Assessment of Depression in Cancer Patients

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It is widely known that depression exists in patients with cancer. The prevalence, however, varies widely by study and is often attributable to differences in assessment procedures. Attempts to identify accurate methods of assessing depression in cancer patients have employed different diagnostic approaches, assessment methods (e.g., self-report versus interview), and inclusion criteria. Unfortunately, all of these variables affect conclusions that can be drawn regarding the presence of depression in cancer patients. Other variables that can further affect the assessment of depression in cancer patients include individual differences such as the patient's age, gender, race/ethnicity, hospitalization status, and type and stage of cancer. Finally, the specific assessor and the timing of the assessment also likely affect conclusions about depression in cancer patients. This review was designed to succinctly address all of the above issues and identify several areas for future research, including refining diagnostic criteria for depression in cancer patients; creating cancer-specific depression measures with appropriate cutoffs; focusing on the issues of age, race, ethnicity, subculture, and type and stage of cancer in creating depression assessment tools; and exploring the issues of clinical versus subclinical depression, who and when to assess, and timely and cost-effective ways to assess. [J Natl Cancer Inst Monogr 2004;32:80–92]

As effective treatments for cancer continue to be identified and refined, increasing numbers of patients are obtaining either a cure or increased longevity, and more attention is being paid to the psychological issues that can accompany the diagnosis of and treatments for cancer. Studies have reported the presence of psychological disorders (i.e., anxiety, depression, adjustment disorders) in approximately 30% of patients *(1–5),* although this percentage varies depending on the specific disorder and study. The prevalence of depression, in particular, ranges from 1.5% to over 53% *(6,7).* Bukberg et al. *(8)* reported that roughly 25% of cancer patients report severe depressive symptoms, with the prevalence increasing in those with advanced illness to 77%. Additional information regarding the prevalence of depression in cancer has been reported by Massie *(9).*

Factors contributing to the variability in the prevalence of depression are many and include age and gender of the patient, hospitalization status, cancer diagnosis, and stage of cancer (i.e., diagnosis through end of life) (10). These issues also contribute to the difficulty in assessing depression in cancer patients. Other issues that are important when assessing for depression in this population include the diagnostic approach (e.g., inclusion, substitution), type of measure (i.e., diagnostic interviews versus self-report measures), and inclusion criteria (clinical versus subclinical) employed. This article discusses these issues, in addition to who should assess for depression and how it can be accomplished effectively. The ultimate goal is to be able to fully understand important issues in assessing depression in cancer patients to provide interventions to those who are most likely to benefit.

Diagnostic Approaches

Depression is defined through the DSM-IV [*Diagnostic and Statistical Manual of Mental Disorders–Fourth Edition (11)*] as the presence of depressed mood or loss of interest or pleasure in nearly all activities for a period of at least 2 weeks. The individual must also present with four of the additional symptoms (Table 1). They include symptoms that can be conceptualized as encompassing somatic (e.g., weight/appetite, fatigue) and cognitive (e.g., poor concentration, guilt) changes from normal functioning that result in significant distress or impairment.

The diagnosis of depression in physically ill patients is difficult because symptoms of depression are often similar to those of the physical illness or its treatments. This is especially true when diagnosing depression in the cancer patient. Treatments for cancer (e.g., chemotherapy, biological therapy) often result in many of the symptoms needed for a diagnosis of depression such as fatigue, weight loss, anhedonia, and psychomotor retardation. As such, it is difficult to determine with reasonable accuracy the source of these symptoms. In an attempt to identify an accurate method of assessing depression in medical patients, and cancer patients in particular, researchers have employed four different approaches: inclusive, etiologic, substitutive, and exclusive *(12,13).* These approaches are summarized in Table 2.

Inclusive

The inclusive approach uses all of the symptoms of depression, regardless of whether they may or may not be secondary to a physical illness *(14),* and is reflected in such interviews as the Schedule for Affective Disorders and Schizophrenia (SADS) and the Research Diagnostic Criteria. The result of employing this approach is high sensitivity (i.e., the ability to correctly identify those who are depressed), but lower specificity (i.e., the ability to correctly identify those who are not depressed). In other words, the tendency with this approach is to overdiagnose depression because of the lack of discrimination regarding the cause of the symptoms. This finding was observed by Kathol et al. *(15),* who reported an 8% drop in the prevalence of depression between an inclusive approach and removal of symptoms caused by cancer.

Etiologic

In contrast, the etiologic approach (that used in the Structured Clinical Interview for DSM and Diagnostic Interview Schedule (DIS), as well as the DSM-III-R/IV) counts a symptom of depression only if it is clearly not the result of the physical illness *(16).* This approach has been suggested by Rodin et al.

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DOI: 10.1093/jncimonographs/lgh013
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Table 1. DSM-IV symptoms of depression

Depressed mood*
Anhedonia*
Insomnia/hypersomnia
Fatigue/loss of energy
Significant weight/appetite change (increase or decrease)
Psychomotor agitation/retardation
Worthlessness/guilt
Reduced concentration, ability to think, or indecisiveness
Recurrent thoughts of death or suicide

*Either of these must be present for a diagnosis of major depressive episode by the DSM-IV criteria.

(17) as the best solution because it provides a more accurate view of the presence of depression. Unfortunately, as Cohen-Cole et al. *(12)* have pointed out, it is unlikely that the average psychiatrist can become familiar enough with all diseases to reliably determine whether a symptom of depression (e.g., fatigue) was a normal or excessive result of the physical illness. The result becomes a reliance on inference, a method of assessment that is typically unreliable. If such a determination is difficult for psychiatrists, it is likely to be close to impossible for other professionals dealing with depressed physically ill individuals.

Substitutive

In an attempt to reduce confusion over the symptoms' cause, the substitutive approach replaces symptoms that may be related to the physical illness (e.g., fatigue) with additional cognitive symptoms (e.g., indecisiveness, hopelessness, pessimism) *(18–20).* Specific modified criteria were provided by Endicott *(20),* although other symptoms could be used. This approach has resulted in similar prevalence rates of depression when compared with the inclusive approach *(15)* and lower rates when compared with the etiologic approach (29% versus 49%). Others have noted that replacing somatic with psychological criteria offers no obvious advantage *(21–23).* An issue with this approach is that it affords great variability in the choice of the specific criteria that could be substituted and whether criteria will (or should) differ depending on the physical illness. As such, Endicott *(20)* notes that if alternative symptoms are used, several issues should be considered. In particular, it is important to train evaluators thoroughly in the new symptoms to ensure consistent application of criteria to all patients, rationale for using the alternative symptoms should be provided to evaluators, and publication of results should occur with descriptions of the criteria used. This last point is most important when attempting to compare results.

Exclusive

Finally, the exclusive approach eliminates two common symptoms of depression (i.e., fatigue and appetite/weight changes) that are frequently the result of a physical illness and uses only the other symptoms of depression *(8,24).* Although equally as pure as the inclusive approach, the exclusive approach suffers from the opposite problem; namely, increased specificity, but lowered sensitivity. The end result is a lower prevalence of depression with an increased likelihood of missed cases (false negatives) and fewer individuals meeting the restricted criteria *(25).*

Given the issues associated with each approach, it is difficult to conclude which of the four approaches is best for being able to correctly identify those individuals with cancer who are depressed and may benefit from an intervention. Although a combination of these approaches is likely in clinical practice, a focus on a single approach is more likely in research studies. This practice is perhaps unfortunate given that a recent study that used both the etiologic and substitutive approaches to assess depression obtained a lower prevalence rate than when using either one alone *(26).* This finding would indicate that a more comprehensive approach is more accurate in identifying individuals who are depressed, although it could be criticized as being an overly restrictive definition of depression. Unfortunately, busy nonpsychiatric clinic practices, effectiveness research studies, and time constraints often limit the practicality of conducting in-depth, comprehensive assessments. Employing approaches that can quickly and consistently identify depression in cancer patients would make it possible to overcome these practical limitations.

Table 2. Criteria for depression by each diagnostic approach

Symptoms	Approach			
	Inclusive	Etiologic	Substitutive	Exclusive
General				
Depressed mood	X	X	X	X
Anhedonia	X	X	X	X
Physical				
In/hypersomnia	X	X	X	X
Weight/appetite change	X	X		
Psychomotor agitation/retardation	X	X	X	X
Fatigue/loss of energy	X	X		
Psychological				
Worthlessness/guilt	X	X	X	X
Poor concentration/indecisiveness	X	X	X	X
Suicidal ideation/thoughts of death	X	X	X	X
Brooding			X	
Indecision			X	

*Etiologic differs from Inclusive in that it requires that a symptom count only if it is clearly not caused by a physical condition.

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How to Assess: Clinical Interview versus Written Self-Report Measures

How to assess for depression can best be addressed by the following questions: What are the methods used for clinical assessment of depression throughout the course of cancer? And what is the evidence for their reliability and validity in cancer patients? In response to this, there are two approaches commonly used: clinical interviews and written self-report measures.

Clinical Interviews

Structured clinical interviews have traditionally been considered the gold standard for identifying the prevalence, clinical significance, and potential treatment of depression because of their rigorous criteria. Common interviews include the SADS *(27)*, Structured Clinical Interview for DSM *(16)*, Research Diagnostic Criteria *(25)*, and DIS *(28)*. In addition, researchers and clinicians have used unstructured clinical interviews in which they diagnose depression based on DSM *(29,30)* or Endicott *(26)* criteria. Table 3 provides a sample of the most commonly used interviews for assessing depression in cancer patients.

Although they possess rigorous criteria, the problems with diagnosing depression using structured clinical interviews stem from the fact that the interviews were developed from one of the diagnostic approaches previously discussed. Thus, the problems with misclassification based on somatic symptoms would apply to the SADS, whereas arguments against the substitutive approach would apply to interviews using the Endicott criteria. In addition, structured clinical interviews have been criticized for the length of time they take to administer and the amount of training that they require for proficiency in administration and scoring *(31)*, as well as for having little reliance on contextual information. Finally, they were developed and validated on a population devoid of significant comorbid physical illness. Hall et al. *(32)* point out that even clinical interviews are not completely reliable. As such, there can be some doubt as to whether they actually are the gold standard for all patients, particularly those patients with significant medical comorbidities.

Nevertheless, clinical interviews constitute the only way to obtain a diagnosis of depression and can be argued as essential in determining the true prevalence of a disorder. Interestingly, the aforementioned criticisms of structured clinical interviews are less applicable from a clinical perspective. For example,

Table 3. Commonly used clinical interviews for assessing depression in cancer patients*

Author (ref)	Clinical interview	N	Age range, y	Cancer diagnosis
Payne et al. *(113)*	SCID (all versions)	279	NR	Breast cancer
Passik et al. *(47)*	MINI (DSM-IV criteria)	60	58 ± 12	Mixed
Maunsell et al. *(114)*	DIS (DSM-III criteria)	205	22–85	Breast
Ciaramella and Poli *(25)*	Endicott criteria; SCID (DSM-III-R)	100	28–86	Mixed
Worden *(115)*	Semistructured interview	120	30–80	Mixed
Levine et al. *(116)*	Interview (DSM-III criteria)	100	<50–>70	Mixed
Massie et al. *(117)*	Interview (DSM II criteria)	334		Mixed
Massie and Holland *(118)*	Interview (DSM-III criteria)	546	10–>70	Mixed
Razavi et al. *(50)*	Clinical interview (Endicott criteria)	128	55 ± 14	Mixed
Desai et al. *(119)*	DIS (DSM-III criteria)	72	61 ± 16	Breast
Golden et al. *(21)*	Semi-structured interview (DSM-III criteria)	65	20–86	Gynecological
Silberfarb et al. *(120)*	Structured interview	146	30–80	Breast
Plumb and Holland *(23)*	Structured interview	80		Mixed
Derogatis et al. *(1)*	DSM-III criteria	215	50 ± 15	Mixed
Bukberg et al. *(8)*	Interview: Exclusive approach DSM-III criteria	62	23–70	Mixed
Morton et al. *(121)*	DSM-III criteria	48	>60	Oropharyngeal
Baile et al. *(122)*	Clinical interview (DSM-III criteria)	89	NR	Head and neck
Lansky et al. *(88)*	RDC (DSM-III criteria)	500	17–80	Mixed
Evans et al. *(123)*	DSM-III criteria	83	20–86	Gynecological (excluding ovarian)
Joffe et al. *(124)*	SADS-Lifetime	21		Pancreatic and gastric
Grandi et al. *(125)*	DSM-III criteria	18	37–75	Breast
Devlen et al. *(126)*	Semistructured interview	90	17–73	Hodgkin's and non-Hodgkin's lymphoma
		120	40 ± 16	
Hardman et al. *(127)*	Structured interview (ICD criteria)	126	NR	Mixed
Kathol et al. *(14)*	DSM-III/III-R; RDC; Endicott criteria	808	16–88	Mixed
Jenkins et al. *(128)*	CIDI (DSM-III criteria)	22	40–75	Breast
Hall et al. *(31)*	PSE	269	< 79	Breast
Colon et al. *(129)*	DSM-III criteria	100	NR	Acute leukemia
Hopwood et al. *(52)*	CIS (DSM-III criteria)	81	NR	Breast
Alexander et al. *(28)*	Clinical Interview (DSM-III-R criteria)	60	53 ± 14	Mixed
Sneeuw et al. *(130)*	DIS (DSM-III criteria)	556	NR	Breast
Chochinov et al. *(22)*	SADS	200	60–80	Mixed (Advanced cancers)
Hosaka and Aoki *(131)*	Interview (DSM-IV criteria)	50	57 ± 14	Mixed
Spiegel et al. *(87)*	SCID (DSM-III criteria)	96	51 ± 15	Mixed
Ibbotson et al. *(48)*	PAS (DSM-III criteria)	513	16–86	Mixed
Berard et al. *(29)*	SCID (DSM-IV criteria)	100	< 40–>59	Mixed

*SCID = Structured Clinical Interview; DSM = Diagnostic and Statistical Manual; DIS = Diagnostic Interview Schedule; SADS = Schedule for Affective Disorders and Schizophrenia; RDC = Research Diagnostic Criteria; PSE = Present State Exam; CIS = Clinical Interview Schedule; PAS = Psychiatric Assessment Schedule.

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Massie *(33)* has reported that a good assessment of depression includes symptom assessment, mental status, physical status, treatment effects, and laboratory data. Support for the presence of depression comes from a personal or family history of depression or suicide, concurrent life stresses, and the absence of social support. Consistent with the substitutive approach, Massie stresses that it is likely that the symptoms of weight/appetite change, insomnia, loss of energy, fatigue, psychomotor slowing, and decreased libido are less valuable in the diagnosis of depression in cancer patients given that they are likely confounders of the disease or treatment. Instead, a focus on the severity of dysphoric mood; degree of feelings of hopelessness, guilt, and worthlessness; and presence of suicidal thoughts are likely to be more effective *(33)*. In essence, Massie notes that a thorough clinical interview that focuses less on the somatic and more on the cognitive symptoms of depression, in addition to variables such as family history and so on, is important for identifying depression in the patient with cancer.

Although this information is almost always obtained in a thorough clinical interview before treating a patient, it is less likely to be obtained as part of a research study that uses a structured clinical interview. As such, for patients who are subsequently going to be receiving treatment, it would appear that the clinical interview is an important and necessary step for generating hypotheses about the cause of depression. In addition, because the individual who does the assessment is likely to be the one providing the treatment, there would be less concern for some of the drawbacks of this approach (e.g., clinician bias, questionable psychometrics, potentially incomplete inquiries). Neither the unstructured nor the structured clinical interview, however, appear to be the best approach for identifying individuals who may be at increased risk for depression and who would potentially benefit from a psychological intervention. This latter goal seems better served by written self-report measures.

Written Self-Report Measures

Written self-report measures constitute another approach for assessing depression in cancer patients. Their use in the assessment of depression in cancer patients is strengthened by their ease of administration and scoring by individuals who have not received extensive training, and the speed with which they can be completed by patients. In addition, written self-report instruments are further strengthened by their ability to obtain a gross assessment before a direct interview, quantify severity of depression, identify changes over time, and be used in busy practices *(34)*.

A variety of written self-report measures are commonly used to identify symptoms of depression in cancer patients. These include the Hospital Anxiety and Depression Scale (HADS) *(35)*, the Rotterdam Symptom Checklist (RSCL) *(36)*, the Beck Depression Inventory (regular and short forms) *(37,38)*, the Brief Symptom Inventory-Depression scale *(39–41)*, Center for Epidemiologic Studies Depression Scale (CES-D) *(42)*, and the Zung Self-Rating Depression Scale (both full and brief forms) *(43,44)*. Table 4 presents several of the more frequently used written self-report measures used to assess depression in cancer patients.

For written self-report assessments to be helpful in the identification of depression, they must demonstrate acceptable reliability, criterion validity, sensitivity, and specificity. In brief, reliability refers to the ability of a measure to obtain the same score on multiple occasions, or the consistency with which responses are made to the instrument, and must occur before assessing validity. The criterion validity of a measure refers to its correlation with an accepted standard (e.g., a clinical interview). Sensitivity and specificity have been previously discussed *(45)*. Two other issues, the misclassification rate and the positive predictive value are also important in identifying the usefulness of a measure. The misclassification rate is the number of people who are identified as either false positives or false negatives, whereas the positive predictive value of a test refers to the probability of a score at or above a chosen cutoff point being a true case. The latter takes into account only true cases and false positives. Given these definitions, it can be seen that cutoff scores are directly related to the issue of sensitivity and specificity, as a high cutoff score decreases sensitivity and increases specificity and a low cutoff score increases sensitivity and decreases specificity *(31)*. As such, an optimal cutoff score must be identified on each screening measure of depression. Failure to choose an appropriate cutoff score or to use a measure with low sensitivity and specificity results in inaccurate classification of depressed individuals, as well as significant differences in the number of subjects needed to find clinically important differences *(32)*.

As with the structured clinical interviews, written self-report measures have been created consistently with one of the aforementioned diagnostic approaches. For example, the HADS removes the somatic symptoms of depression, whereas the Beck Depression Inventory and the Zung include them; interestingly, the Brief Zung has removed the somatic symptoms of depression. The arguments for and against including somatic items, as previously noted, focus on the desire to reduce the number of false positives and to remove potentially confounding items. There is equivocal sentiment, however, over which instruments should be used *(46,47)*.

Regardless of the measure used, given the complicated issue of balancing false positives with false negatives and sensitivity with specificity, it is clear that choosing the correct or optimal cutoff score for identifying depressed patients is critical. From a practical perspective, on some measures this equates to choosing a score one or two standard deviations above the mean as a cutoff score. Ideally, choosing the "best" cutoff, some of which are presented in Table 5, would allow for a balance, thereby allowing the most efficacious treatments to be provided to those most in need. The importance of the choice of cutoff score was reflected by Passik et al. *(48)* in their study of the characteristics of the full and brief Zung Self-Rating Depression Scale. They noted that although there is no right or wrong cutoff, they subsequently identified the best choices for cutoffs on the full and brief Zung for reducing false positives.

The majority of research on depression in cancer patients has used the HADS, with much of this research focused on identifying the optimal cutoff scores for depressed patients with cancer. Often this has been done in combination with the RSCL or clinical interviews. Unfortunately, which cutoff score to use has often varied by study. For example, using a HADS unitary scale cutoff score of 14, Ibbotson et al. *(49)* noted that the HADS performed well in identifying depression for patients who were disease free or with stable disease, but not with progressive disease. In contrast, focusing on women with early breast cancer, Ramirez et al. *(50)* used the HADS as a unitary scale with 11 as the threshold and found

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Table 4. Written self-report measures for assessing depression in cancer patients and the cutoffs employed*

Author (ref)	Measure	Cutoffs	% depressed	Cancer population
Lloyd-Williams et al. *(132)*	HADS	8	63	Mixed metastatic
		11	32	
		(D subscale)		
Payne et al. *(113)*	HADS	10	33	Breast (43% no cancer; 11% Stage I; 31%
		13	27	stage 2; 7% stage III; 51% Stage IV)
Hopwood et al. *(132)*	HADS	8–10	21	Breast
		11+	9	
		(D subscale)		
Pinder et al. *(89)*	HADS	11	12	Breast (advanced disease)
		(D subscale)		
Razavi et al. *(50)*	HADS	19	NR	Mixed
		(total scale)		
Maraste et al. *(6)*	HADS	8–10	10	Breast (conservation and mastectomy
		11+	3	surgery)
		(D subscale)		
Lees and Lloyd-Williams *(134)*	HADS	19	40	Mixed malignant disease
		(total scale)		
Hosaka and Aoki *(131)*	HADS	8	28	Mixed
		(D subscale)		
Berard et al. *(29)*	HADS	>7	14	Mixed
		>9	8	
	BDI	>13	20	
		>15	14	
Hall et al. *(31)*	HADS	7	18.4	Breast (early stage)
		8	16.5	
		11	7.5	
		(D subscale)		
	RSCL	7	43.1	
		8	32.2	
		11	18.5	
Ibbotson et al. *(48)*	HADS	14	NR	Mixed
	RSCL	7	NR	
Dugan et al. *(33)*	ZSRDS	SDS index score:		Mixed (half with early stage disease)
		50–59 mild	21.5	
		60–69 moderate	12.5	
		70+ severe	1.9	
	BZSRDS	SDS index score:		
		22–32 mild	17.9	
		33–38 moderate	8.4	
		39–44 severe	4.8	
Passik et al. *(47)*	ZSRDS	SDS Raw score:	NR	Mixed (convenience sample)
		40–47 mild		
		48–55 moderate		
		56–80 severe		
	BZSRDS	SDS Raw score:	NR	
		22–32 mild		
		33–38 moderate		
		39–44 severe		
Ciaramella and Poli *(25)*	HRSD	7+ presence	NR	Mixed
		16+ moderate-severe		
Middelboe et al. *(135)*	HRSD	13–17	33	Mixed (patients undergoing chemotherapy)
		>17	14	
Lansky et al. *(88)*	HRSD *and* ZSRDS	20 HRSD *and* 50 ZSRDS	5.3	Mixed
Kurtz et al. *(136)*	CES-D	16+	38.9 @ T1	Lung (geriatric patients)
			32.5 @ T2	
			34.3 @ T3	
			30.9 @ T4	
Vernon et al. *(137)*	CES-D	16+	24	Colorectal
Spiegel et al. *(87)*	CES-D *and* BDI	NR	NR	Mixed
McLachlan et al. *(138)*	BDI-SF	8–15 moderate	12	Mixed, any clinical stage
		16+ severe	3	
Frost et al. *(139)*	BSI	NR	NR	Breast
Epping-Jordan et al. *(140)*	SCL-90-R	T score = 63	34	Breast

*HADS = Hospital Anxiety and Depression Scale; D = Depression; ZSRDS = Zung Self-rating Depression Scale; BZSRDS = Brief Zung Self-rating Depression Scale; RSCL = Rotterdam Symptom Checklist; HRSD = Hamilton Rating Scale for Depression; BDI-SF = Beck Depression Inventory-Short Form; CES-D = Center for Epidemiological Studies-Depression Scale; BSI = Brief Symptom Inventory; SCL-90-R = Symptom Checklist-90-Revised; NR = not reported.

a sensitivity of 70% in identifying psychiatric disorder preoperatively. This varied by the age of the woman, however, as women <50 years of age demonstrated a 90% sensitivity and a 40% false positive rate using 11 as the threshold, but in women >50 years of age the sensitivity was 57% and the false positive rate was 3%. Razavi et al. *(51)* used ROC curves on the HADS and reported that for screening for major depression, the optimal cutoff score was 19, associated with

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70% sensitivity and 75% specificity for screening major depressive disorders only in a sample of inpatients. Interestingly, a lower cutoff point was found as optimal in a population of lymphoma outpatients *(52)*.

In contrast to the use of the HADS as a unitary scale (which includes both anxiety and depression subscales), others have focused on the HADS depression scale only. As an example, Hopwood et al. *(53)* reported that the HADS had optimal sensitivity and specificity with a threshold of 11 on the depression scale, correctly identifying 75% of those suffering from an affective disorder; however, misclassification of patients using this scale was 25%. Hall et al. *(32)* used the HADS, RSCL, and Present State Exam (PSE) and found that only 14 women were classified as depressed on both the HADS and PSE when using a threshold of 11 on the depression scale of the HADS. In contrast, 99 (37.2%) women had been assessed as depressed using the PSE. Thus, the sensitivity was 14.1% and the specificity was 98.2%. Sensitivity was increased, but specificity decreased as the threshold was lowered. The authors conclude that using a threshold of 11 on the HADS scales yielded unacceptably low sensitivity and that lowering the threshold to 7 did not result in reasonably accurate screening for depression, although they qualify this by noting that the PSE may have identified too many cases. Although this finding was in contrast to others who have used the HADS *(49,51,53)*, it led to the conclusion that the HADS may be inappropriate for screening in the cancer population *(32)*. Should the HADS continue to be used as a screening tool, Aapro and Cull *(10)* suggest that it should be followed by further assessment designed to assess the number and severity of depressive symptoms relative to recognized diagnostic criteria; a recommendation that could be applied to any self-report measure.

Table 5 presents the sensitivity, specificity, misclassification rate, and positive predictive value for several written self-report measures used with cancer patients. As can be seen, there is noticeable variability in the findings that may be attributable to differences in validation measures, sample studied, or other issues specific to the particular study. This makes choosing instruments even more difficult, even when attempts have been made to use the literature to inform those choices.

Despite their ease of use and other strengths, written self-report measures have some limitations. Among them is the fact that written self-report instruments measure depressive symptomatology but do not provide diagnoses. Comparison of findings from written self-report measures with those from structured and unstructured clinical interviews has prompted some authors to note that significant numbers of patients report the presence of symptoms of depression, but relatively few have symptoms that are indicative of severe depression *(34,54)*. It remains debated as to the disruptive effects depressive symptomatology has on individuals *(55)*. In addition, written self-

Table 5. Cut-off points on self-report measures with associated sensitivity, specificity, misclassification rate, and positive predictive value (PPV)*

Author (ref)	Measure	Validation measure	Cutoff	Sensitivity, %	Specificity, %	Misclassification rate, %	PPV, %
Lloyd-Williams et al. *(132)*	HADS	PSE (ICD-10)	19 (unitary scale)	68	67	NR	36
			11 (depression subscale)	54	74	NR	37
Payne et al. *(113)*	HADS	SCID (DSM-III-R)	13	NR	NR	NR	75
Ramirez et al. *(49)*	HADS	Diagnostic rating criteria	11 (unitary scale)	70	NR	NR	NR
Ibbotson et al. *(48)*	HADS	DSM-III	14	80	76	NR	41
	RSCL		7	83	71		37
Razavi et al. *(50)*	HADS	Endicott criteria	19 (unitary scale)	70	75	NR	NR
Hopwood et al. *(52)*	HADS	Clinical Interview Schedule (DSM-III)	11 (depression subscale)	75	75	25	55.6
	RSCL		11	75	80	21	42.9
Hall et al. *(31)*	HADS	PSE (DSM-III)	11 (depression subscale)	14.1	98.2	34.2	82
	RSCL		11	30.6	95.9	29.9	90
Berard et al. *(29)*	HADS	DSM-IV criteria	8	71	95	10	79
			10	43	96	15	75
	BDI		14	90	90	13	63
			16	86	86	7	82
	HADS & BDI		8 and 16	95	91	8	74
Passik et al. *(47)*	ZSRDS	MINI	>40	55.56	100	26.7	NR
			>48	86.11	66.67	21.7	
			>56	100	33.33	26.7	
	BZSRDS		>22	41.67	95.83	36.7	
			>33	97.22	29.17	30	
			>39	100	0	40	
Doetch et al. *(141)*	GDS	NR	11	84	95	NR	NR
Schein and Koenig *(77)*	CES-D	DSM-III-R criteria	20	61.5	94	NR	84

*HADS = Hospital Anxiety and Depression Scale; ZSRDS = Zung Self-rating Depression Scale; BZSRDS = Brief Zung Self-rating Depression Scale; RSCL = Rotterdam Symptom Checklist; GDS = Geriatric Depression Scale; CES-D = Center for Epidemiological Studies-Depression Scale; PSE = Present State Exam; ICD = International Classification of Disease; SCID = Structured Clinical Interview; DSM = Diagnostic and Statistical Manual; NR = not reported.

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report measures are limited by their lack of rigorous criteria and potential to lead to overdiagnosis and high false positives *(31)*.

Conclusions

Both structured and unstructured clinical interviews and written self-report measures are available for assessing depression. These approaches are limited by the fact that they follow a diagnostic approach that was initially developed to assess depression in patients without comorbid physical illness. Despite that, the HADS represents a written self-report measure explicitly developed for assessing depression with patients in an outpatient medical setting *(35)*, with confirmation of its factor structure obtained in patients with cancer *(56)*. The limited validation of measures (written self-report and interviews) on cancer patients specifically indicates that there is clearly a need for future research. There is also the need for identifying carefully calibrated screening methods and their cutoff scores for the setting in which they are applied *(10)*. This issue is related to that of clinical versus subclinical levels of depression. It is perhaps premature to conclude that symptoms of depression present in the absence of a clinical syndrome do not require further examination and perhaps treatment. Potential research strategies to resolve these issues include determining the effect of subclinical and clinical depression on the quality of life of the patient, medical use, and adherence to medical regimens. In addition, comparing the efficacy of interventions for reducing depressive symptoms in both of the populations would potentially identify the optimal intensity or duration of an intervention. Finally, additional research is needed to determine cutoffs on screening measures that reliably and validly differentiate individuals with subclinical versus clinical depression. Until research studies are designed to resolve these issues, when treating depression in cancer patients, screening instruments should be followed by more detailed medical assessments (and one would assume psychological assessments) *(31)*.

Developmental Issues Pertinent To Assessing Depression

The majority of the studies in the preceding discussion assessed depression in adult cancer patients, although the age ranges varied widely and often included individuals who could be classified as elderly or old age. A separate body of literature focuses on depression in children with cancer. Both children and the elderly, however, have issues that need to be considered when assessing depression in the cancer patient.

Depression in Children

The diagnosis of depression in children without cancer is made difficult by the fact that the clinical picture is frequently different from that of adults. In particular, younger children are more likely to demonstrate anxiety and somatic symptoms, temper tantrums, and behavioral problems, whereas the traditional cognitive components of depression (e.g., low self-esteem, guilt, and hopelessness) are not observed until middle to late childhood *(57)*. In addition, recognition of depression in adolescents is difficult because there is the expectation that teens will be "moody." Important symptoms in adolescents include sleep and appetite disturbance, irritability, and impairment in functioning. Further difficulty assessing depression stems from the fact that depression may be masked by anger/irritability, cutting behaviors, or eating disorders, and that younger children may have difficulty verbalizing thoughts and feelings (C.A. Dittner, personal communication, 12 March 2002).

Given the difficulties with assessing depression in children, it has been argued that the best approach is to use a structured clinical interview, such as the Schedule for Affective Disorders and Schizophrenia for School-Age Children (KSADS) *(58)* or Diagnostic Interview Schedule for Children *(59)*, with multiple informants, given that teachers and parents observe different behaviors in children that may be associated with depression. Similar to the SADS, the KSADS is a structured clinical interview for diagnosing psychiatric disorders in childhood. Both the child and the caregiver are interviewed. The KSADS has been reported to be too long to administer in clinical settings, and like the SADS, it requires extensive training. In addition, low correlation between parent and child reports makes it a poor approach for assessing depression in younger children *(60)*. Likewise, little information is available on the ability of the Diagnostic Interview Schedule for Children to correctly identify children with true major depression, as well as on its concurrent validity *(61)*.

Written self-rating scales have also been identified for assessing depressive symptoms in children and include such measures as the Child Depression Inventory (CDI) *(62,63)*, Center for Epidemiological Studies Depression Scale for Children *(64)*, and Youth Self Report *(65)*. As with the adult measures, these are good for screening symptoms, checking the severity of depressive symptoms and monitoring progress in treatment. Both the CDI and the Youth Self Report, however, are rated by the child and as such require certain levels of reading comprehension and metacognitive ability. The ability to reflect on the self is a quality not present in children under the age of 8 years. Indeed, the majority of assessment instruments does not address the level of child competence and potentially limit the accuracy of the measure *(62)*. In addition, Fristad et al. *(66)* found that studies using the CDI frequently misused the instrument (e.g., as a diagnostic tool) and noted that caution in the administration and interpretation of self-report measures of depression in children is needed. Additional problems with written self-report measures in children include low specificity and the potential for random responses by adolescents. All of these problems require that additional reports be obtained by parents/teachers and behavioral observations of the children.

The issues of assessing depression in children are compounded when the child has been diagnosed with cancer. Added to the aforementioned issues are those concerning whether the symptoms observed in the child are the result of the disease or treatment, isolation from friends and family, or change in daily routine that frequently accompanies treatment for cancer. Interestingly, in studies that have assessed depression in children, a consistent finding is that depression in children and adolescents with cancer is no more prevalent than in the general population *(67–72)*. Explanations for this finding have included the increased use of avoidance or defensive coping strategies *(73–75)* and have led to suggestions that specific symptoms of depression (e.g., anhedonia) be investigated *(76)*. Despite the use of measures such as the CDI in pediatric cancer populations, however, there are few, if any, studies that have specifically undertaken the task of validating a measure of depression in a pediatric cancer sample.

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Depression in the Elderly

As with children, the diagnosis of depression in older adults (>65 years of age) without cancer is occasionally made difficult by variations in symptom presentation. The presence of somatic symptoms that occur frequently in elderly individuals such as changes in appetite, sleep, and fatigue increase the possibility of obtaining higher false-positive rates *(77,78).* In addition, issues such as the presence of dementia, delirium, cognitive impairments, or a performance status that does not allow one to provide responses on their own make the assessment of depression more challenging *(79).* In individuals who are able to complete questionnaires, in terms of symptoms of depression endorsed, Passik et al. *(80)* found that significantly higher scores were obtained on the cognitive factor of the Zung by individuals over 80 years when compared with 50–69 year olds.

In addition to the written self-report measures that are used with adults, there are additional questionnaires that have been created specifically for assessing depression in the elderly. These have been designed to reduce the focus on somatic concerns. Most notable among them is the Geriatric Depression Scale (GDS) *(81),* a 30-item questionnaire with binary (yes/no) response choices. The GDS was developed by expressly eliminating the somatic items commonly included in other depression measures. Cutoff scores with acceptable sensitivity and specificity have been identified *(81),* with a score between 10 and 20 representing "mild" depression and a score ≥20 representing "severe" depression *(77).* A shorter, 15-item, version of the GDS has also been created with cutoff scores that provide adequate sensitivity and specificity *(82).*

The concern that was previously noted in removing somatic items from the assessment of depression in cancer patients has also been expressed with assessments of depression in the elderly, the argument being that the profile of depression in the elderly is as likely to include somatic symptoms as it is cognitive and that excluding such items may result in missed symptom information and cases of depression *(78).* Attempts to determine the veracity of this position have resulted in attempts to validate self-report measures that include somatic items (such as the CES-D) in physically ill elderly patients. Evaluation of the CES-D by Schein and Koenig *(78)* revealed that a cutoff score of 16 resulted in an unacceptably high false-positive rate. Their findings did not support the use of the stringent cutoff of 27 identified by some researchers *(83,84)* and noted that a score of 20 resulted in the highest hit rate and provided an accurate proxy for a diagnosis.

To sum, there appear to be several assessment approaches that can be used to identify depression in the elderly, including those who are physically ill. Of note is the fact that functional deficits may make it difficult to obtain an accurate assessment of depression. In such cases, the use of additional informants, such as caregivers, children, or staff, may be necessary to further clarify the presence of depression. Research is needed that specifically validates measures of depression on elderly depressed cancer patients.

Disease Status and Depression

Equivocal findings have been reported on whether the prevalence of depression varies by cancer type or stage. Although Zabora et al. *(85)* found differences in depression prevalence between cancer diagnoses, many have failed to identify significant amounts of variation by either type or stage of cancer *(2,86,87).* Despite this, two areas that frequently vary by stage of cancer have been related to an increased presence of depression: increased pain and decreased performance status. Increased pain, and specifically increased pain with metastasis (which occurs with stage IV disease), has been associated with increased depression and may play a causal role, as individuals with high levels of pain had significantly lower previous histories of major depression *(88).* Ciaramella and Poli *(26)* in their study of 100 cancer outpatients, 30 of whom had metastases and 37 of whom had pain, found that depression and pain were related, with about half of pain patients having a major depressive episode. They hypothesized that depression follows pain and metastasis, and used as confirmation the fact that their patients with current depression did not have more lifetime depressive episodes than those without depression. As such, they concluded that depression is not endogenous to cancer patients, but follows from the presence of other stressors such as pain. Their findings indicate that an assessment of depression should also include an assessment of pain, especially in those individuals with metastatic cancer.

Decreased performance status is also a potential concomitant to advanced cancer stage and has been found to be related to the presence of depression. Bukberg et al. *(8)* in their study of hospitalized patients found that of those with a score on the Karnofsky Performance Rating Scale of 40 or less (bed restriction), 77% met criteria for major depression. Karnofsky performance status as well as a history of depression were found to be factors associated with comorbid depression *(89).* Similar findings were also reported by Pinder et al. *(90)* in a sample of patients with advanced breast cancer. Specifically, patients confined to bed at least 50% of the day (International Union Against Cancer [UICC] scale 3 and 4) had an odds ratio of 9.1 of being clinically depressed when compared with those who had no symptoms.

In addition to the presence of pain and decreased performance status, which clearly are related to the prevalence of depression, there are issues pertinent to the assessment of depression that may vary by type or stage. For example, individuals with head and neck cancer may find it very difficult to complete structured interviews because of changes in their ability to speak. In such cases, identification of alternative methods of assessment, such as questionnaires or observer ratings, may be necessary.

Race, Ethnicity, and Subcultural Issues

Of ever-increasing importance, although still underrepresented in the literature, is the identification of issues when assessing depression in cancer patients that may be specific to different racial, ethnic, or subcultural groups. A limited review of the literature on the assessment of depression over the past 10 years revealed that the racial breakdown of the sample was only provided in approximately 25% of the studies. In additional studies, results were reported as not differing by racial status without providing the racial composition of the sample *(91).* In those studies that did provide a racial distribution, Caucasians made up between 50% and 99% of the sample, with the majority of studies being >85% Caucasian. The exceptions were studies

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with pediatric cancer patients by Varni et al. *(92)* and Frank et al. *(75),* who reported that 50% and 59% of their samples, respectively, were Caucasian.

Often, the issues of race and ethnicity are confused. As an example, in the two aforementioned studies, African-American and Caucasian races are included in sentences that describe "other ethnic groups" as being Hispanic, Asian, Indian, Vietnamese, and American Indian *(75,92).* Thus, it would appear that in these studies, Caucasian and African-American are considered ethnic groups. This is somewhat misleading, given that ethnicity refers to a "common ancestry through which individuals have evolved shared values and customs" *(93)* and interacts with issues such as race, religion, geography, and so forth. On the basis of this definition, studies often assume equality among racial groups that are inherently different based on this definition as evidenced by the various groups that are classified in the "other" category. As a result, assessing depression in these groups using measures/instruments that have been standardized on Caucasian samples may be ignoring individual differences that could affect the reporting of symptoms, severity of symptoms, and validity of symptom patterns within all of these groups. Finally, acculturation and generational issues are likely important in assessing depression in cancer patients of different cultures. It is unlikely that a new immigrant and a fifth-generation citizen from the same country of origin will have similar presentations of depression, even if they are of similar age and gender.

Who Should Assess?

The question of who should assess for depression is more than academic because traditionally, nonpsychiatric physicians have difficulty identifying depression, patients are reluctant to spontaneously report symptoms of depression, and as noted before, symptoms associated with cancer (fatigue, sleep difficulties, loss of appetite) are also symptoms of depression, but are frequently attributed to the physical illness instead *(80).* The identification of depression becomes additionally important because depression may decrease motivation and adherence with chemotherapy *(94).* Unfortunately, although screening instruments meant to identify patient depression are often self-report and easy to administer, they generally are not a standard part of current clinical medical practice. More often, it is an informal assessment of depression by health care providers (e.g., nurses, physicians) that prompts a referral to a psychologist or psychiatrist for formal assessment.

Informal assessments by nonpsychiatric medical staff, however, may not be an effective method of screening for depression. This is in part because less than one-quarter of depressed cancer patients are likely to report their symptoms to nonpsychiatric medical staff *(95–98).* In addition, the concordance between patient and staff evaluations of depression are not encouraging. When associations between patient and staff ratings have been examined, correlations ranging from 0.21 to 0.50 have been reported *(99,100).* Agreement between patient and staff ratings of depression using Cohen's kappa statistic has been reported between 0.07 and 0.23 *(101).* Although interpretations of these associations may vary [see Lampic and Sjoden *(102)* for a review], it is clear that the agreement between patient and provider ratings of depression is less than perfect. Some studies have noted that staff tend to overestimate depression in their patients *(101–105),* whereas others have found that this is not the case *(106,107).* As an example, a recent study by Sollner et al. *(108)* examined the ability of oncologists to identify depression in their patients and found better detection of moderate than high levels of depression, resulting in overall poor agreement between oncologist and patient ratings on the HADS. This discrepancy implies that staff may identify some aspects of depression more easily than others *(109–110).* Additional research has found that the patient ratings of depression on self-report scales that are most highly correlated with physician ratings are the obvious symptoms of depression such as irritable mood, crying, or statements concerning thoughts or death or suicide *(80).* The tendency for physicians to assess depression based on the observable symptoms and not on cognitive factors led Passik et al. *(80)* to conclude that further training and education among oncologists is needed if they are to accurately assess for mood disturbances in their patients. If mental health professionals are not an integral part of the oncology team, the aforementioned suggestion is of utmost importance if depression and other mental health issues are to be recognized.

When To Assess

Equally as important as who should assess is the issue of when to assess. In the majority of clinical research studies, patients are assessed before or following an intervention, or as part of long-term follow-up of cancer survivors. Using bone marrow transplantation as an example, patients are routinely assessed before undergoing the procedure. Additional assessment frequently occurs at 100 days posttransplant, although this varies by center and research project. Depression has been identified as prevalent at each of these occasions *(111–113).* Given the nature of the procedure, it would appear that these assessment points should be standard, although depression is not usually formally assessed unless patients are part of a research protocol. Thus, there is clearly a need for consistent assessment of depression in all cancers and procedures, not just BMT, throughout the treatment process. Recently, Trask et al. *(47)* have suggested that assessment of depression and distress in general should occur even earlier for some patient populations. Examining the presence of depression in patients who were presenting at a consultation to determine if they would be appropriate for a BMT, they found a 20% prevalence of depression using the HADS, but a 50% prevalence of anxiety and distress. This finding, coupled with those of other studies of cancer patients, strongly indicates that routine assessment of depression is valuable and necessary.

Future Directions

This review has discussed the issues of how, who, and when to assess for depression in cancer patients. It has also presented the importance of considering issues such as age, ethnicity, or stage/site of cancer that may influence the assessment of depression. Based on this discussion, there are several issues that are important to address in future studies. First, to effectively identify depression, there is the need to refine diagnostic criteria for depression in cancer patients. This could be accomplished through studies that assess patients using a combination of the inclusive and substitutive approaches previously discussed and examine which symptoms of depression are most common in

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cancer patients. It is possible that the result would be two separate depression subtypes, somatic and cognitive, which may have very different effect on disease course, morbidity, or quality of life, and that may respond quite differently to interventions. Second, it would be helpful to create cancer-specific depression measures with appropriate cutoffs. This could occur through the creation of a new measure from a combination of existing measures of depression or by obtaining a set of items through interviews with cancer patients. Both approaches would require a demonstration of adequate psychometrics but would reflect a measure that was generated and tested on a specific population.

Third, there is a need to focus on the issues of age, race, ethnicity, subculture, and type/stage of cancer in creating depression assessment tools. Increased efforts are needed to include diverse groups in depression studies, create norms on existing measures for those groups, or create new measures sensitive to the variations that could occur because of ethnicity or subculture. Finally, there is the need to explore the issues of clinical versus subclinical depression, who and when to assess, and timely and cost-effective ways to assess for depression. Devising studies to look at the effect of clinical and subclinical depression on outcomes to determine whether differences exist, as well as to determine whether those groups have similar responses to interventions, is an important first step. Longitudinal studies that use various personnel to assess depression could provide information on when depression is most problematic and whether there are discrepancies between assessors that may be amenable to future training. Finally, developing quick, few-item measures with sound psychometric properties that can be administered through kiosks in waiting rooms, personal digital assistants, or paper and pencil may identify cost-effective assessment techniques. Exploring these issues will result in a better understanding of the specific ways depression is manifested in cancer patients and may lead to the development of more effective interventions.

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