

# When Does Early Palliative Care Influence Aggressive Care At The End of Life?

Mellar P Davis (✉ [mdavis2@geisinger.edu](mailto:mdavis2@geisinger.edu))

Geisinger Medical Center <https://orcid.org/0000-0002-7903-3993>

**Erin vanenkevort**

Geisinger Medical Center

**Alexander Elder**

Geisinger Medical Center

**Amanda Young**

Geisinger Medical Center

**Irina Correa Ordonez**

Geisinger Medical Center

**Mark Wojtowicz**

Geisinger Medical Center

**Halle Ellison**

Geisinger Medical Center

**Carlos Fernandez**

Geisinger Medical Center

**Zankhana Mehta**

Geisinger Medical Center

**Bertrand Behm**

Geisinger Medical Center

**Glen Digwood**

Geisinger Medical Center

**Rajiv Panikkar**

Geisinger Medical Center

---

## Research Article

**Keywords:** Aggressive, Care, End-of-Life, Palliative, Advance Directives

**Posted Date:** September 1st, 2021

**DOI:** <https://doi.org/10.21203/rs.3.rs-806612/v1>

**License:**  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

---

# Abstract

## Background

Early palliative care improves patient quality of life and influences cancer care. The time frame of early has not been established. Eight quality measures reflect aggressive care at the end of life. We retrospectively reviewed patients who died with cancer between January 1, 2018 through December 31, 2019, and compared the timing of palliative care consultation, advance directives (AD), and home palliative care with aggressive care at the end of life (ACEOL).

## Methods

Patients without ACEOL indicators were compared to patients with one or more than one indicator of ACEOL. The proportion of patients who received palliative care, completed AD, and the timing of palliative care and AD (less than 30 days, 60–90 days, and greater than 90 days prior to death) was compared for patients who had ACEOL versus those who did not. Chi-square analysis was used for categorical data, one-way ANOVA for continuous variables, and odds ratio (OR) with confidence intervals (CI) was reported as a measure of effect size. A p-value  $\leq 0.05$  was considered significant.

## Results

1727 patients died, 46% were female, and the mean age was 69 (SD 11.91). 71% had a palliative care consult, 26% completed AD, 888 (51.4%) had at least one indicator of ACEOL. AD completed at any time reduced ACEOL (OR 0.80, 95%CI 0.64–0.99). Palliative care was associated with a greater risk of ACEOL at 30 days (OR 5.32, 95% CI 3.94–7.18) and between 30 and 90 days (OR 1.39, 95% CI 1.07–1.80), but dramatically reduced ACEOL at > 90 days (OR 0.46, 95% CI 0.38–0.57). The most common indicator of ACEOL was new chemotherapy within 30 days of death, in 571 of 888 (64%) of patients experiencing ACEOL.

## Discussion

AD reduce ACEOL and often reflect goals of care and end-of-life discussions in the transition of care away from tumor directed therapy. Palliative care paradoxically in our experience is associated with greater ACEOL in the first 90 days since consultation occurs late in the course of illness and the focus is on crisis management in patients who are frequently utilizing the health care system. If palliative care consultation occurs greater than 90 days before death, there is the opportunity for both aggressive symptom management and end of life discussions which may influence aggressive care at the end of life.

# Conclusions

An initial palliative care consult greater than 90 days before death and ADs completed at any time during the disease trajectory significantly impacts care at the end of life. Both should become quality metrics for good cancer care.

## Introduction

Aggressive cancer care is considered poor quality care which includes chemotherapy at the end of life, multiple emergency department visits, rehospitalizations, intensive care unit (ICU) admissions and hospital mortality. A retrospective review of the National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) database dating from 1993 to 1996 identified characteristics of aggressive care at the end of life (ACEOL) (Table 1).<sup>1,2</sup> These seven indicators, and hospitalization for 14 days within the last month of life,<sup>1</sup> were identified as poor outcomes to cancer care.

**Table 1 Indicators of Aggressive Care at the End of Life**

New chemotherapy initiated within 30 days of death
Chemotherapy administered within 14 days of death
Greater than 1 hospitalization within 30 days of death
Greater than 2 emergency room visits within 30 days of death
An intensive care admission within 30 days of death
Death within the hospital
No hospice admission or hospice services of less than 3 days in duration

One third of patients are reported to have at least one indicator of ACEOL.<sup>3</sup> Several studies have found that early palliative care, reduces ACEOL.<sup>4,5</sup> Intrinsic to an early palliative care referral is a prognostic understanding of the patient's cancer.<sup>6,7</sup> Definitions and timeframe of early palliative care are not established.<sup>3</sup> Timely palliative care has been defined as more than 30 days before death, greater than eight weeks before death, and within eight weeks of diagnosis of metastatic disease.<sup>3,4,8,9</sup> Benefits to palliative care are reported to occur regardless of the trajectory of advanced cancer.<sup>10-12</sup> Paradoxically, palliative care has been associated with ACEOL if consultations are late in the disease course or patients are transferred to an inpatient palliative care unit.<sup>3</sup>

The multiple studies find that the time to palliative referral for the most part is late; the time between consultation and death ranges from five to fifty-four days.<sup>13-15</sup> In a recently published systematic review

and meta-analysis, the median time between palliative care consultation and death was 18.9 days (IQR 0.1).<sup>16</sup>

The purpose of this retrospective study was to primarily determine the the proportion of patients who underwent ACEOL. We wanted to understand the influence of a comprehensive palliative care program which consists of inpatient and outpatient services as well as an inpatient unit on ACEOL and the influence and timing of ADs on ACEOL. Our hypothesis was that palliative care service consultations first instituted greater than 30 days prior to death and preferably greater than 90 days before death and completed ADs would be associated with reduced ACEOL.

## Methods

This is a retrospective cohort study of patients ages 18–99 diagnosed with cancer, followed within the Geisinger Health System, who died in the years 2018 and 2019. Data were collected from the electronic medical record within the dates of 01/01/2018 to 12/31/2019. The study inclusion criteria included patients ages 18–99 with a diagnosis of cancer who received chemotherapy and died in 2018–2019. All patients had available to them inpatient and outpatient palliative care services but was dependent on the referring oncologist or primary care physician. The Geisinger Health Plan also has a community-based palliative care program for members; patients could receive Geisinger at Home Palliative services were included in the study.

Exclusion Criteria included patients who died within 30 days of the diagnosis of cancer. The primary outcome was the proportion of patients having indicator(s) of ACEOL as outlined and included the metric of 14 days of hospitalization in the last 30 days of life. Data for hospice referrals and duration of hospice services could not be obtained, therefore this indicator was excluded. The other outcome of interest was the completion and timing of ADs.

Demographic and clinical characteristics were summarized and compared across aggressive care groups defined as receiving no indicators of ACEOL compared to one or more indicators. Demographic and clinical data included sex, age at death, organ site of primary disease, Charlson Comorbidity Index (CCI), Geisinger Health Plan insurance, and clinical visit with hematology or oncology within 12 months before death. Frequencies and percentages were reported for categorical variables; for continuous variables mean and standard deviations were reported. To assess differences among patients who had one or more indicators of ACEOL to those who did not have any, Chi-square analyses were conducted on dichotomous and categorical data (e.g., sex) and one-way analysis of variance (ANOVA) tests were conducted for continuous outcome variables (e.g., age at death). Odds ratios from the Chi-square analysis were used as a measure of effect size. 95% confidence intervals and associated p-values are also reported. A p-value less than or equal to 0.05 indicated statistical significance. Statistical analyses were conducted using SOFTWARE VERSION\*\*\*.

This study was approved by the Geisinger Institutional Review Board.

## Results

Of the 1,727 eligible patients, 790 (46%) were female; the average age was 69 (SD = 11.9). Thirty-five percent (n = 611) had Geisinger Health Plan, 27% had lung cancer (n = 473), the majority (88%) of patients had hematology or oncology visits within 12 months prior to death. The average CCI score was seven (SD = 3.7).

There were no significant differences in sex or CCI scores between those receiving palliative care services and those not. There was a significant difference between patients who had no indicators of aggressive care at end of life, one indicator of aggressive care, and more than one indicator of aggressive care on type of cancer and age at death. Patients who received no aggressive care were older, and those with more than one indicator were younger than those who only had one indicator of aggressive care (Table 2).

Table 2  
Demographic Characteristics by Aggressive Care Indicators

	<b>Total</b>	<b>No aggressive care</b>	<b>One indicator of aggressive care</b>	<b>More than one indicator of aggressive care</b>	<b>P-Value</b>
	<b>(N = 1727)</b>	<b>(N = 839)</b>	<b>(N = 314)</b>	<b>(N = 574)</b>	
Female, N (%)	790 (45.7%)	387 (46.1%)	141 (44.9%)	262 (45.6%)	0.932
Age at Death, Mean (SD)	69.0 (11.91)	70.5 (12.01)	68.9 (11.82)	66.8 (11.48)	< .0001
Disease, N (%)					<b>0.024</b>
Bladder / Kidney	72 (4.2%)	32 (3.8%)	16 (5.1%)	24 (4.2%)	
Breast	113 (6.5%)	58 (6.9%)	18 (5.7%)	37 (6.4%)	
Colon / Rectum	137 (7.9%)	75 (8.9%)	24 (7.6%)	38 (6.6%)	
Esophageal	63 (3.6%)	27 (3.2%)	15 (4.8%)	21 (3.7%)	
Female Reproductive	99 (5.7%)	48 (5.7%)	22 (7.0%)	29 (5.1%)	
Head & Neck	76 (4.4%)	48 (5.7%)	12 (3.8%)	16 (2.8%)	
Liver & Bile Duct	28 (1.6%)	18 (2.1%)	1 (0.3%)	9 (1.6%)	
Lung	473 (27.4%)	220 (26.2%)	82 (26.1%)	171 (29.8%)	
Lymphoma	89 (5.2%)	39 (4.6%)	16 (5.1%)	34 (5.9%)	
Melanoma and other Skin	43 (2.5%)	19 (2.3%)	7 (2.2%)	17 (3.0%)	
Pancreas	112 (6.5%)	56 (6.7%)	26 (8.3%)	30 (5.2%)	
Prostate	95 (5.5%)	61 (7.3%)	15 (4.8%)	19 (3.3%)	
Thyroid	10 (0.6%)	5 (0.6%)	1 (0.3%)	4 (0.7%)	

	<b>Total</b>	<b>No aggressive care</b>	<b>One indicator of aggressive care</b>	<b>More than one indicator of aggressive care</b>	<b>P-Value</b>
Other	317 (18.4%)	133 (15.9%)	59 (18.8%)	125 (21.8%)	
Geisinger Health Plan, N (%)	611 (35.4%)	303 (36.1%)	118 (37.6%)	190 (33.1%)	0.339
HemOnc a year before, N (%)	1528 (88.5%)	741 (88.3%)	276 (87.9%)	511 (89.0%)	0.864
Charlson Score, Mean (SD)	7.1 (3.75)	7.2 (3.91)	7.0 (3.55)	7.0 (3.63)	0.454

Twenty-six percent had completed ADs documented. Patients who had no indicators had a greater percentage of documented ADs compared to patients who had ACEOL, but the difference was not statistically significant (Table 3). Ads were categorized as completed within 30 days, between 30 and 90 days, and more than 90 days before death. There were no significant group differences. Completed ADs reduced chemotherapy utilization within 30 days of death and ICU admissions (Table 4).

Table 3  
Advanced Directives by Aggressive Care Indicators

	<b>Total</b>	<b>Aggressive Care</b>	<b>No Aggressive Care</b>	<b>P-value<sup>1</sup></b>	<b>Odds Ratio (OR) (95% CI)</b>
	<b>(N = 1727)</b>	<b>(N = 888)</b>	<b>(N = 839)</b>		
Any Advanced Directive	443 (25.7%)	209 (23.5%)	234 (27.9%)	0.038	0.80 (0.64, 0.99)
Advanced Directives 30–90 days	4 (0.2%)	4 (0.5%)	0 (0.0%)	0.052	-
Advanced Directives > 90 days	439 (25.4%)	205 (23.1%)	234 (27.9%)	0.022	0.78 (0.62, 0.96)
<sup>1</sup> Chi-Square p-value					



Table 4  
The Influence of Advance Directives on Aggressive Care at the End of Life

Indicator	No Advanced Directives (n = 1284)	Advanced Directives (n = 443)	P-value <sup>1</sup>
New chemotherapy initiated within 30 days of death	448 (34.8%)	123 (27.8%)	0.006
Chemotherapy given within 2 weeks of death	204 (15.9%)	59 (13.3%)	0.194
An ICU admission within 30 days of death	54 (4.2%)	9 (2.0%)	0.035
Greater than 1 ED visit within 30 days of death	205 (16.0%)	67 (15.1%)	0.675
Greater than 1 hospitalization visit within 30 days of death	163 (12.7%)	59 (13.3%)	0.735
Death within the hospital	251 (19.5%)	84 (19.0%)	0.788
Admission greater than 14 days in last 30 days before death	107 (8.3%)	43 (9.7%)	0.376
<sup>1</sup> Chi-Square p-value			

Seventy-one percent had a palliative care consultation. This frequency differed among the groups. Specifically, 78% of patients who had more than one indicator of aggressive care, 70% of those who had one indicator, and 66% of those who did not receive ACEOL had palliative care services (Table 5). The odds of having a palliative care consultation for patients with one or more than one indicator of aggressive care was 1.20 (95% CI: 0.90, 1.59) and 1.78 (95% CI: 1.40, 2.27) fold greater than those with no indicators. This pattern was consistent with a large proportion of palliative care consultations within 30 days of death and palliative care consultations 30–90 days before death. However, those who had no indicators of aggressive care (45%), and one indicator of aggressive care (33%) were more likely to receive a palliative care consultation greater than 90 days before death compared to those who had more than one indicator of aggressive care (25%). The odds of a palliative care consult being initiated more than 90 days before death for those with one or more than one aggressive care indicator was 0.59 (95% CI: 0.45, 0.78) and 0.40 (95% CI: 0.32, 0.51) times the odds of those with no aggressive care indicators, respectively.

Table 5  
Palliative Care Services by Aggressive Care Indicators

	Total (N = 1727)	Aggressive Care (N = 888)	No Aggressive Care (N = 839)	P-value <sup>1</sup>	Odds Ratio (OR) (95% CI)
Any Palliative Care Services	1221 (70.7%)	666 (75.0%)	555 (66.2%)	< .0001	1.53 (1.25, 1.89)
Palliative Consult within 30 days	318 (18.4%)	258 (29.1%)	60 (7.2%)	< .0001	5.32 (3.94, 7.18)
Palliative Consult 30–90 days	278 (16.1%)	162 (18.2%)	116 (13.8%)	0.012	1.39 (1.07, 1.80)
Palliative Consult > 90 days	625 (36.2%)	246 (27.7%)	379 (45.2%)	< .0001	0.46 (0.38, 0.57)

<sup>1</sup>Chi-Square p-value

Seven percent received Geisinger at Home Palliative services which did not differ among groups. Geisinger at Home Palliative services within 30 days of death, 30–90 days before death, and more than 90 days before death also did not differ among groups.

Supportive services included completed Ads, palliative care services, and Geisinger at Home Palliative services. There was a significant difference in the number of supportive services across groups. Specifically, fewer patients who had more than one indicator of ACEOL received no supportive services compared to those with one indicator or no indicators. A greater percentage of patients who had more than one indicator received one supportive service compared to those who had one or no indicators. Patients with one indicator of aggressive care had the greatest percentage of receiving two supportive services, and those with no indicators had the greatest percentage of receiving all three supportive services. The odds of having one or more supportive services for those with one or more than one indicator of aggressive care was 0.98 (95% CI: 0.76, 1.22) and 0.88 (95% CI: 0.72, 1.08) relative to no aggressive care indicators, respectively (Table 6). To determine the impact of palliative care services, Geisinger at Home Palliative and palliative care inpatient and outpatient consultations were combined to create a “palliative care service” indicator. Table 6 demonstrates the differences across groups; no supportive services, palliative care services only, palliative care services and ADs, or only ADs. There is a significant difference among groups ( $p = 0.0003$ ) where the odds of supportive services for patients with one or more than one indicator of ACEOL of 0.84 (95% CI: 0.66, 1.07) and 0.61 (95% CI: 0.50, 0.75) fold less than those with no indicators, respectively (Table 6). We also examined the influence of any supportive services that included palliative care services compared to those who only completed ADs or no supportive services (Supplementary Table 1). There was a significant group difference ( $p = 0.0001$ ). The odds of any supportive services that included palliative care for those with one or more than

one indicator was 1.18 (95% CI: 0.88, 1.57) and 1.71 (95% CI: 1.33, 2.19) fold the odds of those with no indicators, respectively.

Table 6  
Supportive services by Indicators of Aggressive Care.

	<b>Total</b>	<b>Aggressive Care</b>	<b>No Aggressive Care</b>	<b>P-value<sup>1</sup></b>	<b>Odds Ratio (OR) (95%CI)</b>
	<b>(N = 1727)</b>	<b>(N = 888)</b>	<b>(N = 839)</b>		
<b>Number of Supportive Services</b>				0.052	0.91 (0.76, 1.10)
No Supportive Services	370 (21.4%)	173 (19.5%)	197 (23.5%)		
1 supportive service	956 (55.4%)	511 (57.5%)	445 (53.0%)		
2 supportive services	366 (21.2%)	191 (21.5%)	175 (20.9%)		
3 supportive services	35 (2.0%)	13 (1.5%)	22 (2.6%)		
<b>Palliative Care vs. Advanced Directives</b>				0.0002	0.69 (0.57, 0.82)
no supportive services	370 (21.4%)	173 (19.5%)	197 (23.5%)		
advanced directives only	98 (5.7%)	34 (3.8%)	64 (7.6%)		
palliative care only	914 (52.9%)	506 (57.0%)	408 (48.6%)		
palliative care and advanced directives	345 (20.0%)	175 (19.7%)	170 (20.3%)		
<b>Any Palliative Care vs. Advanced Directives</b>				0.0001	0.66 (0.53, 0.81)
no supportive services	370 (21.4%)	173 (19.5%)	197 (23.5%)		
advanced directives only	98 (5.7%)	34 (3.8%)	64 (7.6%)		
palliative care services	1259 (72.9%)	681 (76.7%)	578 (68.9%)		
<b>Palliative Care vs. No Palliative Care</b>				0.0003	1.49 (1.20, 1.84)
no palliative care services	468 (27.1%)	207 (23.3%)	261 (31.1%)		

	Total	Aggressive Care	No Aggressive Care	P-value <sup>1</sup>	Odds Ratio (OR) (95%CI)
	(N = 1727)	(N = 888)	(N = 839)		
palliative care services	1259 (72.9%)	681 (76.7%)	578 (68.9%)		
<sup>1</sup> Chi-Square p-value					

Three hundred fourteen of 888(35.4%) patients had one ACEOL indicator and 574 (64.6%) had more than one indicator ( Supplementary Table 1,2). The most common indicator was chemotherapy within the last 30 days of life, which occurred in 571 of 888 (64.3%) patients. Younger patients were more likely to receive chemotherapy within the last 30 days of life. Neither sex nor CCI influenced chemotherapy at 30 or 15 days before death. ( Supplementary Table 3). Approximately 20% of patients died in the hospital. The least common indicator was ICU admissions, which occurred in 63 of 888 patients (7%). Compared with no palliative care services, palliative care initiated at greater than 90 days reduced new chemotherapy within 30 days of death and chemotherapy administered within 15 days of death ( Supplementary Table 4). Palliative care services initiated greater than 90 days before death was associated with decreased emergency department utilization and hospital admission compared with palliative care initiated at less than 90 days but not less than those who were not seen by palliative care. However, patients who had a palliative consult greater than 90 days before death had significantly less chemotherapy initiated within 30 days of death and less chemotherapy continued within 2 weeks of death then those who had not had a palliative care consult (Supplementary Table 4).

## Discussion

Half of patients who died in the years 2018 and 2018 had at least one indicator of ACEOL; only 1/3 were seen greater than 90 days prior to death. A quarter of the patients had completed ADs, most were completed > 90 days prior to death. Documented ADs reduced ACEOL by reducing the number of patients receiving chemotherapy at the end-of-life and ICU admission. ADs completed at any point in time did reduce ACEOL though few though were completed < 90 days before death. Palliative care consultation > 90 days before death reduced ACEOL by reducing chemotherapy given in the last month of life.

Completion of ADs reduces aggressive care at the end of life. This requires discussions about patient values and an understanding of prognosis. End-of life-discussions are more likely to have occurred for those with an AD. Prognostic awareness occurs in 49% of patients with an advanced illness but this varied based upon country.<sup>17</sup> Lack of prognostic awareness and inaccurate prognostication are associated with ACEOL.<sup>6,18-21</sup> Oncologists tend to be optimistic in their prognostication.<sup>22</sup> Hence, they may put off AD discussions until late in the course of cancer. “ Hoping for the best but planning for the worst” may be an important way of approaching patients about personal values in light of an incurable

illness with completion ADs in a timely fashion even if a timeframe of survival is not discussed or does not want to be discussed by patients.<sup>23</sup>

In a retrospective review of patients with advanced cancer, completion of ADs greater than 90 days before death reduced rehospitalization within 90 days of death (odds ratio 0.21:90 5% CI 0.12 to 0.37).<sup>24</sup> A second retrospective study of women with advanced ovarian cancer found that end-of-life discussions greater than 30 days before death reduced chemotherapy in the last 14 days of life, reduced hospitalizations within 30 days of death and increased the number of hospice days.<sup>25</sup> In a large cohort study of lung and colon cancer patients, 39% of end-of-life discussions took place in the last 30 days of death. For the subset in which discussions took place greater than 30 days before death there was a reduction in all indicators of ACEOL except ICU admissions.<sup>6</sup> The Cancer Care Outcomes Research and Surveillance Consortium study found that the median time between end-of-life discussions and death was 33 days suggesting that for many there is a lost opportunity to discuss choices at the end-of-life.<sup>26</sup> Also, a significant proportion of patients do not engage or do not want to engage in end of life discussions and a significant proportion of end of life discussions occur under crisis conditions in the last 30 days of life. Less than half of physicians know their patients' preferences for end-of-life care including resuscitation.<sup>6,27-30</sup> Completion of ADs prior to hospitalization is preferred. Most patients prior to admission have decision-making capacity but half of advanced cancer patients lose decision making capacity in hospital. If then a surrogate becomes the decision-maker in the place of patient, there is a greater risk that ACEOL will take place.<sup>31</sup> Decisions regarding resuscitation prior to hospitalization reduces the number resuscitations that occur after hospitalization, reduces intensive care unit length of stay and hospital mortality.<sup>32</sup>

Our findings are consistent with two systematic reviews.<sup>33,34</sup> Both reviews demonstrated that end-of-life discussions and advanced care planning reduces ACEOL and healthcare expenditures. Reduction in intensive care utilization (odds ratio 0.26–0.68) and chemotherapy (odds ratio 0.41–0.57) were two major benefits.

Many patients have end- of-life discussions but not recorded in the medical record. One study found that only 48% were recorded in the medical record and 23% were known only through interviewing the surrogate decision-maker.<sup>6</sup> It is possible that more patients had Ads in our study but were not documented in the medical record

Seventy percent of patients who died of were cancer were seen by our palliative care service but only 1/3 were seen greater than 90 days prior to death. Palliative care consultations within 90 days of death were associated with increased ACEOL ; only those patients initially seen greater than 90 days prior to death had a significant reduction in ACEOL.

Half of patients dying of cancer in our study had at least one indicator of aggressive care and is consistent with a retrospective study of women with gynecological cancers. In this study 41% had at least one indicator.<sup>35</sup> Younger patients are more likely to receive chemotherapy at the end of life. Comorbidities

and gender did not play a role in ACEOL in our study Comorbidity has been published as a risk factor for ACEOL.<sup>36</sup> Gender in several other studies was found to be different with males undergoing more aggressive care and women received less ACEOL.<sup>2,3,10</sup> This may reflect differences in referral and individual oncologist's practice style.

A small study of patients with cervical cancer found that the median time frame for palliative care referral before death was 2.3 months with 34% referred within the last month of life.<sup>37</sup> A systematic review found the average time from palliative care consultation to death was 18.9 days.<sup>16</sup>

In a large review of patients with advanced gastrointestinal cancers (n = 34,630) the median time from palliative care to death was 76 days and 46% had palliative care services initiated greater than 90 days prior to death. Twelve percent had services initiated within 7 days of dying.<sup>12</sup> A retrospective review of patients with pancreatic cancer found the median survival time from palliative consultation was 75 days, only 52% had palliative care consultations.<sup>10</sup>

We uniquely found that palliative care consultations within 90 days of death was associated with more ACEOL which differs from previously published studies.<sup>10,12</sup> Few studies have looked at the time-frame of palliative care and ACEOL. This likely reflects crisis intervention at the end-of-life in patients who have had multiple hospitalizations, emergency room visits and may be in the ICU in which primary services feel a goals of care discussion is needed or a transition to hospice or comfort care is needed. Patients are often seen by our service for the first time after several emergency department visits or readmission after receiving chemotherapy or for reasons of cancer. Our experience is not unique<sup>3</sup>. A retrospective study of patients with pancreatic cancer found that late palliative care consultations defined as occurring less than 90 days prior to death was associated with an 18% greater use of the emergency department, a 12.5% greater number of hospitalizations and increased chemotherapy in the last 30 days of life.<sup>38</sup>

We observed a robust reduction in ACEOL when a palliative care consultation took place greater than 90 days before death. Though there is no universal definition of "early palliative care", we believe that > 90 days before death has practical utility. Others have defined "early palliative care" as consultations > 90 days to death to within 8 weeks of the diagnosis of metastatic disease.<sup>3,4,11</sup> Two studies suggest that the number of contacts may be an important factor to early palliative care.<sup>10,39</sup> Increased contacts between the patient and palliative services reduce ACEOL and with > 90 days of time, the number of contacts are likely to increase which allows for the development of trusting relationship, time for symptom management and end-of-life discussions. Two studies suggest that the number of contacts are an important factor in early palliative care.<sup>10,39</sup> A systematic referral of patients with incurable cancer facilitates early referral and is more likely reduce ACEOL.<sup>9</sup>

We found that 64% of patients who experience ACEOL receive new chemotherapy within 1 month of death and nearly 30% continue chemotherapy within 2 weeks of death. Frequency of other indicators is consistent with the literature.<sup>40</sup> A retrospective study of patients who received chemotherapy within 3

months of death found that 52% were treated with chemotherapy in the last month of life and 29% in the last 2 weeks of life.<sup>41</sup> Another study, contrary to ours, found that though hospital deaths were more frequent than ours (47.7%), chemotherapy within 14 days of death was only 12.9%, 9.1% had new chemotherapy started within 30 days of death.<sup>42</sup> Maltoni and colleagues found that early palliative care defined as palliative care within 8 weeks of diagnosis reduced chemotherapy from 27.8–18.7% in the last month of life.<sup>9</sup> A second study demonstrated a reduction in late chemotherapy from 24.5–16.7% with early palliative care defined as palliative care greater than 90 days before death.<sup>38</sup> Multiple other studies have demonstrated the same though not consistently.<sup>10–12, 37</sup>

. Even though the prognosis may be the same regardless of age, younger patients are more likely to receive anti-cancer therapy within the last month of life. A Finnish study found that 33% of patients less than 50 years old received chemotherapy in the last month of life versus 10% of those 80 years or older.<sup>43</sup>

The use of chemotherapy within 14 days of death has increased over 2 decades.<sup>1</sup> One reason, is that there are more treatment options. There can be unrealistic expectations of chemotherapy or fear of “doing nothing” on the part of the patient and physician.<sup>21</sup> A

This study has several weaknesses. We defined advanced cancer patients by their diagnosis and by receiving chemotherapy. Some patients may have received adjuvant chemotherapy and died from other causes rather than their cancer. The association of ACEOL with palliative care < 90 days may reflect a referral pattern of sicker patients though the CCI did not differ between groups. We were unable to obtain hospice referral data which is one of the indicators of ACEOL and hence some patients in the “nonaggressive care” group may actually have been referred to hospice later or not at all and would have been part of the group experiencing ACEOL. The use of palliative care services early in the course of advanced cancer and completed ADs may reflect a patient’s value which emphasizes quality of life and less ACEOL. Finally, there could be unmeasured confounders that we did not include that could have influenced the results. This was a single institution study and so may not be generalizable.

## Conclusions

Half of patients who died with cancer experience at least one indicator of ACEOL.. Palliative care consultations greater than 90 days before death significantly reduces ACEOL as does completion of ADs. The most frequent indicator of aggressive care is new chemotherapy within 30 days of death. In our experience early palliative care should be defined as palliative care consultations occurring more than 90 days before death. Early palliative care and completion of ADs should be quality metrics within cancer programs.

## Declarations

**Funding:** None



**Conflicts of interest/Competing interests:** None

**Availability of data and material:** NA

**Code availability:** NA

**Authors' contributions:**

Manuscript development and writing; Mellar Davis, Erin A. Vanenkevort, Alexander Elder, Amanda Young, Irina D. Correa Ordonez, Mark J Wojtowicz, Halle Ellison, Carlos Fernandez, Zankhana Mehta, Bertrand Behm, Glen Digwood, Rajiv Panikkar

**Ethics approval:** NA

**Consent to participate:** NA

**Consent for publication:** NA

## References

1. Earle CC, Landrum MB, Souza JM, Neville BA, Weeks JC, Ayanian JZ (2008) Aggressiveness of cancer care near the end of life: is it a quality-of-care issue? *J Clin Oncol* 26(23):3860–3866
2. Earle CC, Neville BA, Landrum MB, Ayanian JZ, Block SD, Weeks JC (2004) Trends in the aggressiveness of cancer care near the end of life. *J Clin Oncol* 22(2):315–321
3. Hui D, Kim SH, Roquemore J, Dev R, Chisholm G, Bruera E (2014) Impact of timing and setting of palliative care referral on quality of end-of-life care in cancer patients. *Cancer* 120(11):1743–1749
4. Temel JS, Greer JA, Muzikansky A et al (2010) Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med* 363(8):733–742
5. Zimmermann C, Swami N, Krzyzanowska M et al (2014) Early palliative care for patients with advanced cancer: a cluster-randomised controlled trial. *Lancet* 383(9930):1721–1730
6. Mack JW, Cronin A, Keating NL et al (2012) Associations between end-of-life discussion characteristics and care received near death: a prospective cohort study. *J Clin Oncol* 30(35):4387–4395
7. Yoong J, Park ER, Greer JA et al (2013) Early palliative care in advanced lung cancer: a qualitative study. *JAMA Intern Med* 173(4):283–290
8. Chow E, Abdoell M, Panzarella T et al (2008) Predictive model for survival in patients with advanced cancer. *J Clin Oncol* 26(36):5863–5869
9. Maltoni M, Scarpi E, Dall'Agata M et al (2016) Systematic versus on-demand early palliative care: results from a multicentre, randomised clinical trial. *Eur J Cancer* 65:61–68
10. Jang RW, Krzyzanowska MK, Zimmermann C, Taback N, Alibhai SM. Palliative care and the aggressiveness of end-of-life care in patients with advanced pancreatic cancer. *J Natl Cancer Inst.*

2015;107(3)

11. Lees C, Weerasinghe S, Lamond N, Younis T, Ramjeesingh R (2019) Palliative care consultation and aggressive care at end of life in unresectable pancreatic cancer. *Curr Oncol* 26(1):28–36
12. Merchant SJ, Brogly SB, Goldie C et al (2018) Palliative Care is Associated with Reduced Aggressive End-of-Life Care in Patients with Gastrointestinal Cancer. *Ann Surg Oncol* 25(6):1478–1487
13. Good PD, Cavenagh J, Ravenscroft PJ (2004) Survival after enrollment in an Australian palliative care program. *J Pain Symptom Manage* 27(4):310–315
14. Bennett MI, Ziegler L, Allsop M, Daniel S, Hurlow A (2016) What determines duration of palliative care before death for patients with advanced disease? A retrospective cohort study of community and hospital palliative care provision in a large UK city. *BMJ Open* 6(12):e012576
15. Lamont EB, Christakis NA (2002) Physician factors in the timing of cancer patient referral to hospice palliative care. *Cancer* 94(10):2733–2737
16. Jordan RI, Allsop MJ, ElMokhallalati Y et al (2020) Duration of palliative care before death in international routine practice: a systematic review and meta-analysis. *BMC Med* 18(1):368
17. Chen CH, Kuo SC, Tang ST (2017) Current status of accurate prognostic awareness in advanced/terminally ill cancer patients: Systematic review and meta-regression analysis. *Palliat Med* 31(5):406–418
18. Tang ST, Wen FH, Hsieh CH et al (2016) Preferences for Life-Sustaining Treatments and Associations With Accurate Prognostic Awareness and Depressive Symptoms in Terminally Ill Cancer Patients' Last Year of Life. *J Pain Symptom Manage* 51(1):41–51 e41
19. Liu LN, Chen CH, Liu TW, Lin YC, Lee SC, Tang ST (2015) Preferences for Aggressive End-of-life Care and Their Determinants Among Taiwanese Terminally Ill Cancer Patients. *Cancer Nurs* 38(3):E9–E18
20. Weeks JC, Catalano PJ, Cronin A et al (2012) Patients' expectations about effects of chemotherapy for advanced cancer. *N Engl J Med* 367(17):1616–1625
21. Weeks JC, Cook EF, O'Day SJ et al (1998) Relationship between cancer patients' predictions of prognosis and their treatment preferences. *JAMA* 279(21):1709–1714
22. Kao SC, Butow P, Bray V, Clarke SJ, Vardy J (2011) Patient and oncologist estimates of survival in advanced cancer patients. *Psychooncology* 20(2):213–218
23. Nogler AF (2014) Hoping for the best, preparing for the worst: strategies to promote honesty and prevent medical futility at end-of-life. *Dimens Crit Care Nurs* 33(1):22–27
24. Emiloju OE, Djibo DAM, Ford JG (2020) Association Between the Timing of Goals-of-Care Discussion and Hospitalization Outcomes in Patients With Metastatic Cancer. *Am J Hosp Palliat Care* 37(6):433–438
25. Lopez-Acevedo M, Havrilesky LJ, Broadwater G et al (2013) Timing of end-of-life care discussion with performance on end-of-life quality indicators in ovarian cancer. *Gynecol Oncol* 130(1):156–161
26. Mack JW, Cronin A, Taback N et al (2012) End-of-life care discussions among patients with advanced cancer: a cohort study. *Ann Intern Med* 156(3):204–210

27. Narang AK, Wright AA, Nicholas LH (2015) Trends in Advance Care Planning in Patients With Cancer: Results From a National Longitudinal Survey. *JAMA Oncol* 1(5):601–608
28. Lund S, Richardson A, May C (2015) Barriers to advance care planning at the end of life: an explanatory systematic review of implementation studies. *PLoS One* 10(2):e0116629
29. Rocque GB, Dionne-Odom JN, Sylvia Huang CH et al (2017) Implementation and Impact of Patient Lay Navigator-Led Advance Care Planning Conversations. *J Pain Symptom Manage* 53(4):682–692
30. A controlled trial to improve care for seriously ill hospitalized patients (1995) The study to understand prognoses and preferences for outcomes and risks of treatments (SUPPORT). The SUPPORT Principal Investigators. *JAMA* 274(20):1591–1598
31. Zaros MC, Curtis JR, Silveira MJ, Elmore JG (2013) Opportunity lost: end-of-life discussions in cancer patients who die in the hospital. *J Hosp Med* 8(6):334–340
32. Marcia L, Ashman ZW, Pillado EB, Kim DY, Plurad DS (2018) Advance Directive and Do-Not-Resuscitate Status among Advanced Cancer Patients with Acute Care Surgical Consultation. *Am Surg* 84(10):1565–1569
33. Abedini NC, Hechtman RK, Singh AD et al (2019) Interventions to reduce aggressive care at end of life among patients with cancer: a systematic review. *Lancet Oncol* 20(11):e627–e636
34. Starr LT, Ulrich CM, Corey KL, Meghani SH (2019) Associations Among End-of-Life Discussions, Health-Care Utilization, and Costs in Persons With Advanced Cancer: A Systematic Review. *Am J Hosp Palliat Care* 36(10):913–926
35. Schneiter MK, Karlekar MB, Crispens MA, Prescott LS, Brown AJ (2019) The earlier the better: the role of palliative care consultation on aggressive end of life care, hospice utilization, and advance care planning documentation among gynecologic oncology patients. *Support Care Cancer* 27(5):1927–1934
36. Wright AA, Keating NL, Ayanian JZ et al (2016) Family Perspectives on Aggressive Cancer Care Near the End of Life. *JAMA* 315(3):284–292
37. Bercow AS, Nitecki R, Haber H et al (2021) Palliative care referral patterns and measures of aggressive care at the end of life in patients with cervical cancer. *Int J Gynecol Cancer* 31(1):66–72
38. Michael N, Beale G, O'Callaghan C et al (2019) Timing of palliative care referral and aggressive cancer care toward the end-of-life in pancreatic cancer: a retrospective, single-center observational study. *BMC Palliat Care* 18(1):13
39. Maltoni M, Scarpi E, Dall'Agata M et al (2016) Systematic versus on-demand early palliative care: A randomised clinical trial assessing quality of care and treatment aggressiveness near the end of life. *Eur J Cancer* 69:110–118
40. Bylicki O, Didier M, Riviere F, Margery J, Grassin F, Chouaid C (2019) Lung cancer and end-of-life care: a systematic review and thematic synthesis of aggressive inpatient care. *BMJ Support Palliat Care* 9(4):413–424
41. Urvay S, Civelek B, Ozaslan E, Surel AA (2021) Chemotherapy at the End of Life. *J Palliat Care* 36(2):73–77

42. Garcia-Martin E, Escudero-Vilaplana V, Fox B et al (2021) Aggressiveness of end-of-life cancer care: what happens in clinical practice? *Support Care Cancer* 29(6):3121–3127
43. Rautakorpi LK, Seyednasrollah F, Makela JM et al (2017) End-of-life chemotherapy use at a Finnish university hospital: a retrospective cohort study. *Acta Oncol* 56(10):1272–1276

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [SupplementaryTable1.docx](#)
- [SupplementaryTable2.docx](#)
- [SupplementaryTable3.docx](#)
- [SupplementaryTable4.docx](#)