

Integrative Oncology – What oncology clinicians need to know

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Comprehensive Hematology and Oncology Review
University of Washington CME
August 2020

Complementary and Integrative Medicine Use among Cancer Patients and Survivors

High use by cancer patients and survivors

- 17+ million cancer survivors in the US
- 60-80% of US cancer survivors use complementary, alternative and integrative medicine
- \$6.7 Billion spent in 2012

Patient reasons for use

- Increase survival
- Increase efficacy of conventional cancer therapies
- Prevent & treat side effects of conventional therapies
- Treat existing comorbidities
- Improve quality of life
- Decrease stress

**What works?
What doesn't work?
What is safe?**

Definitions

Traditional therapies

- *Culturally-based health practices*

Alternative therapies

- *Used in place of conventional medicine*

Complementary therapies

- *Used with conventional medicine*

Integrative medicine

- *Evidence-based use of complementary and supportive therapies in conjunction with conventional therapies*

What is Integrative Oncology?

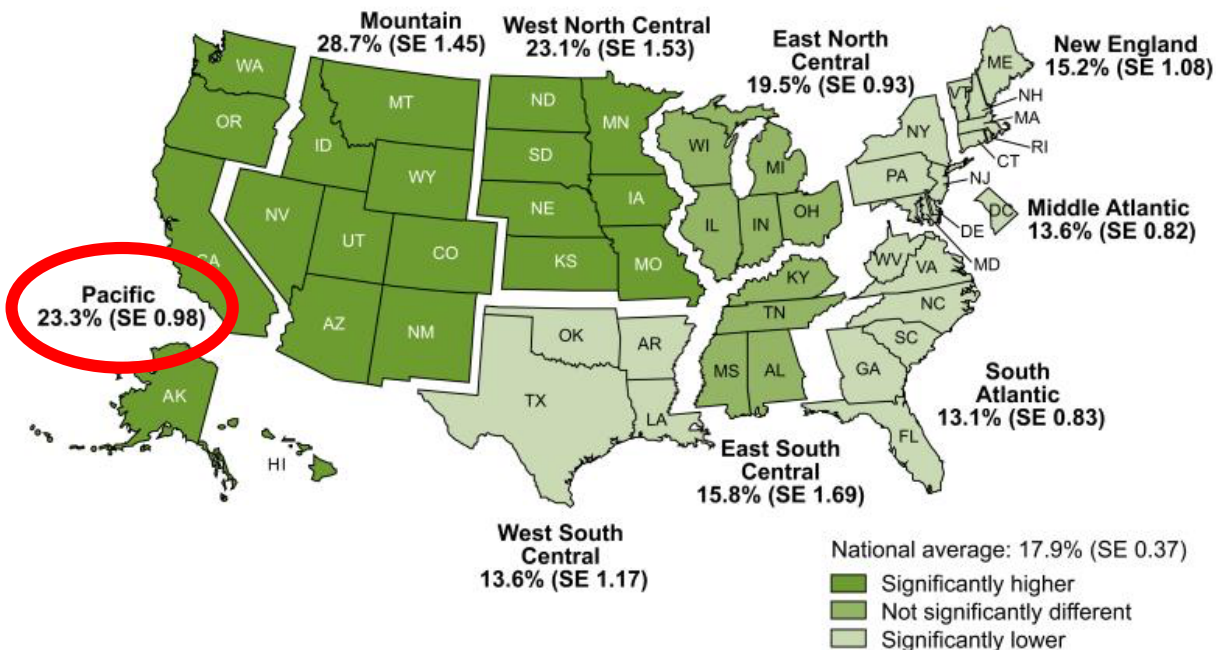
Integrative oncology is a **patient-centered**, evidence-informed field of cancer care that utilizes mind and body practices, natural products, and/or lifestyle modifications from different traditions **alongside conventional cancer treatments**.

Integrative oncology aims to **optimize health, quality of life, and clinical outcomes** across the cancer continuum and to empower people to prevent cancer and become active participants before, during and beyond cancer treatment.

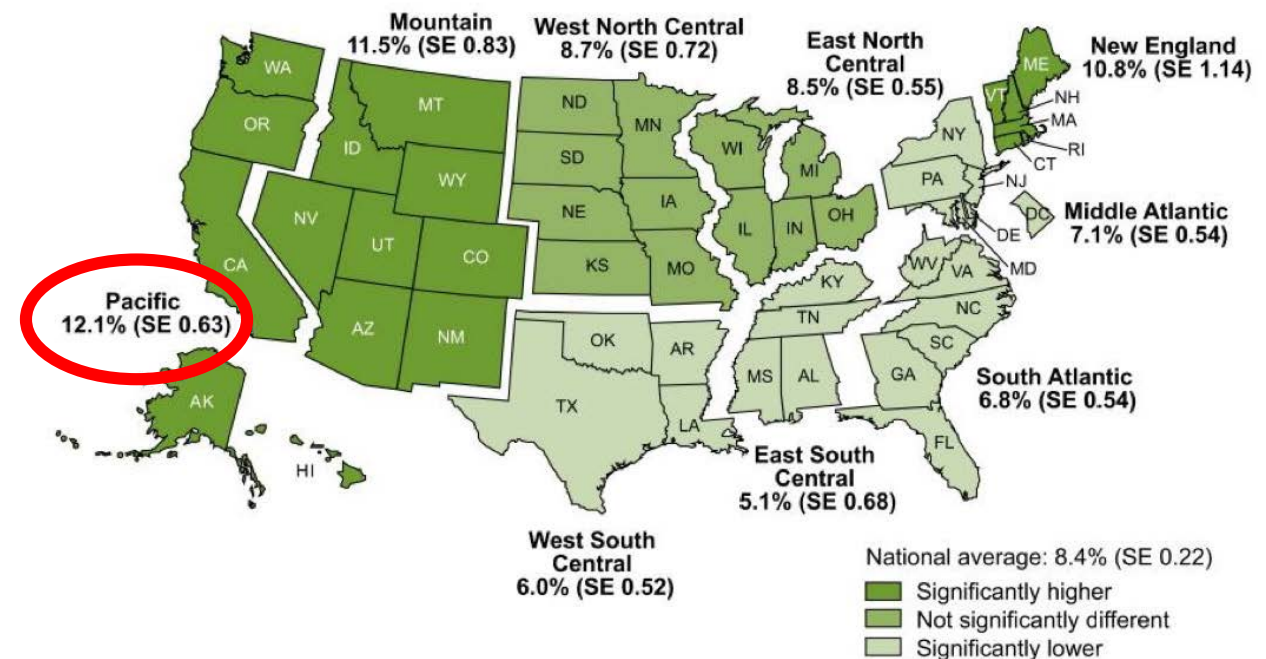
**Using cohort studies to examine
predictors, patterns and outcomes of use**

Use of complementary health approaches in US adults

Use of non-vitamin, non-mineral dietary supplements



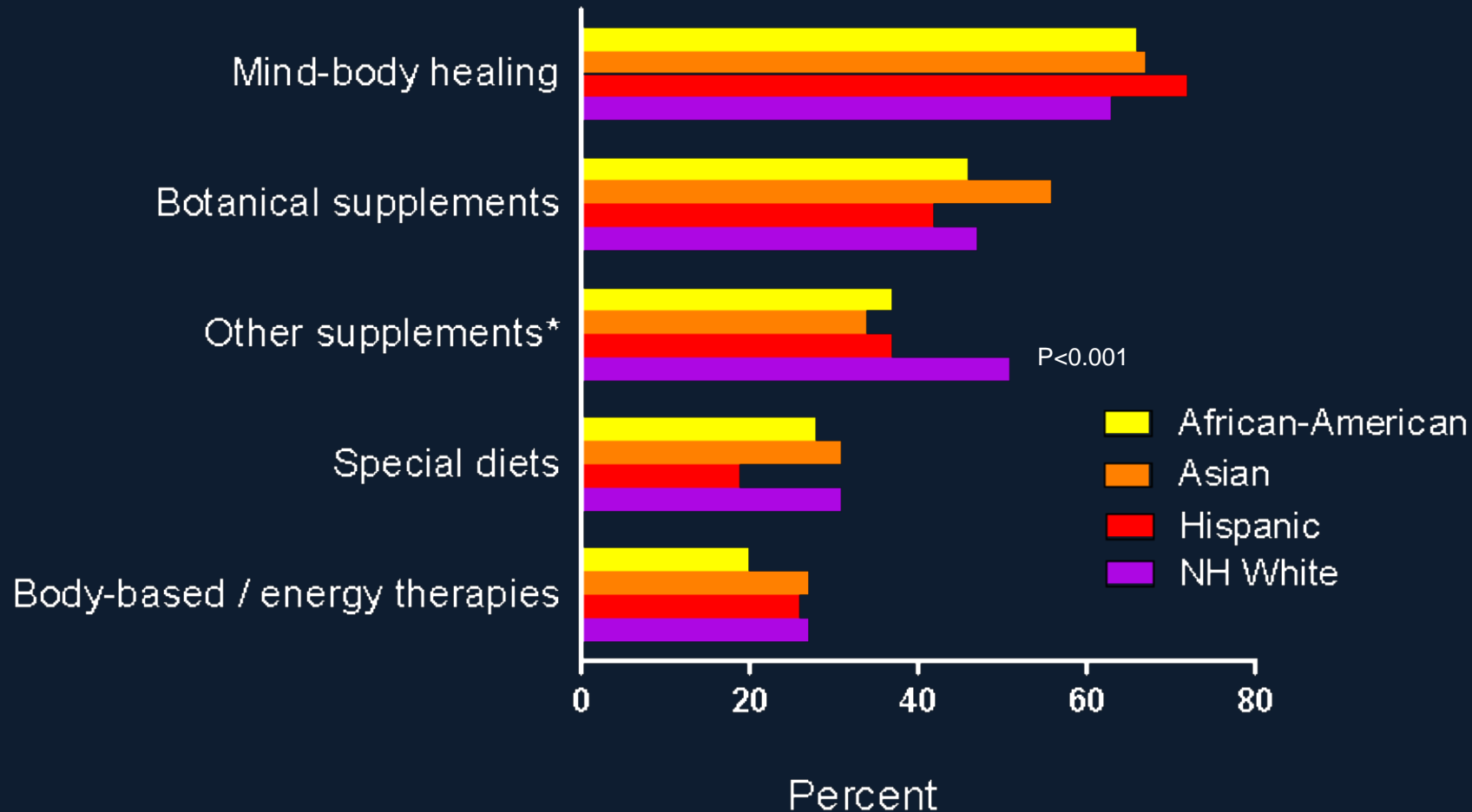
Use of yoga and meditation



CAM use in newly diagnosed Br CA patients

Kaiser Permanente Northern California Pathways Study (n=1,000)

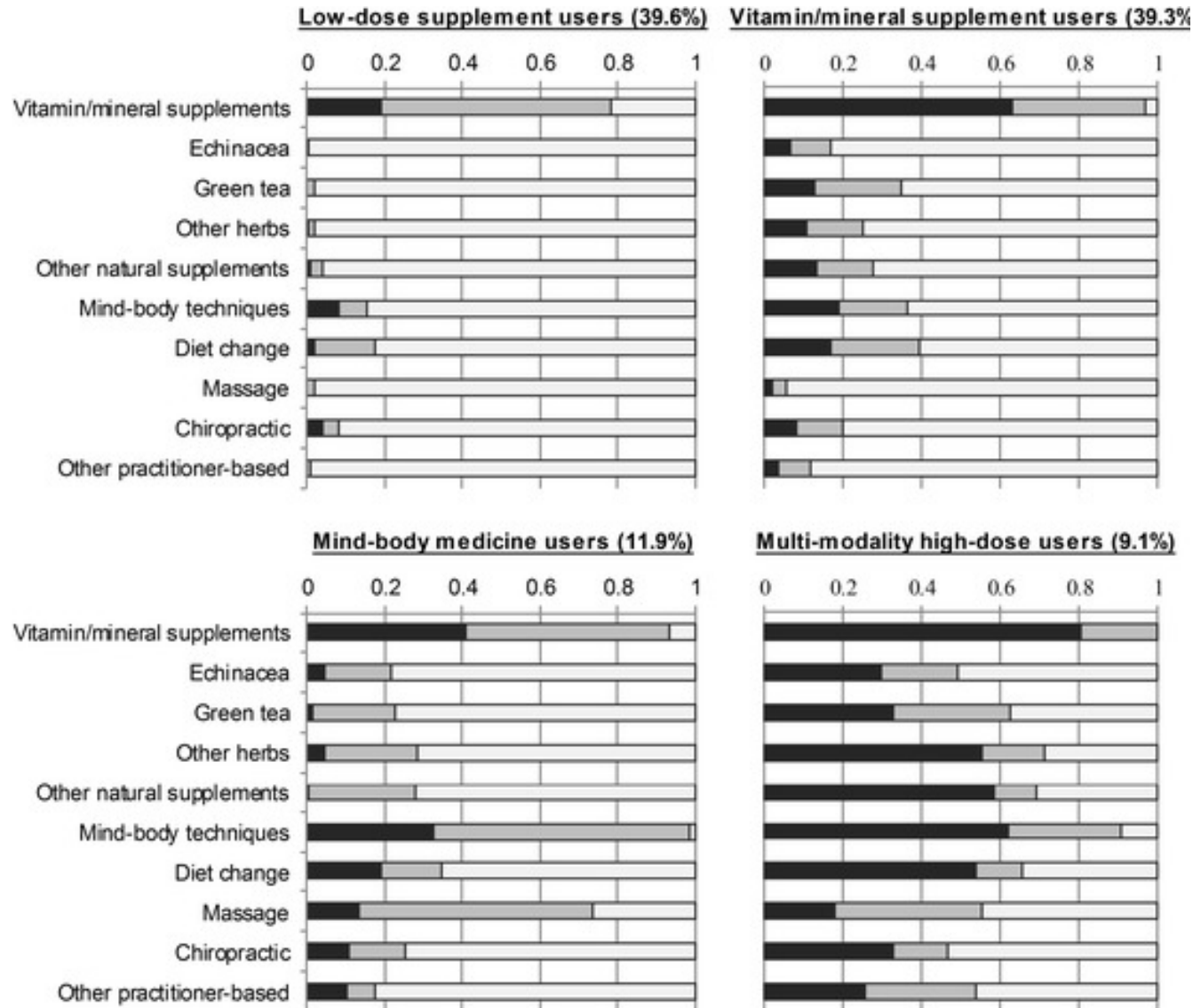
PI: Kushi, R01CA105274



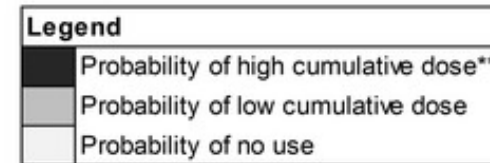
*non-botanical, non-vitamin

Greenlee *Br Cancer Res Treat* 2009

Latent class analysis: Probability of CAM use



Long Island Breast Cancer Study Project (n=764)
PI: M Gammon, UNC



Complementary & Alternative Medicine Use by US Cancer Survivors

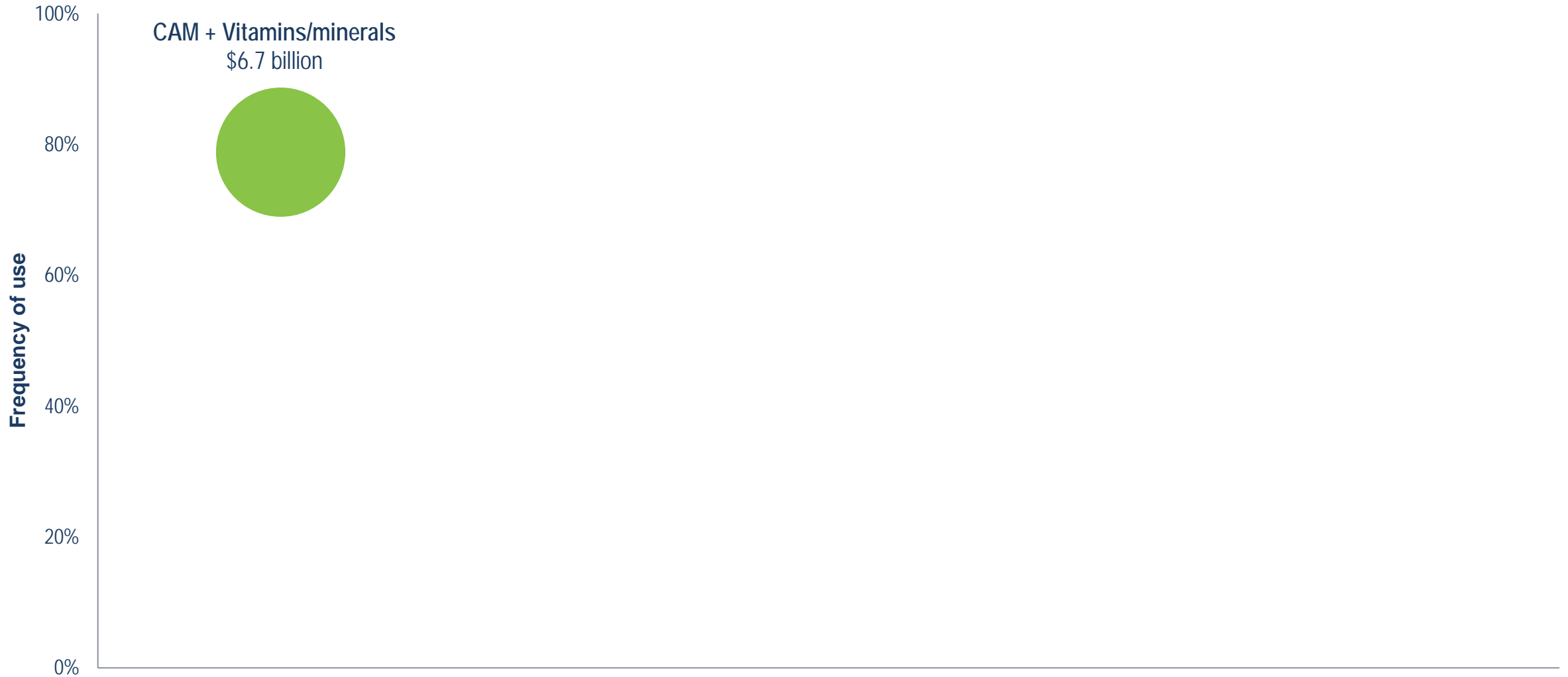
US National Health Interview Survey (NHIS)

- Annual survey by CDC
- Questions on CAM use since 2002

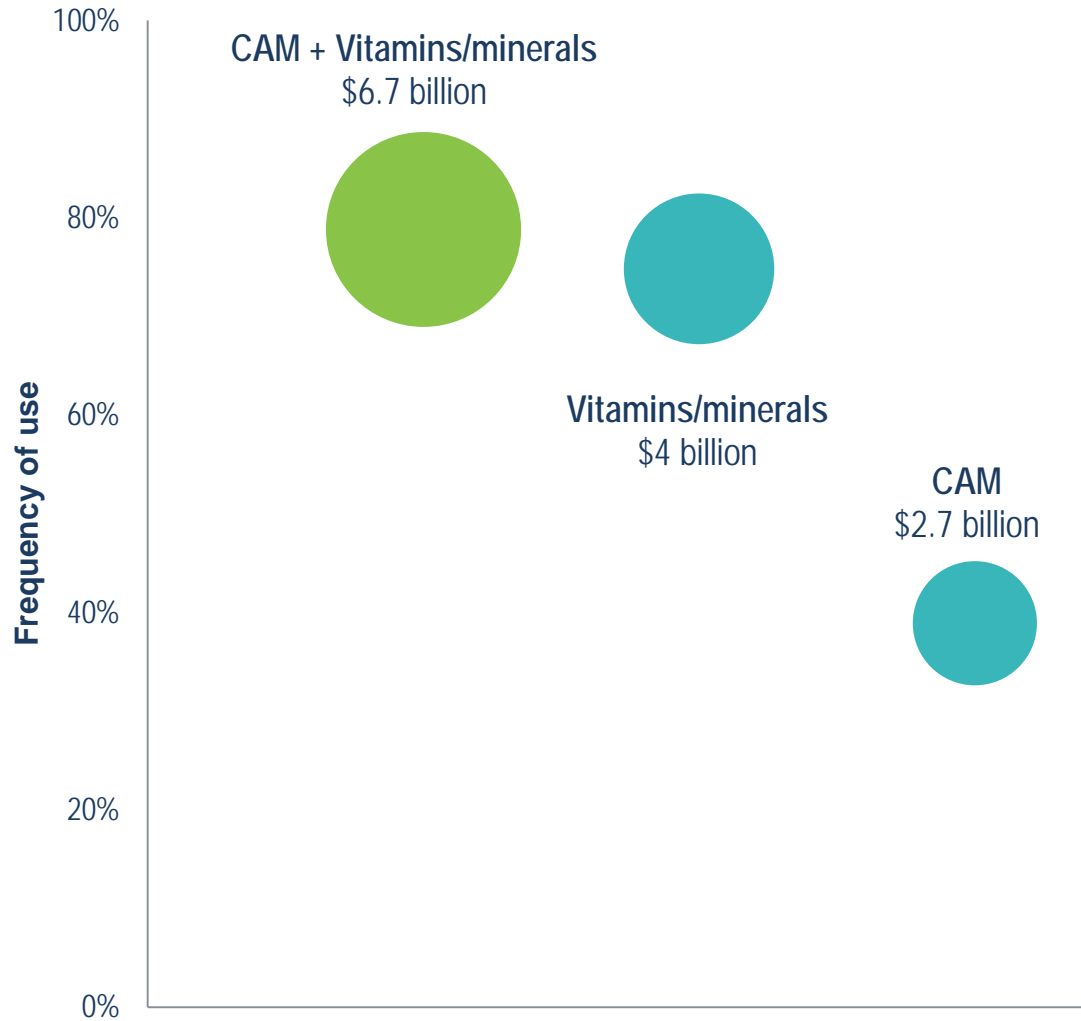
NHIS 2012

- 2,977 adult cancer survivors and 30,551 non-cancer adults
- Self-reported CAM use in past 12 months
- **79%** of cancer survivors used ≥ 1 vitamin/mineral and/or CAM modality

Cost of CAM Use by US Cancer Survivors

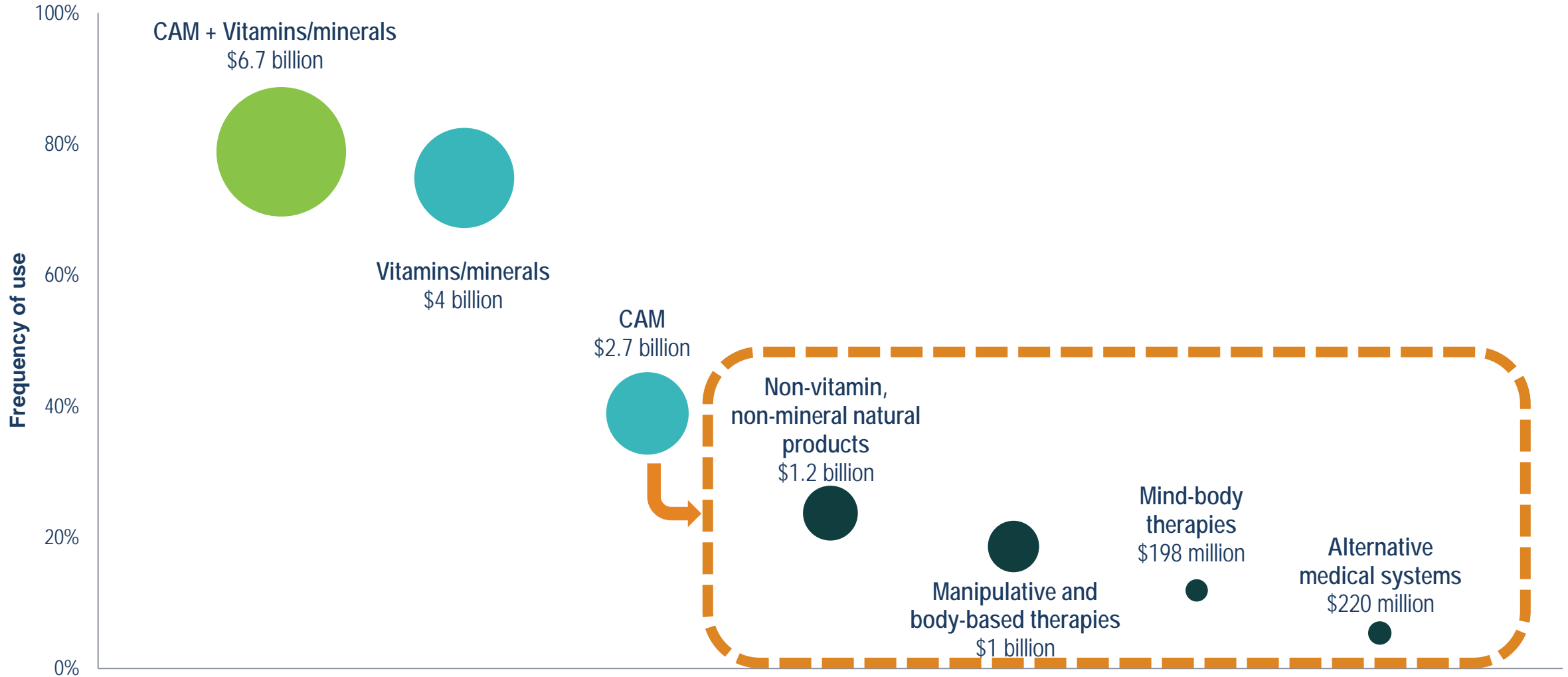


Cost of CAM Use by US Cancer Survivors



Annual expenditure by US cancer survivors (2012)

Cost of CAM Use by US Cancer Survivors



Annual expenditure by US cancer survivors (2012)

Breast Cancer Quality of Life (BQUAL) Study

Aim: To examine association of CAM use with breast cancer chemotherapy initiation

Setting

- Multi-center prospective cohort study of early stage invasive breast cancer patients
- Recruitment sites: New York (Columbia), N California (KPNC), Detroit (Henry Ford)

Methods

- Assessed baseline CAM use (2006-2010):
 - **Dietary supplements** (n=3 types): vitamin/minerals, botanicals, other products
 - **Mind-body** (n=2 types): mind-body based, and body/energy based treatments
 - **CAM use index:** sum of CAM use (1 point for each type, range 0-5)
- Data collection on clinical characteristics and treatment received
- Used NCCN guidelines/dates to determine if clinically indicated treatment was initiated
- Analyses included women <70 years eligible to receive chemotherapy (n=685)

Results: CAM & Chemotherapy Initiation

CAM use at baseline

- **87%** of women reported current CAM use; **38%** reported current use of ≥ 3 modalities

Chemotherapy initiation of clinically indicated treatment

- **89%** initiated chemotherapy; **11%** did not initiate chemotherapy

Association between CAM use and chemo initiation

- Dietary supplement users less likely to initiate (**OR=0.16, 95% CI: 0.03-0.51**)
- High CAM index score less likely to initiate (**OR per unit CAM index=0.64, 95% CI: 0.46-0.87**)
- Mind-body practices not associated with chemotherapy initiation

Antioxidant use since diagnosis & Br CA outcomes

LACE Cohort (n=1,829 antioxidant users)

	All Cause Death HR (95% CI)*	Death from BC HR (95% CI)*	BC Recurrence HR (95% CI)*
Multivitamins			
No Use	Ref	Ref	Ref
Frequent use	1.0 (0.7-1.4)	0.8 (0.5-1.3)	0.9 (0.6-1.3)
Vitamin C alone			
No use	Ref	Ref	Ref
Frequent use	0.8 (0.6-1.1)	0.9 (0.6-1.3)	0.7 (0.6-0.9)
Vitamin E alone			
No use	Ref	Ref	Ref
Frequent use	0.8 (0.6-1.0)	0.9 (0.6-1.3)	0.7 (0.6-1.0)
Combination carotenoids			
No use	Ref	Ref	Ref
Frequent use	1.8 (1.1-2.7)	2.1 (1.2-3.6)	1.3 (0.8-2.2)

*Adjusted for age at diagnosis, race/ethnicity, education, stage at diagnosis, # positive lymph nodes, hormone receptor status, chemotherapy, radiation therapy, hormonal therapy, BMI, smoking, alcohol, physical activity, fruits/vegetables, and comorbidity score at enrollment.

Effects of integrative therapies on decreasing treatment toxicities

Effects of dietary supplements on toxicities

Aromatase inhibitor induced arthralgias in breast cancer patients

- Glucosamine & Chondroitin / Phase II single arm → Null (Greenlee *Support Care Cancer* 2013)
- Fish Oil / RCT SWOG S0927 → Null (Hershman *J Clin Oncol* 2015)

Chemotherapy-induced peripheral neuropathy in breast cancer patients

- Acetyl-L-Carnitine / RCT SWOG S0715 → Harmful (Hershman *J Clin Oncol* 2013)

Anthracycline-induced cardiotoxicity in breast cancer patients

- Coenzyme Q10 / Phase I dose-finding trial → Closed early (unpublished)

Hepatic function in liver cancer patients

- Milk thistle / Phase I dose-finding trial → Closed early (Siegel *Integr Cancer Ther* 2014)

JAMA | **Original Investigation**

Effect of Acupuncture vs Sham Acupuncture or Waitlist Control on Joint Pain Related to Aromatase Inhibitors Among Women With Early-Stage Breast Cancer

A Randomized Clinical Trial

Dawn L. Hershman, MD, MS; Joseph M. Unger, PhD, MS; Heather Greenlee, ND, PhD; Jillian L. Capodice, MS, LAc; Danika L. Lew, MA; Amy K. Darke, MS; Alice T. Kengla, MD; Marianne K. Melnik, MD; Carla W. Jorgensen, MD; William H. Kreisle, MD; Lori M. Minasian, MD; Michael J. Fisch, MD; N. Lynn Henry, MD; Katherine D. Crew, MD, MS

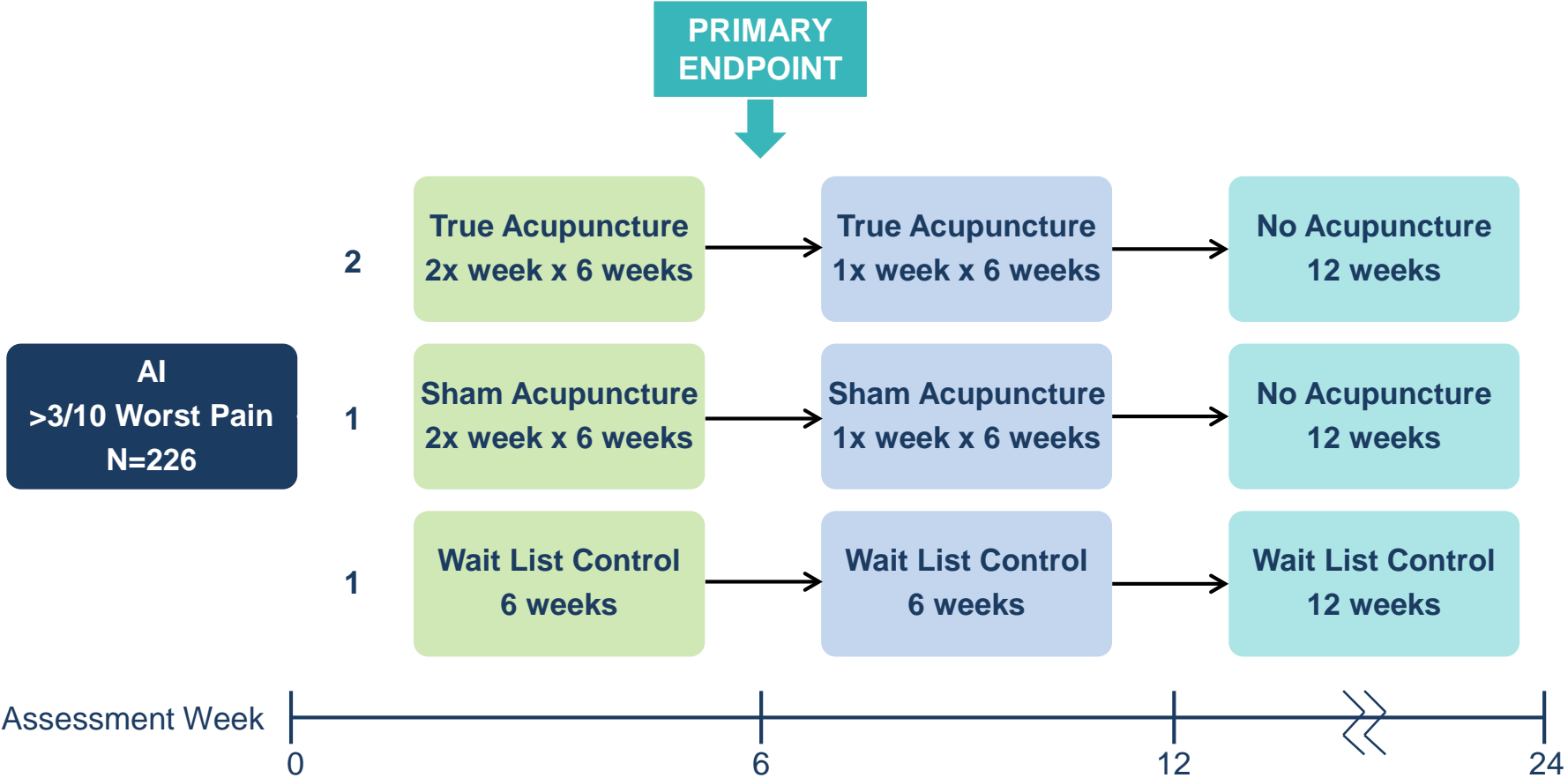
IMPORTANCE Musculoskeletal symptoms are the most common adverse effects of aromatase inhibitors and often result in therapy discontinuation. Small studies suggest that acupuncture may decrease aromatase inhibitor–related joint symptoms.

OBJECTIVE To determine the effect of acupuncture in reducing aromatase inhibitor–related joint pain.

 [Supplemental content](#)

 [Related article at
jamaoncology.com](#)

S1200 Study design

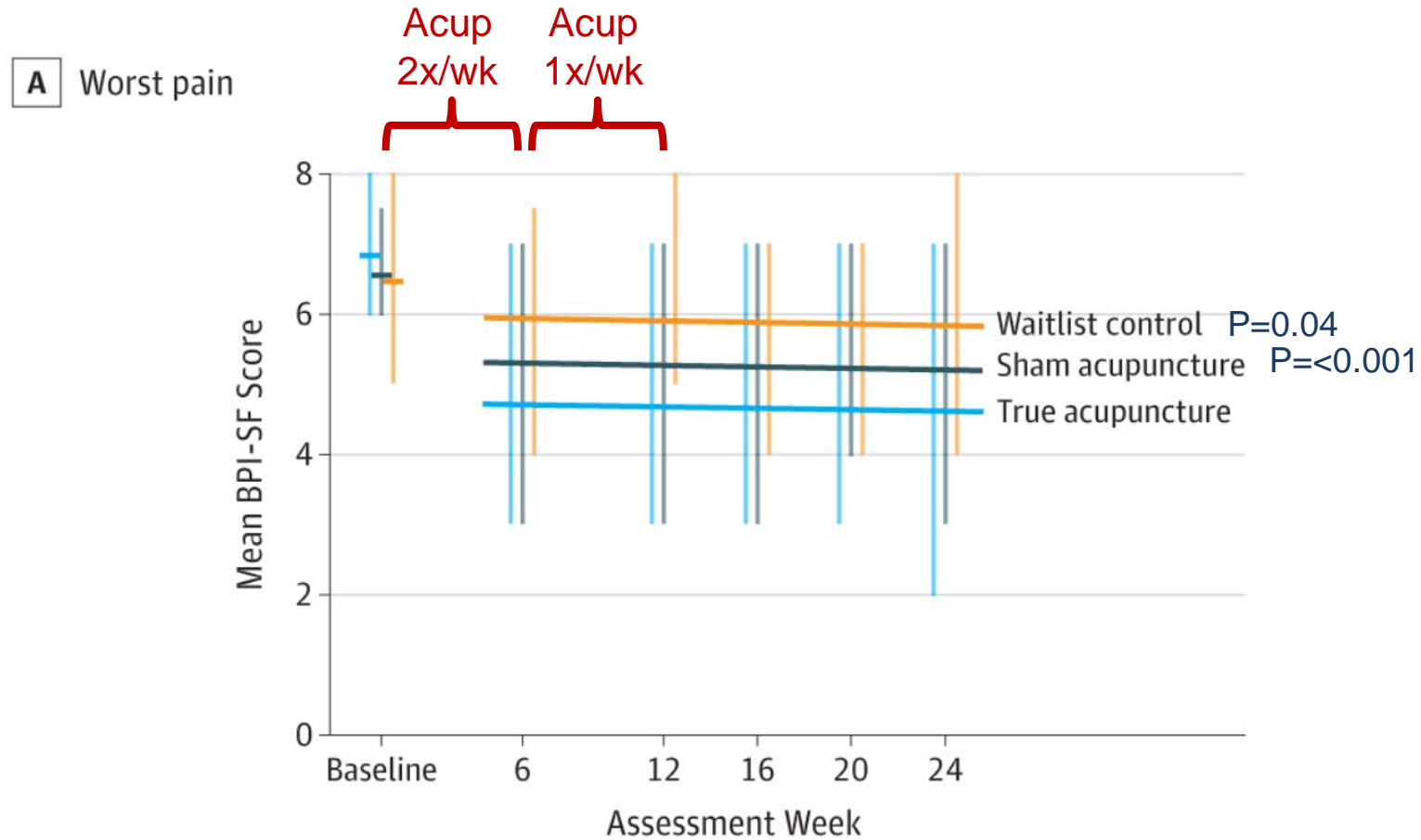


Acupuncturist training

- Interventions provided by licensed acupuncturists (n=60) at 11 sites
- In-person / on-site acupuncturist training
- Online training modules
 - Videos
 - Visuals acupoint location
- Training manuals
- Monthly teleconference
- Annual quality assurance
 - Quality assurance training
 - Web-based quiz
 - Practical demonstration – video-based (Skype or Recorded)

Randomized Blinded Sham- & Waitlist-Controlled Trial of Acupuncture for Joint Symptoms Related to Aromatase Inhibitors in Women with Early Stage Breast Cancer (SWOG S1200)

Linear Mixed Model Results



No. of patients

Waitlist control	56	51	51	48	45	50
Sham acupuncture	59	54	54	53	52	54
True acupuncture	109	100	101	94	97	97

January 2020 – CMS covers acupuncture for back pain



Centers for Medicare & Medicaid
Services

Press release

CMS finalizes decision to cover Acupuncture for Chronic Low Back Pain for Medicare beneficiaries

Jan 21, 2020 | Coverage, Opioids

Today the Centers for Medicare & Medicaid Services (CMS) finalized a decision to cover acupuncture for Medicare patients with chronic low back pain. Before this final National Coverage Determination (NCD) reconsideration, acupuncture was nationally non-covered by Medicare. CMS conducted evidence reviews and examined the coverage policies of private payers to inform today's decision.

“We are dedicated to increasing access to alternatives to prescription opioids and believe that covering acupuncture for chronic low back pain is in the best interest of Medicare patients.”

CMS Principal Deputy Administrator of
Operations and Policy Kimberly Brandt

Developing clinical practice guidelines

OUR MISSION:

TO ADVANCE EVIDENCE BASED, COMPREHENSIVE,
INTEGRATIVE HEALTHCARE TO IMPROVE THE LIVES
OF PEOPLE AFFECTED BY CANCER.



SIO 2020 Virtual Conference is October 16-17, 2020

Please visit our [Conference Home Page](#) for more information and to register.

SIO Offers Membership Scholarship

SIO is pleased to offer 2020 membership scholarships for patient advocates, trainees and students. Please visit [this link](#) to learn more.

Navajo Nation's Regional Healthcare Facility Needs Our Help

The current COVID-19 pandemic has acutely affected the Navajo Nation, which lives in a region spanning parts of Arizona, Utah and New Mexico. Historically, the Navajo People have suffered high rates of diabetes, cardiovascular disease and cancer, all of which contribute to increased risk for poorer COVID-19 outcomes.

For decades, tribal land has been left without basic infrastructure such as running water, electricity and

Events Calendar

Oct 16	SIO 2020 Virtual Conference
Sep 24	SIO 2021 18th International Conference

Interventions of Interest

Natural products (e.g., botanicals, vitamins, minerals)

Mind-body practices

Meditation

Yoga

Hypnosis

Imagery/Relaxation

Creative Therapies

Stress Management

Tai Chi/Qigong

Acupuncture/acupressure/electro-acupuncture

Massage therapy

Whole systems (e.g., naturopathy, traditional Chinese medicine)

* Due to previous reviews by ACS, AICR, and the American College of Sports Medicine, did not include: Diet, Physical Activity, Energy Balance



Clinically relevant outcomes of interest

Fatigue

Gastrointestinal

Gynecological

Hematological

Lymphedema

Neurological

Neuromuscular

Psychological

Quality of life

Vasomotor symptoms

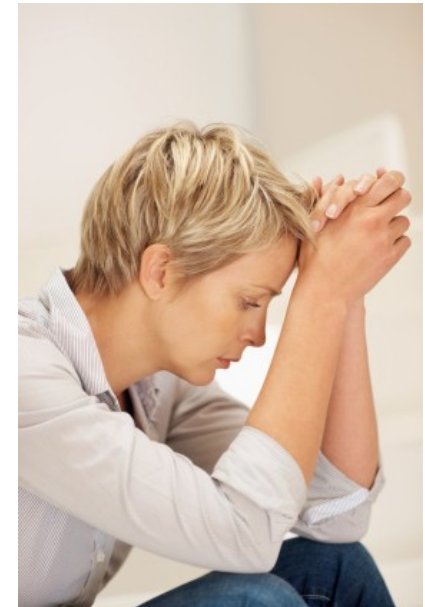
Skin

Renal

Sleep

Pain

Note: Immune parameters were not included





Clinical Practice Guidelines on the Evidence-Based Use of Integrative Therapies During and After Breast Cancer Treatment

Heather Greenlee, ND, PhD, MPH^{1,2}; Melissa J. DuPont-Reyes, MPH, MPhil³; Lynda G. Balneaves, RN, PhD⁴; Linda E. Carlson, PhD⁵; Misha R. Cohen, OMD, LAc^{6,7}; Gary Deng, MD, PhD⁸; Jillian A. Johnson, PhD⁹; Matthew Mumber, MD¹⁰; Dugald Seely, ND, MSc^{11,12}; Suzanna M. Zick, ND, MPH^{13,14}; Lindsay M. Boyce, MLIS¹⁵; Debu Tripathy, MD¹⁶

CME

CNE

¹Assistant Professor, Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY; ²Member, Herbert Irving Comprehensive Cancer Center, Columbia University, New York, NY; ³Doctoral Fellow, Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY; ⁴Associate Professor, College of Nursing, Rady Faculty of Health Sciences, Winnipeg, MB, Canada; ⁵Professor, Department of Oncology, University of Calgary, Calgary, AB, Canada; ⁶Adjunct Professor, American College of Traditional Chinese Medicine at California Institute of Integral Studies, San Francisco, CA; ⁷Clinic Director, Chicken Soup Chinese Medicine, San Francisco, CA; ⁸Medical Director, Integrative Oncology,

Abstract: Patients with breast cancer commonly use complementary and integrative therapies as supportive care during cancer treatment and to manage treatment-related side effects. However, evidence supporting the use of such therapies in the oncology setting is limited. This report provides updated clinical practice guidelines from the Society for Integrative Oncology on the use of integrative therapies for specific clinical indications during and after breast cancer treatment, including anxiety/stress, depression/mood disorders, fatigue, quality of life/physical functioning, chemotherapy-induced nausea and vomiting, lymphedema, chemotherapy-induced peripheral neuropathy, pain, and sleep disturbance. Clinical practice guidelines are based on a systematic literature review from 1990 through 2015. Music therapy, meditation, stress management, and yoga are recommended for anxiety/stress reduction. Meditation, relaxation, yoga, massage, and music therapy are recommended for depression/mood disorders. Meditation and yoga are recommended to improve quality of life. Acupressure and acupuncture are recommended for reducing chemotherapy-induced nausea and vomiting. Acetyl-L-carnitine is not recommended to prevent chemotherapy-

Integrative Therapies During and After Breast Cancer Treatment: ASCO Endorsement of the SIO Clinical Practice Guideline

Gary H. Lyman, Heather Greenlee, Kari Bohlke, Ting Bao, Angela M. DeMichele, Gary E. Deng, Judith M. Fouladbakhsh, Brigitte Gil, Dawn L. Hershman, Sami Mansfield, Dawn M. Mussallem, Karen M. Mustian, Erin Price, Susan Rafté, and Lorenzo Cohen

Author affiliations and support information (if applicable) appear at the end of this article.

Published at jco.org on June 11, 2018.

G.H.L. and L.C. were Expert Panel co-chairs.

Clinical Practice Guideline Committee Approved: March 8, 2018.

Editor's note: This American Society of Clinical Oncology (ASCO) Clinical Practice Guideline provides recommendations, with the understanding that individual

A B S T R A C T

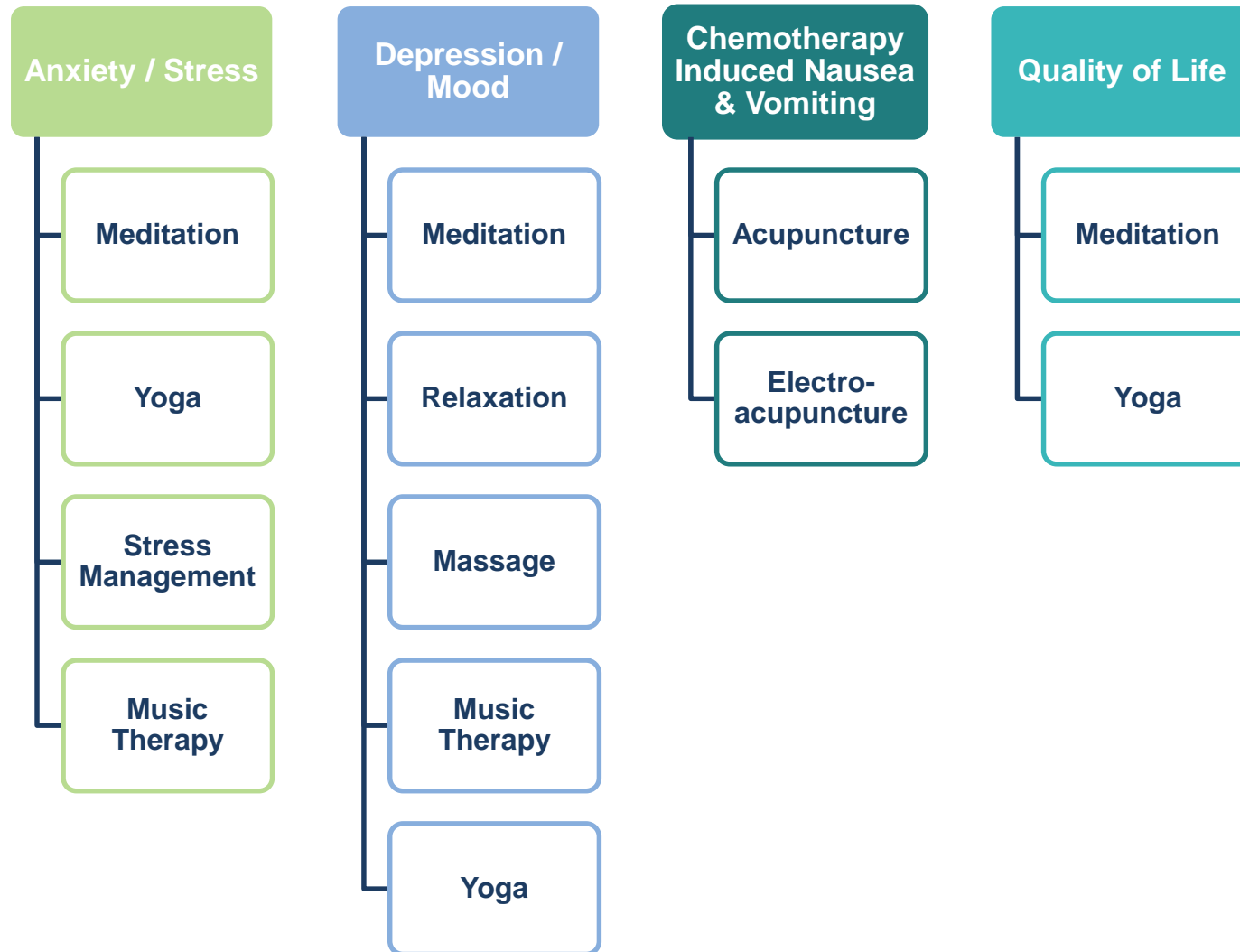
Purpose

The Society for Integrative Oncology (SIO) produced an evidence-based guideline on use of integrative therapies during and after breast cancer treatment that was determined to be relevant to the American Society of Clinical Oncology (ASCO) membership. ASCO considered the guideline for endorsement.

Methods

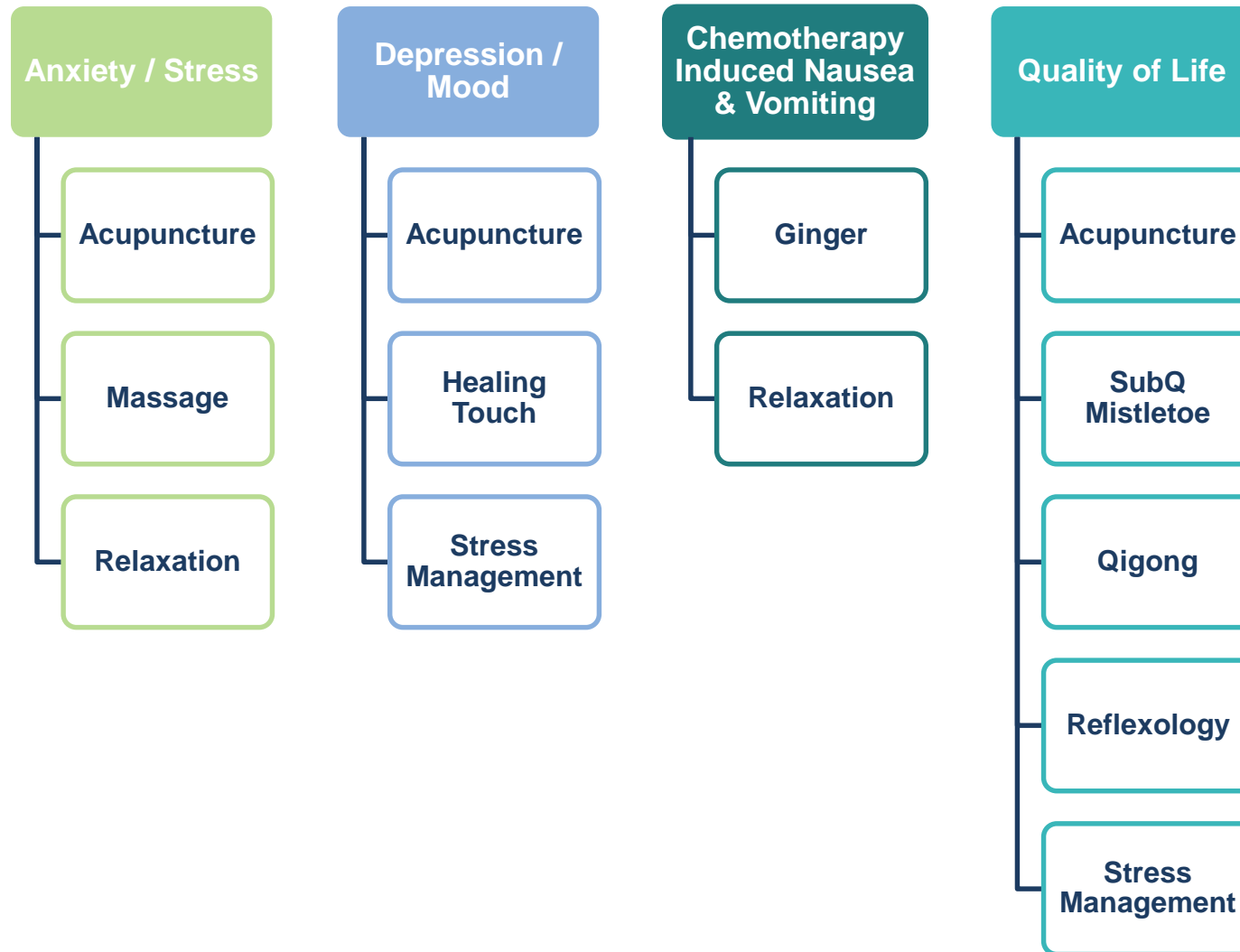
The SIO guideline addressed the use of integrative therapies for the management of symptoms and adverse effects, such as anxiety and stress, mood disorders, fatigue, quality of life, chemotherapy-induced nausea and vomiting, lymphedema, chemotherapy-induced peripheral neuropathy, pain, and sleep disturbance. Interventions of interest included mind and body practices, natural products,

Recommended Therapies



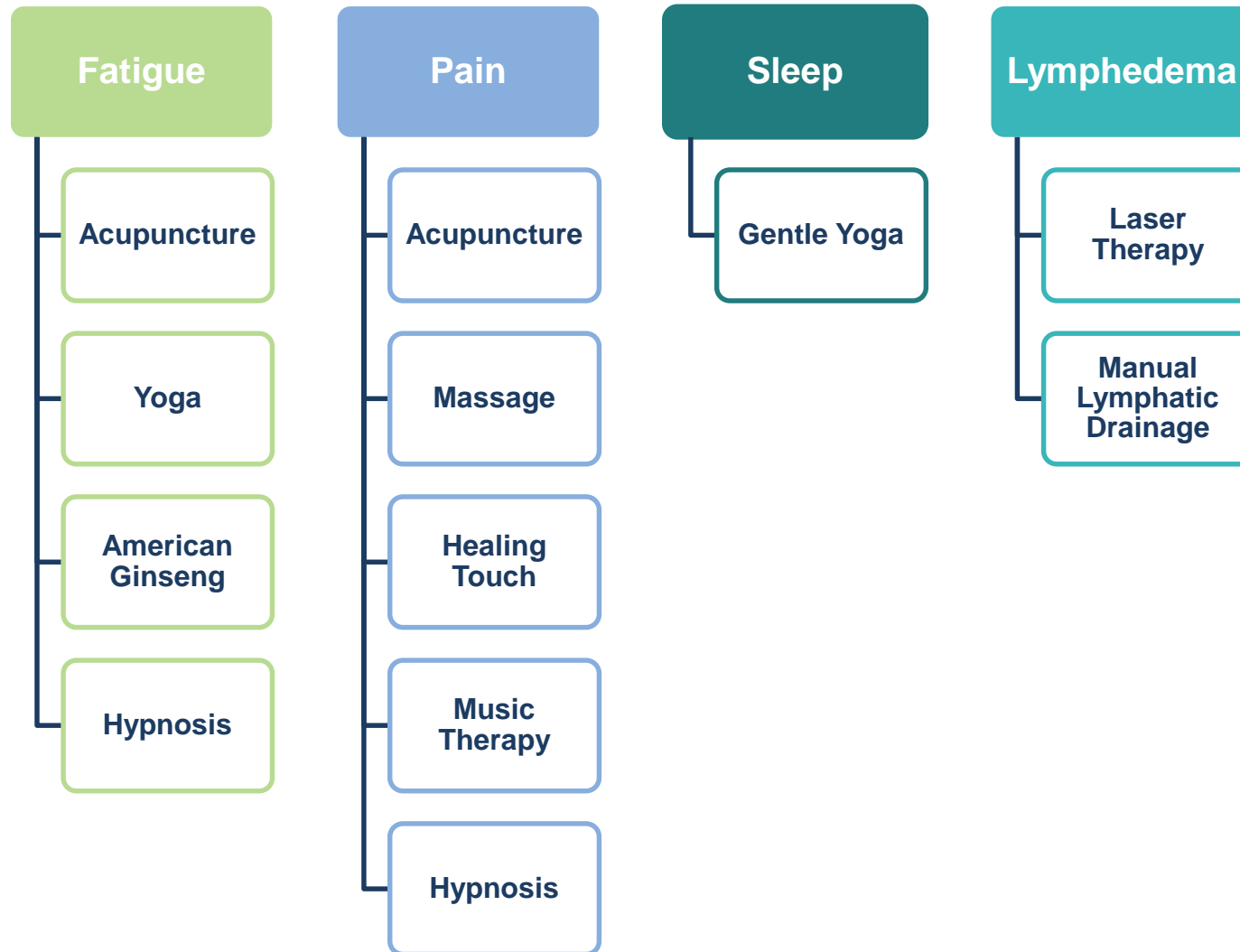
High certainty that the net benefit is substantial or moderate to substantial

Therapies to Consider



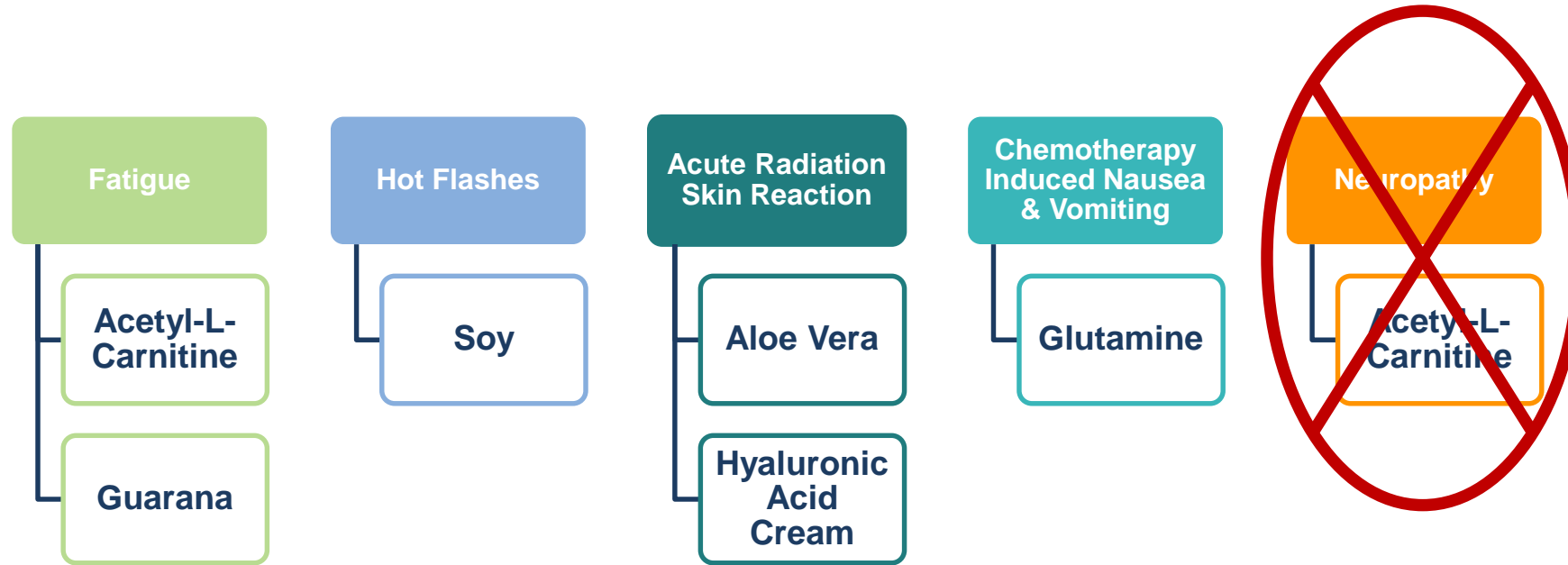
At least ***moderate certainty*** that the net benefit is small

Therapies to Consider



*At least **moderate certainty** that the net benefit is small*

Therapies with *No Benefit* or Harm



Not recommended due to *no benefit or harm*

Integrative Therapies During and After Breast Cancer Treatment: ASCO Endorsement of the SIO Clinical Practice Guideline

ASCO endorses the SIO guideline, Clinical Practice Guidelines on the Evidence-Based Use of Integrative Therapies During and After Breast Cancer Treatment, with some added discussion points.

ASCO Discussion Point 1: The Grade B recommendations for **acupressure and electroacupuncture** differ from the 2017 ASCO antiemetic guideline, which states that evidence remains insufficient for a recommendation for or against complementary therapies for chemotherapy-induced nausea and vomiting. The ASCO Expert Panel feels that Grade C would be more appropriate given the limitations of the available evidence.

ASCO Discussion Point 2: The safety and efficacy of **ginseng** may vary by type of ginseng, and patients should seek guidance from a health care professional before using a dietary supplement. Some ginseng preparations may have estrogenic properties. The ginseng studies cited by the SIO guideline used American ginseng (*Panax quinquefolius*) that was tested for quality and potency; the duration of treatment in these studies was short (8 weeks), and the safety and efficacy of ginseng over longer periods remains uncertain.

ASCO Discussion Point 3: The **mistletoe** trials cited by the SIO guideline evaluated subcutaneous delivery only. Subcutaneous mistletoe is not currently approved by the US Food and Drug Administration. Orally available mistletoe is available in the United States, but ingestion of high doses of mistletoe berry or leaf is known to cause serious adverse reactions.

Conclusions - clinical practice guidelines

- Guidelines improve the ability for patients and clinicians to make healthcare decisions
- Body of evidence supports routine use of selected integrative therapies in the oncology setting
- Recommended clinical practice regarding CAM use:
 - CAM use needs to be discussed upfront and monitored
 - Patients need to be advised about evidence
- Clinical practice guidelines provide an aid to making complex clinical decisions
- SIO aims to be the leader in developing trustworthy guidelines focused on integrative oncology

Identifying effective strategies to improve diet, physical activity & weight management



Effects of Exercise on Health-Related Outcomes in Those with Cancer

What can exercise do?

- **Prevention of 7 common cancers***


Dose: 2018 Physical Activity Guidelines for Americans: 150-300 min/week moderate or 75-150 min/week vigorous aerobic exercise

- **Survival of 3 common cancers****

Dose: Exact dose of physical activity needed to reduce cancer-specific or all-cause mortality is not yet known; Overall more activity appears to lead to better risk reduction

*bladder, breast, colon, endometrial, esophageal, kidney and stomach cancers

**breast, colon and prostate cancers

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
Moderate Evidence			
Bone health	Insufficient evidence	2-3x/week of moderate to vigorous resistance training plus high impact training (sufficient to generate ground reaction force of 3-4 time body weight) for at least 12 months	Insufficient evidence
Sleep	3-4x/week for 30-40 min per session of moderate intensity	Insufficient evidence	Insufficient evidence

Citation: bit.ly/cancer_exercise_guidelines

serve or VO₂R) is recommended.

Cook for Your LIFE



Cookforyourlife.org

We teach healthy cooking to people touched by cancer



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Recipe of the day

Mango Avocado Salsa



VIDEO



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Integrative Medicine at the Seattle Cancer Care Alliance (SCCA)

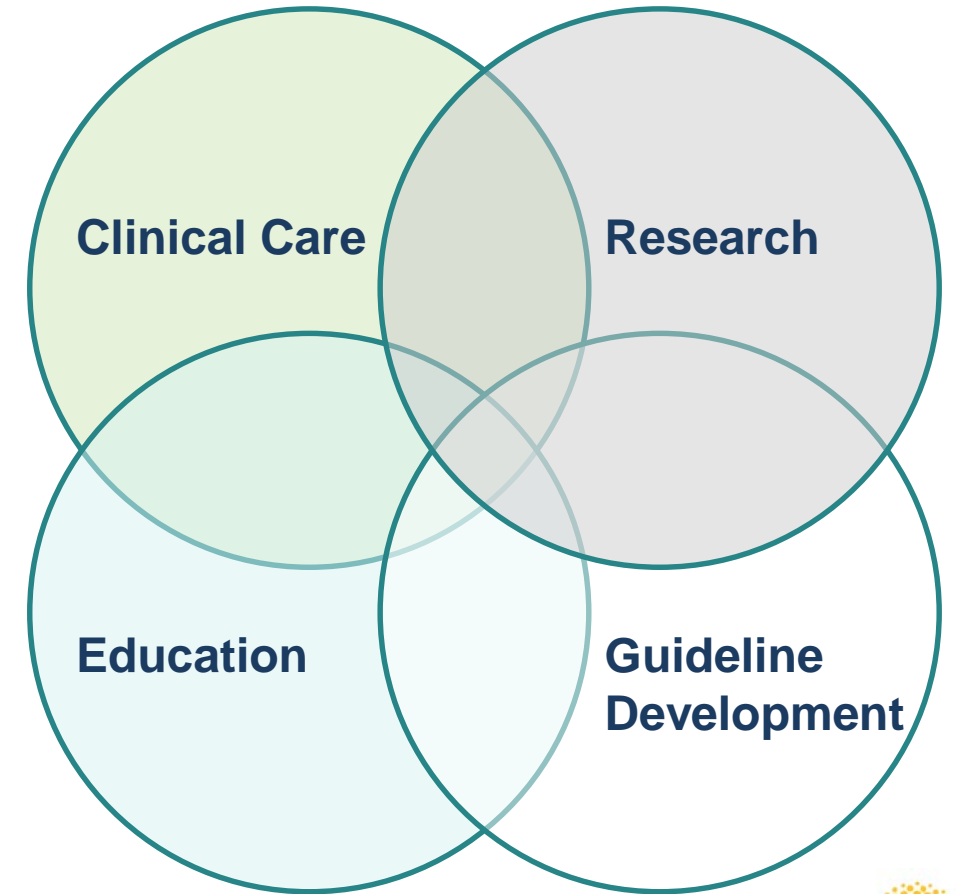
SCCA Integrative Medicine Vision

Effective Integrative Medicine therapies will be integrated into all aspects of cancer care and will become standard of care.

Focus is on improving quality of life and increasing resiliency from the time of diagnosis, through treatment, survivorship and end of life.

Emphasis on acupuncture, mind-body therapies, lifestyle behaviors, and dietary supplement counseling.

Integrative Medicine is highly interdisciplinary in the oncology setting.



Integrative Medicine at SCCA

New SCCA service – launched in January 2018

Interdisciplinary team of clinicians

- Integrative Nurse Practitioner
- Naturopathic physician
- Acupuncturists

Billable services

Shared electronic health record

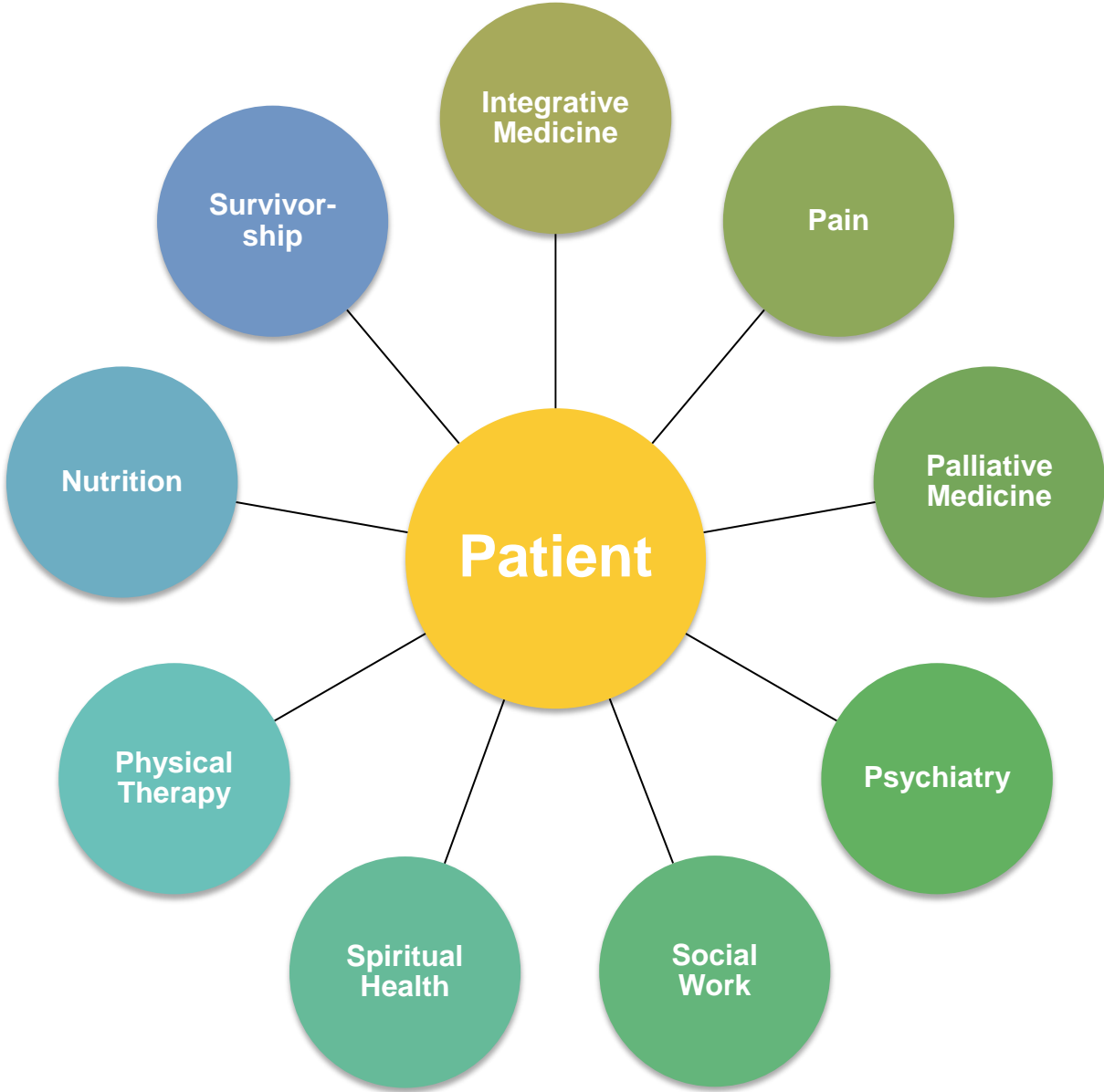
Co-located with SCCA outpatient oncology clinics

Research platform



Fred Hutch · Seattle Children's · UW Medicine

Interdisciplinary Supportive Care at SCCA



Dietary supplement working group

Collaboration between:

- Pharmacy
- Medical Nutrition Therapy
- Integrative Medicine

Purpose: To harmonize and publish recommendations on use of dietary supplement use by SCCA patients

The future of integrative oncology

- Integrative oncology is highly interdisciplinary
- Growing body of evidence supporting select use of integrative therapies for oncology symptom management
- Further need for clinical practice guidelines
- Patients are simultaneously using multiple therapies, need to understand combined use
- Need for observational studies and clinical trials with recurrence and survival endpoints
- Clinical programs and cooperative groups can provide excellent infrastructure to conduct cutting-edge research

THANK YOU



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