

# Integrative Cancer Care

Donald I. Abrams, MD

Professor Emeritus of Medicine

*University of California San Francisco*



# Integrative Cancer Care

“It is more important to know what sort of patient has a disease than what disease a patient has.”

Moses Maimonides and  
Sir William Osler



The patient we see and the person we may not

Although we treat the patient in front of us proficiently, we sometimes can be oblivious to the person behind the patient. While the patient carries the diagnosis, it is the person within who carries the patient. This becomes important because it is the person and the vicissitudes of his or her life that determine the patient's presence, absence, and behavior.

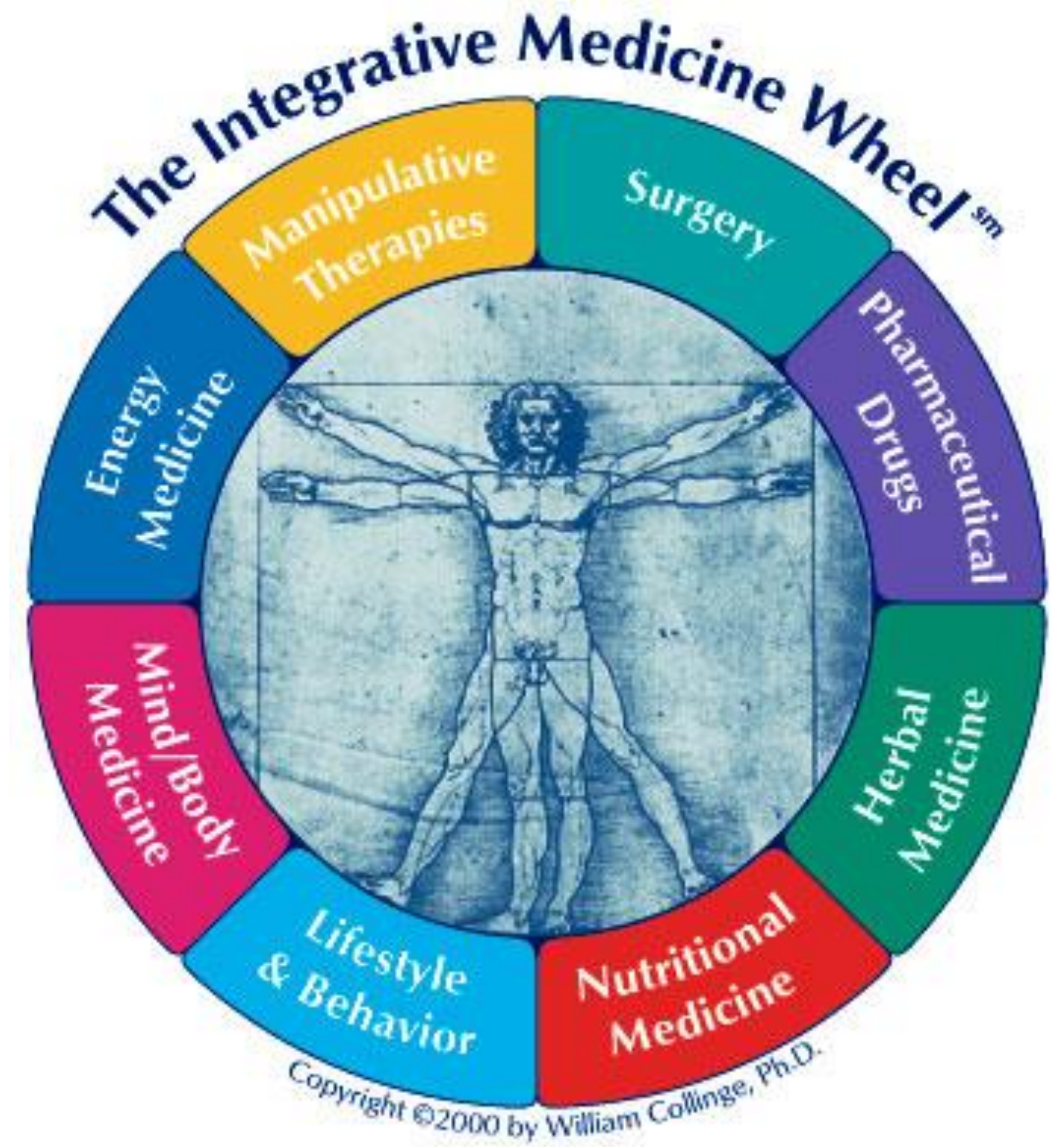
Chandrakanth Are, MBBS, MBA, FRCS, FACS, ASCO Post August 10, 2021





## What is Integrative Cancer Care?

**The rational, evidence-*informed* combination of conventional therapy with complementary interventions into an individualized therapeutic regimen that addresses the whole person (body, mind, spirit) with cancer**



# Integrative Oncology

- Provides relationship-centered care
- Integrates conventional and complementary methods of treatment and prevention
- Aims to activate the body's innate healing response
  - Uses natural, less invasive interventions when possible



# Integrative Oncology

- Engages mind, body, spirit and community
  - Encourages providers to model healthy lifestyles for their patients
  - Focuses attention on lifestyle choices for disease prevention & maintenance of health
  - Maintains that healing is always possible even when curing is not

# Integrative Oncology Patient Subsets

- Seeking alternatives to conventional cancer therapy
- Seeking complementary therapies while undergoing conventional therapy
  - To mitigate symptoms of cancer or treatment
  - To prolong remission
- Seeking optimal survivorship care
- Seeking any possible salvage therapy
- Seeking integrative end-of-life care

# Goals of Integrative Oncology

- Increase patient's sense of control
- Decrease ongoing inflammation
- Increase body's innate immunity in fight against cancer
- Decrease stress
- Increase hope



# Increasing Sense of Control

- Control weight
- Alter diet
- Increase physical activity
- Use appropriate supplements
- Become aware of breathing
- Consider guided imagery or self-hypnosis
- Connect with family and friends
- Engage spirituality and religion



## The Weed and the Garden



Cancer is like a weed. Someone else is taking care of your weed. It's my job to work with the garden to make your soil as inhospitable as possible to growth and spread of the weed.



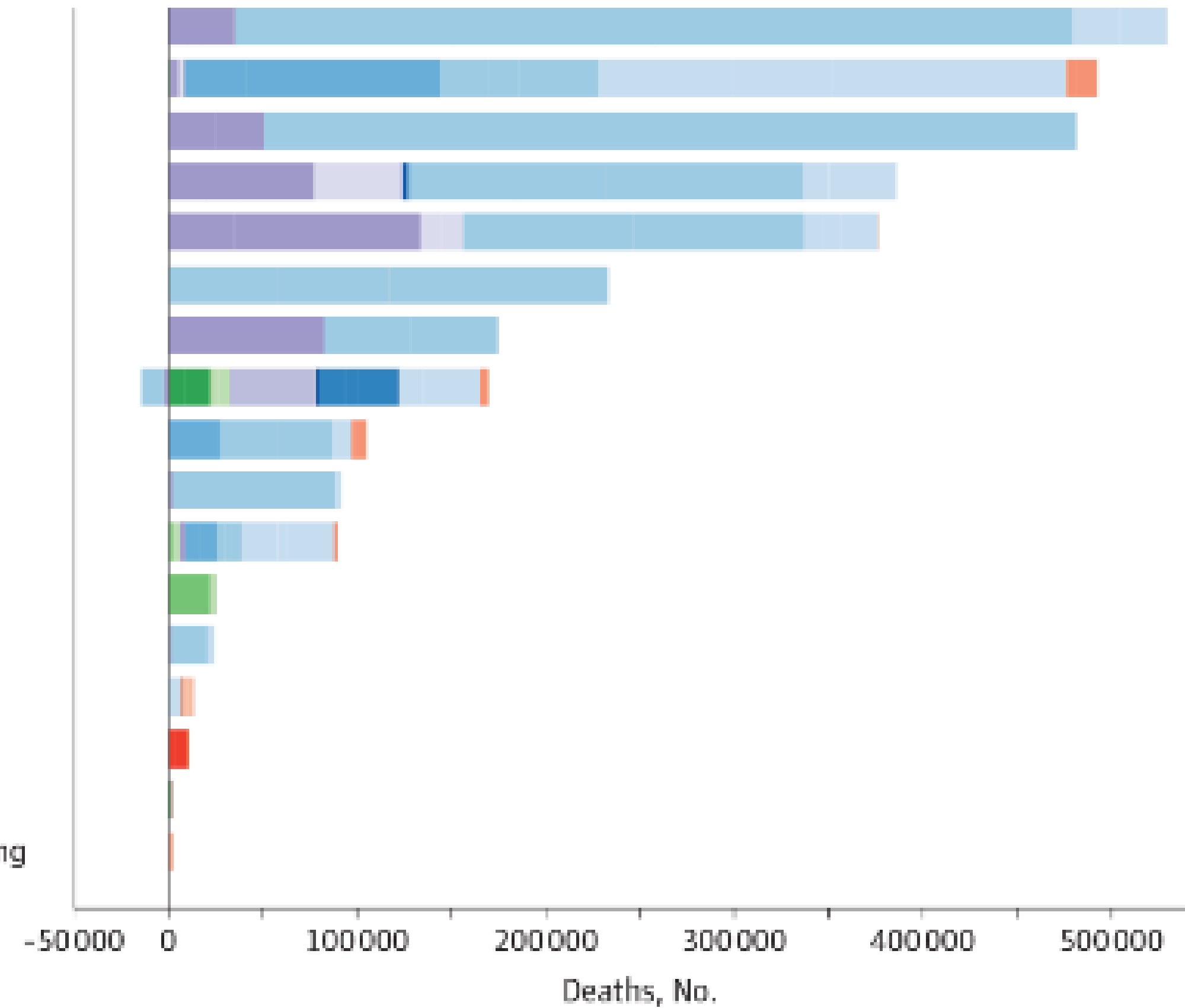
From: **The State of US Health, 1990-2016 Burden of Diseases, Injuries, and Risk Factors Among US States**

JAMA. 2018;319(14):1444-1472. doi:10.1001/jama.2018.0158

**A** Risk factors and related deaths

**Risk factors**

- Dietary risks
- Tobacco use
- High systolic blood pressure
- High body mass index
- High fasting plasma glucose
- High total cholesterol
- Impaired kidney function
- Alcohol and drug use
- Air pollution
- Low physical activity
- Occupational risks
- Low bone mineral density
- Residential radon and lead exposure
- Unsafe sex
- Child and maternal malnutrition
- Sexual abuse and violence
- Unsafe water, sanitation, and handwashing



**Communicable, maternal, neonatal, and nutritional diseases**

- HIV/AIDS and tuberculosis
- Diarrhea, lower respiratory tract, and other common infectious diseases
- Maternal disorders
- Neonatal disorders
- Nutritional deficiencies
- Other communicable maternal, neonatal, and nutritional diseases

**Noncommunicable diseases**

- Neoplasms
- Cardiovascular diseases
- Chronic respiratory diseases
- Cirrhosis and other chronic liver diseases
- Digestive diseases
- Neurological disorders
- Mental and substance use disorders
- Diabetes, urogenital, blood, and endocrine diseases
- Musculoskeletal disorders
- Other noncommunicable diseases

**B** Risk factors as a percentage of disability-adjusted life-years

**Risk factors**



## •Diets low in:

- Fruits
- Vegetables
- Whole grains
- Nuts and seeds
- Milk
- Fiber
- Calcium
- Seafood omega 3s
- PUFA's

## •Diets high in:

- Red meat
- Processed meat
- Sugar-sweetened beverages
- Trans fatty acids
- Sodium



# AICR RECOMMENDATIONS FOR CANCER PREVENTION

## A Blueprint to Beat Cancer

To prevent cancer, people should aim to follow as many of the 10 Cancer Prevention Recommendations as possible. However, any change you make that works toward meeting the goals set out in the Recommendations will go some way to reducing your cancer risk.

### BE A HEALTHY WEIGHT

Keep your weight within the healthy range and avoid weight gain in adult life



### BE PHYSICALLY ACTIVE

Be physically active as part of everyday life – walk more and sit less



### EAT A DIET RICH IN WHOLE GRAINS, VEGETABLES, FRUITS AND BEANS

Make whole grains, vegetables, fruits and pulses (legumes) such as beans and lentils a major part of your usual daily diet



### LIMIT CONSUMPTION OF RED AND PROCESSED MEAT

Eat no more than moderate amounts of red meat, such as beef, pork and lamb. Eat little, if any, processed meat



### LIMIT CONSUMPTION OF SUGAR-SWEETENED DRINKS

Drink mostly water and unsweetened drinks

### LIMIT CONSUMPTION OF "FAST FOODS" AND OTHER PROCESSED FOODS HIGH IN FAT, STARCHES OR SUGARS

Limiting these foods helps control calorie intake and maintain a healthy weight



### LIMIT ALCOHOL CONSUMPTION

For cancer prevention, it's best not to drink alcohol



### DO NOT USE SUPPLEMENTS FOR CANCER PREVENTION

Aim to meet nutritional needs through diet alone



### FOR MOTHERS: BREASTFEED YOUR BABY, IF YOU CAN

Breastfeeding is good for both mother and baby



### AFTER A CANCER DIAGNOSIS: FOLLOW OUR RECOMMENDATIONS, IF YOU CAN

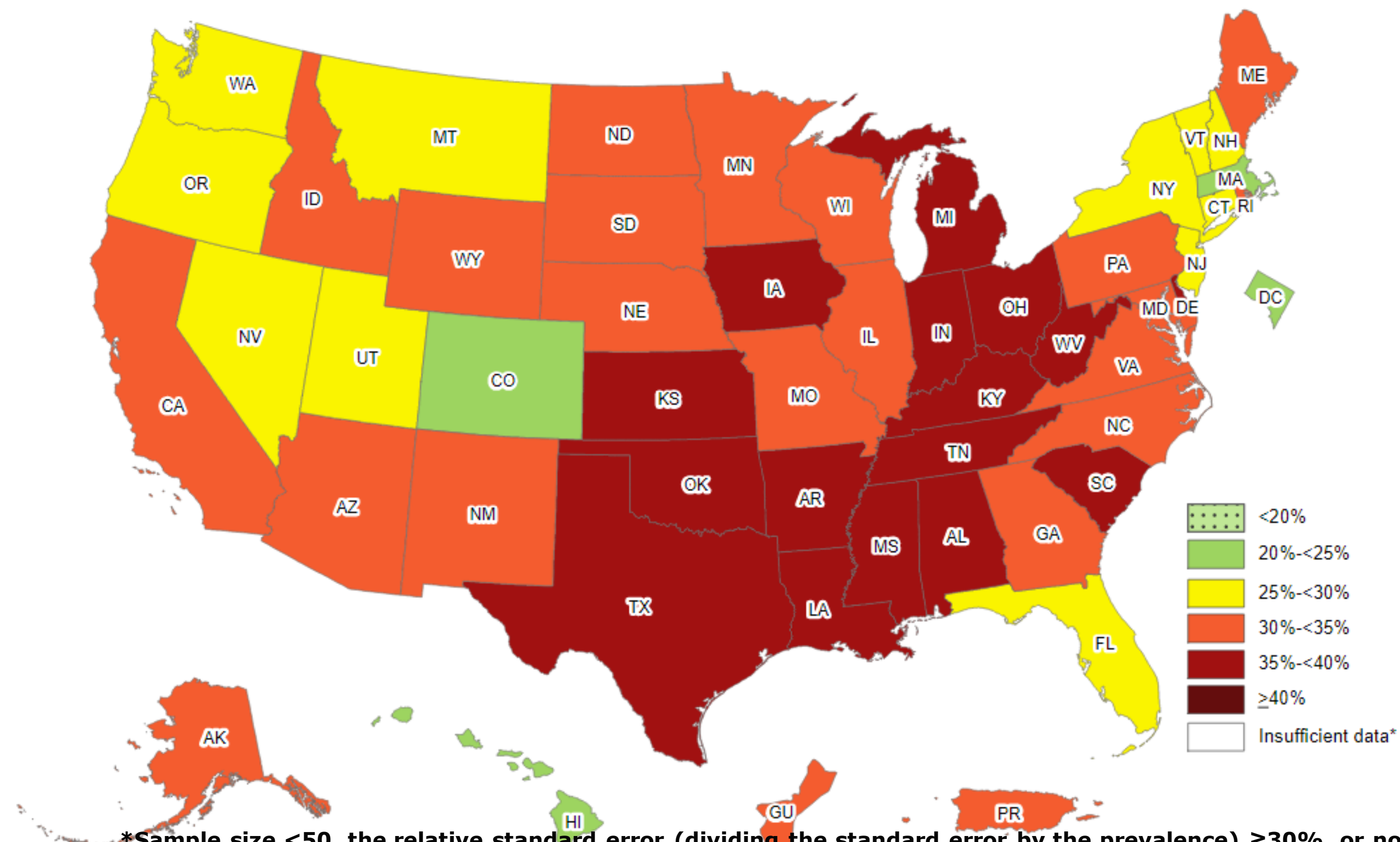
Check with your health professional about what is right for you





# Prevalence<sup>†</sup> of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2020

<sup>†</sup> Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.



\*Sample size <50, the relative standard error (dividing the standard error by the prevalence) ≥30%, or no data in a specific year.



# Obesity-Associated Malignancies

- CDC estimates that overweight/obesity now associated with 40% of all cancer in US
  - Accounts for 55% all cancer in women
  - Accounts for 24% all cancer in men
  - Accounts for 2/3 of all cancer in adults 50 to 74 years old
- More than 630,000 Americans diagnosed with an overweight/obesity associated CA

• CDC.gov 2018





# Obesity-Associated Malignancies

## Estimated Percentages of Annual US Cancers Caused by Excess Body Fat

Breast: 17% , 33,000 cases  
Esophagus: 35%, 5,800 cases  
Pancreas: 28%, 11,900 cases  
Gallbladder: 21%, 2,000 cases  
Colorectal: 9%, 13,200 cases  
Endometrial: 49%, 20,700 cases  
Kidney: 24%, 13,900 cases

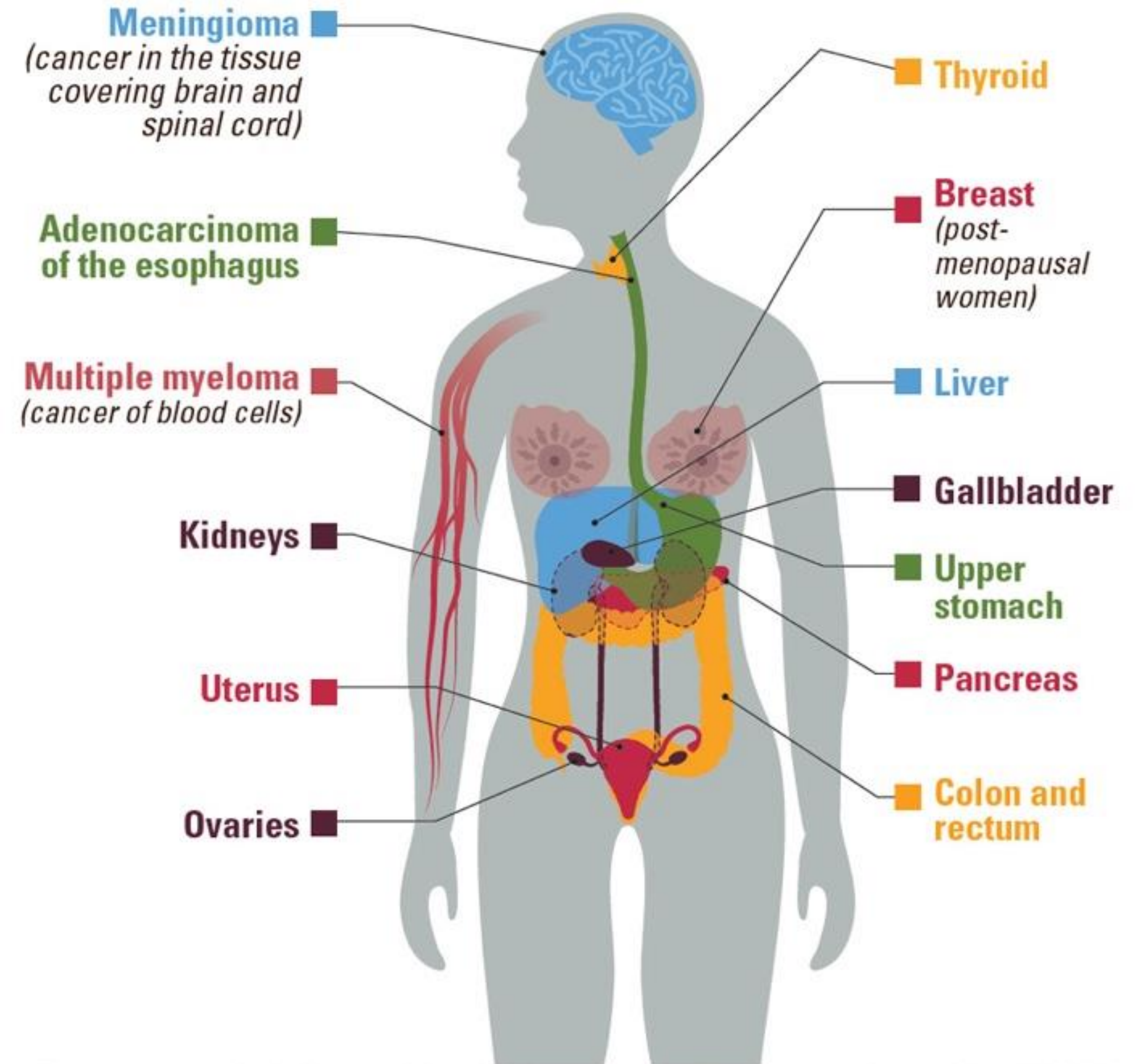
*Source: AICR/WCRF "Policy and Action for Cancer Prevention" report, 2009*

AICR report estimates that obesity-related excesses of these 7 cancers account for ~ 115,000 preventable deaths a year in the US



## AICR Body Weight and Cancer

- Probable increases risk
  - Mouth, pharynx, larynx
  - Stomach
  - Gallbladder
  - Ovary
  - Prostate
- Suggestive increases risk
  - Cervix
- Probable decreases risk
  - Breast premenopause



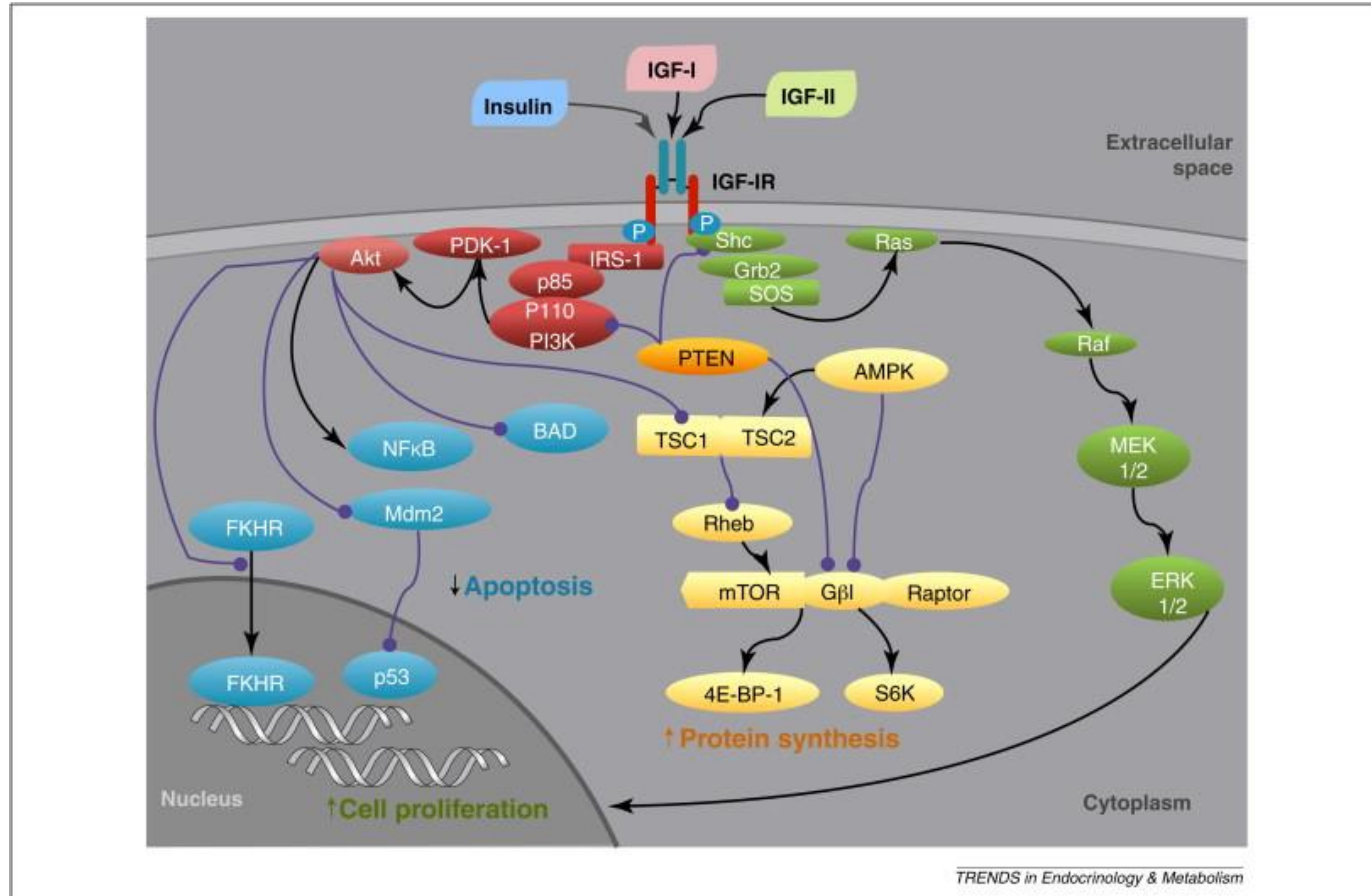
Most cancers associated with overweight and obesity increased while other cancers decreased from 2005-2014

## Body Fat Increases CA Risk

- Fat increases estrogen production
- Body fat secretes cytokines that promote inflammation
- Increase in body fat may impair immunity
- Too much body fat triggers insulin resistance, raising levels of insulin and growth factors that promote cancer



# Insulin and IGF-1 and Cancer



- Meta-analysis of 16 breast and 7 CRC studies with ~50,000 survivors
  - The most active breast CA survivors had lower rates of death from breast CA (RR, 0.72; (0.60-0.85) and other causes (RR, 0.52; 0.42-0.64)
  - The most active CRC survivors had lower rates of death from CRC (RR, 0.61; (0.40-0.92) and other causes (RR, 0.58; 0.48-0.70)
  - Survivors reporting an increase in activity after diagnosis had lower risk of death (RR, 0.61; 0.46-0.80) than those who did not



## The Role of The Oncologist

- Majority of non-small cell lung cancer survivors desired advice re: PA with 80% preferring face-to-face rec from an MD; 92% preferring under CA Center auspices

- Philip et al, Support Care Cancer, 2014

- Survey of Canadian oncologists showed 62% agreed that PA was safe and beneficial, but only 42% ever recommended it and only 26% within past month

- Jones et al, Support Care Cancer, 2005

- Oncologist recommending PA resulted in increase of 60 min vigorous walking/week

- Jones et al, Ann Behav Med 2004

# WCRF/AICR Recommendations to Reduce Cancer Risk 2018

Be a healthy weight

Be physically active for at least 30 minutes every day

Limit consumption of fast foods

Particularly processed foods high in added sugar, low in fiber or high in fat

Avoid sugary drinks





“Processed foods high in fat, starches or sugars embody a cluster of characteristics that encourage excess energy consumption, for example, by being highly palatable, high in energy, affordable, easy to access and convenient to store”







# WCRF/AICR Recommendations to Reduce Cancer Risk 2018

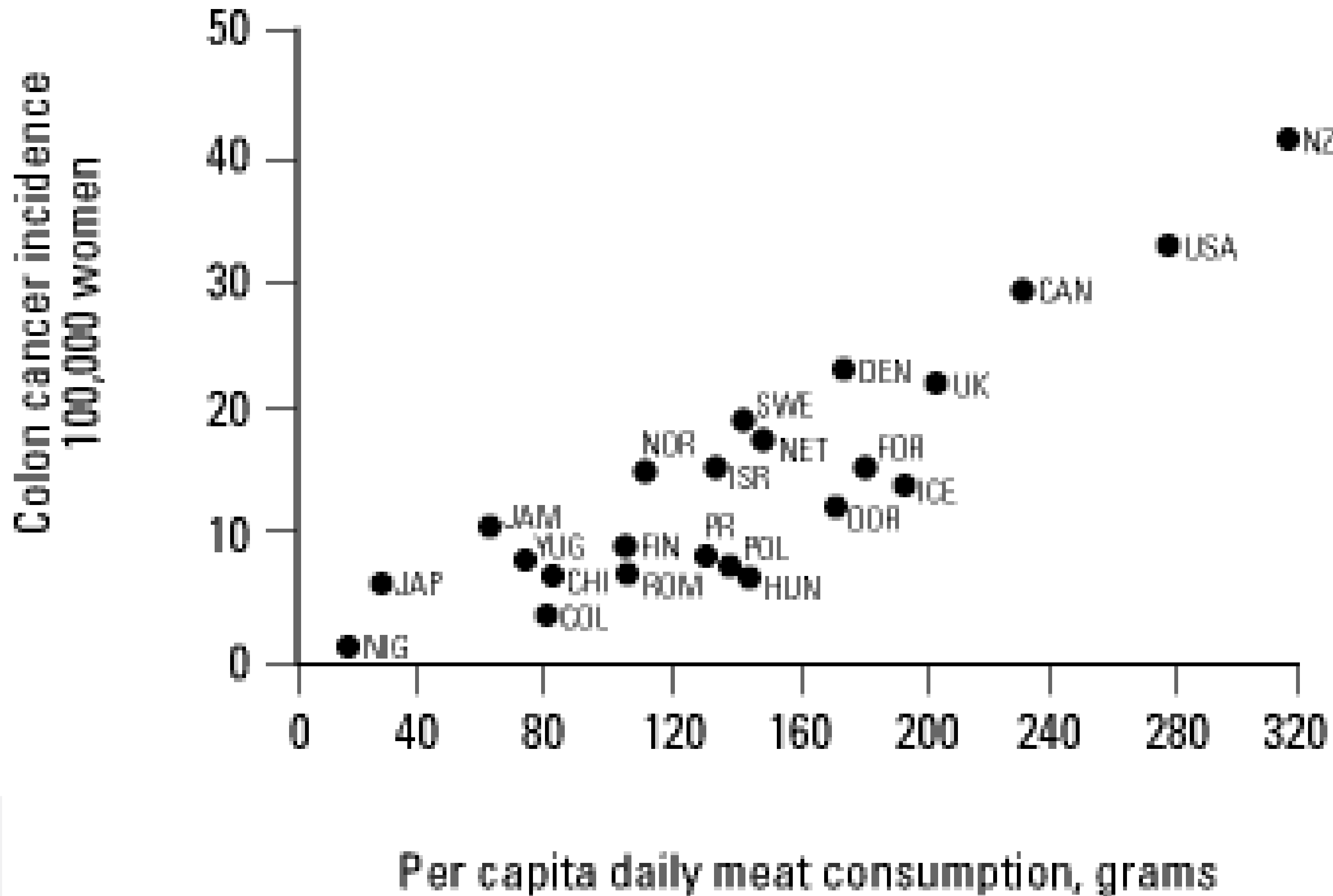
## 5. Eat more of a variety of vegetables, fruits, whole grains and legumes

- Phytoestrogens
  - Soy foods
  - Flaxseed
- Cruciferous vegetables
- Garlic and onions
- Turmeric and ginger
- Green tea
- Omega 3 fatty acids



# WCRF/AICR Dietary Recommendations to Reduce Cancer Risk

## 6. Limit consumption of red (beef, pork and lamb) and processed meats





# Dietary Fats & Inflammation

## OMEGA-6 FATS

Commercially-raised meat, poultry, dairy and eggs (yolk).  
Also nuts, seeds, vegetable oils (corn, safflower, soy, etc.)

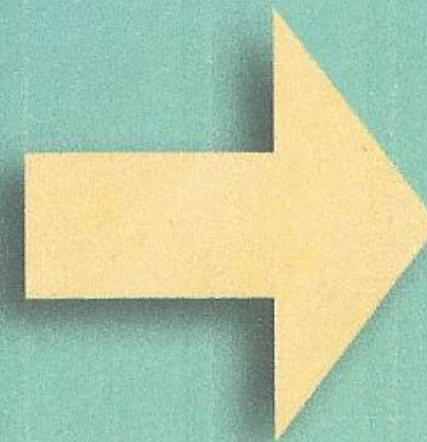


## PRO-INFLAMMATORY Compounds

foster tumor growth & progression,  
promote angiogenesis, suppress  
immune function

## OMEGA-3 FATS

Cold-water fish, flax, hempseed oil, grass-fed meat, poultry, dairy & eggs. Small amounts in canola oil, black walnuts, and leafy greens



## ANTI-INFLAMMATORY Compounds

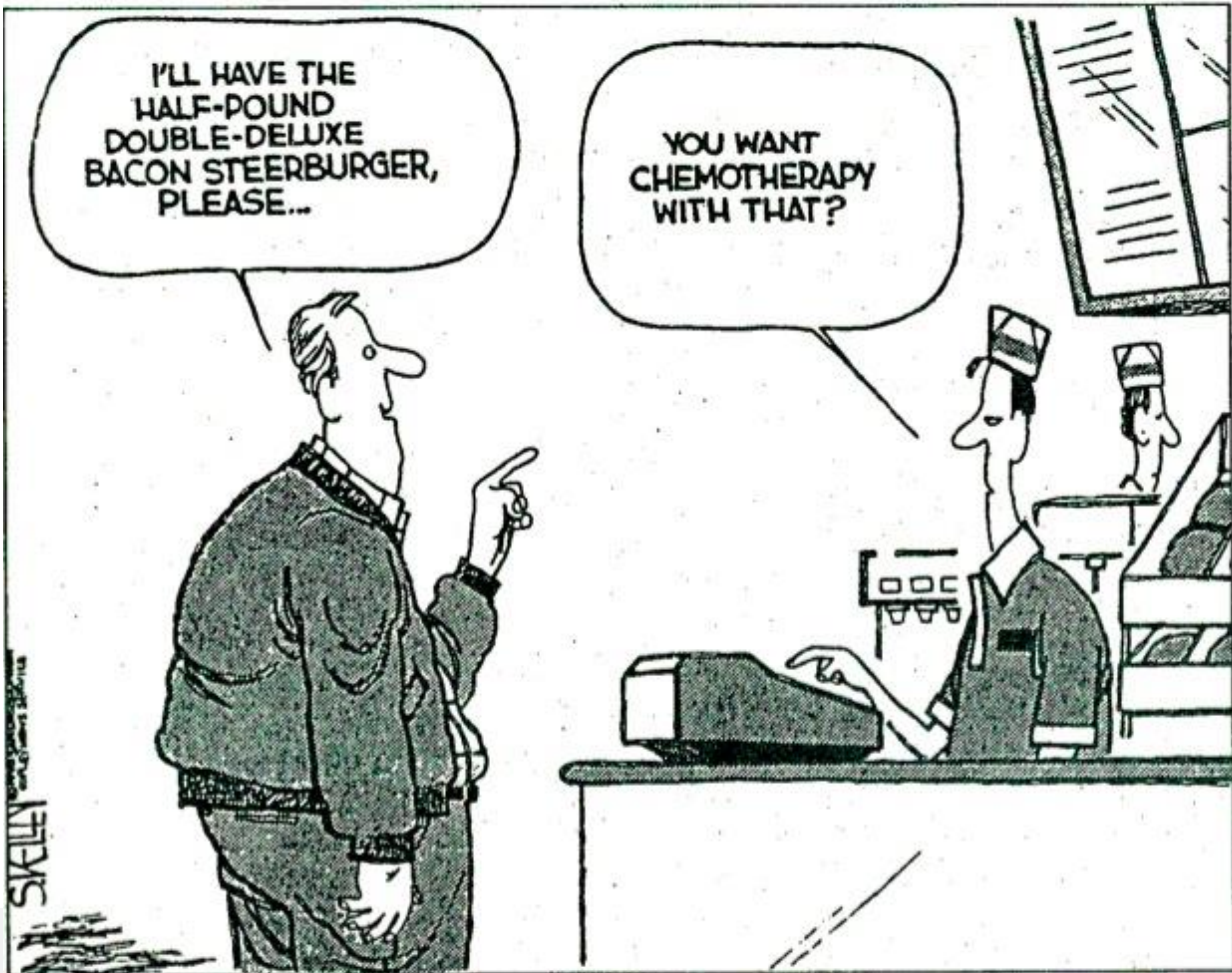
inhibit tumor growth,  
complement RT+chemo,  
anti-angiogenesis



## Meat and Colorectal Cancer

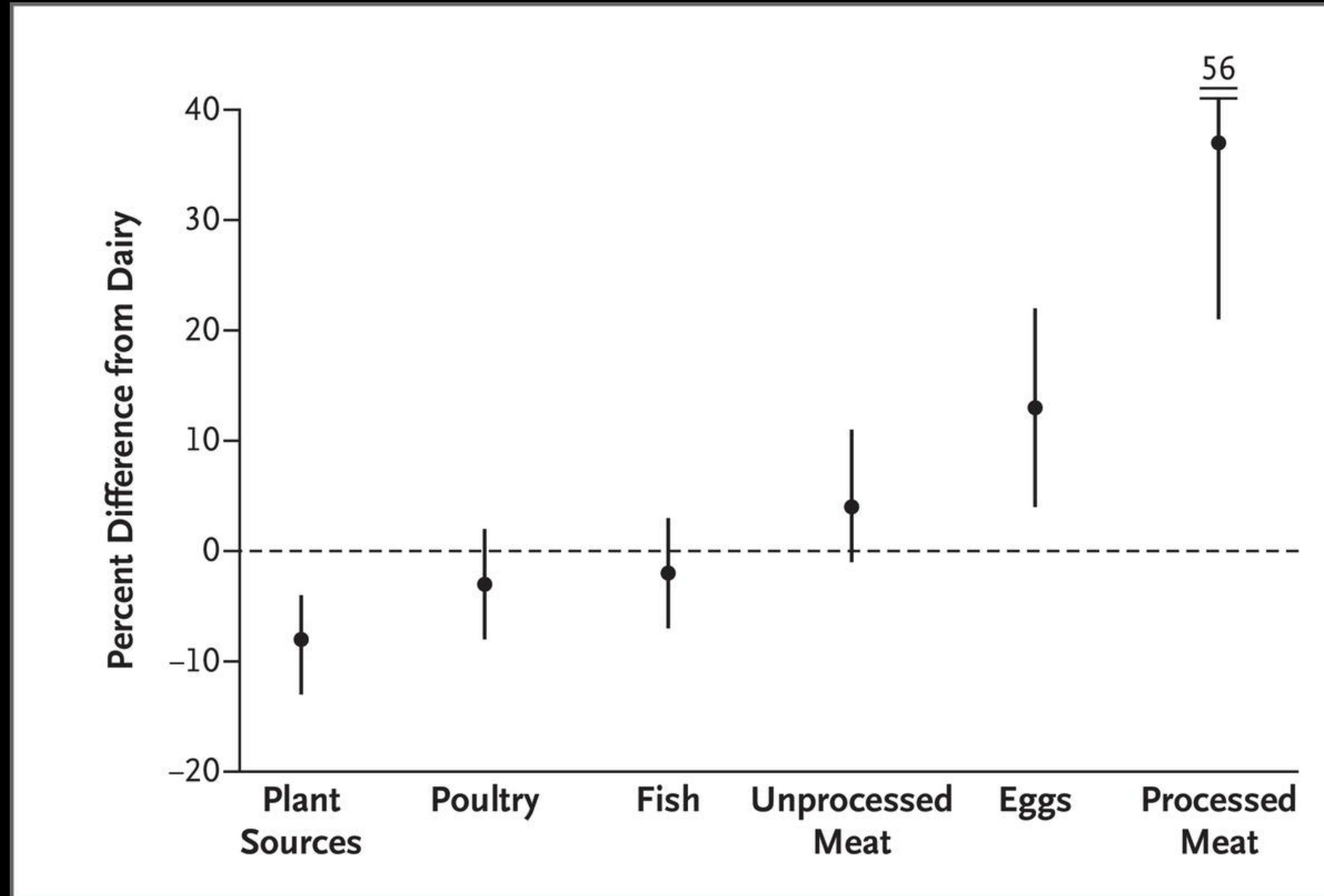
- Total iron intake and dietary iron both inversely associated, although the more bioavailable **heme iron** was positively associated
- **Nitrate** intake from processed meat positively associated; **nitrite** not ( $p=0.055$ )
- **Heterocyclic amine** intake (MeIQx and DiMeIQx) positively associated but only associated with colon, not rectal CA





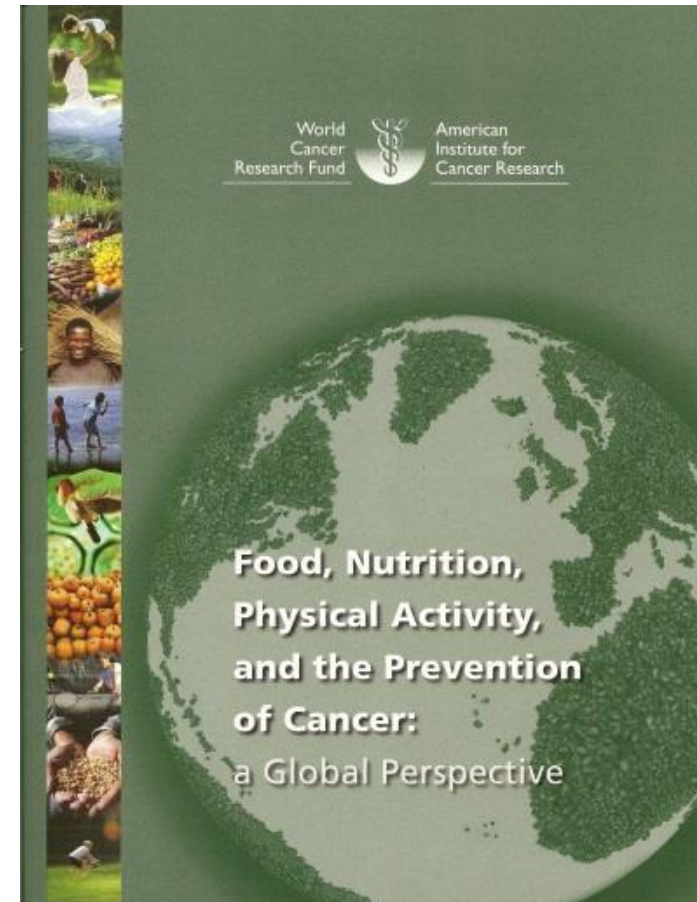


# All-Cause Mortality Associated with Protein Sources.



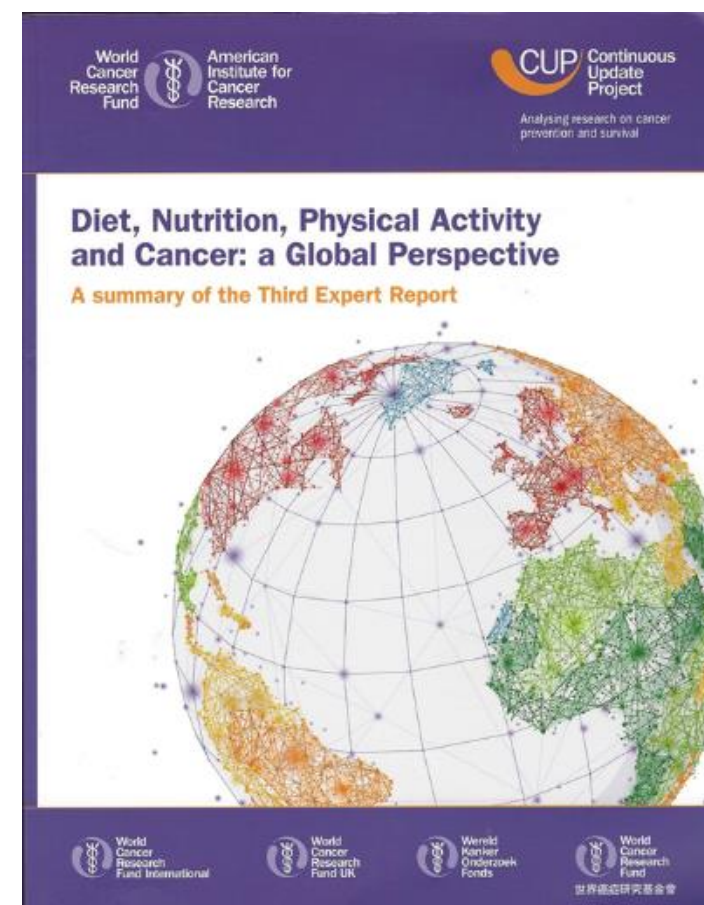


# ALCOHOL GUIDELINES



**2007**

***If consumed at all***, limit alcohol to 2 a day for men and 1 a day for women.

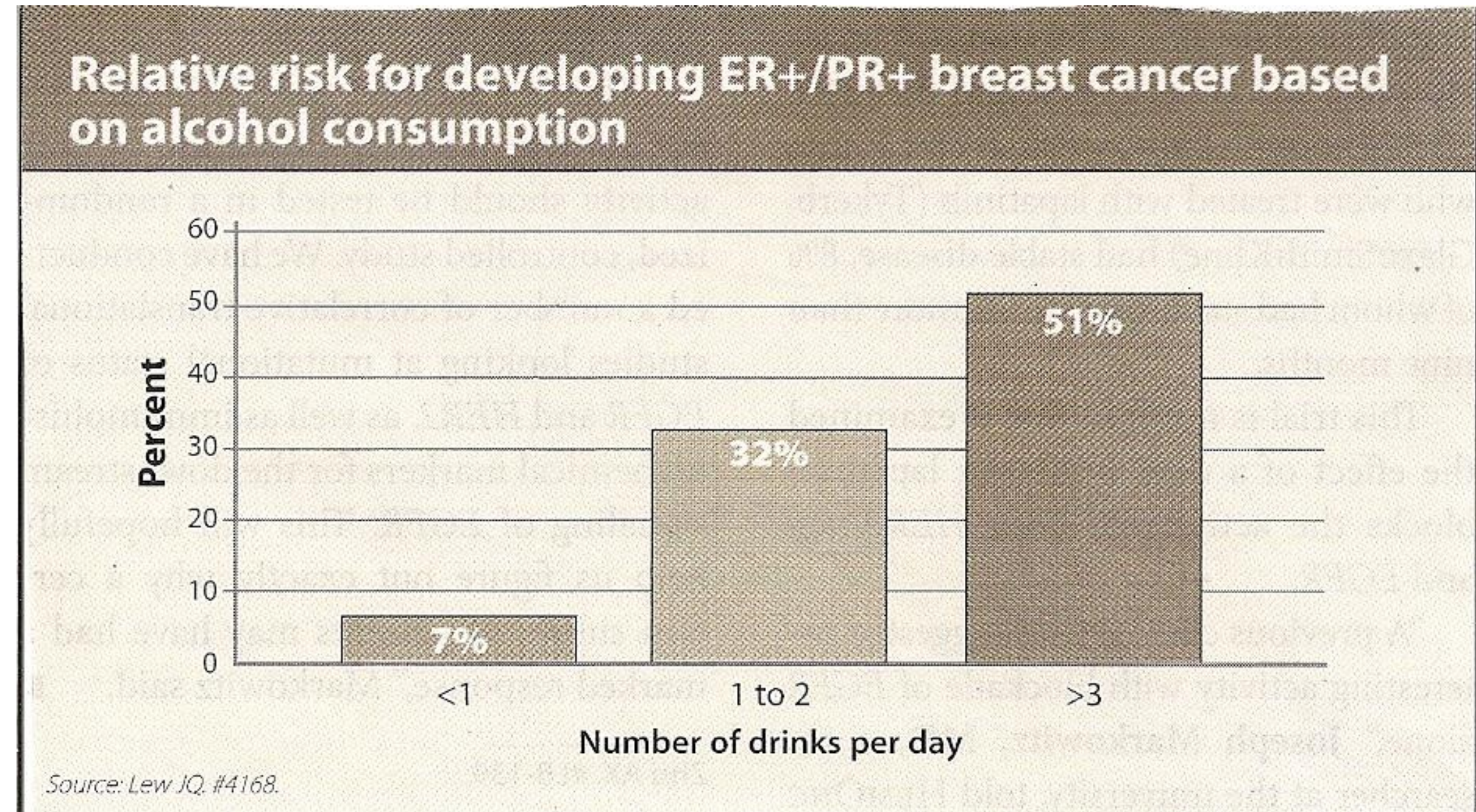


**2018**

For cancer prevention, it's best not



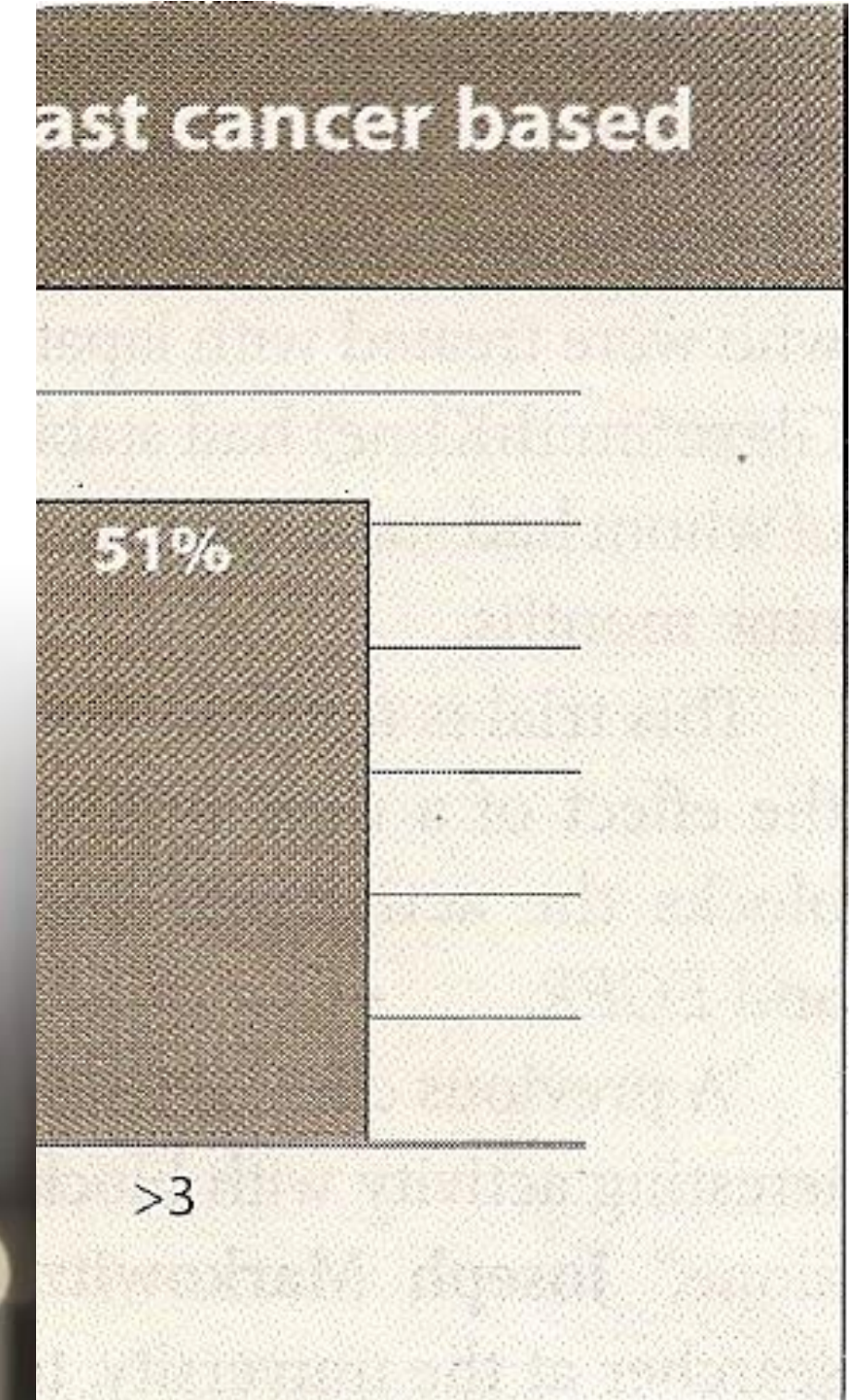
- Convincing increases risk
  - Mouth, pharynx, larynx
  - Esophagus
  - Liver
  - Colorectum
  - Post menopausal breast
- Probable increases risk
  - Stomach
  - Premenopausal breast
- Suggestive increases risk
  - Lung
  - Pancreas
- Probable decreases risk
  - Kidney





- Convincing i
  - Mouth, phar
  - Esophagus
  - Liver
  - Colorectum
  - Post menop
- Probable inc
  - Stomach
  - Premenopau
- Suggestive i
  - Lung
  - Pancreas
- Probable de
  - Kidney

**“If even light drinking can cause cancer, why don’t doctors warn their patients about it?”**





- 41,543 NutriNet-Sante Cohort participants developed 1489 cancers over 6.5 years
- Study investigated 3 validated and 1 new score (only WCRF/AICR cancer-specific)
  - WCRF/AICR, Alternate Healthy Eating Index, French Nutrition and Health Program-Guidelines Score and MEDI-LITE score
- A 1-point increment in WCRF/AICR score
  - 12% decrease in overall CA risk (8-16%,  $P < 0.0001$ )
  - 14% decrease in breast CA risk (6-21%,  $P = 0.001$ )
  - 12% decrease in prostate CA risk (0-22%,  $P = 0.05$ )
  - For colorectal CA,  $HR = 0.86$  [0.72-1.03;  $P = 0.09$ ]



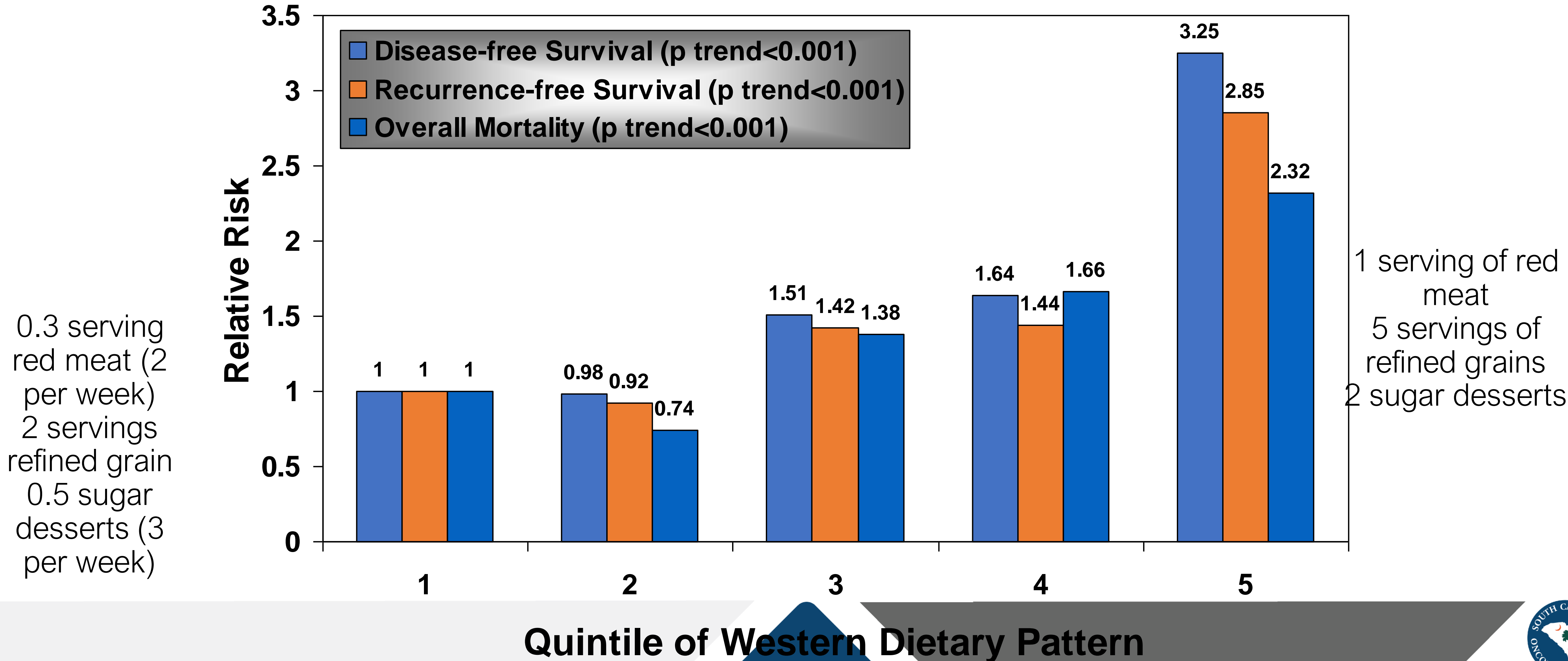
# Does It Really Matter After A Cancer Diagnosis?





# CALGB Prospective Observational Study: Western Dietary Pattern and Cancer Outcomes

•F/U 5.3 years, 324 patients recurred, 223 died with recurrence and 28 died without CA





# Men's Choices of Complementary Therapies

- Survey of 34 men with CaP using complementary Rx in the UK
- Choice of particular therapies was based on forms of “evidence” that were personally meaningful
  1. Personal stories of people helped by the therapy
  2. Long history and enduring popularity of the therapy
  3. The plausibility of the mechanism of action
  4. A belief or trust in individual therapies or their providers
  5. Scientific evidence
- Must acknowledge the different standards of evidence used by patients and clinicians to evaluate the benefits or not of complementary therapies



# Doc, Can I Take This?

Real Questions is:  
Will this interfere with  
my cancer treatment via

- 1) CYP 450 or
- 2) Oxidant/Antioxidant  
effect



Photo by Lawenda





## Anticancer Agents

- Camptothecins
- Cyclophosphamide
- EGFR-TK inhibitors
- Epipodophyllotoxins
- Taxanes
- Vinca alkaloids

## Botanicals

- CYP3A induction
  - SJW
  - Echinacea
  - Grape seed
  - Kava
  - ?Garlic
- CYP3A inhibition
  - Gingko
  - Grapefruit



## The Great Antioxidant Debate

- Antioxidants may interfere with the mechanism of action of cytotoxic chemotherapy or radiotherapy
- Use of antioxidants causes diminished treatment effect and protection of tumor
- Oxidation supports malignant proliferation
- Oxidation may interfere with standard Rx, diminishing therapeutic benefit
- Antioxidants improve Rx efficacy and protect from toxicity of treatments



## **Strongly Oxidative Chemo**

- Cisplatin, et al
- Alkylating agents
  - Cyclophosphamide
  - Ifosfamide
  - Melphalan
- Antitumor antibiotics
  - Doxorubicin
  - Daunorubicin
  - Bleomycin

## **Useful Antioxidants**

- Vitamin A, C, E
- Selenium
- Melatonin
- N-acetylcysteine
- Glutathione
- CO-Q 10
- Alpha-lipoic acid



## My Antioxidant Approach

- Individual advice depends on goal of Rx
  - If cure, err on side of caution
    - Delay antioxidants until end of Rx
    - Discontinue day before, of, after chemo cycle
    - Antioxidant rich foods probably ok
  - If palliation, encourage use for protection of normal tissue, optimization of QOL
- Antioxidant radio- and chemoprotectants (mesna, amifostine) do not interfere with anti-tumor effects of Rx



## Recommended Supplements

- Vitamin D3 (depending on 25OHD level)
- Calcium/Magnesium
- Omega 3's
- Medicinal Mushrooms
- Turmeric
- Probiotic



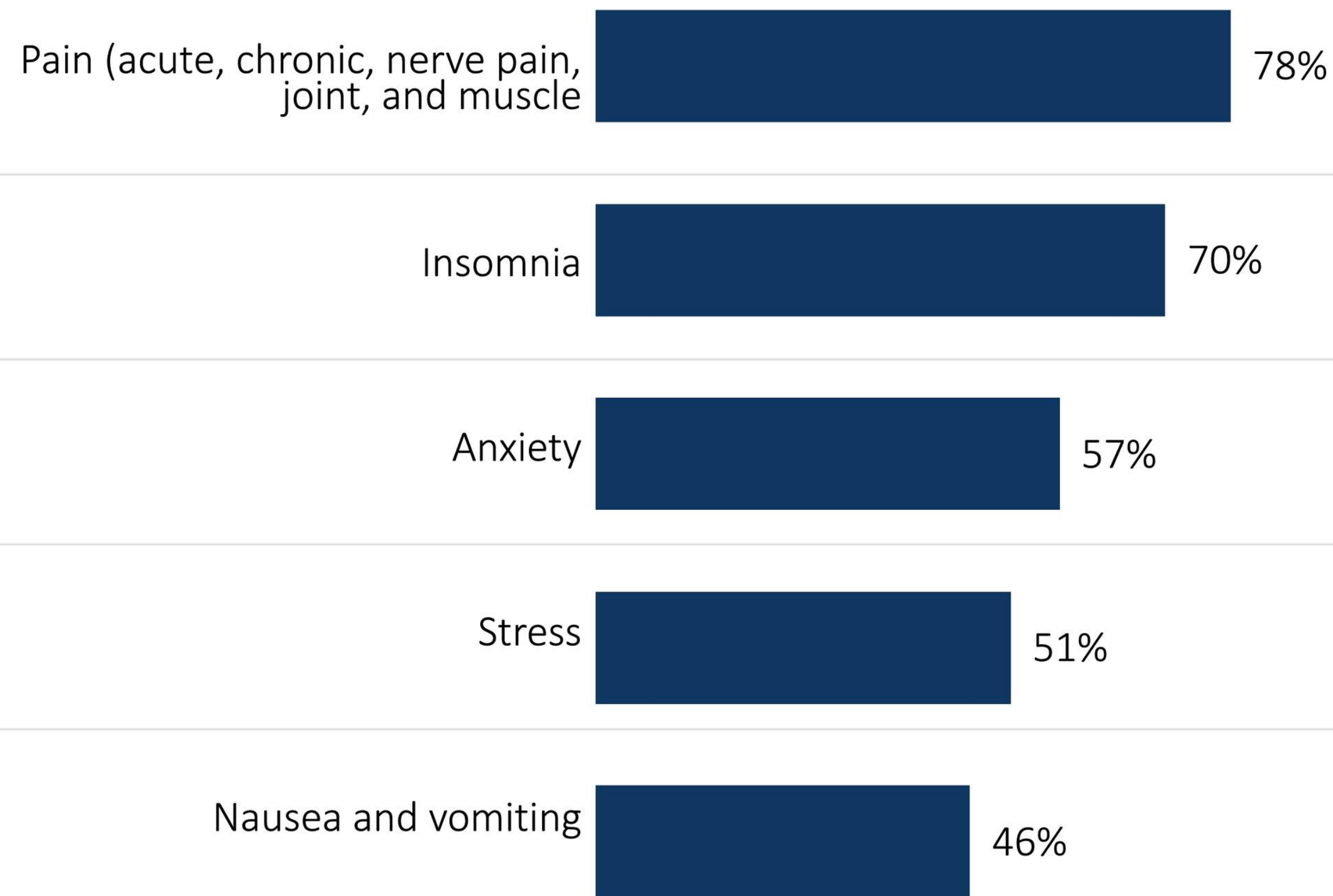
## Recommended Supplements

- Vitamin D3 (depending on 25OHD level)
- Calcium/Magnesium
- Omega 3's
- Medicinal Mushrooms
- Turmeric
- Probiotic
- Cannabis





# Cannabis Use in Breast Cancer Patients



- 612 patients responded to survey; mean age 57

- 42% used cannabis for medical purposes; only 23% strictly medical

- 75% reported extremely or very helpful at relieving sx

- 79% used during Rx; 54% after completion of treatment

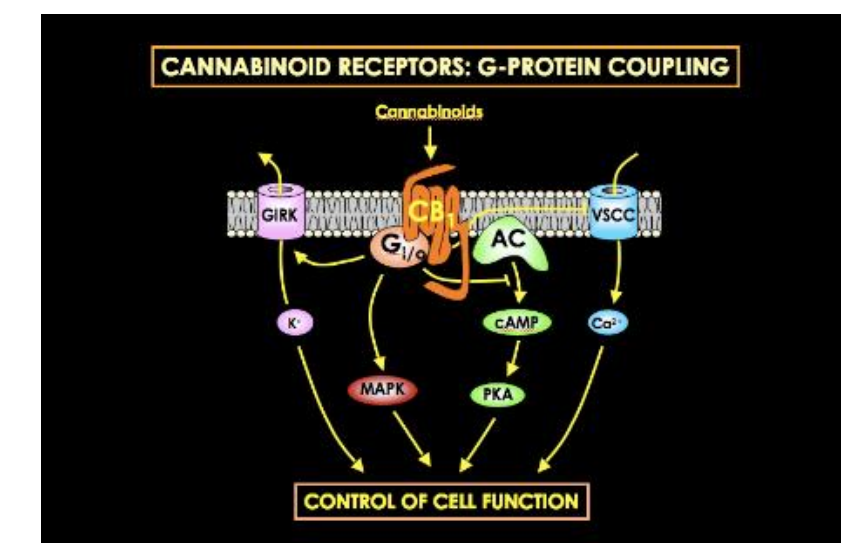
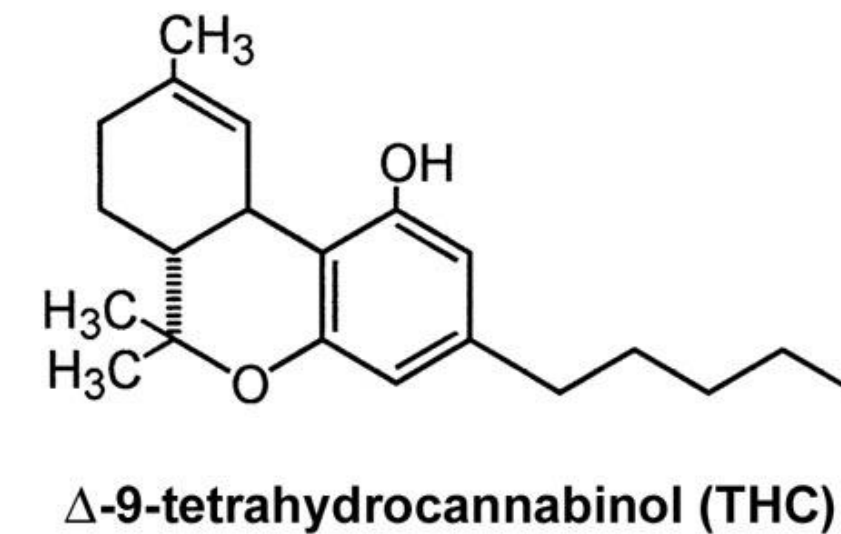
- 49% said cannabis also being used to treat the cancer itself

Cancer, First published: 12 October 2021, DOI: (10.1002/cncr.33906)



## Cannabis 101

- Versatile botanical used for millennia removed from US Pharmacopeia in 1942; placed in Schedule I in 1970
- Contains over 400 chemicals including ~120 cannabinoids as well as terpenoids and flavonoids
  - Delta-9-tetrahydrocannabinol (THC) most psychoactive; cannabidiol (CBD) modulates activity of THC; cannabinol (CBN), cannabigerol (CBG), tetrahydrocannabivarin (THCV) and delta-8-THC are other cannabinoids of note
- Cannabinoid receptors 1 and 2 (CB1 and CB2) present in brain and throughout body to complex with endocannabinoids as well as phytocannabinoids (THC, but *NOT* CBD)





# Therapeutics

- In adults with chemotherapy induced nausea and vomiting, oral cannabinoids are effective antiemetics.
- In adults with chronic pain, patients who were treated with cannabis or cannabinoids are more likely to experience a clinically significant reduction in pain symptoms
- In adults with multiple sclerosis (MS) related spasticity, short-term use of oral cannabinoids improves patient-reported spasticity symptoms.
- For these conditions the effects of cannabinoids are modest; for all other conditions evaluated there is inadequate information to assess their effects.



# Cannabis as an Anti-Cancer Agent

- In 1975 VCU investigators reported that delta-9-THC, delta-8-THC and CBN inhibited Lewis lung adenocarcinoma cell growth in vitro and in mice; CBD did NOT!
- Increasing body of preclinical evidence suggests cannabinoids may have anti-cancer activity
- Anti-oxidant and anti-inflammatory effects may contribute as well
- Possibility of anti-tumor activity via cannabinoid receptors inducing apoptosis and impairing tumor vascularization
- Multiple tumor cell lines inhibited *in vitro*
- Cannabinoid administration to nude mice curbs growth of various tumor xenografts
  - Lung, breast, colorectal and pancreas carcinoma
  - Skin carcinoma
  - Melanoma
  - Lymphoma
  - Thyroid epithelioma
  - Glioma

• Velasco et al, Neuropharmacology 2004





### No or Insufficient Evidence

- Cancers, including glioma (**cannabinoids**)
- 34 *in vitro* and/or *in vivo* experimental studies and one pilot human trial included
  - All but one study showed that cannabinoids selectively kill tumor cells
  - Antitumor activity
    - Antiproliferative effects (cell cycle arrest)
    - Decreased viability
    - Cell death via toxicity, apoptosis, necrosis, autophagy
  - Antiangiogenic effects
  - Antimigratory effects
    - Machado Rocha et al, 2014



## Nabiximols in Glioblastoma Trial

- A phase 1b randomized trial of nabiximols (12) compared with placebo (9), with dose dense temozolomide in patients with recurrent glioblastoma multiforme
  - Nabiximols used for median 22.1 wks; placebo 19.1 wks
- 33% of both groups were progression-free at 6 months
- 83% one year survival c/w 44% (p=0.042) [not powered for survival endpoint]; OS at 2 yrs 50% vs 22% (p=0.134)
  - Median OS estimated at 21.8 mos was not calculable for nabiximols and 12.1 months for placebo
    - Twelves et al, Br J of Cancer, 2021



## Stress and Cancer

- Women with ovarian cancer interviewed pre-op
- In women who lacked social support and had higher levels of distress, tumor had higher levels of VEGF
- First association between a psychological factor and a cytokine involved in tumor angiogenesis
  - Cole et al, Nature Reviews Cancer 2006
- 42 newly diagnosed head & neck pts with squamous cell CA surveyed
- Poorer psychosocial functioning (depressive sx, stress, anxiety, social support) was significantly associated with greater VEGF expression in HPV negative pts (OR=5.50, 95% CI = 1.68, 17.3,  $p < 0.01$ ) but not HPV positive pts
  - “Intense” VEGF expression had mean PSS 47% higher than pts with “weak” expression
  - Associations strongest for early stage pts
  - High VEGF more than 2.5 times more likely to die

• Fang et al, Head Neck 2014





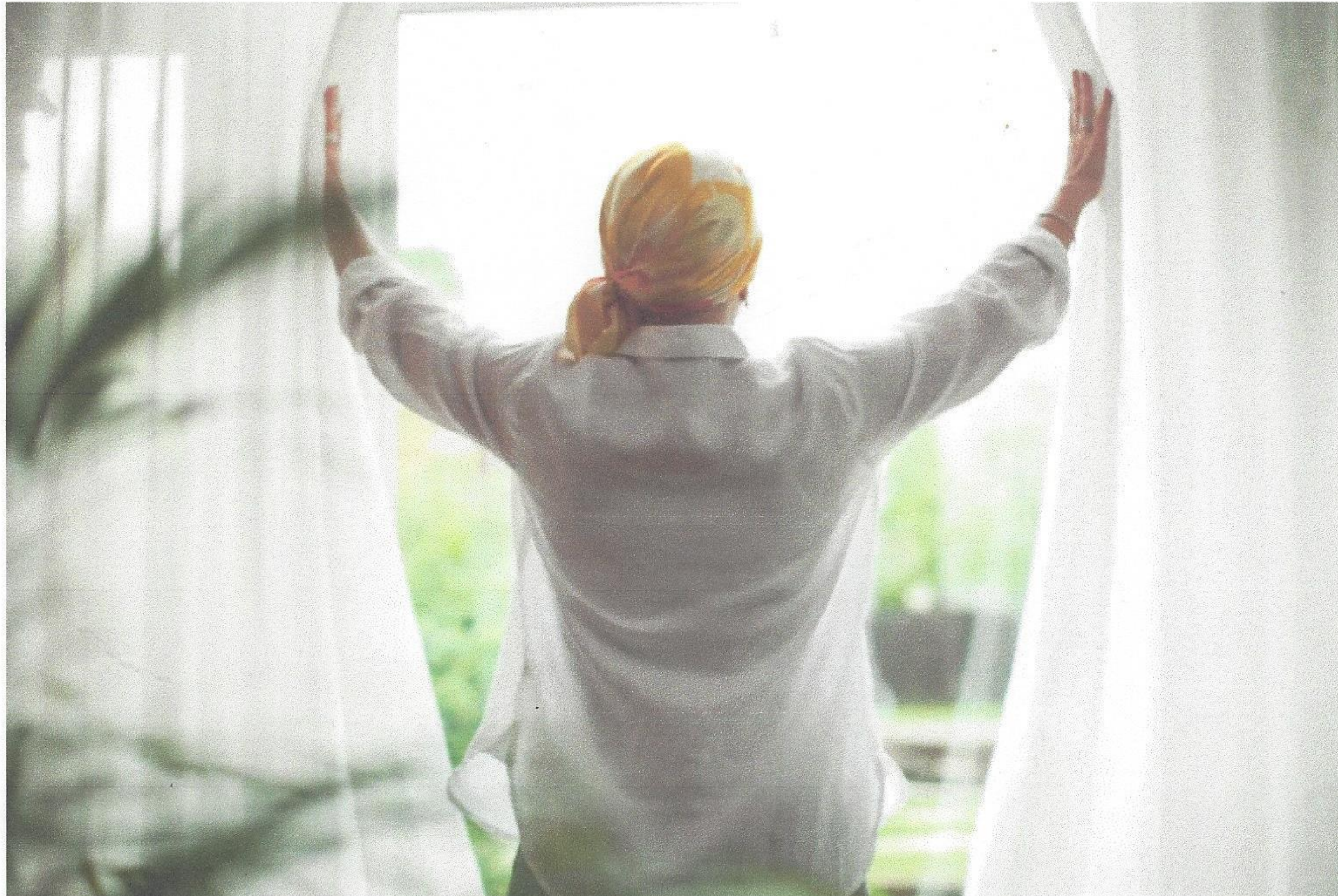
# Mind-Body Interventions

- Support Groups
- Journaling
- Disclosure
- Guided Imagery
- Hypnosis
- Breathwork
- Therapy
- MBSR
- Yoga





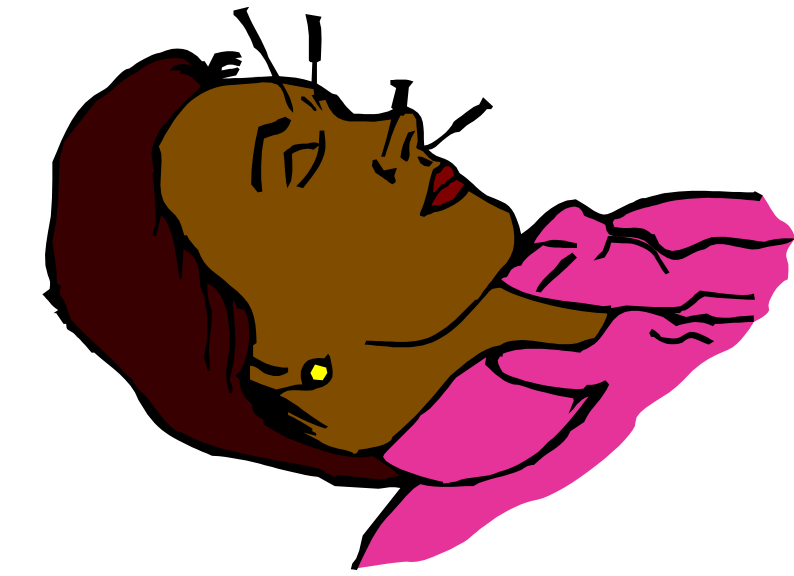
## Can Complementary Therapies Ease Cancer Treatment Symptoms? What the Science Says



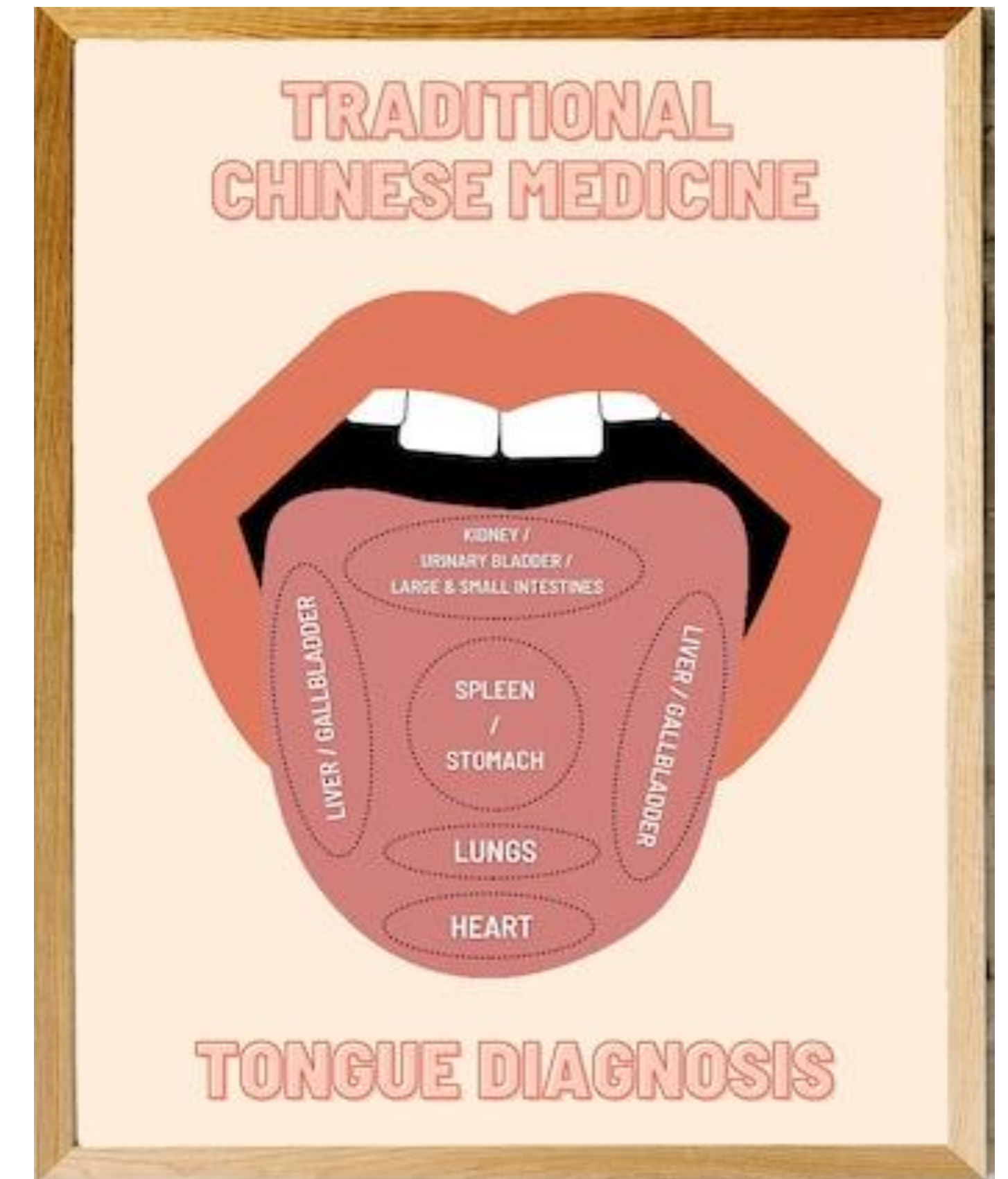
Jonathan Chapman—Cavan Images/Getty Images



## Acupuncture in Cancer



- Antiemetic during chemotherapy
- Pain control, including neuropathy
- Anxiety/Depression
- Breathlessness
- Xerostomia after radiation therapy
- Hot flashes secondary to hormonal therapy
- Chronic post-chemotherapy fatigue
- Constipation/diarrhea
- Sleep disturbance
- Immune enhancement
- Aromatase inhibitor musculoskeletal symptoms





# Benefits of Acupuncture

- Equal to venlafaxine in relief of hot flashes
  - Walker et al, JCO 2010
- Effective in hot flashes in men undergoing ADT for prostate cancer
  - Beer et al, Urology 2010
- Effective for cancer-related fatigue in breast cancer
  - Molassiotis et al, JCO 2012
- Decreases chronic xerostomia symptoms
  - Simcock et al, Annals of Oncology 2013
- Safe in children with cancer Rx related thrombocytopenia
  - Ladas et al, Support Care Cancer 2010



## Survivorship and Level of IM

- Attempt to link level of institutional involvement with IM and outcomes in breast cancer patients
- Institutions scored on efforts to educate, support and provide 12 IM interventions
  - Nutrition, Exercise, Support Groups, Spiritual care, Psycho-Oncology, Massage therapy, Meditation, Yoga, Acupuncture, Music or Art, Reiki, Tai chi or Qi gong
- Of 2430 oncologists invited, 103 participated; analysis included 173 of their patients
  - Median age 51, 8% metastatic, 40.5% South, 36.4% Midwest

Crudup et al, Journal of Oncology 2021





# Breast Cancer Survivorship and Level of Institutional Involvement Utilizing Integrative Oncology

Crudup et al, Journal of Oncology, 2021

**Table 5**

5-year survival across varying levels of institutional integrative involvement.

Institution integrative oncology score	Oncologist sample	Patient sample	Survival rate (%)
Low	25	35	89
Low-mid	26	48	96
Mid-high	23	26	96
High	29	64	95
Total	103	173	94



Working with the whole person

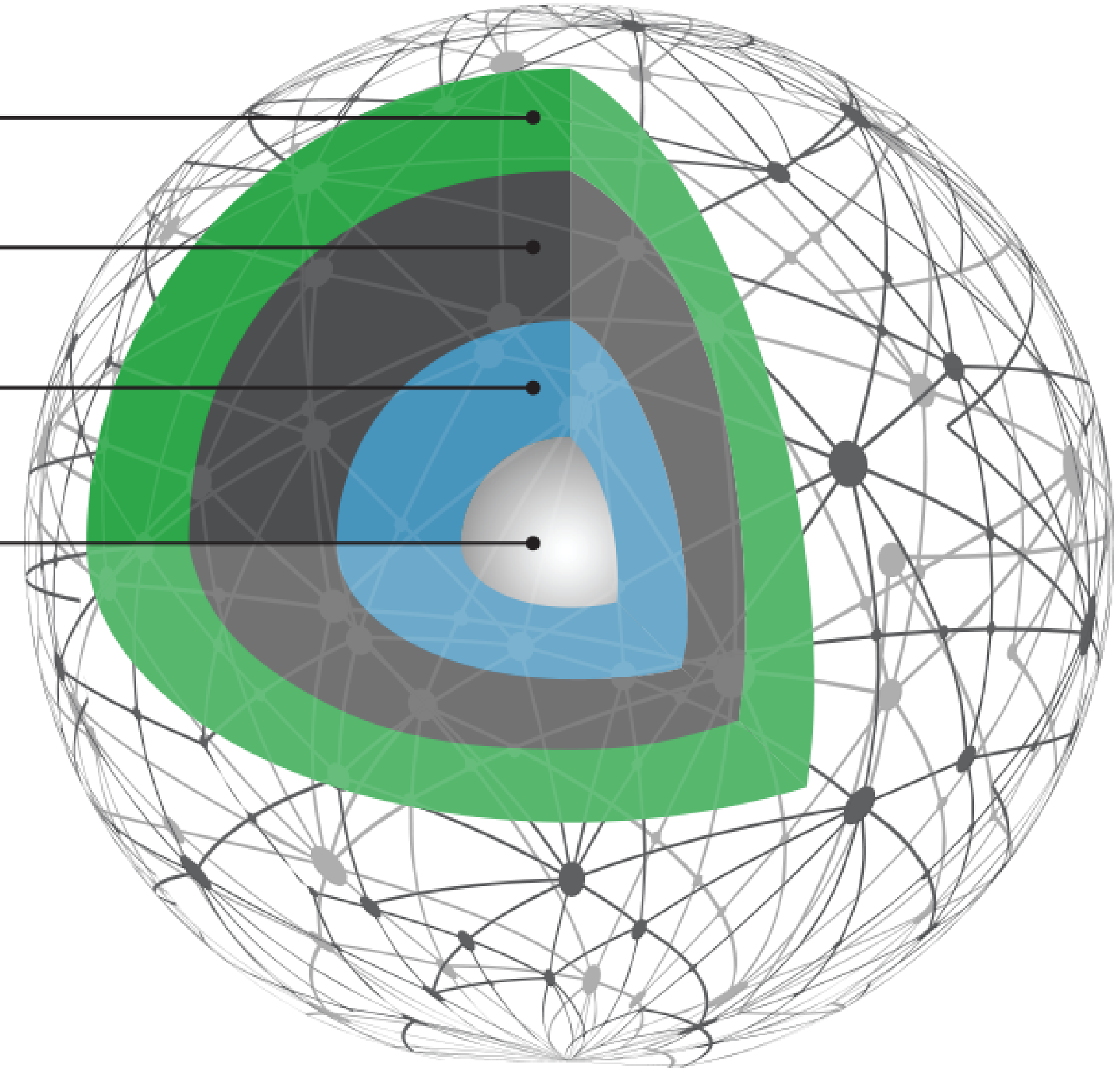
Hope = hEALING ORIENTED PRACTICES AND ENVIRONMENTS

**BODY & EXTERNAL**

**BEHAVIOR & LIFESTYLE**

**SOCIAL & EMOTIONAL**

**SPIRITUAL & MENTAL**



*Asking "What Matters"*

Exploring a patient's personal  
determinants of healing



# Three Closing Questions

- What brings you joy?
- What are your hopes?
- Where does your strength come from?



“The role of the  
physician is to cure  
sometimes, heal often,  
support always.”  
*Ambroise Pare*

