

EPEEC-O

Education in Palliative and End-of-life Care - Oncology

Participant's Handbook

Module 3h:

Symptoms – Depression

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Case*

B.H. is a 72-year-old married man with metastatic lung cancer; he has a three month history of fatigue, insomnia, nausea with decreased appetite, and poorly controlled pain. He also reports feelings of sadness and hopelessness. His wife reports that he often states he is helpless and no longer enjoys his hobbies or spending time with her. She states he has had these feelings for at least two months, and they have been getting progressively worse. His medications include ranitidine, dexamethasone, gabapentin, and lorazepam. He uses opiate analgesics as needed for pain. Examination reveals non-specific neurological abnormalities. His vital signs are normal. CT scan shows cerebral metastases. An initial Folstein Mini-Mental State Examination is normal.

* This case is not on an EPEC-O Curriculum trigger tape.

Introduction

Major depression is *an episode during which the patient complains or is noted to have depressed mood or the loss of interest or pleasure in nearly all activities for a period of at least two weeks*. In children and adolescents, their mood may be irritable rather than sad. Patients also experience a host of other symptoms, including changes in appetite or weight, sleep, and psychomotor activity; decreased energy; feelings of worthlessness or guilt; difficulty thinking, concentrating, or making decisions; or recurrent thoughts of death or suicidal ideation, plans, or attempts.¹ Depression is often viewed by patients as something to be ashamed of, or as a sign of weakness. Through patient and family education, the physician can help correct this misconception.

As depression is a source of intense suffering, oncologists will want to be particularly diligent at assessing and detecting associated signs and symptoms. Persistent depression is not 'normal' for patients with a serious illness or at the end of life. It is a myth that feeling helpless, hopeless, depressed, and/or miserable are inevitable consequences of advanced life-threatening illnesses.²

Risk factors

In patients with cancer, there are many risk factors for major depression. Poorly controlled pain and other physical symptoms contribute to depression and are particularly important because they are remediable (see EPEC-O Module 2: Cancer Pain Management and EPEC-O Module 3: Symptoms).² Progressive physical impairment and an advanced stage of disease also correlate with a higher incidence of depression.³ With some medications, eg, steroids, benzodiazepines, various chemotherapeutics, depression is a potential adverse effect.⁴ A few cancers, eg, pancreatic, breast, and lung, are associated with a higher incidence of depression.² Age may also play a role, with younger cancer patients being more prone to depression.^{5,6} Finally, spiritual pain and conflicts over issues of meaning, guilt, and fear may manifest as depression.²

Risk factors for depression that occur within the general population, eg, prior episodes of depression or mania or a family history of psychiatric illness, also apply to patients with

cancer.⁷ Patients are also at increased risk when they lack social supports or are experiencing other stressful life events that are unrelated to or consequences of their illness.²

Issues of grief and bereavement may also be important risk factors.² (See EPEC-O Module 4: Loss, Grief, and Bereavement).

Prevalence

Most patients with a serious illness experience periods of intense sadness or hopelessness. These feelings are usually present for a relatively short period, and then resolve. For some patients, a major depressive illness occurs. The prevalence of depression ranges from 1-40% in palliative care settings.² It occurs in up to 58% of cancer patients.^{8,9}

Unfortunately, it has been found that most professionals who work with these populations are unable to appropriately estimate the level of psychological distress of their patients.^{10,11,12}

Prognosis

Depression has been demonstrated to be associated with poor prognosis. This has mostly been studied related to increased risk of suicide. However, length of life and quality of life are both influenced by depression. When depression is treated, overall prognosis improves.

An issue of concern to oncologists has been, if the patient knows the true extent of disease and an accurate prognosis, will that lead to depression and adverse outcomes? In a survey of 106 advanced cancer patients at home, no such correlation was found.¹³

Pathophysiology

A biological understanding of depression is still in development. Recent pharmacological advances in the treatment of depression point to the involvement of norepinephrine, serotonin and dopamine. Electroconvulsive therapy, effective for the treatment of major depression, induces seizure which in turn releases increase amounts of these neurotransmitters in the brain. However, just how and why these neurotransmitters are involved is not yet clear.

Genetic and environmental influences play a role in the pathogenesis of depression.¹⁴ A number of conditions have been associated with depression, including cancer. Some medications, including corticosteroids, procarbazine, vincristine, and vinblastine are also associated with depression.¹⁵ A causal link has not been established, but the association is clear.

Assessment

The earlier depression is diagnosed, the more responsive to treatment it is likely to be. Treatment for depression may help patients feel better and have the energy and interest to pursue further anticancer therapy, live life to the fullest, and achieve final goals before they die. This applies to teenage and young adult patients as well.^{2,16}

Focus assessment on psychological and cognitive symptoms that are indicative of the diagnosis. Reliable symptoms of major depression include persistent dysphoria, anhedonia (loss of pleasure), feelings of helplessness, hopelessness, worthlessness, and loss of self-esteem. Other symptoms include feelings of excessive guilt, pervasive despair, bothersome ruminations about death, and thoughts of suicide. Pain not responding as expected, sad mood with flat affect and anxiety, irritability, or unpleasant mood may also be significant signs of depression.^{2,17,18}

Somatic symptoms, eg, changes in appetite, weight, energy level, libido, or sleeping, are important when making a diagnosis of depression in a non-medically ill population.² However, somatic symptoms are almost invariably present in patients with advanced cancer, making it difficult to discern their etiology.² Often these symptoms in depression are indistinguishable from these same symptoms in fatigue, cachexia, or weakness.

The following question appears to be a sensitive and specific question in this population:¹⁹

- Do you feel depressed most of the time?

Requests to hasten death may be a marker of undiagnosed depression (see EPEC-O Module 14: Physician-Assisted Suicide). Asking about the severity and time course of the aforementioned psychological and cognitive symptoms may help make the diagnosis.

Mental health professionals may use more specific screening tools, eg, the Beck Depression Inventory or the Hospital Anxiety and Depression Scale for the identification of depression.¹⁷

Where possible, enquire about the observations of family, friends, and other members of the health care team, as they may provide considerable information about baseline behaviors and add to the history.

It is important and often difficult to distinguish depression from grief reaction, adjustment disorders, delirium, or dementia. Be aware that depression can present with either psychomotor retardation or agitation. Depression that occurs in response to a psychosocial stressor is distinguished from an adjustment disorder with depressed mood in that the full criteria for a major depressive episode are not met in adjustment disorder.¹ After the loss of a loved one, or even after obtaining a diagnosis with a poor prognosis, attribute depressive symptoms to grief or bereavement rather than to a major depressive episode, unless they persist for more than two months or include significant functional impairment, severe preoccupation with worthlessness, psychotic symptoms, psychomotor

retardation, or suicidal ideation.¹ Hypoactive delirium is often mistaken for and difficult to distinguish from depression (see EPEC-O Module 3g: Symptoms - Delirium). A detailed history of onset and time course of both mood and cognitive symptoms is essential. Often in delirium, the cognitive impairment is much more profound and pervasive, and the onset is more abrupt.²⁰ Similarly, an individual with a major depressive episode is much more likely to have a relatively normal premorbid state and abrupt cognitive decline associated with the depression, compared with a dementia, where there is often a protracted history of declining cognitive function.¹

Whenever you are uncertain how to complete a detailed assessment of depression, or the situation appears to be complex, ask a psychiatrist or a psychologist for assistance.

Suicide

Suicidal thoughts are an important sign of depression, even in patients with advanced life-threatening illness. It is a myth that asking about suicide will ‘put the idea into someone’s head.’ To the contrary, allowing patients to discuss the thoughts they are having may reduce the likelihood they will actually commit suicide, particularly if the physician acknowledges their feelings and desires, and addresses the root causes of their distress (see EPEC-O Module 14: Physician-Assisted Suicide).

Assess all patients with depressive symptoms for thoughts and plans to commit suicide. Ask questions like:

- Have you ever thought of committing suicide?
- Do you have a plan?

Consider patients with recurrent thoughts of suicide or serious plans to be at high risk. Consult a mental health specialist experienced in this area immediately.²

Management

Treat depressed cancer patients with a combination of supportive and other psychotherapy modalities, alternative medicine approaches, and pharmacotherapy. Lack of improvement within a few weeks suggests a need for more aggressive therapy or a psychiatric consult. There are a number of reviews on the management of depression:^{2,21} Consensus Guidelines from the American Psychiatric Association²² and Clinical Practice Guidelines from the American Medical Directors Association.²³

Counseling

Individual and group counseling have both been shown to reduce depressive symptoms.^{24,25} Weave supportive counseling that uses aspects of brief supportive psychotherapy into routine interventions. Spend time educating the patient and family members about modifiable factors that contribute to anxiety and depression. Supportive counseling has many goals. The interaction itself may be therapeutic. During the discussions, provide the patient with an improved understanding of his or her prognosis,

potential treatments, and outcomes. These may help the patient put perceptions, expectations, needs, fears, and fantasies about his or her illness and death into a different perspective. Discuss short-term goals. Identify and reinforce the patient's previously demonstrated strengths and successful coping techniques. This will help the patient and family to establish or reestablish the patient's sense of self-worth and meaning (see EPEC-O Module 9: Negotiating Goals of Care).

In addition to formal sessions—with the oncologist, psychiatrists, psychologists, or other mental health professionals—nurses, social workers, and chaplains may also be able to conduct both formal and informal sessions, depending on their training.

Time spent talking with patients about their feelings and reframing their ideas may be very helpful.

These approaches can be used by the primary physician, as well as other colleagues.

Complementary therapies

Relaxation therapy, distraction therapy with pleasant imagery, etc., have been shown to reduce depressive symptoms in patients with mild to moderate levels of depression.²⁶

Other helpful techniques may include meditation training, guided imagery, massage therapy, aromatherapy, or self-hypnosis. If possible for the patient, exercise and exposure to sunlight can help to lift depressed moods.

Pharmacological management

The principal medications used for the treatment of depression include tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs), psychostimulants, and other classes of antidepressants.

The time available for treatment will strongly influence the choice of medication for initial therapy. When reversal of depression is an immediate short-term goal, a rapid-acting psychostimulant is the best choice. If a response in 2 to 4 weeks is acceptable, a selective serotonin reuptake inhibitor, tricyclic or other antidepressant may be an appropriate choice.² When they are available, selective serotonin reuptake inhibitors are preferred over tricyclic antidepressants as the risk of adverse effects is significantly less, even though they may not be as effective as tricyclic antidepressants.

Often patients will respond to specific antidepressants if they have a family member who has had a positive response to that same antidepressant.

With all antidepressant medications, 'start dosing low and go slow.' Titrate the dose to effect and tolerability. Warn patients about possible adverse effects, which will usually ameliorate within a few days. If patients are not responding as expected, consult a psychiatrist.

Tricyclic antidepressants

Amitriptyline is the tricyclic antidepressant listed by the World Health Organizations (WHO) as an Essential Medicine.²⁷ It is also used as an analgesic to manage neuropathic pain. Doxepin and imipramine were also considered to have similar clinical effects by the WHO. Other second-generation tricyclic antidepressants to consider are desipramine and nortriptyline.

When other antidepressants are available, tricyclic antidepressants are not recommended as first-line therapy to manage depression due to their adverse effect profile, unless they are being used as adjuvants to control neuropathic pain.

Titration to achieve an adequate dosage may take 3 to 6 weeks, delaying the onset of therapeutic action.

Anticholinergic adverse effects, eg, dry mouth, constipation, orthostatic hypotension, blurred vision, urinary retention, delirium, and cardiac conduction delays (proarrhythmic) are all seen with some frequency. If a tricyclic antidepressant is to be used, the secondary amines desipramine and nortriptyline are often preferable as they tend to have fewer adverse effects, but these may be activating instead of sedating. Dose all TCAs similarly. Common starting doses are:

- Amitriptyline (or any other tricyclic antidepressant), 10-25 mg PO nightly. Every 3-5 days, increase by 10-25 mg PO nightly. Maintenance dose is typically 50-100 mg PO nightly. Maximum dose is 150 mg/day. When using doses of 100 mg or more, follow blood levels to anticipate and minimize the risk of adverse effects.

Selective serotonin reuptake inhibitors

When selective serotonin reuptake inhibitors, eg, fluoxetine, paroxetine, sertraline, citalopram, and escitalopram are available and affordable, they are recommended over TCAs as they are 1) almost as effective antidepressants, 2) their onset of action is usually faster, and 3) there is much less risk of adverse effects.

Low doses may be sufficient in advanced illness, and once-daily dosing is possible. Use caution, as most of these medications (except for citalopram and escitalopram) have significant effects on hepatic metabolism and possible drug interactions, particularly with psychotropic medications. Evaluate all possible drug interactions before starting a selective serotonin reuptake inhibitor for any patient, especially those on many medications, but certainly when psychotropic medication is involved. Selective serotonin reuptake inhibitors cause significantly less constipation, sedation, and dry mouth than the tricyclic antidepressants, though nausea may be worse with the selective serotonin reuptake inhibitors.²⁸ Expect to see results within two to four weeks. At that time, increase the dose if there is partial effect. If there is no effect, try an alternate medication or consult a psychiatrist. Do not increase doses faster than once weekly. Citalopram and escitalopram are good choices in this population as they have a few drug-drug interactions and often a better adverse effect profile. Paroxetine can be used if night time sedation is a

welcome side-effect. Note that all selective serotonin reuptake inhibitors can either be activating or sedating, but some tend to be more of one than the other. If a selective serotonin reuptake inhibitor is activating to the patient, give the dose in the morning, if it is sedating, give the dose nightly. Fluoxetine is generally not recommended due to its long half-life, but it does come in liquid form, which may be useful in this population. Common starting doses are:

- Citalopram, 10–20 mg PO daily. Increase weekly by 10–20 mg PO daily. Usual target is 40 mg PO daily. Maximum dose is 60 mg/day.
- Escitalopram, 5–10 mg PO daily. Maintenance and maximum dose is 10–20 mg PO daily.
- Paroxetine, 10–20 mg PO daily. Target dose is 20–40 mg PO daily. Maximum dose is 50 mg/day. To reduce the risk of adverse effects, consider an extended-release formulation.

Psychostimulants

The psychostimulants methylphenidate, dextroamphetamine, and pemoline are underappreciated for their antidepressant qualities.^{2,29} They act quickly, hours to days, and produce minimal adverse effects. Some patients report increased energy and an improved sense of well-being within 24 hours.

Psychostimulants can be used alone or in combination with other antidepressants. They may be continued indefinitely as their antidepressant effect persists over time. Tolerance to the antidepressant effect does not appear to develop. They may also be used to diminish opioid-induced sedation, and they may potentiate opioid analgesia.^{30,31}

Psychostimulants may produce psychosis, dependence, tremulousness, anxiety, anorexia, increased blood pressure, tachycardia, and insomnia. Monitor for these adverse effects.

If discontinued, taper psychostimulants off slowly. Monitor liver function tests if the use of pemoline will be prolonged.

Methylphenidate or dextroamphetamine are the medications of first choice as they are inexpensive and have a low risk of adverse effects. Common starting doses are:

- Methylphenidate, 5 mg PO q AM and q Noon. Increase every 1–2 days by 5 mg PO q AM and q Noon. Maximum dose is 30 mg twice a day. To improve tolerability, consider an extended-release formulation.
- Dextroamphetamine, 5 mg PO q AM and q Noon. Increase every 1–2 days by 5 mg PO q AM and q Noon. Maximum dose is 30 mg twice a day.

Pemoline is a stimulant unrelated to amphetamine, and is somewhat less potent. It offers the advantage of decreased sympathomimetic effects, little abuse potential, and absorption through the buccal mucosa.

- Pemoline, start with 18.75 mg PO q AM and q Noon. Increase by 18.75 mg PO q AM and q Noon. Maximum dose is 150 mg/day.

Modafinil is a novel non-stimulant agent that improves lethargy. This agent may help with lethargy in depression and improve response to antidepressants.^{32,33}

- Modafinil, start with 100 mg PO daily. Titrate to desired effect. The maximum dose of 400 mg/day.

Other antidepressants

A diverse group of old and newer medications that affect depression is growing quickly, including mirtazapine, bupropion, trazodone, and venlafaxine. Like selective serotonin reuptake inhibitors, they are thought to be about as effective as tricyclic antidepressants, but most have less risk of adverse effects.

Trazodone, though not considered a potent antidepressant, may have a role in cancer patients for adjunct analgesia due to serotonergic properties. It can also be highly sedating in low doses, making it an effective sedative hypnotic.^{2,28} A common starting dose is:

- Trazodone, 50 mg PO nightly. Increase every 7 or more days by 50 mg PO nightly. Maximum dose is 400 mg/day.

Bupropion and venlafaxine may have a positive impact on pain syndromes, and can be energizing in patients with fatigue or psychomotor retardation.²⁸ Common starting doses are:

- Bupropion, start with 100 mg PO bid for a few days. Increase 100 mg PO tid for a few weeks. Maximum single dose is 150 mg. Maximum daily dose is 450 mg. To simplify dosing and reduce the risk of adverse effect, consider an extended-release formulation, eg, Bupropion XL.
- Venlafaxine, 37.5 mg PO bid or Venlafaxine SR, 75 mg daily nightly to start. Begin with 37.5 SR daily for one week, then increase to 75 mg SR for one week, then 110.5 mg SR for one week, then 150 mg SR and continue for 4 weeks. Dose may be increased to 300 mg SR daily.

Mirtazapine may help with pain syndromes, is an effective antidepressant, tends to be sedating at lower doses, and has been associated with increased appetite. It may be particularly helpful in patients who are depressed, have trouble sleeping, but also have a suppressed appetite. If sedation is too great, try *increasing* the dose to ameliorate this adverse effect.

- Mirtazapine, start with 15 mg PO daily. Increase every 1–2 weeks by 15 mg PO daily. Maximum dose is 45 mg/day.

Summary

Depression is common among those with advanced, life-threatening illnesses. It is often overlooked and/or not aggressively treated. Attention to depression will improve outcomes of anti-cancer therapies, quality of life, psychosocial and family stress, and ultimately quality of death. Psychotherapy, psychopharmacology, and alternative medicine approaches all have a role to play in the treatment of depression, and treatments can be tailored to an appropriate time frame to best help the patient. Do not hesitate to consult with mental health professionals, including psychiatrists, psychologists, nurses, social workers, and chaplains if there is a question of a role for depression in one's illness or if simple interventions do not yield improvement. Suicidal ideation or a wish to hasten one's own death is cause for serious concern, and a psychiatric consult is warranted.

Key take-home points

1. Depression is treatable, even in patients with advanced cancer.
2. The screening question, "Do you feel depressed most of the time" is sensitive and specific.
3. The earlier depression is treated, the better the prognosis.
4. If the therapeutic goal is rapid reversal of depression, a psychostimulant is indicated.
5. Psychostimulants (for rapid effect) can be started at the same time as antidepressants (such as the SSRIs) that take longer to work.
6. Counseling plus pharmacotherapy is more effective than either alone.

Pearls

1. If you feel sad and depressed when in the presence of a patient, it may indicate the patient is depressed (counter-transference).
2. Aggressively titrate psychostimulants to lift depression in days.

Pitfalls

1. Adopting standard outpatient psychiatry models for treatment where the time course may be months for effects.
2. Not escalating doses to effective levels.
3. Thinking a psychiatrist or other trained therapist is the only one who can do brief supportive psychotherapy.

References

- ¹ *Diagnostic and statistical manual of mental disorders*. 4th, text revision ed. Washington, DC. American Psychiatric Association. 2000.
- ² Wilson KG, Chochinov HM, de Faye BJ, Breitbart W. Diagnosis and Management of Depression in Palliative Care. In: Chochinov HM, Breitbart W, eds. *Handbook of psychiatry in palliative medicine*. New York: Oxford University Press; 2000:435.

Review of impact, risk factors, assessment, and treatment of depression.
- ³ Derogatis LR, Morrow GR, Fetting J, et al. The prevalence of psychiatric disorders among cancer patients. *JAMA*. 1983;249(6):751-757. [PMID: 6823028](#).

Two hundred fifteen randomly accessed cancer patients who were new admissions to three collaborating cancer centers were examined for the presence of formal psychiatric disorder. Each patient was assessed in a common protocol via a psychiatric interview and standardized psychological tests. Results indicated that 47% of the patients received a DSM-III diagnosis, with 44% being diagnosed as manifesting a clinical syndrome and 3% with personality disorders. Approximately 68% of the psychiatric diagnoses consisted of adjustment disorders, with 13% representing major affective disorders (depression). The remaining diagnoses were split among organic mental disorders (8%), personality disorders (7%), and anxiety disorders (4%). Approximately 85% of those patients with a positive psychiatric condition were experiencing a disorder with depression or anxiety as the central symptom.
- ⁴ Stiefel FC, Breitbart WS, Holland JC. Corticosteroids in cancer: neuropsychiatric complications. *Cancer Invest*. 1989;7(5):479-491. [PMID: 2695230](#).

Corticosteroids have become an integral part of many cancer treatment regimens. Early reports of severe affective disorders appear less frequent today in patients receiving steroids, though controlled studies are rare. Minor mood changes are common, ranging from the euphoria of initial treatment to depressive symptoms on withdrawal. The most common severe disturbances seen clinically in cancer patients are the organic mood disorders and delirium. A more careful clinical delineation of the mental changes with steroids is desirable not only for the clinical relevance, but for the potential understanding of the etiology of mood disorders and mental changes seen in delirium.
- ⁵ Kathol RG, Noyes R, Jr., Williams J, Mutgi A, Carroll B, Perry P. Diagnosing depression in patients with medical illness. *Psychosomatics*. 1990;31(4):434-440. [PMID: 2247573](#).
- ⁶ Levine PM, Silberfarb PM, Lipowski ZJ. Mental disorders in cancer patients: a study of 100 psychiatric referrals. *Cancer*. 1978;42(3):1385-1391. [PMID: 698920](#).

Records of 100 consecutive hospitalized cancer patients referred for psychiatric consultation were reviewed. Fifty-six percent of the referred patients were diagnosed as depressed and 40% as having organic brain disease. Twenty-six of the 100 patients were misdiagnosed by the referring physician as depressed but were classified by the staff psychiatrist as suffering from organic brain syndrome. When referral was studied by primary site of cancer, only patients with breast cancer were referred at a significantly higher than expected rate (p less than .001). The importance of the mental status examination as a routine procedure in all cancer patients is stressed so that an organic brain syndrome will not be missed.
- ⁷ Kaplan HI, Sadock BJ. *Kaplan and Sadock's synopsis of psychiatry : behavioral sciences, clinical psychiatry*. 8th ed. Baltimore: Williams & Wilkins; 1998.

- ⁸ Pirl WF. Evidence Report on the Occurrence, Assessment, and Treatment of Depression in Cancer Patients. *J Natl Cancer Inst Monographs*. 2004;2004(32):32-39. [Full Text](#)

Rates of major depressive disorder and depressive symptoms comorbid with cancer appear to be 10%-25%. Although multiple instruments are available for assessing depressive symptoms, a clinical interview using Diagnostic and Statistical Manual of Mental Disorders criteria is the standard to which assessments are compared.

- ⁹ Massie MJ. Prevalence of Depression in Patients with Cancer. *J Natl Cancer Inst Monographs*. 2004;No.32:57-71. [Full Text](#)

Although many research groups have assessed depression in cancer patients since the 1960s, the reported prevalence (major depression, 0%-38%; depression spectrum syndromes, 0%-58%) varies significantly because of varying conceptualizations of depression, different criteria used to define depression, differences in methodological approaches to the measurement of depression, and different populations studied. Depression is highly associated with oropharyngeal (22%-57%), pancreatic (33%-50%), breast (1.5%-46%), and lung (11%-44%) cancers. A less high prevalence of depression is reported in patients with other cancers, such as colon (13%-25%), gynecological (12%-23%), and lymphoma (8%-19%).

- ¹⁰ Derogatis LR, Abeloff MD, McBeth CD. Cancer patients and their physicians in the perception of psychological symptoms. *Psychosomatics*. 1976;17(4):197-201. [PMID: 1005638](#).

- ¹¹ Lampic C, Wennberg A, Schill JE, Brodin O, Glimelius B, Sjoden PO. Anxiety and cancer-related worry of cancer patients at routine follow-up visits. *Acta Oncol*. 1994;33(2):119-125. [PMID: 8204268](#).

Anxiety and cancer-related worry were assessed in 197 consecutive cancer patients attending follow-up visits. Results show that while a majority of patients feel no or only mild anxiety in conjunction to the follow-up visit, about one-fifth report moderate or strong anxiety. Many patients (46%) worry about suffering a recurrence and about overlooking symptoms of new cancer (33%). Patients who were not in complete remission reported higher levels of cancer-related worry concerning the follow-up visit than did patients in remission. Among patients in remission, those who recently terminated treatment reported more overall distress than patients two or more years since treatment termination.

- ¹² Rathbone GV, Horsley S, Goacher J. A self-evaluated assessment suitable for seriously ill hospice patients. *Palliat Med*. 1994;8(1):29-34. [PMID: 7514069](#).

In an attempt to measure QOL in these patients a simple assessment was piloted (PEPS--patient evaluated problem score) in which patients were asked to identify and grade major problems as they perceived them and also to grade problems previously identified by the medical and nursing staff. Overall, a mean of 5.6 problems per patient were identified, of which 14% were psychosocial. Of those patients who completed questionnaires, 58% identified problems not picked up by the nursing and medical staff; 52% of these were psychosocial problems. PEPS has proved very useful in the management of patients, enabling the identification of previously unrecognized or underrated problems, particularly of a psychosocial nature, and also as a means of evaluating progress.

- ¹³ Barnett MM. Does it hurt to know the worst?-psychological morbidity, information preferences and understanding of prognosis in patients with advanced cancer. *Psychooncology*. 2005 Mar 7; [Epub ahead of print] [PMID: 15750997](#). [Full Text](#)

106 advanced cancer patients were interviewed at home. When understanding of prognosis was compared with psychological distress, a significant difference was observed between those with realistic versus unrealistic time-scales. Although patients with deteriorating health are more likely to be psychologically distressed, awareness of prognosis does not itself cause depression.

¹⁴ Sullivan PF, Neale MC, Kendler KS. Genetic epidemiology of major depression. *Am J Psychiatry*. 2000;157:1552-62. [PMID: 11007705](#).

¹⁵ Massie M, Holland J, Lesko L. Management of common psychiatric syndromes in elderly patients with cancer. In: *Cancer and aging*. Zenser T, Coe R (eds). New York, NY: Springer Publishing Company, 1998.

¹⁶ Passik SD, Breitbart WS. Depression in patients with pancreatic carcinoma. Diagnostic and treatment issues. *Cancer*. 1996;78(3 Suppl):615-626. [PMID: 8681300](#).

Depression and anxiety occur more frequently in patients with cancer of the pancreas than they do in patients with other forms of cancer. Diagnosis and treatment of depressive disorders as they applied to patients with cancer of the pancreas were reviewed, and psychologic and pharmacologic treatment strategies to deal with these issues were outlined.

¹⁷ Trask PC. Assessment of Depression in Cancer Patients. *J Natl Cancer Inst Monographs*. 2004;(32):80-92. [PMID: 15263046](#). [Full Text](#)

This review was designed to succinctly address and identify several areas for future research, including refining diagnostic criteria for depression in cancer patients; creating cancer-specific depression measures with appropriate cutoffs; focusing on the issues of age, race, ethnicity, subculture, and type and stage of cancer in creating depression assessment tools; and exploring the issues of clinical versus subclinical depression, who and when to assess, and timely and cost-effective ways to assess.

¹⁸ Endicott J. Measurement of depression in patients with cancer. *Cancer*. 1984;53(10 Suppl):2243-2249. [PMID: 6704912](#).

The recognition or detection of depressive symptoms and syndromes in patients with cancer is of value to the patient because his mental distress may respond to treatment, and to the clinician because some of the clinical complications or difficulties in diagnosis and treatment of the patient may be reduced. Many factors militate against the diagnosis of depressive syndromes in patients with cancer. These include problems with the application of standard sets of criteria for depression, the assumption on the part of medical staff, family, and patients that depression is a "natural" response and therefore not treatable, and the pressure on all involved to "think positive." Some ways of modifying the usual screening and diagnostic procedures for depressive disorders are suggested.

¹⁹ Chochinov HM, Wilson KG, Enns M, Lander S. "Are you depressed?" Screening for depression in the terminally ill. *Am J Psychiatry*. 1997;154(5):674-676. [PMID: 9137124](#).

This study compared the performance of four brief screening measures for depression in a group of terminally ill patients. The methods included 1) a single-item interview assessing depressed mood, 2) a two-item interview assessing depressed mood and loss of interest in activities, 3) a visual analog scale for depressed mood, and 4) the Beck Depression Inventory-Short Form. Single-item interview screening correctly identified the eventual diagnostic outcome of every patient, substantially outperforming the questionnaire and visual analog measures.

²⁰ Breitbart W, Cohen K. Delirium in the Terminally Ill. In: Chochinov HM, Breitbart W, eds. *Handbook of psychiatry in palliative medicine*. New York: Oxford University Press; 2000:435.

²¹ Fisch M. Treatment of Depression in Cancer. *J Natl Cancer Inst Monographs*. 2004;2004(32):105-111. [PMID: 15263050](#). [Full Text](#)

Depression occurs in about 15% of the general population and is at least two to three times more common in patients with cancer. Depression is often difficult to diagnose in these patients because of the complexity and constraints of cancer care, patient and family reluctance to acknowledge distress, and the

presence of multiple other symptoms. Both antidepressants and psychotherapy are effective in treating depression in patients with cancer, much like in patients with other significant medical problems. Precise assessments of the benefits of treating depression in these patients are important in weighing them against the costs and potential adverse effects. There is an emerging trend toward simplifying the assessment of depression in outpatient cancer care settings and studying depression therapies in cohorts of patients with cancer other than those with fully characterized depressive disorders.

- ²² Practice guideline for the treatment of patients with major depressive disorder (revision). American Psychiatric Association. *Am J Psychiatry*. 2000;157(4 Suppl):1-45. [PMID: 10767867](#).
- ²³ Clinical Practice Guideline: Depression. Columbia, MD: American Medical Directors Association, 2003. Available at <http://www.ama-assn.org/ama/pub/info/cpg/depression.htm>. Accessed March 19, 2005.
- ²⁴ Edmonds CV, Lockwood GA, Cunningham AJ. Psychological response to long-term group therapy: a randomized trial with metastatic breast cancer patients. *Psychooncology*. 1999;8(1):74-91. [PMID: 10202785](#).

Research has demonstrated that short-term psychological interventions improve the quality of life of cancer patients. However, there is much less evidence for the efficacy of long-term interventions. We report the psychometric results from a randomized clinical trial (n = 66) assessing the effects of an 8 month, weekly psychological intervention on 30 metastatic breast cancer patients. Results demonstrated little psychometric difference between the control (n = 36) and intervention groups over this length of time, in spite of the fact that when the intervention subjects attended a weekend of support and training in coping skills, the usual significant, short-term changes were observed. However, profound clinical changes were observed by the therapists, similar to those noted by Spiegel et al. (1981). We conclude that many of the psychological changes made by subjects in long-term interventions may elude conventional psychometric assessment.

- ²⁵ Spiegel D, Bloom JR, Yalom I. Group support for patients with metastatic cancer. A randomized outcome study. *Arch Gen Psychiatry*. 1981;38(5):527-533. [PMID: 7235853](#).

The effects of weekly supportive group meetings for women with metastatic carcinoma of the breast were systematically evaluated in a one-year, randomized, prospective outcome study. Eighty-six patients were tested at four-month intervals. The treatment group had significantly lower mood-disturbance scores on the Profile of Mood States scale, had fewer maladaptive coping responses, and were less phobic than the control group. This study provides objective evidence that a supportive group intervention for patients with metastatic cancer results in psychological benefit.

- ²⁶ Spiegel D, Bloom JR. Group therapy and hypnosis reduce metastatic breast carcinoma pain. *Psychosom Med*. 1983;45(4):333-9. [PMID: 6622622](#).

The pain and mood disturbance of 54 women with metastatic carcinoma of the breast were studied over the course of one year. A random sample was offered weekly group therapy during the year, with or without self-hypnosis training directed toward enhancing their competence at mastering pain and stress related to cancer. Both treatment groups demonstrated significantly less self-rated pain sensation (t = 2.5 p less than 0.02) and suffering (t = 2.17, p less than 0.03) than the control sample. Those who were offered the self-hypnosis training as well as group therapy fared best in controlling the pain sensation (F = 3.1, p less than 0.05). Changes in pain measures were significantly correlated with changes in self-rated total mood disturbance on the Profile of Mood States and with its anxiety, depression, and fatigue subscales.

- ²⁷ World Health Organizations Essential Medicines Library accessed February 16, 2005: <http://mednet3.who.int/Eml/modellist.asp>

²⁸ Schatzberg AF, Cole JO, DeBattista C. *Manual of clinical psychopharmacology*. 4th ed. ed. Washington, D.C.: American Psychiatric Pub.; 2003.

²⁹ Fernandez F, Adams F, Holmes VF, Levy JK, Neidhart M. Methylphenidate for depressive disorders in cancer patients. An alternative to standard antidepressants. *Psychosomatics*. 1987;28(9):455-461. [PMID: 3432548](#).

³⁰ Bruera E, Watanabe S. Psychostimulants as adjuvant analgesics. *J Pain Symptom Manage*. 1994;9(6):412-415. [PMID: 7963794](#).

Psychostimulants have multiple roles in the adjuvant treatment of pain. Studies are discussed that demonstrate the efficacy of these drugs in potentiating opioid analgesia, counteracting opioid-induced sedation and cognitive impairment, allowing dose escalation in difficult pain syndromes, and alleviating symptoms of depression. Practical guidelines are suggested, and areas for future research indicated.

³¹ Bruera E, Driver L, Barnes EA, et al. Patient-controlled methylphenidate for the management of fatigue in patients with advanced cancer: a preliminary report. *J Clin Oncol*. 2003;21(23):4439-4443. [PMID: 1464534](#).

Assessment of the effects of patient-controlled methylphenidate for cancer-related fatigue. In this prospective open study, 31 patients with advanced cancer and fatigue who scored ≥ 4 on a scale of 0 to 10 received methylphenidate 5 mg by mouth every 2 hours as needed for 7 days (maximum, 20 mg/d). Anxiety, appetite, pain, nausea, depression, and drowsiness all improved significantly ($P < .05$). All patients took afternoon or evening doses, and 28 patients (93%) took three or more doses daily. All patients chose to continue taking methylphenidate after 7 days of treatment. No serious adverse effects were reported.

³² Fava M, Thase ME, DeBattista C. A multicenter, placebo-controlled study of modafinil augmentation in partial responders to selective serotonin reuptake inhibitors with persistent fatigue and sleepiness. *J Clin Psychiatry*. 2005;66(1):85-93. [PMID: 15669893](#).

Up to one half of depressed patients have partial or no response to antidepressant monotherapy. This multicenter, placebo-controlled study evaluated the efficacy of modafinil augmentation in major depressive disorder (MDD) patients with fatigue and excessive sleepiness despite selective serotonin reuptake inhibitor (SSRI) monotherapy. Findings suggest that modafinil is a well-tolerated and potentially effective augmenting agent for SSRI partial responders with fatigue and sleepiness.

³³ DeBattista C, Lembke A, Solvason HB, Ghebremichael R, Poirier J. A prospective trial of modafinil as an adjunctive treatment of major depression. *J Clin Psychopharmacol*. 2004;24(1):87-90. [PMID: 14709953](#).

Preliminary evidence indicates that modafinil may improve fatigue and excessive sleepiness associated with a variety of conditions. The purpose of this study was to investigate the utility of modafinil as an adjunctive treatment of depressed patients. All subjects endorsed complaints of significant fatigue and/or excessive sleepiness on clinical assessment. Modafinil was added to their existing regimen at a dose of 100 to 400 mg/d for 4 weeks. Significant improvements were seen across all 3 measures of depression (HDRS, BDI, CGIS) and both measures of fatigue (VASF, FSI). Modafinil may be a useful and a well-tolerated adjunctive agent to standard antidepressants in the treatment of major depression.