A Pan-Canadian Practice Guideline: Screening, Assessment and Care of Psychosocial Distress (Depression, Anxiety) in Adults with Cancer

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Conflict of Interest Disclosures
Each member of the National Advisory Working Group acting in the role of the guideline expert panel completed a Conflict of Interest Document. No conflicts of interest were identified by members of the practice guideline writing team that could have compromised the recommendations contained within this document.
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Summary of Practice Guideline

Question
What are the optimum screening, assessment and psychosocial-supportive care interventions for adults with cancer who are identified as experiencing symptoms of depression and/or anxiety? Outcomes of interest include general emotional distress, anxiety, depression, appropriate screening and/or assessment, and management of depression and/or anxiety in adults with cancer.

Objective
The objective of this practice guideline is to inform Canadian health authorities, program leaders, administrators and professional health care providers about the optimum screening, assessment and psychosocial-supportive care of adult patients with cancer who are identified as experiencing depression and/or anxiety using the Edmonton Symptom Assessment System (ESAS).

Target Population
This practice guideline pertains to adults with cancer (age 18 years and older) at any phase of the cancer continuum and regardless of cancer type, disease stage or treatment modality. It does not focus on management of depression or anxiety in adults prior to a cancer diagnosis but recognizes these as risk factors in the assessment process.¹

Target Users
This practice guideline is intended to inform Canadian health authorities, program leaders and administrators, as well as professional health care providers engaged in the care of adults with cancer. The guideline is interprofessional in its focus, and the recommendations are applicable to direct-care care providers (e.g., nurses, social workers, family practitioners) in diverse care settings. The scope of practice for different professions may vary according to regulatory standards set by provincial professional colleges and it is expected that professionals using this guideline will exercise skill and judgement to determine if recommendations are within their scope of practice. Users may wish to adapt this guideline to local health care processes and context. Depending on the factors contributing to distress, additional written guidelines and resources should be considered for more detailed evidence-based recommendations (i.e., pain or depression guidelines that focus on pharmacological management). It is not the intent of this guideline to make recommendations for specialist practitioners (e.g., psychologists or psychiatrists). Operational definitions to clarify processes of assessment embedded in the guideline and to clarify scope based on existing guideline definitions¹ are described in the following section of this report.
Assessment Processes and Scope

Screening
Screening is a brief process that provides a “snapshot” of a patient’s problems or concerns. Short or ultra-short psychometrically valid measures are used to quickly flag a problem or concern to identify patients who are at risk for a poor health outcome. ESAS depression and anxiety item scores are used as the screening tool for the algorithm and for the depression and anxiety care maps included herein. Screening, however, is a relatively crude indicator of a problem. Further elaboration is essential, using a more comprehensive assessment approach with valid cut-offs to target appropriate intervention strategies.¹ ²

Comprehensive Assessment
In contrast to screening, a comprehensive assessment is a detailed appraisal of many factors that may contribute to a particular problem such as depression or anxiety. A comprehensive assessment may involve a combination of procedures, checklists and measurement tools to identify specific problem areas and contributing factors. Domains may include health status, coping skills, risk factors, pertinent history, co-morbidities, and current relief or management of symptoms, as well as the patient’s values, preferences and social circumstances. Assessment is expected of direct-care providers, such as family physicians, oncologists and nurses, following identification of problems and/or their severity from an initial screen. A comprehensive assessment is typically followed by a more focused assessment once specific problem areas have been identified.

Focused Assessment
A focused assessment is a more targeted appraisal to clarify the extent of a particular problem identified through screening or earlier assessments, to identify new or overlooked problems and to facilitate subsequent management. Once a patient with cancer has been identified as experiencing symptoms of depression or anxiety using valid and reliable screening tools, a more focused assessment will help identify those patients that are at high risk of a poor outcome and thus should be referred to a specialist. Obtaining a definitive clinical diagnosis may be a component of a focused assessment and is typically conducted by a direct-care health care provider assessing for symptoms such as pain. However, a definitive clinical diagnosis of depression or anxiety can only be made by practitioners specifically trained and skilled in the use of DSM diagnostic criteria and if within their scope of practice.
Introduction

All adults diagnosed with cancer experience some level of emotional distress, but about a third experience more serious distress measured as the presence of symptoms of anxiety and/or depression. Periods of vulnerability include the time of diagnosis, the start of active treatment, recurrence, and transition to palliative and end-of-life care. Determinants of psychosocial distress (anxiety and depression) are multifactorial and can include younger age, unrelieved pain, prior depression or anxiety, a change in life events and/or support system, pre-existing chronic co-morbid conditions and mental health problems. Cancer can therefore both cause and exacerbate depression and anxiety. Those experiencing symptoms may require a definitive clinical diagnosis by appropriately skilled practitioners. A definitive diagnosis of major (clinical) depression or other adjustment or mood disorder is determined using a structured clinical interview for DSM disorders (SCID).

The practice guideline discussed in this report gives practical information and guidance for organizing the assessment process and for providing services. This guideline also provides guidance to health care professionals in the identification and management of depression and anxiety in adult patients with cancer. Screening, assessment, treatment and psychosocial-supportive care recommendations are informed by empirical evidence embedded in current provincial and international guidelines, systematic reviews, guidance documents, and consensus of national and international interprofessional psychosocial and guideline development experts.

Methodology

Practice Guideline Development

The aim of developing this practice guideline was to produce algorithms and recommendations that would facilitate uptake into practice by Canadian health care professionals. This practice guideline is a synthesis of evidence embedded in current evidence-based guidelines. Further aims were to express the recommendations as action statements, to develop a knowledge product as an initial step in an implementation process to facilitate its use in practice of direct-care interprofessional providers.

This practice guideline was developed based on the systematic ADAPTE methodology (www.adapte.org) with assessment of the quality of guidelines in accordance with the AGREE II reporting convention (www.agreetrust.org).

Literature Search

A systematic search of clinical practice guideline databases, guideline developer websites and the published literature was conducted to identify clinical practice guidelines, systematic reviews and other guidance documents that address screening, assessment and/or management of psychosocial distress (depression and anxiety) in adults with cancer. The search of the published literature included searches of the MEDLINE, EMBASE, CINAHL and Cochrane Library databases recent to December 2009.

Literature Search Strategy

The guideline and literature search used separate or combined terms: cancer, neoplasm, depression, mental health, anxiety, distress, anxiety or depressive disorders.
in oncology, screening, assessment, interventions, guidelines, recommendations, practice guidelines, management of anxiety or depressive symptoms, pharmacological and non-pharmacological treatments.

Inclusion Criteria
Guidelines and other practice guidance documents published after 2003 and in the English language were included. The key areas of interest were guidelines, evidence-based practices and best practices focused on screening and/or assessment and/or treatment (pharmacological and non-pharmacological) and/or overall management of depression and anxiety symptoms or disorders in adults diagnosed with cancer.

Literature Search Results
Five clinical practice guidelines and a number of supporting documents were identified for the evidence base of this practice guideline.

Critical Appraisal
The five practice guidelines were assessed for reporting quality using the AGREE II Instrument. At least two independent reviewers scored each practice guideline.

Results

Screening and Assessment for Depression and Anxiety

Of the five guidelines, two recommended that all trained health care professionals should be alert for signs of depression and anxiety and able to screen and assess for the presence of depression and/or anxiety symptoms as part of routine practice during the course of treatment and follow-up.\(^4\) These recommendations were based on expert consensus. Cancer Care Ontario (CCO)\(^8a\) and the Oncology Nursing Society (ONS)\(^9a,10a\) did not report recommendations for screening and assessment; however, ONS (Depression) cites the National Comprehensive Cancer Network (NCCN) standards of care for distress management (i.e., supporting routine screening for distress).\(^9a,9b\) Routine screening for distress followed by assessment was also recommended by the recently released Pan-Canadian Psychosocial Health Care Needs Assessment Guideline.\(^1\)

A synthesis of recommendations across the reviewed guidelines showed consensus in favour of the components of a comprehensive assessment, such as risk factors and the need to use a valid tool to assess symptoms of depression and anxiety. Three guidelines indicated that DSM-IV criteria were necessary to obtain a definitive clinical diagnosis of depression and/or anxiety prior to treatment and referral decisions.\(^4,5,8a\) ONS (Depression) cites the NCCN standards of care for distress management (i.e., supporting the assessment and management of distress according to clinical guidelines).\(^9a,9b\) The DSM-IV criteria can be used by a range of health professionals with specific training and skills (e.g., advanced practice nurses, specialist nurse social workers, mental health professionals and family physicians).\(^11\) The present recommendations suggest all health care professionals, as part of routine practice, screen for depression and anxiety, and if necessary, assess for the presence of symptoms, pertinent history and risk factors. National Breast Cancer Centre (NBCC) and NCCN recommend referral to and assessment by a clinical psychologist or psychiatrist if the anxiety or depressive symptoms are severe.\(^4,5\) Hence, these guidelines also recommend referral to appropriate health care professionals (e.g., physician, psychologist or psychiatrist) for a definitive diagnosis if the anxiety or depression symptoms are present and meet cut-offs for psychosocial referral.
**Treatment and Care of Depression and Anxiety**

Level I (randomized controlled trial or RCT) evidence from four guidelines support the benefit of psycho-educational and psychosocial interventions in the management of depression and anxiety in cancer patients.\(^4^,5^a,9^b,10^a,10^b\) Acknowledging that it may not be the case for all patients, four guidelines agreed that the optimal management of clinical depression involves combined pharmacological and non-pharmacological interventions rather than one or the other on their own.\(^4^,5^a,8^a,9^a\) There was agreement across the reviewed guidelines regarding the benefits of pharmacological agents in the management of anxiety and depressive disorders. The guidelines report equal efficacy between antidepressant medications, with the side effect profiles being a key factor in professional decision-making and choice of agent. All of the guidelines acknowledge that patients should be informed of any potential harms (refer to Appendix D for an information guide to antidepressants).

**Conclusions**

The evidentiary base (five practice guidelines and supporting documents) informing this practice guideline ranges from the highest level (Level I, RCTs) to expert consensus. Based on the evidence, the expert working group concluded that it appears reasonable to screen adult cancer patients for depression and anxiety on a routine basis. The use of screening scores to denote the need for further assessment is consistent with the reviewed guidelines and consensus opinions of the National Advisory Working Group. Consensus by the expert working group supports comprehensive and focused assessment to establish the extent and nature of the depression or anxiety. Assessment and response should be a shared responsibility among members of the interprofessional clinical team. When symptoms are identified, the clinical team must decide when referral to a psychiatrist, psychologist or equivalently trained professional is needed based on the factors contributing to distress or using established cut-offs in valid and reliable tools. The management of depression or anxiety must be tailored to the individual patient, who should be fully informed of the options and have the opportunity to take part in decision-making.\(^5^,12\) The choice of an antidepressant and/or anxiolytic agent should be informed by the side effect profiles of the medications, tolerability of treatment, including the potential for interaction with other current medications, response to prior treatment and patient preference. Patients should be warned of any potential harm. Moreover, patients with cancer who are prescribed antidepressants should be monitored closely for adverse side effects. Each practice setting should have agreed protocols for depression and anxiety management that include expectations or standards for referral, including processes for referral to psychosocial specialists.
Recommendations

The following recommendations and algorithms on the optimum screening, assessment and supportive care of adult patients with cancer who experience depression and/or anxiety are based on the expert consensus of the National Advisory Working Group of the Cancer Journey Action Group, Canadian Partnership Against Cancer and are informed primarily by five clinical practice guidelines and a number of supporting documents. The five guidelines are:

- Clinical practice guidelines for the psychosocial care of adults with cancer, National Breast Cancer Centre and National Cancer Control Initiative
- Clinical Practice Guidelines in Oncology - Distress Management, V.2.2009, National Comprehensive Cancer Network
- The management of depression in cancer patients: A clinical practice guideline, Cancer Care Ontario
- Putting Evidence into Practice (PEP): Depression, Oncology Nursing Society
- Putting Evidence into Practice (PEP): Anxiety, Oncology Nursing Society

The supporting documents are:

- A Pan-Canadian clinical practice guideline: Assessment of psychosocial health care needs of the adult cancer patient; the Partnership and CAPO
- International Consensus Group on Depression and Anxiety, Consensus Statement on Depression, Anxiety and Oncology
- NICE clinical guidelines. Depression in adults with a chronic physical health problem; National Institute for Health and Clinical Excellence
- Guide to implementing screening for distress, the 6th vital sign: Moving toward person-centered care. Part A: Background, recommendations and implementation; The Partnership
- Symptom Guidelines: Depression in the Terminally Ill; Fraser Health Hospice Palliative Care Program

Depression Recommendations

1. Screening for Depression

(Based on the expert consensus of the National Advisory Working Group and informed by NBCC evidence Level III-3, NCCN category 2A, CCO expert consensus, ONS expert opinion)

- All health care providers should routinely screen for the presence of emotional distress and specifically symptoms of depression from the point of diagnosis onward.

- All patients should be screened for distress at their initial visit, at appropriate intervals and as clinically indicated, especially with changes in disease status (i.e., post-treatment, recurrence, progression) and when there is a transition to palliative and end-of-life care.

  - The Canadian Association of Psychosocial Oncology (CAPO) and the Canadian Partnership Against Cancer (the Partnership) guideline “Assessment of Psychosocial Health Care Needs of the Adult Cancer Patient” suggests screening at initial diagnosis, start of treatment, regular intervals during treatment, end of treatment, post-
Practitioner Guideline: Depression, Anxiety

treatment or at transition to survivorship, at recurrence or progression, advanced disease, when dying, and during times of personal transition or re-appraisal such as family crisis, during post-treatment survivorship and when approaching death.1

- Screening should identify the level and nature (problems and concerns) of the distress as a red flag indicator.
- Screening should be done using a valid and reliable tool that features reportable scores (dimensions) that are clinically meaningful (established cut-offs).
  - For example, the Partnership’s Screening for Distress tool, which includes the Edmonton Symptom Assessment System (ESAS) and the Canadian Problem Checklist as per the CAPO/Partnership guideline Assessment of Psychosocial Health Care Needs of the Adult Cancer Patient.1

2. Assessment of Depression
(Based on the expert consensus of the National Advisory Working Group and informed by NBCC evidence Level I, NCCN category 2A, CCO expert consensus, ONS expert opinion)

- Specific concerns such as risk of harm to self and/or others, severe depression or agitation, or the presence of psychosis or confusion (delirium) may require an urgent referral to a psychiatrist, psychologist, physician or equivalently trained professional.
- When moderate or severe depression is detected through screening (ESAS depression item score of 4 or higher), individuals should have an immediate assessment to identify the nature and extent of the depressive symptoms.
- Medical and substance-induced (e.g., Interferon administration) causes of depression should be ruled out.
- As a shared responsibility, the clinical team must decide when referral to a psychiatrist, psychologist or equivalently trained professional is needed (i.e., all patients with an ESAS score in the severe range, with certain accompanying factors and/or symptoms, or with a cut-off identified using valid and reliable tools for assessment of symptoms of depression).
- Assessments should be a shared responsibility of the clinical team, with designation of those who are expected to conduct assessments as per scope of practice.
- The assessment should identify signs and symptoms of depression, the severity of relevant symptoms (e.g., fatigue), possible stressors, risk factors and times of vulnerability, and should also explore underlying problems or causes (common measurement tools include BDI, BSI, CES-D and HADS; see table on page 29).
- A patient considered to have depressive symptoms following the further assessment should, where possible, have confirmation of a clinical diagnosis of depression before any pharmacological treatment or care options are initiated (e.g., DSM-IV, which may require making a referral).
3. Treatment and Care Options for Depression

(Based on the expert consensus of the National Advisory Working Group and informed by NBCC evidence Levels I and II, NCCN category 2A, CCO expert consensus using Level I and II evidence, ONS “recommended for practice” and “likely to be effective”, ONS expert opinion)

- For any patient who is identified as at risk of harm to self and/or others, consider URGENT referral to appropriate services for emergency evaluation. Facilitate a safe environment and one-to-one observation, and initiate appropriate harm-reduction interventions to reduce risk of harm to self and/or others.

- First treat medical causes of depression (e.g., unrelieved symptoms such as pain and fatigue) and delirium (e.g., infection or electrolyte imbalance).

- Optimal management of moderate to severe depression combines pharmacological and non-pharmacological interventions delivered by appropriately trained individuals (e.g., psychotherapy and psycho-educational therapy, cognitive-behavioural therapy).

- These guidelines make no recommendations about specific antidepressant pharmacological regimes being better than another. The choice of an antidepressant should be informed by the side effect profiles of the medications, tolerability of treatment, including the potential for interaction with other current medications, response to prior treatment and patient preference. Patients should be warned of any potential harm or adverse effects (see Appendix D for an antidepressant information guide).

- Offer support and provide education and information about depression and its management to all patients and their families and what specific symptoms warrant a call to the physician or nurse.
Screening and Assessment - Depression* in Adults with Cancer

Screen for distress¹ at entry to system, critical times, periodically during patient care, or other stressful times²

Assessment of risk of harm to self and/or to others (all patients)

- If YES > URGENT referral to appropriate services for emergency evaluation; Facilitate safe environment; One-to-one observation; Initiate appropriate harm reduction interventions to reduce risk of harm to self and/or others. (*The presence of other symptoms such as psychosis, severe agitation and confusion (delirium) may also warrant referral to appropriate services for emergency evaluation).
- If NO > continue with algorithm

Depression identified on ESAS screening (Depression item)

Mild Distress
ESAS Depression Score 1-3

Moderate Distress
ESAS Depression Score 4-6

Severe Distress
ESAS Depression Score 7-10

Assessment to clarify nature and extent of depressive symptoms

- Review problem checklist and all ESAS scores in conversation³ with patient/family and discuss expectations and beliefs about support needs (e.g., Canadian Problem Checklist)
- Identify most distressing ESAS symptom(s) and or problem(s) contributing to depression (e.g., life events, insomnia, pain, fatigue, other co-morbid illness) and daily interference
- Assess effectiveness of current symptom and or co-morbid condition management
- Psychomotor agitation or slowing

Identify pertinent history / Specific risk factors for depression

- Recurrent, advanced, progressive disease (i.e., vulnerable points)
- History: Depression, substance abuse, other mental health problems (e.g., dysthymia)
- Current use of depression medication or seeing a psychologist or psychiatrist
- Perceived lack of social support
- Other factors (e.g., younger age, female, live alone, dependent children, financial problems, prior coping issues)

Focused assessment: Specific to problem of depression

- HCP with appropriate training and skills to complete a depression symptom checklist using validated tool (e.g., CES-D; PHQ-9) or assess for presence of: depressed mood, loss of pleasure, feelings of worthlessness/guilt, diminished concentration, recurrent thoughts of death, fatigue, significant change in appetite and sleep patterns, impaired functioning in daily living⁴
- Assess if symptoms persist for 2 weeks or longer (almost all day, every day)⁴

Mild Distress
ESAS Depression Score 1-3

Moderate Distress
ESAS Depression Score 4-6

Severe Distress
ESAS Depression Score 7-10

*In this algorithm the use of the word depression refers to the ESAS screening scale and not to a clinical diagnosis

1. Use Screening for Distress Tool (SDT), which includes Edmonton Symptom Assessment System (ESAS) and Canadian Problem Checklist (CPC)
2. At initial diagnosis, start of treatment, regular intervals during treatment, end of treatment, post-treatment or at transition to survivorship, at recurrence or progression, advanced disease, when dying, and during times of personal transition or re-appraisal such as family crisis, during survivorship, when approaching death (CAPO/CPAC guideline: “Assessment of Psychosocial Health Care Needs of the Adult Cancer Patient” by Howell et al., 2009; Cancer Care Nova Scotia Distress Management Pathways, draft 2010).
3. The health care team for cancer patients may include surgeons, oncologists, family physicians, nurses, advanced practice nurses, social workers, psychologists, patient navigators and other health care professionals (HCPs)
4. DSM-IV criteria - The DSM-IV criteria can be used by a range of health professionals with specific training and skills.
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**Care Map - Depression in Adults with Cancer**

**Mild Distress**
- ESAS Depression Score 1-3
  - No or minimal symptoms of depression
  - Recent life event(s) such as bereavement or loss
  - Level of grief appropriate for loss ("normal" response, NCCN) with gradual resolution over weeks / months
  - Effective coping skills and access to social support

**Moderate Distress**
- ESAS Depression Score 4-6
  - Moderate to high levels of distress (does not meet criteria for high risk but two or more symptoms present for two weeks) and / or impairment of functioning in daily living
  - Risk factors (e.g., gaps in social support or effective coping mechanisms)

**Severe Distress**
- ESAS Depression Score 7-10
  - Depressed mood and / or loss of pleasure for 2 weeks
  - 4 additional symptoms: Feelings of worthlessness and / or guilt, Insomnia or hypersomnia, Weight gain or loss
  - Psychomotor agitation or retardation
  - Fatigue
  - Risk factors
  - Risk of harm to self and / or to others > URGENT referral to appropriate services; Facilitate safe environment; One-to-one observation; Initiate harm reduction interventions to reduce risk of harm to self and / or others

**Care Pathway 1**
- Prevention and Supportive Care
  - Offer referral to psychosocial support (e.g., counseling, support groups, individual)

**Care Pathway 2**
- Psychosocial Care and/or consider referral to Physician/Psychologist/Psychiatrist
  - Intervention Options
    - Combine non-pharmacological and pharmacological interventions as appropriate
    - Referral to other services as required (e.g., psychosocial team, physician, psychologist, psychiatrist)

**Care Pathway 3**
- Referral to Physician/Psychologist/Psychiatrist
  - Definitive Diagnosis Needed
    - Referral to appropriate services for evaluation and definitive diagnosis
  - Intervention Options
    - Psychiatric standard of care

**Non-Pharmacological**
- Psycho-education and psychosocial interventions (specifically cognitive-behavioral therapy and patient education and information, counseling and individual or group psychotherapy, behavioral therapy, and social support); Relaxation therapy (ONS)

**Pharmacological**
- A number of anti-depressants are recommended for treatment of depression with choice informed by side effect profiles, interactions, response, patient preference. (see appendices). Monitor for adverse effects.

**Supportive care interventions for all patients, as appropriate**
- Offer referral to psychosocial support (e.g., counseling, peer-led support groups, individual)
- Provide education (verbal plus any relevant materials) for the patient and family about:
  - How common emotional distress is in the context of cancer and differing responses
  - Benefits of support groups and other support services
  - Sources of informal support, resources available to patients and families (e.g., accommodation, transportation, financial assistance, additional health/drug benefits)
  - Need for additional psychosocial support if signs and symptoms of depression worsen with specific information regarding symptoms to warrant a call to the physician or nurse.
  - Coping with stress and specific strategies (i.e. relaxation approaches)
  - How to effectively manage symptoms contributing to depression (e.g., fatigue, sleep disturbance)

**Follow-up and ongoing re-assessment**
- and change (reduction) from previous score

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*Refer to the full technical guideline document for the evidentiary support for this algorithm on the Canadian Association of Psychosocial Oncology website (www.capo.ca)

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Anxiety Recommendations

1. Screening for Anxiety
   (Based on the expert consensus of the National Advisory Working Group and informed by NBCC evidence grading Level III-3, NCCN category 2A)
   - All health care providers should routinely screen for the presence of emotional distress and specifically symptoms of anxiety from the point of diagnosis onward.
   - All patients should be screened for distress at their initial visit, at appropriate intervals and as clinically indicated, especially with changes in disease status (i.e., post-treatment, recurrence, progression) and when there is a transition to palliative and end-of-life care.
     - The Canadian Association of Psychosocial Oncology (CAPO) and the Canadian Partnership Against Cancer (the Partnership) guideline “Assessment of Psychosocial Health Care Needs of the Adult Cancer Patient” suggests screening at initial diagnosis, start of treatment, regular intervals during treatment, end of treatment, post-treatment or at transition to survivorship, at recurrence or progression, advanced disease, when dying, and during times of personal transition or re-appraisal such as family crisis, during post-treatment survivorship and when approaching death.¹
   - Screening should identify the level and nature (problems and concerns) of the distress as a red flag indicator.
   - Screening should be done using a valid and reliable tool that features reportable scores (dimensions) that are clinically meaningful (established cut-offs).
     - For example, the Partnership’s Screening for Distress tool, which includes the Edmonton Symptom Assessment System (ESAS) and the Canadian Problem Checklist as per the CAPO/Partnership guideline Assessment of Psychosocial Health Care Needs of the Adult Cancer Patient.¹

2. Assessment of Anxiety
   (Based on the expert consensus of the National Advisory Working Group and informed by NBCC evidence Level I, NCCN category 2A)
   - Specific concerns such as risk of harm to self and/or others, severe anxiety or agitation, or the presence of psychosis or confusion (delirium) may require an urgent referral to a psychiatrist, psychologist, physician or equivalently trained professional.
   - When moderate or severe anxiety is detected through screening (ESAS anxiety item score of 4 or higher), individuals should have an immediate assessment to identify the nature and extent of the anxiety symptoms.
   - Medical and substance-induced causes of anxiety should be ruled out.
   - As a shared responsibility, the clinical team must decide when referral to a psychiatrist, psychologist or equivalently trained professional is needed (i.e., all patients with an ESAS score in the severe range, with certain accompanying factors and/or symptoms, or with a cut-off identified using valid and reliable tools for assessment of symptoms of anxiety).
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- Assessments should be a shared responsibility of the clinical team, with designation of those who are expected to conduct assessments as per scope of practice.
- The assessment should identify signs and symptoms of anxiety (e.g., panic attacks, trembling, sweating, tachypnea, tachycardia, palpitation and sweaty palms), severity of symptoms, possible stressors (e.g., impaired daily living), risk factors and times of vulnerability, and should also explore underlying problems/causes (common measurement tools include BAI, GAD-7; see Appendix C).
- A patient considered to have severe symptoms of anxiety following the further assessment should, where possible, have confirmation of a clinical diagnosis of anxiety disorder before any pharmacological treatment or care options are initiated (e.g., DSM-IV, which may require making a referral).

3. Treatment and Care Options for Anxiety
(Based on the expert consensus of the National Advisory Working Group and informed by NBCC evidence grading Level I, NCCN category 2A)

- For any patient who is identified as at risk of harm to self and/or others, consider URGENT referral to appropriate services for emergency evaluation. Facilitate a safe environment and one-to-one observation, and initiate appropriate harm-reduction interventions to reduce risk of harm to self and/or others.
- First treat medical causes of anxiety (e.g., unrelieved symptoms such as pain and fatigue) and delirium (e.g., infection or electrolyte imbalance).
- Optimal management of moderate to severe anxiety combines pharmacological and non-pharmacological interventions delivered by appropriately trained individuals (e.g., supportive psychotherapy and anxiolytics for PTSD). Management must be tailored to individual patients, who should be fully informed of their options.
- For a patient with mild to moderate anxiety, the primary oncology team may choose to manage the concerns by usual supportive care management.
- These guidelines make no recommendations about specific antidepressant pharmacological regimes being better than another. The choice of an antidepressant should be informed by the side effect profiles of the medications, tolerability of treatment, including the potential for interaction with other current medications, response to prior treatment and patient preference. Patients should be warned of any potential harm or adverse effects (see Appendix D for an antidepressant information guide).
- Offer support and provide education and information about anxiety and its management to all patients and their families and what specific symptoms warrant a call to the physician or nurse.
Practice Guideline: Depression, Anxiety

Screening and Assessment: Anxiety* in Adults with Cancer

Screen for distress¹ at entry to system, critical times, periodically during patient care, or other stressful times²

Assessment of risk of harm to self and/or to others (all patients)
• If YES > URGENT referral to appropriate services for emergency evaluation; Facilitate safe environment; One-to-one observation; Initiate appropriate harm reduction interventions to reduce risk of harm to self and/or others. (The presence of other symptoms such as psychosis, severe agitation and confusion (delirium) may also warrant referral to appropriate services for emergency evaluation).
• If NO > continue with algorithm

Anxiety identified on ESAS screening (Anxiety item)

Mild Distress
ESAS Anxiety Score 1-3

Moderate Distress
ESAS Anxiety Score 4-6

Severe Distress
ESAS Anxiety Score 7-10

Assessment to clarify nature and extent of anxiety symptoms

☐ Review problem checklist and all ESAS scores in conversation³ with patient/family and discuss expectations and beliefs about support needs (e.g., Canadian Problem Checklist)
☐ Identify most distressing ESAS problem or symptom and assess extent of daily life interference
☐ Review ESAS scores for other contributing symptoms (e.g., dyspnea or other medical/medication issue).
☐ Identify other concerns contributing to distress (e.g., life events, sleep deprivation)
☐ Identify other symptoms and current management of relevant symptoms (e.g., pain, fatigue, and/or sleep interference/chronic insomnia)

Identify pertinent history: Specific risk factors for anxiety
☐ History of anxiety problems (e.g., panic attacks, Generalized Anxiety Disorder (GAD)), depression, other mental health problems
☐ Current medication associated with anxiety or depression or seeing a specialist
☐ Disease recurrence, advanced or progressive disease (i.e., vulnerable points)
☐ Withdrawal state (e.g., alcohol, substance use)
☐ Other factors (e.g., younger age, female, live alone, dependents, financial problems)

Focused assessment: Specific to problem of anxiety
☐ HCP with appropriate training and skills to complete an anxiety symptom checklist using a validated tool (e.g., BAI; STAI; GAD-7) or assess for presence of: tension, uncontrollable or excessive worry, agitation, restlessness, panic attacks, poor concentration, nausea/vomiting, reassurance seeking, significant change in sleep patterns, impaired functioning in daily living (e.g., hypervigilance, scanning, irritability, unable to relax, ruminations)
☐ In what ways do anxiety symptoms affect daily functioning (e.g., sleep, appetite)

Mild Distress
ESAS Anxiety Score 1-3

Moderate Distress
ESAS Anxiety Score 4-6

Severe Distress
ESAS Anxiety Score 7-10

*In this algorithm the use of the word anxiety refers to the ESAS screening scale and not to a clinical diagnosis

1. Use Screening for Distress Tool (SDT), which includes Edmonton Symptom Assessment System (ESAS) and Canadian Problem Checklist (CPC).
2. At initial diagnosis, start of treatment, regular intervals during treatment, end of treatment, post-treatment or at transition to survivorship, at recurrence or progression, advanced disease, when dying, and during times of personal transition or re-appraisal such as family crisis, during survivorship, when approaching death (CAPO/CPAC guideline: “Assessment of Psychosocial Health Care Needs of the Adult Cancer Patient” by Howell et al., 2009; Cancer Care Nova Scotia Distress Management Pathways, draft 2010.
3. The health care team for cancer patients may include surgeons, oncologists, family physicians, nurses, advanced practice nurses, social workers, psychologists, patient navigators and other health care professionals (HCPs)
Care Map - Anxiety in Adults with Cancer

**Mild Distress**
ESAS Anxiety Score 1-3
- No or minimal anxiety symptoms
- Typical symptoms - fear, worry, uncertainty about future, concerns about illness, sadness about loss of good health, anger and feeling life is out of control, poor sleep, appetite and/or concentration, preoccupied with thoughts of illness and death, treatment effects and side effects (NCCN)
- Gradual resolution over weeks/months

**Moderate Distress**
ESAS Anxiety Score 4-6
- Maladaptive response (out of proportion to the stressors); disruption of usual or desirable functioning
- Unable or less able to control anxiety without intervention
- Risk factors
- Nature of anxiety disorder established (e.g., generalized anxiety disorder, panic disorder, post-traumatic stress disorder, obsessive-compulsive, phobia(s))

**Severe Distress**
ESAS Anxiety Score 7-10
- High or elevated level of worry or difficult to control anxiety about several things most days
- Re-experiencing events in a distressing way (e.g., dreams, intense recollections, flashbacks, physical reactions)
- One or more occasion of spells or attacks of sudden fear, discomfort, anxiousness or uneasiness
- Risk factors
- Risk of harm to self and/or to others > URGENT referral to appropriate services; Facilitate safe environment; One-to-one observation; Initiate harm reduction interventions to reduce risk of harm to self and/or others

**Care Pathway 1**
Prevention and Supportive Care
Offer referral to psychosocial support (e.g., counseling, support groups, individual, etc.)

**Care Pathway 2**
Psychosocial Care and/or consider referral to Physician/Psychologist/Psychiatrist

**Care Pathway 3**
Referral to Physician/Psychologist/Psychiatrist

**Intervention Options**
Combine non-pharmacological and pharmacological interventions as appropriate (e.g., combined education, supportive psychotherapy and anxiolytics for PTSD)
Referral to other services as required (e.g., psychosocial team, physician, psychologist, psychiatrist, social work, spiritual care provider)

**Non-Pharmacological:**
Psychosocial interventions (CBT (level 1), psychotherapy, individual or group counseling, support groups); Psycho-educational (e.g., about services/resources, symptom management, self-care strategies); Crisis interventions as appropriate.

**Pharmacological:**
benzodiazepines, anxiolytics, antipsychotics, antihistamines; and antidepressants as for moderate depression; SSRIs in longer term management of panic. Monitor adverse effects.

Proceed to other associated algorithms if necessary (e.g., sleep, fatigue, pain)

Supportive care interventions for all patients, as appropriate
- Offer referral to psychosocial support (e.g., counseling, peer-led support groups, individual)
- Provide education (verbal plus any relevant materials) for the patient and family about:
  - How common anxiety is in the context of cancer and differing responses
  - Benefits of support groups and other support services
  - Sources of informal support, resources available to patients and families (e.g., accommodation, transportation, financial assistance, additional health/drug benefits)
  - The need for additional psychosocial support if signs and symptoms of anxiety worsen
  - Coping with stress and specific strategies (i.e. relaxation, breathing techniques, mindfulness)
  - How to effectively manage symptoms contributing to anxiety (e.g., pain, tension)

Follow-up and ongoing re-assessment and change (reduction) from previous score

Disclaimer
Care has been taken in the preparation of the information contained in this practice guideline document. Nonetheless, any person seeking to apply or consult the practice guideline is expected to use independent clinical judgment and skills in the context of individual clinical circumstances or seek out the supervision of a qualified clinician. The Canadian Partnership Against Cancer and the Canadian Association of Psychosocial Oncology (CAPO) make no representation or warranties of any kind whatsoever regarding the content, use or application of this practice guideline and disclaim any responsibility for their application or use in any way.

Refer to the full technical guideline document for the disclaimer statement on the Canadian Association of Psychosocial Oncology website (www.capo.ca)
## ESAS Screening Tool and Canadian Problem Checklist

### Edmonton Symptom Assessment System (ESAS)

**Date of Completion:**____________________  **Time:** _________________

Please circle the number that best describes:

<table>
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<th>Symptom</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
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</thead>
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</tbody>
</table>

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### Canadian Problem Checklist

Please check all of the following items that have been a concern or problem for you in the past week including today:

**Practical:**
- Work/School
- Finances
- Getting to and from appointments
- Accommodation

**Social/Family:**
- Feeling a burden to others
- Worry about family/friends
- Feeling alone

**Emotional:**
- Fears/Worries
- Sadness
- Frustration/Anger
- Changes in appearance
- Intimacy/Sexuality

**Informational:**
- Understanding my illness and/or treatment
- Talking with the health care team
- Making treatment decisions
- Knowing about available resources

**Spiritual:**
- Meaning/Purpose of Life
- Faith

**Physical:**
- Concentration/Memory
- Sleep
- Weight

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Completed by:
- Patient
- Health Professional
- Family
- Assisted by family or health professional
Question
What are the optimum screening, assessment and psychosocial-supportive care interventions for adults with cancer who are identified as experiencing symptoms of depression and/or anxiety? Outcomes of interest include general emotional distress, anxiety, depression, appropriate screening and/or assessment, and management of depression and/or anxiety in adults with cancer.

Objective
The objective of this practice guideline is to inform Canadian health authorities, program leaders, administrators and professional health care providers about the optimum screening, assessment and psychosocial-supportive care of adult patients with cancer who are identified as experiencing depression and/or anxiety using the Edmonton Symptom Assessment System (ESAS).

Target Population
This practice guideline pertains to adults with cancer (age 18 years and older) at any phase of the cancer continuum and regardless of cancer type, disease stage or treatment modality. It does not focus on management of depression or anxiety in adults prior to a cancer diagnosis but recognizes these as risk factors in the assessment process.

Target Users
This practice guideline is intended to inform Canadian health authorities, program leaders and administrators, as well as professional health care providers engaged in the care of adults with cancer. The guideline is interprofessional in its focus, and the recommendations are applicable to direct-care care providers (e.g., nurses, social workers, family practitioners) in diverse care settings. The scope of practice for different professions may vary according to regulatory standards set by provincial professional colleges and it is expected that professionals using this guideline will exercise skill and judgement to determine if recommendations are within their scope of practice. Users may wish to adapt this guideline to local health care processes and context. Depending on the factors contributing to distress, additional written guidelines and resources should be considered for more detailed evidence-based recommendations (i.e., pain or depression guidelines that focus on pharmacological management). It is not the intent of this guideline to make recommendations for specialist practitioners (e.g., psychologists or psychiatrists). Operational definitions to clarify processes of assessment embedded in the guideline and to clarify scope based on existing guideline definitions are described in the following section of this report.
Assessment Processes and Scope

Screening
Screening is a brief process that provides a “snapshot” of a patient’s problems or concerns. Short or ultra-short psychometrically valid measures are used to quickly flag a problem or concern to identify patients who are at risk for a poor health outcome. ESAS depression and anxiety item scores are used as the screening tool for the algorithm and for the depression and anxiety care maps included herein. Screening, however, is a relatively crude indicator of a problem. Further elaboration is essential, using a more comprehensive assessment approach with valid cut-offs to target appropriate intervention strategies.¹,²

Comprehensive Assessment
In contrast to screening, a comprehensive assessment is a detailed appraisal of many factors that may contribute to a particular problem such as depression or anxiety. A comprehensive assessment may involve a combination of procedures, checklists and measurement tools to identify specific problem areas and contributing factors. Domains may include health status, coping skills, risk factors, pertinent history, co-morbidities, and current relief or management of symptoms, as well as the patient’s values, preferences and social circumstances. Assessment is expected of direct-care providers, such as family physicians, oncologists and nurses, following identification of problems and/or their severity from an initial screen. A comprehensive assessment is typically followed by a more focused assessment once specific problem areas have been identified.

Focused Assessment
A focused assessment is a more targeted appraisal to clarify the extent of a particular problem identified through screening or earlier assessments, to identify new or overlooked problems and to facilitate subsequent management. Once a patient with cancer has been identified as experiencing symptoms of depression or anxiety using valid and reliable tools, a more focused assessment will help identify those patients that are at high risk of a poor outcome and thus should be referred to a specialist. Obtaining a definitive clinical diagnosis may be a component of a focused assessment and is typically conducted by a direct-care health care provider assessing for symptoms such as pain. However, a definitive clinical diagnosis of depression or anxiety can only be made by practitioners specifically trained and skilled in the use of DSM diagnostic criteria and if within their scope of practice.

Introduction
All adults diagnosed with cancer experience some level of emotional distress, but a portion also experience major (clinical) depression and anxiety disorders.¹,⁴,⁵ Periods of vulnerability include the time of diagnosis, the start of active treatment, recurrence,²,³ and transition to end-of-life care.¹ Determinants of psychosocial distress (anxiety and depression) are multi-factorial and can include younger age, unrelieved pain, prior depression or anxiety, a change in life events and/or support system,⁴,⁵ pre-existing chronic co-morbid conditions and mental health problems.⁵ Cancer can therefore both cause and exacerbate depression and anxiety.
Moderate to severe depression has been estimated at two to four times more common in individuals with cancer than the general population.\textsuperscript{5,8b} Estimates of major (clinical) depression range from 35\% to 40\% across studies, with higher rates noted for those with advanced disease.\textsuperscript{15} Anxiety, another common psychological response to the cancer experience, can be disabling and can interfere with treatment response and psychosocial functioning.\textsuperscript{10b,10b} Estimates for anxiety in cancer patients range from 25\% to as high as 50\% in those recently diagnosed.\textsuperscript{3,10b,14} For this document, moderate to severe depression and moderate to severe anxiety (moderate to high risk) refer to patients with a diagnosis of major (clinical) depression or anxiety disorders through use of a structured clinical interview for DSM disorders (SCID).\textsuperscript{5,4,8a} None to mild depression or anxiety (mild risk) refers to those that do not meet the criteria for major depression or anxiety disorders. Those with mild risk may still experience anxiety or depressive symptoms and some impairment to functioning.\textsuperscript{5} Symptoms below the threshold for a diagnosis of depression can be distressing and disabling,\textsuperscript{1,5,12} pointing to the need for direct-care providers to be able to provide psychosocial and supportive care to minimize adverse consequences of cancer and treatment.\textsuperscript{2}

In terms of managing depression and anxiety problems, there is increased awareness that psychosocial care is an important part of comprehensive cancer care.\textsuperscript{2} In Canada, a new standard expects emotional distress to be checked routinely as the Sixth Vital Sign alongside blood pressure, pain, pulse, temperature and respiration.\textsuperscript{1,16} Early recognition and timely treatment of symptoms of depression and anxiety is essential to ensure patients get the help that they need and to reduce the likelihood of problems worsening.\textsuperscript{2,4,5,12}

The practice guideline discussed in this report gives practical information and guidance for organizing the assessment process and for providing services, and also helps health care professionals identify and manage depression and anxiety in adult patients with cancer. Screening, assessment, treatment and psychosocial-supportive care recommendations are informed by empirical evidence embedded in current provincial and international guidelines, systematic reviews, guidance documents, and consensus of national and international interprofessional psychosocial and guideline development experts.

**Methodology**

**Practice Guideline Development**

The aim of developing this practice guideline was to produce algorithms and recommendations that would facilitate uptake into practice by Canadian health care professionals. This practice guideline is a synthesis of current evidence embedded in evidence-based guidelines. Further aims were to express the recommendations as action statements, to develop a knowledge product as an initial step in an implementation plan and to guide practice of direct-care interprofessional providers.

This practice guideline was developed based on the systematic ADAPTE methodology (www.adapte.org)\textsuperscript{6,7} with assessment of quality of guidelines in accordance with the AGREE II reporting convention (www.agreetrust.org). A thorough search of relevant clinical practice guidelines (current to December 31, 2009) was conducted to provide the evidentiary base.
Prior to completion, the report was distributed on several occasions to the National Advisory Working Group of the Cancer Journey Action Group for feedback concerning the collection, interpretation and synthesis of the evidence, as well as the development and content of the recommendations and related evidence-based algorithms. Members of the advisory group also reviewed and discussed the final version of the guidelines. The advisory group comprises nurses, psychologists, an administrator, a patient education specialist, a dietitian, researchers, a coordinator of provincial oncology guidelines with content expertise in each of the topic areas, a research coordinator, and a methodologist. Two members of the group are cancer survivors to ensure that consumers’ views also inform the development of this practice guideline. In addition, content experts and key stakeholders across the country were invited to review and provide input on the document. Final consensus on the recommendations was reached through a formal voting process (see Appendix E). The final report will be distributed to key stakeholders across the country. The literature will be reviewed periodically and the practice guideline will be updated as new or compelling evidence is identified.

Literature Search
A systematic search of clinical practice guideline databases, guideline developer websites and the published literature was conducted to identify clinical practice guidelines, systematic reviews and other guidance documents addressing screening, assessment and/or care of psychosocial distress (depression and anxiety) in adults with cancer. The search of the published literature included searches of the MEDLINE, EMBASE, CINAHL and Cochrane (Systematic Reviews and Clinical Trials Register) Library databases recent to December 2009.

The following electronic databases were searched for published guidelines:
- Guidelines International Network (G-I-N; www.g-i-n.net)
- National Institute for Health and Clinical Excellence (NICE)
- Scottish Intercollegiate Guideline Network (SIGN)
- National Comprehensive Cancer Network (NCCN)
- Provincial guideline organizations, including Cancer Care Ontario, Fraser Health in British Columbia and Cancer Care Nova Scotia
- The Canadian Partnership Against Cancer “SAGE” Inventory of Cancer Guidelines (www.cancerview.ca)

As a quality control measure, results from an environmental scan of psychosocial, supportive and palliative care standards and guidelines completed by the Partnership in 2007 were also consulted.17

Literature Search Strategy
The guideline and literature search used separate or combined terms: cancer, neoplasm, depression, mental health, anxiety, distress, anxiety or depressive disorders in oncology, screening, assessment, interventions, guidelines, recommendations,
Practice guidelines, management of anxiety or depressive symptoms, pharmacological and non-pharmacological treatments.

**Inclusion Criteria**
Guidelines and other practice guidance documents published after 2003 and in the English language were included. The key areas of interest were guidelines, evidence-based practices and best practices focused on screening and/or assessment and/or treatment (pharmacological and non-pharmacological) and/or overall management of depression and anxiety symptoms or disorders in adults diagnosed with cancer.

**Literature Search Results**
Five clinical practice guidelines were identified for the evidence base of this practice guideline. The five guidelines were selected for their evidence base, currency and quality. A further 24 guidelines and other guidance documents were retrieved and examined. Of these, 12 were excluded because they were either published before 2003 or were not guidelines for practice (e.g., lay information, articles about guidelines, protocol for future review), five were not specific to cancer patients, and two did not guide depression and anxiety assessment and management in a comprehensive manner (e.g., proceedings, guidelines focused on a different topic, with small mention of psychological morbidity, need for counselling services, etc.).

Despite the inclusion criteria for guidelines published after 2003, the Australian guidelines (2003) are evidence-based and were included in an attempt to comprehensively cover appropriate information. The NCCN guidelines are recent, comprehensive and based on expert consensus. The CCO guideline is current, based on expert consensus and informs depression treatment options. The ONS Depression and ONS Anxiety guides to practice provide information about evidence-based interventions and are current.

In addition to the five guidance documents, a number of supporting documents were identified to help inform the evidence-based algorithm and development of recommendations. The five supporting documents consisted of consensus statements and guidelines that offer best practice advice (e.g., to improve end-of-life care).

**Clinical Practice Guidelines**
- Clinical practice guidelines for the psychosocial care of adults with cancer, National Breast Cancer Centre and National Cancer Control Initiative
- Clinical Practice Guidelines in Oncology - Distress Management, V.2.2009, National Comprehensive Cancer Network (NCCN)
- The management of depression in cancer patients: A clinical practice guideline, Cancer Care Ontario
- Putting Evidence into Practice (PEP): Depression, Oncology Nursing Society
- Putting Evidence into Practice (PEP): Anxiety, Oncology Nursing Society

**Supporting Evidence**
- A Pan-Canadian clinical practice guideline: Assessment of psychosocial health care needs of the adult cancer patient; the Partnership and CAPO
• NICE clinical guidelines. Depression in adults with a chronic physical health problem; National Institute for Health and Clinical Excellence\textsuperscript{12}

Although not specific to depression in patients with cancer, the guidelines consider physical impairments due to chronic disease and assist with information about screening, assessment and interventions.

• Guide to implementing screening for distress, the 6\textsuperscript{th} vital sign: Moving toward person-centered care. Part A: Background, recommendations and implementation; The Partnership\textsuperscript{18}

• Symptom Guidelines: Depression in the Terminally Ill; Fraser Health Hospice Palliative Care Program\textsuperscript{19}

This guideline provides assessment, risk factor and treatment information to improve palliative care at the end of life.

• International Consensus Group on Depression and Anxiety, Consensus Statement on Depression, Anxiety and Oncology\textsuperscript{3,13,14}

Although published in 2001, these documents are foundational and include the views of both oncologists and psychiatrists.

**Critical Appraisal**

The five practice guidelines were assessed for reporting quality using the AGREE II Instrument. AGREE II is a critical appraisal tool and an important aid in the selection of the best-quality guidelines for use in practice (www.agreecollaboration.org).

**Quality of Practice Guidelines based on AGREE II**

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<tr>
<th>Domains</th>
<th>NBCC (Australia, 2003)\textsuperscript{5}</th>
<th>NCCN (v.2.2009)\textsuperscript{4}</th>
<th>CCO (2006)\textsuperscript{8a}</th>
<th>ONS (2008) Depression\textsuperscript{9a}</th>
<th>ONS (2008) Anxiety\textsuperscript{10a}</th>
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<td>1. Scope and Purpose</td>
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<td>2. Stakeholder Involvement</td>
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<td>3. Rigour of Development</td>
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<td>4. Clarity of Presentation</td>
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<td>77.8%</td>
<td>80.6%</td>
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<td>31%</td>
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<tr>
<td>6. Editorial Independence</td>
<td>20.8%</td>
<td>41.7%</td>
<td>79.2%</td>
<td>29%</td>
<td>29%</td>
</tr>
</tbody>
</table>

No of reviewers* 4 2 2 2 2

* Please note that the recommended number of reviewers ranges from two to four.

**Characteristics of the Included Guidelines**

A decision was made to include all five guidelines because two scored high on rigour (≥60\%) and those that scored lower are used to inform practice in large organizations such as Comprehensive Cancer Centers in the United States. The level of evidence is clear in those guidelines, they are based on prominent expert consensus and they are currently in widespread use.

**National Breast Cancer Centre (NBCC)**\textsuperscript{5}

**Scope and Content:** Comprehensive, evidence-based guidelines developed to assist health care professionals provide optimal psychosocial care. The guideline is
multidisciplinary, with recommendations applicable to diverse treatment settings. Content includes general interactional skills, discussing prognosis and treatment options, preparing patients for potentially threatening procedures and treatments, providing emotional and social support, ensuring continuity of care, and providing support toward the end of life.

**Patient Groups:** Adults with cancer. If differences apply (e.g., depending on age, gender, type of cancer, social circumstances, stage of treatment), any modifications are noted.

**Intended Users:** All members of the diagnostic and treatment team, which may include surgeons, radiation oncologists, medical oncologists, general practitioners, nurses, social workers, psychologists, psychiatrists, physiotherapists and occupational therapists.

**Levels of Evidence:** The series of recommendations are accompanied by identification of the levels and sources of research support. Evidence is presented using Levels I, II, III-1, III-2, III-3 and IV, with Level I (all relevant RCTs) representing the gold standard.\(^{20}\)

*Nationa Comprehensive Cancer Network (NCCN)*\(^4\)

**Scope and Content:** This practice guideline was developed by an expert committee and is reviewed and updated annually. The guideline consists primarily of recommendations for evaluation, treatment and follow-up care of identified conditions. The recommendations are organized in terms of clinical pathways. Recommendations for the management of anxiety and depression appear primarily in sections of the guideline focusing on anxiety and mood disorders.

**Patient Groups:** Patients with cancer.

**Intended Users:** Physicians and other health care professionals, such as the primary oncology team (oncologist, nurse, social worker) and the mental health team (psychiatrist, nurse, clinical nurse specialist, social worker, spiritual care provider).

**Levels of Evidence:** The search strategy was not described. Most recommendations represent a uniform consensus among panel members based on lower-level evidence, such as clinical experience, as opposed to higher-level evidence (e.g., RCTs). All recommendations are category 2A unless otherwise indicated.

*Cancer Care Ontario (CCO)*\(^6a\)

**Scope and Content:** The guideline is based on a consensus of expert panel members, informed by evidence reviewed and feedback from Ontario health care providers (peer review and external review). The topic that that is incorporated in the guideline described in the current report is the examination of the efficacy of pharmacological and non-pharmacological treatments for major depression and other depressive disorders in cancer populations. The CCO guideline does not address cancer patients that have anxiety or non-syndromal depression symptoms.

**Patient Groups:** Adult cancer patients with depression diagnosis (via structured interview with clinician or scoring >14 on the first 17 items of HDRS or ≥8 HADS or above cut-off on another valid assessment scale).
Intended Users: Oncology health professionals and mental health professionals engaged in the treatment of cancer patients.

Levels of Evidence: The search strategy included systematic reviews and RCTs. Categories of confidence were not provided. Based on the identified evidence, the recommendations are primarily consensus in nature (Expert Consensus Committee).

Oncology Nursing Society (Depression)

Scope and Content: What can oncology nurses do to assist people with cancer who also have depressive symptoms or a major depressive disorder? The interventions are within the scope of nursing practice and integral to the processes of nursing care. They do not address screening or assessment directly.

Patient Groups: Patients experiencing depressive symptoms and/or depression during and following cancer treatment.

Intended Users: Primarily oncology nurses, but also intended for other health professionals engaged in the care of cancer patients.

Levels of Evidence: ONS critically appraised evidence sources from strongest (multiple, well-designed, randomized, controlled trials with samples of more than 100 subjects) to weakest (e.g., qualitative designs, case studies, opinions). From there, interventions were classified using a weight-of-evidence schema.

Oncology Nursing Society (Anxiety)

Scope and Content: What interventions are effective for preventing and treating anxiety in people with cancer? The interventions are within the scope of nursing practice and integral to the processes of nursing care. They do not address screening or assessment.

Patient Groups: Patients with cancer.

Intended Users: Primarily oncology nurses, but also intended for other health professionals engaged in the care of cancer patients.

Levels of Evidence: ONS critically appraised evidence sources from strongest (multiple, well-designed, randomized, controlled trials with samples of more than 100 subjects) to weakest (e.g., qualitative designs, case studies, opinions). From there, interventions were classified using a weight-of-evidence schema.
Synthesizing the Evidence and Developing the Recommendations

A recommendation matrix was first created to summarize and compare the five guidelines. The comparisons presented (e.g., Scope and Content, Intended Users, Levels of Evidence, Harms) are based on the recommendation matrix template used by the National Guidelines Clearinghouse (www.guideline.gov) and the adaptation methodology. AGREE scores and contributing (risk) factors were added.

Descriptions of the evidence were written to summarize and highlight key evidence-based statements from the five guidelines, covering the areas of screening, assessment, contributing factors, treatment and care options. The key evidence-based statements were used as a base to identify relevant information in the supporting documents and to help build and populate the algorithm frameworks. A series of action statements (screening, assessment, treatment and care options) for both depression and anxiety were also developed from the key evidentiary base and recommendations.

The supporting documents were included to clarify background information and issues in the guidelines, and to cover any gaps. A formal assessment of systematic review quality was not conducted; however, checks were made to ensure the systematic reviews were explicit in how studies were selected (clear inclusion and exclusion criteria) and assessed, and clear about attempts to minimize biases and how studies were integrated to form the recommendations.

Thus, the algorithms and recommendations or action statements are based on the best available current evidence or expert consensus. Any evidence underlying the original practice guidelines was left unchanged and the evidence base for the synthesized recommendations was described in totality.

Discussion of Evidence

Screening for Depression and/or Anxiety

Patients and their families experience emotional distress (including depression and/or anxiety) associated with cancer and its treatment. Early detection and treatment of distress leads to better adherence to treatment, better communication, fewer calls and visits based on anxiety, avoidance of patients’ anger and developing severe anxiety, and greater coping. Exacerbation of distress can be moderated if preventive measures are taken.

NBCC recommends screening all patients with broad open-ended questions and identifying risk factors (Level III-3). Initial questions are the same for depression and anxiety (risk factors and asking about general psychological and emotional well-being). Asking about specific clinical issues such as anxiety and depression follow. This guideline suggests regular screening and monitoring of symptoms, particularly at known times of risk (e.g., diagnosis of recurrence). NBCC does not recommend administration of specific survey tools at this time (because of inconsistent evidence, p. 99).

NCCN recommends screening all patients on initial visit, at appropriate intervals and as clinically indicated (e.g., if status changes). This guideline recommends that patients complete the Distress Thermometer followed by a problem checklist.
(recommendation 2A). The tool is a visual analogue as well as a paper-pencil section to identify areas of concern for patients. The Distress Thermometer is valid and measures overall distress, including anxiety.4 NCCN reports Distress Thermometer cut-off scores: mild distress is less than a visual analogue score of 4, moderate to severe distress is identified as a score of 4 or more.

CCO does not include screening recommendations in the management of depression guideline, and anxiety is not part of its guideline. The CCO perspective, however, is that self-assessment is the gold standard. “Screening instruments may be used to increase the rate of detection of depressive symptoms.” Three instruments widely used to screen for depression in the medically ill are CES-D, HADS and BDI-IA and II.8b CCO reports it is good practice to screen patients using ESAS once per day, or weekly if there are no predominant issues (ESAS Description, www.cancercare.on.ca). The CCO Palliative Care Strategy and Ontario Cancer Plan reports ESAS as a standardized patient assessment tool (www.cancercare.on.ca).

Assessment is beyond the scope of the ONS guideline9a,10a; however, ONS expert opinion recommends that health care professionals “Assess patients and family members for depression and depressive symptoms at every encounter; assess patient’s and family’s understanding of depression and its role in cancer recovery, as well as the meaning of depression to the patient and his or her family.”9b(p.139) In addition, “Oncology nurses can play a significant role in recognizing visual and verbal cues of anxiety and depression and screening for depressive symptoms with the many valid screening tools available.”9b

From the supporting documents, NICE12 suggests two questions that refer to the past month to screen for depression in adults with chronic physical health problems.12 The International Consensus Group on Depression and Anxiety reports screening is crucial to identify patients who need treatment and recommends using the Hospital Anxiety and Depression Scale (HADS).3,13,14 A range of screening tools and self-report assessments are available (see table on following page).
## Selected Screening Tools for Depression and Anxiety

<table>
<thead>
<tr>
<th>Tool</th>
<th>Domains or Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beck Depression Inventory (BDI; short form: BDI-SF)</td>
<td>Widely used. 21 items. Behavioural, cognitive and somatic components of depression; focuses on negative attitudes of the patient toward self. Short-form 13 items.</td>
</tr>
<tr>
<td>Brief Symptom Inventory (BSI)</td>
<td>BSI measures the experience of symptoms in the past 7 days. 53-item self-report scale measures 9 primary symptom dimensions (somatization, obsessive-compulsive behaviour, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism).</td>
</tr>
<tr>
<td>Center for Epidemiological Studies–Depression Scale (CES-D; short form: CES-D-SF)</td>
<td>CES-D is one of the most common screening tests for depression and is in the public domain (10 items or 20 items). A quick self-test measures depressive feelings and behaviours during the past week (frequency of depressive symptoms). Four factors: negative affect and mood, positive mood or well-being, somatic, interpersonal.</td>
</tr>
<tr>
<td>Distress Thermometer (DT). Single item. Identifies distress coming from any source, even if unrelated to cancer.</td>
<td>A visual analogue scale (0-10). The patient answers the question: “How distressed have you been during the past week on a scale of 0 to 10?” 0=no distress 10=extreme distress. Responding with a 4 or higher indicates moderate or higher distress. Below 4 = mild distress to none. DT often completed prior to a brief problem checklist that asks patients to identify problems in five areas: practical, family, emotional, spiritual/religious, physical (NCCN 2009, MS-4).</td>
</tr>
<tr>
<td>Generalized Anxiety Disorder Assessment (GAD-7)</td>
<td>A 7-item anxiety scale, considered a useful screening tool for generalized anxiety disorder (see Appendix C for items).</td>
</tr>
<tr>
<td>Geriatric Depression Scale (GDS; short form: GDS-SF)</td>
<td>Positive and negative affective domains of depression.</td>
</tr>
<tr>
<td>Hamilton Rating Scale for Depression (HAM-D)</td>
<td>21 items. Rates the severity of symptoms observed in depression, such as low mood, insomnia, agitation, anxiety and weight loss. Commonly used and in public domain.</td>
</tr>
<tr>
<td>Hospital Anxiety and Depression Scale (HADS)</td>
<td>Self-screen to rate severity of depression and anxiety (two separate dimensions). Excludes questions about physical symptoms.</td>
</tr>
<tr>
<td>Patient Health Questionnaire PHQ-9 for Depression (PHQ-9).</td>
<td>PHQ-9 is in the public domain and is the nine item depression scale of the Patient Health Questionnaire. Two components: assessing symptoms and functional impairment to make a tentative depression diagnosis; deriving a severity score to help select and monitor treatment. PHQ-9 is based directly on the diagnostic criteria for major depressive disorder in DSM-IV. Patient responses are scored by the primary care clinician or office staff.</td>
</tr>
<tr>
<td>Profile of Mood States (POMS; short form: POMS-SF)</td>
<td>Six subscales: tension-anxiety, depression-dejection, anger-hostility, vigour-activity, fatigue-inertia, and confusion-bewilderment.</td>
</tr>
<tr>
<td>Spielberger State Trait Anxiety Inventory (STAI)</td>
<td>Two 20-item scales (20 state items = how respondents feel &quot;right now, at this moment&quot;; 20 trait items = how respondents feel &quot;generally&quot;). Indicator of state and trait anxiety and measures overall level of anxiety; helps distinguish anxiety from depression.</td>
</tr>
</tbody>
</table>

Sources: 4, 9b, 10b; PHQ-9 from MacArthur Initiative on Depression and Primary Care, http://www.depression-primarycare.org/
In Canada, the Edmonton Symptom Assessment System (ESAS) is a commonly administered screening tool followed by the Canadian Problem checklist (see page 18). The ESAS was initially developed by Dr. Eduardo Bruera and colleagues as a brief symptom assessment tool in palliative patients. The ESAS is a valid and reliable assessment tool and screens for nine common symptoms experienced by cancer patients (pain, tiredness, nausea, depression, anxiety, drowsiness, appetite, well-being and shortness of breath). The severity of each symptom at the time of screening is rated on a numerical scale from 0 to 10, with 0 meaning that the symptom is absent and 10 that it is the most severe; results are trended over time. A systematic review of cancer symptom assessment instruments found that the ESAS is a psychometrically sound instrument. The ESAS has been validated in a variety of populations, including both advanced cancer patients and patients earlier in the cancer trajectory.

The ESAS cut-off scores are assumed to mirror the NCCN Distress Thermometer cut-offs (mild less than 4, moderate to high 4 to 10), but this requires further research to fully validate. For further information about ESAS, see the Partnership’s Guide to implementing screening for distress, the 6th vital sign: Moving toward person-centered care.

To sum up, patients respond to stressors, such as cancer, based on many factors, including their own personality, life experiences, prior coping strategies, circumstances and support systems. Because depression and/or anxiety may go undetected and thereby untreated in oncology practice, the importance of appropriate assessment and screening tools has been emphasized. Screening typically involves one to three question(s) about thoughts and symptoms over the previous week or two. Although there are differences in suggested approaches (e.g., to use a screening tool or not, specific questions to ask, tools to use), the synthesis of recommendations across the reviewed guidelines agree that regular screening for depression and/or anxiety remains a useful approach for all patients. The supporting documents concur.

**Assessment of Depression and/or Anxiety**

If a patient is red-flagged during screening, they require further assessment to clarify the nature and extent of their depression or anxiety. NCCN recommends asking a second level of questions if there is clinical evidence of moderate to severe distress or a score of 4 or more on the Distress Thermometer. According to NBCC, further exploration of the nature, severity and impact of the patients concerns depends on the initial information gained about risk factors and responses to the open-ended screening questions (general psychological and emotional well-being). CCO does not include assessment recommendations. Underlying its treatment recommendations, however, is the assumption that patients have a clinical diagnosis of major depression or other non-bipolar depressive disorders. Assessment is also beyond the scope of the ONS depression guideline; however, ONS expert opinion recommends that health care professionals “Assess patients and family members for depression and depressive symptoms at every encounter; assess patient’s and family’s understanding of depression and its role in cancer recovery, as well as the meaning of depression to the patient and his or her family.”
There is consistency across the reviewed guidelines and supporting documents regarding the necessary components of further assessment if depression or anxiety concerns are red-flagged during screening.\textsuperscript{4,5,8a,8b,9a,10a,12,19} The further assessment should be comprehensive and identify:

- The severity of relevant symptoms,
- Possible stressors (e.g., life events such as recent bereavement or loss, change in home setting or support system),
- Clinical observation,
- Risk factors,
- Times of vulnerability,
- Underlying problems or causes (e.g., consider pain\textsuperscript{14} and fatigue\textsuperscript{27}).

**Depression Symptoms**

The synthesis of recommendations across the reviewed guidelines agree on the signs and symptoms of major depression and are consistent with the DSM-IV criteria:\textsuperscript{4,5,8a,9a,12}

- A depressed mood for most of the day and on most days
- Diminished pleasure or interest in most activities
- Significant change in appetite and sleep patterns
- Psychomotor agitation or slowing
- Fatigue
- Feelings of worthlessness, hopelessness or excessive, inappropriate guilt
- Poor concentration
- Recurrent thoughts of death or suicide

Assessment tools or checklists can help to assess for the presence of symptoms and to identify patients in need of treatment (see table on page 29). The synthesis of recommendations across the reviewed guidelines also agree on the DSM-IV criterion that experiencing symptoms for two weeks or more confirms the presence of depression problems.\textsuperscript{4,5,8a,9a,9b} In a qualifying statement, CCO suggests referral to a mental health specialist where the diagnosis of depression is unclear, the syndrome is severe, the patient is not responding to treatment or there are other complicating factors that may affect the choice of treatment.\textsuperscript{8a,8b}

**Anxiety Symptoms**

Summarizing common anxiety symptoms is less straightforward because of the different types of anxiety. State anxiety is relatively transient compared to longer standing trait anxiety. Generalized anxiety disorder (GAD) is usually pre-existing (trait).\textsuperscript{10a} Panic disorder may also recur during illness in a person with previous panic disorder. Post-traumatic stress disorder (PTSD) is characterized by re-experiencing a traumatic event (state) and heightened arousal, and may involve exaggerated reactions and avoidance of stimuli associated with the trauma.\textsuperscript{4,10a,10b} Obsessive-compulsive disorder (OCD) and phobias were also highlighted by NCCN.\textsuperscript{4}
Anxiety may be manifested by psychological and physical symptoms and it is often a challenge to distinguish “normal” anxiety from pathological anxiety. Most people with mild anxiety feel anxious about a specific event or situation (e.g., time of cancer diagnosis, complications related to their cancer). Anxiety in patients with cancer can include: 4,5,10a

- Feeling restless or on edge, irritable
- Sense of dread
- Physical symptoms such as dry mouth, heart palpitations, excessive sweating, stomach ache, headache, diarrhea
- Sleep difficulties
- Tired easily
- Difficulty concentrating
- Tension in muscles

Those experiencing anxiety due to a phobia or panic disorder usually know the cause of their anxiety. With GAD, however, the underlying triggers are not always known or clear.4 For DSM-IV, the anxiety needs to be “excessive” and “uncontrollable.” Pathological or maladaptive anxiety is characterized by:

- Worry or anxiety out of proportion to the level of threat
- Persistence or deterioration without intervention
- A level of symptoms that is unacceptable to the level of threat
- A disruption of usual or desired day-to-day life functioning

Consequent behaviours can also be disruptive, such as avoidance, repetitive checking of health and excessive reassurance seeking.

To best understand patient experiences, identify problems, etiology and decide appropriate interventions, the comprehensive assessment for anxiety (as noted above) should include both psychological and physical symptoms, as well as possible medical causes, and should identify and document contributing risk factors.10a,10b It is important to rule out other causes of anxiety (such as alcohol and drug withdrawal, medications, medical conditions) and focus on disruption of function and impairment to identify maladaptive anxiety.4,5 To determine the most appropriate referrals and resource options, further questions can be framed to identify patient concerns, difficulties, hopes and expectations (National Advisory Group of the Cancer Journey Action Group, personal communication, 2010).

The Canadian Problem Checklist is commonly used in Canada. Suggested tools10a,10b include the Beck Anxiety Inventory (BAI), the Hospital Anxiety and Depression Scale (HADS), the Brief Symptom Inventory (BSI), Visual Analog Scale (Distress Thermometer) and the Spielberger State Trait Anxiety Inventory (STAI) (see table on page 29).

In terms of who should carry out the comprehensive assessment for depression or anxiety, the NBCC report notes: “It is prudent for all health care professionals to be alert for signs of depression and anxiety and to actively assess adjustment and mood during the course of treatment and follow-up.”5 The guideline recommends consultation before enduring and disabling conditions develop (Level I).5(p.89)

Assessment by a clinical psychologist or psychiatrist is recommended for people...
reporting intrusive or difficult-to-manage anxiety. Prompt consultation is recommended when an acute anxiety state or panic threatens to impede or complicate treatment. People experiencing severe concerns or disorders should be referred to specialist services.  

NCCN indicates that the oncology nurse is the most likely to review the distress screening and the problem checklist. However, any member of the primary oncology team (oncologist, nurse, social worker) may conduct the assessment if they are trained in evaluation. Patients are then referred to appropriate services (e.g., social work, spiritual care provider, mental health) depending on the problems identified. Jones agrees with NBCC, stating that the entire health care team can play a role in identifying (and ensuring treatment of) depression and anxiety in cancer patients. Two guidelines recommend urgent referral to appropriate services for those at risk of harm to self and/or others.

To sum up, early identification and ongoing monitoring are key. The psychological or psychiatric evaluation (i.e., further evaluation or focused assessment) may be conducted by any suitably trained health or mental health professional (consensus). There is consistency across the reviewed guidelines in terms of the necessary components of a comprehensive assessment. Further evaluation should identify the severity of relevant symptoms (e.g., fatigue), possible stressors, risk factors, and times of vulnerability; should explore underlying problems/causes; and should ultimately lead to a diagnosis (directly or following referral to other services). Four guidelines agree that, before initiating any treatment with patients considered at moderate or high risk, there should be confirmation of a diagnosis of depression or anxiety. Fraser Health and NICE concur. The clinical interview (DSM-IV criteria) is the standard of care for diagnosing major depression and other depressive syndromes in people with cancer. NCCN used DSM-IV-TR to identify the disorders (including anxiety disorder and mood disorder). Specific concerns such as suicide risk, severe problems or unclear diagnosis require referral to appropriate specialist mental health services.

Oncology care providers must, therefore, educate themselves about depression and anxiety in adult patients and can select one of many, well-established assessment tools to incorporate into their practices.

**Contributing (Risk) Factors**

NBCC lists factors associated with increased risk of psychosocial problems and NCCN lists psychosocial distress characteristics.  

ONS lists vulnerable points for higher anxiety. Although several are common with the NBCC, NCCN and CCO guidelines, ONS includes other times of vulnerability: change in functioning or roles, during follow-up and screening tests, disease progression or metastases, waiting for recurrence, moving toward palliative or hospice care. NICE highlights history of depression, co-morbidity (with functional impairment) and younger age (younger than 30 years) for depression. A recent systematic review concluded there was a correlation of cancer-related fatigue with depression and anxiety. Ballenger et al. list the following psychosocial risk factors for depression and anxiety: history of mood disorder, poor communication with the health care team, lack of supportive network, poor control of pain or other symptoms, prolonged treatment phase, surgical
interventions and treatment side effects. Jones has a similar list for anxiety and depression. Berard adds family history of psychiatric disorder, advanced disease and poor socioeconomic status as risk factors for psychological morbidity.

The guidelines separate characteristics of the individual from characteristics of the stage of disease or treatment. The NBCC, NCCN and ONS labels were similar (e.g., financial problems vs. financial hardships vs. economic adversity; young or dependent children vs. children younger than 21 years; existential or spiritual crisis vs. spiritual/religious concerns).

**Risk Factors for Psychosocial Distress**

<table>
<thead>
<tr>
<th>Characteristics of the Individual</th>
<th>NBCC5</th>
<th>NCCN4</th>
<th>CCO 6a,6b</th>
<th>ONS Anxiety 10a,10b</th>
</tr>
</thead>
<tbody>
<tr>
<td>Younger</td>
<td>✓ (III-1)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Single, separated, divorced or widowed</td>
<td>✓ (III-2)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Living alone</td>
<td>✓ (III-3)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Children younger than 21 years</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Economic adversity</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Lack of social support or perceived poor social support</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Poor marital or family functioning</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>History of psychiatric problems (e.g., depression, anxiety)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Cumulative stressful life events</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>History of alcohol or substance abuse</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Female gender</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Co-morbidity (severe illnesses)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Communication barriers (language, literacy, physical)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Family/caregiver conflicts</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Change in family status</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Spiritual/religious concerns</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>
Practice Guideline: Depression, Anxiety

<table>
<thead>
<tr>
<th>Characteristics of stage or treatment</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>At the time of diagnosis and recurrence (III-2)</td>
<td></td>
</tr>
<tr>
<td>During advanced stage of the disease (III-3)</td>
<td></td>
</tr>
<tr>
<td>Beginning or ending treatment; change in treatment</td>
<td></td>
</tr>
<tr>
<td>Poorer prognosis (IV)</td>
<td></td>
</tr>
<tr>
<td>Side effects of treatment</td>
<td></td>
</tr>
<tr>
<td>Greater functional impairment and disease burden</td>
<td></td>
</tr>
<tr>
<td>Experiencing lymphoedema</td>
<td></td>
</tr>
<tr>
<td>Experiencing chronic pain</td>
<td></td>
</tr>
<tr>
<td>Fatigue[^1]</td>
<td></td>
</tr>
</tbody>
</table>

[^1] Also reported in a systematic review by Brown and Kroenke. ^27

**Treatment and Care Options**

Before initiating any treatment with patients considered at moderate or high risk, there should be confirmation of a diagnosis of depression. ^4, ^5, ^8a, ^12 The clinical interview (DSM-IV criteria) is the standard of care for diagnosing major depression and other depressive syndromes in people with cancer. ^4

The majority of the NBCC recommendations for depression and anxiety are based on a systematic review of all relevant RCTs (Level I) or on at least one properly designed RCT (Level II).

**NBCC Anxiety and Depression Treatment and Care**

<table>
<thead>
<tr>
<th>Treatment and Care Options</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Offer referral to relevant services early in the course of treatment</td>
<td>I</td>
</tr>
<tr>
<td>(e.g., social worker, psychological services).</td>
<td></td>
</tr>
<tr>
<td>High-risk (depression) patients should be referred to specialized psychological services to minimize the likelihood of developing significant distress.</td>
<td>I</td>
</tr>
<tr>
<td>Treatment of anxiety and depression must include attention to relevant physical problems such as pain, which is a major risk factor for depression.</td>
<td>III-2</td>
</tr>
<tr>
<td>Cognitive, behavioural, psycho-educational and supportive interventions, as well as combinations of education and behavioural or non-behavioural interventions and cognitive behavioural interventions and antidepressants are effective in the treatment of depression.</td>
<td>I</td>
</tr>
<tr>
<td>Depression can be managed by incorporating a combination of supportive psychotherapy, cognitive and behavioural techniques, and pharmacotherapy.</td>
<td>I</td>
</tr>
<tr>
<td>There is no evidence that any particular antidepressant is superior to another in the management of depression in people with cancer.</td>
<td>I</td>
</tr>
<tr>
<td>Cognitive behavioural, psycho-educational and crisis interventions, as well as combinations of education and anti-anxiety medications, are effective in the treatment of anxiety.</td>
<td>I</td>
</tr>
<tr>
<td>Supportive psychotherapy in combination with antidepressants such as selective serotonin reuptake inhibitors is effective in managing post-traumatic stress disorder (PTSD).</td>
<td>I</td>
</tr>
<tr>
<td>When anxiety or panic impedes or complicates treatment, prompt assessment from a psychiatrist or clinical psychologist is required.</td>
<td>I</td>
</tr>
</tbody>
</table>
The NBCC guideline provides many additional recommendations (supported by Level I and II evidence) to guide psychosocial care. Ensuring continuity of care, interactional skills, preparation for potentially threatening procedures and discussing prognosis are some of the areas.\textsuperscript{(p.8-10)}

**NBCC General Recommendations to Reduce Stress**

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Providing question prompt sheets to patients with cancer during an initial consultation promotes patient questions, reduces anxiety, improves recall and shortens the consultation.</td>
<td>II</td>
</tr>
<tr>
<td>Providing patients with information about the procedure they are about to undergo reduces emotional distress and improves psychological and physical recovery.</td>
<td>I</td>
</tr>
<tr>
<td>Providing patients with practical details about the procedure (procedural information) and a booklet and/or videotape decreases anxiety and psychological distress.</td>
<td>II</td>
</tr>
<tr>
<td>Providing patients with information about what they are likely to experience before, during and after a procedure (sensory information) decreases anxiety.</td>
<td>I</td>
</tr>
<tr>
<td>Providing patients with psychological support before undergoing surgery reduces psychological distress.</td>
<td>I</td>
</tr>
<tr>
<td>The opportunity to discuss feelings with a member of the treatment team or counsellor decreases psychosocial distress.</td>
<td>I</td>
</tr>
<tr>
<td>Interventions that provide support for partners of patients are effective in reducing distress in both patients and partners.</td>
<td>I</td>
</tr>
</tbody>
</table>

Underlying the NCCN recommendations is the assumption that, before initiating treatment for depression or anxiety, patients will have been referred to a mental health professional for psychological/psychiatric evaluation.\textsuperscript{4} Psychosocial interventions are included within descriptions of social work services (e.g., education, support, counselling, psychotherapy).

**NCCN Anxiety and Depression Treatment and Care**

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression: modify factors potentially contributing to mood disorder symptoms first (such as concurrent medications, pain and withdrawal states).</td>
<td>2A</td>
</tr>
<tr>
<td>Depression: initiate antidepressant medication and psychotherapy (with or without concurrent initiation of anxiolytic medication), and consider referral to social work and/or spiritual care services before follow-up and re-evaluation.</td>
<td>2A</td>
</tr>
<tr>
<td>Anxiety: provide cognitive behavioural therapy to reduce symptoms and psychotherapy (with or without anxiolytic medication and/or antidepressant medication) before follow-up or re-evaluation\textsuperscript{5}.</td>
<td>1</td>
</tr>
</tbody>
</table>

There are two main forms of treatment for generalized anxiety disorder (GAD), psychological therapy (cognitive behavioural therapy, or CBT) and antidepressants and/or anxiolytics. A patient may require either of these types of treatment or a combination of both. CBT helps to replace unrealistic and unhelpful beliefs and behavioural patterns with more balanced and realistic ones.
### CCO Depression Treatment and Care (in agreement with NBCC\(^5\) and NCCN\(^4\))

<table>
<thead>
<tr>
<th>Task</th>
<th>Level of Evidence*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treat pain and other reversible symptoms prior to initiating antidepressant treatment.</td>
<td>I, Consensus</td>
</tr>
<tr>
<td>Antidepressants should be considered to treat moderate to severe depression.</td>
<td>I, Consensus</td>
</tr>
<tr>
<td>No antidepressant is superior to another.</td>
<td>I, Consensus</td>
</tr>
<tr>
<td>Cancer patients with depression may benefit from a combined modality approach (psychosocial and pharmacological).</td>
<td>I, Consensus</td>
</tr>
</tbody>
</table>

* CCO reported an absence of clear evidence from RCTs.\(^{8b}\) Although its recommendations are based on Level I evidence, they reflect expert consensus. CCO adds that the choice of an antidepressant should be informed by the side effect profiles of the medications, tolerability of treatment, including the potential for interaction with other current medications, response to prior treatment and patient preference. Psychosocial treatment approaches that may be of value include those that provide information and support and that address emotional, cognitive and/or behavioural factors.\(^{8a,8b}\)
## ONS Depression and Anxiety Treatment and Care

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Level of Evidence*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression: Psycho-educational and psychosocial interventions to reduce depressive symptoms (e.g., CBT).</td>
<td>RFP</td>
</tr>
<tr>
<td>Depression: Psycho-educational and psychosocial interventions for treating depression.</td>
<td>RFP</td>
</tr>
<tr>
<td>Depression: Medications such as Methylphenidate (Ritalin)</td>
<td>LTBE</td>
</tr>
<tr>
<td>Depression: Complementary therapies are gaining popularity and some interventions (e.g., relaxation therapy) show promise in reducing stress, pain and other symptoms.</td>
<td>LTBE</td>
</tr>
<tr>
<td>Anxiety: Educational: patient-centered materials about the types of cancer and treatments; patient orientation to staff and contact information; teaching symptom management and self-care strategies.</td>
<td>RFP</td>
</tr>
<tr>
<td>Anxiety: Psychosocial: cognitive behavioural therapy to teach distraction and other techniques; individual or group counselling and psychotherapy sessions; support group meetings.</td>
<td>RFP</td>
</tr>
<tr>
<td>Anxiety: Medications</td>
<td>LTBE</td>
</tr>
<tr>
<td>- Benzodiazepines (lorazepam, diazepam, alprazolam)</td>
<td></td>
</tr>
<tr>
<td>- Azapirones (buspirone)</td>
<td></td>
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<tr>
<td>- Antihistamines (hydroxyzine)</td>
<td></td>
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<tr>
<td>- Antidepressants (paroxetine, sertraline, escitalopram, venlafaxine, mirtazapine)</td>
<td></td>
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<tr>
<td>- Atypical neuroleptics (olanzapine, risperidone)</td>
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<tr>
<td>- Other (propofol)</td>
<td></td>
</tr>
<tr>
<td>Anxiety: Massage therapy</td>
<td>LTBE</td>
</tr>
</tbody>
</table>

* RFP: recommended for practice (based on at least two RCTs); LTBE: likely to be effective (based on single RCT and consensus). Definitions of the interventions and full ONS citations: www.ons.org/outcomes.

Self-management includes modifying lifestyle if appropriate (e.g., stop smoking, reduce alcohol and caffeine, increase physical activity), relaxation techniques and attending support groups.

ONS reports that initial studies of some types of complementary and alternative interventions have shown promise in the treatment of depression. ONS notes that more studies are needed before practice recommendations can be made. It therefore reports that effectiveness is not established (depression) for complementary and alternative therapy such as massage therapy, hypnotherapy and other complementary interventions (e.g., yoga, acupuncture, aromatherapy, meditation). Similarly, effectiveness is not established (anxiety) for art therapy, exercise, meditation, progressive muscle relaxation, therapeutic touch, reiki, foot reflexology, homeopathy, and complementary and alternative medicine.

### Depression and Anxiety Treatment: Key Points

- For depression and anxiety, treat unrelieved symptoms such as pain and fatigue first.
- For patients with no depression to mild depression, offer psychosocial interventions (education and support) as a preventive measure. Support can include group-based counselling and individual self-help. NICE suggests offering a structured group physical activity program (if patient prefers). Education areas can include signs and symptoms, self-management, coping strategies, sources of informal support, resources available to patients and families (e.g., accommodation, transportation, financial assistance and additional health/drug benefits).
• Psycho-educational and psychosocial interventions, particularly cognitive behavioural therapy, are beneficial in managing depressive symptoms and treating depression in patients with various types of cancer.

• The guidelines agree that cancer patients with moderate to severe depression may benefit from a combination of pharmacological and psychosocial interventions, finding it more effective than either alone (e.g., antidepressant medication alongside supportive psychotherapy or cognitive behavioural techniques (group-based or individual)). Fraser Health also supports a combination of treatments for palliative patients with depression.19

• Antidepressants have been shown to have benefits in physically ill patients (including cancer) with moderate to severe depression.18 For example, there are data that show that selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants are effective. Serotonin-norepinephrine reuptake inhibitors (SNRIs) and psycho-stimulants are also given as examples.

• The guidelines agree that no antidepressant is superior to another in terms of efficacy.4,5,8a Ballenger et al. 3 and NICE12 concur. Fraser Health agrees for palliative care.19

• When depression is accompanied by symptoms of anxiety, treat depression first; when an anxiety disorder is accompanied by symptoms of depression, consider treating anxiety first.12

• There is evidence that psychosocial interventions are also beneficial for anxiety symptoms in cancer patients. Psychosocial interventions have generally been defined as non-pharmacological interventions that include a variety of psychological and educational components. Typical components include relaxation training,10a,10b cognitive and behavioural coping strategies, cancer education/information sessions, and individual or group social support.

• Those with anxiety disorders benefit from combined approaches of psychosocial interventions and pharmacological agents where appropriate (pharmacotherapy can include antidepressants with or without anxiolytics).

• Pharmacological management of anxiety includes benzodiazepines (e.g., alprazolam [short acting] and diazepam [longer acting]; if hepatic disease consider oxazepam), anti-psychotics (e.g., if extreme agitation, small doses haloperidol), antihistamines and antidepressants as for moderate depression; SSRIs can be used for longer term management of panic (Level IV).5

To sum up, management of depression or anxiety must be tailored to the individual patient, who should be fully informed of the options. Patients should be aware of options and have the opportunity to take part in decision-making.5,12 The choice of an antidepressant and/or anxiolytic should be informed by the side effect profiles of the medications, tolerability of treatment, including the potential for interaction with other current medications, response to prior treatment and patient preference. Patients should be warned of any potential harm (see Appendix D). Each practice setting should have agreed protocols for depression and anxiety management that include recommendations for referral and care pathways.
Strengthenes and Weaknesses of the Body of Evidence

The NBCC guideline is based on available evidence, with identification of the levels and research support for each recommendation.5 Levels of evidence vary from systematic reviews of all RCTs (Level I) to case studies (Level IV). Level I evidence includes prompt referral to relevant services early in the course of treatment for those with depression and anxiety symptoms; psychological therapies and psychosocial interventions for the treatment of depression and anxiety (e.g., counselling, supportive psychotherapy, group therapy, psycho-education and cognitive behavioural approaches [guided imagery, relaxation therapy]); supportive psychotherapy with cognitive behavioural therapy (CBT) and antidepressants for PTSD; effectiveness of pharmacological agents in the management of anxiety or depressive disorders.

CCO’s evidentiary base primarily comprises RCTs (Level I) that assess pharmacological and non-pharmacological treatments for patients with clinically significant depression.8a CCO systematically reviewed the quality of the evidence and this is explicitly stated in its guideline.5a

The ONS Depression9a,9b and Anxiety10a,10b guidelines include systematic reviews, meta-analyses, RCTs, case studies, expert opinion and consensus in their evidentiary bases. The grade and quality of evidence was systematically evaluated and stated clearly by ONS using a weight of evidence classification schema.9a,10a ONS Level I evidence includes psycho-educational or psychosocial interventions in the management of anxiety and depressive symptoms during and following cancer treatment (e.g., CBT, patient education and information, social support); antidepressant medications in the treatment of depression; relaxation therapy for depression.

NCCN recommendations were primarily based on consensus among respected authorities, clinical experience or evidence from phase II to large cohort studies, and included case series to reports from expert committees to individual practitioner experience.4 There was some consensus based on RCTs (category I) in the area of psychotherapy with or without an anxiolytic or an antidepressant for the treatment of anxiety. It should be noted that there was some overlap between the depression and anxiety evidence as some studies and guidelines (e.g., NCCN) place them on a continuum and address and/or assess both.

Weaknesses in the body of evidence include a relative lack of studies on certain populations (e.g., men with cancer, marginalized populations and patients with a clinically significant level of anxiety or depression), which influences the external validity of findings. In addition, some of the NBCC supporting research was conducted on general populations (i.e., not all cancer patients) and assumes that the evidence from the other populations generalizes to cancer.5 NBCC acknowledges that, at present, data from general populations are needed to derive guidelines because evidence in cancer populations is limited.

Inconsistent findings are a further limitation, largely due to a lack of standardization. Several studies may measure a common intervention strategy, for example, but follow different designs (e.g., varying sample characteristics, outcome measures, timing of data collection). These weaknesses are acknowledged by the present sources of evidence.
Although Ballenger et al. mention that how a patient copes with the stress of cancer will affect their psychological morbidity, the extent to which prior coping strategies and experiences are a contributing factor is not covered by the guidelines. Further limitations in the body of evidence include the lack of specific guidance details pertaining to aboriginal populations, geographic dispersion and tertiary versus community hospitals (i.e., the opportunity to implement some of the recommendations may be limited due to local circumstances and the availability of resources).

**Recommendations**

The following recommendations and algorithms on the optimum screening, assessment and supportive care of adult patients with cancer who experience depression and/or anxiety are based on the expert consensus of the National Advisory Working Group of the Cancer Journey Action Group, Canadian Partnership Against Cancer and are informed primarily by five clinical practice guidelines and a number of supporting documents.  

**Depression Recommendations**

1. **Screening for Depression**

   *(Based on the expert consensus of the National Advisory Working Group and informed by NBCC evidence Level III-3, NCCN category 2A, CCO expert consensus, ONS expert opinion)*

   - All health care providers should routinely screen for the presence of emotional distress and specifically symptoms of depression from the point of diagnosis onward.
   - All patients should be screened for distress at their initial visit, at appropriate intervals and as clinically indicated, especially with changes in disease status (i.e., post-treatment, recurrence, progression) and when there is a transition to end-of-life care.
     - The Canadian Association of Psychosocial Oncology (CAPO) and the Canadian Partnership Against Cancer (the Partnership) guideline “Assessment of Psychosocial Health Care Needs of the Adult Cancer Patient” suggests screening at initial diagnosis, start of treatment, regular intervals during treatment, end of treatment, post-treatment or at transition to survivorship, at recurrence or progression, advanced disease, when dying, and during times of personal transition or re-appraisal such as family crisis, during post-treatment survivorship and when approaching death.¹
   - Screening should identify the level and nature (problems and concerns) of the distress as a red flag indicator.
   - Screening should be done using a valid and reliable tool that features reportable scores (dimensions) that are clinically meaningful (established cut-offs).
     - For example, the Partnership’s Screening for Distress tool, which includes the Edmonton Symptom Assessment System (ESAS) and the Canadian Problem Checklist as per the CAPO/Partnership guideline *Assessment of Psychosocial Health Care Needs of the Adult Cancer Patient.*¹
2. Assessment of Depression
(Based on the expert consensus of the National Advisory Working Group and informed by NBCC evidence Level I, NCCN category 2A, CCO expert consensus, ONS expert opinion)

- Specific concerns such as risk of harm to self and/or others, severe depression or agitation, or the presence of psychosis or confusion (delirium) may require an urgent referral to a psychiatrist, psychologist, physician or equivalently trained professional.

- When moderate or severe depression is detected through screening (ESAS depression item score of 4 or higher), individuals should have an immediate assessment to identify the nature and extent of the depressive symptoms.

- Medical and substance-induced (e.g., Interferon administration) causes of depression should be ruled out.

- As a shared responsibility, the clinical team must decide when referral to a psychiatrist, psychologist or equivalently trained professional is needed (i.e., all patients with an ESAS score in the severe range, with certain accompanying factors and/or symptoms, or with a cut-off identified using valid and reliable tools for assessment of symptoms of depression).

- Assessments should be a shared responsibility of the clinical team, with designation of those who are expected to conduct assessments as per scope of practice.

- The assessment should identify signs and symptoms of depression, the severity of relevant symptoms (e.g., fatigue), possible stressors, risk factors and times of vulnerability, and should also explore underlying problems or causes (common measurement tools include BDI, BSI, CES-D and HADS; see table on page 29).

- A patient considered to have depressive symptoms following the further assessment should, where possible, have confirmation of a clinical diagnosis of depression before any pharmacological treatment or care options are initiated (e.g., DSM-IV, which may require making a referral).

3. Treatment and Care Options for Depression
(Based on the expert consensus of the National Advisory Working Group and informed by NBCC evidence Levels I and II, NCCN category 2A, CCO expert consensus using Level I and II evidence, ONS “recommended for practice” and “likely to be effective”, ONS expert opinion)

- For any patient who is identified as at risk of harm to self and/or others, consider URGENT referral to appropriate services for emergency evaluation. Facilitate a safe environment and one-to-one observation, and initiate appropriate harm-reduction interventions to reduce risk of harm to self and/or others.

- First treat medical causes of depression (e.g., unrelieved symptoms such as pain and fatigue) and delirium (e.g., infection or electrolyte imbalance).

- Optimal management of moderate to severe depression combines pharmacological and non-pharmacological interventions delivered by appropriately trained individuals (e.g., psychotherapy and psycho-educational therapy, cognitive-behavioural therapy).
These guidelines make no recommendations about specific antidepressant pharmacological regimes being better than another. The choice of an antidepressant should be informed by the side effect profiles of the medications, tolerability of treatment, including the potential for interaction with other current medications, response to prior treatment and patient preference. Patients should be warned of any potential harms and adverse effects (see Appendix D for an antidepressant information guide).

Offer support and provide education and information about depression and its management to all patients and their families and what specific symptoms warrant a call to the physician or nurse.

**Algorithm: Screening, Assessment and Care of Depression in Adults with Cancer**

*See following page for detailed algorithm components.

Refer to the full technical guideline document for the disclaimer statement on the Canadian Association of Psychosocial Oncology website (www.capo.ca)
Practice Guideline: Depression, Anxiety

Screening and Assessment - Depression* in Adults with Cancer

Screen for distress¹ at entry to system, critical times, periodically during patient care, or other stressful times²

Assessment of risk of harm to self and/or to others (all patients)
- If YES > URGENT referral to appropriate services for emergency evaluation; Facilitate safe environment; One-to-one observation; Initiate appropriate harm reduction interventions to reduce risk of harm to self and/or others. (The presence of other symptoms such as psychosis, severe agitation and confusion (delirium) may also warrant referral to appropriate services for emergency evaluation).
- If NO > continue with algorithm

Depression identified on ESAS screening (Depression item)

Mild Distress
ESAS Depression Score 1-3

Moderate Distress
ESAS Depression Score 4-6

Severe Distress
ESAS Depression Score 7-10

Assessment to clarify nature and extent of depressive symptoms
- Review problem checklist and all ESAS scores in conversation³ with patient/family and discuss expectations and beliefs about support needs (e.g., Canadian Problem Checklist)
- Identify most distressing ESAS symptom(s) and or problem(s) contributing to depression (e.g., life events, insomnia, pain, fatigue, other co-morbid illness) and daily interference
- Assess effectiveness of current symptom and/or co-morbid condition management
- Psychomotor agitation or slowing

Identify pertinent history / Specific risk factors for depression
- Recurrent, advanced, progressive disease (i.e., vulnerable points)
- History: Depression, substance abuse, other mental health problems (e.g., dysthymia)
- Current use of depression medication or seeing a psychologist or psychiatrist
- Perceived lack of social support
- Other factors (e.g., younger age, female, live alone, dependent children, financial problems, prior coping issues)

Focused assessment: Specific to problem of depression
- HCP with appropriate training and skills to complete a depression symptom checklist using validated tool (e.g., CES-D; PHQ-9) or assess for presence of: depressed mood, loss of pleasure, feelings of worthlessness/guilt, diminished concentration, recurrent thoughts of death, fatigue, significant change in appetite and sleep patterns, impaired functioning in daily living⁴
- Assess if symptoms persist for 2 weeks or longer (almost all day, every day)⁴

*Mild Distress
ESAS Depression Score 1-3

Moderate Distress
ESAS Depression Score 4-6

Severe Distress
ESAS Depression Score 7-10

*In this algorithm the use of the word depression refers to the ESAS screening scale and not to a clinical diagnosis

1. Use Screening for Distress Tool (SDT), which includes Edmonton Symptom Assessment System (ESAS) and Canadian Problem Checklist (CPC)
2. At initial diagnosis, start of treatment, regular intervals during treatment, end of treatment, post-treatment or at transition to survivorship, at recurrence or progression, advanced disease, when dying, and during times of personal transition or re-appraisal such as family crisis, during survivorship, when approaching death (CAPO/CPAC guideline: “Assessment of Psychosocial Health Care Needs of the Adult Cancer Patient” by Howell et al., 2009; Cancer Care Nova Scotia Distress Management Pathways, draft 2010).
3. The health care team for cancer patients may include surgeons, oncologists, family physicians, nurses, advanced practice nurses, social workers, psychologists, patient navigators and other health care professionals (HCPs)
4. DSM-IV criteria - The DSM-IV criteria can be used by a range of health professionals with specific training and skills.
Practice Guideline: Depression, Anxiety

**Care Map - Depression in Adults with Cancer***

- **Mild Distress**
  - ESAS Depression Score 1-3
  - No or minimal symptoms of depression
  - Recent life event(s) such as bereavement or loss
  - Level of grief appropriate for loss ("normal" response, NCCN) with gradual resolution over weeks / months
  - Effective coping skills and access to social support

- **Moderate Distress**
  - ESAS Depression Score 4-6
  - Moderate to high levels of distress (does not meet criteria for high risk but two or more symptoms present for two weeks) and / or Impairment of functioning in daily living
  - Risk factors (e.g., gaps in social support or effective coping mechanisms)

- **Severe Distress**
  - ESAS Depression Score 7-10
  - Depressed mood and / or loss of pleasure for 2 weeks
  - 4 additional symptoms: Feelings of worthlessness and / or guilt, Insomnia or hypersomnia, Weight gain or loss
  - Psychomotor agitation or retardation
  - Fatigue
  - Risk factors
  - Risk of harm to self and / or to others > URGENT referral to appropriate services; Facilitate safe environment; One-to-one observation; Initiate harm reduction interventions to reduce risk of harm to self and/or others

**Care Pathway 1**
- Prevention and Supportive Care
  - Offer referral to psychosocial support (e.g., counseling, support groups, individual)

**Care Pathway 2**
- Psychosocial Care and/or consider referral to Physician/Psychologist/Psychiatrist
  - Intervention Options
    - Combine non-pharmacological and pharmacological interventions as appropriate
    - Referral to other services as required (e.g., psychosocial team, physician, psychologist, psychiatrist)

**Care Pathway 3**
- Referral to Physician/Psychologist/Psychiatrist
  - Definitive Diagnosis Needed
  - Referral to appropriate services for evaluation and definitive diagnosis
  - Intervention Options
    - Psychiatric standard of care

**Non-Pharmacological**: Psycho-education and psychosocial interventions (specifically cognitive-behavioral therapy and patient education and information, counseling and individual or group psychotherapy, behavioral therapy, and social support); Relaxation therapy (ONS)

**Pharmacological**: A number of anti-depressants are recommended for treatment of depression with choice informed by side effect profiles, interactions, response, patient preference. (see appendices). Monitor for adverse effects.

With care team, review the plan for management of depression and other physical symptoms and need for referral unless automatic red flag generated for severe depression (e.g., pain)

**Supportive care interventions for all patients, as appropriate**
- Offer referral to psychosocial support (e.g., counseling, peer-led support groups, individual)
- Provide education (verbal plus any relevant materials) for the patient and family about:
  - How common emotional distress is in the context of cancer and differing responses
  - Benefits of support groups and other support services
  - Sources of informal support, resources available to patients and families (e.g., accommodation, transportation, financial assistance, additional health/drug benefits)
  - Need for additional psychosocial support if signs and symptoms of depression worsen with specific information regarding symptoms to warrant a call to the physician or nurse.
  - Coping with stress and specific strategies (i.e. relaxation approaches)
  - How to effectively manage symptoms contributing to depression (e.g., fatigue, sleep disturbance)

**Follow-up and ongoing re-assessment** and change (reduction) from previous score

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*Refer to the full technical guideline document for the evidentiary support for this algorithm on the Canadian Association of Psychosocial Oncology website (www.capo.ca)

Disclaimer
Care has been taken in the preparation of the information contained in this practice guideline document. Nonetheless, any person seeking to apply or consult the practice guideline is expected to independent clinical judgment and skills in the context of individual clinical circumstances or seek out the supervision of a qualified clinician. The Canadian Partnership Against Cancer and the Canadian Association of Psychosocial Oncology (CAPO) make no representation or warranties of any kind whatsoever regarding the content, use or application of this practice guideline and disclaim any responsibility for their application or use in any way.
Anxiety Recommendations

1. Screening for Anxiety
(Based on the expert consensus of the National Advisory Working Group and informed by NBCC evidence grading Level III-3, NCCN category 2A)

- All health care providers should routinely screen for the presence of emotional distress and specifically symptoms of anxiety from the point of diagnosis onward.
- All patients should be screened for distress at their initial visit, at appropriate intervals and as clinically indicated, especially with changes in disease status (i.e., post-treatment, recurrence, progression) and when there is a transition to end-of-life care.
  - The Canadian Association of Psychosocial Oncology (CAPO) and the Canadian Partnership Against Cancer (the Partnership) guideline “Assessment of Psychosocial Health Care Needs of the Adult Cancer Patient” suggests screening at initial diagnosis, start of treatment, regular intervals during treatment, end of treatment, post-treatment or at transition to survivorship, at recurrence or progression, advanced disease, when dying, and during times of personal transition or re-appraisal such as family crisis, during post-treatment survivorship and when approaching death.¹
- Screening should identify the level and nature (problems and concerns) of the distress as a red flag indicator.
- Screening should be done using a valid and reliable tool that features reportable scores (dimensions) that are clinically meaningful (established cut-offs).
  - For example, the Partnership’s Screening for Distress tool, which includes the Edmonton Symptom Assessment System (ESAS) and the Canadian Problem Checklist as per the CAPO/Partnership guideline Assessment of Psychosocial Health Care Needs of the Adult Cancer Patient.¹

2. Assessment of Anxiety
(Based on the expert consensus of the National Advisory Working Group and informed by NBCC evidence Level I, NCCN category 2A)

- Specific concerns such as risk of harm to self and/or others, severe anxiety or agitation, or the presence of psychosis or confusion (delirium) may require an urgent referral to a psychiatrist, psychologist, physician or equivalently trained professional.
- When moderate or severe anxiety is detected through screening (ESAS anxiety item score of 4 or higher), individuals should have an immediate assessment to identify the nature and extent of the anxiety symptoms.
- Medical and substance-induced causes of anxiety should be ruled out.
- As a shared responsibility, the clinical team must decide when referral to a psychiatrist, psychologist or equivalently trained professional is needed (i.e., all patients with an ESAS score in the severe range, with certain accompanying factors and/or symptoms, or with a cut-off identified using valid and reliable tools for assessment of symptoms of anxiety).
• Assessments should be a shared responsibility of the clinical team, with designation of those who are expected to conduct assessments as per scope of practice.

• The assessment should identify signs and symptoms of anxiety (e.g., panic attacks, trembling, sweating, tachypnea, tachycardia, palpitation and sweaty palms), severity of symptoms, possible stressors (e.g., impaired daily living), risk factors and times of vulnerability, and should also explore underlying problems/causes (common measurement tools include BAI, GAD-7; see Appendix C).

• A patient considered to have severe symptoms of anxiety following the further assessment should, where possible, have confirmation of a clinical diagnosis of anxiety disorder before any pharmacological treatment or care options are initiated (e.g., DSM-IV, which may require making a referral).

3. Treatment and Care Options for Anxiety
(Based on the expert consensus of the National Advisory Working Group and informed by NBCC evidence grading Level I, NCCN category 2A)

• For any patient who is identified as at risk of harm to self and/or others, consider URGENT referral to appropriate services for emergency evaluation. Facilitate a safe environment and one-to-one observation, and initiate appropriate harm-reduction interventions to reduce risk of harm to self and/or others.

• First treat medical causes of anxiety (e.g., unrelieved symptoms such as pain and fatigue) and delirium (e.g., infection or electrolyte imbalance).

• Optimal management of moderate to severe anxiety combines pharmacological and non-pharmacological interventions delivered by appropriately trained individuals (e.g., supportive psychotherapy and anxiolytics for PTSD). Management must be tailored to individual patients, who should be fully informed of their options.

• For a patient with mild to moderate anxiety, the primary oncology team may choose to manage the concerns by usual supportive care management.4

• These guidelines make no recommendations about specific antidepressant pharmacological regimes being better than another. The choice of an antidepressant should be informed by the side effect profiles of the medications, tolerability of treatment, including the potential for interaction with other current medications, response to prior treatment and patient preference. Patients should be warned of any potential harm or adverse effects (see Appendix D for an antidepressant information guide).

• Offer support and provide education and information about anxiety and its management to all patients and their families and what specific symptoms warrant a call to the physician or nurse.
Algorithm: Screening, Assessment and Care of Anxiety in Adults with Cancer

Screening

e.g., Edmonton Symptom Assessment System (ESAS)

1-3 ESAS "GREEN"

≥ 4 ESAS denotes need for further assessment
(4-6 moderate risk; 7-10 high risk)

Assessment* to clarify nature and extent of anxiety symptoms:
1. Generic Assessment
2. Focused Assessment
3. Pertinent History (Risk Factors)

Mild Risk*

Moderate Risk*

High Risk*

Care Pathway 2*

Care Pathway 3: Risk of harm to self and/or others

Care Pathway 1*

Follow-up and Ongoing Re-assessment

* See following page for detailed algorithm components

Refer to the full technical guideline document for the disclaimer statement on the Canadian Association of Psychosocial Oncology website (www.capo.ca)

Refer to the full technical guideline document for the disclaimer statement on the Canadian Association of Psychosocial Oncology website (www.capo.ca)
**Screening and Assessment: Anxiety* in Adults with Cancer**

**Screen for distress** at entry to system, critical times, periodically during patient care, or other stressful times.

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**Assessment of risk of harm to self and/or to others (all patients)**
- **If YES** > URGENT referral to appropriate services for emergency evaluation; Facilitate safe environment; One-to-one observation; Initiate appropriate harm reduction interventions to reduce risk of harm to self and/or others. *(The presence of other symptoms such as psychosis, severe agitation and confusion (delirium) may also warrant referral to appropriate services for emergency evaluation).*
- **If NO** > continue with algorithm

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**Anxiety identified on ESAS screening (Anxiety item)**

- **Mild Distress**
  - ESAS Anxiety Score 1-3

- **Moderate Distress**
  - ESAS Anxiety Score 4-6

- **Severe Distress**
  - ESAS Anxiety Score 7-10

---

**Assessment to clarify nature and extent of anxiety symptoms**

- Review problem checklist and all ESAS scores in conversation with patient/family and discuss expectations and beliefs about support needs (e.g., Canadian Problem Checklist)
- Identify most distressing ESAS problem or symptom and assess extent of daily life interference
- Review ESAS scores for other contributing symptoms (e.g., dyspnea or other medical/medication issue).
- Identify other concerns contributing to distress (e.g., life events, sleep deprivation)
- Identify other symptoms and current management of relevant symptoms (e.g., pain, fatigue, and/or sleep interference/chronic insomnia)

**Identify pertinent history: Specific risk factors for anxiety**

- History of anxiety problems (e.g., panic attacks, Generalized Anxiety Disorder (GAD)), depression, other mental health problems
- Current medication associated with anxiety or depression or seeing a specialist
- Disease recurrence, advanced or progressive disease (i.e., vulnerable points)
- Withdrawal state (e.g., alcohol, substance use)
- Other factors (e.g., younger age, female, live alone, dependents, financial problems)

**Focused assessment: Specific to problem of anxiety**

- HCP with appropriate training and skills to complete an anxiety symptom checklist using a validated tool (e.g., BAI; STAI; GAD-7) or assess for presence of: tension, uncontrollable or excessive worry, agitation, restlessness, panic attacks, poor concentration, nausea/vomiting, reassurance seeking, significant change in sleep patterns, impaired functioning in daily living (e.g., hypervigilance, scanning, irritability, unable to relax, ruminations)
- In what ways do anxiety symptoms affect daily functioning (e.g., sleep, appetite)

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*In this algorithm the use of the word anxiety refers to the ESAS screening scale and not to a clinical diagnosis*

1. Use Screening for Distress Tool (SDT), which includes Edmonton Symptom Assessment System (ESAS) and Canadian Problem Checklist (CPC).
2. At initial diagnosis, start of treatment, regular intervals during treatment, end of treatment, post-treatment or at transition to survivorship, at recurrence or progression, advanced disease, when dying, and during times of personal transition or re-appraisal such as family crisis, during survivorship, when approaching death (CAPO/CPAC guideline: "Assessment of Psychosocial Health Care Needs of the Adult Cancer Patient" by Howell et al., 2009; Cancer Care Nova Scotia Distress Management Pathways, draft 2018).
3. The health care team for cancer patients may include surgeons, oncologists, family physicians, nurses, advanced practice nurses, social workers, psychologists, patient navigators and other health care professionals (HCPs).
**Care Map - Anxiety in Adults with Cancer**

**Mild Distress**
ESAS Anxiety Score 1-3

- No or minimal anxiety symptoms
- Typical symptoms - fear, worry, uncertainty about future, concerns about illness, sadness about loss of good health, anger and feeling life is out of control, poor sleep, appetite and/or concentration, preoccupied with thoughts of illness and death, treatment effects and side effects (NCCN)
- Gradual resolution over weeks/months

**Care Pathway 1**
Prevention and Supportive Care

Offer referral to psychosocial support (e.g., counseling, support groups, individual, etc.)

**Care Pathway 2**
Psychosocial Care and/or consider referral to Physician/Psychologist/Psychiatrist

Intervention Options
Combine non-pharmacological and pharmacological interventions as appropriate (e.g., combined education, supportive psychotherapy and anxiolytics for PTSD)
Referral to other services as required (e.g., psychosocial team, physician, psychologist, psychiatrist, social work, spiritual care provider)

**Care Pathway 3**
Referral to Physician/Psychologist/Psychiatrist

Definitive Diagnosis Needed
Referral to appropriate services for evaluation and definitive diagnosis

Intervention Options
Psychiatric standard of care

**Supportive care interventions for all patients, as appropriate**

- Offer referral to psychosocial support (e.g., counseling, peer-led support groups, individual)
- Provide education (verbal plus any relevant materials) for the patient and family about:
  - How common anxiety is in the context of cancer and differing responses
  - Benefits of support groups and other support services
  - Sources of informal support, resources available to patients and families (e.g., accommodation, transportation, financial assistance, additional health/drug benefits)
  - The need for additional psychosocial support if signs and symptoms of anxiety worsen
  - Coping with stress and specific strategies (i.e. relaxation, breathing techniques, mindfulness)
  - How to effectively manage symptoms contributing to anxiety (e.g., pain, tension)

**Follow-up and ongoing re-assessment’ and change (reduction) from previous score**

**Moderate Distress**
ESAS Anxiety Score 4-6

- Maladaptive response (out of proportion to the stressors); disruption of usual or desirable functioning
- Unable or less able to control anxiety without intervention
- Risk factors
- Nature of anxiety disorder established (e.g., generalized anxiety disorder, panic disorder, post-traumatic stress disorder, obsessive-compulsive, phobia(s))

**Severe Distress**
ESAS Anxiety Score 7-10

- High or elevated level of worry or difficult to control anxiety about several things most days
- Re-experiencing events in a distressing way (e.g., dreams, intense recollections, flashbacks, physical reactions)
- One or more occasion of spells or attacks of sudden fear, discomfort, anxiousness or uneasiness
- Risk factors
- Risk of harm to self and/or to others > URGENT referral to appropriate services; Facilitate safe environment; One-to-one observation; Initiate harm reduction interventions to reduce risk of harm to self and/or others

High or elevated level of worry or difficult to control anxiety about several things most days
Re-experiencing events in a distressing way (e.g., dreams, intense recollections, flashbacks, physical reactions)
One or more occasion of spells or attacks of sudden fear, discomfort, anxiousness or uneasiness
Risk factors
Risk of harm to self and/or to others > URGENT referral to appropriate services; Facilitate safe environment; One-to-one observation; Initiate harm reduction interventions to reduce risk of harm to self and/or others

**Non-Pharmacological:**
Psychosocial interventions (CBT (level 1), psychotherapy, individual or group counseling, support groups); Psycho-educational (e.g., about services/resources, symptom management, self-care strategies); Crisis interventions as appropriate.

**Pharmacological:**
benzodiazepines, anxiolytics, antipsychotics, antihistamines; and antidepressants as for moderate depression; SSRIs in longer term management of panic. Monitor adverse effects.
**Next Steps**

Implementation of the recommendations in this document will involve co-ordination with a wide range of interprofessional service providers and agencies. Field-testing the care map is beyond the scope of this practice guideline. As a next step, patient versions of the recommendations are being developed.
References


5. National Breast Cancer Centre (NBCC) and National Cancer Control Initiative. Clinical practice guidelines for the psychosocial care of adults with cancer. Sydney, Australia; National Breast Cancer Centre; April 2003. 246 p. [776 references]


8a. Cancer Care Ontario (CCO). The management of depression in cancer patients: A clinical practice guideline; October 2006. (www.cancercare.on.ca)


Canadian Partnership Against Cancer. Literature Review and Environmental Scan - Psychosocial, Supportive and Palliative Care Standards and Guidelines. An Initiative of the Guidelines, Standards and Indicators Committee of Rebalance Focus Action Group, Canadian Strategy for Cancer Control (CSCC); March 2007.


Fraser Health Hospice Palliative Care Program. Symptom Guidelines: Depression in the Terminally Ill (www.fraserhealth.ca)


Appendix A: Levels of Evidence from Original Guidelines; ONS Schema

NHMRC Levels of Evidence

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level I</td>
<td>Evidence is obtained from a systematic review of all relevant randomized controlled trials.</td>
</tr>
<tr>
<td>Level II</td>
<td>Evidence is obtained from at least one properly designed randomized controlled trial.</td>
</tr>
<tr>
<td>Level III-1</td>
<td>Evidence is obtained from well designed pseudo randomized controlled trials (alternate allocation or some other method).</td>
</tr>
<tr>
<td>Level III-2</td>
<td>Evidence is obtained from comparative studies with concurrent controls and allocation not randomized (cohort studies), case control studies, or interrupted time series with a control group.</td>
</tr>
<tr>
<td>Level III-3</td>
<td>Evidence is obtained from comparative studies with historical control, two or more single arm studies, or interrupted time series without a parallel group.</td>
</tr>
<tr>
<td>Level IV</td>
<td>Evidence is obtained from case studies, either post-test or pre- and post-test.</td>
</tr>
</tbody>
</table>

Categories of Evidence and Consensus (accessed from www.nccn.org)

The NCCN Guidelines Steering Committee has devised a set of Categories of Evidence and Consensus. These annotations contain two dimensions: the strength of the evidence behind the recommendation and the degree of consensus about its inclusion. Unless indicated, all recommendations for distress management are category 2A.

<table>
<thead>
<tr>
<th>Category of Evidence and Consensus</th>
<th>Quality of Evidence</th>
<th>Level of Consensus</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>High</td>
<td>Uniform</td>
</tr>
<tr>
<td>2A</td>
<td>Lower</td>
<td>Uniform</td>
</tr>
<tr>
<td>2B</td>
<td>Lower</td>
<td>Non-uniform</td>
</tr>
<tr>
<td>3</td>
<td>Any</td>
<td>Major disagreement</td>
</tr>
</tbody>
</table>

NCCN Category 1: The recommendation is based on high-level evidence (i.e., high-powered randomized clinical trials or meta-analyses), and the NCCN Guideline Panel has reached uniform consensus that the recommendation is indicated. In this context, uniform means near unanimous positive support with some possible neutral positions.

NCCN Category 2A: The recommendation is based on lower level evidence, but despite the absence of higher level studies, there is uniform consensus that the recommendation is appropriate. Lower level evidence is interpreted broadly and runs the gamut from phase II to large cohort studies to case series to individual practitioner experience. Importantly, in many instances, the retrospective studies are derived from clinical experience of treating large numbers of patients at a member institution, so NCCN Guideline Panel Members have first-hand knowledge of the data. Inevitably, some recommendations must address clinical situations for which limited or no data exist. In these instances the congruence of experience-based judgments provides an informed if not confirmed direction for optimizing patient care. These recommendations carry the implicit recognition that they may be superseded as higher level evidence becomes available or as outcomes-based information becomes more prevalent.
**NCCN Category 2B:** The recommendation is based on lower level evidence and there is non-uniform consensus that the recommendation should be made. In these instances, because the evidence is not conclusive, institutions take different approaches to the management of a particular clinical scenario. This non-uniform consensus does not represent a major disagreement, rather it recognizes that given imperfect information, institutions may adopt different approaches. A Category 2B designation should signal to the user that more than one approach can be inferred from the existing data.

**NCCN Category 3:** Including the recommendation has engendered a major disagreement among the NCCN Guideline Panel Members. The level of evidence is not pertinent in this category because experts can disagree about the significance of high level trials. Several circumstances can cause major disagreements. For example, if substantial data exist about two interventions but they have never been directly compared in a randomized trial, adherents to one set of data may not accept the interpretation of the other side’s results. Another situation resulting in a Category 3 designation is when experts disagree about how trial data can be generalized. An example of this is the recommendation for internal mammary node radiation in post-mastectomy radiation therapy. One side believed that because the randomized studies included this modality, it must be included in the recommendation. The other side believed, based on the documented additional morbidity and the role of internal mammary radiation therapy in other studies, that this was not necessary. A Category 3 designation alerts users to a major interpretation issue in the data and directs them to the manuscript for an explanation of the controversy.

**ONS Putting Evidence into Practice Weight-of-Evidence Classification Schema**

ONS critically appraises evidence sources from strongest (multiple, well-designed, randomized, controlled trials with samples of more than 100 subjects) to weakest (e.g., qualitative designs, case studies, opinions). From there, interventions are classified using a weight-of-evidence schema.⁹⁶

<table>
<thead>
<tr>
<th>Weight of Evidence Category</th>
<th>Description</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommended for practice</td>
<td>Effectiveness is demonstrated by strong evidence from rigorously designed studies, meta-analyses or systematic reviews. Expected benefit exceeds expected harms.</td>
<td>At least two multi-site, well-conducted, randomized, controlled trials (RCTs) with at least 100 subjects. Panel of expert recommendation derived from explicit literature search strategy; includes thorough analysis, quality rating and synthesis of evidence.</td>
</tr>
<tr>
<td>Likely to be Effective</td>
<td>Evidence is less well established than for those listed under recommended for practice.</td>
<td>One well-conducted RCT with fewer than 100 patients or at one or more study sites. Guidelines developed by consensus or expert opinion without synthesis or quality rating.</td>
</tr>
<tr>
<td>Benefits balanced with harms</td>
<td>Clinicians and patients should weigh the beneficial and harmful effects according to individual circumstances and priorities.</td>
<td>RCTs, meta-analyses or systematic reviews with documented adverse effects in certain populations.</td>
</tr>
<tr>
<td>Effectiveness not established</td>
<td>Data currently are insufficient or are of inadequate quality.</td>
<td>Well-conducted case control study or poorly controlled RCT. Conflicting evidence or statistically insignificant results.</td>
</tr>
</tbody>
</table>
### Weight of Evidence Category

<table>
<thead>
<tr>
<th>Description</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effectiveness unlikely</td>
<td>Lack of effectiveness is less well established than those listed under not recommended for practice. Single RCT with at least 100 subjects that showed no benefit. No benefit and unacceptable toxicities found in observational or experimental studies.</td>
</tr>
<tr>
<td>Not recommended for practice</td>
<td>Ineffectiveness or harm is clearly demonstrated, or cost or burden exceeds potential benefit. No benefit or excess costs or burden from at least two multi-site, well-conducted RCTs with at least 100 subjects. Discouraged by expert recommendation derived from explicit literature search strategy; includes thorough analysis, quality rating and synthesis of evidence.</td>
</tr>
</tbody>
</table>

**ONS definition of Expert Opinion:** Low-risk interventions that are (a) consistent with sound clinical practice, (b) suggested by an expert in a peer-reviewed publication (journal or book chapter) and (c) for which limited evidence exists. An expert is an individual with peer-reviewed journal publications in the domain of interest. 

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Appendix B: Recommendations Matrix

## 1. Screening/Assessing Symptoms

**NBCC (Australia)**

Recommended protocol (p.38): All patients are screened for clinically significant anxiety and depression (III-3) as part of routine clinical practice (i.e., prudent for all health care professionals to be alert for signs of depression and anxiety and to actively assess adjustment and mood during the course of treatment and follow up).

No recommendation to administer questionnaires (e.g., GHQ28, GHQ12, HADS, RSCL).

**Screen Protocol**

1. Identify and document high-risk factors (e.g., younger, single, living alone, economic adversity, chronic pain, etc. (Levels III-1 to III-3, see Table 3.7D, p.98).
2. Assess levels of distress. Broad, open-ended questions about general psychological and emotional well-being (Table 3.7B, p.92).
   - How have you been feeling emotionally?
   - Could you tell me how your mood is?
   - How would you say the diagnosis and treatment has affected you?

Depending on the initial information, the nature, severity and impact of their concerns can be further explored. High-risk patients should be referred to specialized psychological services to minimize the likelihood of developing significant distress (Level I). Urgent psychiatric consultation should be considered for any patient who appears at risk of suicide (p.91).

**Specifically Anxiety**

- Not surprisingly, many people with cancer experience some level of anxiety. Often it settles over time, but sometimes it can make things very hard for people. Do you feel that anxiety has been an issue for you?

**Specifically Depression**

Clinicians can indicate they are interested in the patient’s adjustment and coping by making statements such as:

- Apart from the physical effects of cancer, we’re aware of the emotional toll it can take on you and your family. We know that coping with cancer isn’t just about physical issues, and we now recognize that the emotional impact is also very important.

This can then be followed with open-ended questions, such as:

- Could you tell me about what the cancer has meant emotionally?
- How would you say you are feeling?
- Would you say that you had ever felt really sad or depressed?
NCCN\textsuperscript{4}
All patients should be screened for distress at their initial visit. The distress thermometer (0-10 visual analog scale) is recommended as a brief screening measure. Possible causes should be ascertained using a problem list that includes practical, family, emotional, spiritual/religious and physical problems.

CCO\textsuperscript{8a}
No specific recommendations are provided for screening within this guideline but it gives HADS and HDRS as examples of tools to assess symptoms.

ONS\textsuperscript{9a,10a}
No specific recommendations are provided about screening, which is beyond the scope of these guidelines.

2. Assessment/Further Investigations/Tools (In-Depth Assessment)

NBCC (Australia)\textsuperscript{5}

\textit{Anxiety (p.89)}
For the person who raises concerns, further questions will clarify the extent of anxiety symptoms and their impact:

- Are there any particular things that make you feel anxious?
- Are there any specific times when you feel more anxious?
- How often do you feel this way?
- Are there any times when the anxiety is almost overwhelming?
- How would you say these feelings affect your life?
- Do these feeling affect your relationship?
- Is there anything you’re avoiding because of this anxiety?

\textit{Depression (p.90)}
Open-ended questions can be followed with clarifying questions about the depth of any mood disturbance. In severe cases, patients often describe their feelings in terms such as “hopeless” or “helpless”. It is also important to inquire about whether these feelings are transient (a bad day) or more frequent and lasting. In assessing depression, clinicians also need to recognize the contribution of disease burden and pain.

If a member of a patient’s health care team is becoming concerned that a patient may be becoming clinically depressed, the clinician can explain that depression is common and that there are many effective treatments. Assessment, preferably conducted by a psychiatrist or clinical psychologist, is recommended (DSM diagnosis).
NCCN

If there is clinical evidence of moderate to severe distress or a patient scores 4 or more on the distress thermometer, the primary oncology team (oncologist, nurse, social worker) must ask a second level of questions. Common symptoms that require further evaluation include excessive worries and fears, excessive sadness, unclear thinking, despair and hopelessness, severe family problems and spiritual crises.

In the second phase of questioning, clinicians should evaluate the following:

- High-risk patients (risk factors for distress such as living alone, co-morbidity, history of depression, and periods of vulnerability)
- Practical problems
- Family problems
- Spiritual/religious concerns
- Physical problems

The second phase should prompt referral to oncology social workers, spiritual care providers or mental health professionals, depending on the problems identified in the problem list. A psychiatric consultation should be implemented for patients at suicidal risk.

The supportive care professional who receives the referral for a patient’s distress management should evaluate the patient using the clinical practice guidelines for that discipline (e.g., mental health, social work or spiritual care).

**Mental Health Services:** A psychological or psychiatric evaluation includes an assessment of the nature of distress, behaviour, psychological symptoms, psychiatric history, use of medications, control of pain and other physical symptoms, body image and sexuality, decision-making capacity and safety. A psychiatrist, psychologist, nurse, clinical nurse specialist or social worker may perform the evaluation (i.e., skilled in mental health assessment and treatment). DSM-IV-TR should be used to identify the disorders (including anxiety disorder and mood disorder).

**Social Work Services:** Support from a social worker should be recommended when a patient has a psychosocial (e.g., coping, communication skills, social isolation) or practical problem (e.g., illness-related concerns or concrete needs, such as housing, financial assistance, help with daily living activities, transportation, etc.).

**Spiritual Care Services:** All patients should be referred to spiritual care counselling when their problems are spiritual or religious or when they request it (e.g., loss of faith, purpose of life, conflict between beliefs and recommended treatments, etc.).

**CCO**

This guideline assumes patients are already diagnosed with anxiety or a mood disorder (a structured diagnostic interview has been completed by a trained clinician or the patient shows depressive symptoms >14 on first 17 items of HDRS or equivalent on other validated assessment scale of depression).
ONS\textsuperscript{9a,10a}

No specific recommendations are provided about assessment, which is beyond the scope of these guidelines. However, expert opinion recommends that patients and family members be assessed for depression and depressive symptoms at every encounter. Patient's and family's understanding of depression and its role in cancer recovery should be assessed, and the meaning of depression to the patient and his or her family should be understood\textsuperscript{9b}.

3. Treatment and Care Options

NBCC (Australia)\textsuperscript{5}

\textit{Emotional and Social Support}

- Appropriate counselling improves the well-being of people with cancer (I).
- The opportunity to discuss feelings with a member of the treatment team or counsellor decreases psychosocial distress (I).
- Participation in psycho-educational programs decreases anxiety and depression and increases knowledge (II).
- Participation in peer support programs is beneficial for patients with poor perceived social support (II).
- Successful strategies for meeting psychosocial support needs may differ for men and women, and when the delivery method is inappropriate or insensitive, men may not participate or not gain a benefit (II).
- Interventions that provide support for partners of patients are effective in reducing distress in both patients and partners (I).
- Supportive psychotherapy, in combination with antidepressants such as selective serotonin reuptake inhibitors (SSRIs), is effective for the management of post-traumatic stress disorder (I).
- Cognitive behavioural, supportive and crisis interventions and relaxation techniques are beneficial for people experiencing body image concerns (II).
- Personal and/or couple therapy is beneficial for people experiencing sexuality concerns (II).

\textit{Anxiety and Depression (Tables 4.1A,B,C; p.103-107)}

It is important that all health professionals involved in the care of patients with cancer are aware of the effective treatment modalities that exist for anxiety and depression. Treatment of anxiety and depression must include attention to relevant physical problems such as pain, which is a major risk factor for depression (III-2).

Psychotherapy, along with pharmacotherapy, is regarded as an integral part of treatment of anxiety and depression, with demonstrated positive effects on depression in cancer patients (II). A range of pharmacological agents is effective in managing anxiety and depressive disorders (see benefits below).
**Depression**

Cognitive behavioural techniques and stress management techniques have been demonstrated to be beneficial in reducing depressive symptoms (III.2).

Effective strategies that can be used by treatment teams to improve depression symptoms include relaxation therapy, guided imagery, psycho-education, problem-solving and other supportive interventions (I).

Other therapies that may improve depression are art therapy, music, painting, reading, poetry, wellness programs, meditation, hypnosis, acupuncture, relaxation, exercise, prayer and laughter (levels I, II, III.3, IV).

**Specialized Interventions**

- There is clear evidence of the efficacy of antidepressant medication in treating depression in patients with cancer (I).
- There is no evidence that any particular antidepressant is superior to another in the management of depression in people with cancer (I).
- Electroconvulsive therapy (ECT) may be considered in severe cases, particularly if suicidal ideation is prominent, with careful consideration of the individual’s particular symptoms and disease stage. ECT has demonstrated efficacy in the treatment of severe depression and is generally well tolerated even in those with concurrent medical conditions (I).
- Patients with advanced cancer may experience some improvement in depressed mood, appetite and well-being when treated with low-dose psycho-stimulants. They are generally well tolerated and the onset of action tends to be rapid, which is a particular benefit for terminally ill patients.

**Anxiety**

Treatments that are effective for anxiety include cognitive behavioural techniques (e.g., relaxation therapy and guided imagery), supportive and crisis interventions (e.g., problem solving), and combinations of education and behavioural or non-behavioural interventions and anti-anxiety medications (I, II, p.107). However, when anxiety or panic impedes or complicates treatment, prompt assessment by a psychiatrist or clinical psychologist is required (I).

**NCCN**

“Mild” distress (score less than 4) can be managed by the primary oncology team. Clear and appropriate communication, meeting information needs, demonstrating empathy and ensuring the patient is aware of relevant support options and resources.

**Anxiety or Depression**

Before initiating any treatment, patients will have been referred to a mental health professional for psychological/psychiatric evaluation (DSM-IV-TR classification). The three main intervention areas are mental health services, social work, spiritual care services.
Mental Health Services

Depression: Research suggests that antidepressants and anti-anxiety drugs are beneficial in the treatment of depression and anxiety in adult cancer patients. In RCTs, alprazolam (benzodiazepine) and fluoxetine (SSRI) have been effective in improving depressive symptoms in cancer patients. The SSRIs are widely used for depression and anxiety symptoms. Psycho-stimulant drugs help in the management of fatigue. (p.MS-8)

- Mood disorder managed with an antidepressant and psychotherapy with or without anxiolytics. Referral to social work services and spiritual care counselling may be considered.
- No medications with mild adjustment disorder (mixed anxiety and depressive symptoms).
- Moderate to severe adjustment disorder treated with medication and psychotherapy.
- If suicidal risk, should have safety measures implemented by removal of sharp objects and psychiatric consultation. Psychiatric treatment and hospitalization may sometimes be necessary.

Anxiety: Psychotherapy with or without an anxiolytic or an antidepressant (category 1) should be considered after eliminating medical causes. If responds to initial treatment, follow-up with primary oncology team. No response, reevaluate and treat with different medications (consider neuroleptics) with continued psychotherapy, support and education. Still no response, evaluate for depression and other psychiatric co-morbidity.

Social Work Services

Recommended when a patient has psychosocial or practical problem(s). Interventions vary according to the severity of the problem. Social work services include counselling, education, psychotherapy, support groups and suggesting local resources.

Spiritual Care Services

All patients should be referred for spiritual care counselling when their problems are spiritual or religious or when they request it.

CCO8a

- Treatment of pain and other reversible physical symptoms should be instituted prior to the initiation of specific antidepressant treatment.
- Antidepressant medications should be considered to treat moderate to severe major depression in cancer patients. Current evidence, however, does not support the relative superiority of one pharmacological modality of treatment over another or the superiority of pharmacological versus psychosocial interventions. The choice of an antidepressant should be informed by the side effect profiles of medication, tolerability of treatment, including the potential for interaction with other current medications, response to prior treatment and patient preference.
- Cancer patients diagnosed with major depression may benefit from a combined modality approach that includes both psychosocial and pharmacological
interventions. Psychosocial treatment approaches that may be of value include those that provide information and support and that address emotional, cognitive and/or behavioural factors.

ONS⁹⁻¹⁰

Practices for Managing Depression

ONS⁹ᵇ recommends psycho-educational and psychosocial interventions during and following cancer treatment. Psycho-educational and psychosocial interventions include cognitive-behavioural therapy, patient education and information, counselling and psychotherapy, behavioural therapy, and social support (provided by patients with cancer, family members or laypeople but not professionals). Of the interventions studied, the most evidence is for cognitive-behavioural therapy.

Cognitive-behavioural therapy is defined as any specific psychological or psychosocial intervention that is relatively brief, goal-oriented, based on learning principles of behaviour change and directed at effecting change in a specific clinical outcome. Patient education and information are defined as sensory, procedural or medical information about cancer or cancer therapy regarding illness or symptom(s), symptom management and/or discussion of treatment options. They may include the use of booklets, videos or other education materials, but do not include active rehearsal of new behaviours. Counselling or psychotherapy is defined as interactive verbal interventions, including nondirective, psychodynamic, existential, supportive, general or crisis interventions.

ONS also recommends pharmacologic interventions with antidepressant medications. Pharmacology with antidepressants is an effective intervention and is recommended for practice. Treatment studies of patients with cancer and depression support use of tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs) and others. ONS also reports that there is no evidence to show that any particular antidepressant is superior to another.

Examples of antidepressant medications used in patients with cancer include:

- Selective serotonin reuptake inhibitors: Fluoxetine (Prozac); Fluvoxamine (Lvox)
- Tricyclic antidepressants: Amitriptyline (Elavil), Imipramine (Tofranil)
- Serotonin-norepinephrine reuptake inhibitors: Venlafaxine (Effexor), Duloxetine (Cymbalta)
- Other antidepressants: Mirtrazapine (Remeron), ᵉᵇ lorazepam

Methylphenidate (Ritalin) is likely to be effective.⁹ᵇ The advantage of this central nervous system stimulant is its reported safety and rapid onset of action. It is issued more often in advanced cancer and palliative situations. Methylphenidate has been used to treat depression and is also used to address opioid-induced somnolence, augment opioid effects and improve cognitive functioning in patients with cancer; in addition, some have found a decrease in pain scores. These benefits may contribute to mood improvement.⁹ᵇ

Relaxation therapy is likely to be effective.⁹ᵇ Techniques that focus on inducing a relaxed physical and mental state include progressive muscle relaxation with or
without guided imagery, hypnosis and autogenic training have been found to have significant impact on reducing cancer treatment-related side effects, including emotional adjustment variables (depression, anxiety and hostility).

**Effectiveness not established for massage therapy and other complementary interventions.** Complementary and alternative therapies used to treat depression in patients with cancer are gaining popularity and prevalence. Unfortunately, few randomized, controlled studies of complementary interventions have been conducted in people with cancer and depression. Included in this category are massage therapy, hypnotherapy and others (e.g., yoga, acupuncture, aromatherapy, meditation). Although some studies show promising results and benefits in reducing mood disturbance, stress, pain and other symptoms, effectiveness in decreasing depressive symptoms in patients with cancer has not been established.

**ONS Anxiety Interventions**

**Psycho-educational interventions:** Various psycho-educational interventions have been studied to prevent or treat anxiety in patients with cancer. Psycho-educational interventions can be categorized into three main groups: information regarding a cancer diagnosis and treatment; information about the treatment facility, staff and contacts; and information focusing on self-care and symptom management. These interventions employ a wide range of mediums, including pamphlets and brochures, formal educational sessions, interactive computer-generated information, and video or audio tapes. Anxiety also may be decreased by other types of educational information, including information on relaxation techniques, nutrition and exercise to manage side effects.

**Psychosocial interventions:** Types of psychosocial interventions include cognitive behavioural therapy (CBT), behavioural therapies, individual counselling and support groups. Examples of cognitive therapies include distraction, thought monitoring, cognitive restructuring and coping self-statements. Examples of behavioural therapies include systematic desensitization, biofeedback and various relaxation training techniques.

CBT may be offered in counselling sessions by trained therapists in individual or group settings or delivered individually using a videoconference format. Individualized, interpersonal counselling via telephone has also been shown to decrease anxiety. Oncology nurses may facilitate referrals for CBT, but this specialized therapy requires advanced educational training.

Evidence at the highest level supports CBT as an intervention for patients with cancer who are experiencing symptoms of anxiety and is recommended for practice. Additional high-level evidence substantiates the use of support groups as another form of psychosocial interventions.

**Massage therapy:** Is likely to be effective.

**Pharmacotherapy:** Is likely to be effective. Medications used to treat anxiety in patients with cancer include: Alprazolam, Antidepressants, Antihistamines, Atypical neuroleptics, Azapirones, Benzodiazepines, Buspirone, Diazepam, Excitalopram, Hydroxyzine, Lorazepam, Midazolam, Mitrazapine, Olanzapine and other (Paroxetine, Propofol, Risperidone, Sertraline, Venlafaxine).
Harms and Benefits

Benefits

NBCC (Australia)$^5$

Benefits of Psychological Therapies (p.101)

There is clear evidence that psychosocial interventions are effective in reducing distress and promoting adjustment in patients with cancer, much of the data being Level I or II evidence. In some cases such interventions may also reduce the severity of physical symptoms suffered by the cancer patient (I).

In a meta-analysis of 45 randomized controlled trials in adults with cancer, those receiving psychological therapies showed statistically significant mean improvements of 12% in emotional adjustment, 10% in social functioning, 14% in treatment- and disease-related symptoms, and 14% in overall improvement in quality of life, compared to those not receiving psychological therapy (I).

In most trials, the therapy was provided by a specially trained counsellor, nurse, social worker or psychologist. However, greater effects have been demonstrated when psychological therapies were conducted by more highly trained therapists and continued for longer periods of time (I).

Although many interventions have been directed toward patients themselves, a recent review highlights that interventions that provide support for partners of patients with cancer are likely to be effective in reducing distress. Furthermore, there may be indirect benefits for patients whose partners have participated in such a program. In a study evaluating a six-week weekly psycho-educational group program for partners of 36 patients with cancer, three-month follow-up evaluation showed reduced mood disturbance in patients (who did not attend the program themselves) as well as partners (II).

Most of the studies of psychosocial interventions have evaluated face-to-face individual or group support. Information about novel service delivery methods is now emerging. A small study evaluated a telephone counselling service in 14 women receiving high-dose chemotherapy and 10 male partners. On average the women received 16 sessions, the male partners 11 sessions. Although participants appeared satisfied, rating the service as good to excellent, as yet there is no data about other outcomes such as mood and anxiety (III-3).

Trials comparing the relative effectiveness of different types of psychological interventions have indicated that most therapies have a similar effect (I). It is evident, for example, that professionally led group therapies are as effective as individual-based therapy (I). It may be that the features of therapy common to all psychological interventions, such as empathetic manner, listening, affirmation, reassurance and support, generate the observed outcome.
Benefits of Pharmacological Agents

A range of pharmacological agents have been shown to have an effective role in the management of anxiety or depressive disorders (Level I) (p.108, 109).

For anxiety:
- Benzodiazepines
- SSRIs (longer term management of panic Level IV)
- Neuroleptics (if extreme agitation)

For depression:
- Tricyclic antidepressants
- SSRIs (Level I): Fluoxetine (Level II), selective noradrenergic reuptake inhibitors (SNRIs)
  - SSRIs: Fluoxetine demonstrated as effective in patients with cancer (Level II), including depression in women with advanced cancer (Level II). SSRIs associated with fewer anticholinergic or cardiovascular side effects and less sedating than tricyclics.
  - SNRIs associated with fewer anticholinergic, histaminic, adrenergic effects than tricyclics and no MAO inhibition.

There is no evidence that any particular antidepressant is superior to another (Level I, p.109). Selection of the particular medication involves a careful risk-benefit analysis matching the properties of the drug against the patient’s physical status, the potential for drug interactions and key symptoms that are of concern to the patient. In many instances, a psychiatrist will initiate treatment with these medications (p.108).

NCCN

None reported.

CCO

One systematic review, 10 randomized trials and one comparative cohort study were included in this systematic review of the evidence. Six of the trials compared pharmacologic treatments, four trials compared various non-pharmacological therapies and one trial compared pharmacologic therapy to relaxation. The treatment period and follow-up were short in the trials of pharmacological treatments (10 days to 12 weeks), which limits the conclusions that can be reached regarding long-term treatment.

The systematic review of 24 studies in cancer patients—six focused on antidepressant agents and 18 on psychosocial interventions—found limited evidence in favour of both treatments. However, few studies in the review focused on patients diagnosed with a depressive disorder; most were preventive studies or included patients with mild depressive symptoms.

Two drug trials, which compared mianserin to placebo, detected a significant benefit with treatment. In another trial, alprazolam was found to be superior to progressive muscle relaxation in reducing depressive symptoms.
Four of the drug trials found no significant difference between groups on a measure of depression. Two of those trials compared low-dose fluoxetine to placebo, one compared fluoxetine to desipramine, and one compared paroxetine to amitriptyline. In these latter two studies, there were significant pre-post treatment effects for both active comparators, but the significance of these findings in the absence of placebo comparators is limited. Only one of the pharmacologic trials assessed outcome based on remission of depressive symptoms to within the normal range as opposed to response, which is a less stringent outcome.

Two of the four trials that assessed non-pharmacological therapies for the management of depression found a significant difference between treatment groups. One trial found a benefit in using a multi-component nurse delivered intervention with a reduction in the number of patients diagnosed with major depression, and the other positive trial found the use of an orientation program to be beneficial in reduction of depressive symptoms. In both trials, the control group received usual care. Neither group psychotherapy nor adjuvant psychological therapy (cognitive behavioural therapy) was found to significantly reduce depressive symptoms in the other two non-pharmacological trials.

Four of the 11 trials included only patients diagnosed with major depression through structured diagnostic interview. The remaining seven trials included patients with depressive symptoms above a predefined cut-off score using a validated assessment tool. Significant benefit on depression measures were found in two of the former studies and in three of the latter studies.

**ONS (2008)**

Benefits were the interventions categorized by ONS as “Recommended for Practice” and “Likely to Be Effective” (ONS Depression 2008, ONS Anxiety 2008).

**Harms**

**NBCC (Australia)**

The NBCC guideline document does not detail the adverse effects from individual studies (reported in supporting documents). Potential harms with various medications, however, are summarized.

**Anxiety**

Shorter-acting benzodiazepines (e.g., alprazolam) are safest, but breakthrough anxiety can occur, requiring substitution with long-acting medications (e.g., diazepam). With hepatic disease, selection of an agent for which blood levels are minimally affected by the liver metabolism is recommended (e.g., oxazepam). Long-term use of benzodiazepines is associated with dependence. Benzodiazepines should never be ceased abruptly because of risk of withdrawal symptoms that may include seizures (p.108).

Neuroleptics: Low doses of antipsychotics (e.g., haloperidol) may be used in cases of extreme agitation; patients require close monitoring for risk of extrapyramidal adverse effects.
Depression

“The concern that antidepressant therapy poses an unacceptable side-effect burden is not supported by research. In one study, about 80% of patients showed a good clinical response, the majority had no significant adverse effects (Level IV). Starting with a low dose of the drug and increasing the dose slowly is likely to minimize the occurrence of side effects” (p.109).

**Tricyclic antidepressants:** Anti-cholinergic side effects may aggravate stomatitis secondary to chemotherapy and may exacerbate constipation. Tricyclics have potential to affect cardiac rhythm and patients with pre-existing interventricular conduction delays are at increased risk. Patients with cancer may respond to tricyclics at a lower dose than physically healthy people.

**SSRIs:** Although effective (see benefits), the half-life of fluoxetine is long with active metabolites and, in those with hepatic or renal dysfunction, short-acting drugs such as sertraline and paroxetine are preferable (p.109). SSRIs may be associated with some exacerbation of anxiety or insomnia. Nausea may be a limiting side effect in patients with cancer. Potential for drug interactions (e.g., warfarin) may limit the use of SSRIs.

**SNRIs:** In patients with hepatic disease, venlafaxine may be less likely to disturb protein-binding to other medications than the SSRIs.

**Psychostimulants:** Side effects include nervousness, over-stimulation, mild increases in blood pressure and pulse rate and tremor. Long-term use is associated with tolerance and dependence (p.109).

NCCN

None reported.

CCO

Pharmacological Trials

Adverse effects were reported in all of the pharmacological trials. In three of the four trials in which an antidepressant was compared to placebo, adverse effects were more frequent in the antidepressant arm, while they were more common in the placebo arm in the fourth trial. The most frequent adverse effect of mianserin in one trial was drowsiness, which was reported in six patients in the first week. Although there was a significant difference between groups in the overall number of withdrawals from two of the trials, there was no significant difference in withdrawals due to adverse effects (p=0.704). Initial effects related to mianserin (that disappeared later in the study) included sedation, tiredness, drowsiness and slowed thinking.

The two studies that compared fluoxetine to placebo reported similar adverse effects. Digestive and neuropsychiatric toxicities were more common in the fluoxetine group (24% and 49%, respectively) compared to placebo (13% and 35%, respectively), but these differences were not statistically significant (p=0.16 and p=0.17, respectively). One study reported a significantly higher frequency of emesis in fluoxetine-treated patients compared to placebo. No other toxicities were reported.

There was no significant difference in withdrawals due to adverse events in the trial comparing fluoxetine against desipramine. Six patients withdrew in the fluoxetine
group because of adverse effects, which included somnolence, tachycardia, abnormal thinking, symptoms of depersonalization and pain. Four desipramine-treated patients withdrew because of symptoms such as dyspepsia, abnormal thinking, pain and somnolence. The only significant difference was in the incidence of dry mouth, which was more frequent in fluoxetine-treated patients (p=0.008).

In the trial comparing alprazolam with progressive muscle relaxation, five of the 70 patients in the alprazolam arm required a dose reduction to 0.25mg due to drowsiness and sedation. Additional drug-related adverse effects included light-headedness (eight patients), sleepiness/grogginess (two patients), nightmares (one patient), facial edema (one patient), and nausea and vomiting (one patient), although none of these patients required a dose reduction.

There was a high incidence of adverse effects in the paroxetine vs. amitriptyline trial, but no statistically significant difference between drug treatment groups was reported. Nine of the 88 patients in the paroxetine group were withdrawn from the trial because of adverse effects. For six of these nine patients, the adverse effects included abdominal pain, tremor, dry mouth, insomnia, agitation, confusion, dizziness, headache and abnormal thinking. Between 10 and 12 patients in the amitriptyline group were also withdrawn due to adverse effects, and in six of these patients effects included abdominal pain, tremor, dry mouth, insomnia, anxiety, asthenia, depersonalization, nervousness, somnolence and vertigo. The most frequent adverse effects overall were nausea (13.6%) and leukopenia (10.2%) in the paroxetine group, and dry mouth (14.6%) and constipation (11.2%) in the amitriptyline group.

Non-pharmacological Trials

Adverse effects were not evaluated in the four trials assessing non-pharmacologic interventions.

ONS\textsuperscript{9a,10a}

There were no interventions listed “Not Recommended for Practice”. Adverse effects from the ONS sources of evidence (e.g., NCCN\textsuperscript{4} or NBCC\textsuperscript{5}) were not reported in detail but several were highlighted. For example:

- “The long half-life of fluoxetine makes it less desirable in patients with hepatic or renal dysfunction. In such cases, another antidepressant is preferable - NBCC (2003) guideline.”\textsuperscript{9b (p.134)}

- “Although few adverse effects were reported overall, reports were made of patients that were unable to enter a deep trance or who were frightened by the treatment.”\textsuperscript{9b (p.135)}

- “St. John’s Wort, an herb known to treat mild to moderate depression, should be avoided during chemotherapy or radiation or when surgery is planned because it can adversely impact the efficacy of some chemotherapeutic agents and prescription medications.”\textsuperscript{9b (p.135)}

- “Certain medications such as midazolam, a potent benzodiazepine, and propofol, an anesthetic agent, should only be used when patients are monitored closely, such as in an intensive care unit or during medical procedures.”\textsuperscript{10b (p.793)}
Appendix C: Generalized Anxiety Disorder (GAD-7) Screening Questions

During the past 2 weeks, how often have you been bothered by the following problems?

<table>
<thead>
<tr>
<th></th>
<th>not at all</th>
<th>several days</th>
<th>more than half the days</th>
<th>nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Feeling nervous, anxious or on edge</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2. Not being able to stop or control worrying</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3. Worrying too much about different things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4. Trouble relaxing</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>5. Being so restless that it is hard to sit still</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6. Becoming easily annoyed or irritable</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>7. Feeling afraid as if something awful might happen</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

Total score: ________ = Add columns: ________ + ________ + ________ + ________

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home or get along with other people?

<table>
<thead>
<tr>
<th>Not difficult at all</th>
<th>Somewhat difficult</th>
<th>Very difficult</th>
<th>Extremely difficult</th>
</tr>
</thead>
<tbody>
<tr>
<td>[]</td>
<td>[]</td>
<td>[]</td>
<td>[]</td>
</tr>
</tbody>
</table>

Scoring and Interpretation of Scores

GAD-7 Anxiety Severity: This is calculated by assigning scores of 0, 1, 2 and 3 to the response categories of “not at all,” “several days,” “more than half the days,” and “nearly every day,” respectively. GAD-7 total score for the seven items ranges from 0 to 21.

Scores of 5, 10 and 15 represent cut-off points for mild, moderate and severe anxiety, respectively. Though designed primarily as a screening and severity measure for generalized anxiety disorder, the GAD-7 also has moderately good operating characteristics for three other common anxiety disorders: panic disorder, social anxiety disorder and post-traumatic stress disorder. When screening for individual or any anxiety disorder, a recommended cut point for further evaluation is a score of 10 or greater.

Using the threshold score of 10, the GAD-7 has a sensitivity of 89% and a specificity of 82% for generalized anxiety disorder. It is moderately good at screening three other common anxiety disorders - panic disorder (sensitivity 74%, specificity 81%), social anxiety disorder (sensitivity 72%, specificity 80%) and post-traumatic stress disorder (sensitivity 66%, specificity 81%).
## Interpreting GAD-7 scores

<table>
<thead>
<tr>
<th>Score Range</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>5–9</td>
<td>mild anxiety</td>
</tr>
<tr>
<td>10–14</td>
<td>moderate anxiety*</td>
</tr>
<tr>
<td>15–21</td>
<td>severe anxiety</td>
</tr>
</tbody>
</table>

*When screening, a recommended cut-point for further assessment is a score of 10 or greater.*

### Appendix D: Information Guide to Antidepressants
(MacArthur Initiative on Depression and Primary Care)

<table>
<thead>
<tr>
<th>Anti-depressant*</th>
<th>Therapeutic Dose Range (mg/day)</th>
<th>Initial Suggested Dose**</th>
<th>Titration Schedule</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Selective Serotonin Reuptake Inhibitors (SSRIs)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Citalopram (Celexa)</td>
<td>20-40</td>
<td>20mg in the morning with food (10mg in elderly or those with panic disorder)</td>
<td>Maintain initial dose for 4 weeks before dose increase. If no response, increase in 10mg increments every 7 days as tolerated.</td>
<td>Helpful for anxiety disorders. Few drug interactions. Generic available.</td>
<td></td>
</tr>
<tr>
<td>Escitalopram (Lexapro)</td>
<td>10-30mg</td>
<td>10mg</td>
<td>Increase to 20mg if partial response after 4 weeks.</td>
<td>More potent s-enantiomer of citalopram, 10mg dose effective for most. FDA labeling for general anxiety disorder. Reduces all three symptom groups of PTSD.</td>
<td>More expensive than citalopram.</td>
</tr>
<tr>
<td>Fluoxetine (Prozac)</td>
<td>10-80</td>
<td>20mg in the morning with food (10mg in elderly and those with co-morbid panic disorder)</td>
<td>Maintain 20mg for 4-6 weeks and 30mg for 2-4 weeks before additional dose increases. Increase in 10mg increments at 7-day intervals. If significant side effects occur within 7 days, lower dose or change medication.</td>
<td>Helpful for anxiety disorders. Long half-life good for poor adherence, missed doses; less frequent discontinuation symptoms. Reduces all three symptom groups of PTSD. Generic available.</td>
<td>Slower to reach steady state and eliminate when discontinued. Sometimes too stimulating. Active metabolite has half-life ~10 days and renal elimination. Inhibitor of cytochrome P450 2D6 and 3A4. Use cautiously in the elderly and others taking multiple medications.</td>
</tr>
<tr>
<td>Fluoxetine Weekly (Prozac Weekly)</td>
<td>90</td>
<td>Initiate only after patient stable on 20mg daily.</td>
<td>Start 7-days after last dose of 20mg.</td>
<td></td>
<td>No generic available.</td>
</tr>
<tr>
<td>Medication &amp; Dose</td>
<td>Dosing</td>
<td>Side Effects</td>
<td>Interactions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------------------</td>
<td>--------</td>
<td>-------------</td>
<td>-------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paroxetine (Paxil) 10-50 (40 in elderly)</td>
<td>20mg once daily, usually in the morning with food (10mg in elderly and those with co-morbid panic disorder)</td>
<td>Maintain 20mg for 4 weeks before dose increase. Increase in 10mg increments at intervals of approximately 7 days up to maximum dose of 50mg/day (40 elderly).</td>
<td>FDA labeling for most anxiety disorders. Reduces all three symptom groups of PTSD. Generic available.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paroxetine (Paxil CR) 25-62.5 (50 in elderly)</td>
<td>25mg daily (12.5mg in elderly and those with panic disorder)</td>
<td>Increase by 12.5mg at weekly intervals; maintain 25mg for 4 weeks before dose increase.</td>
<td>May cause less nausea and GI distress.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sertraline (Zoloft) 25-200</td>
<td>50mg once daily, usually in the morning with food (25mg for elderly)</td>
<td>Maintain 50mg for 4 weeks. Increase in 25-50mg increments at 7-day intervals as tolerated. Maintain 100 mg for 4 weeks before further dose increase.</td>
<td>FDA labeling for anxiety disorders including PTSD. Safety shown post myocardial infarction. Generic available.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serotonin and Norepinephrine Antagonist (SNRAs)</td>
<td>Mirtazapine (Remeron) 15-45</td>
<td>15mg at bedtime</td>
<td>Increase in 15mg increments (7.5mg in elderly) as tolerated. Maintain 30mg for 4 weeks before further dose increase.</td>
<td>Few drug interactions. Less or no sexual dysfunction. Less sedation as dose increases. May stimulate appetite.</td>
<td></td>
</tr>
<tr>
<td>Norepinephrine and Dopamine Inhibitor</td>
<td>Bupropion † (Wellbutrin) 200-450</td>
<td>100mg twice a day (once a day in elderly)</td>
<td>Increase to 100mg three times a day after 7 days (slower titration for elderly). After 4 weeks, increase to maximum 150mg three times a day if necessary. Hepatic impairment: 75mg/day.</td>
<td>Can be stimulating. Less or no sexual dysfunction. Generic available.</td>
<td></td>
</tr>
<tr>
<td>Bupropion SR † (Wellbutrin SR) 200-400mg</td>
<td>150mg once a day (100mg in elderly)</td>
<td>Increase to 150mg twice a day after 7 days (100bid elderly). Increase to 200mg twice a day after 4 weeks (150bid elderly) if insufficient response. Hepatic impairment: 100mg daily.</td>
<td>Wellbutrin also approved for the treatment of smoking cessation as Zyban. Generic available.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*† Indicates sustained release products.*
### Practice Guideline: Depression, Anxiety

<table>
<thead>
<tr>
<th><strong>Bupropion XL † (Wellbutrin XL)</strong></th>
<th>300-450mg</th>
<th>150mg once daily (in the morning)</th>
<th>Increase to 300mg daily after 7 days. Increase to 450mg per day after 4 weeks if necessary. Hepatic impairment: 150mg.</th>
<th>Generic XL not available.</th>
</tr>
</thead>
</table>

#### Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs)

| **Venlafaxine (Effexor, Effexor XR)** | 75-375 | 75mg with food; 37.5mg if anxious, elderly or debilitated. | Immediate release (IR) dose should be divided two or three times a day. For extended release (XR) give 37.5mg in the morning, then increase to 75mg in the morning after 1 week, 150mg in the morning after 2 weeks. If partial response after 4 weeks, increase to 225mg in the morning. Norepinephrine effect only occurs above 150mg. | Helpful for anxiety disorders, neuropathic pain and vasomotor symptoms. XR version should be taken once a day. May reduce all three symptom groups of PTSD. Generic available (IR and XR). |
| **Desvenlafaxine (Pristiq)** | 50-400 | 50mg once daily | No evidence that higher doses associated with greater effect. | Active metabolite of venlafaxine. Dose adjustment if CrCl <30ml/min. Gradually increase dosing interval when discontinuing when taken for ≥6 weeks (taper dose if dose >50mg/day). Sexual dysfunction. Generic not available. |
| **Duloxetine** | 40-60 | 40 or 60mg as a single or divided dose (20 or 40mg elderly) | Dose can be increased after 1 week. Maximum dose 120mg/d although doses >80mg/d have not been shown to be more effective. | Also approved for general anxiety disorder and pain associated with diabetic neuropathy and fibromyalgia. Dose adjustment if CrCl <30ml/min. Urinary hesitancy. Sexual dysfunction. Generic not available. |
## Practice Guideline: Depression, Anxiety

### Tricyclic Antidepressants: Secondary Amines

<table>
<thead>
<tr>
<th>Tricyclic Antidepressant</th>
<th>Starting Dose</th>
<th>Description</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desipramine ‡ (Norpramin)</td>
<td>100-300 (25-100 in elderly)</td>
<td>Increase by 25 to 50mg every 3 to 7 days to initial target dose of 150mg (75 or 100mg elderly) for 4 weeks. Target serum concentration: &gt;115ng/mL</td>
<td>More effect on Norepinephrine than Serotonin. Effective for diabetic neuropathy and neuropathic pain. Compliance and effective dose can be verified by serum concentration. Generic available. Can be stimulating, but sedating to some patients. Anticholinergic, cardiac and hypotensive (less than tertiary amines); caution in patients with BPH or cardiac conduction disorder or CHF.</td>
</tr>
<tr>
<td>Nortriptyline ‡ (Pamelor)</td>
<td>25-100</td>
<td>Increase to 10-25mg increments every 5-7 days as tolerated to 75mg/day. Obtain serum concentration after 4 weeks; target range: 50-150ng/mL</td>
<td>Less orthostatic hypotension than other tricyclics. Compliance and effective dose can be verified by serum concentration. Generic available. Anticholinergic, cardiac and hypotensive (less than tertiary amines); caution in patients with BPH or cardiac conduction disorder or CHF.</td>
</tr>
</tbody>
</table>

**Other Tricyclics include:** amitriptyline (Elavil), clomipramine (Anafranil), desipramine (Norpramin), doxepin (Sinequan), imipramine (Tofranil). Common antimuscarinic or anticholinergic effects include dry mouth, blurred vision, constipation and urinary retention. Although patients may eventually develop tolerance to these effects with repeated medication use, symptoms may not completely resolve until the drug is discontinued.

* There are more antidepressants than those listed in this table; however, this list provides a reasonable variety of drugs that have different side effects and act by different neurotransmitter mechanisms. The January 29, 2009, issue of *The Lancet* includes a meta-analysis and an editorial concluding that sertraline (Zoloft) offers the best balance among efficacy, acceptability and costs compared to 11 other agents (Parikh, 2009; Cipriani et al., 2009).

Treatment of Parkinson’s disease may include selegiline (Eldepryl), which is a selective monoamine oxidase inhibitor (MAOI) at low doses only. Because the use of many antidepressants is contraindicated in conjunction with a nonselective MAOI, caution with or discontinuation of Eldepryl may be in order. Selegiline is also available as a higher dose and nonselective transdermal patch (Emsam) approved for the treatment of major depressive disorder.

** For SSRIs, venlafaxine and the tricyclic antidepressants, start at the beginning of the therapeutic dosing range. If side effects are bothersome, reduce the dose and increase more slowly. In the elderly, the debilitated or those sensitive to medications, start lower. For all antidepressants, allow four weeks at a therapeutic dose, then assess for response. If only partial or slight response but well tolerated, then increase the dose. If no response, worse symptoms or intolerable side effects, switch antidepressants.
For treatment of depression in pregnancy, TCAs and SSRIs (particularly fluoxetine) are generally the agents of choice. However, the SSRIs have been associated with persistent newborn pulmonary hypertension with maternal use after 20 weeks of gestation, a slight decrease in gestational age, lower birth weight, and neonatal withdrawal or adaptation syndrome. Paroxetine has been associated with first-trimester cardiovascular malformations (ventricular and atrial septal defects); hence the use of paroxetine should be avoided during the first trimester. TCAs have been associated with neonatal withdrawal symptoms and anticholinergic adverse effects. There are insufficient data about other newer antidepressants, although there may be a link between bupropion and spontaneous abortion.

Parikh SV. Antidepressants are not all created equal. The Lancet, Early Online Publication, January 29, 2009. DOI:10.1016/S0140-6736(09)60047-7


For women planning to breast feed, an antidepressant with the lowest excretion into breast milk (i.e., lowest infant serum concentrations and fewer adverse reactions) should be considered. These include sertraline, paroxetine and nortriptyline. Citalopram and fluoxetine have the highest concentrations in breast milk and more reports of infant adverse effects. A 40% decrease in breast milk concentration can be achieved by switching to escitalopram at 25% of the citalopram dose. Venlafaxine is detectable in the serum and associated with less weight gain in breast-fed infants. Less information is available about bupropion, mirtazepine and trazodone, although the concentrations in breast milk infant serum are low. The TCAs are nearly undetectable in infant plasma concentrations and low concentrations are found in breast milk but have less advantageous side effect profiles.

† Avoid bupropion in patients with a history of seizures, eating disorders, significant central nervous system lesions or recent head trauma.

‡ Tricyclic antidepressants (TCAs) have lower costs but somewhat higher discontinuation rates compared to SSRIs and second-generation antidepressants due to side effects. The TCAs are more lethal in overdose than SSRIs. TCAs may be contraindicated in patients with certain physical co-morbidities, such as recent myocardial infarction, cardiac conduction defects, urinary retention, narrow angle glaucoma, orthostatic hypotension and cognitive impairment.

Appendix E: Summary of External Review

Methods

A diverse panel of 26 external reviewers from across Canada was invited to provide survey feedback. The panel members were purposely selected to participate on the basis of clinical, content and/or methodological expertise. Effort was made to ensure that the external review panel reflected perspectives from a range of clinical settings and geographical locations. Ten provinces were represented and the areas of expertise are listed in the results below. Three people (rural-based nurse, haematologist/paediatric expert, psychologist) from the original survey sample (29) declined the request to participate as they were either retired, on maternity leave or declined for personal reasons. The survey consisted of a total of 35 items and evaluated the methods used to assemble the evidence, agreement with the recommendations and the potential application of the guidelines. Depression and anxiety were both reviewed within the same survey but had separate questions. Written comments were invited. The survey was sent by email on April 6, 2010. Follow-up reminders were emailed on May 3 and follow-up telephone calls were made from May 3 to May 21.

The members of the Ontario Cancer Symptom Management Collaborative (OCSMC) were also asked to review the guideline report, which was sent to them by email. Feedback was also provided by a member of the National Advisory Working Group who had been on sabbatical until May 2010.

Results

Responses were received from 17 of the 26 qualified individuals (65% response rate). In terms of their roles in the psychosocial care of patients with cancer, the 17 respondents reported a total of 22 roles, including five administrators, one guideline methods expert, two family physicians, one oncologist, three psychiatrists, three psychologists, two social workers, one vocational rehabilitation counsellor, one guideline writer and one professional spiritual care provider. Four respondents indicated multiple (2 or 3) roles. One respondent described their role as administrator and social worker; one as oncologist, administrator and guidelines methods; one as administrator, social worker and researcher; and one as an administrator and psychologist.

Eight respondents indicated that they currently follow a practice guideline on depression, and seven of those eight respondents also currently follow a practice guideline on anxiety. Respondents reported the following regarding guidelines they follow:

- Canadian Psychological Association (CPA),
- Pscan (Psychological screening for cancer),
- Cancer Care Ontario (CCO) Management of Depression in Cancer guideline,
- Canadian Network for Mood and Anxiety Treatment (CANMAT) guidelines,
- National Comprehensive Cancer Network (NCCN), DSM,
- A general guideline provided by our psychiatrist;
- www.cancer.gov;
- Combination (e.g., Both the CCO guideline and CANMAT guidelines).
Guidelines currently followed on anxiety were the same as for depression (i.e., BCCA policy, CPA, NCCN, CCO, CANMAT, a general guideline provided by our psychiatrist), with one addition: Canadian Psychiatric Association Journal, special edition on Anxiety Disorders.

Responses from the original survey sample (n=17) to specific questionnaire items about the Pan-Canadian practice guideline on screening, assessment and care of psychosocial distress (Depression, Anxiety) in adults with cancer are summarized in the table on the following page.

**Reviewers Comments: Depression and Anxiety**

Eleven respondents (65%) said “yes” to barriers or challenges in using the depression guideline and 12 said “Yes” to barriers for anxiety. Barriers and challenges to use of the depression guideline included staff availability (for screening, assessment and care options), resources in general, training staff to conduct screening, staff buy-in, “incorporating a routine screen for depression into the daily practice of the clinic” and time issue in a busy clinic. Barriers and challenges for the anxiety guideline were the same as depression, plus “in rural areas treatment options may be limited.”

Overall, the respondents believed that the depression and anxiety practice guidelines were similar or exceeded the recommendations in their current clinical practice. Differences reported between current practice and the guideline document included screening and assessment tools used and health care provider roles (e.g., who confirms a diagnosis of depression; “I use different screening tools, but otherwise, conceptually the recommendations are consistent with my practice—except the involvement of the medical team in structured assessment at present”).

Although the respondents did not disagree specifically with the depression or anxiety recommendations, one respondent believed that describing tricyclic antidepressants as a “promising” option for the treatment of depression was not consistent with the suggestion that no pharmacological agent was superior to any other. Another respondent indicated that the care map text regarding the care of individuals at risk of harm to self and/or others should be repeated in the recommendation text (bullet points).

**Written feedback**

Seventeen respondents from the original survey sample (65%) provided written comments. Feedback suggesting substantive changes to the draft guideline report was synthesized and distributed to the guideline development panel members. Substantive changes include changing the title to psychosocial (larger and more holistic frame) rather than psychological distress, adding further details about scopes of practice, clarifying assessment processes, changing the order of the recommendations to ensure the more urgent concerns appear first, editing the text in the recommendations to be more consistent with the algorithms and placing urgent referral details before the ESAS scores in the algorithms. The feedback was discussed and an action plan was developed for addressing the concerns and suggestions arising from the review, as appropriate. Revisions based on this discussion were integrated into the final iteration of the practice guidelines.
## Practice Guideline: Depression, Anxiety

### Responses to Feedback Survey:
**External Review Depression and Anxiety, Number (% of 17)**

<table>
<thead>
<tr>
<th>Selected Items</th>
<th>Agree*</th>
<th>Undecided</th>
<th>Disagree*</th>
</tr>
</thead>
<tbody>
<tr>
<td>The overall objective of the DEPRESSION guideline is specifically described.</td>
<td>17 (100%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>The overall objective of the ANXIETY guideline is specifically described.</td>
<td>17 (100%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>The target population for the DEPRESSION guideline is clearly described.</td>
<td>17 (100%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>The target population for the ANXIETY guideline is clearly described.</td>
<td>17 (100%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>The target users of the DEPRESSION guideline are clearly defined.</td>
<td>17 (100%)</td>
<td></td>
<td></td>
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<tr>
<td>The target users of the ANXIETY guideline are clearly defined.</td>
<td>17 (100%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systematic search methods for identifying relevant guidelines for adaptation were used for the DEPRESSION guideline.</td>
<td>17 (100%)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>The methods for formulating the DEPRESSION recommendations are clearly described.</td>
<td>17 (100%)</td>
<td></td>
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</tr>
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<td></td>
<td></td>
</tr>
<tr>
<td>The recommendations for DEPRESSION are easily identifiable.</td>
<td>16 (94%)</td>
<td>1 (6%)</td>
<td></td>
</tr>
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<td></td>
</tr>
<tr>
<td>The recommendations for DEPRESSION are appropriate.</td>
<td>15 (88%)</td>
<td>1 (6%)</td>
<td>1 (6%)</td>
</tr>
<tr>
<td>The recommendations for ANXIETY are appropriate.</td>
<td>17 (100%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>The recommendations for DEPRESSION are feasible.</td>
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<td></td>
<td></td>
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<tr>
<td>The recommendations for ANXIETY are feasible.</td>
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<td></td>
<td></td>
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<tr>
<td>When applied, the DEPRESSION guideline will produce more benefits for patients than harm.</td>
<td>17 (100%)</td>
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<tr>
<td>The DEPRESSION guideline is supported with tools for application.</td>
<td>16 (94%)</td>
<td>1 (6%)</td>
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</tr>
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<td>The ANXIETY guideline is supported with tools for application.</td>
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<tr>
<td>How likely would you be able to apply the recommendations in the DEPRESSION guideline to clinical practice?</td>
<td>15 (88%)</td>
<td>1 (6%)</td>
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</tr>
<tr>
<td>How likely would you be able to apply the recommendations in the ANXIETY guideline to clinical practice?</td>
<td>15 (88%)</td>
<td>1 (6%)</td>
<td>1 (6%)</td>
</tr>
</tbody>
</table>

*“Agree” includes responses Strongly agree, Somewhat agree, Agree; “Disagree” includes responses Somewhat disagree, Disagree, Strongly disagree; “Likely” includes responses Very likely, Likely, Somewhat likely.*