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Palliative and Supportive Care (J Hardy, Section Editor)

Integrating Palliative Care into Oncology Care Worldwide: The Right Care in the Right Place at the Right Time

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Opinion statement

While the benefits of early palliative care are indisputable, most of the current evidence has emerged from resource-rich settings in urban areas of high-income countries, with an emphasis on solid tumors in outpatient settings; this model of palliative care integration is not currently scalable internationally. A shortage of specialist palliative care clinicians means that in order to meet the needs of all patients who require support at any point along their advanced cancer trajectory, palliative care must also be provided by family physicians and oncology clinicians who require training and mentorship. Models of care that facilitate the timely provision of seamless palliative care across all settings (inpatient, outpatient, and home-based care), with clear communication between clinicians, are crucial to the provision of patient-centred palliative care. The unique needs of patients with hematological malignancies must be further explored and existing models of palliative care provision modified to meet these needs. Finally, care must be provided in an equitable and culturally sensitive manner, recognizing the challenges associated with the delivery of high-quality palliative care to both patients in high-income countries who live in rural areas, as well as to those in low- and middle-income countries. A one-size-fits-all model will not suffice, and there is an urgent need to develop innovative context-specific models of palliative care integration worldwide, in order to provide the right care, in the right place, and at the right time.

Introduction

Palliative care is defined as an approach that improves the quality of life of patients and their families facing problems associated with life-threatening illness through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial, and spiritual [1]. The domains covered by palliative care include not only physical and psychological symptom control, but also other aspects of care, including social and family supports, financial and practical considerations, and spiritual or religious preferences, as well as goals of care and advance care planning.

Compelling evidence from multiple randomized controlled trials (RCTs) and meta-analyses has demonstrated that early, specialist palliative care improves quality of life and satisfaction with care in patients with advanced solid tumors and hematological malignancies [2••, 3–5]. As a result, international cancer societies recommend integrating palliative care early in the management of patients with advanced cancer [6, 7]. However, most evidence in support of early palliative care originates from resource-rich settings with comprehensive interdisciplinary teams, and from trials conducted in patients with solid tumors attending specialist cancer centres [8–14]. Although the benefits of early palliative care have been demonstrated clearly in these high-resource settings, the results may not be generalizable to settings with limited resources. Moreover, there remain considerable global inequities in access to palliative care based on geography (high-income versus low- and middle-income countries; urban versus rural settings) and type of malignancy (solid tumor versus hematological malignancy). Indeed, it is estimated that up to two-thirds of the world's population currently do not have access to palliative care supports or medications such as opioids for symptom relief [15].

Here, we review recent evidence regarding palliative care provision throughout the course of a cancer illness. We argue that in order to ensure that patients worldwide have access to palliative care, all available resources will need to be utilized, including primary care clinicians as well as specialists, practicing in home, inpatient and outpatient settings, and providing care in rural areas in addition to urban centres. This is summarized in Table 1, which shows the timing and nature of palliative care according to the place of care and level of care provided, based on available evidence. While our premise is that for any given setting, the aim of palliative care should be to provide the right care at the right place at the right time, models of palliative care will need to be flexible and scalable, depending on the health care system and the resources available.

The right care: primary, secondary, and tertiary palliative care

Primary palliative care

Primary palliative care involves integration of the fundamental aspects of palliative care (basic symptom management and advance care planning) into the primary care delivered by non-specialist clinicians [16], and may be provided in inpatient, outpatient and home settings by physicians, nurses, and other

Table 1. Timing and nature of palliative care according to place of care and level of care provided

Level of care	Place of palliative care			
	Outpatient	**Inpatient oncology wards**	**Palliative care unit or hospice**	**Home**
Primary (family physicians, general practitioners)	All patients with cancer; basic palliative care with support by palliative care specialists	Rural and community settings; with support by palliative care specialists	Rural settings; with support by palliative care specialists	Ideally all patients with cancer who have difficulty with mobilization, but most common in rural settings; best provided by primary care teams with support from specialists
Secondary (oncologists)	All patients with cancer; basic palliative care with support by palliative care specialists	Urban and rural settings; with support by palliative care specialists	–	Rarely provided
Tertiary (palliative care physicians)	Evidence for patients with most solid tumors for consultation upon diagnosis of advanced cancer or with prognosis 6–24 months; feasibility demonstrated for targeted model based on symptom control	Evidence for routine consultation early upon admission to hospital for patients with solid tumors and aggressive hematological malignancies	Interdisciplinary care for patients and their families in a specialized setting; acute palliative care units provide short admissions for symptom management, while community units and hospices provide end-of-life care	Ideally support primary home palliative care providers, although there is also emerging evidence for specialized home palliative care teams

interdisciplinary health care professionals. Given the shortage of specialist palliative care clinicians internationally, along with the increasing incidence of cancer in an aging population and the prolonged illness trajectory now typical of most cancers [17, 18], upscaling primary palliative care is crucial [17, 18, 19••].

Compared with specialist palliative care, strong evidence in support of primary palliative care is lacking. A recent meta-analysis comparing primary and specialist palliative care interventions identified a high risk of bias in all included primary palliative care studies [19••]. While primary palliative care may improve quality of life, evidence in support of its impact on symptom burden and survival is limited [20]. Barriers to the delivery of high-quality primary palliative care include poor communication between oncology teams and primary care providers, leading to lack of understanding around illness trajectories, especially at the end-of-life; time constraints within primary care; lack of reimbursement for the delivery of primary palliative care which often involves home visits and out-of-hours support of patients and lack of training in primary palliative care competencies [21]. In the outpatient oncology setting, many patients lose touch with their primary care providers after entering the cancer system. Travel time to the office, a positive perception of care, and a 24-h support service have been associated with outpatients with cancer seeing their family physician for palliative care [22•].

In order to improve primary palliative care delivery, core elements of palliative care may need to be extrapolated from specialist models and integrated into the educational curricula of all primary healthcare providers. Models of care that support mentorship or supervision of primary palliative care providers by specialist clinicians should be considered. One existing model of a primary palliative care educational initiative is Pallium, in Canada [23]. This not-for-profit organization is committed to expanding primary palliative care capacity nationally through its accredited "Learning Essential Approaches to Palliative Care" program, and has trained over 28,000 professionals through 1600 courses from 2015 to 2019.

Secondary palliative care

Secondary palliative care refers to care provided by oncology specialists to inpatients and outpatients in hospital settings. As with primary palliative care, secondary palliative care should be interdisciplinary and include care delivered by medical, radiation, and surgical oncologists and hematologists; oncology nurses; radiation therapists; and allied health professionals such as social workers, physical and occupational therapists, and spiritual care providers [21, 24]. Elements that constitute high-quality secondary palliative care have been defined by a partnership between the American Society of Clinical Oncology (ASCO) and the American Association for Hospice and Palliative Medicine [25]. These include end-of-life care; communication and shared decision-making; advance care planning; referral to palliative care or hospice when appropriate; symptom assessment and management; caregiver supports; care coordination and continuity; psychosocial assessment and management; spiritual care; and cultural considerations [25].

ASCO has published a statement endorsing individualized care for patients with advanced cancer that includes specific attention to symptom management and quality of life issues [26]. In order to ensure providers are well equipped to incorporate these elements into their clinical care, mandatory rotations with specialist palliative care teams should form part of oncology training programs across all disciplines; it has been shown that oncologists who have completed these rotations are more likely to appropriately refer patients to palliative care services [27]. Despite this, a recent survey of hematology-oncology fellowship programs in the United States revealed that only 68% of respondents offered such rotations, with lectures and seminars making up the majority of palliative care education in most programs [28].

Beyond education, additional barriers to secondary palliative care delivery include time constraints within busy oncology practices, as well as remuneration models that often favour patient volumes over time spent with individual patients. As an incentive, both the European Society for Medical Oncology (ESMO) and the Multinational Association of Supportive Care in Cancer (MASCC) have highlighted designated centres of integrated oncology and palliative or supportive care, respectively, based on criteria related to educational, clinical and research domains [29, 30].

Tertiary palliative care

Tertiary palliative care refers to the care provided by clinicians with specialist postgraduate training in palliative care, including physicians, nurses, social workers, spiritual care providers, occupational and physical therapists, and pharmacists, among others [31]. Although tertiary palliative care should ideally be widely available, including in inpatient, outpatient and community settings in rural and urban areas, it is disproportionally represented in tertiary comprehensive cancer settings. In addition to providing palliative care to patients with complex needs, these providers should also be available to provide mentorship and clinical support to primary and secondary palliative care providers and to help support capacity-building for these clinicians.

At this time, the strongest evidence around the benefits of palliative care is derived from RCTs and meta-analyses of tertiary palliative care interventions: structured interdisciplinary outpatient palliative care consultations have been shown to improve patient symptom burden, quality of life, mood, and survival, and caregiver satisfaction and quality of life [8–14, 32]. Early referral to specialist palliative care is now endorsed by ASCO, ESMO, and other international cancer organizations, but worldwide shortages of specialist trained clinicians limit the ability to meet the needs of all patients with advanced cancer [33]. Funding to support expansion of tertiary palliative care within cancer centers appears to be limited internationally, even within tertiary centers [34].

The right place: settings of palliative care

Outpatient clinics

The outpatient setting is ideally suited for early tertiary palliative care delivery [35]. In this setting, palliative care is typically offered concurrently with disease-modifying cancer therapies to support attending clinics longitudinally [31]. While these clinics are for patients with a variety of cancer diagnoses, referrals tend to come more often from medical oncologists who specialize in solid tumors than malignant hematologists. Several different clinic models have been described, based on available palliative care resources and oncology structures [32]. The two main models are embedded clinics, where palliative care is provided within an existing oncology clinic, and stand-alone clinics, where the palliative care clinic has its own designated clinic space [36]. Both models were traditionally provided in person, although virtual care has become increasingly common during the COVID-19 pandemic, particularly for patients seen in follow up [37]. This new method of communication could potentially overcome some of the factors that limit in person attendance to stand-alone clinics, particularly distance to the hospital [38]. However, evidence regarding virtual care delivery models is limited [32], and further trials are needed.

Embedded models are ideal for smaller palliative care teams working in centres where oncology clinics are not cancer site specific. The ability to see the oncologist and palliative care provider in the same clinic on the same day, and to pool resources between teams, may be advantageous, but the ability to expand or grow embedded palliative care clinics is often limited [36]. Stand-alone palliative care clinics independent of the oncology clinic are more commonly offered at comprehensive cancer centres or centres with sufficient clinician support [8, 11, 39]. Referrals from oncologists are triaged based on urgency, with prioritization of highly symptomatic patients for same-day visits while those with less urgent concerns are booked into a visit that coincides with a future clinic visit to their oncologist [31]. While stand-alone clinics require upfront funding and independent administrative and other resources, they offer greater potential to customize the clinic space, to grow and expand based on demand, and to incorporate interdisciplinary team members in a more comprehensive way than an embedded model typically allows. Because no trials have compared an embedded versus a stand-alone model, the decision to adopt one over the other is pragmatic, based on factors such as cancer center size, palliative care team composition, clinic space availability, and financial considerations [36].

Inpatient consultation services

Compared with outpatient studies, where RCTs have focused on patient-reported outcomes, much of the research involving care provided by inpatient specialist palliative care consultation services has been retrospective, focusing on administrative outcomes and economic benefits. In a study of five US hospitals with comprehensive palliative care teams, consultations within 2 and 6 days of admission were shown to reduce hospitalization costs by 24% and 14%, respectively [40]. Similar findings were reported in a meta-analysis of economic evaluations of interdisciplinary palliative care consultations for hospitalized patients with advanced illness [41]. Most of these cost savings appear to come from reduced length of stay and reduced intensity of treatment, and tend to be greater for patients with more comorbidities (four or more), compared with two or fewer [42].

Clinical benefits of inpatient specialist palliative care have also been demonstrated [43]. A systematic review of the impact of palliative care consultations for inpatients showed improvements in pain, quality of life, satisfaction with care and advance care planning discussions [44]. In addition, patients seen by inpatient palliative care teams were more likely to receive home care supports after discharge from hospital and less likely to be readmitted to acute care. Although the emergency department is not an ideal location for a first palliative care consultation, it has nevertheless been demonstrated that emergency department-initiated palliative care consultation in advanced cancer improves quality of life [45].

Palliative care at home

For patients whose performance status has declined, those with limited mobility, or older patients who have difficulty going to the hospital or to clinics, in-home palliative care is most practical [31]. A recently published Cochrane review of home-based palliative care demonstrated an increased likelihood of dying at home and an association with improved satisfaction with care; effects on symptom control were unclear from the limited and heterogeneous data [46]. Key elements of home-based palliative care, as identified by patients and caregivers, include the ability to access care 24 h a day, seven days per week, as well as expertise in communication and symptom management [47]. Although home palliative care is ideally provided by primary care providers, logistical issues related to time and traveling to provide home visits, particularly outside regular office hours, represent prominent barriers [48, 49]. In a survey among family doctors and general practitioners, younger primary care physicians were more engageable to provide home palliative care; this was particularly the case if they were provided sufficient remuneration and resources, and if working in a team-based model with access to advice from specialist palliative care colleagues [49].

In recent years, efforts have been made to integrate home-based palliative care earlier into the cancer trajectory [50]. The advantages of early palliative care delivery in the home setting include the ability to focus on information-sharing; psychosocial elements of care; structured and systematic follow up; and future goal setting, whereas late involvement tends to be characterized by crisis-initiated visits and a need to focus on immediate problem-solving. RCTs investigating the feasibility and acceptability of early palliative care offered at home are ongoing [51•].

Palliative care units and residential hospices

Inpatient hospices and palliative care units provide a specialist setting to support patients with advanced cancer and their families [52]. Some palliative care units within comprehensive cancer centers provide acute symptom management, such as access to bloodwork, diagnostic imaging, intravenous antibiotics, and blood transfusions, and are suitable for patients who may require a brief admission to optimize their symptoms with a goal to return home[53, 54]. Others focus more on providing symptomatic relief for patients in the last days, weeks, or short months of life, and for whom remaining at home is not feasible or not aligned with their goals of care. Many hospices and palliative care units have admission criteria that include accepting a "do not resuscitate" order, and have limited abilities to support patients who continue to receive active anticancer therapies [55]. Interdisciplinary care is a key component of the support provided in inpatient hospices or palliative care units, provided by specialized palliative care nurses, physicians, social workers, spiritual care providers, physiotherapists, occupational therapists, music therapists, art therapists, pharmacists, and others.

Inpatient palliative care units within cancer centres may facilitate increased cancer-directed activities and reduced deaths on inpatient oncology units by supporting the timely transfer of patients to a specialized palliative care setting [56]. Palliative care units also have financial benefits by reducing overall direct costs associated with an acute hospital admission [57].

The right time: evidence from trials in solid tumors and hematological malignancies

Most of the evidence demonstrating the benefits of outpatient palliative care interventions comes from trials of patients with solid tumors attending comprehensive cancer centres; less is known about the impact of early palliative care on patients with hematological malignancies (Table 2). This section will summarize the evidence in support of early palliative care for patients with both solid tumors and hematological malignancies, highlighting the differences between the two groups as well as areas where further research may be needed.

Timing of palliative care for patients with solid tumors

Although the right time for palliative care intervention will depend on the setting of care and the resources available, the most compelling evidence has been from RCTs of "early" palliative care. In these trials, "early" was defined either as within 8–12 weeks of diagnosis of advanced cancer [9–11] and/or a clinical prognosis of between 6 and 24 months [8, 12, 14]. All of these trials utilized a specialized palliative care model and in most, the intervention

Table 2. Early palliative care trials for patients with solid tumors and hematologic malignancies

Author/ year	Type of cancer	Timing of intervention	Team delivering specialized palliative care	Delivery method	Primary outcome(s)
Solid tumors					
Bakitas, 2009 [12]	Breast, GI, GU, lung	Prognosis ≤ 1 year and within 8 weeks of diagnosis	APN with PC specialty training	Telehealth	QOL (+), symptom intensity (−), resource utilization (−)
Temel, 2010 [9]	Non-small cell lung	Within 8–12 weeks of diagnosis	Palliative care physician and APN	Outpatient	TOI at 12 weeks (+)
Zimmermann, 2014 [8]	Breast, GI, GU, Gyn, lung	Prognosis 6–24 months	Specialized PC physician and nurse	Outpatient	QOL at 3 months (−) [QOL at 4 months (+)]
Temel, 2017 [10]	Lung, GI	Within 8 weeks of diagnosis	Palliative care physician and APN	Outpatient	QOL at 12 weeks (−) [QOL at 24 weeks (+)]
Maltoni, 2016 [11]	Pancreas	Within 8 weeks of diagnosis	PC physician	Outpatient	QOL at 12±3 weeks (+)
Groenvold, 2017 [86]	Any solid tumor malignancy	Not specified	Multidisciplinary team (doctor, nurse, psychologist, among others	In person, telephone	Change in primary need from QOL questionnaire at 3 and 8 weeks (−)
Vanbutsele, 2018 [14]	Any solid tumor malignancy	Prognosis ≤ 1 year, and within 12 weeks of diagnosis or progression	Specialized PC nurse with PC physician referral if required	Inpatient, outpatient	Global health status/QOL (+) at 12 weeks
Scarpi, 2019 [39]	Gastric	Within 8 weeks of diagnosis	PC physician	Outpatient	QOL at 12 weeks (−)
Franciosi, 2019 [87]	Lung, GI	Within 8 weeks of diagnosis	Oncologist specialized in PC and PC nurse	Inpatient, outpatient	QOL at 12 weeks (−)
Hematologic malignancies					
El-Jawahri, 2016 [3]	Hematologic malignancy receiving allogenic or autologous stem cell transplantation	Within 72 h of hospital admission	PC physician or APN	Inpatient visits at least twice weekly	QOL at 2 weeks (+)
Loggers, 2016 [69]	Acute leukemia, myelodysplastic syndrome, Hodgkin lymphoma	During the 2-week evaluation period immediately before HCT	APN or RN trained in PC	Outpatient	Feasibility study 69% provided consent to participate
Rodin, 2020 [58••]	ALL/AML within one month of admission for induction treatment	Within 1 month of hospital admission	Therapist trained in EASE; Specialized PC physician and nurse triggered by ESAS-AL symptoms	Inpatient and outpatient	Traumatic stress symptoms at 4 weeks (+)
El-Jawahri, 2021 [2••]	High-risk AML receiving intensive chemotherapy	Within 72 h of receiving chemotherapy	PC physician, APN, or physician assistant	Inpatient visits at least twice weekly	QOL at 2 weeks (+)

(+) indicates that outcome was met; (−) indicates that outcome was not met; *APN* Advanced Practice Nurse, *GI* gastro-intestinal, *GU* genito-urinary, *Gyn* gynecological, *QOL* quality of life, *TOI* trial outcome index, *ALL* acute lymphoblastic leukemia, *AML* acute myeloid leukemia, *ESAS-AL* Edmonton Symptom Assessment System-Acute Leukemia version, *EASE* Emotion and Symptom-Focused Engagement, *ED* emergency department, *HCT* hematopoietic cell transplant, *RN* registered nurse, *PC* palliative care was interdisciplinary, utilizing at minimum a palliative care physician and advanced practice nurse. The mode of delivery was generally in the outpatient setting, although some trials also enrolled inpatients [2••, 3, 58••], and one utilized telehealth [12]. Studies have often been limited to patients with lung and/or gastrointestinal cancers, with only three studies with positive results also including other solid tumor malignancies [8, 12, 14]. Overall, these studies demonstrated that early involvement of specialized palliative care resulted in improved quality of life, satisfaction with care and mood, albeit with small effect sizes. These trial results have been corroborated by meta-analyses [5, 59]; in addition, largescale retrospective studies in real-world settings have shown that early palliative care is associated with a lower risk of dying in hospital, an increased possibility of receiving home-based end-of-life care, and reduced healthcare system costs [60••, 61].

The evidence presented above appears to have resulted in earlier referral to palliative care services in cancer centers [62•, 63••], but barriers to early referral remain. These include a lack of trained specialists to provide palliative care and persistent stigma associating palliative care with end-of-life care [64]. Ultimately, systematic screening of all patients with advanced cancer with targeted early referral for patients with particular need may be a more scalable model than uniform early palliative care for all patients with advanced cancer. A secondary analysis of an RCT showed that the benefit of early palliative care was greatest for patients with higher symptom burden [65•], and a recent phase II trial of symptom screening with targeted early specialized palliative care intervention demonstrated the feasibility of this model [66]. However, this model assumes that oncologists and primary care providers will be able to provide basic palliative care, which necessitates better education than is currently provided [27, 48]. As well, a public health strategy is needed to educate and engage policymakers, stakeholders and the public about the relevance and importance of early palliative care [64].

Timing of palliative care for patients with hematologic malignancies

Hematologic malignancies (acute and chronic leukemias, lymphomas, and multiple myeloma) are often considered more heterogenous and unpredictable in terms of disease course and prognosis than solid tumors [67]. Patients with hematological malignancies may often experience high physical symptom burden, as well as increased levels of psychosocial distress [68]. Despite this, referrals to specialized palliative care tend to be later for patients with hematological malignancies compared to solid tumors. As a result, there is a relative paucity of evidence in support of early palliative care for patients with hematological malignancies.

Unlike trials of early palliative care for patients with solid tumors, most RCTs enrolling patients with hematological malignancies have been conducted in the inpatient setting, and timing of intervention for these studies has been based on timing of admission rather than on prognosis. Two trials of palliative care in outpatient [13] or emergency department [45] settings included patients with haematological malignancies in addition to solid tumors, but the percentage of patients with hematologic malignancies for both of these was only approximately 5% and thus the results cannot be extrapolated to hematologic malignancy populations. Other RCTs exclusive to haematologic malignancies have all recruited inpatients shortly after admission for stem cell transplantation [3] or admission for induction or re-induction chemotherapy [2••, 58••], although a nonrandomized pilot study included outpatients awaiting admission for allogeneic or autologous stem cell transplantation [69]. These trials have all demonstrated the feasibility [58••, 69] of early palliative care and its effectiveness for improving quality of life, mood, and post-traumatic stress for patients with aggressive hematological malignancies such as acute leukemia who are awaiting or have received intensive treatment regimens for their disease [2••, 3, 58••, 70].

Thus, the available evidence for patients with hematologic malignancies supports immediate referral to palliative care for patients with aggressive hematologic malignancies such as acute leukemia who are admitted for intensive treatment for their disease, or those awaiting hemopoietic stem cell transplantation. Further trials are necessary in outpatient populations and for patients with bone marrow failure and indolent hematologic malignancies that are not immediately life-threatening, but are nonetheless associated with a high burden of symptoms.

Global equity in palliative care provision: models of palliative care outside of urban settings in high-income countries

Specialist palliative care services tend to be disproportionately located in large urban academic centers and in high-income countries. With more than half of the world's population residing in rural areas (which make up to 80% of most countries' landmasses), there is an urgent need to improve access to palliative care in these areas [71]. In low- and middle-income countries, cancer rates are increasing at an alarming rate: 50% of cancer diagnosed annually are in low- and middle-income countries where they are associated with high rates of morbidity and mortality. Policies and strategies that are tailored to resource-limited settings must be developed to maximize access to palliative care [72], recognizing that the nature, place and time of palliative care will often differ from those in high-income and urban settings.

Trials of palliative care interventions in rural settings

Patients with advanced cancer who live in rural settings have been shown to be less likely to access palliative care services compared to those residing in urban settings [73]. In addition, living further from a palliative care program is associated with a higher likelihood of dying in hospital and higher costs at the end of life [74]. Identified barriers to specialist palliative care provision in rural settings include lack of cohesive services and communication between clinical settings, demand for services that exceeds supplies of specialist teams where available, and educational gaps for both providers and patients alike

[75]. Primary care physicians are important providers of palliative care in rural communities; this includes providing palliative care at home as well as through cohorted inpatient beds designated for palliative care on hospital medical wards [48, 55].

Only a few RCTs of early palliative care have actively sought to include patients from rural settings. The ENABLE II and III trials, which utilized predominantly telehealth interventions delivered by a specialist nurse, recruited participants from three rural-serving cancer centres in the USA, and approximately 60% of participants came from rural communities [12, 13]. *Apoyo con cariño* was a tailored randomized trial that included urban and rural communities in the state of Colorado in the USA aiming to enhance access to palliative care services among the Latino population [76]. Culturally tailored resources and lay navigator home visits were offered as part of the intervention, which demonstrated improved rates of advance care planning documentation, but there were no significant differences in pain, hospice utilization, or aggressiveness of care at the end of life. In addition, a lay navigator program to improve access to palliative care in 12 rural-serving cancer services in the USA demonstrated less aggressive end-of-life care [77].

Several elements of successful palliative care provision for patients with advanced cancer in rural communities have been identified [75–78]. These include developing local partnerships with healthcare, cultural, spiritual, and religious groups to appropriately support the needs of patients within each community, offering telehealth visits to minimize the direct and indirect costs associated with travelling to comprehensive cancer centers, utilizing models of care that foster local expertise with support from academic centres (e.g., virtual case conferences, mentorship programs), and initiatives that incentivize oncologists and palliative care specialists working in rural areas.

Trials of palliative care interventions in low- and middle-income countries

Palliative care is considered a human right based on two principles: the right to health, and the right to be free from cruel, inhuman, or degrading treatment [79]. Based on these principles, several international cancer organizations and societies have advocated for the integration of palliative care services into routine oncology care [6, 7]. In 2018, ASCO published a resource-stratified guideline to provide guidance on the implementation of palliative care in resource-limited settings [80]. The guideline listed seven recommendations, each subclassified based on the setting (basic, limited, or enhanced), intended to be used alongside local documents or policies.

Globally, only half of countries currently include palliative care within their national Noncommunicable diseases (NCDs) policies, and only 68% have dedicated funding for palliative care, with a gap of 43% between high-income (91%) and low-and-middle-income countries (48%) [15]. The level of palliative care development within countries is highly associated with each country's ranking within the World Bank Group, the Human Development Index, and the presence or absence of universal health coverage; and it is classified in 6 groups according to the level of palliative care integration (Table 3). In recent years, trials proposing models to enhance access to early palliative care in resource-limited settings have been published. Here we highlight studies from Latin America, Africa, and India as examples of successfully completed RCTs and public health initiatives from low- and middle-income countries.

An RCT conducted in a tertiary hospital in Mexico found that a structured navigation program led to a significant increase in accessing specialized palliative care services (74% of the patients enrolled in the intervention arm, compared to 24% from the usual care group) [81••]. Additionally, 48% of patients enrolled in the intervention group completed advanced directives compared to none in the usual care group and patients in the intervention group experienced better pain relief. In Ethiopia, an RCT demonstrated that early home-based palliative care delivered by palliative care-trained nurses for patients with newly diagnosed cancer significantly reduced health care costs compared with standard oncology care [82•].

In India, feasibility criteria were not met for a trial of early palliative care in patients with advanced lung cancer in a tertiary care center. Only 48% received follow-up at the palliative care clinic, with the remainder not followed up due to being fatigued, busy receiving chemotherapy, or returning to their hometown; however, quality of life and symptoms tended to improve, especially for pain and anxiety [83]. In another RCT of patients with head and neck cancer in India, there was no difference in quality of life, symptom burden or survival at three months between patients randomized to receive early specialized palliative care and those receiving systemic therapy alone [84•], although the standard care arm received some elements of palliative care and 18% received a palliative care consultation. Elsewhere in India, the feasibility of home-based palliative care delivered by community health workers was successfully demonstrated, although additional training may be needed to improve pain and provide psychosocial supports [85].

Finally, Panama represents a good example of a low- and middle-income country where the successful development of a sustainable national palliative care program has been possible [15]. Through universal health coverage that includes palliative care, and the integration of health networks across all clinical settings, successful milestones have been possible; these include the accreditation of a specialist palliative medicine program and an amendment to the "Controlled Substances Act" to facilitate access to essential palliative care medicines.

Conclusions

Although the scope of palliative care has expanded over the past decade to support early integration alongside cancer care, most evidence in support of this model comes from high-income, resource-rich settings and in patients with solid tumors. This model may not be easily applied in other settings, where challenges related to the patient population, as well as workforce shortages and lack of public policy in support of palliative care, must be acknowledged. Instead, the "best model" will inevitably vary between settings and must be one that allows maximum impact for patients with the greatest needs, starting at the end of life and expanding towards full integration only when

Table 3. **State of palliative care integration worldwide**

Group according to WHPCA	Level of palliative care	No. of countries [region] % of worldwide population
Group 1	No known palliative care activity	24 countries [Africa, America, Eastern Mediterranean, Europe, South-East Asia, Western Pacific] 3.1%
Group 2	Initiative, but no services established	7 countries [Africa, America, Eastern Mediterranean, Europe, Western Pacific] 1.7%
Group 3a	Localized hospice and/or palliative care activities	65 countries [Africa, America, Europe, South-East Asia, Western Pacific] 47.7%
Group 3B	Regional palliative care led by activism	22 countries [Africa, America, Eastern Mediterranean, Europe] 5.7%
Group 4a	Preliminary integration into mainstream service provision	21 countries [Africa, America, Europe, South-East Asia] 27.6%
Group 4b	Advanced integration in the mainstream system	30 countries [Africa, America, Europe, Western Pacific] 14.2%

Source: WHPCA. WHPCA: Worldwide Hospice Palliative Care Alliance [15] the basic needs of dying patients are adequately met. Public health strategies aimed at developing local, sustainable policies integrated into national healthcare plans, as well as comprehensive training programs for healthcare providers across all clinical settings are needed to bridge the current gaps in care across national and international settings, and to ensure that patients can receive the right care, at the right place, and at the right time.

Compliance with Ethical Standards

Conflict of Interest

The authors declare no competing interests.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

References and Recommended Reading

Papers of particular interest, published recently, have been highlighted as:
- • Of importance
- •• Of major importance

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