

The Prevalence of Depression in People with Cancer

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Depression is amongst the main causes of disability worldwide, leading to personal suffering and increased mortality. The US National Comorbidity Survey revealed a 12-month prevalence of major depressive disorder of 6%, with a lifetime prevalence of 16%, while high comorbidity exists with anxiety disorders, substance use disorders and impulse control disorders [1]. In any twelve-month period, more than half the patients with major depressive disorder are diagnosed with an additional anxiety disorder. Patients with comorbid

depression and anxiety disorders experience more severe symptoms, have a longer time to recovery, use more healthcare resources and have poorer outcome than do those with a single disorder [2]. Seedat *et al.* [3] found that, across cohorts from 15 countries, women developed depression almost twice as frequently as men.

When comorbid with medical illness, depression increases the symptom burden and functional impairment, and worsens medical outcomes [4]. Early studies of depression in the medically ill used patient self-report and varied measures, with a heterogeneous mix of hospitalized medical and surgical patients, and reported prevalence rates ranging from 20 to 30% [5]. In 1987, a retrospective review of 263 000 patients from 327 hospitals found that 24% of those receiving a psychiatric consultation were depressed [6]. However, Snyder *et al.* [7], using both clinical interview and DSM-III-R criteria reported less depression (6%), but more adjustment disorder with depressed mood (14%), in 944 medically ill patients referred for psychiatric consultation.

Wells *et al.* [8] examined Epidemiological Catchment Area Study data regarding mental disorders amongst persons with at least one of eight chronic medical conditions. Six-month and lifetime prevalence rates of mental disorders were increased in those with versus without medical illness (25 and 42% versus 17 and 33%). Thirteen per cent of the chronically medically ill had a lifetime diagnosis of affective disorder versus 8% of those free from medical illness.

Lifetime rates of depression in patients with neurological conditions range from 30 to 50% [9]. Prevalence rates of depression in patients with other medical or systemic illnesses show a variable picture, with the highest rates observed with endocrine disturbances such as Cushing's disease and surprisingly low rates documented in end-stage renal disease.

PREVALENCE OF DEPRESSION IN CANCER PATIENTS

Using DSM-III criteria through a structured clinical interview, the Psychosocial Collaborative Oncology Group (PSYCOG) was one of the first groups to carefully determine the prevalence of mental disorders in 215 randomly selected hospitalized and ambulatory adult

cancer patients in three cancer centres [10]. Forty-seven per cent of the patients evaluated had clinically apparently psychiatric disorders. Of these patients, over two-thirds (68%) had adjustment disorders with depressed or anxious mood, 13% had a major depression, 8% had an organic mental disorder, 7% had a personality disorder, and 4% had a preexisting anxiety disorder. The authors concluded that nearly 90% of the mental disorders observed were reactions to or manifestations of disease or treatment. Personality and anxiety disorders can complicate cancer treatment, and were described as antecedent to the cancer diagnosis. This epidemiologically sound study has remained the gold standard for many years.

Many research groups have assessed depression in cancer patients along the years [10–69], and the reported prevalence varies quite widely (major depression 3 to 38%; depression spectrum syndromes 1.5 to 52%). The following databases were searched to retrieve references published between 1965 and 2009: PubMed, Embase, CINAHL (nursing), PsycINFO, Scopus, Science Citation Index/Social Sciences Citation Index, Cochrane Evidence Based Medicine database. The searches were limited to English language references and to studies with more than 100 subjects, where this information was indicated. Table 1.1 shows the 60 studies with more than 100 patients that provided information about the number of patients interviewed and cancer type(s), evaluation methods, and per cent with depression or affective syndromes. Most authors reported patient gender and hospitalization status. The reported prevalence 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.

In early, typically cross-sectional studies, the rate of depression was usually reported for adults with mixed types and stages of cancer. Depression was reported by severity (borderline, mild, moderate, severe, and extreme), or by a symptom such as depressed mood, or by some of these diagnostic categories: major depression, minor depression, depressive disorder, adjustment disorder with depressed mood, or dysthymia, limiting our ability to compare studies. Although many research groups reported the gender and age (usually older) of study subjects, findings usually were not reported by demographic variables, and racial minorities were always underrepresented.

Table 1.1 Representative studies of the prevalence of depression in cancer patients (adapted from Massie [5])

Study	N	Patients	Method	Percent depressed	Specific findings
Fras <i>et al.</i> [11]	110	Pancreatic and colon cancer	Semi-structured interview; MMPI	50% (pancreas); 13% (colon)	76% psychiatric symptoms in those with pancreatic cancer; psychiatric symptoms appeared before other symptoms in patients with pancreatic cancer
Morris <i>et al.</i> [12]	160	Breast biopsy and mastectomy patients; British cohort	Interview; HRSD	22% depression in mastectomy	Mastectomy patients had persistent depression (22%) at 2 yr compared to benign biopsy patients (8%)
Maguire <i>et al.</i> [13]	201	117 ambulatory breast cancer patients; 89 benign disease; British cohort	Clinical interview	26% moderate or severe depression after mastectomy	Control benign patients had 12% depression
Silberfarb <i>et al.</i> [14]	146	Hospitalization status not indicated; 34% primary disease; 36% recurrent; 30% advanced; all breast cancer; US cohort	Structured interview; open-ended questions; modified psychiatric status scale	10% depression in primary cancer diagnosis; 15% in recurrent; 4.5% in advanced cancer	Physical disability did not relate to emotional disturbances; first recurrence of breast cancer most disturbing time; advanced patients had the least depression

Derogatis <i>et al.</i> [10]	215	Half hospitalized, half ambulatory; all sites and all stages, randomly selected; US cohort	DSM-III criteria; SCL-90; RDS; GAIS; Karnofsky Rating Scale	6% major depression 12% adjustment disorder with depressed mood; 13% adjustment disorder with mixed emotional features	Excluded severely ill (Karnofsky < 50); 47% received DSM-III diagnosis; 68% of these diagnoses were adjustment disorder
Farber <i>et al.</i> [15]	141	Ambulatory; primarily breast cancer	SCL-90	19% severe; 21% moderate; 14% mild	A comparison of males and females with clinical and global scales of the SCL-90 showed no significant differences
Hughes [16]	134	Lung cancer	Structured clinical interview	16% depressed	Most of the depressed patients were depressed before physical symptoms began
Lansky <i>et al.</i> [17]	500	85% ambulatory; 43% survivors with no evidence of disease; 34% early stage	DSM-III, organic brain syndrome section of the PDI; HRSD, Zung SDS; visual pain analogue line	5.3% (using HRSD and SDS); 4.5% (using DSM-III criteria)	
Holland <i>et al.</i> [18]	218	Ambulatory; 107 advanced pancreatic, 111 advanced gastric; US cohort	POMS	21 median POMS gastric; 38 median POMS pancreatic scores	Pancreatic cancer patients had higher depression than gastric cancer amongst men only
Devlen <i>et al.</i> [19]	120	Ambulatory; Hodgkin's disease and non-Hodgkin's lymphoma	Semi-structured interview	8% depressed in year after treatment	Prospective study with interviews at baseline, 2, 6, and 12 mo after diagnosis

(continued)

Table 1.1 (Continued)

Study	N	Patients	Method	Percent depressed	Specific findings
Lasry <i>et al.</i> [20]	123	Hospitalized breast cancer	CES-D	50% mastectomy; 50% lumpectomy with radiation; 41% lumpectomy	Depression varied with treatment
Stefanek <i>et al.</i> [21]	126	Ambulatory; mixed; US cohort	BSI	33% depressed; 9% severe; 24% moderate	20% high psychiatric distress in general
Pettingale <i>et al.</i> [22]	168	Hospitalized early breast cancer and lymphoma; all stages; British cohort	Interview; STAI; Wakefield	Major depression not cited	In lymphoma patients, the more advanced the disease, the higher the depression. No correlation with disease state and depression in breast cancer
Grassi <i>et al.</i> [23]	196	Hospitalized and ambulatory; recent diagnosis of cancer; mixed, 18–70 yr; Italian cohort	HRSD; IBQ; interview	24–38% depressed depending on threshold used	38% depression with HRSD cutoff of 17; 24% with HRSD of 21
Hardman <i>et al.</i> [24]	126	Hospitalized; mixed; British cohort	Structured interview GHQ	3% pure depression; 23% mixed anxiety and depression	Psychiatric symptoms related to feeling moderately or severely ill and previous psychiatric illness; but not with awareness of having cancer

Fallowfield <i>et al.</i> [25]	269	Stage I and II breast cancer assessed 2 wk, 3 mo, 12 mo after surgery; British cohort	Interview	21% mastectomy; 19% lumpectomy	Less depression in mastectomy and lumpectomy patients given treatment choice
Kathol <i>et al.</i> [26]	152	Mixed; US cohort	DSM-III and DSM-III-R criteria; RDC; Endicott substitution criteria; HRSD; BDI	25–38% major depression, depending on diagnostic system; 19% (depressive symptoms)	Authors concluded that self- and observer-rated scales are sufficient to screen at risk patients but not to diagnose
Colon <i>et al.</i> [27]	100	Hospitalized acute leukaemia; US cohort	DSM-III-R criteria	1% major depression; 2% organic affective syndrome; 8% adjustment disorder	Illness status, depressed mood and perceived social support independently affected outcome; depressed patients had poorer outcome
Hopwood <i>et al.</i> [28]	222	Ambulatory; advanced breast cancer; British cohort	HADS; RSCL	9% depression and 9% anxiety using HADS; 22% affective disorder using RSCL	HADS and RSCL detected different groups of cases; one third of depressed patients persisted for 1–3 mo (continued)

Table 1.1 (Continued)

Study	N	Patients	Method	Percent depressed	Specific findings
Goldberg <i>et al.</i> [29]	320	Newly diagnosed, hospitalized for breast cancer surgery	Modified RSCL; pre-operative, 6 and 12 mo post-operatively	32% depressed malignant; 24% depressed benign biopsys	At 1 yr depression had decreased (21% depressed) in both groups
Maraste <i>et al.</i> [30]	133	Ambulatory; adjuvant radiotherapy; breast cancer	HADS	1.5% depressed; 14% anxiety	Age and surgery-related anxiety; anxiety in ages 50–59 was 44% in mastectomy vs. 4% in conservative surgery
Sneed <i>et al.</i> [31]	133	Hospitalized; newly diagnosed; mixed sites and stages	BSI; HIS-GWB	Major depression not cited	Women with gynaecological and breast cancer had less depression, anxiety, hostility, somatization, psychological distress than men and women with other cancers
Carroll <i>et al.</i> [32]	809	Various cancer sites; US cohort	HADS	17.7% anxiety disorder 9.9% depressive disorder	
Cathcart <i>et al.</i> [33]	257	Ambulatory; women with node negative breast cancer; 155 women received tamoxifen; 102 received no tamoxifen	Clinical interview	15% in tamoxifen treated group; 3% in those not receiving tamoxifen	4.5% of 155 women receiving tamoxifen had to discontinue it secondary to depression

Pinder <i>et al.</i> [34]	139	86 hospitalized, 53 ambulatory advanced breast cancer; British cohort	HADS interview	13% depressed; 25% anxiety or depression	Depression more prevalent in low socioeconomic class, in poor performance states, and closer proximity to death
Sneeuw <i>et al.</i> [35]	556	Ambulatory stage I and II breast cancer; interviewed at least 1.5 yr after treatment	DSM-III criteria; DIS; CES-D; SCL-25	4.5% depressed; 6.3% generalized anxiety disorder; 8.8% phobic disorder	Depressive symptoms at one and a half years after treatment and longer; no significant differences in patients who had mastectomy vs. conservative treatment
Kelsen <i>et al.</i> [36]	130	Pancreatic cancer; US cohort	BDI; BHS; MPAC; FLIC	38% depressed (scores ≥ 15 BDI)	
Aass <i>et al.</i> [37]	716	Various cancer sites; Norwegian cohort	HADS, EORTC QLQ03, HOC Questionnaire	9% depression; 15% anxiety	
Berard <i>et al.</i> [38]	456	Breast; head and neck; lymphoma	HADS; BDI; Structured psychiatric Interview	14% depression overall; 8% depression (overlap with both scales)	
Kissane <i>et al.</i> [39]	303	Early stage breast cancer; Australian cohort	MILP; HADS; EORTC-QLQ	45% DSM psychiatric disorder; 42% depression and/or anxiety; 27.1% minor depression; 9.6% major depression	8.6% DSM anxiety disorder

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Table 1.1 (Continued)

Study	N	Patients	Method	Percent depressed	Specific findings
Montazeri <i>et al.</i> [40]	129	Lung cancer; Scottish cohort	HADS (administered at baseline and follow-up); QLQ	Baseline: 6% borderline anxiety; 10% severe anxiety; 11% borderline depression; 12% severe depression Follow-up: 11% borderline anxiety; 10% severe anxiety; 22% borderline depression; 32% severe depression	
Hammerlid <i>et al.</i> [41]	357	Head and neck cancer; Swedish & Norwegian cohort	HADS (administered at 6 different times)	19%–71% probable anxiety; 18%–51% probable depression	
Bodurka-Bevers <i>et al.</i> [42]	246	Epithelial ovarian cancer	CES-D; state anxiety sub-scale of STAI; QOL	21% CES-D depression; 29% anxiety	
Chen <i>et al.</i> [43]	203	Solid and liquid tumours; Taiwanese cohort	HADS	12% anxiety; 20% depression	
DeLeeuw <i>et al.</i> [44]	197	Head and neck cancer	Social Provisions Scale; CES-D; EORTC QOL C30+3	29% possible depression (before treatment); 28% possible depression (after 6 mo)	

Hopwood <i>et al.</i> [45]	987	526 small cell lung cancer; 461 non-small cell lung cancer; British cohort	HADS, Quality of Life Form	33% depression, self-reported; 21% depression and anxiety	Higher prevalence for small cell lung cancer patients
Kugaya <i>et al.</i> [46]	107	Head and neck cancer; newly diagnosed; Japanese cohort	Clinical interview with DSM-III; SCID; HADS	13.1% adjustment disorder 3.7% major depression 15.9% past history of major depression 33.6% alcohol dependence	6.5% alcohol abuse 32.7% nicotine dependence
Pascoe <i>et al.</i> [47]	504	Various cancer sites; Australian cohort	HADS	11.5% anxiety 7.1% depression	
Skarstein <i>et al.</i> [48]	568	Various cancer sites; European	HADS; EORTC QLQC33	9% depression, 13% anxious, 17% psychiatric distress, 5% depression and anxiety	HADS more accurate for depression; EORTC-QLQ good for anxiety, but underdiagnosed depression
Akechi <i>et al.</i> [49]	148	Post operative ambulatory breast cancer; Japanese cohort	HADS	23% psychiatric morbidity; 5% depression	
Akechi <i>et al.</i> [50]	129	Non-small cell lung cancer; Japanese cohort	Clinical Interview, DSM-III	4.7% major depression; 13.9% adjustment disorders	

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Table 1.1 (Continued)

Study	N	Patients	Method	Percent depressed	Specific findings
Ciaramella <i>et al.</i> [51]	100	Various cancer sites	Interview; SCID; Endicott HAM-D	49% all DSM depressive disorders with SCID; 29% depression with Endicott;	28% depression with both diagnostic criteria
DeLeeuw <i>et al.</i> [52]	197 initially; 123 at the end of 3 yr	Head and neck cancer	CES-D; EORTC QOL C30 +3	42% depression between 6 mo and 3 yr after treatment	
Sharpe <i>et al.</i> [53]	3938 screened 570 interviewed	Various cancer sites; breast cancer over-represented; UK cohort	HADS – all patients SCID for HADS high scorers	23% 15 or more on HADS; 34% of HADS high scorers had major depression	8% of entire sample had major depression
Atesci <i>et al.</i> [54]	117	Various cancer sites	SCID, HADS, GHQ	13.7% major depression	
Kissane <i>et al.</i> [55]	503	Breast cancer (303 early stage; 200 advanced); Australian cohort	MILP, HADS	37% DSM depressed (major depression, dysthymia, adjustment disorder) early stage; 31% advanced disease	Early stage: 9.6% major depression, 27.1% minor depression; Metastatic: 6.5% major depression, 24.5% minor depression
Nan <i>et al.</i> [56]	108	Mixed digestive tract cancers	Zung SDS	50% SDS index > 50	

Litofsky <i>et al.</i> [57]	598	High-grade gliomas	SF-36 Mental Health scores	93% patient-reported depressive symptoms; 15% physician-reported depression in postoperative period;	Patient-reported depressive symptoms persisted at 3 and 6 mo; physician-reported depression increased to 22% at 3 and 6 mo
Thomas <i>et al.</i> [58]	236	Various cancer sites; Indian cohort	HADS	20% depressed (8% definite cases)	
Montazeri <i>et al.</i> [59]	177	Breast cancer	HADS	29% severe depression	
Wedding <i>et al.</i> [60]	213	Various cancer sites	BDI	8% major depression; 19% mild to moderate depressive symptoms	
Steel <i>et al.</i> [61]	101	Hepatobiliary	CES-D	37% at diagnosis	
Lueboontha-vatchai. [62]	300	Breast cancer; Thai cohort	Thai HADS	9% depressive disorder; 16.7% depressive symptoms	
Arnold <i>et al.</i> [63]	363	Primary brain tumours	Modified Brief PHQ	41% depression 48% generalized anxiety disorder	
Wedding <i>et al.</i> [64]	175	Various cancer sites	BDI	16.6% mild to moderate depression; 9.1% major depression	

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Table 1.1 (Continued)

Study	N	Patients	Method	Percent depressed	Specific findings
Singer <i>et al.</i> [65]	250	Laryngeal cancer	HADS	9.7% depressed; 5.2% major depression, 4.5% dysthymia	
Nuhu <i>et al.</i> [66]	210	Various cancer sites; Nigerian cohort	SCID interview, MADRS	30% major depression	Significantly higher prevalence in patients with late stage disease
Mhaidat <i>et al.</i> [67]	208	Various cancer sites; Jordanian cohort	HADS	51.9% depressed	High prevalence of depression possibly related to negative perception of prognosis
Christensen <i>et al.</i> [68]	3321	Breast cancer; Danish cohort	BDI	13.7% major depression	
Den Oudsten <i>et al.</i> [69]	223	Breast cancer	CES-D	40.9% before diagnosis; 27.8% 1 yr later	

BDI, Beck Depression Inventory; BHS, Beck Hopelessness Scale; BSI, Brief Symptom Inventory; CES-D, Center for Epidemiology Self-report Depression Scale; DIS, Diagnostic Interview Schedule; EORTC-QLQ, European Organization for Research and Treatment of Cancer-Quality of Life Questionnaire; FLIC, Functional Living Index of Cancer; GAI, Global Adjustment to Illness Scale; GHQ, General Health Questionnaire; HRSD, Hamilton Rating Scale for Depression; HADS, Hospital Anxiety and Depression Scale; HIS-GWB, Rand Health Insurance Study-General Well-Being Schedule; IBQ, Illness Behaviour Questionnaire; MADRS, Montgomery-Asberg Depression Rating Scale; MILP, Monash Interview for Liaison Psychiatry; MMPI, Minnesota Multiphasic Personality Inventory; MPAC, Memorial Pain Assessment Card; PHQ, Patient Health Questionnaire; POMS, Profile of Mood States; QOL, Quality of Life questionnaire; RDC, Research Diagnostic Criteria; RDS, Raskin Depression Screen; RSL, Rotterdam Symptom Checklist; SCID, Structured Clinical Interview for DSM; SCL-25, SCL-90, SCL-90R, Hopkins Symptom Checklist 25, 90, and 90-Revised; SDS, Self-rated Depression Scale; SF-36, Medical Outcomes Study 36-Item Short Form Survey; STAI, State-Trait Anxiety Inventory.

A limitation of many studies is that the effects of cancer treatments and non-cancer related variables that affect mood are not accounted for. For example, although drugs can cause depression in some people, research groups usually have not presented data about cytotoxic drug or hormone use when describing their findings.

Several papers from Nemeroff's group [70–72] acknowledge the many reasons why it is difficult to compare studies (different definitions of depression, cancer type or stage, time since diagnosis, varying cancer treatments, personal history of depression and treatment for depression), but importantly, they underscore several general observations. The severity of medical illness, as manifested by significant pain, declining performance status, or the need for ongoing treatment, is associated with a high risk of comorbid depression. Whether high rates of depression associated with some cancers are due to the pathophysiologic effect of the tumour (i.e. cytokine or paraneoplastic syndromes associated with breast, pancreas, testis or lung cancers), treatment effects or other unidentified factors remain to be discerned. Nonetheless, we confidently conclude that cancer, exclusive of site, is associated with a rate of depression that is higher than in the general population.

Cancer types highly associated with depression include brain (41–93%) [57, 63], pancreas (up to 50%) [11], head and neck (up to 42%) [52], breast (4.5–37%) [45, 55], gynaecological (23%) [74] and lung (11%) [40]. A large cross-sectional study of 8265 adult outpatients revealed higher levels of mixed anxiety/depression symptoms in patients with stomach (20%), pancreatic (17%), head and neck (15%) and lung (14%) cancers [73]. A lower prevalence of depression is reported in patients with other cancers, such as colon (13%) [11] and lymphoma (8%) [19].

DeFlorio and Massie reviewed 49 studies of the prevalence of depression in individuals with cancer with a particular emphasis on gender differences [75]. Twenty-three studies found no gender differences in the prevalence of depression at a significance level of $p < 0.05$. However, 10 research groups found either gender differences in subsets of patients, non-significant trends, or differences in other parameters such as psychiatric morbidity, anxiety and denial.

In their study of 808 cancer patients, Kathol *et al.* [26] found women were more depressed than men using Research Diagnostic Criteria;

however, this finding did not persist when DSM-III criteria were applied. Sneed *et al.* [31] found no gender differences in depression, anxiety, hostility, somatization, general psychological distress, or psychological well-being. Fife *et al.* [76] also found no significant differences in depression in male and female cancer patients; however, they found that women made a more positive adjustment to cancer.

DEPRESSION BY CANCER TYPE

Depression in Women with Breast Cancer

Breast cancer is the cancer most studied in terms of psychosocial effects. The reported prevalence of depression ranges from 4.5% to 37%. One of the larger studies [68], examining 3321 early stage Danish breast cancer patients, recently found a 13.7% prevalence of major depression 12–16 weeks after surgery (17.9% in 18–35 year olds and 11.2% in 60–69 year olds). Independent risk factors for the development of depression included younger age, social status, ethnicity, comorbidity, psychiatric history, physical functioning, smoking, alcohol use and body mass index (BMI). Kissane *et al.* [39], in 303 early stage and 200 metastatic breast cancer patients, found prevalence rates of major depression of 9.6 and 6.5% respectively. Fatigue, a past history of depression, and cognitive attitudes of helplessness, hopelessness or resignation were significantly associated with depression in both groups.

Some research groups have assessed the duration of psychological distress in breast cancer patients. In a prospective study of 160 women awaiting breast surgery, Morris *et al.* [12] found a 22% prevalence of depression in women who had a mastectomy for breast cancer. This prevalence persisted at two years, compared to an 8% prevalence of depression in those with benign disease. One five-year observational cohort study of 222 early stage breast cancer patients [77] revealed prevalence rates for depression and anxiety of 33% at diagnosis, 15% after one year and 45% after a recurrence was diagnosed.

Few researchers have correlated patients' history of depression with current depression and/or functioning. In a study of 303 relatively young (mean age 46) women with early (Stage I or II) breast cancer at

3 months after breast surgery, using a structured diagnostic interview, Kissane *et al.* [39] found that a past history of depression was associated with current depression. They also noted that women with few psychological symptoms and good emotional adjustment to cancer may have refused participation in the study, because these women were also being recruited into an intervention study. Pasacrete [78] reported findings on a homogenous sample of 79 women evaluated with the Diagnostic Interview Schedule and the Center for Epidemiological Studies Depression Scale, three–seven months after their diagnosis of breast cancer. Women with elevated depressive symptoms had more physical symptom distress and more impaired functioning than subjects without depression.

Depression in Women with Gynaecological Cancer

In a systematic review which included 18 studies of psychological distress in ovarian cancer patients, Arden-Close *et al.* [79] found strong evidence for a relationship of younger age, more advanced disease at diagnosis, more physical symptoms and shorter time since diagnosis with increased levels of anxiety and/or depression. In the 12 studies rated as methodologically good, 21–25% of patients scored above the clinical cut-off for depression. In examining depression in ovarian cancer patients, Goncalves *et al.* [80] noted that persistent clinical depression tended to be not prevalent (6%), and that the highest prevalence was at the beginning of treatment. Neuroticism and the use of antidepressants were independent predictors of depression. For women with gynaecologic cancer, Evans *et al.* [74] found a 23% prevalence of depression and a 24% prevalence of adjustment disorder with depressed mood.

Depression in Patients with Head and Neck Cancer

Head and neck malignancies carry high risks of morbidity and mortality, with disease and treatment factors contributing substantially to disfigurement and loss of vital functions, such as eating, breathing and communicating. A systematic review of 52 studies

found that depression is present throughout the trajectory of illness in patients with oropharyngeal cancers. Depression rates were highest at the time of diagnosis (13–40%), during treatment (25–52%), and at six-month follow-up (11–45%); the levels decreased three years after diagnosis (9–27%) [81]. Other correlates of depression in this review included: patient characteristics (male, unmarried, less education, history of past and current smoking, young age, lower physical functioning and low social supports); patient physical symptoms (pain, fatigue, insomnia and anorexia); and treatment characteristics (combined and aggressive treatments).

de Leeuw *et al.* assessed the predictive values of numerous pre-treatment variables [52]. Tumour stage, gender, depressive symptoms, openness to discuss cancer in the family, available support, received emotional support, tumour related symptoms, and size of an informal social network were calculated six months to three years after treatment. They concluded that these variables could be used to accurately predict which head and neck cancer patients were more likely to become depressed up to three years after treatment.

Hammerlid *et al.* [41], studying 357 head and neck cancer patients, found that those who reported a higher level of mental distress had lower performance status and more advanced disease.

Depression in Patients with Lung Cancer

Lung cancer has often been associated with higher levels of distress and depression than other tumour sites. In a study of depression and anxiety in 129 lung cancer patients, before and after diagnosis, Montazeri *et al.* [40] found that 10% of patients had severe anxiety symptoms and 12% had symptoms of depression at first presentation to their pulmonary physician. Depression, but not anxiety, increased by 10% at follow-up. Hopwood and Stephens [45] studied 987 lung cancer patients and found that depression was common and persistent, and that it was more prevalent for those patients with more severe symptoms and functional limitations. Depression was also more prevalent in patients with small cell lung cancer than non-small cell lung cancer.

In a study of 129 newly diagnosed patients with non-small cell lung cancer, using a clinical interview that generated a DSM diagnosis, Akechi *et al.* [50] reported a high prevalence of mental disorders. The most common psychiatric disorder at baseline was nicotine dependence (67%), followed by adjustment disorders (14%), alcohol dependence (13%), and major depression (5%).

Depression in Patients Undergoing Stem-Cell Transplantation

Loberiza *et al.* [82] prospectively studied 193 adults who received autologous or allogenic hematopoietic stem-cell transplantation using the Short Form-36 and the Spitzer Quality of Life Index Scale. The authors controlled for patient, disease and transplantation prognostic factors, but unfortunately, no standardized measure of depression was utilized. Thirty-five per cent of the patients satisfied the authors' criteria for depressive syndrome, which was associated with high mortality in the 6–12 month period after transplantation.

Depression in Brain Tumours

In addition to the difficulty adjusting to an illness that contributes to considerable morbidity and mortality, psychiatric problems in brain tumour patients can also be directly caused by the disease process as well as by treatment, including chemotherapy, radiation and corticosteroids. Arnold *et al.* [63] found that 41% of 363 brain tumour patients had depressive symptoms, as assessed by a modified version of the Brief Patient Health Questionnaire. Female gender, lower education, lower tumour grade and previous psychiatric disorder were predictors of depression. Although not significant, being unmarried and having a past/current medical illness trended toward being predictors of depression. Although based on symptoms, Litofsky *et al.* [57] found that 93% of 598 high-grade glioma patients reported depressive symptoms in the early post-operative period, compared to 15% recognized by their physicians, highlighting the potential for underdiagnosis of depression in this population. Of 60 brain tumour

patients, Pelletier *et al.* [83] found that 38% scored in the clinically depressed range on the Beck Depressive Inventory-II. Although depression, fatigue, emotional distress and existential problems were interrelated, depression was the most important independent predictor of quality of life, emphasizing the importance of its recognition and treatment.

Depression in Patients with Lymphoma, Pancreatic, Gastric and Colon Cancer

Studies of the prevalence of depression in adults with lymphoma, pancreatic, gastric and colon cancers are fewer in number [84]. Wide ranges in the reported prevalence of depression are noted but, in general, patients with lymphoma, gastric and colon cancer have a lower prevalence of depression than those with pancreatic cancer.

DEPRESSION IN ADVANCED CANCER AND PALLIATIVE CARE

Depression is common in patients with advanced cancer [85], yet all too often remains underdiagnosed and undertreated [86]. The barriers facing healthcare professionals in this area are considerable. One of them is the common misconception that it is normal for patients with advanced cancer to be sad. Yet, despite such barriers, we must not lose sight of the fact that depression is an independent predictor of poor survival in advanced cancer [87]. Furthermore, it reduces quality of life and prolongs hospitalization [88]. Most importantly, depression in advanced cancer is treatable, and validated assessment tools have been developed to facilitate diagnosis.

Due to variation in diagnostic criteria, prevalence estimates vary widely from 5 to 26% for major depression and from 7 to 26% for minor depression in those with advanced cancer [89–91]. The highest prevalence rates of depression have been observed in patients with cancers of the pancreas, head and neck, and breast [92]. Brintzenhofe-Szoc *et al.* [73] conducted a large cross-sectional study in an outpatient setting to determine the cancer specific prevalence of both pure depression and mixed anxiety/depression. The highest prevalence of

pure depression was in patients with pancreatic cancer, while the highest prevalence of mixed anxiety/depression was in those with cancer of the stomach.

A past history of depression is the greatest risk factor for developing major depression in advanced cancer [90]. Pain, poor functional status, limited social network and younger age are also important risk factors [91]. Psychological concomitants promoting depression include the emotional impact of the advanced diagnosis, medication side effects, progression of cancer with its associated disability, and cerebral dysfunction [92].

Depression in advanced cancer not only reduces quality of life, but also shortens survival time, reduces compliance with treatment and prolongs hospitalization [87, 93, 94]. It also places a considerable psychological burden on carers and family members [95]. It can lead to a desire to hasten death in terminally ill cancer patients [96, 97]. Recent studies have suggested that depression is not only associated with interest in physician-assisted suicide, but also instability of this interest. When confronted with a request for assisted suicide, the possibility of depression should always be considered [98].

There are no universally accepted criteria for diagnosing depression in the terminally ill patient. Given the neurovegetative features associated with advanced cancer, difficulties arise when deciding which of the somatic symptoms identified in the DSM-IV criteria are attributable to depression and which are due to cancer [93]. Endicott suggested that the somatic symptoms should be replaced by other criteria in the cancer setting [94]. Others encourage an inclusive approach to somatic symptoms if they are severe and proportionate to the illness [99].

Patients often find it difficult to disclose emotional concerns with medical professionals, who themselves may find it difficult to raise such issues [97, 100]. As a result, depression frequently goes undetected in advanced cancer. Given these difficulties, there has been an increasing interest in the development of assessment tools [101]. Such screening instruments are not diagnostic and only serve to identify those patients with symptoms suggestive of depression. When patients are identified by screening, further assessment may be required before treatment is commenced.

Although there remains no ideal screening questionnaire for identifying depression in advanced cancer, the Hospital Anxiety

and Depression scale (HADS) devised by Zigmond and Snaith [102] remains one of the most widely used tools. The HADS is a concise, self-reported questionnaire with 14 items, and was originally intended as a screening tool for medical patients. The HADS excludes physical and emotional indicators of depression and instead focuses on those relating to anhedonia – the inability to experience pleasure from normally pleasurable experiences. Although the HADS appears to perform well in those receiving active anti-cancer treatment, it performs less well in those with progressive disease [103]. This in turn results in a limited sensitivity and specificity when the HADS is used alone as a screening tool [104].

The Edinburgh Depression Scale (EDS), an assessment tool originally designed to screen for postnatal depression in the community, has also shown much promise [105]. This tool also excludes somatic symptoms of depression and replaces those with questions on worthlessness, subjective sadness, and suicidal ideation. The inclusion of questions relating to self harm may be particularly discriminating and represents an independent indicator of depression [106]. One study of palliative care patients using the EDS found that a cut-off threshold of 13 had a sensitivity of 0.79, a specificity of 0.81 and a positive predictive value of 0.53 using ICD-10 criteria for depression [107]. This compares with a sensitivity of 0.77 and a specificity of 0.85 for the HAD scale [108]. More recently, a Brief Edinburgh Depression Scale (BEDS) has been validated, which is more discriminating for depression in patients with advanced cancer than the original 10-item scale. The BEDS has a sensitivity of 0.72, a specificity of 0.83 and a positive predictive value of 0.65 [109]. This tool is now widely used in the palliative care setting when screening for depression [87].

There is strong evidence to suggest that depression is not only underdiagnosed but also undertreated in advanced cancer [110]. There remains a weak correlation between detection of a depressive disorder and actual treatment [111]. The single most important barrier to treatment is the common misconception that it is normal for patients with advanced cancer to be sad. Other barriers to effective treatment of depression in advanced cancer include pre-conceived ideas that psychological treatment is better than pharmacological measures, and attitudes of therapeutic nihilism, that is, nothing works at this stage [112]. In those situations where antidepressant medication is

commenced, it is frequently done so at inadequate doses or too late for a therapeutic effect to take place [113]. One survey conducted in UK palliative care units found that 76% of antidepressants were started in the last two weeks of life [113].

DEMORALIZATION

Despite the increasing focus on mood disorders in cancer care, the role of meaning in understanding the illness experience has been somewhat neglected. Here the concept of demoralization comes to the fore. Frank [114] described demoralization as a persistent inability to cope, together with feelings of helplessness, hopelessness, meaninglessness, subjective incompetence and diminished self-esteem. Obviously, depression and demoralization are closely related, both in their phenomenology and our understanding of how they develop. Although demoralization may be a precursor or even co-exist with depression, the two are essentially different constructs. The central feature of depression is pervasive anhedonia and a loss of consummatory pleasure in the present moment. This contrasts with demoralization, where the individual retains the capacity to enjoy the present moment, but the future is perceived to be without value – there is a loss of anticipatory pleasure [115]. The demoralized feel inhibited in action by not knowing what to do, feeling helpless and incompetent; the depressed have lost motivation and drive even when an appropriate direction of action is known.

Frankl [116] noted that, for life to have meaning, it must offer the experience of self-transcendence. He recognized that meaning can also be found in suffering by transcending the moment to understand the fullest impact of the experience. Engel [117] presented lucid descriptions of demoralization in his ‘giving up-given up syndrome’. While studying psychological states that predispose people to become sick, he and his colleagues observed this syndrome, which was thought to precede physical illness. This was commonly precipitated by a loss and was characterized by a physiological slowing of bodily functions such as reduced heart rate and the affects of helplessness and hopelessness. But does physical illness lead to demoralization or vice versa? The available evidence appears to suggest that both may

occur [118]. Frank emphasized the central importance of mobilizing hope to induce healing and described a restoration of morale as the critical aspect underpinning success [114].

Although several possible diagnostic criteria have been proposed for demoralization, it has not yet been defined in the DSM. de Figueiredo [119] highlighted that, in this multi-axial system, demoralization includes symptoms of anxiety and depressive disorders (axis I), is affected by personality traits (axis II), is clearly to be associated with physical health problems (axis III) and is related to the level of functioning (axis V). Many demoralized individuals are inadequately labelled as suffering from ‘adjustment disorders’ for lack of a better term and to satisfy third-party payers who demand a diagnostic label. This type of confusion occurs because our current diagnostic systems fail to recognize four perspectives of every person: his/her disease, behaviour, illness and life story. Demoralization is intimately related to a person’s life story. One suggestion was made that demoralization could replace stressful life events in axis IV [119]. But such events are circumstances that are external to the individual, and simply listing them under axis IV, or reducing demoralization to a V-code, tells us nothing about the internal struggle of the person exposed to the stress [120].

Morale can vary across a spectrum of mental attitudes, ranging from disheartenment (a mild loss of confidence) to despondency (starting to give up) and despair (losing hope), before eventually reaching the state of demoralization (having given up) [121]. Whilst the initial stages of this spectrum represent a comprehensible response to adversity, the later stages are pathological through their maladaptiveness, the extent of personal distress and the potential to generate greater harm through further deterioration.

Kissane *et al.* [121] emphasized the clinical importance of demoralization as a concept. Contrary to the original definition of Frank, Clarke and Kissane’s review [122] concluded that demoralization can be distinct from depression – depressed patients experience anhedonia, whereas demoralized patients experience subjective incompetence. Kissane *et al.* [121] proposed criteria for the demoralization syndrome (see Table 1.2).

This concept was aided by the development of a tool to measure demoralization, the Demoralization Scale [123]. In a cohort of

Table 1.2 Proposed diagnostic criteria for the demoralization syndrome (adapted from Kissane *et al.* [122]).

- A. Affective symptoms of existential distress including loss of meaning and purpose in life or hopelessness
 - B. Cognitive attitudes of pessimism, helplessness, sense of being trapped, personal failure, or lacking a worthwhile future
 - C. Conative absence of motivation to cope differently
 - D. Associated features of social alienation or isolation and lack of support
 - E. Allowing for fluctuation in emotional intensity, these phenomena persist across more than two weeks
 - F. A major depressive or other psychiatric disorder is not present as the primary condition
-

patients with advanced cancer, this 24-item, self-report questionnaire demonstrated good reliability and strong concurrent validity with measures of existential distress, hopelessness and depression. Of particular interest was the observation that the two items closest in content to suicidal ideation, 'life is no longer worth living' and 'I would rather not be alive', load strongly on the loss of meaning subscale. The dimensions of the phenomenology of demoralization are captured in the tool's subscales: dysphoria, disheartenment, loss of meaning, helplessness and sense of failure. Other cohorts of palliative care patients have permitted the differentiation of depression with anhedonia from depression with demoralization [124].

Clarke *et al.* [125] compared 125 patients with metastatic cancer and 126 patients with motor neurone disease (MND) on a range of physical and psychosocial measures as they approached the end of life. The MND patients were younger, had greater social contacts, but were more physically impaired, while the cancer patients had more pain and were on more medication (opioids, steroids, and other analgesics). Although the Beck Depression Inventory scores were similar in the two groups, MND patients had significantly higher scores for demoralization, hopelessness, and suicidal ideation. Cancer patients, on the other hand, scored significantly higher on anhedonia. This difference in the quality of depression was argued to represent a difference in illness experience of the two groups, which has relevance for the ways we treat depression in the medically ill.

The concept of demoralization clearly has profound implications for clinical practice [126, 127]. Recent evidence suggests that, when allowance is made for demoralization to be comorbidly present with depression, prevalence rates between 20 and 30% for demoralization are seen across studies, with higher rates in advanced cancer than in early cancer states [128]. In the UK, a multi-centre, longitudinal study into the prevalence of depression and demoralization in patients with advanced cancer has recently been undertaken by Lloyd-Williams *et al.* A sample of 629 patients, aged from 21 to 94 years, was recruited from hospice and palliative care day units in the northern part of England and parts of North Wales. Thirty-two per cent of patients had a diagnosis of breast cancer, 17% of gastrointestinal cancers and 17% cancers of the lung; 67% were female. On Eastern Cooperative Oncology Group (ECOG) performance scores, 69% had scores of 1 or 2, indicating that they were ambulatory patients. Thirty-four per cent of the cohort stated they had experienced depression previously and 32% of participants scored 10 or more on the Patient Health Questionnaire, indicating a diagnosis of major depression. Patients also completed the Royal Free Spirituality Scale. Preliminary findings confirm that demoralization and depression are strongly positively correlated, while negatively correlated with spirituality. Spirituality appears to provide the meaning to counter demoralization.

CONCLUSIONS

Depression is common in adults with cancer, and frequently co-exists with anxiety and pain. It has been challenging to study because symptoms occur on a spectrum that ranges from sadness to major affective disorder, and mood change is often difficult to evaluate when a patient is confronted by repeated threats to life, is receiving complex cancer treatments, is fatigued, and/or is experiencing pain. Untreated depression, nevertheless, results in significant morbidity and mortality. Although the prevalence of depression varies across the 60 studies of at least 100 cancer patients cited in this chapter, ranging between 1.5 and 52%, there should be no doubt that cancer is associated with a high degree of depression.

Depression is especially common in patients with advanced cancer, in whom it is frequently missed and therefore not treated. The diagnosis of depression in this population represents a particular challenge given the vegetative features associated with advanced cancer. The impact of the illness on the morale of the patients allows insight to be gained into sources of meaning in their life, which informs the choice of treatment.

Future research must focus on establishing diagnostically reliable criteria, developing standard instruments for measuring depression, correlating past psychiatric history of depression and anxiety with current mood, characterising the causative role of antineoplastics in depression, and identifying biological markers for depression. There is much to do to enhance the quality of life of patients with cancer and prevent the onset of depression.

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