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Integrative Oncology Care of Symptoms of Anxiety and Depression in Adults With Cancer: Society for Integrative Oncology–ASCO Guideline

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ABSTRACT

PURPOSE To provide evidence-based recommendations to health care providers on integrative approaches to managing anxiety and depression symptoms in adults living with cancer.

METHODS The Society for Integrative Oncology and ASCO convened an expert panel of integrative oncology, medical oncology, radiation oncology, surgical oncology, palliative oncology, social sciences, mind-body medicine, nursing, methodology, and patient advocacy representatives. The literature search included systematic reviews, meta-analyses, and randomized controlled trials published from 1990 through 2023. Outcomes of interest included anxiety or depression symptoms as measured by validated psychometric tools, and adverse events. Expert panel members used this evidence and informal consensus with the Guidelines into Decision Support methodology to develop evidence-based guideline recommendations.

RESULTS The literature search identified 110 relevant studies (30 systematic reviews and 80 randomized controlled trials) to inform the evidence base for this guideline.

RECOMMENDATIONS Recommendations were made for mindfulness-based interventions (MBIs), yoga, relaxation, music therapy, reflexology, and aromatherapy (using inhalation) for treating symptoms of anxiety during active treatment; and MBIs, yoga, acupuncture, tai chi and/or qigong, and reflexology for treating anxiety symptoms after cancer treatment. For depression symptoms, MBIs, yoga, music therapy, relaxation, and reflexology were recommended during treatment, and MBIs, yoga, and tai chi and/or qigong were recommended post-treatment.

DISCUSSION Issues of patient-health care provider communication, health disparities, comorbid medical conditions, cost implications, guideline implementation, provider training and credentialing, and quality assurance of natural health products are discussed. While several approaches such as MBIs and yoga appear effective, limitations of the evidence base including assessment of risk of bias, nonstandardization of therapies, lack of diversity in study samples, and lack of active control conditions as well as future research directions are discussed.
Additional information is available at www.asco.org/survivorship-guidelines.

ACCOMPANYING CONTENT

Listen to the podcast by Dr Rowland at guideline.libsyn.com

Appendix

Data Supplement

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INTRODUCTION

Worldwide rates of cancer occurrence continue to rise, along with overall improvements in survival, such that by 2040, the 5-year prevalence of all cancers is estimated to become 50.5 million people across the globe,[1] with approximately 26 million living with and beyond cancer in the United States alone.[2,3] Among this expanding cohort of cancer survivors (referred to throughout this guideline as people with cancer to include those living with any stage of cancer), mental

THE BOTTOM LINE

Integrative Oncology Care of Symptoms of Anxiety and Depression in Adults With Cancer: Society for Integrative Oncology–ASCO Guideline

Guideline Questions

1. What integrative therapies are recommended for managing symptoms of anxiety experienced after diagnosis or during active treatment in adults with cancer?
2. What integrative therapies are recommended in managing symptoms of anxiety experienced post treatment in adults with cancer?
3. What integrative therapies are recommended for managing symptoms of depression experienced after diagnosis or during active treatment in adults with cancer?
4. What integrative therapies are recommended in managing symptoms of depression experienced post treatment in adults with cancer?

Target Population

Adults with cancer experiencing symptoms of anxiety and/or depression.

Target Audience

Clinicians who provide care to people with cancer, people with cancer, their family members, and other informal caregivers.

Methods

An Expert Panel was convened to develop clinical practice guideline recommendations based on a systematic review of the clinical oncology literature.

Recommendations

Anxiety

Active treatment.

Recommendation 1.1. Mindfulness-based interventions (MBIs) should be offered to people with cancer to improve anxiety symptoms during active treatment (Type: Evidence based; Quality of evidence: High; benefits outweigh harms; Strength of recommendation: Strong).
Recommendation 1.2. Yoga may be offered to people with breast cancer to improve anxiety symptoms during active treatment (Type: Evidence based; Quality of evidence: Intermediate; benefits outweigh harms; Strength of recommendation: Moderate).
Qualifying statement: For people with cancer types other than breast, the quality of evidence is low, and the strength of recommendation is weak.
Recommendation 1.3. Hypnosis may be offered to people with cancer to improve anxiety symptoms during cancer-related diagnostic and treatment procedures (Type: Evidence based; Quality of evidence: Intermediate; benefits outweigh harms; Strength of recommendation: Moderate).
Recommendation 1.4. Relaxation therapies may be offered to people with cancer to improve anxiety symptoms during active treatment (Type: Evidence based; Quality of evidence: Intermediate; benefits outweigh harms; Strength of recommendation: Moderate).
Recommendation 1.5. Music therapy or music-based interventions may be offered to people with cancer to improve anxiety symptoms during active treatment (Type: Evidence based; Quality of evidence: Low; benefits outweigh harms; Strength of recommendation: Moderate).
Recommendation 1.6. Reflexology may be offered to people with cancer to improve anxiety symptoms during active treatment (Type: Evidence based; Quality of evidence: Low; benefits outweigh harms; Strength of recommendation: Weak).
Recommendation 1.7. Lavender essential oil inhalation may be offered to people with cancer to improve anxiety symptoms during cancer-related diagnostic and treatment procedures (Type: Evidence based; Quality of evidence: Low; benefits outweigh harms; Strength of recommendation: Weak).

Post treatment.

Recommendation 2.1. MBIs should be offered to people with cancer to improve anxiety symptoms post treatment (Type: Evidence based; Quality of evidence: High; benefits outweigh harms; Strength of recommendation: Strong).
Recommendation 2.2. Yoga may be offered to people with breast cancer to improve anxiety symptoms post treatment (Type: Evidence based; Quality of evidence: Intermediate; benefits outweigh harms; Strength of recommendation: Moderate).
Qualifying statement: For people with cancers types other than breast the quality of evidence is low, and the strength of recommendation is weak.

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THE BOTTOM LINE (CONTINUED)

Recommendation 2.3. Acupuncture may be offered to women with breast cancer to improve anxiety symptoms post treatment (Type: Evidence based; Quality of evidence: Intermediate; benefits outweigh harms; Strength of recommendation: Weak).
Recommendation 2.4. Tai chi and/or qigong may be offered to women with breast cancer to improve anxiety symptoms post treatment (Type: Evidence based; Quality of evidence: Intermediate; benefits outweigh harms; Strength of recommendation: Weak).
Recommendation 2.5. Reflexology may be offered to people with cancer to improve anxiety symptoms post treatment (Type: Evidence based; Quality of evidence: Low; benefits outweigh harms; Strength of recommendation: Weak).
Inconclusive. There is inconclusive evidence to make recommendations for or against music therapy and music-based interventions to improve anxiety symptoms in people with cancer who are post treatment. There is also inconclusive evidence for nutritional interventions, light therapy, psilocybin, massage, dance/movement therapy, laughter therapy, healing touch, expressive writing, acupressure, biofeedback, autogenic training, energy healing, melatonin, or other natural products and supplements to improve anxiety symptoms in people with cancer, regardless of when in the course of care the intervention is provided.

Depression

Active treatment.

Recommendation 3.1. MBIs should be offered to people with cancer to improve depression symptoms during active treatment (Type: Evidence based; Quality of evidence: High; benefits outweigh harms; Strength of recommendation: Strong).
Recommendation 3.2. Yoga may be offered to people with breast cancer to improve depression symptoms during active treatment (Type: Evidence based; Quality of evidence: Intermediate; benefits outweigh harms; Strength of recommendation: Moderate).
Qualifying statement: For people with other cancers the quality of evidence is low, and the strength of recommendation is weak.
Recommendation 3.3. Music therapy or music-based interventions may be offered to people with cancer to improve depression symptoms during active treatment (Type: Evidence based; Quality of evidence: Low; benefits outweigh harms; Strength of recommendation: Moderate).
Recommendation 3.4. Relaxation therapies may be offered to people with cancer to improve depression symptoms during active treatment (Type: Evidence based; Quality of evidence: Low; benefits outweigh harms; Strength of recommendation: Weak).
Recommendation 3.5. Reflexology may be offered to people with cancer to improve depression symptoms during active treatment (Type: Evidence based; Quality of evidence: Low; benefits outweigh harms; Strength of recommendation: Weak).

Post treatment.

Recommendation 4.1. MBIs should be offered to people with cancer to improve depression symptoms post treatment (Type: Evidence based; Quality of evidence: High; benefits outweigh harms; Strength of recommendation: Strong).
Recommendation 4.2. Yoga may be offered to people with breast cancer to improve depression symptoms post treatment (Type: Evidence based; Quality of evidence: Intermediate; benefits outweigh harms; Strength of recommendation: Moderate).
Qualifying statement: For people with other cancers the quality of evidence is low, and the strength of recommendation is weak.
Recommendation 4.3. Tai chi and/or qigong may be offered to people with breast cancer to improve depression symptoms post treatment (Type: Evidence based; Quality of evidence: Intermediate; benefits outweigh harms; Strength of recommendation: Weak).
Recommendation 4.4. Expressive writing should not be offered to people with cancer to improve depression symptoms at any point in the course of care (Type: Evidence based; Quality of evidence: Intermediate; no net benefit; Strength of recommendation: Moderate).
Inconclusive. There is inconclusive evidence to make recommendations for or against reflexology to improve depression symptoms in people with cancer who are post treatment. There is also inconclusive evidence for nutritional interventions, light therapy, psilocybin, massage therapy, biofeedback, autogenic training, energy healing, melatonin, and other natural products and supplements to improve depression symptoms in people with cancer, regardless of when in the course of care these therapies are provided.

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THE BOTTOM LINE (CONTINUED)

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

Additional Resources

Definitions for the quality of the evidence and strength of recommendation ratings are available in Appendix Table A1, online only. More information, including a supplement with additional evidence tables, slide sets, and clinical tools and resources, is available at https://integrativeonc.org/practice-guidelines/guidelines and www.asco.org/survivorship-guidelines. The Society for Integrative Oncology (SIO) Guidelines Methodology Manual (available at https://integrativeonc.org/practice-guidelines/sio-guidelines-guidelines-methodology) and the ASCO Methodology Manual (available at www.asco.org/guideline-methodology) provide additional information about the methods used to develop this guideline. Patient information is available at https://integrativeonc.org/knowledge-center/patients and www.cancer.net.

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

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health concerns have become more prominent. Indeed, the 12-month prevalence rates for mental disorders are higher in people with cancer compared with the general population (odds ratio, 1.28 [95% CI, 1.14 to 1.45]).[4] A systematic review (SR) of 210 studies reported the mean prevalence of clinical depression as 21.2%, across all types of cancers.[5] Rates of depressive disorder diagnoses were reported at 24.6% across 24 studies of people diagnosed with advanced cancers in palliative care settings.[6] Similarly, a meta-analysis of 40 studies across 15 low- and middle-income countries reported a pooled prevalence of 21% for major depression among people with cancer.[7] Rates of anxiety symptoms are similar, with a meta-analysis of 44 studies in over 50,000 longer-term cancer survivors reporting a 17.9% prevalence of self-reported elevated anxiety symptoms,[8] consistent with other SRs, one of which reported rates ranging from 3.4% to 43% in longer-term survivors (pooled prevalence: 21%).[9] Rates of anxiety and distress tend to be even higher around the time of diagnosis, as patients are experiencing the initial shock and implications of their diagnosis, decreasing somewhat as they move into active treatment.[10] Importantly, research shows that people with mental health conditions who have a concurrent general medical condition (including cancer), have increased risk of death and shorter life expectancy than the general population.[11]

Despite their ubiquity, psychologic symptoms among people with cancer often remain undertreated.[10] With the added burden of the COVID-19 pandemic, many people with cancer have had decreased access to mental health support at a time when there is even more uncertainty, fear, and anxiety than prior to the pandemic.[12,13] This has culminated in a mental health crisis, not only among people with cancer but more broadly in society since the onset of the pandemic in 2020.[14,15]

A recently published ASCO guideline addressed the question "What are the recommended psychosocial, behavioral, and psychopharmacologic treatment approaches in the management of anxiety and/or depression in survivors of adult cancer?"[16] This represented an update of the earlier 2014 ASCO guideline on the optimum screening, assessment, and care of anxiety and depressive symptoms in adults with cancer.[17] This current Society for Integrative Oncology (SIO)–ASCO guideline addresses the question of which integrative therapies are also recommended for treating these symptoms. Taken together, these guidelines provide a comprehensive set of recommendations for assessing and treating anxiety and depression in adults with cancer.

Integrative oncology is defined by SIO as "a patient-centered, evidence-informed field of cancer care that uses mind and body practices, natural products, and/or lifestyle modifications from different traditions alongside conventional cancer treatments. Integrative oncology aims to optimize health, quality of life, and clinical outcomes across the cancer care continuum and to empower people to prevent cancer and become active participants before, during, and beyond cancer treatment."[18(p7)] Grouped together, these therapies are sometimes called complementary therapies; however, they are referred to as integrative therapies throughout this guideline to emphasize the point that for optimal patient-centered care, they are intended to be fully integrated into routine oncology practice.

Integrative therapies such as those mentioned in the definition are commonly used by people with cancer, with worldwide usage in approximately half of all people with cancer in both developed[19,20] and low- and middle-income regions.[21] A review of studies from 18 countries with over 65,000 people with cancer found the highest usage rates in the United States and the lowest in Italy and the Netherlands. Globally, integrative therapy use rose from an estimated 25% in the 1970s and 1980s to more than 32% in the 1990s and to 49% after 2000.[22] Another 2019 SR of 61 research articles from around the world included people with all types of cancers and reported an average complementary therapy usage rate of 51%.[23]

Given the high usage of integrative therapies by people diagnosed with cancer, and the growing evidence base to support their use in this context, development of this

guideline was jointly convened by SIO and ASCO to critically review the current evidence and produce recommendations on the use of integrative therapies for treating anxiety and depression symptoms in people with cancer across the disease trajectory. Specific objectives are described in the Bottom Line Box.

GUIDELINE QUESTIONS

This clinical practice guideline addresses four overarching clinical questions: (1) What integrative therapies are recommended for managing symptoms of anxiety experienced after diagnosis or during active treatment in adults with cancer? (2) What integrative therapies are recommended in managing symptoms of anxiety experienced post treatment in adults with cancer? (3) What integrative therapies are recommended for managing symptoms of depression experienced after diagnosis or during active treatment in adults with cancer? and (4) What integrative therapies are recommended in managing symptoms of depression experienced post treatment in adults with cancer?

METHODS

Guideline Development Process

This SR-based guideline was developed by an international multidisciplinary Expert Panel, which included a patient representative and a health research methodologist (Appendix Table A2). The Expert Panel met via webinar and corresponded through e-mail. Based on the evidence, the authors were asked to contribute to the development of the guideline, provide critical review, and finalize the guideline recommendations. The guideline recommendations were available for an open comment period of 2 weeks, allowing the public to review and comment on the recommendations after submitting a confidentiality agreement. These comments were taken into consideration while finalizing the recommendations. Members of the Expert Panel were responsible for reviewing and approving the penultimate version of the guideline, which was then circulated for external review by the SIO Clinical Practice Guidelines Committee and the ASCO Evidence Based Medicine Committee. Upon their approval, it was submitted to the *Journal of Clinical Oncology* for editorial review and consideration for publication. All funding for the administration of the project was provided by SIO.

The recommendations were developed through a SR of the evidence identified via online searches of PubMed (1990-November 2021) and Cochrane Library (1990-November 2021) of phase III randomized clinical trials (RCTs), SRs, and meta-analysis. An updated search of PubMed was done from November 2021 to January 2023. Articles were selected for inclusion in the SR based on the following criteria:

- Population: Adults with cancer experiencing symptoms of anxiety and/or depression during any stage of their cancer trajectory
- Interventions: Integrative interventions for anxiety and depression management (see details in the Data Supplement, online only)
- Comparisons: No intervention, waitlist, usual care or standard care, guideline-based care, active control, attention control, placebo, or sham interventions
- Outcomes: Changes in symptoms of anxiety and depression measured by valid tools reported as primary or secondary outcome
- Sample size: Minimum total sample size of 50

Articles were excluded from the SR if they were (1) meeting abstracts not subsequently published in peer-reviewed journals; (2) editorials, commentaries, letters, news articles, case reports, and narrative reviews; or (3) published in a non-English language. Ultimately, the Expert Panel used effect sizes computed in the SRs to inform the recommendations and in cases where the SRs did not pool data based on outcomes of interest, the primary studies were evaluated individually.

The guideline recommendations were crafted, in part, using the *Guidelines into Decision Support* methodology and accompanying BRIDGE-Wiz software (Yale University, New Haven, CT).[24] Ratings for type and strength of the recommendation and evidence quality are provided with each recommendation. The project methodologist in collaboration with the Expert Panel co-chairs and the full Expert Panel evaluated the quality of the evidence for each trial using the Cochrane risk-of-bias tool,[25] and SRs and meta-analyses were assessed for quality using the assessment of multiple SRs (AMSTAR-2) tool.[26]

The SIO and ASCO Expert Panel and guidelines staff will work with co-chairs to keep abreast of any substantive updates to the guideline. Based on formal review of the emerging literature, SIO will determine the need to update the guideline in the future. The SIO Guidelines Methodology Manual (available at https://integrativeonc.org/practice-guidelines/sio-guidelines-guidelines-methodology) provides additional information about the guideline update process.

OPEN COMMENT REVIEW

The draft recommendations were released to the public for open comment from October 25 through November 8, 2022, with invitations distributed to 34 organizations. There were 17 respondents in total, representing integrative oncology (seven), medical oncology (two), clinical psychology (two), guideline methodology (two), nursing (two), family medicine (one), and patient advocacy (one). Response categories of "Agree as written," "Agree with suggested modifications," and "Disagree. See comments" were captured for every proposed recommendation, with 79 written comments received. A total of 88% of the responses either agreed or

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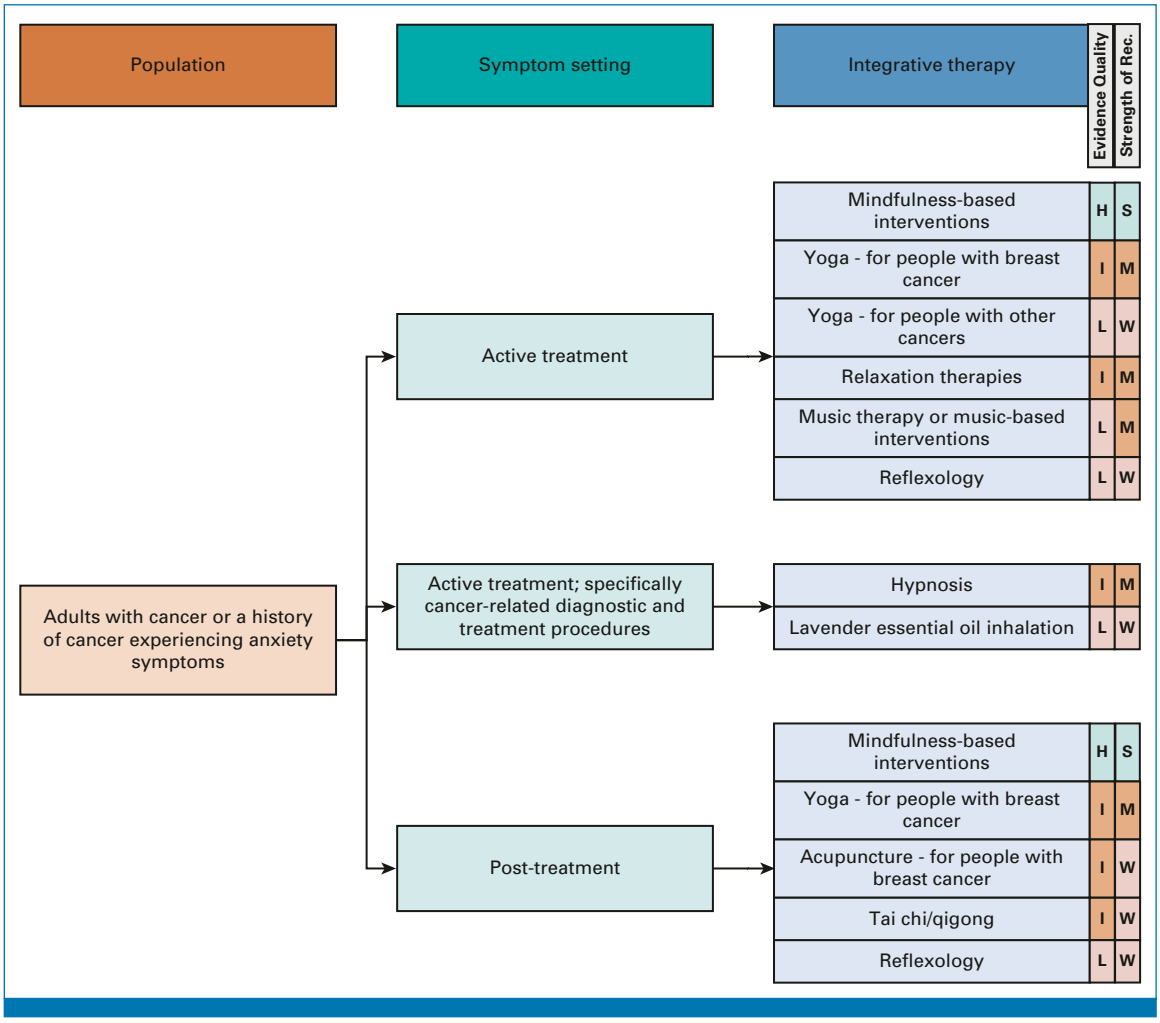

FIG 1. Integrative therapies algorithm for anxiety symptoms.

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agreed with slight modifications to the recommendations and 12% of the responses disagreed. 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 prior to SIO and ASCO review and approval.

Guideline Disclaimer

The Clinical Practice Guidelines and other guidance published herein are provided by the SIO and ASCO to assist health care providers in clinical decision making alongside the people diagnosed with cancer that they serve. 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 clinician to select other courses of action in individual cases. In all cases, the selected course of action should be considered by the treating provider in the context of treating the individual patient. Use of the information is voluntary. SIO and ASCO do not endorse third party drugs, devices, services, therapies, apps, or programs used to diagnose, treat, monitor, manage, or alleviate health conditions. SIO and ASCO provide this information on an "as is" basis and make no

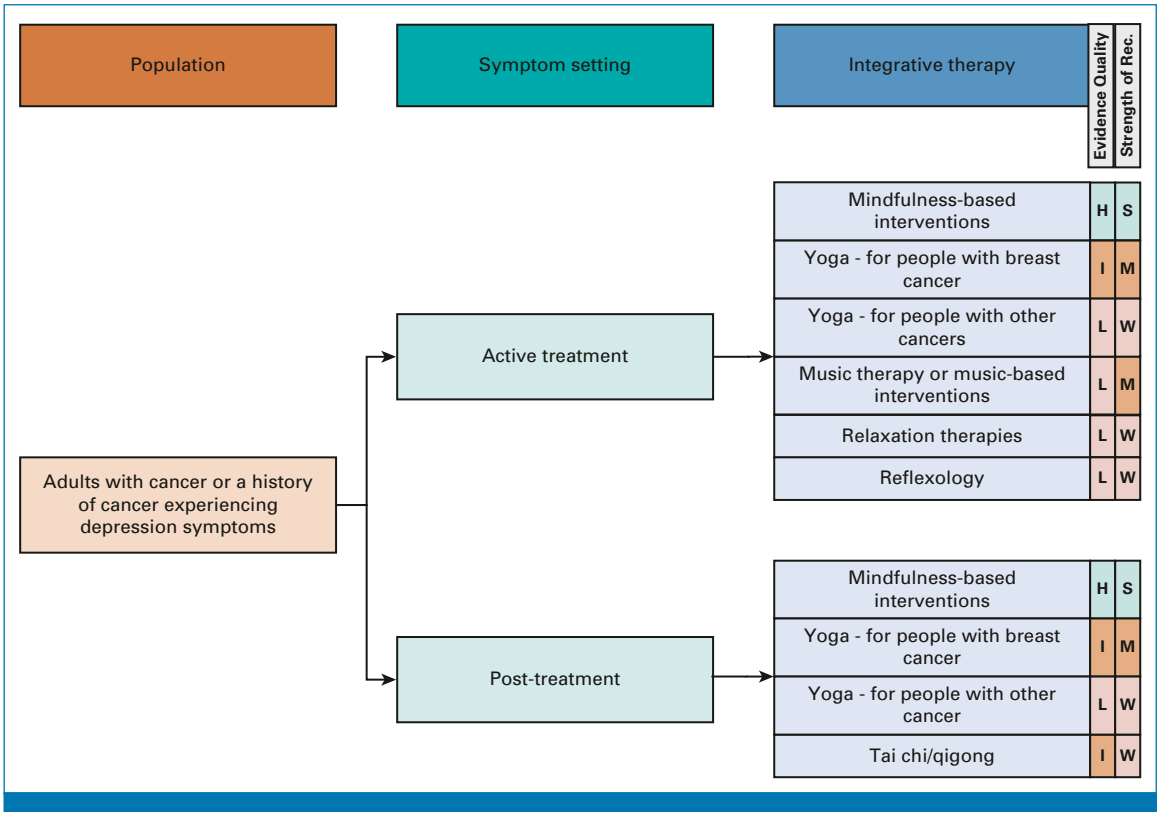

FIG 2. Integrative therapies algorithm for depression symptoms.

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Guideline and Conflicts of Interest

The Expert Panel was assembled in accordance with SIO's and ASCO's Conflict of Interest Policy Implementation for Clinical Practice Guidelines ("Policy," found at https://integrativeonc.org/practice-guidelines/sio-guidelines-guidelines-methodology and https://www.asco.org/guideline-methodology). All members of the Expert Panel completed SIO'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 because 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 disclosed no relationships that would constitute conflict under the Policy.

RESULTS

Characteristics of Studies Identified in the Literature Search

A total of 5,144 publications were identified in the literature search. After applying the eligibility criteria, 30 SRs and meta-analyses and 80 RCTs remained, forming the evidentiary basis for the guideline recommendations. Table 1[27-102] and Table 2[103-136] include a breakdown of the included studies by integrative therapies and anxiety or depression symptoms outcome. Studies were also classified as including participants in active treatment, post treatment (those who had completed their definitive therapy but who, in the case of breast cancer survivors, might remain on adjuvant hormonal therapy), or in the palliative care setting (stage IV cancer or hospice). The SRs included a mix of populations, while a small number of the RCTs were mixed as well (Appendix Tables A3 and A4).

The identified studies were published between 1990 and 2023. The RCTs compared various integrative therapies to standard of care, placebos, sham interventions, other interventions, or active controls. The primary outcome for most of the studies included change in anxiety and depression symptoms, which were measured with some commonly used standardized tools (Appendix Table A5).

Characteristics of the included studies and the PRISMA flow diagram for the SR are provided in the Data Supplement.

Study Quality Assessment

Study design aspects related to individual study quality and risk of bias were assessed. Thirty SRs and meta-analyses were assessed for quality using the AMSTAR-2 tool.[26] The rating for the overall confidence in the results of the review was critically low in 73% (22/30); low in 10% (3/30); moderate in 7% (2/30); and high in 10% (3/30). The AMSTAR-2 critical domains that contributed to the critically low rating for most studies included a priori protocol, list of excluded studies with reason, potential impact of risk of bias, and heterogeneity or publication bias. Design elements, such as masking, allocation concealment, sufficient sample size, intention-to-treat, and funding sources, were assessed for each RCT using the Cochrane risk-of-bias tool.[25] The assessment result ranged from low risk of bias for randomization in 78% (62/80) of trials to high risk of bias for blinding of participants and personnel in 79% (63/80) of the trials. In addition, 53% of the studies reported allocation concealment, while 29% reported masking of outcome assessors. The included studies were also heterogeneous with respect to patient populations, sample size, methodologic quality, treatment duration, and outcome measures. Refer to the Data Supplement for quality rating scores and the Methodology Manual for more information and for definitions of ratings for overall potential risk of bias.

RECOMMENDATIONS

Anxiety

Clinical Question 1

What integrative therapies are recommended for managing symptoms of anxiety experienced after diagnosis or during active treatment in adults with cancer?

Recommendation 1.1. Mindfulness-based interventions (MBIs) should be offered to people with cancer to improve anxiety symptoms during active treatment (Type: Evidence based; Quality of evidence: High; benefits outweigh harms; Strength of recommendation: Strong).

Literature review and clinical interpretation. This recommendation is based on seven SR papers published since 2017,[48-54] which reviewed 7-29 individual RCTs including 1,094-3,476 individual participants. However, some of these do not apply to people with cancer during treatment, as many of the studies included individuals post treatment. For example, in the largest SR by Oberoi et al,[48] 10 of 29 studies enrolled participants both during and after treatment, but only two included participants solely during active treatment, who had thyroid cancer (n = 120)[137] and leukemia (n = 65).[138] These studies had particularly large standardized mean differences (SMDs) favoring the MBI of 0.94[137] and 2.4[138] compared with control groups. Additionally, in the studies that included mixed groups of participants both during and after treatment SMDs were in the medium sized range of about 0.2-0.5, with some higher outliers (eg, Lorca et al,[139] SMD, 1.33).

Recommendation 1.2. Yoga may be offered to people with breast cancer to improve anxiety symptoms during active treatment (Type: Evidence based; Quality of evidence: Intermediate; benefits outweigh harms; Strength of recommendation: Moderate).

Qualifying statement: For people with cancer types other than breast, the quality of evidence is low, and the strength of recommendation is weak.

Literature review and clinical interpretation. Six SRs have evaluated the effect of yoga on anxiety in people with cancer.[96-101] Most SRs and multiple RCTs included a mix of participants on active treatment and post-treatment survivors. Few studies included active control conditions (exceptions include Banerjee et al and Porter et al).[140,141] In one SR, subgroup analyses revealed medium effects of yoga on anxiety in studies conducted during treatment (N = 7, g = −0.508) and in those using active controls (N = 3, g = −0.441).[96] The evidence base includes a preponderance of studies of women with breast cancer. One SR[99] focused on yoga for women undergoing chemotherapy for breast cancer only and reported moderate effects, without heterogeneity, on anxiety (five RCTs, n = 412). Only minor adverse events have been reported.[96] Thus, despite weak evidence overall and intermediate evidence in women with breast cancer, the potential benefits outweigh risk of harm, such that yoga may be offered to patients to reduce anxiety during cancer treatment.

SRs have reported benefits of yoga interventions immediately or up to approximately 6 months post-intervention. Few studies have included people with metastatic cancer (eg, Porter et al).[141] Thus, the benefits of yoga for people with metastatic cancer and intervention duration in people with localized or regionally advanced cancer requires further study.

Recommendation 1.3. Hypnosis may be offered to people with cancer to improve anxiety symptoms during cancer-related diagnostic and treatment procedures (Type: Evidence based; Quality of evidence: Intermediate; benefits outweigh harms; Strength of recommendation: Moderate).

Literature review and clinical interpretation. This recommendation is based on nine RCTs published between 2005 and 2021.[39-47] Notably, the moderate strength of this recommendation is based on sample sizes that range from 50 to 201 participants per study. Overall, studies that applied hypnosis to address anxiety in the context of a diagnostic or treatment procedure, such as central venous port implantation, showed the greatest effectiveness. For instance, a recent RCT conducted by Etienne et al[45] investigated the effects of hypnotherapy on anxiety during placement of a capsaicin patch, compared with music or usual care in a sample of 69 patients with cancer (n = 23 per group) experiencing post-treatment neuropathic pain. While hypnotherapy and music

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TABLE 1. Studies on Interventions With Sufficient Evidence to Inform Recommendations

Interventions	Study Type	No.	Symptom Categories
Acupuncture	RCT	3	Anxiety and depression[27-29]
Aromatherapy (inhalation)	RCT	6	Anxiety[30-34] Anxiety and depression[35]
Expressive writing	SR	1	Depression[36]
	RCT	2	Depression[37,38]
Hypnosis	RCT	9	Anxiety[39-45] Anxiety and depression[46,47]
Mindfulness-based interventions	SR	7	Anxiety and depression[48-54]
	RCT	7	Depression[55,56] Anxiety and depression[57-61]
Music therapy and music-based interventions	SR	4	Anxiety and depression[62-65]
	RCT	4	Anxiety[66-68]
Reflexology	RCT	9	Anxiety[69-72] Anxiety and depression[73-77]
Relaxation techniques	SR	4	Anxiety and depression[78-81]
	RCT	5	Anxiety and depression[82-86]
Tai chi and qigong	SR	4	Depression[87,88] Anxiety and depression[89,90]
	RCT	5	Depression[91,92] Anxiety and depression[93-95]
Yoga	SR	6	Anxiety and depression[96-101]
	RCT	1	Depression[102]

NOTE. RCTs already included in the meta-analyses are not included in this count.
Abbreviations: RCT, randomized controlled trial; SR, systematic review.

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were both found to reduce procedural anxiety, hypnotherapy was superior in alleviating anxiety post-procedure. Evidence also supports the use of digital tools for the application of hypnosis in alleviating anxiety. Specifically, research by Sánchez-Jáuregui et al[46] used pre-recorded hypnotherapy provided in MP3 format, which suggests the use of such technology can improve accessibility of this modality. Cumulatively, the evidence regarding the use of hypnosis for anxiety in people undergoing procedures in the context of cancer care indicates benefit with minimal risk of adverse effects.

Recommendation 1.4. Relaxation therapies may be offered to people with cancer to improve anxiety symptoms during active treatment (Type: Evidence based; Quality of evidence: Intermediate; benefits outweigh harms; Strength of recommendation: Moderate).

TABLE 2. Studies on Interventions With Inconclusive Evidence to Inform Recommendations

Interventions	Study Type	No.	Symptom Categories
Acupressure	RCT	1	Anxiety[103]
Dance/movement therapy	SR	1	Anxiety and depression[104]
	RCT	1	Anxiety and depression[105]
Dietary supplements	RCTs	4	Anxiety and depression[106-109]
Healing touch or therapeutic listening	RCTs	3	Anxiety and depression[110-112]
Laughter therapy	RCT	1	Anxiety and depression[113]
Light therapy	RCTs	1	Depression[114]
Massage	SRs	2	Anxiety and depression[115,116]
	RCTs	4	Anxiety and depression[117-120]
Natural products	SR	1	Anxiety and depression[121]
	RCTs	9	Anxiety and depression[122-130]
Nutritional interventions	RCTs	3	Anxiety and depression[131-134]
Psilocybin-assisted therapy	RCTs	2	Anxiety and depression[135,136]

NOTE. RCTs already included in the meta-analyses are not included in this count.
Abbreviations: RCT, randomized controlled trial; SR, systematic review.

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Literature review and clinical interpretation. The strongest data supporting this recommendation comes from studies during active treatment, often postsurgically or during chemotherapy or radiation therapy. Of the relaxation therapies, most evidence supports progressive muscle relaxation (PMR) and a combination of guided imagery, relaxation, and breathing interventions. A 2022 SR of 12 RCTs of PMR included nine studies in a meta-analysis.[78] All of the studies were conducted during chemotherapy, radiation, or recovery from surgery, and included patients with lung, breast, colorectal, and mixed cancer types. Six of the RCTs (n = 742) measured anxiety and found a large overall SMD of −1.32 comparing PMR to various controls, including usual care, education, and exercise. Among these was a large study from China where 400 women with breast cancer received either PMR once daily for 30 minutes over 5 weeks, or usual care.[142] A SMD in anxiety of −1.18 was reported for PMR compared with usual care control.

An earlier 2018 SR of seven different RCTs (conducted only with individuals with breast cancer) of PMR and visualization therapies during chemotherapy similarly reported improvements in three of four studies that measured anxiety.[79] One of the largest studies in this group included PMR with guided imagery and visualization over 3 weeks during chemotherapy for 236 people with breast or prostate cancer, and found significantly greater improvements in anxiety in the relaxation group with a large effect (d = 0.83).[143] Finally, a third SR of PMR for people undergoing chemotherapy included five different RCTs than the previous SR, and reported significantly greater reductions in anxiety across all four studies that included anxiety as an outcome (but meta-analysis was not conducted).[80]

Another SR and meta-analysis included 15 RCTs assessing breathing exercises for people undergoing treatment for lung cancer; of these, five studies (total n = 189) measured anxiety as secondary outcomes.[81] Three of the five found significantly greater improvements in anxiety in the breathing intervention groups compared with control, with large effect sizes. However, the overall meta-analysis was not statistically significant due to large variability among studies (SMD, −1.18 [95% CI, −2.65 to 0.28]). These studies were also rated with a high risk of bias.

Five other RCTs not included in any of the SRs assessed relaxation in 53 women with gynecologic cancers postsurgically[82]; 51 women after breast cancer surgery[83]; 52 people in Iran with mixed cancer diagnoses undergoing active treatment[84]; 81 people undergoing chemotherapy assigned to either biofeedback or relaxation therapy[85]; and 66 women with gynecologic or breast cancer receiving brachytherapy.[86]

Recommendation 1.5. Music therapy or music-based interventions may be offered to people with cancer to improve anxiety symptoms during active treatment (Type: Evidence based; Quality of evidence: Low; benefits outweigh harms; Strength of recommendation: Moderate).

Literature review and clinical interpretation. There were three recent SRs[62-64] and three RCTs[66-68] investigating the effect of music therapy and music-based interventions on anxiety in people with cancer during active treatment. A SR from 2021[62] examined the effects of music interventions on psychologic and physical outcomes in people with cancer and included a total of 81 trials. The SR included two meta-analyses related to anxiety, one for 17 trials (N = 1,381) that used the Spielberger State-Trait Anxiety Inventory–State version (STAI-S) and one for nine trials (N = 882) that used other standardized measures of anxiety. Trial interventions included music therapy sessions offered by a trained music therapist and listening to pre-recorded or live music. Both meta-analyses suggested large effect sizes for music therapy and music-based interventions compared with standard care controls (mean difference [MD], −7.71 for trials that used STAI-S and SMD, −0.76 for non-STAI-S trials). A subgroup analysis comparing music therapy with listening to pre-recorded music suggested that music therapy interventions offered by a trained music therapist may lead to more consistent results.

Another SR[64] reported a large treatment effect (SMD, −1.51) of music therapy and music-based interventions on anxiety (seven trials, N = 447). A third SR[63] summarized the effects of eight trials (N = 630) that examined if a traditional five-element Chinese music intervention can help reduce anxiety. No evidence of an effect was found for this traditional Chinese music intervention. In these three SRs, most trials were rated as having low methodologic quality. However, it is important to note that for music interventions, as in most other integrative therapies, participants cannot be masked to the intervention, and since anxiety is measured using self-report, outcome assessment cannot be masked either. As a result, integrative therapy intervention trials typically receive low-quality ratings for methodology, even if common criteria used to determine methodologic quality (eg, masking of participants and outcome assessors) cannot be met.

One RCT,[68] examining the effects of a music therapy protocol delivered by a trained music therapist compared with standard care on anxiety in 108 participants with cancer during chemotherapy, resulted in a large effect size for music therapy (SMD, −1.87). A three-arm RCT[67] with 137 Muslim patients with cancer compared listening to pre-recorded music with listening to the Quran and a standard care control group during chemotherapy. The results suggested large treatment effects for music listening and listening to the Quran compared to the control group. Finally, one RCT[66] examined the effects of listening to patient-selected pre-recorded music versus standard care on anxiety in 125 women with cancer during the first session of radiotherapy. No significant difference was found between the two treatment arms.

Based on the large effect sizes reported in the two SRs,[62,64] music therapy and music-based interventions may be recommended to help manage anxiety in people with cancer.

Recommendation 1.6. Reflexology may be offered to people with cancer to improve anxiety symptoms during active treatment (Type: Evidence based; Quality of evidence: Low; benefits outweigh harms; Strength of recommendation: Weak).

Literature review and clinical interpretation. There were six RCTs evaluating the effectiveness of reflexology to reduce anxiety during active treatment.[69,70,73-76] Two trials evaluated patients with breast cancer (N = 286, 183),[73,74] two trials evaluated patients with gynecologic cancers (N = 66, 62),[75,76] and one trial included patients with multiple cancers (N = 60),[70] all undergoing chemotherapy; one trial evaluated postoperative patients with gastrointestinal cancers (N = 61).[69] Reflexology interventions varied regarding the number and length of sessions, as well as the qualifications of reflexology providers. Control procedures also varied across studies (eg, lay foot massage,[73] reading,[70] usual care,[69,73,74,76] and delayed intervention[69]). Reduction in anxiety was reported in postoperative patients with gastrointestinal cancers, although the 1.1-point difference on the Hospital Anxiety and Depression Scale (HADS) score may not be clinically meaningful. For people with gynecologic cancers undergoing chemotherapy, small and medium effect sizes were reported on the HADS (2.46-point difference) and Beck Anxiety Inventory (BAI) (11.03-point difference), respectively, although both trials had several important limitations including masking, allocation concealment, and analysis plans. Two well-conducted trials in people with breast cancer did not show benefit. In participants with multiple cancer types, one trial reported a 2.3-point improvement in anxiety measured on an 11-point visual analog scale (VAS). However, study groups at baseline may have been imbalanced and there was no reporting of masking.[70,76]

Overall, four studies demonstrated at least small benefits of foot reflexology with short-term interventions. No study reported significant adverse events. Although the net benefit may be small, without evidence of important harms, reflexology may be beneficial for anxiety in some patients.

Recommendation 1.7. Lavender essential oil inhalation may be offered to people with cancer to improve anxiety symptoms during cancer-related diagnostic and treatment procedures (Type: Evidence based; Quality of evidence: Low; benefits outweigh harms; Strength of recommendation: Weak).

Literature review and clinical interpretation. There were six RCTs with sample sizes ranging from 70 to 313, examining the effectiveness of lavender essential oil aromatherapy inhalation to reduce anxiety.[30-35] Four of the six trials evaluated people during clinical procedures such as biopsy,[31-34] and the other two trials evaluated people with cancer during active treatment, such as receiving chemotherapy or radiotherapy.[30,35] Three trials evaluated people with multiple cancers (unspecified),[30,32,35] and three trials evaluated people with breast cancer.[31,33,34] Control procedures also varied across studies (eg, health education, wound care, scar massage, no aromatherapy, and placebo tablets). Some aromatherapy treatments were also paired with other interventions such as music listening and other essential oil aromatherapy.[33] Reduction in anxiety was reported in five trials, with only three recording statistically significant differences between the aromatherapy inhalation versus the control.[31,32,34]

Clinical Question 2

What integrative therapies are recommended in managing symptoms of anxiety experienced post treatment in adults with cancer?

Recommendation 2.1. MBIs should be offered to people with cancer to improve anxiety symptoms post treatment (Type: Evidence based; Quality of evidence: High; benefits outweigh harms; Strength of recommendation: Strong).

Literature review and clinical interpretation. This is the strongest recommendation in the guideline, supported by seven meta-analytic reviews published since 2017[48-54] that summarize a range of 7-29 individual RCTs including 1,094-3,476 participants, all of which were included in a meta-analysis for anxiety. Overall SMDs for anxiety reduction in the short term ranged from 0.28[53] to 0.54,[52] with a high of 0.92.[54] Most values fell into the medium-sized range of effect. A subset of RCTs in the SRs reported medium-term (up to 6 months postintervention) or long-term (>6 months) anxiety, but those that did reported SMDs of 0.28 (seven trials)[51] to 0.43 (nine trials)[48] for the medium term, which was slightly smaller than immediately post-intervention. Not enough studies reported on long-term anxiety to conclude efficacy beyond the medium term.

Most studies compared an MBI to either usual care or waitlist control groups, limiting conclusions largely to the effect of MBIs versus no other active intervention. Exceptions to this are five well-designed studies that compared an MBI to supportive-expressive group therapy,[144,145] psychoeducation,[146] or cognitive behavioral therapy.[60] Effect sizes favoring the MBI in these studies are typically smaller than those with a usual care or waitlist control (in the 0.3 range), but still show significantly greater improvements in anxiety in the MBI groups over active control.

Of the individual studies included within these SRs, the largest was by Würtzen et al[147] in Denmark, which included 336 women with nonmetastatic breast cancer both on and off

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treatment, compared with a usual care control. Similarly, Lengacher et al[148] in the United States included 322 women with nonmetastatic breast cancer who had completed treatment, compared with usual care. Würtzen et al[147] found a significant within-group effect size of 0.36 over the entire 12-month follow-up period in the MBI group, with greater benefit for those with higher baseline anxiety. Lengacher et al similarly reported a between-groups effect size of 0.27 over a 12-week period pre-post intervention, with those experiencing more anxiety at baseline improving the most. Carlson et al[144,145] randomly assigned a sample of 271 distressed women with breast cancer post-treatment to either an MBI or supportive-expressive group therapy. While both active interventions improved anxiety significantly pre- to post-intervention, the MBI group improved more, with a between-group effect on anxiety of 0.39 favoring the mindfulness group. These greater benefits of the MBI were maintained over 12 months of follow-up.

A majority of the studies included in these SRs enrolled participants after treatment, with a minority also including samples receiving MBIs both during and after treatment. Hence, the strength of the evidence and the recommendation during the post-treatment phase is strongest. Similarly, most participants in these studies were women, and the majority were diagnosed with breast cancer. Hence, the recommendations are stronger for women with breast cancer, but there are enough male participants and people with other types of cancers to include all people with cancer broadly within the recommendation.

Most of the interventions were offered in-person, with a few notable exceptions such as Compen et al[149] who separately compared in-person and online mindfulness-based cognitive therapy (MBCT) to usual care in a post-treatment sample of 245 people with a variety of cancer types, showing superiority of each modality to usual care alone (combined Hedges' g = 0.56), but the two modalities were not directly compared with one another. Zernicke et al[150] also found online videoconferencing Mindfulness-Based Cancer Recovery superior to usual care in a sample of rural and remote people with cancer both on and off treatment (n = 63; between groups Hedges' g = 0.45). By contrast, however, Chambers et al[151] delivered MBCT via teleconference for men with prostate cancer compared with enhanced usual care (N = 189) to no effect. Currently, the Expert Panel cannot strongly recommend digital health MBIs for treating anxiety in people with cancer, but this question should be answered more conclusively in coming years with the increase in remotely delivered mindfulness applications necessitated by the COVID-19 pandemic.

Recommendation 2.2. Yoga may be offered to people with breast cancer to improve anxiety symptoms post treatment (Type: Evidence based; Quality of evidence: Intermediate; benefits outweigh harms; Strength of recommendation: Moderate).

Qualifying statement: For people with cancer types other than breast, the quality of evidence is low, and the strength of recommendation is weak.

Literature review and clinical interpretation. Two SRs focusing specifically on yoga in women with breast cancer reported significant effects for anxiety (k = 8, n = 505, SMD, −1.35; k = 10, SMD, −0.98)[98,101] as did the SR of yoga or mindfulness-based stress reduction (MBSR) for women with breast cancer.[97] Only minor adverse events were reported.[98] Therefore, the Expert Panel made a moderate recommendation for use of yoga to decrease post-treatment anxiety in women with breast cancer. A SR of yoga for people with any type of cancer at any phase in the cancer trajectory included 16 studies that measured anxiety. While the overall meta-analysis showed a significant medium effect on anxiety (N = 977, g = −0.347), subgroup analysis found no significant effect of yoga for anxiety in post-treatment survivors (n = 4, g = −0.164, P = .157) or in studies that included both active cancer treatment and post-treatment participants (n = 4, g = −0.234, P = .141).[96]

Recommendation 2.3. Acupuncture may be offered to women with breast cancer to improve anxiety symptoms post treatment (Type: Evidence based; Quality of evidence: Intermediate; benefits outweigh harms; Strength of recommendation: Weak).

Literature review and clinical interpretation. Three RCTs evaluated the effectiveness of acupuncture for relieving anxiety symptoms in patients with stage I-III breast cancer following treatment.[27-29] All three studies, including 52-302 participants, reported a statistically significant improvement in anxiety as measured by the HADS with small-to-moderate effect sizes, corresponding to improvements on HADSs for anxiety (HADS-A) of approximately two points. However, interventions were heterogeneous regarding controls and methods used (standard, electroacupuncture, and auricular[28] acupuncture over 8 weeks).[28] Further adequately powered studies with appropriate sham controls are needed, as well as the inclusion of other eligible populations of people with cancer post treatment.

Recommendation 2.4. Tai chi and/or qigong may be offered to women with breast cancer to improve anxiety symptoms post treatment (Type: Evidence based; Quality of evidence: Intermediate; benefits outweigh harms; Strength of recommendation: Weak).

Literature review and clinical interpretation. A 2021 SR[89] specific to individuals with breast cancer reviewed five RCTs with 439 patients and concluded there was a significant benefit of qigong on anxiety measures (SMD, −0.71 [95% CI, −1.32 to −0.10]; P = .02). An additional RCT of 86 breast cancer survivors not included in the SR because of heterogeneity of instrument used found no difference in anxiety after 6 months of medical qigong intervention compared with usual physical activity.[93] On the other hand, a mixed cancer RCT involving 162 people with a variety of cancer types (30% breast cancer) showed significant improvement in Profile of Mood State (POMS) scores in the tension/

anxiety subscale at 10 weeks postintervention when comparing treatment and control groups.[95]

Recommendation 2.5. Reflexology may be offered to people with cancer to improve anxiety symptoms post treatment (Type: Evidence based; Quality of evidence: Low; benefits outweigh harms; Strength of recommendation: Weak).

Literature review and clinical interpretation. Three RCTs of reflexology demonstrated reduction of anxiety in participants with a variety of different cancer types who had metastatic cancer or were in a palliative care program.[71,72,77] None of these studies reported whether participants were receiving active cancer treatments or were post-treatment. All three trials (N = 80-86) reported decreased anxiety in their study populations, but effect sizes were small (1.8-point difference on 11-point VAS, 4.5-point difference on STAI, and 0.8-point difference on HADS-A) and may have been below clinically meaningful differences in two of three trials. All three trials had elements at high risk of bias, including unclear randomization, lack of masking, and unclear intervention protocol.

Given the late-stage cancers represented in these trials and the low likelihood of harm due to reflexology, there is indirect evidence of the potential of a small net benefit of reflexology for anxiety symptoms in the post-treatment phase.

Inconclusive. There is inconclusive evidence to make recommendations for or against music therapy and music-based interventions to improve anxiety symptoms in people with cancer who are post treatment. There is also inconclusive evidence for nutritional interventions, light therapy, psilocybin-assisted therapy, massage, dance/movement therapy, laughter therapy, healing touch, expressive writing, acupressure, biofeedback, autogenic training, energy healing, melatonin, or other natural products and supplements to improve anxiety symptoms in people with cancer, regardless of when in the course of care the intervention is provided.

Literature review and clinical interpretation. Music therapy, music-based interventions. Many RCTs included in two SRs[62,64] that examined the effects of music therapy and music-based interventions on anxiety in people with cancer included people along the cancer care continuum, including those who were post treatment. However, the literature search did not identify any RCTs that met our inclusion criteria that only included people with cancer who were post treatment.

Nutritional interventions. Three eligible trials of nutritional interventions, including a residential nutritional rehabilitation program for people with head and neck cancer, hospital-based nutritional education sessions for people with nonmetastatic breast cancer, and mixed motivational interviewing or pamphlet or newsletter intervention in people with colorectal cancer, that examined effects on anxiety symptoms were analyzed,[131-133] two of which incorporated both dietary and physical activity interventions.[132,133] Two of three eligible trials did not show a significant effect on anxiety outcomes but due to significant heterogeneity of methodology, including the nature and duration of nutritional interventions given in the trials, as well as variability in the patient groups who received the intervention, it is not possible to draw robust conclusions. Further research should focus on specific and well-defined dietary interventions studied in adequately powered trials that monitor for nutritional compliance, as well as measuring both anxiety and depression outcomes during and after the intervention.

Light therapy. There is insufficient evidence to recommend for or against the use of light therapy for treating anxiety symptoms in people with cancer. Light therapy has largely been investigated in this population for the treatment of fatigue; hence anxiety, when measured, has been a secondary outcome. For example, Johnson et al[114] compared 4 weeks of daily bright white light to dim red light in 84 fatigued people living with cancer post-treatment and found both groups improved significantly on fatigue and mood with generally large effect sizes, but there was no usual care comparison group.

Psilocybin-assisted therapy. This is a promising modality for the treatment of existential anxiety and depression in cancer care. Currently, however, only two small RCTs have been published on its use. In the largest trial to date, Griffiths et al[135] compared low- to high-dose psilocybin with supportive psychotherapy in 51 people with advanced cancer in a crossover design. They found large decreases in multiple measures of anxiety, which persisted at 6-month and 4-year follow-up assessments. Ross et al[136] conducted a similar trial with 29 people living with advanced cancer, also finding large effect sizes on anxiety and depression. Many other larger RCTs are currently underway, but at this point, the evidence is inconclusive.

Massage. There were three RCTs of massage therapy to reduce anxiety symptoms in participants undergoing active treatment, including chemotherapy in two trials[117,118] and port placement in one trial.[119] Two SRs also reported on massage or oil aromatherapy massage to reduce anxiety.[115,116] Two trials during active chemotherapy reported no improvement in anxiety symptoms. One SR (eight studies; N = 498)[115] reported no evidence of a treatment effect for anxiety in patients with breast cancer undergoing chemotherapy (SMD, −0.08 [95% CI, −0.44 to 0.28]; I^2 = 72%). A second SR compared massage or aromatherapy massage to no massage or massage without aromatherapy.[116] There was no evidence of a treatment effect of massage studies (three studies, n = 98; MD STAI, −5.4 [95% CI, −16.1 to 5.3]; I^2 = 88%) and aromatherapy massage versus standard massage (two studies; n = 145; no meta-analysis performed). Two trials (n = 253) of oil aromatherapy massage versus no massage reported a pooled MD (STAI-S) of −4.5 (95% CI, −7.7 to −1.3). Strength of evidence for all comparisons was rated as very low. There were no studies of massage that included anxiety in post-treatment phase patients.

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Natural products. Multiple eligible trials tested a variety of natural products and supplements with one negative trial of probiotics,[122] one negative trial of chamomile tea,[123] one positive trial of fermented red Panax ginseng extract,[124] one negative trial of white P. ginseng extract[125] with significant dose variation, one positive low-risk-of-bias trial of 30 mg crocin (found in crocus flowers and saffron),[126] and one negative trial for Yokukansan extract.[127] The use of rigorous methodology and rational formulation, dosing, and strain specificity and their appropriate application to specific patient groups are needed to provide clinically relevant guidance.

Melatonin. In a clinical trial of 128 participants with colorectal cancer, 6 mg of melatonin at bedtime was tested against zolpidem for sleep during chemotherapy, with anxiety considered as a secondary outcome.[106] This study demonstrated no impact on anxiety; however, the trial was not designed for individuals with this condition. One RCT[107] found no impact on anxiety with the use of perioperative melatonin for breast cancer in a small sample of 54 women. This study tested the use of 6 mg of melatonin over the course of 1 week preoperatively and 3 months postoperatively with depression as the primary outcome and anxiety among other outcomes a secondary consideration. This trial, which overall had a low risk of bias, did suffer from a disproportionate number of dropouts in the placebo group compared with the melatonin group.[107] Another RCT tested the impact of melatonin among patients with lung cancer post resection and found no impact on anxiety in a small subset of participants.[108] The subset that was assessed for anxiety consisted of <10% (67/709) of the total sample. In addition, anxiety was a relatively minor secondary outcome that was not a presenting concern for the participants upon enrollment, and thus, the intensity of anxiety among the group was relatively low.

Dance/movement therapy. One SR[104] and one RCT[105] were identified that examined the effect of dance/movement therapy on anxiety and/or stress. The 2015 Cochrane Review by Bradt, Shim, and Goodill[104] included two RCTs and one quasi-experimental study (N = 207) that compared the effect of various types of dance/movement therapies to standard care on psychologic and physical outcomes among women with breast cancer who were within 5 years of diagnosis. The SR included two meta-analyses related to anxiety and stress that pooled the results of two of the three studies (n = 170). No evidence of effect was found for the dance/movement interventions regarding anxiety (SMD, 0.21 [95% CI, −0.09 to 0.51]; P = .18; I^2 = 0%). All three studies included in the SR were rated as being at high risk of bias, mainly due to lack of masking of study participants and outcome assessors. The RCT conducted by Ho et al[105] compared the effect of a 90-minute dance/movement session offered twice a week over 3 weeks to standard care on anxiety and stress among 139 Chinese women living with breast cancer receiving adjuvant radiotherapy treatment. No significant difference between study arms was found for anxiety. Overall, there has been limited high-quality research evaluating the effect of dance/movement interventions on anxiety and/or stress, especially in cancer populations beyond women living with breast cancer.

Laughter therapy. One study[113] was identified that evaluated the impact of a laughter program on people with cancer undergoing active treatment and the effect on anxiety and depression. The pilot trial[113] evaluated patients with breast cancer (N = 62) undergoing postoperative radiation therapy assigned to a therapeutic laughter program (TLP) consisting of periods of loud, prolonged laughter with information about the effects of TLP compared with a control arm. The authors observed that as the number of TLP sessions attended increased, numeric rating scale scores for anxiety and depression significantly decreased.

Healing touch. There is insufficient evidence to recommend for or against the use of healing touch or therapeutic touch for treating anxiety symptoms in people with cancer. In many of these studies, anxiety is a secondary outcome. These studies have been conducted preoperatively and postoperatively and post-treatment. Post-White et al[110] performed a randomized prospective two-period crossover intervention study in a mixed cancer population, testing therapeutic massage and healing touch. The massage therapy group showed a lowering of anxiety post-treatment ($t(61) = 2.3$, P = .023). There was no lowering of anxiety symptoms from healing touch.

Acupressure. One RCT evaluated the effects of acupressure at LI4 and HT7 in people with cancer who were undergoing bone marrow biopsy and aspirate with both sham and usual care controls (N = 90, 30/30/30 group split).[103] Acupressure, compared with sham or usual care, resulted in a statistically significant reduction in anxiety as measured by the STAI, with no serious side effects reported. This protocol may offer a practical short-term intervention for consideration in the periprocedural setting but further research is needed, and study results must be interpreted with caution, given the high risk of bias in two domains.

Depression

Clinical Question 3

What integrative therapies are recommended for managing symptoms of depression experienced after diagnosis or during active treatment in adults with cancer?

Recommendation 3.1. MBIs should be offered to people with cancer to improve depression symptoms during active treatment (Type: Evidence based; Quality of evidence: High; benefits outweigh harms; Strength of recommendation: Strong).

Literature review and clinical interpretation. This recommendation is based on seven SRs published since 2017,[48-54] which reviewed a range of 7-29 individual RCTs including from 1,097 to 3,476 individual participants. These same SRs support Recommendation 1.1, management of symptoms of anxiety during active treatment, and the same comments regarding study composition apply. In the largest SR by Oberoi et al,[48] two studies that solely enrolled

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patients during active treatment were included in the analysis of the association of MBIs with depression in the short and medium term. These studies[137,152] exclusively enrolled patients with nonmetastatic cancer in 8-week MBIs (MBSR and MBCT). The larger study, Liu et al, reported SMDs of 1.24 and 1.55, favoring the MBI for management of depression in the short and medium term, respectively, compared with the control group. In the studies that included mixed groups of participants both on and off treatment for metastatic or nonmetastatic cancer,[149,153,154] SMDs for depression in the short term were in the medium size range of about 0.4-0.7, in favor of the MBI.

Recommendation 3.2. Yoga may be offered to people with breast cancer to improve depression symptoms during active treatment (Type: Evidence based; Quality of evidence: Intermediate; benefits outweigh harms; Strength of recommendation: Moderate).

Qualifying statement: For people with cancer types other than breast, the quality of evidence is low, and the strength of recommendation is weak.

Literature review and clinical interpretation. The SR of yoga in women undergoing chemotherapy for breast cancer included six RCTs with 446 total participants and reported a significant effect on depression (SMD, −0.50).[99] Notably, only one of these RCTs included an active control group (supportive education).[155] Two SRs that examined yoga in women with breast cancer, regardless of treatment phase, also reported benefits for depression (k = 12, n = 761, SMD, −0.98; k = 10, SMD, −0.17).[98,101] The evidence for yoga to improve depression during treatment for breast cancer was, therefore, graded as intermediate. Fewer studies have been conducted in people with other cancer types, but one SR including mixed cancer types conducted a subgroup analysis of the effects of yoga on depression during active treatment and reported a medium effect (n = 11, g = −0.384)[96]; only two of the 11 RCTs in this subgroup analyses enrolled participants with types of cancer other than breast (central nervous system, thoracic). Because most studies focused on women with breast cancer, the overall evidence for yoga to improve depression symptoms during active treatment was graded as low quality. In trials reporting adverse events, no serious events occurred. Therefore, the Expert Panel recommends that clinicians may offer yoga to improve depressive symptoms during active cancer treatment.

Recommendation 3.3. Music therapy or music-based interventions may be offered to people with cancer to improve depression symptoms during active treatment (Type: Evidence based; Quality of evidence: Low; benefits outweigh harms; Strength of recommendation: Moderate).

Literature review and clinical interpretation. There were three SRs on music therapy and music-based interventions that reported treatment effects for depression.[62-64] A SR from 2021[62] that examined the effects of music interventions on psychologic and physical outcomes in people with cancer included a meta-analysis of 12 trials with 1,021 participants for depression. Interventions included music therapy with a trained music therapist and listening to prerecorded music. The pooled effect size of the included trials suggested that music therapy and music-based interventions may have a small-to-moderate treatment effect on depression (SMD, −0.41). Another SR[64] including six trials with 555 participants reported a large treatment effect (SMD, −1.12) for depression. Finally, an SR[63] only including the use of traditional Chinese five-element music also reported a large treatment effect (SMD, −1.11) for depression. Because of the treatment effects reported in these SRs, music therapy and music-based interventions may be recommended to help manage depression in people with cancer during active treatment.

Recommendation 3.4. Relaxation therapies may be offered to people with cancer to improve depression symptoms during active treatment (Type: Evidence based; Quality of evidence: Low; benefits outweigh harms; Strength of recommendation: Weak).

Literature review and clinical interpretation. The evidence for relaxation therapies during treatment for depression symptoms is not as strong as for anxiety, but enough studies exist to make a weaker recommendation. In the 2022 SR of PMR,[78] two included studies (n = 492) measured depression as an outcome during active treatment and saw statistical improvements, but meta-analysis could not be performed due to variability in outcome measures.

The 2018 review of seven different RCTs only in breast cancer (n = 255) of PMR and/or visualization therapies during chemotherapy similarly reported improvements in depression symptoms and mood in the five studies that included that outcome, but meta-analysis was not conducted.[79] The SR and meta-analysis of 15 RCTs assessing breathing exercises for people undergoing treatment for lung cancer included four studies of 159 people that measured depression as a secondary outcome; but while half of them showed benefit, the results were highly heterogeneous and the overall SMD did not significantly favor the treatment.[81]

Individual studies not included in the SRs also found greater improvements in depression in treatment over control conditions.[82,84,86]

Recommendation 3.5. Reflexology may be offered to people with cancer to improve depression symptoms during active treatment (Type: Evidence based; Quality of evidence: Low; benefits outweigh harms; Strength of recommendation: Weak).

Literature review and clinical interpretation. Four RCTs reported on the benefit of reflexology for treatment of depressive symptoms in participants receiving active cancer treatment. Two trials with low risk of bias reported no benefit of reflexology in patients with breast cancer undergoing chemotherapy (N = 286)[73] and surgery (N = 183).[74] One trial of hospitalized patients (N = 66) with a variety of

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gynecologic cancers conducted in Korea reported a small benefit (0.38-point difference on HADS-depression) of aromatherapy and self-performed reflexology over 6 weeks (moderate risk of bias).[75] A second trial of patients (N = 62) with gynecologic cancers receiving outpatient chemotherapy in Turkey reported a small benefit (18% reduction in BAI) in depressive symptoms after 4 weeks of reflexology (high risk of bias).[76]

Reflexology may be considered as an adjunct treatment for depressive symptoms for patients with an interest in this therapy. However, larger, high-quality studies are needed before recommending widespread implementation.

Clinical Question 4

What integrative therapies are recommended in managing symptoms of depression experienced post treatment in adults with cancer?

Recommendation 4.1. MBIs should be offered to people with cancer to improve depression symptoms post treatment (Type: Evidence based; Quality of evidence: High; benefits outweigh harms; Strength of recommendation: Strong).

Literature review and clinical interpretation. This is the second strongest recommendation in the guideline, supported by seven SRs published since 2017,[48-54] summarizing a range of 7-29 individual RCTs including from 1,097 to 3,476 individual participants. These same meta-analyses support Recommendation 2.1, management of symptoms of anxiety post-treatment, and the same comments regarding study design and composition apply. Overall SMDs for depression reduction in the short term ranged from 0.34[53] to 0.74.[54] Most values fell into the medium-sized range. Fewer of the original RCTs reported on medium-term (up to 6 months post-intervention) or long-term (>6 months) management of symptoms of depression, but those that did reported SMDs of 0.26 (four studies),[53] 0.32 (seven studies),[51] and 0.85 (eight studies)[48] for the medium term. Not enough studies reported on the long-term management of depressive symptoms to conclude efficacy beyond the medium term.

Of the individual studies included within these meta-analyses, the largest was by Würtzen et al,[156] which found a significant within-group effect size of 0.55 on depression over the entire 12-month follow-up period in the MBI group. Most studies compared an MBI to either usual care or waitlist control groups. A notable exception is Bower et al,[55] which focused on addressing depressive symptoms in 247 younger (age ≤50 years at diagnosis) breast cancer survivors. Both the MBI and survivorship education significantly reduced depressive symptoms relative to the waitlist control, with a trend toward greater and more durable reduction with the MBI.

As with Recommendation 2.1, the recommendations are strongest for women with breast cancer, but there are enough male participants and people with other types of cancers to include all people with cancer broadly within the recommendation.

Recommendation 4.2. Yoga may be offered to people with breast cancer to improve depression symptoms post treatment (Type: Evidence based; Quality of evidence: Intermediate; benefits outweigh harms; Strength of recommendation: Moderate).

Qualifying statement: For people with other cancers the quality of evidence is low, and the strength of recommendation is weak.

Literature review and clinical interpretation. In an SR and meta-analysis of effects of yoga on depressive symptoms, regardless of cancer type, subgroup analysis (n = 8, g = −0.428) of post-treatment studies identified a significant medium effect.[96] However, only two of the eight RCTs included in this analysis included people with types of cancer other than breast (one trial of people with head and neck cancer, one with people with breast and other types of cancer). In addition, two SRs have focused on yoga for women with breast cancer.[98,101] Although neither conducted subgroup analyses for different treatment phases, both included multiple post-treatment trials and identified overall significant effects in depressive symptoms. The Expert Panel rated the evidence for yoga to improve post-treatment depression as low overall and intermediate in women with breast cancer. Adults with any cancer type, therefore, may be offered yoga as an approach to reduce symptoms of depression post-treatment.

Recommendation 4.3. Tai chi and/or qigong may be offered to people with breast cancer to improve depression symptoms post treatment (Type: Evidence based; Quality of evidence: Intermediate; benefits outweigh harms; Strength of recommendation: Weak).

Literature review and clinical interpretation. A 2018 SR and meta-analysis[87] including 15 RCTs (n = 1,283) evaluating qigong and/or tai-chi exercises showed significant improvement in depression scores (ES = −0.27; P = .001), despite heterogeneity of comparison groups. Cancer-related depression was specifically evaluated by seven RCTs (N = 783). Many different standardized questionnaires were used to measure depression, and a variety of cancers were studied, mostly breast cancer. A 2021 SR and meta-analysis[89] specific to patients with breast cancer reviewed six studies with 540 participants and concluded there is significant effect of qigong on depression symptoms (n = 540, SMD, −0.32 [95% CI, −0.59 to −0.04]; P = .02). On the other hand, two other meta-analyses found no difference (Zeng et al: three RCTs, N = 314[90] and Cheung et al[88]: four RCTs, N = 326), due primarily to significant heterogeneity in effects across studies such that confidence intervals were wide and crossed zero.

Two adequately powered studies included in the 2018 SR and meta-analysis by Wayne et al[87] showed an effect on measures of depression with use of qigong compared with conventional care; however, these are considered low-quality

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studies due to lack of masking, confounding factors (such as extra care *v* none), and high drop-out rates. One RCT of medical qigong in patients with a variety of cancers, including breast cancer (34%), colorectal (12%), lung (9%), and prostate cancer (9%), compared with usual care, involving 162 patients, showed significant improvement in POMS scores in the depression domain at 10 weeks postintervention.[95] A recent prospective, RCT involving 80 patients with gastrointestinal cancer[92] used a specific form of Chinese traditional qigong exercise known as monkey-frolic in the intervention group. Conventional care included coping strategies, routine education, emotional support, cognitive therapy, and stress management. All patients were considered high risk of depression based on questionnaire scores. After 4 weeks, statistically significant improvements in depressive symptoms were reported for those participating in five weekly qigong exercise sessions, compared with controls.

Recommendation 4.4. Expressive writing should not be offered to people with cancer to improve depression symptoms at any point in the course of care (Type: Evidence based; Quality of evidence: Intermediate; no net benefit; Strength of recommendation: Moderate).

Literature review and clinical interpretation. There was one SR[36] that included 16 studies (total n = 2,392), and two RCTs[37,38] of expressive writing interventions (also part of the SR) that examined its specific effect on depression in cancer. The writing interventions used largely followed the original paradigm developed by Pennebaker[157] in which participants are instructed in three to four home- or lab-based sessions across 2-3 weeks to write about their cancer or some other traumatic experience. Control participants are instructed to write about neutral topics such as daily activities, health behaviors, or time management. Participants varied by age, sex, cancer type, and stage, and ranged across the survivorship trajectory from active treatment to end-of-life care. Expressive writing failed to produce significant improvement in overall psychologic well-being, anxiety, or depressive symptoms in any of the studies reviewed. At this point, the Expert Panel does not advise the use of expressive writing interventions to manage anxiety or depression in cancer.

Inconclusive. There is inconclusive evidence to make recommendations for or against reflexology to improve depression symptoms in people with cancer who are post treatment. There is also inconclusive evidence for nutritional interventions, light therapy, psilocybin-assisted therapy, massage therapy, biofeedback, autogenic training, energy healing, melatonin, and other natural products and supplements to improve depression symptoms in people with cancer, regardless of when in the course of care these therapies are provided.

Literature review and clinical interpretation. Reflexology. One randomized trial (N = 86) demonstrated a moderate effect of six weekly reflexology sessions compared with a relaxation control.[77] Participants with multiple cancer types were recruited from an outpatient palliative care unit in Greece. It is unclear if participants were receiving active cancer treatment during the trial. High risk of bias elements included lack of masking and unclear randomization and allocation concealment methods.

Nutritional interventions. Four eligible trials (combined n = 604) of nutritional interventions that examined effects on depression symptoms in people with cancer were analyzed.[131-134] Two of the trials incorporated both dietary and physical activity interventions and showed positive effects on improvement in depression outcomes.[132,133] While three out of four trials showed a positive effect on depression outcomes, due to significant heterogeneity of methodology, including the nature and duration of nutritional interventions given in the trials, as well as variability in the patient groups who received the intervention, it is not possible to draw robust conclusions. Further research should focus on specific and well-defined dietary interventions studied in adequately powered trials that monitor for nutritional compliance, as well as measuring both anxiety and depression outcomes during and after the intervention to assess the likely duration of effects.

Light therapy or psilocybin-assisted therapy. The same caveats apply to depression as anxiety outcomes for both light therapy and psilocybin-assisted therapy as summarized in the anxiety section. The trials are few and small, but both therapies show some promise and require further research.

Massage. One RCT of massage therapy investigated a 2-week intervention (three 30-minute sessions per week by a licensed massage therapist) versus a simple touch control in patients with a variety of metastatic cancers undergoing palliative care.[120] Although the study reported immediate benefits in mood, those improvements were not sustained over time. There was no difference in improvements in symptom distress compared with the control group. Two RCTs[117,118] and two SRs (eight trials, 540 participants[115]; and nine trials, 582 participants[116]) reported on the benefits of massage for depressive symptoms. No studies found statistically significant results in favor of massage. Although most trials had unclear or high risk of bias, further studies are unlikely to demonstrate a clear benefit of massage for depressive symptoms in this patient population.

Natural products and supplements. Multiple trials tested a variety of natural products and supplements, including two negative trials of probiotics with variable formulations,[122,128] one negative trial of 1-g L-carnitine BD,[129] one poor-quality positive trial of chamomile tea,[123] three trials of *P. ginseng* with variable quality and outcomes and significant differences in preparation and dosing,[124,125,130] one positive low-risk-of-bias trial of 30-mg crocin,[126] and one meta-analysis examining 18 RCTs testing 12 types of Chinese herbal medicine formulae with significant methodologic limitations (including lack of masking), heterogeneity in prescribing method, patient population, and formulae used.[121] It

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is important to note that analyses combining different Chinese herbal medicine formulae given to different patient populations within a different framework (personalized *v* generic prescriptions) in different doses are usually of little clinical utility. Adequately powered trials that explore promising areas with rigorous methodology, attention to formulation, dosing, and probiotic strain specificity and their appropriate application to specific patient groups are needed to provide clinically relevant guidance.

Melatonin. In one small RCT (N = 54), there was a significant reduction in the number of women with depression according to the Major Depression Inventory[107] in the perioperative period for women with breast cancer. This trial, which had a low overall risk of bias, did suffer from a disproportionate number of dropouts in the melatonin group. When different sensitivity analyses were applied, however, the effect was still found to be significant. In another trial, melatonin given at 6 mg once daily at night was tested against zolpidem for sleep among 128 participants with colorectal cancer while receiving chemotherapy.[106] In this trial, depression was assessed as a secondary outcome with no changes observed during the 30-day application. One clinical trial tested the impact of melatonin among a subset of patients with lung cancer post resection and found no impact on depression.[108] The subset assessed for depression was small at <10% of the total sample (67/709) and was tested as a secondary outcome where this was not a major presenting concern. In a trial exploring melatonin for sleep, mood, and hot flashes, 3 mg of melatonin taken daily did not show any effect on depression; however, the sample was not selected based on this condition and not powered to demonstrate an effect for this outcome.[109] A small multicomponent, multifactorial trial tested the effect of melatonin on depression as a secondary outcome in patients with advanced cancer. This trial did not demonstrate a difference in depression among this group, but it was not powered to assess this outcome and was designed to approximate effect size for a larger future planned trial.[158]

Multimodal interventions. Two trials of multicomponent, complex interventions were identified. Because each trial was composed of vastly different components, it was not possible to draw broad conclusions about the effectiveness of multicomponent interventions. In one trial of 116 individuals with colorectal cancer undergoing chemotherapy in India, participants were randomly assigned to yoga plus bundled naturopathic interventions including diet, manipulative therapy, massage, mudpack, and bathing versus standard psychosocial counseling over an 18-month period.[159] Although authors reported statistically significant between-group differences for secondary outcomes such as anxiety (STAI) and depression (Beck Depression Inventory), the values reported in table and graphic formats are inconsistent. Additional important limitations to the study are poorly defined intervention procedures, large postrandomization exclusions, unclear blinding, unclear balance of groups at baseline, and multiple testing. Another multicomponent trial investigated the effects of PMR plus Chinese medicine five-element music versus peaceful rest over 8 weeks in participants with a variety of cancer types in China.[160] Although authors reported greater improvements in anxiety and depression for the intervention group compared with the control group, individual HADS component scores were not reported and differences in composite HADS scores did not appear to be clinically meaningful. Additional important limitations included poorly defined interventions, lack of blinding, and multiple testing.

Based on the current body of evidence, no recommendations can be made regarding multimodal interventions. Due to significant methodologic concerns of the studies identified, it is unlikely additional studies similar to the ones currently available can be performed due to the poorly described interventions.

DISCUSSION

These guidelines summarize recommendations for integrative therapies that should or may be used in conjunction with conventional care to improve symptoms of anxiety and depression in people with cancer, either during or after treatment, with MBIs, music therapy, yoga, relaxation, hypnosis, tai chi and qigong, and reflexology among those being recommended. This is important not only for improving overall psychosocial adjustment and quality of life, but because untreated depression and anxiety symptoms are consistently associated with higher overall mortality in people with cancer.[161,162] Interest among those diagnosed and treated for cancer in these complementary forms of care has grown steadily in the past decade.[23] From the perspective of the individual with cancer, these therapies offer a measure of perceived control over the impact of illness and/or side effects, have few if any side effects, and can be received in a variety of settings. Although many of these therapies may be readily available in some urban and suburban settings, some are still not universally available. Furthermore, out-of-pocket costs can limit their uptake. A survey of 45 National Cancer Institute–designated cancer centers found that the most commonly offered integrative therapies were acupuncture and/or massage (73.3% each), meditation and/or yoga (68.9% each), and consultations about nutrition (91.1%), dietary supplements (84.4%), and herbs (66.7%). Compared with 2009, there was a statistically significant increase in the number of websites mentioning acupuncture, dance therapy, healing touch, hypnosis, massage, meditation, qigong, and yoga.[163]

One of the strongest recommendations in this guideline is for the use of MBIs in the management of anxiety and depression in adults with cancer. This finding is synergistic with the updated ASCO guideline review of the psychosocial, behavioral, and pharmacologic management of anxiety and depression in adult cancer survivors in which MBSR interventions, among other cognitive-behavioral and individual psychologic therapies, were strongly recommended by the review committee.[16] The acknowledged utility of yoga for management of anxiety and depression across care could be

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considered paralleling the support found for the role of exercise for this purpose in this latter updated guideline, if considering the physical activity aspect of yoga.

Given the appeal of their use, the lack of support for expressive writing interventions was a surprise. Although no adverse effects were reported, the large numbers of participants (n = 2,392) involved in the 16 studies reviewed, diversity of samples involved, use of well-accepted psychologic measurement tools, and the consistency of findings suggest that pursuing more studies in this area is not likely to change outcomes. Arguably, this type of intervention may be helpful for individuals with cancer in processing, and more deeply exploring the impact or meaning of their illness. However, the brevity of the intervention is not well matched to more chronic conditions, such as depression, whose symptoms tend to persist over weeks and months. If expressive writing were to become a habit, which takes weeks to establish, it is possible that this might prove more useful in managing longer-term emotional distress. But such studies remain to be conducted. It is also noted that keeping diaries of symptoms, side effects, and treatments received can help organize cancer care.[164,165]

The current guideline has many consistencies with the prior 2017 SIO integrative therapy guidelines created for people with breast cancer.[166] In those guidelines, the US Preventive Services Task Force grading system was used,[167] which is different from the currently used system in that it assigns grades to the evidence base, but both assess strength of evidence as determined by the number of trials, quality of trials, magnitude of effect, statistical significance, sample size, and consistency of results across studies. For anxiety, only meditation (including MBIs) received a grade A recommendation, followed by music therapy, stress management, and yoga, all of which received a grade B recommendation, and acupuncture, massage, and relaxation received a grade C. Similarly, for depression and mood disturbance, MBIs and relaxation received grade A recommendations, yoga, massage, and music therapy grade B, and acupuncture, healing touch, and stress management received grade C recommendations. Similarly, in the current guidelines, with the inclusion of all cancer types and a review of the updated literature, MBIs received the strongest recommendations. Other therapies remained equivalent to the grade B category at this time, receiving recommendations of "may be offered" rather than "should be offered." While in some cases the lower grade is related to low study quality scores influenced by the inability to mask participants to integrative interventions, there continues to be a paucity of research among people with cancer other than breast.

There are also many gaps in the evidence base, and the Expert Panel was unable to make recommendations for or against several popular treatment modalities, as not enough studies have been conducted. The Expert Panel specifically recommends more research be conducted in the areas of promising as well as commonly used and accessible therapies such as yoga during active treatment, healing touch and therapeutic touch, tai chi and qigong, natural health products, and creative arts-based therapies, such as art therapy and dance/movement therapy. Studies are also significantly lacking in people with cancers other than breast, in the context of metastatic disease, and among people from diverse backgrounds.

PATIENT AND CLINICIAN COMMUNICATION

For most people, cancer is the most difficult and frightening experience they have ever encountered. Anxiety and depression associated with cancer are largely centered around feelings of guilt from past lifestyle choices, hopelessness, and helplessness in the face of a cancer diagnosis, and fear and uncertainty about the future. These feelings can affect the way a person thinks, acts, interacts with others, and even the way their body functions during and after cancer treatment. The research synthesized in these guidelines suggests various integrative approaches that can be applied to manage anxiety and depression during and after cancer treatment. People with cancer will need to find their own level of comfort with these approaches based on their belief systems and personal ways of coping and their choices of therapies to use or not use should be respected by their families, cancer care team, and others who support them through the cancer experience.

Moreover, it is critical that the cancer care team monitor people at each stage of diagnosis, treatment, and survivorship to discuss and offer different types of emotional, social, and physical support as needs change and evolve throughout the cancer journey. For example, a person newly diagnosed with cancer may benefit from relaxation techniques while undergoing chemotherapy but might benefit from a more active therapy such as yoga once treatment is over, to relieve symptoms from side effects. People who have completed treatment may feel they need the social support of a group or one-on-one counseling to deal with their fear and uncertainty of their cancer returning. At times of critical treatment and diagnostic junctures, for example, at the time of first diagnosis, when diagnosed with recurrent or metastatic disease, and at the start and end of treatments, cancer care teams should be routinely screening for anxiety and depression symptoms to ensure patients follow-through with cancer treatment, and to support use by these individuals of self-management strategies that improve quality of life.

Advances in cancer treatment suggest that a diagnosis does not equal a death sentence, but for many people, cancer does equate to a chronic condition that influences their quality of life and needs to be managed mentally, emotionally, and physically. People with cancer and advocates of integrative oncology strategies will need to continue to raise awareness among mainstream physicians for the need to address and treat the psychiatric consequences of cancer. For recommendations and strategies to optimize patient-clinician communication, see the ASCO guideline by Gilligan et al.[168]

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HEALTH DISPARITIES

Although SIO-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 have limited access to medical care or receive fragmented care. The same is true of participants in research studies, with inequities in research participation across social determinants of health such that marginalized groups are under-represented in clinical trials.[169] Disparities in mental health care are significantly exacerbated by a lack of uniform insurance coverage for behavioral care and ongoing societal stigma. Individual factors such as race, ethnicity, age, socioeconomic status, sexual orientation, gender identity, geographic location, education, literacy (including digital), numeracy, environmental exposure, insurance access, and lack of trust in the health care system are known to impact cancer care outcomes.[170] Clinician factors such as unconscious and conscious bias can contribute to missed diagnoses and differences in care.[171] Despite similar access, prescription treatment for major depression and frequency of treatment has been documented to be lower in minoritized Black and Latino communities.[172] Health system barriers can also disproportionately impact minoritized communities who may experience the intersection of multiple identities and structural inequities.

A review of racial and socioeconomic factors related to the use of complementary therapies for cancer pain management found lower income and educational levels had a greater influence on complementary therapy use than race. People who had a higher educational degree and income typically used body manipulation techniques or practitioner-based therapies that cost money or required insurance, whereas users with inadequate financial resources reported greater use of free methods for symptom management, such as meditation and relaxation techniques. Prayer and spirituality, when included as complementary modalities, were also more often used by racial minority groups. A general limitation of the included studies was the lack of integration between race and socioeconomic factors, wherein social determinants of health and the link between minority status and socioeconomic status were essentially overlooked.[173] People with cancer who are members of minoritized communities may also be more likely to seek care from someone who looks like them. The lack of diversity in the health professional workforce serves as another source of health inequity. These same individuals who are experiencing substantial obstacles to care may also be at greater risk for concurrent illnesses and comorbidities.[170,174] This clinical practice guideline should be considered with awareness and understanding of the patient, clinician, and health system factors that contribute to inequitable care and limit access to care. Even in countries with universal health care, integrative approaches are not uniformly covered leaving access to those who can pay out of pocket.

As discussed in the previous section, disparities in cancer care treatment can be caused or exacerbated by a lack of open and supportive patient-provider communication. It is extremely important that cancer care teams diligently focus on those diagnosed with rare cancers, minoritized groups (including people with cancer from Black and indigenous communities, sexual and gender minorities), and adolescents as their symptoms of anxiety and depression are less likely to be addressed.

Health professionals are committed to delivering the highest level of care to each person living with cancer. All stakeholders are called to work together to ensure equitable access to both high-quality cancer care and cancer clinical research and address the structural barriers that maintain health inequities.[170]

MULTIPLE CHRONIC CONDITIONS

Creating evidence-based recommendations to inform treatment of individuals with additional chronic conditions, a situation in which a person may have two or more such conditions—referred to as multiple chronic conditions (MCC)—is challenging. In the setting of cancer, a disease of aging, MCC is also the norm. US population-based statistics estimate that of the adult population (those age 18 years and older), 23.1% have two or more chronic conditions. For those age 65 years and older, this figure rises dramatically to 63.7%.[175] Of the estimated 18.1 million cancer survivors in the United States in January 2022, 67% were age 65 years or older.[176] As cancer survivors live longer and the world population ages, the number of older people with cancer will continue to climb.

People with MCC are a complex and heterogeneous population, making it difficult to account for all the possible permutations to develop specific recommendations for care. In addition, the best available evidence for treating index conditions, such as cancer, is often from clinical trials whose study selection criteria frequently exclude these very same individuals, in order to avoid potential interaction effects or confounding of results associated with MCC. As a result, the reliability of outcome data from these studies may be limited, thereby creating constraints for expert groups to make recommendations for care in this heterogeneous population.

As many individuals with cancer for whom guideline recommendations apply present with MCC, any treatment plan needs to take into account the complexity and uncertainty created by the presence of MCC and highlights the importance of good patient-provider communication and shared decision making regarding guideline use and implementation. Therefore, in consideration of recommended care for anxiety and depression in cancer, clinicians should review all other chronic conditions present and take those conditions into account when formulating treatment and follow-up plans. When planning care for a person with MCC, clinicians often worry about drug-drug interactions or the effects

of polypharmacy. An advantage to the use of nonbiologically based integrative therapies is that few create this particular challenge; however, other limitations may need to be taken into consideration. For example, a person with metastatic disease to the bones may not be able to engage in some standard yoga poses and would need a tailored program. Those with comorbid neurodegenerative diseases may also need to be cautious in the use of movement-based practices, but on the whole, these also seem to have the potential to benefit older adults with movement disorders.[177,178] The use of pragmatic research designs, which are less likely to exclude people with MCC, is also a way to advance the care of this group.

COST IMPLICATIONS

Increasingly, people with cancer are required to pay a larger proportion of their treatment costs out of pocket through deductibles and coinsurance.[179,180] Even in Canada with universal health insurance, out-of-pocket costs for people on treatment averaged almost $800 in Canadian dollars (CAD) *per month*—with an additional $1,700 (CAD) lost in monthly income.[181] Of those costs, complementary therapies were one of the larger expenses (after travel costs). Higher out-of-pocket costs are often a barrier to initiating and adhering to recommended cancer treatments.[182,183]

Out-of-pocket costs may vary depending on where one lives and the type of health insurance coverage one holds. For example, some plans may cover the expense of visiting a naturopathic doctor for consultation and tests, but not the costs of natural health products. Similarly, some plans cover acupuncture for symptom management, but often only for a diagnosis of chronic pain. Unless programs are offered as part of cancer care, mind-body therapies such as yoga, tai chi and/or qigong, and mindfulness are usually accessed through private classes or practitioners in the community. Some medical doctors and cancer care providers offer group support or meditation programs, which can be classified as group medical visits and thereby covered by insurance. Many cancer centers provide financial counseling and will help people apply for grants or bursaries as well as compassionate pricing that may help cover these expenses, but these services vary depending on where individuals receive their cancer care.

Given that some recommendations in this guideline indicate that therapies should be offered to treat symptoms of anxiety and depression, comprehensive cancer centers and governing administrative bodies should consider prioritizing these specific therapies in their financial and operational planning, providing access to people with cancer without significant financial barriers. Research also shows that complementary and supportive therapies can be cost-effective and provide medical cost offsets by preventing future use of services, such as psychoactive medication, emergency room, psychiatry, and family practice visits.[184,185] For example, one RCT of online and face-to-face mindfulness therapy versus usual treatment found lower societal costs and less paid work-related productivity losses in both intervention groups, coupled with net monetary benefits compared with usual care.[149] Increasing awareness of the potential for cost offsets with the use of integrative programs to address anxiety and depression can make them more appealing to clinicians and administrators alike, and even to health insurers.

GUIDELINE IMPLEMENTATION

SIO-ASCO guidelines are developed for implementation across health settings. Key barriers to implementation include the need to increase awareness of the guideline recommendations among point-of-care practitioners and survivors of cancer and their caregivers, and to provide adequate services in the face of limited resources. The guideline Bottom Line Box was designed to facilitate implementation of recommendations, along with other materials generated by both ASCO and SIO, including a pocket guide, visual abstract, and continuing education modules. This guideline will be distributed widely through the ASCO Practice Guidelines Implementation Network. ASCO guidelines are posted on the ASCO website.

Despite these efforts, the Expert Panel understands that implementation of evidence-based interventions is not automatic once guidelines are disseminated, and often fails to happen altogether.[186] The Expert Panel, therefore, encourages researchers in this area to design implementation trials tailored to different settings using implementation science frameworks, such as the Knowledge to Action Framework[187] or the Consolidated Framework for Implementation Research.[188] These frameworks help to identify local contextual factors relevant to implementation in order to develop and test tailored implementation strategies. Strategies must consider the innovation domain itself (practice guidelines), characteristics (barriers and facilitators) of the inner and outer implementation setting (the hospital and broader community, for example), and specific individuals and roles within the setting that are important to achieve implementation. Partnering with experts in implementation science is recommended to avoid the all-too-common trial-and-error approach to implementation.[186]

The Expert Panel also encourages more pragmatic research in domains that already achieve strong recommendations in these guidelines. For example, there is little need for more efficacy trials on MBIs for women with breast cancer in academic settings, but pragmatic research studying the effectiveness and adaptations necessary to facilitate implementation of such interventions in real-world community settings, with existing resources and real-world patients, would be helpful.

PROVIDER TRAINING, LICENSING, AND CREDENTIALING

A critical challenge to the use of integrative interventions broadly is the training and credentialing of those providing

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them. This is in contrast to the more common psychologic, behavioral, and pharmacologic interventions for anxiety and depression, typically provided by licensed mental health practitioners. While some interventions have certified or accredited training and credentialing programs associated with their use (eg, acupuncture, art therapy, music therapy, dance/movement therapy, yoga, MBSR), not all practitioners come with the same experience. Further, training can vary and often is not nationally or internationally standardized.

For all these reasons, it is appropriate to inquire about the credentials, training, and experience of practitioners to whom people with cancer will be referred, including information about the provider's experience with those treated for cancer. One of the roles of the SIO is to promote more research on the use of these interventions, as well as bring providers together to advocate for training standards in the field that will, ideally, lead to both standardization of care and increased access to this care (https://integrativeonc.org/).

In an important step toward this latter goal, SIO conducted a systematic literature review and international consensus process among members of seven relevant professions on professional competencies for integrative oncology care. The process resulted in a total of 37 core competencies in the areas of knowledge (n = 11), skills (n = 17), and abilities (n = 9), combining both fundamental oncology knowledge and integrative medicine competencies that are necessary to provide effective and safe integrative oncology care for people with cancer. The committee agreed that these could be used as a starting point to develop profession-specific learning objectives and to establish integrative oncology education and training programs to meet the needs of people with cancer and health professionals.[189] SIO is currently developing a training curriculum for integrative oncology health care providers based on these competencies, which will serve as a starting point for adaptations to other professional groups of integrative therapy providers.

In the 2017 SIO breast cancer integrative therapy guideline, a detailed table of training, licensure and accreditation regulations, and a listing of professional societies for all grade A and B therapies were included (Greenlee et al[166]; Table 2). This includes relevant information for acupuncture, hypnosis, massage, meditation, music therapy, relaxation and stress management, and yoga.

QUALITY ASSURANCE OF NATURAL PRODUCTS

Efficacy trials of natural products should adhere to the same rigorous standards as other conventional drug intervention trials, including adequate description of all relevant methods pertaining to the natural product under investigation. However, it remains common that intervention methods and details of natural products are sometimes not properly conducted or reported.[190] Improper or poorly reported methods can be important sources of bias in studies of natural products.

Although the complexity and variability inherent in multicomponent natural products exceed that of single-substance natural products, methods describing both types of products share a number of similarities. Common elements include an accurate description of all components within a natural product (eg, botanical and/or scientific names and amount or proportion within the product), methods for creation of the product (eg, plant part used, extraction method), laboratory authentication of the product components including evaluation of potential contaminants (eg, authentication methods, certificate of analysis), and clear descriptions for dosing and dosing rationale.[191] All information necessary to ensure reproducibility and safety of a product must be included in study reports. If commercially produced over-the-counter natural products are used in research (rather than research-specific formulations), production and batch details should also be reported.

LIMITATIONS OF THE RESEARCH AND FUTURE RESEARCH

Throughout these recommendations, notes regarding the limitations of the literature in specific modalities are included. However, many issues cut across multiple modalities and are summarized in this section.

Assessment of Risk of Bias

The issue of the inability to mask participants to many integrative interventions has been raised repeatedly. This is ubiquitous across a range of therapy modalities, as it is sometimes impossible or undesirable to mask participants to interventions. This is particularly the case for many mind-body therapies that require active participation, such as yoga, mindfulness, tai chi and/or qigong, music therapy, and others. It is artificial to ask participants to actively undertake a practice not knowing what it is they are doing and does not mirror real-life program delivery where participants choose preferred modalities. Additionally, whether they know the name of the intervention or not, they are aware that the activities they are engaging in are expected to provide some benefit, which may lead to demand characteristics and subsequent positive reporting biases. Some exceptions, where participants have been masked to treatment with sham interventions, include acupuncture, Reiki, and other healing touch modalities. Typically, in these cases, the setting of the sham treatment is identical to the real intervention in order to elicit expectancy, but with incorrect acupoints or hand positioning, for example.

However, even with the inability to mask participants to the intervention, there are still methods available to protect studies from selection bias (such as allocation concealment) and measurement bias (by masking outcome assessors when possible). Of course, this is not possible when outcomes are measured by self-report, which is often the case in integrative therapy studies. Potential

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steps to try to account for not masking could be taken, for example measuring treatment preference, credibility, and expectancy for benefit prior to randomization, then determining the effects of these on outcomes. Additionally, few studies that do mask evaluate the success of masking by conducting a manipulation check, which is simple to do.

As a result of the inability to mask individuals to the treatments they are receiving, integrative therapy interventions often score poorly on standardized risk-of-bias assessments, as several of the indicators rate methods related to masking of participants and data collectors. The implications of this can be magnified in a ripple-down effect as follows: (1) studies are rated as low or moderate quality because of lack of masking; (2) evidence in SRs are consequently rated as low or moderate quality; (3) guidelines based on these SRs then lower the strength of the recommendation for the modality in question; and (4) the recommendation is then made that more high-quality research is needed to strengthen the recommendation. However, this is impossible to achieve when continuing to use the same tools to rate study quality and risk of bias that penalize lack of masking. Ultimately, this provides payors a reason not to reimburse interventions.

Solutions to this problem include improving study rigor in ways that are possible without masking, as detailed earlier. It would also be optimal to use risk of bias rating scales specifically developed to assess the design of behavioral intervention trials. While scales of this type do exist,[192] they are not yet routinely used in reviews or guideline development. Alternately, risk of bias can be evaluated using tools that highlight important bias domains for consideration and discussion, rather than provide summary scores from rating scales. This can allow a more refined estimation of the effect of specific biases on study effect measures.

The overall issue of whether and how to mask participants in behavioral intervention research is ongoing. One helpful framework to decide how to approach this is by using the explanatory-efficacy continuum described in the section on pragmatic trials in Future Directions. This framework structures decisions around study design depending on the ultimate goal of the research on the continuum.[193,194]

Standardization of Therapies

Lack of intervention standardization is noted in the commentaries of a number of the specific recommendations, and the section on natural health products, but this is a larger issue across many treatment modalities. Lack of intervention standardization makes comparisons across studies and replication difficult, if not impossible, and relates closely to the issue of adequate and standardized training of program facilitators (see section on provider training, licensing, and credentialing) as well as careful documentation of intervention components used and details of their delivery. For optimal internal validity in efficacy studies, treatment fidelity to the manual should also be monitored and reported.

Specific treatment characteristics that should be reported for mind-body therapies include number and duration of sessions, detailed content of each session, format (individual, group), delivery modality (in-person, online), assigned practice (eg, homework assigned) between sessions, and theoretical underpinnings. Ideally, treatments are manualized, and manuals are made available for replication studies. For natural products, source, composition, dose, and duration should be reported, as previously discussed. For yoga, meditation, and tai chi and/or qigong, the specific orientation of the instructor is important to document (eg, Tibetan *v* Hatha yoga; transcendental *v* Vipassana meditation). In yoga, the degree that each of the eight arms of yoga are incorporated (ie, breathing, meditation, ethics, postures) should be documented. If postures (asanas) are incorporated, the specific sequence of postures used should be documented. In this way, the dose of the therapy can be determined and potentially quantified, allowing for assessment of minimally efficacious doses needed for treatment effects for specific conditions and individuals.

There is tension, however, between providing standardized, manualized treatments, and tailoring integrative interventions to each individual's needs. This is not unlike the tension between pragmatic (real-world) and explanatory (efficacy) studies, where there may be a place for both depending on the ultimate goals of the research (to establish causality, determine real-world effectiveness, or something in between). Many traditional practices are individually tailored based on symptoms, goals of treatment, and individual limitations and characteristics, including acupuncture, yoga, and others. This makes manualizing these interventions difficult, artificial, and potentially less beneficial. One compromise is to standardize individualization; that is, part of the manualized treatment is to gauge individual needs and tailor some elements of the treatment specifically to those needs. This has been done in acupuncture studies for pain, for example, where the acupuncturist assesses the location and quality of the pain, then provides treatment to the acupoints appropriate for that type of pain.[195]

Lack of Diversity

Another issue that has arisen repeatedly in our literature review is the lack of diversity in study samples. The bulk of the research across modalities has been conducted on White, educated, middle-aged, upper and middle-class women with breast cancer. In the field of MBIs, a compelling commentary on Wealthy White Western Women summarizes the problem.[196] It is not unique to psychosocial and integrative oncology research, but is a larger problem across oncology and psychology, more generally. Hence, it has been difficult to

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make recommendations for people outside this demographic, as the research is quite simply lacking. Also, in terms of types of cancer, most research included enrolled women with breast cancer, with fewer studies including colorectal, prostate, and mixed groups of people with cancer.

The Expert Panel encourages researchers to begin filling these gaps by focusing on people from more diverse socioeconomic and racial backgrounds, with types of cancer other than breast. This poses challenges to recruitment and retention in trials, but with a recent shift toward developing methods of reaching and partnering with communities of color and other marginalized groups,[197] and a recognition of, and growing emphasis on, this priority from researchers and funders,[198] a cultural shift in this direction is gaining momentum.

Another area where more diversity is needed is in the therapies studied—there are many that fell into the inconclusive list, but are commonly used, accessible, and of interest to people with cancer, such as natural products, healing touch, reflexology, acupressure, and creative therapies. More rigorous study of these therapies is warranted.

Inactive or Usual Care Controls

The bulk of the research included in this work used study designs in which the intervention of interest was compared with either usual care, treatment as usual, or waitlist control—that is, no other active intervention. What this tells us is that these therapies are typically better than usual care (which could range from nothing at all beyond chemotherapy, radiation, and/or surgery, to high-quality psychosocial and supportive care). The usual care or waitlist condition is typically not well described in these studies if it is described at all. One can only assume that usual care includes usual conventional care, but the range of usual care around supportive interventions varies vastly across treatment settings.

Assuming that usual care typically means no additional supportive care, what this evidence tells us is that a range of integrative modalities is better than nothing for treating anxiety and depression in people with cancer. It is time to move beyond this understanding, to determine which modalities may be best, for which patients, which symptoms, and when. Currently, the research is not anywhere near this level of sophistication. Some studies have used comparative effectiveness designs to test different integrative modalities head-to-head, which also enables the ability to assess which intervention may be better for whom, but this approach is rare.[145,199] Studies comparing exercise to yoga or other mind-body therapies, for example, would be interesting and useful, as would comparisons of natural products to mind-body therapies. Comparisons of integrative modalities to conventional antidepressant or antianxiety medications, which many people are prescribed to treat these symptoms, would also be potentially influential. This has been done in the larger context of anxiety disorders, for example, where an MBI proved noninferior to antianxiety medication, with far fewer adverse events and side effects.[200]

Future Directions

In addition to the areas mentioned previously (better treatment reporting and standardization, greater diversity of study participants and interventions, active comparator groups), there are opportunities to enhance use and reach of integrative therapies in addressing anxiety and depression in cancer in the areas of digital health interventions (DHIs), pragmatic designs, and focus on patient-oriented research, as well as incorporation of precision integrative oncology.

DHIs include both asynchronous (individually paced) and synchronous (live, real time) interventions over the Internet, telephone, or mobile device via apps. Many studies are emerging, greatly accelerated by the COVID-19 pandemic, investigating the delivery and efficacy of integrative interventions through DHIs, and a number of the studies included in these guidelines used digital delivery modalities.[58,149,150] SIO conducted an international survey early in the pandemic regarding how programs were adapting interventions for delivery via videoconferencing and other digital platforms and published recommendations on the topic in 2021.[201] These practical guidelines provide suggestions for online treatment and/or consultation, including ethical and medical-legal aspects, preparing the online treatment setting, maintaining effective communication, promoting specific treatment effects, and ensuring continuity of care, among others.

Pragmatic research, broadly defined as research that occurs in real-world settings with real-world patients, has lately been recognized as a better conduit to practice change and implementation than traditional explanatory models of efficacy research. Pragmatic research designs are identified by real-world characteristics across nine domains: the choice of eligibility criteria, recruitment method, setting, study organization, flexibility of treatment delivery, flexibility of treatment adherence, extent of follow-up, choice of primary outcome, and primary analysis methods.[193] Choices in each of these domains can range from very explanatory and tightly controlled, to pragmatic and less controlled. Explanatory research is necessary to determine strict causation by ensuring internal validity, whereas pragmatic research focuses more on external validity. As mentioned in the implementation section, pragmatic designs can help bridge evidence-based treatments from efficacy to implementation.

With greater incorporation of patient-reported outcomes in the oncology setting, the lived experience of growing numbers of people with cancer is being better understood.[202,203] Studies

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show that there can often be a disconnect between clinician- and patient-report of symptoms.[204-206] This has led to awareness of the need to ask people themselves about how they are faring, and importantly, when and for what they would like assistance. In this context, it is of note that while some integrative approaches provide only minimal benefit to the management of anxiety and depression, they may result in significant improvements in other domains, most specifically overall quality of life, which in turn, is a predictor of cancer-related morbidity and mortality.[207,208]

For all of these promising directions to come to fruition, more public and private funding for integrative oncology intervention research is needed. Given that millions of people with cancer seek out and use these modalities every year and institutions are offering access to integrative services, understanding how best to guide and strengthen this investment would benefit both the recipients and providers—and their respective institutions—of this care.

SIO and ASCO believe that cancer clinical trials are vital to inform clinical decisions and improve cancer care, and that all people with cancer 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 and https://integrativeonc.org/practice-guidelines/guidelines. Patient information is available at www.cancer.net and https://integrativeonc.org/knowledge-center/patients.

RELATED SOCIETY FOR INTEGRATIVE ONCOLOGY AND ASCO GUIDELINES

- Integrative Medicine for Pain Management in Oncology[209] (http://ascopubs.org/doi/10.1200/JCO.22.01357)
- Integrative Therapies During and After Breast Cancer Treatment[210] (http://ascopubs.org/doi/10.1200/JCO.2018.79.2721)
- Clinical practice guidelines on the evidence-based use of integrative therapies during and after breast cancer treatment[166] (https://acsjournals.onlinelibrary.wiley.com/doi/full/10.3322/caac.21397)
- Patient-Clinician Communication[168] (http://ascopubs.org/doi/10.1200/JCO.2017.75.2311)
- Complementary therapies and integrative medicine in lung cancer: Diagnosis and management of lung cancer, 3rd ed[211] (https://pubmed.ncbi.nlm.nih.gov/23649450/)
- Evidence-Based Clinical Practice Guidelines for Integrative Oncology: Complementary Therapies and Botanicals[212] (https://integrativeonc.org/docman-library/docs/65-sio-guidelines-2009/file)

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EDITOR'S NOTE

This joint Society for Integrative Oncology and American Society of Clinical Oncology 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 https://integrativeonc.org/knowledge-center/patients and www.cancer.net, is available at https://integrativeonc.org/practice-guidelines/guidelines and www.asco.org/survivorship-guidelines.

EQUAL CONTRIBUTION

L.E.C. and J.H.R. were Expert Panel cochairs.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Integrative Oncology Care of Symptoms of Anxiety and Depression in Adults With Cancer: Society for Integrative Oncology–ASCO Guideline

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APPENDIX

TABLE A1. GLIDES Rating Definitions

Term	Definition
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: 1. Strong evidence for a true net effect (eg, benefits exceed harms). 2. Consistent results, with no or minor exceptions. 3. Minor or no concerns about study quality; and/or 4. 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: 1. Good evidence for a true net effect (eg, benefits exceed harms). 2. Consistent results with minor and/or few exceptions. 3. Minor and/or few concerns about study quality; and/or 4. 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: 1. Limited evidence for a true net effect (eg, benefits exceed harms). 2. Consistent results, but with important exceptions. 3. Concerns about study quality; and/or 4. The extent of panelists' agreement. Other considerations (discussed in the guideline's literature review and analyses) may also warrant a weak recommendation.

Abbreviation: GLIDES, Guidelines into Decision Support.

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TABLE A2. Integrative Oncology Care of Symptoms of Anxiety and Depression in Adults with Cancer Guideline Expert Panel Membership

Name	Affiliation	Discipline
Linda E. Carlson, RPsych, PhD (Cochair)	Division of Psychosocial Oncology, Department of Oncology, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada	Clinical psychology
Julia H. Rowland, PhD (Cochair)	Smith Center for Healing and the Arts, Washington, DC	Psychology
Elizabeth L. Addington, PhD	Northwestern University Feinberg School of Medicine, Chicago, IL	Psychology
Gary N. Asher, MD, MPH	University of North Carolina, Chapel Hill, NC	Family medicine, emergency medicine (herbal, Ayurveda, massage, Tai Chi Chuan)
Chloe Atreya, MD, PhD	University of California, San Francisco, San Francisco, CA	Gastrointestinal oncology
Lynda G. Balneaves, RN, PhD	College of Nursing, University of Manitoba, Winnipeg, MB, Canada	Psychosocial oncology, integrative oncology, cannabis
Joke Bradt, MT-BC, PhD	Drexel University, Philadelphia, PA	Music therapy
Nina Fuller-Shavel, MB BChir, MA	Synthesis Clinic, Winchester, United Kingdom	Nutritionist, herbal medicine, TCM, yoga, mindfulness, integrative oncology
Joseph Goodman, MD	The George Washington University, Washington, DC	Head and neck oncologic surgery and acupuncture
Caroline J. Hoffman, OAM, RN, BSW, PhD	Paul's Cancer Support, London, United Kingdom	Mindfulness, integrative oncology
Alissa Huston, MD	University of Rochester Medical Center, Rochester, NY	Medical oncology
Ashwin Mehta, MD	Memorial Healthcare System, Hollywood, FL	Nutrition, exercise, sleep, yoga, mindfulness
Channing J. Paller, MD	John Hopkins University, Baltimore, MD	Herbal, genitourinary oncology
Kimberly Richardson	University of Illinois Cancer Center, Chicago, IL	Patient representative
Dugald Seely, ND, MSc	University of Ottawa, Ottawa, ON, Canada Canadian College of Naturopathic Medicine, Toronto, ON, Canada	Naturopathic medicine, integrative oncology
Chelsea J. Siwik, PhD	Osher Center for Integrative Health, University of California, San Francisco, San Francisco, CA	Trainee representative
Jennifer S. Temel, MD	Massachusetts General Hospital and Harvard Medical School, Boston, MA	Medical oncology
Nofisat Ismaila, MD	ASCO, Alexandria, VA	ASCO Practice Guideline Staff (Health Research Methods)

Abbreviation: TCM, traditional Chinese medicine.

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TABLE A3. Index of Terms

Term	Definition
Depression	A mood disorder with eight criteria, of which the individual must be experiencing five or more symptoms during the same 2-week period and at least one of the symptoms should be either (1) depressed mood or (2) loss of interest or pleasure. These symptoms must cause the individual clinically significant distress or impairment in social, occupational, or other important areas of functioning.
Depression symptoms	Depressed mood. Markedly diminished interest or pleasure in all, or almost all, activities. Significant weight loss when not dieting or weight gain or decrease or increase in appetite. A slowing down of thought and a reduction of physical movement (observable by others, not merely subjective feelings of restlessness or being slowed down). Fatigue or loss of energy. Feelings of worthlessness or excessive or inappropriate guilt. Diminished ability to think or concentrate, or indecisiveness. Recurrent thoughts of death, recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.
Anxiety (generalized anxiety disorder)	The presence of excessive anxiety and worry about a variety of topics, events, or activities. Worry occurs more often than not for at least 6 months and is clearly excessive and very challenging to control. The anxiety and worry are accompanied with at least three of six physical or cognitive symptoms that include edginess or restlessness, impaired concentration, and difficulty sleeping.
Anxiety symptoms	Excessive anxiety and worry (apprehensive expectation) about a number of events or activities (such as work or school performance). The person finds it difficult to control the worry. The anxiety and worry are associated with three or more of the following six symptoms: Restlessness or feeling keyed up or on edge. Being easily fatigued Difficulty concentrating or mind going blank. Irritability Muscle tension Sleep disturbance (difficulty falling or staying asleep, or restless unsatisfying sleep)
	(continued in next column)

TABLE A3. Index of Terms (continued)

Term	Definition
Adjustment disorders with depressed anxious/mood	Emotional or behavioral symptoms in response to an identifiable stressor(s) occurring within 3 months of the onset of the stressor(s). With (1) low mood, tearfulness, or feelings of hopelessness, or (2) anxiety, nervousness, worry, jitteriness, or separation anxiety in the presence of the major stressor and with significant impairment in social, occupational, or other important areas of functioning.
PTS symptoms	Unwanted upsetting memories Nightmares/night terrors Flashbacks Emotional distress; arousal after exposure to traumatic reminders Physical reactivity after exposure to traumatic reminders; hypervigilance Avoidance of trauma-related stimuli after the trauma, in the following way(s): Trauma-related thoughts or feelings Trauma-related external reminders negative alterations in cognitions and mood Negative thoughts or feelings that began or worsened after the trauma, in the following way(s): Inability to recall key features of the trauma Overly negative thoughts and assumptions about oneself or the world Exaggerated blame of self or others for causing the trauma Negative affect Decreased interest in activities, feeling isolated Difficulty experiencing positive affect Alterations in arousal and reactivity Trauma-related arousal and reactivity
Active treatment	After cancer diagnosis but before or during the course of surgery, chemotherapy, immunotherapy, or radiation therapy.
Post-treatment	After completion of surgery, chemotherapy or radiation therapy. Includes people on long-term maintenance therapies such as hormonal therapies (aromatase inhibitors, tamoxifen, and androgen-deprivation therapies).

Abbreviation: PTS, post-traumatic stress.

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TABLE A4. Interventions

Integrative Therapy	Definition
Acupuncture or acupressure	Acupuncture is a technique originating from TCM in which practitioners insert fine needles into the skin at specific anatomical locations to treat health problems. The needles may be manipulated manually or stimulated with small electrical currents (electroacupuncture). Acupressure uses the same specific locations as acupuncture but instead of using a needle for skin penetration, manual pressure is applied.[213]
Aromatherapy	Aromatherapy is the therapeutic use of essential oils (also known as volatile oils) from plants (flowers, herbs, or trees) for the improvement of physical, emotional, and spiritual well-being. These are generally applied through the skin as a topical application, as part of a massage, an inhalation, or water immersion. The recommendations in this guideline are for inhaled aromatherapy only.[214]
Art therapy Visual arts–based interventions	Art therapy is a psychosocial intervention, facilitated by a professional art therapist, that utilizes art-making as a way for people to explore their subjective experiences and express their thoughts and emotions verbally and nonverbally. Art therapy is used to improve cognitive and sensory-motor functioning, foster self-esteem and self-awareness, enhance coping skills, cultivate emotional resilience, promote insight, enhance social skills, reduce and resolve conflicts and distress, and advance societal and ecological change. Visual arts–based interventions are defined here as visual arts activities offered by a health care professional or volunteer for therapeutic purposes or the use of visual arts to create a healing environment in hospital settings. In contrast to art therapy interventions, no systematic therapeutic process is present.[215,216]
Relaxation techniques	Breathing and relaxation techniques are practices to help elicit the body's relaxation response, which acts counter to the stress response. The relaxation response is characterized by slowed breathing and reduced heart rate. The National Centre for Complementary and Integrative Medicine include the following techniques under this umbrella term: Progressive muscle relaxation: This technique involves progressively tensing and releasing different muscle groups in the body. Autogenic training: Mental exercises involving relaxation and suggestion to oneself (autosuggestions) to focus on the bodily experience of relaxation. Guided imagery or visualization: Using mental imagery to picture objects, scenes, or events that are associated with relaxation or calmness to produce a similar feeling in the body. Biofeedback-assisted relaxation: Learning how to recognize and manage bodily response and induce relaxation through feedback on heart rate, blood pressure, or muscle tension changes from an electronic device. Breathing exercises: Breathing exercises involving taking slow (often paced) deep breaths.[217]
Botanicals	Botanicals are plants or plant parts used for their therapeutic properties.
Chinese herbal formulae	Chinese herbal medicine is part of a larger system of TCM. Chinese herbal medicine formulae utilize several herbs and their composition is usually based on the TCM materia medica and reconstructed classical texts. The formula may be modified by the Chinese herbal medicine practitioner based on individual presentation or they may be used as standard preparations, eg, patent medicines.
Dance/movement therapy	Dance/movement therapy is the psychotherapeutic use of movement to promote emotional, social, cognitive, and physical integration of the individual, for the purpose of improving health and well-being (ADTA). Dance/movement therapy may include a variety of dance/movement methods and is characterized by a goal-oriented, systematic treatment process.[104]
Dietary supplements	Dietary supplements are products that are taken by mouth (such as a tablet, capsule, powder, or liquid), are made to supplement the diet, have one or more dietary ingredients, including vitamins, minerals, amino acids, enzymes etc, and are labeled as being dietary supplements. (Note—NCCIH definition based on federal law)[218]
Expressive writing, journaling, gratitude	In EWI, participants are instructed to write, typically for 15 consecutive minutes, for at least three times spread out over the course of a day or set of days (eg, 4 consecutive days or twice a week for 2 weeks), about their cancer or other traumatic experience. Participants are encouraged to write freely without regard for punctuation, verb concordance, or other technical aspects of writing. Variants may include use of daily journals and specifically journals in which participants record things for which they are grateful (gratitude journals) as alternative formats for eliciting emotional expression about response to illness or trauma.
Humor or laughter therapy	A type of therapy that uses humor to help relieve pain and stress and improve a person's sense of well-being. It may be used to help people cope with a serious disease, such as cancer. Humor therapy may include laughter exercises, clowns, and comedy movies, books, games, and puzzles. Also called laughter therapy.[219]
Hypnosis	Promoting a state of consciousness involving focused attention and reduced peripheral awareness characterized by an enhanced capacity for response to suggestion. Hypnosis can be delivered by a professional hypnotherapist or be self-delivered with training and practice (self-hypnosis).[220]
Light therapy	Intentional daily exposure to direct sunlight or similar-intensity artificial light in order to treat medical disorders, especially SAD and circadian rhythm sleep-wake disorders. In people with cancer, it has also been tested as a treatment for cancer-related fatigue.[221]
Therapeutic massage and bodywork	Therapeutic massage and bodywork involves manipulation of the soft tissues of the body by a licensed professional as a way to maintain or improve health. These therapeutic modalities use a fully designed systematic approach to treatment that follows certain principles and protocols and can be used to meet specific needs for relaxation, pain relief, or to improve health.
Meditation	Meditation is a group of self-regulation practices that focus on training attention and awareness on bringing mental processes under greater voluntary control. Interventions which train participants in meditation practices not derived from MBSR, such as transcendental meditation, Tibetan meditation, or other traditions, are included in this category.[166]
Mindfulness-based interventions	Programs derived from MBSR, based on the work of Jon Kabat-Zinn. MBSR is typically delivered in an 8-week structured group program consisting of a range of meditation practices including a sensate focus body scan, sitting meditation, walking meditation, loving-kindness practice, and gentle Hatha yoga postures. MBIs typically include multiple sessions in which participants learn and practice mindfulness meditation, mindful movement, and include didactic teaching and inquiry. May be offered in groups (more common) or individually, face-to-face, or through digital health platforms.[166]

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TABLE A4. Interventions (continued)

Integrative Therapy	Definition
Multimodality	Programs in which a mix of modalities is combined to treat symptoms of anxiety or depression and/or help with coping.
Music therapy Music-based interventions	Music therapy is the clinical use of music interventions to accomplish individualized goals within a therapeutic relationship by a credentialed professional who has completed an approved music therapy program. Music interventions include listening to live, improvised, or pre-recorded music; playing music instruments and singing; improvising music; and composing music. Music-based interventions are defined here as music listening offered by a health care professional or volunteer for therapeutic purposes such as relaxation. In contrast to music therapy interventions, no systematic therapeutic process is present. Patients are typically offered pre-recorded music to listen to. However, listening to live music offered by musicians is also classified under music-based interventions.[62]
Nutritional or dietary approaches	Approaches that utilize specific nutritional or dietary guidance or intervention to support health outcomes
Probiotics	Probiotics are live microorganisms which when administered in adequate amounts may confer a health benefit when consumed or applied to the body.
Psychedelic-assisted therapy	The use of psychedelic substances (eg, LSD, MDMA, ketamine, psilocybin) in one or more doses, in combination with supportive therapy sessions to treat symptoms such as depression, anxiety, and post-traumatic stress.
Reflexology	Reflexology is a gentle manipulation or pressure, generally applied to the feet, but can include the hands, ears, or face. In reflexology, it is thought that by supporting and stimulating different parts and points on the body, it can help rebalance the mind and body and help relieve symptoms.[222]
Reiki	Reiki is a Japanese form of hands-on healing using gentle touch either directly on or slightly off the body. Subtle healing energy is transferred through the palms of the practitioner to the patient in order to support emotional or physical well-being.[223]
Tai chi and/or qigong	Qigong is a mind-body practice using exercises to optimize energy within the body, mind, and spirit, with the goal of improving and maintaining health and well-being. Qigong has both psychologic and physical components and involves the regulation of the mind, breath, and body's movement and posture. Dynamic (active) qigong techniques primarily focus on body movements, especially movements of the whole body or arms and legs. Meditative (passive) qigong techniques can be practiced in any posture that can be maintained over time and involve breath and mind exercises, with almost no body movement.[224] Tai chi chuan is an internal Chinese martial art practiced for self-defense, meditation, and health. All schools of tai chi hold in common the practice of choreographed postures that are practiced in sequence as a long string of continual motion. There is considerable overlap in the practices of tai chi and qigong due to their shared focus of using the internal energy of the mind to move the body.[225]
Healing touch or therapeutic touch	Healing touch involves the placing of hands either gently on or close to the body with the intention of gently modulating and balancing the energy field of the body with the intention of improving physical and psychologic well-being.
Yoga	Yoga is an ancient and complex practice rooted in Indian philosophy. Although classical yoga also includes other elements, yoga as practiced in most research studies typically emphasizes physical postures *(asanas)*, breathing techniques *(pranayama)*, and meditation *(dyana)*. There are many different yoga styles, ranging from gentle practices to physically demanding ones.[226]

Abbreviations: ADTA, American Dance Therapy Association; EWI, expressive writing interventions; LSD, lysergic acid diethylamide; MBI, mindfulness-based intervention; MBSR, mindfulness-based stress reduction; MDMA, methylenedioxy-methylamphetamine; NCCIH, National Center for Complementary and Integrative Health; SAD, seasonal affective disorder; TCM, traditional Chinese medicine.

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TABLE A5. Commonly Used Standardized Measuring Tools

Acronym	Meaning
CES-D	Center for Epidemiological Studies-Depression
HADS	Hospital Anxiety and Depression Scale
BDI	Beck Depression Inventory
BSI	Brief Symptom Inventory
PHQ-9	Patient Health Questionnaire-9
GAD-7	General Anxiety Disorder-7
STAI	State-Trait Anxiety Inventory
PROMIS	Patient-Reported Outcomes Measurement Information System
POMS	Profile of Mood States
IOC	Impact of Cancer
IES	Impact of Events Scale
PCL-C	Post-Traumatic Stress Disorder Checklist—Civilian
ESAS	Edmonton Symptom Assessment System
FACT-G	Functional Assessment of Cancer Therapy—General
HAMD-17; HAMD-24	Hamilton Rating Scale for Depression
SF-36	Short Form—36 (quality of life measure)
QOL	Quality of Life
MADRS	Montgomery–Åsberg Depression Rating Scale
SCL-90	Symptom Checklist—90 item version

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