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Management of Anxiety and Depression in Adult Survivors of Cancer: ASCO Guideline Update

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abstract

PURPOSE To update the American Society of Clinical Oncology guideline on the management of anxiety and depression in adult cancer survivors.

METHODS A multidisciplinary expert panel convened to update the guideline. A systematic review of evidence published from 2013-2021 was conducted.

RESULTS The evidence base consisted of 17 systematic reviews ± meta analyses (nine for psychosocial interventions, four for physical exercise, three for mindfulness-based stress reduction [MBSR], and one for pharmacologic interventions), and an additional 44 randomized controlled trials. Psychological, educational, and psychosocial interventions led to improvements in depression and anxiety. Evidence for pharmacologic management of depression and anxiety in cancer survivors was inconsistent. The lack of inclusion of survivors from minoritized groups was noted and identified as an important consideration to provide high-quality care for ethnic minority populations.

RECOMMENDATIONS It is recommended to use a stepped-care model, that is, provide the most effective and least resource-intensive intervention based on symptom severity. All oncology patients should be offered education regarding depression and anxiety. For patients with moderate symptoms of depression, clinicians should offer cognitive behavior therapy (CBT), behavioral activation (BA), MBSR, structured physical activity, or empirically supported psychosocial interventions. For patients with moderate symptoms of anxiety, clinicians should offer CBT, BA, structured physical activity, acceptance and commitment therapy, or psychosocial interventions. For patients with severe symptoms of depression or anxiety, clinicians should offer cognitive therapy, BA, CBT, MBSR, or interpersonal therapy. Treating clinicians may offer a pharmacologic regimen for depression or anxiety for patients who do not have access to first-line treatment, prefer pharmacotherapy, have previously responded well to pharmacotherapy, or have not improved following first-line psychological or behavioral management.

Additional information is available at www.asco.org/survivorship-guidelines.

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ASSOCIATED CONTENT

Appendix

Data Supplement

Author affiliations and support information (if applicable) appear at the end of this article.

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INTRODUCTION

In 2023, 1,958,310 new cancer cases are projected to occur in the United States and it is estimated that by 2040, approximately 26 million people will be living with and beyond cancer in the United States alone.[1,2] Worldwide, 5-year prevalence of all cancers is estimated to be 50.5 million people.[3] An often unappreciated aspect of caring for the growing numbers of cancer survivors is the psychological toll of cancer. The 12-month prevalence rate for any mental disorder is significantly higher in patients with cancer compared with general population controls (odds ratio [OR], 1.28; 95% CI, 1.14 to 1.45).[4] Psychological symptoms among patients with cancer are under-recognized and undertreated.[5,6] Symptoms may be trivialized as a normal reaction to cancer diagnosis, or interpreted as secondary to physical symptoms. In an effort to address this problem, American Society of Clinical Oncology (ASCO) in 2014[7] published recommendations for routine screening using validated, published measures to provide guidance for referral and treatment.

Still, identification and treatment of patients with cancer with comorbid psychiatric disorders, either pre-existing or newly arising, remains imperative. As noted

THE BOTTOM LINE

Management of Anxiety and Depression in Adult Survivors of Cancer: ASCO Guideline Update

Guideline Question

What are the recommended treatment approaches in the management of anxiety and/or depression in survivors of adult (≥18 years old) cancer?

Target Population

Survivors of adult cancer, defined as starting from the time of diagnosis to any time thereafter, with anxiety and/or depression.

Target Audience

Health care providers including oncologists, psychologists, psychiatrists, psychosocial and rehabilitation professionals, integrative medicine practitioners, primary care providers, social workers, nurses, and others involved in the delivery of care for cancer survivors, as well as their family members, and caregivers.

Methods

Following specification of the question and search parameters, a systematic review of relevant literature was conducted, and an Expert Panel was convened to develop updated clinical practice guideline recommendations based on review findings and other considerations.

Author's note: This guideline provides detailed and medically sound compilations of updates, insights, advice, and recommendations for depression and/or anxiety in survivors of adult cancer. However, they were developed in the context of mental health care being available and may not be applicable within other resource settings. It is the view of the Expert Panel that health care providers and health care system decision makers should be guided by these recommendations. However, the authors acknowledge that not all recommended interventions for management of depression and/or anxiety in survivors of adult cancer are available in resource-limited environments. When services are not available, clinicians should opt for other accessible interventions.

Recommendations

Please refer to ASCO's 2014 recommendations on screening and assessment (also available in Appendix Table A1 [online only]).

General Management Principles

Recommendation 1.1. All patients with cancer and any patient-identified caregiver, family member, or trusted confidant should be offered information regarding depression and anxiety. They should also be offered resources, such as the providers' contact information for further evaluation and treatment within or external to the facility whenever available (Type: Evidence based; benefits outweigh harms; Evidence quality: Intermediate; Strength of recommendation: Strong).

Qualifying statement. Information should be culturally informed and linguistically appropriate and can include a conversation between clinician and patient, and/or electronic or written material on depression and anxiety. Examples of materials can be found at Cancer.Net, such as ASCO Answers Anxiety and Depression.

Recommendation 1.2. Clinicians should use a stepped-care model, that is, selecting the most effective and least resource-intensive intervention based on symptom severity when selecting treatment for anxiety and/or depression. Other variables which may inform the choice of treatment approach include the following:

- Psychiatric history, that is, prior diagnoses, with or without treatment
- History of substance use
- Prior mental health treatment response
- Functional abilities and/or limitations related to self-care, usual activities, and/or mobility
- Recurrent or advanced cancer
- Presence of other chronic disease(s) (eg, cardiac disease)
- Member of socially and/or economically marginalized group (eg, Black race, low socioeconomic status)

(Type: Evidence based; benefits outweigh harms; Evidence quality: Intermediate; Strength of recommendation: Strong)

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THE BOTTOM LINE (CONTINUED)

Recommendation 1.3. Psychological and psychosocial interventions provided by mental health practitioners should derive from manualized, empirically supported treatments. Manuals for evidence-based treatments specify content, structure, delivery mode, session number, treatment duration, and related topics. Linguistic, cultural, and socio-ecological contexts need to guide any treatment tailoring (Type: Evidence based; benefits outweigh harms; Evidence quality: Intermediate; Strength of recommendation: Moderate).

Recommendation 1.4. When making a referral for further evaluation or psychological care, clinicians should make every effort to reduce barriers and facilitate patient follow-through. Determining follow through to the first appointment is essential as is discovering any barriers that may have arisen for the patient. Thereafter, determining patient satisfaction and assisting with any new and/or continuing barriers would also be helpful (Type: Informal consensus; benefits outweigh harms; Evidence quality: Insufficient; Strength of recommendation: Moderate).

Recommendation 1.5. For patients who have symptoms of both depression and anxiety, treatment of depressive symptoms should be prioritized. Alternatively, treatment with a unified protocol (ie, combining cognitive behavior therapy [CBT] treatments for depression and anxiety) may be used (Type: Evidence based; benefits outweigh harms; Evidence quality: High; Strength of recommendation: Strong).

Recommendation 1.6. For patients referred to and receiving psychological treatment, mental health professionals should regularly assess treatment response (eg, pretreatment, 4 weeks, 8 weeks, and end of treatment). (Type: Evidence based; benefits outweigh harms; Evidence quality: Intermediate; Strength of recommendation: Strong).

Recommendation 1.7. If pharmacologic treatment is used, the treating clinician should regularly (eg, 4 and 8 weeks) assess using standardized validated instruments, the extent of a patient's symptom relief, side effect and adverse event occurrence, and satisfaction. If symptoms are stable or worsening, the treating clinician should re-evaluate the plan and revise (Type: Informal consensus; benefits outweigh harms; Evidence quality: Insufficient; Strength of recommendation: Strong).

Recommendation 1.8. After 8 weeks of treatment for depression and/or anxiety, if there is little improvement in symptoms despite good adherence, the treating clinician should adjust the regimen (eg, add a psychological or pharmacologic intervention to a single treatment; if pharmacologic, change the medication; and if group therapy, refer to individual therapy). The same considerations may apply if patient satisfaction with treatment is low and/or barriers to treatment exist (Type: Informal consensus; benefits outweigh harms; Evidence quality: Insufficient; Strength of recommendation: Moderate).

Author's note: Current evidence supports that the recommended treatment interventions for depression and anxiety are effective therapeutic options. However, it is acknowledged that availability of mental health services, ease of access, time to service provision, and cost are important considerations that may vary across treatment settings. The choice of intervention to offer patients should be based on shared decision making, taking into account availability, accessibility, patient preference, likelihood of adherence, and cost.

Treatment and Care Options for Depressive Symptoms

Recommendation 2.1. For patients with moderate to severe depressive symptoms, culturally informed and linguistically appropriate information should be provided to patients and patient-identified caregivers, family members, or trusted confidants. Information might include the following: the commonality (frequency) of depression, common psychological, behavioral, and vegetative symptoms, signs of symptom worsening, and indications to contact the medical team (with provision of contact information). (Type: Evidence based; benefits outweigh harms; Evidence quality: Intermediate; Strength of recommendation: Strong).

Recommendation 2.2. For a patient with **moderate** symptoms of depression, clinicians should offer individual or group therapy with any one of the following treatment options:

- Cognitive therapy or CBT
- Behavioral activation (BA)
- Structured physical activity and exercise
- Mindfulness-based stress reduction (MBSR)
- Psychosocial interventions using empirically supported components (eg, relaxation, problem solving).

(Type: Evidence based; benefits outweigh harms; Evidence quality: Intermediate; Strength of recommendation: Strong).

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THE BOTTOM LINE (CONTINUED)

Recommendation 2.3. For a patient with **severe** symptoms of depression, clinicians should offer individual therapy with any one of the following treatment options:

- Cognitive therapy or CBT
- BA
- MBSR
- Interpersonal therapy

(Type: Evidence based; benefits outweigh harms; Evidence quality: Intermediate; Strength of recommendation: Strong).

Recommendation 2.4. Treating clinicians may offer a pharmacologic regimen for depression in patients without access to first-line treatment, those expressing a preference for pharmacotherapy, or those who do not improve following first-line psychological or behavioral management. Pharmacotherapy should also be considered for patients with a history of treatment response to medications, severe symptoms, or accompanying psychotic features (Type: Evidence based; benefits outweigh harms; Evidence quality: Low; Strength of recommendation: Weak).

Qualifying statement. Despite the limitations and weak evidence for pharmacologic management, empirically there is some evidence of benefit to warrant their inclusion as an alternative option.

Treatment and Care Options for Anxiety Symptoms

Recommendation 3.1. For patients with moderate to severe anxiety symptoms, culturally informed and linguistically appropriate information should be provided to patients and patient-identified caregivers, family members, or trusted confidants. Information might include the following: commonality (frequency) of stress and anxiety, psychological, behavioral, and cognitive symptoms, indications of symptom worsening, and medical team contact information (Type: Evidence based; benefits outweigh harms; Evidence quality: Intermediate; Strength of recommendation: Strong).

Recommendation 3.2. For a patient with **moderate** symptoms of anxiety, clinicians should offer individual or group therapy with any one of the following treatment options:

- CBT
- BA
- Structured physical activity and exercise
- Psychosocial interventions with empirically supported components (eg, relaxation, problem solving)

(Type: Evidence based; benefits outweigh harms; Evidence quality: Intermediate; Strength of recommendation: Strong).

Recommendation 3.3. For a patient with **severe** symptoms of anxiety, clinicians should offer individual therapy with any one of the following treatment options:

- CBT
- BA
- MBSR
- Interpersonal therapy

(Type: Evidence based; benefits outweigh harms; Evidence quality: Intermediate; Strength of recommendation: Strong).

Recommendation 3.4. Treating clinicians may offer a pharmacologic regimen for anxiety in patients without access to first-line treatment, those expressing a preference for pharmacotherapy, or those who do not improve following first-line psychological or behavioral management (Type: Evidence based; benefits outweigh harms; Evidence quality: Low; Strength of recommendation: Weak).

Please refer to the treatment algorithm in Figures 1 and 2 for symptomatology severity and a visual representation of these recommendations.

Additional Resources

Definitions for the quality of the evidence and strength of recommendation ratings are available in Appendix Table A2 (online only). More information, including a supplement with additional evidence tables, slide sets, and clinical tools and resources, is available at www.asco.org/survivorship-guidelines. The Methodology Manual (available at www.asco.org/guideline-methodology) provides additional information about the methods used to develop this guideline. Patient information is available at www.cancer.net.

ASCO believes that cancer clinical trials are vital to inform medical decisions and improve cancer care, and that all patients should have the opportunity to participate.

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in the prior guideline[7] and reiterated here, stress, depression, and anxiety are prevalent and occur throughout the survivorship trajectory.[8,9] Adults diagnosed with cancer report higher levels of stress than healthy controls, with diagnosis and the start of treatment being the most stressful times. In the short term, stress covaries with depressive and anxiety symptoms, negative quality of life, physical symptoms, and treatment morbidities across patients,[10-12] and in the long term, data show its relationship to cancer mortality.[13]

The most common depressive disorders among patients with cancer are major depression and adjustment disorder, with data for other depressive disorders scarce. Depression is often accompanied by functional impairment, poorer physical health, substance use, and low quality of life, influenced in turn by impaired relationships, reduced physical activity (PA), and other factors. It is unknown how stressors of older adulthood (eg, comorbid illnesses and partner loss) increase risk or severity. Depressive symptoms are elevated for those with advanced disease stage and/or significant symptom burden.[14,15] Depression at diagnosis and throughout the cancer trajectory[16] covaries with lower adherence to treatment and follow-up care, increased inflammation, impaired immunity, and reduced survival.[17,18]

Along with depression, anxiety, of which generalized anxiety disorder is the most prevalent in this population,[19] is common and continues to be an underaddressed condition.[20-22] Elevated anxiety predicts nonadherence to recommended therapies,[23-25] higher use and costs of medical care,[26-28] and possibly cancer recurrence.[29] As is the case for those without cancer, depression and anxiety usually co-occur.[30] Notably, Arch et al[19] found that 31% of patients with cancer with an anxiety disorder also had major depressive disorder (MDD).

In 2023, an estimated two million new cancer cases will be diagnosed.[31] Those with depression or anxiety disorders can be estimated by considering prevalence rates from studies using symptom reports versus diagnostic interviews, which report lower rates. In comparison with a control group, depression prevalence rates among people with cancer are at least two times higher for unipolar mood disorders (major depression: OR, 2.07; 95% CI, 1.71 to 2.51; dysthymia: OR, 2.93; 95% CI, 2.13 to 4.02).[4] Using self-report instruments with specified cutoff points (eg, Patient Health Questionnaire-9 $\geq$ 10), moderate to severe depressive symptom rates between 13% and 27% have been reported.[32-35] When diagnostic criteria for MDD are used, the prevalence is 14.3%. Viewing these estimates in a broader context, the WHO estimates that 4.4% of the world's population, in general, live with depression, which is notably lower than the rate for patients with cancer. Taken together, a conservative estimate (14.3%) of the number of patients with newly diagnosed cancer in 2023 with comorbid MDD will be approximately 286,000 adults.

For anxiety, studies using self-report instruments with specified cutoff points (eg, Hospital Anxiety and Depression Scale $\geq$ 8) find prevalence estimates between 4% and 48%.[36] In studies using diagnostic interviews, the prevalence is approximately 10%.[37] By comparison, the WHO[38] estimates that anxiety affects 3.6% of the global population. Again, a conservative estimate (10%) of the number of new cases having a comorbid anxiety disorder would be 200,000 individuals.

In addition to the psychological, behavioral, and biologic disruption associated with depression and anxiety after cancer, a possible danger exists for depressed patients who are not treated. Clinical depression does not remit, and patients remain at risk for self harm and/or suicide. The risk for self-harm and/or suicide has been reported to be 85% higher (standardized mortality ratio, 1.85; 95% CI, 1.55 to 2.20) than for the general population,[39] with the greatest risk during the first 12 months after cancer diagnosis,[40,41] underscoring the importance of screening for the newly diagnosed.[42,43]

The purpose of this guideline update is to gather and examine the evidence published since the 2014 guideline by Andersen et al.[7] The 2014 guideline was an adaptation of a Pan-Canadian Practice Guideline on Screening, Assessment, and Care of Psychosocial Distress (Depression, Anxiety) in Adults with Cancer,[44] which addressed the following three research questions: What are the optimum screening, assessment, and psychosocial-supportive care interventions for adults with cancer who are identified as experiencing symptoms of depression and/or anxiety? As screening and assessment for depression and anxiety are improving, the research question was revised by the reconvened panel to focus on management and treatment only. Readers are encouraged to review ASCO's 2014 recommendations on screening and assessment (also available in Appendix Table A1), which the panel deemed as still relevant.[7] Of special note, if through screening and further assessment a patient is deemed at risk of harm to self and/or to others, clinicians should refer them for emergency evaluation by a licensed mental health professional and should initiate interventions to reduce risk of harm to self and/or others (Fig 1).

GUIDELINE QUESTIONS

This clinical practice guideline addresses the question: What are the recommended treatment approaches in the management of anxiety and/or depression in survivors of adult cancer? Although the Expert Panel also sought to evaluate the evidence for management of post-traumatic stress disorder in cancer populations for this update, very few trials were identified (Data Supplement, online only). Therefore, no recommendations are made, and the identified evidence will not be discussed further.

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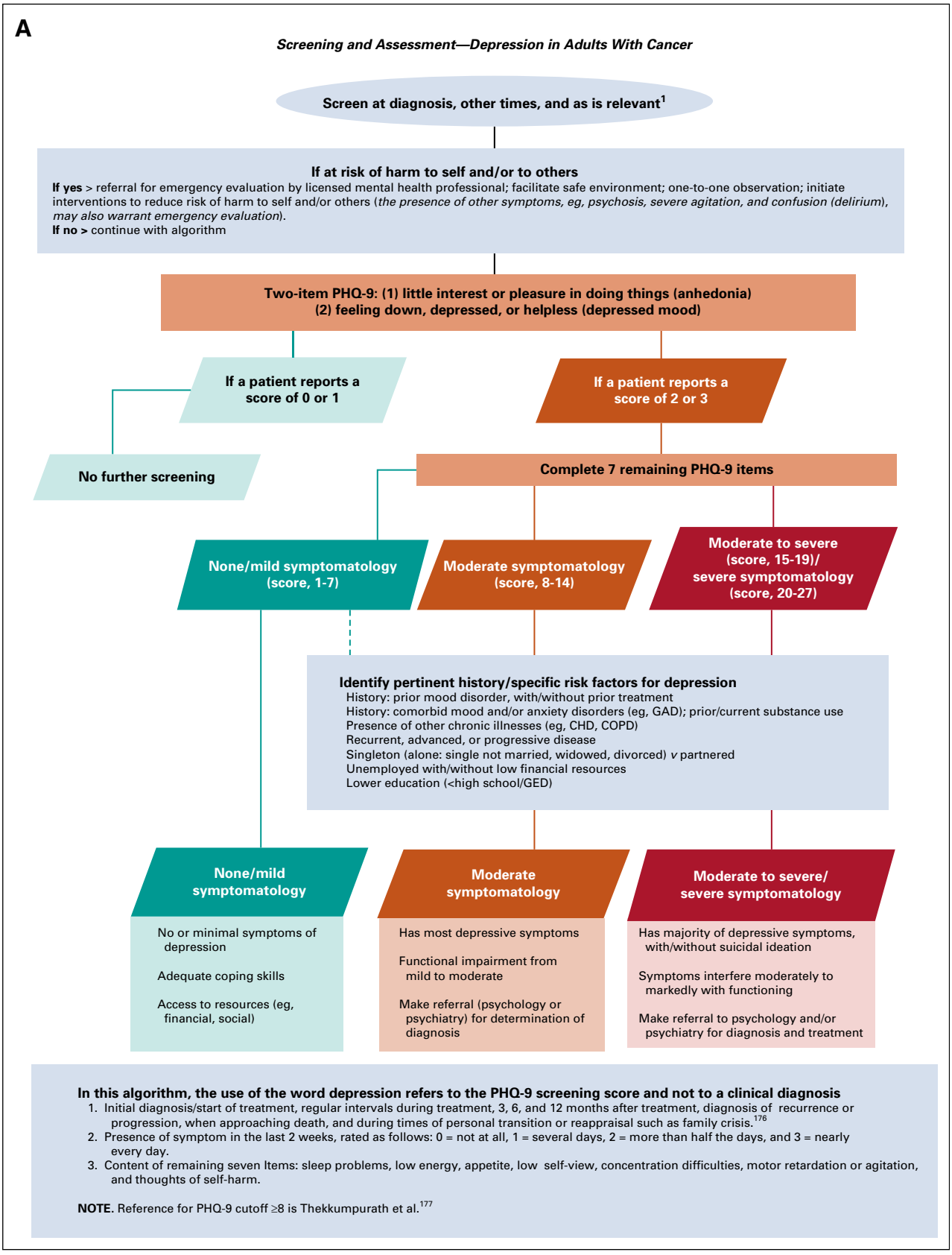

FIG 1. Depression algorithm. (A) Screening and assessment—depression in adults with cancer. (B) Care map—depression in adults with cancer. CBT, cognitive behavior therapy; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; (continued on following page)

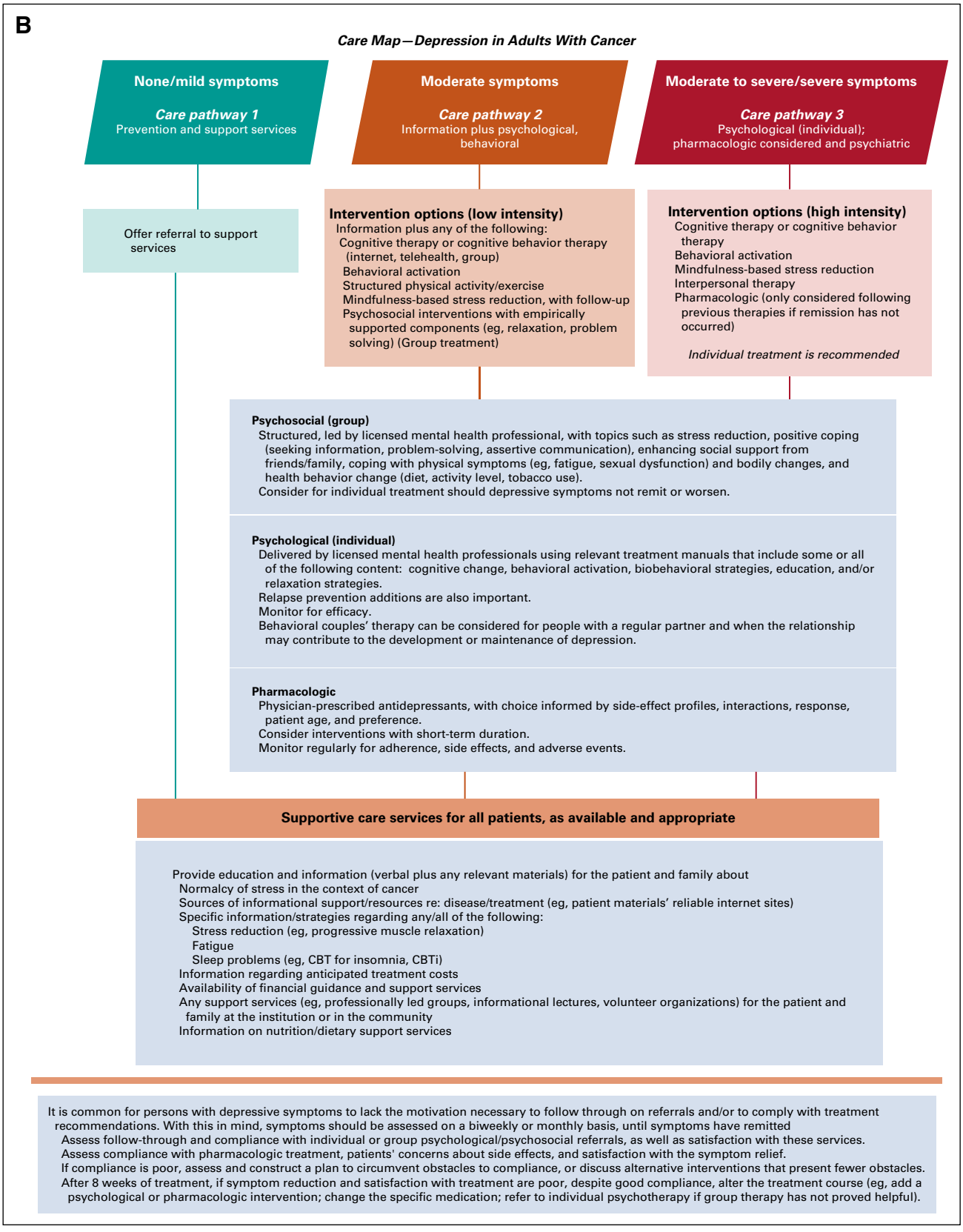

FIG 1. (Continued). GAD, generalized anxiety disorder; GED, General Educational Diploma; PHQ-9, Patient Health Questionnaire-9.

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METHODS

Guideline Development Process

This systematic review–based guideline product was developed by a multidisciplinary Expert Panel comprising professionals in psychology, psychiatry, medical and surgical oncology (cancer center– and community-based), internal medicine, and nursing with clinical and research expertise on the guideline topic. Additional members were a methodologist with expertise in evidence appraisal and guideline development and a patient representative (Appendix Table A3 [online only]). The Expert Panel met via webinar and corresponded through e-mail. The Panel was to contribute to the development of the guideline, consider the evidence, provide critical review, and finalize the guideline recommendations.

The guideline recommendations were written, in part, using the *Guidelines Into Decision Support* methodology and accompanying BRIDGE-Wiz software. In addition, a guideline implementability review was conducted. Based on the implementability review, revisions were made to the draft to clarify recommended actions for clinical practice. Ratings for type and strength of the recommendation and evidence quality are provided with each recommendation. The quality of the evidence for each outcome was assessed based on elements of the Cochrane Risk of Bias tool and the GRADE quality assessment and recommendations development process.[45,46] When evidence was insufficient or of low quality to discern the true magnitude and direction of the net effect, the guideline panel developed expert opinion–based recommendations through an informal consensus process. Employment of formal consensus methodology was deemed unnecessary, with the panel favoring open discussion that allowed for the articulation and full discussion of viewpoints instead.

The guideline recommendations were posted for an open comment period of 2 weeks, allowing the public to review and comment on the recommendations after submitting a confidentiality agreement. The comments were considered as the recommendations were finalized. Members of the Expert Panel were responsible for reviewing and approving the penultimate version of the guideline, which was then circulated for external review, and submitted to the *Journal of Clinical Oncology* for editorial review and consideration for publication. All ASCO guidelines are ultimately reviewed and approved by the Expert Panel and the ASCO Evidence Based Medicine Committee before publication. All funding for the administration of the project was provided by ASCO.

Guideline Disclaimer

The Clinical Practice Guidelines and other guidance published herein are provided by the ASCO to assist providers in clinical decision making. The information herein should not be relied upon as being complete or accurate, nor should it be considered as inclusive of all proper treatments or methods of care or as a statement of the standard of care. With the rapid development of scientific knowledge, new evidence may emerge between the time information is developed and when it is published or read. The information is not continually updated and may not reflect the most recent evidence. The information addresses only the topics specifically identified therein and is not applicable to other interventions, diseases, or stages of diseases. This information does not mandate any particular course of medical care. Further, the information is not intended to substitute for the independent professional judgment of the treating provider, as the information does not account for individual variation among patients. Recommendations specify the level of 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" indicates 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 individual cases. In all cases, the selected course of action should be considered by the provider in the context of treating the individual patient. Use of the information is voluntary. ASCO does not endorse third party drugs, devices, services, or therapies used to diagnose, treat, monitor, manage, or alleviate health conditions. Any use of a brand or trade name is for identification purposes only. ASCO provides this information on an "as is" basis and makes no warranty, express or implied, regarding the information. ASCO specifically disclaims any warranties of merchantability or fitness for a particular use or purpose. ASCO assumes no responsibility for any injury or damage to persons or property arising out of or related to any use of this information, or for any errors or omissions.

Guideline and Conflicts of Interest

The Expert Panel was assembled in accordance with ASCO's Conflict of Interest Policy Implementation for Clinical Practice Guidelines ("Policy," found at https://www.asco.org/guideline-methodology). All members of the Expert Panel completed ASCO's disclosure form, which requires disclosure of financial and other interests, including relationships with commercial entities that are reasonably likely to experience direct regulatory or commercial impact as a result of promulgation of the guideline. Categories for disclosure include employment; leadership; stock or other ownership; honoraria, consulting or advisory role; speaker's bureau; research funding; patents, royalties, other intellectual property; expert testimony; travel, accommodations, expenses; and other relationships. In accordance with the Policy, the majority of the members of the Expert Panel did not disclose any relationships constituting a conflict under the Policy.

Literature Search

PubMed was searched from January 2013 through May 2021. The search was restricted to meta-analyses, systematic reviews, and randomized controlled trials (RCTs) published in English. The ASCO Guidelines Methodology Manual (available

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at www.asco.org/guideline-methodology) provides additional information about the guideline update process. This is the most recent information as of the publication date.

Articles were selected for inclusion in the systematic review based on the following criteria:

- Population: Adult survivors of cancer. Additionally, empirically supported treatments for depressive and anxiety disorder in noncancer groups were considered to supplement or expand upon existing evidence with cancer patients.
- Interventions: Pharmacologic or nonpharmacologic randomized clinical trial designed for the management of anxiety and/or depression symptoms or disorders in adults. Integrative therapies, such as acupuncture, massage, meditation, music, and yoga, are considered in a separate, future guideline.
- Comparisons: Control conditions variously labeled as no treatment, standard of care, or treatment as usual; wait list (ie, no treatment during the time of treatment delivery for the intervention arm, and then treatment delivery to the wait list beginning at the time of post-treatment for the intervention arm); comparison of active treatments (noninferiority trial) with or without a control arm.
- Outcomes: Depressive and/or anxiety symptoms as primary trial outcome(s); diagnoses and/or remission of mood or anxiety disorders, as measured by valid self-reported or interviewer-rated measures and/or diagnostic interview.
- Sample size: ≥ 40 participants
- Time: Any time from cancer diagnosis or thereafter

Articles excluded were the following:

- Meeting abstracts not subsequently published in peer-reviewed journals
- Editorials, commentaries, letters, news articles, case reports, and narrative reviews
- Publication in a non-English language.

Study Quality Assessment

Each included publication was assessed for methodological quality by one methodologist. Systematic reviews and meta-analyses were evaluated using the assessment of multiple systematic reviews rating (Data Supplement). To evaluate RCTs, research design characteristics including random assignment, allocation concealment, blinding of outcome assessment(s), baseline equivalence between groups, extent of loss to follow-up and/or missing data, and the use of intent-to-treat analyses were evaluated (Data Supplement). Each element was rated as having low, uncertain, or high risk of bias.

RESULTS

Characteristics of the Studies, Research Design Elements, and Risk of Bias

A total of 18 systematic reviews with or without meta analyses[47-64] and 48 RCTs,[65-109] one with dual publication,[100,101] met initial eligibility criteria that included post-traumatic stress disorder. Sixteen meta-analyses,[47-50,52-57,59-64] one systematic review,[58] and 44 RCTs[66-91,93,95-109] on management of anxiety and/or depression ultimately formed the updated evidentiary base for the guideline recommendations. It is noted that a substantial proportion (73%) of the RCTs did not originate from the United States, but internationally: Europe (10 studies), Asia (16 studies), Australia (four studies), and Canada (two studies). The studies are heterogeneous with respect to the following: (1) subject characteristics (disease site, stage, time since diagnosis, in active oncologic treatment or not, and with or without palliative care; social determinants of health); (2) timing of accrual and baseline assessment; (3) intervention characteristics (modality of delivery, content, use of manual, duration, and fidelity), (4) patient-reported outcomes assessments in addition to psychological symptoms; (5) comparison conditions, (6) patient intervention adherence and follow-up (presence or absence, and duration), and (7) adequacy of sample size, rigor of analytic methods, and risk of bias. Overall, the diversity in the included studies precluded a quantitative analysis and, as such, a qualitative review was performed. Summary Table 1 outlines the included studies.

Patient Characteristics

Many of the RCTs (36%) included patients with various cancer types and stages, although close to a third of studies were exclusively in patients with breast cancer. Patients with other cancer types included hematologic malignancies, and gynecologic, gastrointestinal, and genitourinary cancers. The time elapsed since cancer diagnosis ranged from less than a month to 5 years. A total of 10 studies[50,76,80,81,89,93,98,102,104,107] focused on patients with advanced cancer and/or in palliative care. The mean age of study participants ranged from 47.5 to 64 years, and the proportion of female participants varied from 11% to 100%, with the exception of one trial exclusively in men with prostate cancer.[97] For the US-based studies, ethnic and/or racial reporting varied in specificity and numbers, and participation of individuals other than European or American ranged from 1% to 73%, with 12 studies reporting <30% ethnic and/or racial minority participation. Most non-US studies did not provide ethnic and/or racial characteristics of the participants.

Research Design Elements

Accrual of study participants occurred during active oncologic treatment in 20% of all included studies and during the post-treatment phase in 41%. A total of 17 studies (28%) did not restrict participation to a particular phase of the cancer continuum and included participants both during and after oncologic treatment. A notable advance in the literature was the use of depression and/or anxiety screening and elevated symptom criteria for enrollment, an important element emphasized in the prior guideline.[7] Of the 44 RCTs,

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TABLE 1. Included Studies

Primary Outcome(s) Interventions	Publication Type and No.	Summary of Results[a]
Depression or depression and anxiety	17 systematic reviews ± meta-analysis[47-50,52-64]	Data Supplement
Depression		
Psychological/social ± educational components or ± pharmacologics	11 RCTs[b,68,69,72,74,77,93,98,100,101,103,105,106]	Data Supplement
Combination psychological + pharmacologic interventions	3 RCTs[99,102,107]	
Physical activity/exercise + diet	1 RCT[96]	
Anxiety		
Psychological/social interventions	3 RCTs[73,76,85]	Data Supplement
Both depression and anxiety		
Psychological/social interventions with or without educational components	19 RCTs[67,70,75,78-84,87,88,90,91,97,104,109-111]	Data Supplement
Physical activity, exercise, and rehab	2 RCTs[71,95]	
Pharmacologic interventions	5 RCTs[66,86,89,108,112]	Data Supplement

Abbreviation: RCT, randomized controlled trial.

[a]Available in the Data Supplement.

[b]One RCT was available in two publications.

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screening criteria of some type were used in 15 studies or 34% (42% [eight of 19] of depression studies; 33% [one of three] of anxiety studies; and 27% [six of 22] of depression plus anxiety studies) and not used in 66% of trials. Sample sizes ranged from 62 to 500 in the RCTs using screening and 74 to 2,140 in RCTs with unscreened participants.

Intervention Characteristics

The included studies used a variety of psychological interventions including, either alone or in combination, cognitive behavior therapy (CBT), information, counseling, education, problem-solving therapy, behavioral activation (BA), psychotherapy, PA, and pharmacologic interventions (Table 2). The majority of the interventions were delivered face-to-face, although 12 studies involved remote options including telephone or virtual sessions. The duration of the interventions in the nonpharmacologic studies ranged from a single session to 24 sessions spanning 12 months.

Comparison Conditions

For the 55 nonpharmacologic studies, the intervention arm was most often compared with a treatment-as-usual (TAU) control (36 studies). However, approximately one third of studies included two or more active treatment arms, either with an additional control arm (seven studies) or without (12 studies).

Assessment of Change

Anxiety and/or depression treatment outcomes were assessed only before and after treatment in 17 RCTs and before, after, and with follow-up in 27 trials. Follow-up was <3 months in seven studies and extended to 3 months or more in 20 studies. An important methodologic advance was inclusion of process measures, that is, assessment during the course of treatment, seen in 17 RCTs, in addition to outcome measures.

Study Quality and Rigor of Analytic Methods

Study quality was formally assessed for all 61 studies identified. For systematic reviews and meta-analyses, assessment of multiple systematic reviews scores ranged from 8 to 11 out of a possible 11 points (higher scores indicate higher quality; Data Supplement). For RCTs, overall risk of bias ranged from low to high (Data Supplement). For the nonpharmacologic RCTs (39 studies), only four (10%) trials had low risk of bias across all domains.[96,97,104,107] Many trials had small sample sizes and/or high attrition rates impacting statistical power and lowering confidence in the findings. Indeed, the most common domain of high-risk bias, found in 53% of RCTs, was missing data from attrition due to drop out, loss to follow-up, or patients continuing in the trial but missing assessments for other causes (eg, illness, administrative error, etc). Data missingness elevates the risk of bias as the listed circumstances are nonrandom, and missingness is made worse by not determining its origins. High mortality can be expected in trials accruing patients with advanced disease and/or in the palliative care setting, but even death is a nonrandom event. Also important is determining if data loss is differential across study arms. Unfortunately, few trials explored the causes of missingness or contrasted patients with complete versus incomplete (missing) data.

All but four studies[67,69,78,102] provided a statistical power calculation and some trials were underpowered to detect change, a situation worsened without screening. Also, the detection of differences between active treatments demands large sample sizes, as the experimental question is degree of improvement, not improvement per se. Despite inclusion of only randomized trials, randomization failed to establish baseline equivalence in 36% of the studies.[67,68,73,75-77,79,80,82,88,91,99,103,105] While small sample sizes substantially increase the likelihood of baseline differences, for some studies, the sample sizes were more than adequate (eg, N > 145) and yet statistically significant baseline differences were found. As is common in psychosocial intervention trials, having truly blind assessors is difficult

TABLE 2. Summary of Findings

Author Year Reference	Primary Intervention	Significant Differences in Outcomes Reported With Intervention Arm Compared With Control: Depression	Anxiety
Nonpharmacologic management			
Psychosocial interventions—CBT, information and counseling, education, psychotherapy			
Evidence from systematic reviews ± meta-analyses			
Chen 2018[48]	Telehealth with education	√	-
Fulton 2018[50]	Psychotherapy	√	√
Jassim 2015[52]	CBT	√	√
Kim 2017[53]	Self-management intervention	-	-
López-López 2019[54]	CBT	√	
Ream 2020[58]	Psychoeducation ± CBT (telephone-based)	√	√
Uphoff 2020[60]	BT (BA and PST)	√	
Wang 2020[108]	Psychoeducation (internet-delivered)	√	
Yang 2014[63]	CBT + education	√	√
Evidence from randomized controlled trials			
Balck 2019[67]	PST	-	√
Beutel 2014[68]	Psychodynamic therapy	√	
Blanco 2019[69]	IPT *v* PST *v* support	-	
Børøsund 2014[70]	Self-management intervention	√	√
Chen 2019[72]	Social skills training with health education	-	
Chow 2020[73]	Psychoeducation		-
Desautels 2018[74]	CT, BLT	√	
Dirkse 2020[a,75]	CBT (internet delivered)	-[a]	-[a]
Greer 2019[76]	CBT (via mobile app)		-
Gudenkauf 2015[77]	CBT *v* RT *v* health education	√	
Halkett 2013[78]	Radiation education	-	-
Ho 2016[79]	Supportive expressive therapy	-	-
Hoek 2017[80]	Specialist palliative care	-	√
Julião 2014[81]	Dignity therapy + palliative care	√	√
Lepore 2014[82]	Support with or without enhancement	X	X
Li 2018[83]	Education	-	-
Li 2019[84]	Education	-	√
Merckaert 2017[85]	CBT + hypnosis		√
Mohd-Sidik 2018[87]	Chemotherapy counseling + education	√	√
Murphy 2020[88]	CBT (internet delivered)	√	√
Nissen 2020[90]	CBT (internet delivered)	√	√
Ren 2019[91]	CBT	√	√
Rodin 2018[93]	Psychotherapy	√	
Schofield 2016[97]	Education and support	√	-
Serfaty 2020[98]	CBT	-	
Sharpe 2014[99]	BT	√	
Stagl 2015,[100] Stagl 2015[101]	CBT	√	
Steel 2016[102]	CBT with psychoeducation	-	

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TABLE 2. Summary of Findings (continued)

Author Year Reference	Primary Intervention	Significant Differences in Outcomes Reported With Intervention Arm Compared With Control: Depression	Anxiety
Syrjala 2018[103]	PST	-	
Tang 2019[104]	Advanced care planning	√	√
Turner 2017[105]	Psychosocial intervention	-	
Meulen 2013[106]	Psychosocial intervention	√	
Walker 2014[107]	BT	√	
Wang 2019[113]	Education	√	√
Wenzel 2015[110]	Psychosocial intervention	√	-
Zhao 2021[111]	Reminiscence therapy	√	√
Physical activity, exercise, and rehab			
Evidence from systematic reviews ± meta-analyses			
Bergenthal 2014[47]	Exercise	√	-
Dennett 2021[49]	Exercise-based rehab	√	-
McGettigan 2020[55]	Exercise	-	-
Singh 2018[59]	Exercise	√	√
Evidence from randomized controlled trials			
Chen 2015[71]	Walking exercise	√	√
Rogers 2017[95]	Physical activity behavior change	√	√
Saxton 2014[96]	Exercise	√	
Mind-body interventions or MBSR			
Evidence from systematic reviews ± meta-analyses			
Oberoi 2020[56]	MBI	√	√
Xunlin 2020[62]	MBI	√	√
Zhang 2019[64]	MBSR	√	√
Pharmacologic management			
Evidence from systematic reviews ± meta-analyses			
Ostuzzi 2018[57]	Antidepressants	-	
Evidence from randomized controlled trials			
Alamdarsaravi 2017[66]	Celecoxib	√	
Mohammadinejad 2015[86]	Celecoxib	√	
Ng 2014[89]	MTZ + MPH	√	
Wang 2020[108]	Ketamine	√	
Zhao 2020[112]	Sufentanil + dezocine	√	-

NOTE. √, difference in outcomes favoring intervention; X, difference in outcomes not favoring the intervention; -, no significant differences reported between groups.

Abbreviations: BA, behavioral activation; BLT, bright light therapy; BT, behavioral therapy; CBT, cognitive behavior therapy; CT, cognitive therapy; IPT, interpersonal therapy; MBI, mindfulness-based intervention; MBSR, mindfulness-based stress reduction; MPH, methylphenidate; MTZ, mirtazapine; PST, problem-solving therapy; RT, relaxation therapy.

[a]Noninferiority trial of self-guided *v* technician-guided therapy.

to achieve, making use of standardized measures and evaluation of rater reliability critical design choices.

Key Outcomes

Data on depression and anxiety outcomes are summarized in Table 2 and reported in detail in the Data Supplement.

RECOMMENDATIONS

Clinical Question

What are the recommended treatment approaches in the management of anxiety and/or depression in survivors of adult cancer?

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General Management Principles

Recommendation 1.1. All oncology patients and any patient-identified caregiver, family member, or trusted confidant should be offered information regarding depression and anxiety. They should also be offered resources, such as the providers' contact information for further evaluation and treatment within or external to the facility whenever available (Type: Evidence based; benefits outweigh harms; Evidence quality: Intermediate; Strength of recommendation: Strong).

Qualifying statement. Information should be culturally informed and linguistically appropriate and can include a conversation between clinician and patient, and/or electronic or written material on depression and anxiety. Examples of materials can be found at Cancer.Net, such as ASCO Answers Anxiety and Depression.

Recommendation 1.2. Clinicians should use a stepped-care model, that is, selecting the most effective and least resource-intensive intervention based on symptom severity, when selecting treatment for anxiety and/or depression. Other variables which may inform the choice of treatment approach include the following:

- Psychiatric history, that is, prior diagnoses, with or without treatment
- History of substance use
- Prior mental health treatment response
- Functional abilities and/or limitations related to self-care, usual activities, and/or mobility
- Recurrent or advanced cancer
- Presence of other chronic disease(s) (eg, cardiac disease)
- Member of socially and/or economically marginalized group (eg, Black race, low socioeconomic status)

(Type: Evidence based; benefits outweigh harms; Evidence quality: Intermediate; Strength of recommendation: Strong).

Recommendation 1.3. Psychological and psychosocial interventions provided by mental health practitioners should derive from manualized, empirically supported treatments. Manuals for evidence-based treatments specify content, structure, delivery mode, session number, treatment duration, and related topics. Linguistic, cultural, and socioecological contexts need to guide any treatment tailoring (Type: Evidence based; benefits outweigh harms; Evidence quality: Intermediate; Strength of recommendation: Moderate).

Recommendation 1.4. When making a referral for further evaluation or psychological care, clinicians should make every effort to reduce barriers and facilitate patient follow-through. Determining follow through to the first appointment is essential as is discovering any barriers that may have arisen for the patient. Thereafter, determining patient satisfaction and assisting with any new and/or continuing barriers would also be helpful (Type: Informal consensus; benefits outweigh harms; Evidence quality: Insufficient; Strength of recommendation: Moderate).

Recommendation 1.5. For patients who have symptoms of both depression and anxiety, treatment of depressive symptoms should be prioritized. Alternatively, treatment with a unified protocol (ie, combining CBT treatments for depression and anxiety) may be used (Type: Evidence based; benefits outweigh harms; Evidence quality: High; Strength of recommendation: Strong).

Recommendation 1.6. For patients referred and receiving psychological treatment, mental health professionals should regularly assess treatment response (eg, pretreatment, 4 weeks, 8 weeks, and end of treatment). (Type: Evidence based; benefits outweigh harms; Evidence quality: Intermediate; Strength of recommendation: Strong).

Recommendation 1.7. If pharmacologic treatment is used, the treating clinician should regularly (eg, 4 and 8 weeks) assess using standardized validated instruments, the extent of a patient's symptom relief, side effect and adverse event occurrence, and satisfaction. If symptoms are stable or worsening, the treating clinician should re-evaluate the plan and revise (Type: Informal consensus; benefits outweigh harms; Evidence quality: Insufficient; Strength of recommendation: Strong).

Recommendation 1.8. After 8 weeks of treatment for depression and/or anxiety, if there is little improvement in symptoms despite good adherence, the treating clinician should adjust the regimen (eg, add a psychological or pharmacologic intervention to a single treatment; if pharmacologic, change the medication; and if group therapy, refer to individual therapy). The same considerations may apply if patient satisfaction with treatment is low and/or barriers to treatment exist (Type: Informal consensus; benefits outweigh harms; Evidence quality: Insufficient; Strength of recommendation: Moderate).

Literature Review Update, Analysis, and Clinical Interpretation

Optimal care of depression and anxiety in cancer survivors should be delivered according to a stepped-care model, which involves assessment of severity of depression, provision of support and education, delivery of lower-intensity interventions for subthreshold, and mild to moderate depression. Higher-intensity interventions are recommended for cancer survivors with moderately severe and severe depression and for individuals who do not remit following lower-intensity intervention.[114] Stepped collaborative care interventions have been used in the primary care setting for the treatment of depression, where a combination of pharmacologic and psychological treatments are customized based on the severity of depression. The treatments are supervised by a psychiatrist, and primary care or oncology providers work collaboratively with a nurse care manager to provide psychological

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interventions and monitor treatment compliance and outcomes. This type of collaborative care is found to be superior to usual care[115] and is more cost-effective than face-to-face and pharmacologic treatment for depression. In addition to efficacy, other benefits of a stepped care model are opportunity for tailoring of patient care and optimized resource allocation.[116]

Although few recent trials investigate the effect of educational sessions, per se, to reduce depression and anxiety, the pattern of response to educational interventions is broadly in line with that identified for depression in people without a chronic physical health problem.[117-119] Effective education in people with cancer and their families includes normalizing the experience, providing information about the nature and symptoms of depression and anxiety, and specifying the nature of symptom worsening that may warrant a call to the health care provider.

Author's note: Current evidence supports that the recommended treatment interventions for depression and anxiety are effective therapeutic options. However, it is acknowledged that availability of mental health services, ease of access, time to service provision, and cost are important considerations that may vary across treatment settings. The choice of intervention to offer patients should be based on shared decision making, taking into account availability, accessibility, patient preference, likelihood of adherence, and cost.

Treatment and Care Options for Depressive Symptoms

Recommendation 2.1. For patients with moderate to severe depressive symptoms, culturally informed and linguistically appropriate information should be provided to patients and patient-identified caregivers, family members, or trusted confidants. Information might include the following: the commonality (frequency) of depression, common psychological, behavioral, and vegetative symptoms, signs of symptom worsening, and indications to contact the medical team (with provision of contact information). (Type: Evidence based; benefits outweigh harms; Evidence quality: Intermediate; Strength of recommendation: Strong).

Recommendation 2.2. For a patient with **moderate** symptoms of depression, clinicians should offer individual or group therapy with any one of the following treatment options:

- Cognitive therapy or CBT
- BA
- Structured PA and exercise
- Mindfulness-based stress reduction (MBSR)
- Psychosocial interventions using empirically supported components (eg, relaxation, problem solving).

(Type: Evidence based; benefits outweigh harms; Evidence quality: Intermediate; Strength of recommendation: Strong).

Recommendation 2.3. For a patient with **severe** symptoms of depression, clinicians should offer individual therapy with any one of the following treatment options:

- Cognitive therapy or CBT
- BA
- MBSR
- Interpersonal therapy

(Type: Evidence based; benefits outweigh harms; Evidence quality: Intermediate; Strength of recommendation: Strong).

Recommendation 2.4. Treating clinicians may offer a pharmacologic regimen for depression in patients without access to first-line treatment, those expressing a preference for pharmacotherapy, or those who do not improve following first-line psychological or behavioral management. Pharmacotherapy should also be considered for patients with a history of treatment response to medications, severe symptoms, or accompanying psychotic features (Type: Evidence based; benefits outweigh harms; Evidence quality: Low; Strength of recommendation: Weak).

Qualifying statement. Despite the limitations and weak evidence for pharmacologic management, empirically there is some evidence of benefit to warrant their inclusion as an alternative option.

Please refer to the treatment algorithm in Figure 1 for symptomatology severity and a visual representation of these recommendations.

Depression: Literature review update, analysis, and clinical interpretation. Interventions for managing depressive symptoms or MDD were evaluated in four meta-analyses and 20 RCTs. Meta-analyses[54,60,61] confirm findings from many prior ones[120-122] that when delivered to adults without cancer, CBT in particular, behavior therapy (BT), and BA are the most efficacious treatments for treating MDD. Moreover, the López-López[54] analyses document robust positive effects for both CBT and internet-delivered CBT, in studies using face-to-face, hybrid, or multimedia formats, in contrast to increased levels of depression found in waitlist control participants.

Depression outcomes in RCTs were assessed in multiple ways, with self-reports (Beck Depression Inventory-Second Edition and Center for Epidemiologic Studies Depression Scale) predominant and some use of structured diagnostic interviews (Hamilton Depression Rating Scale [HAM-D] and Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders). Twelve studies of psychological or social therapies with or without educational components were identified, with half screening patients for enrollment.[68,69,74,98,105,106] In studies using screening, all patients were described as being in the postoncologic treatment phase. In studies with high-quality ratings, RCT evidence supports the benefit of CBT. CBT was also found to be superior to bright light therapy.[74] There was a single RCT support for

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psychosocial interventions[106] and psychotherapy,[68] with no differences in whether the psychotherapy was described and/or delivered as being interpersonal, problem-solving, or supportive.[69] Some studies with null effects were of lower methodological quality[103,105] and/or potentially hampered by using an enhanced TAU control rather than a TAU control.[69,98]

In studies not screening patients for enrollment, CBT plus BT (relaxation)[77,100] and education plus self-care[123] significantly improved depression. Although evidence of long-term benefit has been reported,[101] the generalizability of this finding is limited. Study participants included in the long-term follow-up were older and reported fewer depressive symptoms and greater well-being at the time of diagnosis than those who did not participate.[101] Moreover, a self-report bias may have played a role in the measures collected.[101] Trials of problem-solving therapies alone,[103] or behavior change programs[72] did not show a statistically significant benefit for depression. However, neither of these trials included participants above a threshold for depressive symptoms. One RCT evaluating a combined physical exercise and healthy eating treatment versus usual care for post-treatment female breast cancer patients demonstrated a significant effect on depression at 6 months.[96]

Two trials investigated patients with advanced disease or patients in palliative care settings. In one trial of screened patients with mixed cancer types, no significant difference between CBT versus TAU[98] was found; however, uptake of CBT was limited, reducing the likelihood of detecting a treatment effect. The other trial[93] with unscreened patients found reductions in depressive symptoms with individual supportive psychotherapy compared with TAU.

The effectiveness of collaborative care approaches in the treatment of depression in screened patients with cancer was found in two[99,107] of three trials.[99,102,107] Depression care consisting of individually delivered multicomponent behavioral therapy, including BA and problem-solving, significantly reduced depressive symptoms compared with treatment as usual in patients with nonadvanced cancer,[99] as well as in lung cancer patients with advanced disease.[107] It was shown that depression treatment that was integrated with medical care, intensive, and systematically delivered by a well-trained and supervised team had large and sustained effects. A published meta-analysis,[115] which included these two studies along with five other RCTs, confirmed that collaborative care interventions were significantly more effective than usual care (standardized mean difference, −0.49; $P = .003$), and depression reduction was maintained at 12 months. A less intensive intervention, that is, a collaborative care coordinator and a patient accessed web site providing CBT components, did not produce a significant improvement in depression compared with enhanced usual care for unscreened patients with advanced cancer.[102]

Comparative effectiveness studies indicated similar effects across different models of psychological interventions. As such, the panel does not make a recommendation for a specific therapy for initial treatment among the recommended models of CBT, BA, structured PA, MBSR, and psychosocial interventions with empirically supported components. However, the historical weight of evidence for CBT and BA is most compelling. Combined treatment using CBT or interpersonal psychotherapy with a pharmacologic agent may be an option for partial or nonresponders to initial psychological interventions.[124]

Pharmacologic management was investigated in a 2018 Cochrane review of antidepressant use in cancer patients with MDD and no difference between antidepressants (as a class) and placebo on symptoms of depression at 6-12 weeks was found.[57] The Cochrane review concluded that the evidence for medications compared with placebo was of low certainty based on the limited number and low quality of studies. Also, head-to-head comparisons of selective serotonin reuptake inhibitors versus tricyclic antidepressants showed no difference.[57]

Two RCTs, not included in the Cochrane review, investigated the effect of celecoxib, a nonsteroidal anti-inflammatory drug that acts via the selective inhibition of cyclooxygenase (COX)-2, on depression at 4 and 6 weeks in patients with cancer.[66,86] The RCT by Mohammadinejad found significantly decreased HAM-D scores at 4 and 6 weeks compared with diclofenac, a nonselective COX-1 and COX-2 inhibitor, but no statistically significant different in response rates (<50% reduction in HAM-D scores) at those time points.[86] The RCT by Alamdarsaravi found significantly decreased HAM-D scores at 4 and 6 weeks compared with placebo, and significantly more responders at 6 weeks.[66] However, both trials were small, with 52 and 40 participants, respectively, and included samples in which a COX-2 inhibitor might have also contributed to improved physical symptoms. In terminally ill patients with cancer, methylphenidate as add-on therapy to mirtazapine improved antidepressant response from the third day of treatment onward, and resulted in clinically significant improved response rate, as measured by the Montgomery-Åsberg Depression Rating Scale, from the second week onward.[89] However, this early antidepressant response in terminally ill patients with cancer was associated with an increased risk of nervous system adverse events.

These guidelines make no recommendations about any specific pharmacologic regimen being better than another. The choice of an antidepressant should be informed by current empirical evidence; 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.[44] Patients should be warned of potential harm or adverse effects.

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Treatment and Care Options for Anxiety Symptoms

Recommendation 3.1. For patients with moderate to severe anxiety symptoms, culturally informed and linguistically appropriate information should be provided to patients and patient-identified caregivers, family members, or trusted confidants. Information might include the following: commonality (frequency) of stress and anxiety, psychological, behavioral, and cognitive symptoms, indications of symptom worsening, and medical team contact information (Type: Evidence based; benefits outweigh harms; Evidence quality: Intermediate; Strength of recommendation: Strong).

Recommendation 3.2. For a patient with **moderate** symptoms of anxiety, clinicians should offer individual or group therapy with any one of the following treatment options:

- CBT
- BA
- Structured PA and exercise
- Psychosocial interventions with empirically supported components (eg, relaxation, problem solving)

(Type: Evidence based; benefits outweigh harms; Evidence quality: Intermediate; Strength of recommendation: Strong).

Recommendation 3.3. For a patient with **severe** symptoms of anxiety, clinicians should offer individual therapy with any one of the following treatment options:

- CBT
- BA
- MBSR
- Interpersonal therapy

(Type: Evidence based; benefits outweigh harms; Evidence quality: Intermediate; Strength of recommendation: Strong).

Recommendation 3.4. Treating clinicians may offer a pharmacologic regimen for anxiety in patients without access to first-line treatment, those expressing a preference for pharmacotherapy, or those who do not improve following first-line psychological or behavioral management (Type: Evidence based; benefits outweigh harms; Evidence quality: Low; Strength of recommendation: Weak).

Please refer to the treatment algorithm in Figure 2 for symptomatology severity and a visual representation of these recommendations.

Anxiety: Literature review update, analysis, and clinical interpretation. Interventions for managing anxiety disorders or anxiety symptoms were evaluated in only three RCTs identified in the updated literature search.[73,76,85] None of the interventions could be characterized as testing empirically supported anxiety treatments (eg, BA, exposure) but rather stress reduction strategies (eg, relaxation, hypnosis), with some addition of behavioral therapy strategies (activity planning, problem solving), or education. A group intervention combining CBT, hypnosis, and support yielded significantly reduced anxiety compared with standard care enhanced with support for female breast cancer survivors.[85] A psychoeducational intervention for gynecologic surgery patients[73] and BT provided via a mobile app for patients with metastatic disease had no effect compared with an attention control or mobile health education app control, respectively.[76] Despite the limitations of the new evidence, responses are in accordance with previous research for treatment of anxiety in people with cancer.[125-129] In particular, psychosocial interventions, stress reduction strategies, and a combination of CBT, hypnosis, and support are effective over standard care. With no newer pharmacologic trials identified for management of anxiety, previous evidence[130,131] with noncancer patients supports pharmacologic treatment as an addition or as an alternative in those who do not respond to recommended first-line psychological and/or behavioral management.

Depression and anxiety: Literature review update, analysis, and clinical interpretation. Interventions for managing both depression and anxiety were evaluated in 12 meta-analyses and one systematic review. In 11 of the meta-analyses, CBT was evaluated and all found CBT to result in significant reductions in depressive and anxiety symptoms. This was also the case if additional therapies were included, such as second-wave therapies (MBSR, acceptance, and commitment therapy).[50] A systematic review of 21 studies showed CBT and other interventions, when delivered either face-to-face or by telephone, to improve anxiety and depression in patients with cancer.[58]

Meta-analyses in patients with cancer report that exercise both during and after cancer treatment provides a moderate to large reduction in depression and may offer a reduction in anxiety. In a meta-analysis of 14 studies with over 900 patients, Singh et al[59] reported a large effect in favor of exercise compared with usual care for both depression and anxiety. While evidence from other meta-analyses support the benefit of exercise for depression, no significant benefit was found for anxiety.[47,49] The meta-analysis by McGettigan et al[55] found no significant difference in depression nor anxiety with PA in the short term or medium term. Two additional RCTs not already included in the systematic reviews reported a statistically significant reduction in both depression and anxiety with PA interventions compared with control with no PA intervention.[71,95]

Meta-analyses evaluating the impact of MBSR interventions during and after cancer treatment demonstrate statistically significant improvements in both depression and anxiety compared with usual care.[56,62,64] One of these meta-analyses reported that mindfulness-based interventions were associated with a reduction in the severity of depression and anxiety in both the short term and medium term, but not in the long term.[56]

There were 22 additional RCTs not summarized in the meta-analyses and systematic review. Outcomes were predominantly self-reported depression (Beck Depression Inventory-Second Edition, Center for Epidemiologic Studies

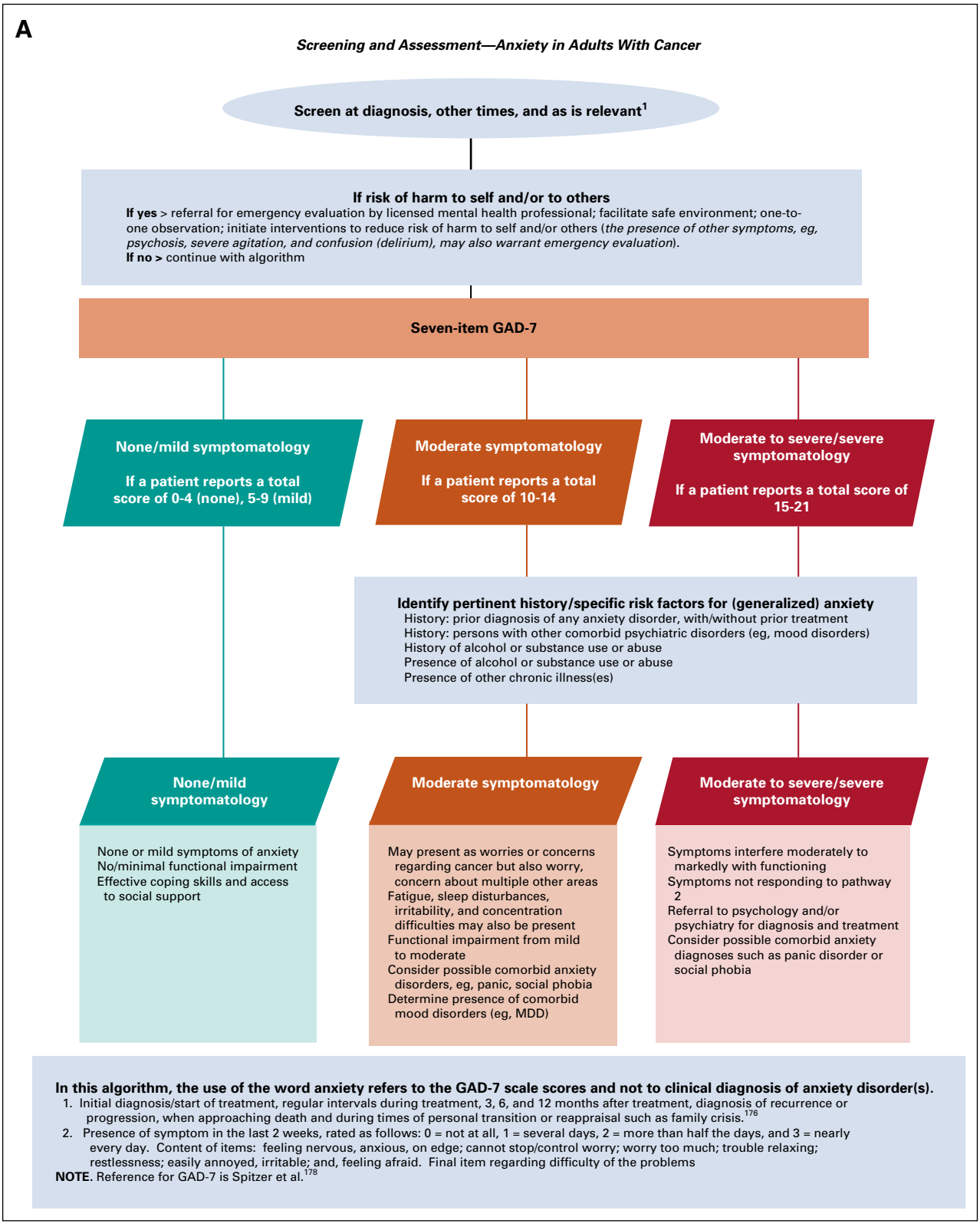

FIG 2. Anxiety algorithm. (A) Screening and assessment—anxiety in adults with cancer. (B) Care map—generalized anxiety in adults with cancer. GAD, generalized anxiety disorder; MDD, major depressive disorder. (continued on following page)

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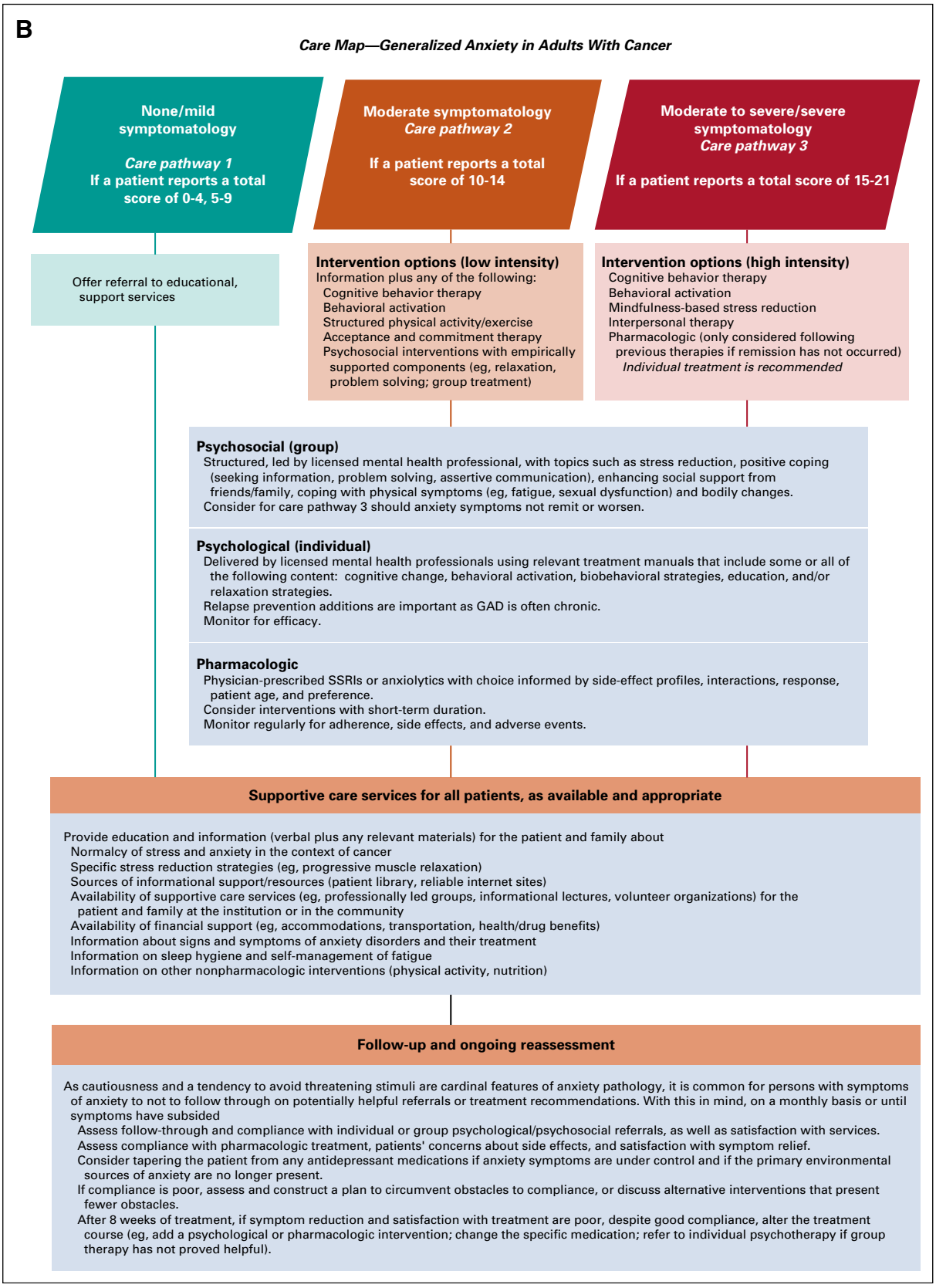

FIG 2. (Continued).

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Depression Scale, and Patient Health Questionnaire-9) and anxiety (Hospital Anxiety and Depression Scale and State-Trait Anxiety Inventory) symptoms or distress (Symptom Checklist-90), with some use of diagnostic interviews (HAM-D, Hamilton Anxiety Rating Scale, and Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders). Statistically significant benefits were seen for various management strategies across the comorbid symptoms. There were two notable improvements in the literature. First, several studies included assessments during the course of treatment (eg, Zhao[111]), and second, post-treatment follow-up data were provided in eight studies (36%) to test for sustained effects of interventions.

Consistent with the meta-analyses, all trials of CBT[75,88,90,91] and BT (ie, problem solving)[67] showed significant effects on anxiety with the majority showing significant effects for depression as well. The Ren study[91] is notable for showing significant effects for CBT in comparison with both attention control and TAU arms. The one noninferiority trial comparing internet-delivered CBT without coaching versus with coaching[75] showed no significant differences and improvements occurred for both groups, contrasting with meta-analyses showing stronger post-treatment effects when coaching is used.[132]

Three RCTs were conducted in palliative care settings or with palliative care specialists. Unique to these studies was the inclusion of multiple assessments (some extending through 12 months) and a final post-treatment assessment. Interventions were similarly themed, including dignity therapy,[81] advanced care planning,[104] and telehealth with a palliative care specialist.[80] All treatments were successful in significantly reducing anxiety and depressive symptoms, with the exception of the Hoek trial,[80] which found null effects on depressive symptoms. Risk of bias was low in one trial,[104] with the others having high risk of bias in two[80] or three[81] key areas.

Excluding the studies of education only, many of the remaining trials are single examples of experimenter-developed treatments. Some components of the tested treatments may have empirical support (eg, problem solving), whereas other components do not (eg, diary keeping). Such approaches limit the interpretation of the findings, and hinder replication by other investigators and the accumulation of knowledge supporting one treatment over another. Studies in this category include efforts by Børøsund,[70] Li,[84] Schofield,[97] Wang,[113] and Wenzel.[110]

It is useful to consider the studies showing null effects, assuming adequate statistical power, as they provide valuable information for future research. For example, both Halkett[78] and Li[83] provided educational sessions to patients about to receive radiotherapy. Noteworthy for each is the brevity of the intervention, one described as a single session and another being 3 hours. It is unknown if the sessions aided patients' understanding of receive radiotherapy, but there is no evidence from RCTs to suggest such efforts would impact anxiety or depressive symptoms. In a noninferiority trial, Lepore[82] used an internet support group context to compare one enhanced support group (members received individual prompts to reach out to help others) to one not enhanced. Analyses showed worsened outcomes for those in the enhanced condition. These data align with earlier trials showing negative effects for peer support conditions,[133] countering assumptions of peer support being uniformly beneficial. Finally, Ho[79] reported null effects for both supportive expressive therapy and a mind-body-spirit intervention compared with an unstructured peer support group.

DISCUSSION

Following the 2014 guideline[7] emphasizing screening and recommending measures for the assessment of depression and anxiety symptoms, this guideline reiterates the importance of screening for mental health conditions and prepares oncology and mental health professionals to take next steps when elevations of symptoms are found—specifically, to conduct further evaluation to determine symptom severity, to refer for treatment if warranted, and to determine choice among empirically supported treatments. Since the 2014 guideline, screening is a care aim that has been disseminated, but the principle and procedures remain to be fully implemented.[134,135] The Expert Panel recognizes that psychological symptom screening remains aspirational for some settings, but considerable progress toward this standard of care has been made,[136] as witnessed by the inclusion since 2015 of screening for distress as an accreditation criterion for cancer centers seeking Commission on Cancer certification. As for management, our systematic review shows CBT and BA achieve robust effects on symptom reduction. This contrasts with the limited, low-quality evidence for pharmacotherapies.

As emphasized in the 2014 ASCO guideline, the following topics remain important in this update. *Education*: Many hospitals or centers provide patient-tailored cancer treatment-related information on surgery, chemotherapy, immunotherapy, and related topics. We recommend that general (first-level) materials on coping with stress, anxiety about treatment, and depression be routinely provided as well. For individuals with elevated symptoms, validation and normalizing patients' experiences is crucial, with provision of information such as common signs and symptoms of anxiety and/or depression, types of treatments used, and pathways for treatment. *Screening timing*: While not the focus of this updated review, it is recognized that how and when patients with cancer and survivors are screened are important determinants of timely management of anxiety and depression.[7] The period between diagnosis and start of treatment is an essential time for first screening, as one third of patients report experiencing significant psychological distress during this period.[35] Yet, the need remains thereafter; many of the interventions reviewed were delivered after primary oncologic treatments were completed. *Risk correlates*: Anxiety and depressive symptoms and disorders are not randomly distributed. Correlates of elevated symptoms include those with a current or prior psychiatric

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diagnosis, other chronic medical conditions, adverse social determinants of health, and poor functional status, among others (Table 3). *Stepped care*: As in the previous version,[7] the guideline defines levels for screening follow-up to achieve patient care that is tailored, efficient, and cost-effective.

It is relevant to note that the focus on depression and anxiety specifically in cancer remains comparatively new, preceded by decades of RCTs of psychological and psychosocial interventions focused on stress reduction and enhancing coping, and, occasionally, improving health behaviors or adherence. Psychological screening for trial entry was rare, with the majority of study participants (60%-70%) likely having no or few symptoms of generalized anxiety or major depression, and patients with the latter were more often excluded from trial participation. Even so, some trials with positive effects on other dimensions (ie, where anxiety or depression were not among the primary outcomes) were also found to effectively treat adults with depression.[137,138] In this context, today's focus on cancer survivors with the greatest psychological need is a significant advance. For them, the predominant affective, cognitive, and behavioral disruptor is depression. This circumstance is recognized by RCT investigators, as 95% of the reviewed studies focused on depression alone or with comorbid anxiety. Our recommendation remains to treat depression first with proven cognitive and/or behavioral therapies, or alternatively, consider the transdiagnostic unified protocol for emotional disorders.[139-141]

TABLE 3. Risk Factors for Anxiety and Depression in Cancer

Risk Factor
Medical
Advanced disease
Intense or aggressive treatment(s); multiple treatments
Higher symptom/side effect, adverse event burden
Comorbid medical conditions
Few rehabilitative options
Poor patient/doctor relationship
Personal
Prior psychiatric history
Past trauma history
Helpless/hopeless outlook
Low education level
Low income
Marital/interpersonal relationship conflict
Younger age (<40 years)
Social
Singleton (without marital or other partner)
Limited social contacts
Insufficient social support
Limited access to service resources
Socioenvironmental stressors
Social stigma

With respect to treatment recommendations, this systematic review enabled confirmation of previous recommendations and reference to new therapies with promising evidence. The prior guideline[7] listed CBTs and BA among the recommended treatments. This review shows these treatments continue to be first-line treatments of choice, with added support for components (eg, problem solving) used alone or in combination. The CBT and BA effects for depression and anxiety are robust, generalizing across sex, age, disease site, time in the cancer trajectory, and patients from the United States, English-speaking countries, Europe, and Asia, all consistent with large-scale population-based US tests.[142] Relevant to cost of treatment, evidence is also confirmatory for multiple modes of delivery including by app, virtually, telephone, and others.

Unlike the prior guideline,[7] pharmacotherapy is not recommended as a first-line treatment, neither alone nor in combination. The evidence is not compelling, a conclusion informed by the 2018 Cochrane review of null findings for antidepressant use for MDD in patients with cancer at 6-12 weeks, a sufficient interval in pharmacologic trials for effects to be detected.[57] The Data Supplement outlines two studies[89,108] reporting positive effects at day 3, a finding of unknown consequence, with other studies having sample sizes just within the cutoff for systematic review inclusion (N = 40). Physician choice of pharmacotherapy may be considered when there is no or low availability of mental health resources, for patients who have responded well to pharmacotherapy for depression or anxiety in the past, for patients with severe neurovegetative or agitated symptoms of depression, patients with depression with psychotic or catatonic features, and/or patient preference. In contrast to the pharmacologic only studies, two rigorous studies from the United Kingdom[99,107] both described a 10-session multicomponent BT treatment for MDD, which achieved depression remission and other gains in which medication management was also provided.

The mental health care crisis is a widespread issue that affects individuals with all types of medical conditions, including patients with cancer. Problems with access to psychological care for cancer patients with depression and/or anxiety can be attributed to organizational and workforce obstacles, such as a shortage of mental health professionals, and limited referral networks for managing depression and anxiety. The choice of intervention to offer patients facing such obstacles should be based on shared decision making, taking into account availability, accessibility, patient preference, likelihood of adverse events, adherence, and cost.

Attention to regular assessment of mental health following initial diagnosis is needed. Finding significant pre-treatment to post-treatment effects is necessary but often not sufficient to confirm treatment effectiveness with depressed or anxious patients. Adequately timed and repeated follow-ups are needed, particularly for disorders such as MDD known not to

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improve or improve and then worsen. Also, use of theoretically relevant process measures—assessments made during the course of treatment that provide confirmatory evidence that the intervention changed relevant aspects of the disorder (eg, change in daily sedentary behavior for an exercise intervention) and/or patients engaged in and/or used intervention components (eg, usage of prescribed relaxation)—enable investigators to determine effective components. To assess change more broadly, other measures could be used (eg, cancer-specific stress, coping strategies, number of sick days, cancer treatment dose received).

There are several known factors that increase the risk of suicide in patients with cancer, including older age at diagnosis, lower level of education, nonpartnered relationship status, living in rural or sparsely populated areas, psychological comorbidity, hopelessness, advanced stages of cancer, and poor performance status.[143,144] Crisis response planning should be readily implemented as a brief, practical strategy for reducing short-term suicide risk.[145] For any acutely suicidal patient, institutional management and referral policies should be followed.

LIMITATION OF THE RESEARCH AND FUTURE RESEARCH DIRECTIONS

This systematic literature review provides an opportunity for a broad consideration of research design and methodology used in the recent past. Studies can be weakened by early research design decisions that reduce the likelihood of detecting reliable and valid effects. In RCTs, screening of patients is essential (used in only one third of studies) and has the potential benefit of reducing sample size. Regarding the latter, many studies (one third) began with baseline group differences, a circumstance less likely when randomizing within strata, as variables potentially correlated with the outcome can reduce nuisance subject variance. Other decisions can reduce statistical power, such as small sample sizes in general, sizes insufficient to detect effects between active treatments, or when any sample size is reduced across time. Data loss threatens the reliability and validity of findings. As noted earlier, high mortality may be anticipated in trials accruing patients with advanced disease and/or in the palliative care setting. Other than the latter, the most common source of bias in the RCTs was attrition.

There are several key points to reflect upon regarding future research and clinical directions. Considering the reliability and generalizability of the effects for CBT, be it with individuals with or without cancer, further demonstrations would not contribute to the literature significantly. Implementation and dissemination research examining treatment guideline uptake among oncology providers generally and in community settings is needed. After screening, several action steps are needed, for example, further assessment to clarify the problem and determine if treatment is needed, identification of mental health providers for referral, and others. The pathway thereafter may not be simple. As noted previously,[7] it is common for persons with depressive symptoms to lack the motivation necessary to follow through on referrals and/or to comply with treatment recommendations. So too is the case for persons with anxiety. With this in mind, the Expert Panel recommends that the mental health professional or another member of the clinical team follow-up with the patient and provider to assure a successful transition to psychological treatment is made. It is a myth that screening takes a long time. Rather, it is the effort thereafter that is time- and resource-intense, and incurs the greatest cost for the patient when not provided.

HEALTH DISPARITIES

Although ASCO clinical practice guidelines represent expert recommendations on the best practices in disease management to provide the highest level of cancer care, it is important to note that many patients from socially or economically marginalized communities have limited access to medical care and may not receive guideline concordant care.[146] Membership in social and economically marginalized groups is defined as facing structural inequity and systemic inequality perpetuated by discriminatory, sexist, racist, homophobic, and classist sociocultural norms and governmental policy.[147] Factors such as race and ethnicity, age, socioeconomic status, sexual orientation and gender identity, geographic location, and access to medical and mental health insurance are known to impact cancer care outcomes.[148] Racial and ethnic disparities in health care contribute significantly to this problem in the United States. Patients with cancer who are members of racial and/or ethnic minorities suffer disproportionately from comorbidities, experience more substantial obstacles to receiving care, are more likely to be uninsured, and are at greater risk of receiving fragmented care or poor-quality care than other Americans.[149-152]

According to the American Association for Cancer Research 2022 progress report on cancer disparities, racial and ethnic minorities and other underserved populations shoulder a disproportionate burden of the adverse effects of cancer and cancer treatment, including physical, emotional, psychosocial, and financial challenges.[153] Survivors who are Black consistently report poorer quality of life and physical and mental health compared with cancer survivors who are White, found in studies of breast, prostate, or colorectal cancer.[153-157] Disparities in survivors' mental health remain even when sociodemographic and psychosocial factors are considered.[153,155] In addition to racial and ethnic minorities, cancer survivors who identify as sexual minorities have two to three times greater risk for depression and/or poor mental health compared with heterosexual counterparts among all races.[153,158-163] This disparity widens in survivors who are also from a racial or ethnic minority, underscoring the influence of intersectionality in cancer health disparities.[153,158]

Awareness of these disparities in access to care should be considered in the context of this clinical practice guideline, and health care providers should strive to deliver the

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highest level of cancer care to these under-resourced populations. Additionally, stakeholders should work toward achieving health equity by ensuring equitable access to both high-quality cancer care and research and addressing the structural barriers that preserve health inequities.[148,164] At the institutional level, documentation of patient descriptive characteristics, for example, race and ethnicity, gender identity, socioeconomic status, is essential. It is known that social determinants of health such as these covary with adverse cancer and mental health outcomes. Collection of such data will enable institutions to monitor their status in achieving timely and equitable cancer treatment and mental health coverage for all.

EXTERNAL REVIEW AND OPEN COMMENT

The draft recommendations were released to the public for open comment from September 19 through October 3, 2022. Response categories of "Agree as written," "Agree with suggested modifications" and "Disagree. See comments" were captured for every proposed recommendation with 126 written comments received from 28 respondents. Two draft statements achieved 100% agreement, 10 achieved >90% agreement, and four draft statements received >85% agreement. None of the draft recommendations achieved <85% agreement. Expert Panel members reviewed comments from all sources and determined whether to maintain original draft recommendations, revise with minor language changes, or consider major recommendation revisions. All changes were incorporated before Evidence Based Medicine Committee review and approval.

The draft was submitted to two external reviewers with content expertise. It was rated as high quality, and it was agreed it would be useful in practice.

GUIDELINE IMPLEMENTATION

ASCO guidelines are developed for implementation across health settings. Each ASCO guideline includes a member from ASCO's Practice Guideline Implementation Network (PGIN) on the panel. The additional role of this PGIN representative on the guideline panel is to assess the suitability of the recommendations to implementation in the community setting, but also to identify any other barriers to implementation a reader should be aware of. Barriers to implementation include the need to increase awareness of the guideline recommendations among front-line practitioners and survivors of cancer and their caregivers, and also to provide adequate services in the face of limited resources. The guideline Bottom Line Box was designed to facilitate implementation of recommendations. This guideline will be distributed widely through the ASCO PGIN. ASCO guidelines are posted on the ASCO website and most often published in the *Journal of Clinical Oncology*.

ASCO believes that cancer clinical trials are vital to inform medical decisions and improve cancer care, and that all patients should have the opportunity to participate.

ADDITIONAL RESOURCES

More information, including a supplement with additional evidence tables, slide sets, and clinical tools and resources, is available at www.asco.org/survivorship-guidelines. Patient information is available at www.cancer.net.

GENDER-INCLUSIVE LANGUAGE

ASCO is committed to promoting the health and well-being of individuals regardless of sexual orientation or gender identity.[164] Transgender and nonbinary people, in particular, may face multiple barriers to oncology care including stigmatization, invisibility, and exclusiveness. One way exclusiveness or lack of accessibility may be communicated is through gendered language that makes presumptive links between gender and anatomy.[172-175] With the acknowledgment that ASCO guidelines may impact the language used in clinical and research settings, ASCO is committed to creating gender-inclusive guidelines. For this reason, guideline authors use gender-inclusive language whenever possible throughout the guidelines. In instances in which the guideline draws upon data based on gendered research (eg, studies regarding women with ovarian cancer), the guideline authors describe the characteristics and results of the research as reported.

RELATED ASCO GUIDELINES

- Screening, Assessment, and Care of Anxiety and Depressive Symptoms in Adults with Cancer[7] (https://ascopubs.org/doi/10.1200/jco.2013.52.4611)
- Exercise, Diet, and Weight Management during Cancer Treatment[165] (https://ascopubs.org/doi/10.1200/JCO.22.00687)
- Screening, Assessment, and Management of Fatigue in Adult Survivors of Cancer[166] (https://ascopubs.org/doi/10.1200/jco.2013.53.4495)
- Integrative Medicine for Pain Management in Oncology[167] (https://ascopubs.org/doi/10.1200/JCO.22.01357)
- Management of Chronic Pain in Survivors of Adult Cancers[168] (https://ascopubs.org/doi/10.1200/JCO.2016.68.5206)
- Interventions to Address Sexual Problems in People With Cancer[169] (https://ascopubs.org/doi/10.1200/JCO.2017.75.8995)
- Integration of Palliative Care into Standard Oncology Care[170] (http://ascopubs.org/doi/10.1200/JCO.2016.70.1474)
- Patient-Clinician Communication[171] (http://ascopubs.org/doi/10.1200/JCO.2017.75.2311)

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EDITOR'S NOTE

This American Society of Clinical Oncology (ASCO) Clinical Practice Guideline provides recommendations, with comprehensive review and analyses of the relevant literature for each recommendation. Additional information, including a supplement with additional evidence tables, slide sets, clinical tools and resources, and links to patient information at www.cancer.net, is available at www.asco.org/survivorship-guidelines.

EQUAL CONTRIBUTION

B.L.A. and J.H.R. were Expert Panel cochairs.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Management of Anxiety and Depression in Adult Survivors of Cancer: ASCO Guideline Update

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Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

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Barbara Given
Patents, Royalties, Other Intellectual Property: Symptom Management Toolkit. The toolkit is an evidence-based guide of self-care strategies to assist patients to manage their cancer and cancer treatment symptoms (side effects) during and following active treatment. This guide is written at a 7th grade reading level. It is organized according to frequently asked questions including strategies to manage symptoms, and what and when symptom status needs to be reported to professionals. This self-care management toolkit has been used with over 1,000 patients who were in active treatment for their cancer. It was licensed with MSU in approximately 2004 and has been used by companies such as Genentech and Anthem who adapted it for a smartphone app.

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APPENDIX

TABLE A1. Recommendations on Screening and Assessment of Depression and Anxiety

Recommendation
Screening for 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 (ie, post-treatment, recurrence, progression) and transition to palliative and end-of-life care.
The CAPO and the Canadian Partnership Against Cancer (the Partnership) guideline Assessment of Psychosocial Health Care Needs of the Adult Cancer Patient suggests screening at initial diagnosis, start of treatment, regular intervals during treatment, end of treatment, post-treatment or at transition to survivorship, at recurrence or progression, advanced disease, when dying, and during times of personal transition or reappraisal such as family crisis, during post-treatment survivorship, and when approaching death.[a]
Screening should be done using a valid and reliable measure that features reportable scores (dimensions) that are clinically meaningful (established cutoffs).[a]
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.
As a first step for all patients, identification of the presence or absence of pertinent history or risk factors (see Depression Algorithm, Fig 1) is important for subsequent assessment and treatment decision making.
As a second step, two items from the PHQ-9 can be used to assess for the classic depressive symptoms of low mood and anhedonia. For individuals endorsing either item (or both) as occurring for more than half of the time or nearly every day within the last two weeks (ie, a score of > 2), a third step is suggested in which the patient completes the remaining items of the PHQ-9. It is estimated that 25%-30% of patients would need to complete the remaining items.
The traditional cutoff for the PHQ-9 is > 10. The Panel's recommended cutoff score of > 8 is based on a study of the diagnostic accuracy of the PHQ-9 with cancer outpatients. A meta-analysis by Manea et al also supports the > 8 cutoff score.
For patients completing the latter step, it is important to determine the associated sociodemographic, psychiatric or health comorbidities, or social impairments, if any, and the duration that depressive symptoms have been present.
Of special note, one of remaining seven items of the PHQ-9 assesses thoughts of self-harm, ie, thoughts that you would be better off dead or hurting yourself in some way. Among patients with moderate to severe or severe depression, such thoughts are not rare. Having noted that, it is the frequency and/or specificity of the thoughts that are most important vis-à-vis risk. Some clinicians/practices may choose to omit the item from the PHQ-9 and administer 8 items. It should be noted, however, that doing so may artificially lower the score, with the risk of some patients appearing to have fewer symptoms than they actually do. Such changes also weaken the predictive validity of the score and the clarity of the cutoff scores. It is important to note that individuals do not typically endorse a self-harm item exclusively or independent of other symptom; rather, it occurs with several other symptom endorsements. Thus, it is the patient's endorsement of multiple symptoms that will define the need for services for moderate/severe to severe symptomatology.
Consider special circumstances in the assessment of depressive symptoms. These include but are not limited to the following: (1) Use culturally sensitive assessments and treatments as is possible, (2) tailor assessment or treatment for those with learning disabilities or cognitive impairments, and (3) be aware of the difficulty of detecting depression in the older adult.
Assessment of depressive symptoms
Specific concerns such as risk of harm to self and/or others, severe depression or 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, with designation of those who are expected to conduct assessments as per scope of practice.[a]
The assessment should identify signs and symptoms of depression, the severity of cancer symptoms (eg, fatigue), possible stressors, risk factors, and times of vulnerability. A range of problem checklists is available to guide the assessment of possible stressors. Clinicians can amend checklists to include areas not represented or ones unique to their patient populations.
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 (eg, interferon administration) should be determined and treated.
As a shared responsibility, the clinical team must decide when referral to a psychiatrist, psychologist, or equivalently trained professional is needed. This includes, for example, all patients with a PHQ-9 score in the severe range or patients in moderate range but with pertinent history/risk factors. Such would be determined using measures with established reliability, validity, and utility (eg, cutoff or normative data available) or standardized diagnostic interviews for assessment and diagnosis of depression.

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TABLE A1. Recommendations on Screening and Assessment of Depression and Anxiety (continued)

Recommendation
Screening for anxiety
All health care providers should routinely screen for the presence of emotional distress and specifically symptoms of anxiety from the point of diagnosis onward.[a]
All patients should be screened for distress at their initial visit, at appropriate intervals and as clinically indicated, especially with changes in disease status (ie, post-treatment, recurrence, progression) and when there is a transition to palliative and end-of-life care.[a]
The CAPO and the Canadian Partnership Against Cancer (the Partnership) guideline Assessment of Psychosocial Health Care Needs of the Adult Cancer Patient suggests screening at initial diagnosis, start of treatment, regular intervals during treatment, end of treatment, post-treatment or at transition to survivorship, at recurrence or progression, advanced disease, when dying, and during times of personal transition or reappraisal such as family crisis, during post-treatment survivorship, and when approaching death.[a]
Screening should be done using a valid and reliable tool that features reportable scores (dimensions) that are clinically meaningful (established cutoffs).[a]
Anxiety disorders include specific phobias and social phobia, panic and agoraphobia, GAD, obsessive compulsive disorder, and 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 (eg, social anxiety disorder).
Use of the GAD-7 scale is recommended.
Patients with GAD do not necessarily present with symptoms of anxiety, per se. The pathognomic GAD symptom, ie, multiple excessive worries, may present as concerns or fears. Whereas cancer worries may be common for many, GAD worry or fear may be disproportionate to actual cancer-related risk (eg, excessive fear of recurrence, worry about multiple symptoms or symptoms not associated with current disease or treatments). Importantly, an individual with GAD has worries about a range of other, noncancer topics and areas of his/her life.
It is important to determine the associated home, relationship, social, or occupational impairments, if any, and the duration of anxiety-related symptoms. As noted above, problem checklists can be used. Clinicians can amend the checklists to include additional key problem areas or ones unique to their patient populations.
As with depressive symptoms, consider special circumstances in screening/assessment of anxiety including using culturally sensitive assessments and treatments and tailoring assessment or treatment for those with learning disabilities or cognitive impairments.
Assessment of anxiety
Specific concerns such as risk of harm to self and/or others, severe anxiety or agitation, or the presence of psychosis or confusion (delirium) requires referral to a psychiatrist, psychologist, physician, or equivalently trained professional.
When moderate to severe or severe symptomatology is detected through screening, individuals 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 (ie, all patients with a score in the moderate to severe or severe range, with certain accompanying factors and/or symptoms, identified using valid and reliable measures for assessment of symptoms of anxiety).
Assessments should be a shared responsibility of the clinical team, with designation of those who are expected to conduct assessments as per scope of practice.[a]
The assessment should identify signs and symptoms of anxiety (eg, panic attacks, trembling, sweating, tachypnea, tachycardia, palpitations, and sweaty palms), severity of symptoms, possible stressors (eg, impaired daily living), risk factors and times of vulnerability, and should also explore underlying problems/causes.[a]
A patient considered to have severe symptoms of anxiety following the further assessment should, where possible, have confirmation of an anxiety disorder diagnosis before any treatment options are initiated (eg, DSM-V, which may require making a referral).

NOTE. Evidence supporting these unchanged recommendations is reviewed in the 2014 guideline publication.[7] The sections that follow present the recommendations adapted from the Pan-Canadian guideline,[44] on screening and assessment for depressive symptoms, followed by recommendations for anxiety symptoms.

Abbreviations: ASCO, American Society of Clinical Oncology; CAPO, Canadian Association of Psychosocial Oncology; DSM, Diagnostic and Statistical Manual of Mental Disorders; GAD, generalized anxiety disorder; PHQ-9, Patient Health Questionnaire-9; PTSD, post-traumatic stress disorder.

[a]Recommendations are verbatim from the Pan Canadian guideline. Otherwise, recommendations are the ones adapted by the ASCO panel.

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TABLE A2. Recommendation Rating Definitions

Term	Definitions
Quality of evidence	
High	High confidence that the available evidence reflects the true magnitude and direction of the net effect (eg, balance of benefits *v* harms) and further research is very unlikely to change either the magnitude or direction of this net effect.
Intermediate	Intermediate confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research is unlikely to alter the direction of the net effect; however, it might alter the magnitude of the net effect.
Low	Low confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research may change the magnitude and/or direction of this net effect.
Insufficient	Evidence is insufficient to discern the true magnitude and direction of the net effect. Further research may better inform the topic. Reliance on consensus opinion of experts may be reasonable to provide guidance on the topic until better evidence is available.
Strength of recommendation	
Strong	There is high confidence that the recommendation reflects best practice. This is based on: Strong evidence for a true net effect (eg, benefits exceed harms); Consistent results, with no or minor exceptions; Minor or no concerns about study quality; and/or The extent of panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a strong recommendation.
Moderate	There is moderate confidence that the recommendation reflects best practice. This is based on: Good evidence for a true net effect (eg, benefits exceed harms); Consistent results with minor and/or few exceptions; Minor and/or few concerns about study quality; and/or The extent of panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a moderate recommendation.
Weak	There is some confidence that the recommendation offers the best current guidance for practice. This is based on: Limited evidence for a true net effect (eg, benefits exceed harms); Consistent results, but with important exceptions; Concerns about study quality; and/or The extent of panelists' agreement. Other considerations (discussed in the guideline's literature review and analyses) may also warrant a weak recommendation.

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TABLE A3. Management of Anxiety and Depression in Adult Survivors of Cancer Guideline Expert Panel Membership

Name	Affiliation	Role or Area of Expertise
Barbara L. Andersen, PhD (cochair)	The Ohio State University, Columbus, OH	Psychology
Julia H. Rowland, PhD (cochair)	Smith Center for Healing and the Arts, Washington, DC	Psychology
Kimlin Ashing, PhD	City of Hope, Duarte, CA	Psychology
Jonathan S. Berek, MD, MMS	Stanford University School of Medicine, Palo Alto, CA	Medical Oncology—Gynecologic Oncology
Barry S. Berman, MD	Florida Cancer Specialists, West Palm Beach, FL	PGIN Representative
Sage Bolte, PhD	Inova Health Foundation, Falls Church, VA	Patient Advocate
Don S. Dizon, MD	Legorreta Cancer Center at Brown University and Lifespan Cancer Institute, Providence, RI	Medical Oncology—Breast and Pelvic Malignancies
Barbara Given, PhD, RN	Michigan State University, East Lansing, MI	Nursing
Larissa Nekhlyudov, MD, MPH	Brigham and Women's Hospital and Dana-Farber Cancer Institute, Boston, MA	Primary Care, Cancer Survivorship
William Pirl, MD, MPH	Dana-Farber Cancer Institute, Boston, MA	Psychiatry
Annette L. Stanton, PhD	University of California, Los Angeles, Los Angeles, CA	Psychology
Christina Lacchetti, MHSc	ASCO, Alexandria, VA	ASCO Practice Guideline Staff (Health Research Methods)

Abbreviations: ASCO, American Society of Clinical Oncology; PGIN, Practice Guideline Implementation Network.