Prevalence and Correlates of Depression Among Patients With Head and Neck Cancer: A Systematic Review of Implications for Research

Mary Ellen Haisfield-Wolfe, PhD, RN, OCN®, Deborah B. McGuire, PhD, RN, FAAN, Karen Soeken, PhD, Jeanne Geiger-Brown, PhD, RN, and Bruce R. De Forge, PhD

Head and neck cancer is a collective term defined on an anatomic-topographic basis to describe malignant tumors of the upper aerodigestive tract. Cancers of the head and neck include lip, oral cavity, pharynx, nasal cavity, paranasal sinuses, larynx, thyroid gland, and salivary gland. Worldwide, head and neck cancer is the eighth most common cause of cancer death (Choong & Vokes, 2008). In North America and Europe, head and neck cancer accounts for 3%–4% of all cancer diagnoses (Ferlay et al., 2007; Jemal et al., 2007). More than 90% of head and neck cancers are squamous cell carcinoma in origin and about 50% occur in the oral cavity (Carr, 2005). Epidemiologic and molecular studies have identified high-risk types of human papillomavirus (HPV) in patients with no common risk factors for head and neck cancer (Haddad, 2007), which suggests HPV is a new etiologic factor in squamous cell carcinoma. HPV-related head and neck cancers are associated with a higher proportion of men, younger age groups, and a more advanced stage at initial presentation (Haddad).

Head and neck cancer is a complex and distressing disease with high mortality and morbidity because of disease and treatment factors that affect vital function, such as eating, breathing, and communicating. Depression often is present for patients with head and neck cancer throughout the course of their cancer experience.

Researchers to date have examined depression in clinical populations at different points in the cancer trajectory but have not specifically focused on head and neck cancer. However, they have studied depression related to cancer from a variety of anatomic sites and used different instruments to measure depression. The purpose of this systematic review is to present a comprehensive summary of existing research literature related to the prevalence and correlates of depression in adult patients with head and neck cancer to establish a knowledge base for future research.

Purpose/Objectives: To present a comprehensive summary of the existing research literature related to prevalence and correlates of depression in adult patients with head and neck cancer to establish a knowledge base for future research.

Data Sources: Quantitative studies in English measuring depression or mood in adults with head and neck cancer published from 1986–2008.

Data Synthesis: A substantial body of knowledge exists regarding prevalence, correlates, and predictors of depression in patients with head and neck cancer. Prevalence rates of depression are high at diagnosis, during treatment, and in the first six months following treatment, and mild to moderate depression may continue for three to six years after diagnosis. Certain patient demographic characteristics (e.g., marital status, education), symptoms, and specific time points in the illness trajectory (e.g., time of treatment) are correlated with depression. Specific patient variables at diagnosis, such as depression, can predict depression at later time points.

Conclusions: Additional research should assess symptoms using consistent depression instruments or clinical interviews based on specific criteria in patients with head and neck cancer. Specifically, multisite studies should be conducted to increase sample sizes. Research related to symptom clusters and the effect of clusters on patients is needed. Longitudinal studies that examine depression and patient characteristics, symptoms, type of treatments, and the correlates of depression across the trajectory of illness are important. Replication of existing research using multiple patient and clinical characteristics to explore predictors of depression may reveal profiles for patients most at risk.

Implications for Nursing: This comprehensive summary of existing research literature related to the prevalence and correlates of depression among adult patients with head and neck cancer provides evidence-based information that can be used by oncology nurses in their practice.

Definition of Depression

Depression is a major mood disorder that is not a unitary phenomenon but exists on a continuum of emotional response ranging from minor mood changes such as feeling sad, helpless, or demoralized (McDowell, 2006) to a major depressive disorder. Given this continuum, a clear definition of depression was essential to this review. As a mood disorder, depression consists of a cluster of symptoms that represent a marked departure from a person's habitual functioning (Sadock & Sadock, 2003). The *Diagnostic and Statistical Manual of Mental Disorders* (American Psychiatric Association [APA], 2005) defined the criteria for clinical diagnosis of major depression. First, the symptoms of major depression must be present for at least two consecutive weeks. Second, the person must exhibit five or more symptoms that include either depressed mood or loss of interest and/or pleasure. Other symptoms may include significant weight loss or gain, appetite disturbance, insomnia or hypersomnia, psychomotor agitation or retardation, fatigue or loss of energy, feelings of worthlessness, inappropriate guilt, impaired concentration, or recurrent suicidal ideas or suicide attempt. Third, symptoms must be newly present or must clearly worsen as compared with the person's pre-episode status. Finally, the episode must be accompanied by clinically significant distress or impairment in social, occupational, or other important areas of functioning. A proportion of cases evaluated for major depression (20%–30%) have some depressive symptoms but do not meet all criteria for major depressive disorder.

The many scales available to measure depression reflect the divergent approaches to conceptualizing the construct of depression. No one symptom is clinically diagnostic of depression; instead, depression is a syndrome identified by its many symptoms. The conceptualization of depression includes two major paradigms: the general phenomenon of depressive symptoms and specific psychiatric disorders. The general medical health professional tends to conceptualize depression according to depressive symptoms, whereas the mental health specialist conceptualizes depression according to a psychiatric diagnosis (Wells, 1998). Researchers who study depression may reflect either one of these two views. In selecting studies for this review, the authors included only studies that used a depression instrument or an interview using the *Diagnostic and Statistical Manual* criteria to identify depression. The term depression is used in this review to denote a variable in a research study that reaches an identified cutoff score on a depression or mood instrument, the presence of a significant number of depressive symptoms, or a diagnosis of depression by a trained individual during an interview using the *Diagnostic and Statistical Manual* criteria. Most researchers in the studies reviewed for this article used self-report depression instruments with a cutoff score to identify depression rather than an interview and mental disorder diagnosis based on *Diagnostic and Statistical Manual* criteria.

Selection of Studies for the Review

A combined computerized and search of medical (MEDLINE®, 1950–2008), health and psychosocial (HAPI, 1985–2008; PsycINFO, 1990–2008), and nursing (CINAHL®, 1992–2008) literature focused on the following terms: *head and neck cancer* paired with *depression, depressive symptoms, psychological distress,* and *distress.* The broad timeframe that was used ensured identification of the vast majority of existing studies. Articles in languages other than English, published abstracts without full articles, qualitative studies, and unpublished dissertations were excluded. The search resulted in 137 articles, which were narrowed down to 52 articles by selecting only descriptive studies that included a depression or mood measurement or a diagnostic interview.

This systematic review included 20 studies in which depression was the main variable and 32 studies in which depression and quality of life were the main variables. The study of depression among patients with head and neck cancer has increased, with 20 articles published from 1984–2000 and 32 articles published since 2001. Table 1 presents the first author, country of origin, publication year, depression measure, and sample characteristics of the studies reviewed. Thirty-eight studies were from countries other than the United States. Nineteen studies had a sample size greater than 100. The majority of patients were men older than 50 years. Race usually was not reported in studies conducted outside the United States. In the studies reviewed, the sites of head and neck cancer included as many as eight anatomic locations. Thirteen studies did not include disease stage, but patients with both early- and late-stage cancer were reported in the majority of studies. The most frequent depression instruments used were Hospital Anxiety and Depression Scale (HADS) (17 studies), Center for Epidemiologic Studies–Depression Scale (CES-D) (15 studies), and Beck Depression Inventory (BDI) (10 studies).

Prevalence of Depression

For this review, prevalence was defined as the number of people with a condition or a disease divided by the total number of people at risk for the condition or disease (Polit & Beck, 2006). Samples from clinical studies rather than population-based samples were used to examine prevalence because epidemiologic studies of depression in head and neck cancer populations are

Table 1. Descriptive Characteristics of Studies Included in the Systematic Review

Study	Country	Design	Measure (Cutoff Score)	Sample	Cancer Site	Disease Stage
Aarstad et al., 2005	Norway	Descriptive, comparison	BDI (more than 7)	79 hospitalized men; race not reported; $\bar{X}$ age = 58 years	32% oral, 23% pharynx, 44% larynx	5% Tis/Tx, 29% stage 1, 32% stage 2, 10% stage 3, 24% stage 4
Baile et al., 1992	United States	Descriptive, cross-sectional	MCMI (75 or more)	45 outpatients; 57% men; 99% Caucasian; age not reported	43% oral or oropharynx, 6% nasopharynx, 9% larynx, 6% salivary gland, 36% other	28% stage 0–1, 23% stage 2, 14% stage 3, 35% stage 4
Braz et al., 2005	Brazil	Descriptive, retrospective	BDI (16 or more)	30 outpatients; 90% men; race not reported; $\bar{X}$ age = 62 years	100% larynx	Not reported
Chawla et al., 1999	India	Descriptive, prospective	BDI-13; BDI-21 (14 or more)	50 outpatient men; race not reported; $\bar{X}$ age = 51 years	22% oral, 14% nasopharynx, 46% oropharynx, 4% hypopharynx, 14% larynx	6% stage 1, 20% stage 2, 54% stage 3, 20% stage 4
Chen & Chang, 2004	Taiwan	Descriptive	HADS (11 or more)	121 hospitalized patients; 55% men; race not reported; $\bar{X}$ age = 52 years	33% head and neck, 40% breast, 27% esophagus	15% stage 2, 17% stage 3, 33% stage 4, 36% not reported
D'Antonio et al., 1998	United States	Descriptive, interview, and chart review	BDI-13; BDI-21 (not reported)	50 outpatients; 76% men; race not reported; $\bar{X}$ age = 67 years	34% oral, 14% pharynx, 44% larynx, 8% other	12% stage 1, 14% stage 2, 30% stage 3, 34% stage 4, 10% unknown
Davies et al., 1986	United Kingdom	Descriptive	SADS (more than 6)	72 hospitalized patients or outpatients; 59% men; race not reported; $\bar{X}$ age = 54 years	53% positive HNC biopsy; 47% negative biopsy	Not reported
de Graeff, de Leeuw, Ros, Hordijk, Battermann, et al., 1999	Netherlands	Descriptive	CES-D (16 or more)	65 outpatients; 89% men; race not reported; median age = 61 years	100% larynx	3% Tis, 58% stage 1, 31% stage 2, 8% stage 3
de Graeff, de Leeuw, Ros, Hordijk, Blijham, et al., 1999	Netherlands	Descriptive, longitudinal	CES-D (16 or more)	75 outpatients; 73% men; race not reported; median age = 60 years	84% oral, 13% oropharynx, 3% other	28% stage 1, 21% stage 2, 13% stage 3, 38% stage 4
de Graeff et al., 2000a	Netherlands	Descriptive, longitudinal	CES-D (16 or more)	107 outpatients; 80% men; race not reported; median age = 60 years	46% oral, 6% oropharynx, 3% hypopharynx, 43% larynx, 2% other	2% stage 0, 42% stage 1, 22% stage 2, 12% stage 3, 22% stage 4
de Graeff et al., 2000b	Netherlands	Descriptive, longitudinal	CES-D (16 or more)	153 outpatients; 80% men; race not reported; 46% were aged 20–59 years; 54% were aged 60–76 years	Oral, oropharynx, hypopharynx, larynx (Percentages were not reported.)	65% stages 0–2, 35% stages 3–4
de Graeff et al., 2001	Netherlands	Descriptive	CES-D (16 or more)	208 outpatients; 78% men; race not reported; $\bar{X}$ age = 60 years	41% oral, 7% oropharynx, 5% hypopharynx, 45% larynx, 2% other	1% stage 0, 33% stage 1, 25% stage 2, 6% stage 3, 35% stage 4

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Table 1. Descriptive Characteristics of Studies Included in the Systematic Review (Continued)

Study	Country	Design	Measure (Cutoff Score)	Sample	Cancer Site	Disease Stage
de Leeuw, de Graeff, Ros, Bilijham, et al., 2000	Netherlands	Descriptive, longitudinal	CES-D (16 or more)	155 outpatients; gender and race not reported; age was younger than 80 years	Oral, throat, larynx (Percentages were not reported.)	Not reported
de Leeuw, de Graeff, Ros, Hordijk, et al., 2000	Netherlands	Descriptive	CES-D (16 or more)	197 outpatients; 78% men; race not reported; X̄ age = 59 years	Oral, throat, larynx (Percentages were not reported.)	Not reported
de Leeuw et al., 2001	Netherlands	Descriptive	CES-D (16 or more)	197 outpatients; 78% men; race not reported; aged 80 years or older	Oral, throat, larynx (Percentages were not reported.)	Not reported
Derks et al., 2004	Netherlands	Descriptive, comparison	CES-D (16 or more)	121 outpatients; 64% men; race not reported; age range = 40–60 or 70 years and older	49% oral, 35% pharynx, 17% larynx	30% stage 2, 27% stage 3, 43% stage 4
Duffy et al., 2002	United States	Descriptive, pilot	GDS-SF (more than 3)	81 patients; 83% men; 86% Caucasian; 12% African American; 3% other; X̄ age = 62 years	14% oral, 9% oropharynx, 18% hypopharynx, 46% larynx, 13% other	25% stage 1, 18% stage 2, 19% stage 3, 38% stage 4
Duffy et al., 2007	United States	Descriptive, cross-sectional	GDS-SF (not reported)	973 outpatients; 83% men; 88% Caucasian; 11% non-Caucasian; X̄ age = 61 years	33% oral and other, 33% oropharynx and hypopharynx, 34% larynx	33% in situ and stages 1–2, 67% stages 3–4
El-Deiry et al., 2005	United States	Descriptive, cross-sectional	BDI (10 or more)	52 outpatients; 69% men; race not reported; X̄ age = 56 years	56% oropharynx, 15% hypopharynx, 30% larynx	26% stage 3, 74% stage 4
Espie et al., 1989	United Kingdom	Descriptive	HADS (9 or more)	39 outpatients; 66% men; race not reported; X̄ age = 64 years	39% oral, 61% oropharynx	Not reported
Gritz et al., 1999	United States	Descriptive, longitudinal	POMS (not reported)	105 outpatients; 70% men; 73% Caucasian; 18% African American; X̄ age = 58 years	51% oral, 6% pharynx, 42% larynx	37% stages 1–2, 46% stage 3, 17% stage 4
Hammerlid et al., 1997	Sweden	Descriptive, longitudinal	HADS (8 or more)	105 outpatients; 68% men; race not reported; X̄ age = 60 years	10% oral, 28% oral and oropharynx, 25% tonsils, 10% hypopharynx, 4% epipharynx, 15% floor of mouth, 9% gingiva	20% stage 1, 25% stage 2, 21% stage 3, 34% stage 4
Hammerlid et al., 1998	Sweden	Descriptive, longitudinal	HADS (more than 10)	57 outpatients; 86% men; race not reported; X̄ age = 63 years	100% larynx	47% stage 1, 23% stage 2, 16% stage 3, 14% stage 4
Hammerlid et al., 2001	Sweden	Descriptive, longitudinal	HADS (8 or more)	232 outpatients; 70% men; race not reported; X̄ age = 61 years	32% oral, 27% pharynx, 19% larynx, 22% other	39% stages 1–2, 53% stages 3–4, 8% not reported
Humphris & Rogers, 2004	United Kingdom	Descriptive, longitudinal	HADS (not reported)	87 outpatients; 70% men; race not reported; X̄ age = 58 years	82% oral, 14% oropharynx, 4% maxillary sinus	61% stages 1–2, 39% stages 3–4
Hutton & Williams, 2001	United Kingdom	Descriptive, two-group comparison	HADS (more than 8)	18 outpatients; 72% men; race not reported; X̄ age = 67 years	100% HNC	Not reported

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Table 1. Descriptive Characteristics of Studies Included in the Systematic Review *(Continued)*

Study	Country	Design	Measure (Cutoff Score)	Sample	Cancer Site	Disease Stage
Karnell et al., 2006	United States	Descriptive, longitudinal	BDI (10 or more)	14 outpatients; 70% men; race not reported; 68% older than 55 years	35% oral cavity, 39% pharynx, 26% larynx	29% stages 1–2, 64% stages 3–4, 7% not reported
Karnell et al., 2007	United States	Descriptive, retrospective	BDI (not reported)	394 outpatients; 68% men; race not reported; median age = 58 years	100% HNC (squamous cell carcinoma)	33% stages 1–2, 69% stages 3–4
Katz et al., 2003	Canada	Descriptive	CES-D (16 or more)	82 outpatients; 70% men; race not reported; X̄ age = 59 years	52% oral, 16% sinus, 11% salivary and parotid, 8% pharynx, 5% skin, 4% sarcoma, 2% thyroid, 1% ear	53% stages 3–4, 7% Tx
Katz et al., 2004	Canada	Descriptive	CES-D (16 or more); BDI (16 or more); HADS (8 or more); SADS	60 outpatients; 78% men; race not reported; X̄ age = 61 years	22% oral, 7% nasopharynx, 30% oropharynx, 15% larynx, 8% salivary gland, 7% nasal cavity, 11% unknown	8% stage 1, 15% stage 2, 23% stage 3, 38% stage 4, 16% unknown
Kelly et al., 2007	United Kingdom	Descriptive, longitudinal	HADS (not reported)	118 outpatients; 73% men; race not reported; age not reported	20% oral, 3% nasopharynx, 20% oropharynx, 11% hypopharynx, 41% larynx, 2% paranasal sinus, 1% nasal cavity	Not reported
Kohda et al., 2005	Japan	Descriptive, longitudinal	HADS (not reported); DSM interview	20 outpatients; 97% men; race not reported; X̄ age = 67 years	11% pharynx, 69% larynx, 20% other	69% stage 1, 31% stage 2
Krouse et al., 1989	United States	Descriptive, longitudinal	BDI (not reported)	33 outpatients; 91% men; race not reported; X̄ age = 58 years	40% oral or pharynx, 51% larynx, 9% other	Not reported
Kugaya et al., 1999	Japan	Descriptive	POMS depression subscale (not reported)	99 outpatients; 61% men; race not reported; X̄ age = 59 years	25% oral, 21% pharynx, 20% larynx, 20% thyroid, 13% other	18% stage 1, 23% stage 2, 23% stage 3, 19% stage 4, 16% other
Kugaya et al., 2000	Japan	Descriptive, cross-sectional	HADS (15 or more); DSM	107 outpatients; 76% men; race not reported; X̄ age = 61 years	57% oral, 26% pharynx, 17% larynx	61% stages 3–4, 39% not reported
Lambert et al., 2005	United States	Descriptive	GDS-SF (4 or more)	684 outpatients; 86% men; race not reported; X̄ age = 62 years	31% oral, 31% hypo and oropharynx, 38% larynx	36% stages 0–2, 65% stages 3–4
Llewellyn et al., 2006	United Kingdom	Descriptive	HADS (not reported)	55 outpatients; 71% men; 94% Caucasian; X̄ age = 59 years	100% HNC	20% stage 1, 20% stage 2, 16% stage 3, 27% stage 4, 17% not reported
McCaffrey et al., 2007	United States	Descriptive, cross-sectional	SCID; DSM	24 outpatients; 83% men; race not reported; X̄ age = 73 years	Oral, oropharynx, hypopharynx, larynx)	38% stage 3, 62% stage 4
McDonough et al., 1996	United States	Descriptive, retrospective	BDI (not reported)	30 outpatients; 50% men; 70% Caucasian; 30% African American; X̄ age = 62 years	10% oral, 10% nasopharynx, 17% oropharynx, 17% hypopharynx, 37% larynx, 3% thyroid, 6% not reported	17% stage 1, 37% stage 2, 23% stage 3, 17% stage 4, 6% other

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Table 1. Descriptive Characteristics of Studies Included in the Systematic Review (Continued)

Study	Country	Design	Measure (Cutoff Score)	Sample	Cancer Site	Disease Stage
Morton et al., 1984	United Kingdom	Descriptive	DSM	48 outpatient men; race not reported; X̄ age = 70 years	100% bucco-pharynx	27% stage 1, 27% stage 2, 27% stage 3, 21% stage 4
Nordgren et al., 2003	Germany	Descriptive, longitudinal	HADS (8 or more)	86 outpatients; 84% men; race not reported; X̄ age = 66 years	100% larynx	64% stages 1–2, 36% stages 3–4
Pandey et al., 2007	India	Descriptive, cross-sectional	HADS (8 or more)	123 outpatients; 76% men; race not reported; X̄ age = 54 years	100% HNC	22% stage 1, 29% stage 2, 19% stage 3, 13% stage 4, 18% stage Tx
Reisine et al., 2005	United States	Descriptive	CES-D (16 or more)	401 outpatients; 52% men; 95% Caucasian; X̄ age = 63 years	58% oral epithelial dysplasia, 41% oral cancer	Not reported
Rogers, Courneya, et al., 2006	United States	Descriptive	CES-D (not reported)	83% men; 92% Caucasian; 5% African American; X̄ age = 58 years	24% oral, 37% oropharynx, 25% larynx, 14% not reported	20% stage 1, 7% stage 2, 19% stage 3, 54% stage 4
Rogers, Rajlawat, et al., 2006	United Kingdom	Descriptive, cross-sectional	CES-D (16 or more); HADS (8 or more)	197 outpatients; 56% men; race not reported; age = 30% younger than 55 years and 70% 55 years and older	89% oral, 10% oropharynx, 2% maxillary sinus	27% stage 1, 34% stage 2, 8% stage 3, 23% stage 4, 7% Tis, 1% Tx
Rose & Yates, 2001	Australia	Descriptive, longitudinal	HADS (8 or more)	58 outpatients; 71% men; race not reported; X̄ age = 62 years	14% hypopharynx, 12% tongue, 17% larynx, 57% not reported	Not reported
Rozniatowski et al., 2005	France	Descriptive, group comparison	HADS (8 or more)	100 outpatients; gender, race, and age not reported	Oral, oropharynx (Percentages were not reported.)	50% stages 1–2, 50% stages 3–4
Sehlen et al., 2003	Germany	Descriptive	SDS (50 or more)	133 outpatients; 80% men; race not reported; X̄ age = 58 years	11% oral; 21% tongue and mouth; 40% pharynx; 12% larynx; 15% nose, nasal cavity, and salivary glands	17% stage 1, 26% stage 2, 12% stage 3, 37% stage 4, 7% not reported
Tesch et al., 2004	Brazil	Descriptive, comparison	SCL90-R (not reported)	40 outpatients; 35% men; race not reported; X̄ age = 46 years	100% HNC	Not reported
van der Schroeff et al., 2006	Netherlands	Descriptive, comparison	CES-D (16 or more)	266 outpatients; 67% men; race not reported; age = 56% were 45–60 years and 44% were older than 70 years	43% oral, 40% pharynx, 18% larynx	22% stage 2, 23% stage 3, 56% stage 4
Veronck-de Leeuw et al., 2007	Netherlands	Descriptive, matched pairs	HADS (12 or more)	41 patients and spouses; 63% men; X̄ age = 61 years	61% oral and oropharynx, 32% larynx, 7% parotid	46% stages 1–2, 54% stages 3–4
Westin et al., 1988	Sweden	Descriptive	CPRS (9 or more)	59 outpatients; 83% men; race not reported; X̄ age = 64 years	100% HNC	Not reported

BDI—Beck Depression Inventory; CES-D—Center for Epidemiological Studies–Depression Scale; CPRS—Comprehensive Psychopathological Rating Scale; DSM—Diagnostic and Statistical Manual; GDS-SF—Geriatric Depression Scale–short form; HADS—Hospital Anxiety Depression Scale; HNC—head and neck cancer; MCMI—Million Clinical Multi-Axial Inventory; POMS—Profile of Mood States; SADS—Schedule for Affective Disorders and Schizophrenia; SCID—Structural Clinical Interview for Depressive Disorders; SCL90-R—Symptom Checklist 90–Revised; SDS—Zung Self-Rating Depression Scale

Note. Because of rounding, not all percentages total 100.

nonexistent. Prevalence rates are presented in Table 2. The data clearly show that depression is present in patients with head and neck cancer throughout the course of the cancer trajectory at time points prior to diagnosis (premorbid); at diagnosis; during treatment with surgery, radiation, or chemotherapy; and after treatment. Davies, Davies, and Delpho (1986) noted that 29% of patients with biopsy-proven carcinoma of the oral cavity were depressed at initial evaluation even before biopsy results were known. Depression rates of studies reviewed were particularly high at diagnosis (13%–40%, n = 21 studies), during treatment (25%–52%, n = 7 studies) and at six-month follow-up (11%–45%, n = 11 studies); however, the levels decreased three years after diagnosis (9%–27%, n = 4 studies). Although methodologic limitations hinder comparison of rates from individual studies, a clinical picture of depression in head and neck cancer was able to emerge, with depression peaking at time of treatment and declining after treatment but continuing at mild to moderate levels for years after diagnosis.

Correlates of Depression

Patient Characteristics

Demographic characteristics of age, gender, marital status, and education have been correlated with depression. Depression has been associated with younger age in eight studies (Derks, de Leeuw, Winnubst, & Hordijk, 2004; Duffy et al., 2007; Espie, Freedlander, Campsie, Soutar, & Robertson, 1989; Hammerlid, Silander, Hornestam, & Sullivan, 2001; Hutton & Williams, 2001; Lambert, Terrell, Copeland, Ronis, & Duffy, 2005; Reisine et al., 2005; Rogers, Courneya, et al., 2006). However, in two other studies that compared patients aged 40–60 years to patients older than 70 years, no significant difference was found between these age groups (Derks et al.; van der Schroeff, Derks, Hordijk, & de Leeuw, 2006).

Gender also has been correlated with depression. Women were noted to be more depressed in one study (Katz, Irish, Devins, Rodin, & Gullane, 2003), whereas in four other studies, men were noted to be more depressed (D'Antonio et al., 1998; Katz, Kopek, Waldron, Devins, & Tomlinson, 2004; Tesch, Denardin, Baptista, & Dias, 2004; Westin, Jansson, Zenckert, Hallstrom, & Edstrom, 1988). Being unmarried or living alone was found to be correlated with more depression by several researchers (Baile, Gibertini, Scott, & Endicott, 1992; Duffy et al., 2007; Kugaya, Akechi, Okamura, Mikami, & Uchitomi, 1999; Kugaya et al., 2000; Lambert et al., 2005) but not by others (D'Antonio et al.; Sehlen et al., 2003). Decreased social support has been correlated with increased levels of depression (Karnell, Christensen, Rosenthal, Magnuson, & Funk, 2007; Reisine et al., 2005;

Verdonck-de Leeuw et al., 2007) and available social support predicted depression in one study at six months and three years (de Leeuw et al., 2001). In another study, depression was less common among patients who attended support groups (Hutton & Williams, 2001). Persistently high levels of depressive symptoms after treatment have been associated with more social disruption (odds ratio = 1.219; p = 0.008) (Karnell et al., 2007), and a lower education level has been correlated with more depression (Sehlen et al.). People with fewer than 9 (Kugaya et al., 2000) or 12 years (Duffy et al., 2007; McCaffrey et al., 2007) of education appear to have more depression than patients with a college education (Lambert et al.).

Patient characteristics related to depression include comorbidities, cancer stage, smoking, employment, and effects of cancer treatment. A high number of comorbidities have been associated with an increased risk for depression (Lambert et al., 2005) as has advanced stage of cancer or larger tumor size (Aarstad, Aarstad, Heimdal, & Olofosson, 2005; Baile et al., 1992; de Graeff, de Leeuw, Ros, Hordijk, Battermann, et al., 1999; Hammerlid et al., 2001; Kugaya et al., 1999, 2000; Rogers, Rajlawat, Goru, Lowe, & Humphris, 2006). At time of biopsy, patients with oral cancer versus dysplasia (Reisine et al., 2005) and positive biopsy for cancer (Davies et al., 1986) were more likely to be depressed. Patients with depression also demonstrated increased levels of smoking (Humphris & Rogers, 2004), and depressive symptoms have been significantly associated with smoking and drinking (Duffy et al., 2007). In addition, depression has been associated with job loss (McDonough, Boyd, Varvares, & Maves, 1996), less employment outside the home (Reisine et al.), more disability from cancer treatment (McDonough et al.), and more disfigurement (Katz et al., 2003).

Several researchers found that depression before treatment predicted depression at later time points (6 months, 12 months, and 3 years), which raises the concern that there may be a subgroup of patients who are consistently depressed over time (Aarstad et al., 2005; de Graeff, 2000a, 2000b; de Leeuw, 2001). Karnell, Funk, Christensen, Rosenthal, and Magnuson (2006) found that persistently high levels of depressive symptoms after treatment were associated with a trend toward higher levels of depression scores before treatment (odds ratio = 1.737; p = 0.09).

An overlap between depression and anxiety has been noted in several studies (Espie et al., 1989; Gritz et al., 1999; Hammerlid, Mercke, Sullivan, & Westin, 1998; Pandey et al., 2007). Hammerlid et al. (1997) found that the number of patients scoring high on the depression scale exceeded the number scoring high on the anxiety scale at all measurement points from before treatment to one year after treatment. Additionally, depression has been found to increase over time from before treatment to treatment completion, but anxiety did not follow this

Table 2. Depression Prevalence, Time Points, and Treatments Coupled With Findings of Studies Included in the Systematic Review

Study	Prevalence	Time Point, Treatment Type, and Sample %	Findings
Aarstad et al., 2005	Not reported	Follow-up (six months plus or minus one year); surgery (100%)	Patients with HNC had higher depression scores than controls (F = 3.99, p < 0.05). Both tumor stage (T) (F = 2.74, p = 0.035) and node stage (N) (F = 4.9, p = 0.004) predicted depression scores. Post-hoc comparison showed differences between T2 and T4 (p < 0.05), N0 and N3 (p = 0.05), and N1 and N3 (p < 0.01). Depression scores at diagnosis correlated with depression scores at follow-up (r = 0.39, p < 0.05). The higher the depression score, the lower the reported QOL levels.
Baile et al., 1992	40%	Before treatment; surgery (100%)	Women with stage 1 or 2 cancers and men with stage 3 or 4 cancers had the highest depression scores (F = 7.69, p < 0.01).
Braz et al., 2005	13%	After treatment (four months or longer); surgery (100%)	Mean and median depression scores of patients with partial laryngectomies were lower than patients with total laryngectomies.
Chawla et al., 1999	37% before treatment; 54% during treatment (three to four weeks); 9% after treatment (three months)	Treatment; radiation (100%)	In weeks 3–4 of radiotherapy, performance and functional status decreased although depression increased, indicating impairment in QOL. Three months after radiotherapy, performance status, functional status, and depression scores improved but were not restored to levels prior to treatment.
Chen & Chang, 2004	25%	Treatment; chemotherapy (76%), not reported (24%)	Depressed patients had more symptoms (p = 0.001). Depressed patients had higher occurrence rates (p < 0.05) than patients who were not depressed of insomnia (83% versus 62%), pain (83% versus 55%), anorexia (63% versus 42%), fatigue (67% versus 32%), and wound pressure sores (30% versus 13%). Patients experiencing multiple symptoms had a significantly higher risk for being depressed (OR = 5.023, 95% CI 1.96–12.93). Among patients who had four symptoms, 52% also were depressed, whereas only 18% were not depressed (X² = 10.74, p = 0.001).
D'Antonio et al., 1998	22%	After treatment; surgery (100%)	Depression was correlated with emotional, physical, and functional well-being and QOL (r = 0.52, p = 0.001). No relationship was found between depression and living situation, age, gender, marital status, employment, and religious denomination.
Davies et al., 1986	29%	Before treatment; biopsy (100%)	A positive biopsy was a significant factor for depression (F = 5.59, p < 0.02).
de Graeff et al., 2000a	27% before treatment; 24% after treatment (6 months); 21% after treatment (12 months)	Before treatment; surgery or radiation (percent not reported)	By using five variables (physical symptoms, depressive symptoms, emotional support, extent of social network, and avoidance coping), predicting depression at 6 (81%) and 12 months (67%) after treatment was possible. Inclusion of physical symptoms increased the percentages (89% and 82%).
de Graeff et al., 2000b	29% before treatment; 28% after treatment (six months)	Before and after treatment (six months); radiation (43%), surgery or radiation (57%)	Before treatment, three types of received social support (emotional support in stressful situations [p < 0.01], informative [p = 0.01], and instrumental [p < 0.01]) were positively related to depressive symptoms. Six months following treatment, these same correlations were not significant. After treatment, more available support was related to fewer depressive symptoms (p < 0.01) and a large informal network (p < 0.01). Multiple regression showed that before treatment health complaints (R² = 28%), and social support (R² = 6%) explained the variance in depressive symptoms.

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Table 2. Depression Prevalence, Time Points, and Treatments Coupled With Findings of Studies Included in the Systematic Review *(Continued)*

Study	Prevalence	Time Point, Treatment Type, and Sample %	Findings
de Graeff, de Leeuw, Ros, Hordijk, Batterman, et al., 1999	28% before treatment; 22% after treatment (6 months); 19% after treatment (12 months)	Treatment; radiation (100%)	Emotional functioning and depression improved gradually at 6 and 12 months. A nonsignificant trend existed toward a lower percentage of patients with a CES-D score of 16 or greater. Patients with T2 tumors were more depressed than patients with T1 tumors ($p < 0.05$).
de Graeff, de Leeuw, Ros, Hordijk, Blijham, et al., 1999	27% before treatment; 27% after treatment (6 months); 25% after treatment (12 months)	Before and after treatment (6 and 12 months); radiotherapy (100%)	Emotional functioning improved gradually at 6 and 12 months, but mood, as measured with the total score of CES-D, did not change.
de Leeuw et al., 2001	29% before treatment	Before and after treatment (three years or longer); surgery (19%), radiation (44%), surgery and radiation (37%)	No relationship was found between emotional functioning or depressive symptomatology and recurrence or survival.
de Leeuw, de Graeff, Ros, Bilijham, et al., 2000	27% before treatment; 23% after treatment (6 months); 21% after treatment (12 months); 20% after treatment (24 months); 19% after treatment (36 months)	Before and after treatment (6, 12, 24, and 36 months); surgery (27%), radiation (45%), surgery and radiation (28%)	The percentage of patients with depression showed a nonsignificant trend ($p = 0.08$) for improvement (decreasing from 27%–19%). When comparing the depression scores at 12 and 36 months, a significant difference (i.e., improvement) existed for the total CES-D score ($p < 0.01$).
de Leeuw, de Graeff, Ros, Hordijk, et al., 2000	26% before treatment; 24% after treatment (6 months); 22% after treatment (12 months)	Before and after treatment (6 and 12 months); surgery and/or radiation (percent not reported)	High levels of depressive symptoms, low performance status, and combination treatments were predictors of increased severity of symptoms and poor functioning after treatment ($p = 0.05$). Patients with a CES-D score of 16 or greater at baseline had worse scores for the total score of CES-D at 6 and 12 months ($p < 0.05$). Depressive symptoms at baseline were the most important predictor at six months of emotional functioning (32%), fatigue (19%), cognitive functioning (18%), role activities (16%), social functioning (12%), pain (11%), and QOL (8%) ($p < 0.05$).
de Leeuw et al., 2001	12% before treatment; 11% after treatment (six months); 9% after treatment (three years)	After treatment; surgery or radiation (percent not reported)	Eight variables (tumor stage, genders, depressive symptoms, openness to discuss cancer with family, available social support, received emotional support, tumor-related symptoms, and size of informal social network) prior to treatment were used to calculate a risk score to determine the patients who might be depressed six months to three years after treatment (positive predictive value 58%; negative predictive value 83%).
Derks et al., 2004	29% before treatment; 42% after treatment (one year)	Before treatment and one year after treatment; surgery (33%), surgery and radiation (67%)	Patients aged 70 years and older had no significant difference from patients aged 45–69 years in depression before treatment; both groups had higher depression scores one year following treatment.
Duffy et al., 2002	44%	From diagnosis and anytime after; treatment type not reported	Smoking and alcohol issues were positively associated ($X^2 = 8.82$, $p < 0.001$) as were smoking and depressive symptoms ($X^2 = 3.84$, $p < 0.05$). No association was noted between alcohol and depression. Screening positive for depression was found to have a strong negative association with QOL. Thirty-eight percent of patients with depression were interested in depression services.

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Table 2. Depression Prevalence, Time Points, and Treatments Coupled With Findings of Studies Included in the Systematic Review *(Continued)*

Study	Prevalence	Time Point, Treatment Type, and Sample %	Findings
Duffy et al., 2007	46%	From diagnosis and anytime after; treatment type not reported	Depressive symptoms, smoking, and drinking were associated with each other (p < 0.05). Patients who were depressed and who smoked were more likely to be younger, not married, have a high school degree or less, and be one year or less removed from diagnosis (p < 0.05). Depressive symptoms were negatively associated with QOL (p < 0.001).
El-Deiry et al., 2005	18% chemotherapy and radiation; 5% surgery and radiation	After treatment (12 months); chemotherapy and radiation (50%), surgery and radiation (50%)	Patients receiving surgery and radiation treatment ($\overline{X}$ = 9.6) versus chemotherapy and radiation ($\overline{X}$ = 11.6) performed better on the BDI, but this was not statistically significant (p = 0.42).
Espie et al., 1989	17%	After treatment (10 months or longer); surgery (100%)	Patients had both anxiety (24%) and depression (17%), which were not mutually exclusive. Depression was correlated with younger age (X^2 = 0.028, p < 0.05). Depression was not correlated with tumor site (p > 0.60).
Gritz et al., 1999	Not reported	Diagnosis to 12 months after treatment; radiation (23%), surgery (27%), surgery or radiation (51%)	Total POMS scores improved over time from baseline to 12 months (p = 0.001). POMS subscales of depression-dejection (p = 0.001), tension-anxiety (p = 0.001), anger-hostility (p = 0.04), confusion-bewilderment (p = 0.02), and vigor-activity (p = 0.01) improved from baseline to 12 months.
Hammerlid et al., 1997	20% before treatment; 15% after treatment (3 months); 14% after treatment (6 months); 13% after treatment (12 months)	Diagnosis to one year; radiation or brachytherapy (100%)	Patients scoring high on the depression scale exceeded the number of patients scoring high on the anxiety scale at all measurement points. Most symptoms, including depression, were at their peak two to three months after the start of treatment. Anxiety trended downward from before treatment to 12 months.
Hammerlid et al., 1998	23% before treatment; 26% after treatment (1 month); 13% after treatment (3 months); 14% after treatment (6 months); 24% after treatment (12 months)	Before and after treatment (1, 2, 3, 6, and 12 months); radiation (68%), chemotherapy and radiation (20%), laryngectomy and radiation (12%)	Patients with larger tumors at diagnosis and at 12 months scored more frequently as depressed (41% and 45%) than patients with smaller tumors (32% and 32%). All patients with laryngectomies were depressed and had low QOL scores at diagnosis and throughout the study.
Hammerlid et al., 2001	24% after treatment (3 months); 19% after treatment (12 months); 9% after treatment (36 months)	After treatment (3, 12, or 36 months); radiation (30%), surgery (5%), surgery and radiation (25%), surgery, radiation, and chemotherapy (9%), radiation and chemotherapy (31%)	Predictors of QOL after three years were physical functioning and depression at diagnosis (p = 0.001). Patients scored highest for anxiety at diagnosis (32%), whereas patients scoring highest for depression were highest just after finishing treatment (three months, 24%). At three years after treatment, depression decreased by 50% (p < 0.001). At three years, a significant difference existed between patients with small and large tumors for depression (p < 0.05). Women's depression scores improved more than the men's scores between assessment points, but, at three years, no significant differences were seen by gender.
Humphris & Rodgers, 2004	Not reported	After treatment (3, 7, 11, or 15 months); surgery (43%), surgery and radiation (54%), surgery and chemotherapy (3%)	Smokers, when compared to nonsmokers, had higher levels of depression and anxiety at seven months or longer after treatment. Smokers exhibited a higher level of depression than nonsmokers (F = 4.40, p < 0.05).

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Table 2. Depression Prevalence, Time Points, and Treatments Coupled With Findings of Studies Included in the Systematic Review *(Continued)*

Study	Prevalence	Time Point, Treatment Type, and Sample %	Findings
Hutton & Williams, 2001	22%	After treatment (eight months or longer); surgery or surgery and radiation (percent not reported)	Depression decreased with age. Depression decreased after onset of illness and was less common among those attending a support group (2 of 9 versus 4 of 9).
Karnell et al., 2006	44% after treatment (3 months); 37% after treatment (6 months); 34% after treatment (9 months); 35% after treatment (12 months)	Before and after treatment (3, 6, 9, or 12 months); surgery (35%), radiation (11%), surgery and radiation or chemotherapy (40%); 14% not reported	Persistent high levels of depressive symptoms after treatment were associated with higher levels of depressive scores before treatment (OR = 1.737, p = 0.0859), lower (worse) HNC-specific scores after treatment in eating (OR = 1.219, p = 0.445), and social disruption (OR = 1.219, p = 0.0077).
Karnell et al., 2007	Not reported	After treatment; treatment type not reported	Higher social support scores were associated with fewer depressive symptoms (p = 0.023), social disruption (p = 0.045), and higher general mental health (p = 0.016).
Katz et al., 2003	26%	After treatment (more than six months); surgery (100%)	Mean CES-D scores for men were 9.88 and 16.18 for women (t = –2.308, p < 0.024). Increased depressive symptoms were reported by women (β = 0.29, p < 0.01) and individuals more disfigured (β = 0.25, p < 0.01).
Katz et al., 2004	20%	After treatment (one month); radiation (100%)	Nineteen percent of men and 23% of women were depressed (X^2 = 0.098, p = 0.754). All cases of major depression were in men.
Kelly et al., 2007	43% before treatment; 32% during treatment; 24% at treatment completion	Treatment; radiation or chemotherapy (100%)	Patients experienced deterioration in QOL (p < 0.001) and an increase in depression scores (p < 0.001) over the course of the treatment.
Kohda et al., 2005	Not reported	Before treatment and treatment (four and eight weeks); radiation (100%)	Depression, anxiety, and pain were more severe at four weeks than at baseline. Depression scores deteriorated at four weeks concomitantly with anxiety, but depression remained elevated at eight weeks although anxiety levels decreased. QOL was explained (R^2 = 0.64) by depression (β = –0.66, p = 0.001) and face rating scale score (β = 0.43, p = 0.013).
Krouse et al., 1989	Not reported	Preoperative and after treatment (three and nine months); surgery (50%), surgery and radiation (50%)	Patients with oral and oropharyngeal cancer had an increase in depression with passage of time compared to all other patient group sites (F = 3.585, p < 0.01). Patients with composite resections had significant increases in depression over time from before treatment through three months after. Scores of all patient group sites remained relatively stable over time (F = 2.722, p < 0.022).
Kugaya et al., 1999	Not reported	After treatment (more than three months); treatment type not reported	The value on the POMS-depression was predicted by stage (local disease versus advanced stage) (t = 2.18, p = 0.03), marital status (married versus unmarried) (t = 2.72, p = 0.008), and helplessness or hopelessness (t = 6.65, p = 0.0001).
Kugaya et al., 2000	17%	Pretreatment; surgical excision (95%), chemotherapy and radiation (5%)	Depression was associated with less than nine years of education (p = 0.014), being unmarried (X^2 = 6.70, p = 0.01), living alone (X^2 = 5.96, p = 0.02), advanced cancer stage (p = 0.009), and alcohol abuse (p = 0.09).

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Table 2. Depression Prevalence, Time Points, and Treatments Coupled With Findings of Studies Included in the Systematic Review *(Continued)*

Study	Prevalence	Time Point, Treatment Type, and Sample %	Findings
Lambert et al., 2005	45%	After treatment (six months); surgery (64%), radiation (84%), chemotherapy (23%) (more than one type of surgery possible)	A decreased risk of depression was predicted by older age (OR = 0.96, 95% CI 0.94–0.98, p < 0.05), college education (OR = 0.64, 95% CI 0.46–0.91, p < 0.05), and being married (OR = 0.62, 95% CI 0.44–0.89, p < 0.05), whereas higher tumor stage (OR = 1.84, 95% CI 1.23–2.75, p = 0.05) and more comorbidity (OR = 1.5, 95% CI 1.30–1.75, p < 0.05) increased depression risk.
Llewellyn et al., 2006	Not reported	Diagnosis to eight months; surgery (24%); radiation (29%); surgery and radiation (24%); radiation and chemotherapy (9%),; surgery, radiation, and chemotherapy (4%)	Depressive symptoms contributed significantly to five of eight QOL domains: physical functioning (β = 2.79, p < 0.05), role physical (β = 3.83, p < 0.01), bodily pain (β = 4.16, p < 0.01), social functioning (β = 4.4, p < 0.01), and role emotional (β = 4.89, p < 0.01).
McCaffrey et al., 2007	26%	Time of treatment, surgery alone, or with radiation or chemotherapy (percent not reported)	Older patients had more depression than younger patients (p < 0.04). Depression was associated with less than 12 years of education (p < 0.01). No association was noted between depression and marital status, alcohol use, or cognitive function.
McDonough et al., 1996	12%	After treatment (six months); surgery (29%), radiation (10%), surgery and radiation (58%), chemotherapy (3%)	Gender differences were not found, but a trend existed for women to score higher on depression. Depression was highest in patients who were disabled because of cancer treatment and who reported experiencing financial hardship because of job losses.
Morton et al., 1984	40%	After treatment (three years or less); radiation (40%), salvage surgery for failed radiation therapy (35%), surgery (25%)	Variability was observed in depression prevalence (33% surgery alone compared to 47% salvage surgery) but the difference between treatment types was not statistically significant (X^2 = 0.6, p > 0.05). Fifty percent of patients had dysphoric mood.
Nordgren et al., 2003	Not reported	After treatment (one and five years); radiation (75%), combined treatment (10%), surgery and radiation with or without chemotherapy (15%)	HADS depression score at one year was not a predictor of QOL at the five-year follow-up.
Pandey et al., 2007	10%	Time of treatment; surgery (32%), radiation (33%), multimodality (35%)	Depression was correlated with emotional distress (r = 0.614, p = 0.001), family distress (r = 0.329, p < 0.001), social distress (r = 0.292, p = 0.001), and anxiety (r = 0.66, p = 0.001). Depression was correlated with education (r = –0.185, p < 0.05), distance travelled (r = –0.188, p < 0.05), and chewing (r = –0.216, p < 0.5). Depression and anxiety were associated with activity of daily living (r = 0.199 and 0.263, respectively, p < 0.001).
Reisine et al., 2005	23%	Diagnosis; initial biopsy (100%)	Depression was 79% higher among patients with oral cancers relative to oral epithelial dysplasia (OR = 1.79, 95% CI 1.03–3.12, p < 0.05). Odds of depression were significantly reduced in patients aged 50 years or older (aged 51–60: OR = 0.38, 95% CI 0.17–0.87; aged 61–70: OR = 0.13, 95% CI 0.05–0.34; aged 71 or older: OR = 0.24, 95% CI 0.10–0.59, p < 0.05), men (OR = 1.73, 95% CI 0.95–3.15, p = 0.07), patients with higher levels of social support (OR = 0.44, 95% CI 0.24–0.79, p < 0.05), and patients employed outside the home (OR = 0.28, 95% CI 0.13–0.59, p < 0.05).

Table 2. Depression Prevalence, Time Points, and Treatments Coupled With Findings of Studies Included in the Systematic Review *(Continued)*

Study	Prevalence	Time Point, Treatment Type, and Sample %	Findings
Rogers, Courneya, et al., 2006	Not reported	Treatment and after treatment (less than six months); chemotherapy or radiation (percent not reported)	The mean depression score on the CES–D was 18.7, which is greater than the cutoff point. Younger age was associated with higher depressive symptoms ($r = -0.26$, $p = 0.05$). No association was found among the absence of comorbidities, alcohol use, activities, and depression.
Rogers, Rajlawat, et al., 2006	19% HADS; 27% CES-D	After treatment; surgery (100%)	Patients with larger tumors, later staging, flap surgery, and adjuvant radiotherapy had worse levels of QOL and depression ($p < 0.05$).
Rose & Yates, 2001	10% before treatment; 41% after treatment (six weeks); 30% after treatment (one month)	Treatment; radiation (100%)	A decrease was noted between pretreatment and six weeks ($t[57] = -5.07$, $p < 0.001$) and between pretreatment and the first time point ($t[57] = -3.38$, $p < 0.001$), but no significant change existed between the six-week time point and the one-month time point ($t[57] = -1.19$, $p = 0.239$).
Rozniatowski et al., 2005	Not reported	Before treatment at time of initial consult for a diagnosis (100%)	Patients with larger tumors had lower HADS scores, lower involvement of a spouse or partner ($p < 0.001$), greater social isolation ($p = 0.0002$), and fewer regular medical visits ($p = 0.00001$). Pain ($p = 0.03$) rather than depression was a factor influencing the seeking of initial consultation for HNC.
Sehlen et al., 2003	34% before treatment; 47% at treatment completion; 39% after treatment (six weeks); 43% after treatment (six months)	Time of treatment; radiation (100%)	Higher depression was associated with lower education level ($p = 0.034$) and aggressive hyper-fractionated-accelerated treatment ($p = 0.015$). No association between depression and marital status, tumor stage, histologic grading, and substance abuse was noted.
Tesch et al., 2004	Not reported	After treatment; treatment type not reported	Depression levels were progressively higher with the degree of the chronic pain. Depression was associated with pain intensity ($r = 0.483$, $p = 0.01$) and chronic pain severity ($r = 0.584$, $p = 0.01$).
van der Schroeff et al., 2006	25% before treatment; 37% after treatment (12 months); 27% after treatment (3–6 years)	Follow-up (three to six years); no treatment (11%), surgery (21%), surgery and radiation (41%), radiation (17%), chemotherapy and radiation (12%)	No difference was noted in CES-D scores 16 and greater before treatment, one year, and three to six years between subjects aged 45–60 years and those older than age 70.
Veronck-de Leeuw et al., 2007	27%	After treatment; parotidectomy or radiation (39%), surgery and radiation (39%), chemotherapy and radiation (22%)	HADS score greater than 12 was related to presence of feeding tube ($p < 0.05$), speech and swallowing issues ($r = 0.42$, $p < 0.01$), fewer social contacts ($r = 0.64$, $p < 0.01$), a passive style of coping ($r = 0.66$, $p < 0.01$), and nonexpression of emotions ($r = 0.36$, $p < 0.05$).
Westin et al., 1988	9%	Treatment and after treatment; receiving treatment (37%), clinical workup for recurrence (27%), and disease free (36%)	Depressed patients all were cachectic men who completed their oncology treatment more than one year previously. Depression was higher among the malnourished ($p < 0.01$).

BDI—Beck Depression Inventory; CES-D—Center for Epidemiological Studies–Depression Scale; CI—confidence interval; HADS—Hospital Anxiety Depression Scale; HNC—head and neck cancer; OR—odds ratio; POMS—Profile of Mood States; QOL—quality of life

Note. Because of rounding, percentages may not total 100.

pattern and decreased over time (Kelly, Paleri, Downs, & Shah, 2007; Kohda et al., 2005).

Summary and implications: Although observed levels of psychological distress cannot be attributed to simple demographic patient characteristics (Espie et al., 1989), knowledge of characteristics associated with depression may guide the clinician in identifying patients at risk for depression (Kugaya et al., 1999; Reisine et al., 2005). This review revealed that, in the head and neck cancer population, being male, being unmarried, having less education, having a history of past and current smoking, being younger (younger than age 40), and having lower physical functioning are associated with depression. The association of larger tumors with more depression at diagnosis (Hammerlid et al., 1998) suggests that depression may depend more on the level of visible disease rather than on the actual extent of disease (Aarstad et al., 2005). Patients with higher levels of social support after treatment appear to have fewer depressive symptoms (Karnell et al., 2007). However the impact of social support can vary by gender: Social support may have a moderating effect on the psychosocial impact of disfigurement on the well-being of men but not women (Katz et al., 2003).

Patient Physical Symptoms

Not surprisingly, patient symptoms have been correlated with depression in several studies. Patients experiencing multiple (more than four) physical symptoms were five times more likely to be depressed (odds ratio = 5.02, 95% confidence interval 1.96–12.93) (Chen & Chang, 2004). In addition, a greater number of depressive symptoms, lower performance status at baseline, and combined modality treatment were significant predictors of increased severity of symptoms and poorer functioning after treatment (de Graeff et al., 2000b). Patients with insomnia, pain, anorexia, fatigue, and presence of wound pressure sore symptoms had significantly more depression (Chen & Chang). Depression also has been significantly correlated with weight loss (Westin et al., 1988), the presence of a feeding tube, and speech or swallowing issues (Verdonck-de Leeuw et al., 2007). When depression levels were across different grades of chronic pain, the levels of depression were progressively higher with increasing pain severity (Tesch et al., 2004).

Summary and implications: Physical symptoms provide information for risk assessment for depression. In one study, physical symptoms prior to treatment predicted increased physical symptoms and poorer physical, psychological, and social functioning at 6 and 12 months after diagnosis (de Graeff et al., 2000b). In another study, patient profiles of simultaneous occurrence of pain, fatigue, insomnia, and anorexia during treatment were highly associated with depression (Chen & Chang, 2004), suggesting that symptoms are inter-related and should not be viewed as a single entity. The concurrence

and inter-relationship of multiple symptoms suggest an underlying dimension that includes psychological and physical symptoms (Kim, McGuire, Tulman, & Barsevick, 2005) and may represent a symptom cluster (Barsevick, 2007) such as pain, fatigue, insomnia, and depression. The presence of individual symptoms within a symptom cluster could result in different symptom outcomes; therefore, assessing patients for evidence of symptom clustering is important to reduce negative patient outcomes (Barsevick).

Patient Well-Being and Quality of Life

Depression has been associated with patient well-being, aspects of quality of life, and distress. Depression also has been significantly correlated with decreased activities of daily living (Pandey et al., 2007). Several investigators have found correlations between depressive symptoms and physical, functional, emotional (D'Antonio et al., 1998), and social well-being (Duffy et al., 2002). These symptoms also may influence physical, role, and social functioning (Llewellyn, McGurk, & Weinman, 2006). Higher depression scores repeatedly have been associated with lower quality of life (Aarstad et al., 2005; Chawla, Mohanti, Rahshak, Saxena, & Rath, 1999; D'Antonio et al., 1998; de Graeff et al., 2000a, 2000b; Duffy et al., 2007; Kelly at el., 2007; Kohda et al., 2005; Llewellyn et al., 2006). However, Nordgren et al. (2003) found that depression scores at one year follow-up were not predictive of quality of life at five years. Depression also has been correlated with global distress levels as well as with emotional, family, and social distress (Pandey et al.). In one study, a relationship did not appear to exist between emotional functioning and depressive symptoms on survival (de Graeff et al., 2001).

Summary and implications: Patient well-being and quality of life are conceptualized and measured in many ways. A relationship clearly exists between depression, well-being, and quality of life, but these are complex and complicated relationships that require more research beyond the scope of this article. Research to date that has examined the many different facets of these variables has found an enormous variation in the way patients experience and adapt to their illness (Llewellyn et al., 2006). Why some patients experiencing depression report good quality of life but others do not still is unclear. Of the studies examining the relationship of quality of life to depression, it appears that baseline depression is a better predictor of depression at later time points than is quality of life (Llewellyn et al.).

Time Points in the Treatment Trajectory

Depression has been associated with specific time points in the illness trajectory and passage of time. Depression did not influence delay in seeking consultation for initial head and neck cancer (Rozniatowski et al.,

2005). Depression has repeatedly been found at diagnosis as well as at 6, 12, 24, and 36 months, and even six years after treatment. Researchers in 10 studies found high levels of depression at the time of diagnosis, followed by improvement after treatment (Chawla et al., 1999; D'Antonio et al., 1998; de Graeff, de Leeuw, Ros, Hordjik, Battermann, et al., 1999; de Graeff, de Leeuw, Ros, Hordjik, Blijham, et al., 1999, de Graeff et al., 2000a; de Leeuw et al., 2001; Gritz et al., 1999; Hammerlid et al., 1997, 2001; Karnell et al., 2006; Kelly et al., 2007). Depression levels increased from before treatment to completion of treatment (Kelly et al.; Rose-Ped, Bellam, Epstein, Trotti, Gwede, & Fuchs, 2002), but a gradual improvement of depressive symptomatology was seen after treatment with the passage of time, even in the face of physical deterioration (de Graeff et al., 2000a; Gritz et al.). Hammerlid et al. (1998) reported that depression levels were high at one year after diagnosis; Hammerlid et al. (2001) also found that depression decreased 50% between diagnosis and three years.

Summary and implications: Patients undergoing curative treatment experience significant morbidity that creates distress associated with more depression (Pandey et al., 2007). Despite physical deterioration, emotional functioning gradually improved and depressive symptomatology decreased with time (de Graeff, de Leeuw, Ros, Hordjik, Battermann, et al., 1999), with an improvement occurring between diagnosis and three years (Hammerlid et al., 2001). However, it cannot be presumed that time will entirely remedy the issue of psychological distress for patients with head and neck cancer (Espie et al., 1989) given that depression has been found up to six years after treatment (Verdonck-de Leeuw et al., 2007). Depression after treatment that persists over time often is the result of issues with depression present at the time of diagnosis or level of concurrent head and neck cancer–specific outcomes, such as symptoms and treatment side effects (Karnell et al., 2006).

Treatment Characteristics

Depression has been examined in relation to type of treatment by several researchers. Krouse, Krouse, and Fabian (1989) found that depression increased over time (three months and one year) after surgical resection of oral and oropharyngeal cancers in patients who underwent composite resections. Morton, Davies, Baker, Baker, and Stell (1984) found no significant difference in depression between patients who had surgery alone versus those who had salvage surgery after failure of radiation therapy. Depression levels for patients following partial laryngectomy were lower than for patients following total laryngectomy (Braz, Ribas, Dedivitis, Nishimoto, & Barros, 2005).

In studies comparing treatments, depression scores were worse for patients receiving flap surgery and surgery plus adjuvant radiotherapy (Rogers et al., 2006). In one study,

patients undergoing surgery and radiation treatment functioned better and had fewer depressive symptoms than patients undergoing chemotherapy and radiation (El-Deiry et al., 2005). Patients with laryngectomies have been found to have higher depression levels from diagnosis to one year after treatment than patients having radiation and chemotherapy (Hammerlid et al., 1998). In patients receiving combined treatment, high depression levels and performance status at baseline predicted severity of symptoms and poor functioning after treatment (de Graeff, 2000b). Additionally, patients treated with aggressive hyperfractionated accelerated radiation therapy were at a higher risk of depression (Sehlen et al., 2003).

Summary and implications: Patients receiving both combined and more aggressive treatments are most at risk for depression. As part of determining the type of treatment for head and neck cancer, an evaluation of the patient's functional status and psychological symptoms is recommended. Selection of treatment should be tailored to the individual patient (El-Deiry et al., 2005). As new treatments for head and neck cancer are developed, research related to the depression levels of patients receiving the treatments must be explored.

Multiple Characteristics Predicting Depression

De Leeuw et al. (2000a, 2001) used a combination of patient variables at diagnosis to predict depression at later time points. Five variables (physical symptoms, depressive symptoms, emotional support, extent of social network, and avoidance coping) predicted depression at 6 and 12 months (de Leeuw, de Graeff, Ros, Blijham, et al., 2000). In subsequent work, eight pretreatment variables (tumor stage, sex, depressive symptoms, openness to discussing cancer in the family, available social support, received emotional support, tumor-related symptoms, and size of informal social network) were used to calculate a risk score to determine patient depression six months to three years following treatment (positive predictive value 58%; negative predictive value 83%) (de Leeuw et al., 2001).

Summary and implications: The presence of depressive symptoms before treatment and at six months is a good indicator of future depression. Depression also is influenced by other factors, such as physical symptoms, amount and type of support, and disease stage. The study of patient variables that are predictors of depression is important for future research so this patient population can receive appropriate screening, repeated monitoring, and early intervention (McDonough et al., 1996; Sehlen, 2003; Verdonck-de Leeuw, 2007).

Limitations

This systematic review had several limitations. First, the majority of studies reviewed assessed depression by using self-report depression instruments instead of an

interview with a trained clinician using the *Diagnostic and Statistical Manual* depression criteria. Second, when used alone, self-report instruments have been questioned in light of their ability to positively identify depression (Kathol, Noyes, & Williams, 1990). Third, different constructs of depression as well as different instruments to assess depressive symptoms used by researchers caused a significant issue in comparing results across studies (Snaith, 1987). Fourth, self-report measures may produce high false-negative diagnostic rates depending on the cutoff points used to indicate depression. These cutoff points may differ in separate investigations even when the same scale is used (Meyers & Weissmann, 1980). Finally, researchers did not consider how dysregulation of stress hormones, physiologic factors, or cytotoxic drugs may have affected depressed patients in their studies (Archer, Hutchison, & Korszun, 2008).

Recommendations for Future Research

The findings of this systematic review suggest the need for additional depression research among patients with head and neck cancer. The fact that researchers from 13 countries have studied depression suggests the need for identification of specific global and regional issues and cultural differences in this population. Because the majority of researchers in the studies reviewed used self-report depression instruments, a need exists for more research in which depressive disorders are identified by trained clinicians using the *Diagnostic and Statistical Manual* criteria to differentiate depressive symptoms from a psychiatric diagnosis. In addition to research that more precisely identifies prevalence rates, several other key areas require more study. Some of these areas overlap with the recommendations made by the National Institutes of Health State-of-the-Science Panel (2004). For example, studies with sufficient sample sizes, studies of the incidence of depression, investigations of occurrence and relation of coexistent conditions such as pain and sleep disorders, studies of screening strategies and diagnostic approaches in clinical practice, and comparison of results from different assessment instruments are needed. Other areas for future studies go beyond these recommendations.

Patient Characteristics

Numerous patient characteristics clearly are associated with depression among patients with head and neck cancers. Existing studies generally involved older patients, but depression in the new head and neck cancer subset of HPV-positive patients has not been studied. Also, because many researchers studied heterogeneous samples of patients, which patient characteristics are associated with depression for each specific anatomic site of head and

neck cancer still are unclear. For example, patients with cancer of the oropharynx have been identified as having a high prevalence of depression (Massie, 2004), but few studies have focused on this particular anatomic site. Low incidence rates and smaller numbers of patients receiving treatment at most clinical sites often account for the difficulty in obtaining sufficient sample sizes to study relationships among cancer and patient characteristics; therefore, multisite studies are needed to address this issue.

Of the studies reviewed, only eight (16%) reported the race of the patients, and neither ethnicity nor subcultural group membership was reported. Because race, ethnicity, and subgroup identity are increasingly important in today's multicultural society, and because different cultural or group behaviors may influence the individual experience of depression, additional research in this area is needed. Researchers are encouraged to report race and ethnicity of their samples and to explore relationships among these variables and other variables of interest.

Patient Symptoms

The co-occurrence of multiple physical symptoms and depression within this population suggests the need to examine and develop patient profiles that reflect these clusters of symptoms (Chen & Chang, 2004). Problematic symptoms for this cancer population include simultaneous occurrence of pain, fatigue, insomnia, anorexia (Chen & Chang), weight loss (Westin et al., 1988), difficulty swallowing (Verdonck-de Leeuw et al., 2007), and pain (Tesch et al., 2004). Also needed are studies that address the consequences and clinical implications of multiple rather than individual symptoms. Future studies must start with the assessment for evidence of clustering (Barsevick, 2007), the key components of which include relationships of symptoms, underlying dimensions, concurrence, stability, and common etiology (Kim et al., 2005).

Patient Well-Being and Quality of Life

Well-being and quality of life have been extensively studied in relation to depression in the head and neck cancer population. Because of conceptual and measurement differences between studies and the individual adaptation of each person, the relationship between depression and these variables is not entirely clear. One area in need of additional study is the association between distress, both symptomatic and psychological, and depression. Also, additional research is needed to examine these variables in relation to communication deficits because patients' ability to communicate may be adversely affected by side effects during treatment and they may experience a long-term loss of the ability to speak. This would affect their ability to communicate with caregivers and receive psychological counseling or support to address any depression they may experience during or following treatment. Qualitative studies are needed to

understand family, occupational, and social role changes that patients experience as a result of having head and neck cancer and the relationship to depression.

Time Points in the Treatment Trajectory

Future studies should consider psychological adjustment in patients at fixed time points during the cancer trajectory (Espie et al., 1989) because patients appear particularly vulnerable to depression at certain time points. Few researchers address depression among patients with head and neck cancer during survivorship and recurrence. This gap indicates a need for more longitudinal studies that investigate depression after treatment, including functional status and disability related to physical and emotional consequences of head and neck cancer and its treatment. A question not specifically addressed in any of the studies reviewed is the influence of demoralization and delirium related to depression in patients receiving intensive treatment over a long period of time. Therefore, future investigators should use a longitudinal research design to examine the full dimensions of the symptomatologic and depressive experiences of patients (Chen & Chang, 2004).

Treatment Characteristics

Treatments for head and neck cancer include surgery, radiation, and chemotherapy, as well as newer more aggressive combined modality regimens. A few studies have examined depression and type of treatment regimen, but they still make up a relatively small body of evidence. As new intensive treatments and regimens are developed, researchers should assess the level of depression for patients receiving these treatments.

Multiple Characteristics Predicting Depression

More work is needed on the patient characteristics and symptoms at diagnosis and follow-up that may influence or predict depression at later time points. In addition, replication of existing studies are needed to strengthen evidence about which patients to target for depression screening, evaluation, and monitoring. Knowing predictors of depression in patients with head and neck cancer has the potential to influence evidence-based clinical practice for prediction of occurrence, assessment, and management.

Three specific recommendations from this systematic review are supported by the Oncology Nursing Research Priorities (Oncology Nursing Society, 2007): focusing on individual and family behavioral and psychosocial aspects of cancer illness in everyday life, research in cancer symptoms and side effects that focus on symptoms clusters and associated outcomes, and research that considers the late effects of cancer treatment and long-term survivorship.

Conclusions

Overall, the findings of this systematic review provide a summary of the current body of knowledge regarding patients with head and neck cancer and depression. Specific recommendations can be used to provide direction for future research that will ultimately strengthen the existing knowledge and guide clinical practice.

Mary Ellen Haisfield-Wolfe, PhD, RN, OCN®, is a student, Deborah B. McGuire, PhD, RN, FAAN, is a professor and director of the oncology graduate program and the Developing Center of Excellence in Palliative Care Research, Karen Soeken, PhD, is a professor emeritus, and Jeanne Geiger-Brown, PhD, RN, and Bruce R. De Forge, PhD, are associate professors, all in the School of Nursing at the University of Maryland, Baltimore.

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