

SYMPTOM MANAGEMENT IN PALLIATIVE CARE

Schwartz Senior Symposium
Southington, CT
April 6th, 2017

Presented by: Rab Razzak, MD- Director, Outpatient Palliative Medicine, Hopkins Medicine

OBJECTIVES

- ▶ List key concepts to treat nausea and vomiting.
- ▶ Discuss the use of non-pharmacological therapy to treat pain, anxiety, and dyspnea.
- ▶ Choose appropriate treatment or therapy based on a patient's symptoms and clinical presentation.

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- ▶ NO CONFLICT OF INTERESTS
- ▶ THIS PRESENTATION WILL INCLUDE USE OF SOME OFF-LABEL APPLICATION OF MEDICATIONS

DISCLOSURES

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What are the most common symptoms in advance illnesses?

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SYMPTOMS IN ADVANCED ILLNESSES

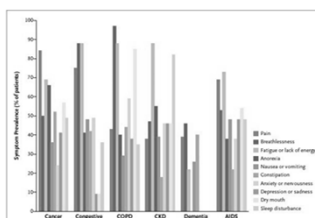


Figure 1. Symptom Prevalence in Advanced Illness.
Data are from representative studies of symptom prevalence among patients with cancer,^{1,2} congestive heart failure,^{3,4} chronic obstructive pulmonary disease (COPD),^{5,6} chronic kidney disease (CKD),^{7,8} or dementia^{9,10} and among patients who received highly active antiretroviral therapy for the acquired immunodeficiency syndrome (AIDS).¹¹ Self-reported data regarding some symptoms were unavailable for patients with dementia.

N Engl J Med 2015;373:747-55

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NON-OPIATES FOR PAIN

- ▶ Acetaminophen
- ▶ NSAIDs
- ▶ Steroids
- ▶ Bisphosphonates
- ▶ Gabapentin/ Pregabalin
- ▶ SNRI / TCAs
- ▶ Nerve blocks
- ▶ XRT

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PEGFILGRASTIM INDUCED BONE PAIN

- ▶ 510 pts U Rochester- Breast CA/Lung CA
- ▶ Naproxen 500 mg po bid vs placebo D1-8
- ▶ Naproxen reduced pain from 3.4/10 to 2.5/10
- ▶ Loratadine 10 mg daily -ppx
- ▶ Histamine release and IL-6/8 is probably involved in the inflammatory process for pegfilgrastim induced bone pain

Severe pegfilgrastim-induced bone pain completely alleviated with loratadine: A case report. J Clin Pharm Pract Med. 2014. J Clin Oncol 2012 Jun 13;30(18):1974-9

CIPN

- ▶ Chemotherapy induced peripheral neuropathy (CIPN) in 40-70% of patients
- ▶ New dose limiting factor
- ▶ Persists long after treatment
- ▶ Can disable the patient

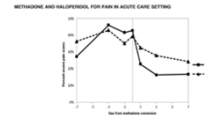
WHAT WORKS FOR CIPN?

- ▶ In RCTs, nortryptiline and amitryptiline do not work.
- ▶ In RCT, Glutamine supplements do not work. (Jacobson SD, J Supp Oncol 2003)
- ▶ In RCT, lamotrigine (Lamictal) does not work (Rao D, Cancer 2008)
- ▶ In RCT, gabapentin (Neurontin) does not work. (Rao D, Cancer 2007)
- ▶ Vitamin E does not work and increases mortality in large studies.
- ▶ In RCT, topical baclofen-amitryptiline-ketamine (BAK) gel works slightly, with NO harm. (Support Care Canc 2011)
- ▶ In RCT, duloxetine (Cymbalta) lowers pain by 1.0 point (CALGB 170601, Smith E, et al. JAMA 2012). "frequently reported adverse events were fatigue, insomnia, nausea, somnolence, and dizziness. Most of the events were moderate, with severe effects reported by 7% of patients."
- ▶ Not much to recommend.

Ames Soc Clin Onc Clinical Practice Guidelines. J Clin Oncol. 2014 Jun 20;32(18):1941-67.

METHADONE + HALDOL

- ▶ Methadone 2.5-15 mg/day + Haldol 1.5 mg/day (NMDA pathway activation, prevention of opioid hyperalgesia)
- ▶ Complete conversion to methadone and haloperidol was associated with a drop of median pain score from 5 to 0



J Palliat Med 2015 Feb;18(2):114-9

PPX BOWEL REGIMEN

"The hand that writes the opioid prescription writes the bowel regimen (or does the disimpaction)."



TURN THE TIDE

www.turnthetiderx.org



BREATHLESSNESS

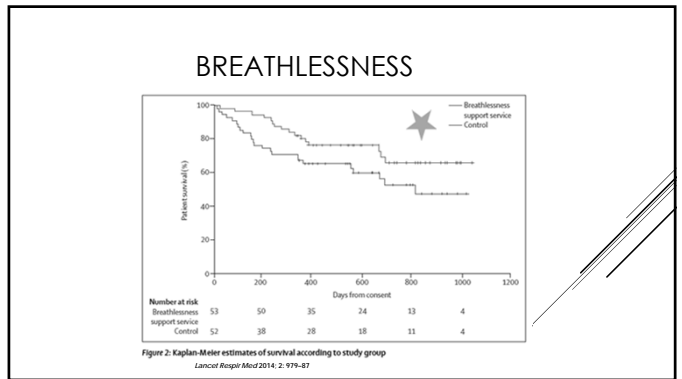
An integrated palliative and respiratory care service for patients with advanced disease and refractory breathlessness: a randomised controlled trial

Background: Breathlessness is a common and distressing symptom, which increases its mean duration as their prognosis and is difficult to manage. We assessed the effectiveness of early palliative care integrated with respiratory services for patients with advanced disease and refractory breathlessness.

Methods: In this single-blind randomised trial, we enrolled consecutive adults with refractory breathlessness and advanced disease from three teaching hospitals and six general practitioners in South London. We randomly allocated 112 patients to receive either a breathlessness support service or usual care. Breathlessness was compared centrally by the independent Clinical Trials Unit in a 1:1 ratio, by minimisation to balance for potential confounders: cancer versus non-cancer, breathlessness severity, presence of an informal caregiver, and ethnicity. The breathlessness support service was a short-term, single point of access service integrating palliative care, respiratory medicine, physiotherapy, and occupational therapy. Research interviews were conducted on a whole patient level in the treatment group. Our primary outcome was patient-reported breathlessness scores, a quality of life domain in the Clinical Respiratory Research Questionnaire, at 4 weeks. All analyses were by intention to treat. Survival was a safety endpoint. This trial is registered with ClinicalTrials.gov, number NCT19102094.

Findings: Between Oct 22, 2009 and Sept 28, 2013, 101 consenting patients were randomly assigned to the breathlessness support service and 12 to usual care. 81 of 101 (80%) patients completed the assessment at week 4. Median in the Lancet Respir Med 2014; 2: 979-87

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NAUSEA AND VOMITING

Gastric stasis-

- ▶ Gastric ca, hepatomegaly or ascites, paraneoplastic neuropathy
- ▶ Opioids, ondansetron
- ▶ Dyspepsia, gastritis, diabetic gastroparesis

Biochemical

- ▶ Hypercalcemia, liver mets, obstructive uropathy, bowel obstruction,
- ▶ Drugs/chemo, organ failure, infections

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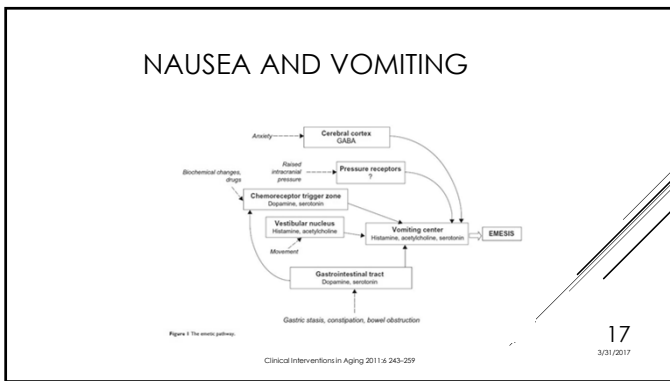
Clinical Interventions in Aging 2011;6:243-259

NAUSEA AND VOMITING

- ▶ Raised ICP- brain/meningeal mets/tumors
- ▶ Vestibular- mets, opioids, motion sickness
- ▶ Bowel dysmotility- bowel primary, secondaries, ascites, adhesions, constipation
- ▶ Other- anxiety

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Clinical Interventions in Aging 2011;6:243-259



NAUSEA AND VOMITING

Table 4: Receptor site affinities of commonly used antiemetics^{13,14,16}

Drug	Dopamine antagonist	Histamine antagonist	Acetylcholine (muscarinic) antagonist	Serotonin type 2 antagonist	Serotonin type 3 antagonist	Serotonin type 4 agonist
Chlorpromazine	█					
Cisapride			█			
Cyclizine		█				
Dopamine	█					
Haloperidol	█					
Hydroxyzine		█				
Lorazepam				█		
Metoclopramide	█					
Phenothiazines	█					
Ondansetron				█		
Prochlorperazine	█					
Promethazine	█					

Notes: Black, high affinity for receptor; dark grey, moderate affinity; light grey, low affinity; white, no known affinity.

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Clinical Interventions in Aging 2011;6:243-259

CHRONIC COUGH

Adults with refractory chronic cough (>8 weeks' duration) without active respiratory disease

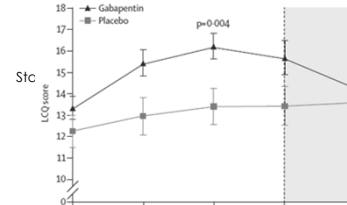
Randomly assigned to receive gabapentin (maximum tolerable daily dose of 1800 mg) or matching placebo for 10 weeks.

Primary: (Leicester cough questionnaire [LCQ] score) from baseline to 8 weeks of treatment

Leicester cough monitor, which consists of a recording device and an external free-field microphone

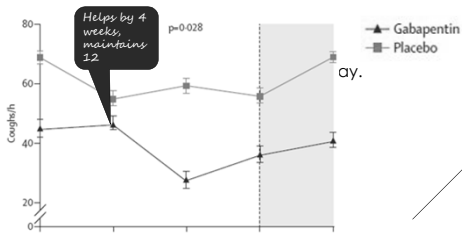
Lancet 2012; 380: 1983-89

CHRONIC COUGH



Ryan NM, Briting SS, Gibson PG. Gabapentin for refractory chronic cough: a randomised, double blind, placebo-controlled trial. Lancet. 2012 Nov;380(9833):1983-9.

CHRONIC COUGH

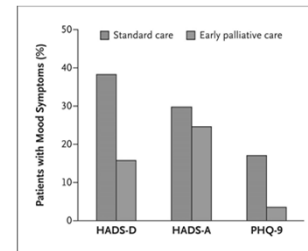


Helps by 4 weeks, maintains 3.2

p=0.028

Lancet. 2012 Nov 3;380(9833):1983-9.

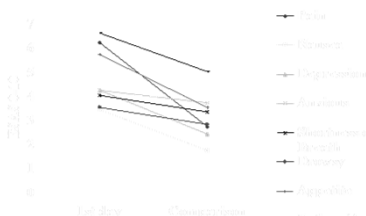
PC ON SYMPTOMS



N Engl J Med 2010;363:733-42

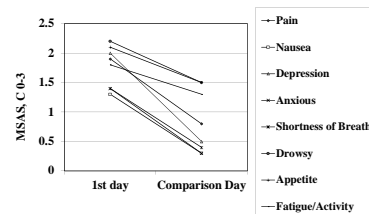
NEW ENGLAND JOURNAL OF MEDICINE

PC ON SYMPTOMS



J Clin Oncol 2004; 22:2088-2014

PC on Symptoms



Hatcherreson J, et al. Oncology, September 2005

PC ON SYMPTOMS

258 Journal of Pain and Symptom Management Vol. 50 No. 6 December 2015

Original Article

Interdisciplinary Palliative Care for Patients With Lung Cancer

Betsy Ferrell, PhD, FAAN, Virginia Sun, RN, PhD, Arif Hattar, MD, Mhaelita Cristea, MD, Dan J. Rao, MD, Jae Y. Kim, MD, Karen Reckamp, MD, Anna Carly Williams, RN, MSN, PHN, Tami Borneman, RN, MSN, CNS, Coeur Usman, PhD, and Mariana Kopyeva, MD
Division of Nursing Research and Education (B.F., V.S., A.C.H., T.B.), Department of Population Sciences, Department of Medical Oncology and Hematology Research (A.H., M.C., K.R., M.K.), Division of Thoracic Surgery (D.J.R., J.Y.K.), Department of Surgery, City of Hope, Duarte, California, and Vial Research, LLC (G.U.), Los Angeles, California, USA

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J Pain Symptom Manage 2015;50:758-767

PC ON SYMPTOMS

FACT-Sp-12: 12-Item Functional Assessment of Chronic Illness Therapy-Spirituality subscale

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J Pain Symptom Manage 2015;50:758-767

PC ON SYMPTOMS

FACT-L: Functional Assessment of Cancer Therapy - Lung Tool

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3/31/2017

J Pain Symptom Manage 2015;50:758-767

DEPRESSION

- ▶ Simply ask- Are you depressed?
- ▶ Remember: not a perfect test, but it is do-able.

**“Are You Depressed?”
Screening for Depression in the Terminally Ill**

Harvey Max Chochman, M.D., Kirk G. Wilson, Ph.D.,
Murray Teas, M.D., and Heidi Laskin, R.N.

Objective: This study compared the performance of four brief screening measures for depression in a group of terminally ill patients. The methods included a single-item screen, a six-item screen, a 10-item screen, and a 15-item screen. The results showed that the six-item screen was the most accurate and easiest to use. *Conclusion:* Brief screening measures for depression are important clinical tools for the terminal patient. For diagnostic purposes, however, they do not approach the validity of a single-item screen that asks, in effect, “Are you depressed?” (Chochman 1991; 1:547-549).

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DEPRESSION

200 outputs with CA and MDD
Usual care vs usual care vs intervention
RN led sessions- 7-10; 45 mins; SCL20

SMArT: RN led sessions

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Lancet 2008; 372: 40-48

DEMORALIZATION

Hopelessness and helplessness caused by a loss of purpose and meaning in life (with loss of anticipatory pleasure)

Single, isolated or jobless

poorly controlled physical sx

Present in 13-18% of time in progressive disease or cancer

Apathy (treat fatigue)

Medical illness (anemia, low cortisol, hypercalcemia, high IL-6 levels, etc.

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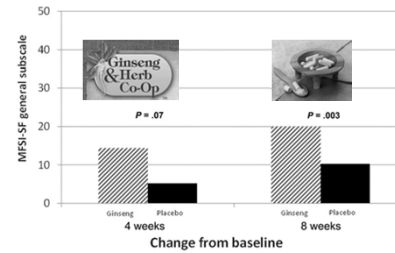
J Pain Symptom Manage 2015;41:595-610

SPIRITUAL ASSESSMENT

- ▶ Is religion or spirituality important to you?
- ▶ Would you like to see a chaplain?
- 87% of patients want us to know their spiritual needs; 6% of us ask.
- People who get spiritual care from chaplains use hospice more, ICU less.

J Clin Oncol 2013 Feb 13; 31(4):461-7; JAMA Intern Med 2013 Jun 24; 173(12):1109-17

FATIGUE



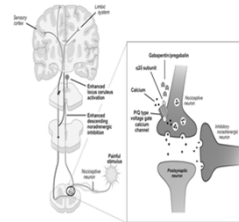
364 patients NCCTG, Oct 6, 1996, 2000 mg a day. J Natl Cancer Inst 2013; 105:1230-1238 JNCI

FATIGUE

- ▶ 84 pts with Cancer related fatigue in advanced cancer
- ▶ Dex 4 mg bid vs placebo
- Improvement in fatigue at day 15 was significantly lower in the dexamethasone than in the placebo group (P = .008)
- Total quality-of-life scores also significantly better for the dexamethasone group at day 15 (P = .03)
- Frequency of adverse effects was not significantly different between groups (41 of 62 v 44 of 58; P = .14)

JCO 2013;31(25):3076-3082

PRURITUS



- Uremia
- Cancer/Heme etio
- Opioids
- Brachioradial
- Burns
- PUO

American Journal of Hospice & Palliative Medicine 30(7) 192-196 Anesthesiology 11 2013, Vol. 119, 1215-1221

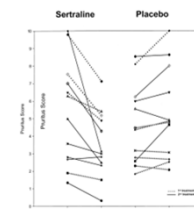
PRURITUS

- ▶ Gabapentin works for some pruritus *but not all*
- ▶ Cholestatic itching.
- ▶ Gabapentin up to 2400 mg a day
- ▶ Placebo was better.

Hepatology 2006;44(1):317-1323

CHOLESTATIC PRURITUS

- ▶ Gabapentin does NOT work.
- ▶ Options include the
 - ▶ anion exchange resin cholestyramine,
 - ▶ the PXR agonist rifampin,
 - ▶ the μ -opioid antagonist naltrexone,
 - ▶ the serotonin reuptake inhibitor sertraline
 - ▶ and paroxetine



Dig Dis 2014;32(5):637-45 Hepatology 2007;45(3):666-674

CIPN

Nerve	Before treatment	After treatment	P
Radial nerve			
Latency (ms)	4.96(2.0)	4.26(1.5)	0.173
Peak amplitude (µV)	3.45(1.4)	5.08(4.7)	0.002
Neural conduction velocity (m/s)	39.73(3.6)	39.82(3.7)	0.938
Median nerve			
Latency (ms)	5.09(1.2)	4.49(1.3)	0.003
Peak amplitude (µV)	3.47(1.4)	5.18(5.2)	0.006
Neural conduction velocity (m/s)	45.76(4.2)	52.68(5.2)	0.001
Ulnar nerve			
Latency (ms)	4.77(1.2)	4.17(1.2)	0.003
Peak amplitude (µV)	3.94(1.3)	5.20(4.7)	0.004
Neural conduction velocity (m/s)	48.45(2.4)	49.44(2.8)	0.229
Tibial nerve			
Latency (ms)	5.45(1.2)	5.16(1.3)	0.662
Peak amplitude (µV)	4.99(1.4)	6.49(5.1)	0.001
Neural conduction velocity (m/s)	37.93(3.6)	32.83(3.7)	0.001
Peroneal nerve			
Latency (ms)	11.89(2.2)	11.99(2.4)	0.862
Peak amplitude (µV)	3.29(1.2)	4.64(4.3)	0.001
Neural conduction velocity (m/s)	36.52(2.9)	34.96(3.3)	0.001

AP, action potential; m/s, meters per second (m/s); ms, before treatment (paired t-test). Data are expressed as the mean (SD) (n = 26).

Comparison of motor nerve conduction between before and after 10 sessions of electroacupuncture on Carotid sinus and local median axons.

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MINDFULNESS

Mindfulness— moderate impact on

- ▶ Anxiety
- ▶ Depression
- ▶ Pain

JAMA Intern Med. 2014;174(3):357-68

MINDFULNESS IN BC

- ▶ 320 patients
- ▶ Stage 0–III post-treatment BCS
- ▶ Six-week MBSR(BC) program vs. usual care
- ▶ Psychological
- ▶ Physical
- ▶ Cognitive symptoms
- ▶ QOL

Reich et al JPSM 2016; 53 (1) 85-95

COMMUNICATION & HOPE

Attribute	Parental Hopefulness		
	OR	95% CI	P
Parent reports high quality physician communication	6.58	3.17 to 13.69	<.0001
Degree of disclosure, per element	1.60	1.05 to 2.42	.03
Physician-rated prognosis, per category of worsening prognosis	0.65	0.48 to 0.88	.005

NOTE. Hopefulness represents parental report that the way oncologist communicates always makes the parent feel hopeful. Model was controlled for diagnostic category, time since diagnosis, parental education, parental sex, and parental race/ethnicity and was adjusted for clustering by physician. Abbreviation: OR, odds ratio.

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COMMUNICATION & HOPE

Figure 1: Herth Hope Index Average Patient Scores Before and After Intervention—Results show that patients with advanced cancer maintained their sense of hope despite receiving honest information about their prognosis.

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COMMUNICATION

EOL care discussions are important as:

- ▶ 30 day cutoff changes 50% to 19% hospital death
- ▶ Patient beliefs did not change chemo use last 30 days of life, but did increase hospice use.

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COMMUNICATION

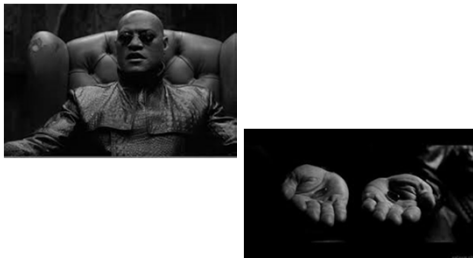
- ▶Paternalism
- ▶Autonomy
- ▶Shared Decision Making

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PATERNALISM



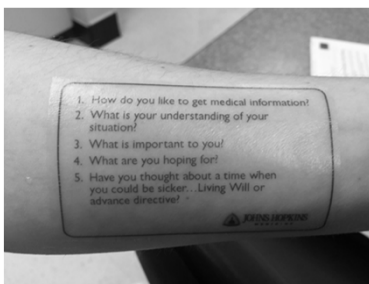
AUTONOMY



SHARED DECISION MAKING



JHM COMMUNICATION TATTOO



SO EASY!



CASE 1

EK is a 56 yo male with metastatic pancreatic cancer who was treated with FOLFIRINOX and after the second cycle developed severe nausea and vomiting, warranting hospitalization. Ondansetron was given every 4 hours as needed with minimal effect. What other agents would be good alternatives for n/v? Which receptors do those meds mediated through?

CASE 2

Ms. TM is a 61 yo woman with hx of left breast ca s/p mastectomy and chemo with Adriamycin, Cytoxan and Taxol; she has been in remission for 6 years and develops acute CHF exacerbations over the next few years. Her meds are optimized with an ACEI, diuretics, and beta blockers. Oxycodone 5 mg po tid prn is used about 1-2 times daily with better controlled. What other non-pharmacological options of care would you recommend?



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