CORE Cancer Outcomes Research & Education

Integrating Palliative and Oncology Care: Past, Present, and Future

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HARVARD MEDICAL SCHOOL

Overview

1. Why did this effort to integrate palliative and oncology care begin?
2. What is the status of the field?
3. What is the future of palliative care for patients with serious cancers?

Why did we start thinking about the possible role for early integration of palliative care for patients with cancer?

Historical Role of Palliative Care in Oncology

- The role of palliative care in the hospital or home setting for patients near the end of life had been established for many decades.

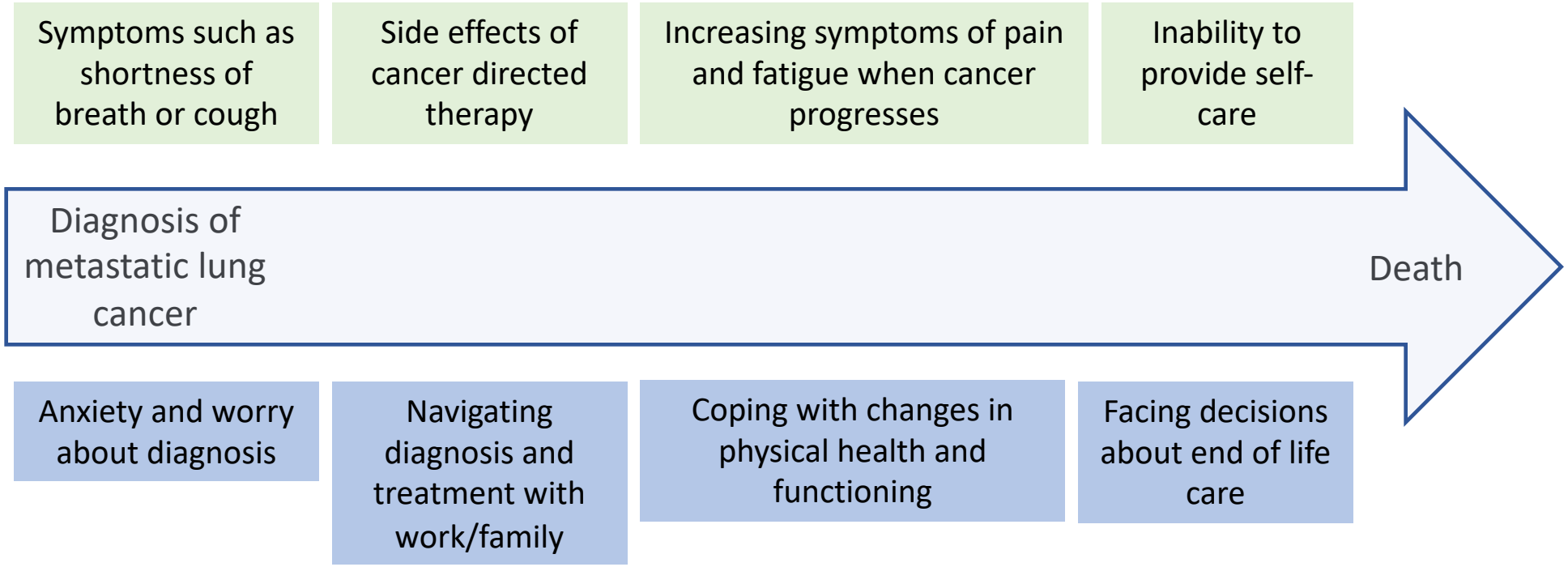
Hospital Setting: Oncology inpatient teams often requested palliative care consultations for hospitalized patients with difficult to control symptoms or challenging end of life care circumstances.

Home Setting: Many patients who died of cancer received hospice services in their home for some period prior to death.

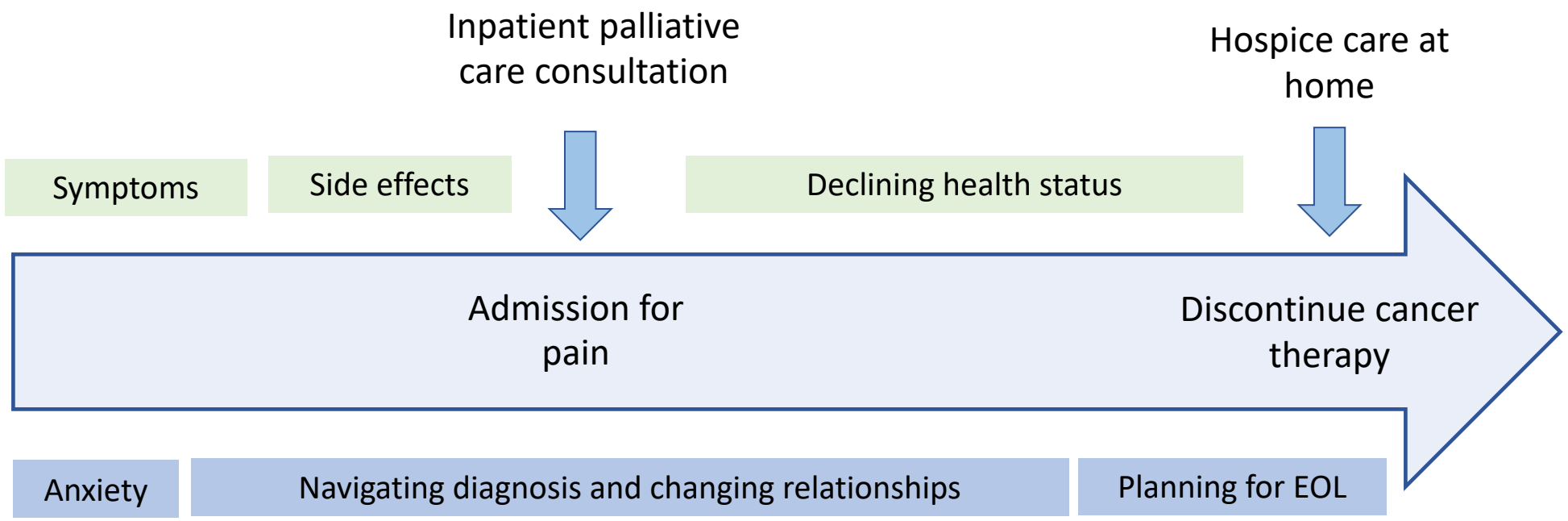
Historical Role of Palliative Care In Oncology

- Inpatient palliative care consultation and hospice left patients and their family members with unmet needs throughout their illness course.
  - Uncontrolled physical and psychological symptoms.
  - Insufficient communication about prognosis, treatment intent, and end of life care.

What is it like for a patient living with a serious cancer, such as metastatic non-small cell lung cancer?

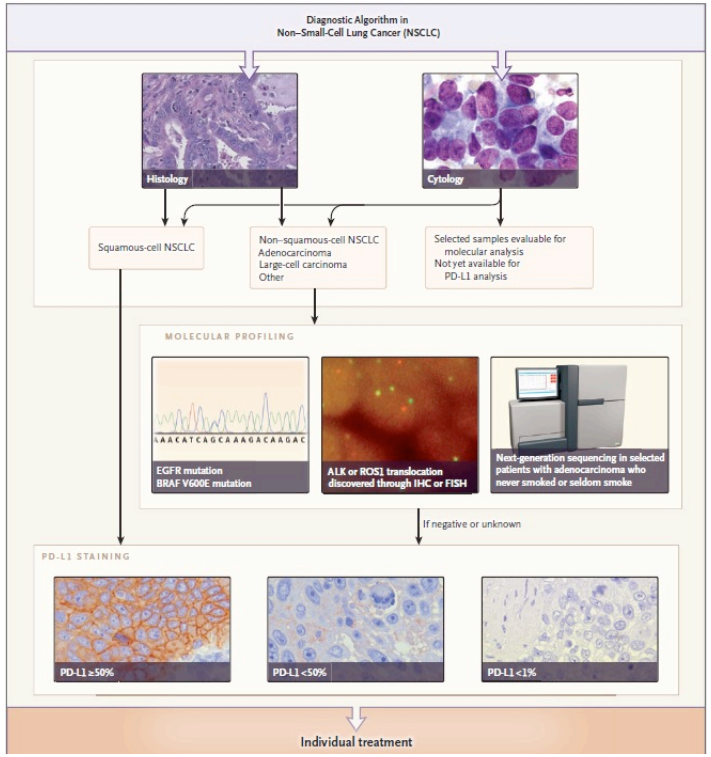


Historical Role of Palliative Care in Oncology



Shouldn't Oncology Clinicians Be Addressing These Issues?

- Of course, oncology is and should be attending to these issues.
- But can we really expect oncology clinicians to be able to do it all?
  - Especially as the complexity of cancer care has increased



Oncology Care Models are Already Complex

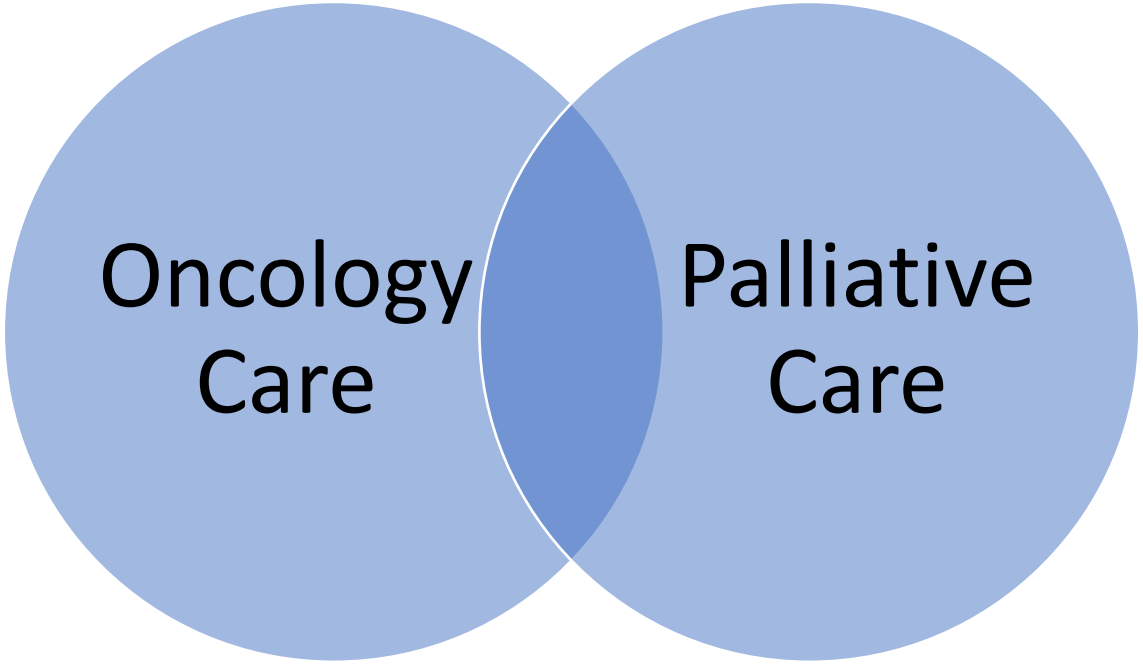
- Oncology follow up visits are often booked for 15 or 20 minutes in which clinicians need to:
  - Discuss genetic/molecular testing results
  - Evaluate patients for clinical trials and optimal treatment regimens
  - Enroll patients on clinical trials (including supportive care studies)
  - Assess and manage treatment related toxicities and adjust treatment regimens

What can palliative care do when they are involved early and throughout the illness?

1. Collaborate with oncology to manage patients' physical and psychological symptoms.
2. Help patient's cope with living with a serious illness.
3. Engage patients and their family in discussions about the illness, prognosis and (eventually) their end-of-life care preferences.
4. Include the family as recipients of care.

While patients are receiving the best possible cancer treatment

Care Should be Collaborative and Integrated



Integrated Palliative and Oncology Care

Historical Model

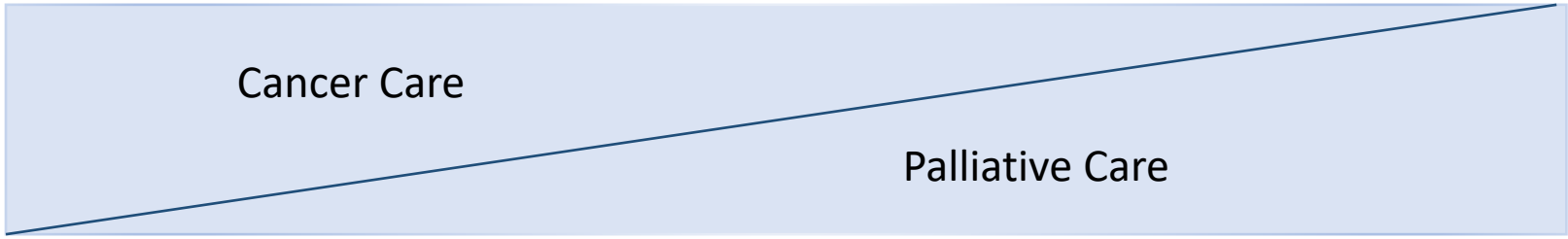
Pros: Less complex

Con: Palliative care too late

Integrated Care Model

Pro: Early palliative care

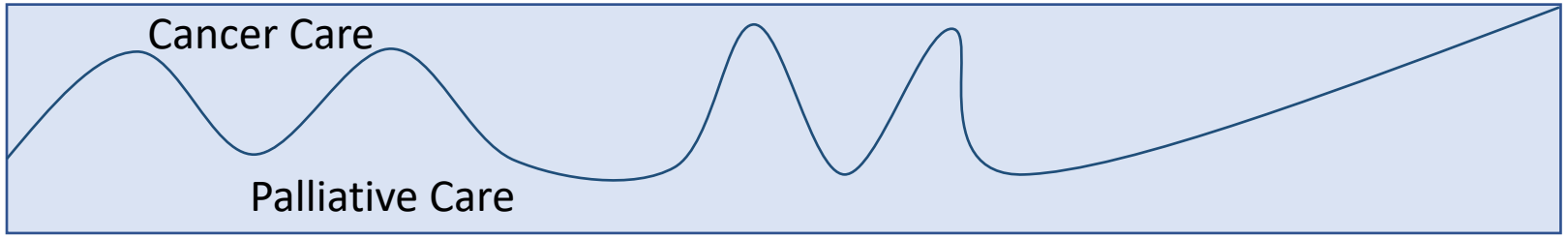
Con: Assumes needs are linear



Personalized Care Model

Pro: Palliative care based upon needs

Con: Most complex



Why is Integrated Care Complex?

- Who will provide palliative care?
- What domains will palliative care address?
- Where will palliative care see patients?
- How will patients be scheduled to see palliative care?
- When will palliative care visits be scheduled?

Randomized Trials of Integrated Palliative Care and Oncology Care

Outpatient Palliative Care Interventions

Telephone-based early palliative care model

In person early palliative care models

Inpatient Palliative Care Interventions

In person early palliative care models

Outpatient Palliative Care Interventions

Telephone-based early palliative care model

In person early palliative care models

Telephone Based Outpatient Early Palliative Care (ENABLE Trials)

- Telephone-based intervention delivered by advanced practice nurses with palliative care training.
- Manualized psycho-education with four weekly structured sessions:
  - Problem solving
  - Communication and social support
  - Symptom management
  - Advance care planning and unfinished business
- Monthly telephone follow up to assess the need for referrals (e.g., to palliative care).

Project ENABLE II

322 patients within 8-12 weeks of a new diagnosis of GI, lung, GU or breast cancer with a prognosis of approximately one year

ENABLE intervention

Usual Care

Outcome Measures

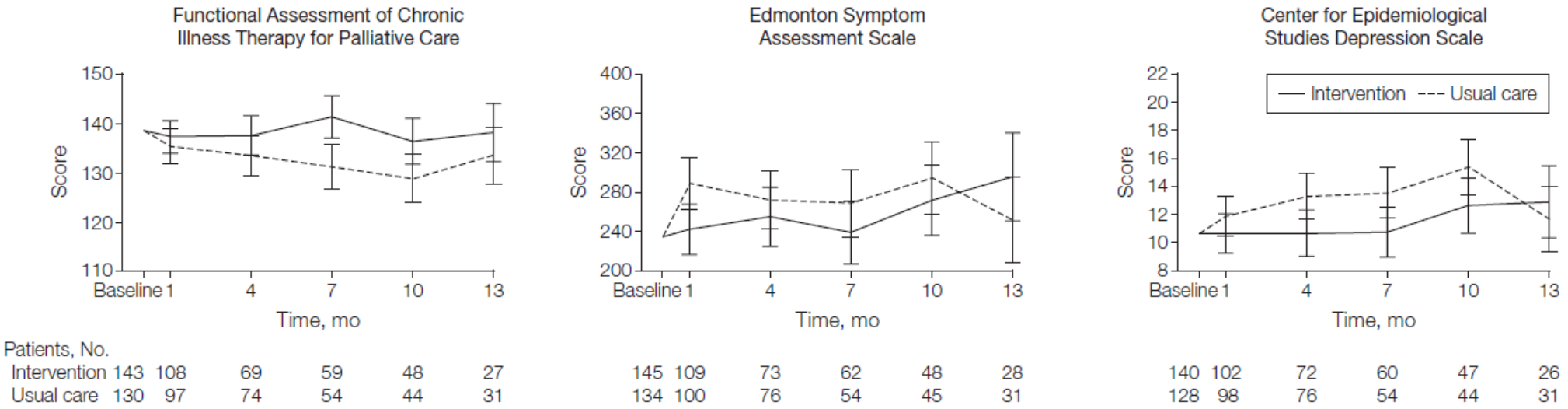
Patient-reported Measures
1. Quality of life
2. Symptoms
3. Depression

Health Service Utilization
1. Completion of advanced directives
2. Referral for palliative care or hospice
3. Days in hospital, intensive care unit and emergency department

Bakitas JAMA 302(7) 2009

ENABLE II – Patient Reported Outcomes

Figure 2. Quality of Life, Symptom Intensity, and Mood Scores for All Patients



Quality of Life
p=0.02

Symptom Burden
p=0.06

Depression
p=0.02

Bakitas JAMA 302(7) 2009

Project ENABLE II

	Full Study Cohort			Deceased Cohort		
	Intervention n=161	Usual Care n=161		Intervention n=161	Usual Care n=161	
Type of advance directive[e]						
Living will	69 (42.9)	76 (47.2)	.50	63 (43.4)	66 (49.2)	.34
Durable power of attorney for health care	68 (42.2)	78 (48.4)	.31	62 (42.8)	67 (50.0)	.23
Do not resuscitate order	13 (8.1)	10 (6.2)	.67	11 (7.6)	7 (5.2)	.47
Referral to hospice[e]	6 (3.7)	4 (2.5)	.75	4 (2.8)	2 (1.5)	.68
Referral to palliative care[e]	42 (26.1)	51 (31.7)	.32	34 (23.4)	39 (29.1)	.34
Resource use in prior 3 mo, mean (median) [maximum][f]						
Hospital days[e]	2.8 (0) [25]	3.1 (0) [25]	.06	2.6 (0) [25]	2.8 (0) [24]	.60
Intensive care unit days[e]	0.02 (0) [2]	0.04 (0) [2]	.41	0.03 (0) [2]	0.05 (0) [2]	.36
Emergency department visits[e]	0.27 (0) [3]	0.41 (0) [5]	.37	0.28 (0) [3]	0.38 (0) [4]	.62

Bakitas JAMA 302(7) 2009

Take Home Points From ENABLE

- Patients are really suffering with uncontrolled physical and psychological symptoms that are impacting their quality of life and it is *not that hard* to make it better.
  - First "proof-of-principal" that early attention to palliative care improves outcomes for patients with cancer
- But….this telephone-based intervention was not sufficient for impacting health care utilization or delivery of end-of-life care.

In Person Outpatient Early Palliative Care

- In-person palliative care with physician or advanced practice provider at least monthly.
  - MGH Model "early integrated palliative care"

    Patients with newly diagnosed incurable cancer receive palliative care until death.
  - Zimmermann Canadian Study

    Patients with a physician estimated limited life expectancy (6-24 months) receive a four-month palliative care intervention.
- Involvement of palliative care when admitted to the hospital.

Operationalizing the MGH Early Integrated Palliative Care Model

- Palliative care visits conducted by physician or advanced practice nurse.
- Palliative care was not manualized, although care followed National Quality Forum guidelines.
- Palliative care visits occurred on the same day as oncology visits.
  - Palliative care visits often take place in the infusion room.
  - Occasionally palliative care and oncology clinicians saw patients in the same room at the same time ("joint visits").
- Telephone calls as needed to maintain monthly contact

Randomized Trial of Early Integrated Palliative Care in Patients with Metastatic Lung Cancer

150 patients within 8 weeks of diagnosis of metastatic NSCLC with an ECOG PS 0-2

Integrated care
- Monthly palliative care visits weeks in conjunction with oncology visits

Standard care
- Palliative care visits only upon request

Study Measures

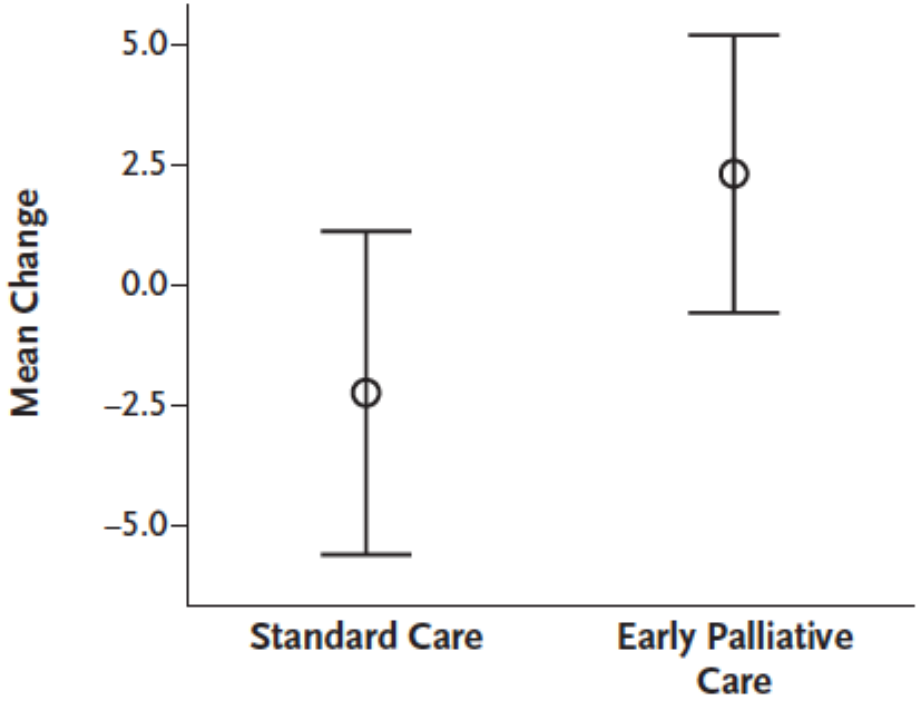
Patient-reported measures
1. Quality of life
2. Mood
3. Prognostic awareness

Health service utilization
1. Documentation of resuscitation preferences
2. Hospice utilization
3. Chemotherapy administration

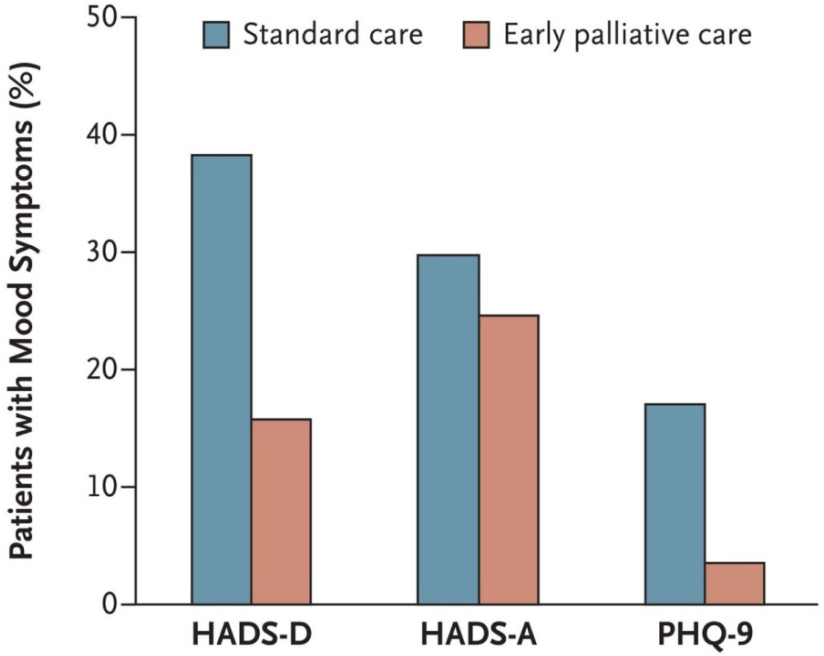
Temel NEJM 363(8) 2010

Lung Cancer Trial – Patient-Reported Outcomes

Quality of life



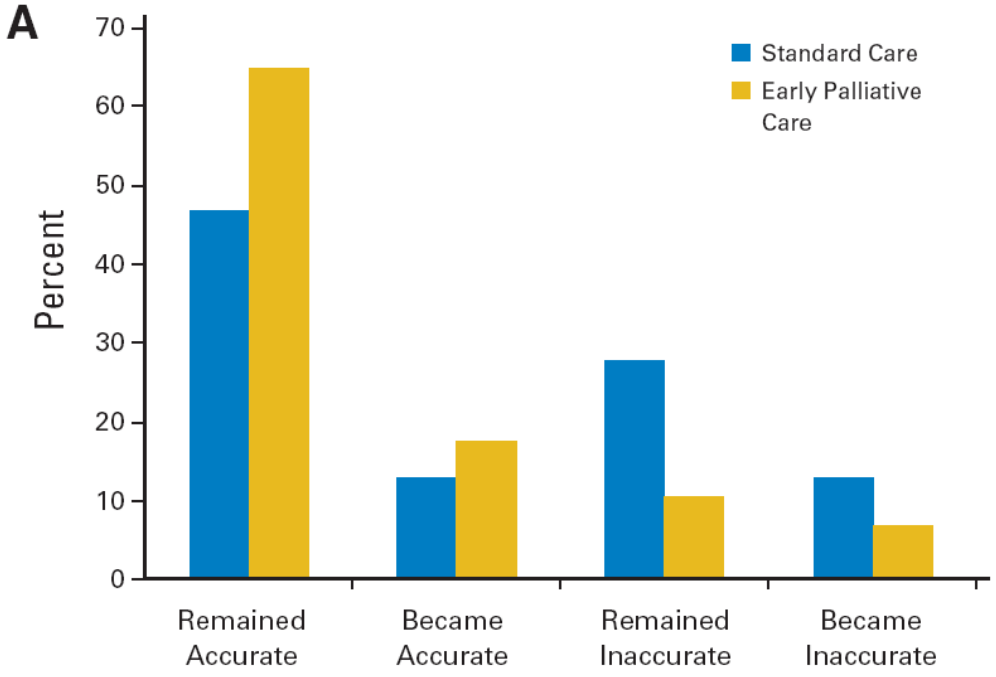
Depression and Anxiety



Temel NEJM 363 (8) 2010

Lung Cancer Trial – Prognostic Awareness

My cancer is curable: Yes or No

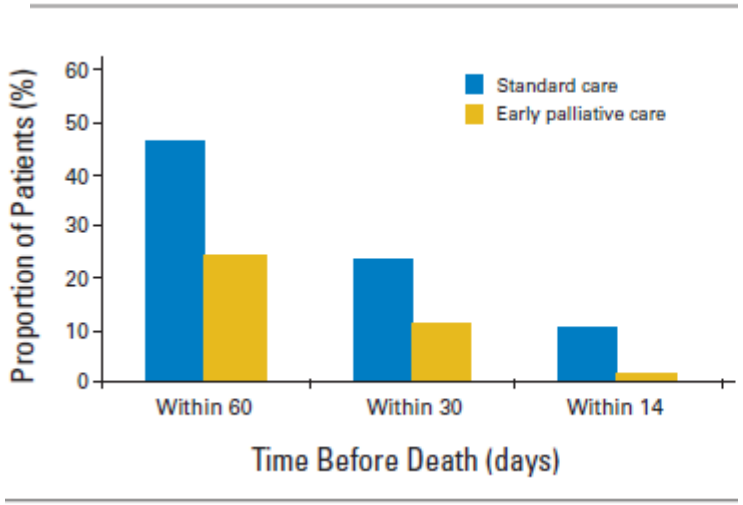


Palliative care v Standard care
82.5% v 59.6%, p=0.02

Temel JCO 29 (17) 2011

Lung Cancer Trial - Health Service Utilization

Variable	Standard Care	Early Palliative Care	*P*
Documented Code Status	11/39 (28)	18/34 (53)	0.05
Hospice Care			
Received hospice care	44/67 (66)	44/62 (71)	0.57
Length of Stay > 7 days	21/63 (33)	36/60 (60)	0.004
Median days	9.5 (1-268)	24 (2-116)	0.02



IV chemo within 60 DOD
46% v 24% p=0.01

Greer JCO 30 (4) 2012

Integrate PC Trial

350 patients within 8 weeks of diagnosis of advanced/incurable lung and non-colorectal GI cancers with an ECOG PS 0-2 (and their family caregivers)

Integrated care
- Palliative care visits every 3-4 weeks in conjunction with oncology visits

Standard care
- Palliative care visits only upon request

Study Measures

Patient-reported measures
1. Quality of life
2. Mood
3. Prognostic awareness
4. Coping

Family-reported measures
1. Quality of life
2. Mood
3. Prognostic awareness

Health service utilization
1. Chemotherapy administration
2. Documentation of resuscitation preferences
3. Hospital utilization

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Integrate PC Trial – Coping and EOL Communication

Measure	Usual Care	Early PC	*P*
"Knowing about prognosis has been very/extremely helpful for"			
- Making decisions about treatment	89.8%	96.5%	0.04
- Coping with the disease	83.6%	97.3%	<0.01
"Discussed wishes about the care you would want to receive if you are dying"	14.5%	30.2%	<0.01

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Early Integrated Palliative Care Decreases Caregiver Distress

Table 2. Effect of early integrated palliative care on caregivers' outcomes at 12 and 24 weeks

	Sample size	Group assignment	Adjusted mean score	95% CI	Adjusted mean difference	95% CI	Effect size *d*	*p* value
Week 12 outcomes[a]								
HADS-Total distress	$n = 227$	Control Intervention	10.48 9.02	9.58–11.38 8.09–9.96	−1.45	−2.76 to −0.15	0.300	**.029**
SF-36 PCS	$n = 228$	Control Intervention	51.40 52.94	49.83–52.98 51.30–54.59	1.54	−0.74–3.82	0.180	.183
SF-36 MCS	$n = 228$	Control Intervention	45.92 47.00	44.25–47.59 45.26–48.74	1.09	−1.33–3.51	0.119	.376

El-Jawahri Oncologist 22 (12)2017

Canadian Study

461 patients with stage IV cancer (including hormone refractory breast and prostate) or stage III with poor prognosis and ECOG PS 0-2 with a clinical prognosis of 6-24 months

Early Palliative Care Intervention

Usual Care

Outcome Measures

Patient-reported Measures
1. QOL
2. Symptoms
3. Quality of Life at EOL
4. Satisfaction

Zimmermann Lancet 383(9930) 2014

Canadian Study – Patient-Reported Outcomes

4 Month Patient Reported Outcomes				
Measure	**Intervention** (mean change from baseline)	**Control** (mean change from baseline)	**Adjusted Difference** (between change)	***P***
Quality of Life (Spiritual)	2.46	-3.95	9.44	0.006
Quality of Life at End of Life	3.04	-0.51	3.51	0.003
Symptom Burden	-1.34	3.23	-4.41	0.05
Satisfaction	3.70	-2.42	6.00	<0.001

Take Home Points From Outpatient In-Person Early Palliative Care Studies

- Similar to the ENABLE intervention, in-person palliative care improves patient's QOL, mood, and symptom burden.
- Early and longitudinal palliative care involvement improves communication about and delivery of end-of-life care.
- But these care models are complex….

Alliance Palliative Care Trial

400 patients at 10 academic and 10 community Alliance sites within 8 weeks of diagnosis of advanced/incurable lung and non-colorectal GI cancers with an ECOG PS 0-2 (and their family caregivers)

Integrated care
- Palliative care contact at least every 4 weeks in conjunction with oncology visits

Standard care
- Palliative care visits only upon request

Study Measures

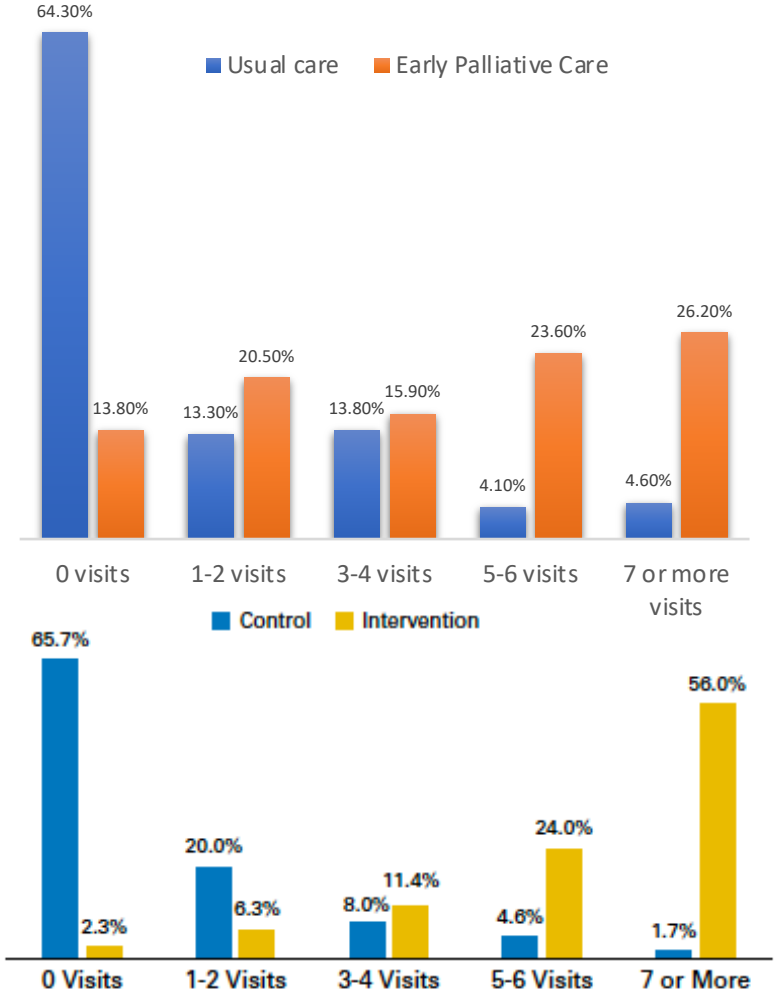
Patient-reported measures
1. Quality of life
2. Mood
3. Prognostic awareness

Family-reported measures
1. Quality of life
2. Mood
3. Prognostic awareness

Health service utilization
1. Chemotherapy administration
2. Documentation of resuscitation preferences
3. Hospital utilization

Temel JPM 23 (7) 2020

Alliance Palliative Care Trial



In addition to experiencing difficult with intervention delivery, this trial faced challenges with data collection with more than 60% missing data at the primary endpoint of week-24

TABLE 3. INTERVENTION EFFECTS ON CHANGE IN OUTCOMES FROM BASELINE TO WEEK 24

	Early palliative care		*Usual care*			
	N	*Mean change from baseline (SD)*	N	*Mean change from baseline (SD)*	*Mean difference between groups (95% CI)*	p
FACT-G	68	3.80 (15.3)	80	0.69 (13.3)	3.12 (−1.54 to 7.77)	0.19
HADS-Depression	75	0.37 (3.8)	84	0.26 (3.6)	0.11 (−1.04 to 1.27)	0.85
HADS-Anxiety	75	−1.23 (3.5)	84	−0.21 (3.3)	−1.01 (−2.07 to 0.05)	0.06

Temel JPM 23 (7) 2020

Inpatient Palliative Care Interventions

In person early palliative care models

Palliative Care for Patients Undergoing Hematopoietic Stem Cell Transplant

160 patients admitted to MGH for autologous or allogeneic hematopoietic transplant and their family caregivers

Palliative Care Intervention
Twice weekly visits during the transplant

Usual Care

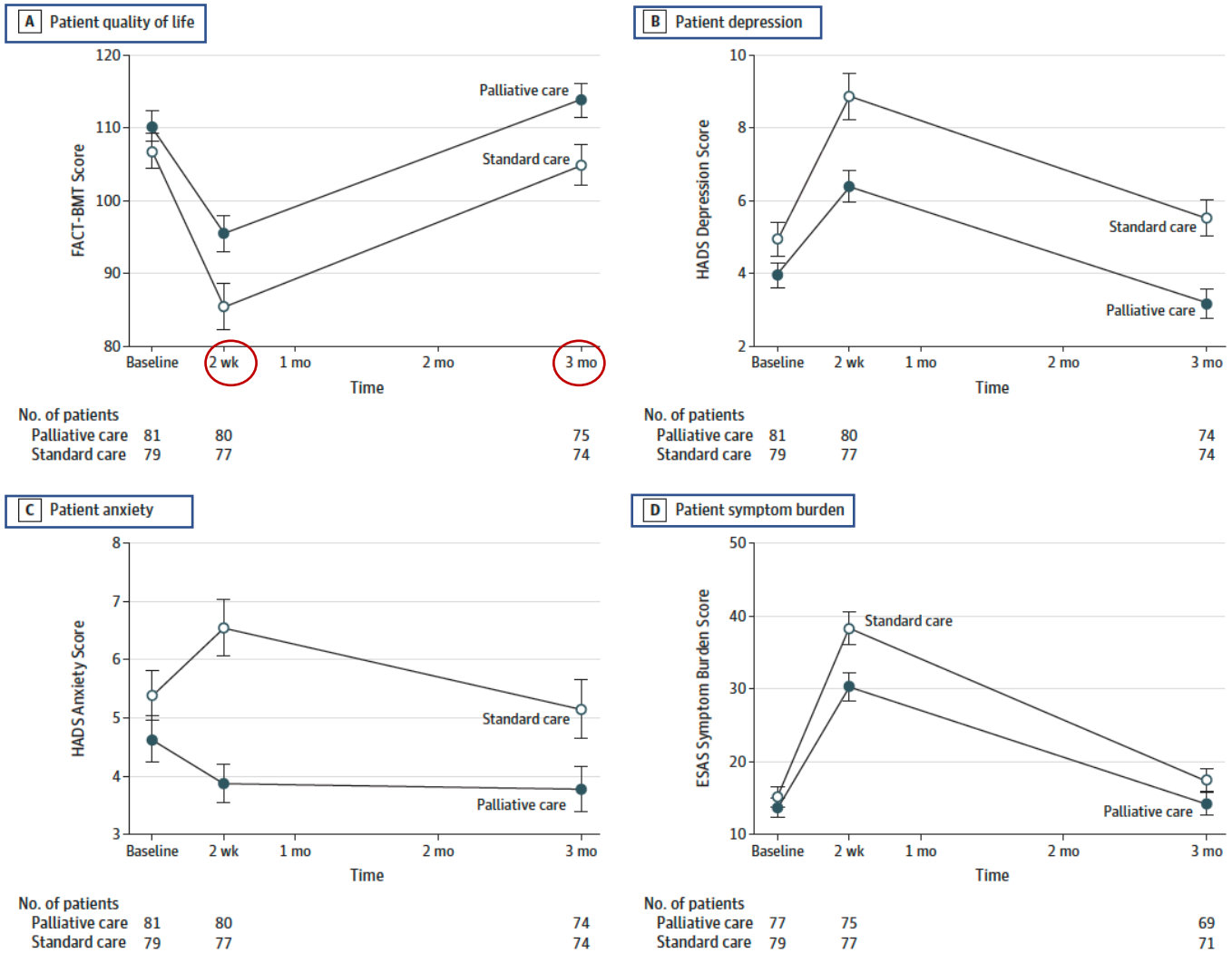
Outcome Measures

Patient-reported Outcomes
1. Quality of life
2. Symptom burden
3. Mood
4. Post-traumatic stress

Family-caregiver Outcomes
1. Quality of life
2. Mood

El-Jawahri JAMA 316(20) 2016

Palliative Care for Patients Undergoing Hematopoietic Stem Cell Transplant



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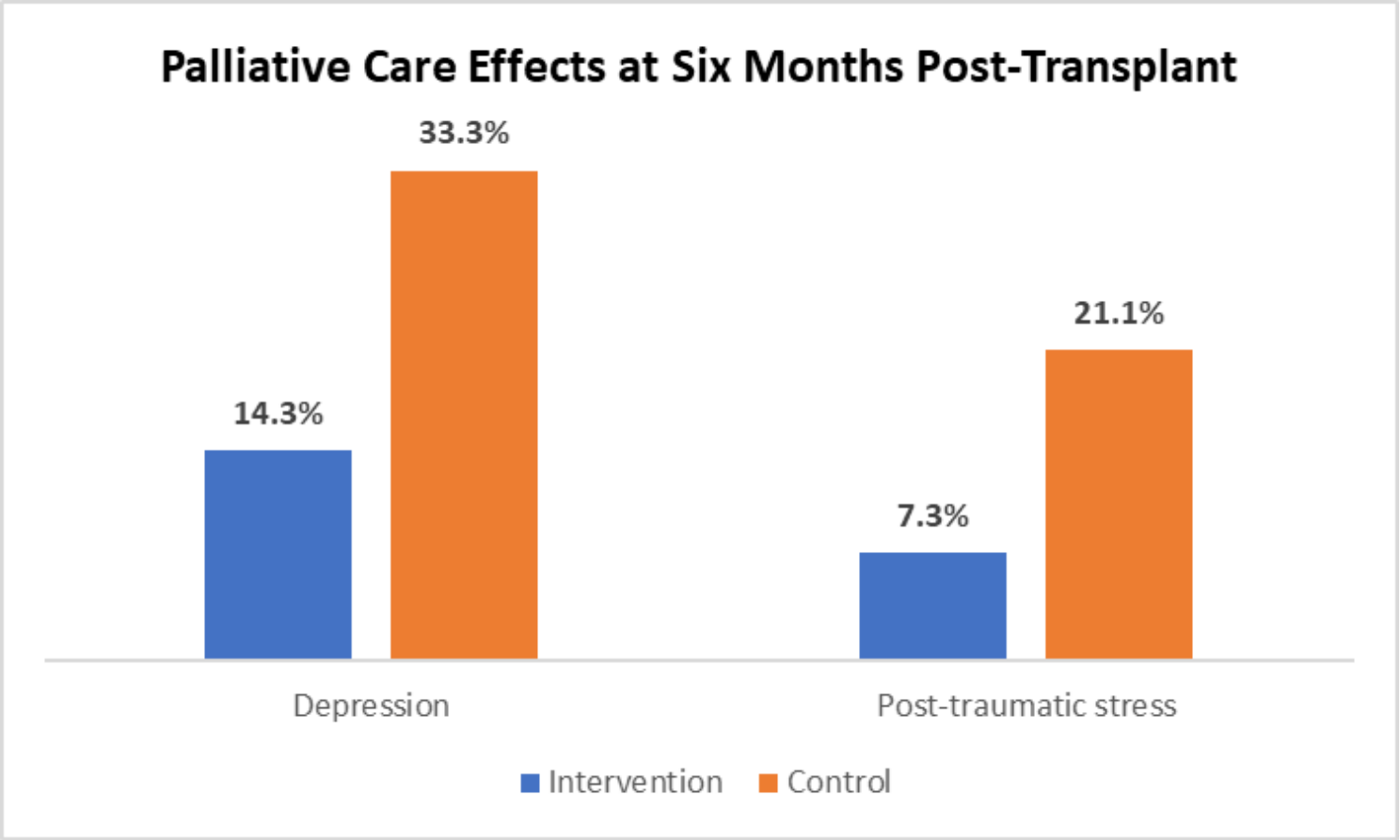
Long Term Effects of Palliative Care During Transplant



El-Jawahri JCO 35(32) 2017

Palliative Care for Patients with Acute Myeloid Leukemia

160 patients admitted to four tertiary care hospitals with newly diagnosed AML receiving intensive chemotherapy

Palliative Care Intervention
Twice weekly visits during hospitalizations

Usual Care

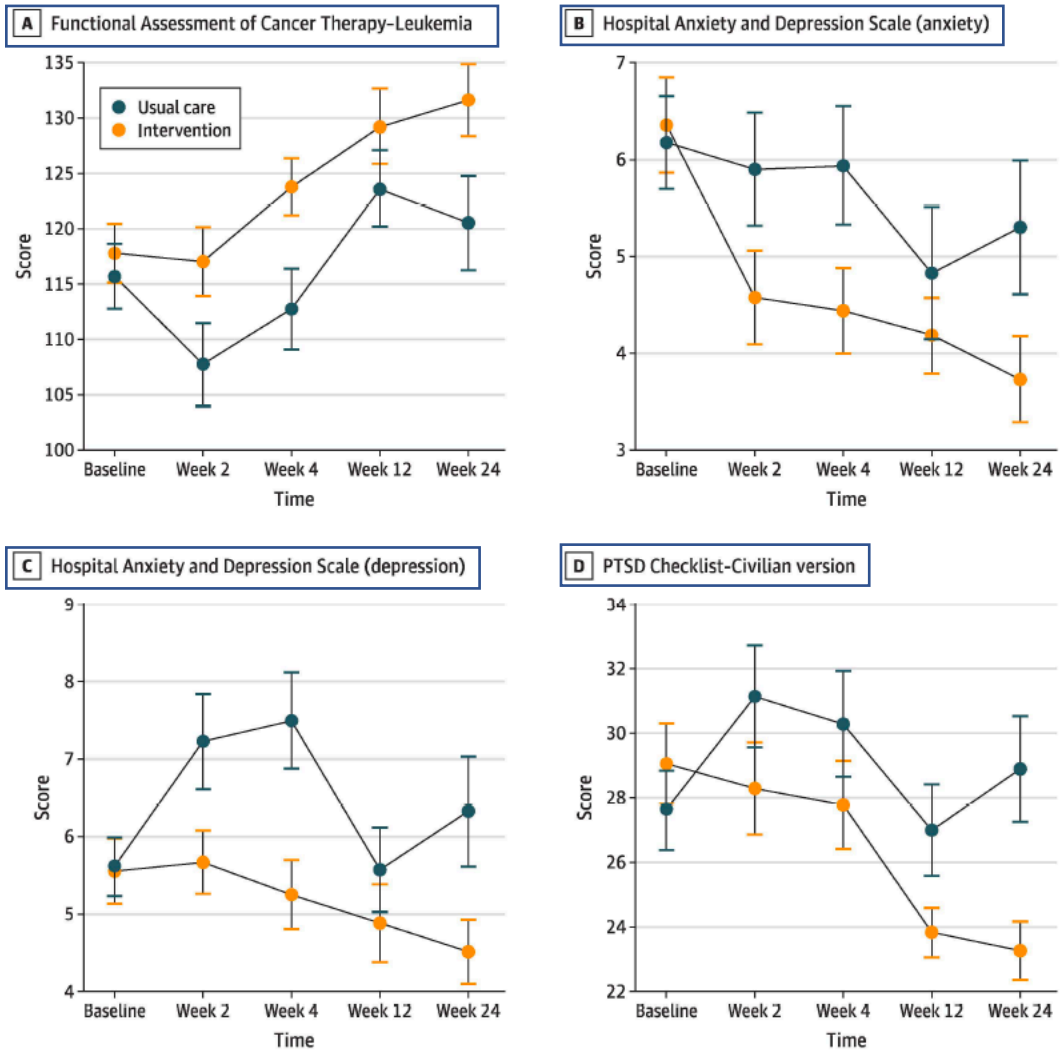
Outcome Measures

Patient-reported Outcomes
1. Quality of life
2. Symptom burden
3. Mood
4. Post-traumatic stress

End of Life Care Outcomes
1. EOL communication
2. Chemotherapy use
3. Hospice use

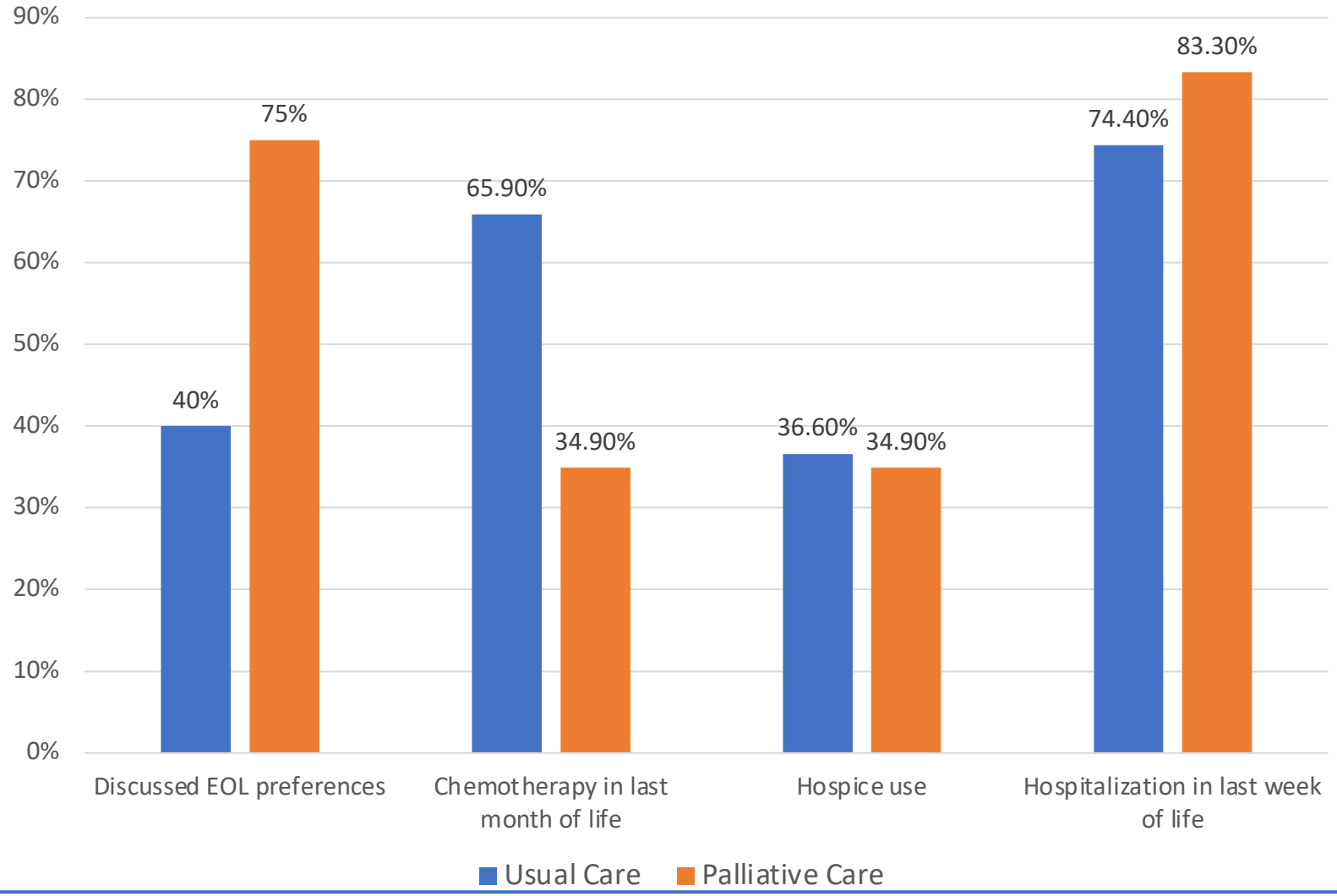
El-Jawahri JAMA Oncology 2020 in press

Palliative Care for Patients with Acute Myeloid Leukemia



El-Jawahri JAMA Oncology 2020 in press

Palliative Care for Patients with Acute Myeloid Leukemia



Take Home Points From Inpatient Palliative Care Studies

- Palliative care improves outcomes for patients with hematologic malignancies being treated with curative intent.
- Even brief/short term exposure to palliative care can have an impact on late outcomes.

"Status of the Field"

1. Transitioning palliative care from the hospital to the outpatient setting is an effective care model and improves the experience and outcomes of patients with serious cancers.
2. Involving palliative care in the care of hospitalized patients receiving intensive cancer treatments with curative intent, such as patients with acute leukemia or those undergoing hematopoietic stem cell transplant, improves their experience and outcomes.


The End.

Not So Fast….

Lack of data on the nature, timing, and dose of palliative care across populations.

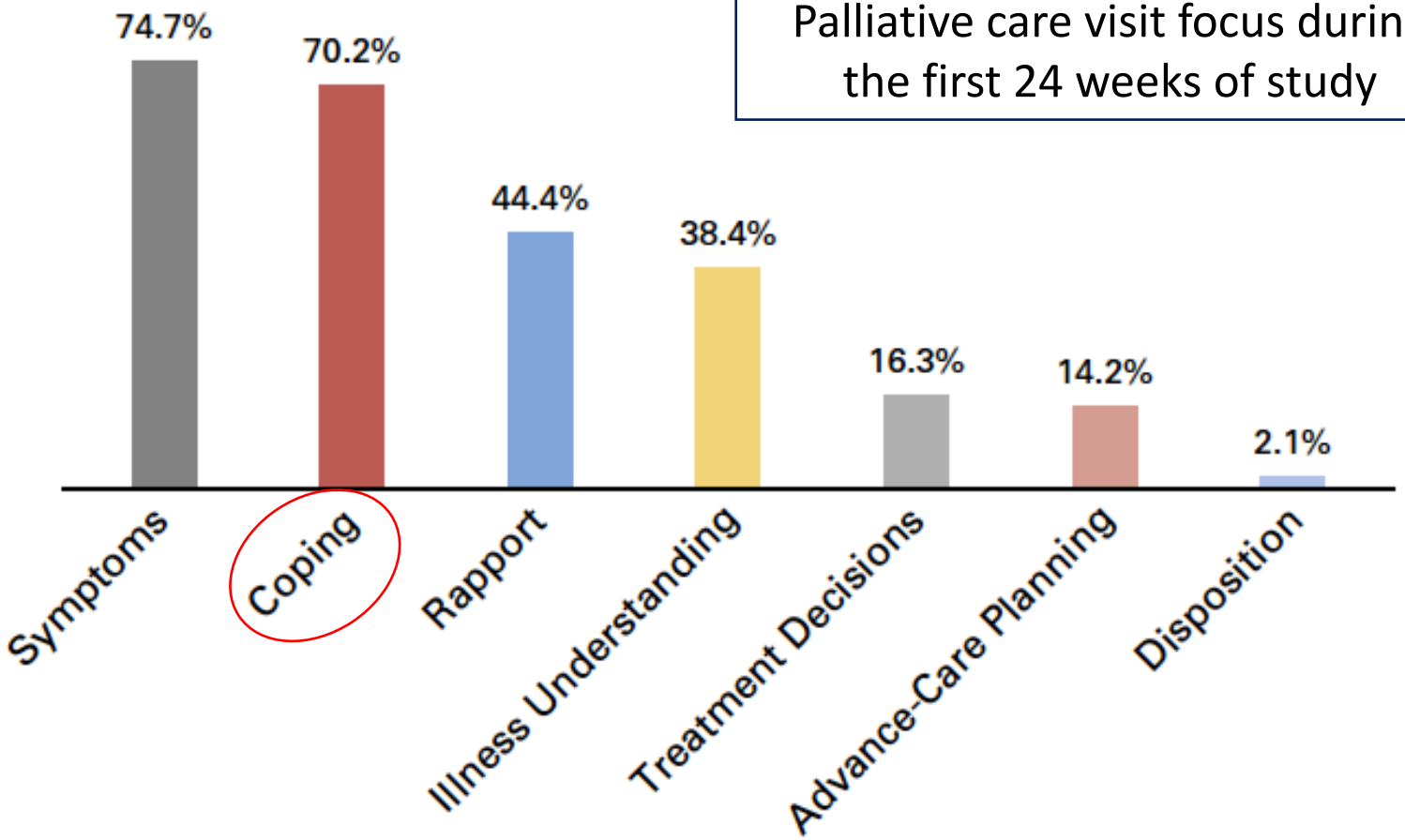
Cancer care is changing rapidly so even with data across populations, does that data still apply?

Inadequate space and resources for palliative care within cancer centers.

Not enough palliative care clinicians to care for all patients with serious cancers.

What is Palliative Care Doing?

Palliative care visit focus during the first 24 weeks of study



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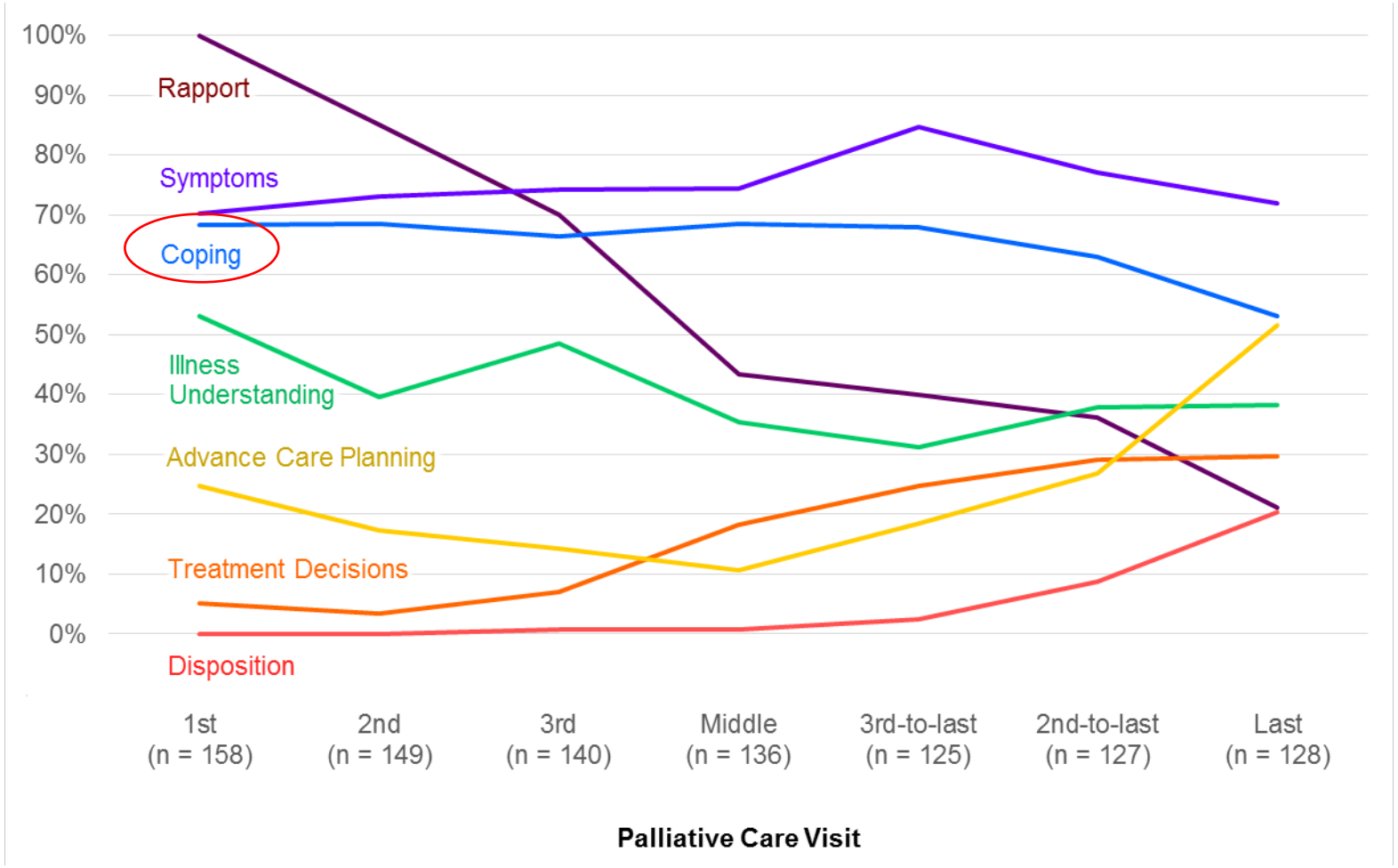
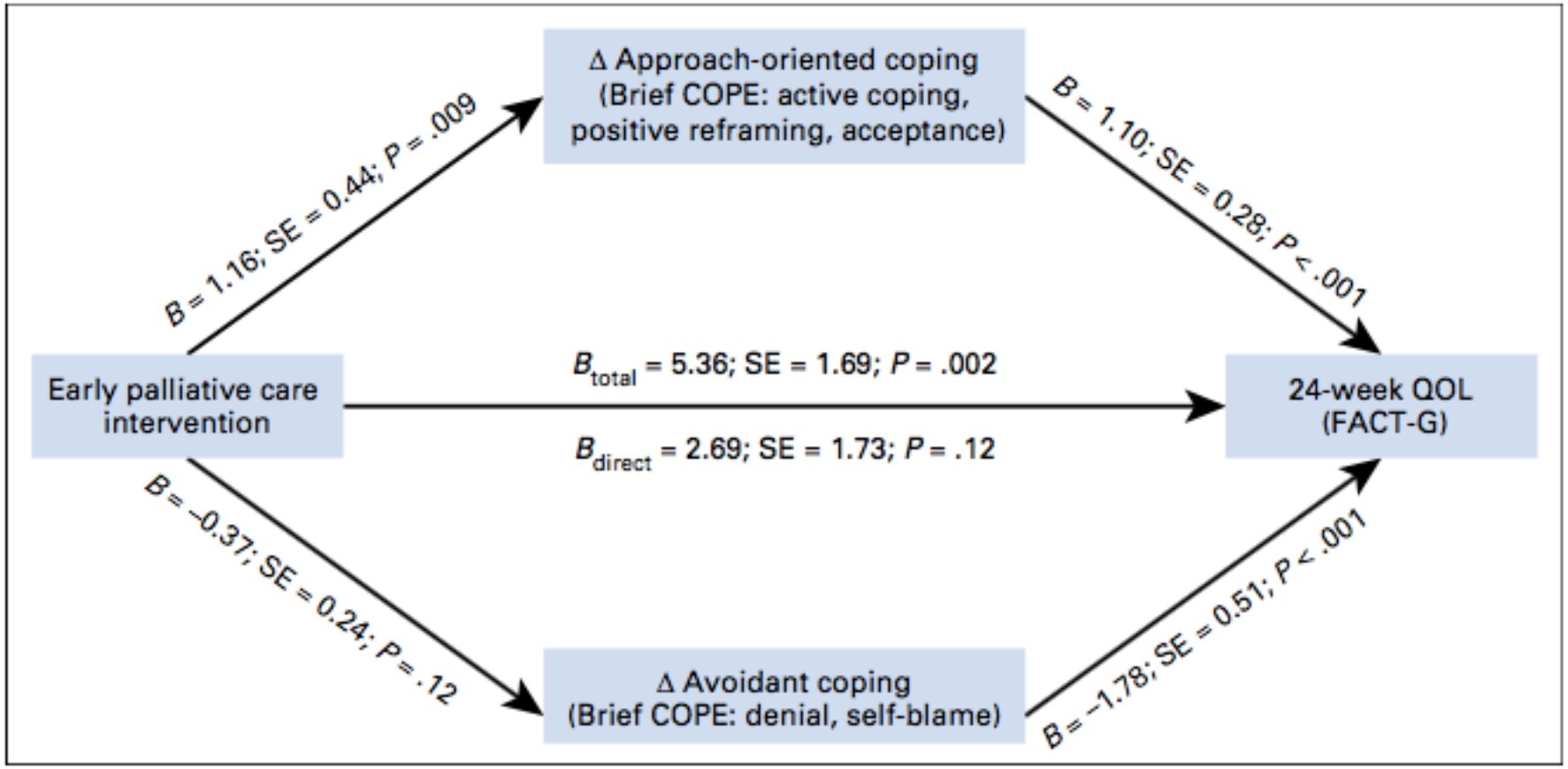
Practice of Early Integrated Outpatient Palliative Care



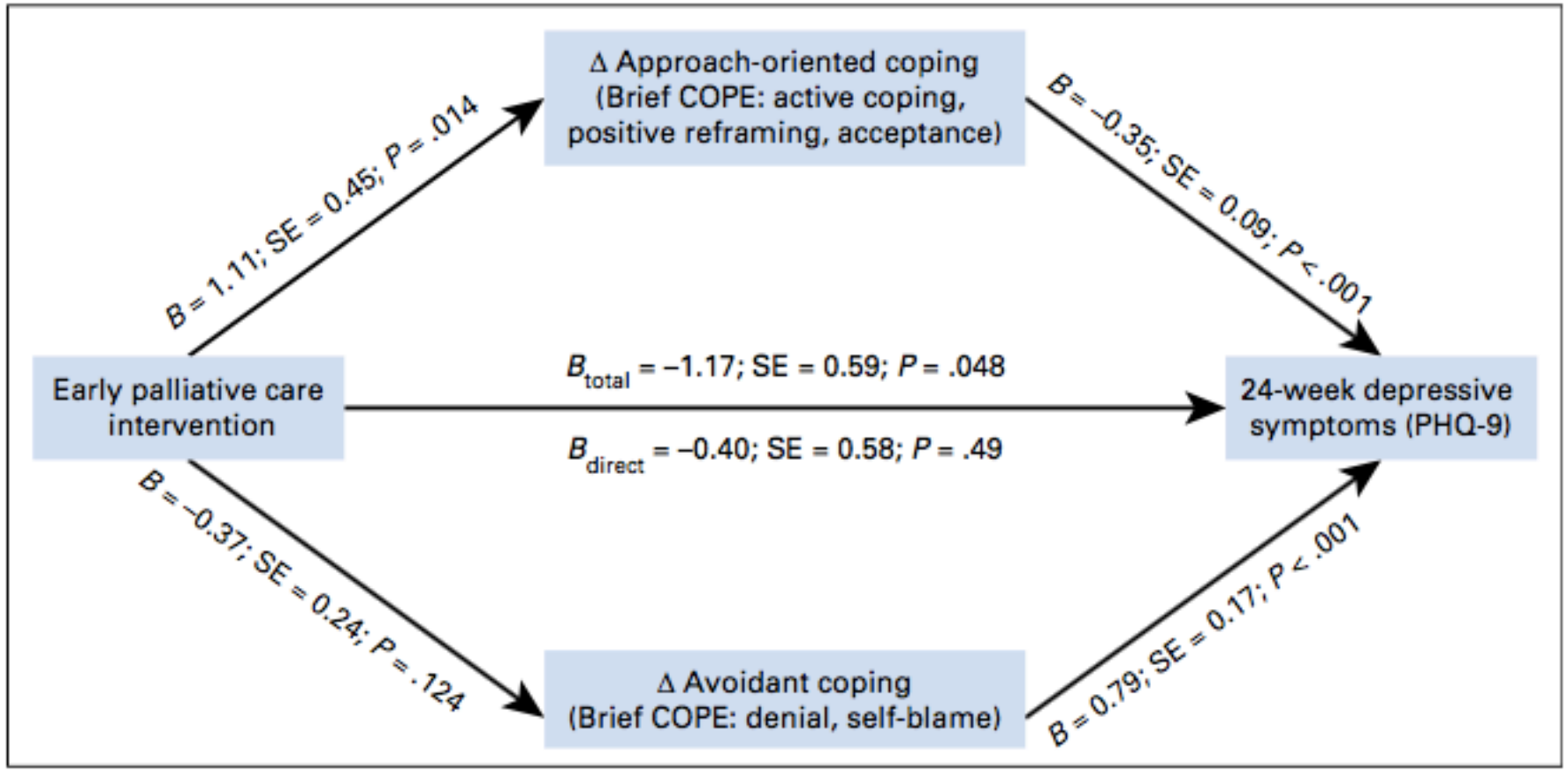
Hoerger JCO 36 (11) 2018

Importance of Coping in Improving QOL



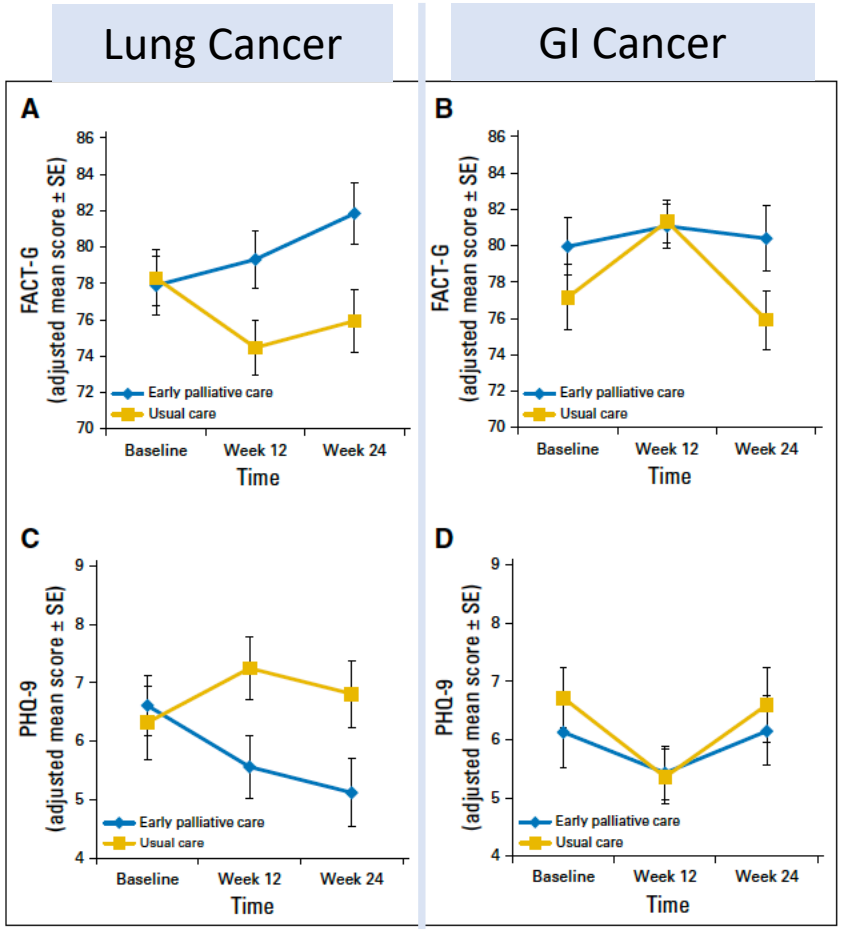
Greer, Jacobs JCO 36 (1) 2018

Importance of Coping in Improving Depression



Greer, Jacobs JCO 36 (1) 2018

But Different Populations May Need Different Palliative Care "Things"



- Monthly outpatient visits from diagnosis until may not be the right timing and interval for all patients with serious cancers.
- A focus on coping may not be the most important element of palliative care for all patients.

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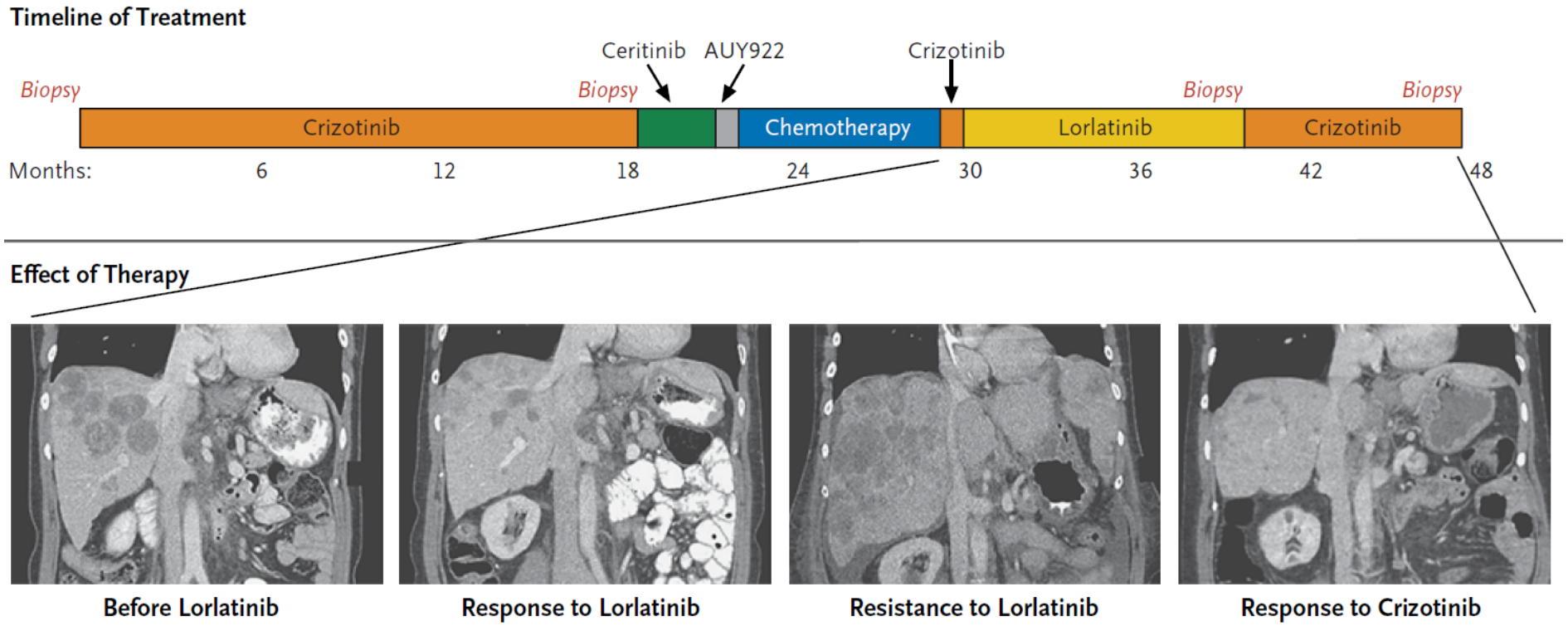
Palliative Care in the Context of a Rapidly Changing Field of Oncology

- Since these palliative care trials were conducted, there have been significant changes in cancer therapeutics which have impacted patients' quality of life and survival.
  - Some groups of patients with advanced cancer are not treated with chemotherapy throughout their illness.
    - Most of the time, novel therapies such as immunotherapy and targeted therapy have less side effects than chemotherapy.
  - Subpopulations of patients with advanced cancer are living significantly longer.

But Novel Therapies Bring About Novel Palliative Care Challenges



Shaw NEJM 374(1) 2016

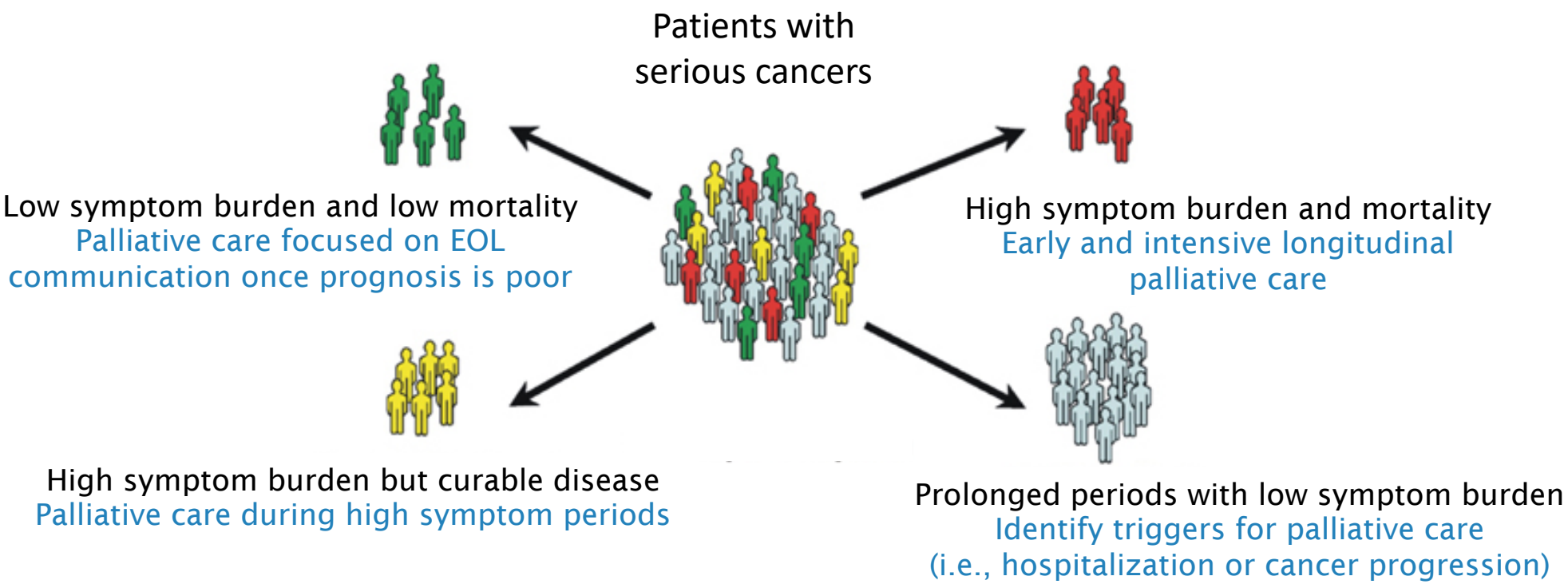
Implications of Novel Therapies on the Practice of Palliative Care

- Palliative care may need to focus less on addressing physical symptoms.
- Palliative care will likely need to play a significant role helping patients and their families manage prognostic uncertainty and the distress associated with it.
- Palliative care will likely need to play a greater role in end-of-life decision making.

Patient-Centered Palliative Care

Patients with
serious cancers

Patient-Centered Palliative Care



Addressing Inadequate Palliative Care Staffing and Resources

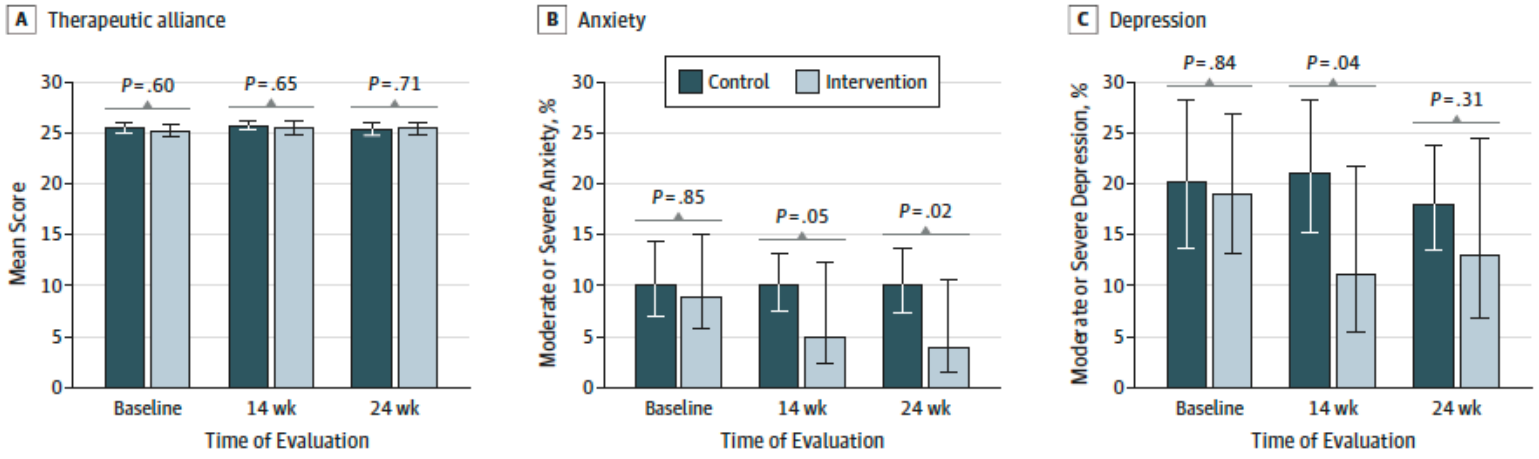
1. Determine whether increasing "primary palliative care" skills in oncology can achieve similar results as specialty palliative care.
2. Develop less resource intensive palliative care delivery models.
   - Utilize novel technologies to provide services
   - Triage services to those who need it most

Serious Illness Communication

Table 3. Achievement of Goal-Concordant Care and Peacefulness Near the End of Life

Outcome	Intervention Arm No.	Intervention Arm Mean (95% CI)	Intervention Arm Median (95% CI)	Control Arm No.	Control Arm Mean (95% CI)	Control Arm Median (95% CI)	Differences (95% CI)[a]
Goal-concordant care[b]							
No. of goals met	38	1.4 (1.0 to 1.7)	0.8 (0.6 to 1.1)	26	1.5 (1.0 to 2.1)	1.2 (0.3 to 2.1)	Median, −0.4 (−1.5 to 0.7)
Sensitivity analysis	29	1.3 (1.0 to 1.6)	0.8 (0.5 to 1.1)	17	1.5 (0.9 to 2.2)	1.2 (0.1 to 2.3)	Median, −0.3 (−1.2 to 0.6)
PEACE							
PA scale	47	16.9 (16.1 to 17.6)	NA	47	16.8 (15.9 to 17.6)	NA	Mean, 0.1 (−1.0 to 1.2)
SI scale	44	14.0 (12.9 to 15.1)	NA	42	14.4 (12.7 to 16.0)	NA	Mean, −0.3 (−2.2 to 1.5)

Figure 2. Outcomes of Assessments of Therapeutic Alliance, Anxiety, and Depression



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JUMPSTART Communication Intervention

Figure 2. Percentage of Patients Reporting Goal-Concordant Care 3 Months After Target Visit

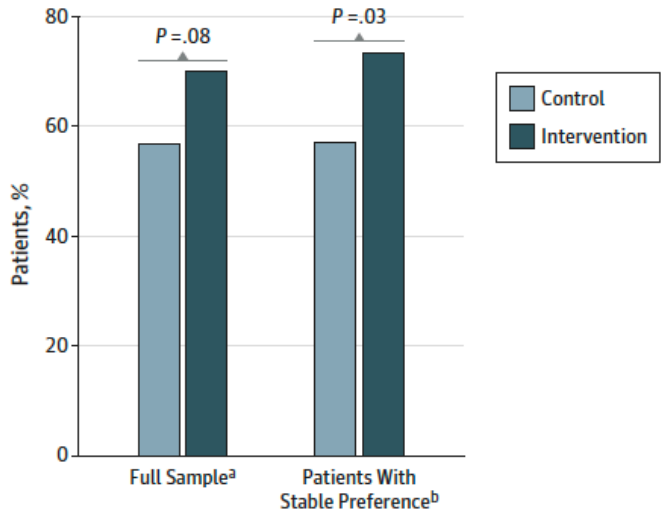

Table 3. Effect of the Intervention on Patients' Symptoms of Depression and Anxiety[a]

Outcome	Patients/Clinicians, No.[b]	Mean Value for Psychological Symptoms (95% CI) at Follow-up[c]		β (95% CI)[d]	P Value
		Control	Intervention		
Depression Symptoms					
3 Months after target visit					
2-Indicator latent variable[e,f]	262/113	0.20 (−0.02 to 0.42)	0.26 (−0.04 to 0.55)	−0.10 (−0.33 to 0.12)	.37
Standard PHQ-8 composite score[g,h]	359/119	4.88 (4.23 to 5.54)	5.92 (5.19 to 6.66)	0.26 (−0.57 to 1.10)	.54
6 Months after target visit					
2-Indicator latent variable[e,i]	262/113	0.24 (0.07 to 0.42)	0.40 (0.11 to 0.69)	0.21 (−0.04 to 0.46)	.11
Standard PHQ-8 Composite Score[g,j]	314/118	4.84 (4.17 to 5.51)	5.927 (5.05 to 6.81)	0.45 (−0.48 to 1.37)	.34
Anxiety Symptoms					
3 Months after target visit					
2-Indicator latent variable[e,h]	277/119	0.22 (0.01 to 0.43)	0.28 (−0.04 to 0.60)	−0.03 (−0.23 to 0.16)	.73
Standard GAD-7 composite score[h,k]	366/122	3.00 (2.44 to 3.57)	3.26 (2.64 to 3.89)	0.04 (−0.95 to 1.03)	.94
6 Months after target visit					
2-Indicator latent variable[e,h]	277/119	0.21 (−0.05 to 0.47)	0.30 (0.00 to 0.59)	−0.04 (−0.25 to 0.16)	.69
Standard GAD-7 composite score[h,k]	327/119	3.08 (2.44 to 3.72)	3.375 (2.67 to 4.08)	−0.11 (−1.20 to 1.00)	.85

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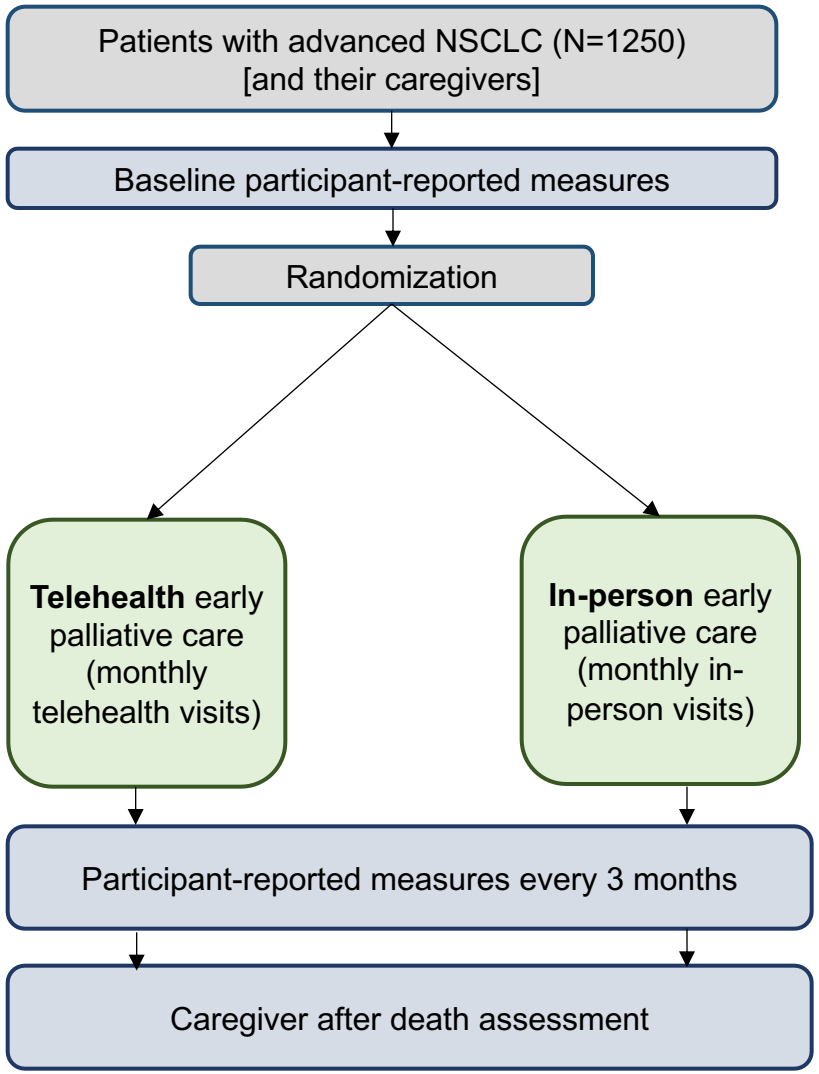
Primary Palliative Care

- With training and support, there should not be a significant downside to oncology clinicians doing what they can to deliver "palliative care".
- We have mixed results on "serious illness communication" improving EOL outcomes for patients but this field is in its infancy and I feel optimistic that as our experience with these interventions grow, these will be effective interventions.
- We do not yet have data on primary palliative care for outcomes other than EOL care but hopefully that is forthcoming.

Less Intensive Palliative Care Delivery Models

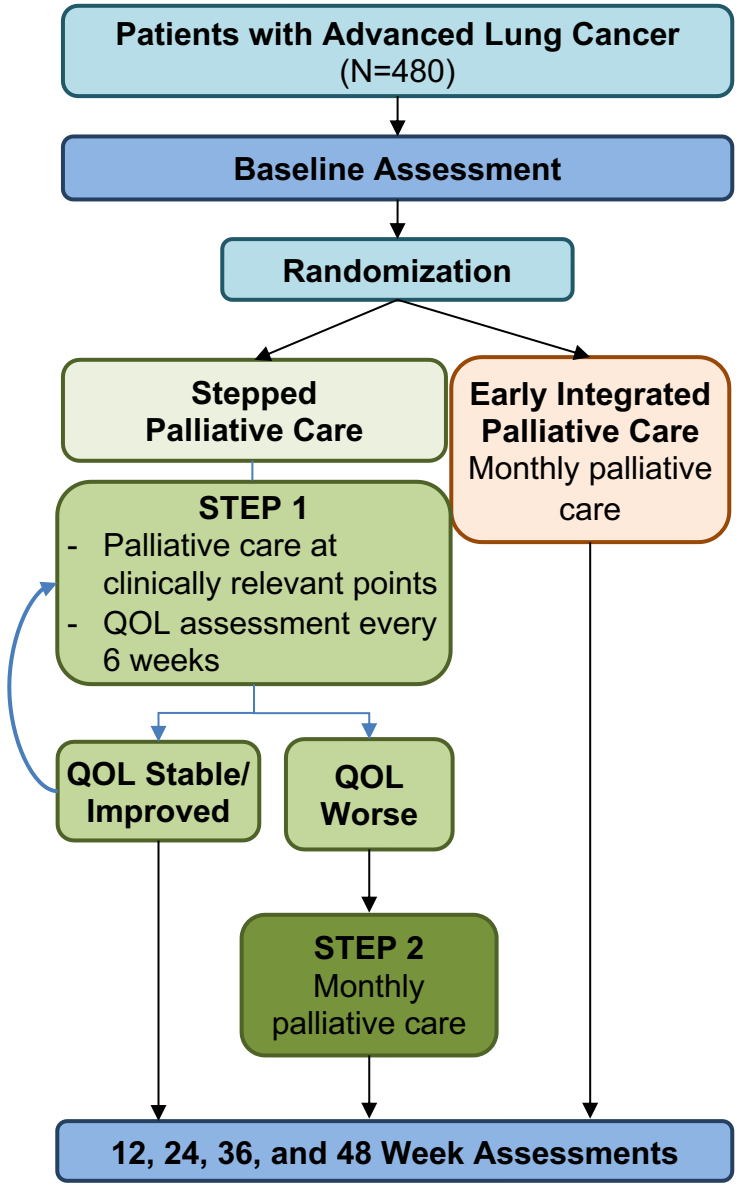
Comparative Effectiveness Trial



Utilizing HIPAA compliant video technology to provide face to face care

STEP PC

- "Stepped care" is an evidence-based method to increase access to and efficiency of health care services.
- With stepped care, all patients receive care low intensity treatment with more intensive intervention reserved for those who have greater needs.



Summary

- The role of early involvement of palliative care for patients with newly diagnosed poor prognosis cancer or those undergoing intensive inpatient treatment is now established.
- While the data from published trials is compelling, implementing these care models can be challenging.
- We must focus our research efforts on how to develop more patient-centered and scalable palliative care models to increase access to this essential aspect of care for patients with serious cancers.

Thank you

- Massachusetts General Hospital Cancer Center
  - Cancer Outcomes Research and Education Program
  - Center for Thoracic Oncology
  - Center for Psychiatric Oncology and Behavioral Science
  - Division of Palliative Care
- National Institute of Nursing Research
- National Cancer Institute
- Patient Centered Outcomes Research Institute
- American Cancer Society
- National Palliative Care Research Center

CORE Team