HELPING PATIENTS COPE WITH EMOTIONAL RESPONSES TO CANCER:

Non-Pharmacological Approaches for Managing Anxiety and Depression

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Definitions

**Distress** has been defined as “an unpleasant experience of an emotional, psychological, social, or spiritual nature that interferes with the ability to cope with cancer treatment. It extends along a continuum, from common normal feelings of vulnerability, sadness, and fears, to problems that are disabling, such as true **depression**, **anxiety**, panic, and feeling isolated or in a spiritual crisis.”

Biopsychosocial Model of Etiology

Cancer-Related Stressors
- Diagnosis
- Treatment
- Diagnostic investigations
- Communication of test results
- Completion of active treatment
- Physical symptoms and disability
- Disease progression and recurrence

Individual Factors
- Coping strategies
- Social support
- Attachment style
- Life stage
- Previous trauma
- Psychiatric history
- Biologic response
- Genetic vulnerability

Distress Response
- Major Disorders
- Subthreshold and Adjustment Disorders
- Normative Distress

Screening for Distress

• Screening is a brief process that provides a “snapshot” of a patient’s problems or concerns
• Uses short or ultra-short psychometrically valid measures
• Used to quickly flag a problem or concern to identify patients who are at risk for a poor health outcome

Edmonton Symptom Assessment System

https://www.cancercare.on.ca/toolbox/symptools/
PRCC Depression Scores

ESAS Depression Score Distribution
PRCC October 2010

- No Symptom (Score = 0) 54%
- Low Severity (Score = 1-3) 27%
- Moderate Severity (Score = 4-6) 13%
- Severe Severity (Score = 7-10) 6%
PRCC Anxiety Scores

ESAS Anxiety Score Distribution
PRCC October 2010

- No Symptom (Score = 0): 41%
- Low Severity (Score = 1-3): 35%
- Moderate Severity (Score = 4-6): 16%
- Severe Severity (Score = 7-10): 8%

(Chart showing the distribution of anxiety scores)
PRCC Wellbeing Scores

ESAS Wellbeing Score Distribution
PRCC October 2010

- Low Severity (Score = 1-3): 34%
- Moderate Severity (Score = 4-6): 25%
- Severe Severity (Score = 7-10): 11%
- No Symptom (Score = 0): 30%
Beyond Screening: Comprehensive and Focused Assessment

Comprehensive Assessment
• detailed appraisal of many factors that may contribute to a particular problem such as depression or anxiety
• may involve a combination of procedures, checklists and measurement tools to identify specific problem areas and contributing factors

Focused Assessment
• targeted appraisal to clarify the extent of a particular problem, to identify new or overlooked problems and to facilitate subsequent management
• will help identify those patients that are at high risk of a poor outcome and thus should be referred to a specialist
• may involve obtaining a definitive clinical diagnosis
Recommended Assessment Tools

Comprehensive Assessment

- PHQ-9
- GAD-7
- Clinical interview
- Other valid tools as needed

Focused Assessment

- Clinical interview
- Diagnostic and Statistical Manual of Mental Disorders (DSM-5)
- Structured Clinical Interview for DSM
**Assessment: Continuum of Depression in Cancer Patients**

<table>
<thead>
<tr>
<th>Normal Sadness</th>
<th>Adjustment Disorder</th>
<th>Subthreshold Depression</th>
<th>Major Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Maintains intimacy and connection</td>
<td>- Marked distress or functional impairment but not meeting other criteria for major depression</td>
<td>- Similar low mood presentation as major depression but not meeting full criteria for symptom number or duration</td>
<td>- Feels isolated</td>
</tr>
<tr>
<td>- Belief things will get better</td>
<td>- Not specifically defined</td>
<td>- Includes persistent depressive disorder if &gt; 2 years duration</td>
<td>- Feeling of permanence</td>
</tr>
<tr>
<td>- Can enjoy happy memories</td>
<td>- Distinction from subthreshold depression may be arbitrary</td>
<td>- Includes episodes lasting &lt; 2 weeks</td>
<td>- Excessive guilt and regret</td>
</tr>
<tr>
<td>- Sense of self-worth</td>
<td>- Often transient and self-limited</td>
<td></td>
<td>- Self-critical ruminations/loathing</td>
</tr>
<tr>
<td>- Fluctuates with thoughts of cancer</td>
<td></td>
<td></td>
<td>- Constant and pervasive</td>
</tr>
<tr>
<td>- Looks forward to the future</td>
<td></td>
<td></td>
<td>- Sense of hopelessness</td>
</tr>
<tr>
<td>- Retains capacity for pleasure</td>
<td></td>
<td></td>
<td>- Loss of interest in activities</td>
</tr>
<tr>
<td>- Maintains will to live</td>
<td></td>
<td></td>
<td>- Suicidal thoughts/behaviour</td>
</tr>
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</table>
State of the Evidence for Treatment of Depression in Cancer

- Striking paucity of research on both psychologic and pharmacologic treatment of major depression in cancer patients

- Controversial evidence for effectiveness of subthreshold depression treatment

- In practice, management of depression is extrapolated from practice guidelines developed for psychiatric and medical populations
## The Stepped-Care Model

<table>
<thead>
<tr>
<th>Focus of the intervention</th>
<th>Nature of the intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>STEP 1:</strong> All known and suspected presentations of depression</td>
<td>Assessment, support, psycho-education, active monitoring and referral for further assessment and interventions</td>
</tr>
<tr>
<td><strong>STEP 2:</strong> Persistent subthreshold depressive symptoms; mild to moderate depression</td>
<td>Low-intensity psychosocial interventions, psychological interventions, medication and referral for further assessment and interventions</td>
</tr>
<tr>
<td><strong>STEP 3:</strong> Persistent subthreshold depressive symptoms or mild to moderate depression with inadequate response to initial interventions; moderate and severe depression</td>
<td>Medication, high-intensity psychological interventions, combined treatments, collaborative care, and referral for further assessment and interventions</td>
</tr>
<tr>
<td><strong>STEP 4:</strong> Severe and complex depression; risk to life; severe self-neglect</td>
<td>Medication, high-intensity psychological interventions, electroconvulsive therapy, crisis service, combined treatments, multiprofessional and inpatient care</td>
</tr>
</tbody>
</table>

NICE Clinical Guideline 91, 2009
Practice Guideline in Practice

• Most cancer patients present with mild to moderate depressive symptoms (Step 2)
  o more challenging to recognize and select treatments for
  o most do not require specialist referral

• When to refer to psychosocial specialists
  1. Risk of harm (Step 4)
  2. Complex psychosocial cases (Step 4)
  3. Persistent symptoms after initial intervention (Step 3)
  4. Unsure of diagnosis
  5. For delivery of specific psychotherapies requiring specialized training
General Management Principles for Depression in Cancer Patients

1. Provide psychoeducation about the nature of depression
   - Consider patient handouts such as those in: MacArthur Toolkit (goo.gl/F4Q6Em), Mood Disorders Canada (goo.gl/J7qhjn), APA (goo.gl/rG8SkK)

2. Inform about the impact of depression on cancer outcomes
   - Reduced quality of life, intensification of physical symptoms, longer hospital stays, reduced survival (Currier, Ann Rev Med, 2014)

3. Many do not have psychiatric history, may require destigmatizing of depression
   - Medical model of depression
General Management Principles for Depression in Cancer Patients

4. Assess and optimize cancer-related physical symptom control

5. Discuss treatment options attending to patients’ preferences and previous treatment experiences

6. Consider use of a validated depression rating scale to monitor change over time
   - e.g. PHQ-9, HADS, BDI-II (Mitchell J Aff Dis, 2012)
Pharmacologic Treatment in Cancer

- Open label, case series studies demonstrate effectiveness of newer SSRIs and SNRIs (Li JCO, 2012)
- No evidence for superiority of any one antidepressant over another
- Insufficient evidence for effectiveness of psychostimulants (e.g., methylphenidate), steroids or benzodiazepines for the treatment of depression
- Meta-analyses of antidepressants for depressive symptoms in cancer patients demonstrate RR=1.56 (Laoutidis BMC Psych, 2013) and Hedges’ g effect size=0.44 (compared to 0.83 for CBT and 0.33 for PST) (Hart JNCI, 2012)
## Commonly Used Antidepressant Medications in Cancer Patients

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Standard Adult Dose</th>
<th>Therapeutic Considerations</th>
</tr>
</thead>
</table>
| Citalopram / (Escitalopram)   | Start: 10-20 mg OD / (5-10 mg qhs)  
Goal: 20–40 mg / (10-20 mg)  
Max: 40 mg OD / (20 mg qhs) | • Consider first-line due to least potential for drug interactions  
• May help with hot flashes  
• Escitalopram more sedating, most rapid onset of all SSRIs (1-3 weeks) |
| Venlafaxine                   | Start: 37.5-75 mg qam  
Goal: 75-225 mg  
Max: 375 mg qam | • Consider for prominent hot flashes  
• Energizing |
| Bupropion                     | Start: 100-150 mg qam  
Goal: 150-300 mg  
Max: 450 mg qam | • Consider for prominent fatigue  
• Pro-sexual function  
• Smoking cessation aide |
| Duloxetine                    | Start: 30 mg qam  
Goal: 30-60 mg  
Max: 90 mg qam | • Consider for neuropathic and chronic pain |
| Mirtazapine                   | Start: 7.5-15 mg PO/SL qhs  
Goal: 15-45 mg  
Max: 60 mg PO/SL qhs | • Consider for prominent insomnia, anorexia/cachexia, diarrhea, pruritis  
• Rapid dissolve formulation available |
| Methylphenidate               | Unclear dosage:  Range of 5-60 mg OD divided BID | • Energizing  
• Rapid onset of action within hours |
Selecting an Antidepressant for a Depressed Cancer Patient

<table>
<thead>
<tr>
<th>Factors to Consider</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Past psychiatric history (e.g. past positive treatment responses to an antidepressant)</td>
</tr>
<tr>
<td>• Concurrent medications (e.g. potential drug-drug interactions)</td>
</tr>
<tr>
<td>• Somatic symptom profile (e.g. sedating antidepressant for those with prominent insomnia; weight gaining antidepressant for cachectic patients)</td>
</tr>
<tr>
<td>• Potential for dual benefit (e.g. duloxetine and TCAs for neuropathic pain, venlafaxine for hot flashes)</td>
</tr>
<tr>
<td>• Type of cancer (e.g. avoid bupropion in those with CNS cancers)</td>
</tr>
<tr>
<td>• Co-morbidities (e.g. avoid psychostimulants or TCAs in cardiac disease)</td>
</tr>
<tr>
<td>• Cancer prognosis (e.g. consider psychostimulants if very short)</td>
</tr>
</tbody>
</table>
Psychosocial Interventions

• Generally the preference for most cancer patients

• Evidence for effectiveness of psychological therapies for major depression in cancer is mixed (Jacobsen 2008 CA Cancer J Clin)

• Large body of research on psychosocial interventions for cancer patients limited by heterogeneity in studies and floor effects (Linden 2012 Psycho-Oncology)

• Should be delivered by healthcare professionals competent in the modality, but non-mental health specialists can be trained
## Types of Psychosocial Interventions

<table>
<thead>
<tr>
<th>Term</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Counseling</td>
<td>Generic term used to refer to supportive psychosocial care provided by a qualified professional</td>
</tr>
<tr>
<td>Psychoeducation</td>
<td>Provision of information designed to increase knowledge and reduce uncertainty and thereby enhance psychological well-being</td>
</tr>
<tr>
<td>Relaxation training</td>
<td>Teaches skills for releasing physical or mental tension using meditative activities, progressive muscle relaxation exercises, or use of guided mental imagery</td>
</tr>
<tr>
<td>Problem-solving</td>
<td>Focuses on generating, applying, and evaluating solutions to identified problems</td>
</tr>
<tr>
<td>Cognitive-behavioral</td>
<td>Focuses on identifying, challenging and changing maladaptive thoughts therapy and behaviors to reduce negative emotions and promote psychological adjustment</td>
</tr>
<tr>
<td>Interpersonal therapy</td>
<td>Focuses on problems within interpersonal interactions and relationships, focusing on areas such as grief, role transitions, disputes or interpersonal deficits to reduce distress and promote psychological adjustment</td>
</tr>
<tr>
<td>Supportive-expressive</td>
<td>Focuses on the communication and processing of subjective experience (psychodynamic) therapy and on the joint creation of meaning within a therapeutic relationship to reduce distress and promote psychological adjustment (e.g. Meaning-Centred therapy, Dignity Therapy and CALM therapy)</td>
</tr>
</tbody>
</table>
### RCTs of Psychological Interventions for Depression in Cancer Patients

<table>
<thead>
<tr>
<th>Study</th>
<th>Cancer Population</th>
<th>Method</th>
<th>Results (Cohen’s $d$ - effect size by time)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evans 1995</td>
<td>Mixed type, stage II, in radiotherapy</td>
<td>Group CBT vs peer support vs usual care</td>
<td>↓ depression with CBT or peer support (-0.6, -1.2)</td>
</tr>
<tr>
<td>Nezu 2003</td>
<td>Mixed type, early stage, active treatment</td>
<td>PST vs couples PST vs wait list control</td>
<td>↓ depression with PST and couples PST (-3.5, -4.8)</td>
</tr>
<tr>
<td>Savard 2006</td>
<td>Breast, stage IV, mixed treatments</td>
<td>CBT vs wait list control</td>
<td>↓ depression with CBT (-1.8)</td>
</tr>
<tr>
<td>Goerling 2011</td>
<td>Mixed type and stage during surgical admission</td>
<td>Individual counseling vs usual care</td>
<td>↓ depression with counseling (-0.6)</td>
</tr>
<tr>
<td>Hopko 2011</td>
<td>Breast, all stages, mixed treatments</td>
<td>Behavioural activation vs PST</td>
<td>↓ depression with activation or PST (-1.6, -1.8)</td>
</tr>
<tr>
<td>Rodriguez Vega 2011</td>
<td>Mixed type, early stage, ambulatory care</td>
<td>Narrative therapy + escital. vs escital.</td>
<td>No added benefit to narrative therapy, both improved</td>
</tr>
<tr>
<td>Kangas 2013</td>
<td>Head &amp; Neck, newly diagnosed, radiotherapy</td>
<td>CBT vs supportive counseling</td>
<td>↓ depression with CBT or support (-0.9, -0.4)</td>
</tr>
<tr>
<td>Beutel 2014</td>
<td>Breast, early stage, active treatment</td>
<td>Brief psychodynamic vs usual care</td>
<td>44% depression remission, OR=7.64 (-0.8)</td>
</tr>
</tbody>
</table>
Nature of Anxiety in Cancer

• Research on anxiety disorders in cancer much less developed than that on depression

• **Unspecified Anxiety Disorder** is the label for sub-threshold anxiety disorders in DSM-5
  - Clinical features and diagnostic threshold not well described

• Anxiety disorders relevant to cancer include Panic Disorder, Specific Phobia, **Generalized Anxiety**, Acute Stress Disorder, **Posttraumatic Stress Disorder**
Guidance on Anxiety (and Depression) Assessment and Management

• Pan-Canadian practice guideline endorsed by CCO outlines assessment and management algorithm based on ESAS scores
• Available in symptom management section of CCO website: goo.gl/mBjQo
• Following slides are based on this guideline

Howell D, Keller-Olaman S, Oliver T, Hack T, Broadfield L, Biggs K, Chung J, Esplen M-J, Gravelle D, Green E, Gerin-Lajoie C, Hamel M, Harth T, Johnston P, Swinton N, Syme A. A Pan-Canadian Practice Guideline: Screening, Assessment and Care of Psychosocial Distress (Depression, Anxiety) in Adults with Cancer, Toronto: Canadian Partnership Against Cancer (Cancer Journey Action Group) and the Canadian Association of Psychosocial Oncology, August 2010
Anxiety Severity and Treatment Planning

ESAS Anxiety Score 1-3

- Proceed to care pathway

ESAS Anxiety Score 4-6

- Comprehensive assessment to clarify nature and extent of anxiety symptoms
  - e.g., identify contributing factors, history, etc.
- Focused assessment specific to problem of anxiety
  - e.g., use validated tool to assess symptoms and severity, impact on function

ESAS Anxiety Score 7-10
# Anxiety Severity and Treatment Planning

<table>
<thead>
<tr>
<th>Mild Anxiety</th>
<th>Moderate Anxiety</th>
<th>Severe Anxiety</th>
</tr>
</thead>
</table>
| • No or minimal anxiety symptoms  
• Typical symptoms – fear, worry, uncertainty about future, concerns about illness, feeling life is out of control, poor sleep, appetite and/or concentration, preoccupied with thoughts of illness and death  
• Gradual resolution over weeks/months | • Maladaptive response (out of proportion to stressors); disruption of functioning  
• Difficulty controlling anxiety without intervention  
• Risk factors present  
• Nature of anxiety disorder established (e.g., specific diagnosis) | • High level of worry or difficult to control anxiety about several things most days  
• Re-experiencing events in a distressing way (e.g., dreams, flashbacks)  
• Spells or attacks of sudden fear, discomfort, anxiousness  
• Risk factors  
• Risk of harm to self and/or to others > URGENT referral to appropriate services; safety planning |

**Care Pathway 1**
Prevention and Supportive Care

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

**Care Pathway 3**
Referral to Physician/Psychologist/Psychiatrist
Anxiety Severity and Treatment Planning

Supportive care interventions for all patients, as appropriate

- Offer referral to psychosocial support (e.g., counseling, support groups)
- Provide education for 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, available resources (e.g., transportation, financial assistance, etc.)
  - Coping with stress and specific strategies (i.e. relaxation, breathing techniques, mindfulness)
  - Managing symptoms contributing to anxiety (e.g., pain, tension)
  - Encourage use of additional supports if symptoms worsen
Anxiety Severity and Treatment Planning

Mild Anxiety

Moderate Anxiety

Severe Anxiety

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

Intervention Options
• Combine non-pharmacologic and pharmacologic interventions as appropriate (e.g., education, psychotherapy, and anxiolytics for PTSD)
• Referral to other services/providers as required

Non-pharmacologic: Psychosocial interventions (CBT [level 1], other psychotherapy, counseling, support – group or individual); psycho-education (about resources, self-management)

Pharmacologic: Benzodiazepines (<4 weeks), antihistamines, antipsychotics; antidepressants as for moderate depression; SSRIs in longer term management of panic. Monitor adverse effects.
Anxiety Severity and Treatment Planning

Mild Anxiety  Moderate Anxiety  Severe Anxiety

Care Pathway 3
Referral to Physician/Psychologist/Psychiatrist

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

Intervention Options
Psychiatric standard of care
Commonly Used Psychological Treatment Components for Depression and Anxiety in Cancer Patients
Behavioural Activation for Depression

• Derived from behavioral theory that not enough environmental reinforcement or too much environmental punishment can contribute to depression
• Goal to increase activities that bring sense of pleasure and/or accomplishment (mastery)
• Token economy (rewards) for moving through hierarchy of reinforcing activities
• Large-scale study found BA to be more effective than cognitive therapy and on a par with medication for treating depression (Dimidjian et al., 2006)

RESOURCES:
• One page patient handout for behavioural activation: goo.gl/IVBcBV
Progressive Muscle Relaxation (PMR)

- For depression and some anxiety disorders
- Progressive tensing and releasing of muscle groups
- Counters the muscle tension symptom of anxiety
- Best as part of multi-component treatment plan
- May improve a number of cancer-related symptoms

**RESOURCES:**
- Relaxation audio files at Trillium Health Partners website: goo.gl/bCJyhN
- PMR patient handout from Anxiety BC: goo.gl/OGRrBe
Cognitive Restructuring

- identification, evaluation, and modification of thoughts that patients experience on particular occasions and that are associated with an increase in an aversive mood state
- Overview of steps in cognitive restructuring:
  - Identification of dysfunctional “automatic thoughts” about self, world, or future
  - Labeling of cognitive distortions
  - Rational disputation of automatic thoughts
  - Develop more helpful thoughts
- Techniques include thought recording, socratic questioning, downward arrow technique, behavioural experiments, etc.

RESOURCES:
- Tools for cognitive restructuring: goo.gl/aWCTMI
- ABCDE method thought diary: goo.gl/nv2kkZ
Problem Solving Therapy (PST)

• A cognitive-behavioural intervention to improve coping with stressful life experiences; PST incorporates:
  o Adjustment of thoughts about problems and ability to solve
  o Application of specific rational problem-solving tasks:
    ▪ Defining problem
    ▪ Generation possible solutions
    ▪ Cost-benefit analysis
    ▪ Implementation of solutions
    ▪ Outcome evaluation

RESOURCES:
• One page patient handout on problem solving: goo.gl/FO6Ocq
Mindfulness

- Roots in Buddhist meditation, brought to mainstream by Jon-Kabat Zinn at U Mass Medical School – “Mindfulness Based Stress Reduction”
- Basis of MBSR is mindfulness – “moment to moment, non-judgemental awareness”
- Opposite of automatic pilot -- focus on being in “here and now,” observing thoughts, feelings, behaviours with a gentle curiosity rather than thinking/analyzing
- Meta-analysis of 209 studies showed large and clinically significant effects in treating depression and anxiety (Khoury et al., 2013)

RESOURCES:
- One page handout for patients on mindfulness: goo.gl/aYh582
Behavioural Exposure

• Similar to evidence-based treatment protocol for PTSD (e.g., “prolonged exposure”)
• Writing can be used for patients who avoid cancer-related cues, talking about cancer – esp. post-treatment
• Structured writing exercise over 4 sessions

RESOURCES:
Take Home Messages

• Comprehensive assessment needed to inform treatment plan – diagnostic clarity important

• Cancer-related contributing factors must be addressed

• Depression/anxiety severity is key
  o Subthreshold or mild: psychosocial interventions
  o Moderate: psychosocial interventions +/- pharmacotherapy
  o Severe: psychosocial interventions + pharmacotherapy

• Choice of psychosocial intervention should be tailored to patient preference and coping style
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