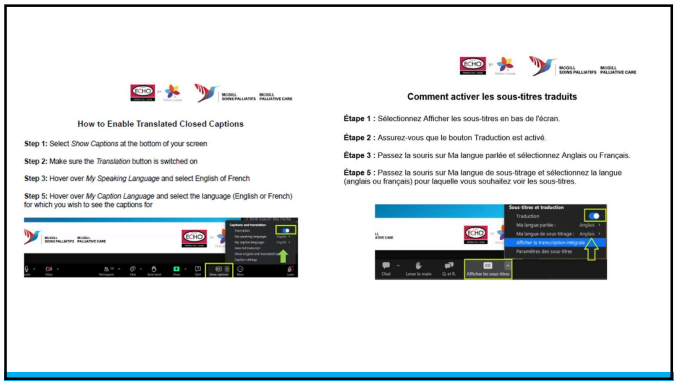


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1



2



3

McGill Palliative Care
National Grand Rounds
2026 Series

J. Craig Miller Lecture
October 21, 2026

Bedside Palliative Care Assessment and Management: What's New?

Eduardo Bruera, MD, FAAHPM
Department Chair, Professor of Medicine, Palliative, Rehabilitation and Integrative Medicine
The University of Texas MD Anderson
Cancer Center, Houston, TX

MCGILL SOINS PALLIATIFS MCGILL PALLIATIVE CARE

Project ECHO Palliative Care - Canada BY Pallium Canada

4

Conflict of Interest Declaration

Eduardo Bruera, MD, FAAHPM

I have no conflicts of interest to declare.

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5

Learning Objectives

By the end of this talk, participants will be able to:

- Review what is new about the assessment and virtual delivery of palliative care.
- Explain which drugs are just new and which ones are new and also good.
- Discuss which communication interventions can have a placebo effect.

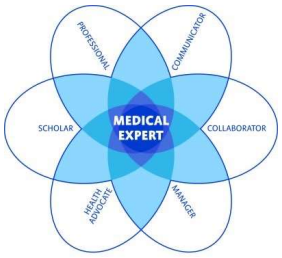
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6

CanMEDS Framework:

The CanMED competencies that will be addressed during this presentation:

- Professional
- Collaborator
- Scholar
- Communicator



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Current bedside assessment and management is :

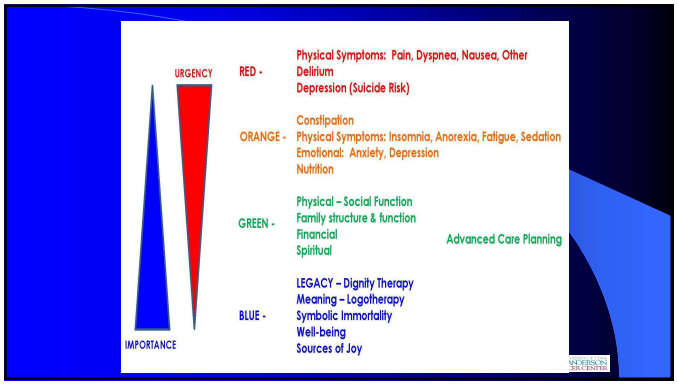
- Multidimensional
- Interdisciplinary
- Personalized

8

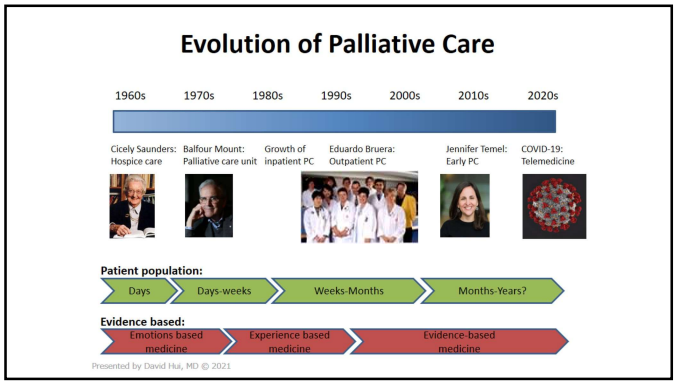
We Address Suffering



9


URGENCY
IMPORTANCE
RED -
Physical Symptoms: Pain, Dyspnea, Nausea, Other
Delirium
Depression (Suicide Risk)
ORANGE -
Constipation
Physical Symptoms: Insomnia, Anorexia, Fatigue, Sedation
Emotional: Anxiety, Depression
Nutrition
GREEN -
Physical – Social Function
Family structure & function
Financial
Spiritual
Advanced Care Planning
BLUE -
LEGACY – Dignity Therapy
Meaning – Logotherapy
Symbolic Immortality
Well-being
Sources of Joy

10


Evolution of Palliative Care
1960s
1970s
1980s
1990s
2000s
2010s
2020s
Cicely Saunders: Hospice care
Balfour Mount: Palliative care unit
Growth of inpatient PC
Eduardo Bruera: Outpatient PC
Jennifer Temel: Early PC
COVID-19: Telemedicine
Patient population:
Days
Days-weeks
Weeks-Months
Months-Years?
Evidence based:
Emotions based medicine
Experience based medicine
Evidence-based medicine
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11


GAP 2019
Pain & Symptom Control Clinic

12

RCTs since 2009

- Bakitas et al. *JAMA* 2009
- Temel et al. *NEJM* 2010
- Zimmermann et al. *Lancet* 2014
- Tattersall et al. *Palliat Care Med* 2014
- Bakitas et al. *J Clin Oncol* 2015
- Grudzen et al. *JAMA Oncol* 2016
- Maltoni et al. *Eur J Cancer* 2016
- Temel et al. *J Clin Oncol* 2016
- El-Jawahri et al. *JAMA* 2016
- Groenvold et al. *Palliat Med* 2017
- Monteiro do Carmo et al. *BMC Cancer* 2017
- Vanbutsele et al. *Lancet Oncol* 2018
- Scarpi et al. *Supp Care Cancer* 2018
- Franciosi et al. *Ann Palliat Care* 2019
- Temel et al. *J Palliat Med* 2020
- El-Jawahri et al. *JAMA Oncol* 2020

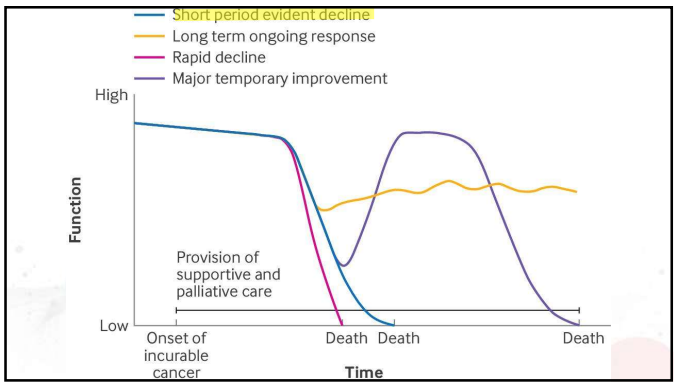
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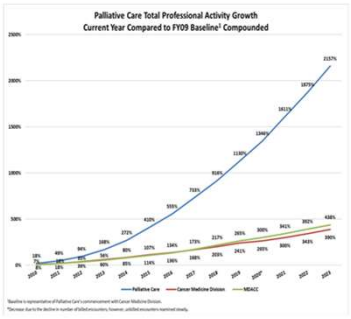
The natural history of advanced cancer has changed

- More longterm survivors
- More and longer response in advanced cancer
- New aggressive treatments (Car-T, immuno-chemo- RT)

14



15



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(A) Kaplan-Meier survival from **initial palliative care consultation** stratified by year (2017–2023). (B) Kaplan-Meier for patients with **advanced** cancer

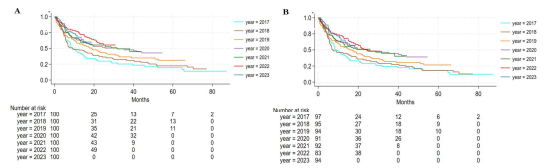


Figure 1

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Need- based has replaced time- based referral

- Time based : " advanced cancer", " no more treatment", " < 12 weeks after recurrence", etc
- Need based : ESAS

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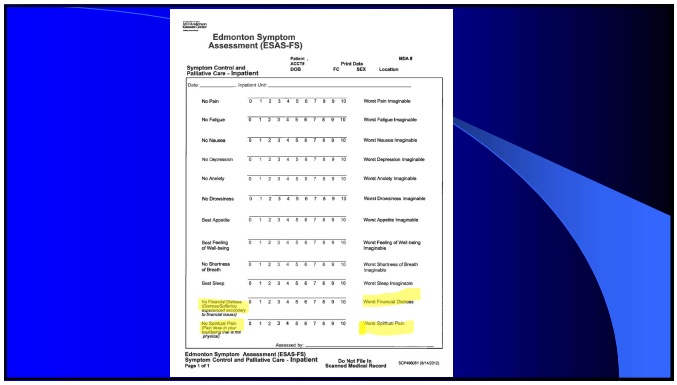
ESAS :No copyright!!!

- Completely free
- Takes 1 minute (RCT Wong A et al)
- More than 60 languages
- Graphic display
- Easy to do virtually/ by remote monitoring
- Introducing ESAS- FS

PC Assessment

MD ANDERSON CANCER CENTER

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Edmonton Symptom Assessment (ESAS-FS)

Symptom Control and Palliative Care - Inpatient

Patient ACCT# DOB | Print Date FC SEX | MDA # Location

Date: Inpatient Unit:

No Pain	0 1 2 3 4 5 6 7 8 9 10	Worst Pain Imaginable
No Fatigue	0 1 2 3 4 5 6 7 8 9 10	Worst Fatigue Imaginable
No Nausea	0 1 2 3 4 5 6 7 8 9 10	Worst Nausea Imaginable
No Depression	0 1 2 3 4 5 6 7 8 9 10	Worst Depression Imaginable
No Anxiety	0 1 2 3 4 5 6 7 8 9 10	Worst Anxiety Imaginable
No Drowsiness	0 1 2 3 4 5 6 7 8 9 10	Worst Drowsiness Imaginable
Best Appetite	0 1 2 3 4 5 6 7 8 9 10	Worst Appetite Imaginable
Best Feeling of Well-being	0 1 2 3 4 5 6 7 8 9 10	Worst Feeling of Well-being Imaginable
No Shortness of Breath	0 1 2 3 4 5 6 7 8 9 10	Worst Shortness of Breath Imaginable
Best Sleep	0 1 2 3 4 5 6 7 8 9 10	Worst Sleep Imaginable
No Financial Distress (Patient may not have experienced term/idiom) Is financial distress?	0 1 2 3 4 5 6 7 8 9 10	Worst Financial Distress
No Spiritual Pain (Patient may not have experienced term/idiom) Is spiritual or not physical	0 1 2 3 4 5 6 7 8 9 10	Worst Spiritual Pain

Assessed by: _____

Edmonton Symptom Assessment (ESAS-FS) Symptom Control and Palliative Care - Inpatient Page 1 of 1

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SCP466501 (9/14/2012)

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JOURNAL OF PALLIATIVE MEDICINE
Volume 29, Number 3, 2026
Mary Ann Liebert, A Part of Sage
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DOI: 10.1177/10966218251401403

Frequency and Correlates of Financial Distress in Patients with Advanced Cancer

Jacqueline Tschanz, MD,* Rida Khan, MD,* Maxine De La Cruz, MD, Minxing Chen, and Eduardo Bruera, MD

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- The InCharge Financial Distress/Financial Well-Being (IFDFW / IFDW) Scale has 8 items.
- FACIT- cost has 12 item
- Can we do a single item F?

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Table 1. Patient Demographics[a]

Characteristic	High financial distress[b] (n = 35) Mean (SD)	N (%)	Average/low financial distress (n = 105) Mean (SD)	N (%)	p-value
Age	55.1 (9.4)		59.3 (10.7)		**0.040**
Gender					0.316
Female		24 (68.6)		62 (59.1)	
Male		11 (31.4)		43 (41.0)	
Ethnicity					0.086
White		19 (54.3)		77 (73.3)	
Hispanic		8 (22.9)		9 (8.6)	
African American		7 (20.0)		12 (11.4)	
Asian		1 (2.9)		5 (4.8)	
Other		0 (0.0)		2 (1.9)	
Marital status					**0.002**
Single/Never married		7 (20.0)		8 (7.6)	
Married		18 (51.4)		87 (82.9)	
Divorced		8 (22.9)		6 (5.7)	
Widowed		2 (5.7)		3 (2.9)	
Separated		0 (0.0)		1 (1.0)	
Involved in caregiving					0.180
No		23 (65.7)		81 (77.1)	
Yes		12 (34.3)		24 (22.9)	
Education level					0.433
Up to high school		10 (28.6)		22 (21.0)	
Vocational/technical school		1 (2.9)		3 (2.9)	
Associate degree/some college		12 (34.3)		25 (23.8)	
Bachelor's degree		7 (20.0)		33 (31.4)	
Advanced degree		5 (14.3)		22 (21)	
Place of residence					0.992
Local		9 (25.7)		27 (25.7)	
Out of town		18 (51.4)		55 (52.4)	
Out of state		8 (22.9)		23 (21.9)	
Homeowner status					0.238
Homeowner with mortgage		15 (42.9)		55 (52.9)	
Homeowner without mortgage		10 (28.5)		14 (13.5)	
Renter		9 (25.7)		14 (13.5)	
Prefer not to answer		1 (2.9)		1 (1.0)	
Employment status					**0.001**
Retired		8 (22.9)		33 (31.4)	
Part-time		2 (5.7)		4 (3.8)	
Unemployed		2 (5.7)		17 (16.2)	
Retired		10 (28.6)		43 (41.0)	
Other		13 (37.1)		8 (7.6)	
Annual household income					**<0.001**
<$40,000		17 (48.6)		14 (13.3)	
$40,000–$80,000		9 (25.7)		23 (21.9)	
>$80,000		4 (11.4)		47 (44.8)	
Prefer not to say		5 (14.3)		21 (20.0)	

[a]All values rounded up to nearest tenth decimal place.
[b]As defined by IFDFW score.
IFDFW, InCharge Financial Distress/Financial Well-Being Scale.

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Table 3. Association Between Financial Well-Being Scale (IFDFW), COST-FACIT, Edmonton Symptom Assessment Scale-Financial Distress (ESAS-FS), Total ESAS Score, and Quality of Life (FACT-G)

	Ordinary least squares results			
Predictors	*Coefficient*	*Robust SE*	*95% CI*	p-*value*
Cost-FACIT	0.18	0.01	(0.16, 0.19)	*<0.001*
Financial distress rating in ESAS-FS	−0.60	0.05	(−0.70, −0.50)	*<0.001*
FACT-G	0.09	0.01	(−0.08, −0.03)	*<0.001*
ESAS-Total	−0.06	0.01	(−0.08, −0.03)	*<0.001*

CI, confidence interval; COST-FACIT, Comprehensive Score for Financial Toxicity-Functional Assessment of Chronic Illness Therapy; SE, standard error.

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https://doi.org/10.1007/s00520-021-06758-w

ORIGINAL ARTICLE

Financial distress and its associated burden in couples coping with an advanced cancer

Juliet L. Kroll[1] · Seokhun Kim[1] · Dalnim Cho[2] · Shiao-Pei Weathers[3] · Aileen B. Chen[4] · Grace Smith[2,4] · Eduardo Bruera[5] · Kathrin Milbury[1]

Received: 27 May 2021 / Accepted: 13 December 2021 / Published online: 3 February 2022
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Table 1 Participant demographics and characteristics

n=76 dyads	Patients		Partners		
	Mean (SD)	Min–max	Mean (SD)	Min–max	χ^2 or paired t
Age (years)	58.19 (12.31)	29–81	57.83 (13.12)	28–88	0.17
Sex, n (% male)	37 (49.3)		37 (51.4)		0.06
Race n (%)					0.65
Asian/Pacific Islander	1 (1.4)		2 (2.6)		
Black	4 (5.7)		3 (3.9)		
White	57 (81.4)		61 (80.3)		
Category not available	2 (2.9)		2 (2.6)		
Ethnicity n (%)					
Hispanic	6 (8.6)		8 (10.5)		
Employment (n, %)					6.07
Full-time employed	24 (33.8)		38 (50.7)		
Part-time employed	8 (11.3)		3 (4.0)		
Retired	33 (46.5)		27 (36.0)		
Unemployed	6 (8.4)		7 (9.3)		
Education n (%)					5.99
Graduate degree	11 (15.3)		16 (21.3)		
Some Graduate school	5 (6.9)		6 (8.0)		
Bachelor's degree	16 (22.2)		19 (21.3)		
Some college	26 (37.5)		20 (29.6)		
High school graduate	12 (16.7)		11 (14.7)		
Some high school	1 (1.4)		3 (4.0)		
Diagnosis n (%)					
Brain tumor	33 (43.4)		–		
Lung cancer	43 (56.6)		–		
Time since diagnosis (yrs)	2.76 (4.6)	0–27	–		
Self-report					
Physical QOL (PROMIS-10)	43.74 (9.3)	19.9–61.9	48.47 (10.7)	4.8–67.7	−3.09*
Mental QOL (PROMIS-10)	50.51 (8.8)	31.3–67.6	51.25 (9.3)	21.2–67.6	−0.95
Anxiety symptoms (BSI-18)	0.31 (0.34)	0–1.67	0.458 (0.45)	0–1.67	−2.77*
Depressive symptoms (CES-D)	10.69 (7.3)	0–37	11.75 (9.0)	0–54	−1.10
CES-D cases ≥ 16 (%)	20.5		21.1		3.61
Illness communication (CICS)	16.74 (3.1)		15.67 (3.6)		2.38*

*$p < .05$, **$p < .001$. Note. Quality of life (QOL), CES-D ≥ 16 indicates clinical levels of depression in the mild to moderate range; ≥ 28 indicates moderate to severe range. PROMIS-10 measures, higher scores indicate more of the concept being measured. CICS, Couples Illness Communication Scale, higher scores indicate greater ratings of ease of illness communication within the couple. Possible scores range from 4 to 20. Race and ethnicity were captured together in a single item

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Table 2 Patient and spousal caregiver self-report of symptoms on ESAS

	Patients			Spousal caregivers				
	Mean (SD)	Min–max	Rank	Mean (SD)	Min–max	Rank	Correlation	Paired t
Fatigue	4.00 (2.71)	0–9	1	2.79 (2.56)	0–10	3	0.70	2.79*
Sleep	3.96 (2.50)	0–8	2	3.79 (2.69)	0–10	1	0.05	0.17
Well-being	3.07 (2.56)	0–10	3	2.76 (2.72)	0–10	4	0.19	0.66
Appetite	3.00 (2.90)	0–10	4	2.13 (2.71)	0–10	6	0.15	2.00*
Pain	2.49 (2.64)	0–10	5	1.49 (2.14)	0–10	8	0.16	2.58*
Shortness of breath	2.45 (2.84)	0–9	6	0.66 (1.37)	0–7	11	0.26*	5.30**
Financial distress	2.32 (2.81)	0–10	7	2.81 (3.11)	0–10	2	0.53**	−1.57
Drowsiness	2.20 (2.59)	0–9	8	1.65 (2.31)	0–10	7	0.06	1.23
Anxiety	1.64 (2.23)	0–9	9	2.41 (2.66)	0–9	5	0.09	−2.04*
Nausea	1.16 (2.07)	0–8	10	0.34 (1.33)	0–8	12	0.29	3.30*
Depression	1.05 (1.88)	0–8	11	1.43 (2.20)	0–10	9	0.09	−1.09
Spiritual pain	0.69 (1.42)	0–7	12	1.19 (2.41)	0–10	10	0.30*	−0.09

*$p < .05$, **$p < .001$. Edmonton Symptom Assessment Scale (ESAS-SF), where scores range from 0 (fewest symptoms) to 10 (greatest extent of symptoms). Partial correlation coefficient

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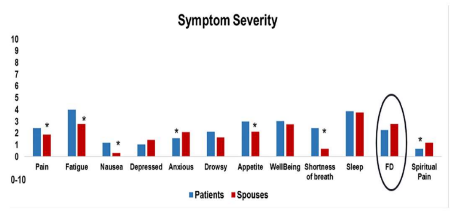


Fig. 1 Relative symptom severity among patients and spouses. Note. $^{*}p < .05$, paired sample *t*-test demonstrates no significant difference between patients and their spouses on financial distress (FD)

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Table 4 Patient self-report rating and spousal caregiver proxy report of symptoms on ESAS

	Patient self-report		Caregiver proxy report of patient's symptoms				Caregiver response style
	Mean (SD)	Rank	Mean (SD)	Rank	Correlation	Paired *t*-test	
Fatigue	4.00 (2.71)	1	5.01 (2.78)	1	0.50^{**}	-2.84^{*}	Overreport^{+}
Sleep	3.96 (2.50)	2	4.18 (2.52)	2	0.40^{**}	−0.95	Overreport
Well-being	3.07 (2.56)	3	3.29 (2.43)	4	0.12	−0.67	Accurate
Appetite	3.00 (2.90)	4	2.61 (2.47)	6	0.27^{**}	0.81	Accurate
Pain	2.49 (2.64)	5	3.49 (3.00)	3	0.66^{**}	-3.31^{**}	Overreport^{+}
Shortness of breath	2.45 (2.84)	6	2.39 (2.84)	8	0.63^{**}	0.25	Accurate
Financial distress	2.32 (2.81)	7	2.21 (2.70)	9	0.23	0.54	Accurate
Drowsiness	2.20 (2.59)	8	2.87 (2.81)	5	0.42^{**}	-2.01^{*}	Overreport
Anxiety	1.64 (2.23)	9	2.73 (2.50)	7	0.52^{**}	-4.39^{**}	Overreport^{+}
Nausea	1.16 (2.07)	10	2.04 (2.57)	11	0.71^{**}	-3.97^{**}	Overreport
Depression	1.05 (1.88)	11	2.17 (2.35)	10	0.38^{**}	-3.82^{**}	Overreport^{+}
Spiritual pain	0.69 (1.42)	12	1.14 (2.00)	12	0.36^{**}	2.38^{*}	Overreport

$^{*}p < .05$, $^{**}p < .001$. Edmonton Symptom Assessment Scale (ESAS), $^{+}$a full point difference between caregiver and patient

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The Oncologist®

Symptom Management and Supportive Care

Inequalities in Financial Distress, Symptoms, and Quality of Life Among Patients with Advanced Cancer in France and the U.S.

Cécile Barbaret,[a,†] Marvin O. Delgado-Guay,[b,†] Stéphane Sanchez,[c] Christelle Brosse,[d] Murielle Ruer,[e] Wadih Rhondali,[e] Léa Monsarrat,[e] Patrick Michaud,[d] Anne Marie Schott,[f] Eduardo Bruera,[b] Marilène Filbet[e]

[a]Department of Supportive and Palliative Care, Centre Hospitalo-Universitaire de Grenoble, La Tronche, France; [b]Department of Palliative, Rehabilitation, and Integrative Medicine, The University of Texas MD Anderson Cancer Center, Houston, Texas, U.S.A; [c]Department of Medical Information, Evaluation and Performance, Hôpitaux Champagne Sud, Troyes, France; [d]Department of Palliative Care, Institut de Cancérologie de la Loire, Saint-Etienne, France; [e]Department of Supportive and Palliative Care, Centre Hospitalier Lyon-Sud, Lyon, France; [f]Pôle IMER, Hospices Civils de Lyon, Lyon, France

[†]Contributed equally

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Table 2. Demographic and clinical characteristics of study participants

Characteristic	Overall, *n* (%) *n* = 292	French medical institution, *n* (%) *n* = 143	U.S. medical institution, *n* (%) *n* = 149	*p* value
Age, years, mean (SD)	59.3 (10)	58 (12)	60 (9)	.192
Sex				
Female	144 (49.3)	70 (49)	74 (50)	.9
Male	148 (50.7)	73 (51)	75 (50)	.9
Cancer				
Breast	75 (26)	36 (25.1)	39 (26)	.9
Colorectal	72 (24)	36 (25.1)	36 (24)	.9
Lung	74 (25)	36 (25.1)	38 (26)	.9
Prostate	71 (24)	35 (24.4)	36 (24)	.9
Metastasis	237 (81)	118 (82)	119 (80)	.4
ECOG status, mean (SD)	1.9 (0.8)	2.2 (0.8)	1.6 (0.8)	**<.001**
Treatment				
Chemotherapy	247 (84.6)	132 (92)	115 (77)	**<.001**
Targeted therapy	38 (13)	8 (6)	30 (20)	**<.001**
Radiation	117 (40.1)	80 (56)	37 (25)	**<.001**
Surgery	107 (37)	74 (52)	33 (22)	**<.001**
Marital status				
Married	165 (57)	87 (61)	78 (52)	.061
Single	48 (16)	16 (11)	32 (11)	.061
Divorced	38 (13)	19 (13)	19 (13)	.061
Widowed	33 (11)	17 (12)	16 (11)	.061
Separated	5 (2)	4 (3)	5 (2)	.061
Education				
Advanced degree	44 (15)	13 (9)	31 (21)	**<.001**
College	63 (22)	23 (16)	40 (27)	**<.001**
High school or less	179 (61)	106 (74)	73 (49)	**<.001**
Government (National) insurance	223 (76)	143 (100)	80 (54)	**<.001**

Bolded *p* values indicate statistical significance.
Abbreviation: ECOG, Eastern Cooperative Oncology Group.

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Table 3. Effects of financial distress on suffering

Statements	Overall, *n* (%)	French medical institution, *n* (%)	U.S. medical institution, *n* (%)	*p* value
n =	288	141	147	
I have more financial distress than physical distress	61 (21)	16 (11)	45 (30)	**<.001**
n =	289	141	148	
I have more financial distress than distress about my physical functioning	82 (28)	18 (13)	64 (43)	**<.001**
n =	289	141	148	
I have more financial distress than social/family distress	82 (28)	18 (13)	64 (43)	**<.001**
n =	289	141	148	
I have more financial distress than emotional distress (anxiety/depression)	73 (25)	18 (13)	55 (37)	**<.001**

Bolded *p* values indicate statistical significance.

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Table 5. Multivariate linear regression mode

Variable	Regression coefficient	*p* value
France residence	−3.376	**.001**
High HADS-D score	1.932	**.001**
Low HADS-A score	−1.224	**.001**
Greater age	−0.052	**.003**
Single status	0.907	**.023**
Functional and social well-being	−0.077	**.031**
Metastasis	1.538	**.036**
Surgery	0.794	**.039**
Physical well-being	−0.045	.101
Government insurance	−0.77	.124

Bolded *p* values indicate statistical significance.

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Similar results with Cancer Center Vs Public hospital in Houston

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Table 2. Perception of the impact of financial distress on other clinical problems among advanced cancer patients

Statements	Overall	Comprehensive cancer center	General public hospital	p value*
I have more financial distress than physical distress	45/147 (30)	23/76 (30)	22/71 (31)	1.0000
I have more financial distress than distress about my physical functioning	46/148 (31)	18/76 (23)	28/72 (39)	.0511
I have more financial distress than social/family distress	64/148 (43)	25/76 (33)	39/72 (54)	.0085
I have more financial distress than emotional distress (anxiety/depression)	55/148 (37)	22/76 (29)	33/72 (46)	.0411

Data given as no./total (%) unless otherwise indicated.
*Fisher's exact test.
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© Cambridge University Press, 2015 1478-9515/15
doi:10.1017/S147895151500108X

Frequency, intensity, and correlates of spiritual pain in advanced cancer patients assessed in a supportive/palliative care clinic

MARVIN OMAR DELGADO-GUAY, M.D.,[1] GARY CHISHOLM, M.S.,[2]
JANET WILLIAMS, M.P.H., C.C.R.P.,[1] SUSAN FRISBEE-HUME, M.S., B.S.N.,[1]
ANDREA O. FERGUSON, M.DIV., M.A., B.C.C.,[1,3] AND EDUARDO BRUERA, M.D.[1]
[1]Department of Palliative Care and Rehabilitation Medicine, The University of Texas MD Anderson Cancer Center, Houston, Texas
[2]Department of Biostatistics, The University of Texas MD Anderson Cancer Center, Houston, Texas
[3]Department of Spiritual Care and Education, The University of Texas MD Anderson Cancer Center, Houston, Texas

(RECEIVED June 19, 2015; ACCEPTED July 21, 2015)

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Edmonton Symptom Assessment Scale (ESAS–FS)

Please circle the number that best describes your symptoms:

No Pain	0 1 2 3 4 5 6 7 8 9 10	Worst Pain
No Fatigue	0 1 2 3 4 5 6 7 8 9 10	Worst Fatigue
No Nausea	0 1 2 3 4 5 6 7 8 9 10	Worst Nausea
No Depression	0 1 2 3 4 5 6 7 8 9 10	Worst Depression
No Anxiety	0 1 2 3 4 5 6 7 8 9 10	Worst Anxiety
No Drowsiness	0 1 2 3 4 5 6 7 8 9 10	Worst Drowsiness
No Shortness of Breath	0 1 2 3 4 5 6 7 8 9 10	Worst Shortness of Breath
Best Appetite	0 1 2 3 4 5 6 7 8 9 10	Worst Appetite
Best Feeling of Well-being	0 1 2 3 4 5 6 7 8 9 10	Worst Feeling of Well-being
Best Sleep	0 1 2 3 4 5 6 7 8 9 10	Worst Sleep
No Financial Distress (Distress/suffering experienced secondary to financial issues)	0 1 2 3 4 5 6 7 8 9 10	Worst Financial Distress
No Spiritual Pain (Pain deep in your soul/being that is not physical)	0 1 2 3 4 5 6 7 8 9 10	Worst Spiritual Pain

Fig. 1. The Edmonton Symptom Assessment Scale–FS (ESAS–FS).

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Table 1. *Characteristics of advanced cancer patients evaluated in our outpatient supportive/palliative care clinic (SCPC) (N = 292)*

Variable	Level	*n*	(%)
Age	Median: 61 years (range = 22–92)		
Gender			
Female		136	(46.6%)
Male		156	(53.4%)
Ethnicity			
White		191	(65.4%)
African American		47	(16.1%)
Hispanic		36	(12.3%)
Asian		15	(5.1%)
Other		3	(1.1%)
Primary cancer			
Head/neck		62	(21.2%)
Gastrointestinal		57	(19.5%)
Breast		40	(13.7%)
Urological		32	(11%)
Lung		32	(11%)
Gynecological		24	(8.2%)
Hematological		2	(0.7%)
Other		43	(14.7%)
Cancer stage			
Metastatic		155	(53.1%)
Local/recurrent		120	(41.1%)
No evidence of active disease		17	(5.8%)
Chemotherapy			
During 2 weeks prior to SCPC appointment		91	(31.2%)
At time of PC evaluation		56	(19.2%)
4 weeks prior		10	(3.4%)
More than 4 weeks		63	(21.6%)
None		72	(24.7%)

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Table 2. *Change in frequency and intensity of symptoms from baseline to follow-up for those patients who have the symptom (ESAS score ≥ 1) at baseline*

	Baseline		Follow-Up			
Symptom	Frequency of Symptom (%)	Intensity, Mean (95% *CI*) for Patients with Symptom	Frequency of Symptom (%)	Intensity, Mean (95% *CI*) for Patients with Symptom	Change in Intensity, Mean (95% *CI*)	*p**
Pain	254/291 (87%)	5.5 (5.2, 5.9)	152/166 (92%)	5.0 (4.6, 5.5)	−0.6 (−1.1, −0.2)	**0.0482**
Fatigue	268/292 (92%)	5.8 (5.5, 6.1)	168/172 (98%)	5.5 (5.2, 5.9)	−0.3 (−0.7, 0.1)	0.2211
Drowsiness	208/291 (71%)	4.7 (4.4, 5.1)	100/130 (77%)	4.8 (4.4, 5.3)	0.1 (−0.4, 0.7)	0.3143
Nausea	147/291 (51%)	4.0 (3.6, 4.4)	65/97 (67%)	4.5 (3.9, 5.0)	0.4 (−0.5, 1.2)	0.3222
Depression	188/289 (65%)	4.6 (4.2, 5.0)	99/124 (80%)	3.7 (3.2, 4.1)	−1.1 (−1.6, −0.7)	**0.0006**
Anxiety	195/291 (67%)	4.8 (4.4, 5.2)	111/131 (85%)	4.2 (3.8, 4.6)	−0.7 (−1.2, −0.2)	0.0066
Appetite	250/292 (86%)	5.3 (5.0, 5.6)	142/154 (92%)	5.3 (4.8, 5.7)	−0.3 (−0.8, 0.3)	0.4153
Dyspnea	168/292 (58%)	4.5 (4.1, 4.9)	83/101 (82%)	4.2 (3.7, 4.7)	−0.7 (−1.2, −0.1)	0.1421
Sleep	262/291 (90%)	5.5 (5.2, 5.8)	143/162 (88%)	5.1 (4.7, 5.5)	−0.6 (−1.0, −0.2)	**0.0279**
Wellbeing	269/291 (92%)	5.3 (5.0, 5.5)	155/165 (94%)	5.0 (4.6, 5.3)	−0.4 (−0.9, 0.1)	0.0714
Financial	187/289 (65%)	4.9 (4.5, 5.3)	89/113 (79%)	4.8 (4.2, 5.4)	−0.3 (−0.8, 0.2)	0.4570
Spiritual pain	123/282 (44%)	**4.0 (3.5, 4.4)**	**41/72 (57%)**	**3.2 (2.5, 3.9)**	**−0.9 (−1.6, −0.2)**	**0.1102**

ESAS–FS = Edmonton Symptom Assessment Scale–Financial Distress/Spiritual Pain; 95% *CI* = 95% confidence interval.
*Sign test for change in intensity different from zero is based on patients with non-missing data at both baseline and follow-up and for whom the symptom was present at baseline.

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Table 3. *Multiple distressing symptoms among advanced cancer patients with mild (≥1/10) to moderate/severe (≥4/10) spiritual pain: Use of the ESAS–FS* in a supportive/palliative care outpatient clinic setting*

ESAS Symptom	Spiritual Pain ≥1/10 ($n = 123$) Mean (95% *CI*)	No Spiritual Pain ≥4/10 ($n = 159$) Mean (95% *CI*)	*p* Value**
Pain	5.5 (4.8, 5.8)	4.4 (3.9, 4.9)	0.0213
Fatigue	5.8 (5.3, 6.2)	5.0 (4.5, 5.4)	0.0230
Nausea	2.6 (2.0, 3.1)	1.6 (1.2, 2.0)	0.0020
Depression	4.2 (3.7, 4.7)	2.0 (1.5, 2.4)	**<0.0001**
Anxiety	4.2 (3.6, 4.7)	2.4 (1.9, 2.9)	**<0.0001**
Drowsiness	4.2 (3.7, 4.7)	2.8 (2.4, 3.3)	**<0.0001**
Appetite	4.7 (4.2, 5.3)	4.3 (3.8, 4.8)	0.2672
Dyspnea	3.1 (2.6, 3.7)	2.3 (1.8, 2.7)	**0.0037**
Sleep	5.4 (4.9, 5.9)	4.5 (4.1, 5.0)	**0.0203**
Well-being	5.4 (4.9, 5.8)	4.5 (4.1, 5.0)	**0.0166**
Financial distress	4.4 (3.9, 5.0)	2.1 (1.7, 2.6)	**<0.0001**
ESAS Symptom	**Spiritual Pain ≥4/10 ($n = 60$) Mean (95% *CI*)**	**No Spiritual Pain ($n = 159$) Mean (95% *CI*)**	***p* Value****
Pain	6.1 (5.4, 6.9)	4.4 (3.9, 4.9)	**0.0005**
Fatigue	6.1 (5.4, 6.8)	5.0 (4.5, 5.4)	**0.0107**
Nausea	2.9 (2.0, 3.7)	1.6 (1.2, 2.0)	**0.0044**
Depression	5.1 (4.4, 5.9)	2.0 (1.5, 2.4)	**<0.0001**
Anxiety	4.8 (3.9, 5.6)	2.4 (1.9, 2.9)	**<0.0001**
Drowsiness	4.4 (3.6, 5.1)	2.8 (2.4, 3.3)	**0.0003**
Appetite	5.0 (4.3, 5.8)	4.3 (3.8, 4.8)	0.1355
Dyspnea	3.5 (2.6, 4.4)	2.3 (1.8, 2.7)	0.0236
Sleep	6.0 (5.3, 6.7)	4.5 (4.1, 5.0)	**0.0017**
Well-being	5.9 (5.2, 6.6)	4.5 (4.1, 5.0)	**0.0012**
Financial distress	5.5 (4.6, 6.3)	2.1 (1.7, 2.6)	**<0.0001**

*ESAS–FS = Edmonton Symptom Assessment Scale—Financial Distress and Spiritual Pain.
**Wilcoxon rank-sum test

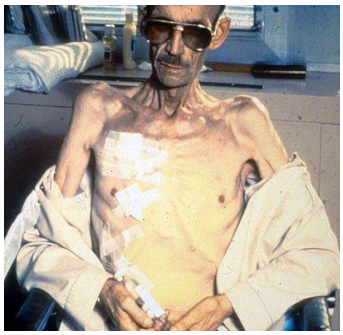
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Table 4. *Correlations between ESAS–FS* symptom distress and spiritual pain (SP) at baseline, at follow-up, and the impact of baseline symptom distress on change in spiritual pain*

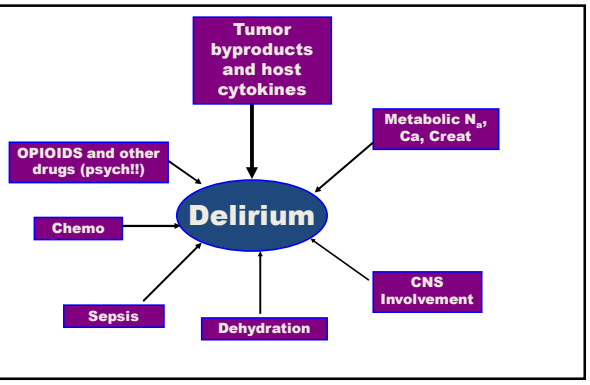
ESAS Symptoms	SP at Baseline ($n = 282$) *r*	SP at Baseline ($n = 282$) *p* Value**	SP at Follow-Up ($n = 162$) *r*	SP at Follow-Up ($n = 162$) *p* Value**	Change of SP ($n = 162$) *r*	Change of SP ($n = 162$) *p* Value**
Pain	0.20	**0.0010**	0.12	0.1260	−0.13	0.1007
Fatigue	0.18	0.0026	0.01	0.9924	−0.01	0.8729
Nausea	0.20	**0.0009**	0.29	**0.0002**	0.07	0.3769
Depression	0.45	**<0.0001**	0.35	**<0.0001**	−0.20	0.0096
Anxiety	0.34	**<0.0001**	0.25	**0.0010**	−0.20	0.0076
Drowsiness	0.26	**<0.0001**	0.15	0.0493	−0.06	0.4165
Appetite	0.10	0.1113	0.07	0.3762	0.04	0.5810
Dyspnea	0.17	0.0033	0.06	0.4299	−0.02	0.7695
Sleep	0.18	0.0026	0.08	0.3329	−0.09	0.2703
Well-being	0.19	**0.0011**	0.27	**0.0006**	−0.05	0.5547
Financial distress	0.44	**<0.0001**	0.42	**<0.0001**	−0.13	0.0969

*ESAS–FS = Edmonton Symptom Assessment Scale—Financial Distress and Spiritual Pain.
**Spearman correlation test.

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Delirium Recall (Bruera E et al, Cancer 2009)

- 99 Patients with Complete resolution < 72hs before
- HYPO 20% ; HYPER 13%; MIXED 67%
- 250 Contributing Factors
- **73/99 Patients (74%) Remembered DELIRIUM !!!!**
- 59/73 Recall expressed distress (81%); vs. 11/26 No Recall (42%); p = 0.01

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Delirium: Bedside Babel

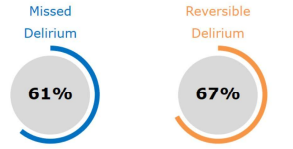
	Patient/ Family Caregiver		Patient/ Nurse		Patient/ PCS		Family Caregiver/ Nurse		Family Caregiver/ PCS		Nurse/ PCS	
Symptoms	n	WK (*P*)	n	WK (*P*)	n	WK (*P*)	n	WK (*P*)	n	WK (*P*)	n	WK (*P*)
Auditory hallucinations	93	0.38 (<.01)	79	0.19 (<.01)	92	0.2 (.02)	78	0.03 (.52)	93	0.18 (.01)	80	0.26 (<.01)
Delusional thoughts	95	0.29 (<.01)	80	0.15 (.09)	93	0.1 (.25)	79	0.08 (.3)	94	0.07 (.36)	80	0.04 (.63)
Time orientation	91	0.28 (<.01)	74	−0.08 (.4)	87	−0.02 (.79)	79	−0.03 (.73)	94	0.01 (.97)	78	0.19 (.03)
Place orientation	91	0.26 (<.01)	74	−0.01 (.93)	87	0.06 (.43)	80	0.09 (.26)	94	0.01 (.93)	79	0.18 (.03)
Psychomotor agitation	94	0.25 (<.01)	79	0.13 (.12)	90	0.09 (.26)	80	0.13 (.06)	95	0.06 (.4)	80	0.08 (.33)
Tactile hallucinations	93	0.19 (.02)	79	0.09 (.37)	91	−0.003 (.97)	79	0.13 (.12)	94	0.07 (.34)	80	0.13 (.16)
Visual hallucinations	96	0.45 (<.01)	78	0.14 (.01)	91	0.21 (.01)	80	0.18 (<.01)	94	0.24 (<.01)	79	0.05 (.38)

PCS indicates palliative care specialist; n, effective sample size; WK, weighted kappa.

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Delirium Assessment

Missed Delirium



252/771 (33%) patients who had an inpatient palliative care consult found to have delirium by the palliative care team. 99 (39%) diagnosed with delirium by oncology team

55/82 (67%) patients with reversible delirium had a missed diagnosis initially

Routine screening is key!

Presented by David Hui, MD © 2023

De La Cruz et al. *Supp Care Cancer* 2015

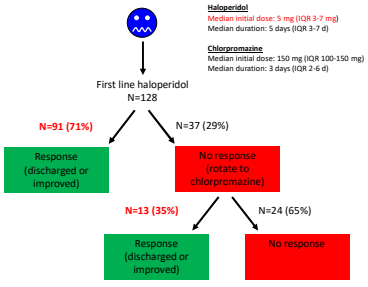
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Shin, HS et al. Frequency and outcome of **neuroleptic rotation** in patients with advanced cancer

- 167/266 consecutive PCU admissions (63%): delirium treated with haloperidol 1st line
- 128 (77%) only haloperidol (71% discharged alive)
- 39 (23%) required neuroleptic rotation (41% discharged alive)
- Median (IQR) H dose: 5 (3-7) mg/day

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Haloperidol Success Rate

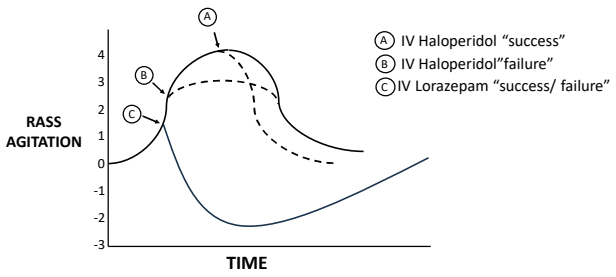


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Multiple RCTs

- Other neuroleptics **not superior** to haloperidol
- Olanzapine, quetiapine, risperidone
- Dexmedetomidine, midazolam, lorazepam: **palliative sedation** (persistent negative RASS)

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Haloperidol drug- drug interactions(DDIs) attack is unjustified

- **ALL** neuroleptics prolong QTc
- Delirium is a cause of great suffering
- Pharmacokinetic **potential** interactions are irrelevant!: **clinical** adverse effects are what matters

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RESEARCH ARTICLE

Major adverse cardiac events with haloperidol: A meta-analysis

Michael Cristian Garcia[1,2*], Mason Anderson[1], Michelle Li[1], Mick Zewdu[1], Tyler Schneider[1,3], Jessyca Matos-Silva[1,4], Genevieve Ramnarine[1], Kassie Rong[1], Lawrence Mbuagbaw[1,4,5], Anne Holbrook[1,4,6]

1 Clinical Pharmacology and Toxicology Research Group, Research Institute of St Joe's Hamilton, Hamilton, Canada, **2** Temerty Faculty of Medicine, University of Toronto, Toronto, Canada, **3** e-Health MSc Program, Faculty of Health Sciences, DeGroote School of Business, Faculty of Engineering, McMaster University, Hamilton, Canada, **4** Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, Canada, **5** Biostatistics Unit, Father Sean O'Sullivan Research Centre, St Joseph's Healthcare, Hamilton, Canada, **6** Division of Clinical Pharmacology and Toxicology, Department of Medicine, McMaster University, Hamilton, Ontario, Canada

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- Randomized controlled trials (RCTs)
- Patients 18 years or older
- Comparing haloperidol to placebo.
- The FDA-adapted MACE composite: death, non-fatal cardiac arrest, ventricular tachyarrhythmia including torsades de pointes, and seizure or syncope

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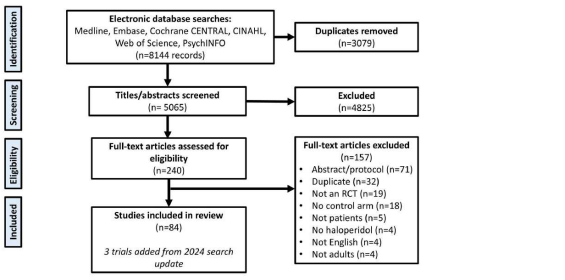


Fig 1. PRISMA flow diagram of the included studies in the meta-analysis. QTPmed: QT interval-prolonging medication; RCT: randomized control trial.

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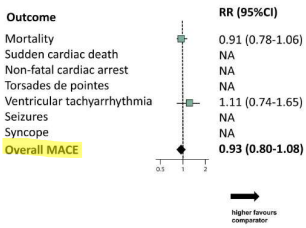


Fig 3. Pooled events for MACE for Haloperidol versus control.
MACE: Major adverse cardiac events; RR: Risk ratio; CI: Confidence interval.

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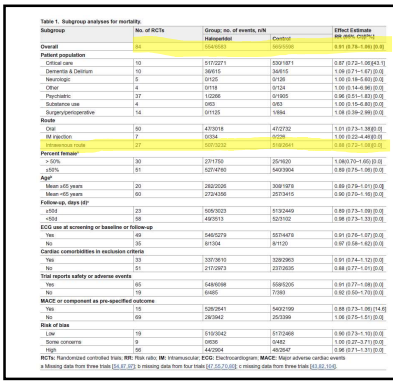


Table 1. Subgroup analyses for mortality.

Subgroup	No. of RCTs	Group; no. of events, n/N		Effect Estimate
		Haloperidol	Control	RR (95% CI)[a] (%)
Overall	84	1044/6663	969/5590	0.91 (0.78–1.06) [0.0]
Patient population				
Critical care	10	517/2271	330/1871	0.87 (0.73–1.06)[43.1]
Dementia & Delirium	10	366/615	348/615	1.09 (0.71–1.67) [0.0]
Neurologic	5	0/125	0/126	1.00 (0.18–5.60) [0.0]
Other	4	0/118	0/124	1.00 (0.14–6.96) [0.0]
Psychiatric	37	1/2266	0/1905	0.96 (0.51–1.83) [0.0]
Substance use	4	0/63	0/63	1.00 (0.15–6.83) [0.0]
Surgery/perioperative	14	0/1125	1/894	1.08 (0.39–2.99) [0.0]
Route				
Oral	50	437/3018	417/2732	1.01 (0.73–1.38)[0.0]
IM injection	7	0/334	0/339	1.00 (0.22–4.49)[0.0]
Intravenous route	27	507/3232	518/2641	0.88 (0.72–1.08)[0.0]
Percent female[c]				
> 50%	30	237/1750	25*/620	1.08(0.70–1.66) [0.0]
≤50%	51	527/4740	540*/3904	0.89 (0.75–1.06) [0.0]
Age[d]				
Mean ≥65 years	20	282/2026	309*/1878	0.88 (0.73–1.01) [0.0]
Mean <65 years	60	272/4356	257/3415	0.96 (0.73–1.16) [0.0]
Follow-up, days (d)[e]				
≤504	23	505/3023	513/2449	0.89 (0.73–1.09) [0.0]
>504	58	49/3513	52/3102	0.96 (0.73–1.33) [0.0]
ECG use at screening or baseline or follow-up				
Yes	49	546/5279	557/4478	0.91 (0.76–1.07) [0.0]
No	35	8/1304	8/1120	0.97 (0.58–1.62) [0.0]
Cardiac comorbidities in exclusion criteria				
Yes	33	337/3810	329/2963	0.91 (0.74–1.12) [0.0]
No	51	217/2973	237/2635	0.88 (0.77–1.01) [0.0]
Trial reports safety or adverse events				
Yes	65	548/6098	559/5205	0.91 (0.77–1.08) [0.0]
No	19	6/485	7/393	0.92 (0.50–1.70) [0.0]
MACE or component as pre-specified outcome				
Yes	15	526/2641	540/2199	0.88 (0.73–1.06) [14.6]
No	69	28/3942	25/3399	1.06 (0.75–1.51) [0.0]
Risk of bias				
Low	19	518/3042	517/2468	0.96 (0.73–1.10) [0.0]
Some concerns	9	0/636	0/482	1.00 (0.27–3.71) [0.0]
High	56	44/2984	45/2947	0.96 (0.71–1.31) [0.0]

RCTs: Randomized controlled trials; **RR:** Risk ratio; **IM:** Intramuscular; **ECG:** Electrocardiogram; **MACE:** Major adverse cardiac events
a Missing data from three trials [54,87,97] b missing data from four trials [67,69,70,88] c missing data from three trials [83,92,104].

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Conclusion

"Our systematic review found that haloperidol, although listed as a known QTP- Med, did not increase the rate of MACE including mortality. This suggests an opportunity to modify QTP-related alerts for haloperidol"

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Conclusions for our team

- IV/SC haloperidol continues to be best for delirium (mixed or agitated)
- Do not use homeopathic doses: 2mg q 6 h po/ IV regular, and dose reduction once RASS episodes stable
- Ask patient's family/ bedside RN for some time before jumping to palliative sedation (lorazepam et al)

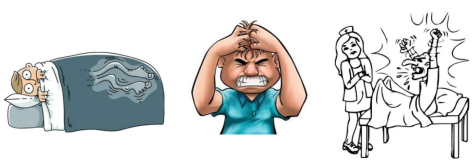
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Should every cancer patient with delirium be on regular haloperidol?

- **Hyperactive and mixed YES**
- In cancer 80 % are MIXED
- In PURE hypo no evidence, prn needed in case of change to mixed

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How about agitation…



RASS +1 Restless | **RASS +2 Agitated** | **RASS +3 Aggressive**

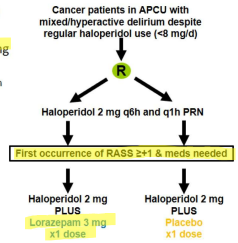
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Haloperidol ± Lorazepam

Palliative Care, Persistent Agitation

- Double-blind, randomized controlled trial
- Single dose instead of repeated dosing
  - Short survival (i.e. hours to days)
  - Uncertain risks associated with lorazepam in a frail population
- Study outcomes:
  - Richmond Agitation Sedation Scale (1°)
  - Use any additional psychotropic agents
  - Perceived patient comfort
  - MDAS, ESAS, DEQ
  - Communication capacity
  - Adverse effects
  - Discharge outcomes, survival



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Haloperidol ± Lorazepam

Richmond Agitation Sedation Scale (RASS)

Score	Description	Criteria
+4	Combative	Overly violent, danger to staff
+3	Very agitated	Pulls on lines/tubes or aggressive
+2	Agitated	Frequent non-purposeful movements
+1	Restless	Anxious but not aggressive, apprehensive appearing
0	Alert and calm	
-1	Drowsy	Response to voice with ≥10 seconds of eye contact
-2	Light sedation	Response to voice with <10 seconds of eye contact
-3	Moderate sedation	Response to voice but no eye contact to voice
-4	Deep sedation	No response to voice but response to physical stimulus
-5	Unarousable	No response to voice or physical stimulus

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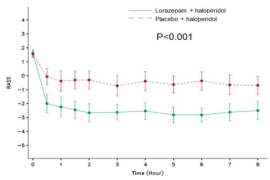
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Haloperidol ± Lorazepam

Palliative Care, Persistent Agitation

- Lorazepam/haloperidol was associated with a significantly greater reduction of RASS compared to placebo
  - 0-30 min: mean Δ -2.0, 95% CI -2.9, -1.1, P<0.001
  - 0-8 h: mean Δ -1.9, 95% CI -2.8, -0.9, P<0.001



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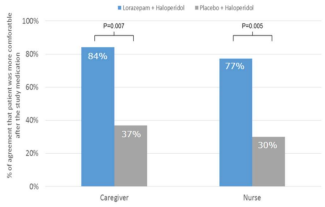
Hui et al. *JAMA* 2017

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Haloperidol ± Lorazepam

Palliative Care, Persistent Agitation

Patients on lorazepam/haloperidol arm were perceived to be more comfortable after the study medication by *blinded* caregivers and nurses



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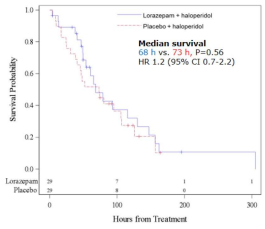
Hui et al. *JAMA* 2017

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Haloperidol ± Lorazepam

Palliative Care, Persistent Agitation

- No significant difference in
  - Delirium recall
  - Communication capacity
  - Adverse effects
  - Discharge outcomes
  - Overall survival



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Escalation, combination, rotation

- Escalation > haloperidol
- Rotation : from haloperidol to chlorpromazine
- Combination : haloperidol + chlorpromazine

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Escalation, Rotation, Combination

Palliative Care, Persistent Agitation

Variables	Escalation Group (N=15)		Rotation Group (N=16)		Combination Group (N=14)		
	N	Mean (95% CI)	N	Mean (95% CI)	N	Mean (95% CI)	P-value
Perceived agitation level							
Patient less agitated as assessed by caregiver, Agree or strongly agree (%)	13	9 (69)	14	10 (71)	10	60 (60)	0·82
Patient less agitated as assessed by nurse, Agree or strongly agree (%)	14	8 (57)	12	8 (67)	11	7 (64)	0·91
Perceived comfort level							
Patient more comfortable as assessed by caregiver, Agree or strongly agree (%)	13	8 (62)	14	10 (71)	10	6 (60)	0·83
Patient more comfortable as assessed by nurse, Agree or strongly agree (%)	14	9 (64)	12	9 (75)	11	7 (64)	0·82

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Hui et al. *Lancet Oncol* 2020

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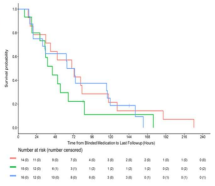
Escalation, Rotation, Combination

Palliative Care, Persistent Agitation

- No neuroleptic adverse effects detected
- Change in systolic blood pressure (95% CI)
  - Escalation: 5·1 mmHg (-7·1, 17·3 mmHg)
  - Rotation: -19·3 mmHg (-33·8, -4·8 mmHg)
  - Combination: -12·6 mmHg (-23·7, -1·4 mmHg)

  P=0.01
- Median overall survival (95% CI)
  - Escalation: 44 h (18, 65 h)
  - Rotation: 68 h (19, 116 h)
  - Combination: 71 h (19, 117 h)

  P=0·47



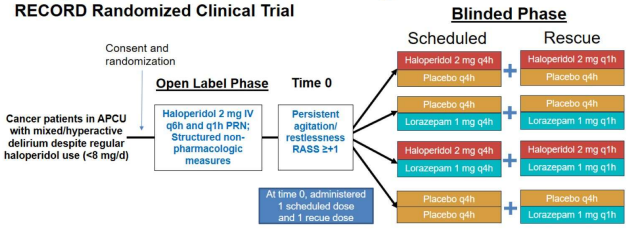
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Hui et al. *Lancet Oncol* 2020

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Proportional Sedation for Agitated Delirium

RECORD Randomized Clinical Trial



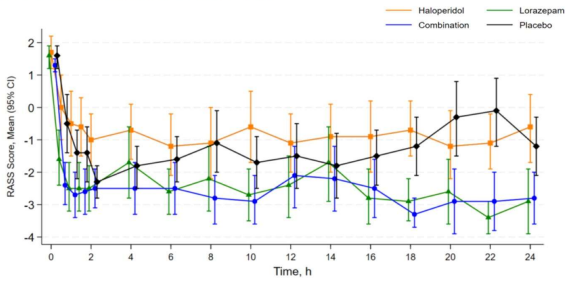
Design: double-blind, randomized trial (MDACC, VCU, NTU)
Primary outcome: RASS at 24 h
Secondary outcomes: rescue medication use, perceived patient comfort, adverse events

Hui et al. *JAMA Oncol* 2025

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Proportional Sedation for Agitated Delirium

RECORD Randomized Clinical Trial

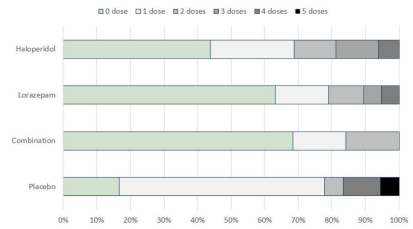


Hui et al. *JAMA Oncol* 2025

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Proportional Sedation for Agitated Delirium

RECORD Randomized Clinical Trial



P=0.006

Hui et al. *JAMA Oncol* 2025

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Proportional Sedation for Agitated Delirium

RECORD Randomized Clinical Trial

- The data support a proactive instead of reactive pharmacologic approach for patients with persistent agitated delirium
- Three potential options to personalize care
  - Haloperidol alone—light
  - Lorazepam alone—moderate
  - Haloperidol + lorazepam—heavy

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A few drugs we are using more often

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Suzetrigine(journavx)

- Selective Na channel blocker in pain sensory nerves
- Only peripheral effects (no CNS)
- FDA approved < 14 days (acute pain smes)
- 2 RCTS in chronic diabetic neuropathy: similar to gabapentin 100 q 8 !! Could not even beat it at that dose.
- 3A4 substrate
-

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Suzetrigine conclusions

- Mild analgesic effect
- Acute pain: biopsy, ostomy, acute Musculo/ skeletal
- About 1 week
- 3A4 metabolism

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Methadone as adjuvant

- Reduce dose escalation/ OIN?
- Potentiate analgesia?
- Prevent hyperalgesia?
- Much easier than rotation

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Methadone adjuvant

- > 50 MEDD: 5 mg q 12h
- < 50 MEDD: 2.5 mg q 12 h
- Give regularly (not prn)
- Escalate in 3-5 days according to pain
- After several titrations the other opioid can be d/c or kept only prn

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Buprenorphine in pall care

- Only the patch q 7 days
- Opioid naïve pts
- Mild first line opioid (similar to tramadol, hydrocodone 5, codeine 30)
- BTP can be any agonist
- 3A4 to norbuprenorphine
- Expensive but getting better at insurance denials

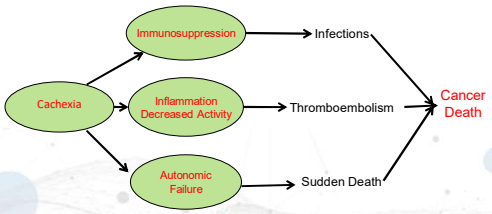
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Oxybutynin (Ditropan)

- Hot flashes in women and men
- Hyperactive bladder
- 2.5- 5 mg qhs/ bid
- Urinary retention (men), CNS penetration and delirium/ sedation, constipation, dry mouth
- 3A4 metabolism
- Works faster than venlafaxine but it is best to start both and then stop the Ditropan after 2 weeks

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Cancer Cachexia – Poor Prognosis



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Cachexia management : a moving target

- Anorexia
- Chronic nausea/ gastroparesis (autonomic failure)
- Body composition
- Functional outcomes
- Quality of life
- Body image distress
- Psychosocial distress
- Treatment response
- Disease free survival
- Overall survival (second primaries, comorbidities)

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The context of cachexia changes everything!

- **Survivor** (after treatment completion)
- **Primary treatment**
- **Advanced cancer on active treatment**
- **Palliative care**

- **Discuss disease status : oncology team + patient + family**

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Survivor

- Lower BMI/ weight reduces recurrence and second primaries
- GLP-1 are here to stay (sarcopenia risk)
- Physical activity reduces recurrence and second primaries
- Nutritional management of co-morbidities (diabetes, cardiovascular)
- Integrative motivational interventions: " I am healthy", " I am fit"

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Primary cancer treatment

- Prehabilitation (surgery, SCT, Car-T)
- Check testosterone/ vitamin D
- Nutritional support (**microbiota**)
- Pharmacological
- Physical activity

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Advanced cancer – active treatment

- Nutritional support
- Check testosterone/ vitamin D
- Gastroparesis (metoclopramide), constipation (laxatives, microbiome prebiotics)
- Olanzapine/ mirtazapine?
- Physical activity
- Body image (objective and subjective support)
- G- tube for dysphagia

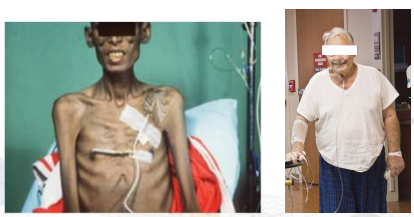
85

Palliative care

- High energy/ protein diet
- Restore testosterone/ vitamin D
- Olanzapine/ mirtazapine ?
- Corticosteroids
- Metoclopramide/ laxatives
- Body image support
- Physical activity
- Goal concordant care : G-tube, ostomies?

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Cachexia management needs context



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Anorexia - Definition

- Loss of appetite
- Present in multiple diseases
  - Cancer
  - COPD “pulmonary cachexia syndrome”
  - Renal Failure
  - Heart Failure
- Increased hospitalization & mortality
- Poor Quality of life
- Assessment Tools
  - (FAACT & FAACT-A/CS-12)

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Appetite Regulation

- Positive
  - Glucocorticoids
  - Dopamine
  - Ghrelin
    - Anamorelin –ghrelin receptor agonist
  - Orexin A and B
  - Endocannabinoids
    - Dronabinol – synthetic THC CB 1&2
    - Nabilone – CB 1
  - Neuropeptide Y
- Negative
  - Pro-opioimelanocortin (POMC)
    - α + β melanocyte-stimulating hormone
    - Adrenocorticotropic hormone (ACTH)
    - B Endorphins
  - α melanocyte-stimulating hormone
    - Cleaved from POMC
    - Binds MC4R to inhibit hunger
    - Drugs in development
  - Serotonin
  - Leptin
  - Tumor necrosis factor alpha
  - Thyrotropin-releasing hormone
  - Growth Differentiating Factor 15
    - Ab GDF 15 Ponsegromab - Phase III Cancer Cachexia

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Prospective Survey – Patients Supportive Care Center MDACC

Dev R, Bramati P, Delgado Guay MO, et al JCSM Communications 2025

Patient Characteristics N=100	No Anorexia n=47	Anorexia n=53	P-value	<10% Weight Loss n=39	≥10% Weight Loss n=60	P-value	<5% Weight Loss/6 Months n=50	≥5% Weight Loss/6 Months n=49	P-value
HADS Anxiety (mean (SD))	3.2 (3.2)	4.4 (3.2)	0.04	4.5 (3.8)	3.4 (2.7)	0.29	3.9 (3.6)	3.7 (2.8)	0.93
HADS Depression	3.5 (2.6)	5.9 (3.8)	0.001	5.1 (4.1)	4.6 (3.1)	0.95	5.1 (3.7)	4.4 (3.3)	0.37
PG-SGA SF	4.6 (3.3)	9.3 (4.0)	<0.001	5.6 (4/2)	8.0 (4.3)	0.005	6.0 (4.2)	8.1 (4.4)	0.01
BIS	4.9 (5.3)	7.2 (6.0)	0.03	6.3 (6.1)	6.1 (5.6)	0.99	6.7 (5.8)	5.5 (5.6)	0.36
ESAS (Total Score 0-100)	17.1 (10.8)	31.1 (12.4)	<0.001	24.0 (14.0)	24.6 (13.3)	0.82	23.0 (14.2)	25.7 (12.7)	0.32
Pain	1.2 (2.0)	1.3 (2.2)	0.91	1.2 (1.7)	1.3 (2.3)	0.80	1.3 (2.1)	1.2 (2.1)	0.57
Fatigue	1.7 (2.2)	2.1 (2.6)	0.55	1.9 (2.6)	1.9 (2.4)	0.85	1.9 (2.3)	1.9 (2.6)	0.80
Nausea	0.0 (0.2)	0.3 (1.1)	0.20	0.20 (1.0)	0.13 (0.7)	0.96	0.2 (0.9)	0.2 (0.8)	0.61
Depression	1.0 (1.7)	1.4 (1.9)	0.32	1.1 (1.9)	1.3 (1.8)	0.57	1.2 (2.0)	1.2 (1.7)	0.67
Anxiety	2.2 (2.4)	2.1 (2.3)	0.98	1.9 (2.1)	2.3 (2.5)	0.55	2.0 (2.1)	2.4 (2.5)	0.56
Drowsiness	1.1 (2.1)	0.7 (1.3)	0.26	0.6 (1.2)	1.1 (2.0)	0.35	0.5 (1.3)	1.3 (2.1)	0.07
Shortness of Breath	0.0 (0.2)	0.4 (1.6)	0.35	0.2 (1.0)	0.2 (1.3)	0.57	0.0 (0.3)	0.4 (1.7)	0.26
Sleep	2.9 (2.6)	2.4 (2.4)	0.40	2.9 (2.6)	2.6 (2.5)	0.53	3.0 (2.6)	2.4 (2.4)	0.20
Appetite	0.6 (1.5)	1.4 (2.0)	0.02	0.8 (1.7)	1.2 (1.9)	0.33	1.1 (1.8)	1.0 (1.8)	0.60
Feeling of Wellbeing	2.2 (2.1)	2.0 (2.1)	0.70	2.0 (1.8)	2.2 (2.2)	0.99	2.2 (2.1)	2.1 (2.0)	0.80

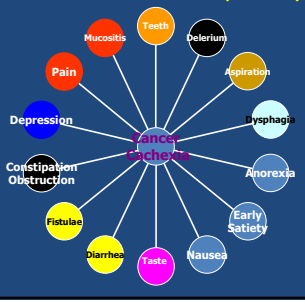
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Anorexia – medications to reduce

- Amphetamines
- Antibiotics
- Chemotherapy
- Digoxin
- Anti-depressants
- Opioids
- Anti-histamines

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Assessment - **Secondary Cachexia**
Checklist: Nutritional Impact Symptoms



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Microbiome and cancer cachexia

- Dysbiosis: “leaky gut”- bacterial LPS into blood- increased IL6/ TNF/ IL1b
- Dysbiosis: cytokine associated proteolysis and lipolysis
- Decreased lumen bacterial produnction of short chain fatty acids and BCAAs increase leaky gut + inflammation.
- **Prebiotics + fiber**. Problem : low nutrient density in severe starvation/ cachexia.
- **Probiotics- engineered new**- Omega 3 FA.
- **Fecal transplant**
- **Minimize ATBs and PPIs!**

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Mirtazapine

- Double-blind placebo-controlled trial – *Hunter JPSM 2021*
- 120 incurable solid tumors with anorexia (≥4/10), cachexia (>5% or >2% +BMI<20)
- 15mg nightly mirtazapine over 8 weeks
- Primary endpoint day 28
- ***Appetite score – no change compared to placebo***
- Mirtazapine arm
  - ***Less depressive symptoms***
  - ***Increased somnolence***

- Arrieta O, et al. JAMA Oncol 2024
  - RCT – placebo controlled
  - Mirtazapine 15-30mg 8 weeks
  - ***No change Appetite Score***
  - Increase fat intake
    - Assessed by Energy Quantification Mexican system of nutritional equivalents
- Almeida OLS, et al. Cancers 2023
  - Mirtazapine (30mg) vs Megestrol (320mg)
  - ***Mirtazapine inferior to megestrol acetate but noted improvement in sub-analysis of women – improved appetite and weight gain***
- Chowdhury IH, et al. Jpn J Clin Oncol 2024
  - Mirtazapine (15mg) vs Megestrol (160mg) - 8-week duration
  - QOL and FACT-ACS
  - ***No statistical difference***

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Olanzapine

	D-2	Ach	H-1	α1-Adr	5-HT3
Olanzapine	+++	++	++	+	++

Antagonistic activity against multiple receptors:

Useful in management of nausea, delirium, anxiety, appetite

- atypical antipsychotic
- potent anti-nausea effects via blocking multiple neuronal receptors.
- 5-HT3 inhibitory effects with a longer half-life than ondansetron
- Antianxiety effects.
- Level 1 evidence:
  - **chemotherapy-related, advanced cancer-related nausea and appetite**

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Randomized Double-Blind Placebo-Controlled Study of Olanzapine for Chemotherapy-Related Anorexia in Patients With Locally Advanced or Metastatic Gastric, Hepatopancreaticobiliary, and Lung Cancer

Lakshmi Sandhya, JCO 2023

- RCT – 63 Olanzapine (2.5mg Qdaily for 12 weeks), 61 placebo
- Adult cancer patients, GI and lUNG malignancies
- >5% weight gain 60% vs 9% p<0.001
- VAS appetite improvement 43% vs 13% P=<0.001
- FAACT ACS scores ≥ 37 22% vs 4% p=0.004

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Management of Cancer Cachexia: ASCO Guideline

Eric J. Roeland, MD[1]; Kari Bohlke, ScD[2]; Vickie E. Baracos, PhD[3]; Eduardo Bruera, MD[4]; Egidio del Fabbro, MD[5]; Suzanne Dixon, MPH, MS, RD[6]; Marie Fallon, MD[7]; Jann Herndon, MD, DMSc[8]; Harold Lau, MD[9]; Mary Platek, PhD, MS, RD[10]; Hope S. Rugo, MD[11]; Hester H. Schnipper, LICSW, BCD, OSW-C[12]; Thomas J. Smith, MD[13]; Winston Tan, MD[14]; and Charles L. Loprinzi, MD[15]

TABLE 1. Summary of Recommendations for the Treatment of Cancer Cachexia in Patients With Advanced Cancer

Intervention	Strength of Recommendation	Strength of the Evidence	Benefits*	Harms*
Nutritional interventions				
Dietary counseling[25,26,37]	Moderate in favor	Low	Moderate	Low
Parenteral or enteral nutrition (routine use)[37,42]	Moderate against	Low	Low	Moderate to high
Omega-3 fatty acids[26,39,40]	No recommendation	Low	Low	Low
Vitamins, minerals, and other dietary supplements[38]	No recommendation	Low	Low	Low
Pharmacologic interventions				
Progesterone analogs[25,33,35,36,43]	Moderate in favor	Intermediate	Moderate	Moderate
Corticosteroids[43]	Moderate in favor	Intermediate	Moderate	Moderate
Anamorelin[25,32,58]	No recommendation (not commercially available)	Intermediate	Moderate	Low
Olanzapine[26]	No recommendation	Low	Moderate	Low
Androgens[25,43,59]	No recommendation	Low	Moderate	Low
Thalidomide[34,36]	No recommendation	Low	Low	Low
NSAIDs[26,44]	No recommendation	Low	Low	Low
Cyproheptadine[44]	No recommendation	Low	None	Low
Cannabinoids[36,45]	Weak against	Low	None	Low
Melatonin[25,43]	Weak against	Low	None	Low
TNF inhibitors[36,43]	Moderate against	Intermediate	None	Moderate
Hydrazine sulfate[43]	Strong against	Intermediate	None	Moderate
Other interventions				
Exercise[27]	No recommendation	Low	Unknown	Unknown

Abbreviations: NSAIDs, nonsteroidal anti-inflammatory drugs; TNF, tumor necrosis factor.
*Categorization of benefits and harms was based on use of the intervention for cancer cachexia in the populations that were enrolled in randomized controlled trials.

Olanzapine status update! 2023

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Growth Differentiating Factor-15 (**very frequent: 90%**!)

- GDF-15 as biomarker: state of the art - Kai Wollert, Germany
- **Distant member of the TGFβ cytokine superfamily**
- **Induced by cellular stress – and acts on GFRAL receptor in hindbrain area postrema (AP) and nucleus of the solitary tract (NTS)**
- **Elevated in many disease states including cancer, chronic cardiac and renal disease**
- **Increases with chronological age and disease burden (Deng Cell 2025; Liu Aging Cell 2024)**
- **Remains low in healthy centenarians (Vincent Maturitas 2018)**

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Highlights – monoclonal antibody targeting GDF-15

Efficacy and safety of ponsegromab in patients with cancer-associated cachexia: results from open-label extension of a randomized, placebo-controlled, phase 2 study. John Groarke, USA

- **1-year, open-label extension (Part B), Patients with Cancer Cachexia + GDF-15 >1500 pg/mL**
- **117 Patients (44% NSCLC, 29% Colorectal CA, 27% Pancreatic: 71% Stage 4)**
- **Increase weight : 2.74, 4.43, and 5.18 kg at weeks 24, 52, and 64, respectively**
- Weights gain lowest in placebo patients
- All cause (84.2%) and Treatment related AEs (4.4%) at weeks 12-72, respectively.

Efficacy and safety of ponsegromab in patients with pancreatic cancer, cachexia, and elevated growth differentiation factor: insights from the Phase 2 PROACC-1 trial (8-05)
John Groarke, USA

- **59 Patients with Pancreatic Cancer**
- 48% BMI<20 and 51% Cancer Cachexia (>10% prior 6 months)
- **At week 12: -0.36kg (placebo), +0.65kg (ponsegromab 100mg), +1.72kg (200mg), +3.37kg (400mg)**
- Generally, well tolerated
  - Nausea (8.9% vs 28.6% placebo)
  - Diarrhea (13.3% vs 21.4% placebo)

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Highlights – monoclonal antibody targeting GDF-15

- Growth differentiation factor 15 (GDF-15)
- GDF-15 targeted antibody – RCT 12-week, double-blind (phase 2) - SC 100, 200, 400mg ponsegromab
  - Improved body weight
  - Improved physical function
  - Improved muscle mass

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Other drugs are being developed against GDF-15

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Exercise Effects – Physical activity

Exercise

- Anti-inflammatory in healthy and cancer patients
- Increased muscle synthesis
- Increased insulin sensitivity (decreased break down!)
- Increased vascularization and oxygenation of the tumor

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Exercise Program – Ideal?

Exercise

- Large Muscle Groups
- Seated if necessary. Standing if safe
- With resistance bands
- Interval Training
- 30 min each day. May be broken into 3x10 min bouts
- **Resistance versus Aerobic? Both!!**
- Adherence issues
  - Script for exercise?
  - Motivational interviewing?
  - Social/Group Interventions?

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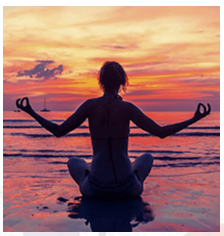
Nonpharmacological-interventions

- **Compassionate communication**
  - Reframe "starving to death" to the more complex one of irreversible (usually) metabolic abnormalities.
  - Body image distress : weight loss main predictor!
  - **Tertiary cachexia**: patient + caregiver interventions (dyadic)
- **Nutritional counseling**
  - Remove dietary restrictions
  - Small and frequent meals (limited data)
  - 25 to 30 calories/kg per day 1.5 to 2.0 g of protein/kg per day
- **Exercise**: aerobics and resistance training

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Psychological Interventions

- *Interventions focusing on functional & sensory awareness – **PT, yoga, or dance therapy** can help people reconnect with their bodies, turn **focus to capabilities over judgement***
- ***Acceptance & Commitment Therapy** (ACT) to promote acceptance of uncomfortable emotions tied to bodily changes*
- ***Mindfulness** to foster gentle awareness*
- ***Journaling** and activities to reconnect with purpose*
- *Support existential growth through **self-compassion exercises***
- ***Couples counseling** to address **intimacy, role changes***
- ***Group programs :" I am healthy" / "I am fit"***



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Management of Anorexia-Cachexia

Single modality/agent unlikely to be successful

Multi-modal recommended and undergoing investigation

- Treat causes of secondary cachexia
- Appetite stimulants for some patients
- Appropriate nutrition
- Identify and treat deficiencies
  - Testosterone , Thyroid, Vitamin D, B-vitamins and other micrornutrients
- Empiric treatment with multivitamin and omega-3 fish oil
- Exercise
- Anti-catabolic/Anti-metabolic agents/*Anabolic agents*

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The Other Side of the Opioid Crisis – Opiophobia

When did we start using the term "Opioid Crisis"?

FIRST WAVE – Increased opioid prescription

Mid-1990s when Purdue Pharma promoted OxyContin, which had received approval. FDA: " reduced abuse liability".

Initial wave of fatalities associated with the legal prescription opioid usage.

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The Other Side of the Opioid Crisis - Opiophobia

Subsequent waves of opioid crisis

SECOND WAVE – Heroin

Began around 2010, resurgent of heroin markets driven by the increasing demand from individuals addicted to prescription opioids.

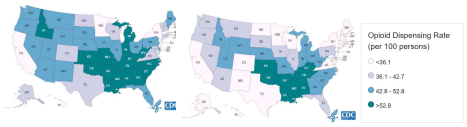
THIRD WAVE – Synthetic opioids

Began around 2013, escalating addiction and fatal overdoses were connected to synthetic opioids, specifically substances like fentanyl, combined with Xylazine, Medetomidine, other tranquilizers that reduce naloxone response

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State opioid dispensing rates comparison (2019 vs 2022)



Centers for Disease Control and Prevention, National Center for Injury Prevention and Control [109]

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Opiophobia

Exaggerated concern about the risks preventing appropriate medical use of opioid analgesics

- **Vast majority of clinicians, patients, and caregivers**.

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Clinician opiophobia

- **Inadequate opioids-related medical knowledge**

-- **Fear of legal ramification: sanctions, prosecutions**

- **Logistical barriers: insurance prior-authorization, dispense quantity limit, ban on mail-in opioids, continuous denials by insurance etc.**

- **Excessive time demand including mandatory annual "training"**

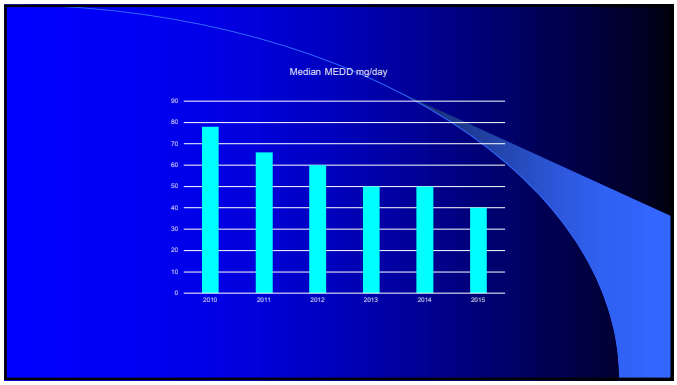
-

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The opioid epidemic has impact on the oncologist's prescription patterns
(Haider et al, J oncol practice 2017)

- Random sample of 750 consults for patients with advanced cancer at the supportive care center between 2010 and 2015

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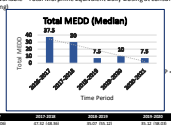
Further MEDD reduction 2016- 2021

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Trend in Total (median) MEDD

Primary Outcome variable – Total Morphine Equivalent Daily Dosing at consult (Long Acting + Short Acting)

2015 Total median MEDD = 40

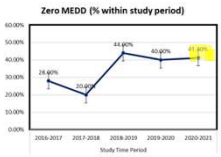


P <0.001

Total MEDD	2016-2017	2017-2018	2018-2019	2019-2020	2020-2021
Mean (SD)	79.55 (129.56)	57.52 (68.46)	26.07 (50.12)	35.42 (58.03)	
Median (IQR, 47%)	37.50 (0.00, 100.00)	30.00 (7.50, 105.00)	7.50 (0.00, 30.00)	10.00 (0.00, 45.00)	

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Trend for Zero MEDD



P=0.008

Multiple patients after 2019 prescribed opioids but were not taking at the time of consult due to fear of opioids

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Depiction of opioids on the TV



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Current " opioid sparing" (opiophobic) cocktails"

- **Gabapentinoids**: poor evidence, fatigue, sedation, addictive. Increased mortality with opioids
- **Carisoprodol/ methocarbamol**: no evidence, fatigue, sedation, weakness, addictive
- **THC**: hallucinations, hyperemesis, addictive
- **Benzodiazepines**: sedation, weakness, fatigue, addictive, increased mortality with opioids
- **High dose NSAIDS**: multiple side effects, especially in cancer pts

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AVOID Opiophobic cocktails

• High dose NSAIDS:	Renal- GI bleed
• Gabapentinoids:	Addictive, sedation, high mortality with opioids
• Carisoprodol/ methocarbamol:	Addictive, fatigue, sedation
• Cannabinoids:	Addictive, sedation, delirium, toxic with opioids
• Benzos:	Addictive, sedation, high mortality with opioids
• Suzetrigine:	Mild, unknown chronic toxicity

Opiophobic cocktails are a major barrier to opioid initiation and titration.

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Managing patient opiophobia

1. Ask pain intensity associated with **physical/ social function**
2. Continuous nociception requires continuous (not prn) opioid
3. Use a non- opiophobic pharmacy, especially initially
4. **Include family** in the conversation (or give recording of the message)
5. Educate and ask for endorsement by referring clinicians

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Placebo

- Intervention not expected to have a therapeutic effect
- Usually a pill or injection
- Used in research but considered unethical in clinical care

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Placebo has clinical effects

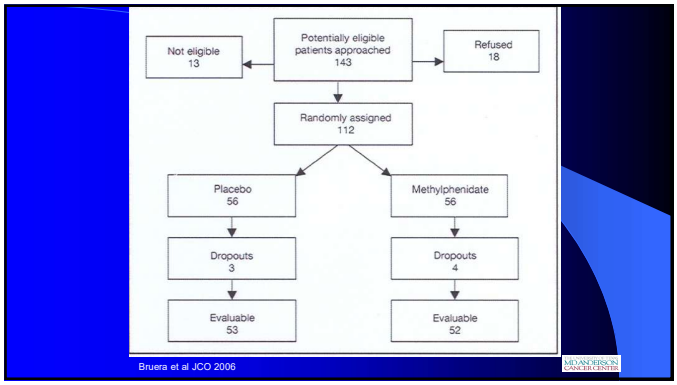
- Increases expectation of improvement
- Pre- frontal activity: understanding
- Limbic activity: positive affect
- Endorphin release

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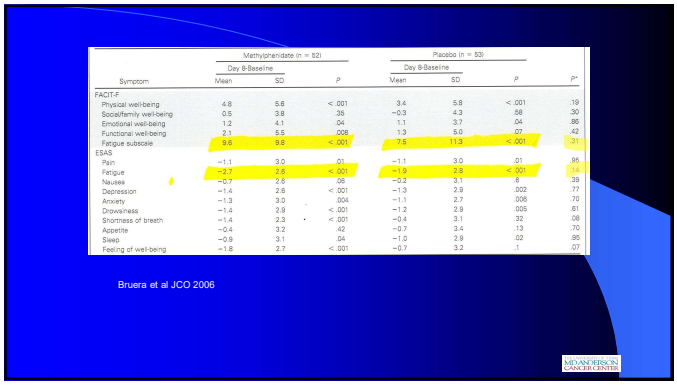
Can we create placebo effect in our palliative care encounters?

- Increasing expectation of relief increases placebo
- Placebo potentiates clinical interventions (opioid, laxative, hypnotic counseling, etc)
- Decreasing expectation of toxicity reduces nocebo
- **We conducted 52 placebo controlled RCTs**

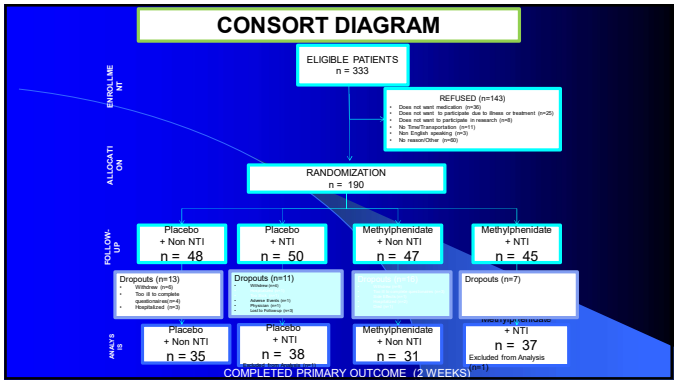
123


Not eligible
13
Potentially eligible patients approached
143
Refused
18
Randomly assigned
112
Placebo
56
Methylphenidate
56
Dropouts
3
Dropouts
4
Evaluable
53
Evaluable
52
Bruera et al JCO 2006
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Methylphenidate (n = 82)
Placebo (n = 53)
Day 8-Baseline
Symptom
Mean
SD
P
Mean
SD
P
P*
FACIT-F
Physical well-being 4.8 5.8 <.001 3.4 5.8 <.001 .19
Social/family well-being 0.5 3.8 .35 −0.3 4.3 .58 .30
Emotional well-being 1.2 4.1 .04 1.1 3.7 .04 .86
Functional well-being 2.1 5.5 .008 1.3 5.0 .07 .42
Fatigue subscale 8.6 9.8 <.001 7.5 11.3 <.001 .31
ESAS
Pain −1.1 3.0 .01 −1.1 3.0 .01 .95
Fatigue −2.7 2.6 <.001 −1.9 2.9 <.001 .16
Nausea −0.7 2.6 .06 −0.2 3.1 .6 .39
Depression −1.4 2.6 <.001 −1.3 2.9 .002 .77
Anxiety −1.3 3.0 .004 −1.1 2.7 .006 .70
Drowsiness −1.4 2.9 <.001 −1.2 2.9 .005 .61
Shortness of breath −1.4 2.3 <.001 −0.4 3.1 .32 .08
Appetite −0.4 3.2 .42 −0.7 3.4 .13 .70
Sleep −0.9 3.1 .04 −1.0 2.9 .02 .95
Feeling of well-being −1.8 2.7 <.001 −0.7 3.2 .1 .07
Bruera et al JCO 2006
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CONSORT DIAGRAM
ENROLLMENT
ELIGIBLE PATIENTS
n = 333
REFUSED (n=143)
Does not want medication (n=36)
Does not want to participate due to illness or treatment (n=25)
Does not want to participate in research (n=8)
No Time/Transportation (n=11)
Non English Speaking (n=3)
No reason/Other (n=60)
ALLOCATION
RANDOMIZATION
n = 190
FOLLOW-UP
Placebo + Non NTI n = 48
Placebo + NTI n = 50
Methylphenidate + Non NTI n = 47
Methylphenidate + NTI n = 45
Dropouts (n=13)
Withdrew (n=5)
Too ill to complete questionnaire(n=4)
Hospitalized (n=3)
Dropouts (n=11)
Withdrew (n=6)
Adverse Events (n=1)
Physician (n=1)
Lost to Follow-up (n=3)
Dropouts (n=7)
ANALYSIS
Placebo + Non NTI n = 35
Placebo + NTI n = 38
Methylphenidate + Non NTI n = 31
+ NTI n = 37
Excluded from Analysis
COMPLETED PRIMARY OUTCOME (2 WEEKS)

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FACIT-F and ESAS fatigue scores at baseline, Day 8 and Day 15 in the four subgroups

	FACIT-F (Fatigue Subscale)						ESAS Fatigue					
	Day 8-Baseline			Day 15-Baseline			Day 8-Baseline			Day 15-Baseline		
	N	Median (IQR)	P	N	Median (IQR)	P	N	Median (IQR)	P	N	Median (IQR)	P
Treatment			.87			.63			.86			.86
Methylphenidate	71	6.00 (0,16.00)		68	5.50 (-1.00, 11.00)		71	-2.00 (-3.00, 0)		66	-2.00 (-4.00, 0)	
Placebo	76	7.00 (0.50, 12.00)		73	6.00 (2.00, 11.00)		76	-2.00 (-3.00, 0		71	-2.00 (-5.00, 0)	
Nursing Intervention			.22			.27			.00			.14
NTI	78	6.50 (1.00, 15.58)		75	6.00 (0, 14.00)		79	-2.00 (-4.00, -1.00)		74	-2.50 (-5.00, 0)	
CTI	69	6.00 (-1.00,12.00)		66	5.50 (1.00, 10.00)		68	-1.00 (-2.50, 1.00)		63	-2.00 (-4.00, 0)	
ALL Groups			.19			.16			.02			.45
MP+ NTI	39	4.00 (0, 16.00)		37	4.00 (-2.00, 11.00)		40	-2.00(-3.00, -1.00)		37	-3.00 (-4.00, -1.00)	
MP+ CTI	32	6.50 (0.50, 16.00)		31	7.00 (2.00, 11.00)		31	-1.00 (-2.00, 0)		29	-1.00 (-3.00, 0)	
P+ NTI	39	10.00 (4.00, 15.00)		38	8.50 (3.00, 17.00)		39	-2.00 (-4.00, -1.00)		37	-2.00 (-5.00, 0)	
P +CTI	37	6.00 (-3.00, 10.00)		35	5.00 (0,6.00)		37	-1.00 (-3.00, 1.00)		34	-2.00 (-4.00, 0)	

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Open labeled Placebo for the treatment of Cancer related fatigue in Advanced cancer: A Randomized controlled Trial:

Sriram Yennurajalingam, Ahsan Azhar, Zhanni Lu, Clark Anderson, Ashley Rodriquez, Adrienne Archinega, Penny Stanton, Clark Anderson, Diana Urbauer, Eduardo Bruera

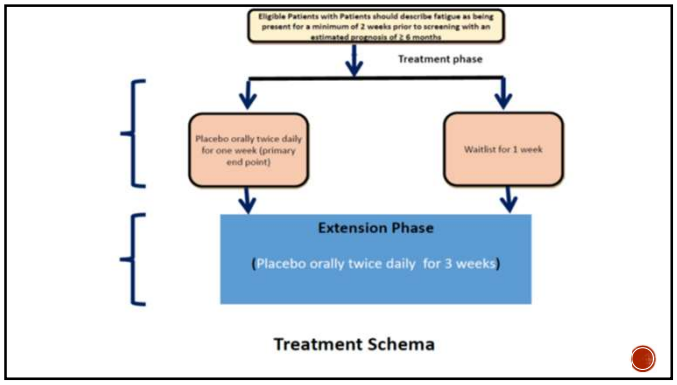
Oncologist. 2022 Dec 9;27

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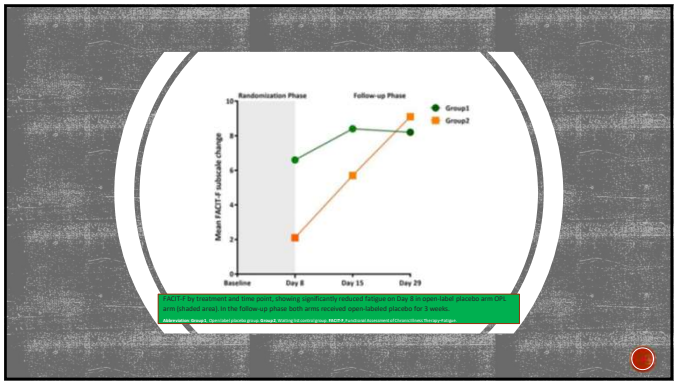
ELIGIBILITY

- Diagnosis of Advanced cancer
- Fatigue >/=4/10 on ESAS fatigue item
- Hb >/=8gm
- No uncontrolled pain

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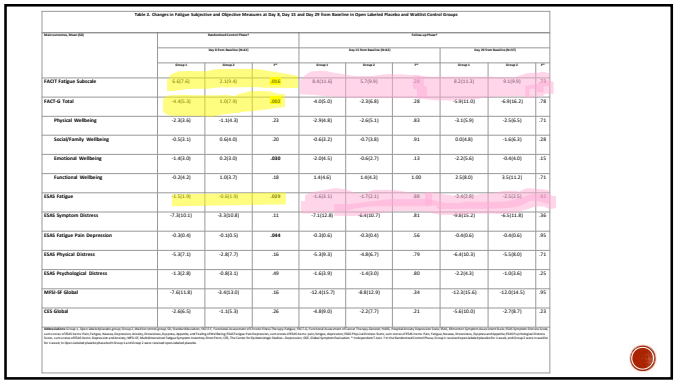


Table 2. Changes in Fatigue Subjective and Objective Measures at Day 8, Day 15 and Day 29 from Baseline in Open Labeled Placebo and Waitlist Control Groups

Outcomes Measures, Mean (SD)	Randomized Control Phase*			Follow-up Phase*					
	Day 8 from Baseline (Week)			Day 15 from Baseline (Week)			Day 29 from Baseline (Week)		
	Group 1	Group 2	p*	Group 1	Group 2	p*	Group 1	Group 2	p*
FACIT Fatigue Subscale	6.4(7.4)	2.1(9.4)	**.004**	8.4(11.6)	5.7(9.9)	.28	8.2(11.3)	9.1(9.9)	.73
FACT-G Total	-4.4(5.3)	1.0(7.9)	**.002**	-4.0(5.0)	-2.3(6.8)	.28	-1.9(11.0)	-6.9(16.2)	.78
Physical Wellbeing	-2.3(3.6)	-1.1(4.3)	.33	-2.9(4.8)	-2.6(5.1)	.83	-3.1(5.9)	-2.5(6.5)	.71
Social/Family Wellbeing	-0.5(3.1)	0.6(4.0)	.20	-0.6(3.2)	-0.7(3.8)	.91	0.0(4.8)	-1.6(6.3)	.28
Emotional Wellbeing	-1.4(3.0)	0.2(3.0)	**.030**	-2.0(4.5)	-0.6(2.7)	.13	-2.2(5.6)	-0.4(4.0)	.15
Functional Wellbeing	-0.2(4.2)	1.0(3.7)	.18	1.4(4.6)	1.4(4.3)	1.00	2.5(8.0)	3.1(11.2)	.71
ESAS Fatigue	-1.5(1.9)	-0.4(1.9)	**.029**	-1.4(0.1)	-1.7(0.1)	.88	-3.4(2.8)	-2.5(2.5)	.32
ESAS Symptom Distress	-7.3(10.1)	-3.3(10.8)	.11	-7.1(12.8)	-6.4(10.7)	.81	-9.8(15.2)	-6.1(11.8)	.36
ESAS Fatigue Pain Depression	-0.3(0.4)	-0.1(0.5)	**.044**	-0.3(0.6)	-0.3(0.4)	.56	-0.4(0.6)	-0.4(0.6)	.95
ESAS Physical Distress	-5.3(7.1)	-2.8(7.7)	.16	-5.3(9.3)	-4.8(6.7)	.79	-6.4(10.3)	-5.5(8.0)	.71
ESAS Psychological Distress	-1.3(2.8)	-0.8(3.1)	.49	-1.6(3.9)	-1.4(3.0)	.80	-2.2(4.3)	-1.0(3.6)	.25
MFSI-SF Global	-7.4(11.8)	-3.4(13.0)	.16	-12.4(15.7)	-8.8(12.9)	.34	-12.3(15.6)	-12.0(14.5)	.95
CES Global	-2.6(6.5)	-1.1(5.3)	.26	-4.8(9.0)	-2.2(7.7)	.21	-5.4(10.0)	-2.7(8.7)	.23

Abbreviations: Group 1, Open-label placebo group; Group 2, Waitlist control group; FACIT, Functional Assessment of Chronic Illness Therapy-Fatigue; FACT-G, Functional Assessment of Cancer Therapy-General; FSMC, Fatigue Symptom Inventory; Multi, Multidimensional Fatigue Inventory; ESAS, Edmonton Symptom Assessment System; MFSI-SF, Multidimensional Fatigue Symptom Inventory-Short Form; CES, The Center for Epidemiologic Studies - Depression; IDD, Global Symptom Evaluation. *Independent T test. †In the Randomized Control Phase, Groups 1 received open-labeled placebo for 1 week, and Group 2 were treated with the 1 week; ‡ Open-labeled placebo placebo/Waitlist control group 2 were received open-labeled placebo.

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OPEN LABEL PLACEBO

- What is the mechanism for open placebo improvement?
- Subjective studies always need a placebo arm
- How can we use placebo in the clinical setting?

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How can we increase expectation of improvement?

1. Communicate (phone the patient)
2. Prepare and give a prompt- sheet
3. Sit when you visit the patient
4. Always examine the patient
5. Offer audio recording of the visit or recommendations
6. Ask how the patient prefers to make decisions
7. Play some music
8. Avoid EHR during encounter.
9. No waiting room, smiling clerk, no exam room, pink light, sign on the ceiling, wellcome pets and weddings

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How can we increase expectation of improvement?

1. Communicate (phone the patient) - Prospective open
2. Prepare and give a prompt- sheet - RCT
3. Sit when you visit the patient - RCT
4. Always examine the patient - Prospective open
5. Offer audio recording of the visit or recommendations - RCT
6. Ask how the patient prefers to make decisions – Prospective open
7. Play some music - Prospective open
8. Avoid EHR during the encounter- RCT
9. No waiting room, no EPIC computer use, pink lighting, signs on the ceiling, introducing counselor, opioid and constipation education: current research

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Thank You!

Please complete your evaluation.

McGill

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