Pan-Canadian Practice Guideline: Screening, Assessment and Management of Psychosocial Distress, Depression and Anxiety in Adults with Cancer

Version 2, 2015

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1 Recommendation Summary

1.A Recommendation Summary-Cancer Related Distress

This guideline is a second edition of, and, replaces the previous guideline, A Pan-Canadian Practice Guideline: Screening, Assessment and Care of Psychosocial Distress (Depression, Global Anxiety) in Adults with Cancer version 1-2010.

Our recommendations are based on two sources of evidence:
First, from existing guidelines, for which we used an expert panel consensus method to evaluate the different levels of evidence and review strategies to produce recommendations reported within these guidelines. Recommendations for screening and assessment for distress, depression, and global anxiety in adults with Cancer were identified based on the application of the ADAPTE methodology[1, 2], a rigorous 24 step method for adapting knowledge from existing guidelines following a quality appraisal in accordance with the AGREE II convention[3]. The ADAPTE methodology is a systematic process for adapting recommendations in existing guidelines to create high quality guidelines tailored for use in a specific health care context [2, 4].(see section 4.B.1.1 for more details)

Second, we identified RCTs through our systematic review process as well as from reviewing other systematic reviews. We formulated standardized 'effectiveness statements' to rate the evidence arising from the systematic review of evidence for the management of Psychosocial Distress, Depression and Global Anxiety in Adults with Cancer, using the overall Strength of the Evidence (SOE) of randomized control trials (RCTs) across the literature using the rating approach as specified by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Methodology [5-7]. See table 1.A.1.

GRADE Methodology

The evidence in RCTs is graded according to whether it is of high quality, moderate quality or low quality or very low quality evidence according to the Grade of Recommendation Assessment, Development and Evaluation system. GRADE offers two strengths of recommendation: strong and weak. The strength of recommendations is based on the quality of supporting evidence, the degree of uncertainty about the balance between desirable and undesirable effects, the degree of uncertainty or variability in values and preferences, and the degree of uncertainty about whether the intervention represents a wise use of resources. We adopted the American Thoracic Society approach to GRADE based on the level of evidence as shown below with various levels of evidence contributing to strong or weak recommendations as shown in Table 1.A.1.[8]

Table1.A.1: Grading the Strength of Recommendations and Quality of Evidence

Grade of Recommendation	Clarity of Risk/Benefit	Quality of Supporting Evidence	Implications
Strong recommendation High-quality	Benefits clearly outweigh harms and burdens, or vice versa	Consistent evidence from well-performed randomized controlled trials or exceptionally strong evidence from unbiased observational studies	Recommendation can apply to most patients in most circumstances. Further research is very unlikely to change our confidence in the estimate of effect
Strong recommendation Moderate-quality	Benefits clearly outweigh harms and burdens, or vice versa	Evidence from randomized controlled trials with important limitations (inconsistent results, methodological flaws, indirect or imprecise), or unusually strong evidence from unbiased observational studies	Recommendation can apply to most patients in most circumstances. Further research (if performed) is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Strong recommendation Low-quality	Benefits clearly outweigh harms and burdens, or vice versa	Evidence for at least one clinical outcome from observational studies, from randomized controlled trials with serious flaws or indirect evidence	Recommendation may change when higher quality evidence becomes available. Further research (if performed) is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Strong recommendation Very-low-quality (very rarely applicable)	Benefits clearly outweigh harms and burdens, or vice versa	Evidence for at least one clinical outcome from unsystematic clinical observations or very indirect evidence	Recommendation may change when higher quality evidence becomes available; any estimate of effect, for at least one critical outcome, is very uncertain
Weak recommendation High-quality	Benefits closely balanced with harms and burdens	Consistent evidence from well-performed randomized controlled trials or exceptionally strong evidence from unbiased observational studies	The best action may differ depending on circumstances or patients or societal values. Further research is very unlikely to change our confidence in the estimate of effect
Weak recommendation Moderate-quality	Benefits closely balanced with harms and burdens	Evidence from randomized, controlled trials with important limitations (inconsistent results, methodological flaws, indirect or imprecise), or unusually	Alternative approaches likely to be better for some patients under some circumstances. Further research (if performed) is likely to have an important impact on our confidence in

		strong evidence from unbiased observational studies	the estimate of effect and may change the estimate
Weak recommendation Low-quality	Uncertainty in the estimates of benefits, harms, and burdens; benefits may be closely balanced with harms and burdens	Evidence for at least one critical outcome from observational studies, from randomized controlled trials with serious flaws, or indirect evidence	Other alternatives may be equally reasonable. Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Weak recommendation Very-low-quality	Major uncertainty in the estimates of benefits, harms, and burdens; benefits may or may not be balanced with harms and burdens	Evidence for at least one critical outcome from unsystematic clinical observations or very indirect evidence	Other alternatives may be equally reasonable. Any estimate of effect, for at least one critical outcome, is very uncertain

Adapted from Schunemann[8]

Summary of Glossary of Terms

Cancer-Related Distress: According to the NCCN, "distress is a multifactorial unpleasant emotional experience of a psychological (cognitive, behavioral, and emotional), social, and/or spiritual nature that may interfere with the ability to cope effectively with cancer, its physical symptoms and its treatment. Distress extends along a continuum, ranging from common normal feelings of vulnerability, sadness, and fears to problems that can become disabling. The terms generalized or global distress is often used interchangeably as an overarching term for cancer-related distress to differentiate general distress from depressive symptomatology.

Fear of Recurrence: Fear of cancer returning or progressing is now identified as a common type of distress in post-treatment survivors. It is characterized as heightened-health related global anxiety, symptom vigilance, worries about risk of recurrence or disease progression, and fears of shortened life span.

Depression (Major Depressive Disorder-MDD):This is defined as follows:

A. At least 5 of the following symptoms, present during the same 2-week period, representing a change from previous functioning, each present nearly every day; at least one of the symptoms is either (1) or (2).
   1. Depressed mood most of the day
   2. Markedly diminished interest or pleasure in almost all activities most of the day
   3. Significant weight loss or gain (change of >5% in a month), or decrease or increase in appetite
   4. Insomnia or hypersomnia

5. Psychomotor agitation or retardation 6. Fatigue or loss of energy 7. Feelings of worthlessness or excessive or inappropriate guilt 8. Diminished ability to think or concentrate, or indecisiveness 9. Recurrent thoughts of death recurrent suicidal ideation, or a suicide attempt or plan **B.** Symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning In this guideline we defined major depressive disorder based on the CCO guideline definition and it was defined as meeting a threshold (cut-offs for significant depression or depression) for depressive disorders based on a validated depression rating scale or based on a clinical interview.
Global Anxiety: The "anxiety" we refer to in this guideline refers to anxiety symptoms measured on a validated self-report scale and not to a clinical diagnosis of general anxiety disorder(s) confirmed by a psychologist or psychiatrist. We have also defined General Anxiety Disorder or GAD as ≥ 6 months of excessive anxiety/worry about multiple events/activities. Worry is difficult to control and is associated with symptoms such as restlessness, fatigue, poor concentration, irritability, tension, poor sleep. Disturbance is impairing and/or distressing.
None or Mild Anxiety: None or mild symptoms of anxiety, no or minimal functional impairment, effective coping skills and access to social support.
Moderate Anxiety: Presents as worries or concerns with fatigue, sleep disturbances, irritability, and concentration difficulties, functional impairment from mild to moderate, anxiety symptoms of panic or social phobia may be present
Moderate to Severe Anxiety: Anxiety symptoms interfere moderately too markedly with functioning, symptoms do not respond to low intensity based on CBT principles, other psychosocial or pharmacological interventions. May have symptoms of GAD.
Panic disorder: Recurrent unexpected panic attacks, ≥ 1 month of persistent worry about future panic or consequences of panic, or behavior change related to panic
Agoraphobia: Fear of places/situations in which escape may be difficult or help for panic may not be available. Places/situations are avoided or endured with distress or fear of having a panic attack
Specific Phobia: Persistent fear of a specific object or situation, Exposure provokes immediate anxiety, Person acknowledges fear as excessive or unreasonable and impairing/distressing
Social anxiety disorder: Persistent fear of social or performance situations Exposure provokes anxiety or panic Patient acknowledges fear as excessive or unreasonable and impairing/distressing

Acute stress disorder: Experience of a traumatic event Persistent and impairing symptoms in four domains 1 month after trauma: • Dissociation (e.g., numbing, derealization) • Re-experiencing (e.g., intrusive thoughts) • Avoidance • Hyper arousal (e.g., tension, hypervigilance) Patient acknowledges disturbance as impairing/distressing
Obsessive-compulsive disorder : Recurrent, intrusive thoughts/images, with persistent attempts to ignore or suppress them via a neutralizing thought or action Repetitive, rigid behaviors that person is driven to perform to reduce distress/threat, although behaviors are not realistically connected to threat Patient acknowledges disturbance as excessive or unreasonable and impairing/distressing
Post-Traumatic Stress Disorder (PTSD): This involves exposure to trauma involving death or the threat of death, serious injury, or sexual violence as per the DSM-IV. DSM-5 proposes four distinctive behavioral symptoms or diagnostic clusters for 1>month 1) intrusion symptoms (instead of re-experiencing), 2) alterations in arousal and reactivity (instead of arousal), 3) avoidance, and 4) negative alterations in cognitions and mood

1.A.1 Recommendations for Screening and Assessment of Distress and Depression in Adults with Cancer

✔	No change was made to the previous recommendation as a result of the 2015 systematic review of the evidence, including clinical practice guidelines and RCTs.
✚	The recommendation and supporting evidence were updated based on the 2015 systematic review evidence, including clinical practice guidelines and RCTs.
NEW	A new recommendation was developed based on supporting evidence from the 2015 systematic review evidence, including clinical practice guidelines and RCTs.

Note: *Minor changes were made to the **screening and assessment** recommendations for improved clarity and consistency. The minor changes also take into account an evaluation of recommendations from high quality evidence-based clinical practice guidelines based on our most recent update in 2015.

Recommendations for screening and assessment of distress in adults with cancer were identified based on the application of the ADAPTE methodology[1, 2]a rigorous 24 step method for adapting knowledge from existing guidelines following a quality appraisal in accordance with the AGREE II convention[3]. The ADAPTE methodology is a systematic process for adapting recommendations in existing guidelines to create high quality guidelines tailored for use in a specific health care context[2, 4], see detail on section 3.A.

Screening and Assessment		Evidence Appraisal Strategy in Guidelines	Strength of Recommendation	Status
1.0 Screening for Distress	1. All cancer patients should be routinely screened for the presence of distress and specific contributing problems/concerns (i.e. Canadian problem checklist); a valid measure should be used as an initial "red-flag" indicator of the level of distress from the point of diagnosis onward and at points of vulnerability along the cancer journey[9-14].	Yu 2012 & Andersen 2014: **expert consensus** Holland(NCCN): **2A** Howell 2010: **2A** Howell 2009: **expert consensus** Howes 2015: **Strong Recommendation Level I*** Level II*** Level III-3*** **	Strong Recommendation-moderate-quality evidence	✔
	2. All patients should be screened for distress at their initial visit, at appropriate intervals, and as clinically indicated, especially with changes in disease or treatment status (i.e. post-treatment, recurrence, progression, transition to palliative and end-of-life care) and other points of vulnerability, i.e.	Andersen 2014: **expert consensus** Howell 2010: **2A** Howell 2009: **expert consensus** Howes 2015: **Strong recommendation, some strong**	Strong Recommendation-moderate quality evidence	✔

	times of personal transition such as family crisis[10, 12-14].	**evidence, benefits clearly exceed harm** **Level I***** **Level II***** **Level III-3*****		
	3. Screening should be done using brief tools to minimize patient burden and maximize use in clinical practice; tools should have adequate sensitivity and specificity and established cut-offs for rapid identification of distress (i.e. ESASr, Distress Thermometer (DT), or PHQ-2 screening questions)[10-17].	Andersen 2014: **expert consensus** Holland(NCCN): **2A** Howell 2010: **2A** Howell 2009: **expert consensus** Howes 2015: **Strong recommendation (Some strong evidence, benefits clearly exceed harm)** **Level I***** **Level II***** **Level III-3*****	Strong Recommendation-moderate quality evidence	✔
2.0 Assessment of Distress	4. Patients who screen positive for distress (score of 4 or higher-signifying moderate or severe distress) on either the ESASr[2] or the DT[1] or a score of 3 or higher on the PHQ-2[2] item screener should have: (a) a comprehensive assessment completed to identify the sources (problems/concerns), nature and extent of distress, risk factors; a specific tool e.g. the Problem or Concerns Checklist or the Social Difficulties Inventory may facilitate systematic assessment of distress and contributing factors; (b) a focused assessment to	Andersen 2014 & Li 2015: **expert consensus & consensus-based/adapted from NICE guideline** Howell 2010: **2A** Howell 2009: **expert consensus** Howes 2015: **Strong Recommendations: (Some strong evidence, Benefits clearly exceed harm)** **Level I***** **Level II***** **Level III-1*****	Strong Recommendation-moderate quality evidence	✚

[1] Distress Thermometer
[2] Patient Health Questionnaire

	identify depressive or anxiety symptomatology [10, 12-14, 18].			
	5. Patients who screen positive for distress should have a focused assessment to identify symptoms of depression or anxiety; use of a validated self-report measure, such as the PHQ-9 and GAD-7[3] or a similar measure (common tools include the BDI[4], BSI[5], CES-D[6] and HADS[7]) is recommended that enables classification of symptoms into mild, moderate or severe to guide interventions and for monitoring intervention effectiveness over time[10-12].	Andersen 2014: **expert consensus** Holland(NCCN): **2A** Howell 2010: **2A**	Strong Recommendation-low quality evidence	✚
	6. All patients at times of transition to post-treatment follow-up care should be assessed for psychosocial support needs, specifically for fear of recurrence. Referral to support services advised[10].	Andersen 2014: **expert consensus**	Strong Recommendation-low quality evidence	NEW
	7. It is recommended that patients be screened for symptoms of global anxiety and assessed for presence of Generalized Anxiety Disorder using validated tools i.e. GAD 7, as it is commonly comorbid with other mood or anxiety disorders[10].	Andersen 2014: **expert consensus**	Strong Recommendation-low quality evidence	NEW
	8. Any patient who expresses specific concerns such as risk of harm to self and/or others, severe depression or agitation, or	Andersen 2014: **expert consensus** Howell 2010: **2A**	Strong Recommendation-moderate quality evidence	✔

[3] Generalized Anxiety Disorder
[4] Beck Depression Inventory
[5] Brief Symptom Inventory
[6] Center for Epidemiological Studies Depression Scale
[7] Hospital Anxiety Depression Scale

	the presence of psychosis or delirium (acute confusion) requires immediate referral to a psychiatrist, psychologist, physician, or equivalently trained professional[10, 12, 14].	Howes 2015: **Strong Recommendations: (Some strong evidence, Benefits clearly exceed harm) Level I*** Level II***		
	9. As a shared responsibility the clinical team must decide when a referral to a psychiatrist, psychologist, or trained psychosocial specialist is required (i.e. social worker) (i.e. all patients with a score on a screening tool indicative of severe distress (4 or above) or based on established cut-offs for symptoms of depression and/or anxiety on valid tools and presence of specific risk factors on secondary assessment (see Risk Factors Text Box 2 pg. 24)[10-12, 14].	Andersen 2014: **expert consensus** Howes 2015: **Strong Recommendations: (Some strong evidence, Benefits clearly exceed harm) Level I*** Level II*** Holland(NCCN): **2A** Howell 2010: **2A** Howell 2009: **expert consensus**	Strong Recommendation-moderate-quality evidence	✔
	10. A patient with symptoms that are clinically significant for depression or severe anxiety, should, have a further diagnostic assessment to identify the nature and extent of depressive symptoms and the presence or absence of a mood disorder before pharmacological treatments are initiated (i.e. DSM-5)[10-12, 14, 18, 19].	Andersen 2014 & NICE 2009: **expert consensus** Howes 2015: **Strong Recommendations: (Some strong evidence, Benefits clearly exceed harm) Level I*** Level II*** Holland(NCCN): **2A** Howell 2010: **2A** Howell 2009: **expert consensus** Li 2015: **consensus-based/adapted from NICE guideline**	Strong Recommendation **moderate-quality evidence**	✚

Recommendation Statements: *Recommendation statements reflect high, moderate or low confidence that the recommendation reflects the net effect of a given course of action. The use of words like "must," "must not," "should," and "should not" indicate that a course of action is recommended or not recommended for either most or many patients, but there is latitude for the treating physician to select other courses of action in certain cases*[10]. **Words such as "likely benefit" show there is low quality evidence of an effect.**
Expert Consensus: *Overall, the final recommendations are based on expert consensus of the pan-Canadian inter-professional panel, after review of the available evidence, guidelines from other groups, and current clinical practice in Canada. Screening for distress should not be limited to depression and anxiety symptoms alone but also include identification of physical, informational, psychological, social, spiritual, and practical domains of psychosocial health care needs or concerns that contribute to distress of cancer and treatment.*

*****Definition for Australian National Breast Cancer Centre and National Cancer Control Initiative (NBCC-NCCI) Categories:** The specific definition of the NBCC-NCCI categories for recommendations are included below:
Level I *Based on a systematic review of randomized controlled trials (RCT).*
Level II *Based on a minimum of one properly designed RCT.*
Level III-1 *Based on well-designed pseudo-randomized controlled trials.*
Level III-2 *Based on "comparative studies with concurrent controls and allocation not randomized (cohort studies), case control studies, or interrupted time series with a control group".*
Level III-3 *Based on "comparative studies with historical control, two or more single-arm studies, or interrupted time series without a parallel group".*
Level IV *Based on "case studies, either post-test or pre- and post-test"* [14].

Definitions for National Comprehensive Cancer Network (NCCN) Categories: The specific definitions of the NCCN categories for recommendations are included below:
Category 1*: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate;*
Category 2A*: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate;*
Category 2B*: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate;*
Category 3*: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.*
For the 'uniform NCCN consensus' defined in Category 1 and Category 2A, a majority Panel vote of at least 85% is required. For the 'NCCN consensus' defined in Category 2B, a Panel vote of at least 50% (but less than 85%) is required. Lastly, for recommendations where there is strong Panel disagreement regardless of the quality of the evidence, NCCN requires a vote from at least three Panel Members (representing at least three different Member Institutions) to include and designate a recommendation as Category 3. The large majority of the recommendations put forth in the Guidelines are Category 2A. Where categories are not specified within the Guidelines, the default designation for the recommendation is Category 2A[11].

1.A.2 Recommendation Summary-Management for Cancer-Related Distress and Depression in Adults with Cancer

✔	No change was made to the previous recommendation as a result of the 2015 systematic review of the evidence, including clinical practice guidelines and RCTs.
✚	The recommendation and supporting evidence were updated based on the 2015 systematic review evidence, including clinical practice guidelines and RCTs.
NEW	A new recommendation was developed based on supporting evidence from the 2015 systematic review evidence, including clinical practice guidelines and RCTs.

Note: Minor changes were made to the recommendations for distress for improved clarity and consistency. The minor change also takes into account an evaluation of recommendations from high quality evidence-based clinical practice guidelines based on our most recent update in 2015. Recommendations for screening and assessment of distress in adults with cancer were identified based on the application of the ADAPTE methodology[1, 2], a rigorous 24 step method for adapting knowledge from existing guidelines following a quality appraisal in accordance with the AGREE II convention[3]. The ADAPTE methodology is a systematic process for adapting recommendations in existing guidelines to create high quality guidelines tailored for use in a specific health care context[2, 4],see detail on section 3.A.

Distress		Evidence Appraisal Strategy in Guidelines	Strength of Recommendation	Status
3.0 Stepped-Care Approach	1. Interventions for distress in cancer should be delivered according to a stepped care model (see Figure 2.1). This involves assessment of the severity of distress for each patient, provision of support and education to all patients, delivery of low intensity interventions for mild to moderate levels of distress (psycho-education, supervised physical activity programs, group-based peer support or self-help programs based on CBT, behavioral activation or problem-solving techniques)[10, 18, 19].	Andersen 2014 & NICE 2009: **expert consensus** Li 2015: **consensus-based/adapted from NICE guideline**	Strong-low quality evidence	**NEW**
4.0 Education and Information	2. All patients should receive basic supportive care such as empathic communication, provision of information on support groups and symptom self-management strategies as part of routine care delivery that can assist	Li 2015: **consensus-based/adapted from NICE guideline** Deng 2013: **Grade 2B**	Strong Recommendation-moderate quality evidence	✚

	them in adjusting to cancer[9, 11, 13, 14, 18, 20-28].	Howell 2010: **2A** Howell 2009: **expert consensus** Howes 2015: **Strong Recommendation: (Some strong evidence, Benefits clearly exceed harm) Level I*** Level II*** Level IV***		
	3. All patients should receive education about the potential for distress in cancer and its impact on the intensification of symptoms and reduced quality of life. Patients should also be counseled on the specific symptoms of depression or anxiety and when distress is severe enough to warrant a call to the physician or nurse, or psychosocial oncology expert. Consider use of patient handouts such as those provided by the MacArthur Depression Management Toolkit, Mood Disorders Cancer, Canadian Mental Health Association, or the American Psychiatric Association, CAPO Emotional Facts of Life (MODIFIED, CCO)[9, 10, 12-14, 18].	Li 2015: **consensus-based/adapted from NICE guideline** Anderson 2014: **expert consensus** Howell 2009: **expert consensus** Howell 2010: **2A** Howes 2015: **Strong Recommendation: (Some strong evidence, Benefits clearly exceed harm) Level I*** Level II*** Level IV***	Strong Recommendation-high quality evidence	✚
	4. All potential underlying causes for distress should be addressed i.e. unrelieved symptoms such as pain or sleep disturbance and medical causes ruled out and corrected for distress (i.e. delirium, electrolyte imbalances, opiates)[12, 13, 18].	Li 2015: **consensus-based/adapted from NICE guideline** Howell 2009: **expert consensus** Howell 2010: **2A**	Strong Recommendation-low quality evidence	✚

5.0 **Low Intensity** **Psychological Interventions**	5. Patients with mild to moderate distress will benefit from low intensity psychological interventions delivered in either group format, individually or self-help programs (i.e. psycho-education, coping skills training, skills based learning, problem-solving, mindfulness based stress reduction), delivered by qualified personal or clinicians who have received specific training [12, 14, 18, 19, 22, 25, 28].	NICE 2009:**Level 1 (RCT)** Li 2015: **consensus-based/adapted from NICE guideline** Howell 2010: **2A** Howes 2015: **Strong Recommendation: (Some strong evidence, Benefits clearly exceed harm)** **Level I***** **Level II***** **Level III-1*****	Strong Recommendation-high quality evidence	**NEW**
	6. Patients with moderate distress who do not respond to initial interventions, or those with severe distress, require referral to psychosocial specialists for high intensity psychological interventions and/or pharmacologic management[9, 11, 12, 14].	Yu 2012: **NR** Holland 2014: **NCCN,1** Howell 2010: **2A** Li 2015: **consensus-based/adapted from NICE guideline** Howes 2015: **Strong Recommendation: (Some strong evidence, Benefits clearly exceed harm)** **Level I***** **Level II***** **Level III-1*****	**Strong recommendation-** moderate quality evidence	**NEW**
	7. Patients with acute stress or post-traumatic disorder may benefit from a multi-component intervention that includes a structured physical activity program, visual	**consensus-based**	**Weak Recommendation-low quality evidence-**	**NEW**

	imagination, and progressive relaxation techniques with instruction regarding diaphragmatic breathing for treatment of insomnia[29].			

Recommendation Statements: *Recommendation statements reflect high, moderate or low confidence that the recommendation reflects the net effect of a given course of action. The use of words like "must," "must not," "should," and "should not" indicate that a course of action is recommended or not recommended for either most or many patients, but there is latitude for the treating physician to select other courses of action in certain cases*[10]. **Words such as "likely benefit" show there is low quality evidence of an effect.**
Expert Consensus: *Overall, the final recommendations are based on expert consensus of the pan-Canadian inter-professional panel, after review of the available evidence, guidelines from other groups, and current clinical practice in Canada. Screening for distress should not be limited to depression and anxiety symptoms alone but also include identification of physical, informational, psychological, social, spiritual, and practical domains of psychosocial health care needs or concerns that contribute to distress of cancer and treatment.*

*** Definitions for National Comprehensive Cancer Network (NCCN) Categories:** The specific definitions of the NCCN categories for recommendations are included below:
Category 1*: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate;*
Category 2A*: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate;*
Category 2B*: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate;*
Category 3*: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.*
For the 'uniform NCCN consensus' defined in Category 1 and Category 2A, a majority Panel vote of at least 85% is required. For the 'NCCN consensus' defined in Category 2B, a Panel vote of at least 50% (but less than 85%) is required. Lastly, for recommendations where there is strong Panel disagreement regardless of the quality of the evidence, NCCN requires a vote from at least three Panel Members (representing at least three different Member Institutions) to include and designate a recommendation as Category 3. The large majority of the recommendations put forth in the Guidelines are Category 2A. Where categories are not specified within the Guidelines, the default designation for the recommendation is Category 2A[11].

Definition for GRADE Categories: The specific definitions of GRADE categories for recommendations are included below:
High: *We are very confident that the true effect lies close to that of the estimate of the effect;*
Moderate: *We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different;*
Low: *Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect;*
Very Low: *Substantially different from the estimate of effect.*

*****Definition for NBCC-NCCI Categories:** The specific definition of the NBCC-NCCI categories for recommendations are included below:
Level I *Based on a systematic review of randomized controlled trials (RCT).*
Level II *Based on a minimum of one properly designed RCT.*
Level III-1 *Based on well-designed pseudo-randomized controlled trials.*
Level III-2 *Based on "comparative studies with concurrent controls and allocation not randomized (cohort studies), case control studies, or interrupted time series with a control group".*
Level III-3 *Based on "comparative studies with historical control, two or more single-arm studies, or interrupted time series without a parallel group".*
Level IV *Based on "case studies, either post-test or pre- and post-test"*[14].

1.B Recommendation Summary- Cancer-Related Depression

1.B.1 Recommendation Summary- Management for Cancer-Related Moderate to Severe Depression

✔	No change was made to the previous recommendation as a result of the 2015 systematic review of the evidence, including clinical practice guidelines and RCTs.
✚	The recommendation and supporting evidence were updated based on the 2015 systematic review evidence, including clinical practice guidelines and RCTs.
NEW	A new recommendation was developed based on supporting evidence from the 2015 systematic review evidence, including clinical practice guidelines and RCTs.

Note: ✓ Minor changes were made to the recommendations for improved clarity and consistency. The minor change also takes into account an evaluation of recommendations from high quality evidence-based clinical practice guidelines based on our most recent update in 2015. Recommendations for screening and assessment of distress in adults with cancer were identified based on the application of the ADAPTE methodology[1, 2], a rigorous 24 step method for adapting knowledge from existing guidelines following a quality appraisal in accordance with the AGREE II convention[3]. The ADAPTE methodology is a systematic process for adapting recommendations in existing guidelines to create high quality guidelines tailored for use in a specific health care context[2, 4], see detail on section 3.A.

Depression		Supporting Evidence in Guidelines	Strength of Recommendation	Status
	1. Any patient who expresses specific concerns such as risk of harm to self and/or others, severe depression or agitation, complex psychosocial issues, or the presence of psychosis or delirium (acute confusion) require urgent referral to a psychiatrist, psychologist, physician, or equivalently trained professional[12, 18, 19].	NICE 2009: **Expert consensus/Level 1 (RCT)** Li 2015: **consensus-based/adapted from NICE guideline** Howell 2010: **2A**	**Strong recommendation-low quality evidence**	✔
	2. Optimal management of moderate to severe depression includes pharmacological and non-pharmacological interventions in combination delivered by appropriately trained individuals (Recommendation Statement Adopted-from CCO Guideline)[18].	Li 2015: **consensus-based/adapted from NICE guideline**	**Strong recommendation-high quality evidence**	**NEW**
	3. Pharmacological interventions are recommended for severe or depression (Recommendation Statement Adopted from CCO Guideline)[12, 14, 17-19].	NICE 2009: **Level 1 (RCT)** Li 2015: **consensus-based/adapted from NICE guideline**	**Strong recommendation-high quality evidence**	**NEW**

		Rayner 2011: **Level of Recommendation : Not Reported** Howell 2010: **2A**		
	4. Collaborative care interventions should be considered for patients with cancer who are diagnosed with depression (Recommendations Statement Adopted from CCO Guideline)[18, 19].	NICE 2009: **Level 1 (RCT)** Li 2015: **consensus-based/adapted from NICE guideline**	**Strong Recommendation-moderate quality evidence**	**NEW**
	5. Clinicians should select pharmacological treatment (i.e. antidepressants) based on knowledge of the side-effect profiles of medications, tolerability of treatment, potential for interaction with other medications, response to prior treatment and patient preferences; patients should be advised of any potential harm or adverse effects[10, 14, 18, 19].	NICE 2009: **Level 1 (RCT)** Li 2015: **consensus-based/adapted from NICE guideline** Andersen 2014: **expert consensus** **Howes 2015: Level III and Level IV**	**Strong Recommendation-moderate quality of evidence**	✔
	6. Antidepressants should not be used routinely to treat sub-threshold depressive symptoms or mild depression, due to the higher risk-benefit ratio at this level of depression severity. Antidepressant medication should be considered first for severe depression. A selective serotonin reuptake inhibitor (SSRI) such as citalopram/escitalopram should be the first resort due to best tolerability and the least potential for drug interactions (Statement of Recommendation Adopted from CCO Guideline)[14, 18].	Li 2015: **consensus-based/adapted from NICE guideline**	**Strong Recommendation-high quality evidence**	**NEW**
High Intensity Inter-ventions	7. High intensity psychotherapeutic interventions should be combined with pharmacological treatment for sub-threshold or depression and include individual or group	NICE 2009: **Level 1 (RCT)** Li 2015: **consensus-based/adapted from NICE guideline**	**Strong Recommendation-high quality evidence**	**NEW**

	CBT, behavioral couples' therapy and individual or group supportive expressive therapies (CCO Modified)[18, 19].			

*** Definitions for National Comprehensive Cancer Network (NCCN) Categories:** The specific definitions of the NCCN categories for recommendations are *included below:*

Category 1*: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate;*

Category 2A*: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate;*

Category 2B*: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate;*

Category 3*: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.*

For the 'uniform NCCN consensus' defined in Category 1 and Category 2A, a majority Panel vote of at least 85% is required. For the 'NCCN consensus' defined in Category 2B, a Panel vote of at least 50% (but less than 85%) is required. Lastly, for recommendations where there is strong Panel disagreement regardless of the quality of the evidence, NCCN requires a vote from at least three Panel Members (representing at least three different Member Institutions) to include and designate a recommendation as Category 3. The large majority of the recommendations put forth in the Guidelines are Category 2A. Where categories are not specified within the Guidelines, the default designation for the recommendation is Category 2A[30].

Definition for NBCC-NCCI Categories: The specific definition of the NBCC-NCCI categories for recommendations are included below:

Level I *Based on a systematic review of randomized controlled trials (RCT).*

Level II *Based on a minimum of one properly designed RCT.*

Level III-1 *Based on well-designed pseudo-randomized controlled trials.*

Level III-2 *Based on "comparative studies with concurrent controls and allocation not randomized (cohort studies), case control studies, or interrupted time series with a control group".*

Level III-3 *Based on "comparative studies with historical control, two or more single-arm studies, or interrupted time series without a parallel group".*

Level IV *Based on "case studies, either post-test or pre- and post-test"..*

1.C Recommendation Summary- Cancer-Related Global Anxiety

1.C.1 Recommendation Summary- Management for Cancer-Related Global Anxiety

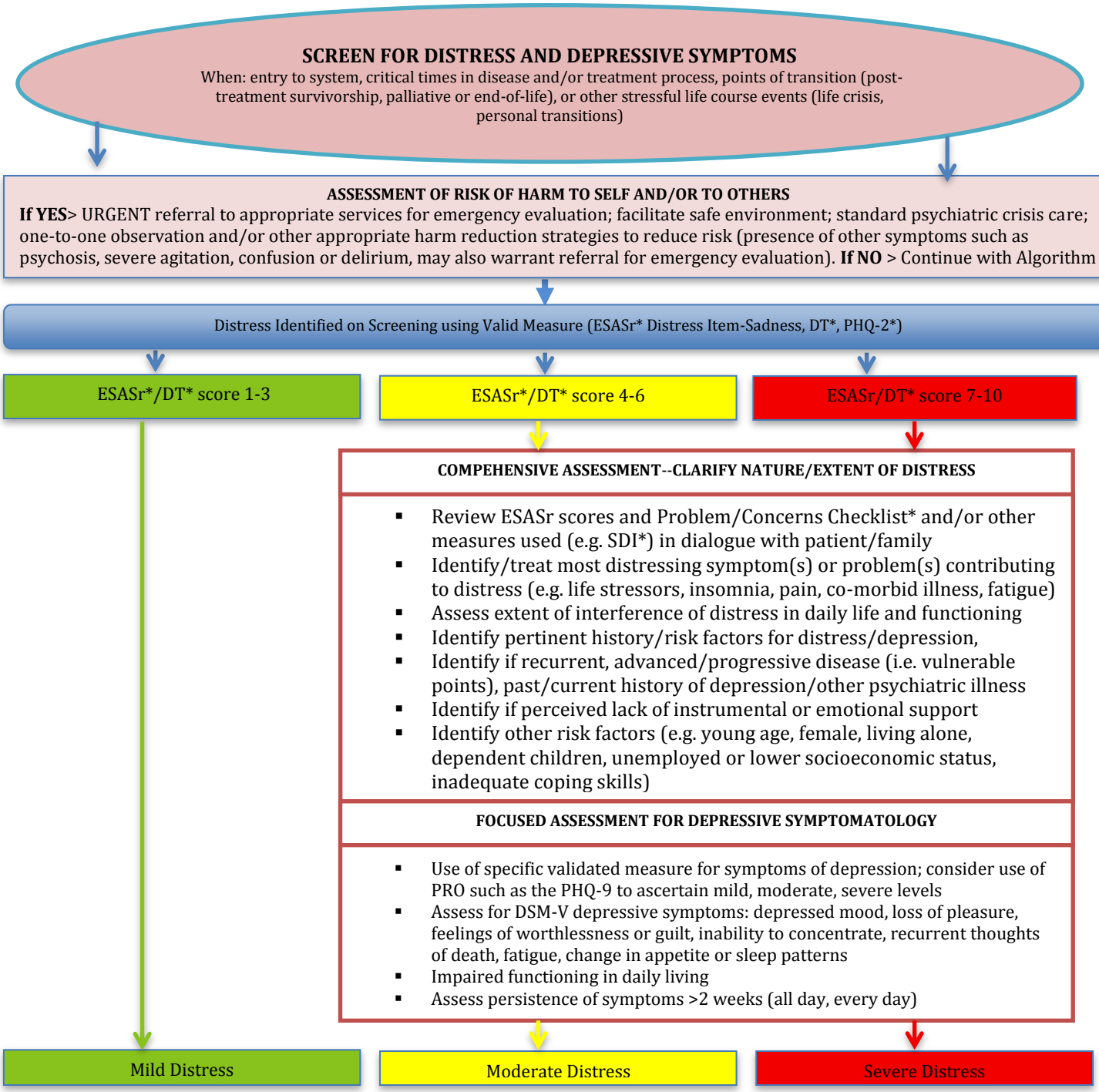
✔	No change was made to the previous recommendation as a result of the 2015 systematic review of the evidence, including clinical practice guidelines and RCTs.
✚	The recommendation and supporting evidence were updated based on the 2015 systematic review evidence, including clinical practice guidelines and RCTs.
NEW	A new recommendation was developed based on supporting evidence from the 2015 systematic review evidence, including clinical practice guidelines and RCTs.

Note: ✓ Minor changes were made to the global **anxiety** recommendations for improved clarity and consistency. The minor change also takes into account an evaluation of recommendations from high quality evidence-based clinical practice guidelines based on our most recent update in 2015. Recommendations for screening and assessment of distress in adults with cancer were identified based on the application of the ADAPTE methodology[1, 2], a rigorous 24 step method for adapting knowledge from existing guidelines following a quality appraisal in accordance with the AGREE II convention[3]. The ADAPTE methodology is a systematic process for adapting recommendations in existing guidelines to create high quality guidelines tailored for use in a specific health care context[2, 4],see detail on section 3.A.

Global Anxiety		Supporting Evidence in Guidelines/RCTs	Strength of Recommendation	Status
Low psycho-logical Intensity Inter-ventions	1. Cognitive Behavior Therapy interventions delivered by psychologists, psychiatrists or appropriately trained clinicians are likely to reduce cancer-related global anxiety[31, 32].	**Very Low**	**Strong Recommendation-low quality of evidence**	**NEW**
	2. Aromatherapy massage may be beneficial to treat global anxiety on a short-term basis[33].	**Moderate**	**Weak Recommendation-low quality of evidence**	**NEW**
	3. Brief cognitive behavioral therapy may be beneficial in reducing fear of recurrence but larger higher quality trials are needed[34, 35].	**Low**	**Strong Recommendation-low quality of evidence**	**NEW**
High intensity psycho-logical inter-ventions	4. Patients with mild or moderate global anxiety who do not respond to initial interventions require referral to psychosocial specialists for high intensity psychological interventions and/or pharmacologic management[9, 11, 12, 14].	**NCCN,1 NCCN,2A** **ADAPTED CCO Guideline**	**Strong Recommendation-high quality evidence**	**NEW**
Pharma-cological Treat-	5. Pharmacological treatment of anxiety may be necessary and the use of medications should be	**Consensus Based**	**Expert Consensus**	**NEW**

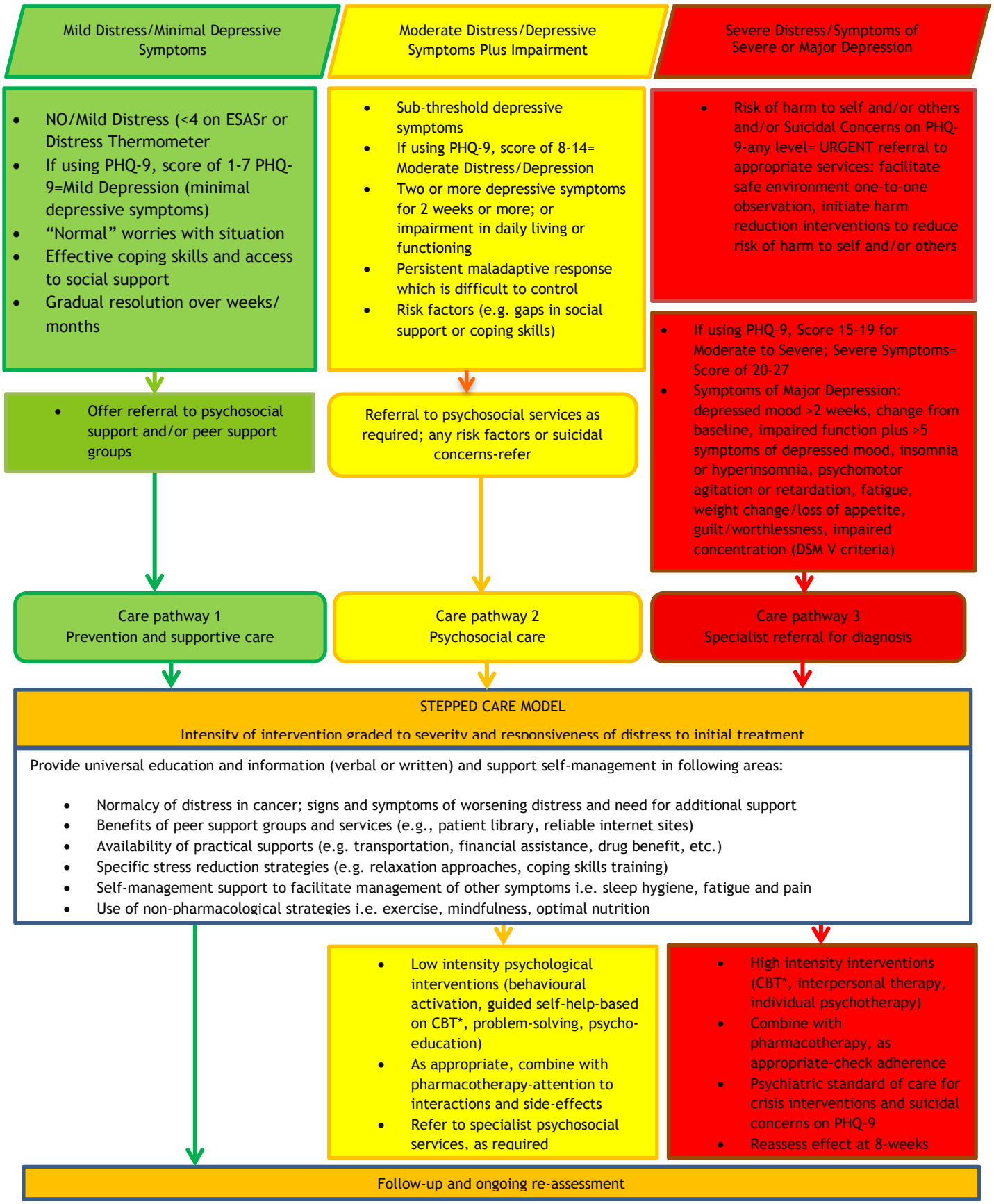
ment of Anxiety	based on severity of anxiety symptoms as well as potential for interaction with other cancer treatment medications[36].			
	6. Patients who exhibit symptoms of moderate to severe generalized anxiety may require a combination of pharmacological and psychological interventions delivered by a psychologist or psychiatrist training or appropriately trained clinicians.	**Consensus Based**	**Expert Consensus**	**NEW**

1.D Algorithms for Cancer-Related Distress, Depression, & Global Anxiety



ESASr=Edmonton Symptom Assessment Scale Revised; PHQ-9=Patient Health Questionnaire- 9 items; PHQ-2=2 item screener for depression; use of algorithm does not substitute for appropriate clinical judgment; Reference: Howell et al. Screening, Assessment and Management of Psychosocial Distress, Anxiety and Depression. Canadian Association of Psychosocial Oncology (CAPO) 2015.

CARE MAP-DISTRESS AND DEPRESSION IN ADULTS WITH CANCER



* CBT-cognitive-behavioral therapy;*major depression based on clinical interview or threshold depression on valid tool

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CANADIAN PARTNERSHIP AGAINST CANCER
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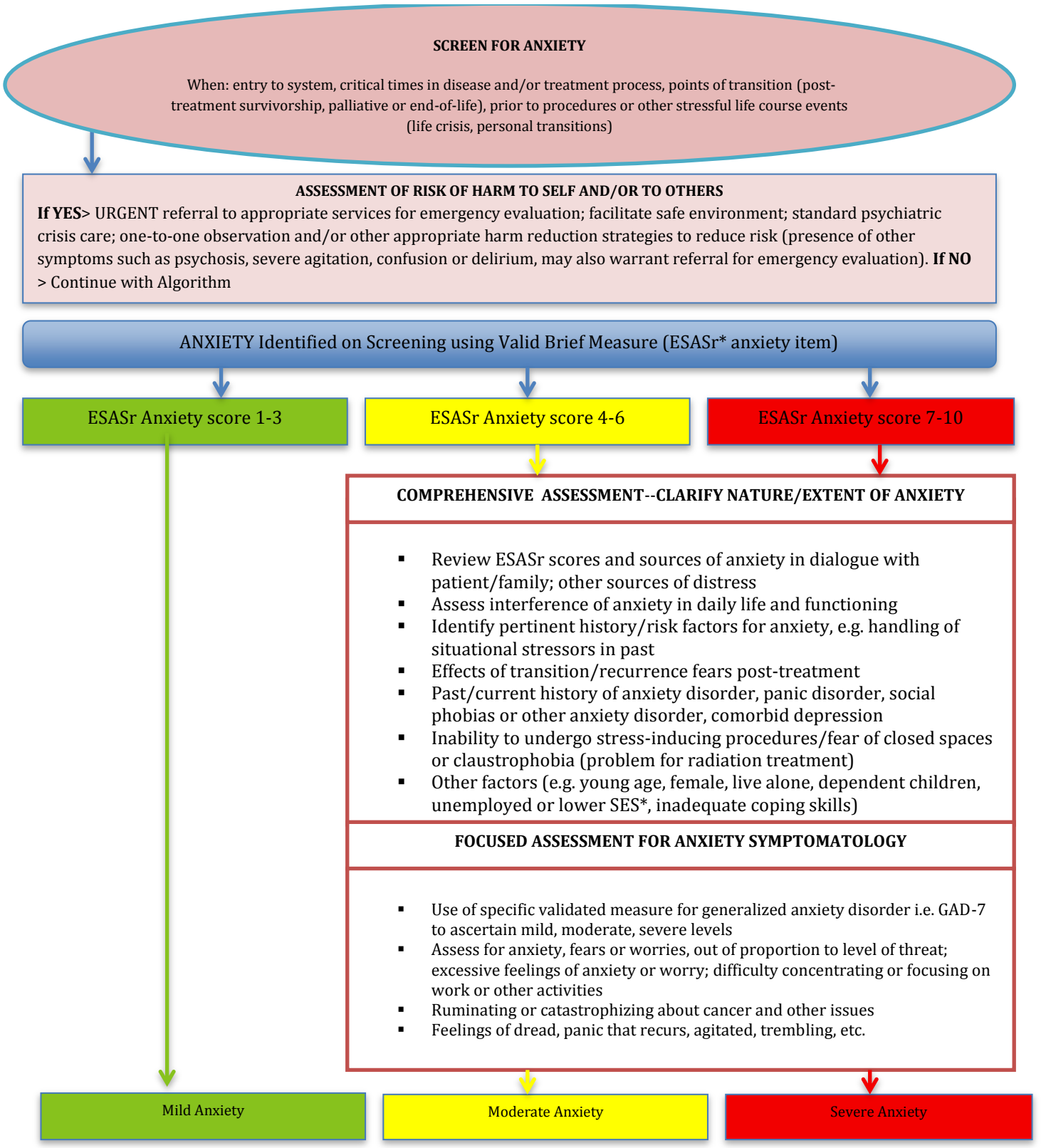

ESASr=Edmonton Symptom Assessment Scale Revised; GAD-7=Generalized Anxiety Disorder 7 items; *Socioeconomic status-SES; Team decides referral standard; Reference: Howell et al. Screening, Assessment and Management of Psychosocial Distress, Anxiety and Depression, Canadian Association of Psychosocial Oncology (CAPO) 2015. Use of algorithm does not substitute for appropriate clinical judgment.

Howell et al. Canadian Association of Psychosocial Oncology, 2015

REFERENCE-Howell et al. 2015 Distress Guideline, Canadian Association of Psychosocial Oncology

Reference: Howell et al. Screening, Assessment and Management of Psychosocial Distress, CAPO

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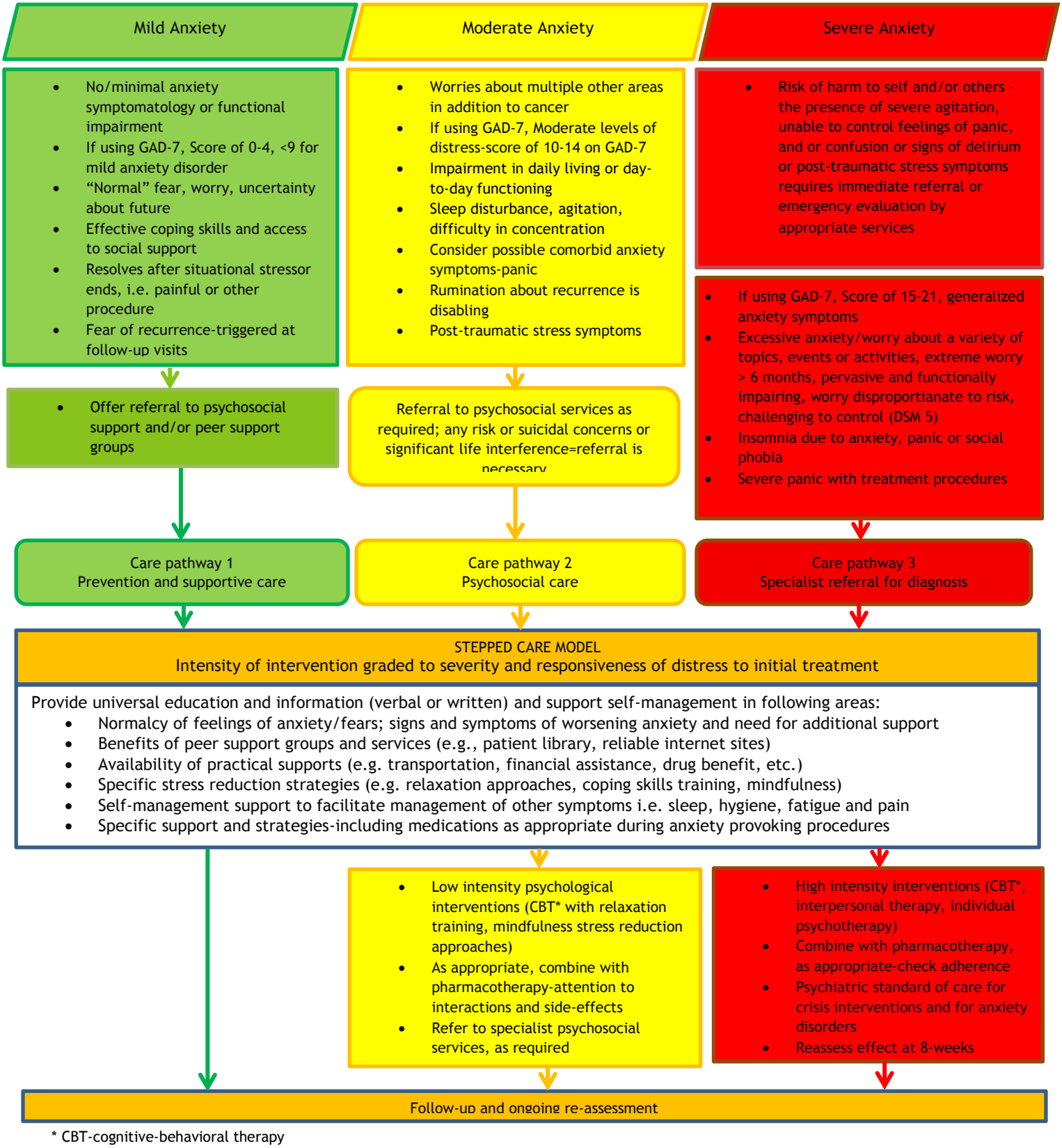
PARTENARIAT CANADIEN CONTRE LE CANCER

CARE MAP-ANXIETY IN ADULTS WITH CANCER



* CBT-cognitive-behavioral therapy

Figure 1.D.1: Algorithm for Cancer-Related Distress, Depression & Global Anxiety

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1.E Executive Summary

Background

A diagnosis of cancer and its treatment represent a significant threat to the well-being of an individual as a result of its life-altering and multi-faceted impact on the life of the individual and their family[37]. All people will experience some level of emotional distress in anticipation of a cancer diagnosis, during the early phases of cancer, and treatment, and at periods of vulnerability along the cancer journey continuum[11, 38]. There is now emerging evidence on early intervention or pre-emptive psychosocial interventions that target the prevention of distress such as preparatory education, and self-help online interventions that may help to support patients in developing adaptive responses to distress earlier[42]. Similarly, in cancer patients with advanced disease, early palliative care team interventions have become a focus to reduce symptom suffering and distress and interventions targeting specific problems such as demoralization and helplessness[43-45]. A review of this literature was beyond the scope of this guideline but future reviews to assess effectiveness of interventions along the continuum of cancer should include this evidence in future guideline updates.

Scope and Purpose of this Review

The objective of this review is to improve the quality and consistency of screening, assessment and management of distress, depression, and global anxiety across the cancer trajectory in adults (≥18 years of age). This guideline pertains to adult cancer patients experiencing cancer-related distress including global anxiety, post-traumatic stress disorder and those individuals with depression based on meeting a threshold for suspected depressive disorder on a validated depression rating scale or diagnosed with depression by structured diagnostic interview.

Intended Users

This practice guideline is intended to inform Canadian health authorities, program leaders and administrators, as well as health care providers engaged in the care of adults with cancer. The recommendations are applicable to care providers (i.e. oncologists, nurses, social workers, clinical counsellors, primary care practitioners) in diverse care settings. Since the scope of practice for various professions varies according to regulatory standards and laws, professionals using this guideline are

advised to exercise the skill and judgment that best reflects their responsibilities to determine if the recommendations are within their scope of practice. In addition, depending on the risk factors of distress, additional written guidelines and resources should be considered for more detailed evidence-based recommendations.

Questions

1. What are the current guideline recommendations for routine screening and assessment of Distress, Depression, and Global Anxiety in adults with Cancer?

2. What is the efficacy of interventions (pharmacological, non-pharmacological, and/or combinations) for reducing Distress, Depression, and Global Anxiety in adults with cancer?

i. Screening and Assessments of Cancer-Related Distress, Depression, and Global Anxiety

The 2010 Version 1 of the Guideline served was the evidentiary foundation of the current guideline that aims to update the previous guideline. Recommendations for screening and assessment for distress, depression, and global anxiety in adults with cancer were identified based on the application of the ADAPTE methodology[1, 2], a rigorous 24 step method for adapting knowledge from existing guidelines following a quality appraisal in accordance with the AGREE II convention[3].

ii. Management of Cancer-Related Distress, Depression and Global Anxiety

Methods

Our aim was to update A Pan-Canadian Practice Guideline: Screening, Assessment and Care of Psychosocial Distress (Depression, Global Anxiety) in Adults with Cancer[12].

Sources of Evidence:

We searched for existing evidence-based guidelines on screening, assessment, and management of Distress and global Anxiety in adults with Cancer from 2009 to May 2015. We selected any guideline published since the last literature update from Version 1 of the 2010 guideline. We also searched for systematic reviews for

potentially relevant citations (RCTs) that may not have been captured by the search. We further performed a systematic search of randomized control trials (RCTs) that evaluated the effects of any intervention on the management of distress and anxiety in adults with all types of cancer from 2009 to May 2015.

Literature Search Strategy

For the evidence-based guidelines and systematic reviews, and RCTs the search strategy was limited to studies published from 2009, to May 11, 2015. The following electronic bibliographic databases were searched: MEDLINE®, Cochrane Central®, PsychINFO, Cochrane Database of Systematic Reviews, EMBASE®, and CINAHL®.

Types of Participants (P)

Adults (aged 18 and over) with a diagnosis of cancer and identified as having clinically significant distress and/or anxiety.

Types of Interventions (I)

Any pharmacological or non-pharmacological (psychosocial, CBT, psychosocial or supportive education, mindfulness meditation, yoga, exercise/activity, complementary medicine, supportive expressive therapies) interventions used for the management of distress and anxiety in adult patients with cancer.

Types of Comparator (C)

Comparison condition is usual care, attention control or other comparator. Studies comparing drug treatment versus no drug treatment or versus alternative drug treatment, or both were also included.

Types of Outcomes (O)

1) Clinically significant improvement in distress and/or anxiety as measured by valid scales (included specific fear or worry-i.e. fear of recurrence) or
2) Clinically significant reduction in distress and/or anxiety as measured by valid scales (measured by severity) or
3) Differences in distress and/or anxiety severity between intervention group and controls using valid self-reported outcome measures for distress, anxiety or depression

Types of Studies

We included evidence-based guidelines based on systematic review evidence, systematic reviews of randomized controlled trials, and RCTs of interventions with cancer related Distress and/or anxiety as an (primary or secondary) outcome.

Assessment of Methodological Quality of Guidelines and Randomized Clinical Trials

We used the AGREE II to assess the variability in the quality of the guideline process[3]. We selected the Risk of Bias Tool by the Cochrane Collaboration[47] to assess RCTs. Criteria for evaluation are standardized for specified domains. Inconsistency amongst raters was minimized by providing adequate training and standardized instructions; disagreements were resolved by consensus.

Qualitative Synthesis

Study results were grouped according to the type of treatment categories and corresponding comparator treatment; the specific grouping of the pharmacological treatment; and nonpharmacological treatment. We grouped study results according to: 1) the specific grouping of the pharmacological treatment; and 2) non-pharmacological treatment.

Quantitative Synthesis

To perform meta-analysis, outcome measurement at the end of intervention or immediate post-treatment data (mean, standard deviation) was utilized. The DerSimonian and Laird random effects models with inverse variance method were utilized to generate the Standard Mean Deviation (SMD) for continuous outcomes[48]. The SMD was used as a summary statistic because the studies in this systematic review often assessed the same outcomes measured in a variety of ways. In this situation, it was necessary to standardize the results of the studies before they could be compared across studies or combined in a quantitative synthesis. SMDs were calculated using change from baseline data, i.e. mean difference between pre-treatment (baseline) and post-treatment (final/end-point) scores along with its standard deviation for both intervention and control groups. The SMD effect sizes with scores of 0.2–0.5, 0.5–0.8, and >0.8 were considered as small, medium, and large effects, respectively[49]. In studies where SD was not reported, we calculated SD from the reported SE of the mean, or 95% CIs. The Cochrane's Q (α=0.10) and I2 statistic were employed to

quantify the statistical heterogeneity between studies, where p<0.10 indicates a high level of statistical heterogeneity between studies.

Rating the Body of Evidence

For CPG, our recommendations are based on two sources of evidence: from existing guidelines we used an expert panel consensus method to evaluate levels of evidence and strategies to produce recommendations reported within these guidelines. Recommendations for screening and assessment for distress, depression, and global anxiety in adults with Cancer were identified based on the application of the ADAPTE methodology[1, 2], for adapting knowledge from existing guidelines following a quality appraisal[3].

For RCTs, we formulated standardized 'effectiveness statements' to rate the evidence found for the management of Psychosocial Distress (Depression and Global Anxiety) in Adults with Cancer, using the overall Strength of the Evidence (SOE) of randomized control trials (RCTs) across the literature using the rating approach as specified by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Methodology [5-7]. We also formulated standardized 'effectiveness statements' to rate the evidence arising from the systematic review of evidence for the management of Psychosocial Distress (Depression and Global Anxiety) in Adults with Cancer, using the overall Strength of the Evidence (SOE) of randomized control trials (RCTs) across the literature using the rating approach as specified by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Methodology[5-7] .The internal panel review independently developed the recommendation statements by consensus, based on a detailed review of the evidence.

Results & Conclusion

Distress

Psychosocial Interventions

The combined data from 8 studies that were identified showed that generic psychosocial interventions had no significant effect on distress among patients with cancer as compared to control group. (SMD = - 0.3029; 95% CI -0.6823 to 0.0765). The overall quality of this evidence was rated as moderate and downgraded due to concerns regarding imprecision.

Low-intensity interventions or psychosocial interventions, such as psycho-education, generally perform well and are mostly beneficial for addressing lower levels of distress[22].

Novel interventions, such as art therapy modes, integrated with interventions including opportunities for emotional expression with some guidance, combined with peer components can address moderate to higher levels of distress[22, 23, 28]. There is also some evidence that online facilitator led-support groups are beneficial in improving distress[27].

Cognitive Behavioral Therapy Interventions

The evidence for efficacy of CBT to reduce emotional distress was inconsistent. The one study identified indicated that when cancer patients are first screened for significant distress at study entry, CBT is effective in improving global anxiety, depression and/or distress.

Complementary Interventions

This systematic review identified no eligible studies for complementary interventions on distress since the previous version of this guideline.

Pharmacotherapy

This systematic review identified no eligible studies for pharmacotherapy of distress since the previous version of this guideline.

<u>Global Anxiety</u>

Fear of Cancer Recurrence – Supportive-expressive therapy (SET)

We identified one clinical controlled trial (CCT) assessing the effect of SET compared to a control group[34] in a sample of cancer patients with significant fear of recurrence. The results from this CCT suggest that brief SET may be effective at reducing fear or cancer progression post cancer treatment. However firm conclusions cannot be drawn in terms of SET effects on global anxiety, depression or QoL given the lack of control data in this study. Further research in this area is required.

Fear of Cancer Recurrence – CBT

Our search identified one CCT that assessed CBT compared to a control group[34] in a sample of cancer patients with significant fear of progression. The results from this

CCT suggest that brief CBT may be effective at reducing fear of cancer progression in cancer patients post-treatment and that the effects may last for up to 1 year. No conclusions can be drawn about CBT effects on global anxiety, depression or QoL given the lack of control data.

Pharmacotherapy

This systematic review identified no eligible studies for pharmacotherapy of global anxiety since the previous version of this guideline.

Cognitive behavioral interventions

Our search identified 2 eligible CBT RCTs for the treatment of cancer-related distress in adults. The combined data from the 2 studies showed that CBT had no significant effect on global anxiety among patients with cancer as compared to control group. (SMD = - 0.3173; 95%CI -0.1400 to 1.3798). The overall quality of this evidence was rated as very low and downgraded due to concerns regarding risk of bias, inconsistency and imprecision.

Pharmacological and Psychological Interventions for Cancer-Related Depression

We identified a recently completed Cancer Care Ontario (CCO) depression guideline entitled *The Management of Depression in Patients with Cancer*[18]; the expert panel adopted recommendations from this guideline in the absence of more recent additional evidence. This systematic review concluded that there is a dearth of high-quality pharmacotherapy or psychotherapy research on the treatment of depression in patients with cancer. Although the meta-analyses indicated cancer patients with depression may benefit from a variety of interventions, there is insufficient evidence at present to support the superiority of any specific treatment over another.

Psychosocial Intervention on Cancer-Related Post-Traumatic Stress Disorder (PTSD)

There is increased focus on providing brief interventions/psychosocial sessions for individuals with cancer-related global anxiety and post-traumatic stress symptoms across the cancer journey. One recent RCT with cancer patients highlight the value of such brief interventions.[55] The study examined the effectiveness of an online cognitive behavioral stress management workbook intervention for breast cancer patients with at least moderate distress, relative to a waitlist control group. The results provide support for the usefulness of internet based psychosocial intervention

for distressed cancer survivors who have cancer-related post-traumatic symptoms. However, the overall quality of this evidence was rated as low and downgraded due to concerns regarding risk of bias.

CBT intervention on Cancer-Related Post-Traumatic Stress Disorder (PTSD)

We identified two studies on the treatment of PTSD in cancer patients that showed that CBT when compared with usual or standard care was not substantially different in terms of reducing PTSD or global anxiety symptoms [31].

1.F Lay Summary

Most patients with cancer experience some levels of emotional distress after their diagnosis that may affect many aspects of their lives. There is some evidence to suggest that early psychosocial interventions to prevent distress may help patients to develop coping strategies in response to distress earlier that may reduce suffering and distress along the cancer journey continuum. The aim of this review is to improve the quality of screening, assessment, and treatment of distress, depression, and global anxiety in adults with cancer. The guideline is aimed at health care professionals including oncologists and nurses as well as patients with cancer and their families to help them learn about the most effective strategies, for dealing with distress and global anxiety due to cancer. We identified studies that tested the effectiveness of pharmacological and non-pharmacological interventions (e.g. exercise, yoga, mindful meditation etc.) in reducing distress and global anxiety due to cancer. We then evaluated the quality of these studies and an expert panel of health care professionals formulated their recommendations based on the results of these studies.

Low-intensity Psychosocial and psycho-educational interventions and especially tailored physical activity interventions (e.g. tailored exercise) have shown some benefit for lower levels of distress in cancer. However they are less effective than more intensive or psychotherapeutic interventions such as cognitive behavioral therapy for those with moderate or severe distress. Moreover, novel therapies such as those that involve emotional expression with some guidance and peer components may help alleviate moderate to higher levels of distress. However, there is dearth of evidence for effectiveness of pharmacotherapy for reducing cancer-related distress. Similarly there is a lack of studies on the effectiveness of pharmacotherapy to manage cancer-related global anxiety. For cancer-related post-traumatic stress disorder (PTSD), internet-based psychosocial interventions has been shown to be somewhat effective but cognitive behavioral therapy was not found to be effective in reducing PTSD symptoms. However, this evidence is based on a very small number of studies. More studies are needed to examine treatment strategies for managing distress and global anxiety in persons with cancer.

2 Introduction

A diagnosis of cancer and its treatment represents a significant threat to the well-being of an individual as a result of its life-altering and multi-faceted impact on all aspects of a person's life and that of their family and/or significant others[37]. All adults will experience some level of emotional distress (also labeled psychosocial distress or distress) in anticipation of a cancer diagnosis, during the early phases of cancer, and treatment, and at periods of vulnerability along the cancer journey continuum[11, 38]. Particular periods of vulnerability to distress include the time of diagnosis, the start of active treatment, recurrence[39, 40] and transition to post-treatment survivorship, particularly when worrying cancer might return (fear of recurrence), and during the palliative care and end-of-life phase of cancer[11, 41].

Most cancer patients will be able to adapt by making the changes necessary to manage a cancer diagnosis and the effects of cancer treatment when they have access to effective, supportive and psychosocial care that assists them to cope well and solve problems related to cancer[21]. These patients may exhibit low levels of emotional distress (normal adjustment) and thus do not meet the diagnostic criteria for any specific mental disorder. Consequently, there is now emerging evidence on early intervention or pre-emptive psychosocial interventions that target the prevention of distress such as preparatory information or education, prompt sheets or use of consultation recordings, and self-help online interventions that may help to prevent or reduce distress and support patients in developing adaptive responses earlier in the cancer journey[83]. Similarly, in cancer patients with advanced disease, interdisciplinary palliative care team interventions has become a focus for intervention earlier in the course of non-curative, life threatening illness to reduce symptom suffering and distress and other interventions targeting specific problems in this phase of the continuum such as demoralization and helplessness[43-45]. A review of this literature was beyond the scope of this guideline but future reviews to assess effectiveness of interventions along the continuum of cancer may be important to future guideline updates.

However, many patients do experience difficulty in adjusting to a cancer diagnosis and treatment, and consequently can experience a variety of difficult emotional responses and more severe levels of distress[84-86]. Adjustment or psychosocial adaptation to cancer has been defined as an ongoing process in which the patient tries to manage emotional distress, solve specific cancer-related problems, and gains mastery or control over cancer-related life events[86]. It is not a unitary, single event but rather a series of ongoing coping responses to the multiple tasks associated with living with a life-threating disease such as cancer[11].

Cancer—related distress is defined as, "a multifactorial unpleasant emotional experience of a psychological (cognitive, behavioral, emotional), social or spiritual nature that may interfere with the ability to cope effectively with cancer, its physical symptoms and its treatment. Distress extends along a continuum, ranging from common normal feelings of vulnerability, sadness, and fears to problems that can become disabling, such as depression, global anxiety, panic, social isolation, and existential and spiritual crisis[11]. The level of distress can vary based on points of vulnerability along the cancer journey, the clinical course and phase of cancer and treatment (diagnosis, treatment, surgery, radiation, chemotherapy, immunotherapy, personalized medicine), life situation, life cycle of the individual and family[41] and other risk factors[12]. Moreover, distress occurs on a continuum from low levels of distress to high levels of distress as shown in Table 2.1.

As noted by Holland (2014) distress exists along a continuum from feelings of sadness and vulnerability to more significant levels of distress or states of clinical depression or global anxiety. Distress may be identified based on the clinical presentation shown in Table 2.1 on a continuum from low to moderate or high distress. Patients with distress may express fear, worry, uncertainty about the illness and future, sadness, anger, poor sleep, poor appetite, poor concentration, pre-occupation with thoughts of illness and death, and concerns about roles and relationships. Such distress may require psychosocial and supportive care or specific medications to manage symptoms[11].

Table 2.1: Psychosocial Distress Continuum

Low Distress	Moderate to High Distress
Feels connected to others	Feels outcast and alone
Belief things will get better	Feeling of permanence
Can enjoy happy memories	Past guilt, regret
Sense of self-worth	Self-deprecating
Comes in waves	Constant and unremitting
Looks forward to things	Hopeless
Can still enjoy things	No interest
Will to live	Suicidal
Specific worries	Unfocussed anxiety
Can see positives and negatives	Catastrophizes
Able to make decisions	Unable to engage in cancer treatment

As noted earlier, many patients will experience distress in the less severe end of this continuum. Prevalence rates for distress vary across studies depending on the measure used; rates range from 22-58% in studies that have used the distress thermometer (DT) using a cut-off score of 4 or 5 and approximately one-third of ambulatory cancer patients report moderate or severe depression (score >3) when the Edmonton Symptom Assessment System revised[87] (Numerical Rating Scale; 0-no depression to 10-worst level of depression) is used[88] across a range of cancer

populations [10, 88-91]. Higher rates are noted for palliative populations[92]. Pooled results from multiple studies suggest that about 40% of patients will experience more significant levels of distress (above 4 or 5 in the DT)[93].

Emotional distress has also been reported for post-treatment survivors with common areas of distress including anxiety about recurrence (or fear of progression), increased sense of vulnerability, post-traumatic stress like symptoms and concerns about body image and sexuality or physical symptoms such as ongoing fatigue[94]. There are certain risk factors for serious distress (Box 1) in cancer populations including cancers associated with a poor prognosis (lung, pancreas, brain), and severe physical symptoms or treatment side effects[12].

Box 1: Some of the Risk Factors for Distress

- **Living/ Family condition:** living alone, dependent, financial problems (poor socioeconomic status), change in family status[12]
- **Marital status:** single, separated, divorced or widowed[12]
- **Withdrawal statues:** alcohol, substance use[12]
- **Vulnerable points:** disease recurrence, advanced or progressive disease (metastases), moving toward palliative or hospice care, cumulative stressful life events, change in functioning or roles[12]
- **Past Medical and Psychological History:** panic attacks, Generalized Anxiety Disorder (GAD), history of depression, history of mood disorder, history of other psychiatric disorder[12]
- **Medical conditions:** co-morbidity (severe illnesses), prolonged treatment phase, cognitive impairment, surgical interventions, treatment side effects, current medication associated with anxiety or depression or seeing a specialist[12]
- **Other factors:** younger age, female, lack of social support, poor marital or family functioning, poor communication with the health care team, lack of supportive network, poor control of pain or other symptoms, family/caregiver conflicts, communication barriers, catastrophizing coping or anxious coping style (language, literacy, physical)[12]

Cancer-related depression can present as several diagnostic entities in the DSM-V. Box 2 aligns the most common DSM-V (Diagnostic and Statistical Manual of Mental Disorders American Psychiatric Association (APA),2013[95]) depressive disorder diagnoses along the depression severity continuum (adapted with permission from Li et al[18]). Sub-threshold depression refers to depressive symptoms that cause significant distress or impairment, but do not meet criteria for the diagnosis of depression in terms of the symptom number and/or duration criteria. These disorders include depressive episode with insufficient symptoms (formerly “minor depression”) and persistent depressive disorder (formerly “dysthymia”). Substance/medication-induced depressive disorder (i.e., often corticosteroids, interferon-alpha or interleukin-2) in cancer patients and depressive disorder due to another medical condition (i.e., cancer) are other relevant diagnoses, although their management is often the same as for depression.

Box 2: Features Distinguishing the Continuum of Depression

Normal Sadness	Adjustment Disorder	Sub-threshold Depression	Major Depression
• Sadness specifically associated with thoughts of cancer • Retains hope and capacity for pleasure • No functional impairment	• Marked distress or functional impairment but not meeting other criteria for depression • Not specifically defined • Distinction from sub-threshold depression may be arbitrary • Often transient and self-limited	• Similar low mood presentation as depression but not meeting full criteria for symptom number or duration • Includes persistent depressive disorder if > 2 years duration • Includes episodes lasting < 2 weeks	• Meets DSM-5 diagnostic criteria of 5/9 depressive symptoms, including either low mood or anhedonia • Symptoms present for at least 2 weeks • Clinically significant functional impairment

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Rates of depression vary across studies based on the measures used, with pooled rates of 8-24% reported. Rates differ by use of self-report instruments or diagnostic interviews, type of cancer and treatment phase[96]. In systematic reviews with meta-analysis, about 10.8%[97] and 12.9%[98] of cancer patients meet DSM diagnostic criteria for major depressive disorder, with about 16% sub-threshold depression [98]. Similar rates have been reported in other studies (range of 5.6% gynecological cancer compared to a lung cancer rate of 13.1% [99]; and 13% across all types of cancer)[100].

Cancer-related global anxiety is a common situational response to the threat of cancer or critical events that can occur across the cancer trajectory, i.e. response to cancer pain, undergoing a screening test or waiting for results of these or follow-up test after cancer treatment, transition from acute phase of treatment to post-treatment survivorship, or anticipating a recurrence[34, 101, 102]. Symptoms of anxiety include feelings of apprehension, powerlessness, and loss of control, worry, fear and dread and often accompanied by physiological symptoms such as accelerated heart rate and respiration, tremor, sweating, muscle tension and gastrointestinal upset[103]. Studies suggest that most patients will experience anxiety at some point along the cancer continuum as part of normal adaptation to cancer; 44% of patients with cancer reported some anxiety with 23% reporting significant anxiety[104]. Anxiety reactions that are more prolonged or intense can be classified as Adjustment Disorder or one of several anxiety disorders. DSM-5 anxiety disorders include specific phobias, panic disorder, agoraphobia, obsessive-compulsive disorder, generalized anxiety disorder-GAD, or social anxiety disorder. These anxiety disorders are not frequently diagnosed

in cancer patients unless they are pre-existing or are based on personality and other life circumstance variables (see definitions)[10].

The more common anxiety associated with cancer may be more accurately diagnosed in the DSM-5 as either Unspecified Anxiety Disorder or Anxiety Disorder due to Another Medical Condition[105], captured in this guideline under the term Generalized Anxiety Distress

Emotional Distress Screening and Management:
It is important to address the psychosocial distress associated with cancer and its treatment at all phases of the cancer continuum. Untreated psychosocial distress that remains high and occurs repeatedly over a long period of time may affect a person's overall health, ability to cope with cancer, and has been shown to be associated with lower rates of treatment adherence, worse physical symptom severity, higher health care costs, suicide, desire for hastened death, worse functioning and higher rates of mortality and distress may worsen over time when left untreated [106-110].

Primary oncology teams need to be able to support cancer patients (and their families) in the management of distress, solving specific cancer-related problems, and support their ability to gain mastery or control over cancer-related events, cope effectively, and manage specific problems, such as situational distress, i.e. anxiety in response to events along the cancer continuum. This requires primary oncology teams to have knowledge and skills to integrate the provision of supportive and psychosocial care into routine cancer practice to prevent and reduce distress as appropriate within their scope of practice. They need to be able to distinguish normal adjustment or cancer sadness issues from more serious mental health problems, such as sub-threshold or depression in order to ensure appropriate referral to specialists for management (i.e. psychologists, psychiatrists, or other mental health professionals).

In Canada, screening for distress has been recommended as a standard of care and the Minimum Data Set for screening programs recommended is the Edmonton Symptom Assessment System Scale Revised (ESASr) and the Canadian Problem Checklist [111, 112]. The ESASr has now replaced the word depression with the word sadness as anchors on one of the 0-10 severity scales. Consequently, this guideline makes recommendations for management of distress and global anxiety to inform the primary oncology team. But has also adopted recommendations from a provincial guideline for the management of depression to ensure pan Canadian recommendations address distress and depression along the continuum, as defined by the NCCN[11] and the American Psychiatric Association.

Stepped Care Model:

Stepped care is a type of health care delivery model, graded to a patient's symptom severity. This system is based on two major principles; the effective intervention which is recommended to the patient should be 1) the least restrictive and; 2) the least costly[19, 113]. Patients with chronic disease may have some problems accessing or receiving the appropriate treatment. A stepped care model was identified by the National Institute for Health and Clinical Excellence for managing patients with depression [19]. Based on the NCCN, 2015 recommendations to reduce the stigma associated with emotional distress and that this was not viewed as a pathological state, the term distress was adopted to replace the word psychological distress or labels such as depression. Thus, the stepped-care model has been adapted for cancer populations using the term distress [114]. See Figure 2.1.

The stepped care model generally suggests low-intensity interventions in the first few steps. However, if the patient's condition does not improve, they will be stepped-up to a higher-intensity intervention. Providing higher level of care to address the increasing level of distress[19]. The initial level of care, or Universal level, which addresses minimal to mild distress for anxiety in CCO Tiered Model of Psychosocial Care, provides informational and practical support; for example, a toll free helpline or support service staffed by oncology nurses and other health professionals. Mild to moderate distress, is addressed by the second level of care, the Supportive care level. Care at this level involves emotional and peer support provided by a nurse counsellor and through a cancer helpline. At the Moderate distress level, extended care, counselling and coping skills training is be provided by a cancer counselling service or a nurse counsellor. At the next level, Specialist Care, for patients experiencing moderate to severe distress is specialized therapy for depression, anxiety, and relationship problems is provided by a cancer counselling service. At the final stage, the Acute care level, that involves the need to manage severe distress, intensive or comprehensive therapy for acute and complex problems is provided by the mental health team and psychiatrists[114].

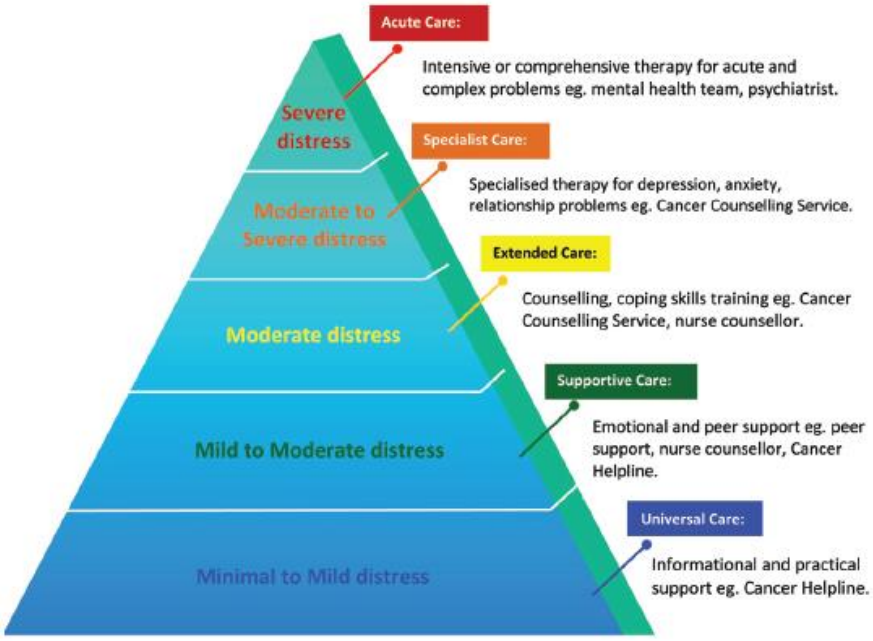

Figure 2.1: Tiered model of psychosocial care[114]

Thus, to provide guidance to interdisciplinary primary oncology providers in the screening, assessment and management of psychosocial distress, this is an update to the previous 2010 guideline, "A Pan-Canadian Practice Guideline: Screening, Assessment and Care of Psychosocial Distress (Depression, Global Anxiety) in Adults with Cancer"[12] was included.

We have updated this earlier guideline by conducting a systematic review of the empirical and grey (guideline specific) literature on the pharmacological and non-pharmacological or psychosocial interventions (i.e. coping skills training, psychosocial, cognitive-behavioral therapy, supportive therapeutic counseling, supportive-expressive therapy, exercise), and complementary therapies (i.e. yoga, mindfulness). This 2015 version of the guideline is focused on the development of recommendations for health care professionals for the screening, assessment and management of distress in cancer including (global distress including global anxiety and more serious levels of distress, (i.e. sub-threshold depressive symptoms or depression). Recommendations for fear of recurrence and post-traumatic stress distress are special form of distress often labeled under the umbrella of global anxiety adjustment disorders, and have also been included within the scope of this guideline when specific interventions were identified for addressing these specific problems. 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 inter-professional psychosocial and guideline development experts.

Glossary of Terms

Cancer-Related Distress: Is defined according to the NCCN as "...a multifactorial unpleasant emotional experience of a psychological (cognitive, behavioral, and emotional), social, and/or spiritual nature that may interfere with the ability to cope effectively with cancer, its physical symptoms and its treatment. Distress extends along a continuum, ranging from common normal feelings of vulnerability, sadness, and fears to problems that can become disabling, such as depression, global anxiety, panic, social isolation and existential and spiritual crisis[11]." The terms generalized or global distress is often used interchangeably in the literature as an overarching term for cancer-related distress. The term distress has become widely accepted in the cancer field, as it is less stigmatizing than the terms psychosocial or psychological distress, and since distress is considered a normal response to a cancer diagnosis and treatment, that can be measured by self-report[11]. We adopted the term distress, as this is a more useful term in the day-to-day practice of clinicians; and may help to sensitize primary oncology teams and primary care physicians regarding the important role they play in management of distress. It is hoped that the updated guidelines will help in recognition of these responses, and the need for early intervention, as well as have the possible impact of reducing secondary disability and the risk of developing a depression. In Canada we have included physical symptoms related to cancer diagnosis and treatment in our screening, assessment and management of distress (e.g. dyspnea, pain, nausea, fatigue)[72, 115].

Fear of Recurrence: Fear of Recurrence is defined as the fear of cancer returning or progressing. This type of distress is commonly reported as an issue for post-treatment survivors. It is characterized as heightened-health related anxiety, symptom vigilance, worries about risk of recurrence, fears of shortened life span[116].

Depression (MDD): depression refers to a syndrome characterized by at least five symptoms, one of which is depressed mood or loss of interest in nearly all activities for at least 2 weeks as per DSM-V (see Box 3). The other symptoms include appetite or sleep disturbance, psychomotor agitation or retardation, decreased energy, feelings of worthlessness or excessive guilt, difficulty thinking or concentrating, and recurrent thoughts of death or suicidal ideation. Depression can manifest in mild, moderate or severe forms, depending on the intensity of the symptoms and functional impairment. Minor depression can be diagnosed when only 2-4 of these symptoms are present for at least 2 weeks. For, dysthymia, 3-4 symptoms are present continuously for a period of at least 2 years. On the milder end of the depressive continuum are adjustment disorder and normative sadness, which do not have specific diagnostic criteria. In this

guideline we defined major depressive disorder based on the CCO guideline definition and it was defined as meeting a threshold (cut-offs or significant depression or depression) for depressive disorders based on a validated depression rating scale or by diagnostic interview. For example, measures such as the PHQ-9, HADS, or BDI-II (cut-offs for or by structured diagnostic interview) that are commonly used to assess for depressive symptomatology and enable classification of depressive symptoms into mild, moderate, severe or other measures of depressive symptomatology[18].

I. Box 3: DSM-5 diagnostic criteria for a major depressive episode (A and B criteria only)*	
C. At least 5 of the following symptoms, present during the same 2-week period, representing a change from previous functioning, each present nearly every day; at least one of the symptoms is either (1) or (2). **Note**: Do not include symptoms that are clearly attributable to another medical condition. **10.** Depressed mood most of the day **11.** Markedly diminished interest or pleasure in almost all activities most of the day **12.** Significant weight loss or gain (change of >5% in a month), or decrease or increase in appetite **13.** Insomnia or hypersomnia **14.** Psychomotor agitation or retardation **15.** Fatigue or loss of energy **16.** Feelings of worthlessness or excessive or inappropriate guilt **17.** Diminished ability to think or concentrate, or indecisiveness **18.** Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation, or a suicide attempt or plan D. Symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning	
II. DSM-5 depression severity criteria	
Sub-threshold depressive symptoms	Fewer than five symptoms of depression
Mild depression	Few, if any, symptoms in excess of the minimum required to make the diagnosis and symptoms result in only minor functional impairment
Moderate depression	Symptom number/intensity or functional impairment are between 'mild' and 'severe'
Severe depression	Most symptoms and the symptoms markedly interfere with functioning. Can occur with or without psychotic symptoms

Global Anxiety: In this guideline we have adopted the term global anxiety and operationally defined anxiety as occurrence of anxiety (score of 4 or higher on the ESASr) or meeting a cut-off for anxiety symptomatology on a validated self-report scale for anxiety symptoms (HADS-A, BAI, GAD-7). The use of the word "anxiety" refers to symptomatology measured as generalized anxiety on a validated self-report scale for anxiety symptoms and not to a clinical diagnosis of anxiety disorder(s) confirmed by a psychologist or psychiatrist. The "anxiety" we refer to in this guideline refers to anxiety, worry, or anxiety-related symptoms that cause clinically significant distress as measured on a validated self-report scale for anxiety symptoms. We have adopted the definitions and classification of anxiety as per the American Society of Clinical Oncology[10] as follows:

None or Mild Anxiety: None or mild symptoms of anxiety, no or minimal functional impairment, effective coping skills and access to social support.

Moderate Symptomatology: Anxiety that presents as worries or concerns re: cancer but also multiple other areas; fatigue, sleep disturbances, irritability, and concentration difficulties may also be present, functional impairment from mild to moderate, may have comorbid anxiety symptoms of panic or social phobia.
Moderate to Severe Symptomatology: Anxiety symptoms interfere moderately too markedly with functioning, symptoms do not respond to low intensity interventions (education, guided self-help (or computerized) based on CBT principles, other psychosocial interventions (i.e. coping skills training or psycho-education), or combined pharmacological treatment.

As noted in the NCCN definition for distress, anxiety is considered one of the emotional responses in a distress response. Anxiety, fear and/or worry are normal adaptive responses to a cancer diagnosis that can increase in severity at different time-points along the continuum of cancer as stressors and perception of threats change. It manifests as an emotional state (symptoms include anxiety, worry, apprehension, and/or dread) and an affect from an observers perspective (nervousness, shakiness, tremulousness). Anxiety, is thus dynamic, and can range from mild to severe and fluctuate at critical points and in response to different situations, such as waiting for a screening test, test results, undergoing treatment or anticipating recurrence (often called situational anxiety)[117]. Situational or existential anxiety is differentiated from psychiatric or organic anxiety[117].

Box 4: Anxiety Symptoms

• **Emotional States**
  ○ Anxiety
  ○ Worry
  ○ Apprehension
  ○ Dread
• **Observer Perspective**
  ○ Nervousness
  ○ Shakiness
  ○ Tremulousness

Anxiety symptoms that become excessive and uncontrollable, require no specific external stimulus, and manifest with a wide range of physical and affective symptoms as well as changes in behavior and cognition, and may meet Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition[95] for an adjustment disorder with anxious mood or a specific anxiety disorder. As outlined in the Diagnostic and Statistical Manual of Mental Disorders, fifth edition, text revision (DSM V-TR), anxiety disorders include a diverse group of disorders: global anxiety disorder, social anxiety disorder

(also known as social phobia), specific phobia, panic disorder with and without agoraphobia, obsessive-compulsive disorder (OCD), posttraumatic stress disorder (PTSD), anxiety secondary to medical condition, acute stress disorder (ASD), and substance-induced anxiety disorder (see Box 4).

Table 2.2: Anxiety Disorders and Example Presentations in Adults with Cancer

Disorder	Summary of DSM-IV Diagnostic Criteria	Example Presentations in Cancer
Generalized anxiety disorder	≥ 6 months of excessive anxiety/worry about multiple events/activities Worry is difficult to control and is associated with symptoms such as restlessness, fatigue, poor concentration, irritability, tension, poor sleep Disturbance is impairing and/or distressing	Cancer-related worries shift from one topic to another, including both major and minor concerns Difficulty focusing on other tasks because of apprehension or worry
Panic disorder	Recurrent unexpected panic attacks ≥ 1 month of persistent worry about future panic or consequences of panic, or behavior change related to panic	Avoidance of physical activity or self-care behaviors that might increase heart rate or shortness of breath
Agoraphobia	Fear of places/situations in which escape may be difficult or help for panic may not be available Places/situations are avoided or endured with distress or fear of having a panic attack	Marked difficulty in leaving home alone and/or traveling to oncology visits
Specific phobia	Persistent fear of a specific object or situation Exposure provokes immediate anxiety Person acknowledges fear as excessive or unreasonable and impairing/distressing	Strong vasovagal response to specific event such as blood draw Panic attack in anticipation of specific medical procedure
Social anxiety disorder	Persistent fear of social or performance situations Exposure provokes anxiety or panic Patient acknowledges fear as excessive or unreasonable and impairing/distressing	Avoidance of situations in which patient may be center of attention Marked fear of embarrassment in front of medical staff
Obsessive-compulsive disorder	Recurrent, intrusive thoughts/images, with persistent attempts to ignore or suppress them via a neutralizing thought or action Repetitive, rigid behaviors that person is driven to	Intrusive, distressing thoughts about medical contamination, with persistent behaviors (e.g., repetition of specific phrases) to

	perform to reduce distress/threat, although behaviors are not realistically connected to threat Patient acknowledges disturbance as excessive or unreasonable and impairing/distressing	neutralize threatening thoughts Compulsive checking or arranging of medications
Acute stress disorder	Experience of a traumatic event Persistent and impairing symptoms in four domains 1 month after trauma: • Dissociation (e.g., numbing, derealization) • Re-experiencing (e.g., intrusive thoughts) • Avoidance • Hyper arousal (e.g., tension, hypervigilance) Patient acknowledges disturbance as impairing/distressing	Derealization or lack of emotional responsiveness during receipt of a cancer diagnosis or news about worsening prognosis Irritability, hypervigilance, and difficulty sleeping soon after a traumatizing cancer-related event
Post-traumatic stress disorder	Experience of a traumatic event Persistent and impairing post-trauma symptoms in three domains for 1>month: • Re-experiencing (e.g., intrusive thoughts) • Avoidance/numbing • Hyper arousal (e.g., tension, hypervigilance) Patient acknowledges disturbance as impairing/distressing	Avoidance of places or situations that trigger reminders of cancer-related events Difficulty discussing cancer-related events with others Marked physical and emotional distress during oncology clinic visits

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Post-Traumatic Stress Disorder- Post-traumatic Stress Disorder (PTSD) is included in DSM-5 as one of the Anxiety Disorders. This is now classified in a section in the DSM-5 called Trauma and Stressor Related Disorders. This involves exposure to trauma involving death or the threat of death, serious injury, or sexual violence as per the DSM-IV. Something is traumatic when it is very frightening, overwhelming and causes a lot of distress. Trauma is often unexpected, and many people say that they felt powerless to stop or change the event. PTSD causes intrusive symptoms such as re-experiencing the traumatic event. DSM-5 proposes four distinctive behavioral symptoms or diagnostic clusters; 1) intrusion symptoms (instead of re-experiencing), 2) alterations in arousal and reactivity (instead of arousal), 3) avoidance, and 4) negative alterations in cognitions and mood[95].

Objective

To improve the quality and consistency of the screening, assessment and management of distress, depression, and global anxiety in adult cancer patients.

Target Population

This guideline pertains to adult cancer patients experiencing cancer-related distress including global anxiety, post-traumatic stress disorder and those individuals with depression based on meeting a threshold for suspected depressive disorder on a validated depression rating scale or diagnosed with depression by structured diagnostic interview.

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 inter-professional in its focus, and the recommendations are applicable to direct-care care providers (i.e. oncologists, nurses, social workers, clinical counsellors, primary care practitioners) in diverse care settings. Since the scope of practice for various professions may vary according to regulatory standards and by laws set by provincial professional colleges, it is expected that professionals using this guideline will exercise the skill and judgment that best reflects their responsibilities to determine if the recommendations are within their scope of practice. Users may also wish to adapt this guideline to local health care processes and context. In addition, depending on the risk factors of distress, additional written guidelines and resources should be considered for more detailed evidence-based recommendations (i.e. pain guidelines or the American Psychiatric Association recommendations for treatment depression).

Guideline Questions

1. What are the recommended screening and assessment strategies for the identification of psychosocial distress, global anxiety and depression in adults with cancer?
2. What is the effectiveness of interventions (pharmacological, psychosocial, and/or combinations) for the management of psychosocial distress, global anxiety and depression in adults with cancer?

3 Methods

Research Objectives

To improve the quality and consistency of the screening, assessment and management of Distress, Depression, and Global Anxiety across the cancer trajectory in adults (≥18 years of age).

Research Questions

1. What are the current guideline recommendations for routine screening and assessment of Distress, Depression, and Global Anxiety in adults with Cancer?

2. What is the efficacy of interventions (pharmacological, non-pharmacological, and/or combinations) for reducing Distress, Depression, and Global Anxiety in adults with cancer?

3.A Methods-Screening and Assessments of Cancer-Related Distress, Depression and Global Anxiety

The 2010 Version 1 of the Guideline served as the evidentiary foundation of the current guideline that aims to update the previous guideline. Recommendations for screening and assessment for distress, depression, and global anxiety in adults with Cancer were identified based on the application of the ADAPTE methodology[1, 2], a rigorous 24 step method for adapting knowledge from existing guidelines following a quality appraisal in accordance with the AGREE II convention[3]. The ADAPTE methodology is a systematic process for adapting recommendations in existing guidelines to create high quality guidelines tailored for use in a specific health care context[2, 4].

The adaptation process began with a systematic literature search to identify only candidate guidelines for adaptation. The systematic search of clinical practice guideline databases, guideline developer websites, and published health literature was conducted to identify clinical practice guidelines, systematic reviews, meta-

analyses, and other guidance documents addressing the screening, assessment, and care of distress, depression, and global anxiety in adults with Cancer. The quality of guidelines identified either through grey literature or empirical data base searches were assessed by two reviewers (DH) and (HK) for this guideline. Recommendations from guidelines with rigor graded as greater than 50% were adapted or were used to clarify or refine recommendations from the original CAPO guideline "A Pan-Canadian Practice Guideline: Screening, Assessment and Care of Psychosocial Distress (Depression, Global Anxiety) in Adults with Cancer[12]. The recommendations were approved by the National Expert Psychosocial Distress Panel by telephone or email vote.

3.B Methods Management of Cancer-Related Distress, Depression and Global Anxiety

Methods-Management for Distress and Global Anxiety in adults with Cancer
Our aim was to update a 2010 previous version of A Pan-Canadian Practice Guideline: Screening, Assessment and Care of Psychosocial Distress, Depression, and Global Anxiety in Adults with Cancer[12]. We developed a three-step approach that we followed concurrently:

3.B.1 Sources of Evidence:

1) We searched for existing evidence-based guidelines on screening, assessment, and management of Distress and Anxiety in adults with Cancer from 2009 to May 2015. We selected any guideline published since the last literature update from Version 1 of the 2010 guideline. We examined the references of the eligible evidence-based guidelines through the searches.
2) We searched for systematic reviews on the management of Distress and Anxiety in adults with Cancer from 2009 to May 2015 for potentially relevant citations (RCTs) that may not have been captured by the search. We examined the references of the articles identified through the searches and relevant reviews and meta-analyses (see appendix 6 section 6.E Table 6.E.1).
3) We performed a systematic search of Randomized Control Trials (RCTs) that evaluated the effects of any pharmacological and/or non-pharmacological intervention on the management of distress and anxiety in adults with all types of cancer from 2009 to May 2015.

3.B.2 Literature Search Strategy

For the evidence-based guidelines and systematic reviews, and RCTs the search strategy was limited to studies published from 2009, to May 11, 2015. The following electronic bibliographic databases were searched: MEDLINE®, Cochrane Central®, PsychINFO, Cochrane Database of Systematic Reviews, EMBASE®, and CINAHL®. The strategies used combinations of controlled vocabulary (medical subject headings,

keywords) and text words. Table 6.A.1 appendix 6.A details the search strategies used to capture relevant citations.

An extensive grey literature search included systematic searches of relevant citations of Web sites: Clinical Trial Registries (ClinicalTrial.gov, WHO Clinical Trials), New York Academy of Medicine's Grey Literature Index, National Comprehensive Cancer Network, and National Institute for Health and Care Excellence.

Review of reference lists of eligible studies at full text screening was performed for relevant citation. Any potentially relevant citations were cross-checked with our citation database and any that were new were retrieved and screened at full text.

In addition, a targeted environmental scan of international guideline developers websites and key organizations for evidence-based clinical practice guidelines, systematic reviews and ongoing trials was conducted (June, 2015) for documents about distress and anxiety in adults with cancer. A listing of the organizations that were examined is given in appendix 6 section 6.A Table 6.A.2. CPGs were limited to those published between 2009 and June 2015. Reference lists of eligible systematic reviews and included CPG[9-14, 17-20, 36, 97, 102, 118-129] were also searched for potentially relevant citations. Similarly, the reference lists of eligible studies at full text screening were reviewed for relevant references. Any potentially relevant citations were cross-checked with our citation database and any that were new were retrieved and screened at full text.

3.B.2.1 Study Selection Criteria [Inclusion and Exclusion Criteria (PICO)]

Types of Participants (P)

Adults (aged 18 and over) with a clinical diagnosis of cancer known to have clinically significant distress and/or anxiety (including those with Post-traumatic Stress disorder symptoms and fear of recurrence).

Types of Interventions (I)

Any pharmacological or non-pharmacological (psychosocial, CBT, psychosocial or education, mindfulness meditation, yoga, exercise/activity, complementary medicine, supportive/expressive therapies) interventions for the management of distress and anxiety (including fear of recurrence as a type of survivor distress) in adult patients with cancer.

Types of Comparator (C)
Comparison condition is usual care, attention control or other comparator. Studies comparing drug treatment versus no drug treatment or versus alternative drug treatment, or both were also included.

Types of Outcomes (O)

Outcomes (either primary or secondary) included:

1) Clinically significant improvement in distress and/or anxiety as measured by valid scales (included specific fear or worry e.g. fear of recurrence) or
2) Clinically significant reduction in distress and/or anxiety as measured by valid scales (measured by severity) or
3) Differences in distress and/or anxiety severity between intervention group and controls using valid self-reported outcome measures for distress, anxiety or depression

Outcomes excluded:

1) Distress and/or anxiety measured during the diagnostic period prior to cancer treatment or those at genetic risk of cancer;
2) Distress and/or anxiety is not the outcome;
3) No validated measure of fatigue distress and/or anxiety

Types of Studies

We included evidence-based guidelines based on systematic review evidence, systematic reviews of randomized controlled trials, and RCTs of interventions with cancer related Distress and/or anxiety as a (primary or secondary) outcome.

Studies excluded:

Publications that were not RCTs, narrative reviews, or guidelines not based on systematic review evidence were excluded. Similarly, editorials, commentaries and student thesis were excluded.

Timing

There were no restrictions on study eligibility with respect to a minimum treatment interval or follow-up post treatment.

Settings

Studies that recruited patients from primary care, outpatient, and inpatient oncology, and palliative care settings were included. There were no exclusions for study setting.

Language Criteria:

All publications were in English. Non-English citations were excluded.

3.B.3 Selection of Clinical Practice Guideline (CPG)

We defined CPG as "systematically developed statements about specific clinical problems intended to assist practitioners and patients in making decisions about appropriate health care"[46]. We included full guidelines and consensus statements but we excluded algorithms with no background or description of the process by which the algorithm was developed, lay information, clinical knowledge summary or articles about guidelines.

3.B.4 Assessment of Study Eligibility

Six reviewers (JY, RT, MW, CW, SR, HN) working independently and in duplicate, screened all titles and abstracts and, upon retrieval of candidate studies, five team members (JY, RT, MW, SR, HN) reviewed the full text to determine eligibility. If the study was eligible, data were abstracted by JY, SR and HN. Any questions arising during data abstraction were resolved by discussion with other team members (DH).

3.B.5 Data Extraction and Management

Through an iterative process, we created a standardized form to extract descriptive, methodological and key variables from all eligible studies. Distiller (Ottawa, Ontario), an online reference management system for systematic reviews, was used to manage study selection and data extraction. Relevant fields of information were extracted from individual studies by trained data extractors using standardized forms and a reference guide. Prior to performing the data extraction, a calibration exercise was undertaken using a convenience sample of five included studies (RCTs and SRs). We collected data on study design, population, demographics, inclusion and exclusion criteria, measurement tool, intervention, and analytical technique. Data were tabulated and categorized according to the type of intervention. Key study elements were reviewed by a second person study investigator (DH) and methodologist (HK) (with respect to study outcomes, population characteristics, interventions, definition of prior "cancer-related distress and stress"), and characteristics of the intervention and outcome. Disagreements were resolved by consensus. We categorized included studies into pharmacological and non-pharmacological interventions (psychosocial-education).

We found relevant studies of fear recurrence and PTSD as our search strategy covered distress and anxiety. Appendix 6.I shows title and abstract, full text, and data abstraction forms.

3.B.6 Assessment of Methodological Quality Guidelines and Randomized Clinical Trials

We addressed two different quality assessments:
1) We used the AGREE II to assess the variability in the quality of the guideline process[3].

2) We selected the Risk of Bias Tool by the Cochrane Collaboration[47] to assess RCTs. The tool contains 12 items that include evaluation of the domains of randomization, blinding, co-intervention, and selective outcome reporting biases. Criteria for evaluation are standardized for these domains. Inconsistency amongst raters was minimized by providing adequate training and standardized instructions; disagreements were resolved by consensus. All tools can be viewed in appendix 6 section 6.I.

3.B.7 Data Synthesis

3.B.7.1 Qualitative Synthesis

We grouped study results according to: 1) the type of treatment categories and the corresponding comparator treatment; 2) the specific grouping of the pharmacological treatment; and 3) nonpharmacological treatment. Forest plots and summary tables were generated to display primary study outcomes of cancer related distress and global anxiety. Summary tables were created for CPGs and RCTs stratified by country of origin, where possible.

For each trial information on population characteristics (sample sizes, setting cancer, type, site, stage and treatment stage, intervention [type, dose, duration], population, assessment tool, interview vs. self-report, outcome measure, outcomes [both of benefit and of harm], statistical analysis, adverse events, and summary results). We have stratified the presentation of results based on the type of intervention. Additionally, we grouped study results according to: 1) the specific grouping of the pharmacological treatment; and 2) non-pharmacological treatment. Forest plots and summary tables were generated to display primary study outcomes of response. Summary tables were created for CPGs stratified by country of origin, where possible.

3.B.7.2 Quantitative Synthesis

To perform meta-analysis, outcome measurement at the end of intervention or immediate post-treatment data (mean, standard deviation) was utilized for continuous outcome measures. The DerSimonian and Laird random effects models with inverse variance method were utilized to generate the summary measures of effect in the form of Standard Mean Deviation (SMD) for continuous outcomes[48]. The SMD was used as a summary statistic because the studies in this systematic review often assessed the same outcomes measured in a variety of ways. In this situation, it was necessary to standardize the results of the studies before they could be compared across studies or combined in a quantitative synthesis. SMDs were calculated using change from baseline data, i.e. mean difference between pre-treatment (baseline) and post-treatment (final/end-point) scores along with its standard deviation for both intervention and control groups. The SMD effect sizes with scores of 0.2–0.5, 0.5–0.8, and >0.8 were considered as small, medium, and large effects, respectively[49]. The studies, where SD was not reported, we calculated the SD from the reported SE of the mean, or 95% CIs using the equations provided in Chapter 9 of the Cochrane Handbook for Systematic Reviews of Interventions. The Cochrane's Q (α=0.10) and I2 statistic were employed to quantify the statistical heterogeneity between studies, where $p<0.10$ indicates a high level of statistical heterogeneity between studies. The analyses were performed using Review Manager Version 5.1 software. For studies not included in the meta-analyses, findings are described narratively in the text[48, 50]. In data analysis section as "For studies where more than one intervention arms were included, the control arm sample size was split to allow comparison with intervention arms and avoid unit of analysis error" [50].

3.B.8 Rating the Body of Evidence

3.B.8.1 Grading of Recommendations on Randomized Controlled Trials

We used the GRADE approach to determine the quality of evidence and strength of recommendations for each important outcome. GRADE has advantages over other approaches. Advantages include: developed by a widely representative group of international guideline developers, explicit and comprehensive criteria for downgrading and upgrading quality of evidence ratings, clear separation between quality of evidence and strength of recommendations that includes a transparent process of moving from evidence evaluation to recommendations, clear, pragmatic interpretations of strong versus weak recommendations for clinicians, patients and policy-makers, explicit acknowledgement of values and preferences, and explicit evaluation of the importance of outcomes of alternative management strategies.

Once the systematic review of RCTs was available from the evidence review team, the internal panel review independently developed the recommendation statements by consensus, based on a detailed review of the evidence. In formulating recommendations, panel review considered both the benefits and harms associated with pharmacological and or non-pharmacological treatment, patient values and preferences, the quality of the evidence and, in some cases; the costs of the intervention (see Box 5 below). The strength of evidence was determined using the GRADE system[5-7] and the draft recommendations developed by the review panel were revised and approved by external expert reviewers.

The evidence in RCTs is graded according to whether it is high quality, moderate quality or low quality or very low quality evidence according to the Grade of Recommendation Assessment, Development and Evaluation system. GRADE offers two strengths of recommendation: strong and weak. The strength of recommendations is based on the quality of supporting evidence, the degree of uncertainty about the balance between desirable and undesirable effects, the degree of uncertainty or variability in values and preferences, and the degree of uncertainty about whether the intervention represents a wise use of resources.

Box 5: Grading of Recommendations

Recommendations are graded as either strong or weak according to the Grades of Recommendation Assessment, Development and Evaluation system (GRADE). GRADE offers two strengths of recommendation: strong and weak. The strength of recommendations is based on the quality of supporting evidence, the degree of uncertainty about the balance between desirable and undesirable effects, the degree of uncertainty or variability in values and preferences, and the degree of uncertainty about whether the intervention represents a wise use of resources.

Evidence is graded as high, moderate, low or very low based on how likely further research is to change our confidence in the estimate of effect.

Category Quality	Definitions	Strong Recommendation	Weak Recommendation
High Quality Evidence	Further research is very unlikely to change our confidence in the estimate of effect.	The work group is confident that the desirable effects of adhering to this recommendation outweigh the undesirable effects. This is a strong recommendation for or against. This applies to most patients.	The work group recognizes that the evidence, though of high quality, shows a balance between estimates of harms and benefits. The best action will depend on local circumstances, patient values or preferences.
Moderate Quality Evidence	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.	The work group is confident that the benefits outweigh the risks but recognizes that the evidence has limitations. Further evidence may impact this recommendation.	The work group recognizes that there is a balance between harms and benefits, based on moderate quality evidence, or that there is uncertainty about the estimates of the harms and benefits of the

		This is recommendation that likely applies to most patients.	proposed intervention that may be affected by new evidence. Alternative approaches will likely be better for some patients under some circumstances.
Low Quality Evidence	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change. The estimate or any estimate of effect is very uncertain.	The work group feels that the evidence consistently indicates the benefit of this action outweighs the harms. This recommendation might change when higher quality evidence becomes available.	The work group recognizes that there is significant uncertainty about the best estimates of benefits and harms.

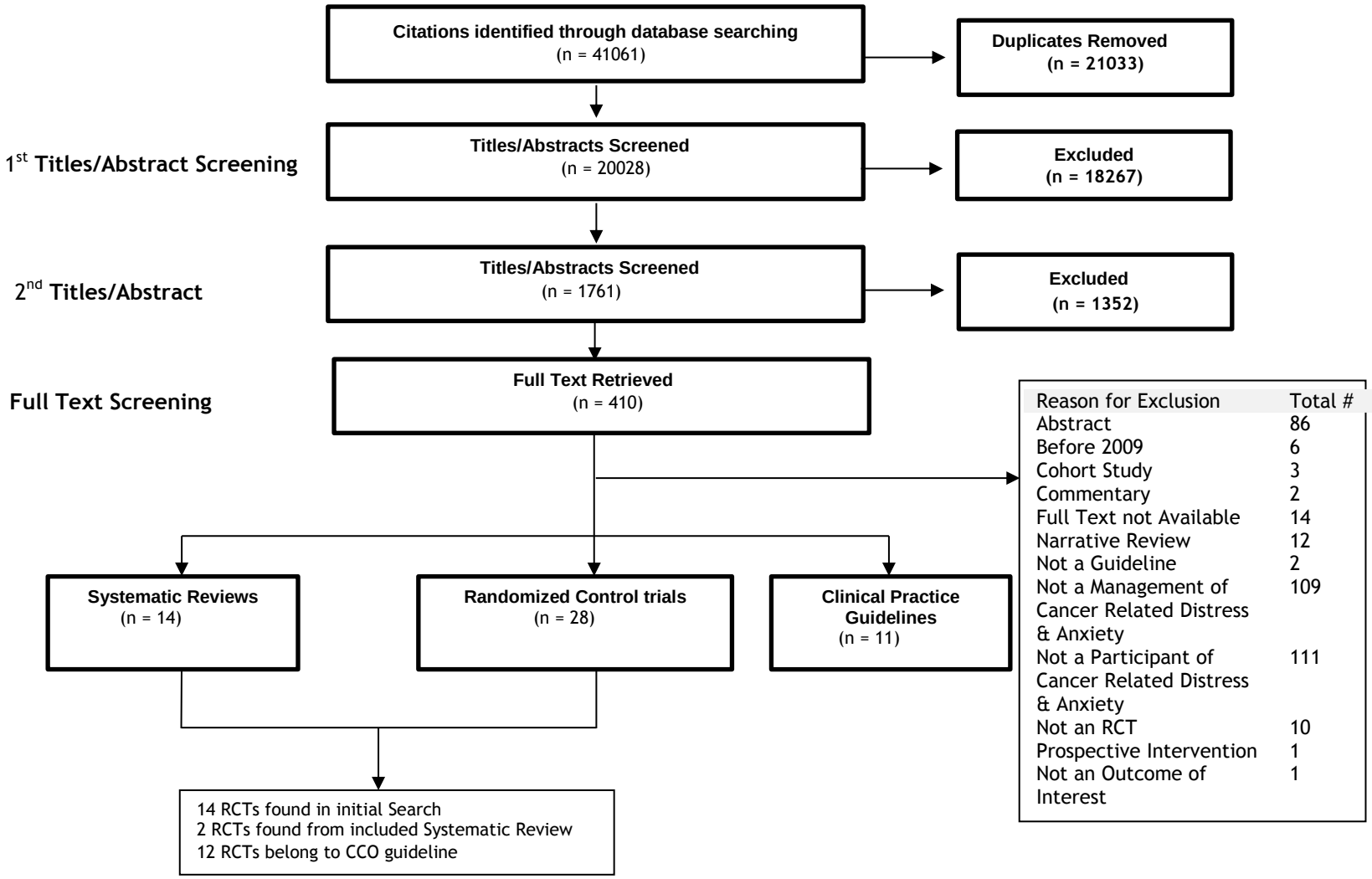
3.B.9 Publication Bias

Although our search strategy is comprehensive and includes a grey literature search including sources for unpublished trials, there is still potential for publication bias. Publication bias is important to assess in reviews with the use of drugs (pharmacological section), as there is evidence to suggest that industry sponsorship may lead to negative trials not being published[130], that reporting of adverse events are more favorable to clinician[131], and that there may be delay in publication of negative findings[132].

4 Results, Conclusion, and Recommendations

4.A Results

We identified 10[9-14, 17-20] clinical practice guidelines in 11 publications, 14[36, 97, 102, 119-129] unique systematic reviews and 28 RCT[22-29, 31-34, 53, 55-57, 65-67, 71, 72, 76-80, 133] randomized clinical trials on distress and anxiety in this practice guideline. (See PRISMA diagram, Figure 4.A.1).



4.A.1.1Figure 4.A.1: PRISMA Diagram for Cancer Related Distress, Global Anxiety, and Depression

4.B Clinical Practice Guidelines

We defined CPG as "systematically developed statements about specific clinical problems intended to assist practitioners and patients in making decisions about appropriate health care"[46]. We included full guidelines and consensus statements if there was an explicit process identified that summarized the evidence that contributed to the statement of recommendation.

There were a total of 10 CPG's in 11 publications, sponsored by unique organizations that were identified in the review[9-14, 17-20]. Appendix 6 section **Error! Reference ource not found.** shows the characteristics of the CPGs as a function of country of origin, scope, and intended users.

4.B.1 Quality Assessment of CPGs for Cancer-Related Distress, Depression, and Global Anxiety

Table 4.B.1.1 shows the domain scores for the AGREE II ratings of the CPGs for cancer-related distress, depression and global anxiety. The AGREE II is based on six domains of methodology for the guideline process and one item with an overall assessment.

All CPGs scored high for *Scope and Purpose* (Domain 1) (range 91 to 100 percent). *Stakeholder involvement* (Domain 2) showed scores varying from 65 to 100 percent, and the lowest score was for a CPG sponsored by Deng[20]**.** For the domain of *Rigor of Development* (Domain 3), scores varied from 40 to 96 percent; all indicated a process for updating the guideline. For the domain of C*larity of Presentation* (Domain 4), scores were generally high and varied from 55 to 98 percent. This domain evaluated whether the recommendations were clear and unambiguous, such that options were clearly presented, and key recommendations easily identifiable. However, the scores for the items within this domain were based on all recommendations within the CPG and were not specific to those applicable to patients who failed to respond to antidepressants for the treatment of depression. When considering the *Applicability* Domain (Domain 5), scores were highly variable from 33 to 86 percent. The majority of CPGs scored poorly for two criteria within this domain: 1) consideration of potential resource implications of applying their recommendations, and 2) presenting, monitoring, or auditing criteria. For the domain regarding *Editorial Independence* (Domain 6), scores were generally highly variable except for one[9] and ranged from 64 to 100 percent. Most systems of grading the strength of the evidence included aspects of study design, number of studies, or confidence of treatment; most included a level that reflected consensus or expert opinion for some recommendations informed by knowledge of the evidence in the field. Potential competing interests of the guideline development group were not consistently recorded. Note that although the AGREE II

evaluates the methodology of the guideline process, it cannot evaluate the clinical merit (taking into account the methods for summarizing the evidence).

Table 4.B.1.1: AGREE Results of Included Guideline

Author	Organization	Scope and Purpose (Domain 1)	Stakeholder Involvement (Domain 2)	Rigor of Development (Domain 3)	Clarity of Presentation (Domain 4)	Applicability (Domain 5)	Editorial Independence (Domain 6)	Overall Rating
Yu,2012[9]	National Cancer Center	91%	74%	40%	55%	33%	64%	33%
Andersen, 2014[10]	American Society of Clinical Oncology	94%	96%	80%	98%	61%	97%	83%
Deng, 2013[20]	American Collage of Chest Physicians	96%	65%	64%	89%	39%	100%	67%
Holland, 2014[11]	National Comprehensive Cancer Network	94%	96%	59%	83%	83%	100%	67%
National Institute for Health and Clinical Excellence, 2009[19]	National Institute for Health and Care Excellence (NICE) Clinical Guideline	100%	100%	94%	98%	79%	100%	100%
Howell, 2010[12]	Canadian Partnership Against Cancer (Cancer Journey Action Group); Canadian Association of Psychosocial Oncology	98%	98%	96%	98%	84%	100%	100%

Rayner, 2011[17]	European Journal of Cancer	94%	89%	70%	87%	62%	100%	83%
Howell, 2009[13]	Canadian Partnership Against Cancer (Cancer Journey Action Group); Canadian Association of Psychosocial Oncology	98%	98%	90%	90%	79%	100%	100%
Li,2015[18]	Cancer Care Ontario	100%	94%	96%	96%	79%	100%	83%
Howes, 2015[14]	Cancer Care Nova Scotia	100%	96%	88%	98%	86%	100%	83%
**Note that the recommended number of reviewers ranges from two to three; however, if two independent reviewers are consistent in their scoring, no further review is necessary.*								

4.B.1.1 Level of Recommendation: Expert Consensus

Key Supporting Evidence:

As noted in appendix 6 section 6.**Error! Reference source not found.**, we identified en[9-14, 17-20] guidelines, seven[9-14, 17-20] of which made recommendations on screening and assessment of distress for depression and anxiety. The National Comprehensive Cancer Care Network (NCCN) uses the term distress in all of their distress management guidelines as they consider this term less stigmatizing than psychological distress[11], whereas others use the term depressive symptoms[10, 18]. All of these guidelines with the exception of Deng[20] made recommendations specific to screening for distress or depression[9, 11-14, 17-19] or depressive symptoms[9-11, 18] and that psychosocial assessment should follow distress screening. The Distress Guideline[12] and the Psychosocial Assessment Guideline[13] also made recommendations that screening for distress should be followed by a comprehensive psychosocial assessment and a focused assessment for depressive symptoms.

The recommendations for screening for distress were primarily based on expert consensus informed by the evidence. For instance, screening for distress is an accepted standard of care for cancer programs in Canada[13] and in the United States. The American College of Surgeons (ACoS) Commission on Cancer (CoC)[51] identified a standard for cancer programs to implement psychosocial distress screening and referral for psychosocial care. The field of psychosocial oncology has advocated for distress screening as part of routine care since the first release of the National Comprehensive Cancer Network (NCCN) Guideline in 1999[134]. The United Kingdom [19]and a Hong Kong Guideline[20] made recommendations for screening for distress as part or routine care.

A specific search of the literature to identify the effectiveness of screening for distress was not conducted in most of the guidelines[9-13, 17-20] with the exception of Howes[14]. Howes documented Level 1 evidence that provided support for their recommendations that all patients should be screened for distress as a standard of care for all cancer program and organizations. Empirical support for the efficacy of screening for distress in terms of improved recognition and treatment of distress and related problems is not yet conclusive regarding its effects on outcomes but it does appear to improve communication between health care providers and patients[135, 136].

Depression and disorders of the depressive spectrum contribute to suffering in cancer, and can lead to disability and poor quality of life and potentially influence longer term survival[52]. They are often under recognized and undertreated and thus screening followed by secondary assessment for distress is now recognized as a standard of care in cancer care delivery[52] and was endorsed as a recommendation in this 2015 guideline.

As shown in Table 4.B.1.1, using the AGREE appraisal tool, the quality of the guidelines were evaluated. Most of the guidelines scored between 40% and 96% for rigor and overall scores between 33% and 100% suggesting the guidelines identified were appropriate for consideration by the expert panel for inclusion of recommendations for this guideline. There was not a substantial overlap of evidence presented between these guidelines.

4.C Randomized Clinical Trials (RCTs) on Distress and Global Anxiety

Applying our eligibility criteria led to the inclusion of 16 randomized clinical trials identified through our systematic review process as well as from reviewing other systematic reviews [22-29, 31-34, 53-57] describing the results of intervention for the management of cancer related distress, and anxiety. These RCTs were not included in the CPGs identified above.

We further categorized included RCTs by pharmacological and non-pharmacological studies. We sub-grouped non-pharmacological interventions into the following categories: 1) psychosocial interventions and 2) CBT. PTSD, and fear of recurrence. We describe these RCTs including their quality rating by intervention type in detail. Each included trial was independently assessed for risk of bias using the criteria described in the Cochrane Hand-Book version 5.1.0[50] by the authors with any disagreements resolved by discussion or consultation by a third member of the expert panel.

4.C.1 Cancer-Related Distress

4.C.1.1 Results from Psychosocial Interventions on Distress

A total of eight RCTs met our inclusion criteria and were incorporated in this guideline[22-28, 57] sample characteristics and results of the 8 studies can be found in Table 6.G.1 appendix 6.G. Newer studies, including well designed RCTs, provide continued support for the role of psychosocial interventions.

Since our last review[12], an additional 8 studies have investigated various psychosocial interventions including, mindfulness-based stress reduction approaches, Supportive Expressive Therapy (SET), telephone-based support and low intensity online support interventions in the form of CBT based self-help, as well as psycho-educational interventions to address psychosocial distress among cancer patients[22-28, 137].

Five studies were conducted with breast cancer patients[23-27], two with mixed populations[22], and one following hematopoietic stem cell transplant[28]. The psychosocial interventions were delivered by a variety of experts, including nurses, psychosocial experts (i.e. psychologists), peers or other health professionals, depending on the nature of the topics[22-28].

Several of the interventions were delivered in a group format[24, 27], however, individual-oriented interventions were also tested[25]. A major component of well-established interventions include an element of peer support, usually through group support to enhance social support, as well as provide an opportunity for vicarious learning that occurs through meeting others dealing with a similar situation[24, 58]

Since the earlier review[12], there is an emerging literature on the superiority of mindfulness-based interventions in addressing stress and quality of life, particularly for cancer patients with higher baseline levels of distress[23, 24]. Such approaches are typically offered over multiple weeks (i.e. 8-week group format), may or may not include booster sessions, and include a strong skill-based training element, requiring commitment to practice and homework in order to acquire skill in mindfulness meditation[138]. One RCT[24] examined the role of Mindfulness Based Cancer Recovery (MBCR) and found that that mindfulness-based stress reduction performed as well as the well-established Supportive Expressive Therapy (SET) on mood (i.e. POMS), among women with stage I—III breast cancer, with a small to medium effect size. However, MBCR was superior for improving stress levels, quality of life, and social support for distressed survivors in comparison to SET. Further, the benefits of MBCR seemed to continue to accumulate after the intervention finished with greater improvements showing at follow-up, in contrast to the other two interventions.

Monti et al. (2013)[23] conducted a novel intervention study among breast cancer patients that added a component of art therapy to the empirically validated mindfulness-based stress reduction model (MBAT). Additional tasks were included to assist participants to identify and organize internal and external representations of stressors, and the art therapy offered an additional mode for creative expression to enhance self-awareness of sensory stimuli. The mindfulness-based art therapy improved overall outcomes compared to a more general breast cancer educational support program of equal intensity and duration. Both groups improved regarding stress scores at the end of the intervention, but the MBAT groups retained better scores in follow-up.

Zernicke et al. (2014)[57], looked at the feasibility of offering MBCR to an underserved population without access to in person MBCR, delivered through the Internet. Women and men who had completed primary treatment for cancer within 3 years and were exhibiting moderate to high distress participated in the study. Feasibility targets and retention were met; participants were satisfied with the intervention and would

recommend the program to others. Mood disturbance and stress symptoms were reduced, and levels of spirituality and mindfully acting were improved as compared to the wait list control group. Larger studies are planned.

Additional novel ways of facilitating expression include the structured use of expressive writing about one's deepest thoughts and feelings concerning the cancer experience[25, 28]. Rini et al. (2013)[28] compared an intervention of emotionally expressive writing followed by peer helping which involved assisting others who prepare for transplant through sharing one's own experience and offering encouragement with written narrative. The intervention was compared to neutral writing alone, expressive writing without peer helping, and to peer assistance alone. The interventions aimed to address survivorship problems following hematopoietic stem cell transplant. The emotional expressive writing and peer helping combination improved physical symptoms and general distress among men and women with moderate to severe general distress and survivorship issues. In contrast, the standard expressive writing alone and peer assistance without the written component did not produce significant benefits. The authors concluded that there are unique benefits in combining both the emotionally expressive writing component with peer helping and encouragement. It was speculated that by having patients first write about their experience and prepare their offer encouragement/ sharing enabled them to better support other survivors possibly through cognitive restructuring or enhanced emotional regulation. Survivors who first wrote with the peer support offer may have thought more about how someone would react to their writing. The peer helping group received instructions to describe the expressive writing exercises as preparing them to help others.

Mosher et al. (2012)[25] also investigated expressive writing among metastatic breast cancer patients who were asked to write about their deepest thoughts and feelings regarding their cancer, they found no significant group differences compared to patients who wrote about daily activities in a factual manner on measures of existential and psychological well-being, fatigue and sleep at 8 weeks follow up. However, the expressive writing group reported significantly greater use of mental health services during the study compared to the neutral writing group, suggesting that the expressive writing played a role in improved uptake of mental health services among distressed patients.

Many distressed patients with cancer and their caregivers may benefit significantly from a single session of a nurse led psychosocial intervention that can be delivered remotely by telephone and supported by self-management materials.
Chambers et al. (2014)[22] compared a nurse-delivered single session psycho-educational intervention delivered over the phone with a psychologist delivered 5-session telephone-based CBT intervention.

For the low-intensity intervention, patients received a kit prior to the telephone follow up by the nurse, which included psycho-education, resources on self-management, stress management skills and problem-solving approaches and strategies for mobilizing personal and community supports to reduce isolation, as well as a relaxation CD. The intervention was tailored in that the nurse provided feedback according to the patients' distress level and specific concerns and offered strategies targeted to patient concern. Study investigators predicted that patients with higher distress would benefit most from the more intensive intervention which included five sessions of telephone-based counseling from a psychologist consisting of core components of CBT and psychosocial related to cancer, coping, stress management and cognitive therapies, as well as strategies to enhance support networks. Principles of CBT were utilized and applied flexibly to respond to the therapy goals of each participant and behavioral homework for core components was suggested to address treatment effects, such as pain or sleep, along with a self-management resource kit. 93% in the nurse intervention arm completed the intervention, compared to 53% in the 5-session intervention.

The researchers found that distress decreased in both arms, with small to large effect sizes, and post-traumatic growth increased over time, with the exception of a subset of the participants with low-education, who benefited most from the psychologist delivered intervention. The authors cautiously concluded that distressed patients with cancer and their caregivers improve over time with a single low intensity psychological intervention. A study limitation was the lack of an inclusion of a "no treatment" control arm. It should be noted that the intervention performed best for cancer-specific distress, versus global distress. Others[26] have reported similar findings. Ashing and her colleagues studied a lay health worker telephone delivered, brief, psycho educational intervention for depression in a Latina breast cancer population. Significant improvements in depression scores were seen in the intervention group in contrast to the control group, as measured by the CES-D.

Online support groups have received interest due to their use of online technology and its potential of providing greater access to psychosocial support, particularly for those individuals who live in remote areas and are unable to attend in person interventions. Lepore et al.[27] compared two types of online support groups offered to women with Stage 1 or II breast cancer. The standard Internet group format consisted of facilitator-led 90-minute sessions over six weeks, and included several mechanisms. For example, live (synchronous) chats with introduction of topics (e.g. fatigue, pain, lymphedema, intimacy and psychosocial concerns and diet/exercise), posting of transcripts for post session review and access, and a discussion board for asynchronous text communication. The standardized format was compared to a more enhanced version, in which an added intervention was an enhanced focus provided for the patients in how to offer support to others (enhanced prosocial internet support group). Patient-oriented written coaching on how to recognize and respond to others'

needs for support was offered along with weekly emails that helped patients prepare text for sharing their experiences and specific ways to offer help through encouraging helping behaviors and praising. The researchers surprisingly found that the standard version performed better on anxiety and depression outcomes as measured by the HADS. They suggested that patients may have hesitated to share concerns due to the potential burdening of others and felt more pressure to increase expression of positive feelings in order to help others. The study suggests that online support groups with chat features and opportunities are beneficial. However, the offering of specific ways to structure the group discussions that highly encourage a focus on helping others may not be useful at least, in a group format. The authors acknowledged that this finding fails to confirm the widely held assumption that helping others is a key active ingredient in support groups. In contrast, Rini et al[28] (above), found that the patient coaching in helping others was beneficial compared to expression of own feelings alone, however the helping behavior was provided to peers through an individually-oriented format. The Lepore et al.[27] online group support study was limited in that it didn't have an arm of standard care for comparison and the outcomes were only collected at one month post-intervention.

4.C.1.1.1 Risk of Bias of Included Studies

The results of the methodological quality assessment is shown in the Tables of Quality Assessment appendix 6 section. 6.F Table 6.F.1 and Characteristics Table (Table 6.G.1 in appendix 6 section 6.G) see Figure 4.C.1.1.1.1.

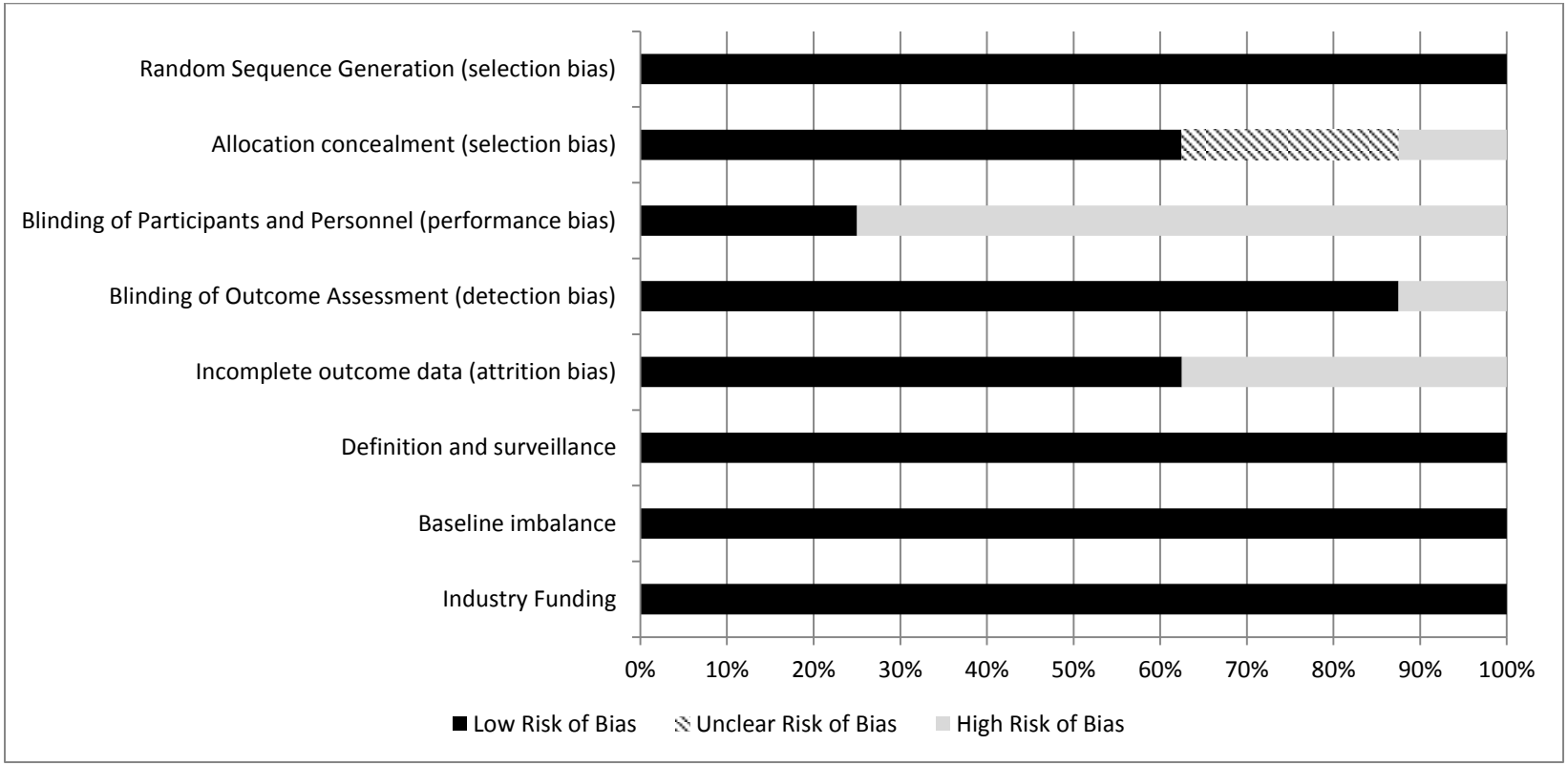


Figure 4.C.1.1.1.1 Risk of Bias Graph: Review Authors' Judgment about Psychosocial Interventions

4.C.1.1.2 Effects of Psychosocial Interventions on Distress:

The combined data from the seven studies, involving 611 patients in the psychosocial arm and 459 patients in the control arm, showed that psychotherapy had no significant effect distress among patients with cancer as compared to control group. (SMD = - 0.3029; 95%CI -0.6823 to 0.0765). The overall quality of this evidence was rated as moderate and downgraded due to concerns regarding imprecision. See Figure 4.C.1.1.2.1.

Review: Psychosocial for distress among cancer patients
Comparison: Psychosocial versus treatment as usual
Outcome: Distress

	Experimental			Control				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Ashing 2014	-7.8	6.147	45	1.2	4.232	39	11.6%	-1.6682 [-2.1688, -1.1676]
Carlson 2013-A	-19.27	18.671	111	-8.87	18.601	27	12.3%	-0.5543 [-0.9801, -0.1286]
Carlson 2013-B	-9.46	18.806	101	-8.87	18.601	27	12.3%	-0.0313 [-0.4559, 0.3934]
Chamber 2014	-1.66	7.355	145	-0.82	7.237	147	13.9%	-0.1148 [-0.3444, 0.1148]
Lepore 2012	-1.5	2.558	88	-2.38	2.501	95	13.4%	0.3466 [0.0544, 0.6388]
Monti 2013	-0.1	0.285	47	-0.13	0.285	50	12.6%	0.1044 [-0.2941, 0.5029]
Mosher 2012	17.99	8.955	44	17.87	8.943	42	12.4%	0.0133 [-0.4095, 0.4361]
Zernicke 2014	-22.87	19.948	30	-7.38	22.759	32	11.5%	-0.7132 [-1.2279, -0.1985]
Total (95% CI)			**611**			**459**	**100.0%**	**-0.3029 [-0.6823, 0.0765]**

Heterogeneity: Tau² = 0.26; Chi² = 56.98, df = 7 (P < 0.00001); I² = 88%
Test for overall effect: Z = 1.56 (P = 0.12)

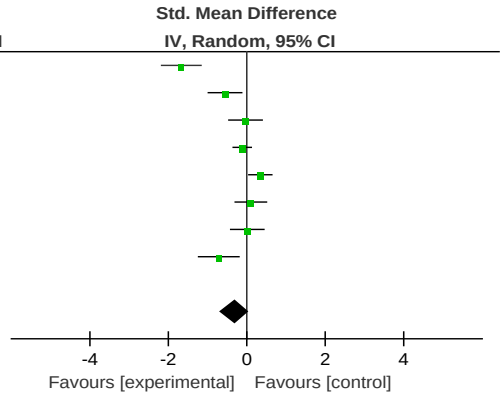


Figure 4.C.1.1.2.1: Effect of Psychosocial Interventions on Cancer-Related Distress

Table 4.C.1.1.2.1: GRADE Tables for Effect of Psychosocial Interventions on Cancer-Related Distress

Quality assessment							No of patients		Effect	Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Education / Psychosocial intervention**	**Control**	**SMD (95% CI)**		
Effect of Education / Psychosocial treatment on distress (Better indicated by lower values)											
7[1]	randomised trials	no serious risk of bias[2]	no serious inconsistency[3]	no serious indirectness[4]	serious[5]	none[6]	611	459	SMD 0.30 lower (0.68 lower to 0.08 higher)	⊕⊕⊕O MODERATE	CRITICAL

Education / Psychosocial intervention for cancer related distress

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk **Control**	Corresponding risk **Education / Psychosocial intervention**				
Effect of Education / Psychosocial treatment on distress		The mean effect of education / psychosocial treatment on distress in the intervention groups was **0.30 standard deviations lower** (0.68 lower to 0.08 higher)		1070 (7 studies[1])	⊕⊕⊕⊖ **moderate**[2,3,4,5,6]	SMD -0.30 (-0.68 to 0.08)

CI: Confidence interval;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the

estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] 1) Ashing et.al., 2014; 2) Carlson et.al., 2013; 3) Chambers et.al., 2014; 4) Lepore et.al., 2014; 5) Monti et.al., 2013; 6) Mosher et.al., 2012; 7) Zernicke et.al., 2014.
[2] Using Cochrane's Risk of Bias tool, for this outcome four studies were rated as low, two as unclear risk and one as high risk. Across studies, there was a lack of certainty (unclear ratings) regarding allocation concealment (14%); and high risk of bias associated with allocation concealment (14%), blinding of participants & outcome assessment (71%) and incomplete outcome reporting (14%). Given that most of the information is from studies at low risk of bias, this body of evidence was not downgraded for serious study limitations.
[3] The statistical heterogeneity is high [Chi2=56.98, df=7 (P<0.00001); I2=88%] but the direction of the effect is consistent across most studies and the confidence intervals overlap. The statistical heterogeneity is most likely due to small versus large treatment effects observed across studies. This body of evidence was not downgraded for inconsistency.
[4] Seven RCTs provided data for this outcome. The studies included mixed gender in two and female population in 5 studies. The mean age ranged from 50 to 55 years. The intervention arm across studies received various types of psychosocial / educational therapies including mindfulness-based cancer recovery, Expressive Writing, Emotionally Focused therapy, Psychologist-Delivered Five-Session Cognitive Behavioral Intervention, telephonic-based psycho-education, and enhanced prosocial Internet support group. The control group across studies received various types of support therapies. Four studies were conducted in USA, two in Canada and one in Australia. All studies were published between 2012 and 2014. The length of intervention across studies ranged from 6 to 16 weeks. There were no serious concerns regarding indirectness for this body of evidence and was not downgraded.
[5] The sample size is adequate i.e. > 300 (611 intervention arm, 459 control arm) and the pooled effect estimate is not precise and confidence interval include the null value "0" [SMD= -0.3029 (-0.6823, 0.0765)]. This body of evidence was downgraded for serious concerns regarding imprecision.
[6] There were too few studies (n<10) to assess publication bias.

4.C.1.1.3 Conclusion and Recommendations

Low-intensity interventions or psychosocial interventions generally perform well and are most beneficial for addressing lower levels of distress[22]. Such interventions generally include psycho-education, information on cancer resources and self-management strategies. There may be added benefit by tailoring specific exercises to address specific concerns and needs, for example through information provision or self-management strategies.

Low-intensity interventions, such as psychosocial may be less effective than more intensive or psychotherapeutic based interventions such as Cognitive Behavioral Therapy[22] for those with greater psychological needs or for specific subgroups, such as those with higher levels of moderate to severe distress (i.e. depression or sub-threshold symptoms of depression[22, 24]).

Mindfulness based stress reduction improves distress and quality of life for those patients who have elevated levels of stress or distress[24, 58]. Mindfulness based stress reduction may have added benefit over the long term in addressing quality of life and stress[24].

Novel interventions, such as art therapy modes integrated with other traditional forms of intervention or narrative expression that include opportunities for emotional expression with some structure/guidance, combined with peer components can effectively address moderate to higher levels of distress[22, 23, 28].

Helpful in addressing access issues, there is evidence that online facilitator led-support groups are beneficial in improving distress[27].

Unfortunately, the vast majority of studies continue to be conducted with breast cancer populations, a limitation in extrapolating findings to other cancer populations and, particularly, men.

4.C.1.2 Results from Cognitive Behavioral Therapy Interventions on Distress

Our search identified one eligible RCT that examined CBT for the treatment of cancer related distress in adults. Researchers[56] examined a brief 10-session individual telephone-based CBT intervention (T-CBT) versus an assessment-only condition on PTSD, distress and depressive symptoms. Eligibility criteria included adult, English speaking hematopoietic stem-cell transplantation (HSCT) patients with significant distress as assessed by PTSD symptom criteria. A sample of 81 hematopoietic stem-cell transplant (HSCT) patients was randomly assigned to either the T-CBT intervention or assessment-only condition. Results showed that patients receiving the

intervention reported less PTSD and general distress symptoms than assessment-only patients.

We found one randomized clinical trial examining the effectiveness of aromatherapy massage versus cognitive behavioral therapy. Although this study did not meet all our inclusion criteria, we included it in the absence of other studies. However, this study was not included in the meta-analysis. The goal of Serfaty's study[33] was to 1) test the feasibility of recruitment into a randomized controlled trial of Aromatherapy Massage (AM) versus CBT in patients with cancer; 2) test and modify the intervention; and 3) determine the extent of change in global anxiety, depression and overall mood as measured by the Profile of Mood States (POMS). Thirty-nine outpatients with cancer were entered onto the trial after scoring 8 or higher (changed to 11 or higher at the 4 month recruitment mark) for global anxiety and/or depression using HADS screening criteria. Patients were randomized to Treatment as Usual (TAU) plus up to 8 weekly sessions of either AM or CBT, offered within 3 months. The POMS was administered at baseline and at 3 and 6 months post-baseline. Significant improvements in POMS (total mood, depressive mood and anxious mood scores) occurred with both interventions. Between-group comparison showed a non-significant trend towards greater improvement in depressive mood with CBT.

4.C.1.2.1 Risk of Bias of Included Studies

The results of the methodological quality assessment are shown in the Tables of Quality Assessment appendix 6 section 6.F Table 6.F.2 and Characteristics Table (Table 6.G.2 in appendix 6 section 6.G) see Figure 4.C.1.2.1.1.

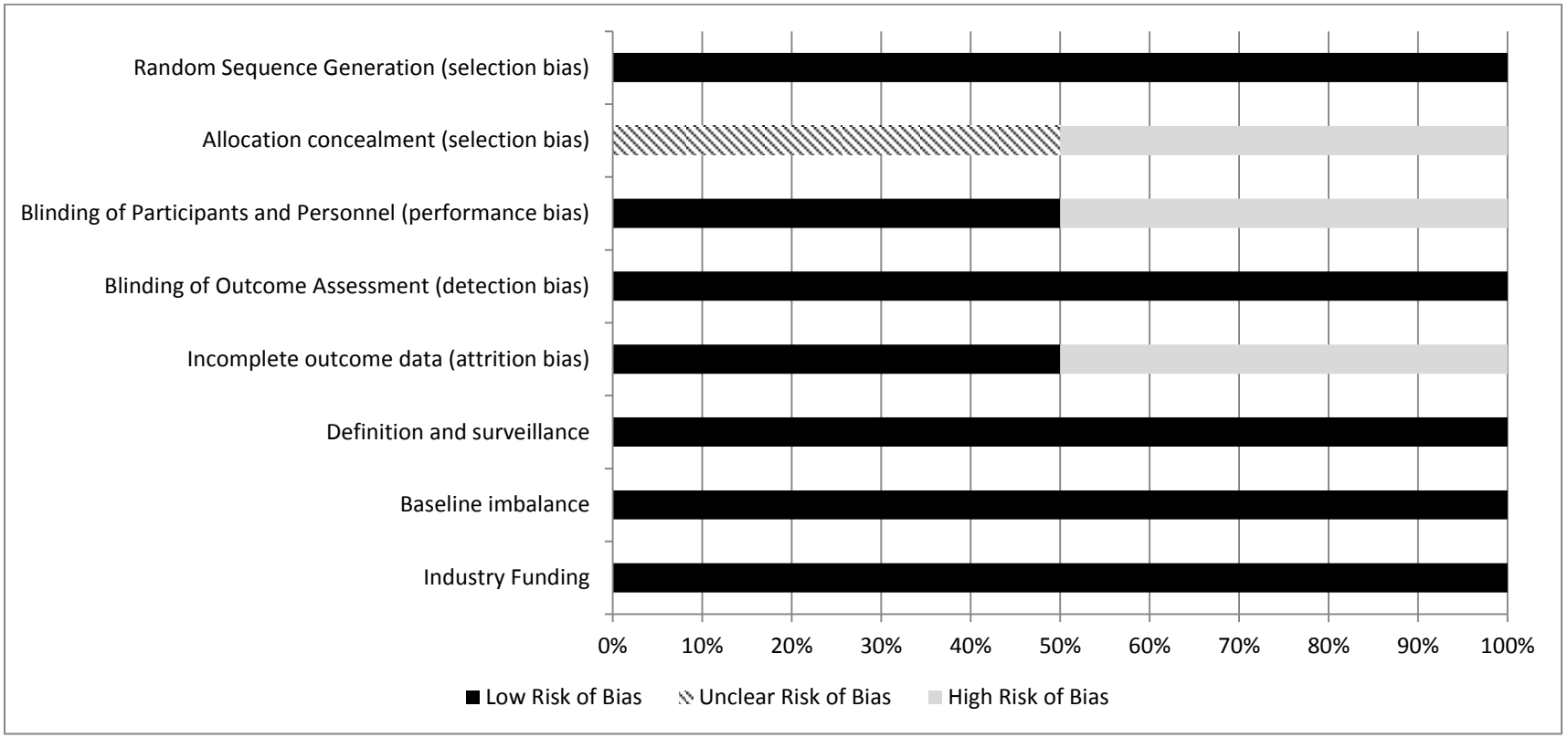


Figure 4.C.1.2.1.1 Risk of Bias Graph: Review Authors' Judgment about CBT Interventions

4.C.1.2.2 Effects of CBT on Distress:

The effect estimate from one study, involving 47 patients in the CBT arm and 34 patients in the control arm, showed that CBT had a significant effect of medium magnitude on distress among patients with cancer as compared to control group. (SMD = - 0.5734; 95%CI -1.0238 to -0.1229). The overall quality of this evidence was rated as high. See Figure 4.C.1.2.2.1.

Review: CBT for distress among cancer patients
Comparison: CBT versus treatment as usual
Outcome: Distress

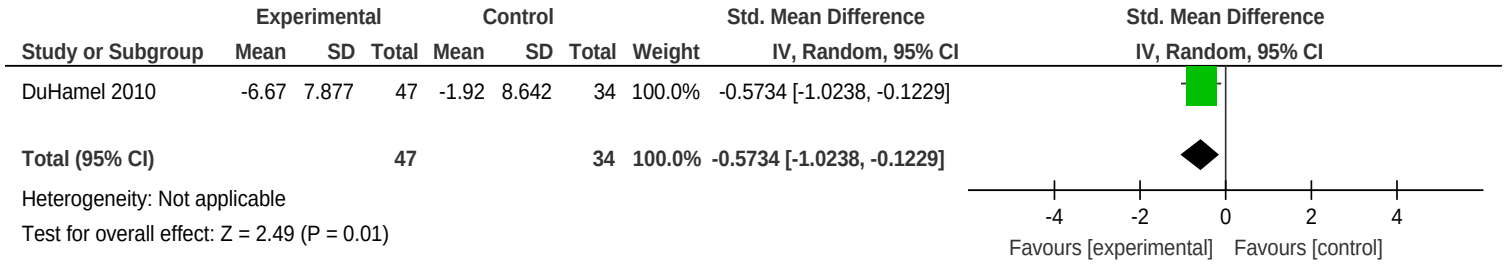


Figure 4.C.1.2.2.1: Comparison of CBT versus treatment as usual Outcome Distress

Table 4.C.1.2.2.1: GRADE Tables for Effect of CBT Interventions on Cancer-Related Distress

Quality assessment							No of patients		Effect	Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT intervention	Control	SMD (95% CI)		
Effect of CBT on distress (Better indicated by lower values)											
1[1]	randomised trials	no serious risk of bias[2]	no serious inconsistency[3]	no serious indirectness[4]	no serious imprecision[5]	none[6]	47	34	SMD 0.57 lower (1.02 to 0.12 lower)	⊕⊕⊕⊕ HIGH	CRITICAL

CBT intervention for cancer related distress

Outcomes	Illustrative comparative risks* (95% CI) Assumed risk Control	Corresponding risk CBT intervention	Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
Effect of CBT on distress		The mean effect of CBT on distress in the intervention groups was **0.57 standard deviations lower** (1.02 to 0.12 lower)		81 (1 study[1])	⊕⊕⊕⊕ **high**[2,3,4,5,6]	SMD -0.36 (-0.88 to 0.17)

CI: Confidence interval;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

[1] 1) DuHamel et.al., 2010
[2] Using Cochrane's Risk of Bias tool, the study was rated as low risk. There was a lack of certainty (unclear ratings) regarding allocation concealment; and high risk of bias associated with blinding of participants & outcome assessment. Given that most of the information is from studies at low risk of bias, this body of evidence was not downgraded for serious study limitations.
[3] The statistical heterogeneity across studies could not be assessed due to only one study providing data for this outcome.
[4] One RCT provided data for this outcome and included female population. The mean age was 52.19 and 49.38 years for intervention and control groups respectively. The intervention arm received Cognitive Behavioral Therapy. The control group received no treatment. The study was conducted in USA and published in 2010. The length of intervention was 16 weeks. There were no serious concerns regarding indirectness for this body of evidence and was not downgraded.
[5] The sample size is not adequate i.e. < 300 (47 intervention arm, 34 control arm) but the pooled effect estimate is precise and confidence intervals do not include the null value "0" [SMD= -0.5734 (-1.0238, -0.1229)]. This body of evidence was not downgraded for serious concerns regarding imprecision.
[6] There were too few studies (n<10) to assess publication bias.

4.C.1.2.3 Conclusion and Recommendation

The efficacy of CBT to reduce emotional distress, such as depression and global anxiety, has produced inconsistent findings. The above study indicates that when cancer patients are first screened for significant distress at study entry, CBT is effective in improving anxiety, depression and/or distress.

4.C.1.3 Results from Pharmacotherapy for Distress

This systematic review identified no eligible studies for pharmacotherapy of distress since the previous version of this guideline.

4.C.2 Global Anxiety- Fear of Cancer Recurrence

4.C.2.1 Results on Global Anxiety- Fear of Cancer Recurrence - Supportive-experiential group therapy (SET)

We identified one clinical controlled trial (CCT) that was conducted assessing the effect of SET compared to a control group[34] in a sample of cancer patients with significant fear of recurrence measured as fear of disease progression. Although this study did not meet our inclusion criteria, we included it, in the absence of any RCTs on the topic. The intervention was group based and delivered over 4 sessions. The main outcome was the Fear of Progression Questionnaire (FoP-Q) measured at baseline (T1), immediately after the intervention (T2), 3 (T3) and 12 (T4) months post discharge. Secondary outcomes included global anxiety, depression, and quality of life. The control group, which received standard of care, were recruited one year later and assessed with the FoP-Q at T1, T2 and T4. Data were not collected for secondary outcomes.

FoP-Q scores decreased significantly over time in the SET intervention group compared to the control group. Scores on the outcomes including global anxiety, depression and quality of life also improved over the time points measured.
The results from this one CCT suggests that brief SET may be effective at reducing fear or cancer progression (fear of recurrence) in cancer patients post-treatment and that the effects may last for up to 12 months. No conclusions can be drawn in terms of SET effects on global anxiety, depression or QoL given that lack of control data.

4.C.2.1.1 Risk of Bias of Included Studies

The results of the methodological quality assessment is shown in the Tables of Quality Assessment appendix 6 section 6.F Table 6.F.6 and Characteristics Table (Table 6.G.6 in appendix 6 section 6.G) see Figure 4.C.2.1.1.1.

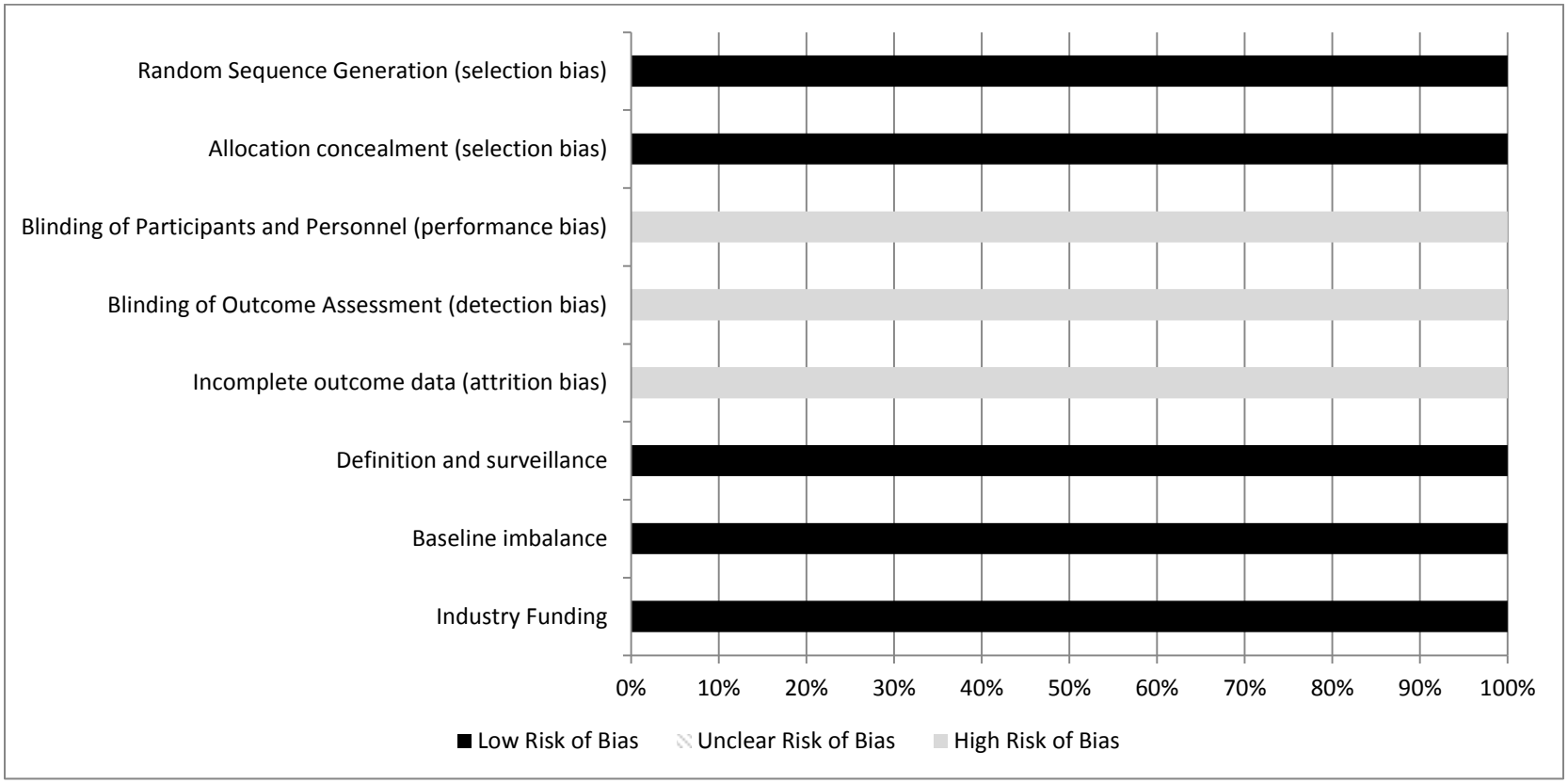


Figure 4.C.2.1.1.1: Risk of Bias Graph: Review Authors' Judgment about SET Interventions

4.C.2.1.2 Effects of SET on Fear: effect estimate

The data from one study, involving 63 patients in the SET arm and 68 patients in the control arm, showed that psychotherapy had no significant effect on fear of cancer recurrence among patients as compared to control group. (SMD = - 0.1445; 95%CI -0.4937 to 0.2047). The overall quality of this evidence was rated as very low and downgraded due to concerns regarding risk of bias and imprecision.

Review: SET for Fear of Recurrence among cancer patients
Comparison: SET versus treatment as usual
Outcome: Fear of Recurrence

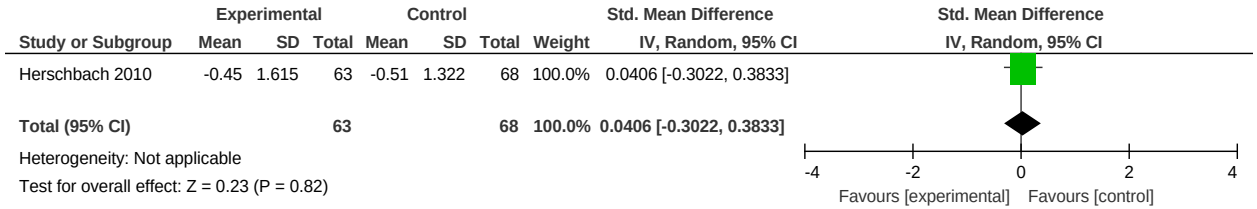


Figure 4.C.2.2.2.1: Effect of SET Interventions on Fear Recurrence

4.C.2.1.3 Conclusions and Recommendation

To date, only one CCT has examined the effect of brief group SET on fear of cancer progression (FoP). Although this study did not meet our inclusion criteria, we included it, in the absence of any RCTs on the topic and given the importance of this as a significant source of distress by the expert panel. The study included a screen for significant FoP to determine eligibility and had an adequate sample size. However, the control group was not recruited at the same time threatening the internal validity of the study. There was a significant improvement in FoP-Q scores over time compared to the control group suggesting that brief group SET is effective a reducing FoP but further studies are needed before a recommendation can be made.

Table 4.C.2.1.3.1: GRADE Tables for Effect of SET Interventions on Fear of Cancer Recurrence

Quality assessment							No of patients		Effect	Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**SET intervention**	**Control**	**SMD (95% CI)**		
Effect of SET on Fear (Better indicated by lower values)											
1[1]	randomized trials	Very serious[2]	no serious inconsistency[3]	no serious indirectness[4]	serious[5]	none[6]	63	68	0.04 higher (0.3 lower to 0.38 higher)	⊕⊕OO LOW	CRITICAL

CBT intervention for cancer related fear

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk **Control**	Corresponding risk **SET intervention**				
Effect of SET on Fear		The mean effect of SET on fear in the intervention groups was **0.04 standard deviations higher** (0.3 lower to 0.38 higher)		131 (1 study[1])	⊕⊕⊖⊖ **low**[2,3,4,5,6]	SMD 0.04 (-0.3 to 0.38)

CI: Confidence interval;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Herschbach et.al., 2010
[2] Using Cochrane's Risk of Bias tool, for this outcome, the study was rated as unclear risk. There was high risk of bias associated with randomization, allocation concealment, blinding of participants & outcome assessment, and incomplete outcome reporting. Given that most of the information is from studies at high risk of bias, this body of evidence was downgraded for very serious study limitations.
[3] The statistical heterogeneity across studies could not be assessed due to only one study providing data for this outcome.
[4] One CCT provided data for this outcome. The study included mixed gender population. The mean age was 53.7 years. The intervention arm received Supportive-Expressive Therapy. The control group received usual care. The study was conducted in Germany and published in 2010. The length of intervention was 2 weeks. There were no serious concerns regarding indirectness for this body of evidence and was not downgraded
[5] The sample size is not adequate i.e. < 300 (63 intervention arm, 68 control arm) and the effect estimate is not precise and confidence interval include the null value "0" [SMD= -0.0406 (-0.3022, 0.3833)]. This body of evidence was downgraded for serious concerns regarding imprecision.
[6] There were too few studies (n<10) to assess publication bias.

4.C.2.2 Results on Global Anxiety- Fear of Cancer Recurrence – CBT

Our search identified only one clinical controlled trial that assessed CBT compared to a control group[34] in a sample of cancer patients with significant fear of progression. The intervention was group based and delivered over 4 sessions. The main outcome was the Fear of Progression Questionnaire measured at baseline (T1), immediately after the intervention (T2), 3 (T3) and 12 (T4) months post discharge. Secondary outcomes included anxiety, depression, and quality of life. The control group, which received standard of care, were recruited one year later and assessed with the FoP-Q at T1, T2 and T4. Data was not collected for secondary outcomes.

FoP-Q scores decreased significantly over time in the CBT intervention group compared to the control group. Scores on the secondary outcomes including anxiety depression and quality of life also improved over the time points measured.
The results from this one clinical controlled trial suggests that brief CBT may be effective at reducing fear or cancer progression (fear of recurrence) in cancer patients post-treatment and that the effects may last for up to 12 months. No conclusions can be drawn in terms of CBT effects on anxiety, depression or QoL given that lack of control data.

4.C.2.2.1 Risk of Bias of Included Studies

The results of the methodological quality assessment is shown in the Tables of Quality Assessment appendix 6 section 6.F Table 6.F.6 and Characteristics Table (Table 6.G.6 in appendix 6 section 6.G) see Figure 4.C.2.2.1.1.

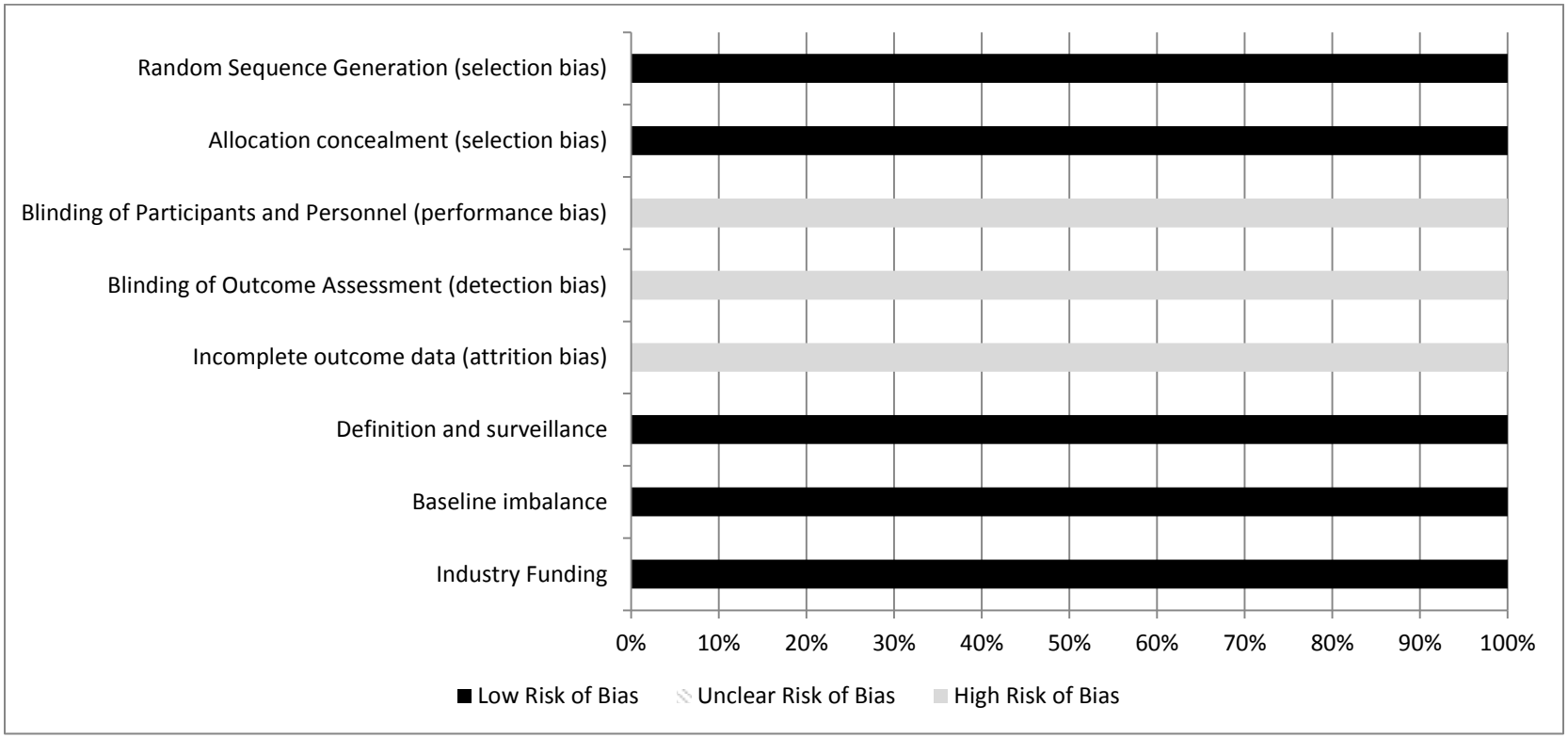


Figure 4.C.2.2.1.1: Risk of Bias Graph: Review Authors' Judgment about CBT Interventions

4.C.2.2.2 Effects of CBT on Fear: effect estimate

The data from one study, involving 63 patients in the CBT arm and 68 patients in the control arm, showed that CBT had no significant effect on fear of cancer recurrence among patients as compared to control group. (SMD = 0.0406; 95%CI -0.3022 to 0.3833). The overall quality of this evidence was rated as very low and downgraded due to concerns regarding risk of bias and imprecision. See Figure 4.C.2.2.2.1.

Review: CBT for Fear of Recurrence among cancer patients
Comparison: CBT versus treatment as usual
Outcome: Fear of Recurrence

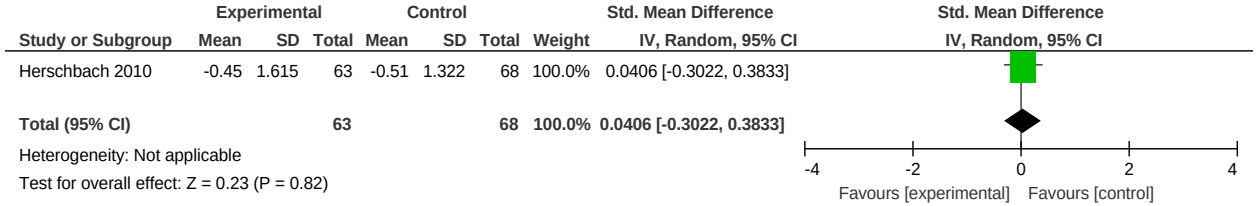


Figure 4.C.2.2.2.1: Effect of CBT Interventions on Fear Recurrence

4.C.2.2.3 Conclusion and Recommendation

To date, only one RCT has examined the effect of brief group CBT on FoP. The study included a screen for significant FoP to determine eligibility and had an adequate sample size. However, the control group was not recruited at the same time threatening the internal validity of the study. There was a significant improvement in FoP-Q scores over time compared to the control group suggesting that brief group CBT is effective a reducing FoP but further studies are needed before a recommendation can be made.

We assessed the overall SOE across the literature using the rating approach as specified by the GRADE tables. See Table 4.C.2.2.3.1.

Table 4.C.2.2.3.1: GRADE Tables for Effect of CBT Interventions on Fear of Cancer Recurrence

Quality assessment							No of patients		Effect	Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT intervention	Control	SMD (95% CI)		
Effect of CBT on Fear (Better indicated by lower values)											
1[1]	randomized trials	serious[2]	no serious inconsistency[3]	no serious indirectness[4]	serious[5]	none[6]	63	68	0.04 higher (0.3 lower to 0.38 higher)	⊕⊕OO LOW	CRITICAL

CBT intervention for cancer related fear

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk Control	Corresponding risk CBT intervention				
Effect of CBT on Fear		The mean effect of CBT on fear in the intervention groups was **0.04 standard deviations higher** (0.3 lower to 0.38 higher)		131 (1 study[1])	⊕⊕⊖⊖ **low**[2,3,4,5,6]	SMD 0.04 (-0.3 to 0.38)

CI: Confidence interval;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Herschbach et.al., 2010
[2] Using Cochrane's Risk of Bias tool, for this outcome, the study was rated as unclear risk. There was high risk of bias associated with blinding of participants & outcome assessment, and incomplete outcome reporting. Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.
[3] The statistical heterogeneity across studies could not be assessed due to only one study providing data for this outcome.
[4] One RCT provided data for this outcome. The study included mixed gender population. The mean age was 53.7 years. The intervention arm received Supportive-Expressive Therapy. The control group received usual care. The study was conducted in Germany and published in 2010. The length of intervention was 2 weeks. There were no serious concerns regarding indirectness for this body of evidence and was not downgraded
[5] The sample size is not adequate i.e. < 300 (63 intervention arm, 68 control arm) and the effect estimate is not precise and confidence interval include the null value "0" [SMD= -0.0406 (-0.3022, 0.3833)]. This body of evidence was downgraded for serious concerns regarding imprecision.
[6] There were too few studies (n<10) to assess publication bias.

4.C.3 Results for Pharmacological and Psychological Interventions for Cancer-Related Depression

In our review of the grey literature, we identified a recently completed Cancer Care Ontario (CCO) depression guideline entitled *The Management of Depression in Patients with Cancer*[18]. This guideline made recommendations for the management of major depressive disorder diagnosed by a structured clinical interview, or a suspected depressive disorder based on meeting a threshold on a validated depression rating scale. The current systematic review searched up to May 2015 and did not identify any additional intervention studies for the treatment of depression in cancer patients beyond those described in the CCO depression guideline. Given the currency and quality of evidence in this guideline as per AGREE[3], the expert panel adopted recommendations from this guideline.

The CCO depression guideline searched from database inception to January 2015, and 25 primary articles met the inclusion criteria of RCTs where individuals in the study population met a cut-off for a suspected depressive disorder on a validated depression rating scale or were diagnosed with a major depressive disorder based on a structured diagnostic interview at study entry. Eight pharmacological[59-65] interventions, 9 psychological [31, 53, 66-72] interventions, and 8 reports of 4 collaborative care[73-80] interventions comprised the evidence base. Detailed descriptions and analyses of these studies can be found in the source guideline[18], where meta-analyses were conducted for each of the intervention types.

Among pharmacological interventions, two studies of mianserin compared with placebo control group[59, 63], and one study of methylphenidate plus mirtazapine compared with placebo plus mirtazapine[65] found significant differences between groups, while a double-blind three-arm trial of paroxetine compared with desipramine or a placebo control did not achieve the required sample size to detect differences between groups[64]. Other trials of fluoxetine[60, 62, 81], desipramine[81], or paroxetine and amitriptyline[61] did not separate from placebo or active comparator. Meta-analysis showed an overall positive effect of pharmacotherapy on depression in cancer patients with an odds ratio of 1.91 (95% CI, 1.09 to 3.36).

The 9 eligible RCTs that assessed psychological interventions, included CBT[31, 68, 70, 71], social support[68], problem-solving therapy (PST) [69], behavioral activation treatment (BAT) [82], "low-threshold" psycho-oncological support[53], narrative therapy[72], and psychodynamic psychotherapy[67], compared with other pharmacological or psychological treatments, or a waiting list or a usual-care control group. Effectiveness was demonstrated in 5 of these studies including CBT[68, 69] social support[68], PST with or without a significant other[69], brief psycho-oncological support[53], and short-term psychodynamic psychotherapy[67]. Meta-analysis of studies comparing treatment groups

with a usual care/no treatment control group[53, 68-72] significantly favored the experimental groups (standardized mean difference [SMD], -1.40 [95% CI, -2.50 to -0.29]).

All collaborative care interventions, which are models of care characterized by active collaboration between psychiatry specialists, primary care or oncology providers, and a care manager who monitors treatment compliance, resulted in significantly better standardized mean depression scores compared with usual care, sustained up to 12 months after initiation of the intervention. These models of care combine psychological interventions (primarily problem solving therapy or telephone support) and pharmacotherapy as needed, with rates of antidepressant use ranging from 35% [74] to 82%[79] in the intervention groups and from 11% [74] to 58%[79] in the comparison groups. The SMD in meta-analyses of studies that reported data for effects at three, six, and twelve months after the initiation of treatment favored the intervention group at all time periods (SMD -0.58, 95% CI -0.91 to -0.25, p=0.00007 at 3 months; SMD -0.53, 95% CI -0.85 to -0.20, p=0.001, at 6 months; SMD -0.49, 95% CI -0.81 to -0.16, p=0.003, at 12 months).

4.C.3.1 Conclusion

Conclusions from the CCO depression guideline systematic review were that there remains a paucity of high-quality pharmacotherapy or psychotherapy research on the treatment of depression in patients with cancer. Although the meta-analyses indicate cancer patients with depression may benefit from either pharmacological or psychological interventions, there is insufficient evidence to support the superiority of any specific treatment over another. In the absence of a strong cancer-specific evidence base, recommendations for management were extrapolated from evidence of treatment efficacy in primary psychiatric and other medical populations.

4.C.3.2 Recommendation

Based on expert opinion and adapting from the National Institute for Health and Care Excellence (NICE) Clinical Guideline 91 (CG91), Depression in Adults with a Chronic Physical Health Problem [19], eight recommendations were made in the CCO depression guideline which were endorsed in the current guideline:

1. Patients with cancer should be screened for depression
2. Seven general principles to guide assessment, investigation, communication and management of cancer patients with depression
3. Patients with cancer who are diagnosed with depression may benefit from pharmacological or psychosocial interventions either alone or in combination

4. Interventions for depression in patients with cancer should be delivered according to a stepped care model tailored according to depression severity
5. Collaborative care interventions should be considered for patients with cancer who are diagnosed with depression
6. Five indications for referral to mental health specialists
7. Selection of psychological should be based on patient factors and local resource availability
8. Antidepressant medication should not be used routinely to treat sub-threshold depressive symptoms or mild depression, but should be considered first for severe depression.

4.C.4 Cancer-Related Global Anxiety

4.C.4.1 Results for Pharmacotherapy for Global Anxiety

This systematic review identified no eligible studies for pharmacotherapy of global anxiety since the previous version of this guideline.

4.C.4.2 Results of Psychosocial-education—Global Anxiety

There is an increased focus on providing brief interventions such as psychosocial sessions for individuals with cancer-related global anxiety in a timely manner across the cancer experience. This is often regarded as a means to meet patient needs by decreasing cancer-related global anxiety and facilitating their coping, thereby improving quality of life. One recent RCT[53] with cancer patients dealing with challenging disease highlights the value of such brief interventions. In a sample of 131 patients, they found a reduction of global anxiety and depression in the high risk cancer patients (according to the HADS) on a surgical ward, who received psycho-oncological intervention up to a year after discharge from the hospital. See Table 4.C.4.2.2.1.

4.C.4.2.1 Risk of Bias of Included Studies

The results of the methodological quality assessment is shown in the Tables of Quality Assessment appendix 6 section 6.F Table 6.F.4 and Characteristics Table (Table 6.G.4 in appendix 6 section 6.G) see Figure 4.C.4.2.1.1.

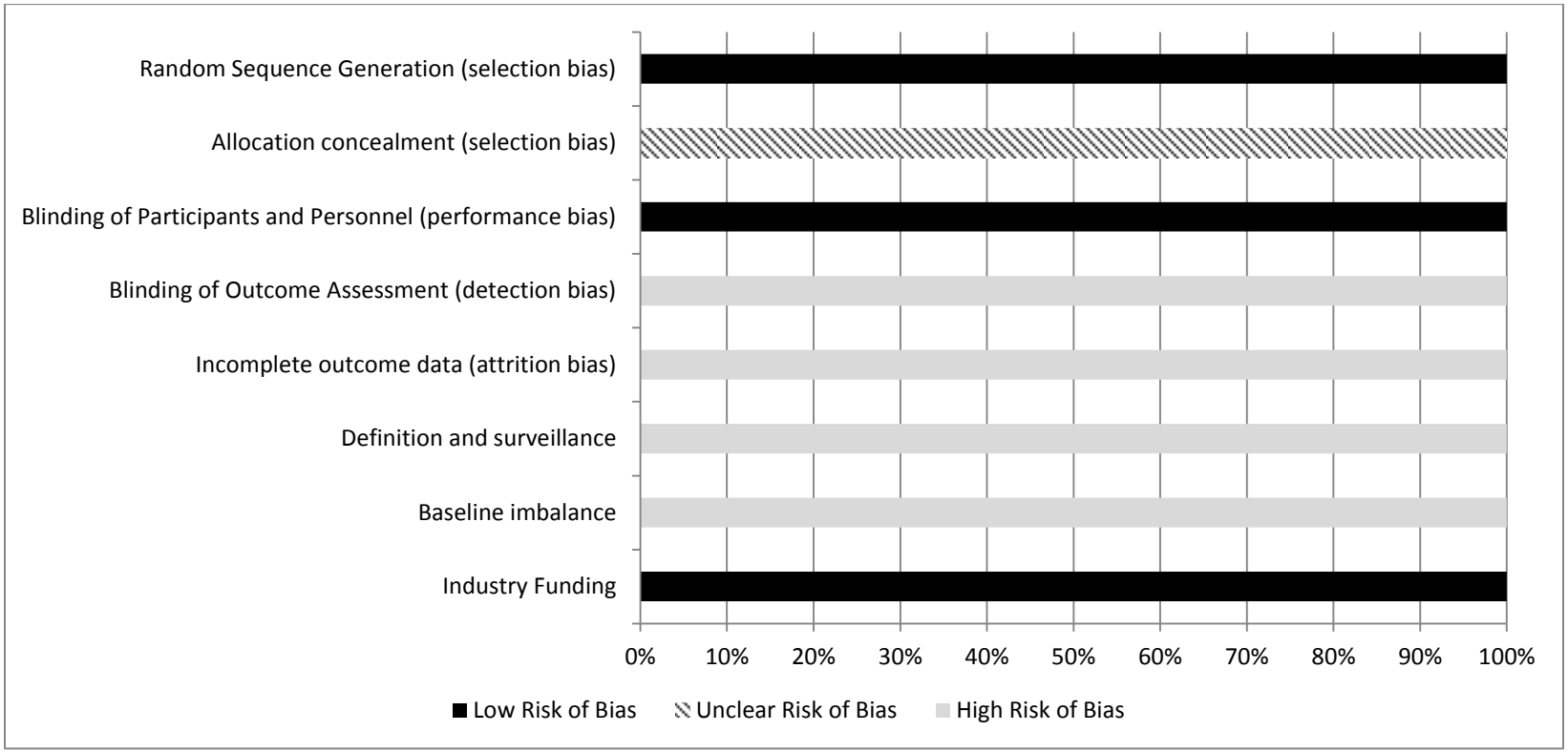


Figure 4.C.4.2.1.1: Risk of Bias Graph: Review Authors' Judgment about Psychosocial Interventions

4.C.4.2.2 Effects of Psychosocial on Global Anxiety:

The effect estimate from one study, involving 65 patients in the Psychosocial/Psycho-educational arm and 65 patients in the control arm, showed that psychotherapy had a significant effect of large magnitude on global anxiety among patients with cancer as compared to control group. (SMD = - 0.8207; 95%CI -1.1791 to -0.4623). The overall quality of this evidence was rated as moderate and downgraded due to concerns regarding risk of bias. See Figure 4.C.3.2.2.1.

Review: Psychosocial for global anxiety among cancer patients
Comparison: Psychosocial versus treatment as usual
Outcome: Global Anxiety

	Experimental			Control				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Goerling 2011	-2.822	2.482	65	-0.568	2.958	65	100.0%	-0.8207 [-1.1791, -0.4623]
Total (95% CI)			**65**			**65**	**100.0%**	**-0.8207 [-1.1791, -0.4623]**

Heterogeneity: Not applicable
Test for overall effect: Z = 4.49 (P < 0.00001)

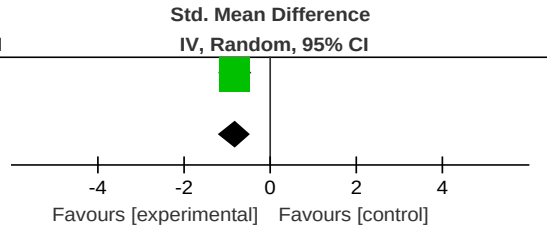


Figure 4.C.4.2.2.1: Effect of Psychosocial Intervention on Global Anxiety

Table 4.B.4.2.2.1: GRADE Tables for Effect of Psychosocial education Interventions on Global Anxiety

Quality assessment							No of patients		Effect	Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Education / Psychosocial intervention	Control	SMD (95% CI)		
Effect of Education / Psychosocial intervention on global anxiety (Better indicated by lower values)											
1[1]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness[4]	no serious imprecision[5]	none[6]	65	65	SMD 0.82 lower (1.18 to 0.46 lower)	⊕⊕⊕O MODERATE	CRITICAL

Education / Psychosocial intervention for cancer related global anxiety

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk **Control**	Corresponding risk **Education / Psychosocial intervention**				
Effect of Education / Psychosocial intervention on anxiety		The mean effect of education / psychosocial intervention on global anxiety in the intervention groups was **0.82 standard deviations lower** (1.18 to 0.46 lower)		130 (1 study[1])	⊕⊕⊕⊖ **moderate**[2,3,4,5,6]	SMD -0.82 (-1.18 to -0.46)

CI: Confidence interval;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] 1) Goerling et.al., 2011
[2] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as high risk. Across studies, there was a lack of certainty (unclear ratings) regarding allocation concealment; and high risk of bias associated with blinding of participants & outcome assessment, incomplete outcome reporting and other sources of bias (i.e., industry funding, baseline differences between groups, insufficiently powered and/or sample size <30 per arm,). Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.
[3] The statistical heterogeneity across studies could not be assessed due to only one study providing data for this outcome.
[4] One RCT provided data for this outcome and included mixed gender population. The mean age was 57 years. The intervention arm received psycho-oncological support. The control group received support / usual care. The study was conducted in Germany published in 2011. The length of intervention was 12 weeks. There were no serious concerns regarding indirectness for this body of evidence and was not downgraded.
[5] The sample size is not adequate i.e. < 300 (65 intervention arm, 65 control arm) but the pooled effect estimate is precise and confidence intervals do not include the null value "0" [SMD= -0.8207 (-1.1791, -0.4623)]. This body of evidence was not downgraded for serious concerns regarding imprecision.
[6] There were too few studies (n<10) to assess publication bias.

4.C.4.3 Results from CBT intervention for Global Anxiety

Our search identified two eligible CBT RCTs for the treatment of cancer-related distress in adults. Kangas et al.[31] examined the benefits of a multi-modal CBT versus a non-directive supportive counselling (SC) program on PTSD, general anxiety and depressive symptoms. The sample included 35 newly diagnosed head and neck cancer patients randomly assigned to either one of the two individually delivered therapies. Results indicated that both programs were equally effective in reducing PTSD, anxiety and depressive symptom severity at 1 and 6 months. However, up to 67% of patients in the CBT program no longer met clinical or sub-clinical PTSD, anxiety and/or depression by 12 months post-treatment compared with 25% of patients who received SC. This study was limited in having a low sample size and no non-intervention (i.e., waitlist) control group.

Greer et al.[32] examined the feasibility and efficacy of an adapted CBT intervention in reducing anxiety symptoms in patients with end stage cancer (terminally ill). Eligibility included a diagnosis of an incurable solid tumor, meeting the criteria of clinically significant anxiety (i.e., scoring ≥14 on the Hamilton Anxiety Rating Scale-HADS). A total of 40 patients were randomly assigned either to an individual CBT intervention or a waitlist control group. Results indicated that the intervention was deemed feasible as 80% of patients in the CBT group completed 5 or more of the 6 sessions. With respect to the primary outcome, results indicated that participants in the CBT intervention reported a 35% reduction in anxiety symptoms compared to 11% in the control group.

4.C.4.3.1 Risk of Bias of Included Studies

The results of the methodological quality assessment is shown in the Tables of Quality Assessment appendix 6 section 6.F Table 6.F.5 and Characteristics Table (Table 6.G.5 in appendix 6 section 6.G) see Figure 4.C.4.3.1.1.

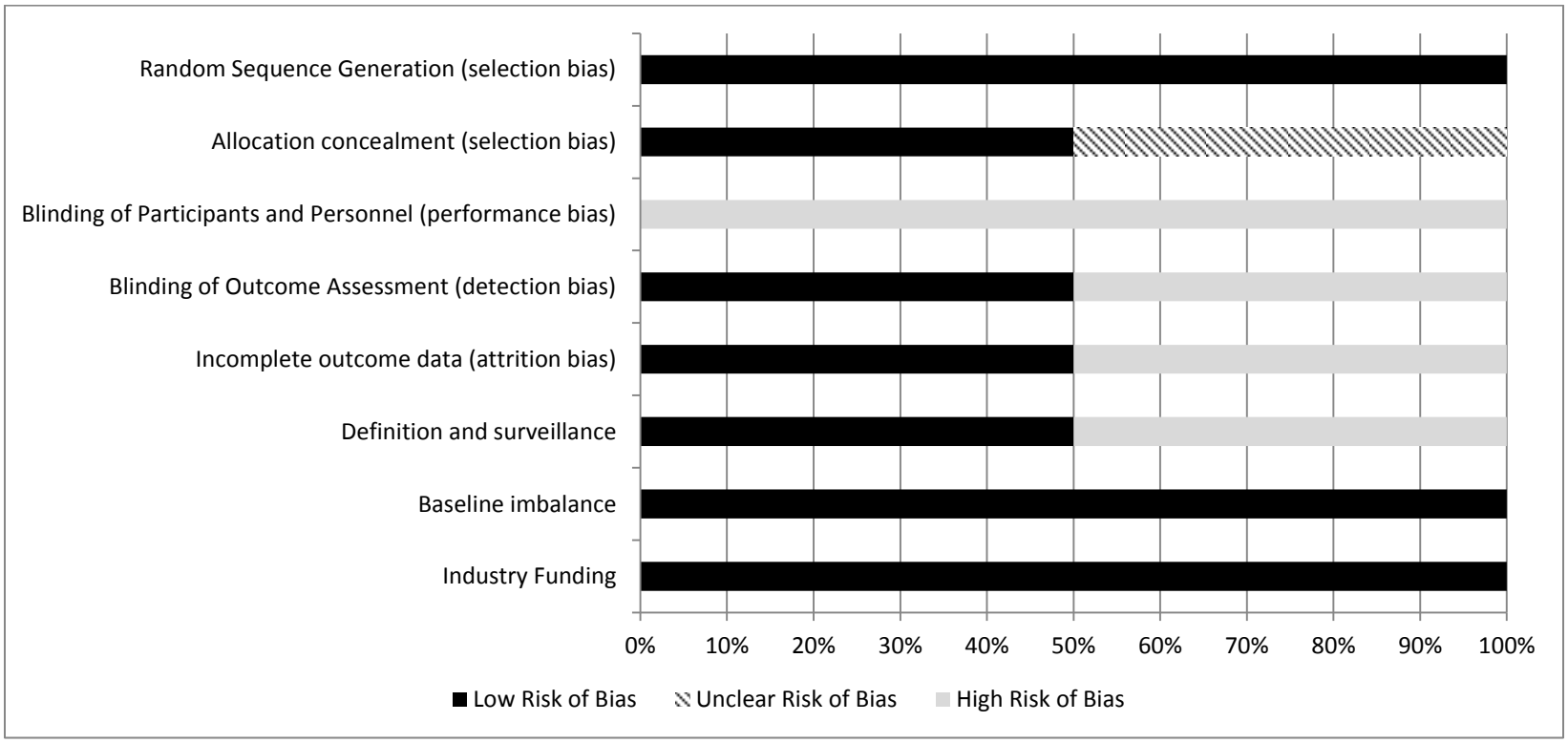


Figure 4.B.4.3.1.1: Risk of Bias Graph: Review Authors' Judgment about CBT Interventions

4.C.4.3.2 Effects of CBT on Global Anxiety: meta-analyses

The combined data from the two studies, involving 41 patients in the CBT arm and 34 patients in the control arm, showed that CBT had no significant effect on anxiety among patients with cancer as compared to control group. (SMD = - 0.3173; 95%CI -0.1400 to 1.3798). The overall quality of this evidence was rated as very low and downgraded due to concerns regarding risk of bias, inconsistency and imprecision. See Figure 4.C.3.3.2.1.

Review: CBT for distress among cancer patients
Comparison: CBT versus treatment as usual
Outcome: Distress

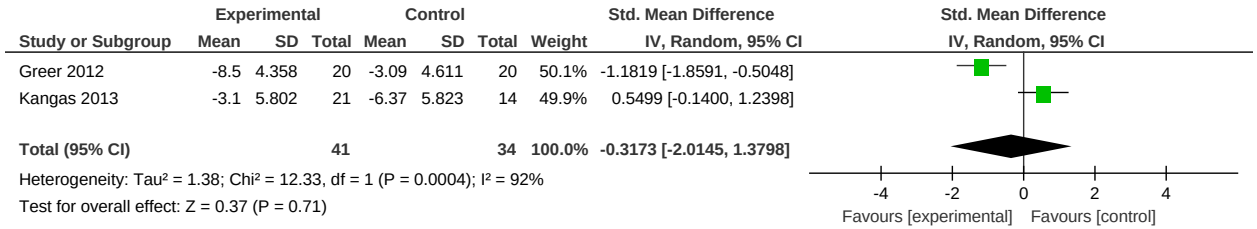


Figure 4.C.4.3.2.1: Effect of CBT Interventions Cancer-Related Global Anxiety

Table 4.C.4.3.2.1: GRADE Tables for Effect of CBT Interventions on Global Anxiety

Quality assessment							No of patients		Effect	Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT intervention	Control	SMD (95% CI)		
Effect of CBT on global anxiety (Better indicated by lower values)											
2[1]	randomized trials	serious[2]	serious[3]	no serious indirectness[4]	serious[5]	none[6]	41	34	0.32 lower (2.01 lower to 1.38 higher)	⊕OOO VERY LOW	CRITICAL

CBT intervention for cancer related global anxiety

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk Control	Corresponding risk CBT intervention				
Effect of CBT on global anxiety		The mean effect of CBT on global anxiety in the intervention groups was **0.32 standard deviations lower** (2.01 lower to 1.38 higher)		75 (2 studies[1])	⊕⊖⊖⊖ **very low**[2,3,4,5,6]	SMD -0.32 (-2.01 to 1.38)

CI: Confidence interval;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] 1) Kangas et al., 2013; 2) Greer et.al., 2012

[2] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as low and one as high risk. Across studies, there was a lack of certainty (unclear ratings) regarding allocation concealment; and high risk of bias associated with blinding of participants & outcome assessment, incomplete outcome and selective reporting. Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.
[3] The statistical heterogeneity is high [Chi2=12.33, df=1 (P=0.0004); I2=92%] and the direction of the effect is not consistent across studies with minimal overlap of confidence intervals. This body of evidence was downgraded for serious concerns regarding inconsistency.
[4] Two RCTs provided data for this outcome. Both studies included mixed gender population. The mean age ranged from 54 to 56 years. The intervention arm across studies received Cognitive Behavioral Therapy. The control group across studies received of support / usual care. One study was conducted in US and one in Australia. All studies were published between 2012 and 2013. The length of intervention across studies ranged from 6 to 8 weeks. There were no serious concerns regarding indirectness for this body of evidence and was not downgraded.
[5] The sample size is not adequate i.e. < 300 (41 intervention arm, 34 control arm) and the pooled effect estimate is not precise and confidence interval include the null value "0" [SMD= -0.3173 (-2.0145, 1.3798)]. This body of evidence was downgraded for serious concerns regarding imprecision.
[6] There were too few studies (n<10) to assess publication bias.

4.C.4.3.3 Conclusion and Recommendation

These two studies were limited by small sample size and the lack of non-intervention (i.e., waitlist) control group. With respect to the primary outcome, results indicated that participants in the CBT intervention reported a 35% reduction in global anxiety symptoms compared to 11% in the control group.

4.C.5 Post-Traumatic Stress Disorder (PTSD)

We identified three RCTs examining the effectiveness of psychosocial and CBT interventions that targeted cancer-related PTSD compared to usual care[29, 31, 55]. This is the first review on PTSD, so there is a need to have a brief introduction.

The diagnosis of cancer, cancer treatment and its sequel, associated lifestyle adjustments, losses, fears of recurrence, and life-threat can be traumatic and life-altering for cancer patients and survivors, as well as their families. In DSM-5[95], Anxiety Disorders were divided into three categories with PTSD and Adjustment Disorders being placed in Trauma-and Stressor-Related Disorders, as both develop following exposure to acute/chronic stressors. In DSM-IV, "being diagnosed with life-threatening illness" potentially met traumatic event criterion for PTSD [139], whereas in DSM-5, "a life-threatening illness or debilitating medical condition is not necessarily considered a traumatic event. Medical incidents that qualify as traumatic events involve sudden, catastrophic events" (p. 274, APA, 2013). There are many aspects of cancer and treatment (i.e., stage and type of cancer; prognosis; invasive medical treatment; treatment complications; impact of cancer and treatment on body image, self-image, self-esteem, and functioning; disease burden) that meet the diagnostic criterion for exposure to a traumatic event for PTSD. The other PTSD diagnostic criteria include intrusion/re-experiencing symptoms, persistent avoidance, negative changes in mood or cognitions related to the trauma, and marked symptoms of arousal and reactivity related to the trauma, with clinically significant distress or impairment in functioning. Although there are some differences between the DSM-IV and the DSM-5 diagnostic criteria for PTSD (i.e., delineation/expansion of negative changes in mood or cognitions in DSM-5; indirect exposure to trauma is now included; removal of person's response of intense fear/horror from trauma criteria), many of the criteria have remained the same.

There is growing clinical literature focusing on Post-Traumatic Stress Disorder (full disorder and sub-threshold/sub-syndromal presentation) in various cancer populations such as breast cancer, hematological cancer, and head and neck cancer (i.e., [31, 140, 141]). Mehnert and Koch (2007)[142] cite literature indicating a varying prevalence range of cancer-related PTSD of up to 32%, with many more patients displaying specific PTSD symptoms. A higher frequency has been noted when sub-threshold symptoms/

symptom clusters, such as re-experiencing symptoms and fear of recurrence, are examined. Some studies have reported findings that indicate PTSD in cancer patients/survivors, similar to some other trauma groups, can be longstanding. For example, Smith et al.[143] reported that 37% of a sample of Non-Hodgkin's Lymphoma survivors experienced persistent or worsening PTSD symptoms over a 5-year period. The many methodological differences between studies regarding the assessment/measurement of Post-Traumatic Stress Disorder and Post-Traumatic Stress features make direct comparisons and the examination of incidence challenging. This is further complicated by the many different types of cancer, treatment protocols, invasiveness of cancer treatments, disease burden of specific cancers, and individual differences/reactions, personal history (i.e., past trauma), and supports that can affect or moderate an individual's cancer experience and emotional reaction. The length of time required treating and dealing with cancer can serve as a constant reminder to the patient, thus keeping the focus on the trauma.

With respect to treatment of PTSD, there are many studies examining the effectiveness of psychotherapeutic approaches with various trauma populations. Studies have been published supporting the effectiveness of CBT and Eye Movement Desensitization and Reprocessing (EMDR) (i.e., Foa, Keane, Friedman, & Cohen[144]; Bisson et al.[145]). Several studies have examined the efficacy of psychosocial interventions in published studies focused on anxiety in cancer patients (i.e., Jacobsen & Jim[146]). There is limited research focused on the efficacy of psychotherapy/psychosocial interventions for cancer patients with full disorder or sub-threshold PTSD. There are few studies that meet criteria for RCT's.

4.C.5.1 Results from Psychosocial Intervention on Cancer-Related Post-Traumatic Stress Disorder (PTSD)

There is increased focus on providing brief interventions/psychosocial sessions for individuals with cancer-related anxiety and post-traumatic stress symptoms in a timely manner across the cancer experience. This is often regarded as a means to meet patient needs by decreasing cancer-related anxiety and post-traumatic stress features and facilitating the patient's ability to cope, thereby improving quality of life. One recent RCT with cancer patients highlight the value of such brief interventions. Carpenter et al.[55] examined the effectiveness of an online cognitive behavioral stress management workbook intervention for breast cancer patients with at least moderate distress, relative to a waitlist control group. They reported that the intervention group patients displayed increased self-efficacy in their ability to cope with cancer and decreased post-traumatic stress symptoms, as measured by the Revised Impact of Event Scale.

4.C.5.1.1 Risk of Bias of Included Studies

The results of the methodological quality assessment is shown in the Tables of Quality Assessment appendix 6 section 6.F Table 6.F.3 and Characteristics Table (Table 6.G.3 in appendix 6 section 6.G) see Figure 4.C.5.1.1.1.

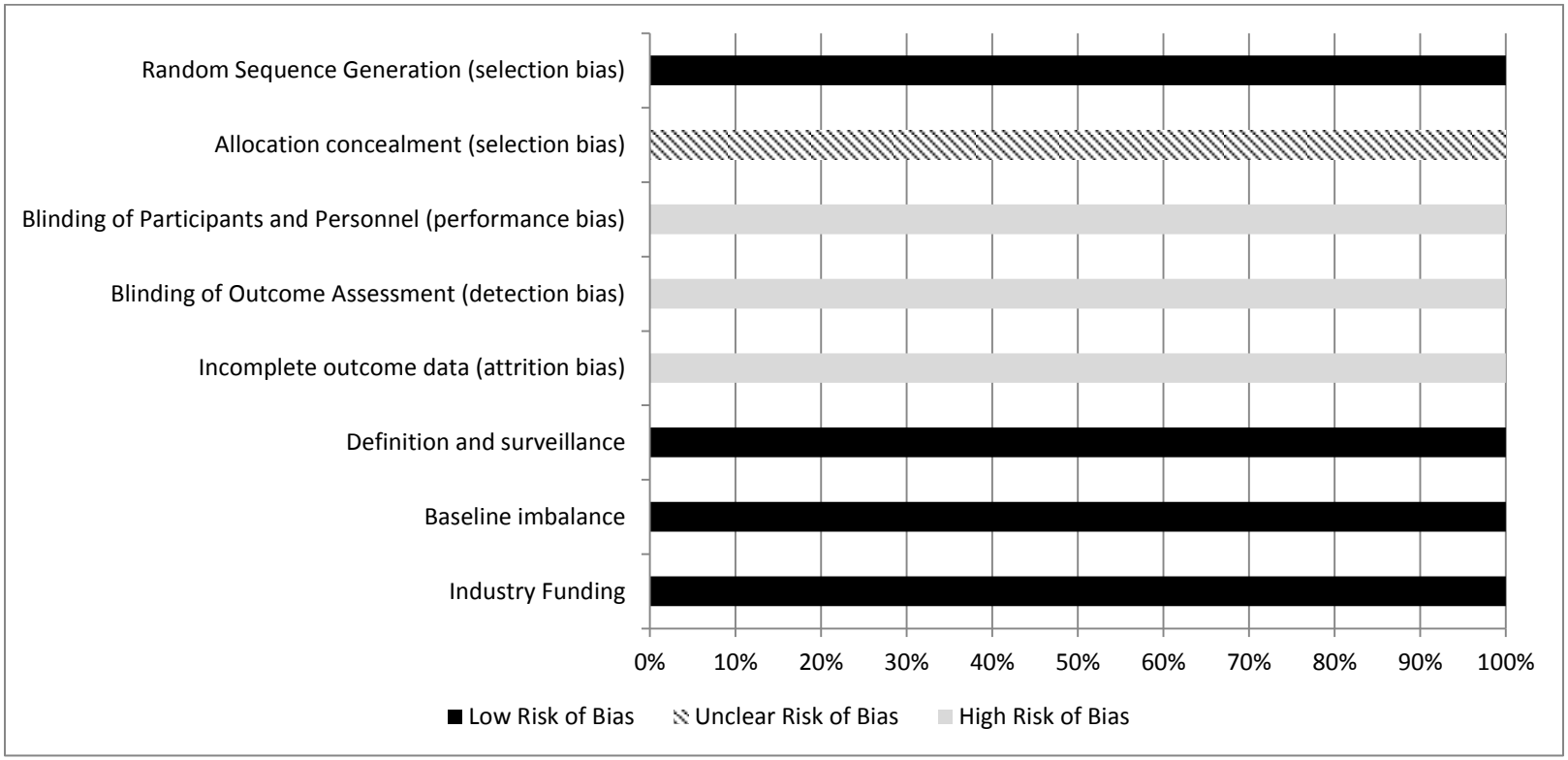


Figure 4.C.5.1.1.1: Risk of Bias Graph: Review Authors' Judgment about PTSD- Psychosocial Interventions

4.C.5.1.2 Effects of Psychosocial Interventions on PTSD:

The data from one study, involving 57 patients in the psychosocial Interventions arm and 59 patients in the control arm, showed that psychosocial Interventions had a significant effect of medium magnitude on PTSD among patients as compared to control group. (SMD = -0.6185; 95%CI -0.9914 to -0.2456). The overall quality of this evidence was rated as low and downgraded due to concerns regarding risk of bias. See Figure 4.C.5.1.2.1.

Review: Psychosocial on PTSD among cancer patients
Comparison: Psychosocial versus treatment as usual
Outcome: PTSD

	Experimental			Control				Std. Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
Carpenter 2014	-1.1	0.955	57	-0.5	0.972	59	100.0%	-0.6185 [-0.9914, -0.2456]
Total (95% CI)			**57**			**59**	**100.0%**	**-0.6185 [-0.9914, -0.2456]**

Heterogeneity: Not applicable
Test for overall effect: Z = 3.25 (P = 0.001)

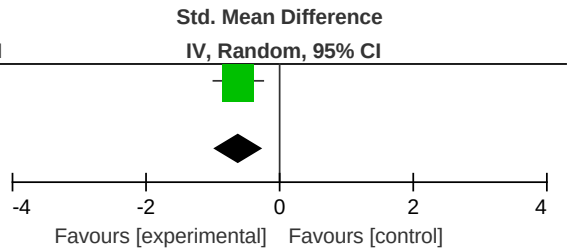


Figure 4.C.5.1.2.1: Effect of Psychosocial Interventions PTSD

Table 4.C.5.1.2.1: GRADE Tables for Effect of Psychosocial Interventions on PTSD

Quality assessment							No of patients		Effect	Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Education/Psychosocial intervention**	**Control**	**SMD (95% CI)**		
Effect of Education/Psychosocial intervention on PTSD (Better indicated by lower values)											
1[1]	randomised trials	very serious[2]	no serious inconsistency[3]	no serious indirectness[4]	no serious imprecision[5]	none[6]	57	59	SMD 0.62 lower (0.99 to 0.25 lower)	⊕⊕OO LOW	CRITICAL

Education/Psychosocial intervention for cancer related PTSD

Patient or population: patients with cancer related PTSD
Settings:
Intervention: Education/Psychosocial intervention

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk **Control**	Corresponding risk **Education/Psychosocial intervention**				
Effect of Education/Psychosocial intervention on PTSD		The mean effect of education/psychosocial intervention on PTSD in the intervention groups was **0.62 standard deviations lower** (0.99 to 0.25 lower)		116 (1 study[1])	⊕⊕⊖⊖ **low**[2,3,4,5,6]	SMD -0.62 (-0.99 to -0.25)

CI: Confidence interval;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] 1) Carpenter et al. 2014
[2] Using Cochrane's Risk of Bias tool, for this outcome, the study was rated high risk. There was a lack of certainty (unclear ratings) regarding allocation concealment; and high risk of bias associated with random sequence generation, blinding of participants & outcome assessment, incomplete outcome and selective reporting. Given that most of the information is from studies at high risk of bias, this body of evidence was downgraded for serious study limitations.
[3] The statistical heterogeneity across studies could not be assessed due to only one study providing data for this outcome.
[4] One RCT provided data for this outcome and included mixed gender population. The mean age was 55 years. The intervention arm received psycho-oncological support. The control group received of support / usual care. The study was conducted in US and published in 2013. The length of intervention was 10 weeks. There were no serious concerns regarding indirectness for this body of evidence and was not downgraded.
[5] The sample size is not adequate i.e. < 300 (57 intervention arm, 59 control arm) but the pooled effect estimate is precise with narrow confidence intervals [SMD= -0.6185 (-0.9914, -0.2456)]. This body of evidence was not downgraded for imprecision.
[6] There were too few studies (n<10) to assess publication bias.

4.C.5.1.3 Conclusion and Recommendation

Psychosocial interventions when compared with usual or standard care was found to be different in terms of reducing PTSD symptoms, as well as anxiety symptoms. The study by Carpenter[55] provides support for the usefulness of Internet based psychosocial intervention for distressed cancer survivors who have cancer-related post-traumatic symptoms. (see Table 4.C.4.1.2.1).

4.C.5.2 Results from CBT intervention on Cancer-Related Post-Traumatic Stress Disorder (PTSD)

Two recent studies are noteworthy in regard to treatment of PTSD in cancer patients. Specifically, Capezzani et al.[29] compared the effectiveness of CBT and EMDR in a sample of cancer patients with different types of cancer with assessed PTSD in the follow-up phase of their disease, as well as examining one group of patients on active treatment who received EMDR. The findings from this pilot study indicated that EMDR and CBT therapies are useful in treating psychological concerns in cancer patients. The results also suggested that EMDR might be more effective for those cancer patients with PTSD, especially in regard to intrusive symptoms. However, the small sample size and lack of fidelity checks in regard to the treatment are limitations of this pilot study. Another noteworthy pilot RCT by Kangas et al.[31] focused on PTSD, global anxiety, and depression in a modest sample of recently diagnosed head and neck cancer patients undergoing radiotherapy. They examined Cognitive Behavior Therapy and a Non-Directive Supportive Counseling (Non-directive SC) intervention. Both interventions were found to be effective in reducing PTSD symptoms, as well as anxiety symptoms. They also noted that up to 67% of patients in the CBT intervention did not meet clinical or sub-clinical PTS, anxiety and/or depression criteria at 12 month follow-up, relative to 25% of patients in the Non-directive SC intervention. These recent studies, in conjunction with earlier reported findings, indicate that some forms of psychotherapy (i.e., SC, CBT, and EMDR) are helpful in addressing cancer-related PTSD symptoms, and reducing specific clusters of symptoms such as intrusion symptoms/re-experiencing.

4.C.5.2.1 Risk of Bias of Included Studies

The results of the methodological quality assessment is shown in the Tables of Quality Assessment appendix 6 section 6.F Table 6.F.3 and Characteristics Table (Table 6.G.3 in appendix 6 section 6.G) see Figure 4.C.5.2.1.1.

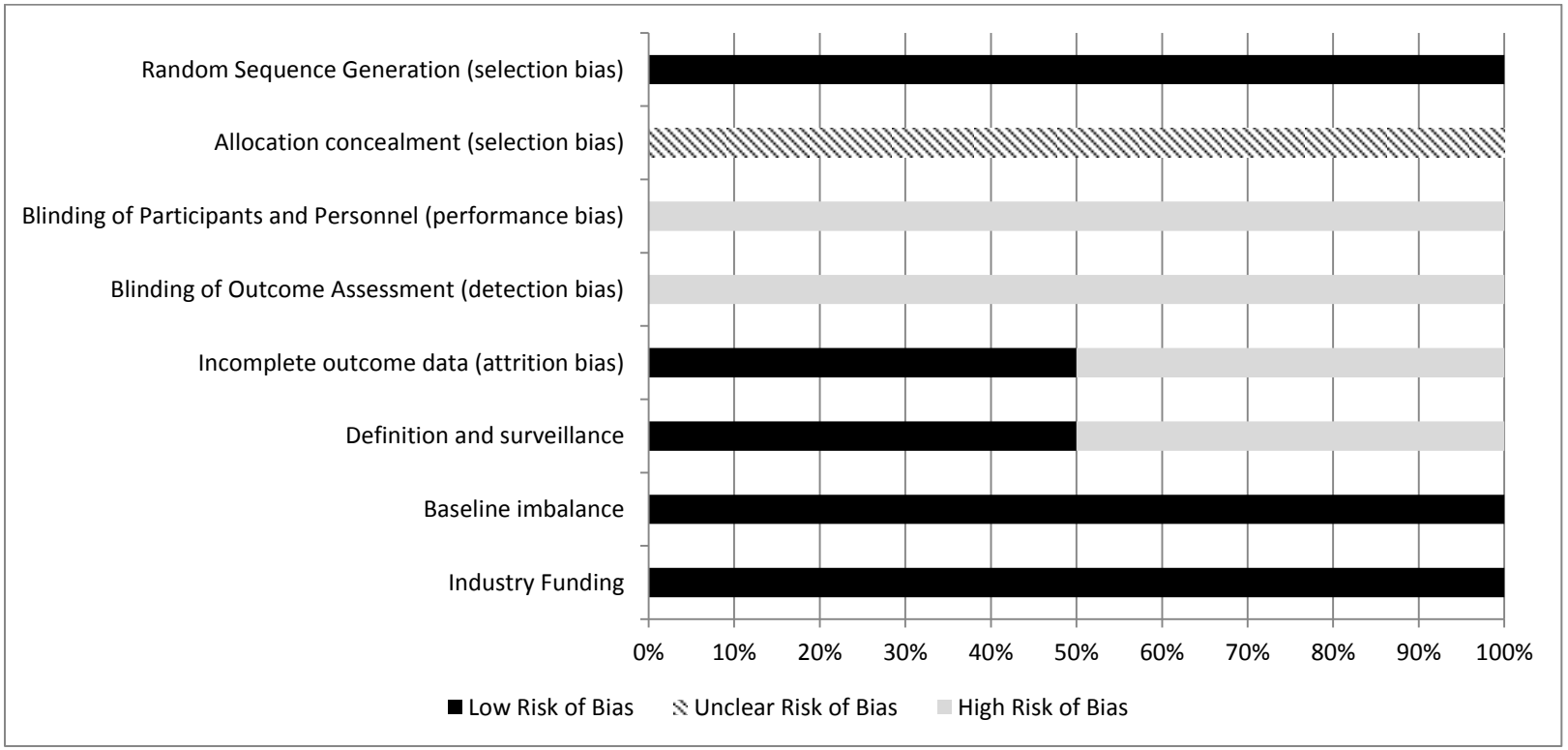


Figure 4.C.5.2.1.1 Risk of Bias Graph: Review Authors' Judgment about PTSD CBT Interventions

4.C.5.2.2 Effects of CBT on PTSD: effect estimate

The data from one study, involving 21 patients in the CBT arm and 14 patients in the control arm, showed that CBT had no significant effect on PTSD among patients with cancer as compared to control group. (SMD = -0.1590; 95%CI-0.8364 to 0.5184). The overall quality of this evidence was rated as very low and downgraded due to concerns regarding risk of bias and imprecision. See Figure 4.C.5.2.2.1.

Review: CBT on PTSD among cancer patients
Comparison: CBT versus treatment as usual
Outcome: PTSD

	Experimental			Control				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Kangas 2013	-4.09	5.581	21	-3.18	5.609	14	100.0%	-0.1590 [-0.8364, 0.5184]
Total (95% CI)			**21**			**14**	**100.0%**	**-0.1590 [-0.8364, 0.5184]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.46 (P = 0.65)

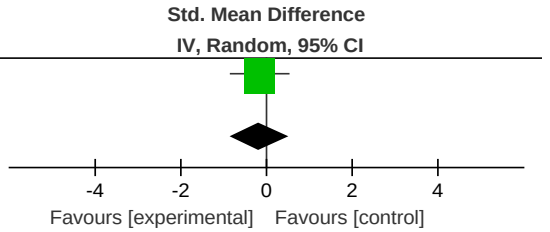


Figure 4.C.5.2.2.1: Effect of CBT Interventions on Cancer-Related PTSD

4.C.5.2.3 Conclusion and Recommendation

CBT when compared with usual or standard care was not substantially different in terms of reducing PTSD symptoms, as well as global anxiety symptoms [31].We assessed the overall SOE across the literature using the rating approach as specified by the GRADE table (see Table 4.C.5.2.3.1).

Table 4.C.5.2.3.1: GRADE Tables for Effect of CBT Interventions on Cancer-Related PTSD

Quality assessment							No of patients		Effect	Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT intervention	Control	SMD (95% CI)		
Effect of CBT on PTSD (Better indicated by lower values)											
1[1]	randomized trials	very serious[2]	no serious inconsistency[3]	no serious indirectness[4]	serious[5]	none[6]	21	14	0.16 lower (0.84 lower to 0.52 higher)	⊕OOO VERY LOW	CRITICAL

CBT intervention for cancer related PTSD

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk **Control**	Corresponding risk **CBT intervention**				
Effect of CBT on PTSD		The mean effect of CBT on PTSD in the intervention groups was **0.16 standard deviations lower** (0.84 lower to 0.52 higher)		35 (1 study[1])	⊕⊖⊖⊖ **very low**[2,3,4,5,6]	SMD -0.16 (-0.84 to 0.52)

CI: Confidence interval;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Kangas et al., 2013
[2] Using Cochrane's Risk of Bias tool, for this outcome, the study was rated as high risk. There was a lack of certainty (unclear ratings) regarding allocation concealment; and high risk of bias associated with random sequence generation, blinding of participants & outcome assessment, incomplete outcome and selective reporting. Given that most of the information is from studies at high risk of bias, this body of evidence was downgraded for serious study limitations.
[3] The statistical heterogeneity across studies could not be assessed due to only one study providing data for this outcome.
[4] One RCT provided data for this outcome. The study included mixed gender population. The mean age was 54.8 years. The intervention arm received multi-modal cognitive behavioral therapy. The control group received supportive care. The study was conducted in Australia and published in 2013. The length of intervention was 6 weeks. There were no serious concerns regarding indirectness for this body of evidence and was not downgraded
[5] The sample size is not adequate i.e. < 300 (21 intervention arm, 14 control arm) and the effect estimate is not precise and confidence interval include the null value "0" [SMD= -0.1590 (-0.8364, 0.5184)]. This body of evidence was downgraded for serious concerns regarding imprecision.
[6] There were too few studies (n<10) to assess publication bias.

Guideline Implementation

To promote the uptake of the guideline across Canada and maximize its dissemination, various steps will be developed and implemented. This includes producing practice protocols for health care professionals, patient versions, translation of the guideline into French, and workshops with key health providers. An important consideration when selecting the inter-professional panel is the ability of the panel members to disseminate and implement the guideline in their respective jurisdictions. The partnership with the Canadian Association of Psychosocial Oncology will also ensure greater exposure for the guideline and support its implementation. In addition, the guideline will be published in a peer-reviewed journal, and posted on the websites of the Canadian Partnership Against Cancer (Cancer Journey Advisory Group) and the Canadian Association of Psychosocial Oncology. Further, the guidance will be disseminated through cancer advocacy survivorship groups, including the Canadian Cancer Action Network and the Canadian Cancer Society, and a summary of the guideline will act as an implementation tool, which will be distributed widely. It is recommended that the implementation of the guidelines in clinical practice follow a systematic knowledge translation process and use best practice strategies tailored to the local contextual health care setting to facilitate uptake.

Much variability in resources across the various Canadian health jurisdictions exists but the potential resource implications of applying the recommendations is unclear as no relevant evidence was identified. Although the resources needed to implement the recommendations are unknown, there are also the resources consumed to offer current services to consider, and it is clear that increasing the health and wellbeing of cancer survivors is an important and worthwhile investment. The guideline recommendations were developed for implementation in a variety of health settings, and criteria to monitor or audit the organization of care or clinical practice are clearly defined throughout the document. In many cases, whether or not the services are offered forms the initial criteria to assess services. With reorganization of services, subsequent program evaluations will be essential for optimizing care for cancer survivors.

Current Research Limitations and Future Direction

Existing studies on the effectiveness of various interventions to manage cancer-related distress, depression and global anxiety are limited by different methodological shortcomings such as small sample size, lack of blinding, and short study duration. Further trials with more robust methodology are clearly required to ascertain the most effective interventions to alleviate distress, depression and global anxiety in patients with cancer. Improving methodological quality of future studies and consensus on issues such as minimum accepted duration of trials and clinically

meaningful change in symptoms are needed to better evaluate effectiveness of interventions and to facilitate inter-study comparisons.

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6 Appendices

6.A Search Strategies, Environmental Scan, PRISMA Chart & Abbreviations and Acronyms

Table 6.A.1: Distress Search Strategy

Psychosocial Distress and Anxiety Search Strategy	
Medline	
Cancer	
1	neoplasm*.hw.
2	exp Neoplasms/
3	cancer*.mp.
4	tumor*.mp.
5	tumour*.mp.
6	carcin*.mp.
7	neoplas*.mp.
8	lymphoma*.mp.
9	melanoma*.mp.
10	melanotic*.mp.
11	metasta*.mp.

Psychosocial Distress and Anxiety Search Strategy	
12	exp Medical Oncology/
13	exp Radiation Oncology/
14	or/1-13
Anxiety	
15	exp Anxiety/
16	exp Anxiety Disorders/
17	Adjustment Disorders/
18	anxiet*.mp.
19	anxious*.mp.
20	nervous*.mp.
21	concern*.mp.
22	worr*.mp.
23	fear*.mp.
24	apprehens*.mp.
25	distress*.mp.
26	panic*.mp.
27	agitat*.mp.
28	stress*.mp.
29	or/15-28
SRs	
30	review/
31	(medline or medlars or pubmed or grateful med or CINAHL or scisearch or psychinfo or psycinfo or psychlit or psyclit or handsearch* or hand search* or manual* search* or electronic database* or bibliographic database* or embase or lilacs or scopus or web of science).mp.
32	30 and 31
33	meta-analysis.mp.
34	meta-analysis as topic/
35	meta-analysis/
36	systematic review*.tw.
37	cochrane database*.jn.
38	or/32-37
Combined Results	
39	14 and 29 and 38
40	limit 39 to (english language and yr="2005-Current")

Psychosocial Distress and Anxiety Search Strategy	
41	remove duplicates from 40
Guidelines	
30	guideline.pt.
31	practice guideline:.mp.
32	or/30-31
Combined Results	
33	14 and 29 and 32
34	limit 33 to (english language and yr="2005-Current")
35	remove duplicates from 34
EMBASE	
Cancer	
1	neoplasm*.hw.
2	exp Neoplasm/
3	exp oncology/
4	exp cancer staging/
5	cancer*.mp.
6	tumor*.mp.
7	tumour*.mp.
8	carcin*.mp.
9	neoplas*.mp.
10	lymphoma*.mp.
11	melanoma*.mp.
12	melanotic*.mp.
13	metasta*.mp.
14	exp Medical Oncology/
15	exp Radiation Oncology/
16	or/1-15
Anxiety	
17	exp fear/
18	exp anxiety disorder/
19	exp anxiety/
20	adjustment disorder/
21	anxiet*.mp.
22	nervous*.mp.

Psychosocial Distress and Anxiety Search Strategy	
23	concern*.mp.
24	worr*.mp.
25	fear*.mp.
26	apprehens*.mp.
27	distress*.mp.
28	panic*.mp.
29	agitat*.mp.
30	stress*.mp.
31	anxious*.mp.
32	or/17-31
SRs	
33	meta analysis/
34	"systematic review"/
35	meta-analysis.tw.
36	systematic review.tw.
37	33 or 34 or 35 or 36
38	16 and 32 and 37
39	limit 38 to embase
40	limit 39 to (english language and yr="2005-Current")
41	remove duplicates from 40
Combined Results **********	
Guidelines	
33	exp practice guideline/
34	guideline?.mp.
35	33 or 34
Combined Results	
36	16 and 32 and 35
37	limit 36 to (english language and yr="2005-Current")
38	limit 37 to embase
39	remove duplicates from 38
Cochrane	
Cancer	
1	cancer*.mp.

Psychosocial Distress and Anxiety Search Strategy	
2	tumor*.mp.
3	tumour*.mp.
4	carcin*.mp.
5	neoplas*.mp.
6	lymphoma*.mp.
7	melanoma*.mp.
8	melanotic*.mp.
9	non small cell.mp.
10	nonsmall cell.mp.
11	(nonsmall adj2 cell).mp.
12	nsclc.mp.
13	adenocarcin*.mp.
14	osteosarcom*.mp.
15	phyllodes.mp.
16	cystosarcom*.mp.
17	fibroadenom*.mp.
18	hepatoma*.mp.
19	hepatoblastom*.mp.
20	plasmacytoma*.mp.
21	myeloma?.mp.
22	blastoma*.mp.
23	lymphangioma*.mp.
24	lymphangiomyoma*.mp.
25	lymphangiosarcoma*.mp.
26	lymphoblastoma*.mp.
27	lymphocytoma*.mp.
28	lymphosarcoma*.mp.
29	lymphoma?.mp.
30	immunocytoma?.mp.
31	angiosarcoma*.mp.
32	astrocytoma*.mp.
33	neuroma?.mp.
34	cytoma?.mp.
35	gist.mp.

Psychosocial Distress and Anxiety Search Strategy	
36	neurocytoma?.mp.
37	oncolog*.mp.
38	staging.mp.
39	squamous cell?.mp.
40	cytosarcoma*.mp.
41	sarcoma*.mp.
42	hodgkin*.mp.
43	non-hodgkin*.mp.
44	nonhodgkin*.mp.
45	incidentaloma?.mp.
46	retinoblastoma?.mp.
47	plasmacytoma*.mp.
48	cholangiocarcinoma*.mp.
49	leiomyoblastoma*.mp.
50	leiomyocarcinoma*.mp.
51	leiomyosarcoma*.mp.
52	melanosis.mp.
53	(hutchinson* adj2 freckle*).mp.
54	melanoameloblastom*.mp.
55	melanoblastom*.mp.
56	melanocarcin*.mp.
57	melanomalign*.mp.
58	naevocarcin*.mp.
59	nevocarcin*.mp.
60	adamantinom*.mp.
61	ameloblastom*.mp.
62	adenosquam*.mp.
63	teratoma*.mp.
64	leukemia*.mp.
65	metaplas*.mp.
66	or/1-65
Anxiety	
67	anxiet*.mp.
68	anxious*.mp.

Psychosocial Distress and Anxiety Search Strategy	
69	concern*.mp.
70	worr*.mp.
71	fear*.mp.
72	apprehens*.mp.
73	distress*.mp.
74	panic*.mp.
75	agitat*.mp.
76	stress*.mp.
77	stress*.mp.
78	or/67-77
SRs **********	
Combined Results	
79	66 and 78
80	limit 79 to last 9 years
81	remove duplicates from 80
PsycINFO	
Cancer	
1	exp neoplasms/
2	exp oncology/
3	cancer*.mp.
4	tumor*.mp.
5	tumour*.mp.
6	carcin*.mp.
7	neoplas*.mp.
8	lymphoma*.mp.
9	melanoma*.mp.
10	melanotic*.mp.
11	metasta*.mp.
12	or/1-11
Anxiety	
13	exp anxiety/
14	exp Anxiety Disorders/
15	exp Fear/

Psychosocial Distress and Anxiety Search Strategy	
16	exp Anxiety Management/
17	exp Anxiety Sensitivity/
18	psychological stress/
19	social stress/
20	distress/
21	anxiet*.mp.
22	anxious*.mp.
23	nervous*.mp.
24	concern*.mp.
25	worr*.mp.
26	fear*.mp.
27	apprehens*.mp.
28	distress*.mp.
29	panic*.mp.
30	agitat*.mp.
31	stress*.mp.
SRs	
32	exp meta analysis/
33	exp literature review/
34	metanalys:.mp.
35	(systematic overview: or systematic review:).mp.
36	(methodologic: overview: or methodologic: review:).mp.
37	(collaborative: overview: or collaborative: review:).mp.
38	integrative research review:.mp.
39	research integration.mp.
40	(handsearch: or hand search: or manual search:).mp.
41	mantel haenszel.mp.
42	peto.mp.
43	(dersimonian or der simonian).mp.
44	fixed effect:.mp.
45	meta analysis.sh.
46	meta-anal*.tw.
47	metaanal*.tw.
48	(systematic* and (review* or overview*)).tw.

Psychosocial Distress and Anxiety Search Strategy	
49	(critical* and apprais*).tw.
50	literature review.sh.
51	or/32-50
52	or/13-31
Combined Results	
53	12 and 51 and 52
54	limit 53 to (english language and yr="2005 -Current")
55	remove duplicates from 54
Guidelines	
32	Treatment guidelines/
33	guideline*.tw.
34	Best practices/
35	32 or 33 or 34
36	or/13-31
37	32 or 33 or 34
Combined Results	
38	12 and 36 and 37
39	limit 38 to (english language and yr="2005 -Current")
40	remove duplicates from 39
CINAHL	
SRs	
#	Query
S1	MW neoplasm*
S2	(MH "Neoplasms+")
S3	(MH "Oncology+")
S4	(MH "Neoplasm Staging")
S5	cancer*
S6	tumor*
S7	tumour*
S8	carcin*
S9	neoplas*
S10	metasta*
S11	oncolog*
S12	malignan*

Psychosocial Distress and Anxiety Search Strategy	
S13	lymphoma*
S14	melanoma*.
S15	melanotic
S16	non small cell
S17	nonsmall n2 cell
S18	nsclc
S19	adenocarcin*
S20	osteosarcom*.
S21	phyllodes
S22	cystosarcom*.
S23	fibroadenom*.
S24	hepatoma*
S25	hepatoblastom*
S26	plasmacytoma*
S27	myeloma?
S28	blastoma*
S29	lymphangioma*
S30	lymphangiomyoma*
S31	lymphangiosarcoma*
S32	lymphoblastoma*
S33	lymphocytoma*
S34	lymphosarcoma*
S35	lymphoma?
S36	immunocytoma?
S37	angiosarcoma*
S38	astrocytoma?
S39	neuroma?
S40	cytoma?
S41	gist
S42	neurocytoma?
S43	staging
S44	squamous cell?
S45	cytosarcoma*
S46	sarcoma*

Psychosocial Distress and Anxiety Search Strategy	
S47	hodgkin*
S48	non-hodgkin*
S49	nonhodgkin*
S50	incidentaloma?
S51	retinoblastoma?
S52	plasmacytoma*
S53	cholangiocarcinoma*
S54	leiomyoblastoma*
S55	leiomyocarcinoma*
S56	leiomyosarcoma*
S57	melanosis
S58	hutchinson* n2 freckle*
S59	melanoameloblastom*
S60	melanoblastom*
S61	melanocarcin*
S62	melanomalign*
S63	naevocarcin*
S64	nevocarcin*
S65	adamantinom*
S66	ameloblastom*
S67	adenosquam*
S68	teratoma*
S69	leukemia*
S70	metaplas*
S71	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54 OR S55 OR S56 OR S57 OR S58 OR S59 OR S60 OR S61 OR S62 OR S63 OR S64 OR S65 OR S66 OR S67 OR S68 OR S69 OR S70
S72	anxiet*
S73	anxious*
S74	nervous*
S75	nervous*
S76	worr*
S77	fear*

Psychosocial Distress and Anxiety Search Strategy	
S78	apprehens*
S79	distress*
S80	distress*
S81	agitat*
S82	stress*
S83	S72 OR S73 OR S74 OR S75 OR S76 OR S77 OR S78 OR S79 OR S80 OR S81 OR S82
S84	(MH "Meta Analysis")
S85	(MH "Literature Review+")
S86	(MH "Literature Searching+")
S87	PT systematic review
S88	PT practice guidelines
S89	PT nursing interventions
S90	PT (care plan OR critical path OR protocol)
S91	metaanaly*
S92	meta analy*
S93	metanalys*
S94	(systematic* OR quantitative OR methodologic*) N3 (overview* OR review*)
S95	Integrative research review*
S96	research integration
S97	handsearch* OR ((hand OR manual) N3 search*)
S98	mantel haenszel
S99	fixed effect*
S100	medline OR cinahl OR psyc?info OR psyc?lit OR embase OR pubmed
S101	pooled N1 data
S102	S84 OR S85 OR S86 OR S87 OR S88 OR S89 OR S90 OR S91 OR S92 OR S93 OR S94 OR S95 OR S96 OR S97 OR S98 OR S99 OR S100 OR S101
S103	S71 AND S83 AND S102
S104	S71 AND S83 AND S102
Guidelines	
S1	MW neoplasm*
S2	(MH "Neoplasms+")
S3	(MH "Oncology+")
S4	(MH "Neoplasm Staging")
S5	cancer*
S6	tumor*

Psychosocial Distress and Anxiety Search Strategy	
S7	tumour*
S8	carcin*
S9	neoplas*
S10	metasta*
S11	oncolog*
S12	malignan*
S13	lymphoma*
S14	melanoma*.
S15	melanotic
S16	non small cell
S17	nonsmall n2 cell
S18	nsclc
S19	adenocarcin*
S20	osteosarcom*.
S21	phyllodes
S22	cystosarcom*.
S23	fibroadenom*.
S24	hepatoma*
S25	hepatoblastom*
S26	plasmacytoma*
S27	myeloma?
S28	blastoma*
S29	lymphangioma*
S30	lymphangiomyoma*
S31	lymphangiosarcoma*
S32	lymphoblastoma*
S33	lymphocytoma*
S34	lymphosarcoma*
S35	lymphoma?
S36	immunocytoma?
S37	angiosarcoma*
S38	astrocytoma?
S39	neuroma?
S40	cytoma?

Psychosocial Distress and Anxiety Search Strategy	
S41	gist
S42	neurocytoma?
S43	staging
S44	squamous cell?
S45	cytosarcoma*
S46	sarcoma*
S47	hodgkin*
S48	non-hodgkin*
S49	nonhodgkin*
S50	incidentaloma?
S51	retinoblastoma?
S52	plasmacytoma*
S53	cholangiocarcinoma*
S54	leiomyoblastoma*
S55	leiomyocarcinoma*
S56	leiomyosarcoma*
S57	melanosis
S58	hutchinson* n2 freckle*
S59	melanoameloblastom*
S60	melanoblastom*
S61	melanocarcin*
S62	melanomalign*
S63	naevocarcin*
S64	nevocarcin*
S65	adamantinom*
S66	ameloblastom*
S67	adenosquam*
S68	teratoma*
S69	leukemia*
S70	metaplas*
S71	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54 OR S55 OR S56 OR S57 OR S58 OR S59 OR S60 OR S61 OR S62 OR S63 OR S64 OR S65 OR S66 OR S67 OR S68 OR S69 OR S70

Psychosocial Distress and Anxiety Search Strategy	
S72	guideline*
S73	standard*
S74	position paper
S75	clinical protocol*
S76	(clinical OR medical) N1 criteri*
S77	(clinical OR medical) N1 polic*
S78	clinical N1 pathway
S79	critical N1 pathway
S80	care map*
S81	algorithm*
S82	(MH "Practice Guidelines")
S83	PT practice guidelines
S84	PT nursing interventions
S85	S72 OR S73 OR S74 OR S75 OR S76 OR S77 OR S78 OR S79 OR S80 OR S81 OR S82 OR S83 OR S84
S86	anxiet*
S87	anxious*
S88	nervous*
S89	nervous*
S90	worr*
S91	fear*
S92	apprehens*
S93	distress*
S94	distress*
S95	agitat*
S96	stress*
S97	S86 OR S87 OR S88 OR S89 OR S90 OR S91 OR S92 OR S93 OR S94 OR S95 OR S96
S98	S71 AND S85 AND S97
S99	S71 AND S85 AND S97
S100	S71 AND S85 AND S97

Searches: Database: Ovid MEDLINE(R)		
randomized controlled trial.pt.		
exp Randomized controlled trial/		
exp Randomized Controlled Trials as Topic/		
clinical trial.pt.		
Double-Blind Method/		
"double blind:".mp.		
Placebos/		
placebo:.mp.		
random:.mp.		
EBM Reviews - Cochrane Central Register of Controlled Trials		
Searches: Database: Embase		
randomized controlled trial.pt.		
exp Randomized controlled trial/		
exp Randomized Controlled Trials as Topic/		
clinical trial.pt.		
Double-Blind Method/		
"double blind:".mp.		
Placebos/		
placebo:.mp.		
random:.mp.		
or/93-101 [****RCT terms****]		
#	**Searches:** Database: PsycINFO	**Results**
93	clinical trials/	8640
94	(single adj blind*).mp.	1642
95	(double adj blind*).mp.	19300
96	(triple adj blind*).mp.	37
97	exp Placebo/	4062
98	random sampling/	648

99	placebo:.mp.	32814
100	(assign* adj2 random*).mp.	29469
101	(assign* adj2 random*).mp.	29469
102	or/93-101 [****RCT terms****]	71728
#	**Query:** CINAHL	**Results**
S86	(MH "Placebos")	7,270
S85	TX (random* n2 allocat*)	7,276
S84	TX placebo*	52,421
S83	(MH "Random Assignment")	32,044
S82	TX randomi* control* trial*	85,799
S81	TX (trebl* n1 mask*)	1
S80	TX (trebl* n1 blind*)	3
S79	TX (tripl* n1 blind*)	212
S78	TX (doubl* n1 mask*)	447
S77	TX (doubl* n1 blind*)	649,578
S76	TX (singl* n1 mask*)	209
S75	TX (singl* n1 blind*)	10,017
S74	TX clinic* n1 trial*	162,725
S73	PT Clinical trial	52,097
S72	(MH "Clinical Trials+")	127,928

Table 6.A.2: Environmental Scan Search Results

Database/Source (Website)	No of Retrieved Papers
National Institute for Health and Clinical Excellence (NICE) (http://www.nice.org.uk/)	0
National Comprehensive Cancer Network (NCCN) (www.nccn.org)	0
World Health Organization (WHO) (http://apps.who.int/trialsearch/Default.aspx)	23
Clinical Trials.gov (https://www.clinicaltrials.gov)	8
The New York Academy of Medicine's Grey Literature Index (http://www.greylit.org)	0
American Society of Clinical Oncology (ASCO) (http://www.asco.org/)	2
Cancer Care Ontario (https://www.cancercare.on.ca/)	1
Multinational Association of Supportive Care in Cancer (MASCC) (www.mascc.org)	0
Cancer Care Nova Scotia (http://www.cancercare.ns.ca/en/home/default.aspx)	2

Table 6.A.3: Abbreviation Table

Abbreviations	
ACoS	American College of Surgeons
ADDM	Adjustment Disorder with Depressed Mood
ADIS	Anxiety Disorders Interview Schedules
AGREE	Appraisal of Guidelines for Research and Evaluation
AM	Aromatherapy Massage
ASD	Acute Stress Disorder
BAT	Behavioral Activation Therapy
BATD	Behavioral Activation Therapy for Depression
BCSG	Breast Cancer Support Group
BDI	Beck Depression Inventory
BSI	Brief Symptom Inventory
CAPO	Canadian Association of Psychosocial Oncology
CAPS	Clinician Administered PTSD Scale
CBT	Cognitive-Behavioral Therapy
CBSM	Cognitive Behavior Stress Management
CC&CRG	Cochrane Consumers and Communication Review Group
CCO	Cancer Care Ontario
CES-D	Center for Epidemiological Studies Depression Scale
CG91	Clinical Guideline 91
CGI	Clinical Global Impression
CGI-S	Clinical Global Impression on- Severity Scale
CI	Confidence Interval
CL	Cluster
CoC	Commission on Cancer
CPG	Clinical Practice Guideline
C-SOSI	Calgary Symptoms of Stress Inventory
CTL	Standard Care as Control
DCPC	Depression Care for People with Cancer (problem-solving therapy and behavioral activation)
DD	Dysthymic Disorder
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders 4th edition
DSM-IV-TR	Diagnostic and Statistical Manual of Mental Disorders 4th edition text revision
DSM-5	Diagnostic and Statistical Manual of Mental Disorders 5th edition

Abbreviations	
DT	Distress Thermometer
Dx	Diagnosis
EFT	Emotionally Focused Therapy
EH	Expressive Helping = Expressive Writing + Peer Helping
ELP	English Language Preferred
EMDR	Eye Movement Desensitization and Reprocessing
ESAS	*Edmonton Symptom Assessment Scale*
ESASr	*Edmonton Symptom Assessment System Revised*
EW	Expressive Writing
FoP	Fear of Progression
FoP-Q	Fear of Progression Questionnaire
FU	Follow up
GAD	Generalized Anxiety Disorder
GCBT	Group Cognitive Behavioral Therapy
GI	Gastrointestinal
GP	General Practitioner
GRADE	Grading of Recommendations Assessment, Development and Evaluation
GSI	Global Severity Index
HADS	Hospital Anxiety and Depression Scale
HADS-A	Hospital Anxiety and Depression Scale - Anxiety
HADS-D	Hospital Anxiety and Depression Scale - Depression
HAM	Hamilton Anxiety Rating Scale
HAM- A	Hamilton Anxiety Rating Scale for Anxiety
HANDS	Harvard National Depression Screening
HLM	Hierarchical Linear Model
HRSD/HAM-D	Hamilton Rating Scale for Depression
HSCL-20	20-item Hopkins Symptom Checklist
HSCT	Hematopoietic Stem Cell Transplantation
IES	Impact of Events Scale
IMPACT	Improving Mood Promoting Access to Collaborative Treatment
ITT	Intent-To-Treat
MADRS	Montgomery-Asberg Depression Rating Scale
MBAT	Mindfulness-Based Art Therapy

Abbreviations	
MBCR	Mindfulness-Based Cancer Recovery
MDD	Major Depressive Disorder
MINI	Mini-International Neuropsychiatric Interview
Mo	Month
Mod	Moderate
MS	Mean of Square
NBCC-NCCI	Australian National Breast Cancer Centre and National Cancer Control Initiative
NCCN	National Comprehensive Cancer Network
NICE	National Institute for Health and Care Excellence
Non-directive SC	Non-directive Supportive Counseling program
NR	Not Reported
NRS	Numerical Rating Scale
NT	Narrative Therapy
NW	Neutral Writing
OCD	Obsessive-Compulsive Disorder
PC	Personal Computer
PCL-C	PTSD Checklist - Civilian Version
PCL-S	Posttraumatic Checklist - Stress specific version
PH	Peer Helping
PHQ-9	Patient Health Questionnaire for Depression
P-ISG	Enhanced Prosocial Internet Support group
POMS	Profile of Mood States
PP	Per Protocol
PST	Problem Solving Therapy
PTS	Post-Traumatic Stress
PTSD	Post-Traumatic Stress Disorder
QoL	Quality of Life
RCT	Randomized Control Trials
SC	Supportive Counselling
SCID	Structured Clinical Interview for DSM Disorders
SCL-90-R	Symptoms Checklist Revised
SD	Standard Deviation
SE	Standard Error
SET	Supportive-Expressive Group Therapy

Abbreviations	
S-ISG	Standard Internet Support Group Intervention
SLP	Spanish Language Preferred
SMD	Standard Mean Deviation
SMG	Symptom Management Guideline
SMS	1-Day Didactic Stress Management Seminar
SOE	Strength of Evidence
SR	Systematic Review
SS	Sum of Square
SSRI	Selective Serotonin Reuptake Inhibitor
STAI	Spielberger State Trait Anxiety Inventory
STPP	Short-Term Psychodynamic Psychotherapy
TAU	Treatment as Usual
T-CBT	Telephone-Based Cognitive-Behavioral Therapy
TMD	Total Mood Disturbance
TMS	Total Mood Score
TQSS	Two Question Screening Survey
Tx	Treatment
WG	Writing Group

6.B Literature Search Results by Intervention

Table 6.B.1: Literature Search Result by Intervention

Author, Year	Title
10 Clinical Practice Guidelines	
Yu,2012[9]	Development of guidelines for distress management in Korean cancer patients.
Andersen,2014[10]	Screening, assessment, and care of anxiety and depressive symptoms in adults with cancer: an American Society of Clinical Oncology guideline adaptation.
Deng,2013[20]	Complementary therapies and integrative medicine in lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines.
Holland,2014[11]	Distress management.
National Institute for Health and Clinical Excellence,2009[19]	Depression in adults with a chronic physical health problem.
Howell,2010[12]	Pan Canadian Practice Guideline Screening, Assessment and Care of Psychosocial Distress (Depression, Anxiety) In Adults with Cancer.
Rayner,2011[17]	The development of evidence-based European guidelines on the management of depression in palliative cancer care.
Howell,2009[13]	A Pan-Canadian clinical practice guideline: Assessment of psychosocial health care needs of the adult cancer patient.
Li,2015[18]	The Management of Depression in Patients with Cancer.
Howes,2015[14]	Best Practice Guideline for the Management of Cancer-Related Distress in Adults.
14 Systematic Reviews	
Hart,2012[122]	Meta-analysis of efficacy of interventions for elevated depressive symptoms in adults diagnosed with cancer.
Matcham,2014[124]	Self-help interventions for symptoms of depression, anxiety and psychological distress in patients with physical illnesses: A systematic review and meta-analysis.
Akechi,2013[119]	Psychotherapy for depression among incurable cancer patients.
Galway,2014[121]	Psychosocial interventions to improve quality of life and emotional wellbeing for recently diagnosed cancer patients.
Candy,2012[36]	Drug therapy for symptoms associated with anxiety in adult palliative care patients [Systematic Review].
Rayner,2010[127]	Antidepressants for depression in physically ill people.
Walker,2014[129]	Treatment of depression in adults with cancer: A systematic review of randomized controlled trials.
Mitchell,2012[125]	Meta-analysis of screening and case finding tools for depression in cancer: Evidence based recommendations for clinical practice on behalf of the Depression in Cancer Care Consensus Group.
Nenova,2013[126]	Psychosocial interventions with cognitive-behavioral components for the treatment of cancer-related traumatic stress

Author, Year	Title
	symptoms: A review of randomized controlled trials.
Carvalho,2014[120]	Major depressive disorder in breast cancer: a critical systematic review of pharmacological and psychotherapeutic clinical trials.
Laoutidis and Mathiak,2013[123]	Antidepressants in the treatment of depression/depressive symptoms in cancer patients: A systematic review and meta-analysis.
Ng,2011[97]	The prevalence and pharmacotherapy of depression in cancer patients.
Simard,2013[102]	Fear of cancer recurrence in adult cancer survivors: a systematic review of quantitative studies.
van Straten,2010[128]	Psychological treatment of depressive symptoms in patients with medical disorders: a meta-analysis.
28 RCTs	
Anxiety- Non-Pharmacological **Psychosocial Intervention**	
Goerling,2011[53]	The impact of short-term psycho-oncological interventions on the psychological outcome of cancer patients of a surgical-oncology department - a randomized controlled study.
CBT	
Kangas,2013[31]	A pilot randomized controlled trial of a brief early intervention for reducing posttraumatic stress disorder, anxiety and depressive symptoms in newly diagnosed head and neck cancer patients.
Greer,2012[32]	A pilot randomized controlled trial of brief cognitive-behavioral therapy for anxiety in patients with terminal cancer.
Distress- Non-Pharmacological **Psychosocial Intervention**	
Chambers,2014[22]	A Randomized Trial Comparing Two Low-Intensity Psychological Interventions for Distressed Patients With Cancer and Their Caregivers.
Monti,2013[23]	Psychosocial benefits of a novel mindfulness intervention versus standard support in distressed women with breast cancer.
Carlson,2013[24]	Randomized controlled trial of Mindfulness-based cancer recovery versus supportive expressive group therapy for distressed survivors of breast cancer.
Mosher,2012[25]	Randomised trial of expressive writing for distressed metastatic breast cancer patients.
Ashing and Rosales,2014[26]	A telephonic-based trial to reduce depressive symptoms among Latina breast cancer survivors.
Lepore,2012[27]	Preliminary findings from a randomized trial of standard versus prosocial online support groups for distressed breast cancer survivors.
Rini,2014[28]	Expressive helping intervention to improve survivorship problems after hematopoietic stem cell transplant: What is the evidence and how is it done?
Zernicke,2014[57]	A randomized wait-list controlled trial of feasibility and efficacy of an online mindfulness-based cancer recovery program: the eTherapy for cancer applying mindfulness trial.

Author, Year	Title
CBT	
Serfaty,2012[33]	The ToT study: helping with Touch or Talk (ToT): a pilot randomized controlled trial to examine the clinical effectiveness of aromatherapy massage versus cognitive behavior therapy for emotional distress in patients in cancer/palliative care.
DuHamel,2010[56]	Randomized clinical trial of telephone-administered cognitive-behavioral therapy to reduce post-traumatic stress disorder and distress symptoms after hematopoietic stem-cell transplantation.
PTSD-Non-Pharmacological Psychosocial Intervention	
Carpenter,2014[55]	An online stress management workbook for breast cancer.
CBT	
Kangas,2013[31]	A pilot randomized controlled trial of a brief early intervention for reducing posttraumatic stress disorder, anxiety and depressive symptoms in newly diagnosed head and neck cancer patients.
Capezzani,2013[29]	EMDR and CBT for cancer patients: Comparative study of effects on PTSD, anxiety, and depression.
Fear- Non-Pharmacological Education/Psychosocial & CBT	
Herschbach,2010[34]	Evaluation of two group therapies to reduce fear of progression in cancer patients.

6.C Characteristics of Included Guidelines

Table 6.C.1: Characteristics of Distress Focused Guidelines

Author, Year **Organization/Guideline publisher (Year):** **Country:**	**Title:** **Intended User:** **Scope:** **Population:**	**Recommendations(s):** **Grading system used for body of evidence = Overall rating**
Howell,2009[13] Canadian Partnership Against Cancer (Cancer Journey Action Group); Canadian Association of Psychosocial Oncology (2009) Canada	A Pan-Canadian Clinical Practice Guideline: Assessment of Psychosocial Health Care Needs of the Adult Cancer Patient All members of the inter-professional health care team. This includes, but is not limited to: primary care providers, oncologists, nurses, social workers, psychiatrists, psychologists, dieticians, rehabilitation	**SCREENING:** - Screening for distress is recommended for use as an initial "red flag" indicator of psychosocial health care needs. It should be followed by a more comprehensive and focused assessment to ensure that interventions are targeted, appropriate, and relevant to the needs and specific problems identified by the individual and family. **Level of recommendation: expert consensus**[1] - Screening for distress is recommended at critical times during the cancer treatment (initial diagnosis, start of treatment, regular intervals during treatment, end of treatment, post-treatment or transition to survivorship, at recurrence or progression, and dying). **Level of recommendation: expert consensus**[1] - Tools used to screen patients should be brief to minimize patient burden and maximize ease of update into clinical practice; and should possess adequate sensitivity and specificity and established cut-offs for rapid identification of high risk population. **Level of recommendation: expert consensus**[1] **ASSESSMENT:**

[1] Overall, the final recommendations are based on expert consensus of the inter-professional panel, after review of the available evidence, guidelines from other groups, and current clinical practice in Canada Screening for distress should not be limited to depression and anxiety symptoms alone but also include identification of physical, informational, psychological, social, spiritual, and practical domains of psychosocial health care needs or concerns that contribute to distress of cancer and treatment.

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
	professionals, counsellors, speech language pathologists, and spiritual care providers. The guideline may also inform the training of professionals and decisions regarding appropriate resource allocation for psychosocial services Provides recommendations on the routine, standardized assessment of domains of person-centered, psychosocial health care needs that are common across cancer population	- Standardized assessment of psychosocial health care needs is recommended as a critical first step in the provision of appropriate, and relevant psychosocial and supportive care interventions and or services. **Level of recommendation: expert consensus**[1] - Standardized assessment of psychosocial health care needs should include physical, informational, emotional, psychological, social, spiritual, and practical domains that are common across cancer population. **Level of recommendation: expert consensus**[1] - Disease, treatment, or phase-specific psychosocial health care needs assessment should be added to routine, standardized assessment across cancer population to treat specific cancer types and treatment modality. **Level of recommendation: expert consensus**[1] - Assessment for distress may be a combination of self-report questionnaires and interview approach and is dependent on effective communication between patient and clinician. **Level of recommendation: expert consensus**[1] - Tools used for assessment should be comprehensive with sound psychometric properties that address all domains of psychosocial health care needs. Focused assessment using a valid and reliable tool should follow a comprehensive assessment and be targeted to identification of the parameters of a specific problem and

[1] Overall, the final recommendations are based on expert consensus of the inter-professional panel, after review of the available evidence, guidelines from other groups, and current clinical practice in Canada Screening for distress should not be limited to depression and anxiety symptoms alone but also include identification of physical, informational, psychological, social, spiritual, and practical domains of psychosocial health care needs or concerns that contribute to distress of cancer and treatment.

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
	Adult cancer patients regardless of cancer type, phase, or treatment.	dimensions of a specific problem. **Level of recommendation: expert consensus**[1] **<u>MANAGEMENT:</u>** - Screening and assessment should be followed by evidence-based interventions and targeted care processes appropriate to the identified need to improve patient outcomes including relief of symptoms, emotional well-being and quality of life. **Level of recommendation: expert consensus**[1] - Ongoing education of all members of the health care team is critical to ensure competent psychosocial health care needs assessment and appropriate clinician response to findings of "red flag" screening for distress, and comprehensive and focused assessment. **Level of recommendation: expert consensus**[1] - Interdisciplinary collaboration is recommended for routine, standardized psychosocial health care needs assessment and screening for distress and targeting of interventions consistent with practice scope to effectively address multidimensional domains of need and/or facilitate appropriate referral to discipline-specific and/or psychosocial oncology specialists and services. **Level of recommendation: expert consensus**[1]

[1] Overall, the final recommendations are based on expert consensus of the inter-professional panel, after review of the available evidence, guidelines from other groups, and current clinical practice in Canada Screening for distress should not be limited to depression and anxiety symptoms alone but also include identification of physical, informational, psychological, social, spiritual, and practical domains of psychosocial health care needs or concerns that contribute to distress of cancer and treatment.

Table 6.C.2 Characteristics of Distress (Anxiety/Depressive Symptoms) Focused Guidelines

Author, Year **Organization/Guideline publisher (Year):** **Country:**	**Title:** **Intended User:** **Scope:** **Population:**	**Recommendations(s):** **Grading system used for body of evidence = Overall rating**
Holland,2014[11] National Comprehensive Cancer Network (2014) USA	Distress management Oncology teams, social workers, certified chaplains, mental health professionals The goal of this guideline was to discuss the identification and treatment of psychosocial problems in patients with cancer. Indented to assist oncology teams, mental health professionals guidance and knowledge of interventions and treatments for patients with mild distress related to patients cancer	**SCREENING:** Each new patient should be assessed for evidence of distress using the DT (0 =no distress to 10 = extreme distress) and Problem List (a 39-item Problem List) as initial rough screen. Score of 4 or more on DT should be evaluated further by oncologist or nurse. A referral to psychological services should be referred if necessary. Patients with practical and psychosocial problems should be referred to social workers; patients with emotional or psychological problems referred to mental health professional. **Level of Evidence: NCCN, 2A** **ASSESSMENT:** -Moderate to Severe Distress (Score of ≥ 4 in screening tool): • First Assessment: The first assessment is a clinical assessment which is done by primary oncologist, team of oncologists, nurses or social workers. They assess the patients for emotional problems, including Anxiety and Depression. • Second Assessment: According to patients' need, they maybe refer to; a) Mental Health Services: evaluated for distress, behavioral symptoms, psychiatric history/medications, pain and symptom control, body image/sexuality, impaired capacity, safety, psychological/psychiatric disorder and any medical causes. If the patients suffer from an Anxiety Disorder, after assessment of the related factors, they will receive treatment. b) If patients refer to social work and counseling services, after patient/family are assessed, their conditions are categorized into two kinds of groups; Psychosocial problems or Practical problems. In both groups, after the type of problem is verified, the patients are separated into severe/moderate or mild. They will then receive social work and counseling interventions. c) In Chaplaincy services, patients are assessed and will receive Chaplaincy services.

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
	Cancer patients with psychosocial problems such as distress.	-Mild Distress (Score < 4 on screening tool): As an assessment, patients refer to Primary oncology team and resources available. If it is necessary, they refer patients to a) Mental Health Services and/or b) Social work and counseling service and/or c) chaplaincy services to evaluate. See part a, b, and c above. If it is not necessary to refer, patients will be evaluated for expected distress symptoms. **Level of Evidence: NCCN, 2A** -Patients with unrelieved physical symptoms will be treated using disease specific or supportive care guideline (see NCCN Guidelines for Supportive care). **MANAGEMENT:** -Moderate to Severe Distress a) Patients who are referred to Mental Health Services and diagnosed with an anxiety disorder after more evaluation, they will receive treatment which includes: Psychotherapy and/or anxiolytic and/or antidepressant. **Level of Evidence: NCCN, 1** b) Patients who are referred to social work and/or counseling services and have Practical or Psychosocial Problems are separated into mild and moderate/severe groups and receive social work and counselling interventions. **Level of Evidence: NCCN, 2A** c) Patients are referred by an oncologist to chaplaincy services. After chaplaincy assessment patients will receive the related counseling (i.e., spiritual, palliative, supportive care, ethics) and supports or are referred to the social work and/or mental health professional, local congregation, and clergy of person's faith. **Level of Evidence: NCCN, 2A**

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
		-Mild Distress Patients should receive or participate in the following interventions: ○ Clarification of diagnosis, treatment options and side effects ○ Ensure patient understands disease and treatment options ○ Refer to appropriate patient education materials ○ Education regarding how the points of transition may bring increased vulnerability of distress ○ Acknowledge distress ○ Build trust ○ Ensure continuity of care ○ Mobilize resources ○ Consider medication to manage symptoms: ○ Analgesics ○ Anxiolytics ○ Hypnotics ○ Antidepressants ○ Support groups and/or individual counseling ○ Family support and counseling ○ Relaxation/ meditation, creative therapies(e.g. Art, dance, music) ○ Spiritual support ○ Exercise. **Level of Evidence: NCCN, 2A**
Yu,2012[9] (2012) Republic of Korea	Development of guidelines for distress management in Korean cancer patients	**SCREENING (DISTRESS/ANXIETY):** Patients will be systematically provided with psychosocial services that would match the level of distress assessed with the screening tool (i.e., the NCC psychological symptom inventory: NCC-PSI). As a screening tool, the Korean version of the Distress Thermometer validated by Shim et al. is proposed. **Level of Evidence: NR**

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
	Primary audience: medical, surgical, and radiation oncologists; anesthetists; nurses; social workers; mental health professionals Distressed Korean adult cancer patients (all phases of cancer care; from diagnosis throughout active treatment to follow-up) Scope: 1. What is the concept of distress in Korean cancer patients (i.e. the manifestations of distress, dimensions of distress, coping strategies, etc).	**ASSESSMENT (DISTRESS/ANXIETY):** Assessment will be provided by the primary-care team (e.g. the patients' oncologists and nurses). This team could provide their patients with detailed medical information and emotional support though various education and counseling interventions and programs that rely on clear and open communication. Despite appropriate management by the primary-care team, referral to psychosocial experts would be recommended if a patient's distress did not decrease. **Level of Evidence: NR** **MANAGEMENT (DISTRESS):** 1- Normal to mild (NCCPSI score <4): (Managed by Primary care Providers) • emotional support 2- Moderate to severe (NCCPSI score ≥4): (Managed by various psychosocial experts, including psychiatrists, clinical psychologists, social workers, advanced practice nurses, and pastoral-service providers). • Non-pharmacological[2]/pharmacological intervention • Social work/mental health counseling • Pastoral care. **Level of Evidence: NR** **MANAGEMENT (ANXIETY):** - Normal to mild (NCCPSI score<4):

[2] Non-pharmacological treatment: psycho-education, supportive psychotherapy, CBT psychotherapy and mindfulness-based stress reduction (MBCR).

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
	2. Which format for the guidelines is more feasible for the current situation in Korea: disease specific guidelines versus symptom-specific guidelines, algorithm-based guidelines versus text-based guidelines, and so on? 3. How do we prioritize what we will produce? 4. What are the key questions that should be in the recommendations? 5. Other issues addressed the purpose of and target audience for the guidelines, the	(Managed by Primary care Providers) • Emotional support • Education • Peer support program. - Moderate to severe (NCCPSI score≥4): (Managed by various psychological experts, including psychiatrists, clinical psychologists, social workers, and pastoral-service providers). ○ Adjustment disorder or mild anxiety disorder: • Non-pharmacological intervention[2] and/or anxiolytic ○ Moderate to severe anxiety disorder: • Anxiolytic, non-pharmacological intervention, antidepressant ○ Delirium or Depression: • Go to the algorithm VII. Delirium or V. Depression. **Level of Evidence: NR** Cognitive-behavioral psychotherapy and MBSR are effective for decreasing anxiety in adult cancer patients[2]. **Grade of recommendation: A** Supportive psychotherapy is provisionally recommended for managing a patient's anxiety[2]. **Grade of recommendation: B**

[2] Non-pharmacological treatment: psycho-education, supportive psychotherapy, CBT psychotherapy and mindfulness-based stress reduction (MBCR).

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
	dissemination and implementation strategy to be used, and how to plan for their evaluation and revision.	
Andersen,2014[10] American Society of Clinical Oncology (2014) USA	Screening, assessment, and care of anxiety and depressive symptoms in adults with cancer: an American Society of Clinical Oncology guideline adaptation Healthcare professional, patients, family members, caregivers The goal of this guideline was to discern the optimum screening, assessment, and treatment approaches in the treatment of adult	**SCREENING (DEPRESSIVE SYMPTOMS):** - All patients should be screened for depressive symptoms at their initial visit, at appropriate intervals, and as clinically indicated, especially with changes in disease or treatment status (i.e., post-treatment, recurrence, progression) and transition to palliative and end-of-life care. - Screening should be done using a valid and reliable measure that features reportable scores (dimensions) that are clinically meaningful (established cut-offs). - When assessing a person who may have depressive symptoms, a phased screening and assessment is recommended that does not rely simply on a symptom count. o As a first step, identification of the presence or absence of pertinent history or risk factors is important for subsequent assessment and treatment decision making. o As a second step, two items from the nine-item Personal Health Questionnaire (PHQ-9) can be used to assess for the classic depressive symptoms of low mood and anhedonia. For individuals who endorse either item (or both) as occurring for more than half of the time or nearly every day within the last 2 weeks (i.e., a score of 2), a third step is suggested in which the patient completes the remaining items of the PHQ-9. o The traditional cut-off for the PHQ-9 is 10. The recommended cut-off score is 8. o For patients who complete the latter step, it is important to determine the associated socio-demographic, psychiatric or health comorbidities, or social impairments, if any, and the duration of depressive symptoms.

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
	patients with cancer who are experiencing symptoms of depression and anxiety Adult cancer patients with Distress (depression and/or anxiety) at any phase of cancer regardless of cancer type, disease stage or treatment modality.	○ One of remaining seven items of the PHQ-9 assesses thoughts of self-harm. Some clinicians may choose to omit the item from the PHQ-9 and administer eight items. It should be noted, that doing so may artificially lower the score, with the risk of some patients appearing to have fewer symptoms than they actually do. Thus, it is the patient's endorsement of multiple symptoms that will define the need for services for moderate to severe symptomatology. - Consider special circumstances in the assessment of depressive symptoms. **Recommendations**[3] **ASSESSMENT (DEPRESSIVE SYMPTOMS):** - Specific concerns such as risk of harm to self and/or others, severe depression, agitation, or the presence of psychosis or confusion (delirium) require immediate referral to a psychiatrist, psychologist, physician, or equivalently trained professional. - Assessments should be a shared responsibility of the clinical team. - The assessment should identify signs and symptoms of depression, the severity of cancer symptoms, possible stressors, risk factors, and times of vulnerability. - Patients should first be assessed for depressive symptoms using the PHQ-9. - If moderate to severe or severe symptomatology is detected through screening, individuals should have further diagnostic assessment to identify the nature and extent of the depressive symptoms and the presence or absence of a mood disorder. - Medical or substance-induced causes of significant depressive symptoms (e.g.,

[3] Recommendations reflect high, moderate or low confidence that the recommendation reflects the net effect of a given course of action. The use of words like "must," "must not," "should," and "should not" indicate that a course of action is recommended or not recommended for either most or many patients, but there is latitude for the treating physician to select other courses of action in certain cases.

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
		interferon administration) should be determined and treated. - As a shared responsibility, the clinical team must decide when referral to psychiatrist, psychologist, or equivalently trained professional is needed. **Recommendations**[3] **MANAGEMENT (DEPRESSIVE SYMPTOMS):** - For any patient who is identified as at risk of harm to self and/or others, refer to appropriate services for emergency evaluation. Facilitate a safe environment and one-to-one observation, and initiate appropriate harm-reduction interventions. - First, treat medical causes of depressive symptoms (e.g., unrelieved symptoms such as pain and fatigue) and delirium (e.g., infection or electrolyte imbalance).[4] - For optimal management of depressive symptoms or diagnosed mood disorder, use pharmacologic and/or non-pharmacologic interventions (e.g., psychotherapy, psycho-educational therapy, cognitive-behavioral therapy, exercise) delivered by appropriately trained individuals. - The choice of an antidepressant should be informed by the adverse 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.[4] - Offer support and provide education and information about depression and its

[3] Recommendations reflect high, moderate or low confidence that the recommendation reflects the net effect of a given course of action. The use of words like "must," "must not," "should," and "should not" indicate that a course of action is recommended or not recommended for either most or many patients, but there is latitude for the treating physician to select other courses of action in certain cases.
[4] Recommendation is taken verbatim from the Pan-Canadian guideline.

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
		management to all patients and their families, including what specific symptoms and what degree of symptom worsening warrants a call to the physician or nurse. - It is recommended to use a stepped care model and tailor intervention recommendations based on variables such as the following: o Current symptomatology level and presence or absence of *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (*DSM*-5) diagnosis o Level of functional impairment in major life areas o Presence or absence of risk factors o History of and response to previous treatments for depression o Patient preference o Persistence of symptoms after receipt of an initial course of depression treatment - Psychological and psychosocial interventions should derive from relevant treatment manuals for empirically supported treatments that specify the content and guide the structure, delivery mode, and duration of the intervention. - Use of outcome measures should be routine (minimally pre and post-treatment) to 1) gauge the efficacy of treatment for the individual patient, 2) monitor treatment adherence, and 3) evaluate practitioner competence. **Recommendations**[3] **SCREENING (ANXIETY SYMPTOMS):** - All health care providers should routinely screen for the presence of emotional distress and specifically symptoms of anxiety from the point of diagnosis onward.[4]

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[4] Recommendation is taken verbatim from the Pan-Canadian guideline.

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
		- All patients should be screened for distress at their initial visit, at appropriate intervals and as clinically indicated, especially with changes in disease status and when there is a transition to palliative and end-of-life care. [4] - Screening should identify the level and nature (problems and concerns) of the distress as a red flag indicator. [4] - Screening should be done using a valid and reliable tool that features reportable scores (dimensions) that are clinically meaningful (established cut-offs). [4] - Anxiety disorders include specific phobias and social phobia, panic and agoraphobia, generalized anxiety disorder (GAD), obsessive compulsive disorder, and post-traumatic stress disorder (PTSD). - It is recommended that patients be assessed for GAD, as it is the most prevalent of all anxiety disorders and it is commonly comorbid with others, primarily mood disorders or other anxiety disorders (e.g., social anxiety disorder). - Use of the Generalized Anxiety Disorder (GAD) -7 scale is recommended. - Patients with GAD do not necessarily present with symptoms of anxiety, per se. - It is important to determine the associated home, relationship, social, or occupational impairments, if any, and the duration of anxiety-related symptoms. Problem checklists can be used. - As with depressive symptoms, consider special circumstances in screening and assessment of anxiety, including using culturally sensitive assessments and treatments and tailoring assessment or treatment for those with learning disabilities or cognitive impairments. **Recommendations**[3]

[3] Recommendations reflect high, moderate or low confidence that the recommendation reflects the net effect of a given course of action. The use of words like “must,” “must not,” “should,” and “should not” indicate that a course of action is recommended or not recommended for either most or many patients, but there is latitude for the treating physician to select other courses of action in certain cases.
[4] Recommendation is taken verbatim from the Pan-Canadian guideline.

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
		ASSESSMENT (ANXIETY SYMPTOMS): - Specific concerns (risk of harm to self and/or others, severe anxiety or agitation, or the presence of psychosis, confusion, or delirium) require referral to a psychiatrist, psychologist, physician, or equivalently trained professional. Moderate to severe or severe symptoms should have a diagnostic assessment to identify the nature and extent of the anxiety symptoms and the presence or absence of an anxiety disorder or disorders. - Medical and substance-induced causes of anxiety should be diagnosed and treated. - As a shared responsibility, the clinical team must decide when referral to a psychiatrist, psychologist or equivalently trained professional is needed. - 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, palpitations, 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. - A patient considered to have severe symptoms of anxiety after the further assessment should have confirmation of an anxiety disorder diagnosis before any treatment options are initiated (e.g., *DSM-5*, which may require a referral). **Recommendations**[3]

[3] Recommendations reflect high, moderate or low confidence that the recommendation reflects the net effect of a given course of action. The use of words like "must," "must not," "should," and "should not" indicate that a course of action is recommended or not recommended for either most or many patients, but there is latitude for the treating physician to select other courses of action in certain cases.

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
		MANAGEMENT (ANXIETY SYMPTOMS): - For any patient who is identified as at risk of harm to self and/or others, clinicians should refer to appropriately trained professionals for emergency evaluation. Facilitate a safe environment and one-to-one observation, and initiate appropriate harm-reduction interventions. - It is suggested that the clinical team making a patient referral for the treatment of anxiety review with the patient, in a shared decision process, the reason(s) for and potential benefits of the referral. It is suggested that the clinical team subsequently assess the patient's compliance with the referral and treatment progress or outcomes. - First treat medical causes of anxiety (e.g., unrelieved symptoms such as pain and fatigue) and delirium (e.g., caused by infection or electrolyte imbalance).[4] - For optimal management of moderate to severe or severe anxiety, consider pharmacologic and/or non-pharmacologic interventions delivered by appropriately trained individuals. 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. [4] - The choice of an anxiolytic should be informed by the adverse 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. Caution is warranted with respect to the use of benzodiazepines in the treatment of anxiety, specifically over the longer term. Use of these medications should be time limited in accordance with established psychiatric guidelines.

[4] Recommendation is taken verbatim from the Pan-Canadian guideline.

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
		- Offer support and provide education and information to all patients and their families about anxiety and its treatment and what specific symptoms or symptom worsening warrant a call to the physician or nurse. - It is recommended to use a stepped care model to tailor intervention recommendations as the following: o Current symptomatology level and presence/absence of *DSM-5* diagnoses o Level of functional impairment in major life areas o Presence/absence of risk factors o Chronicity of GAD and response to previous treatments, if any o Patient preference o Persistence of symptoms after receipt of the current anxiety treatment. - Psychological and psychosocial interventions should be derived from relevant treatment manuals that specify the content and guide the structure, delivery mode, and duration of the intervention. **Recommendations**[3]
Howell,2010[12] Canadian Partnership Against Cancer (Cancer Journey Action Group); Canadian Association of Psychosocial Oncology (2014) Canada	Pan Canadian Practice Guideline Screening, Assessment and Care of Psychosocial Distress (Depression, Anxiety) In Adults with Cancer Canadian health	**SCREENING (ANXIETY):** All health care providers should routinely screen for the presence of emotional anxiety from the point of diagnosis onwards. Patients should be screened for anxiety at initial visit in intervals especially with changes in disease status and in transition to palliative and end-of-life care. Screening should identify the problems and concerns of distress as a red flag indicator. Screening should be done using valid and reliable tools that feature dimension and are clinically meaningful. **Level of Evidence: NCCN, 2A** **ASSESSMENT (ANXIETY):**

[3] Recommendations reflect high, moderate or low confidence that the recommendation reflects the net effect of a given course of action. The use of words like "must," "must not," "should," and "should not" indicate that a course of action is recommended or not recommended for either most or many patients, but there is latitude for the treating physician to select other courses of action in certain cases.

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	authorities, program leaders, administrators, professional health care providers The goal of this guideline was to inform the Canadian health authorities, program leaders, administrators, and professional health care providers about the screening, assessment and psychosocial-supportive care of adult patients with cancer depression and/or anxiety using the Edmonton Symptom Assessment System (ESAS) Adult cancer patients at any phase of cancer regardless of cancer type, disease,	Concerns such as risk of harm to self/others, severe anxiety or agitation may require an urgent referral to psychiatrist, psychologist, physician or equivalently trained professional. When moderate or severe anxiety is detected through ESAS score 4 or higher, individuals should have immediate assessment to identify the nature and extent of anxiety. Medical and substance-induced causes of anxiety should be ruled out. Clinical team must decide when referral to trained professional is needed. Assessment should identify signs and symptoms of anxiety, severity, possible stressors, risk factors, and times of vulnerability. Patient with anxiety symptoms should have confirmation of clinical diagnosis of anxiety before use of pharmacological treatment or care options. **Level of Evidence: NCCN, 2A** **MANAGEMENT(ANXIETY):** Patients with risk of harm to self or others consider URGENT referral to appropriate services. Treat medical causes of anxiety first. Optimal management of moderate to severe anxiety combined with pharmacological and non-pharmacological should be delivered by trained professional. Management of anxiety must be tailored to individual patients who should be informed of their options. For mild to moderate anxiety a primary oncology team may choose to manage the concerns by usual supportive care management. Support, education, and information about depression to patient and family should be provided. **Level of Evidence: NCCN, 2A**

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
	stage, or treatment modality.	
Howes,2015[14] Cancer Care Nova Scotia (2014) Canada	Best Practice Guideline for the Management of Cancer-Related Distress in Adults Primarily intended for: HCPs, working in a variety of clinical and care settings, front-line HCPs. Also: Clinical educators, researchers and administrators The scope and purpose of this guideline is to	**SCREENING:** 1. Cancer services will ensure that individuals affected by cancer understand that identification and management of cancer-related distress is an integral part of cancer care. **Level of evidence: Level I[5]** **NBCC-NCCI =Level III-3[5]** **Level of Recommendation: Strong Recommendation[6]** 2. Psychosocial health services must focus on meeting the individual's physical, social, emotional, nutritional, informational, psychological, spiritual, and practical needs is recommended throughout the cancer experience and into survivorship. **NBCC-NCCI =Level 1[5]** **NBCC-NCCI =Level II[5]** **Level of Recommendation: Strong Recommendation[6]** 3. Adults diagnosed with cancer should be screened for cancer-related distress by health care providers. **NBCC-NCCI =Level I[5]** **NBCC-NCCI =Level II[5]**

[5] Level I = Based on a systematic review of randomized controlled trials (RCT), Level II = Based on a minimum of one properly designed RCT, Level III-1 = Based on well-designed pseudo- randomized controlled trials, Level III-2 = Based on comparative studies with concurrent controls and allocation not randomized (cohort studies), case control studies, or interrupted time series with a control group, Level III-3 = Based on comparative studies with historical control, two or more single-arm studies, or interrupted time series without a parallel group, Level IV = Based on case studies, either post-test or pre- and post-test.
[6] Strong Recommendation: Some strong evidence, benefits clearly exceed harm.

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
	provide guidance and assist health care providers (HCPs) to screen, identify and manage cancer-related distress experienced by individuals diagnosed with cancer and their families (first level care) Adults with cancer who may experience distress at some point during the cancer continuum (i.e., from the time of diagnosis through	**NBCC-NCCI =Level III-3**[5] **Level of Recommendation: Strong Recommendation**[6] 4. Screening for cancer-related distress should occur two months following diagnosis. Re-screening should occur at critical times and times of transition throughout the cancer continuum. **NBCC-NCCI =Level III-3**[5] **Level of Recommendation: Recommendation**[7] 5. Screening should be done with Screening for Distress Tool. Tool consists of: - The Edmonton Symptom Assessment System-revised (ESAS-r) - The Canadian Problem Checklist - The Distress Thermometer. **NBCC-NCCI =Level I**[5] **NBCC-NCCI =Level II**[5] **NBCC-NCCI =Level III-3**[5] **Level of Recommendation: Recommendation**[7] **ASSESSMENT:**

[5] Level I = Based on a systematic review of randomized controlled trials (RCT), Level II = Based on a minimum of one properly designed RCT, Level III-1 = Based on well-designed pseudo- randomized controlled trials, Level III-2 = Based on comparative studies with concurrent controls and allocation not randomized (cohort studies), case control studies, or interrupted time series with a control group, Level III-3 = Based on comparative studies with historical control, two or more single-arm studies, or interrupted time series without a parallel group, Level IV = Based on case studies, either post-test or pre- and post-test.

[6] Strong Recommendation: Some strong evidence, benefits clearly exceed harm.

[7] Recommendation: ; Recommendation: Strength of evidence is mixed, benefits exceed the harm.

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
	to survivorship and death and dying).	6. Patients with high distress (one or more distress scores on the ESAS-r and/or DT of 8 or greater) require urgent decision by health care team to either manage distress directly or make a referral to appropriate health care specialist. **NBCC-NCCI =Level I**[5] **NBCC-NCCI =Level II**[5] **NBCC-NCCI =Level III-1**[5] **Level of Recommendation: Strong Recommendation**[6] 7. Patients with moderate distress (one or more scores on the ESAS-r and/or DT between 4-7) maybe managed by health care team or referred to appropriate health specialist. **NBCC-NCCI =Level I**[5] **NBCC-NCCI =Level II**[5] **NBCC-NCCI =Level III-1**[5] **Level of Recommendation: Strong Recommendation**[6] 8. Patients with mild distress (all scores on the ESAS-r and/or DT less than 4) can be managed by health care team. If distress does not improve referral to an appropriate health care specialist should be considered. **NBCC-NCCI =Level I**[5]

[5] Level I = Based on a systematic review of randomized controlled trials (RCT), Level II = Based on a minimum of one properly designed RCT, Level III-1 = Based on well-designed pseudo- randomized controlled trials, Level III-2 = Based on comparative studies with concurrent controls and allocation not randomized (cohort studies), case control studies, or interrupted time series with a control group, Level III-3 = Based on comparative studies with historical control, two or more single-arm studies, or interrupted time series without a parallel group, Level IV = Based on case studies, either post-test or pre- and post-test.
[6] Strong Recommendation: Some strong evidence, benefits clearly exceed harm.

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
		NBCC-NCCI =Level III-1[5] **NBCC-NCCI =Level III-3**[5] **Level of Recommendation: Recommendation**[7] 9. When the adult affected by cancer needs specialized care (eg. assessment and/or treatment), referral to health care specialist with expertise relevant to the identified distress is recommended. **NBCC-NCCI =Level I**[5] **NBCC-NCCI =Level II**[5] **Level of Recommendation: Strong Recommendation**[6] **MANAGEMENT:** 10. Health care providers should provide information on available resources tailored to the person's specific needs and situation. **NBCC-NCCI =Level I**[5] **NBCC-NCCI =Level II**[5] **NBCC-NCCI =Level IV**[5] **Level of Recommendation: Strong Recommendation**[6] 11. Health care providers screening individuals for cancer-related distress must address the needs of people from diverse communities. **NBCC-NCCI =Level III**[5]

[7] Recommendation: Strength of evidence is mixed, benefits exceed the harm.
[6] Strong Recommendation: Some strong evidence, benefits clearly exceed harm.

[5] Level I = Based on a systematic review of randomized controlled trials (RCT), Level II = Based on a minimum of one properly designed RCT, Level III-1 = Based on well-designed pseudo- randomized controlled trials, Level III-2 = Based on comparative studies with concurrent controls and allocation not randomized (cohort studies), case control studies, or interrupted time series with a control group, Level III-3 = Based on

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
		NBCC-NCCI =Level IV[5] **Level of Recommendation: Recommendation[8]** 12. Health care providers seeing person for managed of cancer-related distress should provide service in an inclusive and sensitive manner. **NBCC-NCCI =Level III[5]** **NBCC-NCCI =Level IV[5]** **Level of Recommendation: Recommendation[8]** **MANAGEMENT(ANXIETY):** - General: psychological, non-pharmacological interventions in the treatment of anxiety, psycho-education, relaxation and guided imagery, cognitive-behavior therapy, supportive therapies, crisis intervention. - Moderate to severe anxiety: may require pharmacotherapy in addition to psychosocial/psychological therapies. There are several medications available to treat anxiety. Individual patient-specific variables and needs, as well as other factors (i.e., nature of anxiety, psychological-mindedness, co-morbid medical conditions, potential side effects of medications, and patient preference) should be considered in choosing pharmacological and/or psychological interventions. **Level of Recommendation: NR**
Deng,2013[20]	Complementary	**SCREENING:**

comparative studies with historical control, two or more single-arm studies, or interrupted time series without a parallel group, Level IV = Based on case studies, either post-test or pre- and post-test.

[6] Strong Recommendation: Some strong evidence, benefits clearly exceed harm.

[8] Recommendation: Overwhelmingly consistent evidence from descriptive studies, benefits clearly exceed the harm.

[8] Recommendation: Overwhelmingly consistent evidence from descriptive studies, benefits clearly exceed the harm.

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
American College of Chest Physicians (2013) USA	therapies and integrative medicine in lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines Physicians, Psychologist, Psychotherapist, Oncologist, Massage therapist, Dietitian, professional health care provides, clinical educators, researchers and administrators The recommendations mostly focused on symptoms (anxiety, nausea, vomiting, pain, and other	- No screening recommendation is found. **ASSESSMENT:** - It is suggested that all lung cancer patients should be asked about their interest in and usage of complementary therapies. Counseling on the benefits and risks of those therapies should be provided. **Level of Recommendation: Grade 2C** **MANAGEMENT:** - In lung cancer patients experiencing symptoms, mind-body modalities are suggested as part of a multidisciplinary approach to reduce anxiety, mood disturbance, sleep disturbance, and improve quality of life (QoL). **Level of Recommendation: Grade 2B** - In lung cancer patients whose anxiety or pain is not adequately controlled by usual care, addition of massage therapy performed by trained professionals is suggested as part of a multi-modality cancer supportive care program. **Level of Recommendation: Grade 2B**

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
	symptoms) which could be shared by all patients with cancer rather than those limited to patients with lung cancer Patients with lung cancer.	

Table 6.C.3: Characteristics of Depression Focused Guidelines

Author, Year **Organization/Guideline publisher (Year):** **Country:**	**Title:** **Intended User:** **Scope:** **Population:**	**Recommendations(s):** **Grading system used for body of evidence = Overall rating**
Howes,2015[14] Cancer Care Nova Scotia (2014) Canada	Best Practice Guideline for the Management of Cancer-Related Distress in Adults Primarily intended for: HCPs, working in a variety of clinical and care settings, front-line HCPs. Also: Clinical educators, researchers and administrators The scope and	**SCREENING:** 1. Cancer services will ensure that individuals affected by cancer understand that identification and management of cancer-related distress is an integral part of cancer care. **NBCC-NCCI =Level I[5]** **NBCC-NCCI =Level III-3[5]** **Level of Recommendation: Strong Recommendation[6]** 2. Psychosocial health services must focus on meeting the individual's physical, social, emotional, nutritional, informational, psychological, spiritual, and practical needs is recommended throughout the cancer experience and into survivorship. **NBCC-NCCI =Level 1[5]** **NBCC-NCCI =Level II[5]** **Level of Recommendation: Strong Recommendation[6]** 3. Adults diagnosed with cancer should be screened for cancer-related distress by health care providers.

[5] Level I = Based on a systematic review of randomized controlled trials (RCT), Level II = Based on a minimum of one properly designed RCT, Level III-1 = Based on well-designed pseudo- randomized controlled trials, Level III-2 = Based on comparative studies with concurrent controls and allocation not randomized (cohort studies), case control studies, or interrupted time series with a control group, Level III-3 = Based on comparative studies with historical control, two or more single-arm studies, or interrupted time series without a parallel group, Level IV = Based on case studies, either post-test or pre- and post-test.

[6] Strong Recommendation: Some strong evidence, benefits clearly exceed harm.

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
	purpose of this guideline is to provide guidance and assist health care providers (HCPs) to screen, identify and manage cancer-related distress experienced by individuals diagnosed with cancer and their families (first level care) Adults with cancer who may experience distress at some point during the cancer continuum (i.e., from the time of diagnosis through to	**NBCC-NCCI =Level I**[5] **NBCC-NCCI =Level II**[5] **NBCC-NCCI =Level III-3**[5] **Level of Recommendation: Strong Recommendation**[6] 4. Screening for cancer-related distress should occur two months following diagnosis. Re-screening should occur at critical times and times of transition throughout the cancer continuum. **NBCC-NCCI =Level III-3**[5] **Level of Recommendation: Recommendation**[7] 5. Screening should be done with Screening for Distress Tool. Tool consist of: - The Edmonton Symptom Assessment System-revised (ESAS-r) - The Canadian Problem Checklist - The Distress Thermometer. **NBCC-NCCI =Level I**[5] **NBCC-NCCI =Level II**[5] **NBCC-NCCI =Level III-3**[5] **Level of Recommendation: Recommendation**[7]

[5] Level I = Based on a systematic review of RCTs, Level II = Based on a minimum of one properly designed RCT, Level III-1 = Based on well-designed pseudo- randomized controlled trials, Level III-2 = Based on comparative studies with concurrent controls and allocation not randomized (cohort studies), case control studies, or interrupted time series with a control group, Level III-3 = Based on comparative studies with historical control, two or more single-arm studies, or interrupted time series without a parallel group, Level IV = Based on case studies, either post-test or pre- and post-test.

[6] Strong Recommendation: Some strong evidence, benefits clearly exceed harm.

[7] Recommendation: Strength of evidence is mixed, Benefits exceed the harm.

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
	survivorship and death and dying).	**ASSESSMENT:** 6. Patients with high distress (one or more distress scores on the ESAS-r and/or DT of 8 or greater) require urgent decision by health care team to either manage distress directly or make a referral to appropriate health care specialist. **NBCC-NCCI =Level I**[5] **NBCC-NCCI =Level II**[5] **NBCC-NCCI =Level III-1**[5] **Level of Recommendation: Strong Recommendation**[6] 7. Patients with moderate distress (one or more scores on the ESAS-r and/or DT between 4-7) maybe managed by health care team or referred to appropriate health specialist. **NBCC-NCCI =Level I**[5] **NBCC-NCCI =Level II**[5] **NBCC-NCCI =Level III-1**[5] **Level of Recommendation: Strong Recommendation**[6] 8. Patients with mild distress (all scores on the ESAS-r and/or DT less than 4) can be managed by health care team. If distress does not improve referral to an appropriate health care specialist should be considered. **NBCC-NCCI =Level I**[5]

[5] Level I = Based on a systematic review of RCTs, Level II = Based on a minimum of one properly designed RCT, Level III-1 = Based on well-designed pseudo- randomized controlled trials, Level III-2 = Based on comparative studies with concurrent controls and allocation not randomized (cohort studies), case control studies, or interrupted time series with a control group, Level III-3 = Based on comparative studies with historical control, two or more single-arm studies, or interrupted time series without a parallel group, Level IV = Based on case studies, either post-test or pre- and post-test.

[6] Strong Recommendation: Some strong evidence, benefits clearly exceed harm.

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
		NBCC-NCCI =Level III-1[5] **NBCC-NCCI =Level III-3**[5] **Level of Recommendation: Recommendation**[7] 9. When the adult affected by cancer needs specialized care (e.g. assessment and/or treatment), referral to health care specialist with expertise relevant to the identified distress is recommended. **NBCC-NCCI =Level I**[5] **NBCC-NCCI =Level II**[5] **Level of Recommendation: Strong Recommendation**[6] **MANAGEMENT:** 10. Health care providers should provide information on available resources tailored to the person's specific needs and situation. **NBCC-NCCI =Level I**[5] **NBCC-NCCI =Level II**[5] **NBCC-NCCI =Level IV**[5] **Level of Recommendation: Strong Recommendation**[6] 11. Health care providers screening individuals for cancer-related distress must address the

[5] Level I = Based on a systematic review of RCTs, Level II = Based on a minimum of one properly designed RCT, Level III-1 = Based on well-designed pseudo- randomized controlled trials, Level III-2 = Based on comparative studies with concurrent controls and allocation not randomized (cohort studies), case control studies, or interrupted time series with a control group, Level III-3 = Based on comparative studies with historical control, two or more single-arm studies, or interrupted time series without a parallel group, Level IV = Based on case studies, either post-test or pre- and post-test.
[6] Strong Recommendation: Some strong evidence, benefits clearly exceed harm.
[7] Recommendation: Strength of evidence is mixed, Benefits exceed the harm.

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
		needs of people from diverse communities. **NBCC-NCCI =Level III**[5] **NBCC-NCCI =Level IV**[5] **Level of Recommendation: Recommendation**[8] 12. Health care providers seeing person for managed of cancer-related distress should provide service in an inclusive and sensitive manner. **NBCC-NCCI =Level III**[5] **NBCC-NCCI =Level IV**[5] **Level of Recommendation: Recommendation**[8] **MANAGEMENT(DEPRESSION):** - General: Psychological and pharmacological interventions have shown efficacy in treating individuals diagnosed with major depression: ○ Psychological intervention: psychosocial and behavioral therapy alone or combined with education. ○ Pharmacological intervention: Many types of anti-depressants are available. The choice of antidepressant will be affected by several factors such as potential side-effects of the medications, co-morbid medical conditions, and patient preference. ○ Mild or Sub-syndromal Depression: Psychological treatment ○ Moderate Depression: Psychological intervention and/or pharmacotherapy ○ Severe Depression: Combined pharmacotherapy and psychological therapy. **Level of Evidence: NR**

[8] Recommendation: Overwhelmingly consistent evidence from descriptive studies, benefits clearly exceed the harm.
[8] Recommendation: Overwhelmingly consistent evidence from descriptive studies, benefits clearly exceed the harm.

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
Howell,2010[12] Canadian Partnership Against Cancer (Cancer Journey Action Group); Canadian Association of Psychosocial Oncology (2014) Canada	Pan Canadian Practice Guideline Screening, Assessment and Care of Psychosocial Distress (Depression, Anxiety) In Adults with Cancer Canadian health authorities, program leaders, administrators, professional health care providers The goal of this guideline was to inform the Canadian health authorities, program leaders, administrators, and professional health care providers about the screening, assessment and psychosocial-supportive care of adult patients with cancer depression	**SCREENING (DEPRESSION):** All health care providers should routinely screen for the presence of emotional distress from the point of diagnosis onwards. Patients should be screened for distress at initial visit in intervals especially with changes in disease status and in transition to palliative and end-of-life care. Screening should identify the problems and concerns of distress as a red flag indicator. Screening should be done using valid and reliable tools that features dimension and are clinically meaningful. **Level of Evidence: NCCN, 2A** **ASSESSMENT (DEPRESSION):** Concerns such as risk of harm to self/others, severe depression or agitation may require an urgent referral to psychiatrist, psychologist, physician or equivalently trained professional. When moderate or severe depression is detected through ESAS score 4 or higher, individuals should have immediate assessment to identify the nature and extent of depression. Medical and substance-induced cause of depression should be ruled out. Clinical team must decide when referral to trained professional is needed. Assessment should identify signs and symptoms of depression, severity, possible stressors, risk factors, and times of vulnerability. - Patient with depression symptoms should have confirmation of clinical diagnosis of depression before use of pharmacological treatment or care options. **Level of Evidence: NCCN, 2A** **MANAGEMENT (DEPRESSION):** Patients with risk of harm to self or others consider URGENT referral to appropriate services. Treat medical causes of depression first. Optimal management of moderate to severe depression combined with pharmacological and non-pharmacological treatment should be delivered by a trained professional. Support, education, and information about depression to patient and family should be provided. **Level of Evidence: NCCN, 2A**

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
	and/or anxiety using the Edmonton Symptom Assessment System (ESAS) Adult cancer patients at any phase of cancer regardless of cancer type, disease, stage, or treatment modality.	
National Institute for Health and Clinical Excellence,2009[19] NICE Clinical Guideline (2009) UK	Depression in adults with a chronic physical health problem: Treatment and management Adults with depression and a chronic physical health problem, health care professionals who have direct contact with these patients, family and community effect by patients with depression and chronic physical	**SCREENING (DEPRESSION):** Be alert to possible depression (particularly in patients with a past history of depression or a chronic physical health problem with associated functional impairment) and consider asking patients who may have depression two questions, specifically: ● During the last month, have you often been bothered by feeling down, depressed or hopeless? ● During the last month, have you often been bothered by having little interest or pleasure in doing things? If a patient with a chronic physical health problem answers 'yes' to either of the depression identification questions but the practitioner is not competent to perform a mental health assessment, they should refer the patient to an appropriate professional. If this professional is not the patient's GP, inform the GP of the referral. If a patient with a chronic physical health problem answers 'yes' to either of the depression identification questions, a practitioner who is competent to perform a mental health assessment should: ● ask three further questions to improve the accuracy of the assessment of depression,

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
	health problem The scope of this guideline is to make recommendations for the treatment and management of depression in adults with chronic physical health problem Adults (18 years and older) with a clinical working diagnosis of a depressive disorder and a chronic physical health problem with associated impact on function. This could include, for example, people with cancer, heart disease, neurological disorders or diabetes, and depression.	specifically: - During the last month, have you often been bothered by feelings of worthlessness? - During the last month, have you often been bothered by poor concentration? - During the last month, have you often been bothered by thoughts of death? ● review the patient's mental state and associated functional, interpersonal and social difficulties ● consider the role of both the chronic physical health problem and any prescribed medication in the development or maintenance of the depression ● ascertain that the optimal treatment for the physical health problem is being provided and adhered to, seeking specialist advice if necessary. When assessing a patient with suspected depression, consider using a validated measure (for symptoms, functions and/or disability) to inform and evaluate treatment. For patients with significant language or communication difficulties, for example patients with sensory impairments or a learning disability, consider using the Distress Thermometer 14 and/or asking a family member or carer about the patient's symptoms to identify possible depression. If a significant level of distress is identified, investigate further. **Level of recommendation: NR** **ASSESSMENT (DEPRESSION):** Conduct a comprehensive assessment that does not rely simply on a symptom count. Consider how the following factors may have affected the development, course and severity of a patient's depression: ● any history of depression and comorbid mental health or physical disorders ● any past history of mood elevation (to determine if the depression may be part of bipolar disorder) ● any past experience of, and response to, treatments

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
		● the quality of interpersonal relationships ● living conditions and social isolation. Be respectful of, and sensitive to, diverse cultural, ethnic and religious backgrounds when working with patients with depression and a chronic physical health problem, and be aware of the possible variations in the presentation of depression. Ensure competence in: ● culturally sensitive assessment ● using different explanatory models of depression ● addressing cultural and ethnic differences when developing and implementing treatment plans ● working with families from diverse ethnic and cultural backgrounds. When assessing a patient with a chronic physical health problem and suspected depression, be aware of any learning disabilities or acquired cognitive impairments, and if necessary consider consulting with a relevant specialist when developing treatment plans and strategies. When providing interventions for patients with a learning disability or acquired cognitive impairment who have a chronic physical health problem and a diagnosis of depression: ● where possible, provide the same interventions as for other patients with depression ● if necessary, adjust the method of delivery or duration of the intervention to take account of the disability or impairment. Always ask patients with depression and a chronic physical health problem directly about suicidal ideation and intent. If there is a risk of self-harm or suicide: ● assess whether the patient has adequate social support and is aware of sources of help ● arrange help appropriate to the level of risk ● advise the patient to seek further help. **Level of recommendation: NR**

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
		MANAGEMENT (DEPRESSION): For patients with persistent sub-threshold depressive symptoms or mild to moderate depression and a chronic physical health problem who have not benefited from a low-intensity psychosocial intervention, discuss the relative merits of different interventions with the patient and provide: ● an antidepressant (normally a selective serotonin reuptake inhibitor [SSRI]) or ● one of the following high-intensity psychological interventions: - group-based CBT or - individual CBT for patients who decline group-based CBT or for whom it is not appropriate, or where a group is not available or - behavioral couples therapy for people who have a regular partner and where the relationship may contribute to the development or maintenance of depression, or where involving the partner is considered to be of potential therapeutic benefit. For patients with initial presentation of moderate depression and a chronic physical health problem, offer group-based CBT or individual CBT or behavioral couple's therapy for people who would benefit from such interventions. For patients with initial presentation of severe depression and a chronic physical health problem, consider offering a combination of individual CBT and an antidepressant. The choice of intervention should be influenced by the: ● duration of the episode of depression and the trajectory of symptoms ● previous course of depression and response to treatment ● likelihood of adherence to treatment and any potential adverse effects ● course and treatment of the chronic physical health problem ● patient's treatment preference and priorities. Antidepressant drugs/choice of antidepressants: When an antidepressant is to be prescribed for a patient with depression and a chronic physical health problem, take into account the following:

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
		● the presence of additional physical health disorders ● the side effects of antidepressants, which may impact on the underlying physical disease (in particular, SSRIs may result in or exacerbate hypernatremia, especially in older people) ● that there is no evidence as yet supporting the use of specific antidepressants for patients with particular chronic physical health problems ● interactions with other medications. When an antidepressant is to be prescribed, be aware of drug interactions and: ● refer to appendix 1 of the BNF and the table of interactions in appendix 16 of the full guideline for information ● seek specialist advice if there is uncertainty ● if necessary, refer the patient to specialist mental health services for continued prescribing. First prescribe an SSRI in generic form unless there are interactions with other drugs; consider using citalopram or sertraline because they have fewer propensities for interactions. When prescribing antidepressants, be aware that: ● dosulepin should not be prescribed ● non-reversible monoamine oxidase inhibitors (MAOIs; for example, phenelzine), combined antidepressants and lithium augmentation of antidepressants should normally be prescribed only by specialist mental health professionals. Take into account toxicity in overdose when choosing an antidepressant for patients at significant risk of suicide. Be aware that: ● compared with other equally effective antidepressants recommended for routine use in primary care, venlafaxine is associated with a greater risk of death from overdose ● tricyclic antidepressants (TCAs), except for lofepramine, are associated with the greatest risk in overdose. Interactions of SSRIs with other medication

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
		Do not normally offer SSRIs to patients taking non-steroidal anti-inflammatory drugs (NSAIDs) because of the increased risk of gastrointestinal bleeding. Consider offering an antidepressant with a lower propensity for, or a different range of, interactions, such as mianserin, mirtazapine, moclobemide or trazodone. If no suitable alternative antidepressant can be identified, SSRIs may be prescribed at the same time as NSAIDs if gastroprotective medicines (for example, proton-pump inhibitors) are also offered. Do not normally offer SSRIs to patients taking warfarin or heparin because of their anti-platelet effect. Use SSRIs with caution in patients taking aspirin. When aspirin is used as a single agent, consider alternatives that may be safer, such as trazodone or mianserin. If no suitable alternative antidepressant can be identified, SSRIs may be prescribed at the same time as aspirin if gastroprotective medicines (for example, proton-pump inhibitors) are also offered. Consider offering mirtazapine to patients taking heparin, aspirin or warfarin (but note that when taken with warfarin, the international normalized ratio [INR] may increase slightly). Do not offer SSRIs to patients receiving 'triptan' drugs for migraine. Offer a safer alternative such as mirtazapine, trazodone or mianserin. Do not normally offer SSRIs at the same time as monoamine oxidase B (MAO-B) inhibitors such as selegiline and rasagiline. Offer a safer alternative such as mirtazapine, trazodone or mianserin. Do not normally offer fluvoxamine to patients taking theophylline, clozapine, methadone or tizanidine. Offer a safer alternative such as sertraline or citalopram. Offer sertraline as the preferred antidepressant for patients taking flecainide or propafenone, although mirtazapine and moclobemide may also be used. Do not offer fluoxetine or paroxetine to patients taking atomoxetine. Offer a different SSRI.

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
		Starting treatment When prescribing antidepressants, explore any concerns the patient with depression and a chronic physical health problem has about taking medication, explain fully the reasons for prescribing, and provide information about taking antidepressants, including: ● the gradual development of the full antidepressant effect ● the importance of taking medication as prescribed and the need to continue treatment after remission ● potential side effects ● the potential for interactions with other medications ● the risk and nature of discontinuation symptoms with all antidepressants, particularly with drugs with a shorter half-life (such as paroxetine and venlafaxine), and how these symptoms can be minimized ● the fact that addiction does not occur with antidepressants. ● Offer written information appropriate to the patient's needs. Prescribe antidepressant medication at a recognized therapeutic dose for patients with depression and a chronic physical health problem (that is, avoid the tendency to prescribe at sub-therapeutic doses in these patients). For patients started on antidepressants that are not considered to be at increased risk of suicide, normally see them after 2 weeks. See them regularly thereafter, for example at intervals of 2 to 4 weeks in the first 3 months, and then at longer intervals if response is good. A patient with depression started on antidepressants who is considered to present an increased suicide risk or is younger than 30 years (because of the potential increased prevalence of suicidal thoughts in the early stages of antidepressant treatment for this group) should normally be seen after 1 week and frequently thereafter as appropriate until the risk is no longer considered clinically important. If a patient with depression and a chronic physical health problem develops side effects early in antidepressant treatment, provide appropriate information and consider one of the following strategies:

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
		● monitor symptoms closely where side effects are mild and acceptable to the patient or ● stop the antidepressant or change to a different antidepressant if the patient prefers or ● in discussion with the patient, consider short-term concomitant treatment with a benzodiazepine if anxiety, agitation and/or insomnia are problematic, but: - do not offer benzodiazepines to patients with chronic symptoms of anxiety - use benzodiazepines with caution in patients at risk of falls - in order to prevent the development of dependence, do not use benzodiazepines for longer than 2 weeks. Continuing treatment Support and encourage a patient with a chronic physical health problem who has benefited from taking an antidepressant to continue medication for at least 6 months after remission of an episode of depression. Discuss with the patient that: ● this greatly reduces the risk of relapse ● antidepressants are not associated with addiction. Review with the patient with depression and a chronic physical health problem the need for continued antidepressant treatment beyond 6 months after remission, taking into account: ● the number of previous episodes of depression ● the presence of residual symptoms ● concurrent physical health problems and psychosocial difficulties ● Failure of treatment to provide benefit If the patient's depression shows no improvement after 2 to 4 weeks with the first antidepressant, check that the drug has been taken regularly and in the prescribed dose. If response is absent or minimal after 3 to 4 weeks of treatment with a therapeutic dose of an antidepressant, increase the level of support (for example, by weekly face-to-face or telephone contact) and consider: ● increasing the dose in line with the SPC if there are no significant side effects or ● switching to another antidepressant as described in Section 1.8 of the

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
		Depression guideline (CG90) if there are side effects or if the patient prefers. If the patient's depression shows some improvement by 4 weeks, continue treatment for another 2 to 4 weeks. Consider switching to another antidepressant as described in Section 1.8 of the Depression guideline (CG90) if: ● response is still not adequate or ● there are side effects or ● the patient prefers to change treatment. When switching from one antidepressant to another is aware of: ● the need for gradual and modest incremental increases in dose ● interactions between antidepressants ● the risk of serotonin syndrome when combinations of serotonergic antidepressants are prescribed. If an antidepressant has not been effective or is poorly tolerated: ● consider offering other treatment options, including high-intensity psychological treatments ● prescribe another single antidepressant (which can be from the same class) if the decision is made to offer a further course of antidepressants. Stopping or reducing antidepressants Advise patients with depression and a chronic physical health problem who are taking antidepressants that discontinuation symptoms may occur on stopping, missing doses or, occasionally, on reducing the dose of the drug. Explain that symptoms are usually mild and self-limiting over about 1 week, but can be severe, particularly if the drug is stopped abruptly. When stopping an antidepressant, gradually reduce the dose, normally over a 4-week period, although some patients may require longer periods, particularly with drugs with a shorter half-life (such as paroxetine and venlafaxine). This is not required with fluoxetine because of its long half-life. Inform the patient that they should seek advice from their practitioner if they experience

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
		significant discontinuation symptoms. If discontinuation symptoms occur; ● monitor symptoms and reassure the patient if symptoms are mild ● consider reintroducing the original antidepressant at the dose that was effective (or another antidepressant with a longer half-life from the same class) if symptoms are severe, and reduce the dose gradually while monitoring symptoms. Psychological interventions Delivering high-intensity psychological interventions For all high-intensity psychological interventions, the duration of treatment should normally be within the limits indicated in this guideline. As the aim of treatment is to obtain significant improvement or remission the duration of treatment may be: ● reduced if remission has been achieved ● increased if progress is being made, and there is agreement between the practitioner and the patient with depression that further sessions would be beneficial (for example, if there is a comorbid personality disorder or psychosocial factors that impacts the patient's ability to benefit from treatment). Group-based CBT for patients with depression and a chronic physical health problem should be: ● delivered in groups (typically of between six and eight patients) with a common chronic physical health problem ● typically delivered over a period of 6 to 8 weeks. Individual CBT for patients with moderate depression and a chronic physical health problem should be: ● delivered until the symptoms of depression have remitted (over a period that is typically 6 to 8 weeks and should not normally exceed 16 to 18 weeks) ● followed up by two further sessions in the 6 months after the end of treatment, especially if treatment was extended.

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
		Individual CBT for patients with severe depression and a chronic physical health problem should be: ● delivered until the symptoms of depression have remitted (over a period that is typically 16 to 18 weeks) ● focused in the initial sessions (which typically should take place twice weekly for the first 2 to 3 weeks) on behavioral activation ● followed up by two or three further sessions in the 12 months after the end of treatment. Behavioral couple's therapy for depression should normally be based on behavioral principles, and an adequate course of therapy should be 15 to 20 sessions over 5 to 6 months. Collaborative care Consider collaborative care for patients with moderate to severe depression and a chronic physical health problem with associated functional impairment whose depression has not responded to initial high-intensity psychological interventions, pharmacological treatment or a combination of psychological and pharmacological interventions. Collaborative care for patients with depression and a chronic physical health problem should normally include: ● case management which is supervised and has support from a senior mental health professional ● close collaboration between primary and secondary physical health services and specialist mental health services ● a range of interventions consistent with those recommended in this guideline, including patient education, psychological and pharmacological interventions, and medication management ● long-term coordination of care and follow-up. COMPLEX AND SEVERE DEPRESSION

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
		Practitioners providing treatment in specialist mental health services for patients with complex and severe depression and a chronic physical health problem should: ● refer to the NICE guideline on the treatment of depression ● be aware of the additional drug interactions associated with the treatment of patients with both depression and a chronic physical health problem ● work closely and collaboratively with the physical health services. **Level of recommendation: NR**
Rayner,2011[17] European Journal of Cancer (2011) UK	The development of evidence-based European guidelines on the management of depression in palliative cancer care All health care professionals involved in the provision of palliative care The guideline aimed to provide evidence-based recommendations on managing depression in palliative care to inform clinical practice, establish policy, promote European	**SCREENING AND ASSESSMENT:** Clinical assessment should involve a thorough psychiatric history and an assessment of the intensity of depressive symptoms, the duration of the episode and the degree of functional impairment. Depression should be diagnosed according to validated diagnostic criteria (i.e. DSM-IV or ICD-10). The Hamilton Depression Rating Scale (HADS) can be used for assessment of severity and response to treatment. The Beck Depression Inventory (BDI) is another commonly used severity assessment scale. **Level of evidence: NR** - Clinicians should prioritize cognitive/affective symptoms in detecting depression as physical symptoms may be caused by physical disease or medical treatment **GRADE: Strong** - Clinicians should consider screening for depression in palliative care patients. **GRADE: Weak** - Clinicians should regularly review depressive symptoms to capture changes in mood. **GRADE: Strong** **MANAGEMENT:**

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
	consensus and ultimately improve patient outcomes Cancer patients with advanced disease/depression who are receiving palliative care.	• Mild Depression: First-line treatment: - Refer to palliative care specialist for symptom control and psychosocial support - Assess quality of relationships with significant others; facilitate communication - Consider a guided self-help program - Consider a brief psychological intervention (i.e., problem-solving therapy, brief CBT) If symptoms persist: - Consider using an antidepressant - Reassess and possibly revise the diagnosis • Moderate Depression: First-line treatment: - Follow recommendations for mild depression - Initiate treatment with antidepressant medication and/or psychological therapy If symptoms persist: - Assess compliance to treatment - Consider combining antidepressant treatment and psychological therapy - After 4 weeks of antidepressant treatment, consider raising the dose of antidepressant or switching to a different drug • Severe Depression: First-line treatment - Follow recommendation for mild depression - Initiate treatment with antidepressants medication and psychological therapy - Consider using a hypnotic or sedative in sleep disturbed or very distressed patients If symptoms persist: - As for moderate depression - Refer to a mental health specialist - Lithium augmentation, electroconvulsive therapy and anti-psychotic drugs may be considered (under supervision of a mental health specialist). **Level of evidence: NR**

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
		- Clinicians should refer patients with depression to specialist palliative care for improved symptom control and psychosocial support. **GRADE: Strong** - Clinicians should consider antidepressants for treatment of depression in palliative care. **GRADE: Strong** - Clinicians should consider psychological therapy for treatment of depression in palliative care. **GRADE: Strong**
Li,2015[18] Cancer Care Ontario (2015) Canada	The Management of Depression in Patients with Cancer: Guideline Recommendations Mental-health care providers (psychiatrists, psychologists), palliative care professionals, oncologists, oncology nurses, psychosocial intervention providers, primary care providers, and	**SCREENING AND ASSESSMENT:** - Patients with cancer should be screened for depression. A clear diagnosis of depression is required to guide treatment, and must be followed by effective intervention. **Level of recommendation: consensus-based/adapted from NICE guideline** **MANAGEMENT:** - Provide psychosocial about depression to cancer patients and consider providing handouts by National Cancer Institute - Inform patients about the impact of depression on cancer outcomes, including reduced quality of life, intensification of physical symptoms, longer hospital stays, and reduced survival rates - Destigmatize clinical depression by framing it as a serious problem - Investigate medical contributors to depression (e.g., hypothyroidism, vitamin B12, iron deficiency) - Assess and optimize cancer-related physical symptoms - Encourage family members involvement, education, communication, and resolution of problems

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
	community nurses The goal of this guideline was to provide recommendations on the effective treatment (pharmacological and/or psychological) for depression in adult cancer population and to improve quality and consistency of the management of depression for patients with cancer Adult patients with cancer who are diagnosed with a major depressive disorder based on a structured diagnostic interview, or who have a suspected depressive disorder based on meeting a	- Discuss treatment options attending to patients preferences and previous treatment experience - Consider use of validated depression rating scale such as Patient Health Questionnaire 2 (PHQ-9), Hospital Anxiety Depression Scale (HADS) or Beck Depression Inventory II (BDI-II). **Level of recommendation: consensus-based/adapted from NICE guideline** Pharmacological or Psychosocial interventions: - Patients may benefit from pharmacological or psychosocial interventions either alone or in combination - The effectiveness of psychosocial and pharmacological interventions for moderate depression is equal • Pharmacologic interventions are most effective for more severe depression • Combined psychosocial and pharmacologic interventions should be considered for severe depression in patients with cancer. **Level of recommendation: consensus-based/adapted from NICE guideline** Depression severity and a stepped care approach: - Interventions should be delivered according to a stepped care model. This involves assessment of severity of depression, provision of support and psycho-education, delivery of lower-intensity interventions for persistent sub threshold and mild to moderate depression (including group physical activity programs, group-based peer support, self-help, guided self-help program based on CBT, behavioral activation, and problem solving techniques), followed by progression to higher intensity intervention for non-responsive or moderate to severe depression (including individual or group CBT, behavioral couples therapy, individual or group supportive-expressive psychotherapies). - Antidepressant medication should be reserved for moderate to severe depression, but can be considered for sub-threshold or mild depressive symptoms persisting after

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
	threshold on a validated depression rating scale.	initial interventions or when depression interferes with engagement in cancer treatment. **Level of recommendation: consensus-based/adapted from NICE guideline** Collaborative care interventions: - For patients with major depression, interventions should be discussed between specialist and primary care providers. Collaborative care interventions include measurement-based care, with a range of intensity levels needed according to stepped care, Follow-up and maintenance are also required. - Within a stepped care approach, collaborative care interventions may be most appropriate for patients with cancer and with sub-threshold/mild depression persisting after other interventions, or with moderate to severe depression. - Implementation of a collaborative care model may require significant reorganization of mental health care service delivery in cancer treatment facilities. **Level of recommendation: consensus-based/adapted from NICE guideline** Specialist referral: - Referral to a mental health specialist should occur in the following circumstances: when there is risk of harm, in complex psychosocial cases, where the patient experiences persistent symptoms after initial intervention, when diagnosis is unclear, for delivery of specific psychotherapies requiring specialized training. **Level of recommendation: consensus-based/adapted from NICE guideline** Selection of psychological therapies: - Selection of psychological therapy should be based on patient factors and local resource availability. - Psychological interventions should be considered first for mild to moderate depression.

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
		- Psychological therapies should be delivered by healthcare professionals competent in the modality. Mental health specialists can be trained in basic psychosocial interventions. Delivery of therapy: - Empathic communication, psycho-education, problem-solving, and behavioral activation are therapeutic techniques which may be delivered by trained healthcare professionals. - Supportive-expressive and structured psychotherapies (e.g., CBT, interpersonal therapy, psychodynamic therapy) require specially trained therapists. Patient factors guiding selection: - CBT may be useful for patients wanting a symptom-based approach. - Supportive-expressive therapies may be of value with more psychologically minded patients. - Individual therapies may be more practical in patients who are in the palliative phase. **Level of recommendation: consensus-based/adapted from NICE guideline** Use of antidepressant medication: - Antidepressant medication should be considered first for severe depression and not used routinely to treat sub threshold depressive symptoms or mild depression. - In clinical practice, a selective serotonin reuptake inhibitor (SSRI) such as citalopram/escitalopram should be the first resort due to best tolerability and the least potential for drug interactions. - Some studies showed interactions between tamoxifen and antidepressants that inhibit cytochrome P450 2D6 (CYP2D6), reducing the conversion of tamoxifen to the active metabolite endoxifen and thereby increasing the risks of recurrence and mortality. However, meta-analyses have suggested that the reductions in endoxifen do not translate into increased breast cancer recurrence rates or mortality rates, possibly because the therapeutic dosing of tamoxifen fully saturates the estrogen receptor. - Existing recommendations have been conservative, cautioning avoidance of potent

Author, Year Organization/Guideline publisher (Year): Country:	Title: Intended User: Scope: Population:	Recommendations(s): Grading system used for body of evidence = Overall rating
		CYP2D6 inhibitors (i.e., paroxetine, fluoxetine, high-dose sertraline, bupropion) with tamoxifen. Although these antidepressants are not recommended as first-line agents, clinical judgment can be exercised in their use with patients for whom safer alternatives are not an option, after discussion with the treating oncologist has occurred and informed consent obtained. More potent CYP2D6 inhibitors may be safer to use in postmenopausal women, or women with a known extensive metabolizer CYP2D6 genotype. When possible, it is prudent to prefer antidepressants with low CYP2D6 inhibition (i.e., citalopram/escitalopram, venlafaxine/desvenlafaxine, or mirtazapine) as first line agents. **Level of recommendation: consensus-based/adapted from NICE guideline**

6.D Definition of Level of Evidence

Table 6.D.1: Definition of Level for Recommendations of Eligible Guidelines

NBCC-NCCI	Levels of Evidence • Recommendations are based on the highest level of evidence, as found through the evidence review process (Refer to Appendix II). The level of evidence is provided for each recommendation. • There is limited research in some areas and when this is the case any major deficiencies are noted. • The evidence used in the guideline is rated using the system developed by the Australian National Breast Cancer Centre and National Cancer Control Initiative (NBCC-NCCI) as described in the Clinical practice guidelines for the psychosocial care of adults with cancer (10). The levels of evidence are as follows: Level I Based on a systematic review of randomized controlled trials (RCT). Level II Based on a minimum of one properly designed RCT. Level III-1 Based on well-designed pseudo- randomized controlled trials. Level III-2 Based on "comparative studies with concurrent controls and allocation not randomized (cohort studies), case control studies, or interrupted time series with a control group". Level III-3 Based on "comparative studies with historical control, two or more single-arm studies, or interrupted time series without a parallel group". Level IV Based on "case studies, either post-test or pre- and post-test". • Level I evidence is the gold standard for recommendations related to clinical interventions. In the absence of this level of evidence, some recommendations have been made based on lower levels of evidence and expert consensus[14].
GRADE	Strong = Strong evidence (i.e., from RCT or meta-analysis) Weak = Weak evidence (i.e., from cross-sectional surveys, case series)[17].
NCCN	Category 1 = Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate. Category 2A = Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate. Category 2B = Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate. Category 3 = Based upon any level evidence, there is major NCCN disagreement that the intervention is appropriate [11].
SIGN recommendation	A = indicated that the recommendation was derived from at least one meta-analysis, systematic review, or RCT rated as 1++ and was directly applicable to the target population; or a body of evidence consisting principally of studies rated as 1+,directly applicable to the target population, and demonstrating overall consistency of results. B = A body of evidence including studies rated as 2++, directly applicable to the target population and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 1++ or 1+. C = A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 2+. D = Evidence level 3 or 4; or extrapolated evidence from studies rated as 2= [147].
Chest Grading	1A = Strong recommendation, high-quality evidence.

System	1B = Strong recommendation, moderate-quality evidence. 1C = Strong recommendation, low-quality or very low-quality evidence. 2A = Weak recommendation, high-quality evidence. 2B = Weak recommendation, moderate-quality evidence. 2C = Weak recommendation, low-quality or very low-quality evidence [148].

6.E Cross References

Table 6.E.1: Cross References of Included Systematic Reviews and Guidelines

All RCTs in eligible SRs and Guideline	Hart,2012[122]	Matcham,2014[124]	Akechi,2013[119]	Galway,2014[121]	Candy,2012[36]	Rayner,2010[127]	Walker,2014[129]	Mitchell,2012[125]	Nenova,2013[126]	Carvalho,2014[120]	Laoutidis and Mathiak,2013[123]	Ng,2011[97]	Simard,2013[102]	van Straten,2010[128]	Yu,2012[9]	Andersen,2014[10]	Deng,2013[20]	Holland,2014[11]	National Institute for Health and Clinical Excellence,2009[19]	Howell,2010[12]	Rayner,2011[17]	Howell,2009[13]	Li,2015[18]	Howes,2015[14]	Included RCTs in current Guideline
Search/ Last date	11	12	05	11	12	09	12	11	10	13	10	10	11	09	08	09	11	NR	09	09	NR	08	15	NR	
Study design	SR	SR	SR	SR	SR	SR	SR	SR	SR	SR	SR	SR	SR	SR	GL	GL	GL	GL	GL	GL	GL	GL	GL	GL	
Banasik *et al.*,2011[148]																	✓								
Beatty *et al.*,2010[149]									✓																
Beatty *et al.*,2010[150]		✓																							

All RCTs in eligible SRs and Guideline	Hart,2012[122]	Matcham,2014[124]	Akechi,2013[119]	Galway,2014[121]	Candy,2012[36]	Rayner,2010[127]	Walker,2014[129]	Mitchell,2012[125]	Nenova,2013[126]	Carvalho,2014[120]	Laoutidis and Mathiak,2013[123]	Ng,2011[97]	Simard,2013[102]	van Straten,2010[128]	Yu,2012[9]	Andersen,2014[10]	Deng,2013[20]	Holland,2014[11]	National Institute for Health and Clinical Excellence,2009[19]	Howell,2010[12]	Rayner,2011[17]	Howell,2009[13]	Li,2015[18]	Howes,2015[14]	Included RCTs in current Guideline
Beutel,2014[67]																							✓		✓
Branstrom *et al.*,2010[151]									✓																
Breitbart *et al.*,2012[152]																		✓							
Breitbart *et al.*,2010[153]																		✓							
Carlson *et al.*,2010[154]																								✓	

All RCTs in eligible SRs and Guideline	Hart,2012[122]	Matcham,2014[124]	Akechi,2013[119]	Galway,2014[121]	Candy,2012[36]	Rayner,2010[127]	Walker,2014[129]	Mitchell,2012[125]	Nenova,2013[126]	Carvalho,2014[120]	Laoutidis and Mathiak,2013[123]	Ng,2011[97]	Simard,2013[102]	van Straten,2010[128]	Yu,2012[9]	Andersen,2014[10]	Deng,2013[20]	Holland,2014[11]	National Institute for Health and Clinical Excellence,2009[19]	Howell,2010[12]	Rayner,2011[17]	Howell,2009[13]	Li,2015[18]	Howes,2015[14]	Included RCTs in current Guideline
Carlson *et al.*,2012[155]																		✓							
Chochinov *et al.*,2011[156]																		✓							
DuHamel,2010[56]									✓																✓
Ell,2011[78]	✓																						✓		✓
Fann,2009[76]																							✓		✓
Goerling,2011[53]																							✓		✓
Greer,2012																		✓							✓

All RCTs in eligible SRs and Guideline	Hart,2012[122]	Matcham,2014[124]	Akechi,2013[119]	Galway,2014[121]	Candy,2012[36]	Rayner,2010[127]	Walker,2014[129]	Mitchell,2012[125]	Nenova,2013[126]	Carvalho,2014[120]	Laoutidis and Mathiak,2013[123]	Ng,2011[97]	Simard,2013[102]	van Straten,2010[128]	Yu,2012[9]	Andersen,2014[10]	Deng,2013[20]	Holland,2014[11]	National Institute for Health and Clinical Excellence,2009[19]	Howell,2010[12]	Rayner,2011[17]	Howell,2009[13]	Li,2015[18]	Howes,2015[14]	Included RCTs in current Guideline
[32]							✓																		
Hopko,2011[66]																							✓		✓
Kangas,2013[31]																							✓		✓
Kroenke,2010[77]																							✓		✓
Menza *et al.*,2009[157]						✓																			
Moorey *et al.*,2009[158]																					✓				
Ng,2014[65]																							✓		✓
Parker *et*									✓																

All RCTs in eligible SRs and Guideline	Hart,2012[122]	Matcham,2014[124]	Akechi,2013[119]	Galway,2014[121]	Candy,2012[36]	Rayner,2010[127]	Walker,2014[129]	Mitchell,2012[125]	Nenova,2013[126]	Carvalho,2014[120]	Laoutidis and Mathiak,2013[123]	Ng,2011[97]	Simard,2013[102]	van Straten,2010[128]	Yu,2012[9]	Andersen,2014[10]	Deng,2013[20]	Holland,2014[11]	National Institute for Health and Clinical Excellence,2009[19]	Howell,2010[12]	Rayner,2011[17]	Howell,2009[13]	Li,2015[18]	Howes,2015[14]	Included RCTs in current Guideline
al.,2009[159]																									
Qiu,2013[71]																							✓		✓
Rodriguez Vega,2011[72]																							✓		✓
Sharpe,2014[79]																							✓		✓
Temel,2010[45]																					✓				
Vadiraja *et al.*,2009[160]																	✓								
Walker *et al.*,2014[161]																							✓		✓

All RCTs in eligible SRs and Guideline	Hart,2012[122]	Matcham,2014[124]	Akechi,2013[119]	Galway,2014[121]	Candy,2012[36]	Rayner,2010[127]	Walker,2014[129]	Mitchell,2012[125]	Nenova,2013[126]	Carvalho,2014[120]	Laoutidis and Mathiak,2013[123]	Ng,2011[97]	Simard,2013[102]	van Straten,2010[128]	Yu,2012[9]	Andersen,2014[10]	Deng,2013[20]	Holland,2014[11]	National Institute for Health and Clinical Excellence,2009[19]	Howell,2010[12]	Rayner,2011[17]	Howell,2009[13]	Li,2015[18]	Howes,2015[14]	Included RCTs in current Guideline
Weintraub *et al.*,2010[162]						✓																			
Zissiadis *et al.*,2010[163]		✓																							
Amodeo *et al.*,2012[164]																									✓
Ashing and Rosales,2014[26]																									✓
Capezzani, 2013[29]																									✓
Carlson,2013[24]																									✓

All RCTs in eligible SRs and Guideline	Hart,2012[122]	Matcham,2014[124]	Akechi,2013[119]	Galway,2014[121]	Candy,2012[36]	Rayner,2010[127]	Walker,2014[129]	Mitchell,2012[125]	Nenova,2013[126]	Carvalho,2014[120]	Laoutidis and Mathiak,2013[123]	Ng,2011[97]	Simard,2013[102]	van Straten,2010[128]	Yu,2012[9]	Andersen,2014[10]	Deng,2013[20]	Holland,2014[11]	National Institute for Health and Clinical Excellence,2009[19]	Howell,2010[12]	Rayner,2011[17]	Howell,2009[13]	Li,2015[18]	Howes,2015[14]	Included RCTs in current Guideline
Carpenter, 2014[55]																								✓	✓
Chambers,2014[22]																								✓	✓
Herschbach,2010[34]																								✓	✓
Lepore,2012[27]																								✓	✓
Monti,2013[23]																								✓	✓
Mosher,2012[25]																								✓	✓
Rini,2014[28]																								✓	✓

All RCTs in eligible SRs and Guideline	Hart,2012[122]	Matcham,2014[124]	Akechi,2013[119]	Galway,2014[121]	Candy,2012[36]	Rayner,2010[127]	Walker,2014[129]	Mitchell,2012[125]	Nenova,2013[126]	Carvalho,2014[120]	Laoutidis and Mathiak,2013[123]	Ng,2011[97]	Simard,2013[102]	van Straten,2010[128]	Yu,2012[9]	Andersen,2014[10]	Deng,2013[20]	Holland,2014[11]	National Institute for Health and Clinical Excellence,2009[19]	Howell,2010[12]	Rayner,2011[17]	Howell,2009[13]	Li,2015[18]	Howes,2015[14]	Included RCTs in current Guideline
Serfaty,2012[33]																								✓	
Zernicke,2014[57]																								✓	

6.F Quality Assessment

Table 6.F.1: Quality Assessment of Included Randomized Control Trials Distress- Psychosocial Intervention

Author, Year	Adequate sequence generation	Allocation concealment	Blinding	Incomplete outcome data addressed	Free of selective reporting	Free of other bias	Declaration of funding	Statistical analysis methods section	Score
Chambers, 2014[22]	+[9]	+	-[10]	+	+	+	+	+	7
Monti, 2013[23]	+	?[11]	-	-	+	+	+	+	5
Carlson, 2013[24]	+	?	+	+	+	+	+	+	7
Mosher, 2012[25]	+	-	-	-	+	+	+	+	5
Ashing and Rosales, 2014[26]	+	+	-	+	-	+	+	+	6
Lepore, 2012[27]	+	+	+	+	+	+	+	+	8
Rini, 2014[28]	+	+	-	-	+	+	+	+	6
Zernicke, 2014[57]	+	+	-	+	+	+	+	+	7

[9] + = Low Risk of Bias
[10] - = High Risk of Bias
[11] ? = Unclear Risk of Bias

Table 6.F.2: Quality Assessment of Included Randomized Control Trials- Distress- CBT Intervention

Author, Year	Adequate sequence generation	Allocation concealment	Blinding	Incomplete outcome data addressed	Free of selective reporting	Free of other bias	Declaration of funding	Statistical analysis methods section	Score
Serfaty, 2012[33]	+[12]	-[13]	+	-	+	+	+	+	6
DuHamel, 2010[56]	+	?[14]	-	+	+	+	+	+	6

[12] + = Low Risk of Bias
[13] - = High Risk of Bias
[14] ? = Unclear Risk of Bias

Table 6.F.3: Quality Assessment of Included Randomized Control Trials- PTSD- Psychosocial & CBT Intervention

Author, Year	Adequate sequence generation	Allocation concealment	Blinding	Incomplete outcome data addressed	Free of selective reporting	Free of other bias	Declaration of funding	Statistical analysis methods section	Score
Kangas, 2013[31]	+[15]	?[16]	-[17]	-	-	-	+	+	3
Capezzani, 2013[29]	+	?	-	+	-	+	+	+	5
Carpenter, 2014[55]	+	?	-	-	-	+	+	+	4

[15] + = Low Risk of Bias
[16] ? = Unclear Risk of Bias
[17] - = High Risk of Bias

Table 6.F.4: Quality Assessment of Included Randomized Control Trials- Anxiety- Psychosocial Intervention

Author, Year	Adequate sequence generation	Allocation concealment	Blinding	Incomplete outcome data addressed	Free of selective reporting	Free of other bias	Declaration of funding	Statistical analysis methods section	Score
Goerling, 2011[53]	+	?	+	-	-	+	-	+	4

Table 6.F.5: Quality Assessment of Included Randomized Control Trials- Anxiety- CBT Intervention

Author, Year	Adequate sequence generation	Allocation concealment	Blinding	Incomplete outcome data addressed	Free of selective reporting	Free of other bias	Declaration of funding	Statistical analysis methods section	Score
Kangas, 2013[31]	+[18]	?[19]	-[20]	-	-	-	+	+	3
Greer, 2012[32]	+	+	-	+	+	+	+	+	7

[18] + = Low Risk of Bias
[19] ? = Unclear Risk of Bias
[20] - = High Risk of Bias

Table 6.F.6: Quality Assessment of Included Randomized Control Trials- Fear- Psychosocial & CBT Intervention

Author, Year	Adequate sequence generation	Allocation concealment	Blinding	Incomplete outcome data addressed	Free of selective reporting	Free of other bias	Declaration of funding	Statistical analysis methods section	Score
Herschbach, 2010[34]	+[21]	+	-[22]	-	-	+	+	+	5

[21] + = Low Risk of Bias
[22] - = High Risk of Bias

6.G Characteristics of Included Randomized Control Trials

Table 6.G.1: Characteristics of Included Randomized Control Trials Distress-Psychosocial Intervention

Author, Year Country (Intervention)	Disease Site/Stage Treatment Stage	Screened (n) Analyzed (n) Intervention IPT	Population Assessment tool Interview vs. Self-report	Outcome Measure Harms, Adverse events, or Side effect	Effect size expressed as Odds Ratios (95% confidence interval) P-value	Summary Result
Carlson,2013[24] Canada (MBCR)	Breast Cancer Stage I-III Completion of all treatment with exception of hormonal or trastuzumab therapy (at least 3 months ago)	956 ITT: 271 MBCR vs SET vs SMS 8-12 weeks	Clinically meaningful distress: Distress Thermometer Score ≥ 4 Distress Thermometer Interview	C-SOSI (stress) NR	ITT analysis: (effect size$^{\eta^2}$)= 0.040 P group = 0.020 P Time <0.001 P Group × Time = 0.015 MBCR, Baseline: Mean =66.84 95%CI = 61.12 to 72.55 MBCR, after intervention: Mean =47.57 95%CI = 41.12 to 54.03 PP analysis: (effect size$^{\eta^2}$)= 0.043 P group = 0.178 P Time <0.001 P Group × Time = 0.009 MBCR, Baseline: Mean =67.42 95%CI = 60.36 to 74.47 MBCR, after intervention: Mean =48.00	Compared with both SET and SMS, MBCR cause greater reduction in stress symptoms, stress level and social support in breast cancer survivors.

Author, Year Country (Intervention)	Disease Site/Stage Treatment Stage	Screened (n) Analyzed (n) Intervention IPT	Population Assessment tool Interview vs. Self-report	Outcome Measure Harms, Adverse events, or Side effect	Effect size expressed as Odds Ratios (95% confidence interval) P-value	Summary Result
					95%CI = 40.88 to 55.13	
Carlson,2013[24] Canada (SET)	Breast Cancer Stage I-III Completion of all treatment with exception of hormonal or trastuzumab therapy (at least 3 months ago)	956 ITT: 271 MBCR vs SET vs SMS 8-12 weeks	Clinically meaningful distress: Distress Thermometer Score ≥ 4 Distress Thermometer Interview	C-SOSI (stress) NR	ITT analysis: (effect size η^2)= 0.040 P group = 0.020 P Time <0.001 P Group × Time = 0.015 SET, Baseline: Mean =73.24 95%CI = 67.26 to 79.23 SET, after intervention: Mean =63.78 95%CI=57.27 to 70.29 PP analysis: (effect sizeη^2)= 0.043 P group = 0.178 P Time <0.001 P Group × Time = 0.009 SET, Baseline: Mean =70.40 95%CI = 63.35 to 77.45 SET, after intervention: Mean =61.72 95%CI = 54.67 to 68.77	Compared with both SET and SMS, MBCR cause greater reduction in stress symptoms, stress level and social support in breast cancer survivors.
Carlson,2013[24] Canada	Breast Cancer	956 ITT: 271	Clinically meaningful distress:	C-SOSI (stress)	ITT analysis: (effect size ŋ2)= 0.040 P group = 0.020	Compared with both SET and SMS, MBCR cause greater reduction in

Author, Year Country (Intervention)	Disease Site/Stage Treatment Stage	Screened (n) Analyzed (n) Intervention IPT	Population Assessment tool Interview vs. Self-report	Outcome Measure Harms, Adverse events, or Side effect	Effect size expressed as Odds Ratios (95% confidence interval) P-value	Summary Result
(SMS)	Stage I-III Completion of all treatment with exception of hormonal or trastuzumab therapy (at least 3 months ago)	MBCR vs SET vs SMS 8-12 weeks	Distress Thermometer Score ≥ 4 Distress Thermometer Interview	NR	P Time <0.001 P Group × Time = 0.015 SMS, Baseline: Mean =66.07 95%CI =57.88 to 74.25 SMS, after intervention: Mean =57.20 95%CI=48.16 to 66.24 PP analysis: (effect size ŋ2)= 0.043 P group = 0.178 P Time <0.001 P Group × Time = 0.009 SMS, Baseline: Mean =63.00 95%CI = 53.06 to 72.90 SMS, after intervention: Mean =54.84 95%CI = 44.92 to 64.76	stress symptoms, stress level and social support in breast cancer survivors.
Mosher,2012[25] USA (Neutral Writing)	Breast Cancer Metastatic NR	521 86 Expressive Writing vs	Significant distress: Distress Thermometer Scores exceeding the cut-off (≥ 4)	Distress Thermometer (Distress) NR	Neutral Writing Group: Mean(SE)= 4.37(0.37) 95% CI = -1.20 to 0.88 Partial η^2 = 0.00	Both Neutral and Expressive writing groups showed their awareness of their distress and condition is elevated.

Author, Year Country (Intervention)	Disease Site/Stage Treatment Stage	Screened (n) Analyzed (n) Intervention IPT	Population Assessment tool Interview vs. Self-report	Outcome Measure Harms, Adverse events, or Side effect	Effect size expressed as Odds Ratios (95% confidence interval) P-value	Summary Result
		Neutral Writing 4-7 weeks	Distress Thermometer Interview			Expressive writing group used the mental health service two times more than neutral writing group.
Mosher,2012[25] USA (Expressive Writing)	Breast Cancer Metastatic NR	521 86 Expressive Writing vs Neutral Writing 4-7 weeks	Significant distress: Distress Thermometer Scores exceeding the cut-off (≥ 4) Distress Thermometer Interview	Distress Thermometer (Distress) NR	Expressive Writing Group: Mean(SE)= 4.53(0.36) 95% CI = -1.20 to 0.88 Partial η^2= 0.00	Both Neutral and Expressive writing groups showed their awareness of their distress and condition is elevated. Expressive writing group used the mental health service two times more than neutral writing group.
Chambers,2014[22] Australia (Psychologist-Delivered Five-Session Cognitive Behavioral Intervention)	Any Type Any Stage NR	3129 292 Nurse Single-Session Self-Management vs Psychologist-Delivered Five-Session	Distress Thermometer Score ≥4 Distress Thermometer Interview	BSI-18 total (Distress) NR	Psychologist-Delivered Five-Session Cognitive Behavioral Intervention Baseline Mean(SD)=14.9(11.95) 3 months Mean(SD)=13.24(11.2)	A single session of a nurse psychosocial intervention could have some significant benefit for distressed patients with cancer. This type of intervention can be delivered remotely by telephone and supported by self-management materials.
				IES total (Distress) NR	Psychologist-Delivered Five-Session Cognitive Behavioral Intervention Baseline	

Author, Year Country (Intervention)	Disease Site/Stage Treatment Stage	Screened (n) Analyzed (n) Intervention IPT	Population Assessment tool Interview vs. Self-report	Outcome Measure Harms, Adverse events, or Side effect	Effect size expressed as Odds Ratios (95% confidence interval) P-value	Summary Result
		Cognitive Behavioral Intervention 1 session or 5 session in 3 months			Mean(SD)=32.16(16.38) 3 months Mean(SD)=24.75(17.05)	
Chambers,2014[22] Australia (Nurse Single-Session Self-Management)	Any Type Any Stage NR	3129 292 Nurse Single-Session Self-Management vs Psychologist-Delivered Five-Session Cognitive Behavioral Intervention 1 session or 5 session in 3 months	Distress Thermometer Score ≥4 Distress Thermometer Interview	BSI-18 total (Distress) NR	Nurse Single-Session Self-Management Baseline Mean(SD)=15.36(11.29) 3 months Mean(SD)=14.54(11.58)	A single session of a nurse psychosocial intervention could have some significant benefit for distressed patients with cancer. This type of intervention can be delivered remotely by telephone and supported by self-management materials.
				IES total (Distress) NR	Nurse Single-Session Self-Management Baseline Mean(SD)=34.32(16.61) 3 months Mean(SD)=25.9(17.33)	
Ashing and Rosales,2014[26]	Breast Cancer Stage 0-III	529 199	At least moderate distress	Depressive Symptoms	Effect of intervention on Depressive symptoms Main effects:	The article's results demonstrate that this psycho- educational

Author, Year Country (Intervention)	Disease Site/Stage Treatment Stage	Screened (n) Analyzed (n) Intervention IPT	Population Assessment tool Interview vs. Self-report	Outcome Measure Harms, Adverse events, or Side effect	Effect size expressed as Odds Ratios (95% confidence interval) P-value	Summary Result
USA (Telephonic-based psycho-educational intervention)	NR	Telephonic-based psycho-educational intervention vs Control Study Condition 16 weeks	and burden levels measured by the CES-D ≥16 CES-D Interview	NR	(study condition) SS = 347.89, df = 1 MS = 347.89, F = 4.73 $p<0.05$, $\eta^2= 0.024$ Effect of intervention on Depressive symptoms Main effects: (Total) SS = 71076.0, df = 198 Baseline ELP, Control Group:Mean(SD)= 9.5(6.4) t-test = -7.73 ($p<0.001$) Baseline ELP, intervention Group:Mean(SD)= 23.5(9.5) t-test = -7.73 ($p<0.001$) Post-treatment ELP, Control Group: Mean(SD)= 10.7(6.9) t-test = -2.65 ($p<0.05$) Post-treatment ELP, intervention Group: Mean(SD)= 15.7(9.9) t-test = -2.65 ($p<0.05$)	telephonic intervention reduced significantly the depressive symptoms in cancer patients.

Author, Year Country (Intervention)	Disease Site/Stage Treatment Stage	Screened (n) Analyzed (n) Intervention IPT	Population Assessment tool Interview vs. Self-report	Outcome Measure Harms, Adverse events, or Side effect	Effect size expressed as Odds Ratios (95% confidence interval) P-value	Summary Result
					Depressive symptom for Intervention group Baseline: (Mean=25.4, SD=10.2) Post-treatment: (Mean=17.2, SD= 10.5) (p<0.001) Depressive symptom for control group Baseline: (Mean=14.8, SD=10.8) Post-treatment: (Mean=14.1, SD= 10.6) (p>0.05)	
Monti,2013[23] USA (BCSG)	Breast Cancer Any Stage NR	260 184 MBAT vs BCSG vs Untreated Group 8 weeks	Psychosocial stress level as determined by the BSI-18. Score of 12 or less to be 'low' stress. Score of 13 or higher to be 'high' stress. The BSI-18 distress cut-off scores:	SCL-90-R (Distress) GSI NR	BCSG Adjusted Mean Score* Week 1= 0.78 Week 9= 0.65, (week 9 p**<0.01) Week 1 & 9 Effect [ΔBCSG-ΔMBAT] (95%CI) = 0.02(-0.04, 0.08) (p=0.54) Untreated versus Control Effect (difference of difference)= -0.17 (-0.23, -0.12) , P<0.001	MBAT has significant benefits in breast cancer patients who suffered high stress level.

Author, Year Country (Intervention)	Disease Site/Stage Treatment Stage	Screened (n) Analyzed (n) Intervention IPT	Population Assessment tool Interview vs. Self-report	Outcome Measure Harms, Adverse events, or Side effect	Effect size expressed as Odds Ratios (95% confidence interval) P-value	Summary Result
			Moderate: 13 Low: 12 or less High: 13 or higher BSI-18 Interview		BCSG Adjusted Mean Score* (BSI Group: Low) Week 1= 0.41 Week 9= 0.27, (week 9 p**<0.01) BCSG Adjusted Mean Score* (BSI Group: High) Week 1= 0.99 Week 9= 0.74, (week 9 p**<0.01) Week 1 & 9 Effect [ΔBCSG-ΔMBAT](95%CI) (BSI Group: Low)= 0.02(-0.07,0.11), P=0.60 (BSI Group: High) = 0.01(-0.23,0.21) p=0.91	
Lepore,2012[27] USA (S-ISG intervention)	Breast Cancer Stage I –II NR	669 183 S-ISG intervention (Standard Internet support group)	Distress Scoring Above normal (≥8) for level of depression or Anxiety on the Hospital Anxiety and Depression Scale	Depression symptoms (HADS) NR	Baseline Mean(SD) = 7.20(3.85) Post-treatment Mean(SD)= 5.77(4.34)	Both interventions were helpful. The hypothesis that demonstrates S-ISG will improve psychological outcomes in distressed survivors of breast cancer was not improved by the results.
				Anxiety symptoms (HADS)	Baseline Mean(SD)= 10.12(3.02) Post-treatment Mean(SD)=	

Author, Year Country (Intervention)	Disease Site/Stage Treatment Stage	Screened (n) Analyzed (n) Intervention IPT	Population Assessment tool Interview vs. Self-report	Outcome Measure Harms, Adverse events, or Side effect	Effect size expressed as Odds Ratios (95% confidence interval) P-value	Summary Result
		vs P-ISG intervention (enhanced prosocial Internet support group) 6 weeks	HADS Interview	NR	7.74(4.14)	
Lepore,2012[27] USA (P-ISG intervention)	Breast Cancer Stage I –II NR	669 183 S-ISG intervention (Standard Internet support group) vs P-ISG intervention (enhanced prosocial Internet support group)	Distress Scoring Above normal (≥8) for level of depression or Anxiety on the Hospital Anxiety and Depression Scale HADS Interview	Depression symptoms (HADS) NR	Baseline Mean(SD)= 6.64(3.80) Post-treatment Mean(SD)= 6.13(4.21)	Both interventions were helpful. The hypothesis that demonstrates S-ISG will improve psychological outcomes in distressed survivors of breast cancer was not improved by the results.
				Anxiety symptoms (HADS) NR	Baseline Mean(SD)= 10.68(3.31) Post-treatment Mean(SD)= 9.18(4.26)	

Author, Year Country (Intervention)	Disease Site/Stage Treatment Stage	Screened (n) Analyzed (n) Intervention IPT	Population Assessment tool Interview vs. Self-report	Outcome Measure Harms, Adverse events, or Side effect	Effect size expressed as Odds Ratios (95% confidence interval) P-value	Summary Result
		6 weeks				
Rini,2014[28] USA	Hematological Cancers Cancer survivors HSCT	437 264 EH (Expressive Helping: Expressive Writing + Peer Helping) vs PH(Peer Helping) vs EW (Expressive Writing) vs NW(Neutral Writing) 4 weeks	At least mild survivorship problems according to published cut-offs or findings in relevant populations: general distress (BSI), cancer-specific distress (IES) BSI, IES Interview	53- item BSI-GSI (General Distress) NR	Writing Group (WG) SS= 0.15,df= 3, M=0.05, F=1.04, partial η^2 = 0.012 p=0.38 Cluster (CL) SS= 0.05,df= 1, M=0.05, F=0.97, partial η^2 = 0.004 p=0.33 WG × CL SS= 0.39, df= 3, M=0.14, F=2.77, partial η^2 = 0.032 p=0.04	Writing alone had no benefit in decreasing the general distress in cancer patients. Expressive writing showed significant therapeutic effects. If cancer survivors completed expressive writing and then go through peer helping writing, it has some benefits on moderate-severe survivorship problems.
Zernicke,2014[57] Canada (MBCR)	Any type Any stage Complete the	180 ITT: 62 Online MBCR	At least moderate distress: Distress Thermometer:	POMS TMD scores (anxiety , depression)	Online MBCR group Baseline: Mean(SE)=39.57(3.67) Online MBCR group Post-	Online MBCR intervention could be effective on total mood and stress symptom scores and spiritual well-

Author, Year Country (Intervention)	Disease Site/Stage Treatment Stage	Screened (n) Analyzed (n) Intervention IPT	Population Assessment tool Interview vs. Self-report	Outcome Measure Harms, Adverse events, or Side effect	Effect size expressed as Odds Ratios (95% confidence interval) P-value	Summary Result
	primary cancer treatment within last 3 years	vs TAU Wait-List Control Condition 8 weeks	score ≥ 4 Distress Thermometer Interview	NR	treatment: Mean(SE)= 18.31(4.10) Group Effect : F(df)[p]= 5.25(113)[0.024] Time Effect : F(df)[p]= 13.89(1,113)[0.000] Group × Time Interaction; F (*df*) [p] 3.95(1,113)[0.049] Online MBCR group Baseline: Unadjusted Mean(SD)=37.43(35.69) Online MBCR group Post-treatment: Unadjusted Mean(SD)=17.16(30.72) Cohen d = 0.44	being after 8 weeks.
				CSOSI (stress) NR	Bas Online MBCR group Baseline: Mean(SE)=62.49(3.12) Online MBCR group Post-treatment: Mean(SE)= 40.29(3.49)	

Author, Year Country (Intervention)	Disease Site/Stage Treatment Stage	Screened (n) Analyzed (n) Intervention IPT	Population Assessment tool Interview vs. Self-report	Outcome Measure Harms, Adverse events, or Side effect	Effect size expressed as Odds Ratios (95% confidence interval) P-value	Summary Result
					Group Effect : F(df)[p]=7.00(1.113)[0.009] Time Effect : F(df)[p]= 21.83(1,113)[0.000] Group × Time Interaction ; F (df) [p] 5.48(1,113)[0.021] Online MBCR group Baseline: Unadjusted Mean(SD)=59.70(32.52) Online MBCR group Post-treatment: group, Unadjusted Mean(SD) =36.83(21.87), Cohen d = 0.49	

MBCR: mindfulness-based cancer recovery, SET: supportive-expressive group therapy, SMS: 1-day stress management seminar, BSI-18: Brief Symptom Inventory -18, SS: Sum of Square, MS: Mean of Square, ELP= English Language preferred, MBAT: Mindfulness-based art therapy, BCSG: Breast Cancer Support Group, HSCT: Hematopoetic Stem Cell Transplant, *: Square root scale, **: Compare with week 1.

Table 6.G.2: Characteristics of Included Randomized Control Trials Distress-CBT Intervention

Author, Year Country (Intervention)	Disease Site/Stage Treatment Stage	Screened (n) Analyzed (n) Intervention IPT	Population Assessment tool Interview vs. Self-report	Outcome Measure Harms, Adverse events, or Side effect	Effect size expressed as Odds Ratios (95% confidence interval) P-value	Summary Result
DuHamel,2010[56] USA (T-CBT)	Leukemia, Lymphoma After HSCT (Hematopoietic stem cell transplantation) HSCT	408 81 T-CBT vs Assessment only 10-16 weeks	Significant distress as indicated by at least one of the following three criteria: probable illness-related PTSD on the PTSD Checklist-Civilian Version (PCL-C) by using the 3 or 4 symptom cluster criteria; subclinical PTSD symptoms as indicated by scores one or more standard deviations greater than the PCL-C mean; or general distress with some PTSD symptoms as indicated by scores exceeding the clinical cut-off on any two subscales of the Brief Symptom Inventory (BSI) or the BSI Global Severity Index &, according to either PCL-C scoring method, scores exceeding the cut-off for at least one PTSD symptom cluster PCL-C, PTSD, Checklist-	Total PCL-C Screening NR	T-CBT group Baseline: Mean(95%CI)= 32.05(28.60 to 35.50) T-CBT group post-treatment: Mean(95%CI)= 25.38(21.69 to 29.07)	A brief, telephone-administered CBT intervention designed for HSCT survivors reduces general distress in Hematopoietic cancer patients after HSCT.
				Global BSI Distress NR	T-CBT group Baseline: Mean(95%CI)= 34.87(26.67 to 43.07) T-CBT group post-treatment: Mean(95%CI)= 21.36(12.56 to 30.17) Adjusted: T-CBT group Baseline Mean(95%CI) =40.97(30.70 to 51.25) T-CBT group Post-treatment Mean(95%CI) = 27.74(16.83 to 38.65)	

Author, Year Country (Intervention)	Disease Site/Stage Treatment Stage	Screened (n) Analyzed (n) Intervention IPT	Population Assessment tool Interview vs. Self-report	Outcome Measure Harms, Adverse events, or Side effect	Effect size expressed as Odds Ratios (95% confidence interval) P-value	Summary Result
			Civilian Version, BSI Global Severity Index Interview			
Serfaty,2012[33] UK (CBT+ TAU)	Any Type Any Stage NR	170 39 randomized 36 post-intervention CBT + TAU vs AM + TAU 10 weeks	HADS scale ≥ 8 for either anxiety or depression HADS Interview	POMS-TMS TMS (Total Mood Score) NR	CBT group Baseline: Mean(SD)= 46.3(21.6) CBT group post-treatment: Mean(SD)= 26.0(21.0) p = Non-Significant	In a short period, both CBT and Aromatherapy massage (AM) may be beneficial for anxiety but CBT showed a long term advantage on depression and emotional distress.
				POMS (Tension-Anxiety) NR	CBT group Baseline: Mean(SD)= 12.3(5.8) CBT group post-treatment: Mean(SD)= 7.9(5.3) p = Non-Significant	

HSCT: Hematopoietic stem-cell transplantation, T-CBT: Telephone-base Cognitive-Behavioral therapy, CBT: Cognitive Behavioral Therapy, TAU: Treatment as usual, AM: Aromatherapy massage, TMS: Total Mood Score.

Table 6.G.3: Characteristics of Included Randomized Control Trials PTSD-Psychosocial, CBT Intervention

Author, Year Country (Intervention)	Disease Site/Stage Treatment Stage	Screened (n) Analyzed (n) Intervention IPT	Population Assessment tool Interview vs. Self-report	Outcome Measure Harms, Adverse events, or Side effect	Effect size expressed as Odds Ratios (95% confidence interval) P-value	Summary Result
Capezzani,2013[29] Italy (CBT)	Any type Follow-up phase & Active treatment phase NR	31 21 EMDR in Follow-up patients vs CBT in Follow-up patients vs EMDR in Active treatment patients 8 weeks	DSM-IV diagnostic criteria for PTSD DSM-IV(PTSD) Interview	CAPS Criterion B NR	CBT group Baseline: Mean (SD)=20.90(7.71) CBT group Post-treatment: Mean (SD)=15.30(5.87) P value* %	Cancer patients who suffered from PTSD and intrusive symptoms could benefit more from EMDR than CBT intervention.
				CAPS Criterion C NR	CBT group Baseline: Mean (SD)=30.30(8.13) CBT group Post-treatment: Mean (SD)=20.50(7.59) P value*	
				CAPS Criterion D NR	CBT group Baseline: Mean (SD)=27.60(6.22) CBT group Post-treatment: Mean (SD)=16.20(9.16) P value*	

Author, Year Country (Intervention)	Disease Site/Stage Treatment Stage	Screened (n) Analyzed (n) Intervention IPT	Population Assessment tool Interview vs. Self-report	Outcome Measure Harms, Adverse events, or Side effect	Effect size expressed as Odds Ratios (95% confidence interval) P-value	Summary Result
Kangas,2013[31] Australia (CBT)	Head & Neck Cancer Any Stage To be recommended to receive primary or adjuvant radiotherapy	460 35 CBT vs SC 6 weeks	Meeting two of three symptom clusters of cancer-related PTSD, assessed by: 1. The Clinician Administered PTSD Scale, and/or 2. sub-clinical or clinical levels of MDD symptoms (scoring a minimum of 14 on the BDI-II) and/or 3. meeting full criteria for MDD as assessed by the SCID-DSM-IV, Depression module, or 4. sub-clinical or clinical levels of general anxiety (scoring a minimum T-score of 60 on the STAI-S) 5. and/or meeting full criteria for a current anxiety disorder as assessed by the SCID-DSM-IV, Anxiety module Clinician Administered PTSD Scale, BDI-II, SCID-DSM-IV, STAI-State, SCID-DSM-IV Interview	PCL-S (Stress) NR	CBT group Baseline: Adjusted mean(SE)= 33.09(1.91) 95%CI = 29.35 to 36.82 CBT treatment effect size(d) = NA Between condition ES:NA Main time effect (significance**) (F=4.18, P<0.001) HLM(hierarchical linear model) Group ×Time interaction (F=1.08, P=0.358) CBT group post-treatment: Adjusted mean(SE)=29.00(1.94) 95%CI = 25.20 to 32.81 CBT group treatment effect size(d) = 0.47 Between condition ES: d=-0.18, Main time effect (significance**)= (T1-T2: T= -2.65;p= 0.008)	Both CBT and SC interventions were effective and improve PTSD, depressive and general anxiety symptoms. The results demonstrate the utility of administering briefer CBT interventions early in the course of patients' cancer treatments for individuals at risk of experiencing more prolonged psychosocial problems.

Author, Year Country (Intervention)	Disease Site/Stage Treatment Stage	Screened (n) Analyzed (n) Intervention IPT	Population Assessment tool Interview vs. Self-report	Outcome Measure Harms, Adverse events, or Side effect	Effect size expressed as Odds Ratios (95% confidence interval) P-value	Summary Result
Kangas,2013[31] Australia (SC)	Head & Neck Cancer Any Stage To be recommended to receive primary or adjuvant radiotherapy	460 35 CBT vs SC 6 weeks	Meeting two of three symptom clusters of cancer-related PTSD, assessed by: 1. The Clinician Administered PTSD Scale, and/or 2. sub-clinical or clinical levels of MDD symptoms (scoring a minimum of 14 on the BDI-II) and/or 3. meeting full criteria for MDD as assessed by the SCID-DSM-IV, Depression module, or 4. sub-clinical or clinical levels of general anxiety (scoring a minimum T-score of 60 on the STAI-S) 5. and/or meeting full criteria for a current anxiety disorder as assessed by the SCID-DSM-IV, Anxiety module Clinician Administered PTSD Scale, BDI-II, SCID-DSM-IV, STAI-State, SCID-DSM-IV Interview	PCL-S (Stress) NR	SC group Baseline: Adjusted mean(SE) =30.58(2.36) 95% CI = 25.96 to 35.21 SC treatment effect size (d)= NA Between condition ES:NA Main time effect (significance**) (F=4.18, P<0.001) HLM(hierarchical linear model) Group ×Time interaction (F=1.08, P=0.358) SC group post-treatment: Adjusted mean(SE) = 27.40(2.38) 95% CI = 22.73 to 32.07 SC treatment group effect size(d)= 0.36 Between condition ES = -0.18, Main time effect (significance**)= (T1-T2: T= -2.65;p= 0.008)	Both CBT and SC interventions were effective and improve PTSD, depressive and general anxiety symptoms. The results demonstrate the utility of administering briefer CBT interventions early in the course of patients' cancer treatments for individuals at risk of experiencing more prolonged psychosocial problems.

Author, Year Country (Intervention)	Disease Site/Stage Treatment Stage	Screened (n) Analyzed (n) Intervention IPT	Population Assessment tool Interview vs. Self-report	Outcome Measure Harms, Adverse events, or Side effect	Effect size expressed as Odds Ratios (95% confidence interval) P-value	Summary Result
Capezzani,2013[29] Italy (EMDR)	Any type Follow-up phase & Active treatment phase NR	31 21 EMDR in Follow-up patients vs CBT in Follow-up patients vs EMDR in Active treatment patients 8 weeks	DSM-IV diagnostic criteria for PTSD DSM-IV(PTSD) Interview	CAPS Criterion B NR	CBT group Baseline: Mean (SD)=19.55(8.15) CBT group Post-treatment: Mean (SD)=6.18(6.95) P value* %	Cancer patients who suffered from PTSD and intrusive symptoms could benefit from EMDR than CBT intervention.
				CAPS Criterion C NR	CBT group Baseline: Mean (SD)=28.36(12.19) CBT group Post-treatment: Mean (SD)=10.45(7.54) P value*	
				CAPS Criterion D NR	CBT group Baseline: Mean (SD)=24.00(8.15) CBT group Post-treatment: Mean (SD)=9.91(5.61) P value*	
Carpenter,2014[55] USA	Breast Cancer Stage 0-III	210 132	Moderate distress: Distress Thermometer scored at least 5 out of 10, or 4-item Perceived Stress	IES NR	Baseline Intervention group: Mean(SE)= 2.5(0.2)	An empirically supported cognitive behavioral stress management

Author, Year Country (Intervention)	Disease Site/Stage Treatment Stage	Screened (n) Analyzed (n) Intervention IPT	Population Assessment tool Interview vs. Self-report	Outcome Measure Harms, Adverse events, or Side effect	Effect size expressed as Odds Ratios (95% confidence interval) P-value	Summary Result
(Online stress management workbook)	Radiation/ chemo-therapy/ surgery	Online stress manage-ment workbook vs waitlist 10 weeks	Scale 6 out of 16 or 5-item brief adjective checklist 7 out of 20 Distress Thermometer, 4-item Perceived Stress Scale, 5-item brief adjective checklist similar to the Profile of Mood States Interview		Condition × time F(1,101)= 10.4 P=0.002 Partial n2= 0.093	intervention could help and improve the breast cancer patient's confidence and enhance their ability to cope with stress.

CBT: Cognitive Behavioral Therapy, SC: Non-directive supportive counseling, BDI: Beck Depression Inventory, PCL-S: Posttraumatic Checklist, Stress-specific version, ** :only significant interaction and main effect reported ($p<0.05$) ,T1: Baseline, T2: Post-treatment, IES: Impact of Event scale, EMDR: eye movement desensitization and reprocessing, * = Significant pre-post effect, independent of the type of treatment (CBT or EMDR), % :Significant group (CBT vs EMDR)-by-time (pre-treatment vs post-treatment) interaction effects, CAPS: Clinical Administered PTSD Scale.

Table 6.G.4: Characteristics of Included Randomized Control Trials Anxiety-Psychosocial Intervention

Author, Year Country (Intervention)	Disease Site/Stage Treatment Stage	Screened (n) Analyzed (n) Intervention IPT	Population Assessment tool Interview vs. Self-report	Outcome Measure Harms, Adverse events, or Side effect	Effect size expressed as Odds Ratios (95% confidence interval) P-value	Summary Result
Goerling,2011 [53] Germany (High Risk Group + intervention)	Any type Any Stage NR	146 131 HR + psycho-oncological support vs HR – psycho-oncological support (control) vs LR + psycho-oncological support vs LR – psycho-oncological support (control) The number of the sessions is varied according to	Adult Patients with malignant tumor. The participants were (t0) presented the Hospital Anxiety and Depression Scale (HADS), a survey for adults with somatic illnesses to self-assess anxiety (A) and depression (D) levels. Patients were classified into either the high-risk group (A + D ≥ 12) or the low-risk group (A + D < 12) HADS-A (Anxiety) self-assessment HADS-D (Depression) self-assessment	HADS (Anxiety) NR	HR + intervention group Baseline: Arithmetic means(SD) =10.67(2.86) (t0-t1)P= 0.001, η2 = 0.442 HR + intervention group post-treatment: Arithmetic means(SD) =7.04(3.68)	Improved score for depression only observable in the high-risk group with psychological intervention. In the high risk group with intervention the anxiety rates were reduced significantly during inpatient treatment. Cancer patients on a surgical ward benefit from psycho-oncological support especially at an early stage of therapy but also over a long time after discharge from the hospital.

Author, Year Country (Intervention)	Disease Site/Stage Treatment Stage	Screened (n) Analyzed (n) Intervention IPT	Population Assessment tool Interview vs. Self-report	Outcome Measure Harms, Adverse events, or Side effect	Effect size expressed as Odds Ratios (95% confidence interval) P-value	Summary Result
		the length of the inpatient care				
Goerling,2011[53] Germany (Low Risk Group + intervention)	Any type Any Stage NR	146 131 HR + psycho-oncological support vs HR – psycho-oncological support (control) vs LR + psycho-oncological support vs LR – psycho-oncological support (control) The number of the sessions is varied	Adult Patients with malignant tumor. The participants were (t0) presented the Hospital Anxiety and Depression Scale (HADS), a survey for adults with somatic illnesses to self-assess anxiety (A) and depression (D) levels. Patients were classified into either the high-risk group (A + D ≥ 12) or the low-risk group (A + D < 12) HADS-A (Anxiety) self-assessment HADS-D (Depression) self-assessment	HADS (Anxiety) NR	LR + intervention group Baseline: Arithmetic means(SD)= 3.53(2.10) (t0-t1)P= 0.764, η2 = 0.007 LR + intervention group post-treatment: Arithmetic means(SD) =3.40(2.38)	Improved score for depression only observable in the high-risk group with psychological intervention. In the high risk group with intervention the anxiety rates were reduced significantly during inpatient treatment. Cancer patients on a surgical ward benefit from psycho-oncological support especially at an early stage of therapy but also over a long time after discharge from the hospital.

Author, Year Country (Intervention)	Disease Site/Stage Treatment Stage	Screened (n) Analyzed (n) Intervention IPT	Population Assessment tool Interview vs. Self-report	Outcome Measure Harms, Adverse events, or Side effect	Effect size expressed as Odds Ratios (95% confidence interval) P-value	Summary Result
		according to the length of the inpatient care				

HR: High Risk, LR: Low Risk, T0: Baseline, T1: Post-treatment, CBT: Cognitive Behavioral Therapy, SC: Non-directive supportive counseling PCL-S: Posttraumatic Checklist— Stress-specific version, **: only significant interaction and main effect reported ($p<0.05$), T1: Baseline, T2: Post-treatment.

Table 6.G.5: Characteristics of Included Randomized Control Trials Anxiety-CBT Intervention

Author, Year Country (Intervention)	Disease Site/Stage Treatment Stage	Screened (n) Analyzed (n) Intervention IPT	Population Assessment tool Interview vs. Self-report	Outcome Measure Harms, Adverse events, or Side effect	Effect size expressed as Odds Ratios (95% confidence interval) P-value	Summary Result
Greer,2012[32] USA (CBT)	Any Type Terminal, Incurable Chemo-therapy Radiation Ambu-latory palliative care	123 40 CBT vs Waitlist 2 mo	Anxiety symptoms: HAM-A score ≥14 HAM-A ≥14 Interview	HAM-A (Anxiety) NR	Adjusted MD(SE) = -5.41(2.61) Effect size (Cohen's d)=0.80 95%CI= -10.78 to -0.04, P = 0.05 HAM-A score on average between-group MD= -5.97, SE= 2.73, 95%CI= -11.40 to -0.18, p=0.04	CBT reduces anxiety symptoms in home care patients with advanced cancer receiving palliative care. Providing brief CBT tailored to the concerns of patients with terminal cancer was not only feasible but also led to significant improvements in anxiety.
				CGI (Anxiety) NR	Adjusted MD(SE)= -0.97(0.41) Effect size (Cohen's d)=0094 95%CI= -1.81 to -0.14, p=0.02 CGI vs control group rating from baseline to post-treatment assessment: between-group MD= -1.00, SE= 0.40, 95%CI= -1.83 to -0.17, p=0.02	
				HADS (Anxiety) NR	Adjusted MD(SE)= -1.78(0.80) Effect size (Cohen's d)=0.84 95%CI= -3.44 to -0.12, p=0.04	
Kangas,2013[31] Australia	Head & Neck Cancer	460 35	Meeting two of three symptom clusters of cancer-related	PCL-S (Stress) NR	CBT group Baseline: Adjusted mean(SE)=33.09(1.91) 95%CI = 29.35 to 36.82 CBT treatment effect size(d) =	Both interventions were found to be equal in their effects in reducing PTSD, depressive and

Author, Year Country (Intervention)	Disease Site/Stage Treatment Stage	Screened (n) Analyzed (n) Intervention IPT	Population Assessment tool Interview vs. Self-report	Outcome Measure Harms, Adverse events, or Side effect	Effect size expressed as Odds Ratios (95% confidence interval) P-value	Summary Result
(CBT)	Any Stage To be recom-mended to receive primary or adjuvant radio-therapy	CBT vs SC 6 weeks	PTSD, assessed by: 1. The Clinician Administered PTSD Scale, and/or 2. sub-clinical or clinical levels of MDD symptoms (scoring a minimum of 14 on the BDI-II) and/or 3. meeting full criteria for MDD as assessed by the SCID-DSM-IV, Depression module, or 4. sub-clinical or clinical levels of general anxiety (scoring a minimum T-score of 60 on the STAI-S) 5. and/or meeting full criteria for a current anxiety		NA Between condition ES = NA Main time effect (significance**) (F=4.18, P<0.001) HLM(hierarchical linear model) Group ×Time interaction (F=1.08, P=0.358) CBT group post-treatment: Adjusted mean(SE)=29.00(1.94) 95%CI = 25.20 to 32.81 CBT treatment effect size(d) = 0.47 Between condition ES: d=-0.18 Main time effect (significance**)= (T1-T2: T= -2.65;p= 0.008)	general anxiety symptoms. The results demonstrate the utility of administering briefer CBT interventions, early in the course of patients' cancer treatments for persons at risk of experiencing more prolonged psychological problems.
				STAI-State (Anxiety) NR	CBT group Baseline: Adjusted mean(SE)=40.86(1.97) 95%CI = 37.00 to 44.72 CBT treatment effect size(d) = NA Between condition ES = NA Main time effect (significance**) (F=3.90, P<0.001)	

Author, Year Country (Intervention)	Disease Site/Stage Treatment Stage	Screened (n) Analyzed (n) Intervention IPT	Population Assessment tool Interview vs. Self-report	Outcome Measure Harms, Adverse events, or Side effect	Effect size expressed as Odds Ratios (95% confidence interval) P-value	Summary Result
			disorder as assessed by the SCID-DSM-IV, Anxiety module Clinician Administered PTSD Scale Interview BDI-II: Min 14 (Depression) Interview SCID-DSM-IV (Depression) Interview STAI-State: Min T- score 60 (Anxiety) Interview SCID-DSM-IV (Anxiety) Interview		HLM(hierarchical linear model) Group ×Time interaction (F=1.38, P=0.248) CBT group post-treatment: Adjusted Mean (SE)=37.76 (2.03) 95% CI = 33.77 to 41.74 CBT treatment effect size(d)= 0.34 Between condition ES: D= -0.40, (T1-T2: T=-2.53; p=0.012)	

PCL-S: Posttraumatic Checklist— Stress-specific version, PTSD: Post Traumatic Stress Disorder, MDD: Major Depressive Disorder, BDI-II: Beck Depression Inventory - Second edition, STAI-S: State Trait Anxiety Inventory -State subscale, **: only significant interaction and main effect reported ($p<0.05$), T1: Baseline, T2: Post-treatment, Min: Minimum.

Table 6.G.6: Characteristics of Included Randomized Control Trials – Fear Recurrence-Psychosocial and CBT Intervention

Author, Year Country (Intervention)	Disease Site/Stage Treatment Stage	Screened (n) Analyzed (n) Intervention IPT	Population Assessment tool Interview vs. Self-report	Outcome Measure Harms, Adverse events, or Side effect	Effect size expressed as Odds Ratios (95% confidence interval) P-value	Summary Result
Herschbach,2010[34] Germany (SET)	Any Cancer Any Type Surgery, Radio-therapy, Chemo-therapy	457 265 CBT vs SET vs TAU 2 weeks	FoP-Q-short form (SF) total score above a critical cut-off point indicating high levels of FoP. The cut-off score was based on an investigation conducted specifically this purpose with comparable sample of cancer patients in the same clinics who completed the FoP-Q-SF FoP-Q-short Form Interview	FoP-Q total score NR	SET Baseline: Mean(SD)= 11.02(2.41) SET post-treatment: Mean(SD)=10.30(2.55) Effect Size=0.56 P value Group=0.244 P value Time= 0.000 P value G×T= 0.591 SET vs control group: MD = 1.46, p<0.01 SET baseline vs post-treatment t-test: SET Group: MD= 0.72, p≤0.001 Control group: MD= 0.50, p≤0.01	Fear of progression can be reduced with short psychotherapeutic interventions both CBT and SET over 12 months. FoP was significantly lower in the SET group compared with the control group.
Herschbach,2010[34] Germany (CBT)	Any Cancer Any Type Surgery, Radiotherapy,	457 265 CBT vs SET vs TAU	FoP-Q-short form (SF) total score above a critical cut-off point indicating high levels of FoP. The cut-off score was based on an	FoP-Q total score NR	CBT Baseline: Mean(SD)= 11.49(2.45) CBT post-treatment: Mean(SD)=11.04(2.63)	Fear of progression can be reduced with short psychotherapeutic interventions both CBT and SET over 12

Author, Year Country (Intervention)	Disease Site/Stage Treatment Stage	Screened (n) Analyzed (n) Intervention IPT	Population Assessment tool Interview vs. Self-report	Outcome Measure Harms, Adverse events, or Side effect	Effect size expressed as Odds Ratios (95% confidence interval) P-value	Summary Result
	Chemotherapy	2 weeks	investigation conducted specifically this purpose with comparable sample of cancer patients in the same clinics who completed the FoP-Q-SF FoP-Q-short Form Interview		Effect Size=0.61 P value Group=NR P value Time= NR P value G×T= NR CBT vs control group: MD =1.12, p<0.05 CBT baseline vs post-treatment t-test: CBT Group: MD= 0.46, p≤0.05 Control group: MD= 0.50, p≤0.01	months. FoP was significantly lower in the CBT group compared with the control group.

CBT: Cognitive Behavioral Therapy, SET: Supportive-Expressive Therapy, FoP: Fear of Progression, TAU: Treatment as usual, Baseline: Before Initial Therapy, Post-treatment: Shortly before discharge.

6.H Assessment Tools

Table 6.H.1: Assessment Tools on Anxiety, Distress and Depression

Selected Tools for Depression and Anxiety	
Tool	**Domains or Factors**
ADIS-IV (Anxiety Disorders Interview Schedules)	Based on diagnostic criteria of the DSM-IV and designed for all anxiety and mood disorders and substance abuse screening and psychotic disorder [66]. Clinical rating from 0 to 8 to indicate the degree of distress and impairment associated with the disorder[165]. 0-8 clinical severity rating (CSR), disorder receiving CSR of 4 or higher is qualified as "official" DSM-IV diagnosis[166].
BDI(Beck Depression Inventory)	Widely used. 21 items. Behavioral, cognitive and somatic components of depression; focuses on negative attitudes of the patient toward self. Short-form 13 items [12]. Minimal: <14, mild: 14-19, moderate: 20-28, severe: >29. Cut-off scores: 18; 22[18].
BSI (Brief Symptom Inventory)	BSI measures the experience of symptoms in the past 7 days. 53-item self-report scale measures 9 primary symptom dimensions (somatization, obsessive-compulsive behavior, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism). 5-point rating scale, 0 = not at all, 4 = extreme [12]. Cut-off T-score = 65[167].
CAPS (Clinician Administered PTSD Scale)	30-item structured interview providing a categorical diagnosis and measure of severity of PTSD symptoms. 5-point scoring scale, 0 = Absent, 1 = Mild/sub threshold, 2 = Moderate/threshold, 3 = Severe, 4 = Extreme. Cut-off score: 2[168].
CES-D (Center for Epidemiological Studies Depression Scale)	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 behaviors during the past week (frequency of depressive symptoms). Four factors: negative affect and mood, positive mood or well-being, somatic, interpersonal [12]. Scoring ranges from 0 to 20. Cut-off score: 16[18].
CGI- S (Clinical Global Impression- Severity Scale)	7-point scale requires clinician to rate the severity of the patient's illness at the time of assessment. Patient is assessed on severity of mental illness at the time of rating. Clinicians answer one question "how mentally ill is the patient at this time" which the response is answered on the following: 1 = normal, not at all ill; 2 = borderline mentally ill; 3 = mildly ill; 4 = moderately ill; 5 = markedly ill; 6 = severely ill; 7 = among the most extremely ill patients [169]. CGI-S optimal cut-off≥3[170].
DSM-IV (Diagnostic and Statistical Manual of Mental Disorders)	Psychiatric Diagnosis manual for children and adults that are categorized by five dimensions; Clinical Syndromes, Developmental Disorders and Personality Disorders, Physical Conditions, Severity of Psychosocial Stressors, and Highest Level of Functioning. Scoring of disorder: mild, moderate, or severe[139].
DT (Distress Thermometer)	Single item. Identifies distress coming from any source, even if unrelated to cancer. 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. [12]. Cut-off score: 4[171].

Selected Tools for Depression and Anxiety	
FoP-Q SF (Fear of Progression Questionnaire Short Form)	43-item questionnaire relating to 5 dimensions: affective reactions, partnership/family, occupation, loss of autonomy and coping with anxiety. The short form (12-item questionnaire) comprises items pertaining to 4 of the 5 dimensions (excluding coping)[172]. Rated on a 5-point scale ranging from never to very often. To date there is no valid cut-off point for FoP-Q[173].
GSI (Global Severity Index)	90-item inventory that assess the best indicator of current level of psychosocial stress on a 5-point scale. 0 = not at all; 4 = extremely[23]. Cut-off T-Score of 63[167].
HADS (Hospital Anxiety and Depression Scale)	14 items self-screen to rate severity of depression and anxiety (two separate dimensions). Excludes questions about physical symptoms[12]. Normal: 0-7, mild: 8-10, moderate: 11-14, severe: 15-21. Cut-off score: 7[18].
HAM-A (Hospital Anxiety and Depression Scale – Anxiety)	14 items. Designed to assess the severity of a patient's anxiety. Each of the items contains a number of symptoms and each group of symptoms is rated on a scale of zero to four (most severe)[174]. Cut-off score: 7[18].
HANDS (Harvard National Depression Screening)	10-item measure assessing core symptoms of major depression. Score range of 0-30 with a cut-off point of 9 or greater[66].
HRSD/HAM-D (Hamilton Rating Scale for Depression)	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[12]. 17-item score, mild: 7-17, moderate: 18-27, and severe: >25. Cut-off score: 10[18].
IES (Impact of Events Scale)	15-item questionnaire used to evaluate the degree of impact experienced in response to a specific stressful event. Response were made on a 4-point scale from *not at* all too *often true* (1,3,and 5)[175]. The cut-off score ≥ 35 is the best one for a probable diagnosis of PTSD[176].
MADRS (Montgomery-Asberg Depression Rating Scale)	10-item questionnaire used to measure severity of depression. Nine of the 10 items are based on patient's report and one item (apparent sadness) is based on external observation of the patient. MADRS are rated on a 0-6 scale (0=no abnormality, 6=severe)[65].A score greater than 30 or 35 on the MADRS indicates severe depression, while a score of 10 or below indicates remission[177].
MINI (Mini-international Neuropsychiatric Interview)	Short structured clinical interview which enables researchers to make diagnoses of psychiatric disorders according to DSM-IV or ICD-10[65]. For depressive disorders, the MINI showed a sensitivity and specificity of 92%, Kappa 0.77, positive predictive value (PPV) 74%, negative predictive value (NPV) 98% and accuracy of 92%[178].
PHQ-9 (Patient Health Questionnaire for Depression)	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 DSMIV. Patient responses are scored by the primary care clinician or office staff[12]. Mild: >5, moderate: >10, moderately severe: >15, severe: >20. Cut-off score: 8[18].
POMS (Profile of Mood States)	37 items. Measures cancer patient's mood. Patients answer in a 5-point Likert scale[33] (*not at all* to *extremely*[179]) pertaining to six subscales: tension-anxiety, depression-dejection, anger hostility, vigour-activity, fatigue-inertia, and confusion-bewilderment[12]. Internal consistency estimates (Cronbach's alpha) range between .76 and .95 for the subscales in POMS-SF and between .63 and .96 for the subscales in POMS. For the total score, the range is between .87 and .92 for POMS-SF and between .75 and .92 for POMS[180, 181].

Selected Tools for Depression and Anxiety	
SCID-DSM-IV (Structured Clinical Interview for DSM Disorders)	An instrument assessing 33 of the more frequently diagnosed Axis I DSM-IV disorders. The interviewer starts by asking closed ended question followed by more elaborate open ended question and gives a score of 1-3 or ?. 1 indicates a symptom described in the criterion is clearly absent or criterion statement is false; 2 indicates a sub-threshold condition that almost meets the threshold for the criterion; 3 the threshold for the criterion is just met or more than met or the criterion statement is true; ? indicates there is inadequate information to code the criterion as either 1,2, or 3[182]. SCID-DSM-IV is a general format of diagnostic criteria assessment tool for several type of psychological disorder. The cut-off score is varies from disease to disease[183].
SCL (Symptoms Checklist Revised)	90-item inventory that assesses nine symptom dimensions and provides a summary score[23]. Self-rating inventory with 9 clinical scales for somatization, interpersonal sensitiveness, obsessive-compulsiveness, hostility, phobic anxiety, paranoid ideation, depression, anxiety and psychoticism. The total scores are considered to be measures of overall psychological symptoms[184]. Patients are asked to rate the severity of their experiences on a 5-point scale ranging from 0= 'not at all' to 4= 'extremely'[185]. Optimal cut-off point=0.9[186].
STAI (Spielberger State Trait Anxiety Inventory)	Two 20-item scales (20 state items = how respondents feel "right now, at this moment"; 20 trait items = how respondents feel "generally"). Indicator of state and trait anxiety and measures overall level of anxiety; helps distinguish anxiety from depression[12]. Scoring is done on a 4-point scale; 1= almost never, 2= sometimes, 3= often, 4: almost always[187]. The optimal cut-off score is 55/54[188]. A cut point of 39–40 has been suggested to detect clinically significant symptoms for the S-Anxiety scale; however, other studies have suggested a higher cut score of 54–55 for older adults[189].
TQSS (Two Question Screening Survey)	Tool to screen for depression in cancer patients with high sensitivity and positive predictive value but with a somewhat limited specificity. Composed of 2 questions: 1. Have you been bothered by little interest or pleasure in doing things? 2. Have you been feeling down, depressed, or hopeless in the last month Each of the items (depressed mood and anhedonia) in the survey has five possible responses that were assigned values of 0 to 4 as follows: 0, not at all; 1, a little bit; 2, somewhat; 3, quite a bit; and 4, very much[60]. [190]. Cut-off score:≥2[191].

6.1 Screening Forms for Title and Abstract, Full Text, Data Extraction, and Quality Assessments

6.1.1 Titles and Abstract - Level 1 Clinical Practice Guidelines

Psychosocial Distress Guideline T&A screening level 1 & 2

1. **Is this report in English?**

- ○ No (stop)

Clear Response

2. **What type of paper is this?**

- ○ Systematic Review
- ◉ Guideline
- ○ RCT
- ○ Neither (Observational, Editorials, commentaries, etc)
- ○ It is not relevant (from title)
- ○ It is not relevant (from title and abstract)

Clear Response

5. **Is this a guideline focused on "treatment" on adult (18 and over) cancer population with ""Anxiety/Stress /Psychosocial distress/Depression"?**

- ○ Yes/cant tell (stop)
- ○ No (exclude)

Clear Response

6. **Note on Guideline**:

Submit Form and go to or Skip to Next

6.I.2 Titles and Abstract - Level 1 RCT

Psychosocial Distress Guideline T&A screening level 1 & 2

1. **Is this report in English?**

- ○ No (stop)

Clear Response

2. **What type of paper is this?**

- ○ Systematic Review
- ○ Guideline
- ◉ RCT
- ○ Neither (Observational, Editorials, commentaries, etc)
- ○ It is not relevant (from title)
- ○ It is not relevant (from title and abstract)

Clear Response

7. **Is this an RCT/CCT focused on "treatment" on adult (18 and over) cancer population with ""Anxiety/Stress /Psychosocial distress/Depression"" ?**

- ○ yes/cant tell
- ○ No (exclude)

Clear Response

8. **Note on RCT**

Submit Form and go to or Skip to Next

6.1.3 Titles and Abstract - Level 1 Systematic Review

Psychosocial Distress Guideline T&A screening level 1 & 2

1. **Is this report in English?**

   ○ No (stop)
   Clear Response

2. **What type of paper is this?**

   ◉ Systematic Review
   ○ Guideline
   ○ RCT
   ○ Neither (Observational, Editorials, commentaries, etc)
   ○ It is not relevant (from title)
   ○ It is not relevant (from title and abstract)
   Clear Response

3. **Is this a systematic review focused on "treatment" on adult (18 and over) cancer population with "Anxiety/Stress /Psychosocial distress/Depression" ?**

   ○ Yes/cant tell (stop)
   ○ No (exclude)
   Clear Response

4. **Note on SR:**

Submit Form and go to or Skip to Next

6.I.4 Full Text – Level 3

Psychosocial Distress Guideline full Text screening level 3

1. **Link:**

2. **Is the attached article match to the title and abstract of this citation?**

- yes(contiue)
- No (stop and send a note to Homa by email please)

Clear Response

3. **what type of study is this citation?**

- SR (continu)
- Guideline (continu)
- RCT (continu)
- narrative review (stop)
- other (specify) and (stop)

Clear Response

4. **Does this article focus on adults (18 years and older) population with cancer who diagnosed with Anexiet/Stress/Distress/ depression/fear recurrent/PTSD (post traumatic stress disorder)?**
(patients with cancer and anxiety/Stress/Psychosocial distress/ depression)

- Yes
- No (exclude)(stop)

Clear Response

5. **Does this article focus on "treatment" and/or "management" of Anexiet/Stress/Distress/ depression/fear recurrent/PTSD (post traumatic stress disorder) in patients with cancer?**

- Yes
- No (exclude)(stop)

Clear Response

6. **Does this article focus on pharmacological treatment?**

- Yes (specify)
- No

Clear Response

7. **Does this article focus on non-pharmacological treatment? (including: psychosocial interventions, exercise, psycho-education, cognitive-behavioural therapy, self-management, exercise/activity)**

- yes (specify)
- No

Clear Response

8. **Does this article focus on alternative treatment?: (specify any alternative treatment component (e.g. Chinese traditional medicine) and/or complementary (e.g. acupuncture))**

- yes (specify)
- no

Clear Response

9. **note:** (specify any alternative treatment component(e.g. Chinese traditional medicine) and/or complementary (e.g. acupuncture))

10. **screener's Note:**

11. **This citaton was excided because of the following Reason:**

- conference abstract
- protocol
- other reason
- full text not available
- chapter in a book

Clear Response

Submit Form and go to or Skip to Next

6.I.5 Data Extraction – Level 4 Clinical Practice Guidelines

1. **Note on this guideline if it is not eligible**

   ○ exclude (reason)

   Clear Response

2. **What organization is responsible for this guideline?**

3. **What country applied this guideline?**

4. **What is the scope & purpose of this guideline/recommendation?** (List all that apply)

   - ☐ Treatment
   - ☐ Diagnosis
   - ☐ Prognosis
   - ☐ Others (specify)

5. **Intended users (check all that apply)**

   - ☐ Primary care physicians (e.g. General practitioners)
   - ☐ Mental health specialist (psychiatrists)
   - ☐ Allied mental health professionals (social workers, mental health nurses, occupational therapists)
   - ☐ Patients
   - ☐ Other (specify)

6. **What is the setting for use of this guideline?** (check all that apply)

   - ☐ Primary care
   - ☐ Oncology outpatient setting
   - ☐ Hospital/ inpatient setting
   - ☐ Other (specify)

7. **What is the target population of this guideline?** (specify as in the guideline)

8. **Does this guideline have a specific recommendation (course of action) for patients who has "Cancer-related distress, stress, anxiety, fear recurrence, PTSD and/or Depression"??**

- ○ Yes
- ○ No
- ○ Not sure

Clear Response

9. **What is the definition of AND method of establishing "Cancer-related distress, stress, anxiety, fear recurrence, PTSD and/or Depression"?** (specify)

10. **Specify the type of pharmacological intervention** (please type in the exact wording)

- ☐ 1
- ☐ 2
- ☐ 3
- ☐ 4

11. **Specify the type of non-pharmacological intervention** (please type in the exact wording)

- ☐ 1
- ☐ 2
- ☐ 3
- ☐ 4

Recommendation #1

12. **Specify Recommendation #1 for populations who has cancer-related fatigue.** (Please type in the exact wording)

13. **Does the recommendation identify or stratify actions or suggestions based on the specific TYPE of intervention?**

- ☐ NO: they do NOT specify
- ☐ YES: they specify the type of intervention

14. **Please specify the type of intervention:**

- ☐ 1-
- ☐ 2-
- ☐ 3-
- ☐ 4-

15. **What type of system was used to grade or evaluate the strength of evidence (i.e. GRADE, or some association specific system)?**

16. **Grading of the recommendation #1:** (i.e. strong recommendation)

17. **Rating of quality of evidence for Recommendation #1 :** (i.e. evidence at high risk of bias, or level I (indicating RCT design))

18. **For the evidence that is cited to support the recommendation, please list the number and type of studies included:** (i.e. 4 RCTs, and 2 observational studies)

19. **What evaluation instrument/tool was used for this Recommendation?**

20. **What is the Grade/Class/Strength of this Recommendation?**

21. **What is the Rating of the quality of the evidence for this Recommendation? (e.g. level1, etc)**

22. **The level of evidence/type of evidence of this Recommendation is based on:**

23. **What type of recommendations are made within this guideline (list all that apply)**

6.I.6 Data Extraction – Level 4 RCT

STUDY CHARACTRISTICS

1. **Country/ies in which study was coducted:**

2. Funding Sources:

3. **Trial ID #**

4. **This RCT focused on the following condition/s:**

- ☐ Anxiety
- ☐ Distress
- ☐ Stress
- ☐ Depression

Population charactristics:

5. **What is the target population in this study? (copy and paste)**
   please provide the definition of population in this trials,if the population of interest is not patient with cancer and diagosed as anxiety, stress, distress, or depression stop and send and email to Homa withthe refid in subject.

6. **what is the definition of condition? (copy & paste)**

- ☐ anxiety
- ☐ stress
- ☐ distress
- ☐ depression

7. **Age of participants:**

- [ ] Adults 18 and over
- [ ] Mean
- [ ] Median
- [ ] SD
- [ ] Minimum
- [ ] Maximum
- [ ] Others(specify)
- [ ] Not Reported

8. **Racial category**

- [ ] Ethnicity_ White %
- [ ] Ethnicity_ Black %
- [ ] Ethnicity_ Asian %
- [ ] Ethnicity_ Other %
- [ ] Not reported

9. **Gender**

- ( ) Male
- ( ) Female
- ( ) Both male & Female
- ( ) Not Reported

Clear Response

10. **% Male**

METHODOLOGY

11. **Cancer site:**

- [ ] 1,
- [ ] 2,
- [ ] 3,

- [ ] All type
- [ ] 4,
- [ ] 5,
- [ ] 6,
- [ ] 7,

12. **Cancer stage:**

- [ ] 1
- [ ] 2
- [ ] 3

13. **Study design**

- ( ) Double blind placebo control
- ( ) Open lable
- ( ) Cross-over double blind placebo control
- ( ) Paralled double blind placebo controlled
- ( ) Single blind
- ( ) parallel trial
- ( ) cross-over trial
- ( ) factorial trial
- ( ) N-of-1 trial
- ( ) cluster trial
- ( ) Other (specified)

Clear Response

14. **Recruitment period: (range-years)**

- [ ] From
- [ ] To
- [ ] duration (months)
- [ ] duration (week)
- [ ] duration (year)

15. **Setting:**

- ( ) Hospital
- ( ) Oncology clinic
- ( ) Outpatient clinic
- ( ) Palliative Care
- ( ) other (specify

Clear Response

16. **Single or multi-center**

- [ ] Single
- [ ] Multi-center(specify)
- [ ] Not Reported
- [ ] # of centers

17. **Duration of treatment** (check one only)

- ( ) Days
- ( ) weeks
- ( ) months
- ( ) years
- ( ) Not Reported

Clear Response

18. **Frequency of treatment** (check 1 only)

- ( ) Time per day
- ( ) Time per week
- ( ) time per month
- ( ) Not reported

Clear Response

19. **Duration of the individual treatment unit** (check 1 only)

- ( ) Weeks
- ( ) Months
- ( ) years
- ( ) Not reported

Clear Response

20. **Lengh of follow up from Randomization:**(specify D,w, M, or Y)

- [ ] Minimum
- [ ] Maximum
- [ ] Median
- [ ] Mean
- [ ] others (specify)

21. **# of Treatment groups/Arm:**

- [ ] Treatment
- [ ] Control

22. **Inclusion criteria**

23. **Exclusion criteria:**

24. **What was the eligibility criteria of Population in this RCT?:** Please describ included population in this study. (copy and paste)

25. **Type of patients' Cancer Treatment:** (check all that apply)

- [ ] Chemotherapy
- [ ] Radiation therapy
- [ ] Hormone therapy
- [ ] Immunotherapy
- [ ] Post treatment/Survivors
- [ ] Post treatment/Disease free
- [ ] Others (specify)

Table: Sample size, Participant Flow throw study:

Number of individual approached to take part in the study?	
Total Patients randomized (raw number)	
Patients randomized (raw number) Treatment group 1	
Patients randomized (raw number) Treatment group 2	

Patients randomized (raw number) Treatment group 3	
Patients randomized (raw number) Control arm	
Lost to follow-up: withdrew consent (raw number)	
33. Lost to follow-up: withdrew due to adverse effects (please specify in details)	
Lost to follow-up: withdrew due to lack of improvement	
Lost to follow-up: withdrew due to loss of contact or migration (raw number)	
Lost to follow-up: withdrew due to Other Reasons (raw number)	

39. **What is the definition of Anxiety, Stress, distress, and/or depression in this study. (please copy and paste)**

- [ ] Anxiety
- [ ] Stress
- [ ] Distress
- [ ] Depresion

40. **What type of tool measurement assessed/screened for eligibility beofre treatment?**

- [ ] FACRT-F /FACT-F
- [ ] PFS
- [ ] BFI
- [ ] SF-36
- [ ] EORTC
- [ ] Quality of Life Questionnaire fatigue scale
- [ ] POMS
- [ ] MFI
- [ ] Other: used a Anxiety, Stress, distress, and/or depression measure not categorized above
- [ ] Not Reported

42. **Baseline Anxiety, Stress, distress, and/or depression cut off point for diagnosis** (T-score or any other measure e.g. at least 4 of 10 on a 0-10 numerical rating scale)

- [ ] Anxiety
- [ ] Stress
- [ ] Distress
- [ ] Depression
- [ ] not reported

43. **Intervention:**

- [ ] Pharmacological
- [ ] Non-pharmacological
- [ ] Alternative

44. **Type of intervention (list all that apply)**

- [ ] 1,
- [ ] 2,
- [ ] 3,

45. **Type of comparison (list all that apply)**

- [ ] 1,
- [ ] 2,
- [ ] 3,

Outcome Measur:

46. **How many outcomes are measured for anxiety/Distress/stress/depression? (specify the condition)** (for example anxiety 2)

- [ ] 1, Anxiety
- [ ] 2, Stress
- [ ] 3, Distress
- [ ] 4, Depression

47. **what type of outcome is specific to anxiety/Distress/stress/depression? (specify the condition) (for example anxiety)**

- [ ] Primary
- [ ] Secondary
- [ ] Tertiary
- [ ] Main
- [ ] Others (speify)
- [ ] condition

RESULTS $ Study Outcomes

48. **What type of tool measurement assessed after treatment?**

- [ ] FACRT-F /FACT=F
- [ ] PFS
- [ ] BFI
- [ ] SF-36
- [ ] EORTC
- [ ] Quality of Life Questionnaire fatigue scale
- [ ] POMS
- [ ] MFI
- [ ] Other: used a anxiety/Distress/stress/depression measure not categorized above
- [ ] Not Rported

49. **sample size:**

- [ ] Total Sample size
- [ ] # of eligible
- [ ] # of Randomized
- [ ] # of included
- [ ] # completed the study
- [ ] # evaluated

50. **Statistical Methods:** (list statistical tests or cut&paste)

- ( ) Yes
- ( ) No

Clear Response

Table1 Outcome: intervention & outcome Groups (please fill all information that apply only to both intervention and outcome groups)

51. Condition: (anxiety, distress, stress, depression)

Type of intervention	Total # intervention	# of events intervention	Total # control	# of events control	Binary/Continuoue outcome	Effect Measures	Measure of Central Tendency	Effect Size	Low CI	Upp. CI	P-value	Frequency of Treatment	Dose/Duration of treatment
T1: condeition/intervention/time/dose													

T2:condeition/intervention/time/dose													
T3:condeition/intervention/time/dose													
T4:condeition/intervention/time/dose													
T5:condeition/intervention/time/dose													

Instruction for table 1 and 2:
Effect measure can be odds ratio (OR), risk ratio (RR), Hazard ratio (HR), or absolut risk reduction (ARD) or risk decreasd (RD).
Measure of central tendency can be Mean, Median, or Mode.
Unit of variance measure can be standard deviation (SD), standard error (SE), 95% CI. IQR, or Range

122. **Note:** specify any important information on the above table

123. **Covariate adjustment for:**

- [ ] 1.
- [ ] 2.
- [ ] 3.
- [ ] 3.

124. **Outcome assessment related anxiety, distress, stress, depression** (e.g. % of reduction of score)

125. **Main results:**

- [ ] 1,
- [ ] 2,
- [ ] 3,
- [ ] 4,

126. **Summary Main Results**

- ○ Benefits
- ○ No effect
- ○ Inconsistent
- ○ others(specify)

Clear Response

127. **Adverse events or any side effects (specify all that apply)**

- ☐ 1
- ☐ 2
- ☐ 3
- ☐ 4

Study Conclusion

128. **Key Conclusion:**

- ☐ 1,
- ☐ 2,
- ☐ 3,
- ☐ 4,

129. Data extractor Note:

130. Extracted data verified by:

- ○ HK
- ○ JY
- ○ MW
- ○ other (specify)
- ○ Saghi

Clear Response

Submit Form and go to or Skip to Next

6.I.7 Quality Assessment – Clinical Practice Guidelines

General Instruction, Rating Scale:

All AGREE II items are rated on the following 7-point scale:

Score of 1 (Strongly Disagree). A score of 1 should be given when there is no information that is relevant to the AGREE II item or if the concept is very poorly reported.

Score of 7 (Strongly Agree). A score of 7 should be given if the quality of reporting is exceptional and where the full criteria and considerations articulated in the User's Manual have been met.

Scores Between 2 and 6. A score between 2 and 6 is assigned when the reporting of the AGREE II item does not meet the full criteria or considerations. A score is assigned depending on the completeness and quality of reporting. Scores increase as more criteria are met and considerations addressed. The "How to Rate" section for each item includes details about assessment criteria and considerations specific to the item. (see instruction)

click here to see the full instruction

1. **The overall objective(s) of the guideline is (are) specifically described.**

   ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 Clear Response

2. **The health question(s) covered by the guideline is (are) specifically described.**

   ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 Clear Response

3. **The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.**

   ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 Clear Response

4. **The guideline development group includes individuals from all the relevant professional groups.**

   ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 Clear Response

5. **The views and preferences of the target population (patients, public, etc.) have been sought.**

   ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 Clear Response

6. **The target users of the guideline are clearly defined.**

   ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 Clear Response

7. **Systematic methods were used to search for evidence.**

   ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 Clear Response

8. **The criteria for selecting the evidence are clearly described.**

   ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 Clear Response

9. **The strengths and limitations of the body of evidence are clearly described.**

1 2 3 4 5 6 7 Clear Response

10. **The methods used for formulating the recommendations are clearly described.**

1 2 3 4 5 6 7 Clear Response

11. **The health benefits, side effects and risks have been considered in formulating the recommendations.**

1 2 3 4 5 6 7 Clear Response

12. **There is an explicit link between the recommendations and the supporting evidence.**

1 2 3 4 5 6 7 Clear Response

13. **The guideline has been externally reviewed by experts prior to its publication.**

1 2 3 4 5 6 7 Clear Response

14. **A procedure for updating the guideline is provided.**

1 2 3 4 5 6 7 Clear Response

15. **The recommendations are specific and unambiguous.**

1 2 3 4 5 6 7 Clear Response

16. **The different options for management of the condition or health issue are clearly presented.**

1 2 3 4 5 6 7 Clear Response

17. **Key recommendations are easily identifiable.**

1 2 3 4 5 6 7 Clear Response

18. **The guideline describes facilitators and barriers to its application.**

1 2 3 4 5 6 7 Clear Response

19. **The guideline provides advice and/or tools on how the recommendations can be put into practice .**

1 2 3 4 5 6 7 Clear Response

20. **The potential resource implications of applying the recommendations have been considered.**

1 2 3 4 5 6 7 Clear Response

21. **The guideline presents monitoring and/ or auditing criteria.**

1 2 3 4 5 6 7 Clear Response

22. **The views of the funding body have not influenced the content of the guideline.**

1 2 3 4 5 6 7 Clear Response

23. **Competing interests of guideline development group members have been recorded and addressed.**

1 2 3 4 5 6 7 Clear Response

24. **Overall Assessment:**

Would you recommend these guidelines for use in practice?

- Strongly recommend
- Recommend (with provisos alteration)
- Would not recommend
- Unsure

Clear Response

25. **Reviewer:**

26. **Appraiser 1:**

- Doris

27. **Appraiser 2:**

- Homa
- Hesam
- Saghi

Submit Form and go to or Skip to Next

6.I.8 Quality Assessment – RCT

1. **This is an RCT on:**

- [ ] Depression
- [ ] Distress
- [ ] Anxiety
- [ ] PTSD
- [ ] Fear

2. Ihis is an RCT on:

- ( ) pharmacological
- ( ) non-pharmacological
- ( ) pharma & nonpharma

Clear Response

3. **this is an RCT focused on:**

- ( ) Exercise
- ( ) CBT
- ( ) Education/Psychosocial
- ( ) Medication
- ( ) Unspecified (any intervention)
- ( ) Pharma + Non-Pharma
- ( ) Sleep Therapy
- ( ) Complementary/Alternative
- ( ) other plus one of the above (spefify both)

Clear Response

Instruction: please click on this link if you need.

Selection Bias

4. RANDOM SEQUENCE GENERATION

- ( ) Low risk of bias
- ( ) High risk of bias
- ( ) Unclear risk of bias

Clear Response

5. ALLOCATION CONCEALMENT

- Low Risk of bias
- High Risk of bias
- Unclear Risk of bias

Clear Response

Performance Bias

6. BLINDING OF PARTICIPANTS AND PERSONNEL

- Low Risk of bias
- High Risk of bias
- Unclear Risk of bias

Clear Response

Detection Bias

7. BLINDING OF OUTCOME ASSESSMENT

- Low Risk of bias
- High Risk of bias
- Unclear Risk of bias

Clear Response

Attrition Bias

8. INCOMPLETE OUTCOME DATA

- Low risk of bias
- High risk of bias
- Unclear risk of bias

Clear Response

Reporting Bias

9. Definition and surveillance

- Low risk of bias
- High risk of bias
- Unclear risk of bias

Clear Response

Baseline imbalance

10. Baseline imbalance

*Look for baseline imbalance (age, gender, race, history of cancer, smoking status, sun exposure (either direct measure or geographic region))

- Low risk of bias
- High risk of bias
- Unclear risk of bias

Clear Response

Funding Source

11. Industry Funding

- Low risk of bias
- High risk of bias
- Unclear risk of bias

Clear Response

12. Note:

6.I.9 Quality Assessment – Systematic Review

Q1. Was an 'a priori' design provided?
The research question and inclusion criteria should be established before the conduct of the review.

- Yes
- No
- Can't answer
- Not applicable

Clear Response

Q2. Was there duplicate study selection and data extraction?
There should be at least two independent data extractors and a consensus procedure for disagreements should be in place.

- Yes
- No
- Can't answer
- Not applicable

Clear Response

Q3. Was a comprehensive literature search performed?
At least two electronic sources should be searched. The report must include years and databases used (e.g. Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found.

- Yes
- No
- Can't answer
- Not applicable

Clear Response

Q4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?
The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc.

- Yes
- No
- Can't answer
- Not applicable

Clear Response

Q5. Was a list of studies (included and excluded) provided?
A list of included and excluded studies should be provided.

- Yes
- No
- Can't answer
- Not applicable

Clear Response

Q6. Were the characteristics of the included studies provided?
In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g. age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported.

- Yes
- No
- Can't answer
- Not applicable

Clear Response

Q7. Was the scientific quality of the included studies assessed and documented?
'A priori' methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo controlled studies, or allocation concealment as inclusion criteria); for other types of studies alternative items will be relevant.

- Yes
- No
- Can't answer

- Not applicable

Clear Response

Q8. Was the scientific quality of the included studies used appropriately in formulating conclusions?
The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations.

- Yes
- No
- Can't answer
- Not applicable

Clear Response

Q9. Were the methods used to combine the findings of studies appropriate?
For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e. Chi-squared test for homogeneity, 2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e. is it sensible to combine?).

- Yes
- No
- Can't answer
- Not applicable

Clear Response

Q10. Was the likelihood of publication bias assessed?
An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test).

- Yes
- No
- Can't answer
- Not applicable

Clear Response

Q11. Was the conflict of interest stated?
Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

- Yes
- No
- Can't answer
- Not applicable

Clear Response

Submit Form and go to or Skip to Next

6.J Excluded Studies

Table 6.J.1: Summary of Excluded Studies

Reason for Exclusion	Total #
Abstract	86
Before 2009	6
Cohort Study	3
Commentary	2
Full Text not Available	14
Narrative Review	12
Not a Guideline	2
Not a Management of Cancer-Related Distress & Anxiety	109
Not a Participant of Cancer-Related Distress & Anxiety	111
Not an RCT	10
Prospective Intervention	1
Not a outcome of Interest	1

Excluded List

1. Aaronson TN, Duijts S, Van Beurden M, Hunter M, Oldenburg H. Cognitive behavioral therapy and physical exercise for climacteric symptoms in breast cancer patients experiencing treatment induced menopause: Final results of a multicenter randomized controlled. Psycho oncology. 2011;20:94-5.
   Excluded: Abstract.
2. Abrahamson K. Dealing with cancer-related distress. Am. 2010;110(4):67-9.
   Excluded: Narrative Review.
3. Abrahm JL, Lobach DF, Halpenny B, Rabin MS, Finn K, Calarese P, Del Fiol G, Zaner K, Berenbaum IL, Johns E, Saunders TA, Berry DL, Cooley ME. Creating evidence-based computable algorithms providing real-time specific symptom management suggestions in both a community and an academic outpatient thoracic oncology setting. Support Care Cancer. 2013;21:S212-S4.
   Excluded: Abstract.
4. Aguado Loi CX, Taylor TR, McMillan S, Gross-King M, Xu P, Shoss MK, Huegel V. Use and helpfulness of self-administered stress management therapy in patients undergoing cancer chemotherapy in community clinical settings. J Psychosoc Oncol. 2012;30(1):57-80.
   Excluded: Not a Management of Cancer-Related Anxiety and Distress.
5. Albrecht TA, Taylor AG. Physical activity in patients with advanced-stage cancer: a systematic review of the literature. Clin J Oncol Nurs. 2012;16(3):293-300.
   Excluded: Not a Participant of Cancer-Related Distress & Anxiety.

6. Apostolo J, Mendes A, Bath-Hextall F, Rodrigues R, Santos J, Cardoso D. The use of non-pharmacological nursing interventions on the comfort of cancer patients: A comprehensive systematic review protocol. JBI Database of Systematic Reviews and Implementation Reports. 2013;11(2):372-88.
Excluded: Not a Participant of Cancer-Related Distress & Anxiety.
7. Archer S, Buxton S, Sheffield D. The effect of creative psychological interventions on psychological outcomes for adult cancer patients: A systematic review of randomised controlled trials. Psycho oncology. 2015;24(1):1-10.
Excluded: Not a Participant of Cancer-Related Distress & Anxiety.
8. Arden-Close E, Gidron Y, Bayne L, Moss-Morris R. Written emotional disclosure for women with ovarian cancer and their partners: Randomised controlled trial. Psycho oncology. 2013;22(10):2262-9.
Excluded: Not a Management of Cancer-Related Anxiety and Distress.
9. Asvat Patel Y. Motivational interviewing to promote physical activity in breast cancer survivors. Dissertation Abstracts International: Section B: The Sciences and Engineering. 2014;74(11-B(E)):No Pagination Specified.
Excluded: Not a Management of Cancer-Related Anxiety and Distress.
10. Baker BS, Harrington JE, Choi BS, Kropf P, Muller I, Hoffman CJ. A randomised controlled pilot feasibility study of the physical and psychological effects of an integrated support programme in breast cancer. Complement Ther Clin Pract. 2012;18(3):182-9.
Excluded: Not a Management of Cancer-Related Anxiety and Distress.
11. Bao T, Cai L, Snyder C, Betts K, Tarpinian K, Gould J, Jeter S, Medeiros M, Chumsri S, Bardia A, Tan M, Singh H, Tkaczuk KH, Stearns V. Patient-reported outcomes in women with breast cancer enrolled in a dual-center, double-blind, randomized controlled trial assessing the effect of acupuncture in reducing aromatase inhibitor-induced musculoskeletal symptoms. Cancer. 2014;120(3):381-9.
Excluded: Not a Participant of Cancer-Related Distress & Anxiety.
12. Beard C, Stason WB, Wang Q, Manola J, Dean-Clower E, Dusek JA, Decristofaro S, Webster A, Doherty-Gilman AM, Rosenthal DS, Benson H. Effects of complementary therapies on clinical outcomes in patients being treated with radiation therapy for prostate cancer. Cancer. 2011;117(1):96-102.
Excluded: Not a Management of Cancer-Related Anxiety and Distress.
13. Beatty L, Oxlad M, Koczwara B, Wade TD. A randomised pilot of a self-help workbook intervention for breast cancer survivors. Support Care Cancer. 2010;18(12):1597-603.
Excluded: Not a Management of Cancer-Related Anxiety and Distress.
14. Bellardita L, Valdagni R, Van Den Bergh R, Randsdorp H, Repetto C, Venderbos LDF, Lane JA, Korfage IJ. How does active surveillance for prostate cancer affect quality of life? A systematic review. Eur Urol. 2015;67(4):637-45.
Excluded: Not a Participant of Cancer-Related Distress & Anxiety.

15. Benney S, Gibbs V. A literature review evaluating the role of Swedish massage and aromatherapy massage to alleviate the anxiety of oncology patients. Radiography. 2013;19(1):35-41.
Excluded: Not a Management of Cancer-Related Anxiety and Distress.
16. Berger AM, Hertzog M, Kuhn BR, Farr L. Values and relationships among circadian activity rhythms with subjective sleep, fatigue, and mood in women one year after the first adjuvant breast cancer chemotherapy treatment. Sleep. 2011;34(11).
Excluded: Abstract.
17. Bergholdt SH, Larsen PV, Kragstrup J, Sondergaard J, Hansen DG. Enhanced involvement of general practitioners in cancer rehabilitation: A randomised controlled trial. BMJ Open. 2012;2(2).
Excluded: Not a Participant of Cancer-Related Distress & Anxiety.
18. Berglund G, Petersson L, Eriksson KC, Wallenius I, Roshanai A, Nordin KM, Sjödén P, Häggman M. "Between men": a psychosocial rehabilitation programme for men with prostate cancer. Acta Oncol. 2007;46(1):83-9.
Excluded: Not a Management of Cancer-Related Anxiety and Distress.
19. Berry DL, Hong F, Halpenny B, Partridge AH, Fann JR, Wolpin S, Lober WB, Bush NE, Parvathaneni U, Back AL, Amtmann D, Ford R. Electronic self-report assessment for cancer and self-care support: results of a multicenter randomized trial. J Clin Oncol. 2014;32(3):199-205.
Excluded: Not a Management of Cancer-Related Anxiety and Distress.
20. Binns-Turner PG, Wilson LL, Pryor ER, Boyd GL, Prickett CA. Perioperative music and its effects on anxiety, hemodynamics, and pain in women undergoing mastectomy. AANA journal. 2011;79(4):S21-S7.
Excluded: Not a Participant of Cancer-Related Distress & Anxiety.
21. Björneklett HG, Lindemalm C, Rosenblad A, Ojutkangas M-L, Letocha H, Strang P, Bergkvist L. A randomised controlled trial of support group intervention after breast cancer treatment: Results on anxiety and depression. Acta Oncol. 2012;51(2):198-207.
Excluded: Not a Management of Cancer-Related Anxiety and Distress.
22. Björneklett HG, Rosenblad A, Lindemalm C, Ojutkangas ML, Letocha H, Strang P, Bergkvist L. Long-term follow-up of a randomized study of support group intervention in women with primary breast cancer. J Psychosom Res. 2013;74(4):346-53.
Excluded: Not a Participant of Cancer-Related Distress & Anxiety.
23. Blackler K, Chambers S, Dunn J, Ritterband L, Aitken J, Scuffham P, Morris B, Baade P, Youl P. Improving access to psychological services for people with cancer: A randomised controlled trial of an interactive web-based intervention. Asia Pac J Clin Oncol. 2014;10(92).
Excluded: Abstract.
24. Bodden G, Uche-Holub E, Wallaeys E, Thierling U, Bodden J, Siegesmund M, Bafteh P, Bogesits-Aufschneider R, Kuerten V, Neumann NJ, Hanneken S, Frank

J. Malignant melanoma in a patient with erythropoietic protoporphyria - A critical appraisal in the light of new treatment strategies. Clinical chemistry and laboratory medicine. 2013;51(5):eA9.
Excluded: Abstract.
25. Boehm K, Bussing A, Ostermann T. Aromatherapy as an adjuvant treatment in cancer care-a descriptive systematic review. European Journal of Integrative Medicine. 2012;4:129.
Excluded: Not a Participant of Cancer-Related Distress & Anxiety.
26. Bomhof-Roordink H, Beekman ATF, Honig A, Hoogendoorn A, Van Der Linden MHM, Meijel B, Mulder CJJ, Van Tulder MW, Neefjes ECW, Van Der Vorst MJDL, Verheul HMW, Dekker J. Screening and treatment of psychological distress in colorectal cancer (CRC) with metastasized disease: The TES-trial. Psycho oncology. 2013;22:295.
Excluded: Abstract.
27. Bower JE, Crosswell AD, Stanton AL, Crespi CM, Winston D, Arevalo J, Ma J, Cole SW, Ganz PA. Mindfulness meditation for younger breast cancer survivors: A randomized controlled trial. Cancer. 2015;121(8):1231-40.
Excluded: Not a Participant of Cancer-Related Distress & Anxiety.
28. Bower JE, Ganz PA, Crosswell AD, Crespi CM, Stanton AL, Winston D, Cole SW. Effects of mindfulness meditation on stress and inflammation in breast cancer survivors: A randomized controlled trial. Psychosomatic medicine. 2014;76(3):A-19.
Excluded: Full text not available.
29. Bradt J, Dileo C, Grocke D, Magill L. Music interventions for improving psychological and physical outcomes in cancer patients [Systematic Review]. Cochrane Database Syst Rev. 2011;9:9.
Excluded: Not a Management of Cancer-Related Anxiety and Distress.
30. Bradt J, Goodill SW, Dileo C. Dance/movement therapy for improving psychological and physical outcomes in cancer patients [Systematic Review]. Cochrane Database Syst Rev. 2014;3:3.
Excluded: Not a Participant of Cancer-Related Distress & Anxiety.
31. Bradt J, Potvin N, Kesslick A, Shim M, Radl D, Schriver E, Gracely EJ, Komarnicky-Kocher LT. The impact of music therapy versus music medicine on psychological outcomes and pain in cancer patients: a mixed methods study. Support Care Cancer. 2015;23(5):1261-71.
Excluded: Not a Participant of Cancer-Related Distress & Anxiety.
32. Brandes K, Linn A, Van Weert J, Butow P. Evaluating the design and effectiveness of question prompt lists in oncology: A systematic literature review. Psycho oncology. 2013;22:131.
Excluded: Abstract.
33. Branstrom R, Kvillemo P, Moskowitz JT. A randomized study of the effects of mindfulness training on psychological well-being and symptoms of stress in

patients treated for cancer at 6-month follow-up. International Journal of Behavioral Medicine. 2012;19(4):535-42.
Excluded: Not a Management of Cancer-Related Anxiety and Distress.
34. Branstrom R, Kvillemo P, Brandberg Y, Moskowitz JT . Self-report mindfulness as a mediator of psychological well-being in a stress reduction intervention for cancer patients--a randomized study. Annals of behavioral medicine. 2010;39(2):151-61.
Excluded: Not a Management of Cancer-Related Anxiety and Distress.
35. Bredal IS, Karesen R, Smeby NA, Espe R, Sorensen EM, Amundsen M, Aas H, Ekeberg O. Effects of a psychoeducational versus a support group intervention in patients with early-stage breast cancer: results of a randomized controlled trial. Cancer Nurs. 2014;37(3):198-207.
Excluded: Not a Management of Cancer-Related Anxiety and Distress.
36. Breitbart W, Rosenfeld B, Gibson C, Pessin H, Poppito S, Nelson C, Tomarken A, Timm AK, Berg A, Jacobson C, Sorger B, Abbey J, Olden M. Meaning-centered group psychotherapy for patients with advanced cancer: a pilot randomized controlled trial. Psycho oncology. 2010;19(1):21-8.
Excluded: Not a Management of Cancer-Related Anxiety and Distress.
37. Brem S, Kumar NB. Management of treatment-related symptoms in patients with breast cancer: Current strategies and future directions. Clin J Oncol Nurs. 2011;15(1):63-71.
Excluded: Narrative Review.
38. Brothers BM, Yang HC, Strunk DR, Andersen BL. Cancer patients with major depressive disorder: testing a biobehavioral/cognitive behavior intervention. J Consult Clin Psychol. 2011;79(2):253-60.
Excluded: Not an RCT.
39. Brown RF, Subnis U, Starkweather A, McCain N. The effect of psychosocial interventions for patients with cancer on psychoneuroimmunologic outcomes: A systematic review. Asia Pac J Clin Oncol. 2012;8:145.
Excluded: Abstract.
40. Bruera E, Willey J, Cohen M, Palmer JL. Expressive Writing in Patients Receiving Palliative Care: A Feasibility Study. Journal of Palliative Medicine. 2008;11(1):15-9.
Excluded: Not a Management of Cancer-Related Anxiety and Distress.
41. Budhrani P. Optimal timing of mindfulness-based stress reduction in cancer: Research synthesis and state of the science. Journal of Alternative and Complementary Medicine. 2014;20(5):A85-A86.
Excluded: Not a Management of Cancer-Related Anxiety and Distress.
42. Buffart LM, van Uffelen JG, Riphagen, II, Brug J, van Mechelen W, Brown WJ, Chinapaw MJ. Physical and psychosocial benefits of yoga in cancer patients and survivors, a systematic review and meta-analysis of randomized controlled trials. BMC Cancer. 2012;12:559.
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6.K External Panel

A draft version of this report was reviewed by 15 health care professionals from across Canada and USA involved in the Cancer Related Distress, Depression & Anxiety and psychosocial and supportive care of cancer survivors. Respondents were asked to complete a survey about the relevance and quality of the guideline and comment on the draft. The Cancer Journey Cancer Related Distress, Depression & Anxiety Expert Panel reviewed the results of the external review, addressed the comments and made modifications accordingly. The findings of the external review are summarized in Table 6.K.1.

Table 6.K.1 shows that all respondents found the guideline's objectives, target population were described clearly. All agreed that appropriate systematic methods were used to identify relevant evidence and the adaptations were appropriate. Most agreed that the supporting evidence for formulating the Distress, Depression & Anxiety recommendations were clearly described and the majority agreed that the recommendations for Distress, Depression & Anxiety were appropriately stated based on the supporting evidence. All respondents rated the overall quality of the guideline as good or of highest quality.

Table 6.K.1: Summary Results of External Review Survey Result

Survey Items	Strongly Disagree (1) N(%)	Disagree (2) N(%)	Neutral (3) N(%)	Somewhat Agree (4) N(%)	Strongly Agree (5) N(%)
The overall objective of the distress guideline is specifically described	0 (0%)	0 (0%)	0 (0%)	1 (6.7%)	14 (93.3%)
The target population for the distress guideline is clearly described	0 (0%)	0 (0%)	0 (0%)	4 (26.7%)	11 (73.3%)
The target users of the distress guideline are clearly described	0 (0%)	0 (0%)	1 (6.7%)	2 (13.3%)	12 (80%)
Systematic search methods for identifying relevant evidence for adaptations to the earlier version of the guideline were appropriate	0 (0%)	0 (0%)	0 (0%)	2 (13.3%)	13 (86.7%)
The supporting evidence for formulating the psychosocial distress (anxiety and depression) recommendations are clearly described	0 (0%)	0 (0%)	0 (0%)	4 (26.7%)	11 (73.3%)
The recommendations for distress are appropriately stated based on the supporting evidence.	0 (0%)	0 (0%)	1 (6.7%)	5 (33.3%)	9 (60%)
I would recommend this guideline for use in practice	0 (0%)	0 (0%)	0 (0%)	7 (46.7%)	8 (53.3%)
When applied the psychosocial distress (anxiety and depression) guideline will produce more benefits than harms	0 (0%)	0 (0%)	1 (6.7%)	4 (26.7%)	10 (66.7%)
I would make use of this guideline in my professional decisions.	0 (0%)	0 (0%)	0 (0%)	6 (40%)	9 (60%)
Survey Items	**Lowest Quality**	**Acceptable Quality**	**Fair Quality**	**Good Quality**	**Highest Quality**
The overall quality of the guideline report on the scale from (1) lowest quality to (5) highest quality.	0 (0%)	0 (0%)	0 (0%)	6 (40%)	9 (60%)