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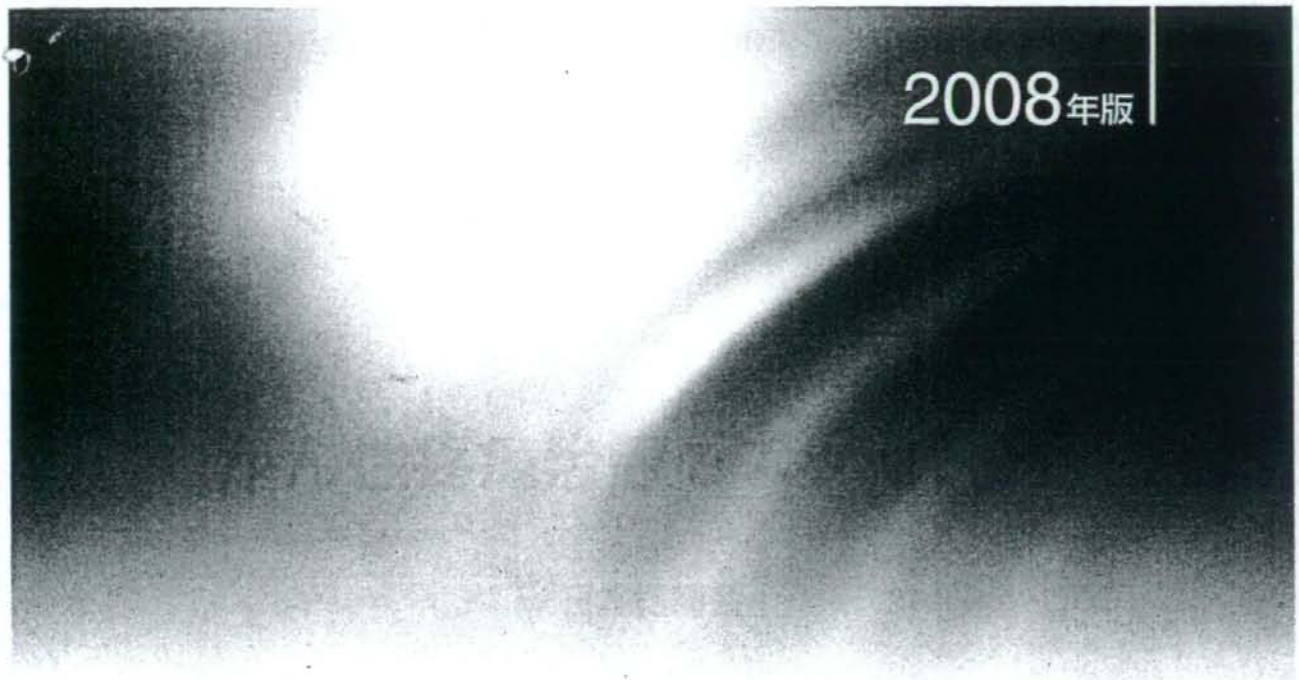


# がん性疼痛治療のエッセンス

監修

日本医師会

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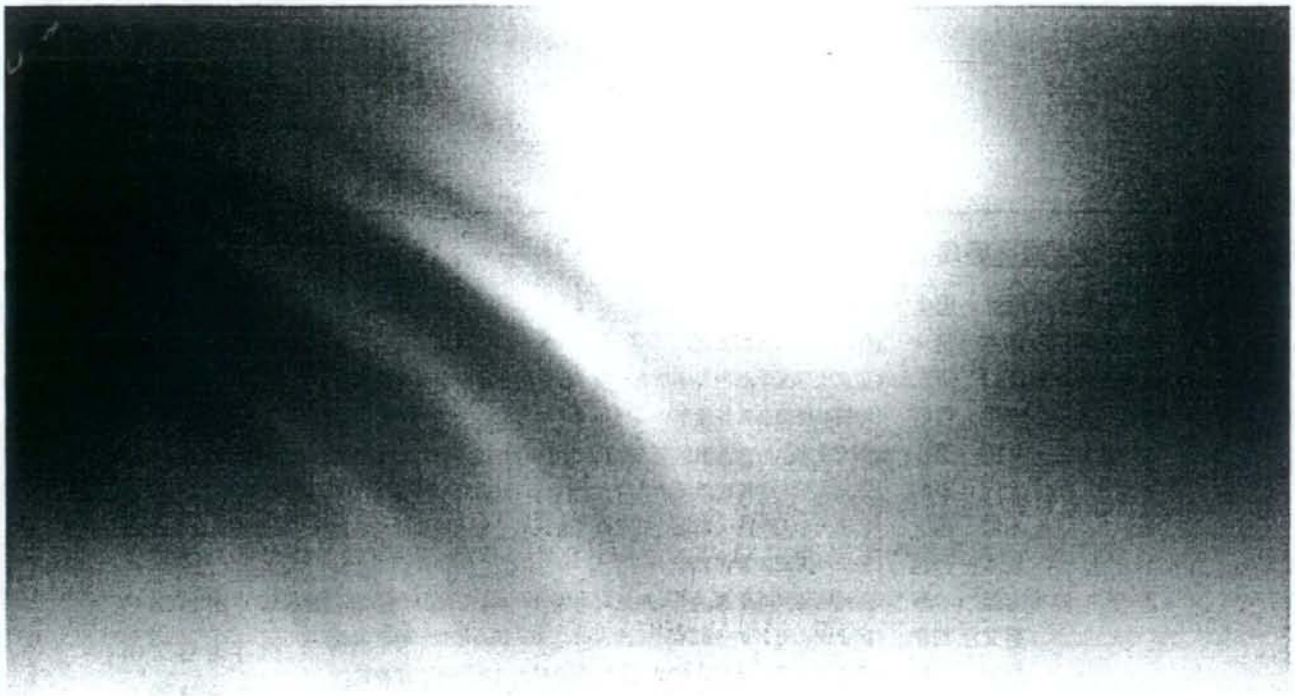

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（担当事務局：地域医療第三課）

2008年3月発行（制作：株式会社 青海社）

本書は，平成19年度厚生労働省科学研究費補助金（第3次対がん総合戦略研究事業）「緩和ケアプログラムによる地域介入研究」で作成された『ステップ緩和ケア』をもとに作成しました。

神疾患の適切な診立てと治療により多くの自殺を防ぐことができる．ただ，精神疾患の多くは精神科を受療しておらず，ほかの診療科において精神症状や精神疾患の診断率を高め，精神科に繋げることが大切である．上記危険因子③との関連で，救急医療施設における自殺企図直後の精神科の介入，あるいは救急処置後の精神医療への繋ぎが重要である．なお精神疾患の診断については他項に詳しい．

**C. 対応と治療の方針**

**1. 患者との面接**　自殺を確実に予測し得るツールは存在しないが，リスクのマージンは広めに取る方がよい．自殺念慮はうつ病の主要症候と認識し，死の願望や自殺の意思については，信頼関係を構築した後に一定の配慮のもと，直接患者に確認すべきである．こうした質問が自殺を惹起することを怖れるよりも，悩める患者への介入を優先すべきである．自殺念慮に対していたずらな叱責は禁忌である．信頼関係を維持し，患者の心理に共感しつつ，精神疾患と自殺念慮の病理に着目した心理教育を行い，「いま，ここで」の対応を患者や家族と話し合う．

**2. 治療**　自殺の危険が切迫している場合は入院の絶対適応であり，患者の安全確保の観点から閉鎖環境での治療導入が考慮される．治療内容はそれぞれの精神疾患によるが，治療の柱は①精神療法，②薬物療法，③ソーシャル・ワーク，④リハビリとなる．②については，合理的治療の観点から，また服薬自殺を回避するためにも，多剤・大量・長期投与を避け，また安全性のより高い薬剤を使用すべきである．気分障害においては，リチウムが自殺予防に効果があることがエビデンスをもって示されている．また抗うつ薬では，毒性の点では三環系よりSSRIの方が安全性が高い．治療は，薬物の工夫だけでは不十分であり，患者の社会心理的背景をよく聴取し，生活困難感の軽減のために③を活用するのがよい．

**■患者説明のポイント**

- 自殺念慮の有無を確認する．
- 自殺念慮は，精神疾患をベースに，極端な思考から生じていることを説明する．
- 治療により自殺念慮が解消されることを説明し，精神科治療を勧める．
- 自殺をしない約束を交わす．
- 危機時の対応窓口や医療機関，社会資源を紹介する．

**■看護・介護のポイント**

- 自殺念慮を打ち明けられてもはぐらかさない，いたずらに批判しない．
- 患者の心情に共感し，そのことばを傾聴する．
- 問題解決の手助けを約束し，自殺をしない約束を交わす．
- 患者の心理状態や行動，自殺の危険性についてスタッフ間で情報を共有する．

## がん患者の精神医学的問題

psychiatric problems among patients with cancer

小早川　誠　広島大学病院・緩和ケアチーム

不眠・不安・抑うつなどの精神症状は，がん患者とその家族のQOLを損なう要因となっている．これらはうつ病，適応障害，せん妄の症状であることが多いが，痛みや吐き気，倦怠感，眠気などがん特有の身体症状や治療のために生じている可能性もある．よって，原因となる身体症状や副作用がないか検討し，対策を行ったうえで精神医学的対応を行う．

**I. 適応障害およびうつ病**

**病態と診断**

米国精神医学会の基準では，①抑うつ気分，②興味・喜びの低下，③食欲低下（亢進），④不眠（過眠），⑤焦燥感または制止，⑥易疲労感，⑦無価値感や罪責感，⑧思考・集中力低下，⑨希死念慮の9つの症状のうち，①または②を含んだ5つ以上の症状が2週間以上持続した場合にうつ病と診断する．うつ病の基準に合わない場合でも，がんに伴う心理的負担により不安や抑うつが生じ，社会生活上支障をきたす場合に適応障害と診断する．

**治療方針**

不眠・不安・抑うつには対症的に薬物療法を行う．特にうつ病と診断された場合には積極的に抗うつ薬使用を考慮する．またこれらの症状は，例えば不安が高じて眠れないなど互いに関連していることがあり，支持的な不安の傾聴や，もし誤解があれば必要な情報提供を行うなど，精神療法的介入で軽減することがある．精神療法に加えて薬物療法を行う際には，身体状況や副作用，薬物相互作用を考慮したうえで慎重に少量から開始する．

**A. 不眠**

**Rp 処方例**　下記の薬剤を症状により選択する．

1) レンドルミンD錠　0.5-1錠　分1　就寝前（寝つきが悪いとき）
2) ロヒプノール錠（1mg）　1-2錠　分1　就寝前（すぐ目が覚めるとき）
3) レスリン錠（25mg）　1-3錠　分1　就寝前（寝た気がしないとき）

**B. 不安**

**Rp 処方例**　下記のいずれかを用いる.

1) ワイパックス錠 (0.5 mg)　1-3錠　分1-3　食後
2) ソラナックス錠 (0.4 mg)　1-3錠　分1-3　食後

**C. 抑うつ**

**Rp 処方例**　下記のいずれかを用いる.

1) パキシル錠 (10 mg)　1-4錠　分1　夕食後
2) トレドミン錠 (15 mg)　2-6錠　分2-3　食後

## II. せん妄

**前提と診断**

せん妄は注意散漫・失見当識・記憶欠損などの認知と記憶の障害である. 短期間に生じ, 時間的な変動があり, 幻覚や妄想を伴うこともある. 脳転移, 呼吸不全, 高カルシウム血症, 脱水, 低栄養, 貧血, オピオイドや抗コリン薬などの薬剤など, 複数の要因が関与しているものと考えられている.

**治療方針**

部屋の明るさの調整やカレンダーを置くなどの環境調整, 電解質補正など身体状況の改善, 原因薬剤の変更・減薬などを考慮する. そのうえで対症的薬物療法を行う. 原則, 夜間の睡眠確保をめざすが, 興奮や焦燥が強い場合には適宜使用する.

**Rp 処方例**　下記のいずれかを用いる. いずれも保険適用外.

1) セレネース錠 (0.75・1・1.5・3 mg)　0.75-3 mg　分1　就寝前
2) リスパダール錠 (1・2 mg)・液 (0.5・1・2 mg)　0.5-2 mg　分1　就寝前
3) セロクエル錠 (25・100 mg)・細粒 (50%)　25-100 mg　就寝前 (糖尿病合併例は禁忌)
4) セレネース注射液 (5 mg/1アンプル)　1/2-1アンプル　生理食塩液などに混ぜて30-60分で静注

*Jpn J Clin Oncol 2008;38(12)867–870*
*doi:10.1093/jjco/hyn115*

**Short Communication**

# Problem-Solving Therapy for Psychological Distress in Japanese Cancer Patients: Preliminary Clinical Experience from Psychiatric Consultations

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Received August 25, 2008; accepted September 22, 2008; published online November 12, 2008

Problem-solving therapy (PST) is a brief, structured psychological treatment. Preliminary clinical findings regarding the effectiveness of PST for treating psychological distress experienced by Japanese cancer patients are presented. Our actual clinical experience in administering PST to four consecutive distressed cancer patients was reviewed. All of the patients were breast cancer survivors who were referred to us after undergoing surgery. Three cases received six PST sessions each and one case received three PST sessions. The depression and anxiety scores decreased after PST. Our preliminary experience suggests that PST is an effective treatment for alleviating psychological distress in Japanese cancer patients and that this treatment should be further examined in a clinical trial.

*Key words: cancer – psychological distress – problem-solving therapy – psychological intervention*

## INTRODUCTION

The experience of cancer causes considerable stress in patients. Depression and anxiety, including adjustment disorders and major depression, are the most prevalent forms of psychological distress experienced by cancer patients (1). Patients sometimes seek psychological treatment to help them cope with their cancer even though their psychological status does not meet the criteria of a formal psychiatric diagnosis (1). Previous Japanese studies investigating the prevalence of psychological distress in cancer patients have reported rates of 15–40% (2,3). Psychological distress not only causes great suffering, but also diminishes quality of life, amplifies pain and other symptoms, and sometimes leads to suicide.

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Regarding therapy for psychological distress, two potentially effective management strategies are available: psychotherapy and pharmacotherapy. A previous Japanese study indicated that psychotherapy is deemed more acceptable than pharmacotherapy by cancer patients (4). Although previous reviews have highlighted the general efficacy of various psychosocial interventions, very few studies have addressed which kinds of psychotherapy are feasible or effective for Japanese cancer patients in actual clinical oncology practice. In this context, we have been interested in the effectiveness of problem-solving therapy (PST), which is a brief, structured psychological treatment (5). PST has been shown to be effective for the treatment of common mental disorders, including depression and anxiety, in primary care and oncology settings in Western countries (5).

The current report introduces our preliminary clinical findings regarding the effectiveness of PST for treating psychological distress experienced by Japanese cancer patients.

## PATIENTS AND METHODS

### Subjects

The subjects were four consecutive cancer patients who were referred to one of the authors for PST. The patients were referred for the treatment of psychological distress and were followed up by one of the authors. The patients received PST for several reasons, such as intolerability and/or reluctance to use medications and refractoriness to general supportive psychotherapeutic approaches. Psychiatric diagnoses were made using the *Diagnostic and Statistical Manual of Mental Disorders*, 4th Edition (DSM-IV). As this study was conducted in the routine clinical setting, treatments of PST were provided under usual health national insurance system (we therefore could not charge the patients any special fee for PST). In the following, several items of personal information were modified to preserve the anonymity of the patients.

### Problem-Solving Therapy

PST focuses on the present and helps patients to use their own skills and resources to function better. The patients are taught how their psychological symptoms may be linked to psychosocial problems that they are facing, and PST provides the patients with a structured strategy to solve them. If these problems can be resolved, their symptoms may improve. PST includes the following seven steps (5): (i) explanation of the treatment and its rationale, (ii) identification, definition and breakdown of the problem, (iii) establishing achievable goals, (iv) generating solutions, (v) evaluating and choosing the solution, (vi) implementing the chosen solution, (vii) evaluating the outcome after the solution has been implemented. We developed a PST manual for Japanese cancer patients. The manual was designed to help the patients list and summarize problems commonly encountered by cancer patients, including cancer treatment, symptoms of cancer, treatment side effects, fear of recurrence/metastasis, relationship with medical staff, family and other people, economic problems, information issues, employment/school issues. The manual also includes tips and worksheets for patients to use while progressing through each step of PST. The first treatment session lasted about 90 min, and subsequent sessions lasted 40–50 min. In principle, six treatment sessions were given. In addition, we incorporated a simple behavioral treatment skill, activity scheduling, into the PST (5). In activity scheduling, we helped the patients find and then engage in pleasurable activities on a more frequent basis to help alleviate their psychological distress.

### Assessment

We used two psychological measures, the Beck Depression Inventory-II (BDI-II) (6) and the Hospital Anxiety and Depression Scale (HADS) (7), to evaluate psychological distress in clinical practice, depending on the patients' psychological status. The BDI-II is a 21-item self-reported questionnaire to evaluate the severity of depression. The total score can range from 0 to 63, with higher scores representing severer depression. The validity and reliability of the Japanese version of the BDI-II has been confirmed (8). Depression severity was assessed according to the following BDI scores (9): 0–13, minimal; 14–19, mild; 20–28, moderate; 29–63, severe. The HADS is a 14-item self-reported questionnaire consisting of an anxiety and depression subscale; the total score can range from 0 to 42. Higher scores indicate severer anxiety and depression. The Japanese version of the HADS has been validated for cancer populations, and the optimal cut-off point for screening for adjustment disorder and major depressive disorder was 10 of 11 (10). In this report, the results of these measures before and immediately after intervention were used.

Because of the small sample size, we presented the descriptive statistics of the BDI-II and HADS scores pre- and post-intervention only.

## RESULTS

All of the patients were breast cancer survivors who were referred to us after undergoing surgery (Table 1). Their psychiatric diagnoses varied, ranging from normal reaction to major depression. Both the BDI-II scores [pre: 26.8 (SD = 14.0); post: 13.3 (SD = 7.7)] and the HADS scores [pre: 17.0 (SD = 2.6); post: 9.7 (SD = 3.5)] improved after PST. Three patients completed all six PST sessions, while one patient received only three PST sessions (one case, a 32-year woman, terminated PST early because she declined further treatment after finding a new job.). Patient adherences with each therapy session, including activity scheduling, was generally excellent for all the four patients.

Here, the clinical process of PST is introduced using one example case (Ms. D). Ms. D was a 52-year-old housewife who lived with her husband and two children. She was diagnosed as having early-stage breast cancer (Stage 0) and received a surgical resection (simple mastectomy). Because the results of a sentinel lymph node biopsy were negative, she was told that she would not need any further adjuvant therapy. However, she became nervous and anxious about the possible recurrence of her breast cancer and its development into a serious physical disease. Consequently, she could not sleep and began to feel several kinds of physical discomfort, including dizziness, tinnitus and palpitations. She visited an otolaryngologist and neurologist, but no evidence of organic disease was found. Three months after her operation, she consulted a psychiatric clinic and began to take psychotropic medications, including antidepressants and benzodiazepines, and was subsequently referred to one of the authors. An initial assessment revealed a depressive mood and a fear of recurrence, and she was diagnosed as having an adjustment disorder with mixed emotional features (BDI-II score, 31). Thereafter, we continued to provide her with general psychosocial treatment, including continuous medication and supportive psychotherapy. However, her condition remained unchanged during the

**Table 1.** Characteristics of the cancer patients

| Age | Sex | Cancer site | Stage | Cancer treatment (period after cancer diagnosis at the start of PST) | Psychiatric diagnosis | PST | BDI-II score | | HADS score | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Pre PST | Post PST | Pre PST | Post PST |
| 32 | Female | Breast | Early | Hormone therapy after left mastectomy (18 months after diagnosis) | Major depression in partial remission | 3 sessions during 4 weeks | 21 | 17 | 19 | 13 |
| 47 | Female | Breast | Early | Hormone therapy after left partial mastectomy + radiation (20 months after diagnosis) | Normal reaction, but having perceived distress | 6 sessions during 10 weeks | 12 | 2 | 14 | 6 |
| 47 | Female | Breast | Locally advanced | None after right mastectomy + chemotherapy (53 months after diagnosis) | Major depression | 6 sessions during 20 weeks | 45 | 15 | NA | 8 |
| 52 | Female | Breast | Early | None after left simple mastectomy (13 months after diagnosis) | Adjustment disorder with mixed emotional features | 6 sessions during 12 weeks | 29 | 21 | 18 | 10 |

BDI-II, Beck Depression Inventory-II; HADS, Hospital Anxiety and Depression Scale; PST, problem-solving therapy; NA, not applicable. One case, a 32-year-old woman, completed only three PST sessions.

next 8 months. We therefore introduced her to the concept of PST and she expressed an interest. At this time, her BDI-II score was 29. During the PST session, various problems were revealed, including a fear of recurrence, dissatisfaction with her communication with her physician, marital discord and tension with her husband, and frequent difficulties with her son. Interestingly, she selected the difficulties with her son as the first problem that she would like to deal with using PST. During the PST session, she stated that much of her distress resulted from quarrels with her son, and these quarrels often began after she had scolded him. Using the PST skills, she defined her problem ('I can't help scolding my son.') and defined an achievable goal ('I will refrain from scolding him for a couple of hours after his return from school.'). She generated nine potential solutions and finally selected three solution strategies. She was able to complete most of the solution strategies. During the evaluation process, she said, 'I feel better because I am having fewer quarrels with my son.' After the third PST session, she stated, 'Lately, I am not so worried about my disease' and 'I feel that I shall see what I shall see'. At this time, her BDI-II score was 19. She next tried to resolve her marital discord. Although this problem was not successfully solved, she understood that her goal was too difficult and that she needed to set a smaller goal. She completed a total of six PST sessions over a period of 3 months. By the completion of the PST, her feelings had improved (Table 1). Although the six sessions were not sufficient to deal with all of her problems and she partly failed to resolve one of her problems, as mentioned, she felt that 'I will be able to cope with my problems using the PST'.

## DISCUSSION

Many types of psychosocial interventions exist for reducing psychological distress among cancer patients. However, very few studies have confirmed the effectiveness of such interventions in Japan, and the available studies were limited to group psychosocial interventions (11,12) and progressive muscle relaxation (PMR) (13). Several barriers to providing such interventions exist in the Japanese medical system and/or culture, including the difficulty of accruing a homogeneous cancer patient group for appropriate interventions, disadvantages of group interventions for some patients (e.g. reluctance to share individual experiences), and the patient's dissatisfaction with simple behavioral interventions such as PMR. Furthermore, although Western studies have systematically reviewed the effectiveness of psychosocial interventions for cancer patients, demonstrating that cognitive behavioral therapy is recommended (14), our clinical experience suggests that most cancer patients do not have extreme distortions of cognition and that traditional cognitive therapeutic interventions are often not appropriate for cancer patients. Additionally, fewer trained clinical psychologists are available to provide formal psychological intervention for cancer patients in Japan, and this situation creates a barrier to its dissemination among them. In this context, we are interested in using PST to alleviate psychological distress in cancer patients within the Japanese medical system, based on the appropriateness and simplicity of PST.

The current findings suggest that PST can be used to alleviate common forms of psychological distress experienced by cancer patients, such as adjustment disorders and/or major depression. In addition, good adherence to the therapy suggests PST is an acceptable therapy for Japanese cancer patients. Furthermore because PST is a brief therapy that consists of six treatment sessions, PST can be a cost effective psychotherapy. The fact that the subjects were cancer survivors, including both short and long duration after cancer diagnosis, who continued to experience psychological distress after cancer diagnosis, suggests that one of possible subjects who benefit from PST may be distressing cancer

survivors, irrespective of duration after cancer. Although many cancer survivors experience a fear of recurrence and a previous Japanese survey indicated that the most common distress experienced by Japanese cancer patients is a fear of recurrence and/or disease metastasis (15), no standard interventions for alleviating this form of distress exist (16). Our experience suggests that PST may be useful for reducing fears of recurrence, although PST does not directly deal with fear or anxiety itself but instead focuses on present daily problems. In addition, a previous study suggested the usefulness of PST for alleviating distress among palliative care patients (17). These findings suggest that PST can be used for a broad range of psychological distress in clinical oncology settings. On the other hand, because we could not find the long-lasting effect of PST (e.g. 6 or 12 months after treatment), whether the effect of PST is persistent or not should be addressed in a future study. In addition, because treatment period ranged widely from 4 to 20 weeks in the current study, we could not determine the best treatment period for cancer patients' illness trajectory. We also need to address this issue in a future study.

The present findings are very limited because our case series is seriously flawed by many methodological weaknesses, especially many types of bias resulting from systematic and random errors. However, our experience indicates that the PST is a promising psychosocial intervention that should be investigated in further well-designed clinical trials in Japanese clinical oncology settings. We are now planning a clinical trial to investigate the effectiveness of PST on fear of recurrence among breast cancer survivors.

## Funding

This study was supported in part by a Grant-in-Aid for Cancer Research from the Japanese Ministry of Labor, Health and Welfare.

## Conflict of interest statement

None declared.

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# Psychotherapy for depression among incurable cancer patients (Review)

Akechi T, Okuyama T, Onishi J, Morita T, Furukawa TA

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**This record should be cited as:**
Akechi T, Okuyama T, Onishi J, Morita T, Furukawa TA. Psychotherapy for depression among incurable cancer patients. *Cochrane Database of Systematic Reviews* 2008, Issue 2. Art. No.: CD005537. DOI: 10.1002/14651858.CD005537.pub2.

**This version first published online:** 23 April 2008 in Issue 2, 2008.
**Date of most recent substantive amendment:** 11 February 2008

## ABSTRACT

**Background**
The most common psychiatric diagnosis among cancer patients is depression; this diagnosis is even more common among patients with advanced cancer. Psychotherapy is a patient-preferred and promising strategy for treating depression among cancer patients. Several systematic reviews have investigated the effectiveness of psychological treatment for depression among cancer patients. However, the findings are conflicting, and no review has focused on depression among patients with incurable cancer.

**Objectives**
To investigate the effects of psychotherapy for treating depression among patients with advanced cancer by conducting a systematic review of randomized controlled trials (RCTs).

**Search strategy**
We searched the Cochrane Pain, Palliative and Supportive Care Group Register, The Cochrane Controlled Trials Register, MEDLINE, EMBASE, CINAHL, and PsycINFO databases in September 2005.

**Selection criteria**
All relevant RCTs comparing any kind of psychotherapy with conventional treatment for adult patients with advanced cancer were eligible for inclusion. Two independent review authors identified relevant studies.

**Data collection and analysis**
Two review authors independently extracted data from the original reports using standardized data extraction forms. Two independent review authors also assessed the methodological quality of the selected studies according to the recommendations of a previous systematic review of psychological therapies for cancer patients that utilized ten internal validity indicators. The primary outcome was the standardized mean difference (SMD) of change between the baseline and immediate post-treatment scores.

**Main results**
We identified a total of ten RCTs (total of 780 participants); data from six studies were used for meta-analyses (292 patients in the psychotherapy arm and 225 patients in the control arm). Among these six studies, four studies used supportive psychotherapy, one adopted cognitive behavioural therapy, and one adopted problem-solving therapy. When compared with treatment as usual, psychotherapy was associated with a significant decrease in depression score (SMD = -0.44, 95% confidence interval [CI] = -0.08 to -0.80). None of the studies focused on patients with clinically diagnosed depression.

**Authors' conclusions**
Evidence from RCTs of moderate quality suggest that psychotherapy is useful for treating depressive states in advanced cancer patients. However, no evidence supports the effectiveness of psychotherapy for patients with clinically diagnosed depression.

## PLAIN LANGUAGE SUMMARY

Psychotherapy for depression among cancer patients who are incurable

Depressive states represent frequent complications among cancer patients and are more common amongst advanced cancer patients. Psychotherapy comprises of various interventions for ameliorating or preventing psychological distress conducted by direct verbal or interactive communication, or both, and is delivered by health care professionals. It is a patient-preferred and promising strategy for treating depressive states among cancer patients. Several systematic reviews have investigated the effectiveness of psychotherapy for treating depressive states among cancer patients. However, the findings are conflicting, and no review has focused on depressive states among patients with incurable cancer. The review authors conducted a systematic review of randomised controlled trials to investigate the effects of psychotherapy on the treatment of depressive states among patients with advanced cancer. The review authors found that psychotherapy was useful for treating depressive states in advanced cancer patients. However, little evidence supports the effectiveness of psychotherapy for patients with clinically diagnosed depression including major depressive disorder. Future studies to investigate and clarify the usefulness of psychotherapy for treating clinically diagnosed depression in terminally ill patients are needed.

## BACKGROUND

Cancer is a life-threatening disease that often impacts on a patient's welfare and well-being; attention to these issues is thus an important aspect of comprehensive patient care. Derogatis *et al.* found that 50% of cancer patients are diagnosed with a psychiatric disorder. The most common psychiatric diagnosis was depressive disorders, including adjustment disorder with depressed mood (12%) or mixed emotional features (13%) or unipolar major depression, (4%) or both (Derogatis 1983). Other studies have consistently indicated that these depressive disorders represent common forms of psychological distress experienced by cancer patients (Akechi 2001; Kugaya 2000; Okamura 2000) and are more common in patients with advanced cancer (Bukberg 1984; Kugaya 2000). Thus depression is one of the most widely recognized psychiatric disorders in cancer patients (McDaniel 1995). Depression not only produces serious suffering (Block 2000), but also worsens quality of life (Grassi 1996), reduces compliance with anti-cancer treatment (Colleoni 2000), can lead to suicide (Henriksson 1995), is a psychological burden on the family (Cassileth 1985), and prolongs hospitalization (Prieto 2002). Thus, the appropriate management of depression in cancer patients is critically important.

One patient-preferred and promising strategy for treating depression among cancer patients is psychotherapy (Okuyama 2007). Here, the term 'psychotherapy' is defined as various kinds of interventions for ameliorating or preventing psychological distress conducted by direct verbal or interactive communication, or both, delivered by health care professionals. Several meta-analyses and systematic reviews investigating the effectiveness of psychosocial treatment for depression among cancer patients have been performed. However, the findings of these reports are conflicting (Devine 1995; Newell 2002; Ross 2002; Sheard 1999), and no review to date has addressed the effectiveness of psychotherapy for treating depression among incurable cancer patients.

## OBJECTIVES

1) The primary objective of this review was to investigate the effectiveness of psychotherapy for treating any kind of depression in incurable cancer patients.
2) The review also evaluated the effectiveness of psychotherapy on:

- anxiety,
- general psychological distress,
- control of cancer symptoms,
- quality of life,
- coping measures for patients,
- severity of physical symptoms such as pain.

## CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

### Types of studies

All relevant randomised controlled trials (RCTs) comparing any kind of psychotherapy with conventional treatment (treatment as usual).

### Types of participants

The study participants were limited to adults (18 years or older) of either sex with any primary diagnosis of incurable cancer. Their depression had to be assessed by validated measures, such as standardized self-report questionnaires or clinical interviews (e.g., Structured Clinical Interview for major depressive episode based on DSM-IV). A concurrent diagnosis of another physical disease was not a criteria for exclusion.

### Types of intervention

Studies involving psychotherapy of any kind were included in the review. We were interested in the effect of a broad range of psychological interventions, including several unique interventions, such as music therapy, that may be used in a palliative care setting. On the other hand, interventions that were not considered as forms of psychotherapy (e.g., aromatherapy, therapeutic touch) were not included. This broad range of non-pharmacological interventions were further divided into:
A: interventions by direct verbal or interactive communication, or both, delivered by health care professionals; and
B: non-pharmacological interventions other than the aforementioned ones.

### Types of outcome measures

The studies had to include at least one measure of the severity of depression, which was set as the primary outcome of this systematic review. Symptom severity could be measured either by self-reporting or rating by an observer.

Effectiveness was to be evaluated using the group mean scores of these continuous depression severity scales (this planned analytical method was modified in the completed review (*See* 'Results')).

Outcomes were to be measured at the end of the study. Where possible, these indices of effectiveness would be pooled at different time points in the course of treatment, such as at one month, three months, six months and so on. In addition, when studies provided data regarding ongoing effectiveness after treatment termination, this data was also to be pooled (this planned method was modified (*See* 'data synthesis').

***Secondary outcomes were as follows:***
1) no of patients who 'responded' to treatment according to the original study authors' definition;
2) anxiety, as measured using scales like the Hamilton Anxiety Rating scale, the State-Trait Anxiety Inventory, and the Hospital Anxiety and Depression Scale;
3) general psychological distress, as measured using scales like the Profile of Mood States (total mood disturbance) and the General Health Questionnaire;
4) quality of life, as measured using scales like the European Organization for Research and Treatment of Cancer (EORTC) quality of life questionnaire, the Functional Assessment of Cancer Therapy-General (FACT-G) scale, and the Medical Outcome Study Short-Form 36-item survey;
5) severity of physical symptoms like pain, as measured using scales like the Brief Pain Inventory (BPI) and visual analogue scale (VAS).

***Tolerability of the treatment was to be evaluated using the following outcome measures:***
1) Number of patients dropping out of the study for any reason.

## SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: Cochrane Pain, Palliative and Supportive Care Group methods used in reviews.

**1. Electronic databases**
To identify studies for inclusion in this review, detailed search strategies were developed for each electronic database searched in September 2005. These strategies were based on the search strategy developed for MEDLINE but were revised appropriately for each database and are included in additional Table 01.

***MEDLINE via OVID search strategy***
1. exp PSYCHOTHERAPY/
2. (psychotherap$ or aromatherap$ or "art therap$" or "autogenic training" or "behavior$ adj6 therap$" or (behaviour$ adj6 therap$) or (biofeedback and psycho$) or (cognitive adj6 therap$) or (desensiti$ and psychol$) or "implosive therap$" or (relax$ adj6 therap$) or (relax$ adj6 techniq$) or (therap$ adj6 touch$) or yoga)
3. (bibliotherapy or (color$ adj6 therap$) or (colour$ adj6 therap$) or (music$ adj6 therap$) or (hypno$ adj6 therap$) or (imagery and psychotherap$) or counsel$ or (group$ adj6 therap$) or "socioenvironmental therap$" or "socio environmental therap$" or "milieu therap$" or "therapeutic communit$" or (famil$ adj6 therap$) or psychosoc$ or psycholog$ or "self help group$" or (support$ adj6 group$) or (guide$ adj6 image$))
4. or/1-3
5. Depression/
6. (depression or depressive$ or depressed)
7. or/5-6
8. exp NEOPLASMS/
9. (tumor$ or tumour$ or cancer$ or carcinoma$ or malignan$ or neoplas$)
10. or/8-9
11. 4 and 7 and 10

The above search strategy was run with the following filter for Controlled Clinical Trials:
Cochrane Sensitive Search strategy for RCTs for MEDLINE on OVID (published in appendix 5b Cochrane Handbook for Systematic Reviews of Interventions. 4.2.5 May 2005)
1. randomized controlled trial.pt.
2. controlled clinical trial.pt.
3. randomized controlled trials.sh.
4. random allocation.sh.
5. double blind method.sh.
6. single blind method.sh.
7. or/1-6
8. (ANIMALS not HUMAN).sh.
9. 7 not 8
10. clinical trial.pt.

11. exp clinical trials/
12. (clin$ adj25 trial$).ti,ab.
13. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab.
14. placebos.sh.
15. placebo$.ti,ab.
16. random$.ti,ab.
17. research design.sh.
18. or/10-17
19. 18 not 8
20. 19 not 9
21. 9 or 19

**2. Reference search**
The references of all selected studies were inspected for more published reports and citations of unpublished studies. In addition, other relevant review papers were checked.

**3. SciSearch**
All the selected studies were sought as a citation in the SciSearch database to identify additional studies.

**4. Personal communication**
To ensure that all RCTs were identified, the authors of significant papers were contacted.

**5. Language**
No language restrictions were applied when selecting studies.

## METHODS OF THE REVIEW

**1. Selection of studies**
In September 2005, two review authors (TA and JO) checked hard copies of the references identified by the search strategy to identify studies meeting the following broad and simple criteria:
i) randomised trials;
ii) incurable cancer patients (this included subjects with incurable, advanced, metastatic, or terminal cancer. When the participants were mixed-stage cancer patients, studies in which more than 80% of the participants had an advanced stage of cancer (stage III, IV, or recurrent) were eligible for inclusion in the review); and
iii) assessment of depression.

The inter-rater reliability of the two raters were evaluated using percentage agreement and kappa coefficient. All studies identified by either of the two raters were then subjected to the next stage of critical appraisal according to the strict eligibility criteria.

**2. Quality assessment**
Two independent review authors (TA and TO) assessed the methodological quality of the selected studies. We used Newell's methodological quality criteria (Newell 2002), which includes the following points:
i) adequate concealment of allocation;
ii) patients randomly selected;
iii) patients blinded to treatment group;
iv) care-providers blinded to treatment group;
v) except for study intervention, equivalence of other treatments;
vi) care-providers' adherence monitored;
vii) detailed lost-to-follow-up information;
viii) percentage of patients not included in analyses;
ix) intention-to-treat analyses; and
x) outcomes measured in a blinding fashion.

The maximum score for each study was 30 points, with higher scores indicating higher quality. As previously reported, the quality of a study was considered to be good if the study had a total score greater than 20 points, fair if it scored 11 to 20 points, and poor if it scored less than 11 points (Newell 2002).

The inter-rater reliability of these validity criteria was evaluated using Cohen's weighted kappa. Those studies with clearly inadequate concealment of random allocation were excluded. The influences of the other quality indices were examined using sensitivity analyses.

**3. Data extraction**
Two review authors (TA and TO) independently extracted data from the original reports using data extraction forms. Any disagreement was resolved by consensus between the two or, where necessary, between all the review authors. Extracted data included the country of origin, the nature and content of psychological intervention and the patient group involved, the duration of the study, the study setting, the sample size, and the key outcomes using validated instruments.

**4. Data synthesis**
***Planned method***
Data were to be entered by JO into Review Manager 4.2.10 twice, using the duplicate data entry feature. For dichotomous outcomes, the relative risk (RR) and their 95% confidence intervals (CI) were to be calculated using the random-effects model, since the RR of the random-effects model has been shown to be superior in clinical interpretability and external generalisability than the fixed-effect models and odds ratios (OR) or risk differences (Furukawa 2002). The heterogeneity among the studies was to be assessed using the I-squared and Q statistics and by visual inspection of the results in the Meta View plots. An $I^2$ greater than 30% or a Q statistic P value of less than 0.1 was to be considered indicative of heterogeneity. If significant heterogeneity was suspected, the sources were to be investigated. For dichotomous outcomes of response, two analytical strategies were to be adopted; first, a 'per protocol' analysis was to be performed according to the values reported by the original authors. When data on dropouts were included, usually by way of the last-observation-carried-forward (LOCF) method, this data was to be analysed according to the primary studies. For continuous outcomes, the standardized mean difference (SMD) was to be pooled using the random-effects model. Continuous outcomes were to be analysed on an endpoint basis, including only patients with a final assessment or with a last

observation carried forward to the final assessment. A strict ITT analysis was not feasible with continuous outcomes, as the studies performed only LOCF or endpoint analyses.

***Actual method***

Data were entered by TA into Review Manager 4.2.10 twice using the duplicate data entry feature. Analysis of dichotomous outcomes was planned, but only one study (Wu 2003) included this. Post-treatment scores were available in three studies (Wu 2003; Liossi 2001; Linn 1982) while change scores were available or could be calculated in six studies (Goodwin 2001; Classen 2001; Edelman 1999; Wood 1997; Linn 1982; Spiegel 1981). We therefore modified the data synthesis method during the review because the data obtained could not be synthesized appropriately using the planned method. The change between the baseline and immediate post-treatment scores was selected as the primary outcome for the meta-analysis (Banerjee 2006). The SMD and 95% CIs were pooled using a random-effects model (Alderson 2004). Two studies provided data on the results of slope analyses (Classen 2001; Spiegel 1981), and we calculated the change scores using these data. One paper provided raw data only (Wood 1997); for these data, we calculated the change score using SPSS 10.0J version software for Windows (SPSS 2003). In addition, because we could not obtain the actual figures for the standard deviations in the change scores for depression, anxiety, and general psychological distress in two studies (Classen 2001; Linn 1982), we calculated the pooled standard deviations in the other available studies that utilized the same measuring instrument (the Profile of Mood States) (MaNair 1992) (Edelman 1999; Goodwin 2001; Spiegel 1981; Wood 1997) and these values were inputted for the missing data (Furukawa 2006).

The heterogeneity among the studies was assessed using the $I^2$ and Q statistics and by visual inspection of the results in Meta View plots. An $I^2$ value greater than 30% or a Q statistic with a P value less than 0.1 were considered indicative of heterogeneity. If significant heterogeneity was suspected, the source of it was investigated.

**5. Subgroup analyses**

Subgroup analyses should be performed and interpreted with caution because multiple analyses can lead to false-positive conclusions (Oxman 1992). However, we performed the following subgroup analyses, if possible, for the following *a priori* reasons:

- A separate analysis was performed for participants who received group psychotherapy, since different modalities of psychotherapy (i.e., group versus individual) could have different effects.
- A separate analysis was performed for breast cancer patients, because many psycho-oncology studies focus on this patient group.
- A separate analysis was performed for participants with clinical depression based on any cut-off points or diagnostic criteria of depression measures, because the effect of psychotherapy on depression may differ according to the baseline depressive status.
- A separate analysis was performed for participants receiving interventions by direct verbal or interactive communication delivered by health care professionals, or both, because this type of psychotherapy may have a different effect on depression.

**6. Funnel plot analysis and sensitivity analyses:**

- A funnel plot analysis was performed to check for any publication bias.
- A sensitivity analysis was performed, if possible, to examine the robustness of the observed findings by repeating all the analyses using only high-quality studies.

## DESCRIPTION OF STUDIES

Two independent review authors checked the studies identified by the search sources, and a total of 176 studies were extracted for possible inclusion. Full copies of these articles were obtained, and the two independent review authors then examined the strict eligibility of these papers. Further reference searches and a SciSearch did not yield any additional studies that satisfied the strict eligibility criteria. The inter-rater reliability of the strict eligibility criteria were as follows: kappa coefficient, 0.84, percent concordance, 95.5%.

First, we identified 16 studies that were potentially suitable for inclusion (Classen 2001; Edelman 1999; Giasson 1998; Goodwin 2001; Laidlaw 2005; Linn 1982; Liossi 2001; Mantovani 1996; North 1992; Sarna 1998; Schofield 2003; Sloman 2002; Soden 2004; Spiegel 1981; Wood 1997; Wu 2003). However, five of these studies (Giasson 1998; North 1992; Sarna 1998; Schofield 2003; Soden 2004) were ultimately dropped after a discussion among the review authors because the interventions in these studies were not forms of psychotherapy. The interventions in these studies were as follows: aromatherapy (Soden 2004), a multisensory environment (Schofield 2003), a structured nursing assessment of symptoms (Sarna 1998), noncontact therapeutic touch (Giasson 1998), and information provided by tape-recordings of consultations (North 1992). In addition, one study was excluded because of the absence of usual care in the control group (Mantovani 1996). Finally we identified ten studies that were suitable for inclusion (total of 780 participants) (Classen 2001; Edelman 1999; Goodwin 2001; Laidlaw 2005; Linn 1982; Liossi 2001; Sloman 2002; Spiegel 1981; Wood 1997; Wu 2003).

The subjects of the meta-analysis were recruited from three main groups: patients with metastatic breast cancer (five studies), patients who had received some form of palliative care (three studies), and various patients with advanced cancer (two studies).

Various types of interventions were utilized in these ten studies. Five studies (Classen 2001; Goodwin 2001; Linn 1982; Spiegel

1981; Wu 2003) mainly used supportive psychotherapy. Three studies mainly investigated the effect of behavioural therapies, either relaxation techniques (Sloman 2002) or hypnosis (Laidlaw 2005; Liossi 2001). The other studies used cognitive behavioural therapy (Edelman 1999) and problem-solving therapy (Wood 1997). The duration of the interventions was variable, ranging from just three to five sessions (Wood 1997) to unlimited and continuing until death (Spiegel 1981). Three of the five studies using supportive psychotherapy and the one study using cognitive behavioural therapy utilized group treatment sessions. Thus, the ten selected studies included several kinds of interventions, all of which involved direct verbal and interactive communication delivered by health care professionals (Classen 2001; Edelman 1999; Goodwin 2001; Laidlaw 2005; Liossi 2001; Linn 1982; Sloman 2002; Spiegel 1981; Wood 1997; Wu 2003). There were no interventions belonging to non-pharmacological interventions other than the aforementioned ones.

## METHODOLOGICAL QUALITY

With regard to study quality, none of the studies met the criteria for a 'good' rating. Three studies met the criteria for a 'fair' rating (Goodwin 2001; Linn 1982; Wu 2003), and the remaining seven studies were judged as having a 'poor' rating. Two studies clearly described the procedure for adequate allocation concealment (Goodwin 2001; Linn 1982).

## RESULTS

Two studies did not report the effects of the interventions on depression (Laidlaw 2005; Wood 1997), although they did measure the severity of depression among the participating subjects. As described above, all of the remaining eight studies used interventions involving direct verbal and interactive communication delivered by health care professionals (Classen 2001; Edelman 1999; Goodwin 2001; Linn 1982; Liossi 2001; Sloman 2002; Spiegel 1981; Wu 2003).

**Effects of psychotherapy on depression: meta-analyses**

Moderate and statistically significant heterogeneity among six studies (see below) was observed ($P = 0.004$, $I^2 = 71\%$). The identified studies were quite heterogeneous with regard to their participants and interventions, and many studies did not include some of the data required for meta-analyses. Consequently, we decided to conduct the meta-analyses by combining the data from studies in which the change scores were available. Thus, we excluded four studies because they did not contain necessary data, such as the change score, the standard deviation of the change score, or the number of participants (Laidlaw 2005; Liossi 2001; Sloman 2002; Wu 2003). The data from the six studies that provided all the information needed to conduct the meta-analyses were combined; all of these studies had used the Profile of Mood States as a measure of depression (Classen 2001; Edelman 1999; Goodwin 2001; Linn 1982; Spiegel 1981; Wood 1997). Among these six studies, four studies used supportive psychotherapy (Classen 2001; Goodwin 2001; Linn 1982; Spiegel 1981), one utilized cognitive behavioural therapy (Edelman 1999) and one utilized problem-solving therapy (Wood 1997). Regarding the data from the study by Linn *et al.*, we decided to use the data obtained one month after intervention to minimize the effects of drop-outs, although the study provided data on depression at five time points during the intervention (Linn 1982).

The combined data from the six studies, involving 292 patients in the psychotherapy arm and 225 patients in the control arm, showed that psychotherapy had a significant effect on the treatment of depression among participants with advanced cancer (SMD = -0.44, 95% CI = -0.08 to -0.80). Visual inspection of the Meta View plots suggested that the study conducted by either Spiegel *et al.* or Wood *et al.* contributed most of the heterogeneity (Wood 1997; Spiegel 1981). While the heterogeneity indicators were similar if the study by Wood *et al* (Wood 1997) was excluded ($Chi^2 = 15.49$, $df = 4$ ($P = 0.004$), $I^2 = 74\%$), the heterogeneity diminished and was no longer statistically significant if the study by Spiegel *et al* was excluded ($Chi^2 = 5.93$, $df = 4$ [$P = 0.20$], $I^2 = 32.6\%$). The source of the heterogeneity was further investigated by examining the patient group, measuring instrument, type and duration of intervention, treatment of control group, outcome data and so on; however, clear factors that might have produced the heterogeneity could not be identified.

**Effect of psychotherapy on anxiety and general psychological distress: meta-analyses**

Since one study did not measure anxiety (Linn 1982), we combined the data from five studies (Classen 2001; Edelman 1999; Goodwin 2001; Spiegel 1981; Wood 1997). The combined data, involving 242 patients in the psychotherapy arm and 169 patients in the control arm, showed that psychotherapy had a borderline effect on anxiety among participants with advanced cancer (SMD = -0.68, 95% CI = 0.01 to -1.37). Strong, statistically significant heterogeneity was observed ($P < 0.00001$, $I^2 = 89.1\%$). Visual inspection of the Meta View plots suggested that the study conducted by Spiegel *et al.* was heterogeneous (Spiegel 1981). When this study was omitted, the significant heterogeneity was no longer observed ($Chi^2 = 3.22$, $df = 3$ [$P = 0.36$], $I^2 = 6.8\%$).

Four studies provided data on general psychological distress, as evaluated using the total mood disturbance score of the POMS (Classen 2001; Edelman 1999; Goodwin 2001; Spiegel 1981). The combined data, involving 237 participants in the psychotherapy arm and 166 participants in the control arm, showed a significant effect for psychotherapy on general psychological distress among participants with advanced cancer (SMD = -0.94, 95% CI = -0.01 to -1.87). A strong, statistically significant heterogeneity was observed ($P < 0.00001$, $I^2 = 94.3\%$). Visual inspection of the Meta View plots again suggested that the study conducted by

Spiegel *et al.* was heterogeneous (Spiegel 1981). When this study was omitted, the significant heterogeneity was no longer observed ($Chi^2$ = 2.43, df = 2 (P = 0.30), $I^2$ = 17.8%).

**Other secondary outcomes**

We deleted some secondary endpoints, including symptom control, quality of life, coping measures for participants, and severity of physical symptoms (like pain), because few studies provided this kind of data. In addition, we stopped checking the tolerability of the treatment and the dichotomous outcomes for the same reason.

**Subgroup and sensitivity analyses**

The two planned subgroup analyses (for participants who underwent group psychotherapy and for breast cancer patients) were conducted using the same four studies that investigated the effectiveness of group psychotherapy among metastatic breast cancer patients (Classen 2001; Edelman 1999; Goodwin 2001; Spiegel 1981). The results demonstrated similar and significant findings for all three targeted psychological symptoms: depression, anxiety, and general psychological distress.

The other subgroup analysis (for participants with clinical depression) was not conducted as none of the studies included the participants with clinically diagnosed depression. In addition, as described in the aforementioned section ('Effects of psychotherapy on depression: meta-analyses'), the planned subgroup analysis for participants receiving interventions via direct verbal and interactive communication delivered by health care professionals was not performed.

As only two studies included in the meta-analysis were judged to be of good or fair quality (Goodwin 2001; Linn 1982), a sensitivity analysis limited to these studies was performed. However, the study conducted by Linn *et al.* did not include anxiety and general psychological distress measures, so we conducted the sensitivity analysis for depression only. The combined data, involving 152 patients in the psychotherapy arm and 101 patients in the control arm, showed that psychotherapy was significantly effective for the treatment of depression (SMD = -0.35, 95% CI = -0.06 to -0.65). Statistically significant heterogeneity was not observed (P = 0.26, $I^2$ = 22.4%).

Although the number of included studies was small, thereby limiting the usefulness of a visual inspection of the funnel plot (Figure 01; Figure 02; Figure 03), a visual inspection did not suggest a prominent publication bias.

## DISCUSSION

**Current findings**

This is the first systematic review, including a meta-analysis so far as we are aware, to show the significant effectiveness of verbal and interactive psychotherapeutic intervention for treating depression among advanced cancer patients. Unfortunately, the effectiveness of other types of non-pharmacological interventions for the treatment of depression could not be analysed because the available data on this topic was insufficient.

Our findings suggest that the effects of psychotherapy are almost comparable to those obtained in antidepressant pharmacotherapy studies in general psychiatry settings (Bech 2000). On the other hand, this effect was not consistent with a previous meta-analysis of 17 clinical trials that investigated the effect of psychological interventions on depression in cancer patients (Sheard 1999). This previous meta-analysis indicated an effect size of 0.19, suggesting a clinically weak or negligible effect. Since the subjects of the majority of the studies included in this previous meta-analysis were not advanced cancer patients and most of the studies had selected their patient populations based on cancer diagnosis, rather than on diagnostic or psychological criteria, or both, differences in the prevalence of clinical depression may be one possible explanation for the discrepancy between their meta-analysis and ours. In other words, since depression is common in patients with advanced cancer (*see* 'Background'), this difference may account for the different findings regarding the effect of the intervention.

Regarding the types of verbal and interactive psychotherapeutic interventions that were included in the meta-analysis, four of the six psychotherapeutic approaches utilized supportive therapy. Probably because of the nature of the study subjects (i.e., people suffering from incurable cancer), all of the approaches involved some form of techniques dealing with the impact of life-threatening disease on patients' lives, including issues of 'dying' or 'existence', or both, in addition to general support (Spiegel 1978; Yalom 1977). In addition, one of the most prominent characteristics of these four studies was the fact that the interventions essentially continued until the patients' deaths. On the other hand, specific types of psychotherapy, especially cognitive behavioural therapy, are widely recommended for the treatment of psychological distress among cancer patients; however, our systematic review highlights the need for more well-designed clinical trials to clarify the effectiveness of cognitive behavioural therapy on depression in patients with advanced cancer.

The findings with regard to anxiety and general psychological distress were similar to those for depression, although the results for anxiety did not reach statistical significance. These findings suggest that the psychotherapy may be useful for ameliorating a broad range of psychological distress, with the exception of anxiety experienced by advanced cancer patients.

**Clinical implications and future research**

The present findings suggest that the depression experienced by advanced cancer patients, who are well-known to be at risk for developing depression or clinically profound psychological distress, or both, can be effectively ameliorated by psychotherapeutic intervention. Although our review could not clarify the cost effectiveness of psychotherapeutic interventions for patients with advanced cancer, and the fact that long-term continuous interven-

tions requiring trained mental health professionals may not be easy to provide for all patients, our findings suggest that psychological interventions should be combined with routine patient care for the treatment of patients with advanced cancer. At the same time, clarifying the cost-effectiveness of psychotherapy and developing cost-effective interventions for treating depression among advanced cancer patients may be important future tasks.

Some relevant questions remain concerning the effectiveness of psychotherapy on depression among patients with incurable cancer. First, because most studies included in the meta-analysis investigated the impact of the interventions just after or during the process of continuous treatment, or both, the persistent effects of the completed interventions were unclear. Second, because most of the subjects were not clinically diagnosed as having depression, the effectiveness of psychotherapy for the treatment of clinical depression could not be clarified in this review. These clinically important issues should be addressed in future studies.

Finally, we would like to comment on the study quality of the psychological interventions. As reported in the previous reviews, the quality of most of the studies was problematic (Newell 2002; Williams 2006). However, given the difficulty of conducting clinical trials in this population, such as in palliative care settings and of evaluating the quality of clinical trials for psychological interventions (Penrod 2004), novel and realistic quality assessment systems may be needed for studies focusing on patients with advanced cancer.

**Methodological advantages of this study**

This systematic review has several major strengths. Firstly, we performed systematic and comprehensive literature searches for relevant studies, whereas previous studies contained several major flaws in their methodology, including a language bias (e.g., typically only English papers), and the combination of randomised and non-randomized clinical trials. Second, the *a priori* planned heterogeneity and sensitivity analyses indicated that the results of the analyses were quite robust.

**Limitations of this study**

Our review also has some limitations. First, the reviewed studies generally had small sample sizes, and only a small number of studies (n = 6) were included in the meta-analysis. These factors may limit the validity of our findings. The existence of a possible outcome reporting bias cannot be negated (Chan 2005; Furukawa 2007). Secondly, although the use of data imputation for missing standard deviations of change scores was found to be valid in one study dealing with pharmacotherapy for depression (Furukawa 2006), whether this procedure was valid in our study sample was not confirmed. Thirdly, while this review included studies on the treatment of depression among advanced cancer patients, the results may not be applicable to advanced cancer patients with clinically diagnosed depression. Additionally, although this study also included meta-analyses for anxiety and general psychological distress, these findings were subsidiary and inconclusive. Finally, because the subjects' physical status (e.g., physical functioning, estimated survival) were not clearly defined *a priori* and the participants were at least not critically terminally ill (i.e. an estimated survival period of less than a few months), the findings may not be applicable to end-stage cancer patients who are nearing death.

Despite these limitations, the obtained findings about the usefulness of psychotherapy for ameliorating depression in advanced cancer patients deserve important consideration, and future studies to investigate and clarify the usefulness of psychotherapy for treating clinically diagnosed depression in terminally ill patients are warranted.

## AUTHORS' CONCLUSIONS

### Implications for practice

Evidence from RCTs of moderate quality suggests that psychotherapy is useful for treating depressive states in advanced cancer patients although little evidence supports the effectiveness of psychotherapy for patients with clinically diagnosed depression including major depressive disorder. The effects of psychotherapy are almost comparable to those observed in antidepressant pharmacotherapy studies of major depressive disorders in general psychiatry settings. Regarding the types of verbal and interactive psychotherapeutic interventions, the most common approach was long-term continuous supportive therapy, typically until the patients' deaths. Although our review could not clarify the cost effectiveness of psychotherapeutic interventions for patients with advanced cancer and considering that long-term continuous interventions requiring trained mental health professionals may not be easy to provide for all patients, our findings suggest that psychological interventions should be combined with routine patient care for the treatment of patients with advanced cancer.

### Implications for research

The continuing effects of the completed interventions and the effectiveness of psychotherapy for the treatment of clinical depression should be addressed in future studies. In addition, clarifying the cost-effectiveness of psychotherapy and developing cost-effective interventions for the treatment of depression among advanced cancer patients are also important future tasks. Specific types of psychotherapy, especially cognitive behavioural therapy, are widely recommended for the treatment of psychological distress among cancer patients; however, our systematic review highlights the need for more well-designed clinical trials to clarify the effectiveness of cognitive behavioural therapy on depression in patients with advanced cancer. The effectiveness of psychotherapy for treating depression in end-stage cancer patients who are nearing death should also be investigated. Finally, given the difficulty of conducting clinical trials in palliative care settings and of evaluating the quality of clinical trials for psychological interventions,