

Literature Review:

Integrating an Early Palliative Approach into Advanced Colorectal Cancer Care

Tumour Teams: Palliative Care and GI

Research Questions:

P: Metastatic colorectal cancer patients (subsequently expanded to include lung and pancreatic cancers)

I: Early palliative care

C: Late or traditional palliative intervention

O: Survival

Table 1: White literature

Author, Year	Type of Study	Methods	Patients & Interventions	Results/Recommendations
Ahluwalia, 2018	Systematic review	Review to synthesize the best current evidence for PC interventions across eight domains that structure the National Consensus Project clinical practice guidelines	N/A	<ul style="list-style-type: none"> • 139 systematic reviews met inclusion criteria • Reviews addressed the structure and process of care; physical, psychological, social, spiritual, religious, existential, and cultural aspects; care of the patient nearing EOL; and ethical and legal aspects • There was low-quality evidence on the impact of early/ integrated PC (i.e. PC provided early in the trajectory of an illness and/or integrated with standard treatment) on most patient outcomes including QoL, physical symptoms, re-hospitalization, patient satisfaction with care, and ACP, mainly due to individual study limitations and inconsistent findings • There was very low-quality evidence for early/integrated PC on patient psychological health and mortality and family psychological health, satisfaction with care, and ACP • A substantial body of evidence exists to support clinical practice guidelines for quality PC, but the quality of evidence is limited
Bagcivan, 2018	Qualitative analysis	Review of outpatient charts with advanced cancer (lung, GI, GU, breast, other) to determine what components of PC are important for early palliative intervention	N=70 early PC N=72 delayed PC	<ul style="list-style-type: none"> • Outpatient PC consultations for newly diagnosed patients with advanced cancer addressed patient needs in the following areas: <ul style="list-style-type: none"> ○ marital status (81.7%) ○ spirituality/emotional well being (80.3%) ○ caregiver/family support (79.6%) ○ symptoms-mood (81.7%) ○ pain (73.9%) ○ cognitive status (68.3%) ○ general treatment recommendations-counseling (39.4%) ○ maintaining current medications (34.5%) ○ initiating new medication (23.9%) ○ symptom specific treatment recommendations-pain (22.5%) ○ constipation (12.7%) ○ depression (12.0%)

Author, Year	Type of Study	Methods	Patients & Interventions	Results/Recommendations
				<ul style="list-style-type: none"> ○ advanced directive completion (43%) ○ identifying a surrogate (21.8%) ○ discussing illness trajectory (21.1%) • Providers were more likely to evaluate general pain (p=0.035), hospice awareness (p=0.005) and recommend hospice (p=0.002) in delayed group vs. early PC group
Boucher, 2018	Survey	Clinicians treating patients with advanced cancers at 4 centres completed a checklist of BSC at eligible patient encounters	N=15 clinicians N=9 advanced care practitioners	<ul style="list-style-type: none"> • 40% noted improved impact using BSC for "overall impact on your delivery of supportive/PC" • 46% noted improved impact using BSC for "overall impact on your documentation of supportive/PC" • 33% noted increased impact of BSC on "frequency of comprehensive symptom assessment" • None noted decreased frequency or worsening impact on any measure with use of BSC • 73% agreed/strongly agreed that checklists could be easily integrated, 73% saw value in integration, and 80% found it easy to use
Collins, 2018	Population cohort study	Patients identified through hospital registration data; statistics collected to identify EOL quality indicators	N=14,759 NSCLC N=2,932 SCLC N=9,445 prostate N=19,564 breast cancer	<ul style="list-style-type: none"> • 80% of patients died in hospital • 83% had suboptimal EOL care • 59% received a palliative approach to care a median of 27 days before death
Hoerger, 2019 (Epub ahead of print in 2018)	Systematic review and meta-analysis	Systematic review and meta-analysis of randomized controlled trials comparing outpatient specialty PC with usual care in adults with advanced cancer	N/A	<ul style="list-style-type: none"> • 9 studies included • In the 3 high-quality studies with long-term survival data (n = 646), patients randomized to outpatient specialty PC had a 14% absolute increase in 1 year survival relative to controls (56% vs. 42%, p < .001). The survival advantage was also observed at 6, 9, 15, and 18 months, and median survival was 4.56 months longer (14.55 vs. 9.99 months). • In the 5 high-quality studies with QoL data (n = 1,398), outpatient specialty PC improved QoL relative to controls (g = .18, p < .001), including for physical and psychological measures
Hoerger, 2018	Secondary analysis of randomized controlled trial	Patients with lung or non-colorectal GI cancer were randomly assigned to receive early PC + standard care	N=171 early PC + standard care	<ul style="list-style-type: none"> • Analysis of 2921 PC visits mostly addressing coping (64.2%) and symptom management (74.5%) • Patients who had higher proportion of visits that addressed coping experience improved QoL (p=0.02) and depression symptoms (p=0.002) • Patients who had a higher proportion of visits addressing treatment decisions were less likely to initiate chemotherapy (p=0.02) or be hospitalized (p=0.005) in the 60 days before death • Patients who had higher proportion of visits addressing ACP were more likely to use hospice (p=0.03)

Author, Year	Type of Study	Methods	Patients & Interventions	Results/Recommendations
Hui, 2018	State-of-the-science review	Review directed at the practicing oncology clinician; discusses 1) the contemporary literature examining the impact of PC on care outcomes, 2) conceptual frameworks on interdisciplinary, timely, and targeted PC, and 3) strengths and weaknesses of innovative care models	N/A	<p><u>Impact of PC on care outcomes:</u></p> <ul style="list-style-type: none"> • Most RCTs demonstrate that PC combined with oncologic care improves QoL and symptom control • Clinical trials involving interdisciplinary PC teams, vs. nurse-led PC, appear to be more likely to be associated with positive findings • 3 recent meta-analyses concluded that PC was associated with improved QoL; however, the effect size was small, maybe related to heterogeneity in trial design • A meta-analysis examining the timing of PC referral supported greater benefits on QoL with earlier referral • PC can improve health care value by reducing costly investigations, interventions, and hospitalizations at the end of life, especially those with questionable benefits <p><u>Conceptual frameworks to define key elements of PC delivery:</u></p> <ul style="list-style-type: none"> • The interconnectedness of symptoms and supportive care needs necessitates a comprehensive interdisciplinary team to provide multidimensional care • Although interdisciplinary PC teams are ideal, single-disciplinary PC may have a role in the provision of primary PC, particularly in resource-limited settings • PC is most effective as a preventive measure when it is introduced early in the disease trajectory (e.g. for patient education, proper symptom management, longitudinal counseling and spiritual care, enhancing illness understanding, ACP) • Timely PC is associated with improved QoL and EOL care • Because of scarce health care resources, it is impossible for all patients to be seen by PC from the time of diagnosis; similar to cancer targeted therapy, a more personalized approach to refer patients with higher current or anticipated supportive care needs may result in better outcomes • Oncologists have an important role in providing primary PC, which includes basic symptom assessment and treatment, communication, decision making, and referral to specialist PC <p><u>Innovative models of care delivery:</u></p> <ul style="list-style-type: none"> • There is strong evidence to support stand-alone PC clinics (ideally staffed with an interdisciplinary team in larger centers) to improve patient outcomes; these clinics represent the current standard of care against which other outpatient models should be measured • Embedded clinics may be more suitable in smaller centers with limited PC resources • Further research is needed to assess the impact of nurse-led PC and how this care model interfaces with specialist PC teams • RCTs have found that oncology teams delivering PC alone resulted in poorer QoL outcomes vs. concurrent care with a specialist PC team; however, it is important that all oncologists are trained in providing a basic level of PC

Author, Year	Type of Study	Methods	Patients & Interventions	Results/Recommendations
				<ul style="list-style-type: none"> Automatic referral to PC may allow for more personalized care; it requires routine screening, standardized referral criteria, and established PC team An international consensus study identified 9 needs-based criteria and 2 time-based criteria for referral to outpatient PC for patients with advanced cancer
Lee, 2018	Retrospective review	Retrospective medical record review of patients with metastatic colorectal cancer who died between 2011 and 2014, comparing use of outpatient PC	N=50 patients used outpatient PC N=82 patients did not use outpatient PC	<ul style="list-style-type: none"> 32% of patients who received outpatient PC were admitted to hospice vs. 17% of patients who did not receive PC (p=0.047) Mean inpatient days within 30 days of death was shorter for PC group (4.02 vs 7.77 days, p=0.032) No difference in proportions of patients who received chemotherapy and visited ED within 30 days from death
Vanbutsele, 2018	Randomized controlled trial	Patients with advanced cancer (GI, GU, lung, breast, head and neck, melanoma) were assigned to either early and systematic integration of PC or standard oncological care	N=94 standard care alone N=92 PC + standard care	<ul style="list-style-type: none"> Overall QoL score at 12 weeks by EORCT QLQ C30 scale=59.39 standard group vs 61.98 PC group (p=0.03) Overall QoL score by MQOL single item scale=5.94 standard group vs. 7.05 PC group (p=0.0006)
Bakitas, 2017	Review	Review of multiple RCTs for common practical elements, methods and techniques that oncologists can use to deliver parts of concurrent interdisciplinary PC	N/A	<ul style="list-style-type: none"> The authors recommend standardized assessment of patient-reported outcomes, including the evaluation of symptoms with such tools as the Edmonton or Memorial Symptom Assessment Scales, spirituality with the FICA Spiritual History Tool or similar questions, and psychosocial distress with the Distress Thermometer All patients should be assessed for how they prefer to receive information, their current understanding of their situation, and if they have considered some ACP Approximately 1 hour of additional time with the patient is required each month If the oncologist does not have established ties with spiritual care and social work, he or she should establish these relationships for counseling as required Caregivers should be asked about coping and support needs Oncologists can adapt PC techniques to achieve results that are similar to those in the RCTs of PC plus usual care compared with usual care alone
Ferrell, 2017	Guideline update	Expert panel review of RCTs, systematic reviews, and meta-analyses	N/A	<ul style="list-style-type: none"> N=9 RCTs, 1 quasi-experimental trial, 5 secondary analyses included in the guideline update Inpatients and outpatients with advanced cancer should receive dedicated PC services early in their disease course concurrent with active treatment; family and friend caregivers of patients with early or advanced cancer should also be referred to PC services

Author, Year	Type of Study	Methods	Patients & Interventions	Results/Recommendations
Gorin, 2017	Systematic review and meta-analysis	Literature search to address cancer care coordination	N/A	<ul style="list-style-type: none"> N=52 studies included in the review, and N=11/52 studies included in the meta-analysis Cancer care coordination approaches led to improvements in 81% of outcomes, including screening, measures of patient experience with care, and quality of EOL care Patient navigation was the most frequent care coordination intervention, followed by home telehealth and nurse case management OR of appropriate health care utilization in cancer care coordination interventions vs. comparison interventions = 1.9 (95 % CI = 1.5-3.5)
Groenvold, 2017	Randomized controlled trial	Multicentre trial comparing early PC + standard care to standard care alone for patients with advanced cancer (lung, GI, breast, other)	N=145 PC + standard care N=152 standard care alone	<ul style="list-style-type: none"> Early PC showed no effect on change in primary need Analysis of secondary outcomes including survival also showed no difference with the exception of nausea/vomiting
Haun, 2017	Systematic review	Review of RCTs and cluster-RCTs on professional PC services that provided or coordinated comprehensive care for adults at early advanced stages of cancer	N/A	<ul style="list-style-type: none"> Included 7 RCTs and cluster-RCTs that together recruited 1614 participants Compared with usual/standard cancer care alone, early PC significantly improved health-related QoL at a small effect size (SMD 0.27, 95% CI 0.15 to 0.38; participants analyzed at post treatment = 1028; evidence of low certainty) No differences in survival or depressive symptoms 7 studies that analyzed 1054 participants post treatment suggest a small effect for significantly lower symptom intensity in early PC compared with the control condition (SMD -0.23, 95% CI -0.35 to -0.10; evidence of low certainty) Current results should be interpreted with caution owing to very low to low certainty of current evidence and between-study differences regarding participant populations, interventions, and methods
Temel, 2017	Randomized controlled trial	Patients with newly diagnosed incurable lung or non-colorectal GI cancer randomized to receive early integrated PC + oncology care or usual care	N=175 early integrated PC and oncology care N=175 usual care	<ul style="list-style-type: none"> Intervention patients (vs. usual care) reported greater improvement in QoL from baseline to week 24 (1.59 vs. 23.40; P=.010) but not week 12 (0.39 vs. 21.13; p=.339) Intervention patients also reported lower depression at week 24, controlling for baseline scores (adjusted mean difference, -1.17; 95% CI, -2.33 to -0.01; p=.048) Intervention effects varied by cancer type, such that intervention patients with lung cancer reported improvements in QoL and depression at 12 and 24 weeks, whereas usual care patients with lung cancer reported deterioration; patients with GI cancers in both study groups reported improvements in QoL and mood by week 12 Intervention patients versus usual care patients were more likely to discuss their wishes with their oncologist if they were dying (30.2% vs. 14.5%; p=.004).
Whitney, 2017	Retrospective review	Review of cancer registry data to	N=25,032	<ul style="list-style-type: none"> 71% of patients with advanced colorectal cancer were hospitalized, 16% had 3 or more hospitalizations, and 64% of hospitalizations originated in the ED

Author, Year	Type of Study	Methods	Patients & Interventions	Results/Recommendations
		calculate hospitalization rates in the year after diagnosis among patients with advanced breast, NSCLC, colorectal, or pancreatic cancer		<ul style="list-style-type: none"> Re-hospitalization rates were significantly lower after discharge from a hospital with an outpatient PC program (IRR=0.90, 95% CI 0.83-0.97) and were higher after discharge from a for-profit hospital (IRR=1.33, 95% CI 1.14- 1.56)
Basch, 2016	Randomized controlled trial	Patients with metastatic breast, GU, gynecologic, or lung cancers were randomized to web-based self-reporting of symptoms (PRO group) vs. usual care	N=441 PRO group N=325 usual care group	<ul style="list-style-type: none"> HRQoL improved in PRO group vs. usual care group (34% vs. 18%) and worsened among fewer (38% vs. 53%) Overall mean HRQoL declined by less in PRO group vs. usual care group (1.4 vs. 7.1 point drop, p<0.001) PRO group less frequently admitted to ED (34% vs. 41%, p=0.02) or hospitalized (45% vs. 49%, p=0.08) and remained on chemotherapy longer (mean 8.2 vs. 6.3 months, p=0.002) 75% of PRO group vs. 69% usual care group alive at 1 year (p=0.05), and mean quality-adjusted survival also higher in PRO group (8.7 vs. 8.0 months, p=0.004)
Kavalieratos, 2016	Systematic review and meta-analysis	Review of trials of PC interventions in adults with a life limiting disease	N/A	<ul style="list-style-type: none"> Review included 12,731 patients and 2,479 caregivers PC interventions associated with improvements in patient QoL and symptom burden Findings for caregiver outcomes inconsistent
Maltoni, 2016	Randomized controlled trial	Comparison of standard care + on-demand early PC vs. standard care + systematic early PC for patients with metastatic or locally advanced inoperable pancreatic cancer	N=100 standard care + on demand early PC N=107 standard care + systematic early PC	<ul style="list-style-type: none"> QoL scores at 12 weeks=84.4 systematic PC vs. 78.1 on-demand PC (p=0.022) Hepatic cancer subscale scores=52.0 systematic PC vs. 48.2 on-demand PC (p=0.008) No OS difference between treatment arms
Seow, 2016	Retrospective cohort study	Examined rates of home care nursing in last 6 months of life vs. standard nursing care in last month of life, and rates of ED admissions in the subsequent week, among patients with advanced cancer	N=54,576	<ul style="list-style-type: none"> 85% of cases had an ED visit and 68% received EOL home care nursing Patients receiving EOL nursing at any week had a significantly reduced ED rate in subsequent week of 31% (RR=0.69, 95% CI 0.68-0.71) compared with standard nursing Receiving EOL nursing and standard nursing in the last month of life at rate of more than 5 hrs/week was associated with a decreased ED rate of 41% (RR=0.59, 95% CI 0.58-0.61) and 32% (RR=0.68, 95% CI 0.66-0.70) respectively compared with standard nursing of 1 hr/week

Author, Year	Type of Study	Methods	Patients & Interventions	Results/Recommendations
		(lung, GI, breast, GU, others)		
Bakitas, 2015	Randomized controlled trial	Comparison of early vs. delayed PC intervention among patients with advanced cancer (lung, GI, GU, breast, other)	N=103 early PC N=104 delayed PC	<ul style="list-style-type: none"> PROs (QoL, symptom impact, mood) not statistically significant after enrolment or before death Resource use in early and delayed PC groups: <ul style="list-style-type: none"> Hospital days (RR=0.73; 95% CI 0.41-1.27, p=0.26) ICU days (RR=0.68; 95% CI 0.23-2.02, p=0.49) ED visits (RR=0.73; 95% CI 0.45-1.19, p=0.21) Chemotherapy in last 14 days (RR=1.57; 95% CI 0.37-6.7, p=0.26) 1 year survival=63% in early PC vs. 48% delayed PC (p=0.038) Rate of home deaths=54% early PC vs. 47% delayed PC (p=0.6)
Cheung, 2015	Retrospective study	Review of population data to identify cancer decedents (lung, GI, breast, prostate, other) who received or did not receive aggressive EOL care and to compare costs of cancer care	N= 83,158 no aggressive care N=24,095 any aggressive care	<ul style="list-style-type: none"> Mean per patient cost over final month=\$18,131 aggressive care group vs. \$12,678 non-aggressive care group (p<0.0001) For patients receiving EOL care in the highest cost quintile, early and repeated PC consultation was associated with reduced costs Chemotherapy in the last 2 weeks of life predictive of increased costs (median increase \$536; p<0.0001) whereas access to PC predictive of lower costs (median decrease \$418; p<0.001)
Dionne-Odom, 2015	Randomized controlled trial	Caregivers of patients with advanced cancer (lung, GI, GU, breast, other) randomly assigned right after randomization (early group) or 3 months after randomization (delayed group) to receive 3 weekly phone coaching sessions, monthly follow-up, and a bereavement call	N=61 caregivers in early group N=61 caregivers in delayed group	<ul style="list-style-type: none"> There were no differences in QoL or burden between groups In decedents' caregivers, a terminal decline analysis indicated between-group differences favoring the early group for depression and stress burden but not for QoL, objective burden, or demand burden Early-group caregivers had lower depression scores at 3 months and lower depression and stress burden in the terminal decline analysis Palliative care for caregivers should be initiated as early as possible to maximize benefits
Ferrell 2015	Prospective quasi-experimental study	Patients with NSCLC were sequentially enrolled into a control group or a concurrent interdisciplinary PC intervention group	N=219 patients in control group N=272 patients in intervention group	<ul style="list-style-type: none"> 491 patients were included in the primary analysis Patients who received the intervention had significantly better scores for QoL (109.1 vs. 101.4; p<0.001), symptoms (25.8 vs. 23.9; p<0.001), spiritual well-being (38.1 vs. 36.2; p=0.001), and lower psychological distress (2.2 vs. 3.3; p<0.001) at 12 weeks, after controlling for baseline scores, compared to patients in the usual care group

Author, Year	Type of Study	Methods	Patients & Interventions	Results/Recommendations
				<ul style="list-style-type: none"> Patients in the intervention group also had significantly higher numbers of completed advance care directives (44% vs. 9%; $p<0.001$), and overall supportive care referrals (61% vs. 28%; $p<0.001$)
Hudson, 2015	Randomized controlled trial	Caregivers of patients with advanced cancer receiving home-based PC were randomized to standard care, or a psycho-educational intervention delivered through 1 home visit and 3 phone calls, or 2 home visits and 2 phone calls	N=57 in 1-visit group N=93 in 2-visit group N=148 in control group	<ul style="list-style-type: none"> There was significantly less worsening in distress between baseline and 8 weeks post-death in the 1-visit intervention group than in the control group; however, no significant difference was found between the 2-visit intervention and the control group
Sun 2015	Two-group, prospective sequential, quasi-experimental design	Family caregivers of patients diagnosed with NSCLC were accrued to a usual care group or intervention group; Caregivers in the intervention group were presented at interdisciplinary care meetings, and received 4 educational sessions	N=157 family caregivers in the usual care group N=197 family caregivers in the intervention group	<ul style="list-style-type: none"> Caregivers who received the interdisciplinary PC intervention had significantly better scores for social well-being (5.84 vs. 6.86; $p<.001$) and lower psychological distress (4.61 vs. 4.20; $p=.010$) at 12 weeks compared to caregivers in the usual care group Caregivers in the intervention group had significantly less caregiver burden compared to caregivers in the usual care group ($p=.008$)
Brinkman-Stoppelenburg, 2014	Systematic review	Review of studies on the effects of ACP	N/A	<ul style="list-style-type: none"> 113 studies assessed and graded 95% of studies were observational, and 81% originated from the United States 49% of studies were performed in hospitals and 32% in nursing homes Do-not-resuscitate orders (39%) and written advance directives (34%) were most often studied ACP was often found to decrease life-sustaining treatment, increase use of hospice and PC and prevent hospitalization
Seow, 2014	Pooled analysis of retrospective cohort study	Comparison of specialist PC vs. standard care	N=3109 patients (~80% with cancer) received specialist PC N=3109 patients received standard care	<ul style="list-style-type: none"> Hospitalization rate=31.2% specialized PC group vs. 39.3% standard care group ($p<0.001$) Rate of ED visits in last 2 weeks of life=28.9% specialized PC group vs. 34.5% standard care group ($p<0.001$) Fewer deaths in hospital for patients in specialist PC group vs. standard care group (N=503 vs. 887, $p<0.001$); pooled RR of dying in hospital=0.46 (95% CI 0.4-0.52)

Author, Year	Type of Study	Methods	Patients & Interventions	Results/Recommendations
Uitdehaag, 2014	Randomized controlled trial	Patients with incurable primary or recurrent esophageal, pancreatic, or hepatobiliary cancer were randomized to nurse-led follow-up at home or conventional medical follow-up in the outpatient clinic	N=36 evaluable patients (i.e. completed at least one follow-up survey) in the nurse-led group N=30 evaluation patients in the conventional group	<ul style="list-style-type: none"> Patients in the nurse-led follow-up group were significantly more satisfied with the visits, whereas QoL and health care consumption within the first 4 months were comparable between the two groups Nurse-led follow-up was less expensive than conventional medical follow-up; however, the total costs for the first 4 months of follow-up in this study were higher in the nurse-led follow-up group because of a higher frequency of visits The results suggest that conventional medical follow-up is interchangeable with nurse-led follow-up
Zimmermann, 2014	Cluster randomized controlled trial	Comparison of early PC consultation + follow-up vs. standard care for patients with advanced lung, GI, GU, breast or gynecological cancers	N=228 early PC N=233 standard care	<ul style="list-style-type: none"> At 3 months, there was a non-significant difference in change score for FACIT-Sp between early PC vs. standard care groups (3.56 points; 95% CI -0.27-7.40], p=0.07), a significant difference in QUAL-E (2.25 points; 95% CI 0.01-4.49, p=0.05) and FAMCARE-P16 (3.79 points; 95% CI 1.74-5.85, p=0.0003) At 3 months, no difference in change score for ESAS (-1.70 points; 95% CI -5.26-1.87, p=0.33) or CARES-MIS (-0.66 points; 95% CI -2.25 -0.94, p=0.40) between early PC vs. standard care groups At 4 months, there were significant differences in change scores for all outcomes except CARES-MIS
Greer, 2013	Review	Review of literature on early integration of PC	N/A	<ul style="list-style-type: none"> Many treatments for cancer but not enough focus on side effects of progressing disease Introducing PC at time of diagnosis of advanced cancer leads to meaningful improvement in experience of patients and caregivers Recommendations: discuss mechanisms by which early PC benefits patients and families, guide the dissemination and application of this model in outpatient settings, and inform health care policy regarding the delivery of high quality cost effective and comprehensive cancer care
McNamara, 2013	Retrospective cross sectional study	Review of death registry data for cancer patients	N=746	<ul style="list-style-type: none"> In final 90 days before death, 31.3% who had early access to PC and 52% of those who did not have access visited an ED (OR=2.86; 95% CI 1.91- 4.30)
Dyar, 2012	Randomized controlled trial	Patients with metastatic breast, lung, prostate, other cancer randomized to standard care or an advanced registered nurse practitioner-directed intervention that included discussions of the benefits of hospice,	N=12 in intervention group N=14 in control group	<ul style="list-style-type: none"> The study closed early due to published data demonstrating the benefits of early PC interventions in the management of metastatic cancer patients and patients wanting the intervention Statistically significant improvements from baseline were noted in the emotional and mental QoL assessments (as determined by the FACT-G and LASA questionnaires) in the intervention group that were not seen in the control group Patients found it useful to have the living will and Five Wishes documents offered as part of the intervention

Author, Year	Type of Study	Methods	Patients & Interventions	Results/Recommendations
		discussions on living wills and advanced directives		
Smith, 2012	ASCO provisional clinical opinion statement	Addresses the integration of PC services into standard oncology practice at a time a person is diagnosed with metastatic or advanced cancer	N/A	<ul style="list-style-type: none"> Statement based on results of 7 RCTs Patients should be offered concurrent PC and standard oncologic care at initial diagnosis While survival benefit from early PC has not yet been demonstrated in other oncology settings, substantial evidence demonstrates that PC combined with standard care or as the main focus leads to better patient and caregiver outcomes, including improvement in symptoms, QoL, patient satisfaction, and reduced caregiver burden Earlier PC leads to more appropriate referral to and use of hospice and reduces the use of futile intensive care No trials have demonstrated harm to patients or caregivers or excessive costs from early PC
Gonsalves, 2011	Retrospective chart review	Assessment of last 100 patients in 2002 and 2008, who died with active cancer; only patients in 2008 had access to a PC team	N=100 patients no PC access (year 2002) N=100 patients PC access (year 2008)	<ul style="list-style-type: none"> In the last 30 days of life, compared to 2002, patients in 2008 had a higher incidence of: chemotherapy administration, >1 hospital admission, >14 days of hospital stay, ICU admissions, and in-hospital deaths Patients with timely PC consults in 2008 appeared to have a lower incidence of: chemotherapy administration, >1 ED visit, >1 hospital admission, >14-day hospital stays, ICU admissions, and deaths in the hospital Timely PC consults were associated with earlier and more frequent hospice referral
Temel, 2010	Randomized controlled trial	Comparison of early PC + standard care vs. standard care alone in patients with metastatic NSCLC	N=77 early PC N=74 standard care	<ul style="list-style-type: none"> Patients assigned to early PC had a better QoL vs. patients assigned to standard care (mean FACT-L score=98.0 vs. 91.5, p=0.03) Fewer patients with depressive symptoms in PC group vs. standard care group (16% vs. 38%, p=0.01) Although fewer patients received aggressive EOL care in the early PC group vs. the standard care group (33% vs. 54%, p=0.05), the median survival was longer (11.6 months early PC group vs. 8.9 months standard care group, p=0.02)
Bakitas, 2009	Randomized controlled trial	Multicomponent, psycho-educational intervention conducted by advanced practice nurses for patients with advanced cancer (GI, GU, lung, breast)	N=161 weekly sessions x 4 + monthly follow-up N=161 usual care	<ul style="list-style-type: none"> Compared with patients receiving usual care, patients receiving nurse-led, PC intervention had higher scores for QoL (p=0.02) and mood (p=0.02), but did not have improvements in symptom intensity scores Intensity of services (days in the hospital/ICU or ED visits) did not differ between the two groups

References

- Ahluwalia SC, Chen C, Raaen L, Motala A, Walling AM, Chamberlin M, O'Hanlon C, Larkin J, Lorenz K, Akinniranye O, Hempel S. A Systematic Review in Support of the National Consensus Project Clinical Practice Guidelines for Quality Palliative Care, Fourth Edition. *J Pain Symptom Manage*. 2018 Dec;56(6):831-870.
- Bagcivan G, Dionne-Odom JN, Frost J, Plunkett M, Stephens LA, Bishop P, Taylor RA, Li Z, Tucker R, Bakitas M. What happens during early outpatient palliative care consultations for persons with newly diagnosed advanced cancer? A qualitative analysis of provider documentation. *Palliat Med*. 2018 Jan;32(1):59-68.
- Bakitas M, Lyons KD, Hegel MT, Balan S, Brokaw FC, Seville J, Hull JG, Li Z, Tosteson TD, Byock IR, Ahles TA. Effects of a palliative care intervention on clinical outcomes in patients with advanced cancer: the Project ENABLE II randomized controlled trial. *JAMA*. 2009 Aug 19;302(7):741-9.
- Bakitas MA, El-Jawahri A, Farquhar M, Ferrell B, Grudzen C, Higginson I, Temel JS, Zimmermann C, Smith TJ. The TEAM Approach to Improving Oncology Outcomes by Incorporating Palliative Care in Practice. *J Oncol Pract*. 2017 Sep;13(9):557-566.
- Bakitas MA, Tosteson TD, Li Z, Lyons KD, Hull JG, Li Z, Dionne-Odom JN, Frost J, Dragnev KH, Hegel MT, Azuero A, Ahles TA. Early Versus Delayed Initiation of Concurrent Palliative Oncology Care: Patient Outcomes in the ENABLE III Randomized Controlled Trial. *J Clin Oncol*. 2015 May 1;33(13):1438-45.
- Basch E, Deal AM, Kris MG, Scher HI, Hudis CA, Sabbatini P, Rogak L, Bennett AV, Dueck AC, Atkinson TM, Chou JF, Dulko D, Sit L, Barz A, Novotny P, Fruscione M, Sloan JA, Schrag D. Symptom Monitoring With Patient-Reported Outcomes During Routine Cancer Treatment: A Randomized Controlled Trial. *J Clin Oncol*. 2016 Feb 20;34(6):557-65.
- Boucher NA, Nicolla J, Ogunseitian A, Kessler ER, Ritchie CS, Zafar YY. Feasibility and Acceptability of a Best Supportive Care Checklist among Clinicians. *J Palliat Med*. 2018 Aug;21(8):1074-1077.
- Brinkman-Stoppelenburg A, Rietjens JA, van der Heide A. The effects of advance care planning on end-of-life care: a systematic review. *Palliat Med*. 2014 Sep;28(8):1000-25.
- Cheung MC, Earle CC, Rangrej J, Ho TH, Liu N, Barbera L, Saskin R, Porter J, Seung SJ, Mittmann N. Impact of aggressive management and palliative care on cancer costs in the final month of life. *Cancer*. 2015 Sep 15;121(18):3307-15.
- Collins A, Sundararajan V, Burchell J, Millar J, McLachlan SA, Krishnasamy M, Le BH, Mileskin L, Hudson P, Philip J. Transition Points for the Routine Integration of Palliative Care in Patients With Advanced Cancer. *J Pain Symptom Manage*. 2018 Aug;56(2):185-194.
- Dionne-Odom JN, Azuero A, Lyons KD, Hull JG, Tosteson T, Li Z, Li Z, Frost J, Dragnev KH, Akyar I, Hegel MT, Bakitas MA. Benefits of Early Versus Delayed Palliative Care to Informal Family Caregivers of Patients With Advanced Cancer: Outcomes From the ENABLE III Randomized Controlled Trial. *J Clin Oncol*. 2015 May 1;33(13):1446-52. doi: 10.1200/JCO.2014.58.7824.
- Dyar S, Lesperance M, Shannon R, Sloan J, Colon-Otero G. A nurse practitioner directed intervention improves the quality of life of patients with metastatic cancer: results of a randomized pilot study. *J Palliat Med*. 2012 Aug;15(8):890-5.
- Ferrell B, Sun V, Hurria A, Cristea M, Raz DJ, Kim JY, Reckamp K, Williams AC, Borneman T, Uman G, Koczywas M. Interdisciplinary Palliative Care for Patients With Lung Cancer. *J Pain Symptom Manage*. 2015 Dec;50(6):758-67.

Ferrell BR, Temel JS, Temin S, Alesi ER, Balboni TA, Basch EM, Firn JI, Paice JA, Peppercorn JM, Phillips T, Stovall EL, Zimmermann C, Smith TJ. Integration of Palliative Care Into Standard Oncology Care: American Society of Clinical Oncology Clinical Practice Guideline Update. *J Clin Oncol*. 2017 Jan;35(1):96-112.

Gonsalves WI, Tashi T, Krishnamurthy J, Davies T, Ortman S, Thota R, Aldoss I, Ganta A, Kalaiah M, Didwaniya N, Eberle C, Ganti AK, Silberstein PT, Subbiah S. Effect of palliative care services on the aggressiveness of end-of-life care in the Veteran's Affairs cancer population. *J Palliat Med*. 2011 Nov;14(11):1231-5.

Gorin SS, Haggstrom D, Han PKJ, Fairfield KM, Krebs P, Clauser SB. Cancer Care Coordination: a Systematic Review and Meta-Analysis of Over 30 Years of Empirical Studies. *Ann Behav Med*. 2017 Aug;51(4):532-546.

Greer JA, Jackson VA, Meier DE, Temel JS. Early integration of palliative care services with standard oncology care for patients with advanced cancer. *CA Cancer J Clin*. 2013 Sep;63(5):349-63.

Groenvold M, Petersen MA, Damkier A, Neergaard MA, Nielsen JB, Pedersen L, Sjøgren P, Strömberg AS, Vejlgård TB, Glud C, Lindschou J, Fayers P, Higginson IJ, Johnsen AT. Randomised clinical trial of early specialist palliative care plus standard care versus standard care alone in patients with advanced cancer: The Danish Palliative Care Trial. *Palliat Med*. 2017 Oct;31(9):814-824.

Haun MW, Estel S, Rücker G, Friederich HC, Villalobos M, Thomas M, Hartmann M. Early palliative care for adults with advanced cancer. *Cochrane Database Syst Rev*. 2017 Jun 12;6:CD011129.

Hoerger M, Wayser GR, Schwing G, Suzuki A, Perry LM. Impact of Interdisciplinary Outpatient Specialty Palliative Care on Survival and Quality of Life in Adults With Advanced Cancer: A Meta-Analysis of Randomized Controlled Trials. *Ann Behav Med*. 2019 Jun 4;53(7):674-685.

Hoerger M, Greer JA, Jackson VA, Park ER, Pirl WF, El-Jawahri A, Gallagher, ER, Hagan T, Jacobsen J, Perry LM, Temel JS. Defining the Elements of Early Palliative Care That Are Associated With Patient-Reported Outcomes and the Delivery of End-of-Life Care. *J Clin Oncol*. 2018 Apr 10;36(11):1096-1102.

Hudson P, Trauer T, Kelly B, O'Connor M, Thomas K, Zordan R, Summers M. Reducing the psychological distress of family caregivers of home based palliative care patients: longer term effects from a randomised controlled trial. *Psychooncology*. 2015 Jan;24(1):19-24.

Hui D, Hannon BL, Zimmermann C, Bruera E. Improving patient and caregiver outcomes in oncology: Team-based, timely, and targeted palliative care. *CA Cancer J Clin*. 2018 Sep;68(5):356-376.

Kavalieratos D, Corbelli J, Zhang D, Dionne-Odom JN, Ernecoff NC, Hanmer J, Hoydich ZP, Ikejiani DZ, Klein-Fedyshin M, Zimmermann C, Morton SC, Arnold RM, Heller L, Schenker Y. Association Between Palliative Care and Patient and Caregiver Outcomes: A Systematic Review and Meta-analysis. *JAMA*. 2016 Nov 22;316(20):2104-2114.

Lee SW, Jho HJ, Baek JY, Shim EK, Kim HM, Ku JY, Nam EJ, Chang YJ, Choi HJ, Kim SY. Outpatient Palliative Care and Aggressiveness of End-of-Life Care in Patients with Metastatic Colorectal Cancer. *Am J Hosp Palliat Care*. 2018 Jan;35(1):166-172.

Maltoni M, Scarpì E, Dall'Agata M, Zagonel V, Bertè R, Ferrari D, Brogna CM, Bortolussi R, Trentin L, Valgiusti M, Pini S, Farolfi A, Casadei Gardini A, Nanni O, Amadori D; Early Palliative Care Italian Study Group (EPCISG). Systematic versus on-demand early palliative care: results from a multicentre, randomised clinical trial. *Eur J Cancer*. 2016 Sep;65:61-8.

McNamara BA, Rosenwax LK, Murray K, Currow DC. Early admission to community-based palliative care reduces use of emergency departments in the ninety days before death. *J Palliat Med.* 2013 Jul;16(7):774-9.

Seow H, Barbera L, Pataky R, Lawson B, O'Leary E, Fassbender K, McGrail K, Burge F, Brouwers M, Sutradhar R. Does Increasing Home Care Nursing Reduce Emergency Department Visits at the End of Life? A Population-Based Cohort Study of Cancer Decedents. *J Pain Symptom Manage.* 2016 Feb;51(2):204-12.

Seow H, Brazil K, Sussman J, Pereira J, Marshall D, Austin PC, Husain A, Rangrej J, Barbera L. Impact of community based, specialist palliative care teams on hospitalisations and emergency department visits late in life and hospital deaths: a pooled analysis. *BMJ.* 2014 Jun 6;348:g3496.

Smith TJ, Temin S, Alesi ER, Abernethy AP, Balboni TA, Basch EM, Ferrell BR, Loscalzo M, Meier DE, Paice JA, Peppercorn JM, Somerfield M, Stovall E, Von Roenn JH. American Society of Clinical Oncology provisional clinical opinion: the integration of palliative care into standard oncology care. *J Clin Oncol.* 2012 Mar 10;30(8):880-7.

Sun V, Grant M, Koczywas M, Freeman B, Zachariah F, Fujinami R, Del Ferraro C, Uman G, Ferrell B. Effectiveness of an interdisciplinary palliative care intervention for family caregivers in lung cancer. *Cancer.* 2015 Oct 15;121(20):3737-45.

Temel JS, Greer JA, El-Jawahri A, Pirl WF, Park ER, Jackson VA, Back AL, Kamdar M, Jacobsen J, Chittenden EH, Rinaldi SP, Gallagher ER, Eusebio JR, Li Z, Muzikansky A, Ryan D P. Effects of Early Integrated Palliative Care in Patients With Lung and GI Cancer: A Randomized Clinical Trial. *J Clin Oncol.* 2017 Mar 10;35(8):834-841.

Temel JS, Greer JA, Muzikansky A, Gallagher ER, Admane S, Jackson VA, Dahlin CM, Blinderman CD, Jacobsen J, Pirl WF, Billings JA, Lynch TJ. Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med.* 2010 Aug 19;363(8):733-42.

Uitdehaag MJ, van Putten PG, van Eijck CH, Verschuur EM, van der Gaast A, Pek CJ, van der Rijt CC, de Man RA, Steyerberg EW, Laheij RJ, Siersema PD, Spaander MC, Kuipers EJ. Nurse-led follow-up at home vs. conventional medical outpatient clinic follow-up in patients with incurable upper gastrointestinal cancer: a randomized study. *J Pain Symptom Manage.* 2014 Mar;47(3):518-30.

Vanbutsele G, Pardon K, Van Belle S, Surmont V, De Laat M, Colman R, Eecloo K, Cocquyt V, Geboes K, Deliens L. Effect of early and systematic integration of palliative care in patients with advanced cancer: a randomised controlled trial. *Lancet Oncol.* 2018 Mar;19(3):394-404.

Whitney RL, Bell JF, Tancredi DJ, Romano PS, Bold RJ, Joseph JG. Hospitalization Rates and Predictors of Rehospitalization Among Individuals With Advanced Cancer in the Year After Diagnosis. *J Clin Oncol.* 2017 Nov 1;35(31):3610-3617.

Zimmermann C, Swami N, Krzyzanowska M, Hannon B, Leighl N, Oza A, Moore M, Rydall A, Rodin G, Tannock I, Donner A, Lo C. Early palliative care for patients with advanced cancer: a cluster-randomised controlled trial. *Lancet.* 2014 May 17;383(9930):1721-30.

Search Strategy

Database	Date	Search Strategy	Limits	Results
PubMed	Aug 15, 2018	<p>“colorectal carcinoma” OR “colorectal neoplasms” OR “lung carcinoma” “small cell lung carcinoma” OR “lung neoplasms” OR “pancreatic carcinoma” OR “pancreatic neoplasms” MeSH OR “colorectal carcinoma” OR “colorectal carcinomas” OR “colorectal cancer” OR “colorectal neoplasm” OR “colorectal neoplasms” OR “colorectal tumour” OR “colorectal tumours” OR “colorectal tumor” OR “colorectal tumors” Ti/ab. AND “palliative care” OR “palliative medicine” OR “palliative therapy” OR “palliative treatment” OR “palliative treatments” OR “terminal care” OR “hospice care” MeSH OR “palliative care” OR “palliative medicine” OR “palliative therapy” OR “palliative treatment” OR “palliative treatments” OR “terminal care” OR “hospice care” OR “early palliative care” OR “early palliative medicine” OR “ early palliative therapy” OR “early palliative treatment” OR “early palliative treatments” OR “early terminal care” OR “early hospice care” Ti/ab.</p>	English language, full text, humans, 2009-current	<p>74 articles identified</p> <p>18/74 articles selected that provided evidence for the impact of early vs. late or no palliative care were</p> <p>19 additional references identified through peer review</p>