clinical review

Putting Integrative Oncology Into Practice: Concepts and Approaches

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abstract

Unmet symptom needs and a desire for holistic health approaches or even cure are among the motivations patients have for seeking out complementary and alternative medicine. Using complementary and alternative medicine instead of conventional cancer treatment can have a negative impact on clinical outcomes and survival. Integrative oncology is a patient-centered, evidence-informed field of comprehensive cancer care that uses mind-body practices, natural products, and lifestyle modifications from different traditions alongside conventional cancer treatments. It prioritizes safety and best available evidence to offer appropriate therapeutic interventions along with conventional care. This review summarizes the underlying principles of integrative oncology and how it is distinct from alternative medicine, and it provides a practical guide for the effective application of evidence-based complementary and alternative medicine interventions in patient-centered care. In addition, we recommend resources for patients and clinicians and provide algorithms for appropriate integrative medicine referrals. Finally, we offer suggestions on developing and implementing an integrative oncology program and addressing current challenges in the field.

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INTRODUCTION

Integrative oncology is a patient-centered, evidence-informed field of comprehensive cancer care that uses lifestyle modifications, mind-body practices, and natural products from different traditions alongside conventional cancer treatments (Fig 1A).[1] Integrative oncology seeks to engage patients and families as active participants in their own care from prevention throughout treatment and survivorship. This principle optimizes health promotion and proactively addresses symptoms and adverse effects that arise from cancer or its treatment.

For many patients, symptoms such as insomnia, pain, fatigue, and anxiety may persist despite standard medical interventions. Unmet symptom needs and a desire for holistic health approaches or even cure are among the motivations patients have for seeking out complementary and alternative medicine (CAM). Although the use of CAM is prevalent among patients with cancer (with estimates of up to 80%), only 14% may communicate their use of CAM to providers.[2,3] In addition, patients are more likely to obtain information about CAM from nonmedical sources. Alarmingly, a recent ASCO 2018 National Opinion Survey[4] found that 40% of Americans believe cancer can be cured solely through alternative therapies; 38% of caregivers and 22% of those with cancer hold this belief. Younger people also tend to have such beliefs.

The practice of integrative oncology stands in contrast to the use of alternative medicine, which is often based on unsubstantiated claims and can involve rejection of conventional medical treatment. The use of alternative medicine in lieu of conventional treatment has been associated with decreased survival in the cancer setting.[5] Integrative oncology prioritizes safety and best available evidence to offer appropriate therapeutic interventions along with conventional care. The commitment to rigorous scientific research and evidence-informed practice in cancer care was strongly emphasized by the foundation of the Society for Integrative Oncology (SIO) in 2003 and the release of the first set of general clinical practice guidelines in 2009, followed by two other cancer-specific guidelines thereafter.[6-9] Most recently, ASCO endorsed SIO clinical guidelines for women with breast cancer.[10]

THERAPEUTIC APPROACHES USED IN INTEGRATIVE ONCOLOGY

Complementary therapies have been established at many major cancer centers to help manage both immediate and delayed cancer-related symptoms, support lifestyle changes, and improve quality of life for patients. The current evidence is strongest for the following interventions to optimize symptom management, address unmet needs, and facilitate positive behavior changes.

ASSOCIATED CONTENT

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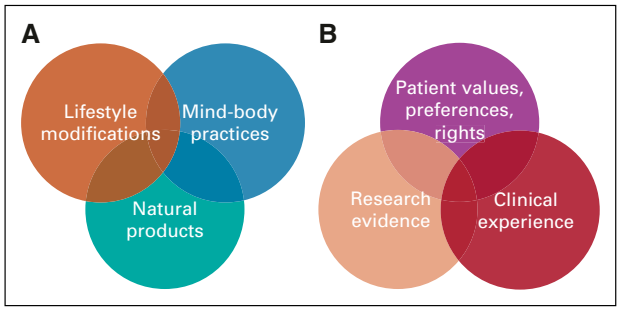

FIG 1. Core components of integrative oncology for evidence-informed patient-centered care: (A) three main therapeutic categories, and (B) components of evidence-informed practice.

Lifestyle Modifications

Diet, exercise, sleep hygiene, stress management, and social environment as well as avoidance of risky behavior are the lifestyle factors that have been shown to have an impact on a wide range of health measures, including lifetime risk of developing or dying from cancer. For cancer survivors, lifestyle factors are relevant in reducing morbidity related to late effects of their disease and its treatment.[11] Cultivated lifestyle habits also have important interactive effects, such as uncontrolled stress that impedes the adoption of healthy behaviors.[12]

Exercise and Physical Activity. American Cancer Society Guidelines on Nutrition and Physical Activity for Cancer Prevention[11] advise patients to pursue at least 150 minutes of moderate-intensity or 75 minutes of vigorous-intensity activity each week. Many patients face barriers to physical activities such as fatigue and pain, and they need guidance on how to implement these guidelines in the face of cancer-related adverse effects or postsurgical changes.[13] During cancer treatment, regular physical activity is effective in addressing fatigue and improving objective measures of physical functioning and cardiovascular fitness.[14-16] In addition, there are well-documented benefits on patient-reported outcomes including self-esteem and quality of life.[14-16] For patients with cancer who have surgical complications or physical limitations, supervised exercise can help prevent injury and declines in physical functioning and quality of life[16] and build confidence for sustained improvements. For patients who are sedentary, movement meditation such as yoga and tai chi can be excellent stepping stones to more robust activity later and can also be customized to optimize individual intensity. Exercise and mind-body movement therapists who are experienced in working with cancer survivors are integral to guiding patients to safely implement sustainable physical activity, prevent falls or injury, and build a regimen that feels right and is even enjoyable.

Diet. At most medical institutions, trained dietitians review nutritional concerns and treatment-related dietary restrictions with patients undergoing cancer treatment. Nonetheless, patients at all disease stages often wonder about whether dietary modifications can modify their cancer risk. Many patients are drawn to pursue popular diets, which are frequently touted as curative regimens for cancer. Although many of these diets (eg, the Alkaline Diet) may be harmless, they lack a scientific basis. Other regimens such as the Gerson Therapy are severely restrictive and can be hazardous to the patient, particularly when paired with a philosophy that rejects conventional care.

For those who may have enduring interests in specialized diets, integrative medicine specialists should work with these patients and their dieticians to help avoid nutritional deficiencies, negative calorie balance, and weight loss during cancer treatment that could be detrimental to overall outcomes. In addition, redirecting patients' focus to appropriate and achievable adjustments in diet and activity are key. In a recent prospective population study (N = 41,543 participants age 40 years or older), better adherence to World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) recommendations significantly contributed to cancer prevention: a one-point increment in WCRF/AICR score was associated with a 12% decreased overall cancer risk, and alcohol avoidance was determined to be an important prevention factor.[17] Encouraging patients to develop regular eating patterns that include more vegetables, fruits, whole grains, and legumes while limiting consumption of red meats and alcohol and avoiding processed foods and sugar should be the touchstone.[18] Increasing evidence links obesity and other modifiable lifestyle behaviors such as physical inactivity and dietary factors to cancer development. For individuals with cancer, there is also evidence supporting the importance of nutrition during and after cancer care for improving quality of life, enhancing recovery, and for health maintenance, as well as for decreasing risk of disease recurrence and increasing survival time.[19,20] Moreover, a strong protective effect is suggested when both diet with higher vegetable-fruit consumption and physical activity are included in treatment.[20]

Sleep. Sleep disturbance and insomnia are highly prevalent in the cancer population, both during and after active treatment. Causes are often multifactorial and include adverse medication effects, disrupted circadian rhythms due to treatment-related fatigue, and psychosocial factors.[21] There are a range of nonpharmacologic treatment options that have been shown to improve sleep quality. Among these, cognitive behavioral therapy for insomnia is the gold standard and should be the first choice when available.[22,23] In recent randomized clinical trials comparing acupuncture, tai chi, or mindfulness-based stress reduction to cognitive behavioral therapy for insomnia for patients with cancer, all of these interventions demonstrated durable and meaningful decreases in the severity of insomnia.[24-26] Clinicians need to help patients recognize

the importance of sleep for good health and engage them in choosing effective therapies to help manage their insomnia.

Stress Management. After a cancer diagnosis, the physical, emotional, and social effects of the disease are overwhelmingly perceived as stressful. Effective coping strategies such as relaxation practices and stress management techniques have been shown to decrease levels of depression, anxiety, and symptoms related to cancer and its treatment.[27,28] Of all the available therapies, mindfulness-based interventions or yoga seem to have the most robust evidence for stress management. However, long-term studies are needed to support ongoing practice.

Mind-Body Interventions

Mind-body therapies include instructor-guided movement practices such as tai chi or yoga or contemplative and relaxation practices such as meditation or guided imagery, as well as provider-dependent interventions such as massage therapy and acupuncture.[29] The practices and their applications harness the intricate relationship between psychological and physical well-being.

Acupuncture. Acupuncture is a therapy that originated from traditional Chinese medicine. It uses sterile thin needles that are inserted at specific points on the body and subsequently stimulated, either manually or electrically, to manage symptoms. Animal studies have found that acupuncture can stimulate the brain to release endogenous opioids, serotonin, and dopamine. Functional imaging studies in humans have also found that acupuncture can modulate multiple brain regions involved in cognition and emotion. The National Comprehensive Cancer Network Guidelines recommend the use of acupuncture for pain, fatigue, nausea, vomiting, and hot flashes, and in the setting of palliative care and survivorship.[30] More than 80% of National Cancer Institute–designated comprehensive cancer centers recommend acupuncture for symptom management.[31]

Massage. Massage therapy in the oncology setting to reduce cancer-related fatigue, pain, mood disturbance, and lymphedema is among the recommended interventions in clinical guidelines.[8,32,33] Adaptations in oncology massage may include changes to applied pressure, site avoidance or restrictions, and precautions related to other relevant history such as recent treatments, surgery, or metastasis. Studies have shown significant reductions in pain, nausea, fatigue, and psychological distress.[34,35] Benefits of massage are likely to be more immediate and of shorter duration than other interventions. More research may help determine optimal massage therapy regimens for patients with cancer.

Mindfulness-Based Interventions. The best researched form of secular meditation is mindfulness-based stress reduction. In the practice of mindfulness meditation, arising thoughts, emotions, and physical sensations are observed with open, relaxed, and nonjudgmental attention. Randomized trials of mindfulness-based stress reduction report decreased fatigue, depression, anxiety, and fear of recurrence.[36,37] In addition, improvements have been noted in sleep,[36,38] quality of life, and psychosocial adjustments,[39] as well as in long-term adverse effects associated with treatment.[40] Although most studies have been conducted in patients with breast cancer, mindfulness-based stress reduction studies in patients with other types of cancer also demonstrate improvements in mood, general well-being, and cancer-related cognitive impairment along with reductions in stress and distress.[41,42] In addition, evidence is emerging that well-studied mindfulness meditation interventions such as mindfulness-based stress reduction are effective adjunct treatments for chronic pain.[43]

Yoga. Yoga is a meditative movement practice that originated from ayurvedic medicine that aims to yoke or join the mind and body. Although there are considerable differences between traditions and schools of practice, all involve the use of physical asanas or postures, breathing techniques, meditation, chanting, and study of philosophical texts and rules of conduct. Several large meta-analyses and systematic reviews summarize the evidence of benefits with yoga on quality of life and emotional health in patients with cancer and cancer survivors.[44-46] In addition, a large multicenter randomized trial of a 4-week restorative yoga program compared with standard care among cancer survivors found that those who participated in the intervention had significantly greater improvements in sleep and reduced their use of sleep medication.[47]

Tai Chi. Tai chi is an ancient movement practice originally based on Chinese martial arts. The practice evolved to be characterized by slow, flowing movement sequences coordinated with the breath and focused attention. As a safe and gentle form of exercise, tai chi is particularly helpful for encouraging debilitated and elderly patients to re-engage in physical activity. In addition, studies have found tai chi to improve balance and reduce risk for falls.[48] In a randomized trial that compared tai chi with physical therapy for knee osteoarthritis, both groups had similar clinically significant improvements, but the tai chi group also showed improvements in depression and quality-of-life scores.[49]

The slow-moving, low-impact sequences of tai chi may be ideal for patients with cancer who are weakened or fatigued and who want to engage in safe exercise. In a randomized controlled trial of patients with lung cancer undergoing chemotherapy, tai chi was found to be effective for managing cancer-related fatigue.[50] In patients with breast cancer who had comorbid insomnia, tai chi produced clinically meaningful improvements and was noninferior to cognitive behavioral therapy (the gold standard) for insomnia.[25]

Natural Products

As defined by the National Center for Complementary and Integrative Health, natural products include “a variety of products, such as herbs (also known as botanicals), vitamins and minerals, and probiotics. They are widely

marketed, readily available to consumers, and often sold as dietary supplements."[29]

Use of herbal products and dietary supplements is the most common CAM approach in more than one third (37%) of patients older than age 50 years who were surveyed.[51] Patients sometimes use natural products to alleviate symptoms; however, they may also have expectations of cure despite the lack of evidence that natural products can alter cancer outcomes. The possibility for harm with natural products is particularly augmented for patients with cancer who are undergoing active treatment. Generally there are four main categories of potential interactions that can occur: high doses of natural products with antioxidant properties may interfere with radiation or chemotherapy efficacy[52,53]; anticoagulant herbs may cause detrimental effects in patients with low platelet levels or when used concurrently with anticoagulant medications[54] or during perioperative periods[55]; phytoestrogenic herbs may interfere with hormonal therapies or exert negative influences on hormone-sensitive cancers[56]; and immunostimulant herbs may alter the efficacy of immunosuppressive therapy.[57] In addition, direct organ toxicity such as renal and hepatic injury has been associated with some natural products.[58]

Quality control issues are a major concern with natural products and herbal supplements because of the potential for product substitutions or fillers, contamination, and inaccurate labeling.[59] Potential issues can be further compounded by lack of dialogue between patients with cancer and their providers regarding the use of natural products.

Recent SIO guidelines endorsed by an ASCO Expert Panel determined that there is generally little evidence for using supplements among patients with breast cancer.[10] In addition, acetyl-L-carnitine may actually cause harm when used for chemotherapy-induced peripheral neuropathy. Aloe vera and hyaluronic acid cream also were not recommended for radiation skin reactions, and glutamine was not recommended for chemotherapy-induced nausea and vomiting, although ginger, when used along with antiemetics, may provide a small benefit.

Given the ubiquitous availability, lack of evidence, and potential for harm posed by many natural products, it is crucial to have a dialogue with patients on this topic. Table 1 provides reliable resources for databases of natural products and evidence-based integrative therapies for both patients and providers.

EVIDENCE-INFORMED PRACTICE

A key feature distinguishing integrative oncology from alternative medicine is its foundation of evidence-informed practice. Evidence-based medicine as a concept emerged in the 1980s and has since transformed medical education and clinical practice.[60] It can be defined as the combined integration of the best available research evidence along with our clinical expertise while considering our patient's values and circumstances (Fig 1B). As research begins to shed light on the safety and efficacy of complementary therapies, critical appraisal of the literature and ongoing learning is needed to incorporate these approaches into clinical practice. Using an evidence-informed approach allows clinicians to incorporate patients' values and preferences along with their own clinical experience and current research evidence for therapeutic approaches (eg, medications or acupuncture for pain) to support a shared decision-making process for patients and families. Figure 2 shows a suggested algorithm of integrative therapy referral options that could help facilitate discussions on evidence-based approaches for patients with cancer.

PATIENT-CENTERED COMMUNICATIONS

Patients with cancer have variable expectations of benefits from integrative therapies. Unrealistic expectations, such as those for cure or life prolongation, can lead to rejection of conventional care or to adverse effects through unsupervised use of CAM.[61-63] Family endorsement of CAM, which is often based on anecdotal information, may significantly shape patients' expectations of CAM's benefits.

In our recent study,[3] patients whose families encouraged CAM compared with those whose families did not also had increased expectations for cancer cure (37% *v* 12%) and prolonged life (61% *v* 24%) from using CAM. Managing individual expectations of what can be achieved with integrative therapies is therefore an important component of integrative oncology care, and sharing evidence-based guidelines, such as the recent ASCO endorsement of SIO clinical guidelines,[10] with patients can help facilitate this conversation. Health care providers are encouraged to foster open and nonjudgmental conversations about their patients' use of CAM. When patients are encouraged to share their health philosophies and interests in complementary treatments, they can then be effectively counseled on their use of CAM. Integrative medicine specialists can empower patients to take part in their care plan by redirecting patients' self-care efforts to treatments and lifestyle changes that are evidence-informed, effective, and safe.

DEVELOPING AN INTEGRATIVE ONCOLOGY PRACTICE

Leading cancer centers such as Memorial Sloan Kettering Cancer Center, MD Anderson Cancer Center, and Dana-Farber Cancer Institute have been building clinical models of integrative oncology for almost 20 years to meet patients' unmet needs and develop rigorous research to further develop the field. Today, a majority of National Cancer Institute–designated cancer centers offer acupuncture (73%), massage (73%), meditation (69%), and yoga (69%), as well as nutrition, supplement, and herbal medicine counseling (91%, 84%, and 67%, respectively).[31]

TABLE 1. Recommended Integrative Oncology Resources for Patients and Providers

Resource	URL
Materials to better help patients understand cancer and its treatment	
American Cancer Society	https://www.cancer.org
National Cancer Institute PDQ Cancer Information Summaries, Dictionaries, and Levels of Evidence	https://www.cancer.gov/publications/pdq
Expertise on integrative medicine therapies	
American Institute for Cancer Research	http://www.aicr.org
American Society of Clinical Oncology endorsement of Society for Integrative Oncology Guidelines	http://ascopubs.org/doi/10.1200/jco.2018.79.2721
Memorial Sloan Kettering Cancer Center Integrative Medicine Service	https://www.mskcc.org/integrativemedicine
Society for Integrative Oncology Clinical Practice Guidelines	https://integrativeonc.org/integrative-oncology-guidelines
University of Texas MD Anderson Cancer Center Integrative Medicine Program	https://www.mdanderson.org/integrativemed
Natural product databases	
About Herbs (Memorial Sloan Kettering Cancer Center)	https://www.mskcc.org/aboutherbs
ConsumerLab	https://www.consumerlab.com (subscription)
National Center for Complementary and Integrative Health	https://nccih.nih.gov
Natural Medicines Comprehensive Database	http://naturaldatabase.com (subscription)
National Cancer Institute Office of Cancer Complementary and Alternative Medicine	https://cam.cancer.gov
Office of Dietary Supplements	https://ods.od.nih.gov
Professional education for health care providers	
MD Anderson Integrative Medicine Conferences	https://www.mdanderson.org/research/departments-labs-institutes/programs-centers/integrative-medicine-program/conferences-events.html
Memorial Sloan Kettering Cancer Center Integrative Medicine Education and Training Programs for Physicians, Healthcare Professionals, and Therapists	https://www.mskcc.org/departments/survivorship-supportive-care/integrative-medicine/programs
Society for Integrative Oncology Annual Conference	https://integrativeonc.org/conference
University of Michigan Integrative Medicine Fellowship training	https://medicine.umich.edu/dept/family-medicine/clinical-services-locations/clinical-focus-areas/integrative-family-medicine-program/education/ifm-fellowship
University of Arizona Center for Integrative Medicine	https://integrativemedicine.arizona.edu/education/index.html

For oncology professionals who seek to develop integrative oncology expertise or build programs in their clinic or cancer centers, the SIO is a research-oriented organization that conducts annual meetings to educate on the emerging evidence base, and it supports career development for junior integrative oncology professionals. Academic cancer centers such as Memorial Sloan Kettering Cancer Center, MD Anderson Cancer Center, the University of Arizona, and the University of Michigan have ongoing training programs for physicians, nurses, and allied health care providers. Table 1 includes resources for clinicians who may want to learn more about integrative medicine.

In addition, the American Academy of Medical Acupuncture represents more than 1,300 physician acupuncturists in North America as well as international members. There are a few specialized training programs for health care providers, including physicians, acupuncturists, yoga instructors, and music therapists, that focus on the specific use of these modalities among patients with cancer (Table 1). Efforts to develop competency-based training models in integrative oncology are also underway. It is important for patients and families to seek providers who are knowledgeable about both complementary therapies and conventional cancer care.

There are additional challenges for integrative oncology, including lack of institution resources or knowledge of existing programs. Patient-level barriers include lack of awareness, demanding treatment schedules, symptom and travel burdens, and lack of financial resources or insurance coverage. Some of these hurdles can be addressed by partnering with nonprofit organizations such as the Cancer Support Community and forming

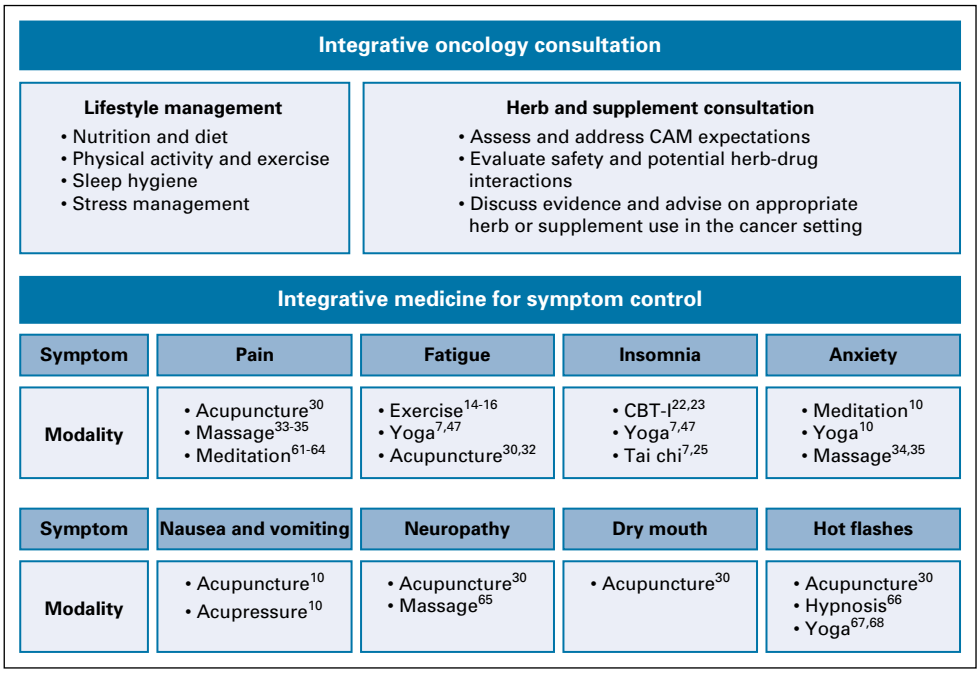

FIG 2. Best approaches and reasons for integrative medicine referrals. CAM, complementary and alternative medicine; CBT-I, Cognitive Behavioral Therapy for Insomnia.

reliable networks of community providers to increase access and reach. Other options include developing programs to incorporate therapies alongside standard treatment or appended to standard care appointments. For example, with our recent implementation of an oncology massage program at our chemo-infusion suites, a majority of patients stated they were satisfied and would recommend it to others undergoing treatment.[35] Providing integrative treatments that are embedded in or vetted by cancer centers can ensure safety, quality of care, and consistent communication about treatment expectations.

In summary, with up to 80% of patients with cancer using CAM, the field of integrative oncology has been developed to use rigorous research and novel clinical programs for evidence-informed patient-centered care. Integrative oncology places the patient at the center of care, and carefully incorporates safe and effective complementary therapies along with conventional cancer treatments to address physical, emotional, and spiritual quality of life. By fostering an open and informed dialogue between patients and their health care providers, integrative oncology specialists work with oncology teams to set realistic expectations, dispel myths regarding natural cancer cures, and guide patients to use specific nonpharmacologic treatments to address symptom burdens caused by cancer or conventional cancer treatments. By doing so, patients do not feel that they have to choose between alternative medicine and conventional care. In turn, appropriate integration of these therapies can lead to more benefit and less harm, and ultimately, improved quantity and quality of life for individuals with cancer.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST AND DATA AVAILABLITY STATEMENT

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Putting Integrative Oncology Into Practice: Concepts and Approaches

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