



University of California
San Francisco

Introduction to Integrative Palliative Care & Symptom Management

Osher Mini Med School for the Public: Integrative Oncology Lecture Series | 25 May 2022

Brieze K. Bell, MD

Assistant Professor of Clinical Medicine

UCSF Division of Palliative Medicine

UCSF Division of Hospital Medicine

1 Questions for Small Group Discussion:

1) What questions come to mind when you think of integrative palliative care or integrative symptom management?

2) What are some key points you are hoping to learn from this session?

Overview of today's talk:

1 Introduction to Integrative Palliative Care

2 Integrative Palliative Care: A Case Study

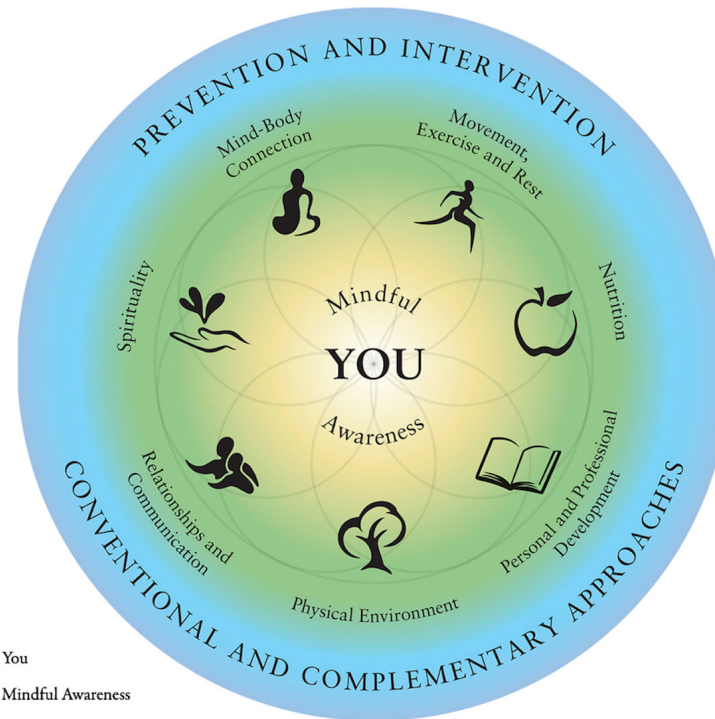
3 Resources for Patients & Providers

1 What does it mean to take an integrative approach to health?

Primary aim is to optimize health & quality of life for people at all stages of their health journeys

Uses a “bigger toolkit” that combines the best of biomedicine with evidence-based holistic therapies to improve health outcomes

Empowers individuals to engage with and enhance their own healing process



Wheel of Health
Duke University Integrative Medicine

Creates individually-tailored therapeutic regimens that address the wellbeing of body, mind, & spirit

Maintains that healing is always possible, even in situations where a “cure” may not be attainable

It is not a rejection of gold standard therapies in favor of alternative treatments

1 What is Integrative Oncology?

“Integrative Oncology is a patient-centered, evidence-informed field of cancer care that utilizes mind and body practices, natural products, and/or lifestyle modifications from different traditions alongside conventional cancer treatments”

*A comprehensive definition for integrative oncology.
Witt CM et al. J Natl Cancer Inst Monogr 2017.*

1 What is Palliative Medicine?



University of California
San Francisco

World Health Organization (WHO):

“An approach that improves the quality of life of patients and their families facing...life-threatening illness, through the prevention & relief of suffering by treatment of pain and other problems, physical, psychosocial, and spiritual.”

Center to Advance Palliative Care (CAPC):

“Specialized medical care for people living with serious illness. It focuses on providing relief from the symptoms and stress of serious illness...to improve quality of life for both patient and family.”

National Consensus Project For Quality Palliative Care (Endorsed by AHA):

“Patient- and family-centered care that optimizes quality of life by anticipating, preventing, and treating suffering...throughout the continuum of illness.”

1 What does it mean to take an integrative approach to palliative care?



University of California
San Francisco

Expanded Toolkit:

Utilizes a broader range of therapeutic tools for symptom relief, including biomedical treatments (e.g., pharmaceuticals) and integrative therapies (e.g., meditation, diet, exercises, supplements when appropriate)

Holistic Approach:

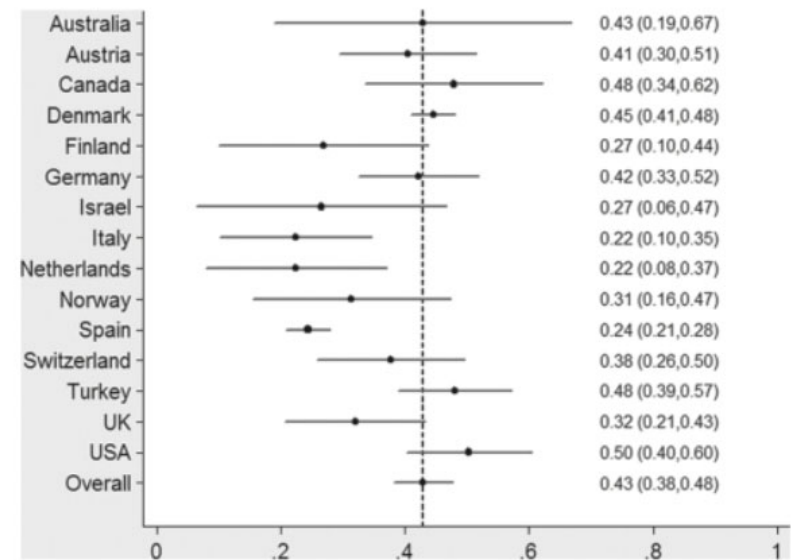
Symptom relief may include therapies that support the wellbeing of the whole person (mind, body, spirit) rather than an isolated physical symptom (e.g., restorative yoga for help with fatigue, mood disorder, pain)

Patient Empowerment:

Some patients may feel more in control of their health when they have the option of using a non-pharmacologic tool for symptom management in lieu of or in addition to a medication

1 Why Consider an Integrative Approach to Palliative Care: Demand

- Cancer remains a huge public health burden in the US
- Disease & treatment often result in significant symptoms that negatively impact quality of life
- Patients' symptom burden & desire for wellbeing have created a demand for integrative medicine (IM)
 - On average, 50% of US patients with cancer use some form of IM
 - This practice pattern extends into the strategies individuals are using to enhance their quality of life in the setting of cancer



*Prevalence of IM use among cancer patients worldwide.
Horneber M et al. Integr Cancer Ther 2012.*

1 Why Consider an Integrative Approach to Palliative Care: Safety

- A 2017 systematic review of 21 studies showed that **up to 95%** of patients surveyed were using some form of complementary or alternative medicine (CAM)* during cancer treatment
- However, **20% to 77%** of patients surveyed did not disclose CAM use to their providers
- **Primary Barriers to Disclosure:**
 1. ***The provider didn't ask***
 2. ***Patients were concerned their provider would disapprove***
 3. ***Patients believed their CAM use was irrelevant to their cancer care***

**Note that CAM is no longer the preferred terminology, which is now “integrative medicine”*

Cancer patient disclosure and patient-doctor communication of CAM use: A systematic review. Davis EL et al. Oncologist 2017.

1 Why Consider an Integrative Approach to Palliative Care: Safety



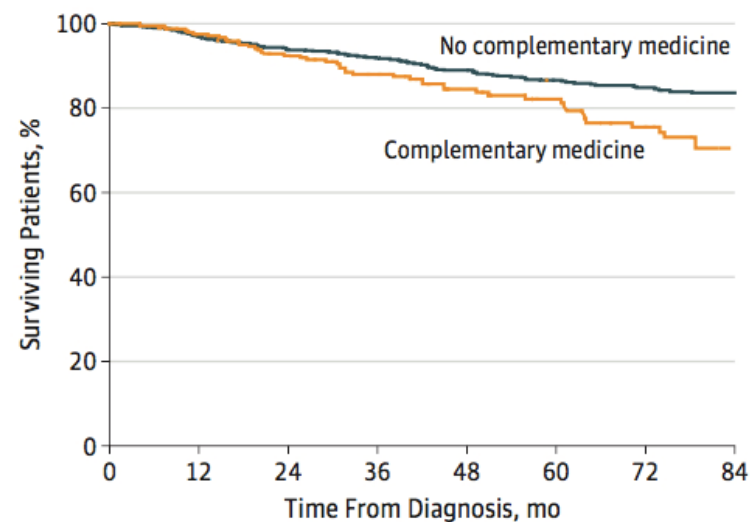
University of California
San Francisco

Key Point:

- *Providers:* Remember to ask patients what herbs, supplements, and botanicals they are using in addition to prescription and OTC biomedicines.
- *Patients:* Disclose this information to your doctor

1 Why Consider an Integrative Approach to Palliative Care: Adherence

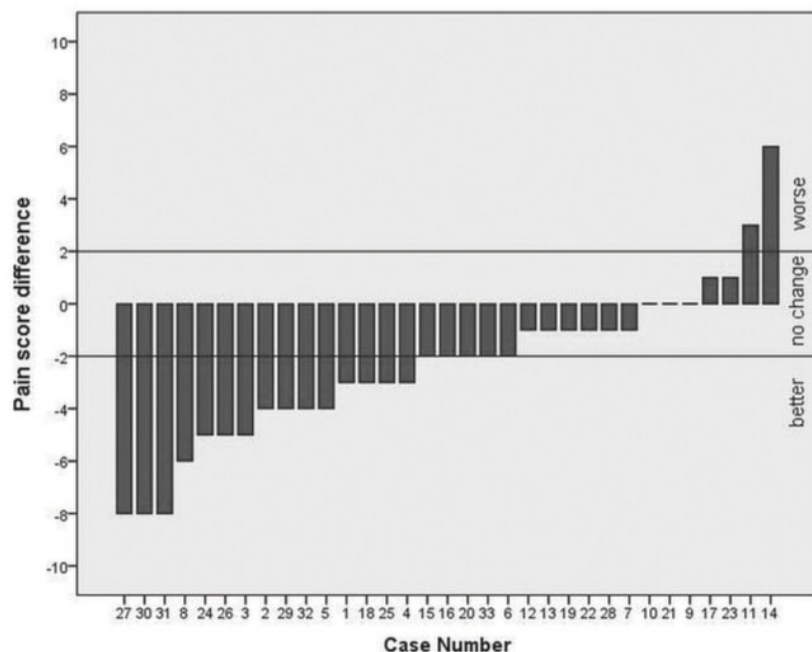
- A 2018 study showed that complementary medicine (CM) use associated with decreased overall 5-year survival & increased risk of death
- Increased mortality mediated entirely by delay or refusal of gold standard therapy
- Working with integrative oncology may increase likelihood that patients will pursue gold standard treatment:
 - Among 357 patients seen at Italian integrative oncology clinic 2013-2017, 21 (6.2%) initially refused conventional tx
 - Of 17 patients who presented for follow-up, 7 (41.2%) accepted standard tx after integrative oncology visit



No. at risk	0	12	24	36	48	60	72	84
No complementary medicine	1022	958	838	691	518	392	294	207
Complementary medicine	256	238	205	167	123	91	72	50

Survival of patients (CM vs no CM) for non-metastatic breast, prostate, lung, and colorectal cancer. Johnson SB et al. JAMA Oncol 2018.

1 Why Consider an Integrative Approach to Palliative Care: Symptom Relief

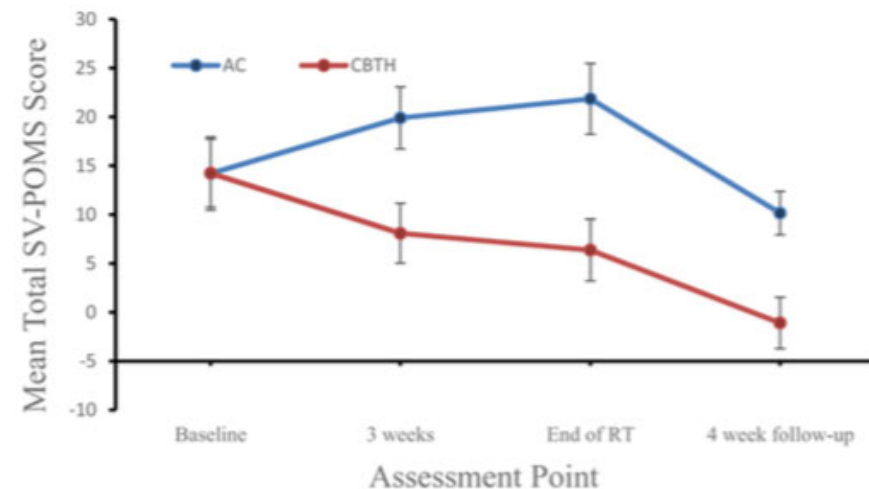
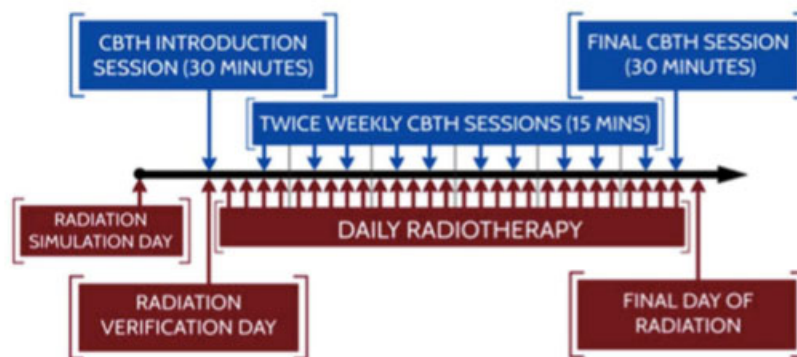


Difference in pain scores pre- and post-intervention.
Kasymjanova G et al. Curr Oncol 2013.

- Integrative therapies can improve cancer-related symptoms
- In a prospective, observational study of 30 patients with advanced lung cancer who underwent 7 sessions of acupuncture in addition to standard tx, researchers noted statistically significant improvements in:
 - Pain
 - Appetite
 - Nausea
 - Anxiety
 - Well-being
- Clinically meaningful improvements in pain for 61% of patients and well-being for 33% of patients

1 Why Consider an Integrative Approach to Palliative Care: Symptom Relief







- A 2017 RCT evaluated cognitive behavioral therapy & hypnosis (CBTH, N = 50) vs. an attention control (AC, N = 50) on emotional distress among 100 women with breast cancer undergoing XRT
- Participants completed a validated questionnaire for emotional distress (SV-POMS) at 4 time points during the study
- Initial 30 minute session, twice weekly 15-minute sessions, & final 30 minute session at completion of XRT
- **Results:** Significant improvement in emotional distress in CBTH group at 3 weeks, end of XRT, and 4 weeks later



1 Why Consider an Integrative Approach to Palliative Care: Symptom Relief



University of California
San Francisco

Outcome	Aerobic Only	Resistance Only	Combination (Aerobic + Resistance)
Strong Evidence	Dose	Dose	Dose
 Cancer-related fatigue	3x/week for 30 min per session of moderate intensity	2x/week of 2 sets of 12-15 reps for major muscle groups at moderate intensity	3x/week for 30 min per session of moderate aerobic exercise, plus 2x/week of resistance training 2 sets of 12-15 reps for major muscle groups at moderate intensity
 Health-related quality of life	2-3x/week for 30-60 min per session of moderate to vigorous	2x/week of 2 sets of 8-15 reps for major muscle groups at a moderate to vigorous intensity	2-3x/week for 20-30 min per session of moderate aerobic exercise plus 2x/week of resistance training 2 sets of 8-15 reps for major muscle groups at moderate to vigorous intensity
 Physical Function	3x/week for 30-60 min per session of moderate to vigorous	2-3x/week of 2 sets of 8-12 reps for major muscle groups at moderate to vigorous intensity	3x/week for 20-40 min per session of moderate to vigorous aerobic exercise, plus 2-3x/week of resistance training 2 sets of 8-12 reps for major muscle group at moderate to vigorous intensity
 Anxiety	3x/week for 30-60 min per session of moderate to vigorous	Insufficient evidence	2-3x/week for 20-40 min of moderate to vigorous aerobic exercise plus 2x/week of resistance training of 2 sets, 8-12 reps for major muscle groups at moderate to vigorous intensity
 Depression	3x/week for 30-60 min per session of moderate to vigorous	Insufficient evidence	2-3x/week for 20-40 min of moderate to vigorous aerobic exercise plus 2x/week of resistance training of 2 sets, 8-12 reps for major muscle groups at moderate to vigorous intensity
 Lymphedema	Insufficient evidence	2-3x/week of progressive, supervised, program for major muscle groups does not exacerbate lymphedema	Insufficient evidence

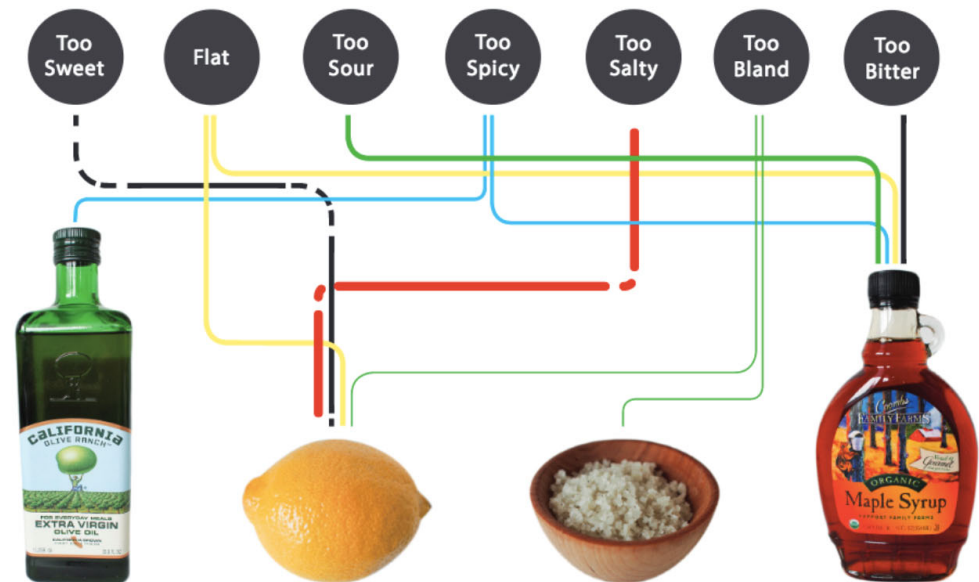
https://journals.lww.com/acsm-msse/Fulltext/2019/11000/Exercise_Guidelines_for_Cancer_Survivors_.23.aspx

1 Why Consider an Integrative Approach to Palliative Care: Symptom Relief

- Cancer treatment commonly leads to dry mouth & taste changes
- These symptoms often improve with time
- Acupuncture during radiation helps prevent dry mouth
- Citrus-infused water can help with dry mouth
- There are several dietary tips to help manage taste changes
- Miracle berries help with bitter taste



Taste, Taste, Taste! Is it too....? Then, play with a pinch or drop of...



MK Garcia et al. *JAMA Network Open*, 2019.

<https://www.rebeccakatz.com/blog/the-elephant-under-the-rug-transient-taste-changes-with-cancer-therapy#>

1 Why Consider an Integrative Approach to Palliative Care: Symptom Relief

Turmeric:

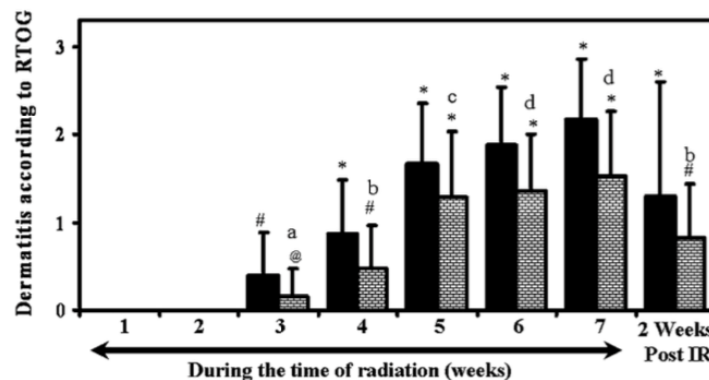
- Plant related to ginger, cultivated throughout India, Asia, & Central America
- Common spice; major ingredient in curry powder
- Turmeric's underground roots (rhizomes) are ground and made into medicinal capsules, tablets, & paste
- Has been widely used in Ayurvedic medicine for centuries: inflammation, arthritis, cancer
- Thought to have antioxidant, anti-inflammatory, anticancer, & cardio-protective properties



1 Why Consider an Integrative Approach to Palliative Care: Symptom Relief

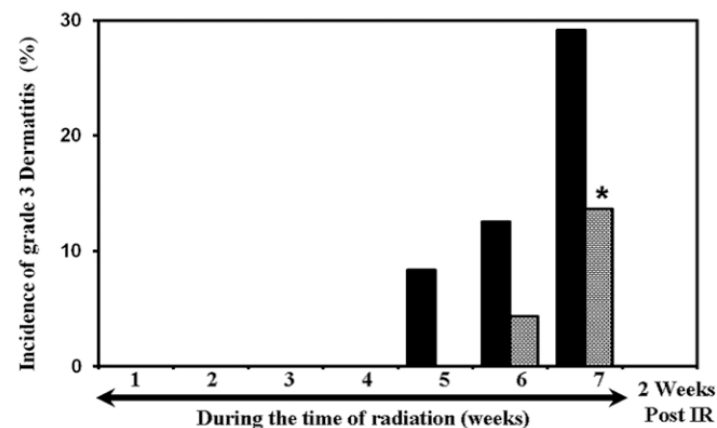
Turmeric & Cancer Symptom Relief

- Oral administration (1000 mg BID) may be helpful for inflammatory pain syndromes
- Topical application may help prevent & improve radiodermatitis during XRT
- 50 patients with H&N cancer assigned to baby oil vs topical turmeric/sandalwood oil applied 5x daily to XRT field during & after radiation treatment
- Intervention group had lower dermatitis rates at all study time points ($p < 0.015$ to $p < 0.001$) and less severe dermatitis ($p < 0.05$)



Incidence of dermatitis throughout study.

Palatty PL et al. Br J Radiol 2014.



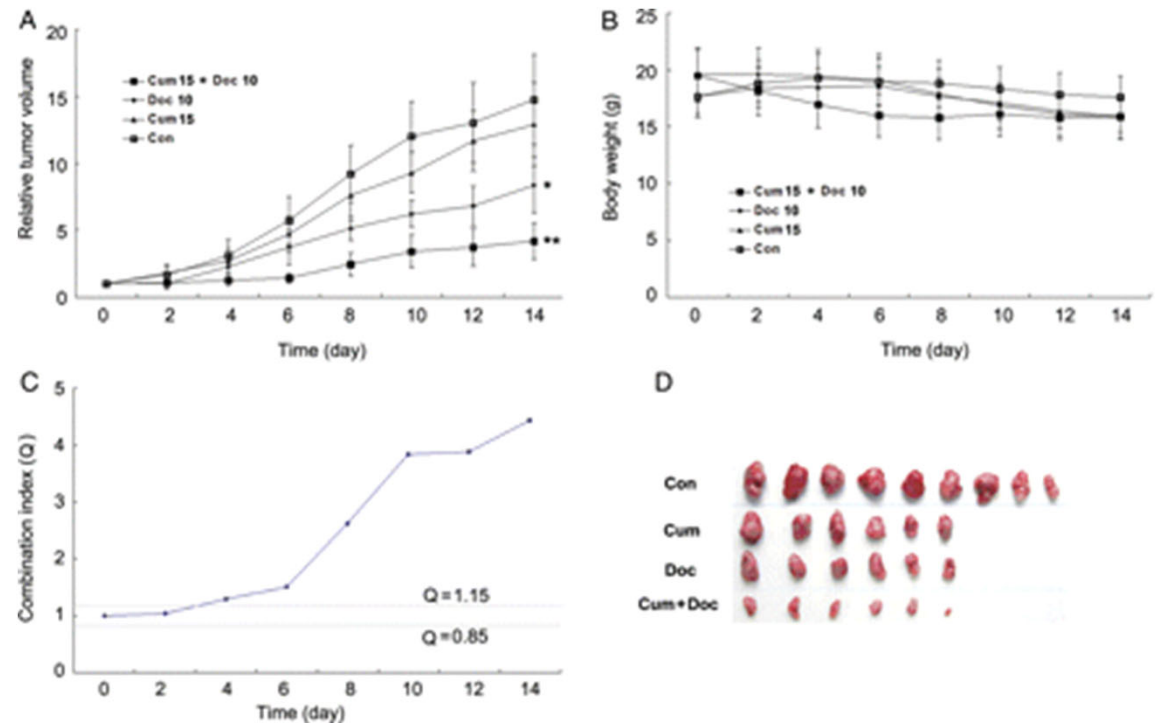
Incidence of grade III dermatitis throughout study.

Palatty PL et al. Br J Radiol 2014.

1 Symptom Relief...and Possible Anti-Cancer Effect?

Anti-Cancer Effects of Turmeric:

- May have anticancer effects, especially for GI tract cancers (colon, pancreas)
- In a phase II human trial of 21 patients with advanced pancreatic cancer who received 8g turmeric per day, 2 showed significant clinical responses (Dhillon N et al, Clin Cancer Res 2008)
- A 2012 mouse study demonstrated synergistic activity of turmeric with docetaxel against non-small cell lung cancer



Variation of tumor volume (A) & tumor volume (D) in mouse models during therapy with different doses of docetaxel & turmeric. Yin H et al. Acta Biochim Biophys Sin 2012.

1 Symptom Relief...and Possible Anti-Cancer Effect?

Cannabis & Cancer:

- The cannabis plant contains over 400 chemical compounds, first reported for medicinal use >3000 years ago
- Pharmacology & half-life varies considerably based on route of administration
- RCTs have shown cannabis to be as effective or superior for treating chemotherapy-induced nausea/vomiting as compared to compazine
- May be helpful for chemotherapy-induced peripheral neuropathy, anorexia-cachexia syndrome. More data is needed.

Can cannabis treat cancer?

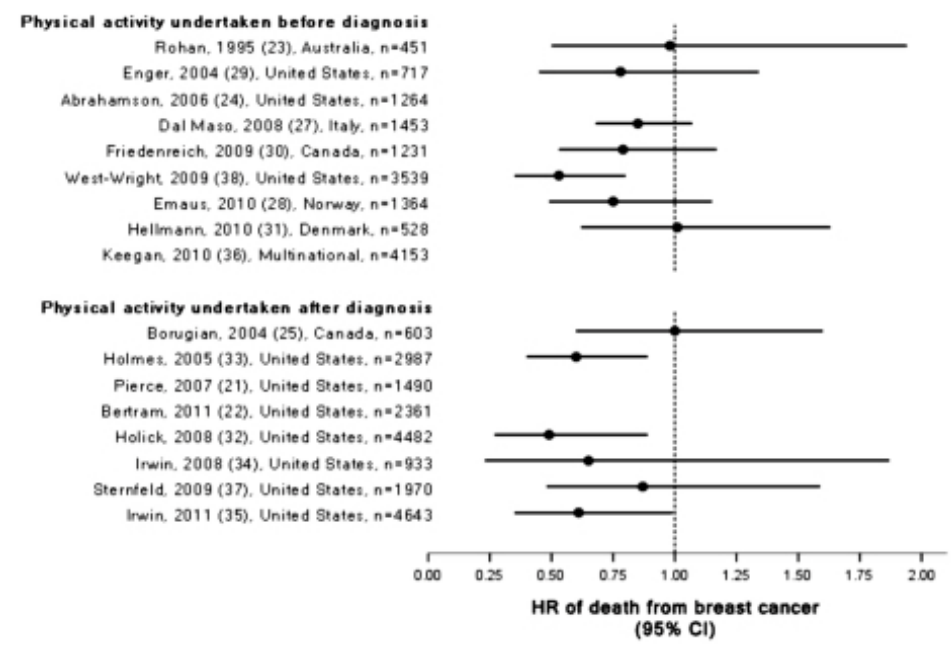
- Growing body of pre-clinical evidence suggests anti-cancer activity, but much more data is needed
- Phase II, proof of concept study in 21 patients with recurrent glioblastoma multiforme (GBM) demonstrated improved survival among patients treated with THC:CBD + temozolomide vs temozolomide alone (83% 1-yr survival vs 53% in controls, $p = 0.042$)
- Clinical trials ongoing



1 Symptom Relief...and Possible Anti-Cancer Effect?

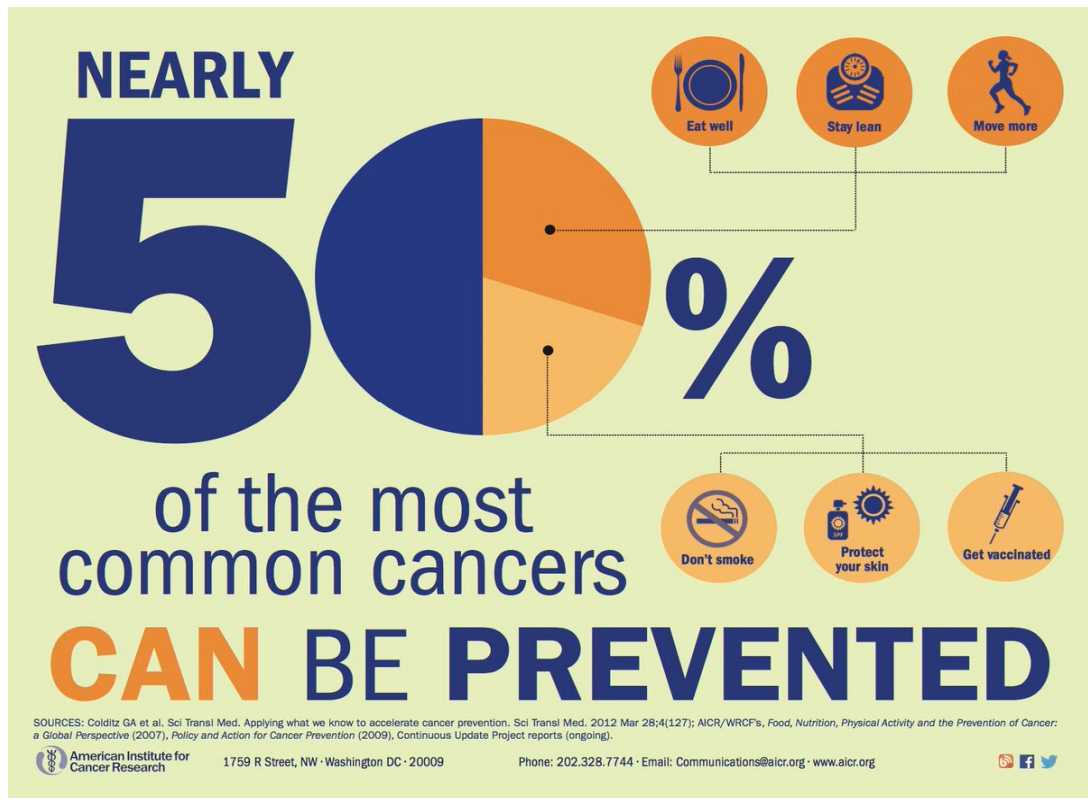
Exercise & Cancer:

- Moderate, regular exercise is consistently associated with improved symptom burden among patients with cancer
- 2012 Cochrane meta-analysis of 27 observational studies shows clear inverse association between physical activity and mortality from breast cancer, colon cancer, & all cancers
- Effect may be dose-dependent



Forest plot of studies of physical activity & breast cancer-related mortality. Ballard-Barbash R et al. J Natl Cancer Inst 2012.

1 Why Consider an Integrative Approach to Palliative Care: Risk Reduction

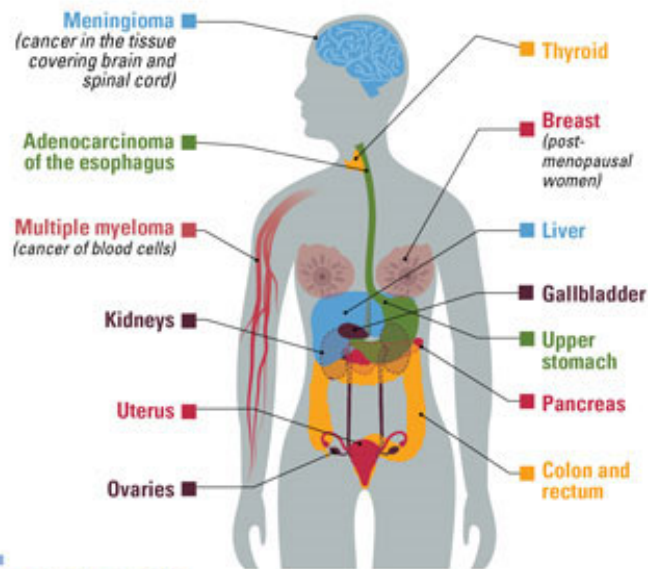


- Abundant evidence that lifestyle influences cancer risk, cancer-related quality of life, recovery, & recurrence
- According to the American Institute for Cancer Research (AICR) and the World Cancer Research Fund (WCRF), nearly 50% of cancers are lifestyle-related and preventable*
- **Great news:** The same tools that help prevent cancer also help with cancer-related quality of life, cancer recovery, and recurrence risk reduction

**Many things contribute to cancer. A person may get cancer even with a very healthy lifestyle. Getting cancer is no one's fault.*

1 Why Consider an Integrative Approach to Palliative Care: Risk Reduction

13 cancers are associated with overweight and obesity



Vitalsigns™

<https://www.cdc.gov/vitalsigns/obesity-cancer>



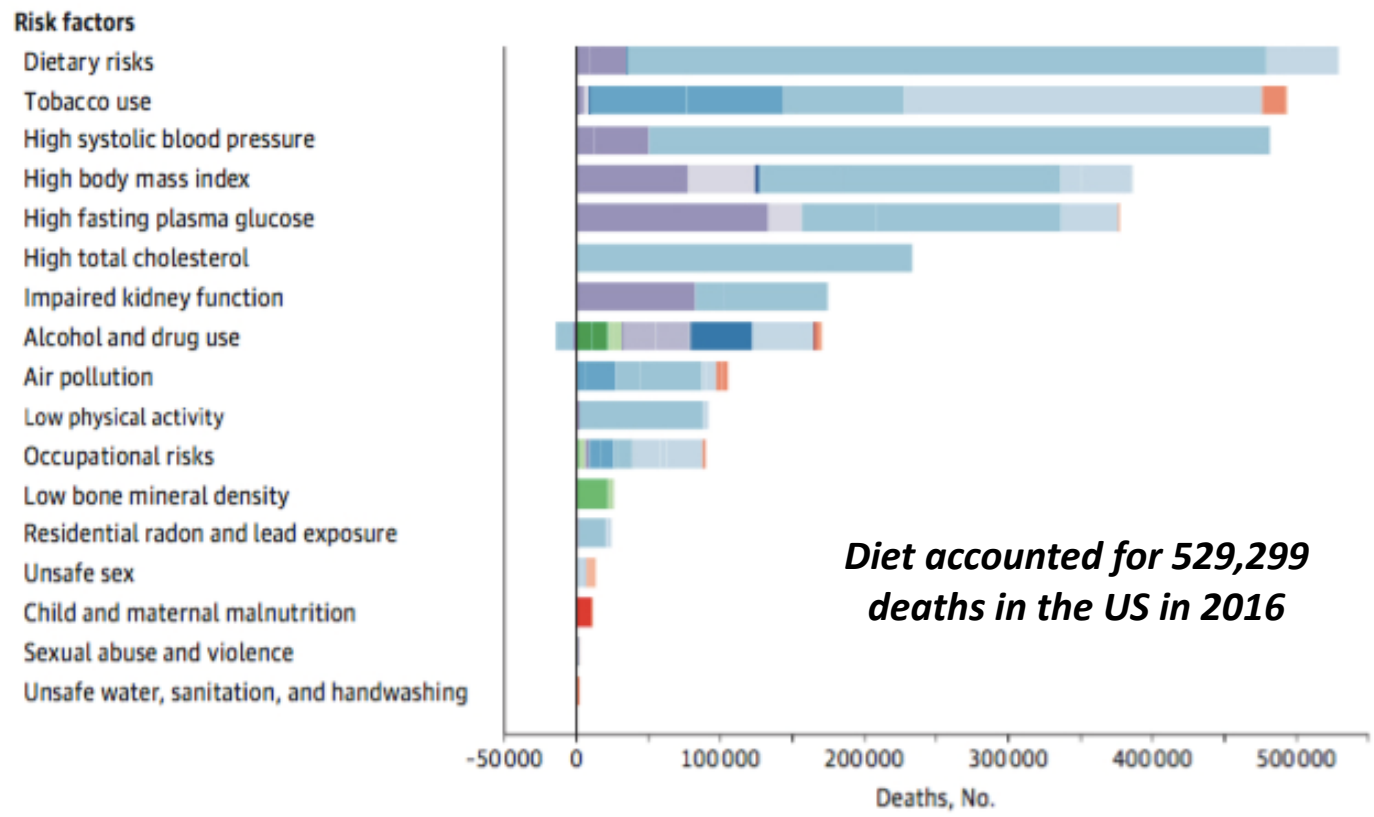
Excess Weight Increases Cancer Risk:

- In 2016, prevalence of obese adults worldwide approached 40% in both sexes
- Excess body weight accounts for ~4% of all cancer incidence worldwide per year (544,300 cases)
- Attributable proportion accounts for nearly 8% in developed nations (USA)
- Burden is greater for women (368,500 cases) than for men (175,800 cases)

Proportions and numbers of cancer cases attributable to excess body weight (BMI > 25) by sex and cancer type worldwide in 2012. Sung H et al. CA J Clin 2019.

1 Why Consider an Integrative Approach to Palliative Care: Risk Reduction

A 2016 study in JAMA found that poor diet is now the number one risk factor for death in the United States



Number of deaths attributable to 17 risk factors in the US in 2016. Mokdad AH et al. JAMA 2018.

1 So How Do We Actually Enhance Quality of Life in the Setting of Cancer?



1 Key Components of Integrative Cancer Care: Dietary Pattern

Where do things currently stand?

- The *2015-2020 Dietary Guidelines for Americans* recommend 1.5-2 cups of fruit & 2-3 cups of vegetables per day
- A 2015 CDC survey of 350,000 US adults found that only **12.2% of adults** met fruit RDA and **9.3% of adults** met vegetable RDA
- Consumption lowest among men, young adults, and adults with lower income

The Standard American Diet (SAD)

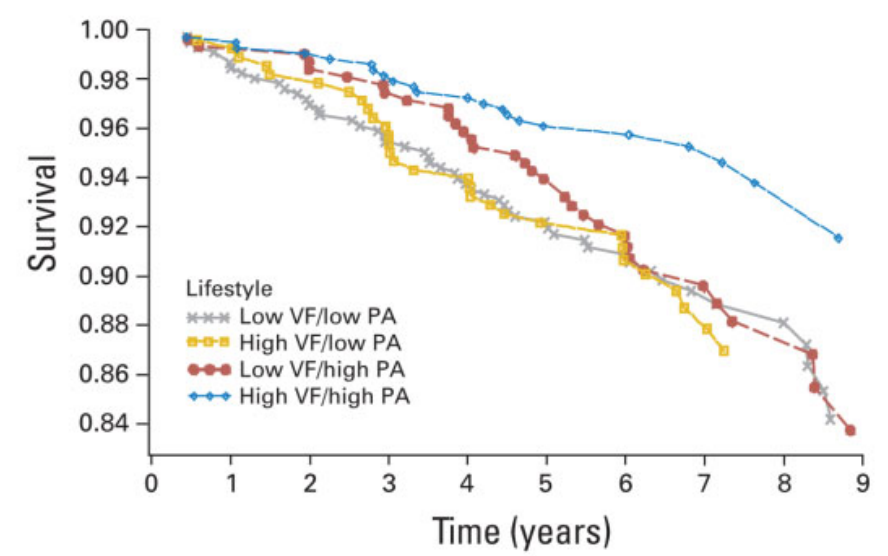
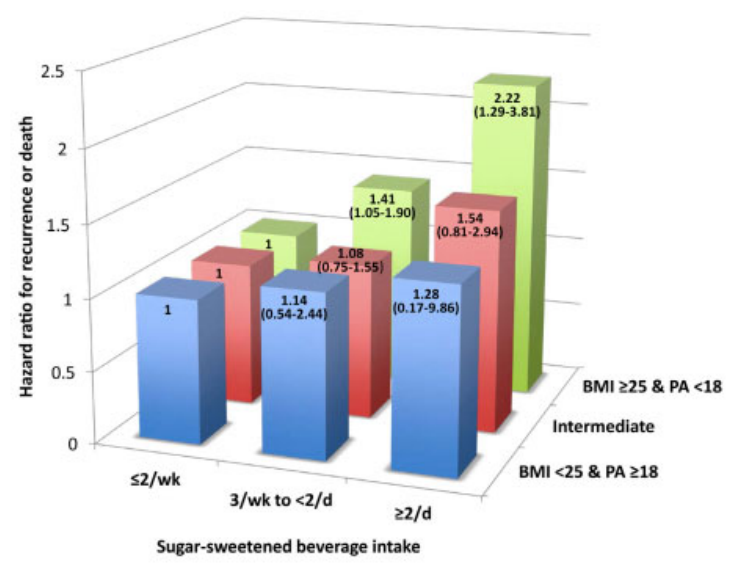


Lee-Kwan SH et al. MMWR Morb Mortal Wkly Rep 2017.

1 Key Components of Integrative Cancer Care: Dietary Pattern

Does eating a “Standard American Diet” influence cancer recurrence and survival?

- Women’s Healthy Eating Study: Prospective observational study of 1,490 women w/early stage breast cancer showed significant survival advantage in women who ate 5+ servings produce and walked 30+ min daily
- A 2014 study of 1,011 patients with stage III colon cancer: Significantly increased risk of cancer recurrence and death w/2+ sugar-sweetened beverages per day; risk greatest for those who were also overweight and inactive



Multivariate HRs for cancer recurrence or death according to BMI, activity, and sugary beverage intake. Fuchs MA et al. PLOS One 2014.

KM Survival curves after WHEL Study enrollment stratified by produce intake and physical activity categories. Pierce JP A et al. J Clin Oncol 2007

1 Key Components of Integrative Cancer Care: Dietary Pattern

Foods to Increase:

- **Vegetables:** Cruciferous, leafy greens, brightly pigmented
- **Fruits:** Especially berries
- **Whole Grains:** Quinoa, millet, brown rice
- **Legumes:** Lentils, black beans, chickpeas
- **Healthy Fats:** Wild fatty fish, ground flax seed, walnuts
- **Antioxidant-Rich Seasonings:** Garlic, onion, ginger, turmeric
- **Asian Mushrooms:** Shiitake, Maitake, Enoki
- **Green tea:** 4-5 cups a day



Foods to Decrease:

- **Sugar-Sweetened Beverages:** Soda, juice
- **Refined Carbohydrates:** Sugar, white flour/rice
- **Red Meat, Pork, Processed Meats, & Dairy:** If consuming, consider organic when possible
- **Processed, Packaged Foods**
- **Alcohol**

<https://www.aicr.org>
<https://www.rebeccakatz.com/cancer-and-food>

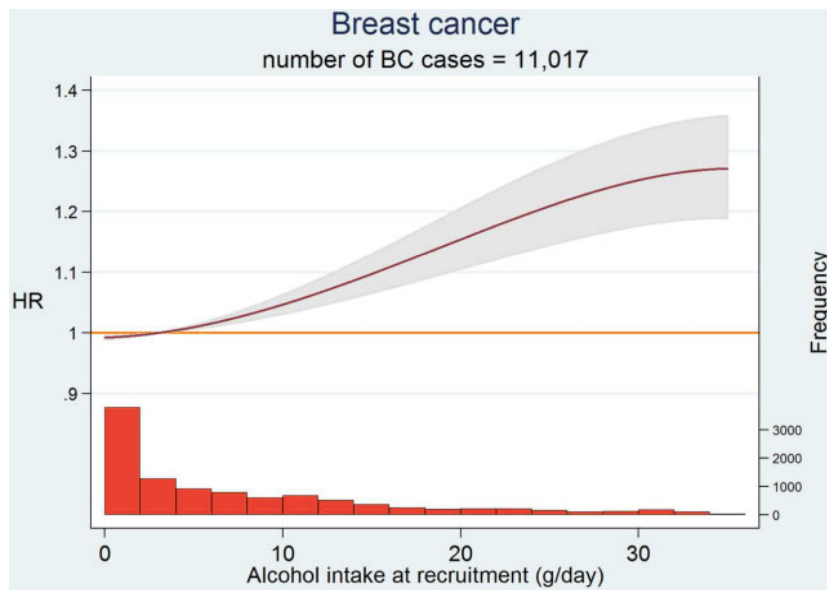
1 Key Components of Integrative Cancer Care: Dietary Pattern

The Benefits of Eating Organic Food:

- **Produce:**
 - Less exposure to pesticides & preservatives
 - Increased vitamin C, minerals, and antioxidant phytonutrients
 - Often fresher (and therefore more nutritious)
- **Animals:**
 - Not given antibiotics, growth hormones, or fed animal by-products
 - Often (though not always) raised in more humane and sanitary conditions
- **May be linked to lower rates of certain cancers:**
 - A 2018 study in *JAMA Internal Medicine* revealed an inverse association between organic food intake and rates of **post-menopausal breast cancer** and **lymphoma** among 68,946 participants
 - Quartile 4 vs Quartile 1 HR 0.75; 95% CI 0.62-0.88, P = 0.001; Absolute risk reduction 0.6%



1 Key Components of Integrative Cancer Care: Minimize Alcohol Use



Dose-Response Curve of BC Risk with Alcohol Intake at EPIC Study Recruitment. Romieu I et al. *Int J Cancer* 2018.

What About Alcohol?

- *Strong correlation* between increased alcohol intake and risk of certain cancers, especially breast, colon, head & neck, liver, & esophageal
- A worldwide systematic analysis for the Global Burden of Disease Study published in *The Lancet* in 2018 concluded:

“Alcohol use is a leading risk factor for global disease burden and causes substantial health loss. We found that the risk of all-cause mortality, and of cancers specifically, rises with increasing levels of consumption, and the level of consumption that minimizes health loss is zero.”

- GBD 2016 Alcohol Collaborators. *Lancet* 2018.

1 Key Components of Integrative Cancer Care: Minimize Alcohol Use



- For cancer prevention & recovery, it's best not to drink alcohol
- If patients are drinking alcohol, encourage moderation
 - ~ Limit to no more than 4 drinks/week
 - ~ Keep some days alcohol-free each week
 - ~ Remember that restaurants & bars often serve larger than standard sizes
 - ~ Alternate alcoholic & non-alcoholic drinks



- Consider encouraging non-alcoholic alternatives:
There are some great options out there now!

<https://www.aicr.org/cancer-prevention/recommendations/limit-alcohol-consumption/>



1 Key Components of Integrative Cancer Care: Exercise

- Exercise decreases cancer risk, improves cancer outcomes, and is associated with longer life
- This is because being active:
 - ~ Regulates hormone levels that influence cancer risk
 - ~ Speeds food through the colon, reducing exposure to dietary carcinogens
 - ~ Helps maintain a healthy weight



<https://www.aicr.org/cancer-prevention/recommendations/be-physically-active/>
<https://www.aicr.org/cancer-prevention/recommendations/be-a-healthy-weight/>

1 Key Components of Integrative Cancer Care: Supplements & Botanicals



AICR/WCRF 2018 Guidelines:

- Do not use supplements for cancer prevention/recovery

Potential exceptions to this rule:

- Organic green tea (up to 5 cups/day)
- Vitamin D (correct deficiency: aim for 25-OH level 40-50)
- Turmeric in some cases (1000 mg BID)
- Medicinal mushrooms



1 Equitable Access to Integrative Medical Care



University of California
San Francisco

Access inequity is a huge challenge:

- Parallels disparities we see in specialty PC and other fields
- Reflects cultural values regarding what we choose to subsidize and insure

National Health Survey Use of IM 2012:

- **Race/Ethnicity:** 37.9% non-Hispanic white; 22% Hispanic; 19.3% non-Hispanic black
- **Education:** Adults w/o high school degree 15.6%; college degree 42.6%
- **Wealth:** Adults below US poverty threshold 20.6%; adults >200% poverty threshold 38.4%

Clarke TC et al. *National Center for Health Statistics 2015.*
Saper R. *Glob Adv Health Med 2016.*

Primary Barriers to IM:

- Awareness
- Availability
- Accessibility
- Affordability

Emerging Solutions...Much more is needed!

- **Increase in insurance coverage:**
 - ~ Acupuncture now covered by MediCal, Medicare for some diagnoses
 - ~ PT; Some exercise training programs
 - ~ Nutrition counseling
- **Educate patients on no/low cost therapies:**
 - ~ Deep breathing, exercise (walking, bodyweight strength), meditation, aromatherapy
- **Explore programs to offset cost:**
 - ~ Foodbanks; food voucher programs
 - ~ Community-based acupuncture; massage schools; grant-funded programs

2 Integrative Palliative Care: A Case Study



University of California
San Francisco

A Case Study:

Mr. H is a 67 y.o. male former smoker (50 pack-year history) w/PMH of COPD (not on home oxygen), and cT4N2(4R)M0 AJCC Stage IIIB squamous cell carcinoma of the right upper lobe who is currently undergoing radiation therapy to the R lung (planned for a total of 60 Gy in 30 fractions) alongside concurrent carboplatin/taxol.

He presents to the UCSF SMS Clinic to get help with the following symptoms:

- Extreme tiredness all day, despite sleeping well at night
- Poor appetite with associated weight loss
- Burning and tingling in both feet
- Significant anxiety related to cancer diagnosis

2 Integrative Palliative Care: A Case Study



University of California
San Francisco

A Case Study:

Mr. H is a 67 y.o. male former smoker (50 pack-year history) w/PMH of COPD (not on home oxygen), and cT4N2(4R)M0 AJCC Stage IIIB squamous cell carcinoma of the right upper lobe who is currently undergoing radiation therapy to the R lung (planned for a total of 60 Gy in 30 fractions) alongside concurrent carboplatin/taxol.

He presents to the UCSF SMS Clinic to get help with the following symptoms:

- **Extreme tiredness all day, despite sleeping well at night**
- Poor appetite with associated weight loss
- Burning and tingling in both feet
- Significant anxiety related to cancer diagnosis

2 Integrative Cancer Symptom Management: Cancer-Related Fatigue

The problem:

- Extremely common among cancer patients; prevalence ranges 50-100%
- Persistent sense of fatigue and poor energy
 - Not relieved by rest
 - Associated with poor function & QOL

First Steps:

- Eliminate sedating drugs
- Correct reversible causes
- Educate & normalize symptom

Contributing Factors:

- Direct effect from cancer and/or therapies
- Sedating medications
- Deconditioning/Malnutrition
- Comorbid psychiatric conditions
- Medical Causes (hypoxemia, anemia, infection, organ failure, electrolyte dysfunction)
- Sleep disturbance
- Pain

2 Integrative Cancer Symptom Management: Cancer-Related Fatigue

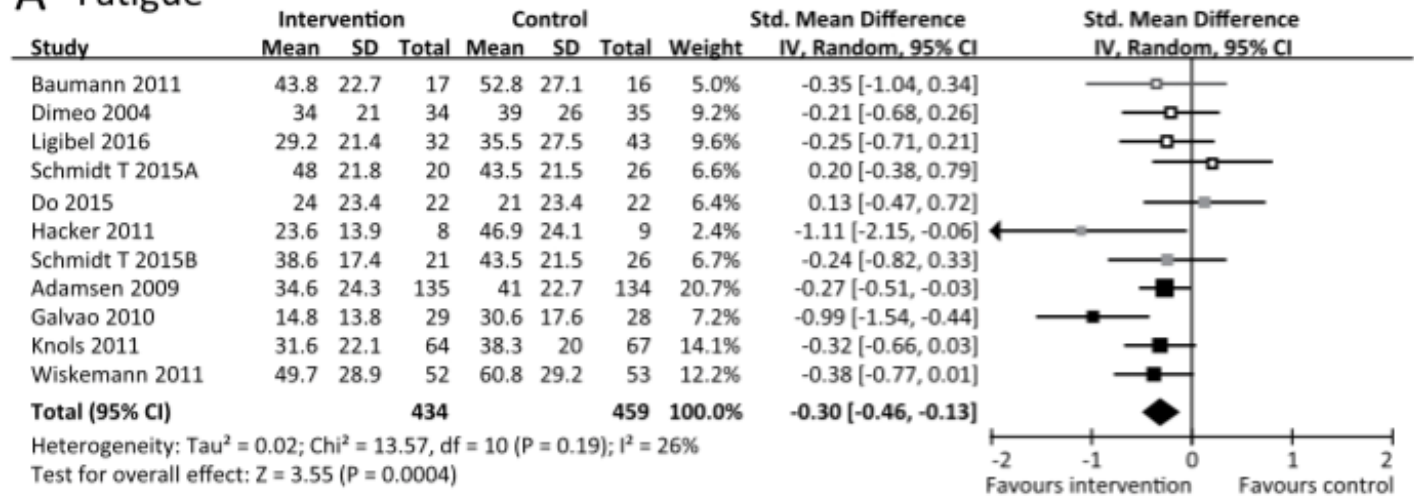


University of California
San Francisco

Physical Activity:

- Multiple meta-analyses demonstrate benefit for CRF symptoms
- Aerobic exercise ideal; resistance training & yoga also effective
- **Goal:** At least 20-30 min/day, 3x per week

A Fatigue



Standard Mean Difference of aerobic exercise on cancer-related fatigue. Nakano J et al. Integr Cancer Ther 2018.

2 Integrative Cancer Symptom Management: Cancer-Related Fatigue



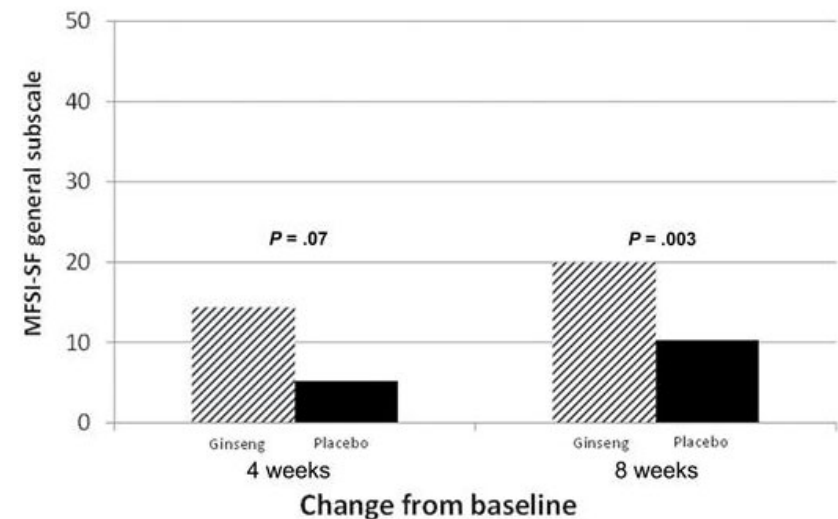
University of California
San Francisco

Multimodal Complementary Therapies:

- *Acupuncture:*
 - A 2015 meta-analysis demonstrated that acupuncture significantly reduced CRF in cancer patients compared to conventional care
 - Pooled SMD -2.12; 95% CI -3.21 to -1.03
- *Dietary Omega-3 fatty acid intake*
 - Increased dietary intake of omega-3 fatty acids associated w/lower rates of CRF among breast cancer patients

Supplements:

- *American Ginseng:*
 - Multisite RCT of 364 patients taking 2000 mg of daily oral American Ginseng vs. placebo showed significant improvement in CRF at 8 weeks with no adverse effects
- *Acetyl L-Carnitine:*
 - Amino acid required for mitochondrial fatty acid oxidation
 - Small, single-arm study of 2g TID demonstrated significant reduction in CRF at 4 weeks with no adverse effect



Fatigue change from baseline at 4 and 8 weeks, ginseng vs placebo.
Barton DL et al. *J Natl Cancer Inst* 2013.

2 Integrative Cancer Symptom Management

A Case Study:

Mr. H is a 67 y.o. male former smoker (50 pack-year history) w/PMH of COPD (not on home oxygen), and cT4N2(4R)M0 AJCC Stage IIIB squamous cell carcinoma of the right upper lobe who is currently undergoing radiation therapy to the R lung (planned for a total of 60 Gy in 30 fractions) alongside concurrent carboplatin/taxol.

He presents to the UCSF SMS Clinic to get help with the following symptoms:

- Extreme tiredness all day, despite sleeping well at night
- **Poor appetite with associated weight loss**
- Burning and tingling in both feet
- Significant anxiety related to cancer diagnosis

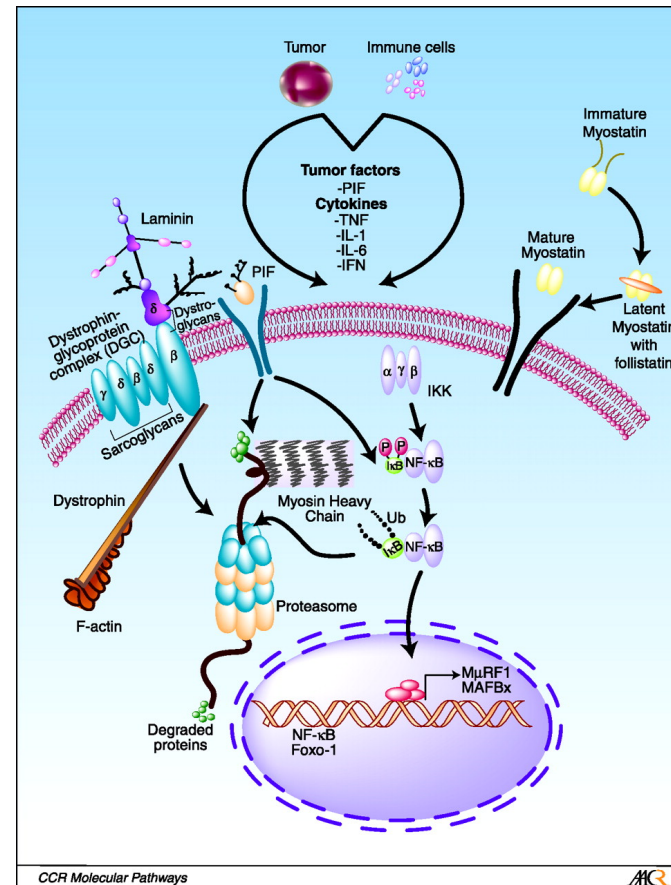
2 Integrative Cancer Symptom Management: Anorexia-Cachexia Syndrome

The problem:

- Affects up to 80% of patients with cancer
- Abnormal weight loss (<5-10% pre-morbid weight)
- Cachexia: Complex signaling pathways mediated by pro-inflammatory cytokines
- Independent risk factor for mortality

First Steps:

- Normalize symptom; educate patient & family
- Refer UCSF patients for dietary counseling at Cancer Center
- Treat associated pain, nausea, GERD, constipation



Emerging signal pathways in cancer cachexia.
Accharya S et al. Clin Cancer Res 2007.

2 Integrative Cancer Symptom Management: Anorexia-Cachexia Syndrome



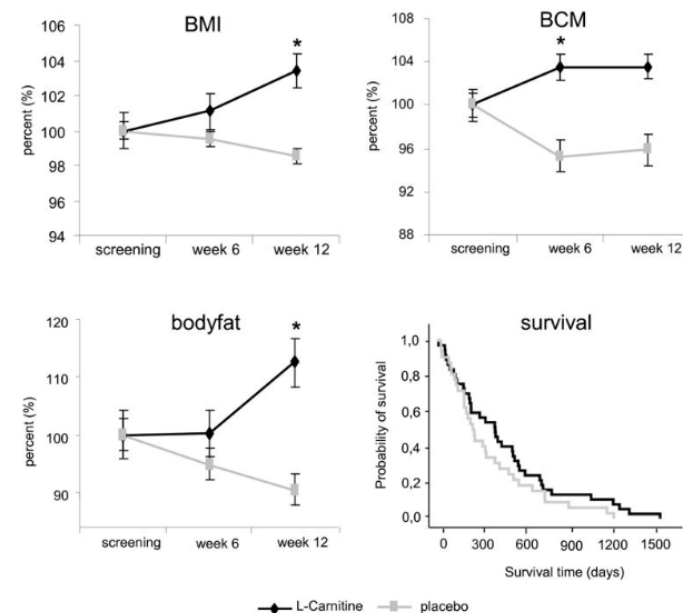
University of California
San Francisco

Multimodal Complementary Therapies

- *Dietary Adjustments:*
 - Smaller, more frequent meals
 - Increase healthy fats, protein
 - Adequate hydration
 - Antioxidant-rich foods (vegetables, fruits)
 - High-quality nutritional supplements (e.g. Kate Farms, Orgain brand)
- *Resistance exercise, PT referral*

Supplements:

- *Acetyl L-Carnitine: CARPAN Trial*
 - Placebo-controlled, randomized, double-blind trial of 72 patients w/advanced pancreatic cancer
 - Receive L-Carnitine 4g QD or placebo for 4 weeks
 - BMI increased ($3.4 \pm 1.4\%$) in intervention arm; decreased ($-1.5 \pm 1.4\%$) in placebo ($p < 0.05$)
 - Non-significant trend towards increased survival



Relevant nutrition parameters and survival, L-Carnitine v. placebo. Kraft M et al. Nutri J 2012.

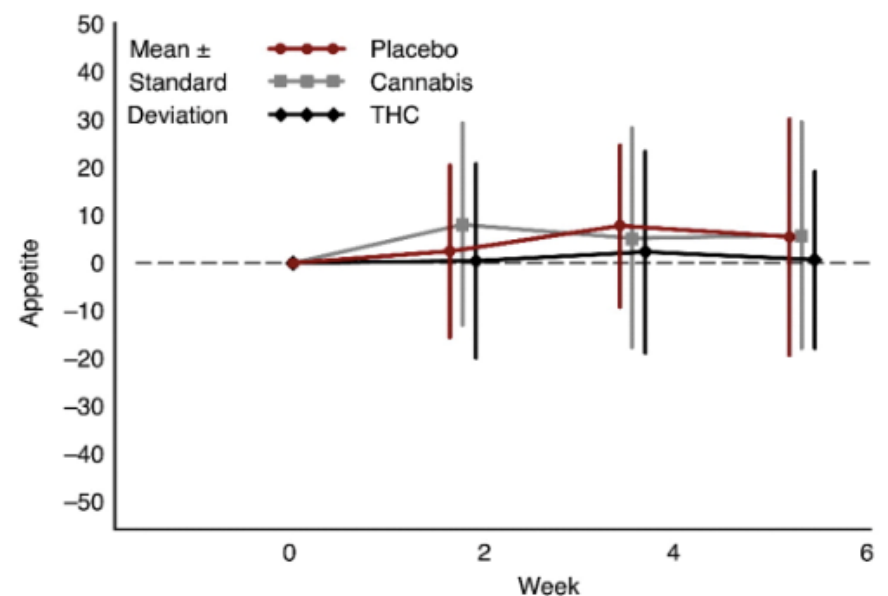
2 Integrative Cancer Symptom Management: Anorexia-Cachexia Syndrome



University of California
San Francisco

Cannabinoids:

- Data is conflicting; more research needed
- Non-randomized trials suggest benefit in terms of appetite & weight gain
- Anecdotal evidence positive for some
- Large, phase III trial found no difference between cannabis, THC, & placebo in terms of appetite, weight gain, or QOL in patients with cancer cachexia over 6 weeks



	0	2	4	6
Placebo	n = 43	42	36	30
Cannabis (CE)	n = 91	88	75	63
THC	n = 92	89	74	62

Daily mean appetite scores for cannabis, THC, & placebo arms.
Cannabis-in-Cachexia-Study-Group et al. J Clin Oncol 2006.

2 Integrative Cancer Symptom Management

A Case Study:

Mr. H is a 67 y.o. male former smoker (50 pack-year history) w/PMH of COPD (not on home oxygen), and cT4N2(4R)M0 AJCC Stage IIIB squamous cell carcinoma of the right upper lobe who is currently undergoing radiation therapy to the R lung (planned for a total of 60 Gy in 30 fractions) alongside concurrent carboplatin/taxol.

He presents to the UCSF Osher Center to get help with the following symptoms:

- Extreme tiredness all day, despite sleeping well at night
- Poor appetite with associated weight loss
- **Burning and tingling in both feet**
- Significant anxiety related to cancer diagnosis

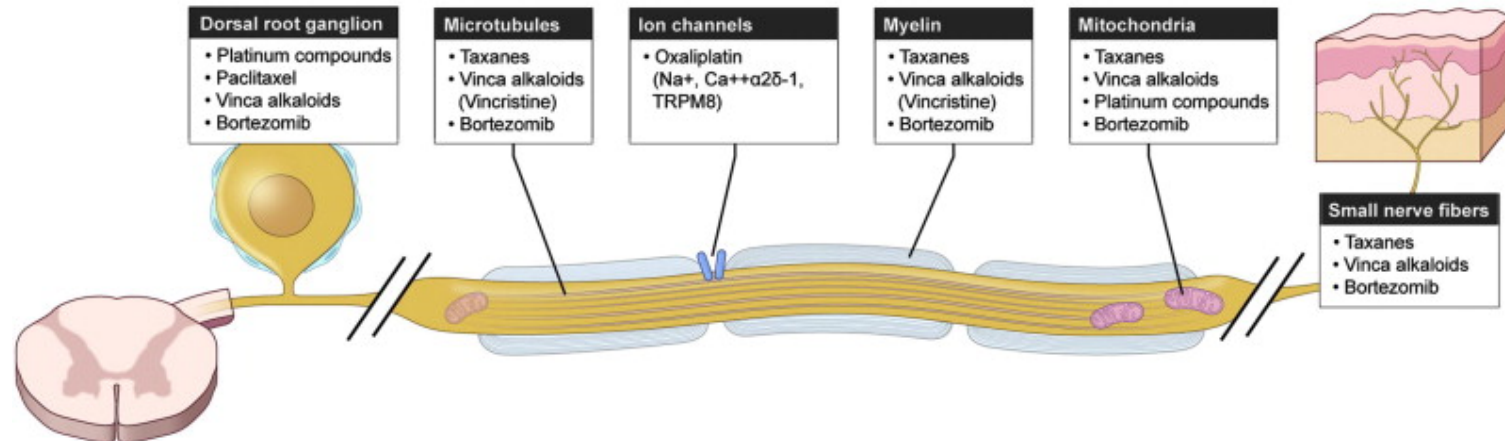
2 Integrative Cancer Symptom Management: Neuropathy

The problem:

- Highly prevalent among patients undergoing chemotherapy (CIPN)
- Exact pathophysiology incompletely understood
- Results from damage to nerves at multiple points
- Tends to improve among most patients over time

First Steps:

- Avoid extreme temperatures
- Consider cold therapy during infusions
- Wear gloves & socks
- Consider PT for patients with gait instability
- Acupuncture for prevention/stabilization of this symptom



*Sites of nerve damage from chemotherapeutic agents.
Wang XM et al. Cytokine 2012.*

2 Integrative Cancer Symptom Management: Neuropathy

Topical Agents: *Capsaicin*

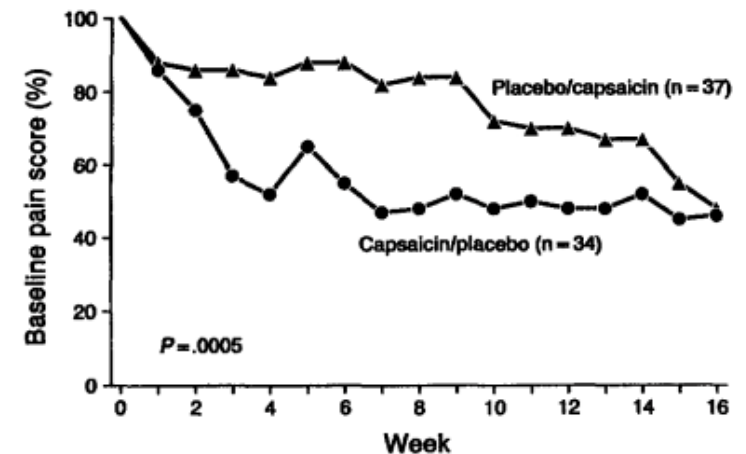
- Phase III, placebo-controlled, randomized crossover trial of capsaicin cream 0.075% vs placebo
- Applied to site of post-surgical pain in cancer patients QID for 8 weeks, followed by crossover
- Capsaicin initially a/w more skin burning, redness, & coughing ($p < 0.0001$ for each)
- Capsaicin arm: significant improvement in pain control after 8 weeks (53% vs 17% reduction, $p = 0.01$)
- Patients preferred capsaicin to placebo by 3:1 margin ($p = 0.001$)

Supplements:

- *2013 Systematic Review*: L-Carnitine, glutamine, vitamin E, glutathione, vitamin B6, Omega-3 fatty acids, magnesium, calcium, alpha-lipoic-acid, N-acetylcysteine
- *Conclusion*: "Currently no agent has shown solid beneficial evidence to be recommended for the treatment or prophylaxis of CIPN"

Acupuncture:

- *2017 Cochrane Systematic Review*: Insufficient evidence to determine efficacy
- Anecdotally, often helpful for *prevention* of CIPN. Recommend starting early during treatment, along with cold therapy.



Changes from baseline pain scores for two study groups .
Ellison N et al. J Clin Oncol 1997.

2 Integrative Cancer Symptom Management

A Case Study:

Mr. H is a 67 y.o. male former smoker (50 pack-year history) w/PMH of COPD (not on home oxygen), and cT4N2(4R)M0 AJCC Stage IIIB squamous cell carcinoma of the right upper lobe who is currently undergoing radiation therapy to the R lung (planned for a total of 60 Gy in 30 fractions) alongside concurrent carboplatin/taxol.

He presents to the UCSF Osher Center to get help with the following symptoms:

- Extreme tiredness all day, despite sleeping well at night
- Poor appetite with associated weight loss
- Burning and tingling in both feet
- **Significant anxiety related to cancer diagnosis**

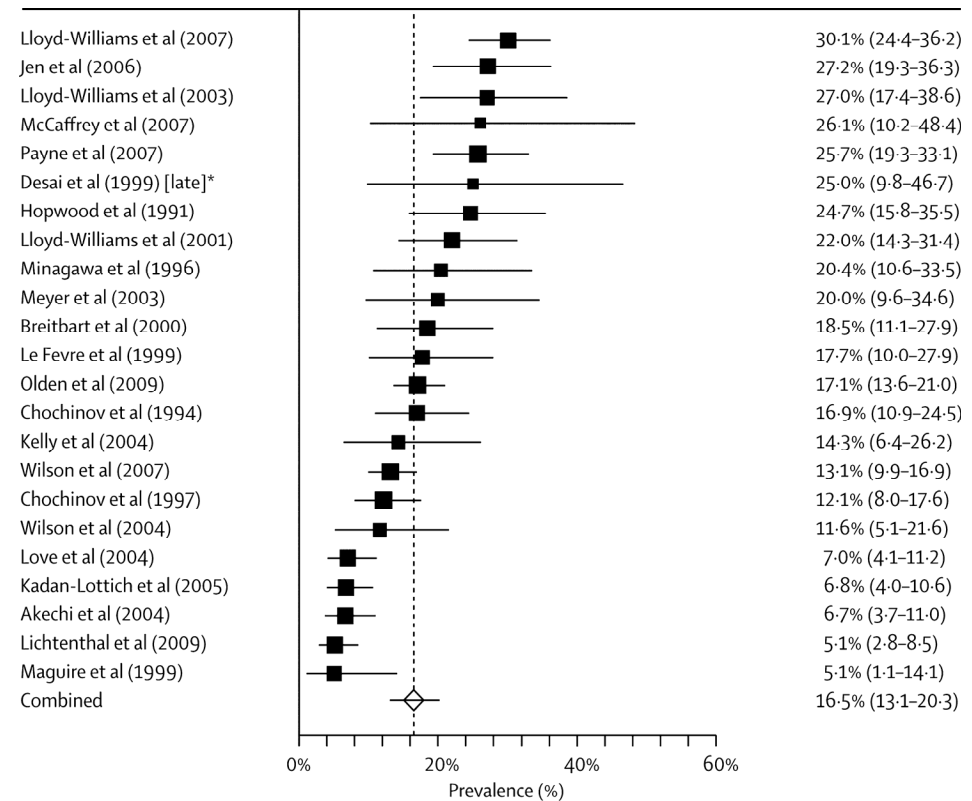
2 Integrative Cancer Symptom Management: Psychological Distress

The problem:

- Includes adjustment disorder, anxiety, depression, PTSD
- Affects nearly 40% of patients with cancer
- Often requires multiple modalities for effective treatment:
 - Pharmacologic Therapy
 - Counseling
 - Support Groups
 - Mind-Body Interventions
 - Supplements

First Steps

- Screen for red flag signs/symptoms
- Discuss referral for counseling (services available through Psycho-Oncology & Osher Center)



Pooled prevalence of depression among patients with advanced cancer.

Mitchell AJ et al. *Lancet Oncol* 2011.

2 Integrative Cancer Symptom Management: Psychological Distress

- Grief, distress, anxiety, & depression are all common challenges after cancer diagnosis
- Studies show that many integrative modalities can improve symptoms, including:
 - ~ Meditation/Mindfulness
 - ~ Supportive Counseling
 - ~ Massage Therapy
 - ~ Acupuncture
 - ~ Exercise
- When combined with counseling, psychedelic treatment with psilocybin and/or ketamine can significantly improve anxiety, depression, & sense of peace in the setting of cancer



Ross S et al. *Psychopharm*, 2016
<https://sageintegrativehealth.org/>

2 Integrative Cancer Symptom Management: Psychological Distress



University of California
San Francisco

Mind-Body Medicine:

- *Meditation:*
 - RCT of 90 cancer patients randomized to weekly meditation group (1.5 hrs) vs. wait-list control for 7 weeks
 - Completed two validated questionnaires before & after intervention: Profile of Mood States (POMS) & Symptoms of Stress Inventory (SOSI)
 - Treatment group experienced a 65% reduction in total mood disturbance over 7 weeks, as compared to 12% reduction in controls ($t(88) = -3.20, p < 0.001$)
- *Massage Therapy:*
 - A 2016 systematic review & meta-analysis found significant reduction in anxiety among cancer patients utilizing massage therapy as compared to controls in pooled analysis of 4 RCTs (MD = - 0.50, 95% CI -0.77 to -0.24)
- Evidence also suggests benefit of yoga, acupuncture, guided imagery for cancer-related mood distress, though more research is needed

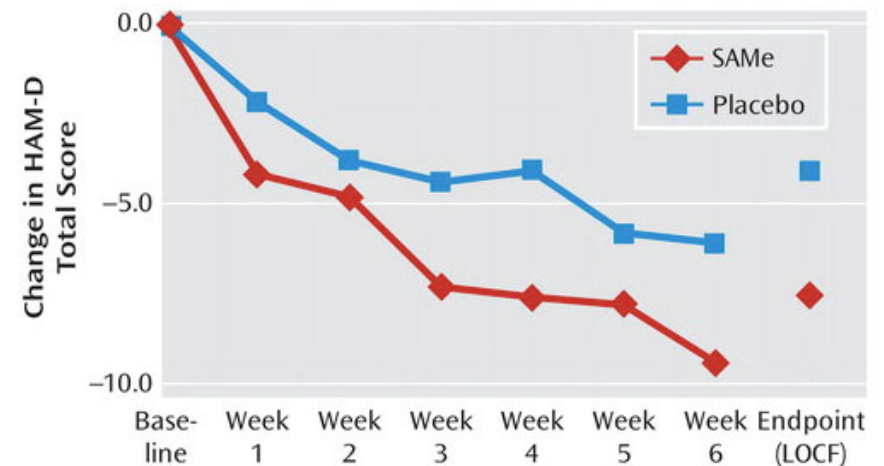
2 Integrative Cancer Symptom Management: Psychological Distress



University of California
San Francisco

Supplements:

- **SAMe:**
 - S-adenosyl methionine (SAMe) is a naturally occurring molecule involved in human cellular metabolism
 - 2010 RCT (73 patients): SAMe superior to placebo as an adjunctive treatment to SSRI in treatment of depression: MD -3.90, 95% CI -6.93 to -0.87; $p = 0.01$
 - 2016 Cochrane review: No difference between TCA or SSRI monotherapy for depression compared to SAMe; fewer side effects with SAMe compared to TCA.
- **CBD:**
 - Associated with anxiolytic effects in both humans and animals
 - A 2010, double-blind RCT of 24 individuals with social anxiety found significant improvement in anxiety symptoms after CBD 600 mg as compared to placebo ($p = 0.009$)
 - More data needed in patients with cancer

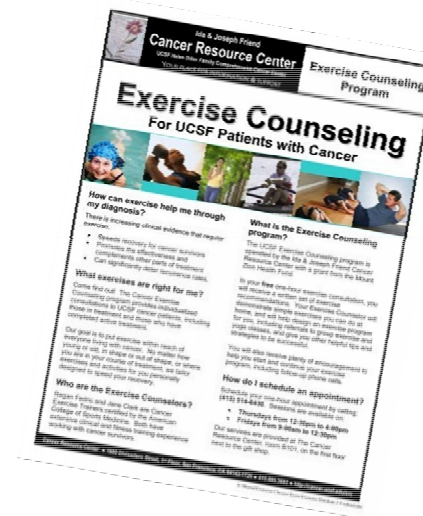


Change in HAM-D scores over 6 weeks among patients randomized to SAMe vs placebo. Papakostas GI et al. *Am J Psychiatry* 2010.

3 Resources for Individuals & Providers: Clinical Services

UCSF Cancer Resource Center:

- Vast array of supportive services for patients in all stages of cancer treatment & recovery
- Events include guest speakers, support groups, classes for patients and caregivers
- Exercise Counseling Service
- Nutrition counseling
- Art for Recovery
- Weekly meditation and guided imagery
- Website: cancer.ucsf.edu/support/crc



UCSF Osher Center for Integrative Medicine:

- Personalized integrative care for patients going through cancer treatment & recovery
- All providers trained in both biomedicine & integrative medicine
- Public classes on integrative health & wellness
- Cancer-related nutrition guide available online
- Website: <http://osher.ucsf.edu>

Hospital-Based Massage Therapy Fellowship

- Founded June 2021
- Led by Carolyn Tague (CMT) & Brieze Bell (MD)
- Free massage therapy available on Wednesdays for inpatients admitted to Parnassus (also Mission Bay and MZ Infusion)
- Place an order by Wednesday morning in Apex (just type “massage” and it will pop up!)

3 Resources for Individuals & Providers: Additional Tools

General Integrative Oncology Lifestyle Support

- Diet: <https://www.rebeccakatz.com/cancer-and-food>
- Lifestyle: <https://www.aicr.org/cancer-survival/>
- Research & Reading: <https://osher.ucsf.edu/patient-care/integrative-medicine-resources/cancer-and-nutrition>

Supplement Quality Control:

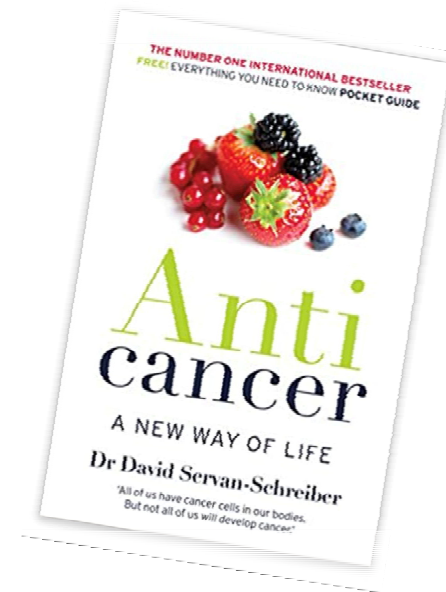
- UCSF Library Natural Medicines Database: <https://naturalmedicines-therapeuticresearch-com.ucsf.idm.oclc.org>
- Consumer Lab: <https://www.consumerlab.com>

Mindfulness Tools:

- Healthy Minds App (free)
- Insight Timer app (free)
- Mindfulness-Based Stress Reduction Course at Osher Center

Acupuncture & Manual Medicine:

- Osher Center acupuncture & massage therapy teams
- Community-based acupuncture
- Massage therapy schools



Psychedelic-Assisted Therapy:

- Polaris: <https://www.polarisinsight.com/>
- Healing Realms: <https://www.healingrealmscenter.com/>
- Sage Institute: <https://sageinst.org/>

Additional References



University of California
San Francisco

- Alfano CM et al. Fatigue, inflammation, and omega-3 and omega-6 fatty acid intake among breast cancer survivors. *J Clin Oncol*. 2012;30(12):1280-7.
- Barton DL et al. Wisconsin ginseng (*panax quinquefolius*) to improve cancer-related fatigue: a randomized, double-blind trial, N07C2. *J Natl Cancer Inst*. 2013;105(16):1230-8.
- Bergamaschi MM et al. Cannabidiol reduces the anxiety induced by simulated public speaking in treatment-naïve social phobia patients. *Neuropsychopharmacology*. 2011;36(6):1219-26.
- Cannabis-in-Cachexia-Study-Group, et al. Comparison of orally administered cannabis extract and delta-9-tetrahydrocannabinol in treating patients with cancer-related anorexia-cachexia syndrome: a multicenter, phase III, randomized, double-blind, placebo-controlled clinical trial from the cannabis-in-cachexia-study-group. *J Clin Oncol*. 2006;24(21):3394-400.
- Ellison N et al. Phase III placebo-controlled trial of capsaicin cream in the management of surgical neuropathic pain in cancer patients. *J Clin Oncol*. 1997;15(8):2974-80.
- Galizia I et al. S-adenosyl methionine (SAmE) for depression in adults. *Cochrane Database Syst Rev*. 2016;10:CD011286.
- Gramignano G et al. Efficacy of l-carnitine administration on fatigue, nutritional status, oxidative stress, and related quality of life in 12 advanced cancer patients undergoing anticancer therapy. *Nutrition*. 2006;22(2):136-45.
- Gullett NP. Nutritional interventions for cancer-induced cachexia. *Curr Probl Cancer*. 2011;35(2):58-90.
- Kraft M et al. L-carnitine-supplementation in advanced pancreatic cancer (CARPAN)—a randomized, multicentre trial. *Nutr J*. 2012;11:52.
- Lee PL et al. Acupoint stimulation, massage therapy and expressive writing for breast cancer: a systematic review and meta-analysis of randomized controlled trials. *Complement Ther Med*. 2016;27:87-101.
- Mitchell AJ et al. Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: a meta-analysis of 94 interview-based studies. *Lancet Oncol* 2011;12(2):160-174.
- Nakano J et al. Effects of aerobic and resistance exercise on physical symptoms in cancer patients: A meta-analysis. *Integr Cancer Ther*. 2018;17(4):1048-1058.
- Papakostas GI et al. S-adenosyl methionine (SAmE) augmentation of serotonin reuptake inhibitors for antidepressant nonresponders with major depressive disorder: a double-blind, randomized clinical trial. *Am J Psychiatry*. 2010;167(8):942-8.
- Schloss JM et al. Nutraceuticals and chemotherapy induced peripheral neuropathy (CIPN): a systematic review. *Clin Nutr*. 2013;32(6):888-93.
- Specia M et al. A randomized, wait-list controlled clinical trial: the effect of a mindfulness meditation-based stress reduction program on mood and symptoms of stress in cancer outpatients. *Psychosom Med*. 2000;62(5):613-22.
- Tian L et al. Effects of aerobic exercise on cancer-related fatigue: a meta-analysis of randomized controlled trials. *Support Care Cancer*. 2016;24(2):L969-983.
- Wu X et al. Effectiveness of acupuncture and related therapies for palliative care of cancer: overview of systematic reviews. *Sci Rep*. 2015;5:16776.