Curr. Treat. Options in Oncol. (2019) 20: 17
DOI 10.1007/s11864-019-0615-8

Palliative and Supportive Care (MP Davis, Section Editor)

Palliative Cancer Care in the Outpatient Setting: Which Model Works Best?

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Published online: 11 February 2019

This article is part of the Topical Collection on *Palliative and Supportive Care*

Keywords Clinical trial · Interdisciplinary health team · Outcome and process assessment (health care) neoplasms · Ambulatory care · Palliative care

Opinion statement

Multiple randomized controlled trials have underscored the importance of timely referral to palliative care for patients with advanced cancer. Outpatient palliative care can facilitate timely referral and is increasingly available in many cancer centers. The key question is which model of outpatient palliative care is optimal. There are currently many variations for how palliative care is delivered in the outpatient setting, including (1) Interdisciplinary Specialist Palliative Care in Stand-Alone Clinics, (2) Physician-Only Specialist Palliative Care in Stand-Alone Clinics, (3) Nurse-Led Specialist Palliative Care in Stand-Alone Clinics, (4) Nurse-Led Specialist Palliative Care Telephone-Based Interventions, (5) Embedded Specialist Palliative Care with Variable Team Makeup, and (6) Advanced Practice Providers-Based Enhanced Primary Palliative Care. It is important to make a clear distinction among these delivery models of outpatient palliative care because they have different structures, processes, and outcomes, along with unique strengths and limitations. In this review article, we will provide a critical appraisal of the literature on studies investigating these models. At this time, interdisciplinary specialist palliative care in stand-alone clinics remains the gold standard for ambulatory palliative care because this approach has the greatest impact on multiple patient and caregiver outcomes. Although the other models may require fewer resources, they may not be able to provide the same level of comprehensive palliative care as an interdisciplinary team. Further research is needed to evaluate the optimal model of palliative care delivery in different settings.

Introduction

Cancer patients often experience a multitude of supportive care issues throughout their disease trajectory, ranging from physical symptoms, psychological distress, spiritual concerns, information needs, decision making, and end-of-life care [1, 2]. These issues interact with each other, fluctuate in intensity over the course of illness, and contribute to decreased quality of life and increased caregiver burden.

Palliative care is a professional discipline with specialized expertise in the management of these complex supportive care issues [2–4]. The past decade has seen particularly significant growth in outpatient palliative care clinics [5–8], supported by a body of literature demonstrating that timely introduction of palliative care can improve patient and caregiver outcomes and avert crises at the end of life with personalized care planning [9, 10••,11,12]. In contrast to inpatient palliative care and community-based palliative care, outpatient palliative care has access to patients much earlier in the disease continuum [5, 13]. These patients are often receiving cancer treatments and have a good performance status. Longitudinal clinic visits translate into greater opportunities for rapport building, counseling, education, optimization of treatments, and crisis prevention [14••]. The presence of a specialist outpatient palliative care clinic is an indicator of integration [15, 16]. An international consensus project has recently defined a set of 11 major criteria for referral to outpatient palliative care [17, 18].

The key question is which model of outpatient palliative care is optimal. There are currently six variations for how palliative care is delivered in the outpatient setting, including (1) Interdisciplinary Specialist Palliative Care in Stand-Alone Clinics, (2) Physician-Only Specialist Palliative Care in Stand-Alone Clinics, (3) Nurse-Led Specialist Palliative Care in Stand-Alone Clinics, (4) Nurse-Led Specialist Palliative Care Telephone-Based Interventions, (5) Embedded Specialist Palliative Care with Variable Team Makeup, and (6) Advanced Practice Providers-Based Enhanced Primary Palliative Care (Table 1 and Fig. 1). In this review article, we provide a critical appraisal of the literature on studies investigating these outpatient models. We discuss the strengths and limitations of each model and which clinical setting(s) they may be particularly appropriate for. Conceptual models of integration have been discussed previously [19, 20].

Interdisciplinary specialist palliative care in stand-alone clinics

To date, the bulk of the evidence on outpatient palliative care for cancer patients has been on stand-alone clinics run by an interdisciplinary team of palliative care specialists (Fig. 1). An international panel recently defined an interdisciplinary team to consist of physicians, nurses, and/or psychosocial professionals [15]. Although actual team makeup varied considerably, studies in this category included at least two disciplines.

The first randomized study examining stand-alone clinic was conducted by Rabow et al., who prospectively examined the impact of outpatient palliative care in one clinic and compared the outcomes to another clinic without palliative care [21]. This study included 90 patients with cancer, advanced emphysema, or heart failure who had a life expectancy of 1 to 5 years. The palliative care outpatient intervention was provided by a comprehensive care team comprised of three physicians, a social worker, nurse, chaplain, pharmacist, psychologist, art therapist, and volunteer coordinator. Pain control was the primary outcome, which did not differ between groups over the 12-month study period [21]. However, the intervention group reported less dyspnea ($P = 0.01$), lower anxiety ($P = 0.05$), improved sleep ($P = 0.05$), and higher spiritual well-being ($P = 0.007$) [21].

Table 1. Comparison of the structures, processes, and outcomes of six service models of outpatient palliative care

Clinic features	Interdisciplinary specialist PC in stand-alone clinics	Physician-only specialist PC in stand-alone clinics	Nurse-led specialist PC in stand-alone clinics	Nurse-led specialist PC telephone-based interventions	Embedded specialist PC with variable team makeup	Advanced practice provider-based enhanced primary PC
Team makeup	PC physician, nurse, and often allied health professional such as psychologist, chaplain, and social worker	PC physician	PC nurse or APP who may or may not consult an interdisciplinary team	PC nurse or APP who may or may not consult an interdisciplinary team	Variable number of members of PC team	Oncology nurse or APP
Location	Stand-alone	Stand-alone	Stand-alone	Telephone based	Embedded in oncology clinic	Embedded in oncology clinic
Level of PC expertise	+++	++	++	++	++ to +++	+
Comprehensiveness of PC services	+++	+ to ++	+ to ++	+ to ++	+ to +++	+
Resources required	+++	++	+	+	+ to +++	+
Level of evidence	5 RCTs	2 RCTs	2 RCTs	2 RCTs	No RCTs	2 RCTs
Positive outcomes	Multiple	Limited	Mixed	Limited	Quality of life	Favors oncology
Unique strengths	Interdisciplinary nature Most likely to have positive outcomes	Less resources needed	Less resources needed	Telehealth useful for rural access Less resources needed	Promote integration of oncology and PC teams	Convenience for patients
Unique weaknesses	More resources needed	Interdisciplinary team not involved	Interdisciplinary team not often involved	Interdisciplinary team not often involved	Limited space for growth	Limited PC training may not be adequate
Most appropriate settings	Appropriate for most centers, particularly the larger ones	Difficulty hiring other members of PC team	Resource limited settings	Rural settings	Small oncology clinics	Role undefined

APP advanced practice provider, PC palliative care, RCT randomized controlled trial

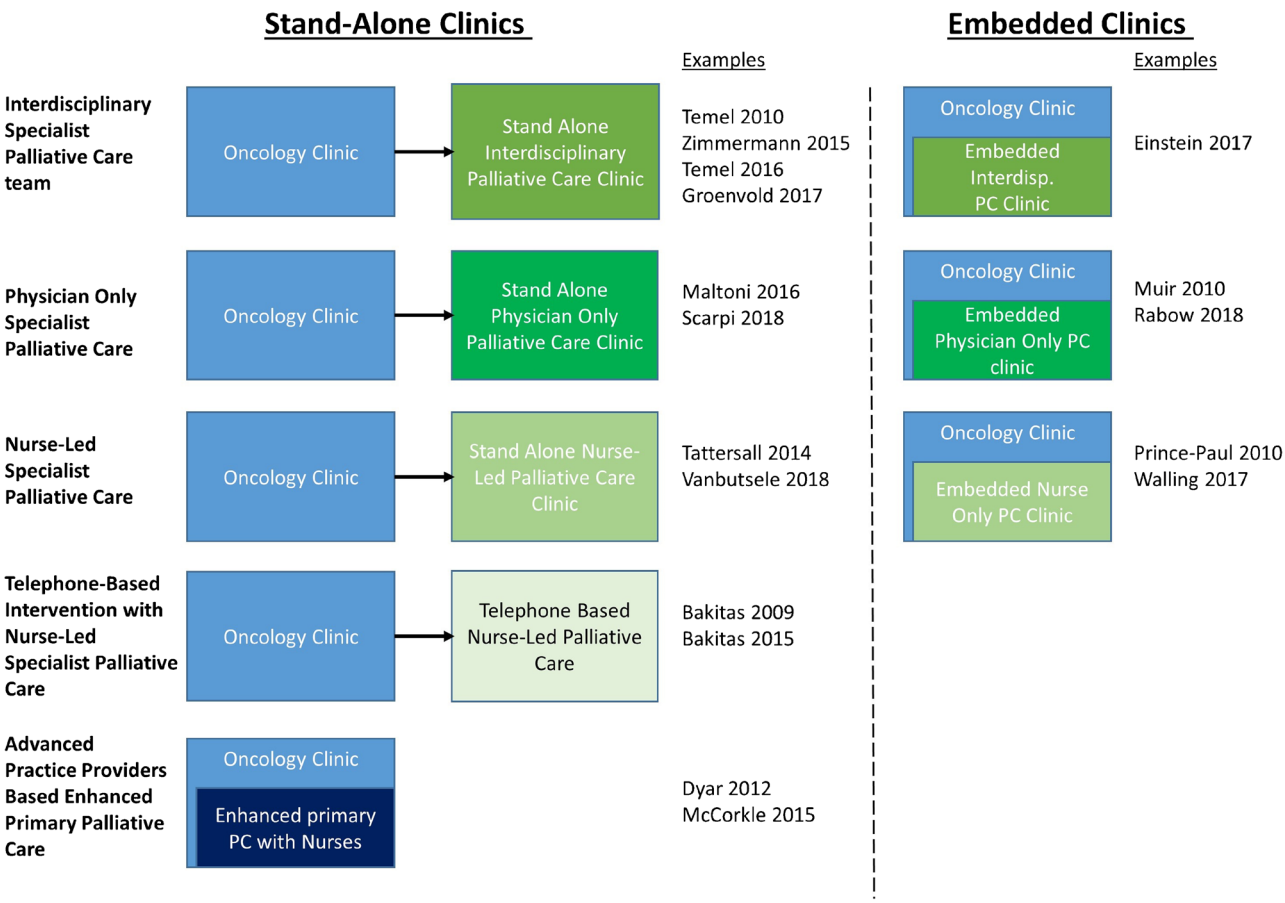

Fig. 1. Service models of palliative care.

Because patients were not randomized at the individual level, there might be some differences between the groups confounding the analysis. This study paved the way for a new generation of stand-alone outpatient clinics.

Temel et al. conducted the landmark clinical trial in which 151 patients with metastatic non-small-cell lung cancer within 8 weeks of cancer diagnosis and performance status of 0 to 2 were randomized to usual oncologic care with or without specialist palliative care [22•]. The intervention consisted of visits with board certified palliative care physicians and advanced practice nurses at least monthly to address symptom management, coping, illness understanding, and decision making [22•]. The palliative care group had significantly better quality of life at 12 weeks (Trial Outcome Index 59 vs. 53, $P = 0.009$), less depressive symptoms (16% vs. 38%, $P = 0.01$), and improved end-of-life care (33% vs. 54%, $P = 0.05$). In post hoc analysis, overall survival was also improved in the palliative care group (11.6 months vs. 8.9 months, $P = 0.02$) [22•]. Further analyses revealed that patients in the palliative care group also had better comprehension of their illness over time [23]. Moreover, better illness understanding was associated with a lower rate of chemotherapy use at the end of life, but only for patients randomized to the palliative care group and not the usual

care group, suggesting an interaction between illness understanding and facilitation of decision making by the palliative care team. This groundbreaking study highlighted the benefits of introducing palliative care early in the disease trajectory and universal referral.

A Canadian study utilized a cluster randomized design to assess the impact of early palliative care, thus allowing for partial blinding of study participants [24•]. This trial enrolled 461 patients from 24 medical oncology clinics. The palliative care intervention consisted of a palliative care physician and nurse in a stand-alone clinic providing monthly follow-up [24•]. Quality of life (Functional Assessment of Chronic Illness Therapy–Spiritual Well-Being Scale [FACIT-Sp]) and symptom burden (Edmonton Symptom Assessment Scale [ESAS]) both improved in the palliative care group and deteriorated in the control group at 3 months, although the difference did not reach statistical significance until 4 months [24•]. Palliative care also increased patient satisfaction, but no difference was observed for patient-clinician communication. This study provided further support for the benefits of stand-alone palliative care clinics beyond patients with lung cancer.

Temel et al. conducted a larger confirmatory trial that involved 191 patients with metastatic lung cancer and 159 with incurable non-colorectal gastrointestinal malignancies [25]. The primary outcome was quality of life (Functional Assessment of Cancer Therapy–General [FACT-G]) at 12 weeks based on the entire sample. Both quality of life and mood improved in the palliative care arm [25]. However, these improvements in quality of life and mood did not reach statistical significance at 12 weeks, and only achieved significance at 24 weeks. Subgroup analysis revealed a greater benefit among lung cancer patients. Moreover, the baseline scores appeared worse in the control group than the palliative care group in gastrointestinal cohort, which may have complicated analysis and interpretation. Overall survival data have not yet been reported.

Groenvold et al. conducted a multicenter randomized trial in Denmark [26]. Unlike previous studies, this trial enrolled patients based on symptom burden instead of time-based criteria. The intervention involved physicians, nurses, and allied health professionals, but was limited in intensity with only one planned consultation visit and only as needed follow-up. Only 31% of patients in the palliative care group had ≥ 2 visits. The primary outcome of change in primary need at 8 weeks was slightly lower in the palliative care group (– 4.9 points, 95% CI – 11.3 to + 1.5), albeit not statistically significant [26]. Importantly, this composite outcome has not been validated and the timing of primary outcome was shorter than other studies. Moreover, there were no significant differences in other secondary outcomes except for nausea. Interpretation of this study was hampered by issues with study design.

do Carmo et al. also conducted a three-arm randomized trial comparing among palliative care plus a psychology intervention, palliative care, and usual care alone [27]. However, this study was terminated prematurely after enrolling 63 of 150 planned patients. This, coupled with the high rates of contamination (32%) and attrition (38%), may explain the lack of difference in a majority of study outcomes among groups.

Taken together, interdisciplinary specialist palliative care clinics represent the gold standard for outpatient palliative care delivery. Their interdisciplinary nature means that they are well suited to fulfill the multidimensional

supportive care needs of patients throughout the disease trajectory in a comprehensive manner [14••].

Physician-only specialist palliative care in stand-alone clinics

Two studies from Italy have examined a physician-only model of specialist palliative care delivery [28, 29]. In a multicenter trial, Maltoni et al. randomized 207 patients with metastatic or unresectable locally advanced pancreatic cancer to either palliative care or usual oncology care [28]. The study design and eligibility criteria were largely similar to the Temel trial. The palliative care intervention consisted of visits with a single palliative care physician every 2–4 weeks until death. The primary outcome, quality of life at 3 months, was significantly better in the palliative care arm compared to control arm (Trial Outcome Index – 0.63 vs. – 4.47, $P = 0.04$); however, the effect size was small and its clinical significance was unclear [28]. No difference was observed in secondary outcomes, including depression, anxiety, a majority of the end-of-life care metrics, or overall survival [30].

The same group of investigators also conducted a randomized trial in patients with advanced gastric cancer with an almost identical design and intervention to the study above [29]. Indeed, the study appeared to have been designed to enroll both pancreatic and gastric cancer patients, but was reported as two separate studies [28, 29]. No significant differences were detected between the two study arms in the primary (quality of life) and secondary outcomes (mood, aggressiveness of care near the end of life, survival) [29].

In both studies, the authors acknowledged that the lack of an interdisciplinary team and lack of standardization of intervention may explain the small effect size; they further postulated that a high level of primary palliative care was provided by the oncology team at the participating sites, although no data were available to support this claim [28, 29]. At this time, there is no formal accreditation process for palliative care in Italy. Based on available data, interdisciplinary clinics are generally preferred over physician-only palliative care, except for settings where it is not possible to hire other team members.

Nurse-led specialist palliative care in stand-alone clinics

In Australia, Tattersall et al. randomized 120 patients with metastatic cancer with a life expectancy of less than 12 months to a palliative care nurse consultant plus usual care or usual care alone [31]. In this study, the nurse "outlined available palliative care services including advice about symptom control, and she offered to arrange review by a palliative care physician, and provided contact details for the palliative care service. The *[palliative care]* PC nurse offered to telephone the patient monthly to check on their well-being…" [31]. Fifty-one patients in the intervention group and 8 patients in the control group had at least one palliative care physician visit, although the timing of this visit was not specified. There was no significant difference in the primary outcome of quality of life over 12 months [31]. However, the palliative care group had greater supportive care needs, worse mean physical symptom scores, worse mean psychological distress scores, and even worse survival compared to control group (7 months vs. 11.7 months, $P = 0.02$). One potential explanation is that

the intervention group had a more aggressive disease course compared to the control group, and thus more symptom distress. The scope and intensity of the "palliative care" intervention appeared to be extremely limited based on the author's description, and may not be adequately developed to address patients' multidimensional issues. Other methodologic issues including under-enrollment, attrition, missing data, and the timing of study outcome also made it difficult to interpret the findings [31].

A Belgium randomized study compared usual oncology care with or without nurse-led palliative care. Outpatients or inpatients were eligible if they were within 3 months of a diagnosis of advanced solid tumor or progression and had a life expectancy of 6 to 24 months [31]. The intervention involved specialist palliative care nurses who met with the patients monthly. Specialist palliative care physicians were available on an as-needed basis only. By 24 weeks, patients on the intervention group had a median of three visits with the palliative care nurse, and 35% had at least one palliative care physician visit. Among the 186 enrolled patients, the investigators reported a statistically significant improvement in the primary outcome, quality of life at 12 weeks (global health status in European Organization for Research and Treatment of Cancer Quality-of-Life Questionnaire Core 30 [EORTC-QLQ-C30] difference 7.6, $P = 0.03$); however, this difference did not meet the 10-point threshold for clinical significance [31]. Secondary analyses revealed no significant differences in overall survival, symptoms, mood, or illness understanding.

In contrast to stand-alone interdisciplinary palliative care clinics, the outcomes associated with nurse-led specialist palliative care with limited physician input have been less impressive. While this could partly be explained by issues with study design, the nature of the intervention may have also played a role. In clinical settings, the lack of an interdisciplinary specialist team may be a marker of lower system resources, lack of infrastructure, and/or inadequate leadership support, all of which could impede implementation of palliative care. Upon further refinement, nurse-led specialist palliative care interventions may have a role, particularly in resource-limited settings such as smaller community clinics.

Nurse-led specialist palliative care telephone-based interventions

Several studies have examined interventions incorporating principles of palliative care delivered predominantly by nurses over the telephone. The main advantages are ease of access and cost-effectiveness. Two randomized controlled trials have examined the outcomes associated with this model of care delivery.

In the Project ENABLE II study, Bakitas et al. randomized 322 patients with advanced solid tumors to a structured nurse-led intervention or usual care alone [32]. This telephone-based intervention involved four manual-based educational and problem-solving sessions and at least monthly telephone follow-up until death, and was delivered by a study advanced nurse practitioner with palliative care specialty training. Among the three co-primary outcomes, the investigators reported significant improvement in quality of life (mean difference in Functional Assessment of Chronic Illness Therapy for Palliative Care 4.6, $P = 0.02$) and non-significant trend for symptom improvement favoring the

nurse-led intervention (mean difference in ESAS − 28, $P = 0.06$), but no difference in resource use such as number of days in the hospital, number of days in the intensive care unit, or number of emergency room visits ($P > 0.05$) [32]. However, the effect sizes for improvements were small and beneath the threshold for clinical significance [11, 33]. The investigators also noted an improvement in mood (Center for Epidemiological Studies Depression Scale − 1.8, $P = 0.02$), and trend toward improved survival in the intervention group (median survival 14 months vs. 8.5 months, $P = 0.14$). Importantly, 26% of patients in the intervention arm and 32% of patients in the usual care group had a referral to specialist palliative care ($P = 0.32$). This study stimulated interest in palliative care, particularly when a relatively low-cost, telephone-based, nurse-led structured model resulted in some clinical benefits.

It also paved the way for Project ENABLE III study by the same group of investigators. This study enrolled 207 patients with advanced cancer [34]. In contrast to the previous study, this trial used a wait-list design in which patients in the control group had a 3-month delay in starting the study intervention. The primary analysis was conducted at 3 months and secondary analyses were at 6 months, 12 months, and from death backward. In addition, the intervention was refined to include an initial in-person visit by a board-certified palliative care clinician and six weekly structured telephone-based sessions delivered by an advance practice nurse focusing on "problem solving, symptom management, self-care, identification and coordination of local resources, communication, decision making, and advance care planning" [34]. This study only enrolled 207 of the 360 planned participants, and had significant contamination in which approximately 66% of patients received a specialist palliative care consultation. The investigators found no significant difference in quality of life, symptom burden, or mood [34]. However, the intervention was associated with 15% improvement in 1-year survival (63% vs. 48%, $P = 0.04$) despite the crossover.

As noted by the investigators, in-person interventions may be more robust than predominantly telephone-based interventions. However, patients enrolled onto these studies were mostly in the rural area, and thus, telephone-based interventions were more feasible. Existing evidence strongly favors interdisciplinary outpatient palliative care clinics over physician-only or nurse-led palliative care. At this time, nurse-led telephone-based interventions are best suited for patients who have difficulty accessing interdisciplinary outpatient palliative care clinics. The survival benefit observed in both studies is intriguing and warrants further research.

Specialist palliative care in embedded clinics

Embedded clinics are defined as "the palliative care team and the oncology team share the same clinic space and see the same patients on the same day" [35]; however, there is much variation in their setup. Embedded specialist palliative care clinics should be distinguished from enhanced primary palliative care in which a dedicated member *of the oncology team* focuses on provision of supportive care (discussed below) [36].

Similar to stand-alone clinics, the nature of the specialist palliative care team also varied widely among centers. Several studies included only palliative care

advanced nurse practitioners [37, 38], some had physicians only [39, 40], and others included both physicians and chaplains [41].

No randomized controlled trials have specifically compared embedded specialist palliative care clinics to stand-alone clinics or usual care. Existing studies mostly employed a retrospective cohort design comparing to historical data or concurrent control [37–41]. The sample size of these studies was typically small and the outcomes varied significantly, which complicates interpretation of these studies. Several studies reported that embedded clinics had greater frequency and/or earlier palliative care referral compared to historical control [39–41].

Embedded clinics offer three main advantages over stand-alone clinics [14••]. They promote communication between the oncology and palliative care teams, create an environment highly conducive for referral, and make it more convenient for patients to be seen on the same day and same location. However, the embedded nature may potentially limit the level of palliative care staffing that can be placed in the available space and restrict growth of the palliative care team over time. Thus, embedded clinics may be more appropriate for smaller community-based oncology practices than larger academic centers with many different clinics.

Advanced practice provider-based enhanced primary palliative care

Some investigators have examined whether palliative care delivered by the oncology team can improve outcomes. This enhanced primary palliative care model typically involves at least one member of the oncology team, such as an advanced practice provider, providing supportive care after some training [36]. We use the term "enhanced" primary palliative care to distinguish these types of interventions from primary palliative care delivered in routine oncology practice. Similar to embedded clinics, such a model could maximize convenience for patients and continuity of care, and may be less expensive. However, the level of expertise and scope of service is often more limited relative to specialist palliative care teams. Administratively, the provider is under the oncology service. Patients may still be referred to specialist palliative care teams; however, the availability of enhanced primary palliative care could potentially increase the threshold for referral.

Dyar et al. randomized patients with metastatic cancer to usual care with or without an oncology advanced nurse practitioner intervention focusing on hospice education, care planning, and needs assessment [42]. The nurse met with the patient twice at baseline and again 1 month later. As part of the eligibility criteria, patients needed to have a strong expectation of hospice enrollment within 12 months, although survival was not reported. This study enrolled 26 of 100 planned patients over 9 months. It was terminated prematurely because "many patients refused study participation as a result of the control arm and their desire to receive the (study) intervention." The primary outcome, time to hospice referral, did not differ. Exploratory analyses of quality of life domains were mostly negative and suffered from multiple comparisons in a small study population [42].

In a second study, McCorkle et al. examined the effect of a structured intervention provided by oncology advanced practice providers and social workers that included five in-person clinic visits and five telephone calls over a 10-week period [43]. These oncology staff received 3 h of training from the study advanced practice nurse. In this cluster randomized clinical trial, 66 patients in the lung and gynecology clinics receive the study intervention, while 80 patients in the gastrointestinal and head and neck clinics received a copy of resource manual that described 28 common symptoms and problems. The investigators assessed symptom distress, health distress, depression, functional status self-rated health, quality of life, anxiety, uncertainty, and self-efficacy over 3 months. With the exception of self-efficacy and uncertainty in illness which favored the control group, none of the outcomes differed [43]. Interpretation of this study was complicated by different baseline characteristics between groups and short duration of intervention. The planned sample size was not reported. At this time, there is inadequate evidence to support enhanced primary palliative care models.

Summary

Similar to other areas of medicine and surgery, palliative care is a specialty with an ever-growing body of knowledge that needs to be acquired through dedicated training and refined through practice. Because the goal of palliative care is to improve quality of life through whole-person care, an interdisciplinary team is essential to address the multidimensional aspects of distress and suffering [14••]. More research needs to be conducted to identify strategies to facilitate timelier referral to specialist palliative care clinics, such as re-branding to supportive care [44, 45], educating oncologists about the role of palliative care [46, 47], developing dually trained palliative oncologists [16, 48], and implementing standardized referral criteria and automatic triggers [17, 18, 49].

In an era of escalating healthcare expenditures, clinicians are often asked to do more with less. Specialist palliative care delivered by a single clinician or enhanced primary palliative care may be an appealing alternative to interdisciplinary palliative care for that purpose. However, it is unreasonable to expect that a single clinician could significantly impact multiple palliative care outcomes after only a few hours to days of palliative care training [50]. Indeed, the evidence supports that palliative care is most effective when it is delivered by an interdisciplinary team of palliative care specialists. These teams have the expertise, time, and clinical resources to provide comprehensive care. Properly delivered, the interdisciplinary palliative care team could improve multiple patient outcomes, such as quality of life, symptom control, mood, patient-clinician communication, illness understanding, quality of end-of-life care, and possibly survival [9,10••,11,12]. As such, the interdisciplinary model of care should be considered the gold standard to which future alternate models are compared against. Although embedded clinics are becoming more popular, they may be more appropriate for smaller centers and more studies are needed to assess their outcomes.

It is important to note that the evidence is still relatively limited and many studies have methodological issues impeding proper interpretation. With further standardization of the palliative care intervention and refinement in

research strategies, the next generation of studies will provide higher-quality evidence to inform practice. In the meantime, meta-analyses and systematic reviews should resist the temptation to combine studies together unless they examined a similar patient population with a similar type of palliative care intervention [51].

Compliance With Ethical Standards

Conflict of Interest

David Hui has received research funding from Insys and Teva. He is also supported in part by grants from the National Cancer Institute (1R01CA214960-01A1, 1R01CA225701-01A1), the National Institute of Nursing Research (1R21NR016736–01), and the American Cancer Society (MRSG-14-1418-01-CCE).

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.

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