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Psychosocial and Integrative Oncology: Interventions Across the Disease Trajectory

Linda E. Carlson

Department of Oncology, Cumming School of Medicine, University of Calgary, Calgary,
Canada; email: lcarlso@ucalgary.ca

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Keywords

psychosocial oncology, integrative oncology, cognitive-behavioral therapy, acceptance-based therapy, mindfulness, mind-body therapies, psychedelic therapy, anxiety, depression, distress

Abstract

This article provides an overview of the fields of psychosocial and integrative oncology, highlighting common psychological reactions to being diagnosed with and treated for cancer, including distress, anxiety, depression, fear of cancer recurrence and caregiver burden, as well as symptoms of fatigue, pain, and sleep disturbance. Patterns of symptomatology across the disease continuum are also discussed. Interventions targeted at treating these symptoms are reviewed, including acceptance-based and mindfulness therapies, mind-body therapies, and meaning-based approaches designed for people with advanced stages of disease, including psychedelic therapy. Common methodological issues and shortcomings of the evidence base are summarized with design recommendations, and a discussion of trends in future research including pragmatic research design, digital health interventions, and implementation science completes the article.



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INTRODUCTION

What Are Psychosocial Oncology and Integrative Oncology?

Cancer is the most common illness in Western countries, with close to two million new cases diagnosed in the United States annually. With recent advances in cancer treatment, approximately 65% of those newly diagnosed are predicated to survive 5 years or longer post-diagnosis, with this number as high as 80% for breast cancer cases. This leaves close to 17 million people currently living with cancer in the United States, many of whom suffer from lingering symptoms and treatment-related side effects. Globally, these numbers include over 19 million people newly diagnosed with cancer in 2020 alone (Sung et al. 2021).

Within the field of health psychology/behavioral medicine, the subspecialty focusing on the behavioral and psychological elements of cancer risk, prevention, response, and treatment is called psycho-oncology, or psychosocial oncology (PON). There are a number of major areas of research and clinical focus within PON, which are thoroughly detailed in a hefty textbook simply called *Psycho-Oncology*, now in its fourth edition (Breitbart et al. 2021). This text, colloquially referred to as *The Bible*, was originated and edited by the psychiatrist Jimmie Holland, of the Memorial Sloan Kettering Cancer Center in New York City. Jimmie was a towering figure in PON (despite her diminutive size), considered the founder of the field in the 1970s, and she worked consistently into her 90s, retiring only when forced to by her eventual death in 2017, which was mourned widely by the PON community.

As such, PON is a relatively new field within behavioral medicine. The textbook description provided by the publisher reads, “Originally published in 1998, *Psycho-Oncology* was the first comprehensive text in the field and remains the gold standard today. The text reflects the interdisciplinary nature and global reach of this growing field. It covers evidence-based clinical practice guidelines from around the world, survivorship issues, psychotherapeutic interventions, and psychopharmacologic interventions” (Breitbart et al. 2021). The fourth edition is well over 800 pages long, and it is recommended reading for anyone wishing to acquire a wide breadth of knowledge in the field.

Integrative oncology (IO), too, is a relatively new subspecialty of oncology defined by the Society for Integrative Oncology (SIO) as “a patient-centered, evidence-informed field of cancer care that utilizes 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” (Witt et al. 2017, p. 3). Hence, there is much overlap between PON and IO approaches to cancer care. In this article I include the mind-body therapies (MBTs) from IO as well as traditional PON therapeutic approaches, since many of these have been integrated into PON programs, are commonly used by people living with cancer, and have a strong evidence base.

As we move into the next sections, some clarity on the terms “cancer patient” versus “cancer survivor” will be helpful, as they are sometimes used interchangeably. Many people diagnosed with cancer prefer the term “survivor” from the point of diagnosis onward, regardless of disease outcome or stage in the cancer treatment trajectory, and this term can be extended to family members and caregivers as well. More conventionally, the medical community tends to call people undergoing active, curative, or primary treatments for cancer, such as surgery, chemotherapy, and radiation therapy, as cancer patients, referring to them as cancer survivors only after the completion of these primary treatments, usually with curative intent.

There are increasing numbers of gray areas, however, as many people continue with maintenance treatments for many years. For example, women with breast cancer often have to take

Psychosocial oncology (PON): a medical subspecialty focusing on the behavioral and psychological elements of cancer risk, prevention, response, and treatment

Integrative oncology (IO): a field of cancer care that utilizes mind and body practices, natural products, and/or lifestyle modifications from different traditions alongside conventional treatments

SIO: Society for Integrative Oncology

Mind-body therapies (MBTs): a group of techniques that enhance the mind’s interactions with bodily function to induce relaxation and improve overall health and well-being



PLWC: people living with cancer

antiestrogen therapies for up to 10 years, and people with more advanced stages of cancer may be on different therapies for the rest of their lives. People may cycle from remission into relapse multiple times over a period of many years. For this reason, and due to some backlash from people not appreciating the connotations of either of these labels, in this article I will refer broadly to “people living with cancer,” or PLWC, and will detail more specifically what sample of people I am referring to as necessary.

Scope of the Review

This article will focus on psychosocial and mind-body interventions within PON and IO for treating a wide variety of psychological symptoms and side effects of cancer diagnosis and treatment, including those of a mainstream nature such as psychoeducation and supportive counseling, but also MBTs such as yoga, meditation, and hypnosis. Cognitive behavioral therapy and similar related interventions are covered in the paper by Antoni et al. (2023) in this volume. Antoni and colleagues also discuss more thoroughly the psychobiological bases of cancer diagnosis and treatment and summarize the biomarker outcome research in psycho-oncology, resulting in two complementary articles covering all of these topics.

This review begins by outlining the general psychological and social impacts of a cancer diagnosis as well as the typical physical symptoms and side effects that either have a psychological or behavioral component or respond to psychosocial therapies, with a breakdown of the types of concerns and symptoms typical of each stage of cancer diagnosis and treatment. This sets the stage for the second major section, a summary of evidence-based interventions to support PLWC, most of which attempt to treat either individual symptoms or a combination of the symptoms summarized in the first section. Finally, a section specifically focusing on interventions in populations of people living with advanced cancer follows. The article concludes with a summary of common limitations in the research literature and recommendations for future directions of study.

IMPACT OF A CANCER DIAGNOSIS

Psychological Impact

When I lecture about PON, I often ask students to imagine the following scenario: “You’ve been having some unusual symptoms and been to see your doctor, had a few tests run. They call you back into the office and break the bad news, ‘You have cancer.’ How do you feel?” For many people, this is not an imaginary scenario, as some form of cancer will be diagnosed in up to half of the male population and one-third of the female population in North America in their lifetime. The first reaction is often of shock. We hear many people say they didn’t hear another word the doctor said after hearing “You have cancer.” They were already distracted imagining their own impending death, leaving behind children and loved ones, and experiencing pain, disability, frightening treatments, hair loss, pity, job loss, you name it. The proverbial house of cards comes crashing down with those three words.

So how do we make sense of this psychologically? One of the most important psychological defense mechanisms, demonstrably false if one ever stops to think about it, is that we have control over the course of our lives. This provides a sense of safety when bad things happen to others; they must have somehow brought it upon themselves. This belief is immediately and irrevocably challenged with a cancer diagnosis. Along with a frightening and even terrifying sense of loss of control is the uncertainty that accompanies it. This can cause an existential angst and challenge the types of coping behaviors that most people have developed through the course of their lives. This forced confrontation with mortality and the often unwelcome pausing of life-as-usual can serve as a catalyst to take a step back and consider one’s values and purpose in life.



In this sense, being diagnosed with cancer provides an ideal, although usually unwelcome, opportunity to consider what brings joy, meaning, and purpose into one's life and the kind of legacy one would like to leave behind. People often come around to using this as an opportunity to fix things that were not working in their lives, and in a sense begin again. The road is often long and fraught, however, as we will see in the next sections reviewing common psychological reactions and symptoms related to cancer.

NCCN: National Comprehensive Cancer Network

DT: Distress Thermometer

Distress

In terms of more concrete psychological constructs, research has consistently shown high levels of psychological distress, anxiety, and depression in PLWC. Distress as a construct has been widely adopted within PON as a way to destigmatize and normalize the typical psychological reactions to a diagnosis. Distress is defined by the National Comprehensive Cancer Network (NCCN) as “a multifactorial, unpleasant experience of a psychologic (i.e., cognitive, behavioral, emotional), social, spiritual, and/or physical nature that may interfere with the ability to cope effectively with cancer, its physical symptoms, and its treatment. Distress extends along a continuum, ranging from common normal feelings of vulnerability, sadness, and fears, to problems that can become disabling, such as depression, anxiety, panic, social isolation, and existential and spiritual crisis” (NCCN 2022).

The recommended tool for assessing distress in oncology is the Distress Thermometer (DT), a 0–10 scale that has been widely used, with norms available for large cancer populations. Typically, a score over 4 on the DT is considered moderate distress, and in many studies across samples of PLWC, 20% to 52% of patients score above this cutoff (Mehnert et al. 2018). There is considerable variability across different types of cancer diagnoses and different stages or severities of illness, as well as across age, gender, and race. Generally, younger PLWC, women, and those from minority groups often reporting higher distress levels (Traeger et al. 2014), as do those with more severe or disfiguring types of cancer, such as head and neck cancers, and in cancers with poorer prognosis such as pancreatic and lung cancers (NCCN 2022). **Table 1**, drawn from the most recent NCCN guidelines (NCCN 2022), lists risk factors for more severe distress.

In many people, distress peaks after diagnosis and then wanes throughout treatment and follow-up, but there are a minority of patients who suffer ongoing symptoms that do not naturally remit (Carlson et al. 2013), and certain transition points are associated with peaks in distress (see **Table 1**).

Depression

Many other studies have looked more specifically at rates of depressive and anxiety disorders, beyond the umbrella measure of distress assessed by the DT. While rates of depression and anxiety are lower than the rates of moderate or higher distress, they are still typically higher than those found in the general population. For example, a recent systematic review of 210 studies reported prevalence rates of clinical depression varying from 7.9% to 32.4%, with a mean rate of 21.2%, across all types of cancers (Riedl & Schuessler 2021). The authors concluded that the risk of suffer from clinical depression during the first year after cancer diagnoses is 15–20%. An earlier meta-analysis of 24 studies of PLWC within palliative care settings reported interview-confirmed rates of depressive disorder diagnoses at 24.6%, combining adjustment disorders and major and minor depression (Mitchell et al. 2011). A further 70 studies in nonpalliative cancer populations reported that all types of depression occurred in 20.7% of PLWC, depression and adjustment disorder in 31.6%, and any mood disorder in 38.2%. Within younger PLWC, a systematic review of depression symptoms in adolescent and young adult groups across 33 studies, with over 55,000



Table 1 Psychosocial distress patient characteristics as defined by the National Comprehensive Cancer Network

Patients at increased risk for distress	Periods of increased vulnerability
<ul style="list-style-type: none"> ■ History of psychiatric disorders or substance use disorder ■ History of depression/suicide attempt ■ Cognitive impairment ■ Communication barriers ■ Severe comorbid illnesses ■ Social issues: <ul style="list-style-type: none"> ○ Family/caregiver conflicts ○ Inadequate social support ○ Living alone ○ Financial problems ○ Limited access to medical care ○ Young or dependent children ○ Younger age ○ History of trauma and/or abuse (physical, sexual, emotional, verbal) ○ Other stressors ■ Spiritual/religious concerns ■ Uncontrolled symptoms ■ Cancer type associated with risk of depression (e.g., pancreatic, head and neck) 	<ul style="list-style-type: none"> ■ Finding and investigating a suspicious symptom ■ During diagnostic workup ■ Finding out the diagnosis ■ Advanced cancer diagnosis ■ Learning about genetic/familial cancer risk ■ Awaiting treatment ■ Increase in symptom burden ■ Significant treatment-related complications ■ Admission to/discharge from hospital ■ Change in treatment modality ■ Treatment failure ■ End of active treatment ■ Medical follow-up and surveillance ■ Transition to survivorship ■ Recurrence/progression ■ Transition to end-of-life care

Table adapted with permission from (NCCN 2022).

participants reporting a pooled prevalence of 16% across depression rating scales (Hong et al. 2022). Another meta-analysis of 40 studies conducted in 15 low- and middle-income countries spanning the regions of East Asia and Pacific, South Asia, Middle East and North Africa, and Sub-Saharan Africa reported a pooled prevalence of 21% for major depression (Walker et al. 2021).

Anxiety

Anxiety and worry are even more common than depressive symptoms, but full-blown anxiety disorders are of similar prevalence to depression. For example, Mitchell et al.'s (2011) study found a 9.8% prevalence of interview-confirmed anxiety disorders across 24 studies in palliative care, and 10.3% across studies of over 10,000 PLWC. The meta-analysis, including over 9,000 PLWC from low- and middle-income countries, reported a prevalence of interview-confirmed anxiety disorders of 18% (Walker et al. 2021). If we consider only anxiety symptoms, a meta-analysis of 44 studies of anxiety prevalence in over 50,000 longer-term cancer survivors reported a 17.9% prevalence of self-reported elevated anxiety symptoms (Mitchell et al. 2013), consistent with other systematic reviews of long-term survivors, one of which reported rates ranging from 3.4% to 43% (pooled prevalence: 21%), depending on how anxiety was assessed (Brandenburg et al. 2019).

Fear of Cancer Recurrence

Recently, more focus has turned toward worry, and specifically worry or fear of cancer recurrence (FCR), defined as “fear, worry, or concern relating to the possibility that cancer will come back or progress” (Mutsaers et al. 2020, p. 672), which many PLWC report haunts them after treatment completion, no matter how positive the prognosis. Every ache or pain becomes a potential



indicator of cancer recurrence, causing worry and anxiety that tend to exacerbate symptoms, thereby confirming their interpretation as a sign of cancer recurrence. This results in a spiral of minor symptoms, worry, symptom escalation, and calls or visits to the physician/oncologist or emergency room. This is often followed by unnecessary tests that in the end show no signs of disease recurrence or progression.

Meta-analytic reviews of the prevalence of FCR show it is very common, with 73% of PLWC experiencing FCR, half of them (49%) with moderate to high intensity, and 7% with high intensity (Simard et al. 2013). FCR seems to cut across all types of cancer, with risk factors including being a women, being younger, not having a partner, having at least one child, being socially isolated, having more (and more severe) physical symptoms, and having lower emotional well-being (Almeida et al. 2019).

Impact of COVID-19

With all these concerns in PLWC's minds, one can only imagine the additional impact of coping with cancer during the time of COVID-19. PLWC are already struggling with feeling scared, alone, and uncertain about the future; this additional stressor may add to their burden by imposing further social isolation and fear of contracting COVID-19, as well as increased stress due to delays in care, bans on bringing support people to appointments, and shifts toward virtual care. Indeed, since the start of the pandemic several large-scale surveys have been conducted investigating the impact of various aspects of the pandemic on people with cancer. Our own study of 41,212 respondents to the iCARE international COVID-19 survey from 175 countries worldwide (Baydoun et al. 2022), found that over the first year of the pandemic, people diagnosed with cancer had higher COVID-19-related feelings of sadness and anxiety, as well as worse overall quality of life compared to healthy people. Cancer patients were also more likely than healthy people or those with other chronic conditions to report maladaptive coping mechanisms, such as increased cigarette smoking, and financial hardships, such as inability to pay rent/mortgage. This illustrates the added burden the pandemic has imposed upon people already coping with one of life's greatest challenges.

Families/Caregivers

It has been said that cancer is a family disease, meaning that when one person in a family has cancer, it inevitably affects everyone in some way or another. This may happen emotionally or practically, resulting in changes in role function and daily routines as well as feelings of fear, shock, anxiety, sadness, and depression. Research shows that acting as an informal caregiver may have detrimental effects on the physical, psychological, and social health of the caregiver and reduce their quality of life (Treanor et al. 2019). This can happen through a range of problems, including back and muscular pain, disturbed sleep patterns, and overall fatigue, as family members try to continue with their previous roles in addition to taking on the caregiving role (Treanor et al. 2019). Psychological difficulties include worry and anxiety about the patient's health and the progression of the cancer. Financially, the time and costs of providing care may lead to gaps in, or loss of, employment and education, reduced income, increased bills, and overall financial strain. One review of the costs of caregiver unpaid time devoted to cancer care reported an average of over \$4,800 per month (Counoundouros et al. 2019).

In terms of psychosocial distress, research on caregivers of adult cancer patients, largely spouses, frequently shows equal and sometimes greater levels of distress in partners compared to the PLWC themselves, as well as high levels of anxiety and reduced quality of life (Treanor et al. 2019). Typically about 30% of caregivers experience elevated levels of distress and depressive and



CINV:
chemotherapy-
induced nausea and
vomiting

CIPN: chemotherapy-
induced peripheral
neuropathy

CRF: cancer-related
fatigue

anxiety symptoms, similar to patients themselves (Caruso et al. 2017). Patients' and partners' distress and other psychological symptoms often mirror one another, resulting in a growing call for interventions that include the dyad as the unit of intervention rather than focusing on just the patient or the partner individually (Caruso et al. 2017).

Physical Symptoms and Treatment Side Effects

Several troubling physical symptoms and cancer treatment-related side effects with a biobehavioral basis are also often targets of psychosocial interventions. These primarily include fatigue, pain, and sleep disturbance, which will be addressed in more detail below. Other symptoms, such as cancer-related cognitive impairment (sometimes called chemo-brain or chemo-fog), vasomotor symptoms (e.g., hot flashes) and pain (arthralgias) related to chemotherapy or hormonal treatments, as well as chemotherapy-induced nausea and vomiting (CINV) and chemotherapy-induced peripheral neuropathy (CIPN), are also commonly experienced and are increasingly the target of psychosocial and biobehavioral interventions.

Fatigue

Fatigue is reported by PLWC as one of the most common and troubling symptoms they experience. The syndrome called cancer-related fatigue (CRF) is defined by the NCCN (2022) as "a distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning." CRF is common in PLWC across the cancer care continuum, from the time of diagnosis, during active treatment, and into long-term survivorship, and it is consistently listed as one of the top three bothersome symptoms, often described as the most distressing (Schmidt et al. 2020). CRF prevalence ranges from 25% to more than 99% among patients who are undergoing cancer treatment (Schmidt et al. 2020), and 19% to 82% among patients post-treatment (Aapro et al. 2017), with a meta-analysis of 84 studies involving over 144,000 subjects estimating an overall pooled prevalence of 52% across the entire disease trajectory (Ma et al. 2020). Significant variability in these estimates is due to a number of factors, including the type of cancer, severity of the cancer, treatments received or ongoing, and the type of measurement tool used for fatigue.

Risk factors for experiencing higher levels of CRF or prolonged CRF identified by the recent large meta-analysis by Ma et al. (2020) include poor performance status (i.e., difficulty undertaking activities of daily living such as walking, housework, personal care, etc.), chemoradiotherapy, female sex, neuroticism, insomnia, pain, and depression. Of note, many of these symptoms cluster together, especially pain, fatigue, insomnia, and depression, and they may feed into one another. For example, experiencing pain interferes with the ability to sleep well, which then contributes to short- and long-term fatigue. In the long run, the ongoing burden of these symptoms can instigate or exacerbate depressive symptoms. This understanding of symptom clusters has led to work defining their prevalence and to the development of interventions meant to target not just one symptom but these common clusters.

There is also a growing body of work attempting to both theoretically and empirically understand and characterize the biobehavioral mechanisms behind the development, maintenance, and potential alleviation of CRF (and other symptoms). CRF is particularly difficult to define, as its mechanisms are not well understood, but is thought to include multifactorial contributions from both the central and peripheral nervous systems, the hypothalamic-pituitary-adrenal (HPA) axis, inflammatory cytokines, and energy metabolism [reviewed by Thong et al. (2020)].

The article from Antoni et al. (2023, in this volume) also delves more into the mechanisms behind these common symptoms, focusing on the psychological and physiological effects of the



various stressors associated with cancer and its treatments across neuroendocrine and immune systems, as well as the biobehavioral effects of adaptation to these challenges. Antoni and colleagues review the data on the role of the HPA axis and the sympathetic nervous system (SNS) in responding to cancer and influencing physical and psychological symptomatology, and they summarize the neuroendocrine-mediated changes in inflammation and antiviral immune regulation that occur, including gene expression and inflammatory biomarkers. They also cover the effects of various interventional strategies, primarily cognitive behavioral therapy (CBT)-derived programs such as cognitive-behavioral stress management (CBSM), on these physiological outcomes.

SNS: sympathetic nervous system

CBSM: cognitive-behavioral stress management

QL: quality of life

Pain

Pain is another common symptom experienced by many PLWC, and one for which the NCCN also has clinical practice guidelines. Pain is technically defined as “an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage” (NCCN 2022). In PLWC, a meta-analysis of 52 studies reported the prevalence of pain at 59% in people undergoing cancer treatments, 64% in people with advanced or metastatic cancer, and 33% in people post-treatment (van den Beuken-van Everdingen et al. 2007). Across studies including patients at all disease stages, 53% of patients reported pain. Of those with pain, more than one-third graded their pain as moderate or severe. Pooled prevalence of pain was >50% in all cancer types, with the highest prevalence in head and neck cancer patients (van den Beuken-van Everdingen et al. 2007). Pain has long been recognized as both a psychological and physical construct in terms of etiology and maintenance, and as such there is latitude for psychological and other nonpharmacological interventions to impact the pain experience.

Sleep Disturbance/Insomnia

Another component of the trifecta of common symptom clusters (along with pain and fatigue) is sleep disturbance; while sleep disorders run the spectrum of conditions including sleep-related breathing disorder/obstructive sleep apnea syndrome, narcolepsy, restless legs syndrome, and REM-sleep behavior disorder, insomnia itself is most common in PLWC (Büttner-Teleagă et al. 2021). Insomnia as a disorder is associated with the following diagnostic criteria: (a) difficulty falling asleep or staying asleep, or having nonrestorative sleep, which (b) is present despite adequate opportunity and circumstance to sleep, (c) is associated with daytime impairment or distress, and (d) occurs at least three times per week and has been a problem for at least 1 month.

As with CRF, the mechanisms and factors instigating and promoting sleep disturbances can be complex, and they may be different in stages of initiation and maintenance. The rate of cancer-related insomnia is reported at nearly three times that of the general population, with different analyses reporting 30–50% of all PLWC experiencing severe sleep difficulties, with a prevalence up to 95% in some studies (Büttner-Teleagă et al. 2021). Typically, insomnia related to cancer is characterized by delayed sleep onset (difficulty falling asleep), problems with sleep maintenance (waking up in the night), and reduced overall total sleep time and/or early morning awakenings, accompanied by daytime sleepiness, fatigue, and impaired well-being. Insomnia is also associated with pain, depression, anxiety, and reduced overall quality of life (QL) (e.g., Savard et al. 2009). These symptoms together interact to exacerbate and often maintain one another, and people can often get stuck in patterns of disorder initiated by the changes wrought by cancer diagnosis and treatment, which are then difficult to resolve once they have become behaviorally established.



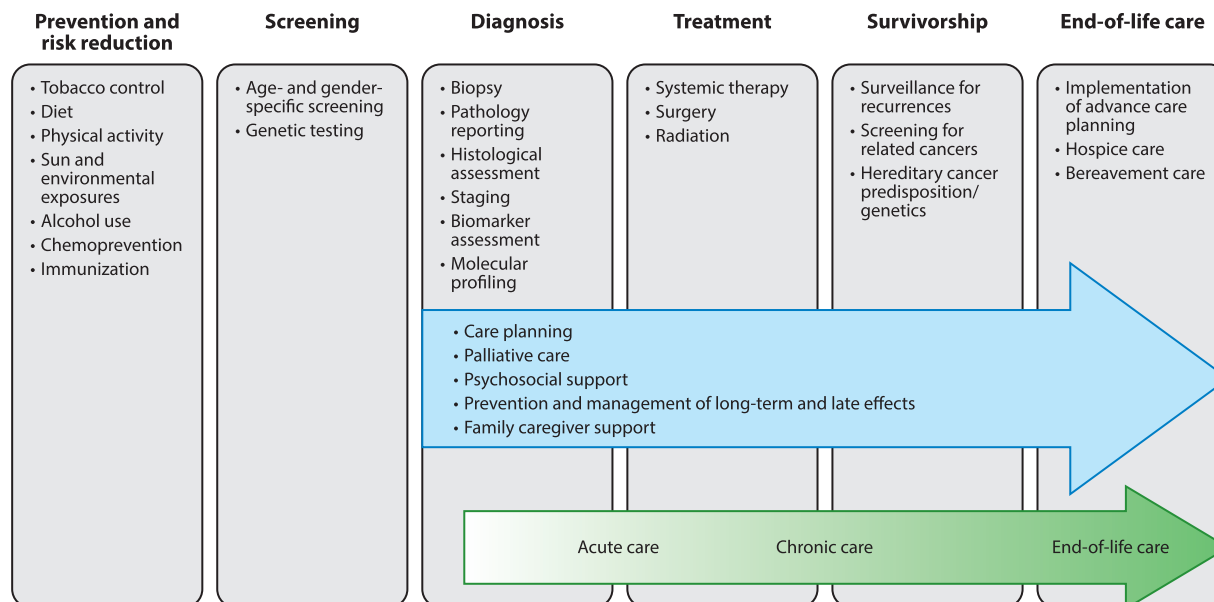


Figure 1

Domains of the cancer care continuum with examples of activities in each domain. The blue arrow identifies components of high-quality cancer care that should span the cancer care continuum from diagnosis through end-of-life care. The green arrow identifies three overlapping phases of cancer care, which is a way of conceptualizing the period of the cancer care continuum that is the focus of this report. Figure adapted with permission from Inst. Med. (2013).

Symptoms Across the Treatment Trajectory

In PON, clinicians and researchers often refer to the treatment trajectory or, more informally, the cancer journey. Across oncology, it is usually referred to as the cancer care/control continuum. There is a typical sequence of stages that most PLWC go through, from prevention, screening/early detection followed by diagnosis, treatment, and survivorship to end-of-life care. Although this sequence has been presented in a linear fashion by the US Institute of Medicine (Inst. Med. 2013) (see **Figure 1**), a circular representation that may more accurately capture the lived experiences of PLWC was proposed by Julia Rowland, the former director of the National Institutes of Health Office of Cancer Survivorship (Rowland 2008). In this model, PLWC may go through successive rounds of testing, diagnosis, and treatment, followed by disease remission and a survivorship phase. This phase of survivorship may be long-lasting or brief, and at any time a person may be diagnosed with advanced or terminal disease, which precedes the end-of-life phase.

Typically, symptoms vary across these stages of the continuum, with anxiety and distress peaking around the time of diagnosis, accompanied by sleep disturbances, and other symptoms like fatigue and pain peaking later, often the result of acute cancer treatments such as surgery, chemotherapy, and radiation therapy. In a study in which we followed close to 900 patients longitudinally from the time of diagnosis through 1 year, levels of distress, depression, and anxiety decreased significantly over time, but no significant changes were found in levels of pain or fatigue (Carlson et al. 2013). Twelve months post-diagnosis, many patients continued to report significantly elevated levels of distress (29%), pain (19%), and fatigue (40%), while levels of anxiety and depression had decreased to below 10% (Carlson et al. 2013).

In addition to experiencing similar or higher symptoms of depression, anxiety, and distress as documented above, people living with advanced forms of cancer also encounter specific issues, including pain management and existential distress at end of life. Palliative care specialists often discuss the importance of meaning making at the end of life in the context of a bio-psychosocial-spiritual framework, recognizing that multiple psychological, social, physical, and spiritual factors may exacerbate the experience of pain and suffering at end of life (and indeed at any time) (Wachholtz et al. 2016). The basis of dignity therapy (Chochinov 2007) and other interventions such as Managing Cancer and Living Meaningfully (CALM) (Mehnert et al. 2020) rests on the centrality of finding a sense of meaning or purpose in one's life through narrative storytelling and interpersonal connection. These are reviewed in the following section.

EVIDENCE-BASED INTERVENTIONS TO SUPPORT PEOPLE LIVING WITH CANCER

Overview

In general, any type of psychosocial intervention designed to support PLWC needs to address some or all of the concerns outlined in the previous sections, ideally by targeting the theoretically proposed or empirically evidenced mechanisms implicated in the etiology or maintenance of these symptoms. Clinical scientists have approached this task from various angles, typically by adopting effective therapies that address troublesome symptoms in other contexts (e.g., CBT for depression), developing interventions specifically tailored to address the unique needs of PLWC (e.g., CALM), or some combination thereof [e.g., Mindfulness-Based Cancer Recovery (MBCR)].

One coping framework that has been helpful in this context is Lazarus & Folkman's model of stress and coping (Biggs et al. 2017). In this conceptualization, coping involves constantly changing cognitive and behavioral efforts to manage external and/or internal demands that are appraised as taxing or exceeding the resources of a person. Coping in this context is process oriented and dynamic, and it involves conscious, purposeful actions taken when an individual appraises a situation as stressful (i.e., posing challenges that may be beyond one's skills or resources to address).

Within this model, specific coping strategies aim to directly manage the stressor itself (called problem-focused coping), regulate emotions arising as a consequence of the stressful situation (called emotion-focused coping), or a mix of the two. Emotion-focused strategies have often received short shrift as they are thought not to be as effective as dealing directly with problems, but for situations characterized by uncontrollability and uncertainty, they may in fact be more effective. Additionally, most people seem to have quite well-developed problem-focused coping strategies but are often less adept at coping with difficult and uncomfortable emotions. It may be the case that both coping strategies have a place in dealing with the myriad of challenges posed to people as they navigate the entire cancer care continuum.

The rest of this section reviews the evidence supporting the efficacy of specific approaches to managing cancer-related psychological sequelae and symptoms. A single summary section at the end detailing common methodological limitations across intervention studies will help avoid redundancy by listing these only once, as the limitations of design, sampling, intervention delivery, and outcome measurement generally cut across therapies.

Acceptance-Based (Third-Wave) Cognitive Behavioral Therapies

Over the last three decades there has been growing interest in the development and application of therapies deemed Third-Wave CBT approaches. Historically, CBT evolved in the 1950s and 1960s as something of a backlash to the predominant behavioral approaches of the time, brought into favor by the work of Skinner and his followers in the earlier decades of the twentieth century.

CALM: Managing Cancer and Living Meaningfully

Mindfulness-Based Cancer Recovery (MBCR):

a mindfulness-based intervention created by Linda Carlson and Michael Speca, adapted from Mindfulness-Based Stress Reduction to the specific needs of people living with cancer



Acceptance and commitment therapy (ACT):

a psychological intervention developed by Steven Hayes that uses acceptance and mindfulness strategies along with commitment and behavior change to increase psychological flexibility

Mindfulness-Based Stress Reduction (MBSR):

an 8-week training program in mindfulness meditation and gentle yoga created by Jon Kabat-Zinn for people with medical conditions

These Skinnerian approaches focused almost solely on behavior, using stimulus-response and conditioning to treat psychological disorders. These paradigms were themselves a backlash to earlier Freudian approaches that emphasized the role of the unconscious in behavior to the exclusion of external forces. Thereafter, behaviorism was considered the first wave in this lineage of therapies. When Ellis & Beck came along in the 1950s, they saw a lack of recognition of the role inner thoughts, stories, and self-talk played in the development and maintenance of psychological disorders. Hence, they added in the emphasis on the “C,” or the role cognitions play, and CBT therapies then evolved to take into account both behaviors and cognitions. Something was still missing, though, as CBT felt a bit cold and harsh to some, and this was highlighted by Rogers, who emphasized the important role of unconditional positive regard and acceptance in his humanistic take on therapy. The third wave, then, evolved over the last three decades to incorporate acceptance-based strategies into the first and second waves, exemplified by Hayes’s acceptance and commitment therapy (ACT) and Kabat-Zinn’s Mindfulness-Based Stress Reduction (MBSR) (see below).

If one is new to acceptance-based approaches, an obvious question might be, What is it that we are advising people to accept? This is really the key question, and it also links back to the previous discussion about problem-focused versus emotion-focused coping strategies. Essentially, one is accepting things the way they are: feelings, situations, other people, the world, being diagnosed with cancer—all sorts of things we don’t have the capacity to control or change.

The focus of the acceptance will vary depending on the problem one is addressing, but let us consider the person newly diagnosed with cancer. From the discussion above we know this person is likely scared, sad, distressed, tired, perhaps in pain, and potentially experiencing a muddy brain, making it hard to focus and think clearly, let alone get off the couch. With an acceptance-based approach, all of this is okay, if not totally normal. A key element is that a person does not have to like a situation or emotion to accept it. One does not have to think what is happening is a good thing, or want it to continue, in order to accept it. Having cancer is awful in so many ways. No one asks for it or wants this to happen to them or their loved ones, but it does happen nonetheless. In this maelstrom, finding a way to simply accept things as they are can be deeply and profoundly healing. It provides space, and it takes off the pressure to be always doing something, fixing something or someone.

Acceptance-based approaches also have other benefits, one of which is allowing people not to feel like they are failing in the societally mandated role of “the good cancer patient” who is “fighting cancer” and “thinking positive.” This is a departure from my main topic, but suffice it to say that these pressures and expectations to behave or think in a mandated way typically have the opposite effect, causing additional worry and distress if one is not able to do so. Acceptance-based approaches allow people to think and feel however they do, recognizing also that the only certainty in life is constant change, and this too will pass. It is also important to distinguish acceptance in this context from self-defeat, fatalism, nihilism, or outright giving up on life.

Acceptance and Commitment Therapy

ACT is a form of individualized CBT that aims to reduce symptomatology by improving psychological flexibility through practices spanning acceptance, mindfulness, commitment, and behavior change (Hayes et al. 2009, Vowles & McCracken 2010). To achieve this end, there are six core therapeutic processes: being present (mindfulness, awareness of present moment experiences); cognitive defusion (deidentifying with thoughts as being always true or relevant); self as process and context [distinguishing thoughts about the self (process) from the larger experiencing self (context)]; acceptance (reducing experiential avoidance of difficult or troubling thoughts and feelings); defining valued directions (identifying chosen qualities of purposive action to serve as



a benchmark against which experiences can be evaluated); and committed action (commitment to living a value-consistent life). ACT was originally developed by Hayes (Hayes et al. 2009) for treating psychological disorders, but it has more recently been adapted for populations experiencing chronic pain and other medical conditions (for a discussion of applying ACT in cancer, see Hulbert-Williams et al. 2015).

ACT has been applied extensively to psychological disorders such as anxiety, traumatic stress, and depression, but the use of ACT for PLWC is a relatively recent application, with most studies published in the last decade. Although ACT was originally delivered individually, adaptations for PLWC have included a mix of group and individual delivery, with both formats usually occurring over six to eight 1.5- to 2-hour sessions. For example, Arch adapted an ACT-based group intervention to focus on three aims: (a) cultivate awareness and acceptance of thoughts and emotions about cancer; (b) disentangle (defuse) from rigid thoughts/beliefs about cancer and themselves, by cultivating flexibility in relating to such thoughts/beliefs; and (c) clarify personal values and commit to pursue meaningful activities aligned with those values (Arch & Mitchell 2016).

A 2019 systematic review of 11 studies of ACT included all study designs, pilot and single-arm as well as randomized controlled trials (RCTs), in 537 PLWC in the post-treatment phase (Mathew et al. 2021). It reported the most promising findings as improvements in anxiety, depression, FCR, and QL. Another meta-analysis of PLWC at all stages of treatment and survivorship (Zhao et al. 2021) included controlled as well as uncontrolled designs. Twenty-five independent trials (of which 17 were RCTs) were identified, including a total of 2,256 participants. Outcomes were broken down by symptom. Psychological distress was measured in 18 trials for a total of 1,324 participants, with a significant large effect size of $g = 0.88$. Psychological flexibility (a key target for ACT) was measured in 10 trials with a significant medium effect size ($g = 0.58$). There was also significant improvement in QL based on 7 trials with 389 patients ($g = 1.19$). Only 3 trials with 83 participants reported changes in hope, and the effect size was $g = 2.17$. In all, although the body of literature is still young, evidence is accumulating to suggest that ACT-based interventions hold significant promise for helping PLWC cope with some of their most distressing issues.

Mindfulness-Based Interventions

Mindfulness-based interventions (MBIs) is the term used to encompass a broad range of programs that derive from the MBSR framework popularized by Kabat-Zinn (1990). MBIs share a lot of similarities with ACT-based interventions, but they have different origins and an approach that has less of a CBT flavor than ACT. The first MBSR program originated in the late 1970s, when Kabat-Zinn and colleagues at the Massachusetts Medical Center combined intensive training in mindfulness meditation based on Eastern practices with cognitive-behavioral stress reduction techniques into a standardized 8-week training program. This program included daily 45-minute home mindfulness meditation and gentle Hatha yoga practice, along with weekly group discussion, inquiry around embodied practice, and didactic learning.

Standard MBSR classes are 2.5 to 3 hours each, and each class begins with experiential practice of a cumulative series of meditations introduced weekly, beginning with body scan meditation, then moving into sitting meditation with awareness of breath, walking meditation, open awareness, imagery (mountain or lake meditation), and eventually loving kindness practices, although the latter may not be included in all MBSR adaptations. Gentle Hatha yoga is added to the experiential practices in the first few weeks, and a series of standardized lying and standing postures are practiced sequentially, which are diagrammed in the *Full Catastrophe Living* book (Kabat-Zinn 1990). Classes typically flow between experiential practice, discussion or inquiry about the preceding practice period in small or large groups, didactic material and discussion, and more practice.

RCT: randomized controlled trial

Mindfulness-based intervention (MBI): a generic term for programs adapted from Mindfulness-Based Stress Reduction, which generally follow the model created by Jon Kabat-Zinn



New didactic content is introduced each week with exercises to illustrate it, including discussions of mindfulness attitudes, mindful eating, the mind-body connection, stress responding versus reacting, and assertive communication. A 6-hour Saturday retreat takes place near the end of the program, during which participants silently engage in all of the practices introduced in the program over an extended period of deep immersion.

The first published applications of MBSR were for people who had comorbid medical and psychological symptoms, including chronic pain and anxiety (Kabat-Zinn 1990). In the 1980s and 1990s MBSR programs became popularized, but it wasn't until the early 2000s that they grew exponentially, along with the research literature evaluating their efficacy. Now there are likely 40 or more distinct MBIs designed to cater to people with recurrent depression (mindfulness-based cognitive therapy being the most popular adaptation), addictions, eating disorders, bipolar disorder, sleep disorders, and many specific medical conditions including cardiovascular disease, diabetes, HIV/AIDS, chronic pain, and many more (Carlson 2021). There are many other applications of MBIs in schools and educational settings, business, law, and so on, such that the concept of mindfulness has permeated the popular vernacular and consciousness to the point of ubiquity.

WHAT IS MINDFULNESS?

Perhaps because of this popularity, there is often confusion about what mindfulness is, how or if it is different from meditation, and how MBIs train people in mindfulness skills. Mindfulness itself is often defined as nonjudgmentally paying attention, on purpose, in the present moment. It can be thought of in two ways: as a way of being in the world, and as a skill or practice one learns over time through meditation. As a way of being, one can be more or less mindful at any given time, no matter what activity one may be engaged in. It doesn't take extra time to live life in a mindful way, and indeed people report feeling happier when they are more fully engaged in the present moment.

The problem is that most people are not socialized, and our minds are not trained, to be mindful of the present moment. Rather, most people spend a good deal of mental energy and focus reliving the past, worrying about the future, or judging and analyzing events. Dwelling in the past can lead to feelings of regret, anger, resentment, and depression. Constantly worrying about the future and all the potential dangers ahead may lead to anxiety and stress. Mindfulness teachers often say that so much time is spent in the past or the future that we often miss the only time we actually have to live our lives, the present.

Hence, in order to train the capacity to become more mindful in everyday life, we turn to the second type of mindfulness, a skill that we build through the practice of mindfulness training, usually in the form of various meditation practices and exercises. One model that encompasses this is called the IAA model of mindfulness (Shapiro & Carlson 2017). The "I" stands for intention, which is the "why" of the practice. To be mindful, we first have to do it on purpose, or intentionally. A beginning intention may be simply to learn to be more present for oneself and in one's relationships; others may desire to learn to be more mindful because they have heard it might help them manage stress, sleep better, cope with pain, gain a sense of meaning and purpose in life, etc. Whatever the intention, lightly holding it serves as motivation and direction for sustaining the practice.

The first "A" stands for attention, the "what" of the practice. The core of the training is building the capacity to direct attention when and where one chooses, for sustained periods of time. Meditation focusing on the breath or the body is often used to train this capacity. Cultivating attention requires repeated sustained practice, most often 20–45 minutes daily, as recommended in standardized mindfulness training programs.



The second “A” is for attitude, the “how” of the practice. It is essential to apply attitudes of kindness, curiosity, openness, patience, nonjudgment, and acceptance to the learning process, because it can be difficult and frustrating and this can lead to discontinuation of mindfulness training if one does not apply these attitudes. People need to recognize that retraining the mind in the capacity to pay kind attention is not easy, despite its simplicity. Without these attitudes, people are much more likely to give up on mindfulness meditation programs. Applying acceptance, nonstriving, and letting go of the need to control life events that are outside of one’s control are also keys to adjusting to serious illness.

MBSR is an 8-week structured group program that incorporates intensive training in mindfulness meditation with group reflection and mindful Hatha yoga practice. The foundations of MBSR stem from Buddhist philosophy and practice, but it is free from any religious context. Participants learn fundamentals of the mind-body connection and how their interpretations of the world can cause both physical and mental suffering. MBSR participants begin to recognize that the amount of mental energy spent regretting the past or worrying about the future has resulted in missing the present moment and can cause depression and anxiety. Through the application of careful attention in this way, a process of re-perceiving can occur whereby the worldview that had perpetuated suffering is diminished. The primary meditation techniques used to cultivate mindfulness in the MBSR program are the body scan, sitting meditation, walking meditation, and loving-kindness meditation, in conjunction with mindful yoga postures.

For people dealing with cancer, many of the issues that arise as described in previous sections are amenable to an MBI approach. Mindfulness training can offer one venue for emotion-focused coping with these often uncomfortable and difficult feelings in a safe and controlled container of one’s own making. By adopting a stance of observers to the overwhelming thoughts and emotions, patients can take a step back and allow themselves to process these experiences at their own pace, seeing their experience as constantly changing and their distressing thoughts simply as mind events that are often untrue. Ultimately, they begin to see that they are more than a cancer patient; they are connected to, and supported by, everyone else who shares this human condition. Hence, there are theoretical reasons to believe that meditation training in general has the potential to be beneficial to PLWC.

Mindfulness-Based Interventions and Cancer Literature Review

In the world of PON, my colleagues and I were the first to publish clinical research on the effects of an intervention adapted from MBSR specifically for PLWC, which we called MBCR. We began this line of work in the late 1990s, adapting the MBSR model to the unique issues of PLWC. Our first publication in 2000 was a wait-list RCT of 89 PLWC with all types and severities of cancer. In it we saw surprisingly (to us) large reductions in symptoms of stress, anxiety, depression, anger, and other psychological and physical symptoms (Specia et al. 2000).

Fast-forward 20 years, and there have been dozens of clinical trials published of a variety of MBIs in PLWC, and many more papers with pre-post, observational, or qualitative designs. By the time I wrote my last review of MBIs in cancer in 2019, published in the fourth edition of the *Psycho-Oncology* textbook (Breitbart et al. 2021), 7 review papers had been published prior to 2014, with another 18 review papers/meta-analyses published between 2015 and 2019. I have often joked that there are now more reviews of MBIs in cancer than original clinical trials. These reviews have primarily covered specific populations (e.g., people with breast cancer or advanced cancer) or specific symptoms (e.g., anxiety, depression, sleep, fatigue, pain, vasomotor symptoms, FCR), or combinations of both.

Much of the literature on MBIs in cancer has been focused on women who have breast cancer—a limitation unfortunately common across much of PON research. For example, Zhang et al.



NK: natural killer

(2019) conducted a meta-analysis of 14 studies with breast cancer patients (8 RCTs and 6 single group pre-post) including over 1,500 participants. The most robust effects were seen on measures of cognitive function [standard mean difference (SMD) of 1.48], emotional well-being (SMD = 1.01), fatigue (SMD = 0.66), depression (SMD = 0.61), distress (SMD = 0.56), anxiety (SMD = 0.54), and stress (SMD = 0.48), representing large to medium effects across most outcomes.

These findings are consistent with those of another 2019 review across all types of cancer that included 29 studies with 3,274 participants; comparison groups were usual care or wait-list control ($n = 18$) or active control (psychoeducation, stress management seminar, supportive expressive group therapy, online mindfulness, nutrition education, or enhanced usual care) ($n = 11$) (Cillessen et al. 2019). Authors reported small to medium effects across outcomes of distress, anxiety, depression, FCR, fatigue, sleep, and pain.

Since 2019 another handful of similar reviews has appeared, with one meta-synthesis of all previously published reviews and meta-analyses combining all these data (Pedro et al. 2021). The authors included only studies with control groups, randomized or otherwise. Ten reviews were included in the meta-synthesis. Results generally supported the conclusions of other papers, that is, that MBIs are effective for decreasing anxiety, depression, and stress, with small to medium effect sizes.

Small effects of MBIs on biomarkers including indices of inflammation, specifically T cell and natural killer (NK) cell activity as well as cytokine counts and function, have also been reported in a number of studies, but in one meta-review effect sizes could not be estimated (Pedro et al. 2021). In the first report on the effects in cancer survivors of an MBI on telomere length, a putative marker of cell aging and risk factor for cancer progression, we found in a sample of 88 breast cancer survivors that those in the MBCR group (and also in a supportive-expressive therapy group) maintained telomere length over the course of 4 months while undergoing interventions, while those randomized to a control condition evidenced shortened telomere lengths (Carlson et al. 2015). These are preliminary data, and at this point we do not know if this would be a long-lasting effect, and what its potential clinical significance would be, if any.

Mind-Body Therapies

MBTs are defined as a group of techniques that enhance the mind's interactions with bodily functions to induce relaxation and improve overall health and well-being. The modalities included in this section have been extensively studied in PLWC, and they include yoga, tai chi/qigong, relaxation/imagery, hypnosis, and creative therapies. The SIO reviewed all integrative therapies for women with breast cancer and generated evidence-based guidelines in 2017 (Greenlee et al. 2017). In these, the highest level of evidence (including data from only RCTs) supported music therapy, meditation, and yoga for anxiety/stress reduction; meditation, relaxation, yoga, and music therapy for depression/mood disorders; and meditation and yoga to improve QL. This evidence is reviewed in more detail in the following sections.

Yoga

Yoga is derived from Indian philosophy, and it traditionally encompasses several branches or practices, which include guidance on ethical lifestyle, spiritual practice, breathing practices (*pranayama*), meditation (*dhyana*), and physical movement postures (*asanas*), which together serve to unite (or “yoke”) mind, body, and spirit. In Western cultures, yoga has become increasingly popular and is most often associated with the physical asanas, but the practice of pranayama is becoming increasingly popular as well.

Research on yoga's effect on a variety of cancer-related symptoms and side effects has proliferated in recent years, with several systematic reviews and meta-analyses available. In one



meta-analysis of 25 RCTs including 1,486 participants, yoga showed beneficial effects on reducing depression ($g = -0.41$) and anxiety ($g = -0.35$) symptoms (Gonzalez et al. 2021) in PLWC at any stage of treatment. Mixed results have been reported for yoga's effect on cognitive impairment (10 studies of various designs found Cohen's d effect sizes ranging from $|0.3|$ to $|0.74|$; Baydoun et al. 2020), fatigue (in 18 RCTs with a nonphysical activity comparator, $SMD = -0.30$; in 6 RCTs with a physical activity comparator, $SMD = -0.17$; O'Neill et al. 2020), and QL (in 18 RCTs with a nonphysical activity comparator, $SMD = -0.27$; in 6 RCTs with a physical activity comparator, $SMD = 0.04$; O'Neill et al. 2020). Notably, even more so that in MBIs, participants in these studies were largely women with breast cancer.

In another review of yoga outcomes based on cancer patients' stage of treatment (29 RCTs, including $n = 13$ undergoing treatment, $n = 12$ post-treatment, and $n = 4$ mixed samples; Danhauer et al. 2019), significant improvements were reported for pain, sleep measured via actigraphy, biomarkers (e.g., inflammation, cortisol), and distress during cancer treatment, as well as significant improvements on self-reported cancer-related side effects (e.g., nausea/vomiting) and sleep following treatment.

Tai Chi/Qigong

Tai chi and qigong are two complementary therapies (CTs) often grouped together, both of which incorporate a range of physical movements, including meditative, flowing, and slow dance-like motions (Wayne et al. 2018), often referred to and studied together as TCQ. Origins date back at least 700 years. Today TCQ is one of the most popular CTs worldwide, with well-documented benefits for a wide range of health conditions and a growing number of recent applications in cancer care, where TCQ has shown the potential to mitigate a range of oncology symptoms and side effects. A 2019 meta-analysis identified 22 RCTs ($n = 1,410$) and found moderate-quality evidence for improving fatigue ($SMD = -0.36$) and limb/muscular function ($SMD = 1.19$), and lower-quality evidence for insomnia ($SMD = -0.37$) and physical ($SMD = 0.34$) and mental ($SMD = 0.60$) well-being (Ni et al. 2019). In another 2018 meta-analysis of 22 studies (15 RCTs and 7 nonrandomized controlled trials; $n = 1,283$), TCQ was associated with significant improvement in fatigue ($g = -0.53$), depression ($g = -0.27$), and QL ($g = 0.33$) (Wayne et al. 2018, Zeng et al. 2014).

Relaxation/Imagery

Relaxation training is often accompanied by the use of imagery. Interventions included under this rubric are varied and include progressive muscle relaxation (PMR), autogenic training, biofeedback, guided imagery, and relaxation programs comprised of multiple components. A recent review of psychosocial interventions (including relaxation techniques) for pain management in advanced cancer reported a small but significant effect on pain ($d = -0.29$) (Warth et al. 2020). Evidence also suggests potential benefits, specifically of PMR, for people with advanced cancer, who reported significantly reduced pain intensity, distress, anxiety, and depression symptoms pre-post PMR (De Paolis et al. 2019). PMR has also been associated with reduced CINV in terms of incidence and frequency, as well as beneficial effects on mood, anxiety symptoms, and depression symptoms during the chemotherapy treatment period (Kapogiannis et al. 2018, Tian et al. 2020).

Hypnosis

Hypnosis is defined as a state of consciousness that involves focused attention and reduced peripheral awareness, characterized by an enhanced capacity for response to suggestion. The first

TCQ: tai chi and qigong

PMR: progressive muscle relaxation



phase of hypnosis is called an induction, and it involves relaxation and usually imagery to become focused on the objective of the session. The second phase is the application phase, during which usually a trained therapist makes suggestions targeted to address specific symptoms or conditions. Among all applications of hypnosis, its effectiveness for improving pain and anxiety is the most well established. In cancer care, a narrative literature review showed positive effects on CINV, anxiety, pain, and, to a lesser extent, fatigue, distress, and hot flashes (Carlson et al. 2018, Cramer et al. 2015).

In another 2017 meta-analysis exploring the effects of hypnosis on anxiety in both pediatric and adult cancer patients, 20 studies including 878 participants were identified (seven single group pre-post and 13 RCTs) (Chen et al. 2017). A moderate effect size ($g = 0.70$) for anxiety was reported, which was maintained at follow-up ($g = 0.64$), and therapist-guided hypnosis was more effective than self-delivered hypnosis (Chen et al. 2017). A 2020 review of controlled trials focusing solely on pain and anxiety included 11 studies with a total of 1,182 participants (of which 968 were women). Most studies were conducted either before or shortly after cancer surgery, or during chemotherapy or radiation therapy, and one was for symptomatic palliative patients. Often only one hypnosis session was provided, and five of the studies included self-hypnosis, while the rest were therapist guided. Results showed efficacy of hypnosis for reducing anxiety and pain compared to usual treatment controls. Of all the MBIs, hypnosis has the most supportive evidence for its usefulness in preparation for surgery and following surgery for management of pain.

Creative Therapies

Creative therapies are designed to facilitate emotional expression beyond words or traditional talk therapy, using various arts-based modalities. The most commonly used and professionally supported approaches include art therapy, writing, sand play, clay modeling, movement therapy, psychodrama, role play, and music therapy. For PLWC, the most well-studied are music therapy, visual arts, and movement therapies. Music therapy can be delivered in several modalities, including songwriting, music and relaxation exercises, lyrics discussion, directed music listening, singing/toning, moving to music, recording and video creation, and adapted instrument lessons, among others. A 2016 meta-analysis of 52 RCTs or non-randomized controlled trials of music therapy for PLWC ($n = 3731$) found positive effects on anxiety (SMD = -0.62 to -0.89), pain (SMD = -0.91), fatigue (SMD = -0.38), and QL (SMD = -0.98), but the quality of the evidence was generally low (Bradt et al. 2016). Additionally, in a 2017 narrative review of the literature on PLWC in palliative care, authors concluded that music therapy may help manage pain in palliative care recipients through its therapeutic effects on emotional and spiritual well-being (McConnell & Porter 2017).

Visual art therapy allows expression of thoughts and feelings through activities involving imagery, color, and shape, facilitating self-exploration and understanding. In a 2017 review, studies on art therapy for PLWC reported improvements in QL, depression, and mood disturbance (Carlson et al. 2017). In another integrative review by Aguilar (2017) evaluating the benefits of art therapy for pediatric cancer patients, six qualitative studies were identified, indicating that children who took part in drawing interventions were able to better express their emotions, developed more effective coping skills, experienced improvements in cancer-related symptoms, and showed enhanced communication with family members and caregivers (Aguilar 2017).

Other creative therapies, such as expressive writing and dance/movement therapy, have also been investigated in PLWC, but the evidence base is still small and inconclusive as to their benefit. For example, a systematic review of 11 RCTs with a total of 1,178 women with breast cancer showed a significant effect of expressive writing on reducing negative somatic symptoms in breast



cancer patients in the short term (<3 months) but not in the longer term, and no significant effects of the intervention on psychological outcomes (Zhou et al. 2015).

ADVANCED CANCERS

There are several psychosocial interventions either specifically targeted to or primarily tested in people diagnosed with advanced, metastatic, or terminal cancers (these are slightly different terminologies meaning the disease has spread or is not curable and will likely progress and lead to loss of life, which may be imminent or sometime in the future). People with these diagnoses are often seen in palliative care (although palliative care specialists will tell you it is more about symptom management than only end-of-life care). Nonetheless, usually when study participants are described as being in palliative care, this means nearing end-of-life and incurable. As mentioned in previous sections, issues around end of life, such as leaving a legacy, tying up loose ends, saying goodbye, and coming to terms with how one has lived one's life are pressing concerns for many people with advanced cancers. Hence, several interventions have been specifically designed for this population.

Supportive Expressive Therapy

Of all the therapies in this section, SET has been around the longest. Developed by Spiegel and Yalom in the 1980s, it is based on principles of existential psychotherapy, and it was designed to build new bonds of social support, encourage expression of emotion, deal with fears of death and dying, help restructure life priorities, improve communication with family members and health care professionals, and enhance control of pain and anxiety. It is delivered in groups of either set duration or ongoing for periods of a year or longer.

A famous (and somewhat controversial) study published by Spiegel et al. (1989) showed that SET not only improved indices of QL in women with metastatic cancer who participated in weekly SET meetings for a year but also resulted in a longer life span, compared to a randomized usual care control group. Replication studies failed to confirm this survival advantage (e.g., Kissane et al. 2007) but supported the effectiveness of the intervention for improving mood and traumatic stress symptoms, psychological symptoms and pain (Goodwin et al. 2001), and QL and depression (Kissane et al. 2007) in women with metastatic breast cancer.

Meaning-Centered Psychotherapy

Meaning-centered psychotherapy was developed by psychiatrist Bill Breitbart in the late 1990s to address the loss of spiritual well-being or sense of meaning in life, and existential distress common in people with advanced cancer (Breitbart 2002). Grounded on the work of Victor Frankl (1959), this intervention is based on the underlying principle that existential distress is due to believing that one's life is meaningless. Therapy, therefore, aims to directly sustain or enhance participants' sense of meaning through reexperiencing and recreating meaning in their lives. It is an eight-session manualized therapy that can be delivered in either group or individual format.

Large RCTs of both group and individual meaning-centered psychotherapy have shown that these programs improve spiritual well-being and QL and significantly reduce depression, hopelessness, desire for hastened death, and physical symptom distress (Breitbart et al. 2015, 2018). For example, 253 people with advanced cancer randomized to an eight-session group meaning-centered therapy program showed significantly greater improvement in spiritual well-being, QL, depression, hopelessness, desire for hastened death, and physical symptom distress compared to those randomized to a support group (Breitbart et al. 2015).

SET: supportive expressive therapy



Dignity Therapy

Dignity therapy was introduced in 2002 by psychiatrist Harvey Chochinov, based on the observation that some people struggle with loss of autonomy and dignity at end of life, while others seem to be able to find peace and serenity and enjoy their final days (Chochinov 2002). It is a brief, individualized psychotherapy that aims to relieve psychoemotional and existential distress for PLWC with advanced illness. This therapy offers people an opportunity to reflect on issues that are important to them and things they would like to recall or transmit to others. The protocol begins by giving the person nine standard questions in advance of meeting with a therapist to consider and reflect upon. The questions cover topics such as a person's life history, things they think are most important about their life, things they would want their family to know about them and remember, important roles they held in life, key accomplishments, things they feel are still left to be said and done, their hopes and dreams for loved ones, lessons in life they would want to pass along to others, advice or words of wisdom for their loved ones, and advice or guidance to help prepare their loved ones for the future. Patients can discuss any of these issues as they choose. They are asked if there are specific things they would like included in the record that is created on the basis of the interview. The session is then recorded, transcribed, and edited, after which a legacy document is produced and delivered to the patient (Manartínez et al. 2017).

In one of the largest RCTs of dignity therapy, Chochinov's group randomized 441 people with advanced disease receiving palliative care to dignity therapy, standard palliative care, or client-centered care (focusing on more practical, here-and-now issues) (Chochinov et al. 2011). Post-intervention, the participants reported that dignity therapy was significantly more likely than the other two interventions to be helpful, improve QL, increase sense of dignity, change how their families saw and appreciated them, and help their families. Dignity therapy was significantly better than client-centered care (but not standard palliative care) in improving spiritual well-being, and it was significantly better than standard palliative care in terms of lessening sadness or depression (Chochinov et al. 2011).

Quite a number of studies have been conducted on dignity therapy since its development, reviewed most recently in 2017 (Martínez et al. 2017). This review included 28 studies, 5 of which were RCTs, of generally high methodological quality. The results were grouped into effectiveness, satisfaction, suitability and feasibility, and adaptability to different diseases and cultures. RCTs showed statistically significant decrease on anxiety and depression, and nonrandomized studies suggested improvements in existential and psychosocial measurements. Patients, relatives, and professionals perceived dignity therapy as improving the end-of-life experience.

Managing Cancer and Leaving Meaningfully

CALM was more recently developed by Rodin and colleagues specifically to help treat depression and existential distress (Hales et al. 2010). CALM is a brief, semi-structured, individual intervention that covers four domains: (a) symptom management and communication with health care providers; (b) changes in self and relations with others; (c) spirituality, sense of meaning, and purpose; and (d) preparing for the future, sustaining hope, and facing mortality. This approach was only developed in the last 10 years, but a series of pilot and feasibility studies culminated in the publication of a large RCT of 305 people with advanced cancer, randomized to either CALM or usual care (Rodin et al. 2018). In this study, CALM participants reported less-severe depressive symptoms than usual care participants at 3 months ($d = 0.23$) and 6 months ($d = 0.29$) post-intervention, and they reported greater end-of-life preparation. However, when compared in another RCT to supportive counseling, the beneficial effects were similar (Mehnert et al. 2020).



It may be the case than any of these types of meaning-focused interventions have similar potential to be efficacious in managing existential distress in people with advanced cancers, but more comparative research is necessary in this relatively new application of psychosocial support.

Complementary Therapies

A range of mind-body and other complementary therapies are also quite often used with people living with advanced cancers. This literature was summarized in a 2021 review, which synthesized the evidence regarding the implementation of complementary therapies on end-of-life outcomes in hospice care (Dingley et al. 2021). Twenty-three quantitative or mixed-method studies across eight countries were included. Most commonly used complementary therapies were music, biofield therapies (reiki, therapeutic touch), and massage therapy. Most studies reported significant findings on physical symptoms (pain, dyspnea, fatigue, gastrointestinal symptoms, agitation) and/or psychosocial/spiritual symptoms (anxiety, depression, spirituality, well-being, QL), but although there were a few adequately powered RCTs, overall study quality was not very high.

Psychedelic Therapies

An exciting new area of investigation is the potential use of psychedelics (such as psilocybin, LSD, MDMA, and ketamine) to help people living with advanced cancer manage existential anxiety, loss of meaning or desire for hastened death, and distress related to end of life. Similarly to the therapies just described, psychedelic experiences often evoke a mystical quality that participants say helps them feel connected and find more meaning and purpose in their lives. Observations from previous research suggest that psychedelics, many of which work through altering tryptamine serotonergic pathways, can produce highly salient spiritual/mystical states of consciousness, which have been associated with enduring positive changes in cognition, affect, behavior, and spirituality. While some of this work was completed decades ago, with the advent of government policies restricting access to psychedelics, the research paused for many decades, only to reignite over the past 10 years.

Clinically, Ross and colleagues completed one of the first RCTs of 31 patients with advanced cancers randomized in a blinded crossover design to a single dosing session of psilocybin versus active control (niacin), administered in conjunction with psychotherapy (Ross et al. 2016). Seven weeks after the original session, participants were crossed over to the other therapy. Compared to the niacin placebo, psilocybin therapy produced rapid and sustained improvements in depression, demoralization, and hopelessness. Secondary analyses of these data 4.5 years later found that psilocybin therapy was also associated with reductions in suicidal ideation that were apparent post-intervention and persisting as well as with large reductions in loss of meaning persisting up to 4.5 years (Ross et al. 2021). Authors emphasize the importance of meaning making for the positive effects of the treatment.

The largest RCT to date included 51 cancer patients with life-threatening diagnoses, randomized to either high- or low-dose psilocybin administered in counterbalanced sequence 5 weeks apart, with a 6-month follow-up. Participants, staff, and community observers all rated participant moods, attitudes, and behaviors. Only the high-dose condition resulted in large decreases in clinician- and self-rated measures of depressed mood and anxiety, along with increases in QL, meaning in life, and optimism and decreases in death anxiety, which were sustained at the 6-month follow-up. Participants attributed these effects squarely to the treatment experience (Griffiths et al. 2016). Finally, in a 2021 review of eight studies of psilocybin in PLWC (four quantitative, two mixed-methods, and two qualitative), the majority of patient experiences were summarized as positive, centering on themes of death acceptance, reflection, and broadened spirituality (Lehto



et al. 2021). While more work remains to be done in this nascent area, it appears very promising as a way to accelerate or supplement the therapeutic process of meaning making with the aid of psychoactive substances.

SUMMARY OF FINDINGS

In general, all of the interventions reviewed herein can be useful for treating a wide range of symptoms in PLWC. The NCCN clinical practice guidelines for distress, pain, fatigue, palliative care, and survivorship (NCCN 2022) provide a useful overview of a full range of interventions. Unfortunately, the literature lacks the specificity necessary to distinguish which among many potentially helpful interventions a PLWC should try or a health care provider should recommend. For example, the NCCN distress guidelines recommend CBT, supportive psychotherapy, psychoeducation, family and couples therapy, relaxation, mindfulness, meditation, creative therapies (art and music), and exercise as evidence-based therapies for treating distress, anxiety, and depression. The recommendations for fatigue are not dissimilar, with perhaps more emphasis on physical activity and yoga but with mention of most of these other modalities as well. For pain, recommendations include CBT, mindfulness, breathing, relaxation, imagery, hypnosis, music therapy, and psychoeducation.

In general, this lack of specificity is due to the fact that very few studies have directly compared the various modalities; most research has used passive or usual care comparators. Moreover, treatment matching studies, wherein individual participant characteristics are tested as moderating factors in treatment efficacy, are scant. When we attempted to do this in one large clinical trial comparing MBCR to SET in distressed women who completed treatment for breast cancer, the only predictor of treatment response was preference—that is, getting assigned to the intervention one was initially hoping for (Carlson et al. 2014)! This reinforces the simple adage that if someone believes an intervention will be of benefit, it most likely will.

Conceptually, at the most basic level, PLWC are seeking ways to cope with a wide range of emotional reactions to the life threat of cancer, the uncertainty it engenders, and the loneliness and pain (physical and emotional) that accompanies this difficult experience. They are seeking to create a sense of meaning and purpose in the face of adversity. So while we may look at the symptoms in isolation, the underlying psychological mechanisms common to many manifestations are appropriate therapeutic intervention targets. These include the importance of meaning making, finding purpose in life, and connecting with others, which are targeted by many of the efficacious therapies reviewed above.

LIMITATIONS TO THE EVIDENCE BASE

Although there is much we know about the efficacy of PON and IO interventions for treating a wide variety of symptoms and side effects for PLWC, there are common limitations to the knowledge base that largely transcend the type of research being studied. These are summarized in **Table 2**. A number of them concern study participants, including small sample sizes, lack of diversity in sociodemographic and cancer-related characteristics, and design issues, such as lack of standardization of intervention delivery and facilitator training, lack of comparison groups, short follow-ups, and measurement and analysis issues. These design and reporting issues impede the ability of future researchers to replicate treatment effects, since without such details it is impossible to recreate tested interventions. In an era of open science and transparency increasingly requiring trial registration and data and protocol sharing, this lack of detail and accountability is becoming unacceptable.



Table 2 Common methodological issues in psycho-oncology research

Issue	Description	Potential remediation
Small sample sizes	Often convenience samples are used and studies are not adequately powered to detect small- or medium-sized effects.	To avoid type II errors, conduct power analyses prior to recruitment to determine the necessary sample size.
Lack of diversity in participant demographic characteristics	Often studies are conducted only with women, and without gender, age, socioeconomic, cultural, geographic, or racial diversity.	To broaden generalizability, strive to test interventions in men and other genders besides women, non-White racial groups, rural and remote or community-based samples, older and younger participants, and lower-SES samples.
Lack of diversity in participant cancer-related characteristics	Often studies include only one type of cancer (often breast), in early stages of disease, and during the survivorship (post-treatment) phase.	Study the effects of interventions separately on people during and after treatment, at end of life in advanced cancer groups, and across types and stages of disease.
Lack of comparison groups	Often studies use only one group in a pre-post intervention design without any comparison group.	Use a comparison group to control for the natural history of changes over time, historical factors, and regression toward the mean.
Lack of randomization	Comparison groups are often convenience samples of patients not interested in the therapy or other patients in the same clinics.	Randomize interested participants into intervention and control groups to establish equivalence at baseline across known and unknown factors.
Lack of therapy standardization and treatment fidelity checks	Therapies within the same category often vary considerably in terms of content, number of sessions, delivery mode, and home practice; therapist behaviors are not routinely monitored.	Create and publish standardized and if possible manualized interventions; monitor treatment fidelity.
Variability in therapist training and credentials	Not all therapists across any given modality have the same level of training or experience.	Choose similarly and highly trained professionals to deliver interventions; describe the training in publications.
Lack of long-term follow-up	Many studies only look at pre-post intervention changes so we know little about the durability of effects.	Follow participants for several months or even years after the intervention; check to see if they are still doing the practice in the interim for skills-based interventions.
Reliance on self-report measures only	Many studies use only self-report questionnaires as outcomes.	Use only appropriate, reliable, and validated questionnaires where they exist; try other methods like qualitative interviews, behavioral observations, proxy reports, or biomarkers.
Use of inappropriate or outdated statistical analyses	Often simple t-tests or ANOVAs are used without controlling for potential confounding variables.	Use linear mixed models or multiple regression and take into account potentially important baseline moderating factors.
Lack of blinding of participants and assessors	Often testers, patients, and intervention providers know which therapy participants are receiving.	It is not always possible or desirable to blind patients or providers to treatment, but assessors can be blinded to study conditions to reduce testing bias.

Abbreviations: ANOVA, analysis of variance; SES, socioeconomic status.

In **Table 2**, strategies to remediate each of these limitations are also suggested. It should be recognized that these recommendations are largely geared toward the conduct of efficacy clinical trials and do not apply to qualitative research and other valuable methodologies outside of these. The issue around lack of diversity in study samples has recently become more salient, with



Digital health intervention (DHI): health services delivered electronically through formal or informal care, ranging from electronic medical records to mobile health apps

disparities in health equity across cancer care being more starkly revealed by the pandemic and other global events. Historically, in many PON studies, participants have been middle-aged, white, educated women. Indeed, I wrote a commentary in 2017 about “wealthy white western women” decrying the lack of diversity, specifically, in MBI research (Carlson 2018). This is an issue across therapeutic modalities, and it highlights the importance of including more diverse samples and targeting lower-SES groups, racialized participants, individuals with sexual orientations other than heterosexual, men and other genders besides women, and both younger and older participants, to name a few areas where this research lacks diversity.

FUTURE DIRECTIONS

Pragmatic Science

In addition to the obvious efforts to address limitations in the existing knowledge base, such as increasing diversity across sociodemographic and cancer-related characteristics in study samples (see **Table 2**), other considerations have become increasingly important when developing, testing, and implementing interventions to help PLWC cope, including using more pragmatic, real-world intervention study design that can better support the sustainability of interventions.

The problem is that traditional research paradigms do not encourage or reward the kind of research that leads to scalability and sustainability of interventions. While the gold standard of tightly controlled efficacy trials is necessary to determine the causal effects of interventions, they are not adequate for changing practice and for actually making these interventions widely available to all PLWC. Ironically, even the literature I have been reviewing in this article largely comes from systematic reviews and meta-analyses of efficacy RCTs. However, to bridge the gap from efficacy to real-world effectiveness, other types of more pragmatic research designs are necessary.

What makes a study pragmatic, and why does this support implementation? There are good resources detailing the explanatory-pragmatic continuum in research design, including the PRECIS-2 guidelines (Loudon et al. 2015), but essentially, the more similar to the real world the research setting and participants, the more pragmatic the design, and the easier to implement following an evaluation of effectiveness. If research is conducted in the same settings as real-world program delivery, with the same staffing models and integrative programs of existing clinic flows, when research support is withdrawn, programs stand a much better chance of continuing and leading to widespread uptake.

Delivery Approaches to Improve Scalability

In pragmatic design, we have to consider the jump from research-funded studies to actual program implementation. For example, resource-intensive interventions that require highly trained facilitators and multiple in-person sessions may not be practical to deliver to many PLWC, and certainly not in busy clinical settings where the rest of care is delivered. In order to truly make an impact for a large number of diverse PLWC, evidence-based interventions need to be scalable, so that they can reach more people without exorbitant costs that health care systems are not willing or able to absorb. Hence, shorter, brief interventions and those utilizing digital technologies can help set the stage for broad future implementation. In response to this need, there has been a growing impetus to develop telephone-based, online, and mobile versions of PON interventions that have shown promise or have proven as efficacious as the traditional face-to-face delivery modalities. These are usually known as eHealth interventions (any remote delivery) or mHealth (mobile apps) interventions, and they can be collectively referred to as digital health interventions (DHIs).

DHIs have begun to proliferate to the extent that several reviews of these interventions have been published. One 2021 systematic review and meta-analysis focused on any type of eHealth



intervention for treating pain, sleep, or fatigue in PLWC (Li et al. 2022). Twenty-five RCTs were included, which utilized a variety of interventions and delivery modalities. Most interventions were delivered online or via telephone, with a few using mobile phone apps. Internet interventions were usually some version of self-paced modules with intermittent professional guidance. Modalities ranged broadly and included CBT-based interventions, exercise, yoga, mindfulness, imagery, symptom management, motivational interviewing, and specific CBT-based interventions for sleep, pain, and fatigue management. Overall, meta-analytic results showed that as a group, these eHealth interventions had a positive impact on pain interference (SMD = -0.37) and sleep disorders (SMD = -0.43) but not on pain severity or fatigue.

Another 2021 meta-analysis reviewed all telehealth interventions for improving quality of life in PLWC, defined as “healthcare service[s] delivered by telecommunication technologies to remotely provide health education, consultation, assessment, and ongoing monitoring for cancer survivors” (Li et al. 2021). This use of terminology is a bit confusing, as usually telehealth refers to telephone or video-based consultation and service delivery. In this case, however, delivery formats included text messages, sound, images, videos, and other multimedia approaches. Twenty-eight RCTs were included, and a meta-analysis found significant effects on QL (SMD = 0.24). The studies included in the analyses tested a wide range of interventions, with 13 studies delivered through a website with modalities including CBT, psychoeducation, symptom tracking, mindfulness, rehabilitation, physical activity, and lifestyle modification. Nine other studies provided telephone-based interventions including mindfulness, ACT, psychoeducation, symptom monitoring, and supportive counseling. The remaining 6 studies used mobile apps to deliver self-management, mindfulness, and symptom monitoring. Of these three delivery modalities, studies using mobile apps had the biggest effect on QL (SMD = 0.41). Whether this was due to the modality of delivery or the interventions themselves is unknown.

In addition, one potentially positive outcome of the COVID-19 pandemic has been the large-scale implementation of virtual care, which has occurred at an unprecedented rate since 2020 and is now commonplace across many cancer care delivery systems. Many people prefer the option to receive care from their own homes, without the added burden of travel and parking time and expenses. Within an IO context, the SIO was quick to survey members and develop practice recommendations for delivering a range of integrative therapies online (Ben-Arye et al. 2021). These online practice recommendations address 10 specific challenges, providing practical suggestions for online treatment and consultation. These include overcoming unfamiliarity, addressing resistance among patients and health care practitioners to online consultation/treatment, exploring ethical and medical-legal aspects, solving technological issues, preparing the online treatment setting, starting the online treatment session, maintaining effective communication, promoting specific treatment effects, involving the caregiver, concluding the session, and ensuring continuity of care. With these guidelines in place, virtual integrative care will only become more commonplace.

Implementation and Dissemination

It is important to develop low-cost, sustainable interventions that are scalable to large numbers of PLWC, but the fact that an intervention has the potential to be scalable does not mean that it will immediately or easily be implemented in real-world settings and reach the intended audience. This requires both dissemination of information about the intervention to key groups and actual implementation of programs among PLWC. Dissemination largely refers to getting the word out, whereas implementation is about uptake: It requires both getting the word out and getting the intervention broadly used by the target audience.

Implementation science is a distinct branch of study that investigates how best to do this, but few clinical scientists are trained in it. This makes purposefully partnering with implementation



specialists and developing knowledge translation plans essential. Implementation is context specific and needs to be designed and evaluated within the context and setting where the intervention is hoped to be adopted. Hence, individual hospitals and health care networks or providers are often the unit targeted by implementation efforts. If interventions can be delivered as stand-alone programs, PLWC themselves may be the target of implementation efforts.

Depending on the target audience and the goal of an implementation activity, different strategies can be effective. Tools for developing knowledge translation strategies for dissemination and implementation activities are available that walk through key questions such as identifying the goals of the activity (e.g., generate awareness, interest, buy-in; share knowledge; inform decision making; inform research; facilitate policy change), the target audience (e.g., researchers, health care providers, the public, media, patients/consumers, decision/policy makers or government, industry, research funders), and the key messages for each audience. Depending on these factors, appropriate materials can be generated such as tool kits, pamphlets, plain language summaries, policy briefs, traditional academic publications, short videos, and infographics and presented in formats ranging from workshops, webinars, and professional training in-services to traditional and social media outlets and platforms.

Engaging with the end users or community members the intervention is trying to reach is also key to generate buy-in and to learn about the types of messages or products that would be well received within specific communities, such as distinct cultural or racial groups. Having partners who can become champions in these communities, help spread the message, and engender trust among community members is also imperative, particularly for communities where trust is low.

CONCLUSION

In this review I have provided an overview of the field of PON in terms of the general experience of living with cancer as well as the potential programs and interventions across a range of modalities that may help people cope with this life challenge. The body of literature in this area is still young, but we know with some certainty that many supportive therapies can help treat a range of common symptoms and side effects such as distress, anxiety, depression, fatigue, pain, and insomnia in PLWC. They can also help people make sense of living with cancer in the context of their own lives, regain a sense of meaning and purpose, and prepare for the eventual end of life so that they can say goodbye feeling calm and at peace. This important work still has a long way to go to address issues of diversity and reach of interventions and to ensure broad implementation in order to help more than a small proportion of the many PLWC who could benefit from access. The task is not small, but enthusiasm within the fields of PON and IO is high, and many clinicians and scientist are dedicated to work directly with PLWC to help them live their best lives, even in the face of cancer.

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