Depression in breast cancer patients: The need for treatment

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Introduction

Sadness, fear, anger, and grief are natural and understandable emotional reactions following a diagnosis of cancer, and are usually overcome by standard social, nursing and medical care. However, there is a need to distinguish between this normal degree of sadness, which patients might describe as depression, and clinical depression which exceeds the normal reaction in duration and/or intensity and which warrants recognition and remedial intervention. Major depression according to DSM-IV criteria [1] needs specialised intervention using adequate psychological and pharmacological treatment approaches. Furthermore, as many as one-fifth of cancer patients may develop chronic depressive illness. Apart from the additional unnecessary suffering this comorbid depression can cause, many studies have suggested that depressed mood has a negative impact on disease outcome. Therefore, diagnosis and treatment of depression among patients treated for cancer may play a crucial role in the prognosis of the disease, in addition to improving the quality of life of the patient.

Prevalence

The prevalence of depression in the general population is approximately 6% [2–4]. However, the incidence of depression in hospitalised medically ill patients is much higher and has been reported in 22%–24% of patients [5, 6]. Massie and Holland [7] reviewed a number of studies assessing the occurrence of comorbid depression in cancer patients and found that the incidence of depression ranged from as high as 58% to as low as 4.5% [8–16]. The wide range in incidences can probably be attributed to variations between studies in patient populations, hospitalisation status, and disease stage and type. In particular, the prevalence rates may be affected by the application of different diagnostic criteria. Standard diagnostic criteria for depression, such as DSM-IV [1], may also contain a number of criteria which reflect the symptoms associated with cancer, leading to difficulties in accurate diagnosis (Table 1).

Using data collected from three cancer centres where the diagnostic criteria were based on DSM-III, Derogatis et al. [13] ascertained that 6% of cancer patients had major affective disorders and an additional 32% had adjustment disorders, comprising 12% with depressed mood, 13% with mixed emotional features, 6% with predominantly anxious mood, and 1% with 'emotion and conduct' disorders. Also applying DSM-III criteria, Massie and Holland [17] found that of 546 cancer patients referred for psychiatric consultations, 9% had major depression and 54% had adjustment disorders, of whom 47% were diagnosed as depressed, 31% had mixed mood disorder, and 22% were primarily anxious. In a study of 50 cancer patients by Hosaka and Aoki [18], 28% were found to meet DSM-IV diagnostic criteria for depression.

The incidence of depression in cancer patients appears to be dependent on the disease severity and level of patient disability. Lansky et al. [15] evaluated 500 women with cancer (190 of whom had breast cancer), and found that Karnofsky performance status and history of depression were the factors most commonly associated with comorbid depression. Similar results in hospitalised

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**Table 1.** DSM-IV criteria for major depressive episode [1].

At least five of the following symptoms to be present during the same two-week period and represent a change from previous functioning: at least one of the symptoms is either (1) or (2).

1. Depressed mood most of the day, nearly every day.
2. Markedly diminished interest or pleasure in all or almost all activities most of the day, nearly every day.
3. Significant weight loss or weight gain.
4. Insomnia or hypersomnia nearly every day.
5. Psychomotor agitation or retardation nearly every day.
6. Fatigue or loss of energy nearly every day.
7. Feelings of worthlessness or excessive or inappropriate guilt nearly every day.
8. Diminished ability to think or concentrate, or indecisiveness nearly every day.
9. Recurrent thoughts of death, recurrent suicidal ideation or suicide attempt.
cancer patients were reported by Bukberg et al. [14]: 77% of patients who scored lower than 40 on the Karnofsky scale (those most severely disabled) met the criteria for major depression, whilst only 23% of those with scores of 60 or above did so.

Assessing the literature, Massie and Holland [7] estimated that a true incidence of major depression among hospitalised cancer patients with significant levels of physical impairment is at least 25%. This incidence of depression in cancer patients is therefore comparable to that seen in patients with other medical conditions. This is contrary to the common assumption that cancer patients are more depressed than patients with other illnesses leading to hospitalisation.

The incidence of depression or anxiety, and subsequent suicide, in patients cured of cancer has been considered in a number of studies. Data indicate that cancer patients in long-standing remission possess similar anxiety rates to patients with active disease, suggesting that anxiety in cancer survivors may be persistent and not related to clinic attendance [19]. A survey of cured cancer patients by Loge et al. [20] identified depression and/or anxiety in 27% of respondents (14.5% anxiety; 4% depression; 8.5% anxiety and depression). Major depression has also been reported to be more common among suicide victims with cancer in remission than in suicide victims with terminal cancer [21]. These data indicate that depression is not only common in cancer patients, but also in patients cured of cancer, who may then commit suicide.

A number of studies have examined the incidence of depression specifically in breast cancer patients and found that the rate was similar to that of depression comorbid with other cancers (10%–55%, Table 2). Pinder et al. [30] studied 139 women with advanced breast cancer; 25% scored 11 or above on either the self-report Hospital Anxiety and Depression Scale (HADS) anxiety or depression subscales, interpreted as indicating probable cases of depression and/or anxiety. In a study of 85 patients with breast cancer [35] 39% were found to be suffering from a depressive disorder, compared with 11% of control patients with benign breast disease (P = 0.0003). In addition, dysthymia was found in 15% of the cancer patients compared with 5% of the control patients (P = 0.03).

Therefore, around a quarter of all breast cancer patients have comorbid depression. Such comorbid depression significantly increases the burden of distress and dysfunction for patients with breast cancer. There is, however, evidence to show that if comorbid depression is recognised, it can be relieved.

### Depression and pain

Control of pain plays a key role in determining quality of life for many patients with cancer. However, the issue of pain and its relationship to depression in cancer patients is still poorly understood. It is not yet clear whether depression is causally related to chronic pain or if pain causes depression. A recent study in patients with cancer indicated that pain may induce clinical depression [36]. This study of 96 patients with either low or high pain symptoms found that the incidence of all depressive disorders was significantly higher in the high pain group than in the low pain group (33% versus 13%, P < 0.05), despite a history of major depression being significantly more common in patients in the low pain group (P < 0.05).

Current scientific concepts of pain emphasise the multidimensional nature of the phenomenon, i.e., nociception (generated by organic pathology) interacting with psychosocial factors to determine behaviour. The cognitive behavioural approach offers a way of thinking about the relationship between pain and depression which has implications for management. It focuses on the role of perceived control over pain and perceived interference of pain in life activities as mediating the relationship between pain and depression [37]. While pain restricts activity, fear and negative thinking about pain may compound the problem. For example beliefs that pain cannot be controlled or anticipation of catastrophic consequences may result in avoidance of activities which were previously associated with pleasure and a sense of achievement. Loss of such activities can act as a stimulus to depress mood, further confirming the cycle of negative thinking. Thus, modifying perceived control of pain and perceived interference of pain in life activ-

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**Table 2. Prevalence of depression in breast cancer patients.**

<table>
<thead>
<tr>
<th>Source</th>
<th>Number of patients</th>
<th>Prevalence (%)</th>
<th>Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maguire et al., 1978 [23]</td>
<td>201</td>
<td>26a</td>
<td>Structured diagnostic interview</td>
</tr>
<tr>
<td>Silberfarb et al., 1980 [24]</td>
<td>146</td>
<td>10a</td>
<td>Structured diagnostic interview</td>
</tr>
<tr>
<td>Faber et al., 1984 [25]</td>
<td>141</td>
<td>19.5a</td>
<td>HSC</td>
</tr>
<tr>
<td>Fallowfield et al., 1990 [26]</td>
<td>269</td>
<td>20</td>
<td>Structured diagnostic interview</td>
</tr>
<tr>
<td>Hopwood et al., 1991 [27]</td>
<td>81</td>
<td>20</td>
<td>HADS, RSCL</td>
</tr>
<tr>
<td>Hopwood et al., 1991 [28]</td>
<td>222</td>
<td>24.5a</td>
<td>HADS, RSCL</td>
</tr>
<tr>
<td>Goldberg et al., 1992 [29]</td>
<td>320</td>
<td>32</td>
<td>RSCL</td>
</tr>
<tr>
<td>Pinder et al., 1993 [30]</td>
<td>139</td>
<td>13</td>
<td>HADS, structured diagnostic interview</td>
</tr>
<tr>
<td>Ramirez et al., 1995 [31]</td>
<td>91</td>
<td>55</td>
<td>HADS, structured diagnostic interview</td>
</tr>
</tbody>
</table>

Adapted from McDaniel et al. [22]. Abbreviations: HSC – Hopkins Symptom Checklist [32], HADS – Hamilton Anxiety and Depression Scale [33], RSCL – Rotterdam Symptom Check List [34].

* Mean prevalence.
The presence of depressive mood in patients with cancer may therefore have a detrimental effect on outcome. Extrapolating from these data, it might be concluded that the long-term prognosis may be seriously affected in breast cancer patients with major depression.

The immune system in cancer and depression

The role of the immune system is to recognise and defend against cells displaying foreign surface proteins, whether from a pathogen or from alteration of normal cell proteins. Thus, the continued growth and spread of cancer cells can result not only from neoplastic transformation, but also from resistance to the host’s immune system. Malignant cells can evade host defences through a variety of mechanisms, including alterations in the host’s T-cell receptor/CD3 complex, or decreased expression of major histocompatibility antigens on the tumour cell, or secretion of suppressive cytokines [52].

Despite growing awareness of functional links between the immune system and the nervous system, and research over the past 20 years into immunological functioning in psychiatric patients, it is still unclear whether depressive illness leads to an impairment in resistance to somatic illness (including cancer), as opposed to depression being secondary to physical illness [53]. A meta-analysis of controlled studies of depressed versus healthy subjects revealed that clinical depression was associated with lowered proliferative response of lymphocytes to mitogens, reduced natural killer cell activity, and alterations in numbers of several white blood cell populations [54]. There appeared to be a relationship between the severity of depression and the degree of changes to immune functioning. Furthermore, in breast cancer patients, the stress of surgery was reported to be associated with reduced lymphocyte-activated killer-cell activity and was related to the severity of concurrent depression and anxiety [55].

Further studies are required to establish the causal relationship between depression, immune system changes, and somatic illness, and to establish the comorbid risk among patients with mood disorders for physical illnesses, including cancer.

Recognition and diagnosis

It has been demonstrated that emotional disturbance in cancer patients commonly goes unrecognised and untreated. Early work by Maguire et al. [23] with mastectomy patients demonstrated that not only did staff fail to recognise affective disorders, but that patients were often reluctant to disclose their concerns. This observation led to a major body of work concerned with improving staff communication and counselling skills. In busy routine practice the most effective way of detecting patients with signs and symptoms of depression is probably through monitoring by specially trained nurses.

The diagnostic criteria for major depression, as defined in DSM-IV [1], include a number of signs and symptoms which may be difficult to distinguish from...
the effects of cancer or that may be attributable to cancer (Table 2). The assessment of patients with cancer is therefore confounded by the difficulty in distinguishing between symptoms of cancer and standard depression markers, such as weight loss, impaired sleep and insomnia, fatigue, and decreased libido [56].

Several systems of diagnosis modified for use in medically ill patients have therefore been proposed. One such system suggests removing anorexia and fatigue from the list of diagnostic symptoms, as these are commonly associated with either the disease or side effects of treatment [57]. However, excluding such markers may decrease the sensitivity of the tests and increase possible misdiagnosis: the authors therefore suggested that for clinical purposes, all criteria may be included even if there is a possibility that the symptoms may be attributed to the disease or treatment. It has also been suggested that more emphasis should be placed on psychological, rather than physical, symptoms, such as feelings of hopelessness, worthlessness, and wishing to die, as primary criteria for depression [58].

Hopwood et al. [27] compared the screening performance of two questionnaires for psychiatric morbidity in patients with advanced breast cancer: the Hospital Anxiety and Depression Scale (HADS) [designed for physically ill patients] and the Rotterdam Symptom Checklist (RSCL) [designed specifically for cancer patients]. Results were compared with those of a psychiatrist who used the Clinical Interview Schedule. Seventy-five percent of patients were correctly identified as suffering from an affective disorder by both the scales: 21% and 26% of 'normal' patients were mis-classified by the RSCL and HADS, respectively. However, the authors concluded that both questionnaires had good predictive value and could be used in patients with advanced cancer to help screen out those with an affective disorder. These data were confirmed by Ibbotson et al. [59] in that both HADS and RSCL questionnaires were found to be effective at detecting major depressive illness and general anxiety disorders in a wide spectrum of cancer types, but noted that the optimal cut-off score varied with the patients disease and treatment status.

Razavi et al. [60] tested the HADS as a screening method for detecting adjustment disorders and major depressive disorders in a sample of 210 cancer inpatients. Receiver operating characteristic (ROC) curves were used to express the relationship between the true positive rate (sensitivity) and the false positive rate (1 - specificity) for each HADS score. This enabled an optimum cut-off point to be chosen that balanced the costs and benefits of treatment of psychological distress. For screening for major depressive disorders only, the optimal cut-off score was found to be 19, associated with 70% sensitivity and 75% specificity. For screening for adjustment disorders and major depressive disorders together, a cut-off score of 13 which gave 75% sensitivity and 75% specificity was optimal in this population. A similar analysis performed in a lymphoma out-patient population resulted in lower cut-off points being identified as optimal [61]. These data underline the need for screening methods and their cut-off scores to be carefully calibrated in the setting in which they are to be applied. It is important to remember the ideal threshold is likely to vary with the prevalence of the disorder in the setting in question.

The RSCL was not designed as a psychiatric screening tool and although the HADS was and is widely used, there are growing concerns about whether or not it is effective for identifying patients in routine oncology practice who warrant intervention. There are a number of case finding instruments (for depression) which warrant further exploration in oncology [62]. When HADS is used as the screening tool, subsequent assessment is required to assess the number and severity of depressive symptoms relative to recognised diagnostic criteria. A briefer screening tool may be at least as effective for the purpose of initial screening, for example the Mental Health Inventory derived from the Medical Outcome Survey, which consists of only five items. The performance of such screening tools might be improved by taking into consideration factors which are known to influence the vulnerability of patients to affective disorders.

A number of vulnerability factors have been identified as increasing the risk of depression in breast cancer patients, including a past history of psychiatric illness, the nature and number of cancer-related concerns, and the lack of a confiding relationship (Table 3). A previous history of being treated for psychiatric illness was shown to be a significant predictor of psychiatric morbidity following mastectomy by Dean [63], and an association between past psychiatric disorder and severe depression in advanced malignant disease has also been demonstrated [12]. More recently, Harrison et al. [64] found that the nature and number of patients' illness-related concerns is a useful marker for affective disorders: using a checklist of concerns, patients with four or more concerns were found to have significantly more anxiety or depression. In community samples, the lack of a confiding relationship has been shown to be associated with an increased likelihood of depression following adverse life events [65]. Although a relationship between confiding concerns and psychological morbidity in cancer patients was not confirmed in a study by Harrison et al. [64], other work does suggest that the perceived quality of support from others is a predictor of psychological adjustment in such patients [66, 67]. The presence of risk factors in patients who are distressed should alert doctors and nurses to the need for more detailed assessment of their mental state. Identification of unresolved

<table>
<thead>
<tr>
<th>Table 3: Factors associated with increased risk of depression in breast cancer patients.</th>
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<td>- Previous history of treatment for psychiatric illness [12. 58].</td>
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<tr>
<td>- ≥4 illness related concerns [59].</td>
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<td>- Lack of confiding relationship [60].</td>
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concerns may be a useful starting point for intervention [64].

Clinicians should also be aware that some drugs used in the treatment of cancer may induce depression e.g., chemotherapeutic agents, vincristine, vinblastine, procarbazine, L-asparaginase, amphotericin B and interferon may cause mood changes of depressive nature [68–70]. Steroids, prednisone and dexamethasone, commonly used with chemotherapy, are also known to cause psychiatric disturbances which may include emotional lability, and depression sometimes with suicidal ideation [71, 72]. Benzodiazepine abuse has also been reported to aggravate or even unmask depression [73, 74].

There is a need for cancer centres to implement routine screening for major depression. Advances in information technology are making this easier but there is still a requirement for a clinical evaluation of patients identified as ‘cases’ by the screening process. This does not obviate the need for all staff in clinical practice to acquire communication skills to elicit patients’ concerns and to have the ability (or access to the resources) to deal with them.

Management of depressed patients with cancer

Pharmacotherapy

As oncology patients receive a high level of concomitant therapy, it is important that effective antidepressant treatment is well tolerated and causes minimum side effects. A low potential for possible drug–drug interactions is also of critical importance. Therefore, emphasis should be placed on prescribing antidepressants with a good tolerability profile. The altered absorption of antidepressants due to mucous membrane thickening or gut atrophy secondary to chemotherapy or radiotherapy must also be taken into account [75]. Thus, antidepressant drugs with a low therapeutic index, such as the tricyclic antidepressants (TCAs), should be used with caution in cancer patients.

Selective serotonin reuptake inhibitors

Selective serotonin reuptake inhibitors (SSRIs) have a similar efficacy to the TCAs in depressed patients [76–80] but are associated with fewer side effects and, in particular, have very few anticholinergic effects [81, 82].

Efficacy and safety

To date, there are few published clinical data evaluating the efficacy of SSRIs in cancer patients, although they have been demonstrated to be effective in depressed patients with other comorbid conditions, such as rheumatoid arthritis [83]. A recent multicentre study assessing the efficacy of fluoxetine in controlling anxiety/depression in patients with cancer [84] did not show fluoxetine to be effective. A total of 45 patients with cancer were randomised to receive fluoxetine (20 mg) and 46 to receive placebo; no differences were observed between the two groups in the primary criterion for efficacy (Hospital Anxiety and Depression Scale score lower than 8 after five weeks), nor for secondary observer-rated assessments (Montgomery and Asberg Depression Rating Scale, HADS or Spitzer Quality of Life Index). Patients receiving fluoxetine did, however, show a better overall psychological assessment than those receiving placebo, when judged by a decrease in the Revised Symptom Checklist (SCL90-R). Significantly more patients dropped out of the study in the fluoxetine group than in the placebo group (15 vs. seven patients, respectively; P = 0.04), although the frequency of side effects was not significantly different between the two treatment groups. A large, randomised, double-blind study of paroxetine (20–40 mg) and amitriptyline (75–150 mg) is currently ongoing in 180 breast cancer out-patients fulfilling the ICD-10 criteria for mild, moderate or severe depression.

SSRIs have a number of properties which may be advantageous in the treatment of cancer patients. Unlike TCAs, SSRIs have the advantage of improving sleep without causing daytime drowsiness. Comparisons of paroxetine and TCAs have shown that whilst both improved sleep by comparison with placebo, TCA use was associated with impaired daytime cognitive and psychomotor functioning [85]. However, agitation has been reported with fluoxetine use in some patients and it may be unsuitable for cancer patients who are agitated or have severe insomnia [81].

Fluoxetine, nefazodone and paroxetine have analgesic properties which may reduce pain [86,87]. Data in patients with chronic headache have confirmed paroxetine’s analgesic efficacy in both open studies [88] and in a double-blind comparison with sulpiride [89].

Although SSRIs are associated with a lower incidence of side effects than the TCAs, they are not free from unwanted effects. Gastrointestinal effects, including nausea, are recognised side effects of SSRIs and may present particular problems in patients undergoing emetic chemotherapy. However, the incidence of nausea with SSRIs is reported to decrease with continued treatment in depressed patients [82].

Some SSRIs are also associated with weight changes. Fluoxetine has been reported to induce appetite suppression/weight loss [90], again an undesirable effect in cancer patients in whom weight loss may occur as a result of the disease, treatment, or nutritional difficulties. However, whilst paroxetine has been shown to reduce weight in overweight patients, no effect was seen in non-overweight individuals [91]. One explanation for this effect might be that appetite suppression/weight loss is apparent in patients whose weight gain is associated with depression.

Paroxetine may have an advantage over TCAs in the management of depressed patients at risk of suicide [92]: a significant reduction in suicidal thoughts (P < 0.01) and significantly fewer emergent suicidal thoughts (P < 0.01) were shown with paroxetine by comparison.
with placebo and TCAs. The wide therapeutic margin of SSRIs also suggests a lower potential for toxic effects in overdose than TCAs and in general SSRIs are thought to be safer in overdose [93]. Prevalence of suicide amongst bone marrow transplant patients has recently been reported as around 3%, so clearly an antidepressant with the potential to reduce suicidal thoughts will be a favourable treatment for cancer patients [94].

**Drug interactions**

All SSRIs inhibit the cytochrome P450 enzyme system to some degree and have the potential for interaction with concomitant drugs, however, the clinical relevance of such potential interactions has yet to be clarified.

SSRIs may interfere with the rate of activation of cyclophosphamide, commonly used in the treatment of breast cancer. However, although activation of cyclophosphamide may be slowed, the rate of activation is not thought to be clinically significant [95]. SSRIs which are highly protein-bound, such as fluoxetine, sertraline, nefazodone and paroxetine, may interact with other highly protein-bound drugs, such as cisplatin. Furthermore, fluoxetine has been reported to decrease the efficacy of a commonly prescribed antiemetic agent, ondansetron [96].

**Venlafaxine**

Venlafaxine is an antidepressant which inhibits both noradrenaline and serotonin reuptake. There are no published clinical data evaluating the efficacy of venlafaxine in cancer patients. Although associated with fewer side effects than the TCAs, venlafaxine has been reported to induce significant weight loss and appetite suppression in patients with major depression compared with placebo (*P* < 0.05) which may be disadvantageous in the cancer patient [97]. However, it is unclear whether or not these patients were initially overweight (i.e., possibly related to depressive symptoms).

**Tricyclic and related antidepressants**

**Efficacy**

Very few trials of TCAs have been carried out in depressed cancer patients, although several studies have evaluated the effects of TCAs in depressed physically ill patients. However, their use was associated with a high incidence of discontinuations due to adverse effects [98, 99]. The efficacy and safety of mianserin 20–30 mg/day has been assessed in 73 depressed women with cancer: patients receiving mianserin showed significant improvement over placebo (Hamilton Rating Scale for Depression [HRSD]: *P* > 0.01 after seven days of treatment [100]. In a more recent study by Van Heeringen and Zivkov [101], 55 women with depression and breast cancer were treated with mianserin 30–60 mg/day for 42 days. HRSD scores were reduced significantly in the mianserin treatment group compared with placebo (*P* ≤ 0.05). An open pilot study in 39 depressed cancer patients indicated that imipramine 25 mg tds improved the HRSD scores of treated patients compared with controls not receiving antidepressant therapy [102]. TCA treatment has also been shown to be effective in relieving chronic pain, both independently of depression and in conjunction with relief of depressive symptoms [45].

**Adverse effects**

Adverse effects commonly associated with TCAs limit their use in this patient population. The most frequently reported adverse effects related to their anticholinergic actions – dry mouth, constipation, tachycardia, blurred vision, urinary retention, and delirium. Orthostatic hypotension and sedation are also common [95, 103]. Such a wide spectrum of adverse effects are potentially hazardous for the cancer patient, who may suffer from narcotic-induced constipation which may be compounded by the anticholinergic effects of TCAs. For volume depleted patients TCA-induced orthostatic hypertension may be a further problem. In addition, orthostatic hypertension may lead to falls and fractures in patients with skeletal weaknesses or bone metastases. Patients with radiation stomatitis will also require an antidepressant relatively free from anticholinergic effects. TCA overdose is potentially fatal as a result of autonomic instability, cardiac arrhythmia or uncontrollable seizures [95].

**Drug interactions**

TCAs are metabolised by at least three major cytochrome P450 enzymes, and therefore have the potential to interact with drugs which interfere with this metabolism. Significant interactions include additive side effects with other anticholinergic drugs (diphenhydramine, phenothiazines); other quinidine-like drugs (quinidine, procainamide); sedatives (ethanol, antihistamines, hypnotics) and hypotensive agents (clonidine, diuretics). Neuroleptics, fluoxetine and methylphenidate may elevate serum TCA levels, whilst oestrogens, smoking and inducers of hepatic microsomal enzymes may depress tricyclic levels [95].

**Monoamine oxidase inhibitors**

Monoamine oxidase inhibitors (MAOIs) are less commonly used antidepressants than the TCAs. There are no reports in the literature on the use of MAOIs in depressed cancer patients and they may be considered unsuitable for this population: dietary restrictions limit the use of MAOIs, as cancer patients may already have nutritional deficiencies and/or dietary restrictions related to their cancer. Pain management may also become an issue, as MAOIs are contraindicated with many narcotic analgesics, especially meperidine, because of the potential for hypertensive reactions.

**Psychotherapy**

Critical review [104, 105] and meta-analysis [106] of published studies have demonstrated that a variety of
Table 4. Psychoeducational and psychotherapeutic interventions.

<table>
<thead>
<tr>
<th>Psychoeducational approaches:</th>
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<tbody>
<tr>
<td>Educational programmes covering pharmacological and psychological aspects of treatment, specifically including misapprehensions.</td>
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<tr>
<th>Psychotherapeutic intervention:</th>
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<tr>
<td>Problem solving – patients learn to use their own skill to cope with problems;</td>
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<tr>
<td>Relaxation training – e.g., muscle relaxation combined with guided imagery;</td>
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<tr>
<td>Behavioural therapies – e.g., activity scheduling;</td>
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<tr>
<td>Cognitive strategies e.g., reattribution, reality testing;</td>
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<tr>
<td>Cognitive-behavioural therapy e.g., adjuvant psychological therapy.</td>
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Psychological intervention techniques, delivered separately or in combination, either to individuals or groups of cancer patients, have a beneficial effect on emotional adjustment. While patients with transient distress are likely to respond to quite limited intervention, those with more intense or more sustained psychological morbidity require more specific psychological intervention and/or psychotropic medication [107]. With minimal additional training, oncologists can deliver some basic psychological interventions in routine oncology practice. Similarly, several techniques can be used by specially trained nurses. More complex psychotherapeutic interventions, however, require referral to a psychiatrist or clinical psychologist.

Most psychological interventions are multifaceted, but they can be broadly classified as psychoeducational or psychotherapeutic [104]. A combination of both is frequently used (Table 4).

Psychoeducational approaches

Education for cancer patients tends to cover disease and treatment information, for example explaining the patient’s experience of symptoms or side effects and challenging misapprehensions about cancer and cancer therapy [105]; the aim of such therapy is to reduce the sense of helplessness and inadequacy which stems from uncertainty, lack of knowledge or mistaken beliefs. Similar attention to information giving is useful in the management of depression. Among patients with major depression, a multifaceted structured treatment programme consisting of pharmacological and psychological elements and including specific education to correct misapprehensions about depression and antidepressant medication led to improved adherence and depression outcomes [108]. A comparable structured approach could prove valuable in the management of depressed cancer patients.

Psychotherapeutic intervention

A number of psychotherapeutic intervention techniques are available, including problem-solving, relaxation training, and cognitive and behavioural therapies.

Problem-solving is a technique in which patients learn to use their own skills and resources to cope with present and future problems. In the primary care setting, problem-solving has been shown to be as effective in the treatment of depression as amitriptyline and more effective than a drug placebo [109]; the intervention was delivered by general practitioners after a brief training and patient satisfaction was high. A comparable strategy could be tailored for depressed patients beset with cancer-related problems.

A variety of relaxation techniques have been successfully used to help patients control anxiety, pain, insomnia and anticipatory nausea and vomiting associated with chemotherapy [110]. In a randomised trial of women with early stage breast cancer, muscle relaxation combined with guided imagery resulted in less mood disturbance than relaxation alone or a control condition in which the women were encouraged to talk about themselves [111].

Behavioural interventions, for example activity scheduling, are designed to encourage patients to experiment with feelings of hopelessness/helplessness in a practical way by engaging in specific tasks which challenge their negative assumptions [112]. Activities are individually selected to foster experiences of mastery and pleasure. A pilot study demonstrated the potential of a behavioural programme in treating psychological distress following mastectomy [113]; the improvement in mood was better maintained when the programme was used in combination with anti-depressant medication.

Cognitive approaches interpret the psychological features of depression as resulting from the patient’s tendency to view the self, the world and the future in a distorted and unrealistically negative way. Therapy seeks to demonstrate to patients the relationship between their emotional distress and underlying negative automatic thoughts, and a variety of techniques are then used to help patients identify and challenge these negative thoughts e.g., reattribution (looking for alternative explanations), reality testing (what is the evidence to support/contradict the negative beliefs?). The aim of these strategies is to foster a more positive attitude and a greater sense of personal control.

Adjuvant psychological therapy (APT) is a cognitive-behavioural therapy developed specifically for cancer patients. In a prospective randomised trial [114, 115], APT reduced the proportion of patients with depression from 40% at baseline to 18% at four months. In the control group, the proportion of patients who were depressed at baseline and four months were 30% and 23%, respectively. At one-year follow-up, 11% of patients who received APT were depressed, compared with 18% of controls.

Supportive group therapy for patients with metastatic breast cancer has been shown to result in improved mood, fewer maladaptive coping responses and reduced pain [116–118]; interestingly, a significant survival advantage was observed in the intervention group.

Combination of psychoeducational and psychotherapeutic intervention. A six-week intervention package developed by Fawzy and Fawzy [119] combines health education with training in stress management and cop-
being skills in the setting of a group which offered social support and opportunity for emotional expression. A distinctive feature of this programme is the use of pictures depicting common scenarios for the woman with breast cancer, including depression: for each scenario, a pair of pictures illustrated examples of adaptive (i.e., active cognitive or behavioural) and maladaptive (i.e., avoidant) coping, as stimulus to group discussion. This intervention model, originally evaluated among patients with malignant melanoma, has been shown to lead to sustained improvement in affective state and coping [120]. Interestingly, this intervention has been shown to be associated with changes in several immune system parameters [121] and with lower rates of recurrence and improved survival [122].

Conclusions

A significant proportion of cancer patients are likely to experience an adjustment disorder in which depressed mood is a significant feature, while only a small proportion develop major depressive illness. There is increasing recognition of the need for medical and nursing staff to have training in communication skills to improve their ability to elicit and respond to patient concerns. Improving such communication may prevent the development of emotional disturbance and improve the detection of those whose distress warrants intervention.

While cancer patients with a major depressive disorder or a complicated psychiatric history would benefit from the specialist intervention of a clinical psychologist or psychiatrist, oncologists should also be prepared to manage the symptoms of depression when they occur using both pharmacological and psychological therapies. Research into antidepressant therapy in cancer patients has shown that TCAs are associated with an unacceptably high incidence of adverse effects. The SSRIs, whilst requiring further evaluation in this patient population, may offer an effective antidepressant therapy with an improved tolerability profile.

There is a growing recognition that quality of life, rather than just quantity, is the most important goal in the management of the patient with cancer. Achieving this goal requires attention to be given to patients’ psychological well being as well as to tumour control and symptom relief.

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