

# Prevalence of Depression in Patients With Cancer

Mary Jane Massie

**Depression is the psychiatric syndrome that has received the most attention in individuals with cancer. The study of depression has been a challenge because symptoms occur on a broad spectrum that ranges from sadness to major affective disorder and because mood change is often difficult to evaluate when a patient is confronted by repeated threats to life, is receiving cancer treatments, is fatigued, or is experiencing pain. 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%). This report reviews the prevalence of depression in cancer patients throughout the course of cancer. [J Natl Cancer Inst Monogr 2004;32:57–71]**

Depression affects 121 million people and is among the leading causes of disability worldwide. Untreated depression leads to personal suffering and increased mortality. Although the prevalence of depression varies considerably globally, the most common symptoms of depression are depressed mood, insomnia, and fatigue, and depressed women outnumber depressed men 2 to 1. Americans have a one in five chance of developing depression in their lifetimes. Weissman and colleagues reported the lifetime rate of major (nonbipolar) depression to be 8%–17% for American women and 3.5%–8.6% for men (1). The 6-month prevalence of depression in adult Americans is 6%. The point prevalence of depression in “healthy community samples” is 4.5%–9.3% for women and 2.3%–3.2% for men.

Although major depression commonly has its onset in the late twenties, one in 10 children have persistent feelings of sadness, one of the hallmarks of depression. The point prevalence of depression in prepubertal children ranges from 1% to 3% and from 3% to 9% in adolescents (2); however, the lifetime prevalence through adolescence is estimated to be as high as 20% (3). Although there is no difference in the prevalence rate between sexes before puberty, females are at higher risk after puberty. Depression in children negatively affects a child’s development and often manifests as behavioral problems or somatic complaints.

Depression commonly coexists with other syndromes and symptoms, such as anxiety disorders (e.g., posttraumatic stress disorder, panic disorder, generalized anxiety disorder) and pain. The National Comorbidity Survey data show that in a 12-month period, 51% of patients with major depressive disorders 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 (4).

The symptoms of depression and personal suffering resulting from this disorder have been well described. The complex biological underpinnings result from disturbances in neurotransmitters and hypothalamic–pituitary–gonadal axis dysregulation. The last two decades have produced exciting science and advances in our understanding of the neurobiology and pathophysiology of depression. Electrophysiologic studies, neuroimaging techniques (i.e., magnetic resonance imaging [MRI]; computed tomography [CT]; single photon emission computed tomography [SPECT]; positron emission tomography [PET]; functional magnetic resonance imaging [functional MRI]), and neuropsychologic studies are providing information about the neuroanatomical substrate of depression as we are learning more about how systemic disease effects vulnerability to depression.

## EARLY STUDIES OF DEPRESSION IN CANCER PATIENTS

When significant numbers of mental health professionals began working in oncology settings, they asked oncologists to describe their perceptions of the prevalence of psychiatric disorders in cancer patients. Common responses ranged from “everyone is depressed, and rightfully so, because they have cancer” to “no one is depressed; these are just normal people” and likely were a reflection of the respondent’s mood and coping style.

One of the first efforts in psychooncology was to obtain objective data on the type and frequency of psychological problems in cancer patients. Using criteria from the *Diagnostic and Statistical Manual of Mental Disorders—Third Edition* (DSM-III) (5) classification of psychiatric disorders, the Psychosocial Collaborative Oncology Group determined the psychiatric disorders in 215 randomly selected hospitalized and ambulatory adult cancer patients in three cancer centers by structured clinical interview (6). Although 53% of the patients evaluated were adjusting normally to stress, the remainder (47%) had clinically apparent psychiatric disorders. Of this 47% with psychiatric disorders, more than 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 psychiatric 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. The finding of 4% anxiety disorders was far below what would have been expected in the general population.

*Correspondence to:* Mary Jane Massie, MD, Department of Psychiatry and Behavioral Science, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY 10021 (e-mail: massiem@mskcc.org).

See “Notes” following “References.”

DOI: 10.1093/jncimonographs/lgh014

*Journal of the National Cancer Institute Monographs*, No. 32, © Oxford University Press 2004, all rights reserved.

Thirty-nine percent of those who received a psychiatric diagnosis experienced significant pain. In contrast, only 19% of patients who did not receive a psychiatric diagnosis had significant pain. The psychiatric diagnosis of the patients with pain was predominately adjustment disorder with depressed or mixed mood (69%), but of note, 15% of patients with significant pain had symptoms of a major depression.

This early study conducted in 1983 was important for several reasons: first, it was a collaborative research effort by groups at three treatment facilities serving patient populations from different socioeconomic and cultural backgrounds (Baltimore, MD; New York City; and upstate New York); second, it was one of the first reviews of the prevalence of psychiatric disorders cancer patients providing useful data for mental health professionals to use to teach oncologists and oncology staff members about the psychological problems of cancer patients and the importance of hiring mental health professionals trained in the assessment and treatment of people with cancer; third, the researchers found support for an association between psychiatric morbidity and the presence of complaints, such as pain, and highlighted the importance of such correlations; and fourth, the findings helped mental health professionals and hospital administrators consider how best to staff clinical settings to effectively treat the psychological problems of cancer patients.

In two other early studies using both DSM-III criteria that were modified to eliminate physical symptoms characteristic of cancer and those that were validated by observer rating scales (Hamilton Rating Scale and Beck Depression Inventory [BDI]), Bukberg and colleagues (7) found a 42% (24% severe, 18% moderate) prevalence among 62 adults (30 female, 32 male) hospitalized on oncology units, and Plumb and Holland (8) found a 33% prevalence of depression among 80 (40 female, 40 male) hospitalized adults with advanced cancer.

## PREVALENCE OF DEPRESSION IN MEDICALLY ILL PATIENTS

To place depression in cancer patients in context, it is helpful to consider the prevalence of depression occurring in association with other medical illnesses. 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% (9). A retrospective review of 263 000 patients from 327 hospitals found that 24% of those receiving a psychiatric consultation were depressed (10). However, Synder and colleagues (11), 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.

Taking a different approach, Wells and colleagues (12) examined Epidemiological Catchment Area Study data regarding psychiatric disorders among persons with at least one of eight chronic medical conditions. Six-month and lifetime prevalence rates of psychiatric disorder were increased in those with medical illness (25% and 42% versus 17% and 33%). Thirteen percent 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% (Table 1) (13). In contrast to

**Table 1.** Secondary depressive disorders in selected neurological diseases\*

Disease	Lifetime prevalence of depression, %
Parkinson's disease	40–50
Huntington's disease	≈40
Cerebrovascular accidents	30–50 (includes major and minor depressions)
Multiple sclerosis	10–50
Alzheimer's disease	15–55

\*Adapted with permission from Oxford University Press (9).

neurological disease, 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 (Table 2) (13). Overall, rates of depression in medical illness appear to be lower than those encountered in neurological illness. Some have hypothesized that this may be a function of the extent of the direct structural compromise of the central nervous system in the neurological conditions as opposed to the medical illnesses.

To what extent depression in the medically ill is a discrete entity, separate from depression arising in patients without comorbid physical illness is controversial. However, factors, including the absence of the usual female preponderance in affective disorder, no indication of genetic loading, treatment outcome, and long-term course, all favor the idea that these disorders are different.

## ASSESSMENT METHODS

Depression has been studied in patients with cancer using a range of assessment methods. The methods (self-report, brief screening instruments, and structured clinical interviews) commonly used are the Hospital Anxiety and Depression Scale (HADS), BDI, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, and DSM criteria. In general, the more narrowly the term is defined, the lower the prevalence of depression that is reported. Please see Dr. Trask's comprehensive discussion of the issues and challenges of assessment in this volume (13a).

## PREVALENCE OF DEPRESSION IN CANCER PATIENTS REFERRED FOR PSYCHIATRIC CONSULTATION

Studies of the prevalence of depression in cancer patients referred for psychiatric consultation are one source of information about depression in cancer patients. Although one might expect to find a higher rate of depression in those noted to be distressed and referred for psychiatric evaluation, the five stud-

**Table 2.** Secondary depressive disorders in selected medical illnesses\*

Illness	Lifetime prevalence of depression, %
Cushing's syndrome	33–67
Type I/type II diabetes mellitus	19–33
End-stage renal disease	5–8 (18% minor depression)
Coronary heart disease	26
Cancer (heterogeneous and single disease status types)	6–42 (current prevalence only)

\*Adapted with permission from Oxford University Press (9).

ies of depression in oncology patients referred for psychiatric consultation report a prevalence of major depression ranging from 9% to 58% (Table 3) (14–18). Although Massie and Holland (17) reported a low prevalence of depression (9%), an additional 26% of the hospitalized and ambulatory patients studied had adjustment disorder with depressed mood according to DSM-III. Lack of standardization in terms of population studied, disease site and stage, sample size, assessment instruments, cutoff score, type of interview, and diagnostic criteria employed (including major depression versus adjustment disorder with depressed mood versus depressive symptoms) all contributed to the large variance in reported prevalence among these studies.

## PREVALENCE OF DEPRESSION IN CANCER PATIENTS

Depression, the psychiatric syndrome that has received the most attention in individuals with cancer, has been a challenge to study because symptoms occur on a spectrum that ranges from sadness to major affective disorder and because mood change is often difficult to evaluate when a patient is confronted by repeated threats to life, is receiving cancer treatments, is fatigued, or is experiencing pain.

However, depression in cancer has been essential to study because comorbid illnesses complicate the treatment of both and may lead to poor adherence to treatment recommendations and to less desirable outcomes of both conditions. Watson and col-

leagues' 1999 report (19) that depression is linked to a reduced chance of survival in women with early stage breast cancer supports the need for further study.

Many research groups have assessed depression in cancer patients since the 1960s, and the reported prevalence (major depression, 0%–38%; depression spectrum syndromes, 0%–58%) varies significantly (Table 4) (6–8,20–104). These databases were searched to retrieve references published between 1965 and 2002 on the prevalence of depression in cancer: Medline, PreMedline, Embase (Excerpta Medica), PsycINFO (Psychological Abstracts), and CINAHL (Cumulative Index to Nursing and Allied Health Literature). Articles in English were reviewed; Table 4 shows the studies that provided information about the number of patients interviewed and cancer type or types, evaluation methods, and percentage with depression or affective syndromes. Most authors reported patient sex and hospitalization status. Please see Dr. Lawrence's evidence report on cancer-related depression in this monograph (104a).

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), by a symptom such as depressed mood, or by some of the 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,

**Table 3.** Psychiatric consultation studies of depression in cancer patients\*

Reference	N	% female	Patients	% depressed	Method	Specific findings	Gender difference
Hinton 1972 (14)	50	72	Hospitalized; terminally ill; mixed neoplasms, one collagen-vascular	58%	Interview	42% anxious; 34% adjustment reaction; 10% confusional state	Not cited for depression; more psychiatric referrals for breast cancer; fewer men with lung cancer referred; low referrals for digestive neoplasms
Levine 1978 (15)	100	51	Hospitalized; all stages and sites	56%	Interview; DSM-II criteria	40% OBS; 26% OBS misdiagnosed as depressed by referring physicians; 58% of depressed had metastases	2:1 female to male ratio to psychiatric referrals; NS trend of more OBS in males than females in under 60
Massie 1979 (16)	334	57	Hospitalized; and ambulatory; all stages and sites	49%; 5% extreme; 24% severe; 71% mild to moderate	Interview; DSM-II criteria	15% organic; all patients with severe or extreme depression had advanced cancer	Women referrals higher than men; 1:13 M:F
Massie and Holland 1987 (17)	546	Not cited	Hospitalized and ambulatory; all stages; all sites; referred for psychiatric consultation	9% major depression; 26% adjustment disorder with depressed mood	Interview; DSM-III criteria	59% of referrals depressed or suicidal; good premorbid functioning with only 11% psychiatric history	Not cited
Razavi 1990 (18)	128	Not cited	Hospitalized; mixed; 88 psychiatric referrals out of total of 210 (141 females 69 males)	26% major depression; 46% adjustment disorder	Semistructured interview from the Diagnostic Interview Schedule; HADS	Depression higher in predeterminal or terminal	Not cited

\*DSM-II, *Diagnostic Manual of Mental Disorders*, 2<sup>nd</sup> edition; OBS, organic brain syndrome; NS, not significant; HADS, Hospital Anxiety and Depression Scale. Adapted with permission from Oxford University Press (9).



**Table 4.** Representative studies of the prevalence of depression in cancer patients

Reference	N	% F	Patients	Method	% depressed	Specific findings
Fras et al. (1967) (20)	110	Not cited	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
Koenig et al. (1967) (21)	36	50	Hospitalized; advanced bowel cancer	MMPI	25%	Cancer patients less psychopathology than depressed psychiatric inpatients
Peck et al. (1972) (22)	50	54	Ambulatory radiotherapy: all sites; all stages	Clinical interview	Major depression-not cited; 74% affective symptoms	10% severe depression; 32% moderate depression; 32% mild depression
Craig et al. (1974) (23)	30	63	Hospitalized; all sites, advanced	SCL-90	53%	13% severe depression; 40% moderate depression; 30% anxious
Morris et al. (1977) (24)	160	100	Breast biopsy and mastectomy patients	Interview; HRSD	22% depression in mastectomy	Mastectomy patients had persistent depression (22%) at 2 years compared with benign patients (8%)
Plumb et al. (1977) (25)	97	52	Hospitalized, all sites, advanced; compared to 99 psychiatric inpatients with recent suicide attempt	BDI	23% cancer patients depressed; 54% psychiatric patients depressed	19% moderate severity; 4% severe; cancer patients and their next of kin were less depressed than physically healthy suicide attempt patients
Maguire et al. (1978) (25)	201	100	117 ambulatory breast cancer patients; 89 benign disease	Clinical interview	26% moderate or severe depression after mastectomy	Control benign patients had 12% depression
Silberfarb et al. (1980) (26)	146	100	Hospitalization status not indicated; 34% primary disease; 36% recurrent; 30% advanced, all breast cancer	Structured interview; open-ended questions; modified psychiatric status scale	10% depression in primary cancer diagnosis; 15% in recurrent; 4.5% advanced cancer	Physical disability did not relate to emotional disturbances; first recurrence of breast cancer most disturbing time; advanced patients had the least depression
Krouse et al. (1981) (27)	21	100	Hospitalized for mastectomy, hysterectomy, or breast biopsy and assessed during hospitalization and ambulatory follow-up at 4 wk to 2 mo	BDI; Rotter Incomplete Sentences; Body Image Questionnaire	Depression-not cited; average Beck Depression Inventory	More severe depression and poorer body image among gynecologic patients. Most mastectomy patients were not depressed and did not have severe body image disturbance
Plumb et al. (1981) (28)	80	50	Hospitalized; all sites; advanced	Structured interview; CAPPS excluding certain physical symptoms	33% 1% extreme; 20% severe; 24% moderate; 33% mild; 16% minimal	Cancer patients less depressed than comparative group of psychiatric patients
Derogatis et al. (1983) (6)	215	51	Half hospitalized; half ambulatory; all sites and all stages	DSM-III criteria; SCL-90; RDS; GAIS; Karnofsky Rating Scale	6% 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
Bukberg et al. (1984) (7)	62	48	Hospitalized on medical oncology units; all sites	Modified DSM-III criteria eliminating physical symptoms; DACL; HRSD; Karnofsky Rating Scale; BDI; McGill Pain Questionnaire	42 depressed 24 severe; 18 moderate; 14 mild; 44 none	Greater physical disability, negative life events, and poor quality of social support associated with depression
Farber et al. (1984) (29)	141	72	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
Lloyd et al. (1984) (30)	40	38	Hospitalized and ambulatory; Hodgkin's or non-Hodgkin's lymphoma; all stages and sites	Semi-structured interview; EPQ; VAS	Major depression-not cited; 38% psychiatric morbidity	26% psychiatric morbidity at 6 mo; one-third patients dissatisfied with information received about illness
Morton et al. (1984) (31)	48	0	Largely ambulatory, oropharyngeal, geriatric; 3 treatment groups; surgery alone, irradiation alone or salvage surgery after failed radiotherapy	DSM-III criteria	40%	Function disability lower in those treated with radiation alone rather than surgery or combination; No significant difference in depression among 3 treatment groups
Hughes (1985) (32)	134	22	Lung cancer	Structural clinical interview	16%	Most of the depressed patients were depressed before physical symptoms began
Lansky et al. (1985) (33)	500	100	85% ambulatory; 43% survivors with no evidence of disease; 34% early stage	DSM-III, organic brain syndrome section of the PDI; HRSD, Zung self-rating depression scale; visual pain analogue line	5.3% (using HRSD and Zung); 4.5% (using DSM-III criteria)	High degree of survivors; HRSD $\geq 20$ and ZUNG $\geq 50$
Robinson et al. (1985) (34)	57	58	Hospitalized and ambulatory	Semi-structured interview; social adjustment self-report; symptom questionnaire	25% both depressed and anxious; 60% depressed or anxious current or past	30% depressed or anxious current or past "not due to cancer," 12% due to cancer; 58% "normal;" depression and anxiety more severe in non-cancer relatives
Starkman et al. (1985) (35)	17	24	Hospitalized pheochromocytoma patients compared with 52 patients with primary anxiety disorder	DSM-III criteria; STAI; SCL-90R	12%	No increased prevalence of anxiety disorder in pheochromocytoma

(Table continues)

**Table 4 (continued).**

Reference	N	% F	Patients	Method	% depressed	Specific findings
Davies et al. (1986) (36)	72	40	Hospitalized; oropharyngeal cancer	Leeds Scale for Self-assessment of Depression; General Health Questionnaire	22%	Patients and investigators were blind to biopsy results; more depression (29 vs. 15%) in those with positive biopsy
Evans et al. (1986) (37)	83	100	All hospitalized women with gynecological cancer (excluding ovarian)	DSM-III; HRSD	23% major depression; 24% adjustment disorder with depressed mood	DST 40% sensitivity, 80% specificity
Holland et al. (1986) (38)	218	36	Ambulatory; 107 advanced pancreatic, 111 advanced gastric	POMS	Major depression-not cited; 21 median POMS gastric; 38 median POMS pancreatic	Pancreatic cancer patients had higher depression than gastric cancer among men only
Joffe et al. (1986) (39)	21	29	Hospitalized; pancreas 12, gastric, 9	SADS-L; SCL-90-R; BDI, STAI, RDC	Major depression: 33% pancreas; 0% gastric; major depression and adjustment disorder: 50% pancreas, 11% gastric	19% of new pancreatic cancer patients had a history of major depression in the year prior to diagnosis; DST: Pancreas 6 of 6 nonsuppression (1 major depression); Gastric: 5 of 6 nonsuppression (0 major depression)
Devlen et al. (1987a) (40)	90	48	Ambulatory; Hodgkin's disease and non-Hodgkin's lymphoma	Semi-structured interview	19% depressed; 27% borderline depression	Retrospective study; with interviews conducted a mean of 32 mo after diagnosis
Devlen et al. (1987b) (41)	120	47	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
Friedrich et al. (1987) (42)	46	48	Hospitalized; 23 twin patients, one with hematologic malignancy, the other a bone marrow donor	MMPI	Major depression-not cited; 62 mean depression MMPI score patients; 54 mean depression score donors	No difference in depression in male twins
Lasry et al. (1987) (43)	123	100	Hospitalized breast cancer	CES-D	50% mastectomy; 50% lumpectomy with radiation; 41% lumpectomy	Depression varied with treatment
Grandi et al. (1987) (44)	18	100	Hospitalized stage II or III breast cancer post-mastectomy or lumpectomy	Paykel's clinical interview for depression; DSM-III criteria	22% depression; 22% anxious	Dexamethasone stimulation test positive in both depressed and non-depressed patients
Stefanek et al. (1987) (45)	126	56	Ambulatory; mixed	BSI	33% depressed; 9% severe; 24% moderate	20% high psychiatric distress in general
Pettingale et al. (1987) (46)	168	Not cited	Hospitalized early breast cancer and lymphoma; all stages	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 et al. (1989) (47)	196	77	Hospitalized and ambulatory; recent diagnosis of cancer; mixed, 18–70 y	HRSD; IBQ; interview	24–38%	38% depression with HDRS cutoff of 17; 24% with HDRS of 21
Hardman et al. (1989) (48)	126	43	Hospitalized; mixed	Structured interview (ICD) General Health Questionnaire	3% depression; 23% anxiety and depression	Psychiatric symptoms related to feeling moderately or severely ill and previous psychiatric illness, but not with awareness of having cancer
Meyer et al. (1989) (49)	58	100	Ambulatory breast cancer patients in Sweden, 5 y after treatment	Clinical interview CPRS depression scale	Major depression-not cited; 30% anxiety or depressive symptoms post-mastectomy	5 year post-treatment anxiety and depression persisted in 30% mastectomy and 29% partial mastectomy
Fallowfield et al. (1990) (50)	269	100	Stage I and II breast cancer assessed 2 wk, 3 mo, 12 mo after surgery	Interview	21% mastectomy; 19% lumpectomy	Less depression in mastectomy and lumpectomy patients given treatment choice
Kathol et al. (1990) (51)	152	59	Mixed	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 et al. (1991) (52)	100	35	Hospitalized acute leukemia prior to BMT	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
Golden et al. (1991) (53)	83	100	Hospitalized; cervical, endometrial, and vaginal cancer	DSM-III criteria; CRS	23% major depression according to DSM-III criteria	—
Hopwood et al. (1991a) (54)	81	100	Ambulatory; advanced breast cancer	HADS; RSCL; Clinical Interview Schedule; DSM-III criteria	20% depression; 15% anxiety	21% of “normal” patients misclassified by RSCL and 26% by HADS; 75% sensitivity of HADS and RSCL together
Hopwood et al. (1991b) (55)	222	100	Ambulatory; advanced breast cancer	HADS; RSCL	9% depression and 9% anxiety using HADS; combined anxiety or depression: 33% (HADS), 22% (RSCL); 40% depressed	HADS and RSCL detected different groups of cases; one third of depressed patients persisted for 1–3 mo
Jenkins et al. (1991) (56)	22	100	Ambulatory breast cancer patients diagnosed with recent local recurrence	DSM-III; EPQ; HAS; MADRS; CIDI	32% depressed; 27% anxiety and depression; 45% depressed or anxious	46% previous major depression; previous psychiatric illness and trait neuroticism predictive of psychiatric morbidity
Baile et al. (1992) (57)	65	43	Ambulatory; head and neck	Semi-structured interview; MCAI; MAST; GARS	40%	Found no relationship between tumor stage and depression

(Table continues)

**Table 4 (continued).**

Reference	N	% F	Patients	Method	% depressed	Specific findings
Goldberg et al. (1992) (58)	320	100	Newly diagnosed, hospitalized for breast cancer surgery	Modified RSCL; pre-operative, 6 and 12 mo post-operatively	32% depressed malignant; 24% depressed benign biopsy	At 1 y, depression had decreased (21% depressed) in both groups
Maraste et al. (1992) (59)	133	100	Ambulatory; adjuvant radiotherapy; breast cancer	HADS	1.5% depressed; 14% anxiety	Age and surgery related anxiety; anxiety in ages 50–59 y was 44% in mastectomy vs. 4% in conservative surgery
Sneed et al. (1992) (60)	133	67	Hospitalized; newly diagnosed; mixed sites and stages	BSI; HIS-GWB	Major depression-not cited	Women with gynecological and breast cancer had less depression, anxiety, hostility, somatization, psychological distress than men and women with other cancers
Alexander et al. (1993) (61)	60	40	Hospitalized on oncology unit in India; mixed sites and stages	DSM-III-R; clinical interview	13% depressed; 20% adjustment disorder; 40% psychiatric disorder; 7% anxiety disorders	Those who were unaware of cancer diagnosis (33%) or considered the treatment curative (82%) had less psychiatric morbidity
Carroll et al. (1993) (62)	809	51	Various cancer sites	HADS	17.7% anxiety disorder 9.9% depressive disorder	
Cathcart et al. (1993) (63)	257	100	Ambulatory; women with node negative breast cancer; 155 women received tamoxifen; 102 received no tamoxifen	Clinical interview	15% tamoxifen treated group; 3% in those not receiving tamoxifen	4.5% of 155 women receiving tamoxifen had to discontinue it secondary to depression
Pinder et al. (1993) (64)	139	100	86 hospitalized, 53 ambulatory advanced breast cancer	HADS interview	13% depressed; 25% anxiety or depression	Depression more prevalent in low socioeconomic class, in poor performance states, and closer proximity to death
Power et al. (1993) (65)	98	49	Terminally ill; various cancer	AMTS, DMS III-R	26% depression with DSMIII-R; 34% cognitive impairment out of 81 patients	35% of cognitive impaired patients also depressed
Rapaport et al. (1993) (66)	55	27	Ambulatory head and neck, all stages, who had completed treatment	Interview with open-ended questions; PAQ	Major depression-not cited; 24% anxious	Psychological problems increased over time
Sneeuw et al. (1993) (67)	556	100	Ambulatory stage I and II breast cancer; interviewed at least 1.5 y 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 1.5 y after treatment and longer; no significant differences in patients who had mastectomy vs. conservative treatment
Middleboe et al. (1994) (68)	36	64	Breast; ovarian; small cell lung cancer	HDS, MES, HAS (all prior to chemotherapy)	HDS-14% major depression; 3 mo after: 10% depression 6 mo after: 9% depression HAS-27% anxious 6 mo after: 9% depression HAS-27% anxious <10% depression	
Mulhern et al. (1994) (69)	99	39	Children various cancers	CDI		Depressive condition is not positively correlated with severity of physical distress
Angelopoulos et al. (1995) (70)	100	41	Various; all ambulatory	Hostility questionnaire; schedule of life experiences and delusions symptoms inventory	Males-49% anxiety; 24% depression Females-58% anxiety; 32% depression	
Ginsburg et al. (1995) (71)	52	25	Newly diagnosed lung cancer	DIS based on DSM III, structured interview	15% psychiatric illness; 4% affective disorder (2% major depression, 2% dysthymia); 12% adjustment disorder; 13% alcohol abuse	
Godding et al. (1995) (72)	69	100	Hospitalized male veteran cancer patients	BDI; KPS; Social provisions scale QOL Index	39% depression; ≈20% clinical depression	
Kelsen et al. (1995) (73)	130	39	Pancreatic cancer	BDI; BHS; MPAC; FLIC	38% depressed (scores ≥15 BDI)	
Sachs et al. (1995) (74)	37	100	Breast cancer	BDI; SADS-LA; Clinical interview DSM III criteria (before surgery)	46% depressive disorders or had depressive disorder earlier in life; 57% depressive symptoms	
Aragona et al. (1996) (75)	85	100	Nontreated breast cancer	Clinical interview; DSMIII-R	2% major depression; 15% dysthymia; 39% depressive disorder; 9% adjustment disorder	
DeWalden-Galuszko (1996) (76)	410	52	Various cancer sites, all terminally ill	Clinical interview with DSM III-R, WHO classification system	37% psychiatric disorders including adjustment disorder and organic mental syndrome	
Grassi et al. (1996a) (77)	86	42	Home care assisted advanced cancer; cancer varied	HADS; EORTC-QLQ-C30	45% depression	
Grassi et al. (1996b) (78)	44	43	Various cancer sites; all undergoing autologous BMT	Self report; symptom questionnaire; Mental Adjustment to Cancer Scale; Social Provision Scale	40.9% depression-before autologous bone marrow transplant; 27.7% depression after BMT	

(Table continues)

**Table 4 (continued).**

Reference	N	% F	Patients	Method	% depressed	Specific findings
Aass et al. (1997) (79)	716	63	Various cancer sites	HADS, EORTC; QLQ-C33; HOC Questionnaire	9% depression; 15% anxious	
Allen et al. (1997) (80)	42	33	Adolescents 12–20 y, cancer variable	BDI, STAI	38% mild to severe depression; 9.5% anxious	
Chochinov et al. (1997) (81)	197	52	Advanced terminally ill cancer	BDI; VAS; Semi-structured diagnostic interview	12.2% depression, 7.6% major depression, 4.6% minor depression	
Pasacrete (1997) (82)	79	100	Breast cancer, 3–7 mo after diagnosis	Interview with DIS; CES-D; Symptom distress scale; ESDS and Cognitive capacity screening test	9% depression disorder 24% depression symptoms	
Berard et al. (1998) (83)	456	75	Breast; head and neck; lymphoma	HADS; BDI, Structured psychiatric Interview	14% depression overall; 8% depression (overlap with both scales)	
Buccheri (1998) (84)	133 initially 95 completed study	Not cited	Newly diagnosed lung cancer	SDS; QOL questionnaire	44.2% moderately or severely depressed	
Kissane et al. (1998) (85)	303	100	Early stage breast cancer	HADS, MILP, EORTC-QLQ	45% psychiatric disorder; 42% depression and/or anxiety; 27.1% minor depression; 9.6% major depression	8.6% anxiety disorder
Montazeri et al. (1998) (86)	129	40	Lung cancer	HADS (administered at baseline and follow-up); QLQ-C30	Baseline: 6% borderline anxiety; 10% severe anxiety; 11% depression borderline; 12% severe depression Follow-up: 11% borderline anxiety; 10% severe anxiety; 22% borderline depression; 32% severe depression	
Hammerlid et al. (1999) (87)	357	28	Head and neck cancer	HADS (administered at 6 different times)	19%–71% probably anxiety; 18%–51% probably depression	
Kramer (1999) (88)	60	Not cited	Inoperable lung cancer	Self administered HADS	50% borderline depression at some point during illness 37% borderline case depression	
Bodurka-Bevers et al. (2000) (89)	246	100	Epithelial ovarian cancer	CES-D; state anxiety sub-scale of Spielberger state trait anxiety inventory; QOL W1 FACT-O	21% CES-D depression w/ 29% anxious	
Breitbart et al. (2000) (90)	92	60	Terminally ill cancer; mixed diagnoses	SAHD	17% depressed; 17% desire for a hastened death	
Chen et al. (2000) (91)	203	50	Solid and liquid tumors	HADS	12% anxious; 20% depression	
DeLeeuw et al. (2000) (92)	197	20	Head and neck cancer	Social Provisions Scale; CES-D; EORTC+; QOL C30+3	29% possible depression (before treatment); 28% (after 6 mo) possible depression	
Hopwood et al. (2000) (93)	987	21	526 small-cell lung cancer 461 non-small-cell lung cancer	HADS, Quality of Life Form	33% depression, self-reported; 21% depression and anxiety	Higher prevalence for small-cell lung cancer patients
Kugaya et al. (2000) (94)	107	22	Head and neck cancer; newly diagnosed	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
Okamura et al. (2000) (95)	55	100	Recurrent breast cancer	Clinical Interview, DSM-III R, POMS	42% depression; 7% major depression; 35% adjustment disorder	
PaScoe et al. (2002) (96)	504	50	Various cancer sites	HADS	11.5% anxious 7.1% depression	
Skarstein et al. (2000) (97)	568	62	Various cancer sites	HADS; EORTC; QLQC33	9% depression, 13% anxious, 17% psychiatric distress, 5% depression and anxiety	HADS more accurate for depression; EORTC QLQ C33 good for anxiety, but underdiagnosed depression
Akechi et al. (2001a) (98)	148	100	Postoperative ambulatory breast cancer	HADS/MAC Scale	23% psych morbidity; 5% depression	
Akechi et al. (2001b) (99)	129	26	Non-small-cell lung cancer	Clinical Interview, DSM-III	4.7% major depression; 13.9% adjustment disorders	
Cavusoglu (2001) (100)	50	38	Children; leukemia, non-Hodgkin's lymphoma, rhabdomyosarcoma, retinoblastoma and Wilms tumor	CDI	22% depression	No gender differences
Ciamarella et al. (2001) (101)	100	50	Various cancer sites	Interview; SCID; Endicott HAMD	49% depression with SCID; 29% depression with Endicott; 28% depression with both	

(Table continues)



**Table 4 (continued).**

Reference	N	% F	Patients	Method	% depressed	Specific findings
DeLeeuw et al. (2001) (102)	197 initially; 123 at the end of 3 y	22	Head and neck cancer	CES-D; EORTC+; QOL C30+3	42% depression 6 mo to 3 y after treatment	
Hutton et al. (2001) (103)	18	28	Head and neck cancer (previously treated)	HADS	22.2% anxious; 22.2% depression; 22.2% psychiatric distress	
Montazeri et al. (2001) (104)	56	100	Breast cancer	HADS — administered before and 1 y after support group	Anxiety: 29% initially 2% after group Depression: 14% initially 0% after group	

\*NS, not significant at  $P = 0.05$ . AMTS: 10-Question, Abbreviated Mental Test Score; BDI, Beck Depression Inventory; BHS, Beck Hopelessness Scale; BSI, Brief Symptom Inventory; CIDI, Composite International Diagnostic Interview; CAPPs, Current and Past Psychopathological Scales; CES-D, Center for Epidemiology Self-report Depression Scale; CPRS, Copenhagen Psychiatric Rating Scale; CRS, Carroll Rating Scale for Depression; CAPPs, Current and Past Psychiatric Adjustment Scale; DACL, Lubin Depression Adjective Check List-form E; DIS, Diagnostic Interview Schedule; DSM-II, *Diagnostic Manual of Mental Disorders*, 2<sup>nd</sup> edition; DMS-III, *Diagnostic and Statistical Manual of Mental Disorders*, 3<sup>rd</sup> edition; EORTC-QLQ-C30, European Organization for Research and Treatment of Cancer-Quality of Life Questionnaire; EPQ Eysenck Personality Questionnaire; ESDS, Enforced Social Dependency Scale; FLIC, Functional Living Index of Cancer; GAIS, Global Adjustment to Illness Scale; GARS, Global Assessment of Recent Stress; HRSD, Hamilton Rating Scale for Depression; HAS, Hamilton Anxiety Scale; HADS, Hospital Anxiety and Depression Scale; HDS, Hamilton Depression Scale; HIS-GWB, Rand Health Insurance Study-General Well-Being Schedule; IBQ, Illness Behavior Questionnaire; KPS, Karnofsky Performance Status Scale; MADRS, Montgomery Asberg Depression Rating Scales; MAST, Michigan Alcohol Screen Test; MCAI, Million Clinical Multiaxial Inventory; MES, Melancholia Scale; MILP, The Monash Interview for Liaison Psychiatry; MMPI, Minnesota Multiphasic Personality Inventory; MPAC, Memorial Pain Assessment Card; PAQ, Patient Adjustment Questionnaire; PDI, Psychiatric Checklist; POMS, The Profile of Mood States; QOL questionnaire, Quality of Life questionnaire; RDC, Research Diagnostic Criteria; RDS, Raskin Depression Screen; RSCL, Rotterdam Symptom Checklist; SADS, Schedule for Affective Disorders and Schizophrenia; SADS-L = Schedule for Affective Disorders and Schizophrenia and Lifetime; SAHD, Schedule of Attitudes Toward Hastened Death; SCL-25, SCL-90, SCL-90R, Hopkins Symptom Checklist 25, 90, and 90-Revised; SDS, Self-rated Depression Scale; STAI, State-Trait Anxiety Inventory; VAS, Visual analog scales; MDNC, major depression not cited. This table was adapted with permission from Oxford University Press (9).

findings usually were not reported by demographic variables, and racial minorities were always underrepresented.

A limitation of many studies is that the effects of cancer treatments and non-cancer-related variables that affect mood often are not accounted for. For example, although the corticosteroids, vincristine, vinblastine, procarbazine, L-asparaginase, amphotericin B, interferon, and tamoxifen cause depression in some people, research groups usually have not presented data about cytotoxic drug or hormone use when describing their findings.

Although Newport and Nemeroff and McDaniel and colleagues (105–107), acknowledged 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), 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 caused by the pathophysiologic effect of the tumor (i.e., paraneoplastic syndromes associated with breast, testis, or lung cancers), treatment effects, or other unidentified factors remains to be described. 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

Cancer types highly associated with depression include oropharyngeal (22%–57%) (36,100), pancreatic (33%–50%) (20,39), breast (1.5%–46%) (67,74), and lung (11%–44%) (84,86). A less high prevalence of depression is reported in patients with

other cancers, such as colon (13%–25%) (20,21), gynecological (12%–23%) (37,53,79), and lymphoma (8%–19%) (40,41).

## GENDER DIFFERENCES

A meta-analysis of 58 studies conducted between 1980 and 1994 demonstrated that cancer patients were significantly more depressed than the general population and that there were significant differences among groups with regard to sex, age, and type of cancer (108). DeFlorio and Massie (109) reviewed 49 studies of the prevalence of depression in individuals with cancer with a particular emphasis on gender differences. Among the 49 studies they reviewed, 30 included both males and females. Six research groups did not examine (or report) gender differences; the remaining 23 found no gender differences in the prevalence of depression at a significance level of  $P < .05$ . However, 10 research groups found either gender differences in subsets of patients, nonsignificant trends, or differences in other parameters such as psychiatric morbidity, anxiety, and denial.

Four studies reported increased depression in the subsets of female patients. Craig and Abeloff (23) found a nonsignificant trend for females to have more psychological symptoms in a study of 30 (63% female) cancer patients. Lloyd and colleagues (30) found significantly higher psychiatric morbidity (anxiety and depression) among women in a study of 40 (38% female) hospitalized and ambulatory patients with different stages of lymphoma.

Pettingale and colleagues (46) studied 168 patients with breast cancer or with lymphoma and found that the women with lymphoma had a tendency to be more depressed and were more anxious than were men with lymphoma and women with breast cancer. Women were more anxious than men at 3 months and 1 year follow-up; women with breast cancer were more anxious



than were other patients at 1 year. Men were more likely to believe their illness was not under their control.

Two studies reported more severe depression in men with cancer. Although Plumb and Holland (28) found no gender differences in overall depression in 80 (50% female) hospitalized patients with advanced cancer, more men than women (12 versus 5) were severely depressed. Males were more likely to have a history of poor impulse control, and females had a history of phobic symptoms. Holland and colleagues (38) found that men with either pancreatic or gastric cancer had depression and distress scores equal or slightly higher than women. Men with pancreatic cancer (but not women) had higher depression scores on the Profile of Mood States than men with gastric cancer. Whether this reflects a gender-based biological mechanism is unknown.

Three research groups reported mixed results depending on subsets of patients or diagnostic criteria. In their study of 808 cancer patients, Kathol and colleagues (51) using Research Diagnostic Criteria found that women were more depressed than men; however, this finding did not persist when DSM-III criteria were applied. Baile and colleagues (57) in a study of 45 (43% female) ambulatory patients with head and neck cancer found increased depression in women with early-stage disease and in men with late-stage disease.

Sneed and colleagues (60) found no gender differences in depression, anxiety, hostility, somatization, general psychological distress, or psychological well-being in 133 (67% female) patients with mixed cancer diagnoses. However, women with gynecological and breast cancer were found to have less depression, anxiety, hostility, somatization, and psychological distress, and greater psychological well-being, than women and men with other types of cancer. The authors believed this was secondary to their perception that their illness was less serious.

Fife and colleagues (110) found no significant differences in depression in male and female cancer patients; however, they found that women made a more positive adjustment to cancer. In a study comparing 46 (45% females) adult twins with a hematological malignancy with their identical twin bone marrow donor, Friedrich and colleagues (42) found that female cancer patients showed more depression and repression of feelings than their nonpatient female twins; no difference was found between the male patients and their nonpatient twins. There was no significant difference in depression between male and female cancer patients.

## DEPRESSION BY CANCER TYPE

### Depression in Women With Breast Cancer

Breast cancer is the cancer most studied in terms of psychosocial effects, and not surprisingly, many studies of the prevalence of depression in cancer are studies of women with breast cancer. The reported prevalence ranges from 1.5% to 46%.

**Longitudinal studies of depression in women with breast cancer.** Some research groups have assessed the duration of psychological distress in breast cancer patients and survivors. In a prospective study of 160 women awaiting breast surgery, Morris and colleagues (24) found a 22% prevalence of depression in women who had a mastectomy for breast cancer. This prevalence persisted at 2 years compared with an 8% prevalence of depression in those with benign disease. Meyer and Asper-

gren (49) found a 30% rate of anxiety or depressive symptoms in a study of 58 ambulatory women who were 5 years posttreatment for breast cancer. Women who had partial mastectomy followed by radiation had better body image but similar amount of anxiety and depression symptoms and fear of recurrence as did women who had modified radical mastectomy.

Watson and colleagues (19) prospectively studied 578 women with early-stage breast cancer using the Mental Adjustment to Cancer Scale, Courtauld Emotional Control Scale, and HADS (4–12 weeks and 12 months after diagnosis) and found that a high helplessness/hopelessness score had a moderate effect on 5-year, event-free survival. However, a high score for depression was linked to a significantly reduced chance of survival. Although the authors cautioned that the latter result was based on a small number of patients and should be interpreted with caution, these findings are provocative and require further study.

**Depression in breast cancer patients by surgical procedure.** In many of these studies, research groups compared psychological outcomes of women undergoing different surgical procedures. Maraste and colleagues (59) found low levels of depression (1.5%) but higher levels of anxiety (14%) in 133 ambulatory breast cancer patients receiving radiotherapy after mastectomy or lumpectomy. Using a cutoff score of 10 on HADS, only two mastectomy patients (1.5%) were considered significantly depressed. If a HADS cutoff score of 8 was applied, then 6.7% (seven mastectomy patients, two conservative surgery patients) were depressed. In contrast, in a study of 123 women with breast cancer, Lasry and colleagues (43) found a high prevalence of depression (50% in mastectomy, 50% in lumpectomy with radiation versus 41% in lumpectomy only). These high percentages may have resulted from a use of a self-report depression scale (Center for Epidemiology Self-report Depression Scale [CES-D]) rather than a DSM-III-R criteria-based clinical interview.

Maguire and colleagues (25) found 26% moderate or severe depression among women who had mastectomy compared with a 12% prevalence of depression in women with benign disease. Grandi and colleagues (44) reported a 22% prevalence of depression and postlumpectomy hospitalized stage II or III breast cancer patients. Similarly, Fallowfield and colleagues (50) found a 21% prevalence of major depression in women who had mastectomy and a 19% prevalence in those who had lumpectomy. Interestingly, there was less depression reported among women whose surgeons allowed them to choose the type of surgery (23% depression reported among women who chose mastectomy versus 38% who had mastectomy based on surgeons' recommendation).

Goldberg et al. (58) found a 32% prevalence of depression in 166 women scheduled for breast surgery that revealed cancer compared with a 24% prevalence of depression in 156 women who were found to have benign disease at the time of breast biopsy. The women with breast cancer were significantly less depressed (21% depressed) at 1 year follow-up. There was no significant difference in depression between mastectomy patients and those who had conservative surgery either preoperatively or at 6 and 12 months postoperatively.

Using the Diagnostic Interview Schedule, the CES-D, and the Hopkins Symptoms Checklist, Sneeuw and colleagues (67) found a 4.5% prevalence of major depression among 556 stage I and II breast cancer patients, 215 treated by radical mastec-

tomy and 341 treated by breast-conserving therapy. At the time of evaluation all women were disease-free. No significant differences were found between women who received mastectomy as opposed to those who were conservatively treated or between patients treated recently (1–2 years before the interview) and those treated longer ago.

### **Prior History of Depression in Women With Breast Cancer**

Few researchers have noted the time of onset of depression or correlated patients' history of depression with current depression or functioning. Notably, Pasacrete (82) reported findings on a homogenous sample of 79 women evaluated with the Diagnostic Interview Schedule and CES-D 3–7 months after their diagnosis of breast cancer. Nearly 18% of this sample had a past or current history of depression according to DSM-III-R criteria. Women with elevated depressive symptoms had more physical symptom distress and more impaired functioning than subjects with depressive disorders and without depression.

In a cross-sectional study of 303 relatively young (mean age 46 years) women with early (stage I or II) breast cancer at 3 months after breast surgery using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire and HADS, Kissane and colleagues (85) found that a past history of depression was associated with depression. They also noted that women with few psychological symptoms and good emotional adjustment to cancer may have refused participation in this study because these women were also being recruited into an intervention study.

### **Hormones and Depression in Women With Breast Cancer**

Cathcart and colleagues (63) studied 257 women with lymph node-negative breast cancer, 155 of whom were treated with tamoxifen and 102 who were not. On the basis of clinical interview, 15% of the tamoxifen-treated group had depression compared with 3% of those not taking tamoxifen. Of the 23 women with depression, eight had mild symptoms and no change in tamoxifen dose was made, eight had significant depression requiring a dose reduction to relieve symptoms, and seven had to discontinue tamoxifen secondary to depression.

Fallowfield and colleagues (112) studied 488 British women, ages 33–67 years, who were at high familial risk of developing breast cancer in a longitudinal, randomized (tamoxifen 20 mg daily), placebo-controlled study. The participants' average General Health Questionnaire score was slightly lower than the average in a large British population study. Using four instruments, including the General Health Questionnaire–30, they found that 16.9% of women taking tamoxifen reported depression as having been somewhat/quite a bit/very much of a problem since taking part in the trial, in comparison with 21.4% of the placebo group. Although this study was of women at high risk (not women with breast cancer), it is of interest because placebo-treated patients had more depression than those taking tamoxifen.

### **Prevalence of Depression in Women With Advanced Breast Cancer**

Studies evaluating the correlation of depression with disease progression in women with breast cancer have shown inconsistent results. Silberfarb and colleagues (26) found less depression

in women with advanced breast cancer (4.5%) than in those with recurrent disease (15%). Physical disability did not relate to emotional disturbance. Hopwood and colleagues (54,55) reported that ambulatory advanced breast cancer patients had a 20% depression prevalence in one study and 9% depression in another. Jenkins and colleagues (56) found a 32% prevalence of depression in 22 women with local recurrence comparable with rates found with mastectomy. Pinder and colleagues (64) found a 13% prevalence of depression in advanced breast cancer patients ( $N = 139$ ); increased levels of depression were found in those with lowest socioeconomic status, poorest performance status, and closer proximity to death.

### **Prevalence of Depression in Women With Gynecological Cancer**

Evans and colleagues (37) studied 83 women with gynecologic cancer and found a 23% prevalence of depression and 24% prevalence of adjustment disorder with depressed mood. Krouse and Krouse (27) found more severe depression (prevalence not cited) and poor body image among gynecologic patients as compared with women with breast cancer undergoing mastectomy. Golden and others (53) found a 23% rate of major depression in 83 hospitalized women with cervical, endometrial, and vaginal cancer.

### **Prevalence of Depression in Patients With Oropharyngeal Cancer**

In a study of 107 newly diagnosed head and neck cancer patients, Kugaya and colleagues (94) reported that 16.8% had major depression or an adjustment disorder and 33.6% met the criteria for alcohol dependence, 6.5% for alcohol abuse, and 32.7% for nicotine dependence. An association of advanced cancer stage and living alone with psychological distress was also found to be significant. Baile and colleagues (57) found that alcohol use was prevalent in patients with both benign and malignant head and neck lesions.

In a study of negative and positive influences of social support on depression in patients with head and neck cancer, de Leeuw and colleagues (92) found that the availability of support led to fewer depressive symptoms, but the effect of received support was equivocal. In another report, de Leeuw and colleagues (102) assessed the predictive values of numerous pretreatment variables. Tumor stage, sex, depressive symptoms, openness to discuss cancer in the family, available support, received emotional support, tumor-related symptoms, and size of an informal social network were calculated 6 months to 3 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 3 years after treatment.

In a study of 18 head and neck cancer patients, Hutton and Williams (103) found that the degree of depression and distress decreased with increasing age. Hammerlid and colleagues (87) studied 357 head and neck cancer patients and found that patients who reported a higher level of mental distress and frequently scored as a possible or probable case of psychiatric disorder were patients who had lower performance status and more advanced disease.

## Prevalence of Depression in Patients With Lung Cancer

In a study of depression and anxiety in 129 lung cancer patients, before and after diagnosis, Montazeri and colleagues (86) found that 10% of patients had severe anxiety symptoms and 12% had symptoms of depression at first presentation to their chest physician. Depression, but not anxiety, increased by 10% at follow-up. Hopwood and Stephens (93) 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 more prevalent in patients with small cell lung cancer than those with non-small cell lung cancer (NSCLC).

In a study of 129 newly diagnosed NSCLC patients, using a clinical interview that generated a DSM-III diagnosis, Akechi and colleagues (98) reported a high prevalence of psychiatric disorders. The most common psychiatric disorder at baseline was nicotine dependence (67%), followed by adjustment disorders (14%), alcohol dependence (13%), and major depression (5%).

Kramer (88) used HADS as an assessment measure and reported that 50% of his sample of 60 patients with inoperable lung cancer were borderline depressed and 37% were depressed. Buccheri (84) reported that depressed lung cancer patients had a significantly lower rate of survival.

**Prevalence of depression in patients undergoing stem-cell transplantation.** Grassi and colleagues (77) studied 44 cancer inpatients with solid tumors undergoing autologous bone marrow transplant and found that depression and anxiety at the time of admission to the hospital and days spent in isolation were the best predictors of depression after the bone marrow transplant.

Loberiza and colleagues (113) prospectively studied 193 adults who received autologous or allogenic hematopoietic stem-cell transplantation, using the SF-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 used. Thirty-five percent ( $N = 65$ ) of the patients studied satisfied the authors' criteria for depressive syndrome. The authors reported that depressive symptoms among patients who have undergone stem-cell transplantation were associated with high mortality in the 6- to 12-month period after transplantation.

**Prevalence of depression in patients with lymphoma, pancreatic, gastric, and colon cancer.** There are fewer studies of

**Table 6.** Prevalence of depression in gastric cancer patients\*

Source	N	Prevalence, %	Assessment
Holland, 1986 (38)	111	MDNC 21 median POMS	POMS
Joffe, 1986 (39)	9	0% MD 11% MD + Adj Dis	SADS-L, SCL-90-R, BDI, STAI, RDC criteria

\*Adj Dis = adjustment disorder; MD = major depression; MDNC = major depression not cited; POMS = The Profile of Mood States; SADS-L = Schedule for Affective Disorder and Schizophrenia and Lifetime; SCL-90-R = Hopkins Symptom Checklist 90-Revised; BDI = Beck Depression Inventory; STAI = State-Trait Anxiety Inventory; RDC = Research Diagnostic Criteria.

the prevalence of depression in adults with lymphoma, pancreatic cancer (Table 5), gastric cancer (Table 6), and colon cancer. Wide ranges in the reported prevalence of depression are noted, but in general, patients with lymphoma, gastric cancer, or colon cancer have a less high prevalence of depression than those with pancreatic cancer. The high prevalence of depression in patients with pancreatic cancer is believed to be related to underlying biologic mechanisms.

## Prevalence of Depression in Terminally Ill Patients

The reported prevalence of depression in patients with advanced cancer varies widely. Bukberg and colleagues (7) found that greater physical disability measured by the Karnofsky Rating Scale (the lower the score, the greater the disability) was associated with depression in their study of 62 patients with cancer. They found a 42% overall prevalence of depression, but a range of from 23% (in those with Karnofsky scores greater than 60) to 77% (in those with Karnofsky scores less than 40).

In the last 10 years, studies reporting the prevalence of depression in the terminally ill have ranged from 12.2% to 26%. In a study of 410 terminally ill cancer patients, De Walden-Galuszko (76) found 37% psychological morbidity, 18% of the 37% resulting from adjustment disorders (Table 7). Regardless of instrumentation (a single-item interview to DSM-III-R criteria), the prevalence of depression in the terminally ill falls within the range of the prevalence of depression in the general cancer population.

In a recent study, Chochinov and colleagues (114) found that depression among terminally ill cancer patients is three times

**Table 5.** Prevalence of depression in pancreatic cancer patients\*

Source	N	Prevalence, %	Assessment
Fras, 1967 (20)	110	50%	Semi-structured interview, MMPI
Holland, 1986 (38)	107	MDNC 38 median POMS	POMS
Joffe, 1986 (39)	12	33% MD 50% MD + Adj Dis	SADS-L, SCL-90-R, BDI, STAI RDC criteria

\*Adj Dis = adjustment disorder; MMPI = Minnesota Multiphasic Personality Inventory; MD = major depression; MDNC = major depression not cited; POMS = The Profile of Mood States; SADS-L = Schedule for Affective Disorder and Schizophrenia and Lifetime; SCL-90-R = Hopkins Symptom Checklist 90-Revised; BDI = Beck Depression Inventory; STAI = State-Trait Anxiety Inventory; RDC = Research Diagnostic Criteria.

**Table 7.** Prevalence of depression in terminally ill cancer patients\*

Source	N	Prevalence, %	Assessment
Power, 1993 (65)	98	26% (out of 81 patients) 34% cognitive impairment	DSM-III, AMTS
DeWalden-Galuszko, 1996 (76)	410	37% psychological disorders	Clinical interview with DM-III- R, WHO classification system
Breitbart, 2000 (90)	92	17% desire for hastened death	SAHD

\*AMTS = 10-question, Abbreviated Mental Test Score; DSM-III = *Diagnostic and Statistical Manual of Mental Disorders*, 3<sup>rd</sup> edition; DSM-III-R = *Diagnostic and Statistical Manual of Mental Disorders*, 3<sup>rd</sup> edition, revised; SAHD = Schedule of Attitudes Toward Hastened Death.



greater among patients who did not acknowledge their terminal prognosis. Breitbart and colleagues (90) found a 17% prevalence of depression and a 17% prevalence for a desire for hastened death in a study of 92 terminally ill cancer patients. Chochinov and colleagues (115) noted that hopelessness significantly contributed to the prediction of suicidal ideation in terminally ill cancer patients, even when the levels of depression were controlled.

### Prevalence of Depression in Children With Cancer

Although there are fewer studies of depression in children and adolescents with cancer, in the last decade several groups have made significant contributions to our understanding of this issue (Table 8). It is commonly reported that children with cancer are no more depressed than are healthy children (80).

Mulhern and colleagues (69) studied the severity of physical and depressive symptoms among 99 children with cancer (0.1–13 years from diagnosis) during a 6-week interval (evaluated at two time points: time 1 and 4–6 weeks later, to coincide with their clinic visit/treatment). Twenty-nine percent of the sample was black. Children were aged 8–16.8 years, with leukemia or solid tumors; all were in remission but were receiving treatment. Using the Children's Depression Inventory (CDI) and a modified CDI (excluding physical symptoms), the authors found that less than 10% of the children exhibited symptoms at or above the threshold for mild depression.

In their first report of their longitudinal study, Allen and colleagues (80) described their assessment of 42 adolescents (12–20 years of age) in the United Kingdom with various cancers (predominately sarcoma, followed by lymphoma, leukemia, and Wilms tumor) who completed the BDI and the State-Trait Anxiety Inventory on their first cancer outpatient visit (median time since diagnosis was 3 months). They found that adolescents with cancer were no more depressed (or anxious) than the control group (composed of 173 like-age students); girls in both groups were significantly more depressed than boys.

Using the CDI, Cavusoglu (100) studied children ages 9–13 years who were 1 or more years following initial cancer diagnosis (leukemia, lymphoma, sarcoma, retinoblastoma, and Wilms's tumor) and compared them with 50 healthy school children. Sixty-six percent of the children were in remission; 34% were being treated. Only 16% reported that they knew they had cancer; 62% could define (or point to) the location of the tumor. Twenty-two percent of the children with cancer had a score of 19 or higher on the depression scales; these scores were significantly higher than those of the healthy children. The children who stated they had cancer had higher depression scores.

**Table 8.** Prevalence of depression in children and adolescents with cancer\*

Source	N	Prevalence, %	Assessment
Mulhern, 1994 (69)	99	<10	CDI
Allen, 1997 (80)	42	38	BDI, STAI
Cavusoglu, 2001 (101)	50	22	CDI

\*CDI = Children's Depression Inventory; BDI = Beck Depression Inventory; STAI = State-Trait Anxiety Inventory.

## MARKERS AND CORRELATES OF DEPRESSION

### Prevalence of Depression in Cancer Patients Who Experience Pain

Consistent with the findings of the 1983 Psychosocial Collaborative Oncology Group study, Chen and colleagues (91) reported that the prevalence of anxiety and depression was significantly higher for Taiwanese cancer patients with pain than for those without pain. In another recent study, Ciaramella and Poli (101) assessed depression among cancer patients using the Structured Clinical Interview for DSM-III-R, Endicott criteria, and Hamilton Depression Rating Scale. They found that depressed patients had more pain and metastasis than nondepressed patients but that depressed patients did not have more lifetime depression than nondepressed patients. Age and sex did not have any influence on the assessment of major depression among the 100 cancer patients studied.

### Do Depressed Cancer Patients Receive Evaluation and Treatment?

Determining whether people who are found to be in need of further evaluation and treatment for depression receive it has been of interest to several groups. Payne and colleagues (116) evaluated 275 women with breast cancer attending ambulatory breast cancer clinics in two sites (New York City and Long Island, NY), using a visual analogue scale, HADS, and Brief Symptom Inventory. A subsegment of the sample was evaluated by use of the Structured Clinical Interview for DSM-III-R. The authors found that the patients at the cancer center most in need of psychiatric services had already been referred for evaluation. In contrast, Berard and colleagues (83) evaluated 456 outpatients with solid tumors (breast cancer, lymphoma, and head and neck cancer), using the HADS, BDI, and structured psychiatric interview, and found that only 14% of the patients identified as depressed had been identified and treated for depression. Using the HADS, Pascoe et al. (96) found that the majority of cancer patients with psychological distress were not receiving counseling or psychological treatment. All of these research groups addressed the need for routine screening for depression in oncology settings and for the implementation of cost-effective treatment for those who need psychiatric services.

## QUALITY OF LIFE

In a study predicting depression among male cancer patients, Godding and colleagues (72) reported that social support and quality of life accounted for 31.5% of the variance in Beck Depression Inventory scores. In another study, Grassi and colleagues (78) found significant correlation between depression scores and impairment in quality of life in advanced, home-care-assisted cancer patients.

### Biological Markers

Several groups have recently studied the association between psychosocial factors, endocrine function, immune function, and survival and mediation by immune mechanisms. Cohen and colleagues (117) examined the association between hormonal profiles before the start of cancer treatment and subsequent psychological symptomatology in 27 patients with renal cell



carcinoma and 18 patients with malignant melanoma. Patients were evaluated by Impact of Event Scale at three time points, and urine cortisol, norepinephrine, and epinephrine levels were measured at baseline. Both baseline cortisol and norepinephrine levels were positively associated with depression at follow-up. Sachs and colleagues (74) studied lymphokine-activated killer cell and natural killer cell activity in breast cancer patients before surgery and reported that lymphokine-activated killer cell activity is a state marker of existing depression before surgery.

### Other Factors Related to Morbidity and Depression in Cancer Patients

In a study of the psychiatric morbidity among cancer patients, Alexander and colleagues (61) reported that psychiatric morbidity was less common in patients unaware of their cancer or in those who considered their treatment as curative.

Aass and colleagues (79) reported that impaired social life, impaired professional work, and previous psychiatric problems were significantly correlated with depression, anxiety, physical function, fatigue, and pain in cancer patients. Depression, but not anxiety, increased in the presence of distant metastases, relapse, or progression and also increased when the diagnosis was made less than 1 month before assessment. They also found gender and age had no influence of the prevalence of depression.

In a recent study of 148 postoperative breast cancer patients undergoing no active cancer treatment except hormones, Akechi and colleagues (98) used the HADS and found that biomedical factors (disease stage, performance status, physical symptoms) were not significant determinants of psychiatric morbidity. In their study, family problems and coping responses were found to be more important.

### CONCLUSION

Depression is common in the general population and in adults and children with cancer and frequently coexists with anxiety and pain. Depression has been challenging to study because symptoms occur on a spectrum that ranges from sadness to major affective disorder and because mood change is often difficult to evaluate when a patient is confronted by repeated threats to life, is receiving cancer treatments, is fatigued, or is experiencing pain. Untreated depression results in significant morbidity and mortality. Although the reported prevalence of depression in more than 100 studies of cancer patients ranges from 0% to 58%, cancer, exclusive of site and stage of illness, is associated with a high degree of depression.

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 depression, characterizing the causative role of antineoplastics in depression, and identifying biological markers for depression.

### REFERENCES

- (1) Weissman MM, Bland R, Joyce PR, Newman S, Wells JE, Wittchen HU. Sex differences in rates of depression. Cross-national perspectives. *J Affect Disord* 1993;29:77–84.
- (2) Waslick BD, Kander R, Kakouros A. Depression in children and adolescents: an overview. In: Shaffer D, Waslick D, editors. *The many faces of depression in children and adolescents*. Washington (DC): American Psychiatric Publishing; 2002. p. 1–36.

- (3) Rushton JL, Forcier M, Schectman R. Epidemiology of depressive symptoms in the national longitudinal study of adolescent health. *J Am Acad Child Adolesc Psychiatry* 2002;41:199–205.
- (4) Grady-Weliky TA. Comorbidity and its implication on treatment: change over the life span. Syllabus and Proceedings Summary, American Psychiatric Association 2002 Annual Meeting. Philadelphia (PA) 2002. p. 295 (abstr 39B).
- (5) American Psychiatric Association. *Diagnostic and statistical manual of mental disorders*. 3rd ed. Washington (DC): American Psychiatric Association, 1980.
- (6) Derogatis LR, Morrow GR, Fetting J. The prevalence of psychiatric disorders among cancer patients. *JAMA* 1983;249:751–7.
- (7) Bukberg J, Penman D, Holland JC. Depression in hospitalized cancer patients. *Psychosom Med* 1984;46:199–212.
- (8) Plumb M, Holland JC. Comparative studies of psychological function in patients with advanced cancer. 1. Self-reported depressive symptoms. *Psychosom Med* 1977;39:264–76.
- (9) Massie MJ, Popkin MK. Depressive disorders. In: Holland, JC, editor. *Psycho-oncology*. New York (NY): Oxford University Press; 1998. p. 518–40.
- (10) Wallen J, Pincus HA, Goldman HH, Marcus SE. Psychiatric consultations in short-term general hospitals. *Arch Gen Psychiatry* 1987;44:163–8.
- (11) Snyder S, Strain JJ, Wolf D. Differentiating major depression from adjustment disorder with depressed mood in the medical setting. *Gen Hosp Psychiatry* 1990;12:159–65.
- (12) Wells KB, Golding JM, Burham MA. Psychiatric disorder in a sample of the general population with and without chronic medical conditions. *Am J Psychiatry* 1988;145:976–81.
- (13) Popkin MK, Tucker GJ. Mental disorders due to a general medical condition and substance-induced disorders; mood anxiety, psychotic, and personality disorders. *DSM-IV sourcebook*. Washington (DC): APA Office of Research; 1994. p. 243–76.
- (13a) Trask, PC. Assessment of depression in cancer patients. *J Natl Cancer Inst Monogr* 2004;32:80–92.
- (14) Hinton JM. The psychiatry of terminal illness in adults and children. *Proc R Soc Med* 1972;65:1035–40.
- (15) Levine PM, Silberfarb PM, Lipowski ZJ. Mental disorders in cancer patients. *Cancer* 1978;42:1385–91.
- (16) Massie MJ, Gorzynski JG, Mastrovito R, Theis D, Holland JC. Proceedings of the AARC and the American Society of Clinical Oncology. The diagnosis of depression in hospitalized patients with cancer. *Proc Am Soc Clin Oncol* 1979;20:432 (abstr).
- (17) Massie MJ, Holland JC. Consultation and liaison issues in cancer care. *Psychiatr Med* 1987;5:343–59.
- (18) Razavi D, Delvaux N, Farvacques C, Robaye E. Screening for adjustment disorders and major depressive disorders in cancer in-patients. *Br J Psychiatry* 1990;156:79–83.
- (19) Watson M, Haviland JS, Greer S, Davidson J, Bliss JM. Influence of psychological response on survival in breast cancer: a population-based cohort study. *Lancet* 1999;354:1331–6.
- (20) Fris I, Litin Em, Pearson JS. Comparison of psychiatric symptoms in carcinoma of the pancreas with those in some other intra-abdominal neoplasm. *Am J Psychiatry* 1967;123:1553–62.
- (21) Koenig R, Levin S, Brennan MJ. The emotional status of cancer patients as measured by a psychological test. *J Chronic Dis* 1967;20:923–30.
- (22) Peck A, Boland L. Emotional reactions to having cancer. *Am Roentgenol Radia Ther Nucl Med* 1972;114:591–9.
- (23) Craig TJ, Abeloff MD. Psychiatric symptomatology among hospitalized cancer patients. *Am J Psychiatry* 1974;131:1323–7.
- (24) Morris T, Greer HS, White P. Psychological and social adjustment to mastectomy. *Cancer* 1977;40:2381.
- (25) Maguire GP, Lee E, Bevington D, Kuchman C, Crabtree R, Cornell C. Psychiatric problems in the first year after mastectomy. *BMJ* 1978;1: 963–5.
- (26) Silberfarb PM, Maurer LH, Crouthamel CS. Psychological aspects of neoplastic disease: I. Functional status of breast cancer patients during different treatment regimens. *Am J Psychiatry* 1980;137:450–5.
- (27) Krouse HJ, Krouse JH. Psychological factors in post-mastectomy adjustment. *Psychol Rep* 1981;48:275–8.

- (28) Plumb M, Holland J. Comparative studies of psychological function in patients with advanced cancer. II. Interviewer-rated current and past psychological symptoms. *Psychosom Med* 1981;43:243–54.
- (29) Farber JM, Weinerman BH, Kuypers JA. Psychosocial distress in oncology outpatients. *J Psychosoc Oncol* 1984;2:109–18.
- (30) Lloyd GG, Parker AC, Ludlam CA, McGuire RJ. Emotional impact of diagnosis and early treatment of lymphomas. *J Psychosom Res* 1984;28:157–62.
- (31) Morton RP, Davies ADM, Baker J, Baker GA, Stell PM. Quality of life in treated head and neck cancer patients: a preliminary report. *Clin Otolaryngol* 1984;9:181–5.
- (32) Hughes JE. Depressive illness and lung cancer. I. Depression before diagnosis. *Eur J Surg Oncol* 1985;11:15–20.
- (33) Lansky SB, List MA, Herrmann CA, Ets-Hokin ED, DasGupta TK, Wilbanks GD, Hendrickson RF. Absence of major depressive disorder in female cancer patients. *J Clin Oncol* 1985;3:1553–60.
- (34) Robinson JK, Boshier ML, Dansak DA. Depression and anxiety in cancer patients: evidence for different causes. *J Psychosom Res* 1985;29:133–8.
- (35) Starkman M, Zelnik T, Nesse R. Anxiety in patients with pheochromocytomas. *Arch Intern Med* 1985;145:248–52.
- (36) Davies ADM, Davies C, Delpo MC. Depression and anxiety in patients undergoing diagnostic investigations for head and neck cancers. *Br J Psychiatry* 1986;149:491–3.
- (37) Evans DL, McCartney CF, Nemeroff CB, Raft D, Quade D, Golden RN, et al. Depression in women treated for gynecological cancer: clinical and neuroendocrine assessment. *Am J Psychiatry* 1986;143:447–51.
- (38) Holland JC, Korzan AH, Tross S, Silberfarb P, Perry M, Corris R, et al. Comparative psychological disturbance in patients with pancreatic and gastric cancer. *Am J Psychiatry* 1986;143:982–6.
- (39) Joffe RT, Rubinow DR, Denicoff KD, Maher M, Sindelar WF. Depression and carcinoma of the pancreas. *Gen Hosp Psychiatry* 1986;8:241–5.
- (40) Devlen J, Maguire P, Phillips P, Crowther D, Chambers H. Psychological problems associated with diagnosis and treatment of lymphomas. I: Retrospective study. *BMJ* 1987;295:953–4.
- (41) Devlen J, Maguire P, Phillips P, Crowther D. Psychological problems associated with diagnosis and treatment of lymphoma. II: Prospective study. *BMJ* 1987;295:955–7.
- (42) Freidrich WN, Smith CK, Harrison SD, Colwell KA, Davis AK, Fefer A. MMPI study of identical twins: cancer patients and bone marrow donors. *Psychol Rep* 1987;61:127–130.
- (43) Larys JCM, Margolese RG, Poisson R, Shibata H, Fleischer D, Lafleur D, et al. Depression and body image following mastectomy and lumpectomy. *J Chronic Dis* 1987;40:529–34.
- (44) Grandi S, Fava GA, Cunsolo A, Gozzetti G, Trombini G. Major depression associated with mastectomy. *Med Sci Res* 1987;15:283–4.
- (45) Stefanek ME, Derogatis LP, Shaw A. Psychological distress among oncology outpatients. *Psychosomatics* 1987;28:530–9.
- (46) Pettingale KW, Burgess C, Greer S. Psychological response to cancer diagnosis-I. Correlations with prognostic variables. *J Psychosom Res* 1987;32:255–61.
- (47) Grassi L, Rosti G, Albieri G, Marangolo M. Depression and abnormal illness behavior in cancer patients. *Gen Hosp Psychiatry* 1989;11:404–11.
- (48) Hardman A, Maguire P, Crowther D. The recognition of psychiatric morbidity on a medical oncology ward. *J Psychosom Res* 1989;33:235–9.
- (49) Meyer L, Aspergren K. Long-term psychological sequelae of mastectomy and breast conserving treatment for breast cancer. *Acta Oncol* 1989;28:13–8.
- (50) Fallowfield LJ, Hall A, Maguire GP, Baum M. Psychological outcomes of different treatment policies in women with early breast cancer outside of a clinical trial. *BMJ* 1990;301:575–80.
- (51) Kathol R, Mutgi A, Williams J, Clamong G, Noyes R Jr. Diagnosis of major depression according to four sets of criteria. *Am J Psychiatry* 1990;147:1021–4.
- (52) Colon EA, Callies AL, Popkin MK, McGlave PB. Depressed mood and other variables related to bone marrow transplantation survival in acute leukemia. *Psychosomatics* 1991;32:420–5.
- (53) Golden RN, McCartney CF, Haggerty JJ, Raft D, Nemeroff CB, Ekstrom D, et al. The detection of depression by patient self-report in women with gynecologic cancer. *Int J Psychiatry Med* 1991;21:17–27.
- (54) Hopwood P, Howell A, Maguire P. Screening for psychiatric morbidity in patients with advanced breast cancer: validation of two self-report questionnaires. *Br J Cancer* 1991;64:353–6.
- (55) Hopwood P, Howell A, Maguire P. Psychiatric morbidity in patients with advanced cancer of the breast: prevalence measured to two self-rating questionnaires. *Br J Cancer* 1991;64:349–52.
- (56) Jenkins PL, May VE, Hughes LE. Psychological morbidity associate with local recurrence of breast cancer. *Int J Psychiatry Med* 1991;21:149–55.
- (57) Baile WF, Gilbertini M, Scott L, Endicott J. Depression and tumor state in cancer of the head and neck. *Psychooncology* 1992;1:15–24.
- (58) Goldberg JA, Scott RN, Davidson PM. Psychological morbidity in the first year after breast surgery. *Eur J Surg Oncol* 1992;18:327–31.
- (59) Maraste R, Brandt L, Olson H, Ryde-Brandt B. Anxiety and depression in breast cancer patients at start of adjuvant radiotherapy. *Acta Oncol* 1992;31:641–3.
- (60) Sneed NV, Edlund B, Dias JK. Adjustment of gynecological and breast cancer patients to the cancer diagnosis: comparisons with males and females have other cancer sites. *Health Care Women Int* 1992;13:11–22.
- (61) Alexander PJ, Dinesh N, Vidyasagar MS. Psychiatric morbidity among cancer patients and its relationship with awareness of illness and expectations about treatment outcome. *Acta Oncol* 1993;32:623–6.
- (62) Carroll BT, Kathol RG, Noyes R, Wald TG, Clamon GH. Screening for depression and anxiety in cancer patients using the hospital anxiety and depression scale. *Gen Hosp Psychiatry* 1993;15:69–74.
- (63) Cathcart CK, Jones SE, Pumroy CS, Peters GN, Knox SM, Cheek JH. Clinical recognition and management of depression in node negative breast cancer patients treated with tamoxifen. *Breast Cancer Res Treat* 1993;27:277–81.
- (64) Pinder KL, Ramirez AJ, Black ME. Psychiatric disorder in patients with advanced breast cancer: prevalence and associated factors. *Eur J Cancer* 1993;29A:524–7.
- (65) Power D, Kelly S, Gilsean J, Kearney M, O'Mahony D, Walsh JB, et al. Suitable screening tests for the cognitive impairment and depression in the terminally ill—a prospective prevalence study. *Palliat Med* 1993;7:213–8.
- (66) Rapaport Y, Kreitler S, Chaitchik S, Alfor R, Weissler K. Psychosocial problems in head and neck cancer patients and their change with time since diagnosis. *Ann Oncol* 1993;4:69–73.
- (67) Sneeuw KCA, Aaronson NK, van Wouwe MCC, Sergeant JA, van Dongen JA, Bartelink H. Prevalence and screening of psychiatric disorder in patients with early stage breast cancer. Paper presented at the International Congress of Psychosocial Oncology, October 12–14, 1992, Beaune, France. *Qual Life Res* 1993;2:50–51 (abstr).
- (68) Middleboe T, Ovesen L, Mortensen EL, Bech P. Depressive symptoms in cancer patients undergoing chemotherapy: a psychometric analysis. *Psychother Psychosom* 1994;61:171–7.
- (69) Mulhern RK, Fairclough D, Douglas SM, Smith B. Physical distress and depressive symptomatology among children with cancer. *Children's Health Care* 1994;23:167–79.
- (70) Angelopoulos NV, Tzivariadou D, Nikolaou N, Pavlidis AN. Mental symptoms, hostility features and stressful life events in people with cancer. *Acta Psychiatrica Scandinavica* 1995;92:44–50.
- (71) Ginsberg ML, Quirt C, Ginsburg AD, MacKillop WJ. Psychiatric illness and psychosocial concerns of patients with newly diagnosed lung cancer. *Can Med Assoc J* 1995; 152:701–8.
- (72) Godding PR, McNulty RD, Wittrock DA, Britt DM, Khansur T. Predictors of depression among male cancer patients. *J Nerv Ment Dis* 1995;183:95–8.
- (73) Kelsen DP, Portenoy RK, Thaler HT, Niedzwiecki D, Passik SD, Tao Y, Banks W, Brennan MF, Foley KM. Pain and depression in patients with newly diagnosed pancreas cancer. *J Clin Oncol* 1995;13:748–55.
- (74) Sachs G, Rasoul-Rockenschaub S, Aschauer H, Spiess K, Göber I, Staffeijn A, et al. Lytic effector cell activity and major depressive disorder in patients with breast cancer: a prospective study. *J Neuroimmunol* 1995;59:83–9.
- (75) Aragona M, Muscatello MRA, Mesiti M. Prevalence of depressive mood disorders in breast cancer patients in southern Italy. *Ann NY Acad Sci* 1996;784:482–5.
- (76) DeWalden-Galuszko K. Prevalence of psychological morbidity in terminally-ill cancer patient. *Psychooncology* 1996;5:45–9.

- (77) Grassi L, Rosti G, Albertazzi L, Marangolo M. Depressive symptoms in autologous bone marrow transplant (ABMT) patients with cancer: an exploratory study. *Psychooncology* 1996;5:305–10.
- (78) Grassi L, Indelli M, Marzola M, Maestri A, Santini A, Piva E, et al. Depressive symptoms and quality of life in home-care-assisted cancer patients. *J Pain Symptom Manage* 1996;12:300–7.
- (79) Aass N, Fossa SD, Dahl AA, Moe TJ. Prevalence of anxiety and depression in cancer patients seen at the Norwegian Radium Hospital. *Eur J Cancer* 1997;33:1597–1604.
- (80) Allen R, Newman SP, Souhami RL. Anxiety and depression in adolescent cancer: findings patients and parents at the time of diagnosis. *Eur J Cancer* 1997;33:1250–5.
- (81) Chochinov HM, Wilson KG, Enns M, Lander S. “Are you depressed?” Screening for depression in the terminally ill. *Am J Psychiatry* 1997;154:674–6.
- (82) Pasacreta N. Depressive phenomena, physical symptom distress, and functional status among women with breast cancer. *Nurs Res* 1997;46:214–21.
- (83) Berard RMF, Boermeester F, Viljoen G. Depressive disorders in an out-patient oncology setting: prevalence, assessment and management. *Psychooncology* 1998;7:112–20.
- (84) Buccheri G. Depressive reactions to lung cancer are common and often followed by a poor outcome. *Eur Respir J* 1998;11:173–8.
- (85) Kissane DW, Clarke DM, Ikin J, Bloch S, Smith GC, Vitetta L, et al. Psychological morbidity and quality of life in Australian women with early-stage breast cancer: a cross-sectional survey. *Med J Aust* 1998;169:192–6.
- (86) Montazeri A, Milroy R, Hole D, McEwen J, Gillis C. Anxiety and depression in patients with lung cancer before and after diagnosis: findings from a population in Glasgow, Scotland. *J Epidemiol Community Health* 1998;52:203–4.
- (87) Hammerlid E, Ahiner-Elmqvist M, Björklund K, Björklund A, Evensen J, Boysen M, et al. A prospective multicentre study in Sweden and Norway of mental distress and psychiatric morbidity in head and neck cancer patients. *Br J Cancer* 1999;80:766–74.
- (88) Kramer JA. Use of the Hospital Anxiety and Depression Scale (HADS) in the assessment of depression in patients with inoperable lung cancer. *Palliat Med* 1999;13:353–4.
- (89) Bodurka-Bevers D, Basen-Engquist K, Carmack CL, Fitzgerald MA, Wolf JK, de Moor C, et al. Depression, anxiety, and quality of life in patients with epithelial ovarian cancer. *Gynecol Oncol* 2000;78:302–8.
- (90) Brietbart W, Rosenfeld B, Pessin H, Kaim M, Funesti-Esch J, Galiotta M, et al. Depression, hopelessness, and the desire for hastened death in terminally ill patients with cancer. *JAMA* 2000;284:2907–11.
- (91) Chen M, Chang H, Yeh C. Anxiety and depression in Taiwanese cancer patients with and without pain. *J Adv Nurs* 2000;32:944–51.
- (92) De Leeuw JRJ, de Graeff A, Ros WJG, Hordijk GJ, Blijham GH, Winnubst JAM. Negative and positive influences of social support on depression in patients with head and neck cancer: a prospective study. *Psychooncology* 2000;9:20–8.
- (93) Hopwood P, Stephens RJ. Depression in patients with lung cancer: prevalence and risk factors derived from quality-of-life data. *J Clin Oncol* 2000;18:893–903.
- (94) Kugaya A, Akechi T, Okuyama T, Nakano T, Mikami I, Okamura H, et al. Prevalence, predictive factors, and screening for psychologic distress in patients with newly diagnosed head and neck cancer. *Cancer* 2000;88:2817–23.
- (95) Okamura H, Watanabe T, Narabayashi M, Katsumata N, Ando M, Adachi I, et al. Psychological distress following first recurrence of disease in patients with breast cancer: prevalence and risk factors. *Breast Cancer Research and Treatment* 2000;61:131–7.
- (96) Pascoe S, Edelman S, Kidman A. Prevalence of psychological distress and use of support services by cancer patients at Sydney hospitals. *Aust N Z J Psychiatry* 2000;34:785–91.
- (97) Skarstein J, Aass N, Fossa SD, Skovlund E, Dahl AA. Anxiety and depression in cancer patients: relation between the Hospital Anxiety and Depression Scale and the European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire. *J Psychosom Res* 2000;49:27–34.
- (98) Akechi T, Okuyama T, Imoyo S, Yamawaki S, Uchitomi Y. Biomedical and psychosocial determinants of psychiatric morbidity among postoperative ambulatory breast cancer patients. *Breast Cancer Res Treat* 2001;65:195–202.
- (99) Akechi T, Okamura H, Nishiwaki Y, Uchitomi Y. Psychiatric disorders and associated and predictive factors in patients with unresectable non-small-cell lung carcinoma. *Cancer* 2001;92:2609–22.
- (100) Cavusoglu H. Depression in children with cancer. *J Pediatr Nurs* 2001;16:380–5.
- (101) Ciaramella A, Poli P. Assessment of depression among cancer patients: the role of pain, cancer type and treatment. *Psychooncology* 2001;10:156–65.
- (102) De Leeuw JRJ, de Graeff A, Ros WJG, Blijham GH, Hordijk G, Winnubst JAM. Prediction of depression 6 months to 3 years after treatment of head and neck cancer. *Head Neck* 2001;23:892–8.
- (103) Hutton JM, Williams M. An investigation of psychological distress in patients who have been treated for head and neck cancer. *Br J Oral Maxillofac Surg* 2001;39:333–9.
- (104) Montazeri A, Jarvandi S, Haghighat S, Vahdani M, Sajadian A, Ebrahimi M, et al. Anxiety and depression in breast cancer patients before and after participation in a cancer support group. *Patient Educ Couns* 2001;45:195–8.
- (104a) Lawrence DP, Kupelnick B, Miller K, Devine D, Lau J. Evidence report on the treatment of pain in cancer patients. *J Natl Cancer Inst Monogr* 2004;32:40–50.
- (105) Newport DJ, Nemeroff CB. Assessment and treatment of depression in the cancer patient. *J Psychosom Res* 1998;45:215–37.
- (106) McDaniel JS, Musselman DL, Porter MR, Reed DA, Nemeroff CB. Depression in patients with cancer. *Arch Gen Psychiatry* 1995;52:89–99.
- (107) McDaniel SJ, Nemeroff CB. Depression in the cancer patient: diagnostic, biological, and treatment aspects. In: Chapman CR, Foley KM, editors. *Current and emerging issues in cancer pain: research and practice*. New York (NY): Raven Press; 1993. p. 1–19.
- (108) Van’t Spijker A, Trijsburg RW, Duivenvoorden HJ. Psychological sequelae of cancer diagnosis: a meta-analytical review of 58 studies after 1980. *Psychosom Med* 1997;59:280–93.
- (109) DeFlorio ML, Massie MJ. Review of depression in cancer: gender differences. *Depression* 1995;3:66–80.
- (110) Fife BL, Kennedy VN, Robinson L. Gender and adjustment to cancer: clinical applications. *J Psychosocial Oncol* 1994;12:1–21.
- (111) Aapro M, Cull A. Depression in breast cancer patients: the need for treatment. *Ann Oncol* 1999;10:627–36.
- (112) Fallowfield L, Fleissig A, Edwards R, West A, Powles TJ, Howell A, et al. Tamoxifen for the prevention of breast cancer: psychosocial impact on women participating in two randomized controlled trials. *J Clin Oncol* 2001;19:1885–92.
- (113) Loberiza Jr, FR, Rizzo JD, Bredeson CN, Antin JH, Horowitz MM, Weeks JC, et al. Association of depressive syndrome and early deaths among patients after stem-cell transplantation for malignant diseases. *J Clin Oncol* 2002;20:2118–26.
- (114) Chochinov HM, Tataryn DJ, Wilson KG, Ennis M, Lander S. Prognostic awareness and the terminally ill. *Psychosomatics* 2000;41:500–4.
- (115) Chochinov HM, Wilson KG, Enns M, Lander S. Depression, hopelessness, and suicidal ideation in the terminally ill. *Psychosomatics* 1998;39:366–70.
- (116) Payne DK, Hoffman RG, Theodoulou M, Dosik M, Massie MJ. Screening for anxiety and depression in women with breast cancer. *Psychosomatics* 1999;40:64–9.
- (117) Cohen L, de Moor C, Devine D, Baum A, Amato R. Endocrine levels at the start of treatment are associated with subsequent psychological adjustment in cancer patients with metastatic disease. *Psychosom Med* 2001;63:951–8.

## NOTE

The author thanks Elaine Bernstein, Theresa Carpenter, Alex Pisani, and Isabel Sulimanoff for their assistance with the preparation of this manuscript and William E. Pelton and Sylvia Rosenberg for their continued generous support of her work.