: a theoretical and empirical review of the literature. *Psycho-Oncology* 2005;14(7): 517–534.
17. Consedine NS, Magai C, Krivoshekova YS, Ryzewicz L, Neugut AI. Fear, anxiety, worry, and breast cancer screening behavior: a critical review. *Cancer Epidemiol Biomarkers Prev* 2004;13(4):501–510.
18. Andersen MR, Smith R, Meischke H, Bowen D, Urban N. Breast cancer worry and mammography use by women with and without a family history in a population-based sample. *Cancer Epidemiol Biomarkers Prev* 2003;12(4):314–320.
19. Andersen MR, Peacock S, Nelson J *et al.* Worry about ovarian cancer risk and use of ovarian cancer screening by women at risk for ovarian cancer. *Gynecol Oncol* 2002;85(1):3–8.
20. Cohen L, Fouladi RT, Babaian RJ *et al.* Cancer worry is associated with abnormal prostate-specific antigen levels in men participating in a community screening program. *Cancer Epidemiol Biomarkers Prev* 2003; 12(7):610–617.
21. Mathews A, Ridgeway V, Warren R, Britton P. Predicting worry following a diagnosis of breast cancer. *Psycho-Oncology* 2002;11(5):415–418.
22. Stefanek ME, Shaw A, DeGeorge D, Tsottles N. Illness-related worry among cancer patients: prevalence, severity, and content. *Cancer Invest* 1989;7(4):365–371.
23. Kitamura T. The Hospital Anxiety and Depression Scale. *Arch Psychiatr Diagn Clin Eval* 1993;4:371–372 (in Japanese).
24. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand* 1983;67(6): 361–370.
25. Weiss DS, Marmar CR. The impact of event scale–revised. In Assessing Psychological Trauma and PTSD, Wilson JP, Keane TM (eds). Guilford Press: New York, 1997; 399–411.
26. Asukai N, Kato H, Kawamura N *et al.* Reliability and validity of the Japanese-language version of the Impact of Event Scale-Revised (IES-R-J): four studies of