

Monitoring of Symptoms: Why Should We?

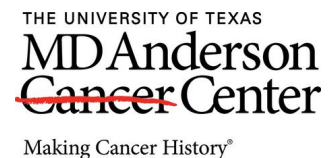
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 - Institutional Research Grant
- Consultancy
 - Eton Pharmaceuticals



Outline



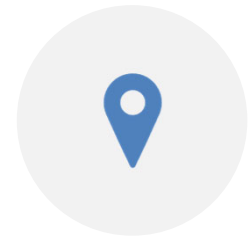
PRINCIPLES



EVIDENCE



PRACTICAL
CONSIDERATIONS



FUTURE
DIRECTIONS

1. Symptoms Occur Frequently

Physical symptoms

- Pain 35-96%
- Fatigue 32-90%
- Anorexia 30-92%
- Delirium 6-93%
- Dyspnea 10-70%
- Insomnia 9-69%
- Nausea 6-68%

Psychological concerns

- Depression 3-77%
- Anxiety 13-79%
- Anger
- Grief
- Frustration
- Fear

Spiritual distress

- Spiritual pain 46%
- Existential concerns
- Loss of meaning
- Hopelessness

Symptom Burden

Incurable Cancer

	Number of Studies	Number of Patients	Pooled Prevalence (%)	95% CI (%)
<i>N</i>	40	25,074		
Fatigue	17	6,727	74	(63; 83)
Pain	37	21,917	71	(67; 74)
Lack of energy	6	1,827	69	(57; 79)
Weakness	18	14,910	60	(51; 68)
Appetite loss	37	23,112	53	(48; 59)
Nervousness	5	727	48	(39; 57)
Weight loss	17	13,167	46	(34; 59)
Dry mouth	20	6,359	40	(29; 52)
Depressed mood	19	8,678	39	(33; 45)
Constipation	34	22,437	37	(33; 40)
Worrying	6	1,378	36	(21; 55)
Insomnia	28	18,597	36	(30; 43)
Dyspnea	40	24,490	35	(30; 39)
Nausea	39	24,263	31	(27; 35)
Anxiety	12	7,270	30	(17; 46)
Irritability	6	1,009	30	(22; 40)
Bloating	5	626	29	(20; 40)
Cough	24	11,939	28	(23; 35)
Cognitive symptoms	9	1,696	28	(20; 38)

	Number of Studies	Number of Patients	Pooled Prevalence (%)	95% CI (%)
Early satiety	5	1,639	23	(8; 52)
Taste changes	11	3,045	22	(15; 31)
Sore mouth/ stomatitis	8	2,172	20	(8; 39)
Vomiting	24	9,598	20	(17; 22)
Drowsiness	16	11,634	20	(12; 32)
Edema	13	3,486	19	(15; 24)
Urinary symptoms	15	12,011	18	(15; 21)
Dizziness	12	3,322	17	(11; 25)
Dysphagia	25	16,161	17	(14; 20)
Confusion	17	11,728	16	(12; 21)
Bleeding	5	8,883	15	(11; 20)
Neurological symptoms	11	10,004	15	(10; 23)
Hoarseness	5	1,410	14	(7; 26)
Dyspepsia	7	3,028	12	(9; 15)
Skin symptoms	7	9,177	11	(6; 20)
Diarrhea	22	16,592	11	(7; 16)
Pruritus	14	6,676	10	(7; 15)
Hiccup	7	3,991	7	(3; 15)

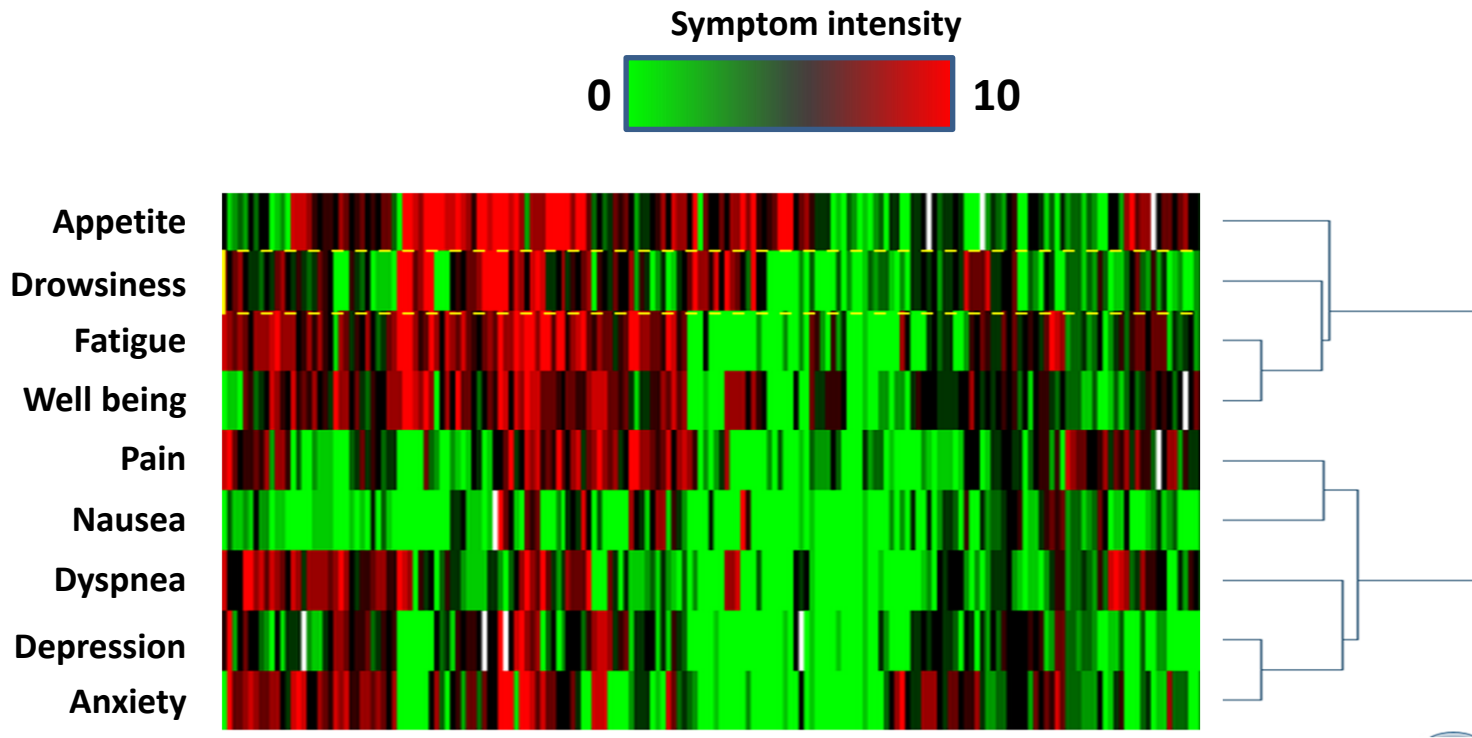
2. Patients Often Have Multiple Symptoms

Symptom	Overall prevalence	Degree of symptom if present		
		Intensity Mod – Vsev (%) ^a	Frequency Freq – Con (%) ^b	Distress QB – VM (%) ^c
Lack of energy	73.4	77.0	55.3	34.2
Worrying	72.4	72.3	38.1	23.2
Feeling sad	67.4	68.7	23.8	21.1
Pain	63.1	74.6	54.3	48.6
Lack of appetite	44.5	82.7	55.1	29.6
Feeling bloated	38.7	81.0	47.6	25.0
Numbness/tingling in hands/feet	36.4	60.3	50.0	26.9
Constipation	33.6	79.5	NE	42.5
Swelling of arms or legs	27.5	66.7	NE	40.0
Problems with sexual interest or activity	23.3	78.0	52.0	22.0
Vomiting	21.1	65.2	32.6	41.3
Difficulty swallowing	10.6	82.6	47.8	52.5

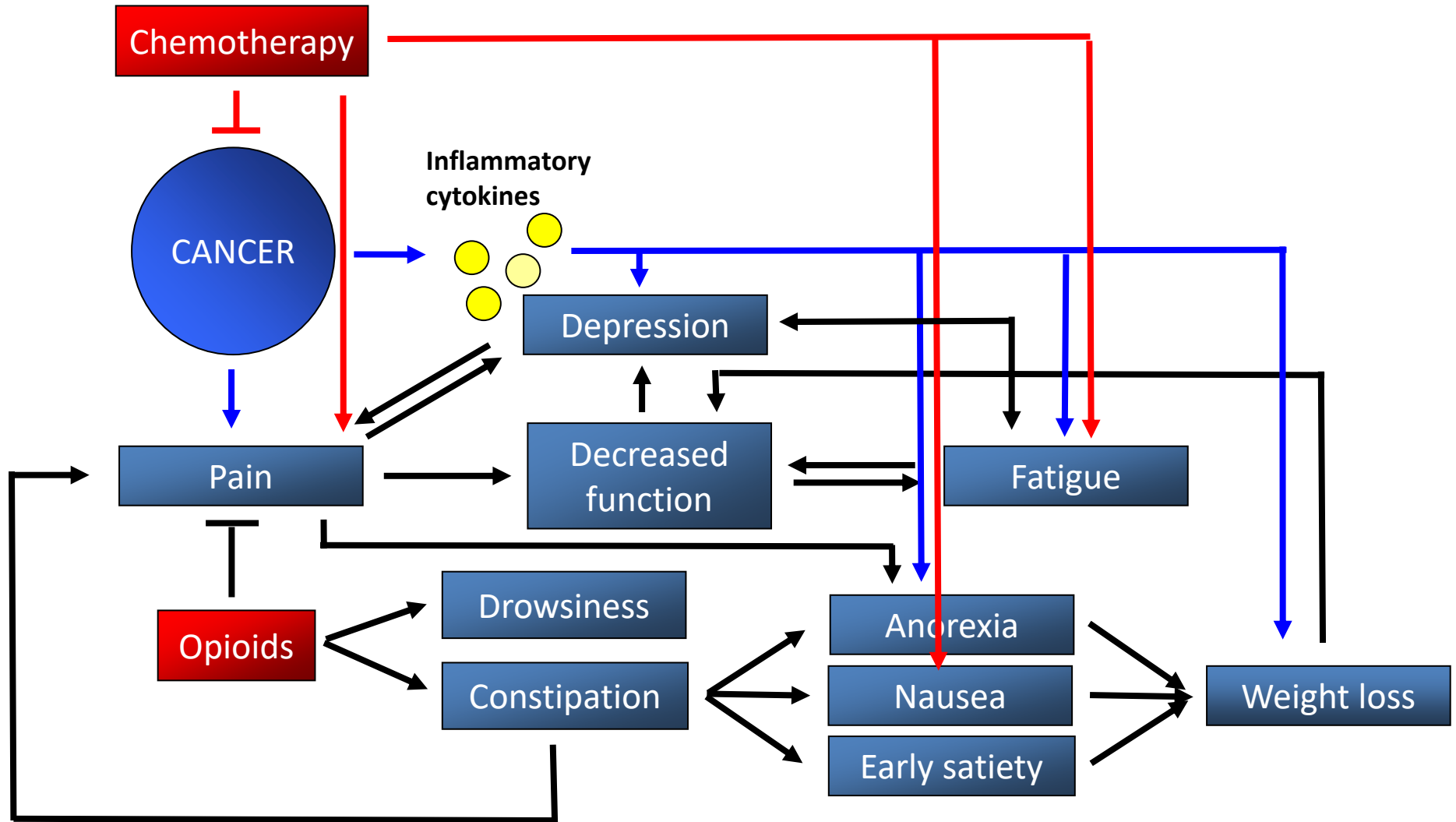
N=243, 2/3 have metastatic cancer

Mean of 11.5±6 symptoms per patient

Symptom Clusters



Symptom Transduction Cascade



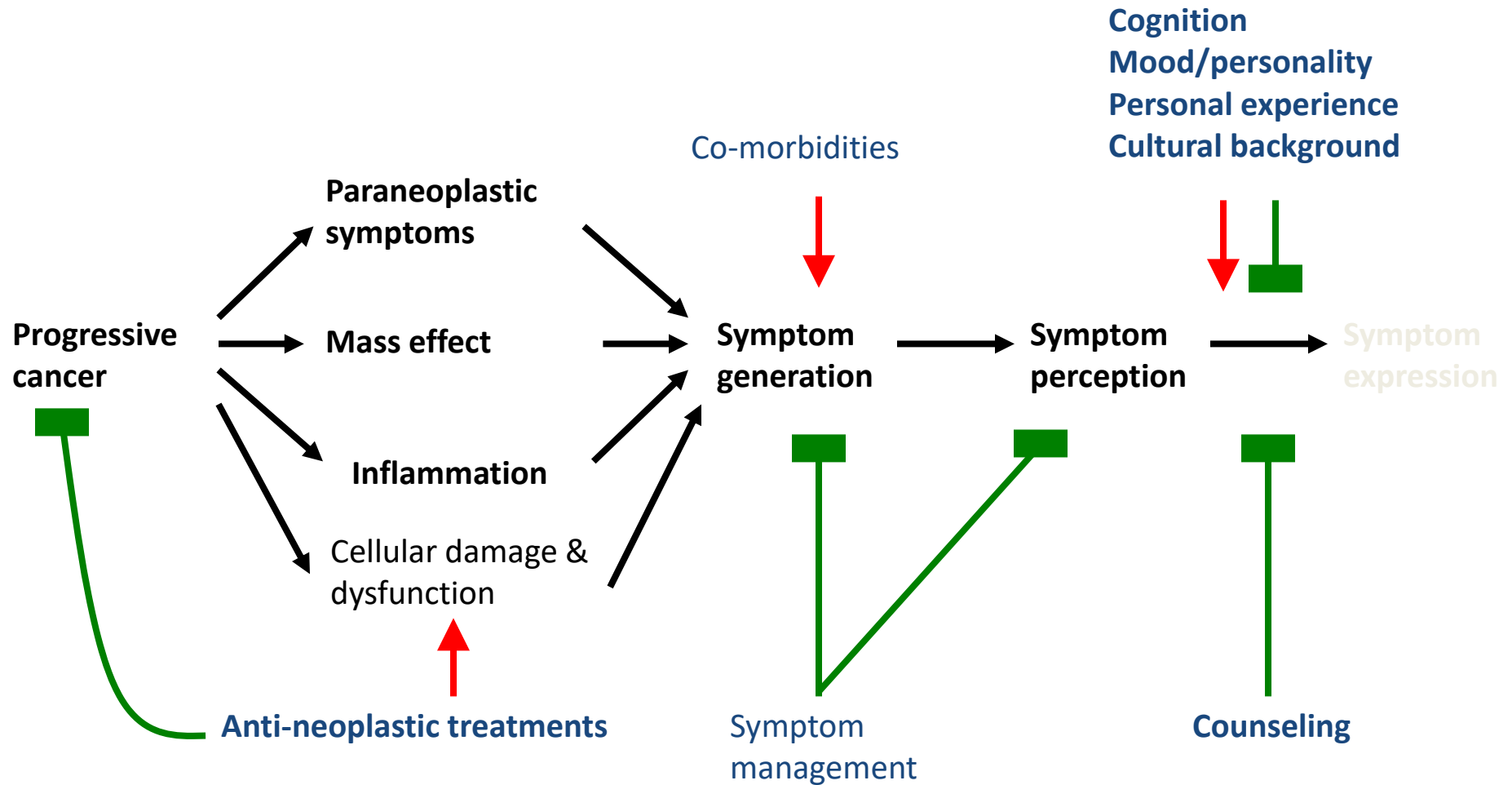
Why Do Symptoms Occur Together?

- Common pathophysiology
 - Cytokines
 - Chemotherapy
- Common associations
 - Dyspnea, fatigue, performance status
 - Nausea, taste changes, anorexia
- Common modulators
 - Anxiety, depression
 - Spiritual distress

3. Symptoms Often Have Multiple Causes

- Cancer
- Cancer treatment side effects
- Other treatment related side effects
- Non-cancer causes
- Modulators
 - Depression and anxiety
 - Spiritual distress
 - Confusion
 - Chemical coping

4. Symptom Expression Modulators



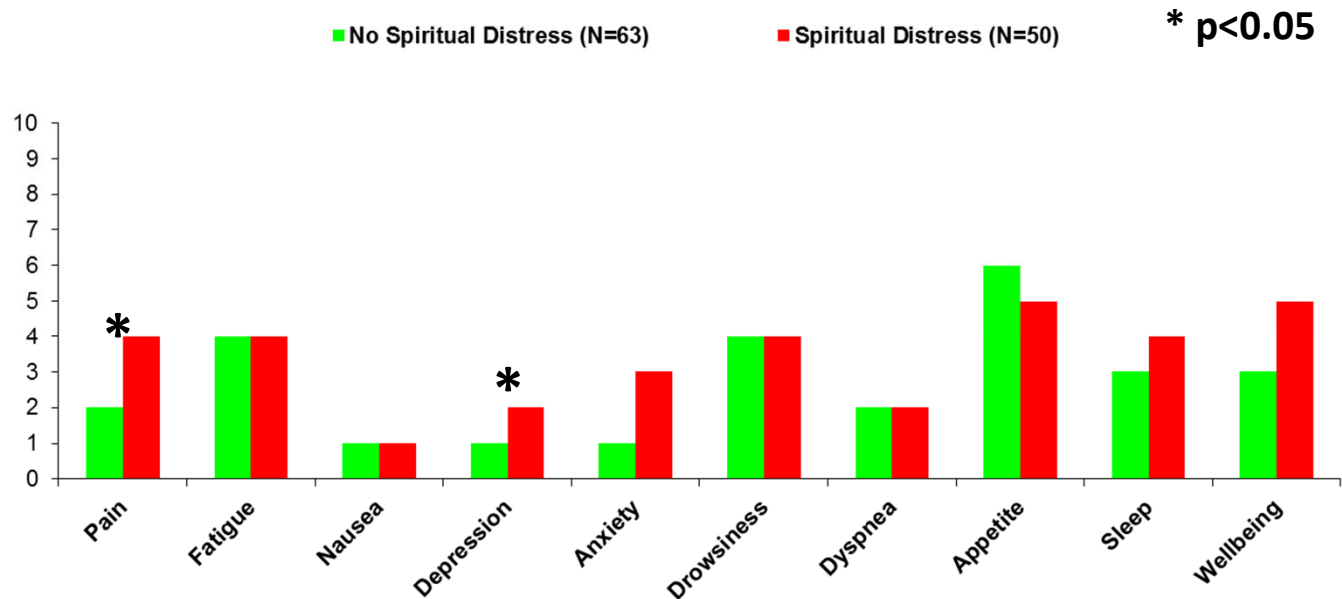
Role of Anxiety/Depression

- 216 cancer patients
- ESAS symptom intensity and HADS

Symptom	Patients without anxiety median ESAS (Q1–Q3, <i>n</i>)	Patients with anxiety median ESAS (Q1–Q3, <i>n</i>)	<i>p</i> value ^a	Patients without depressive mood median ESAS (Q1–Q3, <i>n</i>)	Patients with depressive mood Median ESAS (Q1–Q3, <i>n</i>)	<i>p</i> value*
Appetite	4.5 (3–6, 92)	6 (4–8, 83)	0.0050	5 (3–7, 103)	5 (4–8, 72)	0.0656
Drowsiness	4 (2–5, 81)	5 (3–7, 74)	0.0158	4 (2–6, 87)	4 (3–7, 68)	0.0175
Fatigue	5 (3–7, 115)	6 (5–8, 91)	0.0011	5 (3–7, 131)	7 (5–8, 75)	<0.0001
Nausea	2 (2–4.5, 48)	4 (2–6, 59)	0.0151	3 (2–5, 55)	3 (2–5, 52)	0.5867
Pain	4 (3–7, 96)	6 (3–8, 88)	0.0082	5 (3–7, 110)	5 (3–8, 74)	0.0775
Dyspnea	5 (3–7, 83)	5 (3–7, 84)	0.2368	5 (3–7, 99)	5 (3–7, 68)	0.7209
Well-being	5 (3–7, 105)	5 (3–7, 90)	0.0007	4 (2–6, 117)	6 (5–7, 78)	<0.0001
Anxiety	–	–	–	3 (2–5, 83)	4.5 (3–7)	0.0175
Depression	3 (2–5, 63)	5 (4–7, 79)	<0.0001	–	–	–

Role of Spiritual Distress

- 113 advanced cancer patients in Acute Palliative Care Unit
- Spiritual distress assessed by chaplain



Role of CAGE Positivity

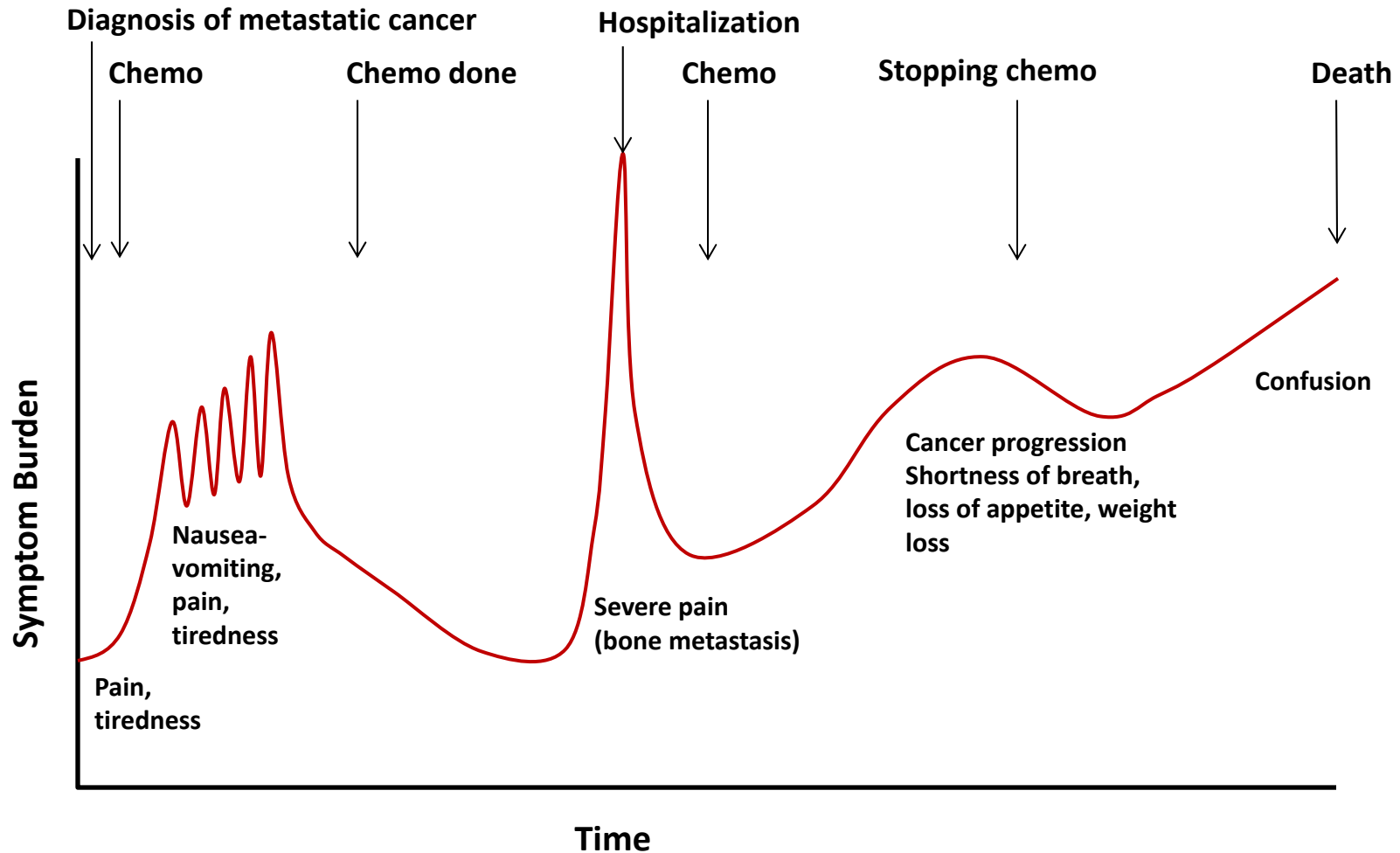
- 598 advanced cancer patients in PC Outpatient Clinic
- 100/598 (17%) were CAGE +ve

<i>Symptom</i>	<i>CAGE negative (n = 100) Median score (interquartile range)</i>	<i>CAGE positive (n = 100) Median score (interquartile range)</i>
Pain	4 (2–7)	6 (4–8) ^a
Fatigue	6 (4–8)	7 (5–8)
Nausea	0 (0–3)	0 (0–3)
Depression	2 (0–5)	3 (0–6)
Anxiety	3 (0–5)	3.5 (0–6)
Drowsiness	4 (1–6)	5 (1–8)
Dyspnea	2 (0–4)	3 (0–6) ^b
Appetite	5 (2–7)	5 (3–8)
Sleep	4 (2–6)	5 (3–7) ^b
Well-being	5 (3–7)	6 (4–8) ^b
Total symptom distress	31 (21–42)	39 (29–51) ^b

^a $p < 0.005$.

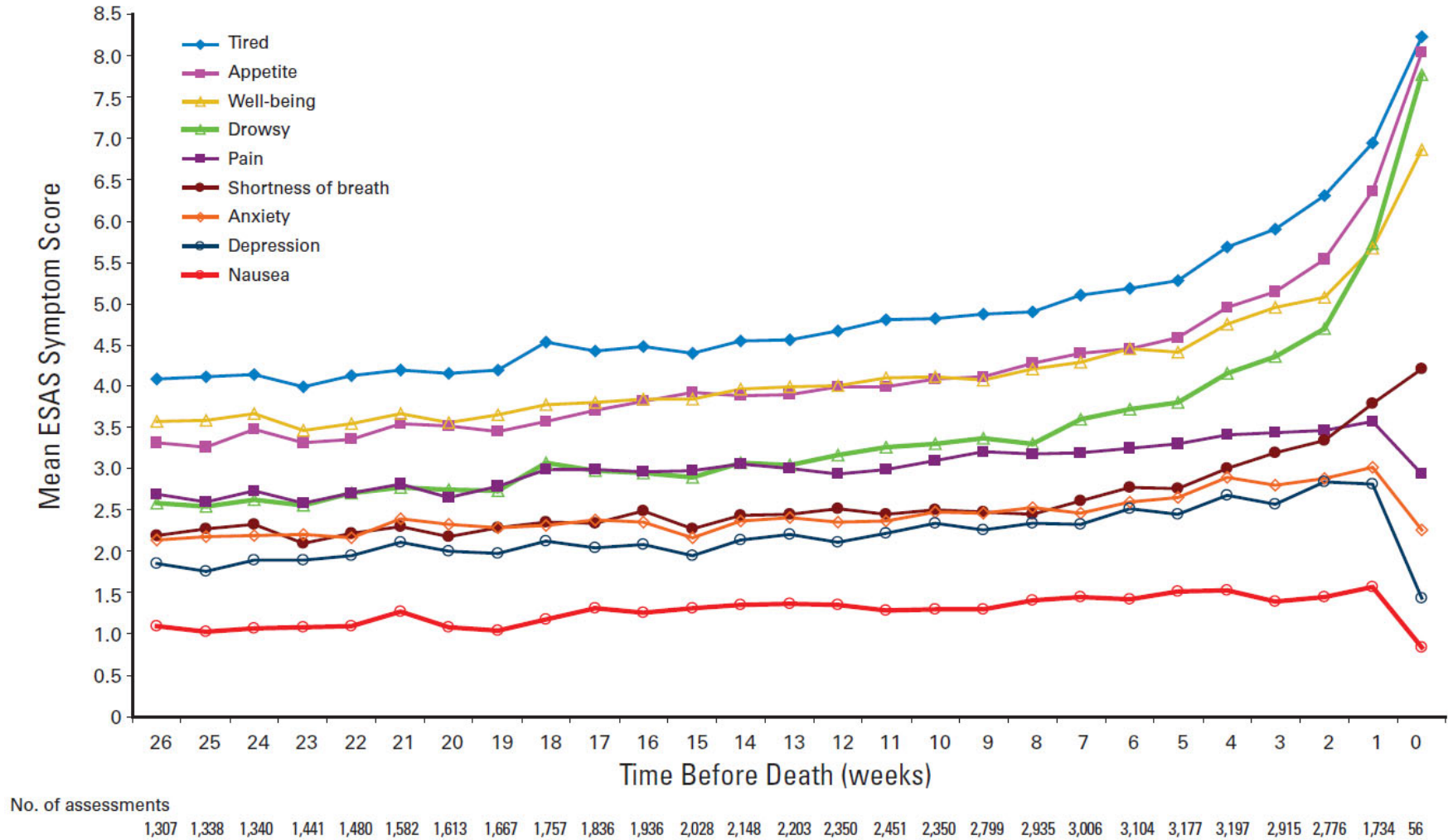
^b $p < 0.05$.

5. Symptom Profile Changes Over Time



Symptom Change

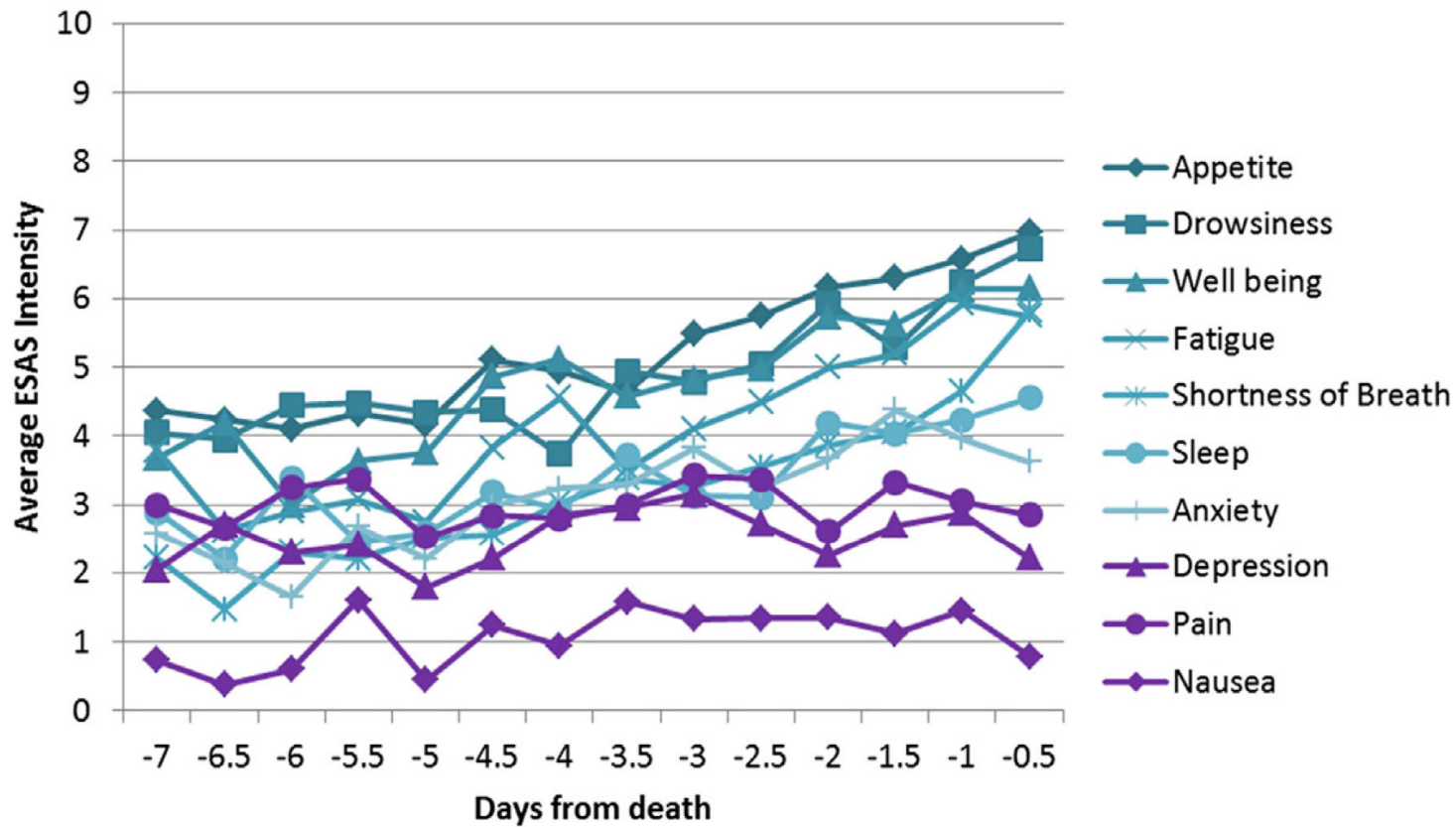
Months before Death



Symptom Change

Days before Death

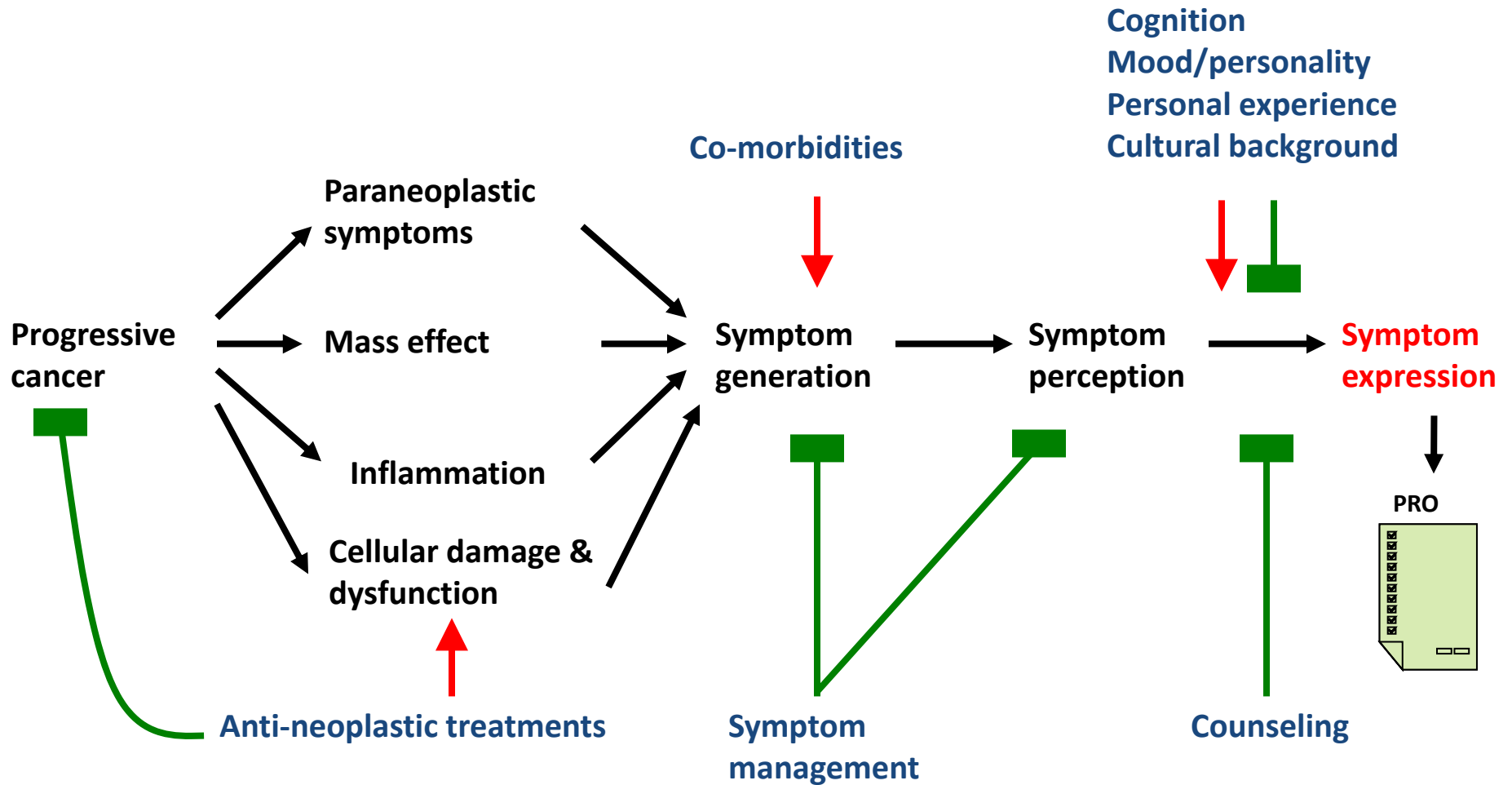
203 patients admitted to Acute Palliative Care Units
(MD Anderson and Barretos Cancer Hospital)



Is This Patient Short of Breath?



6. Patient Report is the Gold Standard



Patient Reported Dyspnea

Subjective and Physiologic Correlates

Characteristics	N	Spearman Correlation Coefficient	P-value
Number of potential causes	299	0.19	0.001
Heart rate	299	0.19	0.001
Respiratory rate	299	0.05	0.36
Oximetry	299	-0.07	0.20
Supplemental oxygen level	299	0.32	<0.001
Respiratory distress observation scale	299	0.35	<0.001
Caregiver's perception	135	0.68	<0.001
Bedside nurse perception	216	0.50	<0.001

Implications for Management

Principles	Implications for assessment	Implications for treatment
1. Symptoms occur frequently	Anticipate, regular screening	Skills in symptom management is essential
2. Symptoms often occur together	Symptom batteries	Multi-targeted treatments
3. Symptoms often have multiple causes	Interdisciplinary assessments	Interdisciplinary treatments
4. Symptom expression is modulated by various factors	Assessment for modulators needed	Management of modulators needed
5. Symptoms fluctuate over time	Longitudinal monitoring	Titration/modification needed
6. Symptom expression is subjective by definition	PROs are gold standard	PROs to define response

Outline



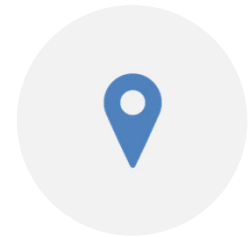
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CONSIDERATIONS



FUTURE
DIRECTIONS



Symptom Assessment Battery

Edmonton Symptom Assessment System (ESAS)

1991

2017

The Edmonton Symptom Assessment System (ESAS): A Simple Method for the Assessment of Palliative Care Patients

EDUARDO BRUERA, NORMA KUEHN, MELVIN J. MILLER, PAL SELMSER, and KAREN MACMILLAN, Edmonton General Hospital, Edmonton, Alberta, Canada

Abstract / We describe a simple method for the assessment of symptoms twice a day in patients admitted to a palliative care unit. Eight visual analog scales (VAS) 0–100 mm are completed either by the patient alone, by the patient with nurse's assistance, or by the nurses or relatives at 10:00 and 18:00 hours, in order to indicate the levels of pain, activity, nausea, depression, anxiety, drowsiness, appetite, and sensation of well-being. The information is then transferred to a graph that contains the assessments of up to 21 days on each page. The sum of the scores for all symptoms is defined as the symptom distress score. The Edmonton Symptom Assessment System (ESAS) was carried out for 101 consecutive patients for the length of their admission to our unit. Of these, 84% were able to make their own assessment sometime during their admission. However, before death 83% of assessments were completed by a nurse or relative. Mean symptom distress score was 410±95 during day 1 of the admission, versus 362±83 during day 5 ($p<0.01$). Mean symptom distress scores throughout the hospitalization were 359±105, 374±93, 359±91 and 406±81 when the ESAS was completed by the patient alone, patient with nurse's assistance ($p=N.S.$), nurse alone ($p=N.S.$), or relative ($p<0.01$) respectively. We conclude that this is a simple and useful method for the regular assessment of symptom distress in the palliative care setting.

Résumé / Cet article décrit une méthode facile pour évaluer les symptômes chez les patients admis dans une unité de soins palliatifs. Il s'agit pour le patient, seul ou avec l'aide de l'infirmière ou d'un proche, de compléter des échelles visuelles analogues deux fois par jour, à 10h00 et à 18h00, et ce, afin d'indiquer ses niveaux de douleur, de nausée, d'anxiété, de somnolence, d'appétit, de dépression, d'énergie et de sensation de bien-être. L'information recueillie est ensuite

transférée sur un graphique, lequel peut inclure 21 jours par page. La somme totale de tous les symptômes évalués se définit comme le score de détresse symptomatique. Le Edmonton Symptom Assessment System (ESAS) a ainsi été administré à 101 patients consécutifs pour la durée de leur hospitalisation à l'unité. Les patients ont été en mesure de compléter l'évaluation seuls dans 84% des cas à un moment ou l'autre durant leur séjour. Cependant, à l'approche de la mort, 83% des évaluations ont été complétées par une infirmière ou un parent. Le score de détresse symptomatique était de 410±95 au premier jour de l'hospitalisation versus 362±83 au cinquième jour ($p<0.01$). Le score de détresse symptomatique durant le séjour était de 359±105 lorsque le ESAS était complété par le patient lui-même, 374±93 lorsque complété par le patient aidé d'une infirmière ($p=N.S.$), 359±91 lorsque complété par l'infirmière seule ($p=N.S.$) et 406±81 lorsque complété par un parent ($p<0.01$). En conclusion, le ESAS s'avère une méthode simple et pratique pour l'évaluation des patients en soins palliatifs et peut être effectué de façon répétitive durant le séjour, même parmi une population très malade.

INTRODUCTION

The proper assessment and management of physical and psychological distress is one of the main components of adequate palliative care (4,5,8,13). Because of the subjective nature of these symptoms, the "gold standard" is the patient's own assessment of their intensity (1,4,6,8,11,13). Several excellent systems for the assessment of symptoms have been described (1-3,6-8,10,11). However, some of these systems are time-consuming and may be expensive and exhausting for very debilitated patients. Other systems such as the visual analog scale (VAS) are simple and effective (6,7,9). However, most

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Review Article

The Edmonton Symptom Assessment System 25 Years Later: Past, Present, and Future Developments



David Hui, MD, MSc, and Eduardo Bruera, MD

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Abstract

Context. Routine symptom assessment represents the cornerstone of symptom management. Edmonton Symptom Assessment System (ESAS) is one of the first quantitative symptom assessment batteries that allows for simple and rapid documentation of multiple patient-reported symptoms at the same time.

Objectives. To discuss the historical development of ESAS, its current uses in different settings, and future developments.

Methods. Narrative review.

Results. Since its development in 1991, ESAS has been psychometrically validated and translated into over 20 languages. We will discuss the variations, advantages, and limitations with ESAS. From the clinical perspective, ESAS is now commonly used for symptom screening and longitudinal monitoring in patients seen by palliative care, oncology, nephrology, and other disciplines in both inpatient and outpatient settings. From the research perspective, ESAS has offered important insights into the nature of symptom trajectory, symptom clusters, and symptom modulators. Furthermore, multiple clinical studies have incorporated ESAS as a study outcome and documented the impact of various interventions on symptom burden. On the horizon, multiple groups are actively investigating further refinements to ESAS, such as incorporating it in electronic health records, using ESAS as a trigger for palliative care referral, and coupling ESAS with personalized symptom goals to optimize symptom response assessment.

Conclusion. ESAS has evolved over the past 25 years to become an important symptom assessment instrument in both clinical practice and research. Future efforts are needed to standardize this tool and explore its full potential to support symptom management. *J Pain Symptom Manage* 2017;53:630–643. © 2016 American Academy of Hospice and Palliative Medicine. Published by Elsevier Inc. All rights reserved.

Key Words

Clinical trial, dyspnea, fatigue, surveys and questionnaires, symptom assessment, personalized medicine, neoplasms, pain, palliative care

Introduction

Patients with advanced diseases experience significant symptom burden from the time of diagnosis, which often increases in intensity over time.^{1,2} In cross-sectional studies, the average cancer patient reports 8–12 symptoms, with fatigue, pain, anorexia, cachexia, dyspnea, anxiety, and depression being particularly common.^{3–5} These symptoms are often multidimensional in nature, and can negatively impact patients' quality of life and function while increasing caregiver burden.⁶

Over the past decades, the specialty of palliative care has acquired substantial expertise in symptom management.⁷ One of the most critical aspects of symptom management is routine symptom assessment and reassessment with patient reported outcomes (PROs)—which allows symptoms to be recognized, diagnosed, treated, and monitored over time. Theoretical frameworks such as the symptom expression pathway have formed the basis for multidimensional symptom management guided by patient-reported outcomes instead of clinician-based assessments.⁸ The symptom transduction cascade illustrates why

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Systematic Symptom Screening

From Detection to Action



Reporting

Evaluation

Clinical actions

Outcomes

Old Face-to-face

Assess and triage

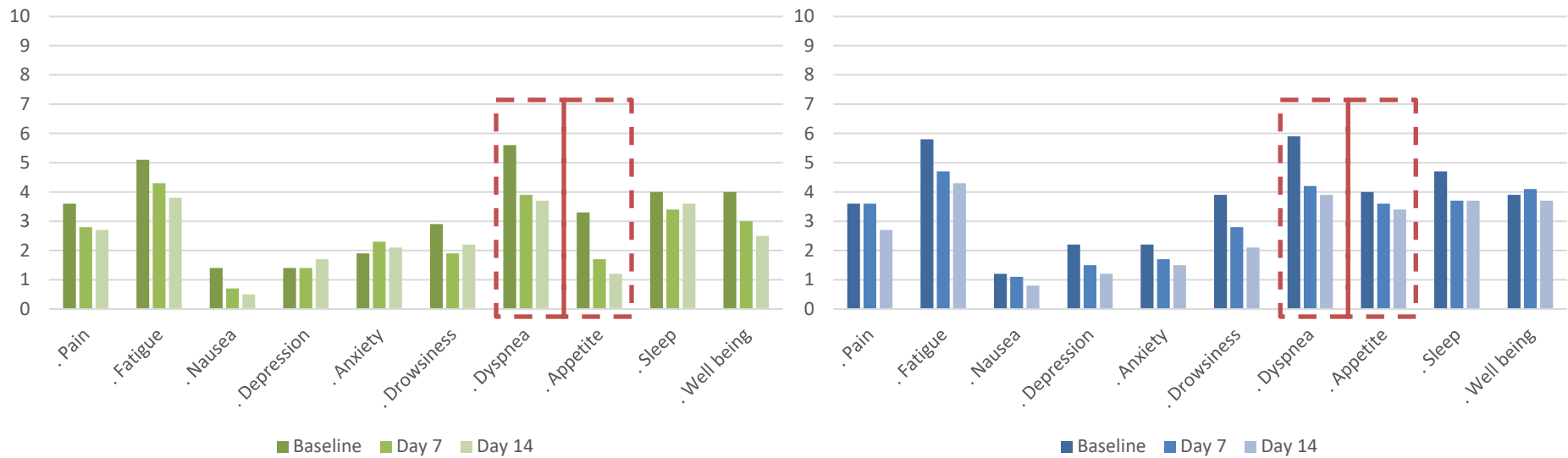
Treatment
recommendations

Symptom control
and quality of life

Symptom Response

Edmonton Symptom Assessment System (ESAS)

What is the effect of high dose dexamethasone on symptoms ?



Dexamethasone Group

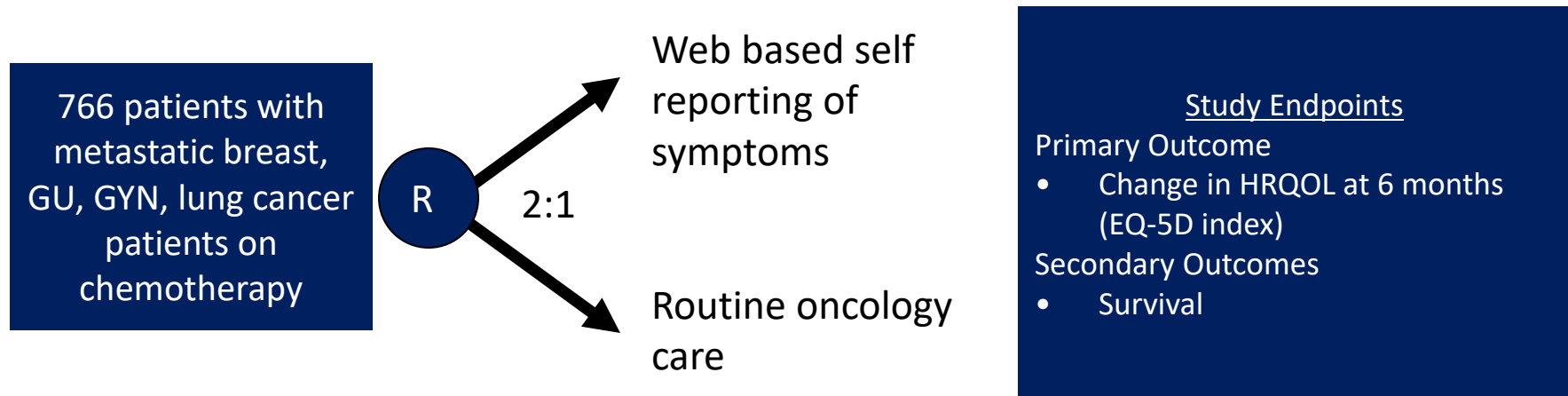
Placebo Group

Clinical Applications

- Symptom screening
 - Increased awareness
 - Clinical actions
 - Improved outcomes
- Symptom monitoring
 - Personalize care longitudinally
 - Response assessment
- Prediction
 - Care needs
 - Survival

Systematic Symptom Screening

Randomized Controlled Trial



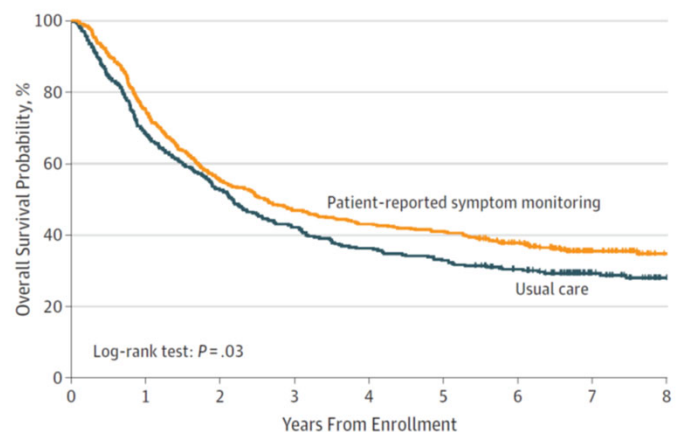
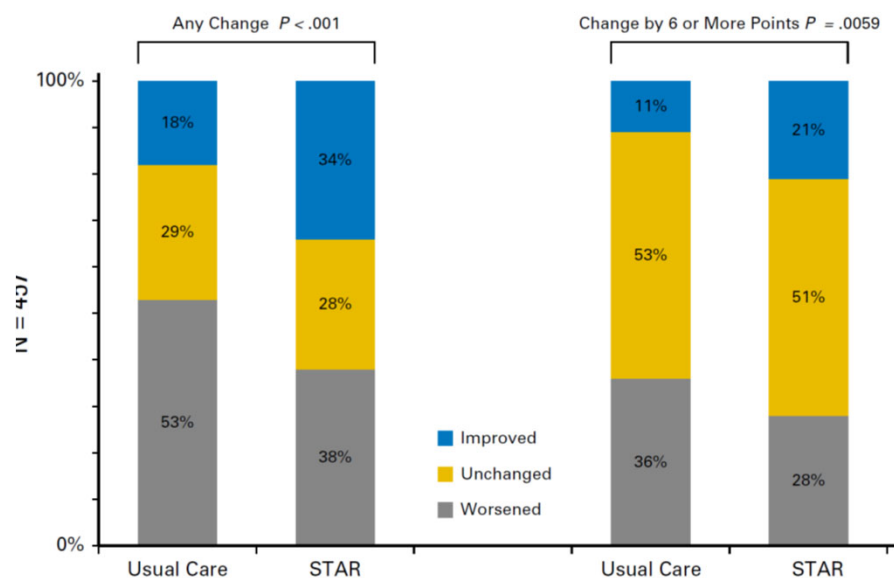
Symptom Tracking and Reporting Web-based interface

- 12 symptoms: Appetite loss, constipation, cough, diarrhea, dyspnea, dysuria, fatigue, hot flashes, nausea, pain, neuropathy, vomiting
- NCI CTCAE grading: 0 (absent) to 4 (disabling)
- Interface: touchscreen tablets or computer kiosks
- Frequency: at clinic visit and between visits (not mandatory)
- Action: e-mail alerts if worsened by 2+ points or absolute value ≥ 3

Basch et al. *J Clin Oncol* 2016

Systematic Symptom Screening

Randomized Controlled Trial



No. at risk	0	1	2	3	4	5	6	7	8
Patient-reported symptom monitoring	441	331	244	207	190	181	148	65	33
Usual care	325	223	171	137	118	107	89	50	27

Secondary outcomes

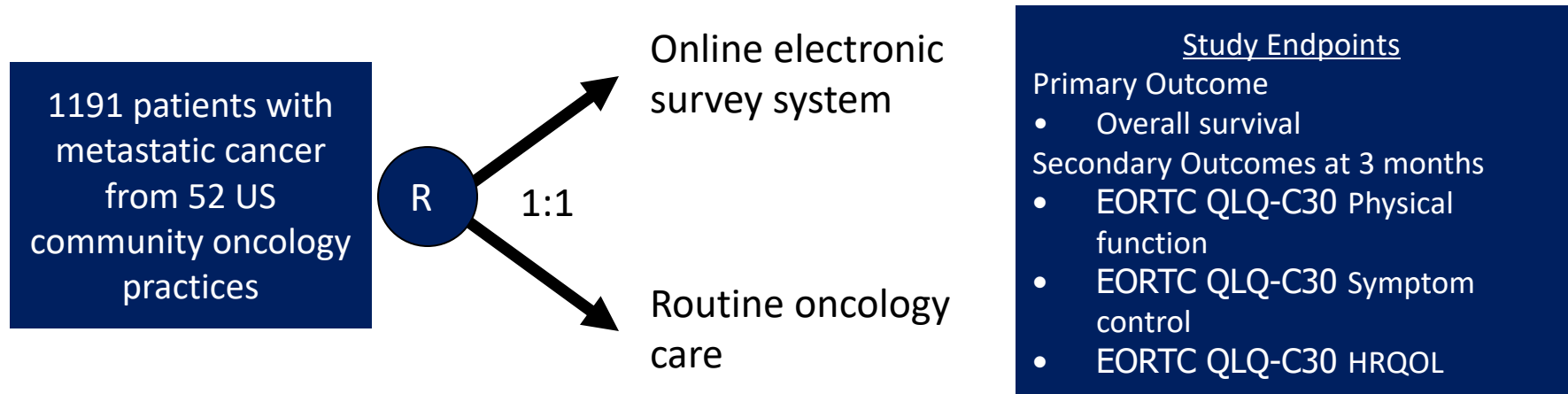
- EQ-5D showed improvement in mobility (P=0.02), self-care (P=0.01), anxiety/depression (P=0.01), pain/discomfort (P=0.05), usual activities (P=0.09)
- Fewer ER visits at 1 year (34% vs. 41%, P=0.02)
- Fewer hospitalized at 1 year (45% vs. 49%, P=0.08)
- Chemotherapy longer (8.2 m vs. 6.3 m, P=0.002)

Median survival

- PRO: 31.2 months
- Control: 26.0 months
- HR 0.83 (95% 0.70-0.99, P=0.04)

Systematic Symptom Screening

Cluster Randomized Controlled Trial



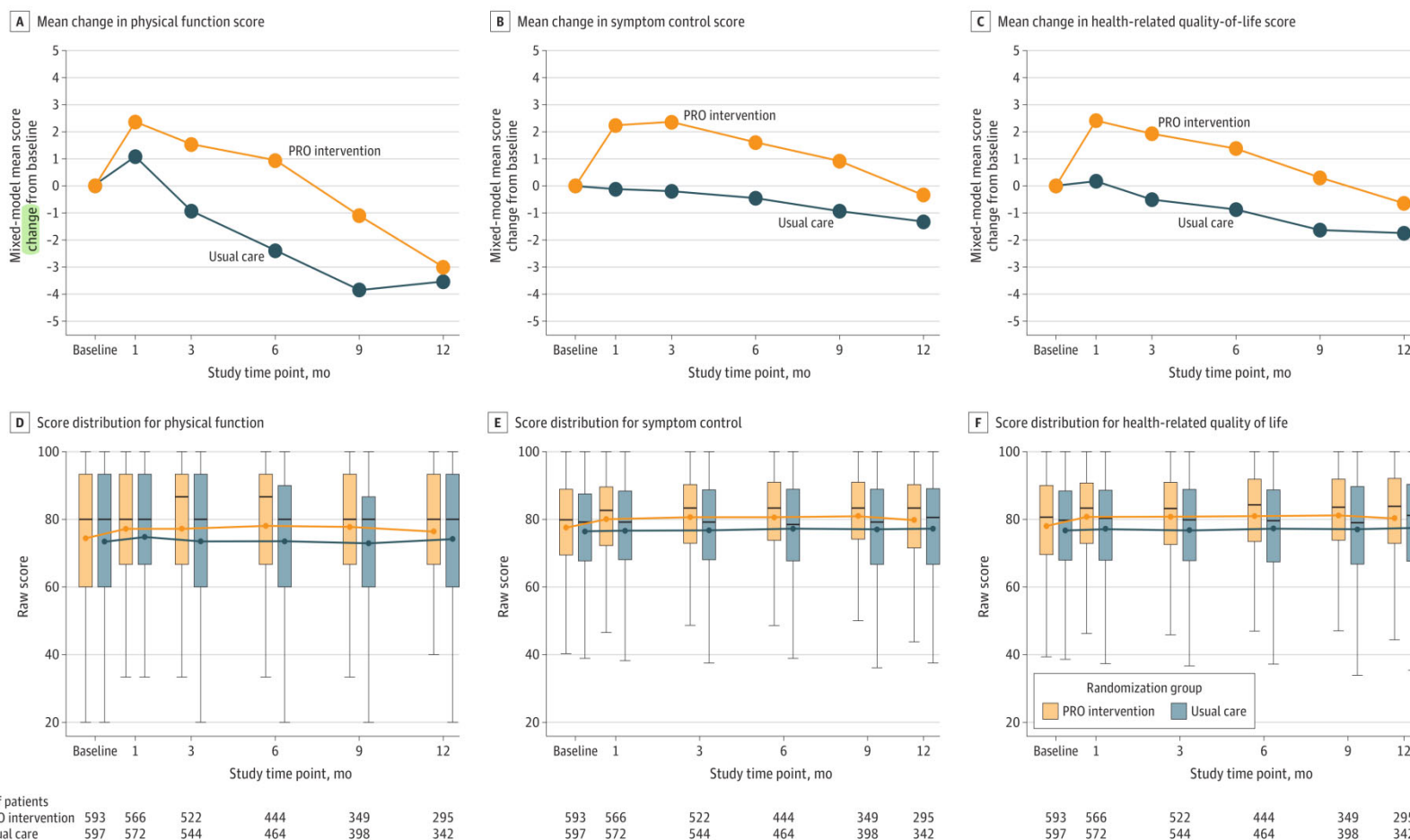
Electronic survey system

- 11 items: PRO-CTCAE pain, nausea, vomiting, constipation, diarrhea, dyspnea, insomnia, depression; oral intake (eating/drinking), performance status (patient-reported ECOG criteria), falls, and financial challenges
- Interface: internet or automatic telephone system
- Frequency: weekly for 1 year or until cancer tx discontinued; reminder
- Action: if threshold met, patient gets info on symptom self management electronically; staff also gets notification and staff email

Basch et al. *JAMA* 2021

Systematic Symptom Screening

Cluster Randomized Controlled Trial

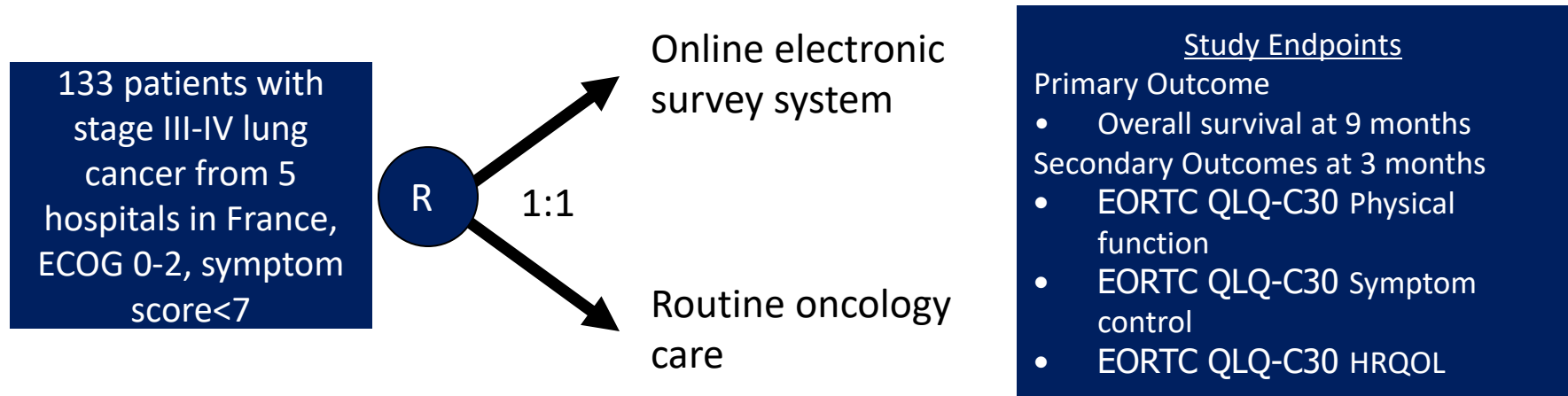


Scores on the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire. PRO indicates patient-reported outcome. Positive values represent improvement. In panels A-C, *P* values for model-based mean change from baseline at 1-, 3-, 6-, 9-, and 12-month assessments, respectively, are as follows: panel A (physical function), *P* = .21, *P* = .02, *P* = .003, *P* = .02, and *P* = .68; panel B (symptom control), *P* = .003,

P = .002, *P* = .02, *P* = .045, and *P* = .32; and panel C (health-related quality of life), *P* = .003, *P* = .002, *P* = .006, *P* = .03, and *P* = .24. In panels D-F, circles indicate means; horizontal bars, medians; box tops and bottoms, IQRs; and whiskers, 1.5× the IQRs. See eTable 5 in Supplement 2 for point estimates and confidence intervals.

Systematic Symptom Screening

Randomized Controlled Trial



Electronic survey system

- 12 symptoms
- Interface: internet
- Frequency: weekly
- Action: e-mail alerts sent to oncologist

Systematic Symptom Screening

Randomized Controlled Trial

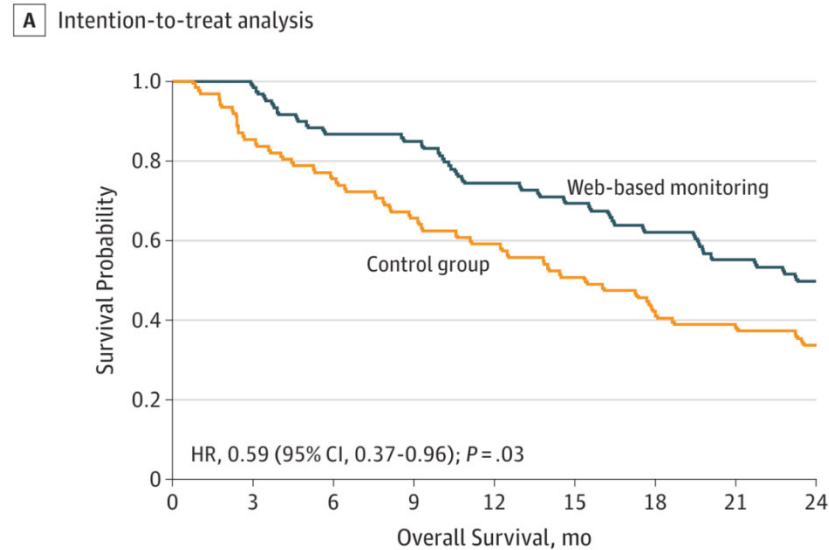


Table 4. Six-month mean changes of quality of life FACT scores from baseline*

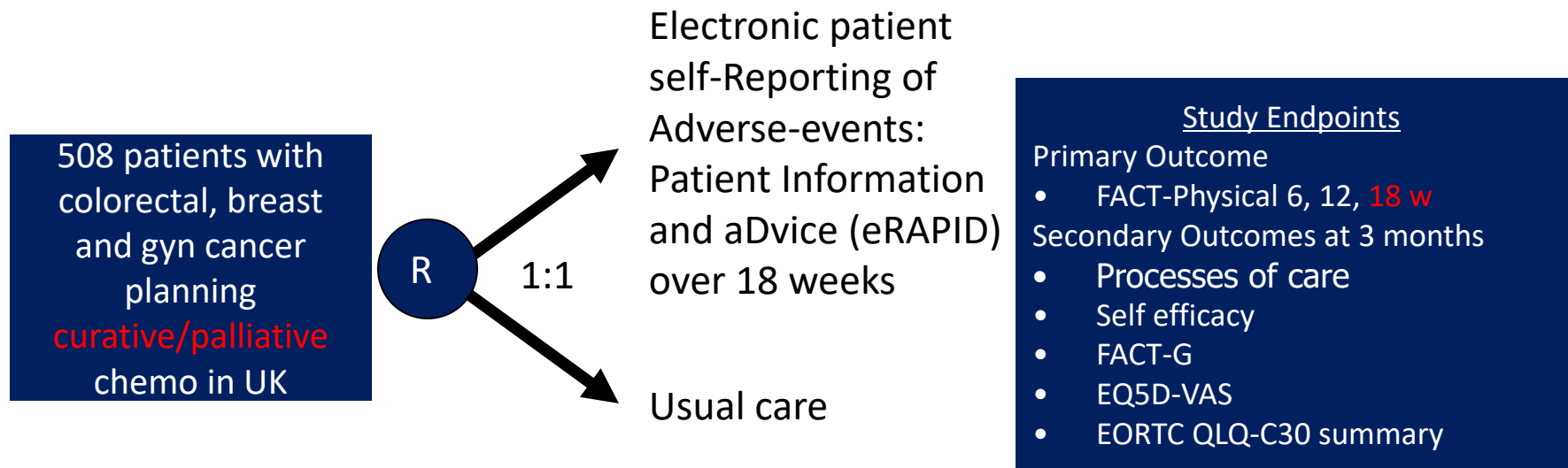
	Control arm No. (%)	Experimental arm No. (%)	Total No. (%)	P†
Mean (SD) baseline FACT score	99.6 (16.3)	91.4 (16.2)	95,6 (16,7)	.01
6-mo evaluation/baseline*				
Improvement or stable	17 (58.6)	25 (80.6)	42 (70.0)	.04
Deterioration	12 (41.4)	6 (19.4)	18 (30.0)	

*Improvement was defined by a six-point increase between the two evaluations. Deterioration was defined by a six-point decrease between the two evaluations; stability is the intermediary situation.

†Two-sided chi-square test.

eRAPID

Randomized Controlled Trial

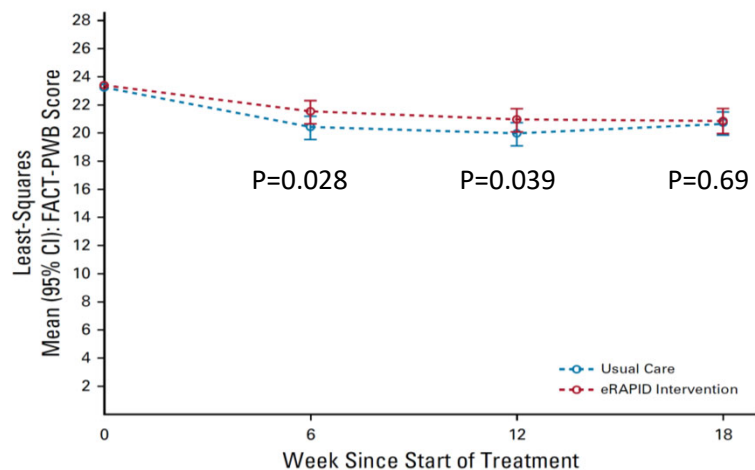


Electronic survey system

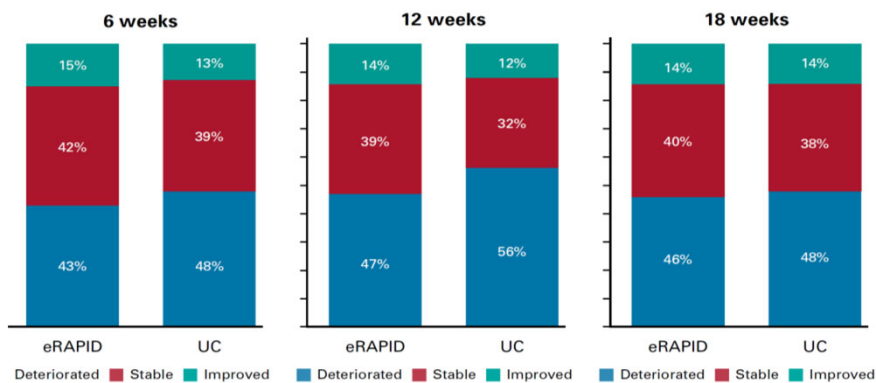
- Key treatment-related symptom (varied by diagnosis)
- Interface: PC/mobile device
- Frequency: weekly
- Self management: immediate severity-dependent advice on symptom management or prompt to contact hospital
- Action: e-mail alerts sent to oncologist

eRAPID

Randomized Controlled Trial



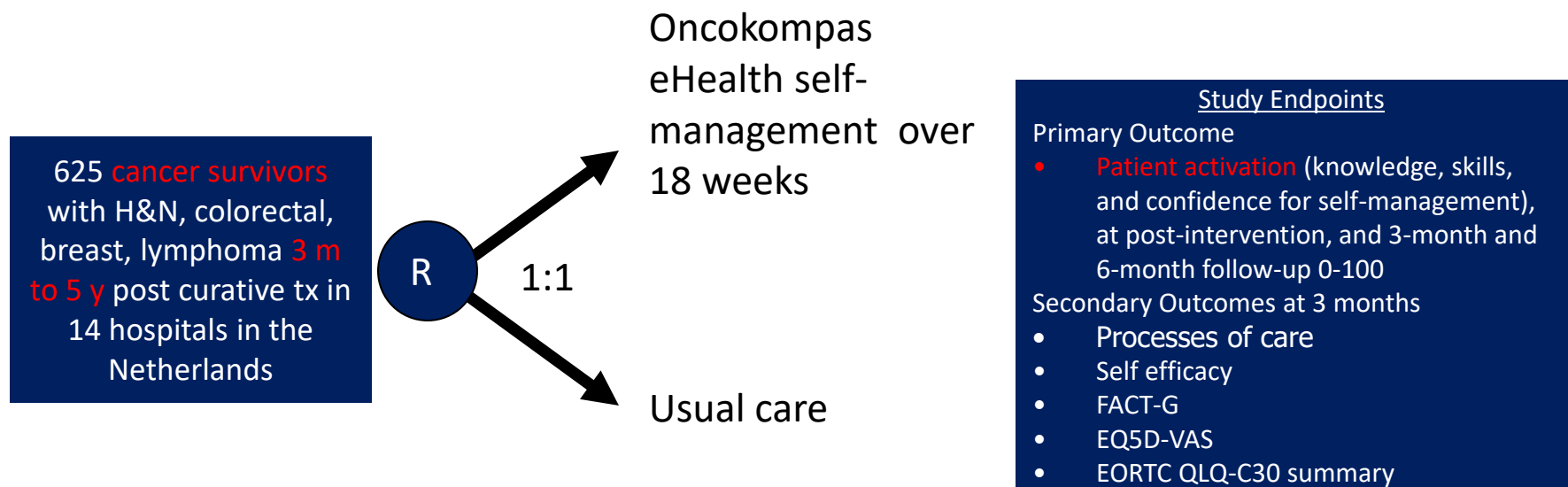
Estimate (95% CI)	eRAPID Intervention	Usual Care
6 weeks	21.48 (20.61 to 22.34)	20.39 (19.56 to 21.23)
12 weeks	20.92 (20.09 to 21.76)	19.91 (19.07 to 20.74)
18 weeks	20.84 (19.95 to 21.72)	20.64 (19.76 to 21.52)



Secondary Patient-Reported Outcome Measures	eRAPID Intervention (n = 256), Mean (SD)	UC (n = 252), Mean (SD)	Adj. Differences in Least Squares Means (95% CI) eRAPID v UC	P
6-item self-efficacy scale (score range 1-10, high score = high self-efficacy)^a				
Baseline	6.85 (1.90) n = 252	6.74 (1.94) n = 247		
Week 18	7.55 (1.83) n = 186	6.96 (2.07) n = 196	0.48 (0.13 to 0.83)	.0073 ^b
Cancer Behavior Inventory (14-item score range 14-126, higher scores = greater coping efficacy)				
Baseline	99.6 (18.4) n ^c = 239	97.8 (19.9) n = 233		
Week 18	102.0 (18.4) n = 181	97.5 (20.7) n = 189	2.83 (-0.53 to 6.18)	.0986
Patient activation measure (score range 0-100 higher scores = higher patient activation)				
Baseline	66.7 (14.6) n = 251	66.1 (16.1) n = 243		
Week 18	64.8 (14.1) n = 182	63.5 (15.7) n = 197	0.30 (-2.34 to 2.94)	.8249
EQ5D-VAS (score range 0-100, 0 = worst possible health; 100 = best possible health)^d				
Baseline	76.3 (18.1) n = 255	75.2 (18.6) n = 248		
Week 6	74.0 (17.3) n = 213	71.4 (19.5) n = 225	1.36 (-1.66 to 4.39)	.3773
Week 12	74.0 (16.6) n = 199	68.9 (19.8) n = 209	3.50 (0.35 to 6.66)	.0302
Week 18	75.6 (18.0) n = 184	68.7 (20.4) n = 199	4.48 (1.11 to 7.86)	.0095
EORTC QLQ-C30 summary score (range 0-100, high = better)^d				
Baseline	79.2 (15.6) n = 207	79.9 (15.0) n = 205		
Week 6	77.7 (13.0) n = 170	75.3 (16.8) n = 185	1.05 (-1.62 to 3.73)	.4420
Week 12	76.3 (13.3) n = 160	71.7 (16.7) n = 168	3.62 (0.84 to 6.40)	.0111
Week 18	76.0 (15.4) n = 148	72.1 (17.9) n = 164	1.91 (-1.17 to 5.00)	.2255
FACT-G (score range 0-108, high = better well-being)^d				
Baseline	82.9 (14.1) n = 251	81.9 (14.1) n = 241		
Week 6	80.0 (15.6) n = 209	76.6 (15.7) n = 226	1.46 (-0.88 to 3.80)	.2218
Week 12	79.2 (15.0) n = 191	74.3 (16.1) n = 204	2.19 (-0.15 to 4.54)	.0679
Week 18	78.8 (16.2) n = 181	75.7 (16.6) n = 200	0.96 (-1.64 to 3.55)	.4712

Oncokempas

Randomized Controlled Trial



Electronic survey system

- Assesses five generic HRQOL domains: physical functioning, psychological functioning, social functioning, lifestyle, and existential issues, and included topics in tumor-specific modules (patient choice of topics to complete)
- Interface: PC/mobile device
- **Frequency:** baseline, 1 w post intervention (2 w post randomization), 3 m and 6 m
- Self-management: advice on symptom management based on green/orange/red system van der Hout et al. *Lancet Oncol* 2020

Oncokempas

Randomized Controlled Trial

	Baseline		1 week post-intervention		3-month follow-up		6-month follow-up		Linear mixed-model analysis (p value)	
	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	Difference (95% CI)	
Intervention	320	..	264	..	231	..	225
Control	305	..	275	..	261	..	251
Patient activation										
Total score, patient activation measure										
Intervention	292	59.2 (12.5)	245	57.2 (12.2)	217	59.5 (12.7)	209	60.0 (13.7)	1.7 (-0.8 to 4.2)	0.41
Control	277	59.5 (12.6)	251	56.9 (11.4)	241	57.9 (12.5)	234	58.3 (12.7)
HRQOL										
Summary score QLQ-C30										
Intervention	320	85.3 (14.9)	259	88.4 (12.1)	228	88.7 (13.2)	223	89.3 (12.3)	2.3 (0.0 to 4.5)	0.048
Control	304	85.4 (13.6)	271	86.2 (12.8)	253	86.5 (13.1)	247	87.0 (12.7)

Summary findings regarding Oncokempas

- No improvement in patient activation
- No improvement in mental adjustment to cancer, supportive care needs, self efficacy, personal control, or perceived efficacy
- Slight improvement in HRQOL
- Overall trend in improving symptoms

Oncokempas

Randomized Controlled Trial

Potential moderator	HRQOL	
	F (3,df) three-way interaction	p value three-way interaction
Socio-demographic factors		
Sex (men, women)	1.214 (1476)	.30
Age (years)	0.647 (1486)	.59
Marital status (no partner, partner)	1.160 (1481)	.32
Education level (low, medium, high)	1.699 (1457)	.12
Employment status (not employed, employed)	1.468 (1478)	.22
Clinical factors		
Tumour type (head and neck, colorectal, breast cancer, lymphoma)	1.780 (1465)	.067
Tumour stage (I or II vs. III or IV)	0.961 (1398)	.41
Time since diagnosis (3–12, 12–24, 24–60 months)	1.633 (1473)	.13
Treatment (0/1, ≥2 treatments)	0.177 (1474)	.91
Comorbidities (0/1, ≥2 comorbidities)	0.960 (1478)	.41
Personal factors		
Self-efficacy	2.903 (1487)	.034
Personal control	3.478 (1481)	.015
Health literacy	2.869 (1478)	.035
Health locus of control		
<i>Internal</i>	0.736 (1475)	.53
<i>Powerful others</i>	1.359 (1476)	.25
<i>Chance</i>	0.762 (1481)	.52
Internet use (<7, >7 h/week)	1.960 (1470)	.12
Patient activation	2.124 (1353)	.095
Mental adjustment to cancer		
Positive adjustment	1.192 (1475)	.31
Negative adjustment	0.699 (1498)	.55
Unmet supportive care needs		
Physical and daily living	1.010 (1479)	.39
Psychological	0.237 (1479)	.87
Sexual	1.474 (1439)	.22
Health system, information and patient support	0.228 (1478)	.88
HRQOL	0.903 (1617)	.44

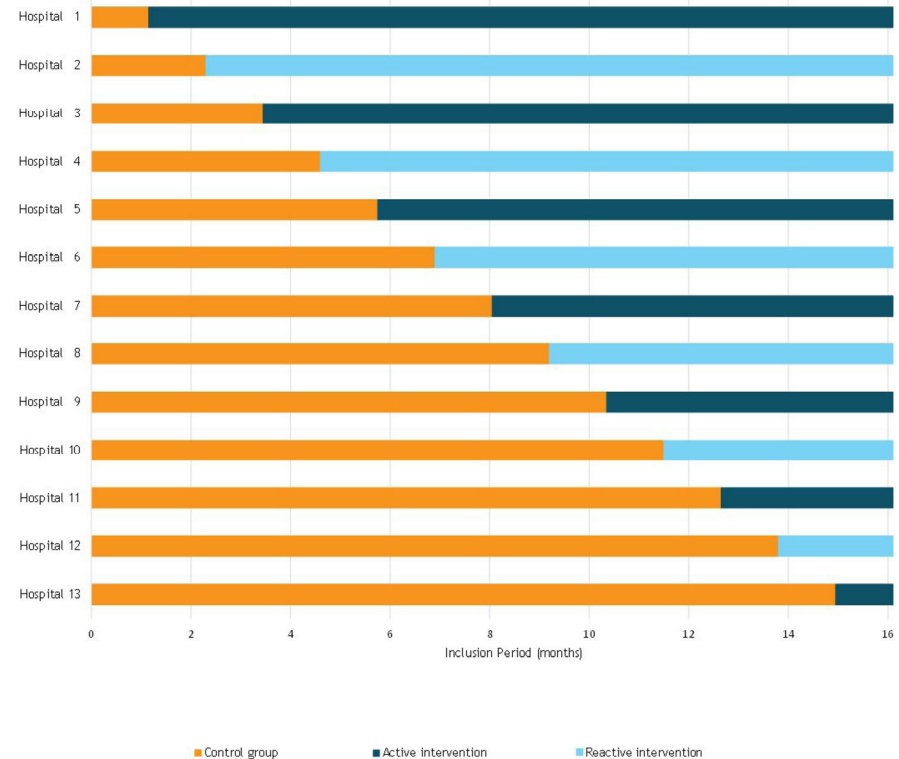
More effective in improving HRQOL in cancer survivors with [lower self-efficacy](#), and in cancer survivors with higher personal control, and higher health literacy

More effective in reducing symptoms in head and neck cancer and colorectal cancer survivors who reported a [higher burden of tumour-specific symptoms](#)

SYMPRO-Lung

Stepped Wedge Cluster Randomized Trial

- Stage I-IV lung cancer starting treatment
- Weekly online PROM symptom monitoring with PRO-CTCAE (n=9) and weight/fever, diarrhea, hemoptysis
 - Active approach with alert for HCP
 - Reactive approach with alert for patient
- Primary outcome: Mean difference between HRQoL at baseline (T0) and 15 weeks (T1), 6 months (T2) and 12 months (T3) post baseline between the intervention and control groups



SYMPRO-Lung

Stepped Wedge Cluster Randomized Trial

- 515 patients were included in the study (266 control, 249 intervention)
 - 244 patients completed 2412 symptom checklists during the first 15 weeks of treatment (mean 10 [SD 4.3])
 - 673 alerts (28%) were triggered (mean 3 [SD 2.1])
- Key findings
 - Compared to control, the intervention group had statistically and clinically significant improvement in **physical functioning** (ES 0.50) and less dyspnea (ES 0.38)
 - Compared to control, the intervention group had statistically but not clinically significant improvement in HRQOL overall summary score (ES 0.34), role functioning (ES 0.31), social functioning (ES 0.26), fatigue (ES 0.27), and constipation (ES 0.16)
 - No significant differences were found in HRQOL **between the two intervention groups**

ESAS Screening

Retrospective Match Cohort Study

- Ontario, Canada; 2007-2015 data
- 128,893 cancer patients with ESAS at least once
- 128,893 cancer patients without ESAS matched based on age, cancer diagnosis date, cancer type, sex

Variables	Recurrent ED (n = 126,106 pairs)						Recurrent Hospitalization (N = 128,893 pairs)					
	Univariate			Multivariable			Univariate			Multivariable		
	RR	LCL	UCL	RR	LCL	UCL	RR	LCL	UCL	RR	LCL	UCL
ESAS (yes or no)	1.15	1.13	1.16	0.92	0.91	0.93	1.14	1.12	1.15	0.86	0.85	0.87
Surgery (yes or no, time dependent) ^a	0.71	0.70	0.72	0.80	0.79	0.81	0.54	0.53	0.55	0.65	0.64	0.66
Chemotherapy (yes or no, time dependent) ^b	2.58	2.54	2.61	1.65	1.62	1.67	2.39	2.35	2.42	1.37	1.35	1.39
Radiation (yes or no, time dependent) ^b	2.12	2.08	2.16	1.59	1.57	1.62	2.08	2.04	2.13	1.43	1.40	1.46
No. of MO or RO visits from diagnosis to index (time invariant)	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.98	0.98	1.015	1.01	1.02
No. of clinic visits from index to current (family, RO or MO, time dependent)	1.02	1.02	1.02	1.01	1.01	1.016	1.02	1.02	1.02	1.76	1.73	1.78
ADG score (≥ 10 v 0-9) ^c	2.42	2.39	2.45	2.05	2.03	2.08	2.10	2.08	2.13	0.98	0.97	0.98
Phase (initial v continuing)	1.24	1.22	1.26	1.11	1.10	1.13	2.08	2.05	2.12	1.89	1.85	1.92
Phase (palliative v continuing)	2.56	2.53	2.60	1.96	1.93	1.99	4.11	4.04	4.17	3.25	3.19	3.30

Summary so far

- Different findings because of
 - Different study designs
 - Different patient populations
 - Different interventions
 - Different time frames
 - Different outcome measures
- Overall in favor!
 - Multiple benefits and no clear harm
 - Scalable interventions
 - Generalizability

Systematic Symptom Screening

Mechanism of Improved Outcomes

Improved awareness

Improved communication

Improved just-in-time recommendations

Improved symptom control

Improved quality of life and quality of care

Improved survival

Outline



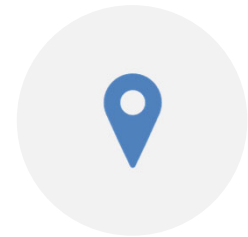
PRINCIPLES



EVIDENCE



PRACTICAL
CONSIDERATIONS



FUTURE
DIRECTIONS

Practical Considerations

- Who? (everyone – almost)
- Where? (appropriate for many settings – primary care, palliative care, other specialists; hospital, home)
- Which questionnaire? (validated, simple)
- How many questions? (depends on patients/settings)
- How frequent? (as often as possible)
- What mode? (paper, electronic)
- What to do? (triggers)

From Paper to Computer

Please select the number that best describes your average symptom intensity over the past 24 hours.

Pain
0-None 1 2 3 4 5 6 7 8 9 10-Worst

Fatigue
0-None 1 2 3 4 5 6 7 8 9 10-Worst

Nausea
0-None 1 2 3 4 5 6 7 8 9 10-Worst

Depression
0-None 1 2 3 4 5 6 7 8 9 10-Worst

Anxiety
0-None 1 2 3 4 5 6 7 8 9 10-Worst

Drowsiness
0-None 1 2 3 4 5 6 7 8 9 10-Worst

Shortness of breath
0-None 1 2 3 4 5 6 7 8 9 10-Worst

Appetite
0-Best 1 2 3 4 5 6 7 8 9 10-Worst

Feeling of Well Being
0-Best 1 2 3 4 5 6 7 8 9 10-Worst

Sleep
0-Best 1 2 3 4 5 6 7 8 9 10-Worst

Financial distress
0-None 1 2 3 4 5 6 7 8 9 10-Worst

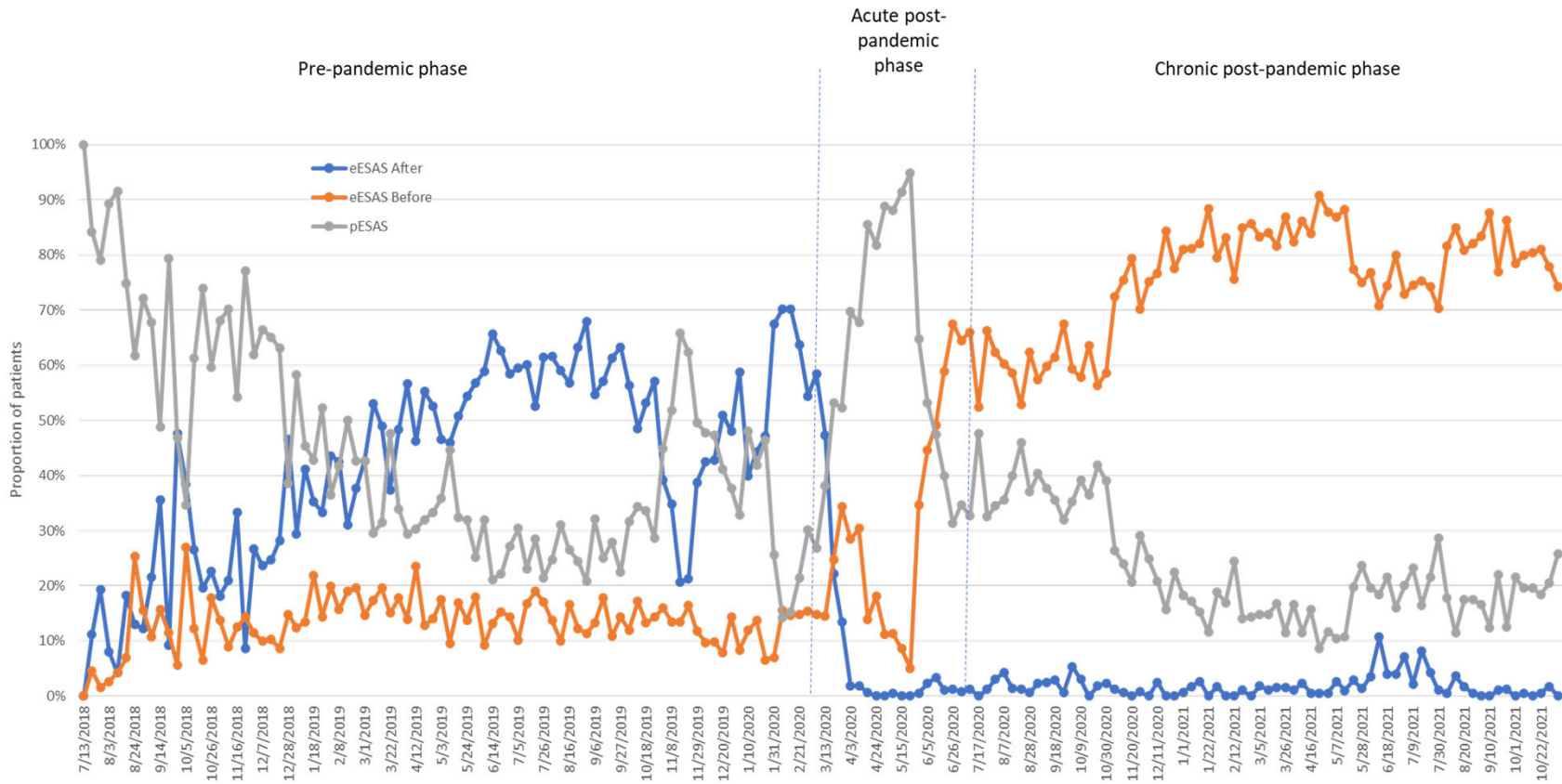
Spiritual pain
0-None 1 2 3 4 5 6 7 8 9 10-Worst

CONTINUE **FINISH LATER** **CANCEL**

- Supportive care center has been administering paper questionnaires since inception
- With implementation of electronic health record in 2016, we transited electronic data capture
- Three approaches
 - Paper ESAS
 - Electronic ESAS – before clinic visit (patient portal, own device)
 - Electronic ESAS – after they showed up to clinic (iPAD in clinic)
- Challenges
 - Patient familiarity
 - Computer access/password
 - Computer literacy
 - Language support

From Paper to Computer

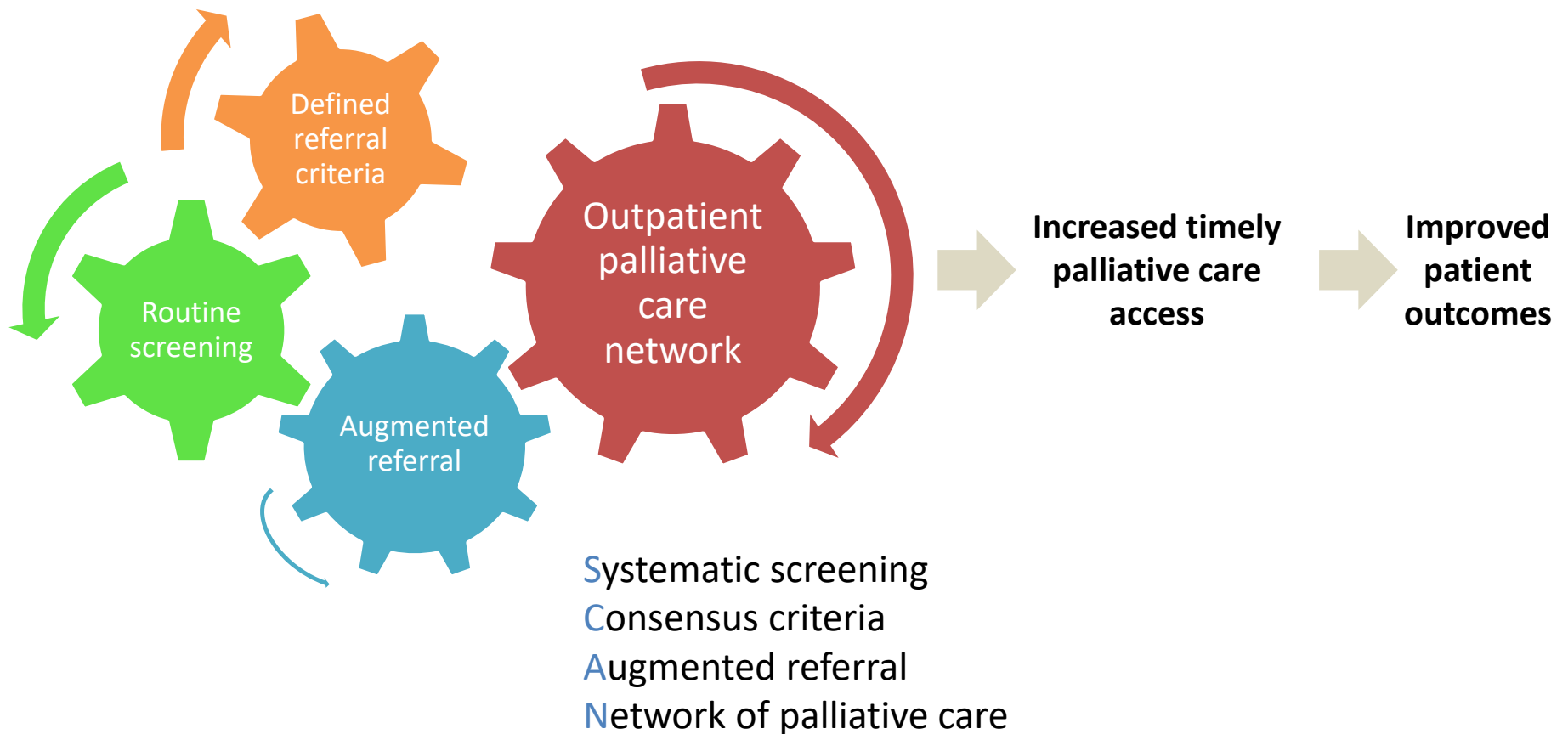
Impact of COVID



Transition takes time, teamwork and patience.
Telehealth has catalyzed adoption of electronic PROs.

Timely Palliative Care

Augmented Referral



Consensus Referral Criteria

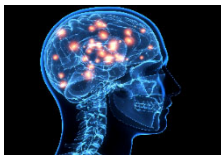
Outpatient Palliative Care for Patients with Advanced Cancer



Severe distress



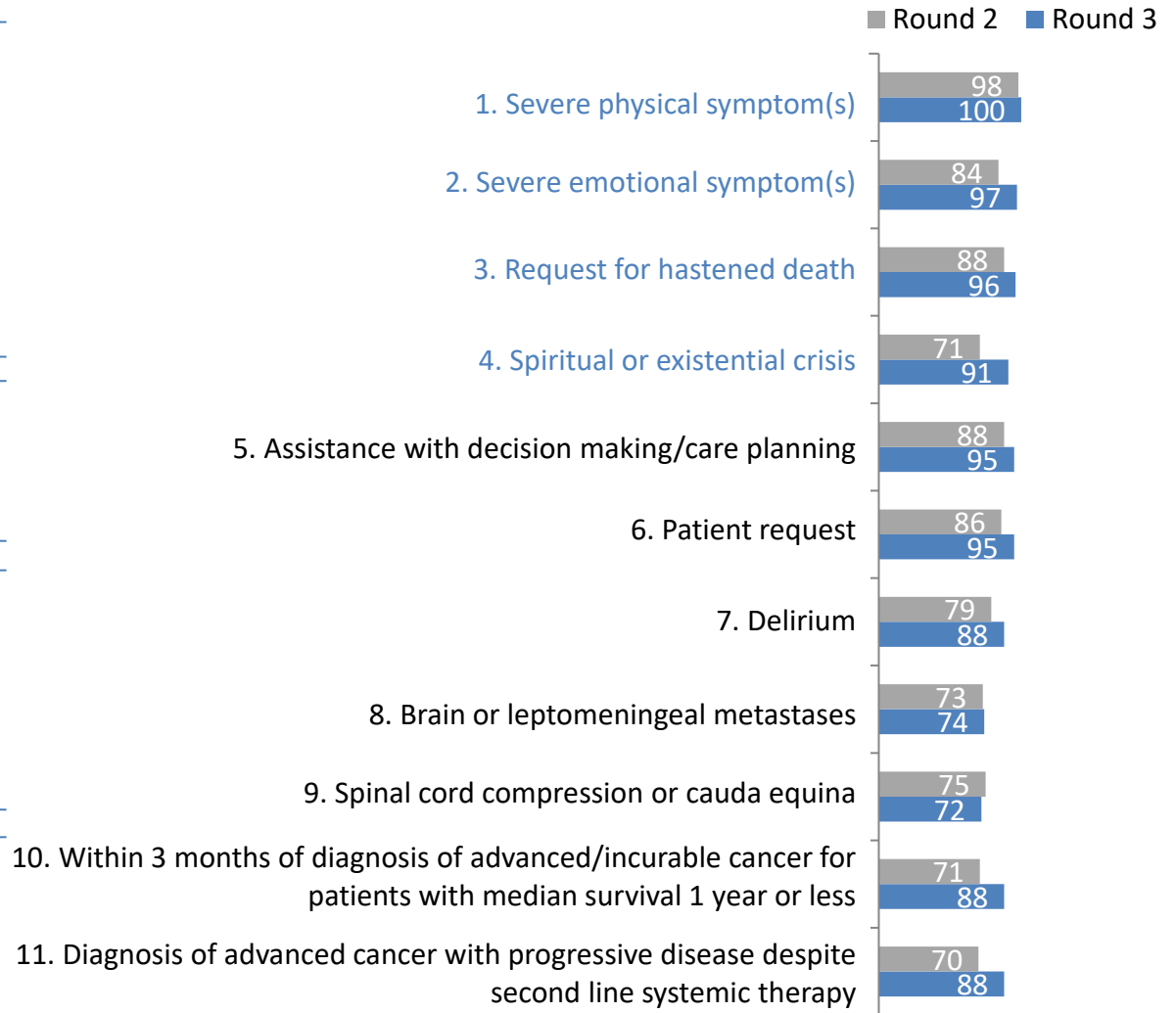
Additional support



Neurologic complications



Proper timing

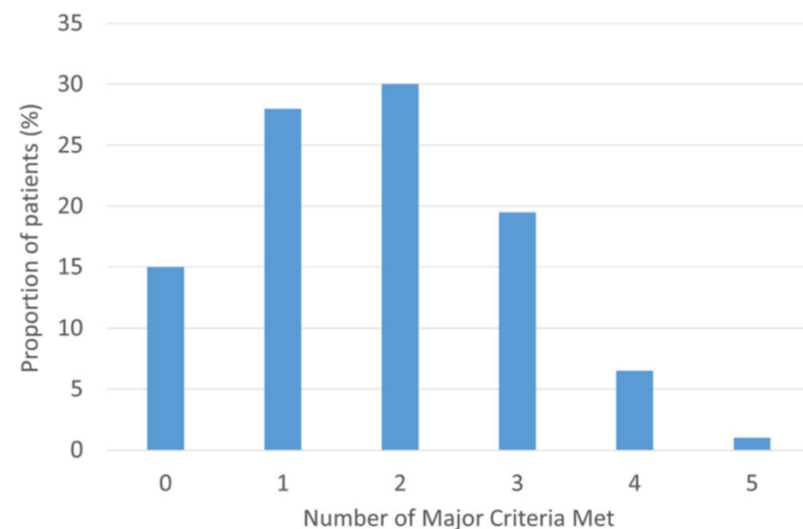


Major Referral Criteria

Performance in Real World

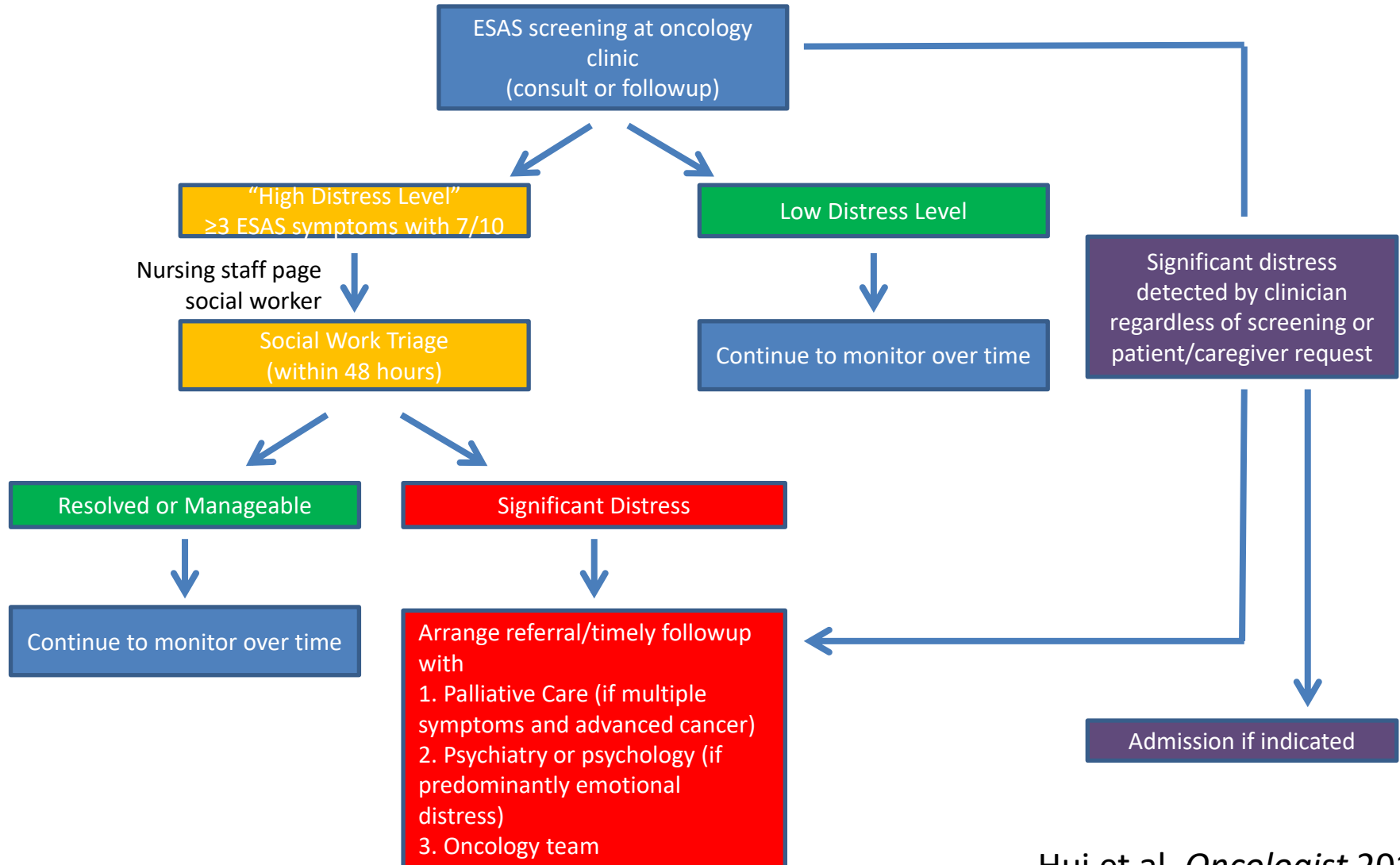
- 200 consecutive consultations at Supportive Care Clinic
- Median survival 14 (95% confidence interval 9.2, 17.5) months
- A majority (85%) met at least 1 major criteria
- The median duration from patient first meeting any criterion to palliative care referral was 2.4 (interquartile range 0.1, 8.6) months

Major criteria	Present (%)
Severe physical symptom(s)	140 (70)
Severe emotional symptom(s)	36 (18)
Request for hastened death	1 (0.5)
Spiritual or existential crisis	2 (1)
Assistance with decision-making/care planning	26 (13)
Patient request	4 (2)
Delirium	0 (0)
Brain or leptomeningeal metastases	25 (12.5)
Spinal cord compression or cauda equine	3 (1.5)
Within 3 months of diagnosis of advanced/incurable cancer for patients with median survival 1 year or less	54 (27)
Diagnosis of advanced cancer with progressive disease despite second line systemic therapy (incurable)	63 (31.5)



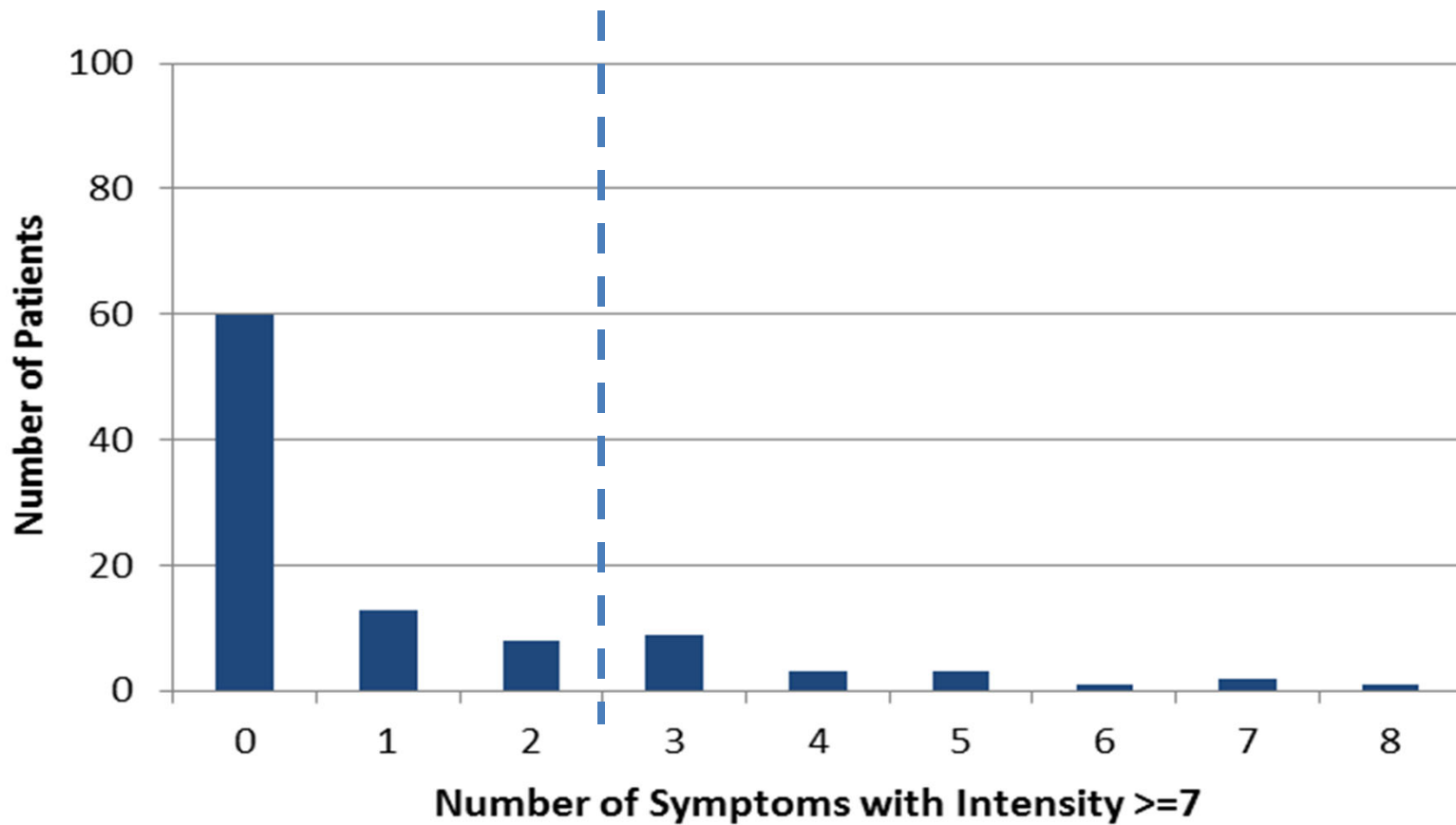
Routine Symptom Distress Screening

General Oncology Clinic



Routine Symptom Distress Screening

Defining Cutoff



Routine Symptom Distress Screening

Referral Outcomes

Screening	Pre-Implementation N (%)	Training N (%)	Post-implementation N (%)	P-value
ESAS completed	316/379 (83)	299/328 (91)	447/465 (96)	<0.001
Severe symptom distress	34/316 (11)	35/299 (12)	58/447 (13)	0.64
Social work referral	7/34 (21)	25/35 (71)	46/58 (79)	<0.001
Palliative care referral	4/34 (12)	7/35 (20)	15/58 (28)	0.21
Hospice care referral	0/34 (0)	2/35 (6)	2/58 (6)	0.54
Psychiatry or psychology referral	3/34 (9)	2/35 (6)	4/58 (7)	0.82

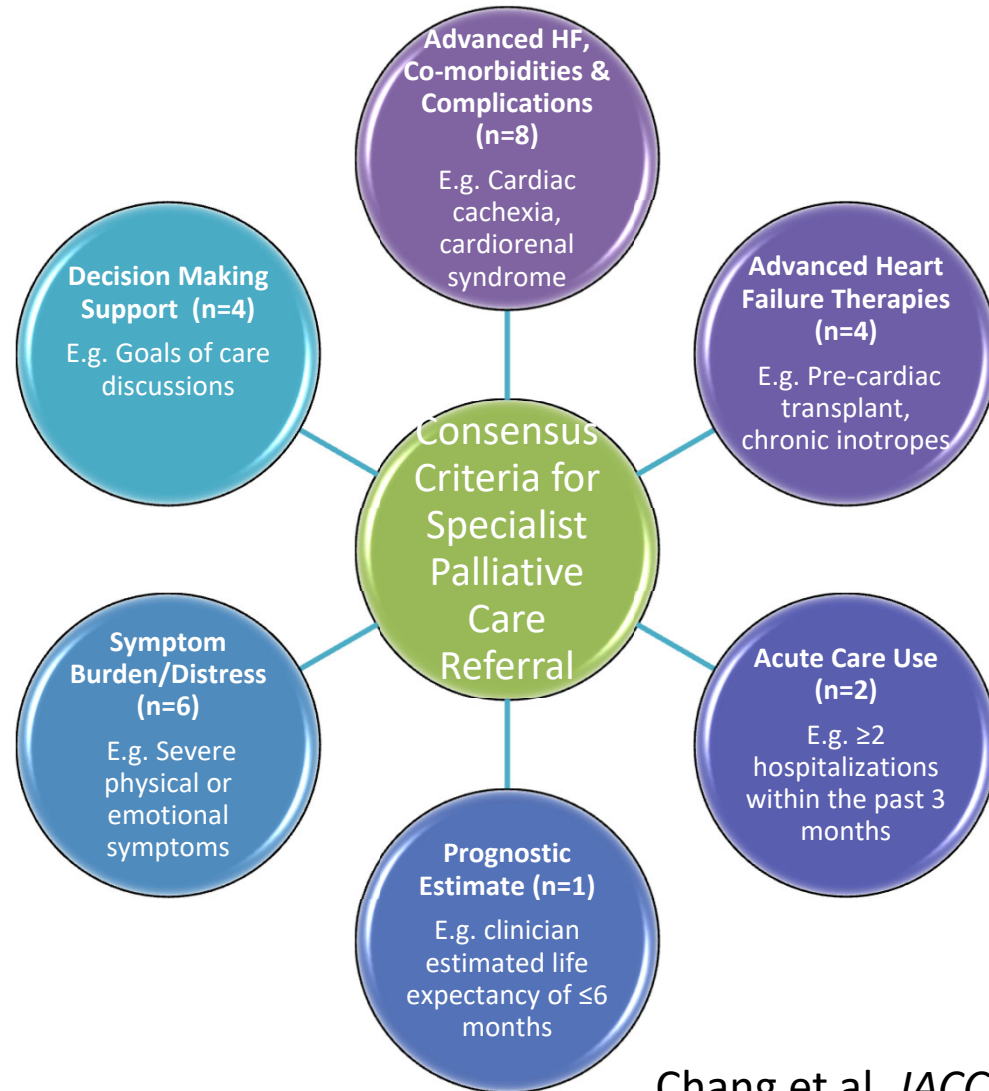
Consensus Referral Criteria

Palliative Care for Patients with Advanced Heart Failure

25 major criteria under 6 themes (one alone is enough to trigger referral)

Advanced heart failure

- ACC/AHA stage D (refractory heart failure requiring advanced intervention e.g. biventricular pacemakers, LVAD, transplantation)
- NYHA III (marked limitation in activity)
- NYHA IV (symptoms at rest)



Outline



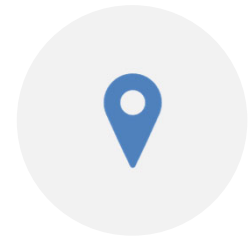
PRINCIPLES



EVIDENCE



PRACTICAL
CONSIDERATIONS



FUTURE
DIRECTIONS

Systematic Symptom Screening

From Detection to Action



Reporting

Face-to-face

Paper questionnaire

Electronic devices/
Wearable sensors

Evaluation

Assess and triage

Review forms

Real time call
Self-management
Just in time alerts

Clinical actions

Treatment
recommendations
Comprehensive plan

Real time advice
Care algorithms
Augmented referrals

Outcomes

Symptom control
and quality of life

ER and
readmission

What? PROs, **vitals**, **PS**
Who? Patients, **CG**
When? Frequency
How? Software,
privacy

When? Triggers
What? Interventions
Who? Availability
How? **AI predictions**

How? Display
How? Implementation
How? **AI**
recommendations

How much? Satisfaction
How much?
Standardization and
implementation
How much? Cost

Research Directions


- Development of better assessments
- Validation of patient reported outcomes
- Personalized symptom goals
- Comprehensive assessment (beyond symptoms)
- Adaptive testing (PROMIS)
- Caregiver assessments
- Remote monitoring
- Linking to clinical action (augmented referral)
- Machine learning

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Editorial

The promise of big data for palliative and end-of-life care research

Lucas Morin ^{1,2} and Bregje D Onwuteaka-Philipsen³

Quality of Life Research (2021) 30:2729–2754
<https://doi.org/10.1007/s11136-021-02925-y>

REVIEW



Minimal important change (MIC): a conceptual clarification and systematic review of MIC estimates of PROMIS measures

Caroline B. Terwee¹  · John Devin Peipert² · Robert Chapman² · Jin-Shei Lai² · Berend Terluin³ · David Cella² · Philip Griffith⁴ · Lidwine B. Mokkink¹

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Original Article

Personalized Symptom Goals and Response in Patients With Advanced Cancer

David Hui, MD, MSc¹; Minjeong Park, PhD²; Omar Shamieh, MD³; Carlos Eduardo Paiva, MD, PhD⁴; Pedro Emilio Perez-Cruz, MD, MPH⁵; Mary Ann Muckaden, MD⁶; and Eduardo Bruera, MD¹

“Monitoring of Symptoms. Why Should We?” as answered by ChatGPT

“Monitoring of symptoms is an important aspect of healthcare, as it allows healthcare providers to assess a patient's condition and make informed decisions about treatment and management.

There are several reasons why monitoring of symptoms is important:

1. **Early detection:** By monitoring symptoms, healthcare providers can detect changes in a patient's condition early on, which can allow for prompt and effective treatment.
2. **Assessment of treatment effectiveness:** Monitoring symptoms can help healthcare providers determine if a treatment is working as intended, and if any adjustments are needed.
3. **Detection of side effects:** Monitoring symptoms can help healthcare providers detect any side effects of a treatment, which can then be addressed.
4. **Improvement of quality of life:** By monitoring symptoms, healthcare providers can help patients manage their symptoms and improve their quality of life.
5. **Management of chronic conditions:** Monitoring symptoms is particularly important for patients with chronic conditions, as it allows healthcare providers to track the progression of the condition and make adjustments to treatment as needed.

Overall, monitoring of symptoms is a critical component of healthcare, as it helps healthcare providers provide the best possible care to patients and improve outcomes.”

“Monitoring of Symptoms. Why Should We?”

- Good symptom management starts with good symptom assessment
- Good evidence to support improved outcomes with systematic symptom assessment
- Advances in electronic health records, remote monitoring, wearable sensors, and machine learning will further augment symptom monitoring
- More research is needed!

Dankjewel

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