

The Evidence Base for Integrative Approaches to Cancer Care



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Objectives

- Definitions
- CAM therapies
- CAM use: who, what, why

Complementary & Alternative Medicine (CAM)

A group of diverse medical and health care systems, practices, and products that are not presently considered part of conventional medicine.

Integrative Medicine

A combination of therapeutic approaches that includes best practices from conventional and CAM medicine

AND

addition to the physical, attempts to address the *intellectual, emotional, and spiritual* aspects of illness.

CAM Practices

Four domains

- Biologically based practices
- Mind/Body medicine
- Manipulative and body-based practices
- Energy medicine

Whole medical systems

- Traditional Chinese Medicine (TCM)
- Ayurveda
- Homeopathy
- Naturopathy

NCCAM - <http://nccam.nih.gov/health/whatscam/#3>

Complementary Health Approaches

- **Natural Products**

- **Mind and Body Practices**

- **Traditional Medical Systems**

NCCIH - <https://nccih.nih.gov/health/integrative-health>

Integrative Oncology

The combination of complimentary health approaches and conventional medicine for cancer treatment, symptom management, and survivorship care.

CAM Use by U.S. Adults and Children

Group	Year	Percentage
Adults	2002	36.0%
Adults	2007	38.3%
Children	2007	11.8%

Use of CAM therapies is common

Source: Barnes PM, Bloom B, Nahin R. CDC National Health Statistics Report #12. Complementary and Alternative Medicine Use Among Adults and Children: United States, 2007. December 2008.

CAM use among cancer patients

Modality	Prevalence n (weighted %)	
	Respondents with cancer ^a (n=1785)	Respondents without cancer (n=21,585)
Alternative medical systems ^b	298 (16.50)*	2567 (11.66)
Biologically based therapy		
Herbal therapies	574 (32.14)*	5021 (24.11)
Vitamins/minerals	1359 (76.64)*	13,644 (64.02)
Manipulation-based therapy		
Chiropractic/osteopathic	596 (34.60)*	4526 (22.07)
Massage	329 (19.56)*	3415 (16.14)
Mind-body therapy		
Meditation	250 (12.94)	2521 (11.78)
Relaxation techniques ^c	345 (19.15)*	2709 (12.72)
Deep-breathing exercises	336 (17.70)*	3151 (14.69)
Yoga / tai chi / qi gong	237 (12.98)	2810 (13.06)
Biofeedback/hypnosis	125 (7.87)*	707 (3.44)
Energy healing therapy	45 (2.53)*	356 (1.52)
Prayer		
Prayer for self	1259 (68.85)*	11,190 (53.19)
Prayer by others	922 (49.22)*	7476 (33.44)

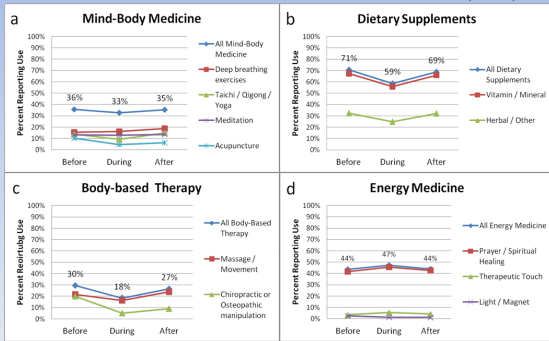
NHIS CAM supplement, 2007
Anderson JG. J Altern Comp Med, 2012;18(3):235-241

CAM use among cancer patients

- Following diagnosis: 54% - 69%
- During treatment: 55-75%
- In children: 84%

Vapiwala N. Cancer J, 2006;12:467
 Ferrucci LM. J Alt Comp Med, 2009;15(6):673
 Hann DM. Integr Cancer Ther, 2005;4(4):294
 Sparber A. J Alt Comp Med, 2001;7(3):281

CAM Therapy Use Before, During, and After Active Cancer Treatment (N=603)



Luo QL, Asher GN. Complementary and Alternative Medicine use at a Comprehensive Cancer Center. Integr Cancer Ther, 2016

Why do patients use CAM treatments?



79% think using CAM *plus* conventional therapies is superior to either alone

Eisenberg DM, et al. Ann Intern Med, 2001;135:344-351

*"The health of my body, mind, and spirit
are related...*

*...and whomever cares for my health
should take that into account."*

Eisenberg DM, et al. Ann Intern Med. 2001;135:344-351
Asch JA, JAMA. 1996;275(19):1548-1553

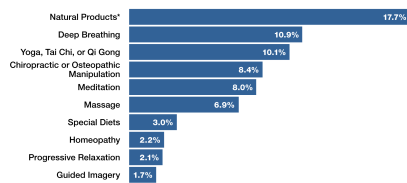
Reasons for CAM use among cancer patients

- Perceived therapeutic response (38%)
 - Enhance conventional tx
 - Improve QoL
- Wanting control (17%)
- Strong belief in CAM (17%)
- Finding hope (10%)
- Last resort (10%)
- Disappointment with conventional treatment or practitioner (4%)

Verhoef MJ. Int Cancer Ther. 2005;4(4):274

Use of Complementary Health Approaches in the U.S. National Health Interview Survey (NHIS)

10 most common complementary health approaches among adults—2012



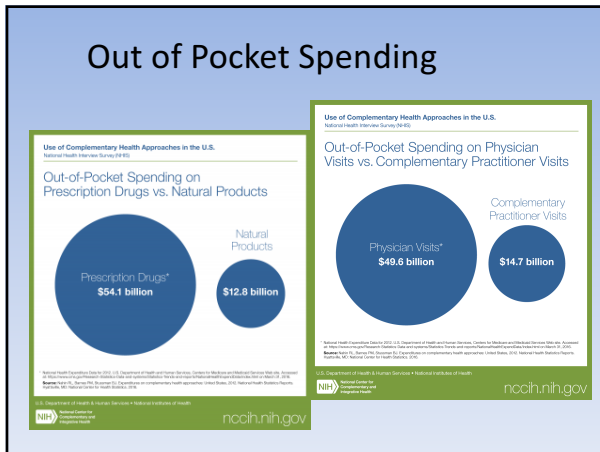
*Dietary supplements other than vitamins and minerals.

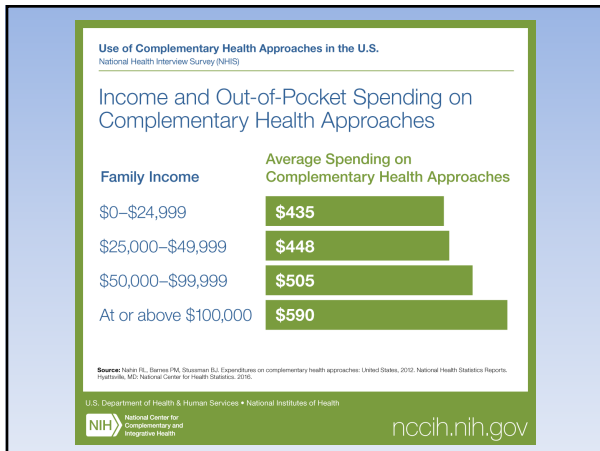
Source: Chou RC, Stock S, Scaumel RL, Clarke RW, Naylor RL. Trends in the use of complementary health approaches among adults—United States, 2002–2012. National health statistics report no. 70. Hyattsville, MD: National Center for Health Statistics; 2016.

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nc.nih.gov





- ### Integrative Oncology Guidelines
- Evidence-based recommendations
 - MBM, Massage, Exercise, Energy Therapies, Acupuncture, Diet, Supplements
 - Safety and Efficacy
 - No deep massage at certain sites
 - Support groups, CBT: anxiety, chronic pain, QoL
 - Acupuncture: pain, N/V, xerostomia
 - MBM: anxiety, pain, mood
 - Specific DS not recommended for prevention
- Greenlee H. JNCI, 2014;50:346
Deng, GE. Chest, 2013;143(5)(Suppl):e420s
Deng, GE. J Soc Int Oncol, 2009;7(13):85

Natural Products (Dietary Supplements)

Botanicals (herbals)



Vitamins & Minerals



Others





Zingiber officinale Ginger

Constituents:
Shogaol
Gingerol


Actions:
TXA \rightarrow platelets
5HT $_3$ antagonist

Uses:
Nausea & vomiting –
pregnancy⁺⁺, chemo⁺⁺, post-op^{+/-}
Coadministered with NSAIDs

Safety:
Bleeding (theoretical)
Heartburn
Asarum canadensis

Panax ginseng, *P. quinquefolius* Ginseng

(American, Chinese, Korean)
Siberian ginseng (*Eleutherococcus senticosus*)



Constituents:
Saponin glycosides – ginsenosides, panaxosides

Actions:
 \uparrow M Φ TNF α production
 \uparrow activity – TH, NK cells

Uses:
Mental & physical performance^{+/},
DM^{+/}, ED⁺, cancer-related fatigue⁺

Safety:
Elevated BP, hypoglycemia, agitation (ginseng abuse syndrome)
Caution with ER⁺ cancers d/t potential estrogenic effects
May reduce efficacy of warfarin (not vitamin K mediated)
No effect on CYP 1A2, 2D6, 2E1, and P-gp. Potential CYP 3A4 induction.

Wisconsin Ginseng (*Panax quinquefolius*) to Improve Cancer-Related Fatigue: A Randomized, Double-Blind Trial, N07C2

Debra L. Barton, Heshan Liu, Shaker R. Dakhl, Breanna Linquist, Jeff A. Sloan, Craig R. Nichols, Travis W. McGinn, Philip J. Stella, Grant R. Seager, Amit Sood, Charles L. Loprinzi

Manuscript received December 21, 2012; revised March 18, 2013; accepted June 13, 2013.

Correspondence to: Debra L. Barton RN, PhD, AOCN, FAAN, Mayo Clinic, 200 First St SW, Rochester, MN 55905 (e-mail: barton.debra@mayo.edu).

Background Safe, effective interventions to improve cancer-related fatigue (CRF) are needed because it remains a prevalent, distressing, and activity-limiting symptom. Based on pilot data, a phase III trial was developed to evaluate the efficacy of American ginseng on CRF.

Methods A multisite, double-blind trial randomized fatigued cancer survivors to 2000 mg of American ginseng vs a placebo for 8 weeks. The primary endpoint was the general subscale of the Multidimensional Fatigue Symptom Inventory-Short Form (MFSI-SF) at 4 weeks. Changes from baseline at 4 and 8 weeks were evaluated between arms by a two-sided, two-sample *t* test. Toxicities were evaluated by self-report and the National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE) provider grading.

Results Three hundred sixty-four participants were enrolled from 40 institutions. Changes from baseline in the general subscale of the MFSI-SF were 14.4 (standard deviation [SD] = 27.1) in the ginseng arm vs 8.2 (SD = 24.8) in the placebo arm at 4 weeks (*P* = .07). A statistically significant difference was seen at 8 weeks with a change score of 20 (SD = 27) for the ginseng group and 10.3 (SD = 26.1) for the placebo group (*P* = .003). Greater benefit was reported in patients receiving active cancer treatment vs those who had completed treatment. Toxicities per self-report and CTCAE grading did not differ statistically significantly between arms.

Conclusions Data support the benefit of American ginseng, 2000mg daily, on CRF over an 8-week period. There were no discernible toxicities associated with the treatment. Studies to increase knowledge to guide the role of ginseng to improve CRF are needed.

J Natl Cancer Inst

Mind-Body Medicine

- Yoga, Tai Chi, Progressive relaxation
- Meditation, Hypnosis, Biofeedback, Guided imagery
- CBT, Support Groups, Expressive therapy



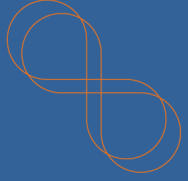

- anxiety, chronic pain
- mood, quality of life, sleep

Use of Complementary Health Approaches in the U.S.

National Health Interview Survey (NHIS)


9.5% of U.S. adults (21 million) used

yoga



	9.5% Yoga
	8.4% Chiropractic or Osteopathic Manipulation
	8.0% Meditation
	6.9% Massage Therapy

Citation: Clarke TC, Black LI, Stussman BJ, et al. Trends in the use of complementary health approaches among adults—United States, 2002–2012. National health statistics reports, no 79. Hyattsville, MD: National Center for Health Statistics; 2015.

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 National Center for Complementary and Integrative Health nccih.nih.gov

Use of Complementary Health Practices in the U.S.
NCHADS System Report 2014

Yoga & Wellness

Did you know? 94% of Americans who practice yoga say that they do it for wellness reasons. And they say that practicing yoga makes them healthier in many ways.

- over 60% of yoga users were motivated to exercise more regularly
- over 40% of yoga users were motivated to eat healthier
- over 55% of yoga users reported improved sleep
- over 85% of yoga users reported reduced stress
- over 12% of yoga users cut back or stopped drinking alcohol
- over 25% of yoga users cut back or stopped smoking cigarettes

YOGA

Moderate-quality evidence as a supportive intervention for:

- improving health-related **quality of life** and reducing **fatigue** and **sleep disturbances** when compared with no therapy
- reducing **depression, anxiety and fatigue**, when compared with psychosocial/educational interventions

Cramer H, Lauche R, Klose P, Lange S, Langhorst J, Dobos GJ. Yoga for improving health-related quality of life, mental health and cancer-related symptoms in women diagnosed with breast cancer. Cochrane Database of Systematic Reviews 2017, Issue 1. Art. No.: CD010802.

nccih.nih.gov

Body-based Therapies

Massage therapy	Lymphedema therapy
	

Pain, Anxiety, Edema

Energy Therapies



- Therapeutic touch, Reiki

	
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- Stress reduction, enhancing quality of life

Acupuncture

- Pain
- Nausea and vomiting
- Xerostomia
- Fatigue, neuropathy, hot flashes



Acupuncture & joint pain

Randomized, blinded, sham-controlled trial of **acupuncture for the management of aromatase inhibitor-associated joint symptoms** in women with early-stage breast cancer.


CONCLUSION: Women with AI-induced arthralgias treated with acupuncture had **significant improvement of joint pain and stiffness**, which was not seen with sham acupuncture

Crew KD, et al. [J Clin Oncol](#). 2010 Mar 1;28(7):1154-60

Traditional Medical Systems

- Ayurvedic medicine
- Traditional Chinese medicine
- Homeopathy
- Naturopathy

Disclosure



The image shows three monkeys sitting in a row. The first monkey on the left has its hands covering its eyes. The middle monkey has its hands covering its ears. The third monkey on the right has its hands covering its mouth. This is a classic illustration of the idiom 'see no evil, hear no evil, speak no evil'.

**Disclosure to
Health Care Providers**

- Among CAM therapy users:
 - 30-35%
- Among patients with cancer or chronic disease:
 - 60%

Eisenberg. NEJM, 1993;328:246.
Barnes. CDC Advance Data, 2004; #343.
Mehta. JACM, 2008; 14:1263.
Eisenberg DM. Ann Intern Med. 2001;135: 344.

Reasons for non-disclosure

My doctor never asked.
It wasn't important for my doctor to know.

It was none of my doctor's business.
My doctor would not understand.

My doctor would disapprove.
My doctor would discourage me.

My doctor might not continue as my provider.

Eisenberg DM. Ann Intern Med. 2001;135: 344-351
Eisenberg DM. JAMA. 1998;280: 1569-1575.

Talking with your patients about CAM

- 1) Providers must initiate conversation
- 2) Be accepting and non-judgmental
- 3) Did not expect provider to be CAM expert

Shelley BM. Annals of Family Med, 2009;7(2):139-147

Summary

- CAM use is common
- Several CAM therapies especially beneficial to cancer survivors
- Many patients willing to pay out-of-pocket

Resources

- Society for Integrative Oncology (SIO)
<https://integrativeonc.org/>
- National Center for Complementary and Integrative Health (NCCIH)
<http://nccih.nih.gov/>
- The Consortium of Academic Health Centers for Integrative Medicine
<http://www.imconsortium.org/cahcm/home.html>
- Natural Medicines: evidence-based information about complementary and alternative therapies
<https://naturalmedicines-therapeuticresearch-com.libproxy.lib.unc.edu/>
- American Botanical Council (ABC): science-based and traditional information to promote the responsible use of herbal medicine
<http://abc.herbalgram.org/site/PageServer>
- UNC Program on Integrative Medicine (PIM)
<http://pim.med.unc.edu/>

Questions?



Integrative Medicine at NC Cancer Hospital

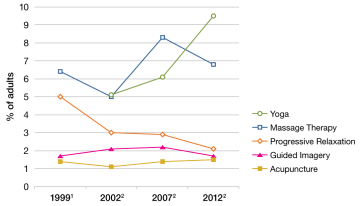
- Integrative Medicine Consultation
- Acupuncture
 - Psycho-oncology
 - Support groups
 - Integrative Health Coaching
- Lymphedema therapy
- Massage therapy
- Yoga classes
- Nutrition

Robin Haring: 966-3494


<http://www.unclineberger.org/ccsp/programs/integrative-medicine>

Use of Complementary Health Approaches in the U.S. National Health Interview Survey (NHIS)

13-year trends for complementary approaches where questions are very similar across years



Year	Yoga	Massage Therapy	Progressive Relaxation	Guided Imagery	Acupuncture
1999	5.5	7.0	2.0	1.5	1.0
2002	5.0	5.5	2.5	1.5	1.0
2007	6.5	8.0	2.5	1.5	1.0
2012	9.5	7.0	2.0	1.5	1.0

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 National Center for Complementary and Integrative Health
nccih.nih.gov



Reference Books

- Complementary and Integrative Medicine in Pain Management, Weintraub MI, Springer. 2008
- Integrative Medicine, Rakel D, Sanders. 2007
- Nutrition by the Numbers, Ramsden C, Appl. Nutritional Biochem (Pub). 2007
- The Desktop Guide to Complementary and Alternative Medicine: An evidence-based approach, Ernst E, Mosby. 2006
- Herb-Drug Interactions in Oncology, Cassilieth BR, Peoples Medical Publishing House, 2010.

Reference Books

- Complementary and Alternative Medicine: An evidence-based approach. Spencer JW and Jacobs JJ, Mosby. 2003
- Integrative Health Care, Sierpina V, FA Davis. 2001
- Clinician's Complete Reference to Complementary and Alternative Medicine, Novey DW, Mosby. 2000
- Herbal Drugs and Phytopharmaceuticals, 3rd ed. Wichtl M, CRC Press. 2004.
- Herb, Nutrient, and Drug Interactions. Stargrove MB, Treasure J, McKee DL. Mosby. 2008.

**Complementary & Alternative
Medicine (CAM)**

Interventions neither taught widely at U.S. medical schools nor generally available in U.S. hospitals.

Therapies from outside of mainstream medicine to be used *in conjunction with or in lieu of* conventional therapies.

SOCIETY FOR INTEGRATIVE ONCOLOGY

Evidence-Based Clinical Practice Guidelines for Integrative Oncology: Complementary Therapies and Botanicals

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Journal of the Society for Integrative Oncology, Vol 7, No 3 (Summer), 2009; pp 85-120

Supplement use among cancer survivors

TABLE 3. VITAMINS AND MINERALS MOST COMMONLY USED WITHIN THE PAST 12 MONTHS

Vitamin/mineral	Prevalence (weighted %)	
	Respondents with cancer ^a (n=1785)	Respondents without cancer (n=21,585)
Calcium	33.70%	22.65%
Folate	5.17%	3.78%
Vitamin B complex	9.35%	8.02%
Vitamin C	19.12%	17.87%
Vitamin E	14.57%	8.53%
Multivitamin	82.75%	84.09%

TABLE 4. HERBS AND SUPPLEMENTS MOST COMMONLY USED WITHIN THE LAST 12 MONTHS

Herb/supplement	Prevalence (weighted %)	
	Respondents with cancer ^a (n=1785)	Respondents without cancer (n=21,585)
Chondroitin	13.81%	11.89%
Coenzyme Q10	11.76%	9.35%
Echinacea	11.31%	17.95%
Fish oil	44.38%	38.33%
Flaxseed oil	15.79%	15.74%
Garlic (pills or gencaps)	15.72%	11.23%
Ginkgo biloba	10.28%	10.64%
Ginseng	7.33%	12.45%
Glucosamine	25.91%	21.40%
Grape seed extract	4.37%	4.32%
Green tea (pills)	3.70%	5.64%
Soy supplements/isoflavones	2.87%	5.08%
St. John's wort	2.64%	3.40%
Valerian	1.95%	3.26%

NHIS CAM supplement, 2007
Anderson JG. J Altern Comp Med, 2012;18(3):235-241

Predictors of CAM use

- Female (74%)
but 62% male
 - White (70%)
but 60% nonwhite
 - Highly educated
HS grad (67%) – graduate degree (78%)
 - Higher income
under \$40k (66%) – over \$75k (71%)
- Stage at dx, age, race, geographic location

Ferrucci LM. J Altern Comp Med. 2009;15(6):673
Fouladbakhsh JM. JCIIM, 2008;5

Interactions: potential & real

Hypericum perforatum
(St. John's Wort)

- Inducer of CYP 3A4, P-gp
- Decreased imatinib, irinotecan concentrations

Izzo AA. Drugs, 2009;69(13):1777
Zhou SF. Drug Met Rev, 2003;35(1):35

Interactions: potential & real

Identification and Exploration of Herb-Drug Combinations Used By Cancer Patients

Silje Engdal, MPharm, Olbjørn Klepp, MD, PhD, and Odd Georg Nilsen, PhD

Conclusion: The large number of in vitro potential herb-drug interactions identified urge for more clinical pharmacokinetic interaction studies in humans.

Integr Cancer Ther 2009; 8; 29

Supplement Use

- National Health Interview Study, 2007
 - 18% adults used NVNMDS
- NHANES, 2003-2006
 - 20% adults used DS containing a botanical

Bailey RL. J Nutr, 2011;141:261

Review

The role of integrative oncology in a tertiary prevention survivorship program

Stephen M. Sagar^{a,b,*}, Brian D. Lawenda^{c,d}

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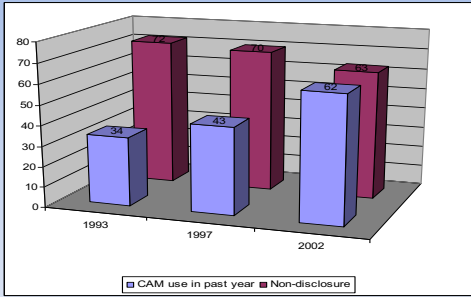
Sagar S. Prev Med, 2009;49:93

What's missing

How do cancer patients use CAM?

- Where do they get their information?
- Actual use vs. instructed use?

Disclosure to Health Care Providers



Eisenberg DM, et al. NEJM, 1993;328:246-252
Barnes PM, et al. CDC Advance Data, 2004;343

Goals for taking supplements

- (A) Disease treatment?
 - Primary treatment
 - Maximize benefits of other treatments
- (B) Symptom management?
- (C) Prevention?
 - Worsening of current disease
 - New disease
- (D) Other priorities?

Safety vs Efficacy

