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Integrative oncology: Addressing the global challenges of cancer prevention and treatment

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Abstract: The increase in cancer incidence and mortality is challenging current cancer care delivery globally, disproportionally affecting low- and middle-income countries (LMICs) when it comes to receiving evidence-based cancer prevention, treatment, and palliative and survivorship care. Patients in LMICs often rely on *traditional, complementary, and integrative medicine* (TCIM) that is more familiar, less costly, and widely available. However, spheres of influence and tensions between conventional medicine and TCIM can further disrupt efforts in evidence-based cancer care. Integrative oncology provides a framework to research and integrate safe, effective TCIM alongside conventional cancer treatment and can help bridge health care gaps in delivering evidence-informed, patient-centered care. This growing field uses lifestyle modifications, mind and body therapies (eg, acupuncture, massage, meditation, and yoga), and natural products to improve symptom management and quality of life among patients with cancer. On the basis of this review of the global challenges of cancer control and the current status of integrative oncology, the authors recommend: 1) educating and integrating TCIM providers into the cancer control workforce to promote risk reduction and culturally salient healthy life styles; 2) developing and testing TCIM interventions to address cancer symptoms or treatment-related adverse effects (eg, pain, insomnia, fatigue); and 3) disseminating and implementing evidence-based TCIM interventions as part of comprehensive palliative and survivorship care so patients from all cultures can live with or beyond cancer with respect, dignity, and vitality. With conventional medicine and TCIM united under a cohesive framework, integrative oncology may provide citizens of the world with access to safe, effective, evidence-informed, and culturally sensitive cancer care.

Keywords: cancer prevention, complementary, alternative, and integrative medicine, global health, health policy, survivorship

Introduction

Cancer is a global health challenge that knows no boundary. Over the next 2 decades, the number of new cancer cases is expected to rise approximately 50% worldwide.[1] Many obstacles stand in the way of successful global cancer care, particularly in low- and middle-income countries (LMICs). In these regions, access to quality affordable care, including cancer screening facilities, trained medical professionals, availability of conventional treatment (such as surgery, chemotherapy, and radiation therapy), and supportive care services, can be extremely limited.[2]

Patients have been using culturally salient, lower cost traditional medicine practices, such as acupuncture, yoga, meditation, and herbal medicine, along their cancer journeys. Collectively, these modalities are classified as part of complementary and alternative medicine (CAM) in the West.[3] Since 2002, the traditional

medicine strategy of the World Health Organization (WHO) has encouraged and strengthened the insertion, recognition, and use of traditional, complementary, and integrative medicines (TCIMs) in national health systems at all levels: primary health care, specialized care, and hospital care.[4] Therefore, we use the term *TCIM* in this article to refer to these practices.

Although TCIM is widely used among populations in high-income countries (HICs)[5] as an adjunct to conventional medicine, TCIM may be considered primary health care in LMICs such as Chile, Brazil, and rural India.[6-8] With economic development and international engagement, growing numbers of LMICs have initiated efforts to provide conventional cancer screening, treatment, and supportive care. Despite the increased use of both TCIM and conventional medicine globally, tension and conflicts between these approaches exist, and systematic integration remains extremely limited. It is precisely for this reason that the growing field of integrative oncology can contribute solutions for patients, families, and practitioners to navigate between the 2 health care paradigms. The Society for Integrative Oncology (SIO) defines this field as a patient-centered, evidence-informed approach to cancer care that uses lifestyle modifications, mind and body therapies, and natural products from different traditions in tandem with conventional cancer treatments.[9] Integrative oncology offers both a bridge and path forward to help deliver culturally sensitive, high-quality care in LMICs.

In October 2020, over 700 participants virtually joined global leaders, researchers, and scholars to learn more about the opportunities and challenges of integrative oncology at the Trans–National Cancer Institute (NCI)-National Institutes of Health (NIH) Conference, *International Perspectives on Integrative Medicine for Cancer Prevention and Cancer Patient Management*. In this review, we have drawn upon the meeting procedures and summarized the key themes that emerged from the presentations and discussions on global integrative oncology, with a particular focus on LMICs. In addition, we performed a scoping review of current clinical guidelines that included integrative oncology treatments. Furthermore, selected conference presenters and moderators formulated recommendations based on the meeting summary. This review includes 6 sections: 1) a synthesis of the global cancer burden and cancer control challenges; 2) a review of the conceptual challenges between TCIM and conventional medicine in cancer care and examples in specific regions, eg, Latin America, Africa, and Asia (China and India); 3) the current evidence base for integrative oncology; 4) research challenges and opportunities in integrative oncology; 5) examples of global integrative oncology research collaborations to increase the evidence base; and 6) the formulation of policy, research, and practice recommendations to advance the global impact of integrative oncology.

Global Cancer Burden

Human and Societal Costs of Cancer

Over 19 million people around the world were diagnosed with cancer and almost 10 million died from cancer in 2020.[10] By 2040, new case and death totals are expected to reach approximately 28 million and 16 million, respectively.[11,12] Cancer treatment alone costs the world approximately US$1.2 trillion annually—nearly 2% of the global gross domestic product in 2019.[13] LMICs account for 80% of the global cancer burden; yet, with only 5% of the global spending to combat this disease, LMICs will continue to fall behind in efforts to provide quality cancer care to their citizens.[14] Furthermore these countries will not remain aligned to achieve the WHO Sustainable Development Goal Target 3.4[14] for the year 2030, which aims to reduce

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by one-third premature mortality from noncommunicable diseases, including cancer, compared with rates from 2015.[15] Countries with a low human development index (a summary measure of key dimensions affected by sustainability and equity) experience significantly higher premature mortality because of delayed diagnosis and access to therapeutic services as well as limited availability of quality treatment.[16] Furthermore, a constellation of dynamics surrounding issues, such as lack of infrastructure, health policies, properly trained professionals to perform evidence-based screening and treatment, trust in providers, and continuity of care across services, underlies and exacerbates these global challenges in cancer care delivery (Fig. 1). For example, premature deaths from noncommunicable diseases that could be prevented through effective policies and public health interventions have increased nearly 50% over a few decades, from 23 million deaths in 1990 to over 34 million deaths in 2017, with one-third of those being cancer-related.[17]

Growing Inequality in Cancer Prevention

Suboptimal implementation of highly effective cancer prevention strategies, such as tobacco-control interventions and vaccination against hepatitis B virus (HBV) and human papillomavirus (HPV) in LMICs, has widened global cancer inequality. More than 80% of global smokers live in LMICs,[18] and many of these countries have not satisfactorily enforced the 6 evidence-based measures identified by the WHO Framework Convention on Tobacco Control.[19] Although the current prevalence of tobacco use is comparatively low in Africa, concerns have been expressed about the impact of lifestyle changes, weak tobacco-control measures, and intensified marketing by tobacco companies. A significant increase in smoking prevalence among men has already been documented in some African countries like Congo.[20] Infection-related cancers constitute disproportionally high rates in LMICs where effective prevention and treatment strategies exist. Chronic HBV infection was responsible for 55% of the hepatocellular cancers occurring in 2018.[21] Coverage of the birth dose of HBV vaccine is <40% globally, with huge disparities across countries.[22] Only 40% of Asian countries and 31% of African countries have introduced HPV vaccination programs as of 2020, although the majority of the global cervical cancer burden is shared by these countries.[23]

Western Lifestyle Contributes to Growing Cancer Incidence

LMICs face additional challenges in responding to the rise of cancer incidence and premature death caused by undesirable lifestyle trends. Cancer incidence changes when people from Asia or Africa migrate to Western countries. Immigrants experience increased obesity and a spike in

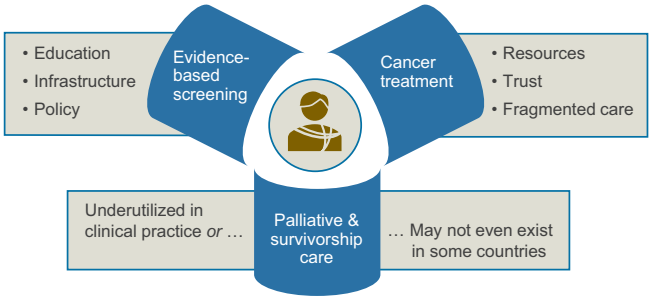

FIGURE 1. Worldwide Challenges in Cancer Care Delivery.

Western lifestyle-associated diseases, including cancer incidence rates higher than those observed in their home countries. Several epidemiological studies found that immigrant cancer rates can match those of their newfound home in as quickly as one generation for Africans and South Asians.[24-26]

In addition, cancer incidence trends in those LMICs that have experienced recent economic development are starting to mirror the trends in Western countries.[27] Whereas breast cancer rates used to be low in China, India, and Brazil, metropolitan areas of these countries now have rates similar to the West because of changes in lifestyles as well as delays in pregnancy and changes in breast-feeding practices.[28-30] Highly processed fast-food diets are common Western exports to LMICs, and obesity rates are increasing alongside Western diseases. In Brazil, for example, almost one-half of people who, in the recent past, were underweight and struggling to consume sufficient calories because of poverty are now overweight, which is linked to physical inactivity and an increased consumption of fast and processed foods that are low in nutrition.[31]

Limited Access to Cancer Treatment

It is well established that lack of resources and fragmented care contribute to global cancer treatment disparities. Despite the rapid development of novel cancer therapies like targeted treatment and immunotherapies in HICs, these treatments are not available to the majority of the population in LMICs. Furthermore, access to older and effective cancer treatment remains extremely limited in the majority of regions in Africa, rural Asia, and rural Latin America.[32] The median density of radiotherapy machines per million population in 2020 was virtually nonexistent at only 0.0 (range, 0.0-0.4) in low-income countries compared with 5.1 (range, 0.4-11.6) in HICs.[33]

A recent *Lancet Oncology* article reported a 25-times difference between LMICs and HICs (3.5% vs 87%) in 5-year survival among women diagnosed with breast cancer. Those authors further estimated that, by implementing a conventional package of screening and treatment (imaging, surgery, radiation, and medical oncology), improving the quality of care delivery can improve survival from 3.5%

to 55.3% in LMICs.[34] Inadequate health care coverage systems can also lead to limitations in cancer treatment.[35] Patients in LMICs often cannot afford conventional medicine options, and out-of-pocket payments dominate health care financing in many of these countries.[36] This has led to elevated risks for adverse financial outcomes, such as medical impoverishment and death, especially in lower income households.[37]

In addition to cost, mistrust of conventional medicine further complicates cancer care in LMICs. More than one-half of patients with cancer in sub-Saharan African countries consulted a traditional healer because of access problems, high cost, stigma, and myths associated with Western cancer treatment.[38] However, an overall lack of cancer education among TCIM practitioners may lead to delayed diagnosis and poor outcomes. For those who do have access to modern cancer advances, early detection and treatment contribute to increases in survival.

Lack of Survivorship and Palliative Care

Growth of the aging population also factors into the rise in cancer survivorship globally, with the WHO reporting that the number of people older than 60 years will increase approximately 2-fold by 2050.[39] The intersection of aging and cancer survivorship can be particularly difficult to navigate for people affected by cancer. Despite progress in supportive care for survivors, gaps still exist in addressing complex symptoms such as anxiety, pain, fatigue, insomnia, neuropathy, and cognitive dysfunction.[40,41] Moreover, the physical, emotional, and social ramifications of cancer may linger years after treatment,[42] further challenging the infrastructure and resources of health care systems.[43]

Early integration of palliative care, which is considered an essential component of universal health care by the WHO to improve quality of life,[44] is also not easily accessible worldwide. For example, only 29% of patients with cancer in middle-income countries and 10% of those in low-income countries have access to oral morphine for pain relief.[45] India and China do not have national policies or government funding that support palliative care,[46,47] and only 12 African countries reported having a stand-alone, nationwide palliative care policy.[48] Therefore, culturally and socioeconomically sustainable solutions are especially needed to support patients and families with advanced disease in LMIC cancer populations.

Challenges of Integrating TCIM Into Conventional Cancer Care

In many LMICs, TCIM practices are deeply rooted in societal cultures and traditions. When used appropriately, TCIM may offer some solutions to address global cancer challenges[6]; however, tensions exist between TCIM and conventional cancer care.

Key differences between conventional cancer care and TCIM perspectives hinder collaboration and integration. Conventional medicine uses a bottom-up, micro-to-macro approach to understand health and disease, examining how structure leads to function. Conversely, TCIM embraces a top-down, macro-to-micro approach, examining how function necessitates structure.[49] Conventional medicine and TCIM have distinct philosophies and treatment approaches (Fig. 2). The conventional oncology paradigm focuses on treating cancer as a biologic disease with identifiable

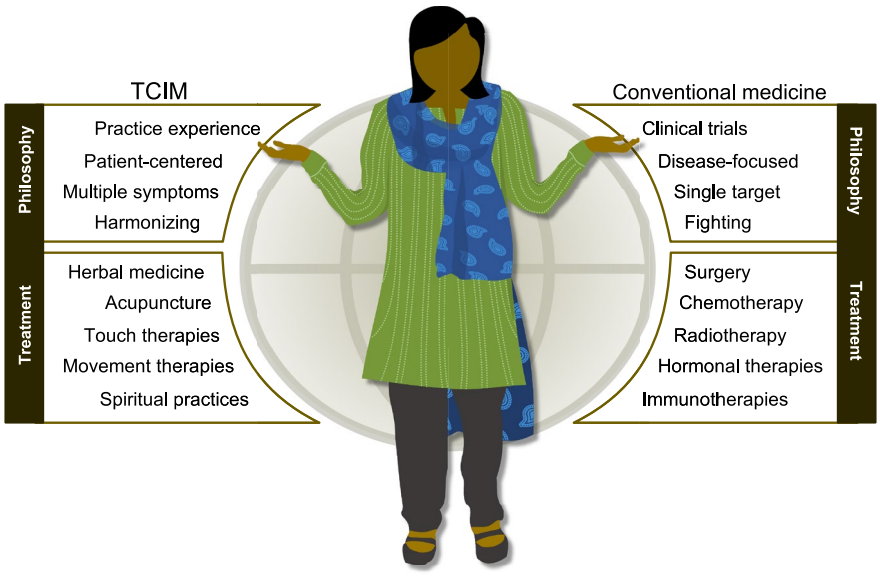

FIGURE 2. Tensions Between Traditional, Complementary, and Integrative Medicine (TCIM) and Conventional Medicine in Low- and Middle-Income Countries.

mutations and targets. Treatments have clear, basic science mechanisms and are evaluated through rigorous clinical trials with well defined end points. As a result, modern anticancer approaches such as surgery, chemotherapy, radiation, hormonal treatment, targeted therapy, and immunotherapy have increased survival for many types of cancer. TCIM, instead, often relies on ancient theory and wisdom as well as thousands of years of empirical practice with people of a particular culture and community. The treatment focuses on the person with the illness rather than the disease itself and embraces the holistic nature of health as the interplay among body, mind, and spirit. The therapeutic approaches, including herbs, acupuncture, touch therapies, and spiritual practices, achieve harmony in the patient regardless of disease status.

Examples of Progress and Challenges of Integrating TCIM and Conventional Medicine in LMICs

Recognizing the tension between TCIM and conventional medical practice, many LMICs are working to integrate their traditional healing practices with conventional cancer care. Below, we provide the examples of Latin America, Africa, and Asia (India and China) to highlight some unique approaches and challenges in health care delivery, research structures, and funding.

Latin America

TCIM is widely used by patients with cancer in Latin American countries.[50-54] It is estimated that between 50% and 90% of adult or pediatric patients with cancer use TCIM.[53,55-62] Natural products and nutritional supplements are most frequently used, followed by spiritual practices. More recognized mind and body therapies, such as meditation, yoga, tai chi, acupuncture, massage, music therapy, dance therapy, mandalas, and horticultural therapy, are also used across Brazil, Argentina, and Chile.[50,53,56,58,59,61,63]

Although widespread use has led to more official recognition, implementation has been mixed. In Argentina, Garrahan Pediatric Hospital and FUNDALEU (Foundation to Fight Leukemia) are 2 examples of health centers that apply TCIM in the clinical setting with medical recommendation. In Chile, the Clinica Alemana, the Arturo Lopez Perez Foundation, the National Cancer Institute, and the Calvo Mackenna Hospital also offer TCIM services integrated with Western conventional therapies to patients with cancer.[64,65] Several Brazilian medical centers have established integrative oncology programs with an academic focus on clinical care, teaching, and research: Hospital Israelita Albert Einstein in Sao Paulo and the Brazilian NCI-Designated Cancer Centers (the National Cancer Institute in Rio de Janeiro and the university hospitals of Sao Paulo and Fortaleza).[66-70] Brazil has a national policy that integrates TCIM within the United Health System, which now includes 29 practices.[71-73] Despite recognition of its policy, these practices are not routinely provided for oncology patients in conventional health centers. In addition, health professionals do not often inquire whether patients are using TCIM; therefore, the extent of benefits or safety issues such as herb-drug interactions are unknown.[59,74,75]

Similarly, the current evidence on TCIM used in Latin America is nascent. Almost all research is preclinical investigation involving plants. Several native and exotic species of Annonaceae, Loranthaceae, and Lamiaceae have been extensively studied.[76-81] Several early phase clinical trials have found preliminary efficacy that plants from the Amazon region, such as *Uncaria tomentosa* and guarana, may help manage adverse effects of cancer treatment (eg, neutropenia, anorexia, fatigue) and improve quality of life.[82-86] The Ministry of Health in Brazil has charged the Brazilian Academic Consortium for Integrative Health, along with the Latin American and Caribbean Center on Health Sciences Information/Pan American Health Organization, with generating clinical guidelines based on systematic reviews that evaluate clinical evidence and treatment outcomes related to cancer symptoms such as fatigue, pain, nausea, and vomiting.[67]

Africa

For most people in Africa, contemporary cancer care is unavailable, inaccessible, or unviable. This is because of the shortage of skilled medical professionals in oncology and scarcity of the required infrastructure. These resources, when available, are concentrated around the few urban centers (mostly national capitals) of the respective countries. The insufficient infrastructure and supply of radiology, diagnostic pathology, therapeutic surgery, chemotherapy, and radiotherapy make conventional cancer care extremely expensive and unviable for the majority of the population. Therefore, TCIM providers are often the first line of health care providers when individuals present with symptoms of cancer, and, for a large segment of the population, they may be the only source of health care that is available and affordable to patients with cancer.[87-90]

African traditional medicine delivered to the community can be classified as divination, spiritualism, and herbalism. Often it is seen as a mixture of these 3 in different proportions, varying from one practitioner to another.[91] In a recent systematic review and meta-analyses, the use of herbs by patients with cancer in Africa was reported to be approximately 40%, the highest of all continents.[92] Because of limited conventional treatment options, many patients with cancer receive herbal medicine alone as monotherapy. Because of a lack of population-based screening and diagnostic capacity,

cancer often presents at an advanced and incurable stage. For these patients, TCIM interventions provide symptom relief and solace until death. Therefore, in the context of Africa, we often find traditional medicine as the first line of treatment for cancer, which is accessible and is introduced as soon as the disease is identified.[90] In urban settings where there are conventional cancer care resources, several hospital-based survey studies in Nigeria, Tunisia, and Morocco found that the use of TCIM treatments among patients receiving treatment was common, which raises the potential for drug-herb interactions.[93-95] TCIM treatments can have side effects and can contribute to renal and hepatic toxicities, which can be a detriment to patients' health; despite common use, physicians rarely inquire about them.[93,94] Considering these drawbacks and the extensive exposure of the African population to TCIM for cancer management and care, it is essential that well defined and focused clinical and experimental investigations are conducted into the safety and effectiveness of these practices to determine their appropriate use in various stages of the cancer care continuum.[87-89]

India

The pluralistic health care system of India offers patients access to TCIM known in the country as AYUSH (Ayurveda, Yoga and Naturopathy, Unani, Siddha, Sowa Rigpa, and Homeopathy). Published estimates of TCIM use among patients who have cancer in India range from 24% to 39%,[96-98] with Ayurveda being the most common.[97] However, these estimates are based on small sample sizes and may not represent behavior of their larger population of patients with cancer. Underreporting raises the possibility of unnoticed harms and benefits and concerns about potential interactions with chemotherapeutic agents. The use of TCIM has been associated with delays in seeking help from oncologists,[96] potentially contributing to delayed diagnosis and treatment and, thus, higher mortality rates. Conversely, benefits from the integration of TCIM therapies into cancer care go unnoticed and are underreported as well.

Despite pluralistic health care systems in India, policies to facilitate cooperation and integration between TCIM and conventional medicine do not exist. Practitioners of these different systems work independently, and integration is challenging because of fundamental distrust in the other.[99] For this reason, integrative oncology is not well developed in India. There have been many scattered and isolated attempts to integrate AYUSH treatments for cancer care in public and private hospitals. For example, several conventional oncology hospitals have established adjunct Ayurveda/AYUSH clinics to integrate relevant treatments with the goals of improving quality of life among patients with cancer. In addition, an Ayurvedic cancer care hospital in Pune, India integrates Ayurvedic drugs in coordination with modern oncology treatments such as chemotherapy, with some reported preliminary benefit.[100]

Research of AYUSH and cancer is predominantly preclinical and focuses on anticancer properties of herbs and formulations, with *Curcuma longa* and *Withania somnifera* being the most studied.[101,102] Some Ayurvedic formulations appear to have chemopreventive, antimetastatic, antiproliferative, chemosensitizing, and radiosensitizing activities.[103-107] To translate any of these findings into effective clinical interventions at the point of care, well designed and rigorous clinical trials are needed. One study of 36 patients with cancer who were undergoing chemotherapy and radiation showed that the Ayurvedic formulation Rasayana Avaleha could reduce adverse events such as vomiting, mucositis, alopecia, and ageusia when used as an adjuvant.[108] Limited funding opportunities, lack of research training, and ethical issues are just some of the challenges faced by researchers in India studying the role of TCIM in cancer management.

China

Traditional Chinese medicine (TCM) is deeply rooted in Chinese culture and everyday life is and held as a symbol of the nation.[109] Approximately 75% to 80% of patients in China use TCM after a cancer diagnosis, with Chinese herbal medicine (55%-75%) used most often and tai chi/qi gong (7%) and acupuncture (1%-5%) used less frequently.[110-112] TCM is widely integrated in oncology departments within China's hospitals in conjunction with conventional cancer treatment.[113] Furthermore, conventional oncology diagnosis (eg, pathology, imaging) and treatment (eg, surgery, chemotherapy, radiation, and hormonal treatment) are available in elite TCM hospital oncology departments in addition to TCM approaches. One medical insurance analysis of oncology inpatients in China showed that 42% used TCM herbs and 25% combined herbs with conventional cancer drugs.[114] In addition, traditional herbal formulas and TCM cancer drugs are listed in China's National Basic Medical Insurance Drug Catalog.

In Hong Kong in 2014, the hospital authority of the Special Administrative Region launched the Integrated Chinese-Western Medicine Pilot Program in 3 public hospitals, which included the integration of acupuncture and Chinese herbal medicine for inpatients with late-stage cancer.[115] The results showed that the practices were safe and feasible, and the program was expanded to 8 hospitals in 2017. Clinical trials conducted in Hong Kong also demonstrated acupuncture benefits in cancer care, including reduced need for postoperative analgesics and improvements in cancer-related cognitive impairment and chemotherapy-induced peripheral neuropathy.[116-118]

In mainland China, with rapid economic growth, government and industry have invested in basic, clinical, and outcomes research of TCM in oncology.[119] For example, in a prospective cohort study, the use of a physician-prescribed TCM formula was associated with improved survival in patients with stage II or III colorectal cancer.[120] In a phase 2 clinical trial, the TCM formula Renshen Yangrong Tang reduced cancer-related fatigue.[121] A systematic review and meta-analysis found that acupuncture was associated with moderate evidence for reducing pain in patients with cancer.[122] Despite progress, TCM often involves complex herbal formulas or individualized prescriptions based on a patient's presentation; therefore, there is a need to increase the quality of TCM clinical trials by developing standardized diagnostic criteria, treatment approaches, and outcome measures according to defining TCM characteristics.[123]

Despite extensive TCM use in China and its surrounding regions, challenges in delivering comprehensive and equitable services exist. One survey of patients that identified barriers to care cited TCM treatment concerns (42%), such as side effects, its hindrance of conventional treatments, and lack of scientific evidence for its use, along with logistical difficulties (42%), including herb decoction, locating a good TCM physician, concerns over treatment cost, and adherence to longer treatments.[124] Furthermore, patients aged 60 years or younger with localized disease had more concerns, and those actively employed reported more logistical difficulties.[124] These findings highlight the need for more basic, clinical, and health services research on TCM treatments, better evidence-based education, and more patient-centered and convenient TCM treatment approaches for patients with cancer.[124]

Current State and Evidence of Integrative Oncology

As shown by the examples above, despite numerous challenges, the practices of conventional medicine and TCIM do not need to be mutually exclusive. By appropriately incorporating specific, evidence-informed TCIM therapies alongside conventional medicine, the field of integrative oncology can overcome tensions and create an inclusive environment in which both philosophies and treatment approaches effectively coexist to produce better patient outcomes. With this goal in mind, it is useful to review the current state of integrative oncology and how it might be used to advance solutions to persistent global challenges in cancer prevention and patient management. Over 20 years ago, leading North American academic cancer institutions, including Memorial Sloan Kettering Cancer Center, Dana-Farber Cancer Institute, and The University of Texas MD Anderson Cancer Center, developed clinical, educational, and research integrative oncology programs in response to the growing demand from patients with cancer to incorporate TCIM into conventional cancer treatment and survivorship care. The NCI also established the Office of Cancer Complementary and Alternative Medicine (OCCAM) to coordinate and enhance activities in TCIM research as it relates to the prevention, diagnosis, and treatment of cancer, cancer-related symptoms, and side effects of conventional cancer treatment.[125] By 2016, the majority of 45 US NCI-designated cancer centers provided integrative medicine information to patients on their websites, including acupuncture/massage (73% each), meditation/yoga (69% each), nutrition consultations (91%), dietary supplements (84%), and herbs (67%), and most also offered these services.[126] Building on 20 years of clinical research, including data from high-quality randomized controlled trials (RCTs), both the SIO and the American Society of Clinical Oncology (ASCO), a leading oncology organization, recommend integrative medicine for supportive care of various disease-related and treatment-related symptoms.[127-129] Furthermore, guidelines from the National Comprehensive Cancer Network (NCCN) include acupuncture, massage, meditation, yoga, music therapy, exercise, and nutrition among their recommendations for alleviating common symptoms, such as fatigue, pain, nausea, hot flashes, and sleep disorders (Table 1).[130-136] A brief summary of the evidence of selected integrative medicine approaches follows.

Lifestyle Management

Promotion of healthy lifestyles is a key component of integrative oncology and a critical component of cancer prevention. Smoking cessation has been a crucial strategy for cancer prevention on a population level.[137-139] Studies that have examined poor diet, insufficient physical activity, and being overweight or obese have been largely observational. However, consistent associations have been demonstrated over time, and it is now well accepted that up to 50% of cancers could be prevented by modifying common lifestyle factors.[140] Reducing alcohol consumption will lower the risk of more than 12 different cancers because alcohol has long been known as a carcinogen.[141] Strategies such as safe sex and vaccinations can decrease the risk of virally mediated cancers caused by HPV, and healthy sun protection practices can reduce the risk of melanoma or other skin cancers.[142]

The same lifestyle risk factors of poor diet, insufficient physical activity, and excess weight are also associated with disease recurrence and mortality after cancer diagnosis for several cancer types.[143] Overweight and obesity are associated with more than 12 types of cancer and account for approximately 5% to 8% of cancer cases.[144-148] Furthermore, they are linked to an increased mortality risk for several common forms of cancer, such as breast, colorectal, and prostate cancers.[149-151] One disturbing observation in LMICs is that the modulation of key biologic pathways associated with

TABLE 1. National Comprehensive Cancer Network Clinical Practice Guidelines for the Use of Integrative Medicine for Supportive Cancer Care[a]

SYMPTOMS	ACUPUNCTURE	MASSAGE	MEDITATION/MBSR	YOGA	MUSIC THERAPY	EXERCISE	NUTRITION
Adult cancer pain	X	X	X	X		X	
Cancer-related fatigue	X	X	X	X		X	X
Sleep disorders			X	X			
Distress (anxiety/depression)			X	X	X	X	X
Cancer-associated cognitive dysfunction			X	X			
Hot flashes/night sweats	X			X		X	
Sexual dysfunction			X	X			
Nausea/vomiting	X			X	X		
Anorexia						X	X

Abbreviation: MBSR, mindfulness-based stress reduction.
[a]Derived from the National Comprehensive Cancer Network (NCCN) clinical practice guidelines for supportive cancer care (NCCN 2021,[130] Denlinger 2021,[131] Swarm 2021,[132] Berger 2021,[133] Ettinger 2021,[134] Riba 2021,[135] Dans 2021[136]).

metabolic syndrome, such as developing diabetes, and with other cancer risk factors in overweight groups is happening at much lower body weights than in the West.[152,153] Obesity also interferes with physical activity goals and makes people less likely to exercise.

Importantly, however, being overweight, being sedentary, having a poor diet, and other high-risk behaviors are modifiable conditions. In the Look AHEAD Study (ClinicalTrials.gov identifier NCT03952728), which evaluated the impact of a weight loss intervention on cardiovascular events in individuals with type II diabetes, participants who were randomized to the weight loss intervention had a 20% reduction in obesity-related cancers compared with those who were randomized to the control group.[154] Other research has demonstrated that people who eat a plant-centered, high-fiber diet have a lower risk of many cancers and that those with cancer who eat such a diet may respond better to treatment and tend to live longer.[140] In addition, recent studies show that replacing 30 minutes of sedentary time with light or moderate physical activity is associated with an 8% and 31% lower risk of cancer mortality, respectively.[155] Large-scale randomized trials are currently ongoing to evaluate the impact of weight loss, increased physical activity, and dietary modification on disease outcomes in individuals with early stage cancers.[156-160]

The global cancer epidemic cannot be overcome with treatment alone. Although billions of dollars each year are invested in precision-based treatments and early detection, cancer prevention through lifestyle modifications remains the cheapest and most effective method to reduce the incidence of cancer.

Mind and Body Interventions

Mind and body interventions, such as acupuncture, meditation, massage therapy, and yoga, have an increased evidence base for improving symptom management during treatment and survivorship.

Acupuncture

Studies indicate that acupuncture, a TCM practice that stimulates specific points on the body with needles, helps control pain in patients who have cancer.[161-163] A systematic review and meta-analysis found moderate evidence that patients with cancer who received acupuncture and/or acupressure also had a decrease in analgesic use and pain.[122] Specifically for breast cancer survivors receiving aromatase inhibitors, one phase 3 RCT demonstrated that acupuncture was associated with reduced joint pain compared with both sham acupuncture and usual care. For example, approximately 60% of those who received acupuncture had a clinically meaningful reduction in pain compared with 30% response rates in sham or usual care groups.[164] More recently, a large RCT (N = 360) among diverse groups of cancer survivors with chronic musculoskeletal pain also showed that both electroacupuncture and auricular acupuncture reduced pain severity (by 1.9 and 1.6 points on the Brief Pain Inventory, respectively), reduced analgesic use, and improved quality of life compared with usual care.[165] Several clinical trials in breast cancer survivors suggest that acupuncture produces lasting benefits for managing hot flashes with fewer adverse events than gabapentin and vanlafaxine.[166-168] Furthermore, SIO, ASCO, and NCCN clinical practice guidelines have recommended acupuncture among options for the treatment of chemotherapy-induced nausea/vomiting and pain management.[128-130,132,134]

Massage therapy

The application of touch therapy to muscles and connective tissue, known as *massage therapy*, has been studied in chemoinfusion settings, where it has been shown to reduce fatigue, pain, nausea, and anxiety in patients, with demonstrated safety during active treatment.[169,170] It has also been widely used for depression, insomnia, and pain in patients with various cancer types.[171-177] A randomized clinical trial

in patients with advanced cancer experiencing moderate to severe pain (N = 380) found that massage was more effective than simple touch for improving pain and mood immediately (mean difference, 0.90 and 0.61 points, respectively; $P < .001$); however, there was no difference over time.[178] In addition, an early phase, randomized study conducted in breast cancer survivors (N = 66) found that 6 weeks of Swedish massage therapy resulted in a clinically meaningful reduction in cancer-related fatigue (−16.50 points on the Multidimensional Fatigue Inventory, which was the primary outcome) compared with an active control (light touch, −8.06 points) and a wait-list control (+5.88 points).[179] A systematic review and meta-analysis that included 12 high-quality and 4 low-quality RCTs of massage therapy for pain management in cancer populations demonstrated that massage therapy was effective for treating pain compared with no-treatment (standardized mean difference [SMD], −0.20) and active (SMD, −0.55) comparators. Compared with active comparators, massage therapy was also identified as beneficial for treating fatigue (SMD, −1.06) and anxiety (SMD, −1.24).[180] In patients with breast cancer, a specialized treatment known as manual lymphatic drainage massage reduced lymphedema[181] and prevented secondary lymphedema.[182,183] ASCO has endorsed SIO massage guidelines for managing depression and mood disorders, and the NCCN includes massage as a treatment option for pain and fatigue.[128-130,132,133]

Meditation

Mindfulness-based interventions like meditation focus on awareness of sensations and feelings in the present moment without judgment or interruption. Meditation can involve breathing techniques and guided imagery, which encourage a deep state of relaxation of the body and mind. Randomized trials have shown that meditation is effective for reducing anxiety, depression, fear of recurrence, and fatigue in patients who have breast cancer.[184,185] It also improves sleep, quality of life, and psychosocial adjustment in this population.[184,186,187] Mindfulness-based stress reduction—a program developed to bring active awareness into daily activities, relationships, and communications—also demonstrated large effect sizes in stress, depression, and anxiety in a meta-analysis of 9 studies of patients with breast cancer.[188] In addition, in a large RCT among breast cancer survivors (N = 322), mindfulness-based stress reduction improved symptoms of anxiety, reduced fear of recurrence, and improved fatigue; however, the effect sizes were generally small to moderate.[185] In another RCT among 271 breast cancer survivors, compared with supportive-expressive group therapy and a one-day stress management control group, the mindfulness-based cancer recovery group significantly reduced stress symptoms and improved quality of life and social support.[189] Recently, an RCT among 247 young breast cancer survivors (aged 50 years and younger) found that both mindful awareness practices and survivorship education significantly improved depressive symptoms from preintervention to postintervention relative to wait-list controls; however, the improvement was persistent only for mindful awareness practices, and not for survivorship education, at the 6-month follow-up. Furthermore, mindful awareness practices, but not survivorship education, improved fatigue, insomnia, and vasomotor symptoms.[190] Given the growing evidence, both the SIO and ASCO suggest meditation for improving quality of life and reducing anxiety, stress, and depression during and after treatment; and the NCCN lists meditation for pain, fatigue, and distress management.[127-130,132,133,135]

Yoga

An ancient Indian practice, yoga involves the incorporation of postures, meditation, and breathing exercises to achieve greater physical and emotional health. Studies show that this modality helps promote stress reduction, a sense of well-being, restful sleep, and better quality of life in patients with recently diagnosed cancer as well as survivors.[191-199] It also improves social functioning and psychological symptoms and reduces stress and fatigue.[189,200-202] In an RCT among 200 breast cancer survivors, compared with usual care, those assigned to 12 weeks of twice-weekly yoga classes experienced a reduction in fatigue (5.4 vs 12.4 on the Multidimensional Fatigue Symptom Inventory–Short Form) and increased vitality (58.1 vs 51.6 on the energy/fatigue [vitality] scale from the Medical Outcomes Study 36-item Short-Form Health Survey) at the 3-month posttreatment visit.[203] In another large, multicenter RCT involving 410 cancer survivors, participants in the yoga group reported overall better sleep quality than those in the usual care group.[197] The effect size in the yoga group for improving sleep quality was large and clinically meaningful. In addition, the yoga group reduced sleep medication use by 21% per week during the intervention period.[197] SIO and ASCO guidelines indicate that yoga may be considered to manage depression, anxiety, and mood disturbances and to decrease stress and enhance overall quality of life.[128,129] According to NCCN guidelines, yoga may be considered for improving some survivorship issues, such as distress, cognitive functioning, menopausal symptoms, and pain.[131] Yoga is also listed in the NCCN guidelines for addressing cancer-related fatigue and anticipatory nausea/vomiting.[133,134]

Natural Products

Herbal medicines are deeply rooted in many cultures and traditions. Interest is also high among patients with cancer, who take herbal supplements more frequently than the general population, with one-third of cancer survivors reporting the use of herbs.[204-206] However, the quality of herbal products

and the lack of robust clinical evidence currently hinders their integration into cancer care practices. The herbal industry faces challenges in consistently formulating products that deliver the promised physiologic effects.[207] Studies show that the content of standardized marker compounds thought to be responsible for medicinal benefits can range from high to nonexistent, even within different batches of the same product.[208] The accessibility of marker compounds or reference standards is another critical issue that hinders the proper biologic and chemical assessment of herbs.[209] Furthermore, the classification of herbal products as *dietary supplements* in some HICs (for example, in the United States under the Dietary Supplement Health and Education Act) has facilitated their haphazard use and does not help address questions on efficacy and safety. Finally, lack of patent protection does not provide any financial incentives for industry to conduct clinical trials. Therefore, despite strong patient interest,[210] conducting high-quality and adequately powered clinical trials of herbal products with limited resources remains difficult, if not impossible.

Research has shown potential herb-drug interactions with chemotherapy, immunosuppressant agents, anticoagulants, and hormonal therapies, all of which are used in cancer care.[211] To educate both physicians and patients on the benefits and risks of supplements, the Integrative Medicine Service at Memorial Sloan Kettering Cancer Center developed and maintains *About Herbs* (aboutherbs.com).[212] This comprehensive database provides reliable, evidence-based information on herbs, vitamins, minerals, and other dietary supplements, including uses, adverse effects, and herb-drug interactions.[212]

Drug development based on compounds derived from natural products has yielded 4 classes of agents available on the market: vinca alkaloids (vinblastine, vincristine, and vindesine), epipodophyllotoxins (etoposide and teniposide), taxanes (paclitaxel and docetaxel), and camptothecin derivatives (camptotecin and irinotecan).[213] However, rigorous research investigating herbal medicine as part of a whole system, as it is used in TCIM for specific cancer outcomes, remains very limited.[123] On the basis of reviewing the available evidence for women undergoing treatment for breast cancer, SIO clinical guidelines consider American ginseng for fatigue, ginger for nausea, and mistletoe for quality of life while recommending against guarana for fatigue, glutamine for nausea/vomiting, and acetyle-L-carnitine for chemotherapy-induced peripheral neuropathy because of lack of efficacy.[127]

Challenges and Opportunities in Research

To guide evidence-informed and patient-centered care, more research on the potential safety, effectiveness, and appropriate integration of TCIM interventions is needed. The design and implementation of integrative oncology studies present several challenges, including the standardization of interventions and the selection of appropriate control conditions. Contrary to clinical trials of pharmaceuticals, it is difficult to blind patients to group assignment when testing the impact of an integrative therapy. This is especially critical in symptom-intervention research, when the outcomes of interest are subjective and prone to the placebo effect. Acupuncture is an example of an integrative therapy intervention with a well established control condition; however, no consensus exists about which sham method is most appropriate for research.[214,215] For integrative interventions with no existing sham, such as yoga or meditation, the selection of a control condition can be more complex. Study strategies range from a comparison of the intervention versus usual care or the development of attention or active control for contact-time and group effect as well as blinding participants to the intent of the trial (comparing 2 behavioral programs when the intent is to test the benefit of yoga, per se).

Intervention standardization is also a challenge for integrative oncology research. By definition, integrative therapies are personalized to the individual. However, research typically involves a standardized intervention that can be tested across a diverse population so that the findings can be easily replicated, generalized to large patient groups, and ultimately implemented in a standardized manner.[123] However, such issues do not just affect the field of integrative oncology. For example, in the field of psychology, cognitive-behavioral interventions follow a specific manual that allows for structured delivery of particular intervention components based on responses of the individual. Careful development and pilot testing of treatments are needed before launching clinical trials to refine intervention components, optimize dose, frequency of delivery, and factors for individualization. Novel research methodologies and whole systems approaches are needed to explore individualization of TCIM interventions. In addition, careful training of interventionists and frequent fidelity testing are needed to ensure treatment fidelity.

Because many TCIM practices exist in the culture and health systems of LMICs, real-world research using surveys, electronic medical records, and qualitative and mixed-methods research can help uncover disparities in utilization, expectations and motivations of patients with cancer, and barriers related to both TCIM and conventional medicine use, all of which can help design more cohesive and integrated care approaches. Systemic documentation and evaluation of existing TCIM integration models with conventional medicine in specific cultural contexts can further identify barriers and facilitators that can contribute to sustainable and effective clinical programs.

In addition, appropriate retrospective and prospective cohort studies incorporating validated patient-reported outcomes and relevant clinical outcomes can inform how these treatments impact populations in real-world settings and potentially generate more specific testable hypotheses that can then be confirmed in clinical trials.[216] Consistent with patient-centered outcomes research, engaging patients and relevant clinical and policy stakeholders in defining research questions and facilitating dissemination efforts are key to generating evidence that actually matters to patients in their specific cultural and societal settings.[217,218]

Global Integrative Oncology Partnerships to Increase the Evidence Base

A global commitment to research is critical to advance evidence-informed integrative oncology programs.[219] Utilization of TCIM in cancer care is highly prevalent in LMICs, but those countries struggle to conduct research in this area.[220] Collaboration and professional associations are key to advancing research, but most have been concentrated in HICs.[220,221] National-level alliances, and bilateral and multinational collaborative endeavors seek to increase research collaborations and training to increase the evidence base of TCIM for cancer prevention, treatment, and symptom management.

National Cancer Institute

The NCI's OCCAM leads initiatives focused on LMICs, facilitating training opportunities, conferences, technical support, and funding for developing and testing novel therapies and applications. OCCAM has focused on medicinal herbs and interventions of traditional Chinese and Indian systems of medicine.[222,223] Partnerships with various Chinese institutions have enabled the investigation of herbal formulations, their components, applications, and effects as part of cancer care. Mechanisms of action are being explored individually or combined with conventional cancer treatments. OCCAM and the Cancer Institute of the China Academy of Chinese Medical Sciences also joined together to hold 2 international conferences in Beijing, China, on cancer research and Chinese medicine. Thereafter, a development committee for the International Consortium for Chinese Medicine and Cancer was established to promote and advance Chinese medicine and cancer research, clinical trials, and symptom management.[223] OCCAM recently signed a Letter of Intent with the Central Council for Research in Ayurvedic Sciences (Ministry of AYUSH, Government of India) aimed to enhance cancer research, research training, and scientific exchanges on the Ayurvedic sciences between US and Indian scientists. The partnership will explore ways of enhancing dialogue and cooperation between scientists and practitioners from both countries.

International Collaborations With Other US-Based Organizations

Large cancer centers around the United States are also collaborating with international partners to advance the field of integrative oncology. Memorial Sloan Kettering Cancer Center's Herbal Education and Research in Oncology program focuses on synthesizing the evidence base of TCM herbs to inform clinical research, education, and practice.[123] The initiative promotes bidirectional learning with Chinese experts to share their knowledge and experience in incorporating TCM approaches in cancer care while the US team trains Chinese physician-scientists on literature review, data analysis, protocol design, and scientific writing in China.[224-228] The University of Texas MD Anderson Cancer Center and its sister institutions have facilitated the documentation of TCIM use in patients with cancer in South America.[62] The MD Anderson team also has collaborations with herbal companies in China and research teams in India. Moreover, these partnerships, along with other mechanisms for promoting research collaborations and training (such as the Brazilian Academic Consortium for Integrative Health[229] or the TCIM Americas Network[230]), could catalyze the expansion of integrative oncology research in LMICs. To highlight the ongoing challenges and opportunities within the field, the SIO led an effort to publish a special *Journal of National Cancer Institute Monograph* titled *Advancing the global impact of integrative oncology*.[231] The SIO also established a global task force to attract and engage international members, expanding to over 600 members representing more than 40 countries across 5 continents.

Specific Recommendations for Advancing the Global Impact of Integrative Oncology

The *Trans–NCI-NIH Conference on International Perspectives on Integrative Medicine for Cancer Prevention and Cancer Patient Management* stimulated rich dialogue about how best to promote the integration of TCIM into conventional cancer care and related research. We identified 3 thematic priorities (Fig. 3): 1) educating and integrating TCIM providers into the cancer control work force to promote risk reduction (ie, reducing initiation of tobacco use and increasing access to tobacco cessation interventions, prevention/treatment of infections such as HIV and HPV) and to promote culturally salient, healthy life styles (diet, physical activities, and overweight/obesity prevention); 2) developing and testing TCIM interventions to address cancer symptoms or treatment-related adverse effects (eg, pain, insomnia, fatigue, psychological distress); and 3) disseminating and implementing evidence-based TCIM interventions as part of comprehensive palliative and survivorship care so patients from all cultures can live with or beyond cancer with

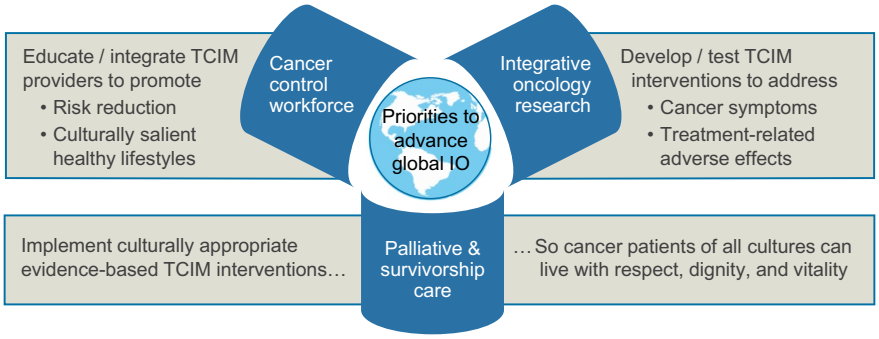

FIGURE 3. Priorities for Global Integrative Oncology (IO). TCIM indicates Traditional, Complementary, and Integrative Medicine.

respect, dignity, and vitality. The long-term goal of integrative oncology is to empower each individual to become an active participant in their health, from prevention and treatment to survivorship and end of life, using high-quality, safe, and effective therapies from both TCIM and conventional medicine in a cohesive and coordinated manner. A concerted global effort as well as changes in perspective and ways of working are needed in the areas of policy, research, clinical practice, and education to achieve these outcomes. Specific recommendations are listed in Table 2.[7]

Policy

Integrative oncology can make a significant contribution to the goal of universal health care by being included in the provision of essential health services. Programs must have support from local institutional leadership and health professionals and must be culturally sensitive to meet the unique needs of their patient population. The WHO is committed to strengthening the contribution of TCIM to universal health care worldwide. Countries integrating TCIM with conventional medicine need to examine not only the differences between the 2 systems but also areas in which they converge to help tackle unique 21st century health challenges. Those with pluralistic health systems, such as South Korea, India, and China, have a natural advantage because they offer a range of health care options.[232,233] Specific societal context has a major influence on the way each system addresses the needs of patients with cancer along the care continuum. Critically evaluating the strengths and weaknesses of each system in specific contexts will allow for more effective collaborations and efficient utilization of resources.

Health Care Disparities

Growing cancer burden and health disparities in cancer care in LMICs require effective and sustainable solutions. Challenges include geographic barriers to receiving care, lack of trained medical professionals, late-stage cancer diagnosis, disease stigma, and treatment affordability.[2] In these countries or regions, TCIM practitioners are often more accessible and affordable than allopathic services, they are often the first point of contact, are more likely to speak the same language, and are trusted by patients, providing an imperative for integration of the 2 approaches.[6] Such integration, facilitated by the WHO's global frameworks, can help address existing health disparities in cancer care in low-resource regions and ensure that treatments are evidence-informed and safe.

TABLE 2. Panel Recommendations to Advance Global Integrative Oncology

FOLLOWING THE 2020 TRANS–NATIONAL CANCER INSTITUTE–NATIONAL INSTITUTES OF HEALTH CONFERENCE ON INTERNATIONAL PERSPECTIVES ON INTEGRATIVE MEDICINE FOR CANCER PREVENTION AND CANCER PATIENT MANAGEMENT, WE RECOMMEND:
• Organization of a working group to address issues surrounding integrative oncology growth worldwide, including strengthening research and training capacity in LMICs
• WHO works with individual member nations to:
○ Develop technical reports on the current state of TCIM in cancer care delivery
○ Propose solutions to foster integration of care for better cancer prevention and outcomes
• TCIM practices be integrated into mainstream health systems per WHO recommendations (WHO 2013[7]) with focused efforts on:
○ Cancer prevention
○ Early detection
○ Survivorship and palliative care
• LMICs provide affordable and equitable access to safe and effective TCIM services for patients affected by cancer
• Rigorous preclinical, translational, clinical, and health services research:
○ Spans the cancer continuum
○ Aims at forming a robust TCIM evidence base
○ Helps reduce cancer burden and health care disparity in LMICs
• Government funding entities assist in the advancement of integrative oncology by:
○ Supporting research training and mentoring
○ Incentivizing research collaborations
• Interprofessional education be fostered so TCIM and conventional medical professionals can work together to care for people affected by cancer
• Evidence-informed, culturally appropriate, and resource-aware clinical guidelines be developed and adopted to improve quality of integrative oncology care

Abbreviations: LMICs, low- and middle-income countries; TCIM, traditional, complementary, and integrative medicine; WHO, World Health Organization.

Cancer Care Delivery

Important areas for the use of TCIM services in LMICs are primary prevention, early detection and screening, public education and outreach, improved accessibility, and promotion of societal acceptance of evidence-based screening, prevention, and conventional cancer treatment and follow-up. Because many TCIM treatments have a rich cultural basis and address the physical, psychological, and spiritual well-being of the individual, they can potentially play a major role in improving cancer-related symptom management, quality of life, mental health, and palliative and survivorship care. Despite extensive historical use, many TCIM interventions have poorly understood mechanisms and lack biologic plausibility as tumor-directed treatments. Therefore, we should guide against the use of TCIM for tumor-directed indications unless they are supported by evidence. The use of TCIM in cancer care must be supported with appropriate synthesis and implementation of policies and must be part of public health programs rolled out by health care systems. It requires concentrated global efforts and partnerships, knowledge sharing, and advocacy to overcome worldview-based biases.

Therefore, it is also critical to re-examine the health financing systems in LMICs. The Declaration of Astana, adopted at the Global Conference on Primary Health Care in October 2018, made clear that the success of primary health care will be driven by applying scientific as well as traditional knowledge and extending access to a range of health care services, which include TCIM.

Research

Rigorous research cannot be performed without an adequate workforce, funding support, and coordinated procedures. The NCI and NIH currently have several funding opportunities that can be applicable to research training or international collaborations in the area of TCIM in LMICs (see Table 3). Despite economic challenges, other countries and regions should also invest in research training and high-quality research and should incentivize collaboration between TCIM practitioners and conventional medical researchers. Agreement on approaches to mapping integrative oncology services provisions at cancer centers and patient-reported outcome measures, as well as a robust approach to recognizing intervention safety and potential interactions, are needed to move forward.[221,234] Standardized platforms for patient-reported outcome assessment selection, delivery, and data collection and interpretation across centers can help facilitate cross-cultural and cross-institutional research efforts.[216] International collaborations for sustained research training and mentoring are important to increase the capacity for conducting high-quality global integrative oncology research.

Education

Addressing gaps in professional training will help support the goal of safe and effective delivery of integrative oncology care. Conventional medical practitioners need to receive more robust education on TCIM and must draw from growing evidence-informed research so they can safely and effectively incorporate these practices into clinical settings to improve cancer outcomes. Similarly, TCIM practitioners can be educated and integrated into routine cancer care settings to more effectively collaborate with the conventional cancer care workforce.[6] It is essential that they receive training in areas such as basic cancer prevention and oncology knowledge, which, in turn, can help them prevent delayed diagnoses, administer some treatments, and work together with conventional medical practitioners. Similar to the HIV/AIDS programs in Africa, TCIM practitioners could help maintain the quality of health care programs and adherence to care.[235] Another example is that, in China, specialized TCM physicians receive additional training in medical oncology or radiation oncology; therefore, they can provide conventional anticancer treatment for those populations that seek out TCM treatment options because of trust, stigma, and preference. Interprofessional organizations like the SIO can play a key role in increasing international representation and engagement of TCIM researchers and practitioners from LMICs.

Clinical Practice Guidelines

To ensure that patients with cancer from around the globe have access to high-quality cancer care, the unique resource limitations and challenges faced by LMICs must be acknowledged. Defining evidence-informed, culturally sensitive, and resource-aware clinical guidelines that help inform careful integration of TCIM into conventional cancer care is key. For example, the SIO and ASCO have established clinical guidelines for integrative oncology.[129] Building on this work, the addition of appropriate cultural context can help LMICs adopt and use these guidelines. Furthermore, in countries with specific TCIM disciplines, such as Ayurveda in India and TCM in China, collaboration between TCIM and conventional medicine societies to establish joint guidelines may help standardize practices and increase the quality of care delivery.

Potential Obstacles and Setbacks

It important to acknowledge that the framework of integrative oncology to systematically bring together TCIM and conventional cancer control and treatment effort can feel aspirational, with challenges and obstacles. Political, economic, cultural, and social norms and beliefs can create obstacles for TCIM and conventional health care providers to collaborate. Some TCIM providers may inaccurately claim adherence to integrative oncology principles as a marketing strategy to promote nonevidence-informed alternative cancer treatment for economic gain. The process of generating research

TABLE 3. Participation and Funding Opportunities for International Traditional, Complementary, and Integrative Medicine in Low- and Middle-Income Countries (TCIM-LMICs) Research Training and Collaboration

FUNDING OPPORTUNITIES	
• NCI Research Funding Announcement (RFA): Strengthening Institutional Capacity to Conduct Global Cancer Research in Low- and Middle-Income Countries, coordinated by the Center for Global Health (CGH) ○ Integrative oncology is an included topic in this RFA	https://grants.nih.gov/grants/guide/rfa-files/RFA-CA-20-031.html
• NCI-NIH CGH funding for global research and training: Provides links to international cancer research/cancer control funding opportunities	https://www.cancer.gov/about-nci/organization/cgh/research-training#current-funding-opportunities
• CGH Short-Term Scientist Exchange Program (STSEP): Promotes collaborative research between NCI and non-US cancer researchers	https://www.cancer.gov/about-nci/organization/cgh/research-training/stsep
• Cancer Research Training Travel Awards for LMIC investigators: Offered intermittently by CRUD-Global, or via NCI-CGH	https://www.crdfglobal.org/funding-opportunities/ncis-cancer-research-training-travel-awards-lmic-investigators
• NIH Fogarty International Center (FIC) Global Health Program for Fellows and Scholars ○ Launching Future Leaders in Global Health (LAUNCH) research training program (RFA-TW-21-004)	https://www.fic.nih.gov/Programs/Pages/scholars-fellows-global-health.aspx https://grants.nih.gov/grants/guide/rfa-files/rfa-tw-21-004.html
PROFESSIONAL EDUCATION FOR LMIC CLINICIANS AND RESEARCHERS	
• IARC postdoctoral fellowships program ○ Contributes to human resources development for cancer research/cancer control worldwide by training early career scientists	https://training.iarc.fr/cards_page/postdoctoral-fellowships/
• Society for Integrative Oncology (SIO)	https://integrativeonc.org/
○ A multidisciplinary global community of oncologists, nurses, psychologists, social workers, nutritionists, complementary therapy practitioners, naturopathic doctors, herbalists, acupuncturists, massage therapists, other health care practitioners, administrators, and patient advocates ○ SIO 2021 International Conference, September 24-26: The Science of Living Well With Cancer	#integrativeonc21
• American Society of Clinical Oncology (ASCO)	https://www.asco.org/about-asco/about-asco-association
○ Provides an array of opportunities for professional development including international programs	https://www.asco.org/international-programs
○ Year-round workshops and scientific sessions with participants worldwide	#ASCO21
○ 2021 ASCO Annual Meeting, June 4-8	2021 Annual Meeting abstracts
• National Comprehensive Cancer Network (NCCN)	https://www.nccn.org/global/what-we-do/harmonized-guidelines
○ NCCN is expanding globally via clinical guideline adaptations and translations, NCCN Harmonized Guidelines™ to utilize regional resources, region-specific coalitions, a Global Policy Webinar series, and other initiatives to advance patient-centered cancer care worldwide	https://www.nccn.org/global/what-we-do/international-adaptations-and-translations https://www.nccn.org/global/opportunities https://www.nccn.org/global/global-events

Abbreviations: IARC, International Agency for Research on Cancer; NCI, National Cancer Institute; NIH, National Institutes of Health.

evidence is both expensive and long, which LMICs with limited resources may not be able to support. Finally, each country or region has a unique political, economic, cultural, and social infrastructure, and it is unlikely that one size can fit all; therefore, the process of integration will likely be specific to its local context and iterative based on progress in both TCIM and conventional oncology approaches.

Conclusion

To address the global challenge of continued increases in cancer incidence, particularly in LMICs, a timely and unified effort is required. Patients with cancer in LMICs face challenges because of limited access to primary prevention strategies, delayed diagnosis because of poor access to screening and gaps in timely referral of symptomatic patients for conventional diagnostic testing, limited treatment options, and very underdeveloped or nonexistent palliative or survivorship care. Many patients with cancer turn to TCIM to address myriad unmet physical, emotional, and spiritual needs. Integrative oncology provides a clear definition and systematic approach to bring TCIM and conventional cancer care together and presents the opportunity to make care more affordable, accessible, and equitable for patients with cancer worldwide, and particularly in LMICs. By developing rigorous research, robust education and research training, high-quality clinical care, and inclusive policies, integrative oncology can be part of the solution to address the current and future global challenges of cancer. ■

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