

# Palliative Care Integration In Hematology

Thomas W. LeBlanc, MD, MA, MHS, FAAHPM,  
FASCO

Associate Professor of Medicine with Tenure  
Division of Hematologic Malignancies

Director, Cancer Patient Experience Research  
Program (CPEP)





# **DOES JEAN NEED PALLIATIVE CARE?**

# **WHAT ARE THE PALLIATIVE AND END-OF-LIFE CARE NEEDS OF HEMATOLOGY PATIENTS?**



54%



81%

# 39%



# 43%







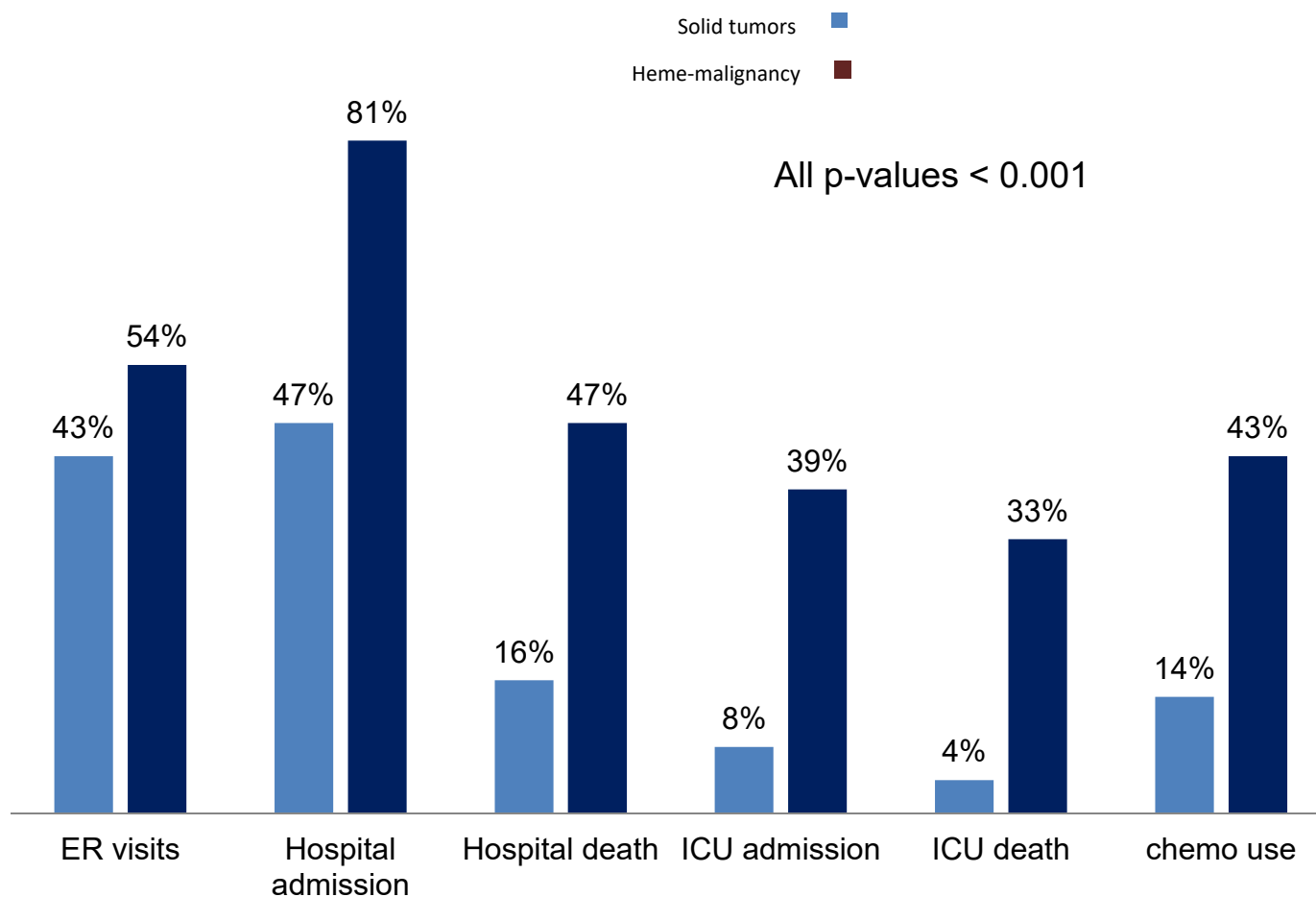
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57,230

40,610

# Unmet End-of-Life Needs in Hematologic Malignancies



## Outcomes: The “Quality Measures” Gap

- Patients with blood cancers are more likely to: <sup>1,2</sup>
  - **receive chemotherapy in the last 14 days of life**
  - **spend time in an ICU in the last 30 days of life**
- Patients with blood cancers are less likely to:
  - **access consultative palliative care services<sup>3</sup>**
  - **use hospice services<sup>4</sup>**
    - Or, are more likely to die within 7 days of enrollment, or within 24 hrs of enrollment <sup>5</sup>
    - Median LOS of 11 days, vs. 19 for solid tumors <sup>5</sup>

1. Howell, DA, et al. “Destined to die in hospital? Systematic review and meta-analysis of place of death in haematological malignancy.” *BMC Pall Care*, 2010.

2. Hui, et al. “Quality of end-of-life care in patients with hematologic malignancies: a retrospective cohort study.” *Cancer* 2014

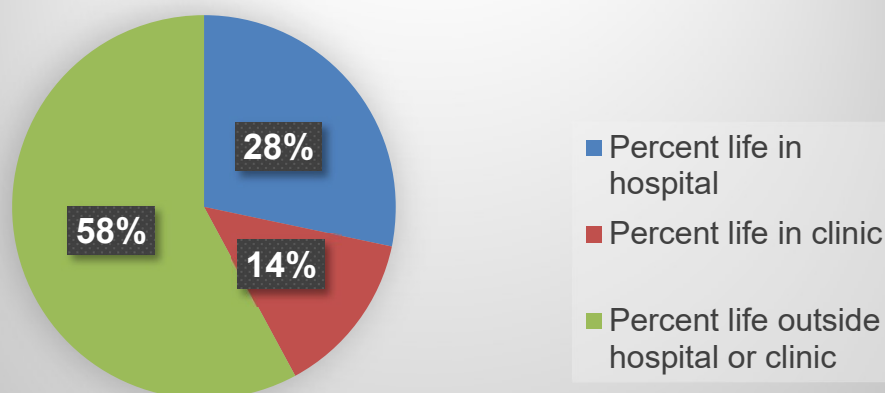
3. Howell DA, et al. Haematological malignancy: are patients appropriately referred for specialist palliative and hospice care? A systematic review and meta-analysis of published data.” *Palliat Med* 2011.

4. Odejide, et al. “Hospice use among patients with lymphoma: impact of disease aggressiveness and curability.” *JNCI*, 2015.

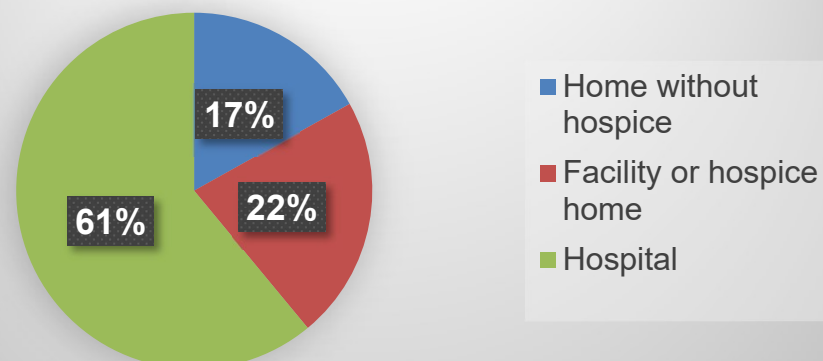
5. LeBlanc TW, Abernethy AP, Casarett DJ. “What Is Different About Patients With Hematologic Malignancies? A Retrospective Cohort Study of Cancer Patients Referred to a Hospice Research Network.” *Journal of Pain and Symptom Management*, 2014

## Burden of Care in AML

### Health care use

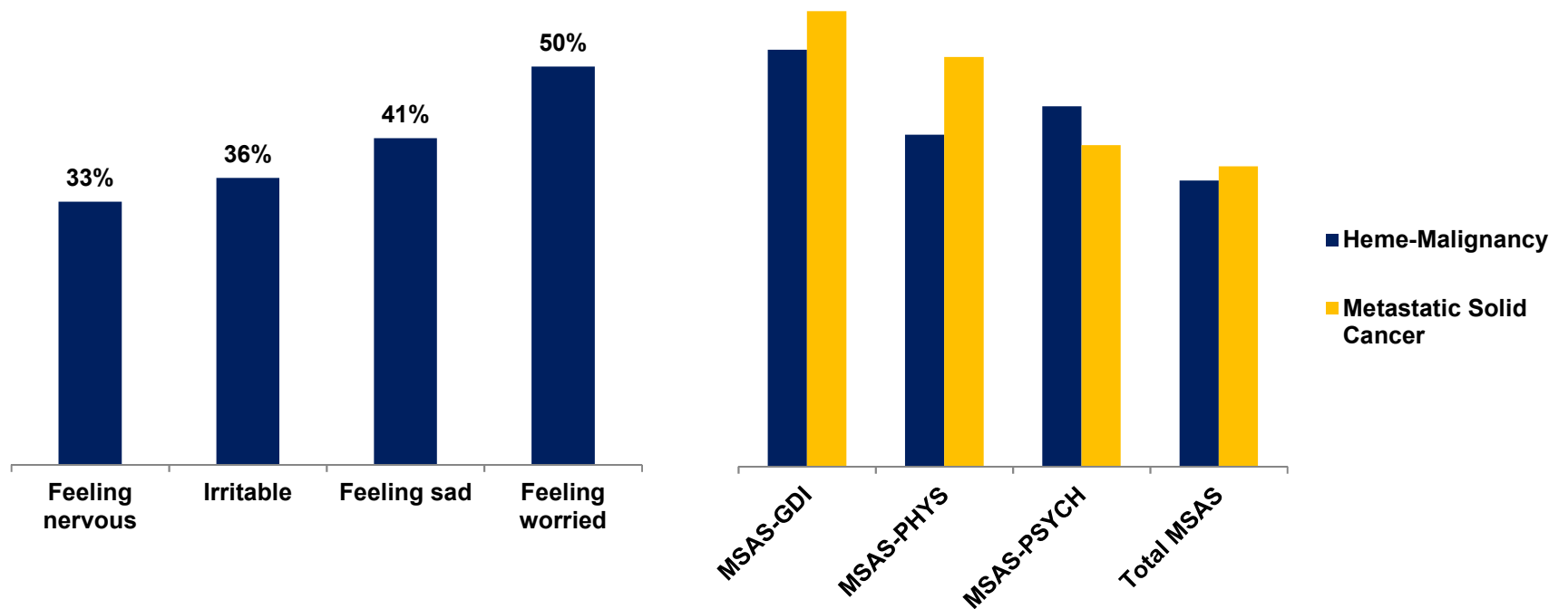


### Place of death

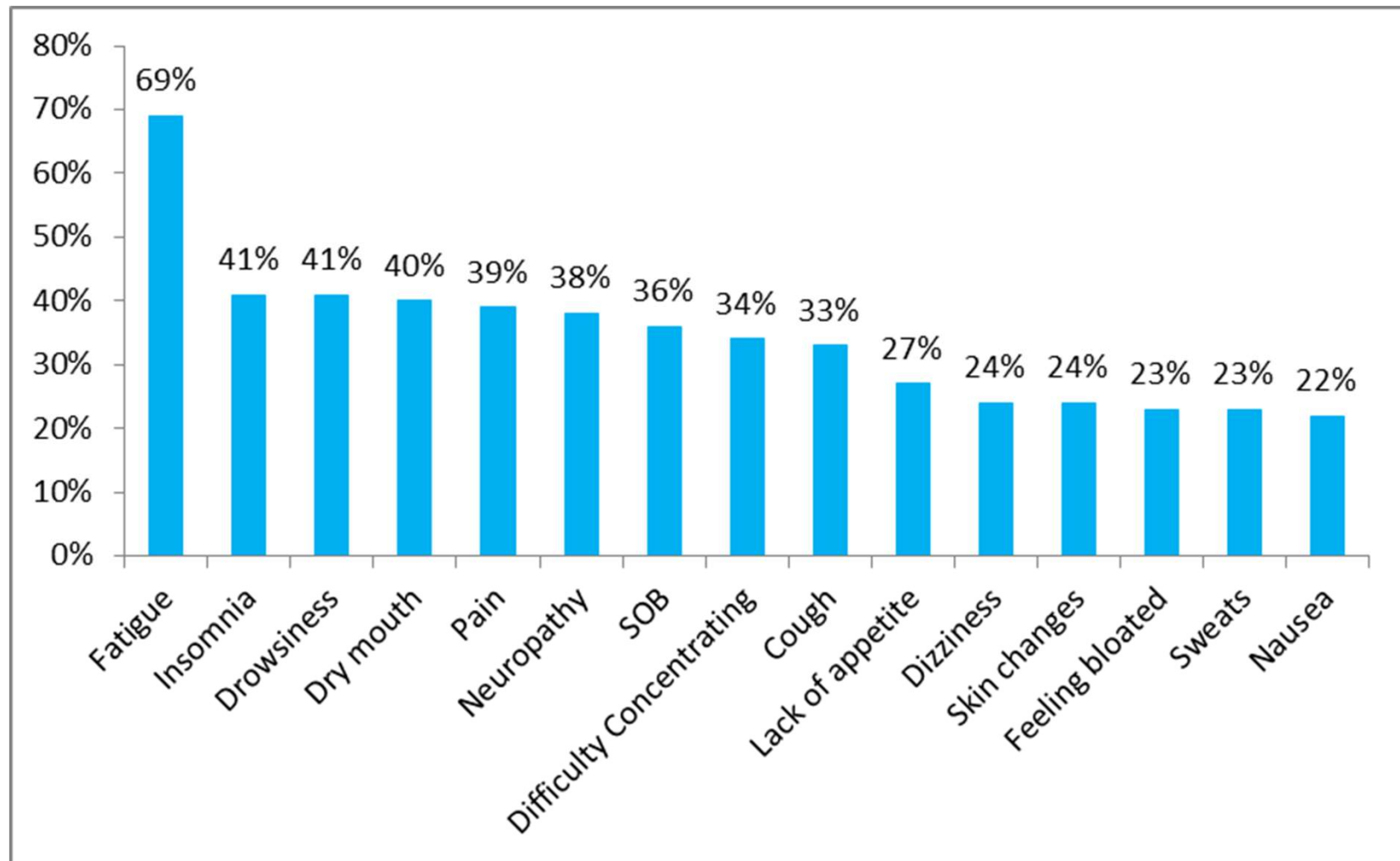


- Median hospitalizations = 4.2
- ICU admissions = 31.7%
- Palliative care consult = 16.2%
- Hospice utilization = 22%

# Unmet Symptom Needs in Hematologic Malignancies



# Symptom Burden







## What the literature tells us...

1. Unique barriers to EOL care
2. Clinicians are different
3. Hospice doesn't work well in hematology

# #1 – Blood Cancers are Different

Remarkable prognostic heterogeneity (uncertainty)

- **Some entirely curable with chemotherapy**
- **Others more like chronic, indolent diseases;**
  - More likely to die of something else

Some confer a dismal prognosis, yet cure remains possible

- **When curative-intent treatments do not work, much misery may result**
  - Sometimes almost kill to cure

# #1 – Unique Barriers to EOL Care

Identifying the end-of-life phase is more difficult<sup>1</sup>

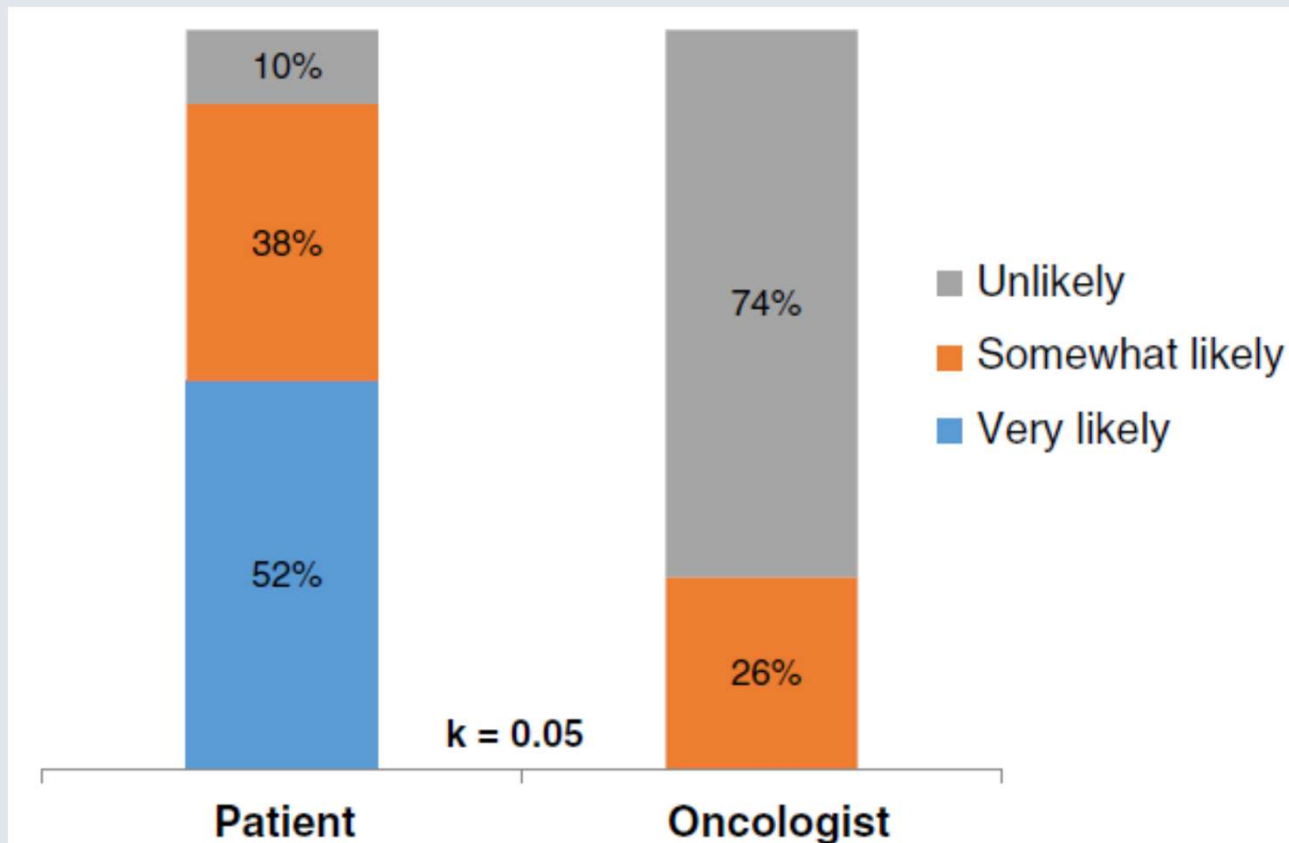
Survey data on heme docs perspectives about barriers to EOL care:<sup>2</sup>

- **Unrealistic patient expectations (97.3%)**
- **Clinician concern about taking away hope (71.3%)**
- **Unrealistic clinician expectations (59%)**

1. Odejide O, et al. "End-of-life care for patients with blood cancers: a series of focus groups with hematologic oncologists." *JOP* 2014

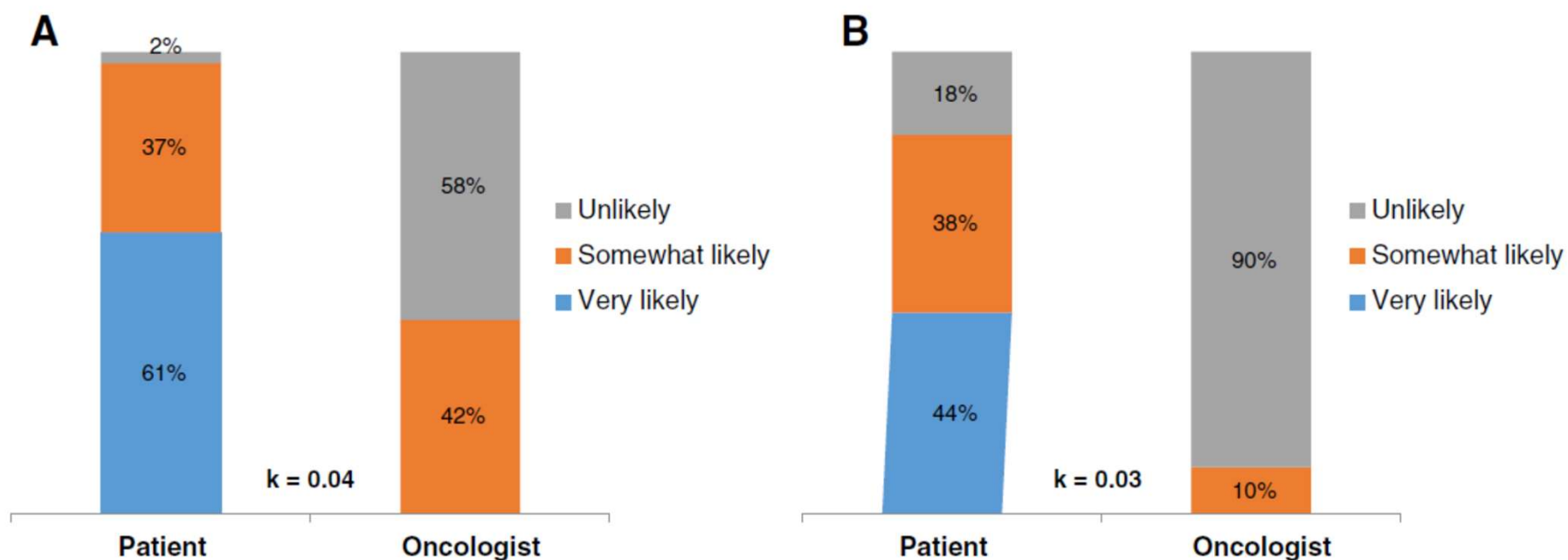
2. Odejide O, et al. "Barriers to quality end-of-life care for patients with blood cancers." *JCO*, 2016

## Illness Understanding – AML



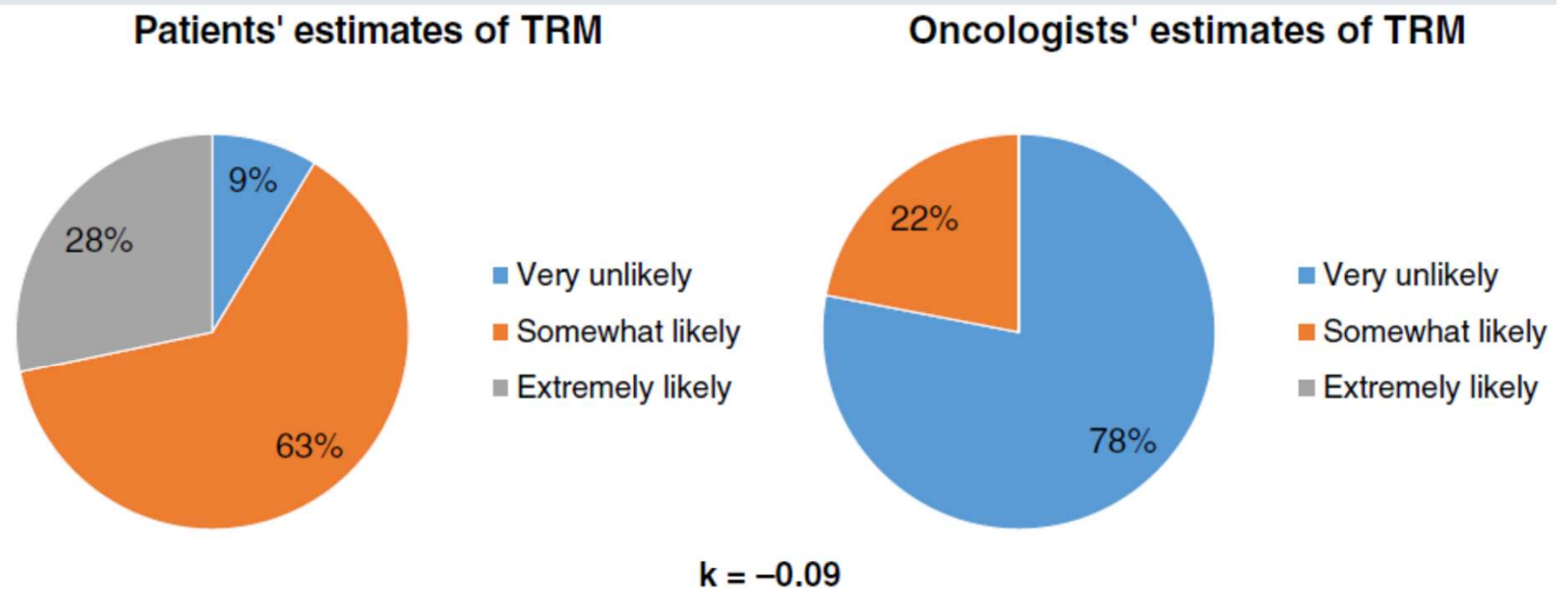
**Figure 3.** Patients' and oncologists' perceptions of the likelihood of cure of leukemia.

## Illness Understanding – AML



**Figure 4.** Patients' and oncologists' perceptions of the likelihood of cure. **(A):** Perceptions among those receiving intensive chemotherapy. **(B):** Perceptions among those receiving nonintensive chemotherapy.

## Illness Understanding – AML



**Figure 2.** Patients' and oncologists' perceptions of the risk of treatment-related mortality.  
Abbreviation: TRM, treatment-related mortality.

## #2 – The Doctors are Different

Survey of 120 hematologic and 120 solid tumor oncologists at MD Anderson Cancer Center (Texas)

Hematologic malignancy specialists are more likely to:

- **Favor systemic therapy with moderate toxicity and no survival benefit**
- **Have a sense of failure with dz progression**

...And are less comfortable discussing:

- **death and dying**
- **Hospice referral**

## #2 – The Doctors are Different

3 tertiary centers w/ established PC programs

- **Surveys and semi-structured interviews to better understand barriers to PC referral**
- **66 interviewees; 23 heme, 43 solid tumor**

Most blood cancer specialists viewed palliative care as just end-of-life care, or hospice

Frequent concerns about philosophical issues:

- non-palliative goals, not wanting another clinician to intrude on the patient-doctor relationship, etc.



## #3 – Hospice Care and Transfusions

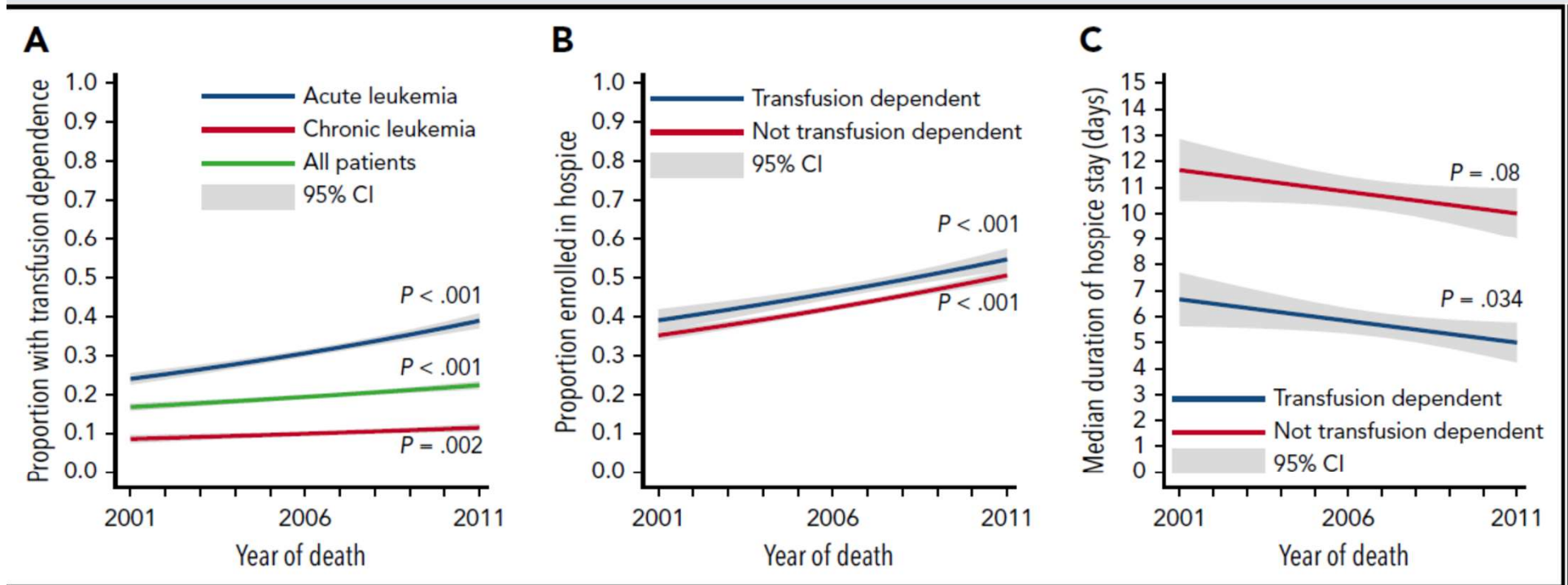
National survey study of 349 hematologic oncologists

Key messages:

- **Hospice care is helpful overall (68.1%)**
- **Home hospice care is inadequate for blood cancer patients' needs (46%)**

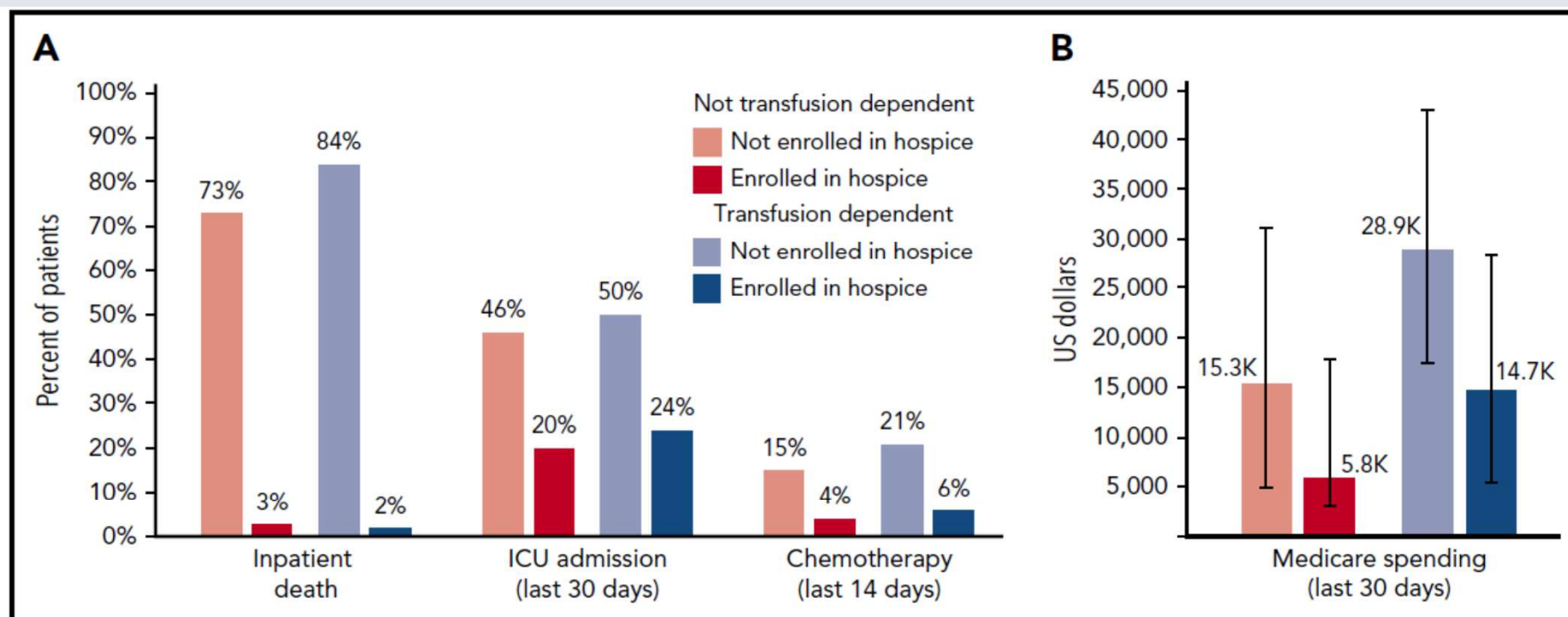
>50% said they would be more likely to refer patients to hospice if transfusions were more available

# Hospice Use in Leukemias



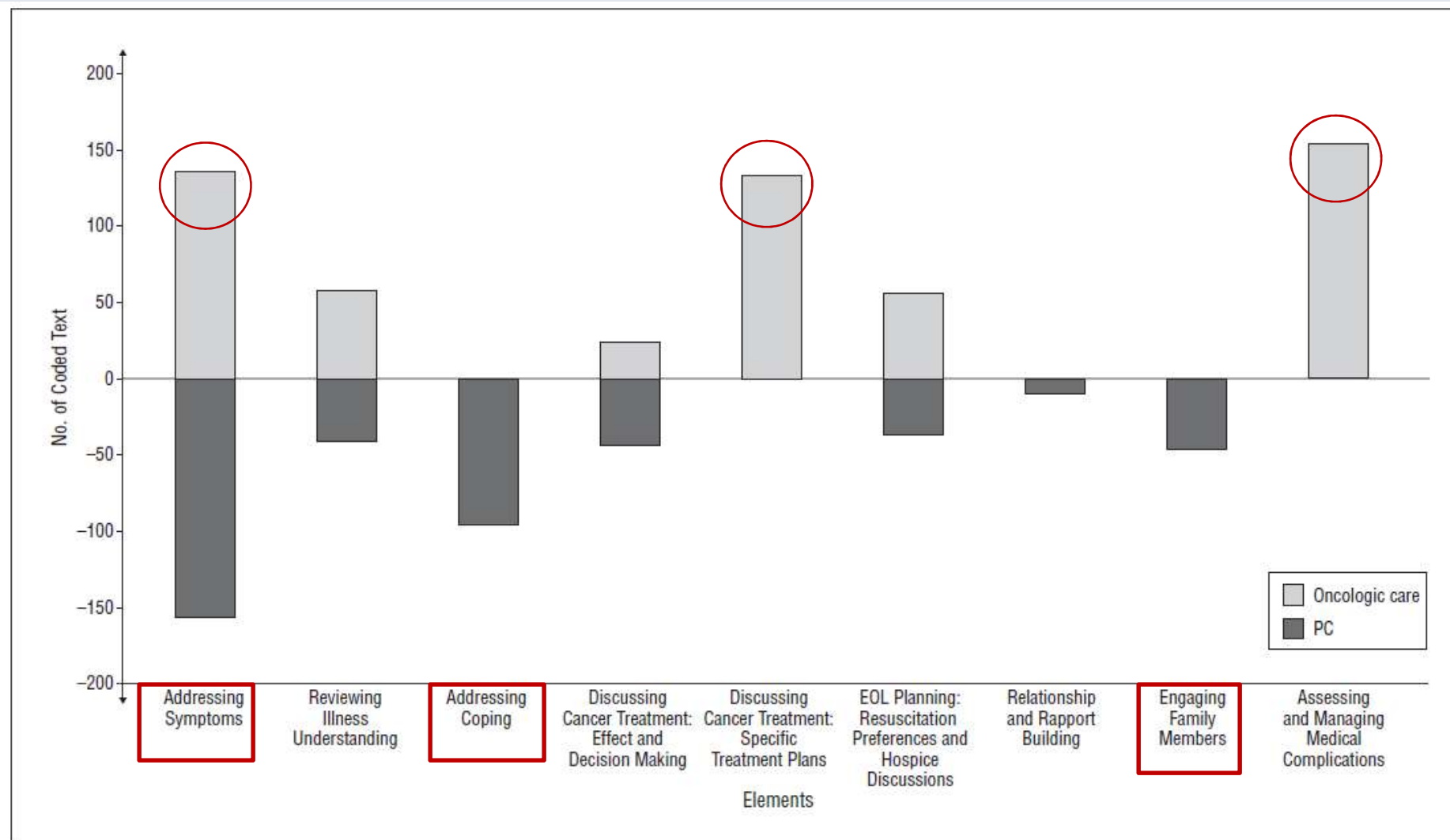
**Figure 2. Trends in transfusion dependence and hospice use.** The panels illustrate proportions of patients who were transfusion dependent at the time of death (A), who were enrolled in hospice at the time of death (B), and in median duration of hospice stay (C). The  $P$  values and CIs were calculated from generalized linear regression (A-B) or quantile regression (C).

# EOL Quality Measures in Leukemias



**Figure 3. Indicators of EOL care quality among Medicare beneficiaries with leukemia, stratified by transfusion dependence and use of hospice at the end of life.** (A) Proportions of patients dying in the inpatient setting, with an ICU admission in the last 30 days of life, or with chemotherapy administration in the last 14 days of life. (B) Median Medicare spending in the last 30 days of life (error bars indicate IQR).

# **DOES PALLIATIVE CARE WORK IN HEMATOLOGY?**



**Figure 2.** Elements of palliative care (PC) vs oncologic care visits at clinical turning points. EOL indicates end of life.

Yoong JAMA IM 17(34) 2013

# Integrated Palliative Care Studies in Oncology

Many randomized clinical trials:

- Bakitas et al, JAMA 2009, ENABLE II study
- Temel et al, NEJM 2010
- Zimmerman et al, Lancet 2014
- Bakitas et al, JCO 2015, ENABLE III study
- Grudzen et al, JAMA Oncology 2016
- Temel et al, JCO 2016
- **El-Jawahri et al, JAMA 2016, SHIELD study**
- Vanbutsele et al, Lancet Onc 2018
- **El-Jawahri and LeBlanc, JAMA Onc 2020, LEAP trial**

Many patient-centered outcome improvements

- **Starting to see long-term and caregiver outcomes improve**

No study has shown harm

## Improved outcomes in these studies

- **Quality of life**
- **Symptom management**
- **Mood/depression**
- **Prognostic understanding**
- **Caregiver outcomes**
- **Utilization/costs**
- **Satisfaction**
- **End-of-life outcomes**
- **Survival**

# Professional Society Recommendations

- American Society of Clinical Oncology
  - “any patient with metastatic cancer and/or high symptom burden”
- American College of Surgeons, Commission on Cancer
  - Accredited programs “required to offer palliative care either on site or by referral”
- National Comprehensive Cancer Network
  - “Institutions should develop processes for integrating palliative care into cancer care, both as part of usual oncology care and for patients with specialty palliative care needs”
- Oncology Nursing Society
  - “All patients with cancer benefit from palliative care”
  - “Palliative care should begin at time of diagnosis”

Smith TJ, et al. “American Society of Clinical Oncology Provisional Clinical Opinion: the Integration of Palliative Care Into Standard Oncology Care.” *Journal of Clinical Oncology*, 2012.  
American College of Surgeons New CoC Accreditation Standards, 2011: <https://www.facs.org/media/press-releases/2011/coc-standards0811>  
NCCN Guidelines Version 2.2015 – Palliative Care: [http://www.nccn.org/professionals/physician\\_gls/PDF/palliative.pdf](http://www.nccn.org/professionals/physician_gls/PDF/palliative.pdf)  
ONS Position Statement: Palliative Care for People With Cancer: <https://www.ons.org/advocacy-policy/positions/practice/palliative-care>



# Randomized Trial of Inpatient Palliative Care Intervention for Patients Hospitalized for Hematopoietic Stem Cell Transplantation (HCT)

Areej El-Jawahri, Thomas LeBlanc, Harry VanDusen, Lara Traeger, Joseph Greer,  
William Pirl, Vicki Jackson, Jason Telles, Alison Rhodes, Thomas Spitzer, Steven McAfee,  
Yi-Bin Chen, Stephanie Lee, Jennifer Temel

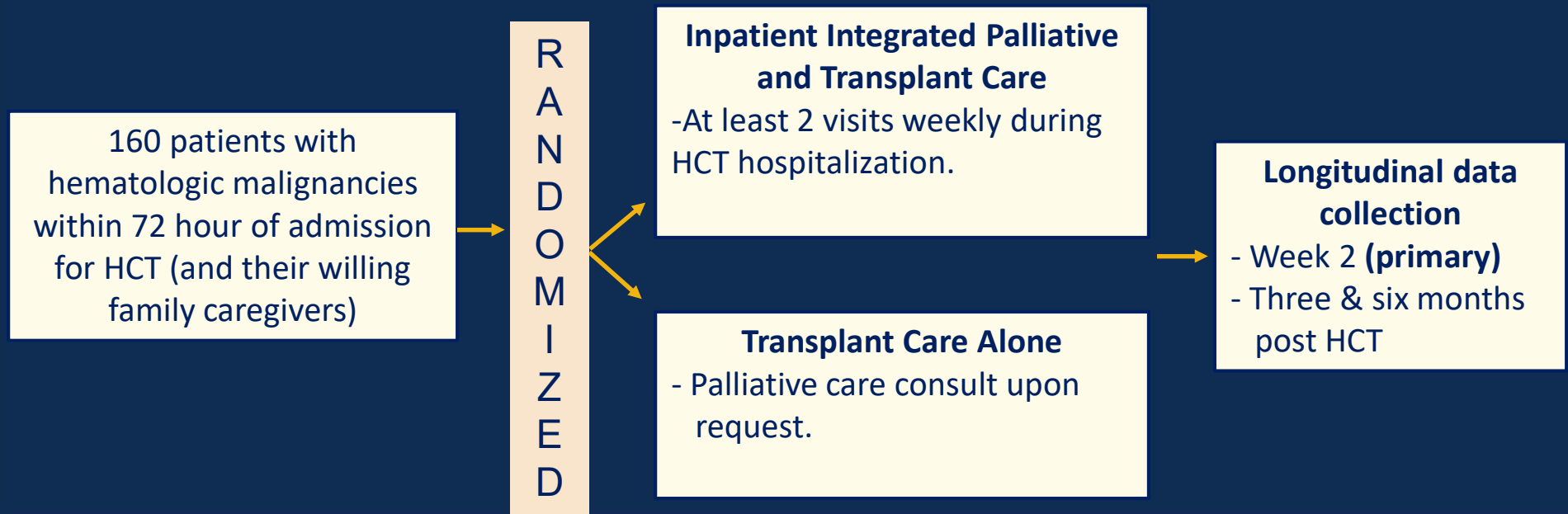


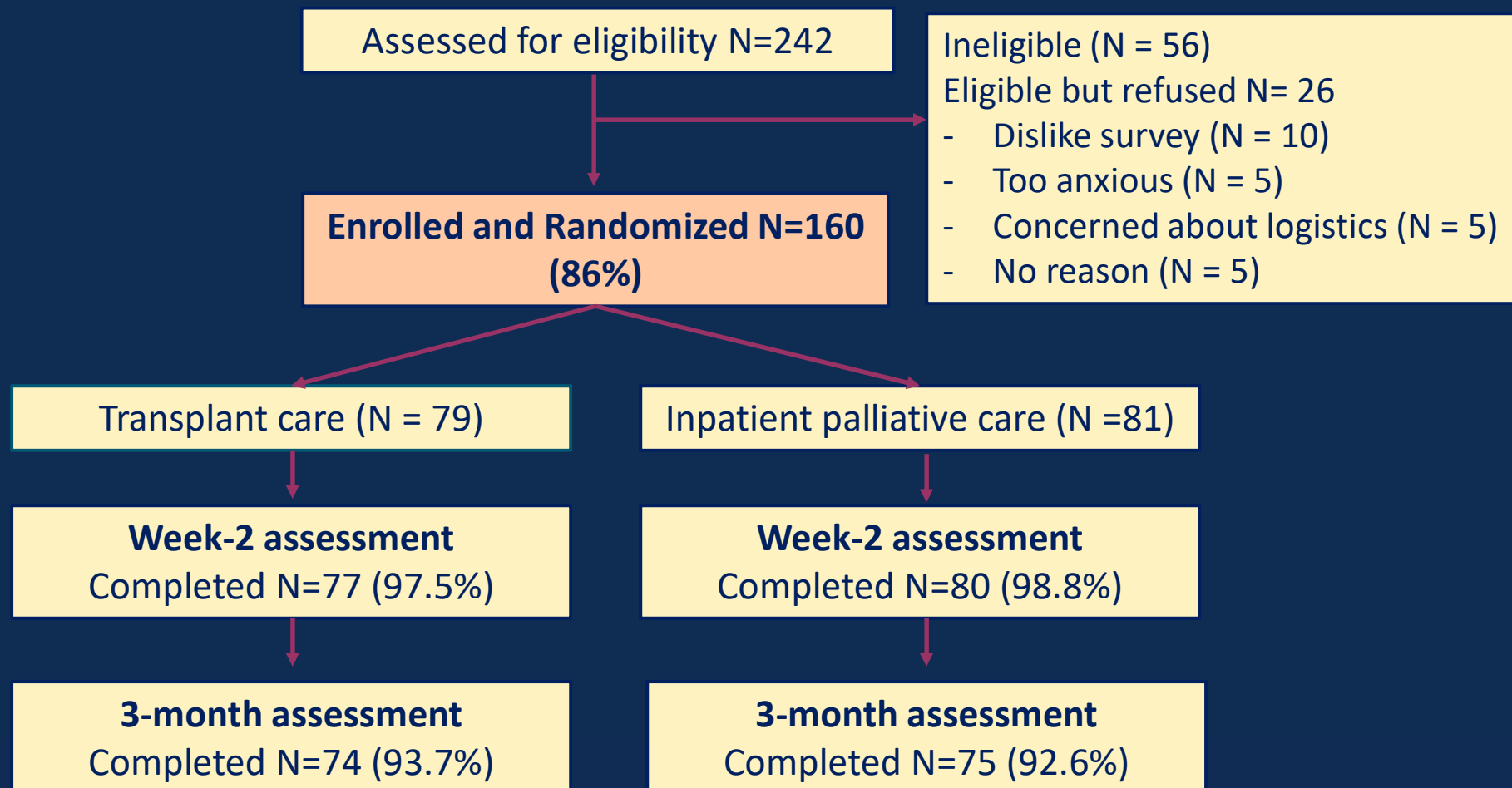
MASSACHUSETTS  
GENERAL HOSPITAL  
CANCER CENTER



CANCER  
OUTCOMES  
RESEARCH

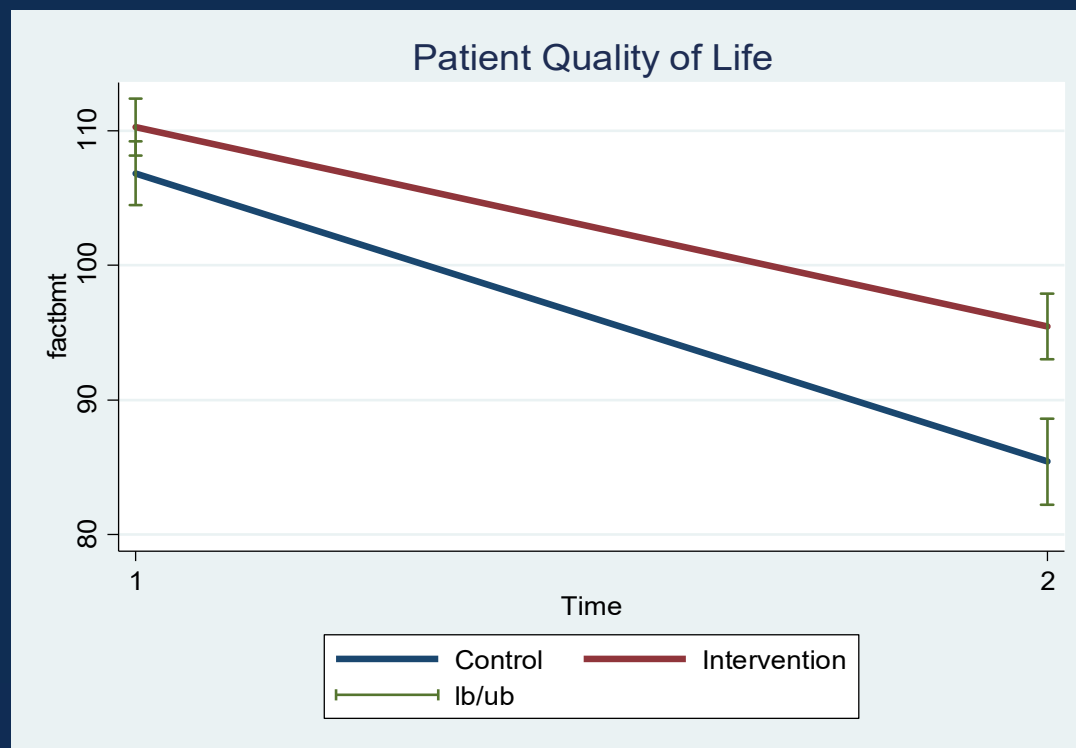
# Study Design





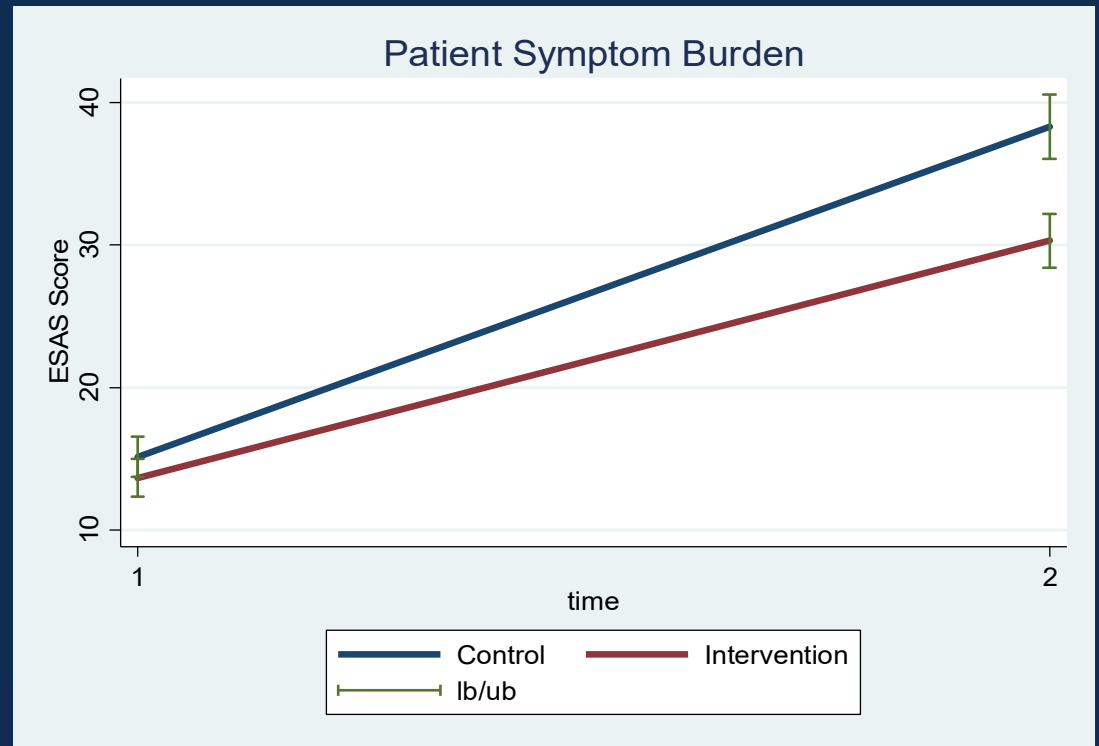
# Patient QOL

$\Delta$  FACT-BMT: -14.7 vs. -21.5  
**P = 0.04**, Cohen's d = 2.9

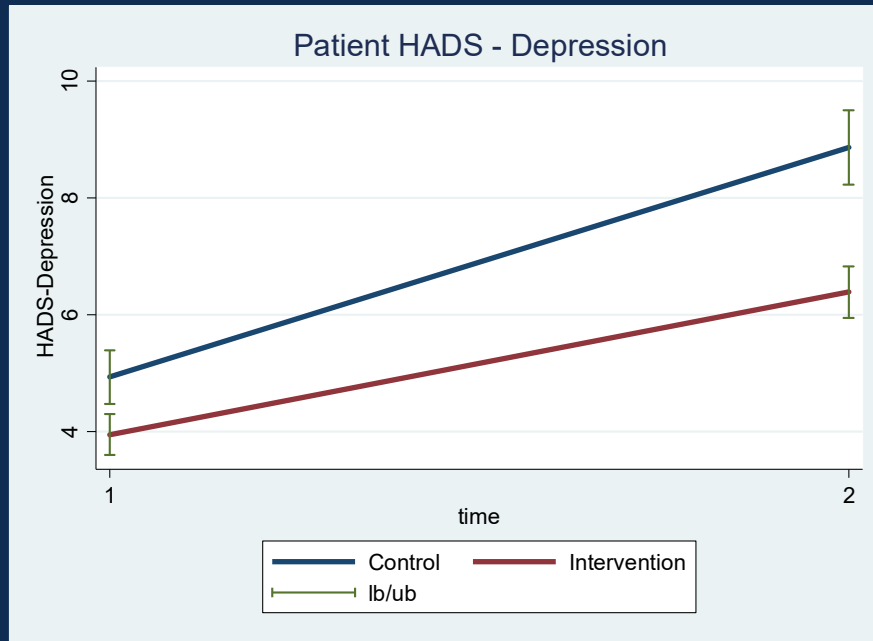


# Patient Symptom Burden

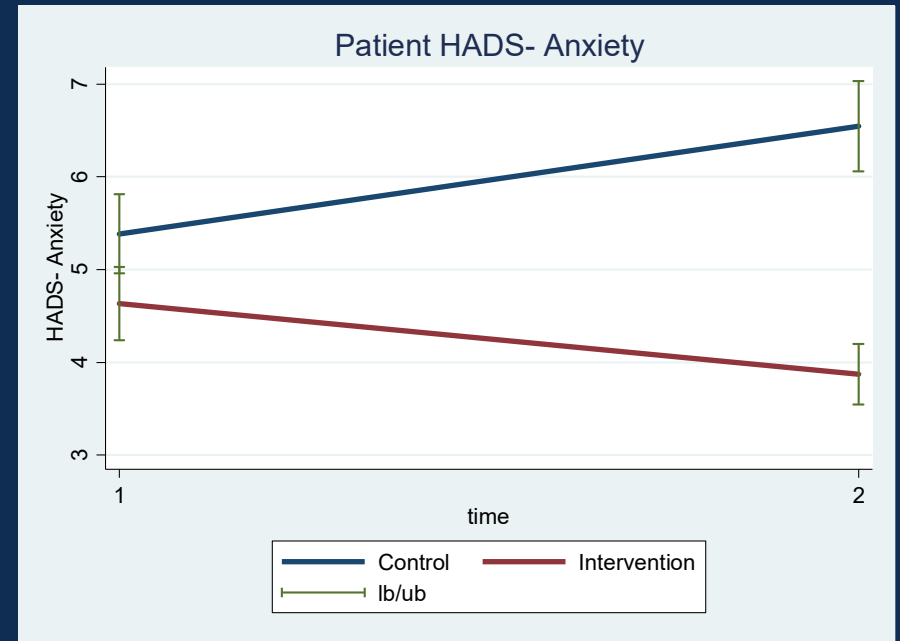
$\Delta$  ESAS: 17.3 vs. 23.1  
**P = 0.03**, Cohen's d = 0.4



# Patient Mood



$\Delta$  HADS-D: 2.4 vs. 3.9,  
**P = 0.02**, Cohen's d = 0.4



$\Delta$  HADS-A: -0.8 vs. 1.1  
**P = 0.0006**, Cohen's d = 0.6



# Week-2 Outcomes

Week-2 Outcomes	Adjusted mean difference	95% CI	P-Value
<b>FACT – BMT (primary outcome)</b>	7.73	1.27 to 14.19	<b>0.019</b>
<b>FACT – Fatigue</b>	3.88	0.21 to 7.54	<b>0.038</b>
<b>ESAS – Symptom burden</b>	-6.26	-11.46 to -1.05	<b>0.019</b>
<b>HADS – Depression symptoms</b>	-1.74	-3.01 to -0.47	<b>0.008</b>
<b>HADS – Anxiety symptoms</b>	-2.26	-3.22 to -1.29	<b>&lt;0.001</b>
<b>PHQ-9 – Depression</b>	-1.28	-2.82 to 0.27	0.104



## 3 Month Outcomes

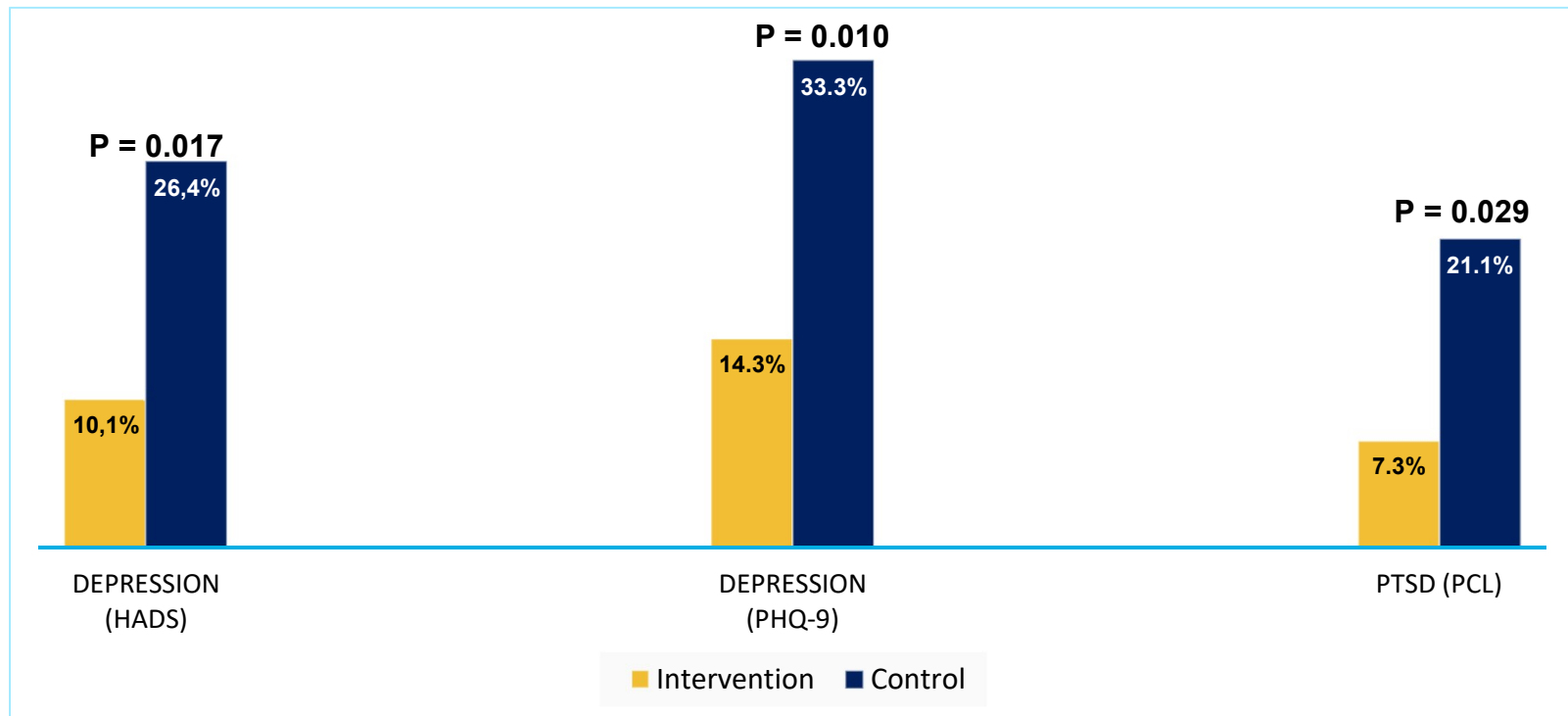
3 Month Outcomes	Adjusted mean difference	95%CI	P-Value
FACT – BMT	5.34	0.04 to 10.65	<b>0.048</b>
FACT – Fatigue	2.00	-1.08 to 5.09	0.202
ESAS – Symptom burden	-2.44	-6.29 to 1.41	0.212
HADS – Depression symptoms	-1.70	-2.75 to -0.65	<b>0.002</b>
HADS – Anxiety symptoms	-0.76	-1.73 to 0.23	0.130
PHQ-9 – Depression	-2.12	-3.42 to -0.814	<b>0.002</b>
PCL – PTSD symptoms	-4.35	-7.12 to -1.58	<b>0.002</b>



## 6-Month Outcomes

6 Month Outcomes	Adjusted Mean Difference	95% CI	P- Value
FACT – BMT	2.72	-2.96 to 8.39	0.346
FACT – Fatigue	0.10	-3.38 to 3.58	.957
HADS – Depression	-1.21	-2.26 to -0.16	<b>0.024</b>
HADS – Anxiety symptoms	-0.61	-1.69 to 0.47	0.267
PHQ-9 – Depression	-1.63	-3.08 to -0.19	<b>0.027</b>
PCL – PTSD Symptoms	-4.02	-7.18 to -0.86	<b>0.013</b>

# Psychological Distress at 6-Months

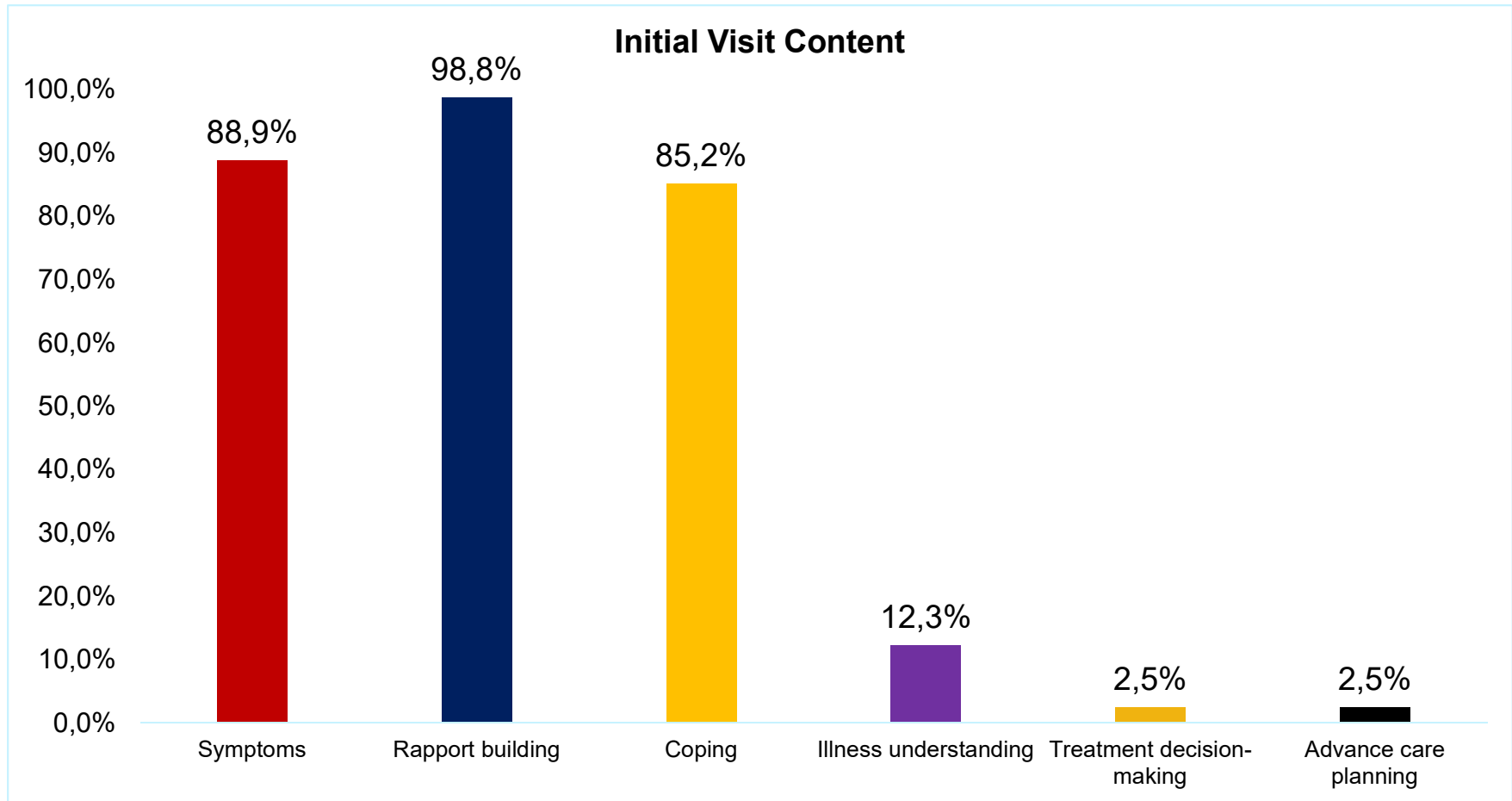


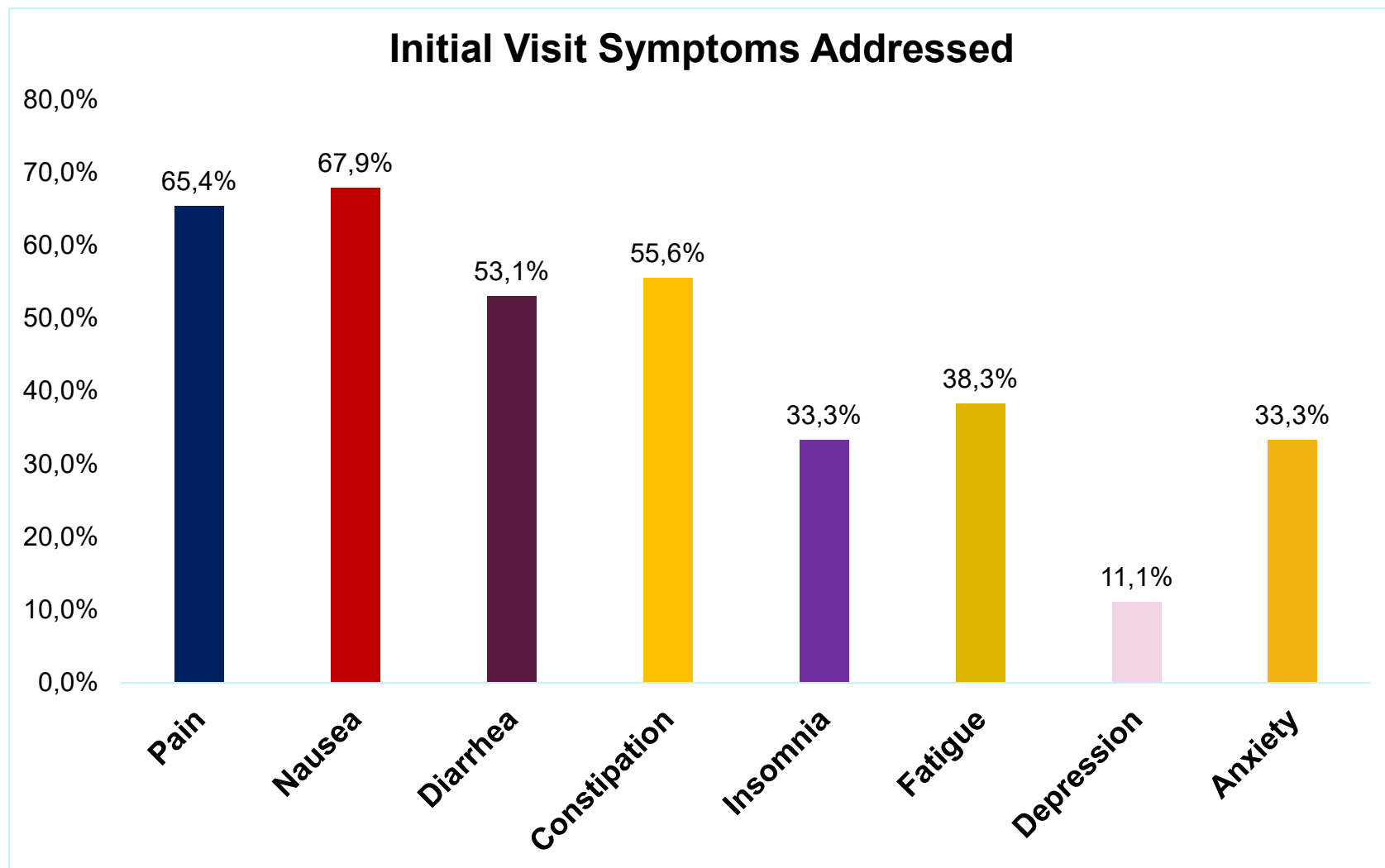
# Caregiver Outcomes

2-week Caregiver Outcomes	Adjusted mean difference	95% CI	P-value
HADS-Depression	-1.65	-3.01 to -0.29	<b>0.018</b>
HADS-Anxiety	-0.14	-1.56 to 1.27	0.84
QOL	3.38	-1.59 to 8.35	0.180

## Improvement in two domains of QOL

- **Coping:** adjusted mean difference = 1.01, **P = 0.009**
- **Administrative/finances:** adjusted mean difference = 0.67, **P = 0.029**







# Multi-Site Randomized Trial of Integrated Palliative and Oncology Care for Patients with Acute Myeloid Leukemia (AML)

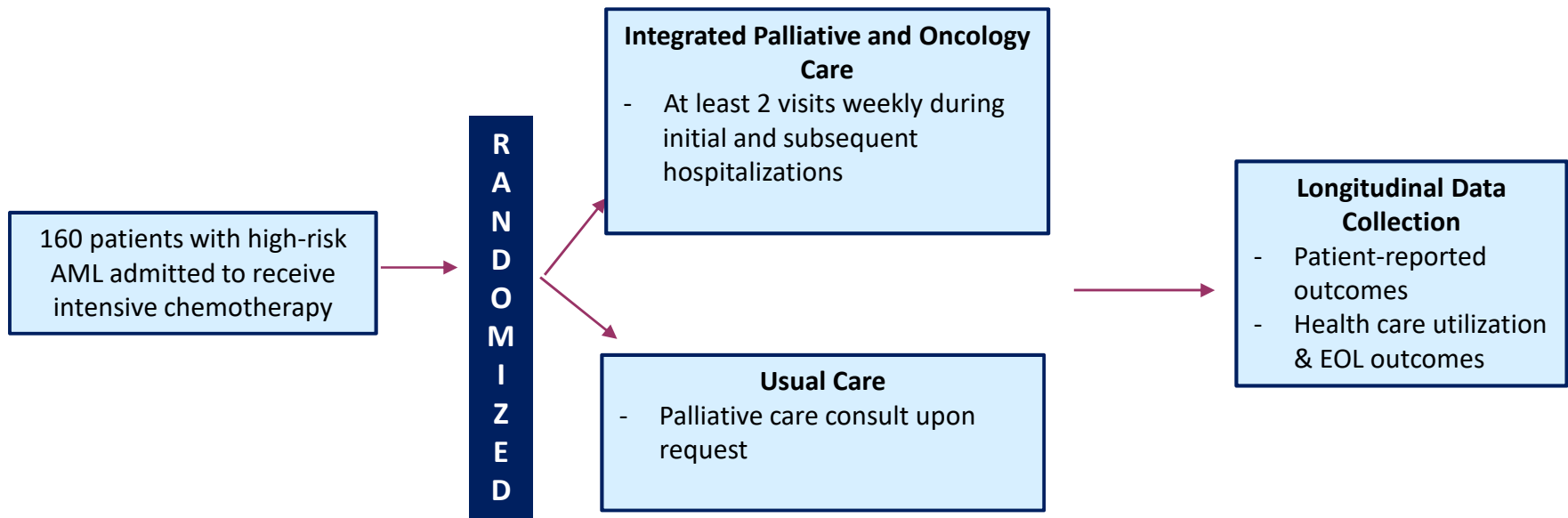
Areej El-Jawahri MD, Thomas W. LeBlanc MD, Alison Kavanaugh NP, Jason A. Webb MD, Vicki A. Jackson MD, Toby Campbell MD, Nina O'Connor MD, Selina Luger MD, Ellin Gafford MD, Jillian Gustin MD, Bhavana Bhatnagar MD, Amir Fathi MD, Gabriela Hobbs MD, Julie Foster NP, Showly Nicholson BS, Debra Davis RN BSN, Hilena Addis BS, Dagny Vaughn BA, Nora Horick MS, Joseph A. Greer PhD, Jennifer S. Temel MD

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# Study Design



- Randomization is stratified by study site, and diagnosis (newly diagnosed vs. relapsed/refractory)
- **Sites:** MGH, Duke, Penn, Ohio State

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## Patient Eligibility Criteria

- Hospitalized patients (age  $\geq 18$ ) with high-risk AML receiving intensive chemotherapy
- **Exclusion criteria:**
  - Patients with APML
  - Patients receiving non-intensive chemotherapy
  - Patients already receiving palliative care
  - Patients with major psychiatric or comorbid conditions

### High-risk AML

- 1) Newly diagnosed  $\geq 60$  years
- 2) Antecedent hematologic disorder or therapy related
- 3) Relapsed or primary refractory AML

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## Study Measures

- Patient-reported outcomes measured at baseline, weeks 2, 4, 12, and 24
- **Primary endpoint:** QOL (FACT-Leukemia) at week-2
- **Secondary endpoints:**
  - Psychological distress (HADS and PHQ-9)
  - Symptom burden (ESAS)
  - PTSD symptoms (PTSD Checklist- Civilian Version)
  - EOL outcomes:
    - Patient-reported discussions of EOL care wishes
    - Hospitalizations in the last week of life
    - Chemotherapy administration in the last 30 days of life
    - Hospice utilization

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## Statistical Analyses

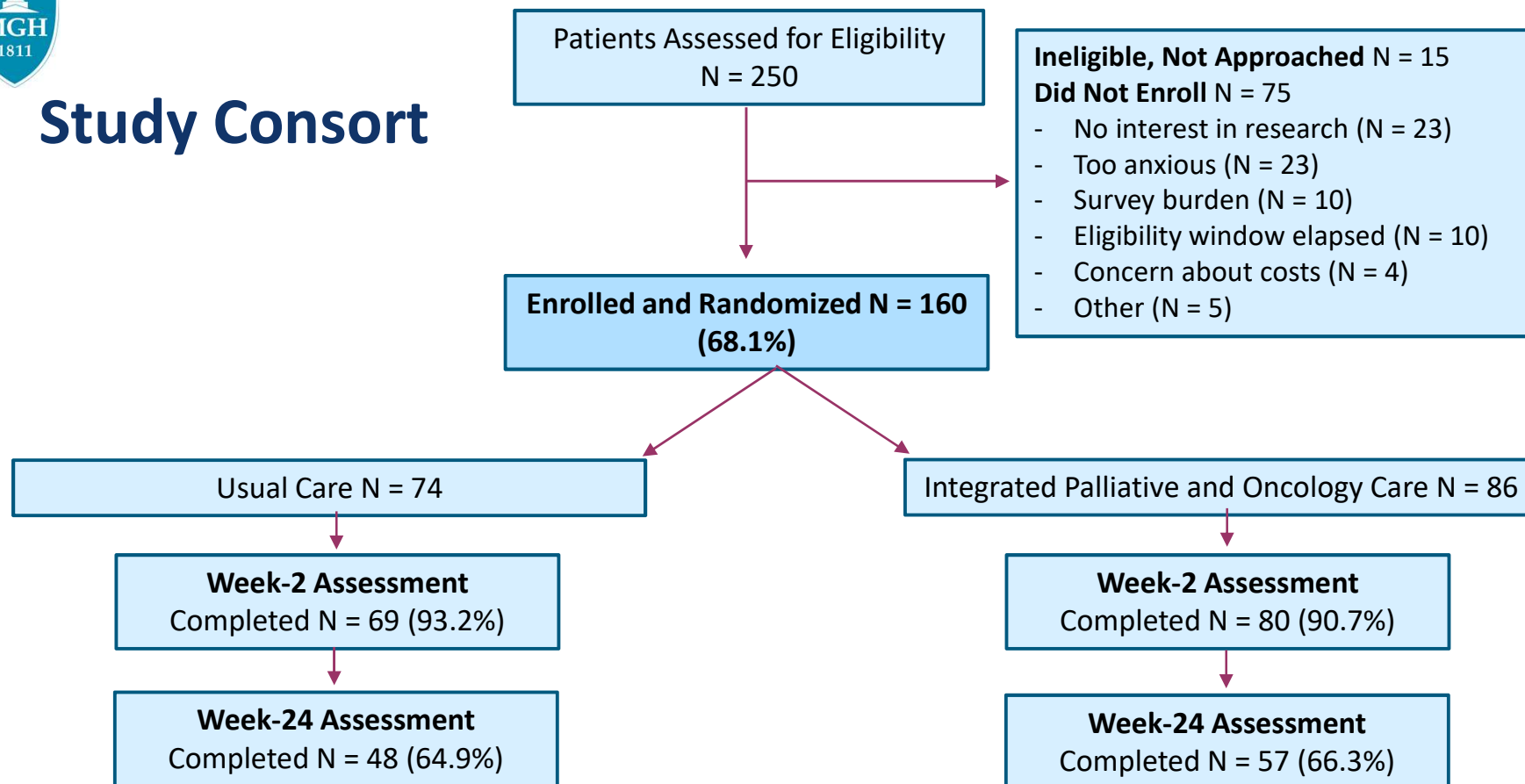
- ANCOVA to assess the impact of the intervention on patient-reported outcomes at week-2 adjusting for baseline scores.
- Mixed linear effect models using Maximum Likelihood to account for missing data to examine the effect of the intervention on patient-reported outcomes longitudinally across all time points (baseline, weeks 2, 4, 12, and 24).
- Fisher's exact test for dichotomous EOL outcomes.

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# Study Consort



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## Baseline Demographics

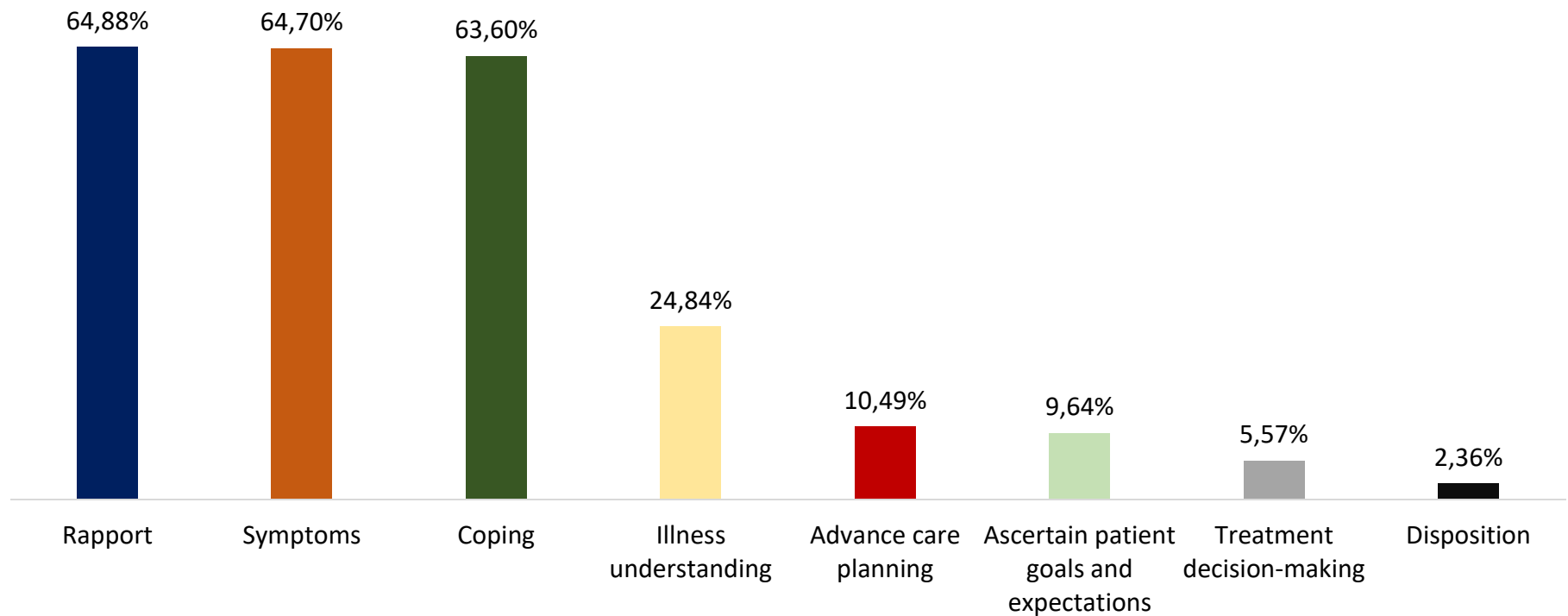
Patient Characteristics	Usual Care (N = 74)	Integrated Palliative and Oncology Care (N = 86)
Age, median (range)	65.2 (22.1-80.1)	63.0 (19.7-77.8)
Female sex, n (%)	27 (36.5%)	37 (43.0%)
Race, n (%)		
White	63 (85.1%)	75 (87.2%)
Black	7 (9.5%)	8 (9.4%)
American Indian	2 (2.7%)	2 (2.3%)
Asian	2 (2.7%)	0
Other	0	1 (1.2%)
Hispanic, n (%)	0 (0.0%)	5 (6.02%)
Diagnosis type, n (%)		
Newly diagnosed AML	50 (67.6%)	59 (68.6%)
Relapsed AML	16 (21.6%)	21 (24.4%)
Refractory AML	8 (10.8%)	6 (7.0%)

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# Palliative Care Intervention Focus During Intensive Chemotherapy Hospitalization

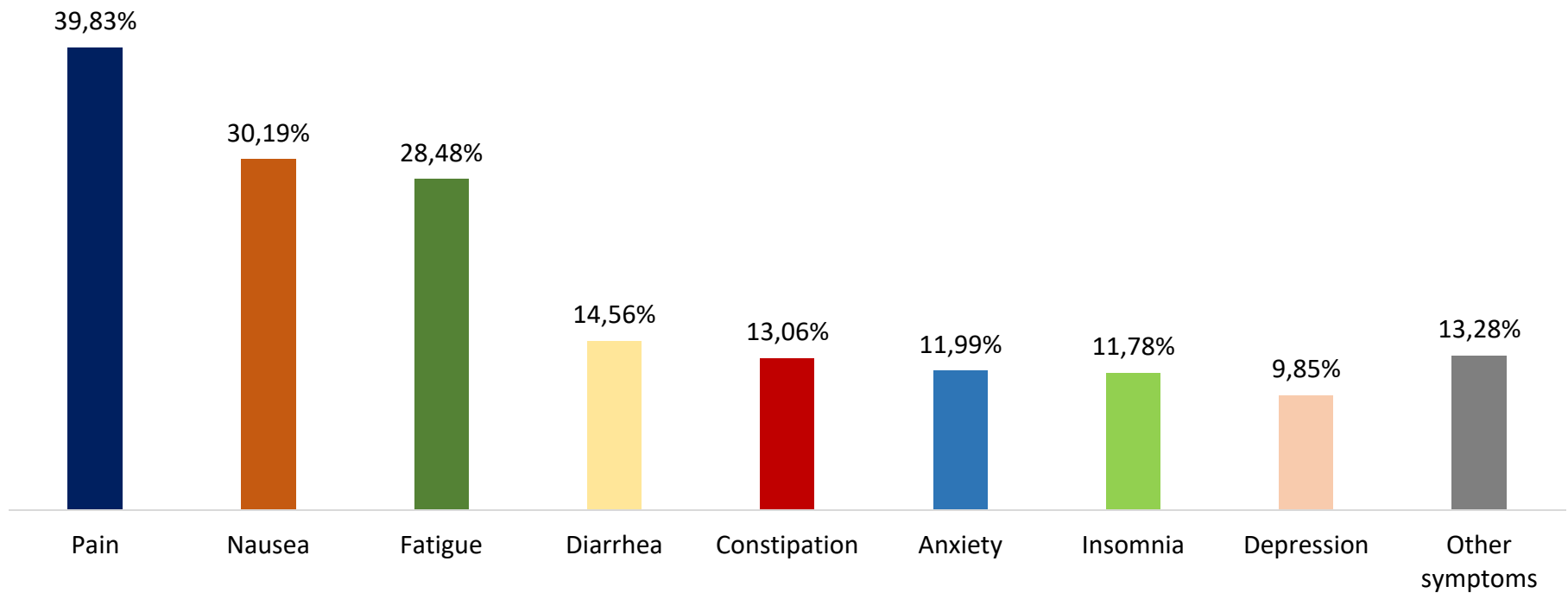


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# Symptoms Addressed During Palliative Care Visits

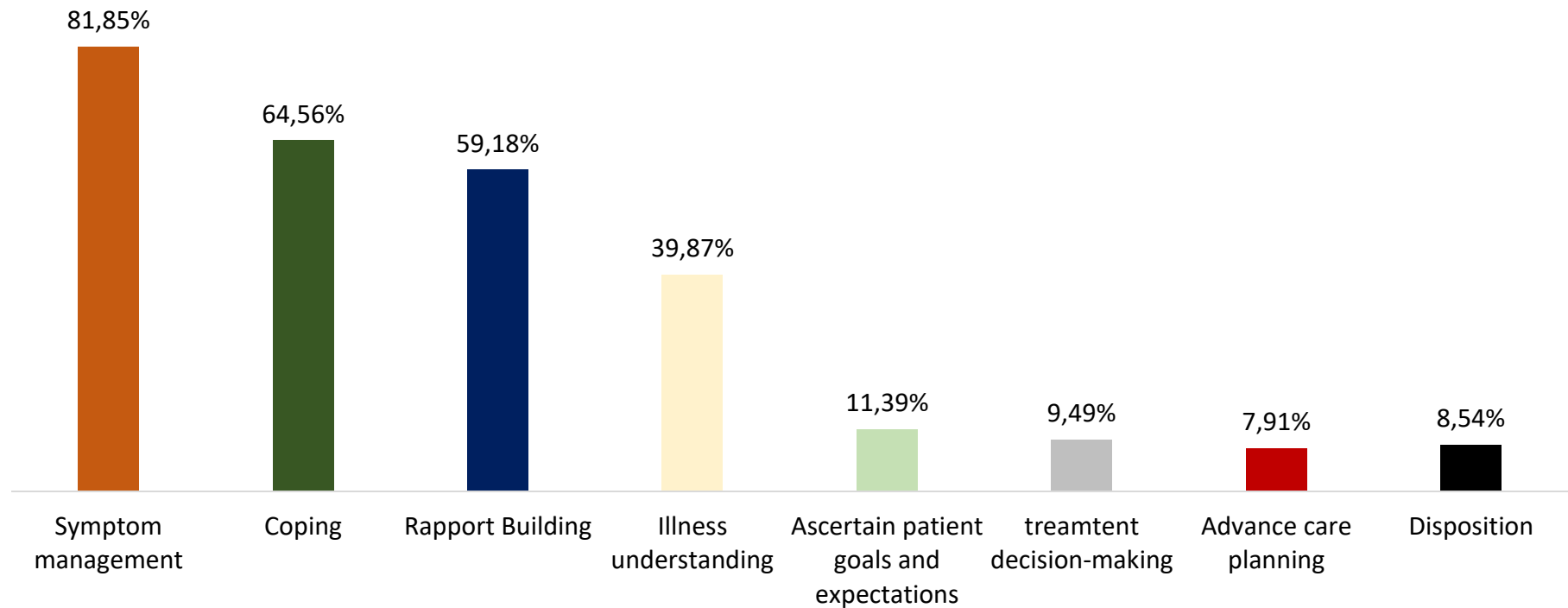


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## Palliative Care Intervention Focus During Subsequent Hospitalizations



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# Results

Week-2	Sample size	Group assignment	Adjusted mean score	95% CI	P-value
QOL (FACT-Leukemia)	139	Usual Care Intervention	107.59 116.45	101.45 - 113.74 110.69 - 122.21	<b>0.039</b>
Anxiety symptoms (HADS-A)	147	Usual Care Intervention	5.94 4.53	5.10 - 6.79 3.74 - 5.34	<b>0.018</b>
Depression symptoms (HADS-D)	147	Usual Care Intervention	7.20 5.68	6.26 - 8.14 4.80 - 6.56	<b>0.021</b>
Depressive syndrome (PHQ-9)	144	Usual Care Intervention	8.00 6.34	6.83 - 9.17 5.23 - 7.44	<b>0.044</b>
Symptom burden (ESAS)	146	Usual Care Intervention	32.82 28.24	28.58 - 37.06 24.23 - 32.25	0.123
PTSD symptoms (PCL- checklist)	146	Usual Care Intervention	31.69 27.79	29.56 - 33.82 27.78 - 29.80	<b>0.009</b>

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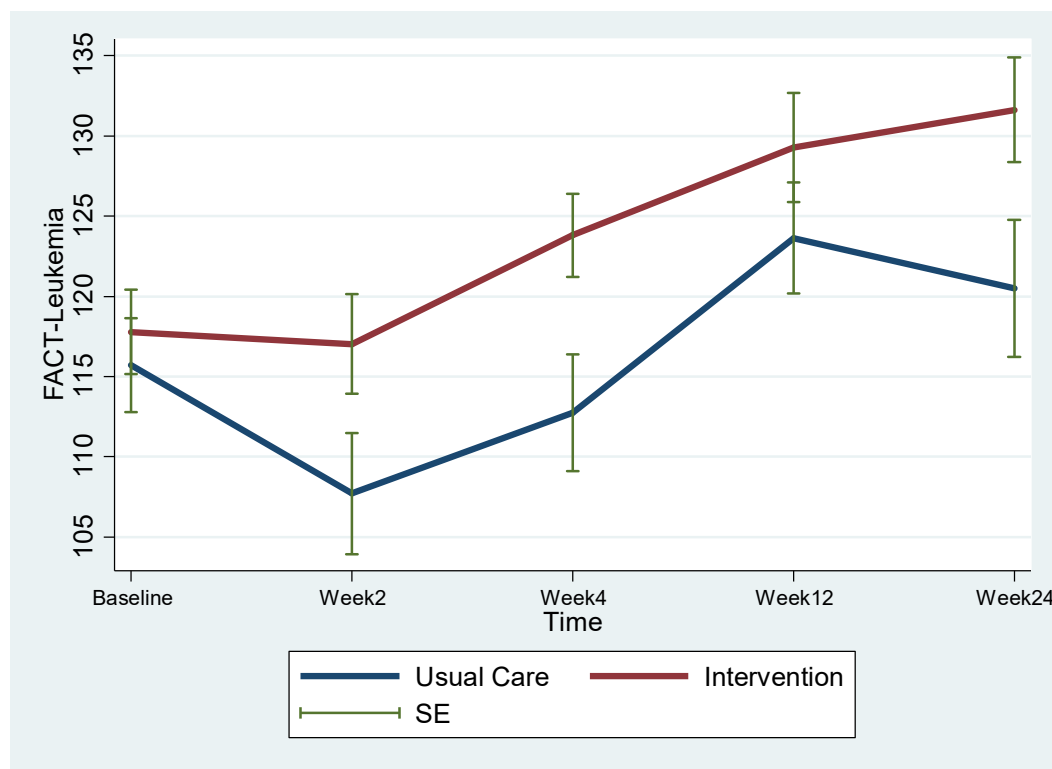


# Results

QOL

Group # Time B = 2.35

95% CI 0.02–4.68, **P = 0.048**



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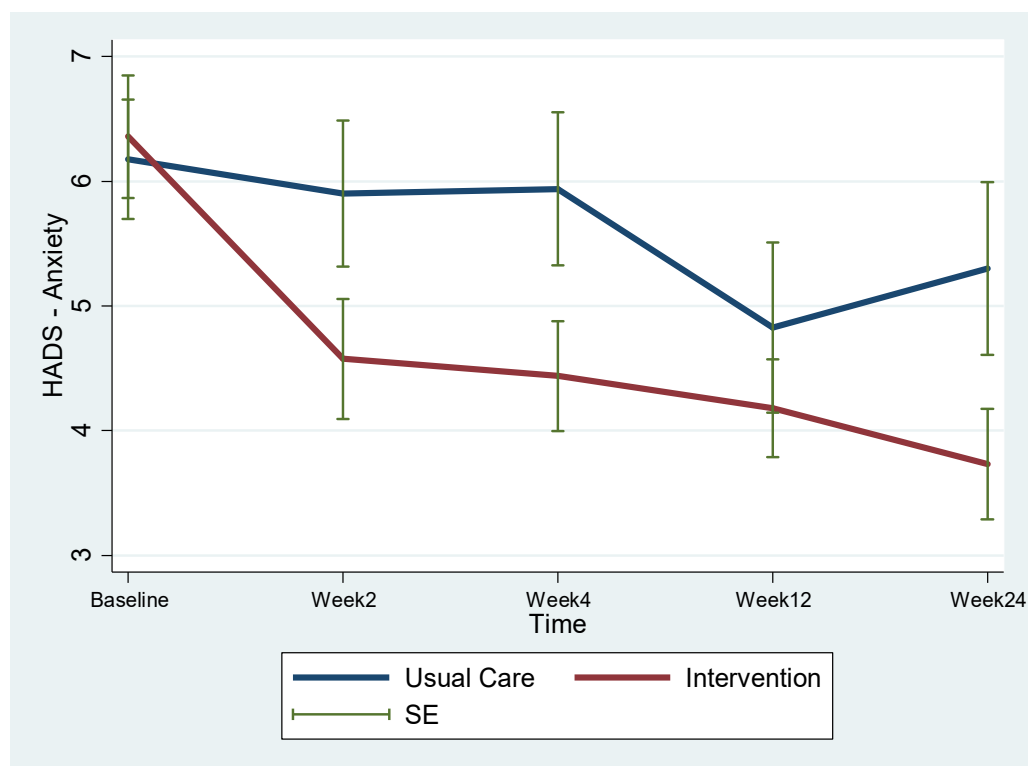
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# Results

## Anxiety symptoms

Group # Time B = -0.38  
95% CI -0.75 – -0.01, P = 0.042



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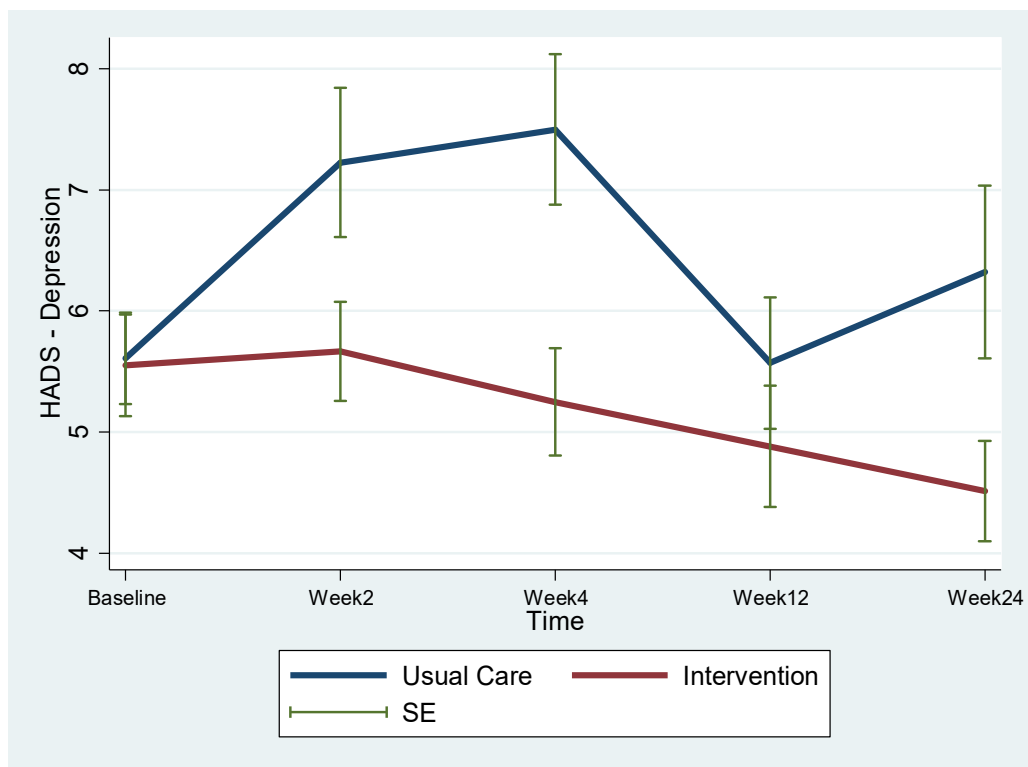
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# Results

## Depression symptoms

Group # Time B = -0.42  
95% CI -0.82 – -0.02, P = 0.039



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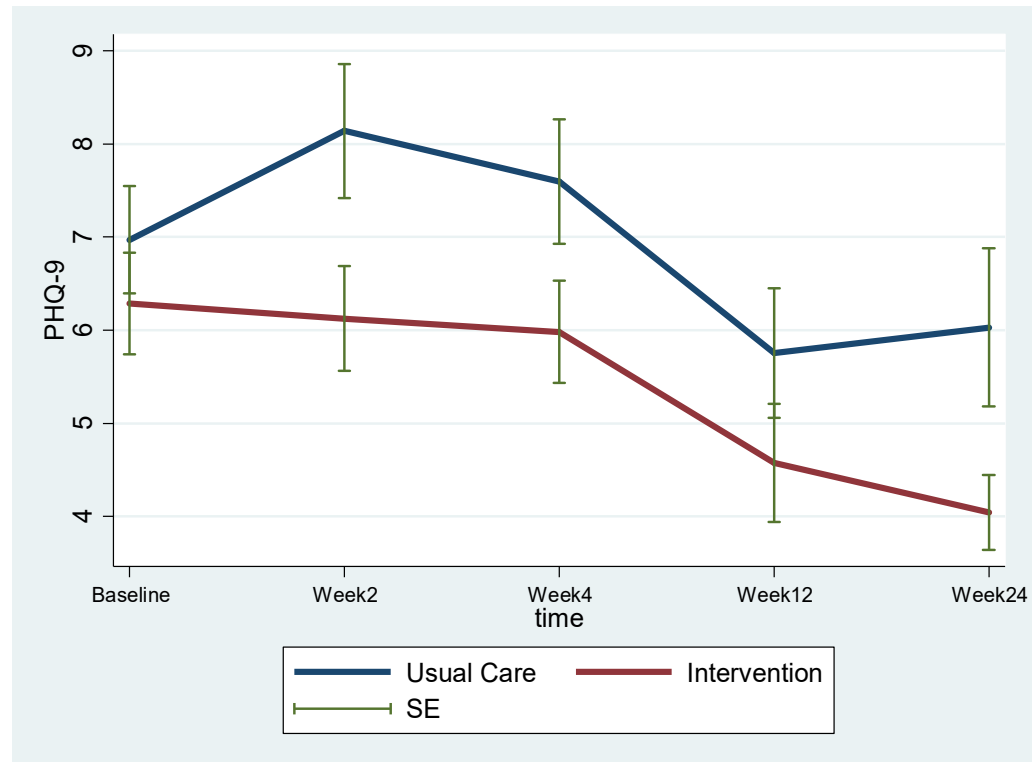


# Results

## Depression syndrome

Group # Time B = -0.21

95% CI -0.67 – 0.25, P = 0.375



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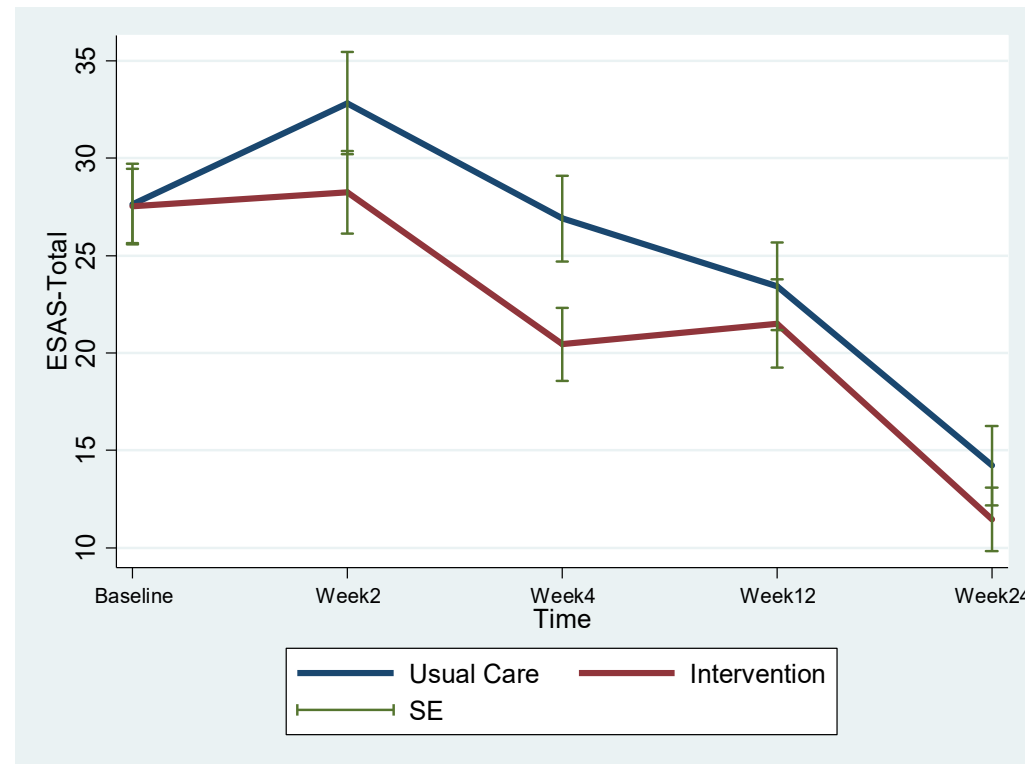


# Results

## Symptom burden

Group # Time B = -0.38

95% CI -2.09 – 1.32, P = 0.659



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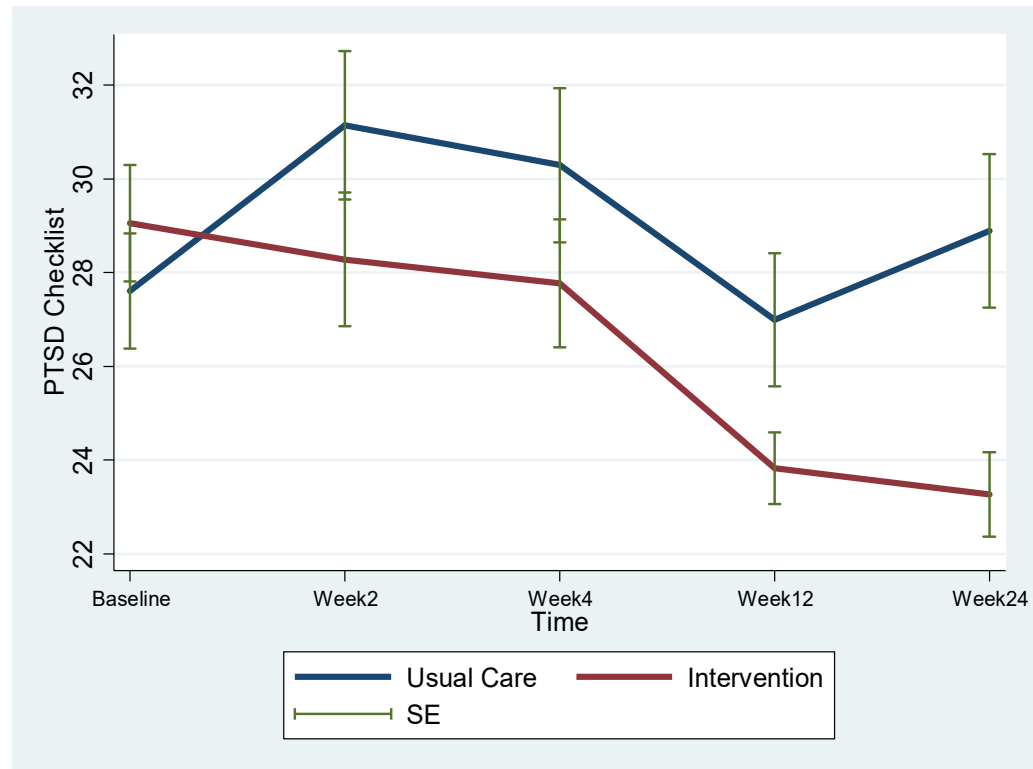
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# Results

## PTSD symptoms

Group # Time B = -1.43  
95% CI -2.34 – -0.54, P = 0.002



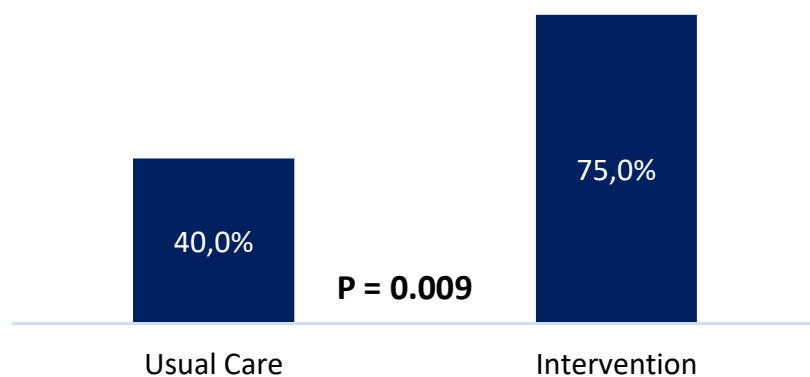
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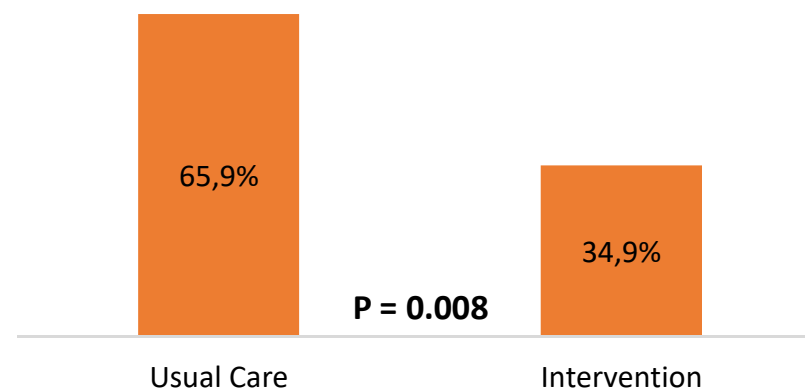


# Results

**Patient-reported discussions of EOL care wishes**



**Receipt of chemotherapy in the last 30 days of life**



- \* 87 participants were deceased at 6-month follow up
- \* No difference in hospitalizations at the EOL or hospice utilization

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## Discussion

- Integrated palliative and oncology care improves QOL, depression and anxiety symptoms, as well as post-traumatic stress symptoms for patients with AML.
- The palliative care intervention led to sustained improvements in QOL and psychological distress six months after initiating chemotherapy in patients with AML.
- Patients receiving the intervention were more likely to discuss their EOL care preferences with their clinicians and less likely to use chemotherapy in the last month of life.

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# Conclusions

Palliative care improves outcomes in hematology too, but we need more evidence

- **Novel intervention development, testing**
- **Other diseases**

Need for clinician education, behavior change

- **...and primary palliative care skill development**

Care model challenges remain; need for policy change

- **Transfusions, chemotherapy and hospice**

Implementation and dissemination is the next big challenge to overcome!

# QUESTIONS AND DISCUSSION